Confidential

SmithKline Beecham

Paroxetine -(PAXIL)

29060

A 38-Week, Two Phase, Multicenter Study to Investigate the Safety and Effectiveness of Paroxetine (10-60 mg/day) in the Treatment of Children and Adolescent Outpatients with Obsessive-Compulsive Disorder

453

Final Clinical Report

xxxxx x. xxxxxxxxx, RPh*
xxxxxxx x. xxxxxxxx*, xxxxx xxxxxxxx, BSc.**, xxxxxxx xxxxxx, MSc**,
xxxxxx xxxxx, Ph.D.

*Clinical Research, Development and Medical Affairs, N.A., **Biostatistics and Data Sciences

SB Document Number: BRL-029060/RSD-100W81/1

Issue Date: August 19, 1999

Signature Page

Report Title: A 38-Week, Two Phase, Multicenter Study to Investigate the Safety and Effectiveness of Paroxetine (10-60 mg/day) in the Treatment of Children and Adolescent Outpatients with Obsessive-Compulsive Disorder

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

Signature Page

Report Title: A 38-Week, Two Phase, Multicenter Study to Investigate the Safety and Effectiveness of Paroxetine (10-60 mg/day) in the Treatment of Children and Adolescent Outpatients with Obsessive-Compulsive Disorder

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

Report Synopsis

Study Title: A 38-Week, Two Phase, Multicenter Study to Investigate the Safety and Effectiveness of Paroxetine (10-60 mg/day) in the Treatment of Children and Adolescent Outpatients with Obsessive-Compulsive Disorder.

Investigators and Centers: Psychiatrist investigators from 26 study centers in the U.S. participated. All were appropriately experienced in the treatment of child and adolescent patients.

Publication: None at the time of study report preparation.

Study Dates: The study was initiated at the first study center on Jan. 13, 1997. The first patient was enrolled (Phase I, open-label paroxetine) on Jan. 23, 1997. The last study visit for the last patient to complete participation occurred on Dec. 28, 1998.

Objective(s): The primary objective was to evaluate the efficacy of paroxetine in children and adolescent outpatients with OCD by assessing the potential for relapse in patients previously responsive to paroxetine (during Phase I), after discontinuation of paroxetine during a 16-week, double-blind, placebo-controlled, randomized phase (Phase II).

The secondary objectives were to establish the clinical effectiveness of paroxetine (10-60 mg/day) in this population during a 16 week, open-label phase of the study (Phase I), and to evaluate the safety and tolerability of paroxetine in this population throughout the duration of the study.

Study Design: Multicenter, two-phase study. During Phase I, eligible subjects received open-label paroxetine for 16 weeks. There were six post-baseline (> Day 0) Phase I visits, which occurred at Weeks 2, 4, 6, 8, 12 and 16. At the end of Phase I, patients who achieved a therapeutic response (defined as $\geq$ 25% improvement in baseline CY-BOCS Total Score and a CGI Global Improvement Item Score of 1 or 2 at Week 16) were eligible to participate in Phase II.

Phase II was a 16-week, double-blind, placebo-controlled phase designed to establish the efficacy of paroxetine in this population by assessing the potential for relapse in previous responders when paroxetine was discontinued. Patients must have completed Phase I and met the response criteria to have been eligible to participate in Phase II. During Phase II, visits were scheduled every two weeks (except week 14) during this phase.

Study Population: Children and adolescent outpatients (8-17 years old) who met DSM-IV criteria for OCD (DSM-IV, 300.30) as their predominant psychiatric diagnosis.

Treatment and Administration: Paroxetine was supplied as white film-coated oval tablets containing 10 mg paroxetine (Batch no. U96157/Lot no. X10-6B10). The placebo tablets

were identical in appearance (Batch no. U96161/Lot no. X9-6B10PL). The tablets were packaged in bottles of 100 for Phase I and were packaged in foil-backed blister packs (60/pack) for Phase II. During Phase I, dosing followed a flexible-dose regimen (paroxetine 10-60mg/day, administered as a single daily dose). Dosing was titrated upward as necessary in 10mg increments no more frequently than once a week. Dose escalation was based on therapeutic response and tolerability. Double-blind dosing (Phase II) was based on the final dosage level reached during Phase I. Patients were randomly assigned (1:1) to paroxetine or placebo. Dose adjustments were not permitted during Phase II.

Evaluation Criteria

The primary efficacy outcome variable was the proportion of patients relapsing during the randomization phase (Phase II), and was defined as any one of the following:

1) Worsening of CGI Global Improvement Score by 1 point for 2 consecutive visits
2) Worsening of CGI Global Improvement Score by ≥ 2 points at any single visit
3) A CGI Global Improvement Score of 5 or greater

The secondary efficacy variables (in Phases I & II) included mean change from Baseline in CY-BOCS Total Score, mean change from Baseline in CY-BOCS obsessive and compulsive subscales, proportion of patients achieving ≥25% improvement in baseline CY-BOCS Total Score, proportion of patients achieving a CGI Global Improvement Score of 1 or 2, time to relapse (Phase II only), change from Baseline in CGI Severity of Illness item, mean change from Baseline in HAMD Score, mean change from Baseline in HAMA Score, the Yale Global Tic Scale - Total Tic Scores, and mean change from Baseline in GAF score.

Safety was assessed through routine adverse experience (AE) monitoring, vital sign (including body weight) determinations, and clinical laboratory evaluations. In addition, a physical examination and a 12-lead ECG were performed at periodic visits.

Statistical Methods: The primary population for the analyses of efficacy was the Phase II intention to treat (ITT) population. This included all patients who received at least one dose of randomized treatment and for whom at least one post-randomization baseline evaluation was available. A Per Protocol Population was identified and analyzed for the primary efficacy variable only. The primary inferences concerning efficacy were made using the last observation carried forward dataset (LOCF) of the Phase II ITT population, defined as the last on-drug assessment during the randomized phase. Two additional datasets were considered to ensure the robustness of the results: 1) an LOCF dataset at the latest time point (Visit) where at least 70% of the patients in each treatment group remained in the study (defined as the 70% endpoint), and 2) an Observed case (OC) dataset at 8 and 16 weeks.

The differences between paroxetine and placebo at study endpoint were estimated from the analysis as paroxetine minus placebo, and 95% confidence intervals were constructed around the estimated differences. All hypothesis tests were two-sided. The effect of interactions (e.g., treatment by center) were assessed at the 10% level of significance. All other statistical tests were performed at the 5% level of significance.

Summary statistics were generated for all efficacy parameters. In addition, statistical analyses were performed for the following efficacy parameters at specified timepoints: proportion of patients relapsing, time to relapse, change from baseline in CY-BOCS total score, and proportion of patients achieving ≥ 25% improvement in baseline CY-BOCS total score. The proportion of patients relapsing and the proportion of patients achieving ≥ 25% improvement in baseline CY-BOCS total score were analyzed using logistic regression, time to relapse was analyzed using the Log Rank test, and change from baseline in CY-BOCS total score was analyzed using ANCOVA. No formal hypothesis testing was conducted on the safety data. Summary tables of adverse experiences, vital signs, and laboratory data were produced.

Patient Disposition and Key Demographic Data: A total of 339 patients entered Phase I and were dispensed open-label paroxetine. Four patients did not return for any post-baseline efficacy evaluations, therefore the ITT population consisted of 335 patients. Of these 335 patients, 194 (57.9%) completed Phase I and were enrolled in Phase II. Of the 141 (42.1%) patients not entering Phase II, 40 (11.9%) were withdrawn due to an AE and 39 (11.6%) were either withdrawn due to lack of efficacy (n=19) or they were not eligible to enter Phase II because they did not meet the efficacy response criteria (n=20). One patient (paroxetine group) in Phase II was excluded from the ITT population because he/she did not return for any post-randomization baseline evaluations, therefore the Phase II ITT consisted of 193 patients. Of these patients, 42 (44.2%) in the paroxetine group and 33 (33.7%) in the placebo group completed Phase II. Lack of efficacy was the primary reason for withdrawal in both treatment groups.

Patient Disposition: Number (%) of Patient Withdrawals by Reason and Study Phase (ITT)

Reasons For Withdrawal	Open-Label Paroxetine N = 335		Double-Blind Paroxetine N = 95		Double-Blind Placebo N = 98	
	N	%	N	%	N	%
Adverse Experience	40	11.9	8	8.4	11	11.2
Lack of Efficacy	39*	11.6	33	34.7	45	45.9
Deviation from Protocol	22	6.6	5	5.3	3	3.1
Lost to Follow-up	8	2.4	3	3.2	0	0.0
Other Reason	32+	9.6	4	4.2	6	6.1
Totals Withdrawn	141*+	42.1	53	55.8	65	66.3

* includes patients who did not meet the protocol-defined response criteria (n = 20)

\+ includes patients eligible for entry into the Double-Blind Phase but who chose not to participate (n = 7).

The mean patient age was approximately 12 years old, with the open-label ITT population evenly split between children (age < 12, n=167/335, 49.9%) and adolescents (age ≥ 12, n=168/335, 50.1%). Most patients were male (198/335, 59.1%), and the majority were caucasian (308/335, 92%). In Phase II, the two treatment groups were generally similar with respect to all demographic characteristics. The mean age at onset of OCD was 10.1 years, with a range of 2 – 18 years. The severity of the illness was rated as moderate or severe at baseline in greater than 95% of the participants.

Efficacy Results

Primary Efficacy Variable

Approximately one-third (33/95, 34.7%) of the paroxetine patients met the relapse criteria, compared to 43.9% (43/98) of the patients randomized to placebo, although this difference was not statistically significant (p=0.136, odds ratio=0.62, C.I. of 0.34,1.16). Similar results were observed for the Per Protocol Population.

Secondary Efficacy Variables

The time to relapse was shorter in the placebo group, however this difference was not statistically significant. In Phase II, the proportion of patients with a decrease in CY-BOCS Total Score ≥ 25% from double-blind baseline was significantly greater for paroxetine than for placebo, both in the Week 16 LOCF dataset and at the 70% endpoint, and the mean increase in CY-BOCS Total Score (indicating an increase in symptoms) from double-blind baseline to Week 16 endpoint was significantly greater in patients switched to placebo than for those maintained on paroxetine, again in both the Week 16 LOCF dataset and at the 70% endpoint.

Furthermore, the data from all of the other secondary efficacy endpoints which were not statistically analyzed numerically favored paroxetine over placebo (i.e., CGI Global Improvement Item Responders, change from randomization baseline in the CY-BOCS subscale scores, CGI Severity of Illness Item rating, HAM-A and HAM-D scores, Yale Global Tic Score and GAF Scale) in the Week 16 LOCF dataset and at the 70% endpoint. However, the Observed Case (OC) datasets generally did not distinguish paroxetine from placebo.

Proportion (%) of Patients With a >= 25% Reduction in CY-BOCS Total Score From Randomization Baseline Double Blind Phase (ITT)

	Paroxetine			Placebo			Pairwise Comparisons*
	n	%	N	n	%	N	Odds Ratio/p-value/(95% CI)
Week 16	17	45.9	37	7	26.9	26	2.31/ 0.130 / (0.78, 6.80)
70% Endpoint**	22	26.5	83	8	8.9	90	3.70/ 0.003 / (1.54,8.86)
Week 16 Endpoint	24	28.9	83	13	14.4	90	2.41/ 0.023 / (1.13. 5.13)

*Unadjusted due to low numbers of patients per treatment/center group combination
**The 70% Endpoint visit is Week 4

CY-BOCS Total Score Mean Change from Randomization Baseline – ITT

	Paroxetine			Placebo			Pairwise Comparisons+
	n	Mean*	SE	n	Mean*	SE	Diff / p-value / (95% CI)
Baseline**	92	9.9	0.67	98	9.6	0.61	-
Week 16	41	- 0.4	1.07	30	1.3	0.93	-0.81 / 0.583 / (-3.73, 2.12)
70% Endpoint ++	92	2.3	0.82	98	6.3	0.82	-4.01 / 0.001/ (-6.30, -.72)
Week 16 Endpoint	92	3.6	0.92	98	6.9	0.86	-3.38 / 0.008 / (-5.88, -.88)

+Adjusted for terms retained in the final model (i.e., center group)
* Mean score at Randomization Baseline; Weeks scores are the mean changes from Baseline
** Baseline is the last open-label value prior to entering the double-blind phase
++ Note: The 70% Endpoint Visit is Week 4

The open-label efficacy data provide further support for the usefulness of paroxetine in treating this patient population. Almost three-quarters of the patients (68.7%) met both of the response criteria at Week 16 Endpoint (LOCF), with 86.2% of the patients who reached Week 16 meeting both response criteria.

Percentage (%) of Patients Meeting the Response Criteria - Open Label Phase (ITT)

	N	n	%
CGI Responders[1]			
Week 16	239	209	87.4
Week 16 Endpoint	315	231	73.3
CY-BOCS Responders[2]			
Week 16	239	217	90.8
Week 16 Endpoint	329	258	78.4
Meets Both Response Criteria[3]			
Week 16	239	206	86.2
Week 16 Endpoint	329	226	68.7

1 Includes patients with score of 1 (Very Much Improved) and 2 (Much Improved) on the CGI Global Improvement Item
2 Reduction of ≥ 25% from Open-Label Baseline
3 Meets both of the above criteria

The overall responsiveness to open-label paroxetine was also demonstrated based on the CGI Severity of Illness Item Score. At Open-Label Baseline, 98% of the patients had a CGI severity of illness rating ≥ 4 (moderately ill or worse [more than half were rated markedly or severely ill]). However, at Open-Label (OL) Week 16, only 28.5% of the patients were rated at least moderately ill.

Safety Results: The safety and tolerability of paroxetine in the age group studied in this trial (8-17 yr olds) were demonstrated. There were no deaths or unexpected safety findings, and in general the nature and incidence of AEs reported were similar to those reported for adult OCD patients who had received paroxetine in controlled trials. Headache (82/335, 24.5%) was the most commonly reported AE in the open-label phase, followed by asthenia (72/335, 21.5%), and insomnia (71/335, 21.2%). Respiratory disorder (54/335, 16.1%), somnolence (49/335, 14.6%), nausea (48/335, 14.3%), nervousness (45/335, 13.4%), trauma (45/335, 13.4%), abdominal pain (40/335, 11.9%), hyperkinesia (38/335, 11.3%), diarrhea (37/335, 11.0%) and weight gain (36/335, 10.7%) were also all reported in at least 10% of the open-label population. Headache was also the most common AE reported in both treatment groups in the double-blind phase (18/95 [18.9%] and 26/98 [26.5%] in the paroxetine and placebo groups, respectively).

Seventeen patients reported a total of 22 SAEs during the study (17/335, 5.1%). Thirteen patients in the open-label phase (3.9%) reported a total of 17 SAEs and four patients in the double-blind phase (2.1%) reported a total of 5 SAEs. Almost all of the SAEs reported (19/22, 86.4%) were CNS-related. Emotional lability (n=5) and hostility (n=4) were the two most common SAEs reported during open-label treatment, and were the only SAEs reported in more than one patient during the open-label phase.

Suicide attempt/ideation was reported in several patients, but could not be reasonably attributed to paroxetine. Some behavioral activation/hyperactivity type AEs (e.g., agitation, hostility, hyperkinesia, manic reaction and concentration impaired) occurred on open-label therapy with greater frequency than have been reported in adults, and summaries by age group suggest these events were more likely to occur in the younger age group (< 12 years). As noted above, some of these particular events were considered serious in a number of patients. One SAE of manic reaction was reported, in a patient who had comorbid ADHD as well as another SAE of hostility. Younger children may be more sensitive to the behavioral activation/disinhibition side effects of SSRIs and therefore should be closely monitored because of the reported risk with antidepressants for hypomanic/manic switch.

A total of 59 patients were withdrawn from the study due to AEs (59/335, 17.6%), 40 patients during the open-label phase (11.9%) and 19 patients during the double-blind phase (9.8%). The majority of the AEs leading to withdrawal were CNS-related. The AEs leading to withdrawal of more than 1% of the open-label phase population included hostility (9/335, 2.7%), hyperkinesia (7/335, 2.1%), agitation (6/335, 1.8%), concentration impaired (5/335, 1.5%), nervousness (4/335,

1.2%) and neurosis (4/335, 1.2%). The most common AEs leading to withdrawal in the DB phase were hostility (3.2% in the paroxetine group, 0.0% in the placebo group), neurosis (3.2% in the paroxetine group, 5.1% in the placebo group), and nervousness (1.1% in the paroxetine group and 2.0% in the placebo group).

Laboratory and vital sign abnormalities of significant clinical concern were few in number and not inconsistent with data generated in adults. Clinically significant weight gain was reported by the investigators in a number of patients, however, in the absence of pre- and post- dose body mass index data, the true clinical relevance of such findings is difficult to establish in an actively growing and maturing population such as this.

In summary, these safety findings suggest that paroxetine is safe and generally well-tolerated in pediatric patients with OCD when administered over the dosage range studied (10-60mg/day).

Conclusion(s): The results of this two-phase, multicenter, relapse-prevention design study provide supportive evidence that paroxetine is beneficial in the treatment of children and adolescents with OCD. Although there was no statistically significant difference between paroxetine and placebo with respect to the protocol-defined primary measurement of efficacy (the proportion of patients meeting relapse criteria during the double-blind phase), almost three-quarters (69%) of all patients enrolled met the response criteria during the OL phase and the proportion of responders in the double-blind phase (based on CY-BOCS Total Score) was statistically significantly greater in the paroxetine group than in the placebo group. The safety data generated in children and adolescents with OCD in this study did not reveal any adverse findings that were unique to this population nor any that would preclude its use in this population.

Table of Contents

List of Tables

List of Figures

List of Appendices

List of Abbreviations & Definitions

Abbreviation	Unabridged Term(s)
ADECS	Adverse Drug Experience Coding System
ADHD	Attention Deficit Hyperactivity Disorder
AE	Adverse Experience
ALT	Alanine Aminotransferase (SGPT)
AP	Alkaline Phosphatase
ART	Adverse Reaction Terminology
AST	Aspartate Aminotransferase (SGOT)
BP	Blood Pressure
BPM	Beats per minute
BUN	Blood Urea Nitrogen
CFR	Code of Federal Regulations
CGI	Clinical Global Impression
CI	Confidence Interval
CRO	Clinical Research Organization
CRF	Case Record Form/Case Report Form
CV	Curriculum Vitae
CY-BOCS	Childrens Yale-Brown Obsessive Compulsive Scale
DB	Double-blind
DSM III/IV	Diagnostic and Statistical Manual of Mental Disorders, Third/Fourth Editions.
DST	Data Source Table
ECG	Electrocardiogram
FU	Follow Up
GAD	Generalized Anxiety Disorder
GAF	Global Assessment of Functioning
GCP	Good Clinical Practice
GGT	Gamma Glutamyl Transferase
HAM-A	Hamilton Rating Scale for Anxiety
HAM-D	Hamilton Rating Scale for Depression
HCT	Hematocrit
HGB	Hemoglobin
HPF	High Power Field

List of Abbreviations & Definitions (continued)

IRB	Institutional Review Board
ITT	Intention to Treat
IUD	Intra-Uterine Device
k	Thousand
Kg	Kilogram
K-SADS-L	Sched. for Affective Disorders and schizophrenia, Lifetime (Kiddie version)
LDH	Lactate Dehydrogenase
LOCF	Last Observation Carried Forward
LOE	Lack of Efficacy
MAOI	Monoamine Oxidase Inhibitor
MCV	Mean Corpuscle Volume
MG	Milligram
mmHg	Millimeters of Mercury
ND	Not Defined/Not Done/Not Determined
NOS	Not Otherwise Specified
OC	Observed Case
OCD	Obsessive Compulsive Disorder
OL	Open-label
OTC	Over-The-Counter
PID	Patient Identifier
PTSD	Post-Traumatic Stress Disorder
PV	Protocol Violator
PVC	Premature Ventricular Contraction
RBC	Red Blood Cell
SAE	Serious Adverse Experience
SBCL	SmithKline Beecham Clinical Laboratories
SD	Standard Deviation
SE	Standard Error of the Mean
SGOT	Serum Glutamic Oxaloacetic Transaminase (AST)
SGPT	Serum Glutamic Pyruvic Transaminase (ALT)
SOP	Standard Operating Procedure
SSRI	Selective Serotonin Reuptake Inhibitor
ths/thou	Thousand
vs	versus
WBC	White Blood Cell
WHO	World Health Organization

List of Abbreviations & Definitions (continued)

WHO ATC	World Health Organization System for Categorizing Medications by Therapeutic Class
Wk	Week
WRC	Worldwide Regulatory Compliance

1 Introduction

Obsessive-Compulsive Disorder (OCD) is a severe, highly prevalent and chronically disabling condition that is characterized by recurrent, ritualized thought patterns (obsessions) and associated repetitive, intentional behavior patterns (compulsions) performed in response to the obsession. The obsessions and compulsions cause marked distress, are time-consuming and may significantly interfere with the person's normal routine, occupational functioning or usual social activities or relationships.

Selective serotonin reuptake inhibitors (SSRIs) such as paroxetine are increasingly viewed as first-line treatment for OCD, and their efficacy has been established in a series of placebo-controlled trials.1 Paroxetine has been shown in double-blind, placebo-controlled trials to be effective in the short-term management2,3 and the long-term management4,5 of adult outpatients with OCD. The minimally effective dose in this population is 40 mg per day, with a daily dose of 60 mg showing additional benefit in some patients. Long-term paroxetine treatment also prevents relapse of OCD. 4

Recent research indicates that OCD is a more common disorder than previously thought, both in adults as well as in children and adolescents. Recent epidemiological studies have consistently found lifetime prevalences of OCD of 1-3% in adults and adolescents, suggesting that previous studies clearly have underestimated its prevalence in the general population.6,7 Children and adolescents are frequently affected by OCD, and in fact the disorder usually emerges during childhood or adolesence, underscoring the importance of developing effective treatments for use in the pediatric population.8 Recent data indicates that 80% of adults with OCD identify their onset of symptoms before age eighteen9, and although prevalence data in teenagers is non-existent6 relatively recent reports of mean age of onset of pediatric OCD have ranged from 9-11 years.8,10,11

Patients who develop OCD later in life appear to have a better chance of responding to drug treatment than patients who become ill earlier, independent of length of illness.12 For this reason, and also because OCD is a chronic and usually disabling condition, has an early onset, and is often comorbid with other psychiatric disorders11, it is essential that intervention be exercised at the earliest stage possible in the disease. Although the presentation of OCD in children can differ from that of adults, and the type and intensity of obsessions and compulsions may change as the child develops, in general the clinical features of

OCD are strikingly similar across age groups and OCD is generally felt to be the same disorder in children, adolescents and adults.13 Consequently, it is reasonable to assume that treatments shown to be effective in adults with OCD may also prove to be effective in children and adolescents with OCD.

The purpose of this trial therefore was to evaluate the safety and effectiveness of paroxetine in children and adolescent outpatients with OCD.

2 Objectives

2.1 Primary

The primary objective of this study was to evaluate the efficacy of paroxetine in children and adolescent outpatients with OCD who were previously responsive to paroxetine (Phase I), by assessing the potential for relapse after discontinuation of paroxetine during a 16 week, double-blind, placebo-controlled randomized phase (Phase II).

2.2 Secondary

The secondary objectives were to establish the clinical effectiveness of paroxetine (10-60 mg/day) in the treatment of children and adolescent outpatients with OCD during a 16 week, open-label phase of the study (Phase I), and to evaluate the safety and tolerability of paroxetine in children and adolescent outpatients with OCD throughout the duration of the study (both open-label and double-blind administration).

3 Methodology

3.1 Study Design

This was a multicenter, two-phase study of paroxetine in the treatment of children and adolescent outpatients with OCD. During Phase I, eligible subjects received open-label paroxetine 10-60 mg/day according to a flexible-dosing regimen for 16 weeks. A total of 375 patients were expected to be enrolled into the open-label phase at a minimum of 24 study centers. Eligibility to enter the open-label phase was determined during an initial screening visit and a subsequent baseline visit prior to initiation of dosing. Open-label dosing was initiated at 10mg/day and could be titrated upward as necessary in 10mg increments at intervals no more frequently than once a week. The maximum daily dose allowed was 60mg. Dose escalation was up to the discretion of the investigator, based on therapeutic response and tolerability to the medication. It was recommended that the daily dose of paroxetine not exceed 40mg/day until after week 6 because of the potential for a delay in response often seen with OCD medication. During Phase I, post-baseline (> Day 0) visits occurred at Weeks 2, 4, 6, 8, 12 and 16 for a total of 6 visits during this phase of the study. At the end of Phase I, patients who achieved a therapeutic response (defined as ≥ 25% improvement in baseline CY-BOCS Total Score and a CGI Global Improvement Item Score of 1 or 2) were eligible to participate in Phase II of the study. For patients withdrawing prematurely, including patients who completed Phase I but did not continue into the double-blind phase, tapering off of the open-label medication was recommended (decreased in 10mg increments per week). If a down titration period was instituted during or at the end of Phase I, a Taper End Visit was to be conducted following cessation of dosing.

Phase II was a 16-week, double-blind, placebo-controlled, randomized phase designed to establish the efficacy of paroxetine in the treatment of OCD in children and adolescents by assessing the potential for relapse after paroxetine was discontinued in patients previously responsive to paroxetine. Patients must have completed Phase I and met the response criteria described above in order to have been eligible to participate in Phase II. It was expected that a minimum of 180 patients would be enrolled in Phase II and randomized to either paroxetine or placebo (1:1 ratio). Downward dose tapering of patients randomized to placebo in Phase II was achieved in blinded fashion (using a double-dummy design) such that decreases occurred in 10mg increments per week beginning at the start of Phase II. Dose adjustments were not permitted in Phase II. Patients not

responding or not tolerating the study medication during Phase II were to be withdrawn from the study. Relapse was based on CGI Global Improvement Item Scores throughout this phase of the study. Patients meeting any of the following criteria for relapse were to have been withdrawn from the study:

- Worsening of CGI Global Improvement Score by 1 point for 2 consecutive visits
- Worsening of CGI Global Improvement Score by ≥ 2 points at any single visit
- A CGI Global Improvement Score of 5 or greater

During Phase II visits were to occur at Weeks 2, 4, 6, 8, 10, 12 and 16 for a total of 7 visits during this phase of the study. Patients experiencing worsening of OCD symptoms between regular visits were to contact the study center in order for an additional clinic visit to be scheduled. This unscheduled visit was to occur within 2 days, if possible, of the worsening of symptoms. Tapering off of study medication was recommended for all patients upon conclusion of Phase II, either upon early termination or completion of the full 16 week period. The recommended down titration regimen was 10 mg increments per week. If a down titration phase was instituted during or at the end of Phase II, a Taper End visit was to be conducted following cessation of dosing. The study design is depicted in Figure 1. Appendix A contains the protocol and sample consent form.

Figure 1 Study Design

Phase I: Open Label	Phase II: Double-Blind
<---------- 16 weeks*---------->	<---------- 16 weeks* ---------->
Paroxetine 10-60 mg daily (upward titration as needed)	16 weeks of paroxetine at the final total daily dosage established in Phase I OR 16 weeks of placebo, or up to 5 weeks paroxetine blinded down titration followed by 11-15 weeks of placebo

*One week Screening Phase and Study End-Taper Phase (up to 5 weeks) not included

3.1.1 Protocol Amendments

Protocol 29060/453 was finalized on Dec. 10, 1996. The protocol was subsequently amended three times over the course of the trial. All three amendments were relatively minor in scope and/or adminstrative in nature. Amendment no. 1, dated April 2, 1997, was implemented primarily to expand the excluded concomitant medication list for consistency with product labeling and to add two additional drugs of abuse to the urine drug screen. Amendment no. 2, dated August 15, 1997, was incorporated in order to add language ensuring continued use of adequate contraception by sexually active females. Amendment no. 3, dated Jan. 30, 1998 was added in order to clarify the procedures which were to occur upon study completion or upon early termination, depending on the circumstances (i.e., down-titration, taper-end visit, and/or follow-up visit, as applicable). Refer to Appendix A of this report for a copy of the protocol and all three amendments.

3.2 Investigators

The study was conducted at 26 centers throughout the United States (28 centers were planned but center number 014 and 028 dropped out before enrolling any patients). Table 1 presents a list of the Principal Investigators, their affiliated institution (center) and number, and their geographic location (centers 014 and 028 are excluded). The investigators were selected because of their interest in the study, their ability to conduct the study according to Good Clinical Practice (GCP) standards, as well as their ability to enroll patients. Appendix A contains the curriculum vitae of each principal investigator.

Table 1 Investigators, the SB Assigned Center Number and the Investigator Hospital or University Affiliation and Location

Investigators	Center	Affiliated Institution	City/State
xxxx xJ. xxxxxxxxx, MD	001	xxxxxxxxx xxxxxxxxxx xx xxx xxxxx xxxxxxxx xx xxxxxxx xxxxxxxxxxx xxxxxxxxxx xxxxxxxxx	xxxxxxxxxxx, xx
xxx x. xxxx, MD	002	xxxxxxxxxx xx xxxxxxxx xxxxxx xx xxxxxxxx	xxxxxx, xx
xxxxxxxx xxxxxxxx, MD/xxxxxx xxxxxxx, MD	017	xxxxxxxxxx xx xxxxxxxx xxxxxx xxxxx	xxxxx, xx
xxxxx xxxxxxxx, MD	022	xxxxxxxxxx xx xxxxxxxxxx xxxxxxx xxxxxx	xxxxxxxxxx, xx
xxxxxx xxxxxxxx, MD	003	xxxxxxxxx xxxxxx	xxxxxx, xx
xxxxxxx x. xxxxx, MD	004	xxxx. xx xxxxxxx xxxxxxx xx xxxxxxxx	xxxxxx, xx
xxxxx x. xxxxxxxx, MD	005	xxxxxxxxxxxxxxxxxx xxxxxx xxxxx	xxxxxxx, xx
xxxxxx xxxxxx, MD	006	xxxxxxxxxx xx xxxxx xxxxxxxxxx xxxxxxx xxxxxx	xxxxxx, xx
xxxxx x. xxxxxxxx, MD	007	xxxxxxxxxxx xxxxxxxx xxxx.	xxxx xxxx xxxx, xx
xxxxxx xxxxxx, MD	027	xxxxxx xxxxxxxx	xxxxxxx, xx
xxxxx xxxxxxx, MD	008	xxxxxxxxxx xx xxxxxxx xxxxxxx xx xxxxxxxx	xxxxxxxxxx, xx
xxxxx x. xxxxxxx, MD	009	xxxx xxxxx xxxxxxxxxx xxxxx xx	xxxx xxxxx, xx
xxxxx xxxxxxxxx, MD	010	xxxxxxxxxx xx xxxxxxxxx xxxxxxx xxxxxx	xxxxxxx, xx
xxxxxx x. xxxxxx, MD	011	xx. xxxxx xxxxxxxxx xxxxxx xx xxxxxxxx	xx. xxxxx, xx
xxxxxxx xxx, MD	012	xxxxx xxxxxxxxx xxxxxx xx xxxxxxxx	xxxxxxx, xx
xxxx xxxxxx, MD	013	xxxxxxxxxx xx xxxxxxxxxx xx xxx xxxxx	xxx xxxxx, xx
xxxxx xxxxxxxxx, MD	015	xxxx xxxxxxxxxxxxxxxxx xxxxxxxxx	xxx xxxxxxx, xx
xxxxxxxx x. xxxxx, MD	016	xxxxxx xxxxxx xxxxxxxx xxxxxxxxxx	xxxxxxxx, xx
xxxx x. xxxxxxxx, MD	026	xxxxxxx xxxxxxx xx xxxxxxxx	xxxxxxxx, xx
xxxxxxxxx xxxxx, MD	018	xxxxxx xxxxxx	xx. xxxx, xx
xxxxxx xxx xxxxxxxx, MD	019	xxxxxxxx xxxxxxxx xxxxxx xxxxxxxxx	xxxxxxx, xx
xxxx xxxxxx, MD	020	xxxxx xxxxxxx xxxxxxx xxxxxxxxx	xxxxxxxxx, xx
xxxxx x. xxxxxxxxx, MD	021	xxxxx xxxxx xxxxxxxxxx	xxxxxxx, xx
xxxxx x. xxxxxxx, MD	023	xxxxxxxxxxxx xxxxx xxxxxxxx xxxxx	xxxxxxxxxxx, xx
xxxxx xxxxxxxxxx, MD	024	xxxxxxxx xxxxxxxxxx	xxxxxxxx, xx
xxxxx xxxxxx xxxxxx, xx	025	xxx xxxxxxxxx xx xxxxx xxxxxxx xxxxxx	xxxxxxxxx, xx

Source Data: Appendix A, Investigator CVs

3.3 Ethics

The study was conducted in accordance with Good Clinical Practices[1] and 21 CFR Part 50 and 56 and the Declaration of Helsinki as amended in Somerset West, Republic of South Africa (October, 1996). The protocol and statement of informed consent were approved by an Institutional Review Board (or Ethics Committee) prior to each center's initiation. Written informed consent[2] from the patient's parent or legal guardian and patient assent to participate were obtained prior to entry into the study. Case report forms were provided for each patient's/subject's data to be recorded.

3.4 Eligibility Criteria

This study enrolled Children and adolescent outpatients (8 to 17 years old) who met DSM-IV criteria for obsessive-compulsive disorder (DSM-IV, 300.30) as their predominant psychiatric diagnosis. The complete list of entrance criteria are provided below.

3.4.1 Inclusion Criteria

Patients were to be included in the study if they satisfied all of the following inclusion criteria:

1 Written informed consent (parent or legal guardian) and assent (patient) to participate obtained.

2 Patient must be at least 8 years old and no more than 17 years old.

3 Met DSM-IV criteria for OCD (300.30) as the principle diagnosis, as determined by the K-SADS-L structured clinical interview.

4 Patient must have a score of 16 or above on the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) at Screening and at Baseline.

---

[1] as stated in EU CPMP for European multi-national studies and 21 CFR for studies filed to the US IND. Note, if this is a local study, the applicable national or regional GCP should be cited.

[2] Appendix A contains the protocol and the sample informed consent is an appendix to the protocol.

5 The patient must have a documented history of OCD for a minimum duration of 3 months.

6 Medically healthy as determined by physical examination, medical history and laboratory screening.

3.4.2 Exclusion Criteria

Patients meeting any of the following exclusion criteria were to be excluded from the study:

1 Patients with any Axis I disorder other than OCD as a predominant diagnosis, especially primary affective disorders, eating disorders, thought disorders, conduct disorders, pervasive development disorders and Tourette's Syndrome.

2 Patients with any serious concomitant medical condition requiring chronic medication management or where the intercurrent illness may interfere with participation in the protocol.

3 Patients with mental retardation or behaviors of sufficient severity which would make them uncooperative or compromise their participation in and completion of the study.

4 Patients with a history of seizure disorders (except for febrile seizures in childhood).

5 Patients requiring concomitant therapy with other psychotropic drugs, L-tryptophan, warfarin, sumatriptan, cimetidine, phenytoin, quinidine or type 1C antiarrhythmics (e.g., propafenone, flecainide and encainide).

6 Patients who meet DSM-IV criteria for substance abuse (alcohol or drugs) within the past 6 months.

7 Patients having clinically significant abnormal laboratory findings at the Screening (Day -7) or Baseline (Day 0) examinations.

8 Patients who, in the investigator's judgement, pose a current, serious suicidal or homicidal risk.

9 Patients who have received other investigational drugs within 30 days of Baseline (Day 0), or within 5 half-lives of the investigational drug (the longer period will apply).

10 Patients who have received other psychotropic drugs (including MAO inhibitors) within 14 days of Baseline (Day 0), or fluoxetine within 42 days of Baseline (Day 0).

11 Patients who have previously failed two or more clinical trials for OCD with an SSRI or cognitive behavioral therapy.

12 Patients with a known hypersensitivity or intolerance to paroxetine.

13 Females of childbearing potential who are lactating or have a positive pregnancy test at Screening.

14 Sexually active females who do not employ adequate means of contraception, i.e., oral contraception, systemic contraception (i.e., Norplant®), or surgical sterilization; I.U.D., and diaphragms in conjunction with spermicidal foam and condom.

15 Behavioral therapy (i.e., exposure and response prevention) or psychotherapy.

3.5 Study Medication and Administration

3.5.1 Study Medication

Paroxetine was supplied as white film-coated oval tablets containing 10 mg paroxetine. For Phase I (open-label), the 10 mg paroxetine tablets were packaged in bottles of 100 for dispensing to the patients. For Phase II (double-blind), all blinded study medication, i.e., paroxetine and placebo, was identical in appearance. The Phase II study medication was dispensed to the patients in foil-backed blister packs (60 tablets per pack).

Table 2 The Appearance, Formulation and Dosage Strength of Drugs Used in this Study (with Batch Numbers)

Study Drug	Dose	Appearance	Batch/(Lot) Numbers
Paroxetine	10mg	White, film coated modified oval tablet	U96157 / (X10-6B10)
Placebo	10mg	White, film coated modified oval tablet	U96161 / (X9-6B10PL)

Source: Appendix A, Certificates of Analysis

3.5.2 Dosage and Administration

Dosing during the 16-week open-label phase (Phase I) followed a flexible-dose (paroxetine 10-60mg/day, administered as a single daily dose) paradigm. Dosing was initiated at 10mg/day and, if necessary, could have been titrated upward in 10mg increments no more frequently than once a week. Dose escalation was to be based on therapeutic response and tolerability of the medication. Dose adjustments in the intervening weeks between scheduled visits were permitted by telephone contact with patient/parent or guardian. Because the response to OCD medication is often delayed (4-6 weeks), it was recommended that the dose of paroxetine not exceed 40 mg/day until after Week 6, unless clinically indicated. The maximum daily dose allowed was 60mg/day.

Dosing during the 16-week, randomized, double-blind, placebo-controlled phase (Phase II) was based on the final dosage level reached during the final visit of Phase I of the study. Dose tapering of patients randomized to placebo was achieved in a blind fashion such that decreases occurred in 10mg increments per week, beginning at the start of Phase II. Dose adjustments were not permitted during this phase of the study. If a dosage increase was indicated due to non-response or a dosage reduction necessary as a result of intolerability, the patient was to be withdrawn from the study.

Tapering of medication was recommended for all patients upon conclusion of the study. For patients not continuing into the double-blind phase (Phase II), it was recommended that medication be reduced in 10mg increments per week. Thus, for patients taking 60 mg/day as their final dose in the study, it was recommended

that the dose be tapered over the next 5 weeks (i.e. 50mg/day for one week, 40mg/day for one week, 30mg/day for one week, 20mg/day for one week and 10mg/day for one week). Patients concluding Phase II were to be down titrated in a double-blind fashion in 10mg increments per week over a six week period.

The maximum paroxetine dose was 60 mg (six tablets) daily. Since the duration of open-label treatment under this protocol (i.e. Phase I) was 16 weeks and the duration of double-blind treatment under this protocol (i.e. Phase II) was 21 weeks (including End Taper), a total of 37 weeks of active treatment was possible during the conduct of this study. Therefore, including the week-long Screening Phase, total duration of the study for any given patient was a maximum of 38 weeks.

3.5.3 Compliance with Study Medication

Every effort should be made to encourage patient compliance with the dosage regimen and to take all medication as instructed. Patients were encouraged to return their current bottle/blister pack of study medication, when they returned for each visit. Adherence to the dosing regimen was assessed at each visit by study site staff by returned tablet counts. Instances of patients taking < 80% or > 120% of the prescribed amount of study medication in a given visit interval were to be discussed with the study sponsor on a case by case basis and a determination made as to whether to remove the patient from the study was to be made. Subjects who missed 5 consecutive doses or more of dosing were considered to be non-compliant and were to have been withdrawn from the study.

3.5.4 Storage and Drug Accountability

Study medication was required to be stored in secure (locked) areas at controlled room temperature (20-25°C) and dispensed according to the protocol udner the supervision of the investigator and his/her designee. Records of all study drug shipped to the study center, dispensed to patients, returned by patients, and returned to the sponsor were to be maintained at the study centers.

3.6 Prior and Concomitant Medication

All psychotropic medication taken during the 6 month period prior to Screening were to be recorded in the case report form (including generic name, dosage, indication, and dates taken). Refer to Section 3.4 for eligibility criteria which pertained to prior medication intake. All concomitant medications taken during the study were likewise to be recorded in the case report form, along with dosage information and start and stop dates.

The concomitant use of L-tryptophan, warfarin, sumatriptan, cimetidine, phenytoin, quinidine or type 1C antiarrhythmics (e.g. propafenone, flecainide and encainide) or other psychotropic drugs was contraindicated during the study, with the exception of Ativan® (lorazepam ½ - 1 mg) for sleep disturbance. However, the use of Ativan® (lorazepam ½ - 1 mg) was not to exceed 3 consecutive days per one week period. Use of Ativan® (lorazepam ½ - 1 mg) was to be recorded in the concomitant medication section of the case report form. Behavioral therapy (i.e., exposure and response prevention) or psychotherapy during the conduct of the study was not permitted.

3.7 Study Procedures

3.7.1 Schedule of Assessments

Tables 3 and 4 present the complete list of study assessments/procedures for the open-label and double-blind phases, respectively.

3.7.2 Prestudy Screening and Enrollment

All patients underwent an initial Screening visit (Visit 1, Day –7) one week prior to the Baseline Visit in order for their eligibility for study entry to be assessed. At the Screening Visit the following were to be performed :

a Written informed consent/assent.

b General patient information.

c A detailed psychiatric, medical and medication history.

d K-SADS-L

e Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS).

f Physical examination.

g Electrocardiogram (ECG)

h Vital signs: systolic and diastolic blood pressure and heart rate to be measured at 3 minutes sitting.

i Body weight determination.

j Clinical laboratory evaluation.

k Baseline adverse experiences.

l Pregnancy test (if applicable).

m Drug screen.

n Inclusion/Exclusion Criteria.

A patient log was to be kept at each site listing all patients considered for the study, including those not entering the trial. The reasons for excluding patients from the study were to be recorded.

Table 3 Flow Chart of Patient Evaluations Phase I

Visits:	Screen	Baseline	Week 2	Week 4	Week 6	Week 8	Week 12	Week 16a	Taper Endb	Follow-Upc
Day/Visit Number	D -7 / V1	Day 0 / V2	V3	V4	V5	V6	V7	V8		
Screening/Baseline Evaluations										
Written Informed Consent/Assent	X									
General Patient Information	X									
K-SADS-L	X									
Psychiatric, Medical, and Medication Histories	X									
ECG	X					X		X	X[d]	X[d]
Pregnancy Test	X			X		X	X	X		
Drug Screen	X					X		X		
Inclusion/Exclusion Criteria	X	X								
Efficacy Evaluations										
CY-BOCS	X	X	X	X	X	X	X	X		
HAMA		X		X		X	X	X		
CGI		X[f]	X	X	X	X	X	X		
HAMD		X		X		X	X	X		
Yale Global Tic Scale		X		X		X	X	X		
Global Assessment of Functioning (GAF) Scale		X		X		X	X	X		
Response Criteria								X[e]		
Safety Evaluations										
Physical Examination	X							X	X	X
Vital Signs/Body Weight	X	X	X	X	X	X	X	X	X	X
Laboratory Evaluation	X	X[d]				X		X	X[d]	X[d]
Adverse Experiences		X	X	X	X	X	X	X	X	X, Y
Miscellaneous Records										
Concomitant Medications	X	X	X	X	X	X	X	X	X	X
Study Medications Record/Accountability			X	X	X	X	X	X	X	
Study Termination Record								X	X	

[a]Completed at week 16 or upon Premature termination. For patients continuing into Phase II, this visit also served as the randomization visit for Phase II.

[b]Conducted after the last dose of study medication if a down-titration

[c]Follow-up for all patients withdrawn from the study due to adverse events or who have an ongoing AE at the time of the last dose of study medication (X's), and for patients who are not entering Phase II and also do not have a Taper End Visit (Y's).

Table 3 Flow Chart of Patient Evaluations Phase I

Visits:	Screen	Baseline	Week 2	Week 4	Week 6	Week 8	Week 12	Week 16a	Taper Endb	Follow-Upc
Day/Visit Number	D -7 / V1	Day 0 / V2	V3	V4	V5	V6	V7	V8		

[d]Repeat evaluation only if values were clinically significantly abnormal at most recent previous visit.

[e]To determine response criteria and eligibility for Phase II of study.

[f]CGI Severity of Illness Item only.
Source Appendix A, Protocol

Table 4 Flow Chart of Patient Evaluations Phase II

Visits: **Vist Number**	**Week 2** V9	**Week 4** V10	**Week 6** V11	**Week 8** V12	**Week 10** V13	**Week 12** V14	**Week 16a** V15	**Taper Endb**	**Follow-upc**
Efficacy Evaluations									
CY-BOCS	X	X	X	X	X	X	X		
HAMA	X	X	X	X	X	X	X		
CGI	X	X	X	X	X	X	X		
HAMD	X	X	X	X	X	X	X		
Yale Global Tic Scale	X	X	X	X	X	X	X		
GAF	X	X	X	X	X	X	X		
Safety Evaluations									
Pregnancy Test		X		X		X	X		
Drug Screen				X			X		
Physical Examination							X	X	X
ECG				X			X	X[d]	X[d]
Vital Signs/Body Weight	X	X	X	X	X	X	X	X	X
Laboratory Evaluation				X			X	X[d]	X[d]
Adverse Experiences	X	X	X	X	X	X	X	X	X
Miscellaneous Records									
Concomitant Medications	X	X	X	X	X	X	X	X	X
Study Medications Record/Accountability	X	X	X	X	X	X	X	X	
Study Termination Record								X	

[a]To be completed at Week 16 or upon premature termination.

[b]To be conducted after the last dose of study medication if a down-titration phase is instituted.

[c]Follow-up for all patients withdrawn from the study due to adverse events, or patients who have an ongoing AE at the time of last dose of study medication.

[d]Repeat evaluation only if value(s) were clinically significantly abnormal at most recent previous visit.
Source: Appendix A, Protocol

3.7.3 Baseline Visit

The following observations/assessments were to be performed at the Baseline Visit (Day 0):

a Hamilton Depression Rating Scale (HAMD)

b Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS).

c Hamilton Anxiety Rating Scale (HAMA).

d Yale Global Tic Scale.

e Severity of Illness item of the Clinical Global Impressions (CGI).

f Global Assessment of Functioning Scale (GAF).

g Vital signs.

h Clinical laboratory evaluations, if abnormal at Screen Visit

i Body weight determination

j Concomitant medication records.

k Baseline adverse experiences.

l Inclusion/Exclusion Criteria.

Patients who continued to satisfy **all** criteria for eligibility at the Baseline evaluation were eligible for participation in the open-label phase of the study (Phase I). Open-label medication for the first two-weeks of treatment were dispensed along with dosing instructions.

3.7.4 Open-Label Treatment Phase

During Phase I, Post-baseline (>Day 0) visits were to be scheduled every two weeks for the first two months and monthly thereafter for the remaining two months, for a total of 6 visits.

The following procedures were to be performed:

a Children's Yale-Brown Obsessive-Compulsive Scale at Weeks 2, 4, 6, 8, 12 and 16.

b Hamilton Anxiety Rating Scale (HAMA) at weeks 4, 8, 12 and 16.

c Severity of Illness and Global Improvement items of the Clinical Global Impressions (CGI) at Weeks 2, 4, 6, 8, 12 and 16.

d Hamilton Depression Rating Scale (HAMD) at Weeks 4, 8, 12 and 16.

e Yale Global Tic Scale at Weeks 4, 8, 12 and 16.

f Global Assessment of Functioning Scale at Weeks 4, 8, 12 and 16.

g Vital signs at each visit.

h Laboratory evaluations at Weeks 8 and 16.

i Body weight determination at each visit.

j Physical examination at Week 16.

k ECG at Weeks 8 and 16.

l Pregnancy Test at Weeks 4, 8, 12 and 16.

m Drug Screen at Weeks 8 and 16.

n Adverse event monitoring at each visit (or ascertained by phone contact with patient).

o Dispense open-label study medication at each visit (except Week 16, unless dispensing study end taper medication) and update study medication record. If dose adjustments were conducted by phone contact with patient/parent or legal guardian in the intervening weeks between study visits, then study medication records were to have been completed accordingly. Update concomitant medication record (including adequate means of contraception for sexually active females).

p Complete the study termination record at final visit (Week 16 or at termination if the patient withdraws from the study), unless the patient proceeds into Phase II of the study.

Upon completion of Phase I, patients who achieved a therapeutic response (defined as ≥ 25% improvement in baseline CY-BOCS Total Score *and* a CGI Global Improvement Item Score of 1 or 2) were eligible to participate in Phase II

of the study. If the patient was to continue into Phase II, the patient was randomized and blinded study medication was dispensed at the Week 16 Visit.

3.7.5 Double-Blind Treatment Phase

During Phase II, visits will were to be scheduled every two weeks (Except Week 14) for a total of 7 visits during this phase of the study. A Taper End Visit was scheduled for the end of the double-blind down-titration phase, if applicable.

The following procedures were to be performed:

a Children's Yale-Brown Obsessive-Compulsive Scale at Weeks 2, 4, 6, 8, 10, 12, and 16.

b Hamilton Anxiety Rating Scale (HAMA) at Weeks 2, 4, 6, 8, 10, 12, and 16.

c Severity of Illness and Global Improvement items of the Clinical Global Impressions (CGI) at Weeks 2, 4, 6, 8, 10, 12, and 16.

d Hamilton Depression Rating Scale at Weeks 2, 4, 6, 8, 10, 12, and 16.

e Yale Global Tic Scale at Weeks 2, 4, 6, 8, 10, 12, and 16.

f Global Assessment of Functioning Scale at Weeks 2, 4, 6, 8, 10, 12, and 16.

g Vital signs at each visit.

h Laboratory evaluations at Weeks 8 and16.

i Body weight determination at each visit.

j Physical examination at Week 16.

k ECG at Weeks 8 and 16.

l Pregnancy Test at Weeks 4, 8, 12 and 16.

m Drug Screen at Weeks 8 and 16.

n Adverse event monitoring at each visit (or ascertained by phone contact with patient).

o Update concomitant medication record (including adequate means of contraception for sexually active females) and study medication records at each visit.

p Complete study termination record at final visit.

3.7.6 End Taper Visit

Tapering of medication was recommended for all patients upon conclusion of the study, either upon premature termination or study completion (including patients who completed Phase I but who did not continue into Phase II). Medication was to be reduced in 10mg increments per week. Thus, for patients taking 60 mg/day as their final dose in the study, it was recommended that the dose be tapered over the next 5 weeks (i.e. 50 mg/day for one week, 40mg/day for one week, 30mg/day for one week, 20mg/day for one week and 10mg/day for one week). Patients concluding Phase II were to be down-titrated in a double-blind fashion in increments of 10 mg/week for a period of up to five weeks.

A Taper End Visit was to be conducted after completion of the down-titration phase and was to consist of a physical exam, including vital signs and body weight determination, and adverse event monitoring. Other evaluations (laboratory, ECG) were also to be repeated at the Taper End Visit if there was an abnormal finding at the most recent prior evaluation or if additional testing was clinically necessary to follow-up an adverse experience.

3.7.7 Interim Visits

In the event that a patient was required to attend the clinic for an unscheduled visit, the following were to be conducted:

a CGI Severity of Illness and Global Improvement items

b Adverse Event monitoring

c Review dosing, update concomitant medication record (including adequate means of contraception for sexually active females) and study medication record.

3.7.8 Early Discontinuation

Patients prematurely discontinued from the study during either phase were to undergo all Week 16 visit procedures/observations for that study phase (i.e., all study endpoint procedures). In addition, for those patients prematurely terminated from the study due to an adverse experience, a follow-up visit was to be conducted within one month of termination for safety assessments (see Section 3.7.9).

3.7.9 Follow-Up Visit

Post-study follow-up must be completed for all patients who are either withdrawn from the study prematurely due to adverse events or who have an ongoing adverse event at the time of the last dose of study medication. Follow up was to occur within 30 days after the last dose of study medication was taken and was to consist of a physical exam, including vital signs and body weight determinations, and adverse event monitoring. Other evaluations (laboratory, ECG) were to be repeated at the Follow-up Visit if there was an abnormal finding at the most recent previous evaluation, or if additional testing was clinically necessary to follow-up the adverse experience.

A Follow-up Visit was also to be conducted for any Phase I patient who did not participate in Phase II, and who did not have a Taper End Visit at the end of Phase I (irrespective of whether they completed Phase I or withdrew prematurely). Phase I patients who did not participate in Phase II but who did taper off of study medication were not required to have a Follow-up Visit if they had no ongoing adverse event(s) at the Taper End Visit.

3.8 Efficacy Assessments

The efficacy assessments were conducted utilizing the following rating scales:

- The Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS)
- Hamilton Anxiety Rating Scale (HAM-A)
- Hamilton Depression Rating Scale (HAM-D)
- Yale Global Tic Scale
- The Clinical Global Impressions (CGI) Severity of Illness and Global Improvement items.

- The Global Assessment of Functioning Scale (GAF).

Refer to Section 3.11.3 for a description of the primary and secondary measures of efficacy.

3.9 Safety Assessments

Safety was assessed primarily through routine adverse experience (AE) monitoring, vital sign (including body weight) determinations, and clinical laboratory evaluations. In addition, a physical examination and a 12-lead ECG were performed at periodic visits (described below).

3.9.1 Adverse Experiences

All AEs (serious and non-serious), whether observed or reported by the patient were evaluated by the investigator and recorded in the AE section of the patient's case report form. Adverse experiences were to be elicited by the investigator asking the patient a non-leading question such as *"Do you feel differently in any way since starting the new treatment?"* If the patient responded "Yes", details of the treatment emergent AE and its severity including any change in study drug administration, investigator attribution to study drug, any corrective therapy given and outcome status were documented on the case report form. Investigators were instructed to follow-up patients with adverse experiences until the event had subsided (disappeared) or until the condition had stabilized. Reports relative to the subject's subsequent course must be submitted to the clinical study monitor. Attribution or relationship to study drug was judged by the investigator to be unrelated, probably unrelated, possibly related, or related. All adverse experiences were coded from the verbatim term according to the WHO Adverse Reaction Terminology (ART) dictionary by body system and preferred term.

The definitions for AEs and serious AEs, as well as the instructions provided to the study sites for assessing AE severity and causality, for reporting serious AEs, and how overdosages, on-study pregnancies, and breaking the study blind should be handled are included in the protocol (Appendix A of this report).

3.9.2 Physical Examinations, Vital Signs and ECGs

Complete physical examinations were required at the Screening visit and at the final visit of each phase of the study. Any adverse changes in the physical examination were to be recorded in the adverse experience pages of the case report forms (CRF). Vital signs, consisting of systolic and diastolic blood pressure and heart rate after 3 minutes sitting and including body weight determination, were conducted at each visit. Likewise, any clinically signicant adverse change in any of these parameters was to be recorded as an adverse experience.

Twelve-lead electrocardiograms (ECGs) were to be performed at the Screening visit and again at Weeks 8 and 16 in each study phase. The investigators were to assess and record whether there were any clinically significant changes from Screening in each ECG. All clinically significant abnormalities were to be recorded in the adverse experience pages of the CRF.

3.9.3 Clinical Laboratory Tests

Clinical laboratory evaluations consisted of hematology, clinical chemistry and urinalysis parameters, and were performed according to the schedule of procedures in Tables 3 and 4. The sample collection procedure is described in the protocol (Appendix A of this report). Any abnormalities considered clinically significant were to be recorded in the adverse experience pages of the CRF.

a. Hematology

The following hematological parameters were evaluated: Hemoglobin (Hb), Hematocrit (HCT), Mean Cell Volume (MCV), Mean Cell Hemoglobin (MCH), Mean Cell Hemoglobin Concentration (MCHC), Red Blood Cell count (RBC), White Blood Cell count (WBC), Platelet count, Differential WBC count (total and segmented neutrophils, bands, lymphocytes, monocytes, basophils and eosinophils).

b. Clinical Chemistry

Serum chemistry parameters evaluated included Sodium, Potassium, Chloride, Phosphorous, Blood Urea Nitrogen (BUN), Creatinine, Glucose (random), Total Protein, Total bilirubin, Asparate Amino Transferase (AST), Alanine AminoTransferase (ALT), Alkaline Phosphatase (AP), Gamma Glutamyl Transferase(GGT), Lactate Dehydrogenase (LDH).

c. Urinalysis

Urinalysis parameters consisted of color and appearance from visual observation. In addition, the following were assessed using dipstick: specific gravity, urine reaction pH, glucose, protein, ketone, occult blood and bilirubin. White blood cells (WBC) and Red Blood Cells (RBC) per high-power field (HPF) were determined by microscopy. Other findings were reported only if observed under microscopic observation. A qualitative drug screen for drugs of abuse (i.e., alcohol, amphetamines, benzodiazapines, cocaine, cannabinoids, opiates, barbituates, propoxyphene, methadone, methaqualone and phencyclidine) was also performed at the specified times.

Lastly, early morning urine samples were collected from females of child-bearing potential for pregnancy testing, at the specified assessment periods.

3.10 Data Quality Assurance

To ensure that the protocol-stipulated study procedures were well-understood and performed as consistently as possible across all investigator sites, the protocol, case report form and safety reporting were reviewed with the investigator and his/her personnel responsible for the conduct of the study by the sponsor representative(s) at the investigator site prior to initiation of the study at that center. In addition, a multicenter Investigators' Meeting was held on Monday, Nov. 18, 1996 in St. Louis, MO, prior to initiation of the study.

Adherence to the protocol requirements and verification of data generation accuracy was achieved through monitoring visits to each study site by sponsor personnel at periodic intervals during the study and at the completion of the study. The monitor verified CRF entries by comparing them with the source documents (hospital/clinic/office records) before retrieving the case report forms. Subsequent data handling and reporting processes were subject to in-process Quality Control and this final clinical report has, in addition, been subject to an end-stage Quality Control review. All the above procedures were performed according to methodologies detailed in SmithKline Beecham Standard Operating Procedures (SOPs).

A Contract Research Organization (Parexel) was employed to perform a variety of data management functions (manual review of the CRFs for completeness and accuracy, CRF data entry, computerized edit/validation checks, generation and issuance of data clarification requests, performing database corrections, and

providing a finalized database to the sponsor) according to an agreed contract. The CRO responsibilities were conducted according to SmithKline Beecham standard data management practices.

Data on serious AEs (SAEs) came from two different databases and were collected at two different timepoints. Although key data in the databases have been reconciled, minor discrepancies in details of the serious AEs between the individual patient narratives and the data source tables may remain. It is considered, however, that these differences were minor in nature and do not change the overall significance or understanding of the serious AE.

This study was subject to audit by SmithKline Beecham's department of Worldwide Regulatory Compliance-GCP (WRC-GCP). A list of audited sites can be found in Appendix A.

3.11 Statistical Evaluation

This section describes the statistical analyses performed on the efficacy and safety data. Statistical aspects of the sample size rationale are also discussed. All analyses were performed in accordance with the protocol unless otherwise stated. No interim analyses were planned or performed in this study. Additional details can be found in the Statistical Report (Section 15).

3.11.1 Target Sample Size

Based on the primary measure of efficacy, i.e., proportion of patients who relapse during the randomized treatment phase, it was estimated that 90 patients per treatment group (total 180) would be sufficient to detect a difference of 25% in relapse rates between paroxetine and placebo. This was based on an assumed relapse rate of 60% for placebo patients. This difference in relapse rates is detectable with a power of 90%, given a significance level of 5% and using a two-sided significance test.

Assuming a response rate of 60% for patients reaching the end of the open- label phase of the study (Phase I), a total of 300 patients were required to complete the 16 weeks of open-label treatment.

Assuming an attrition rate of 20% during the open-label phase, it was estimated that approximately 375 patients would need to be recruited in to the study.

3.11.2 Method of Randomization

Upon entering the double-blind phase (Phase II), patients were randomly assigned in a balanced fashion (1:1) to the two treatment groups using a computer-generated randomization schedule code. The treatment groups were randomly assigned in blocks of four.

3.11.3 Planned Efficacy Evaluations

The primary efficacy outcome variable was the proportion of patients relapsing during the randomization phase (Phase II). Relapse was based on the CGI Global Improvement Item Score, and was defined as any of the following:

- Worsening of CGI Global Improvement Score by 1 point for 2 consecutive visits
- Worsening of CGI Global Improvement Score by ≥ 2 points at any single visit
- A CGI Global Improvement Score of 5 or greater

The secondary efficacy variables (in Phases I & II) included:

1 Time to Relapse (Phase II only).

2 Mean change from Baseline in CY-BOCS Total Score

3 Mean change from Baseline in CY-BOCS obsessive and compulsive subscales.

4 Proportion of patients achieving ≥25% improvement in baseline CY-BOCS Total Score.

5 Proportion of patients achieving a CGI Global Improvement Score of 1 or 2.

6 Change from Baseline in CGI Severity of Illness item.

7 Mean change from Baseline in HAMD Score.

8 Mean change from Baseline in HAMA Score.

9 The Yale Global Tic Scale - Total Tic Scores.

10 Mean change from Baseline in GAF Score.

For the double-blind data (Phase II), summary statistics are presented for all timepoints where the information for that variable was collected, and change from baseline was calculated using the Phase II (randomization) baseline data. In addition, statistical analyses were performed for the primary efficacy variable and secondary variables 1, 2, and 4. Variables 2 and 4 were analyzed at Weeks 8, 16 and study endpoint. For the open-label data (Phase I), summary statistics are presented for all timepoints where the information for that variable was collected, and change from baseline calculated using the Phase I (open-label) baseline data.

The following definitions applied to the efficacy variables:

Endpoint: The endpoint dataset was generated for phase II of the study only, by taking the last valid result between the first visit and the week 16 visit. Only data from assessments made after the start of randomized treatment were extended forward.

Baseline: Baseline was defined as the start date of paroxetine medication in the open label phase (Phase I) of the study.

Randomization Baseline: Randomization baseline was defined as the start date of randomized paroxetine or placebo treatment in Phase II of the study.

Clinical Global Impression (CGI) Global Improvement Item Responder: Patient with a score of 1 (very much improved) or 2 (much improved) at study endpoint.

*Childrens YALE Brown Obsessive Compulsive Scale (CY-BOCS) Total score:*Sum of items 1 to 10 (not including 1b, 6b).

*CY-BOCS Obsessive subscale: S*um of items 1 to 5 (not including 1b)

*CY-BOCS Compulsive subscale: S*um of items 6 to 10 (not including 6b)

*CY-BOCS Responder: P*atient who achieves a ≥25% reduction from baseline in CY-BOCS score at study endpoint.

Hamilton Anxiety Rating Scale (HAMA) Total score: Sum of items 1 to 14

Hamilton Depression Rating Scale (HAMD) Total Score: Sum of items 1 to 17

Yale Global Tic Scale Total Tic Score: Sum of the scores for the items "number", "frequency", "intensity", "complexity", and "interference" of both motor tics and phonic tics.

3.11.4 Patient Populations

The Phase I intention-to-treat population consisted of all patients who were enrolled into the study, who received at least one-dose of open-label treatment and for whom at least one post-baseline evaluation was available. Patients were included in this population regardless of whether the entry criteria were fulfilled or the protocol violated.

The Phase II intention-to-treat population consisted of all patients who were enrolled into the study, who received at least one-dose of randomized treatment and for whom at least one post-randomization baseline evaluation was available. Patients were included in this population regardless of whether the entry criteria were fulfilled or the protocol violated.

The phase II intention-to-treat (ITT) population was the primary population of interest.

The Per-Protocol Population consisted of those Phase II (double-blind) ITT patients for whom all of the following criteria were met:

- No major protocol violation existed with respect to the inclusion/exclusion criteria.
- No major protocol violation occurred between randomization and completion of the 16 week randomized treatment phase.
- The patients do not miss more than 5 consecutive days of randomized study medication.

Patients excluded from the Per-Protocol efficacy analyses were identified before the study was unblinded. Approximately 15% of the ITT population were excluded from the Per Protocol Population for the reasons noted above. Only the primary efficacy variable was analyzed using the Per-Protocol population.

3.11.5 Datasets to be Evaluated

The primary inferences concerning the efficacy of paroxetine in Phase II of the study were made using the last observation carried forward (LOCF) dataset of the ITT population, defined as the last on-drug assessment during the randomized treatment phase.

For the primary efficacy variable, analysis of the proportion of patients relapsing was based on the number of patients relapsing during the entire Phase II period.

For the secondary variables, two additional datasets to the study endpoint dataset were considered to ensure the robustness of the results:

- an LOCF dataset at the latest time point (visit) where at least 70% of the patients in each treatment group remained in the study (defined as the 70% endpoint. The 70% endpoint was the Week 4 Visit.

- an observed cases (OC) dataset at 8 and 16 weeks.

No formal statistical analyses were performed for the open-label treatment phase (Phase I) of the study.

3.11.6 Methods of Analysis

The differences between paroxetine and placebo at study endpoint were estimated from the analysis as paroxetine minus placebo, and 95% confidence intervals were constructed around the estimated differences. All hypothesis tests were two-sided. The effect of interactions (e.g., treatment by center) were assessed at the 10% level of significance. All other statistical tests were performed at the 5% level of significance.

Covariates for Adjustment in the Efficacy Analyses

The following variables were assumed to be associated with response:

- Age at onset of OCD

- Baseline CY-BOCS score

The following variable was assumed to be associated with relapse:

- CY-BOCS Score at randomization baseline

Two analyses were performed for each of the primary and secondary efficacy variables specified for analysis. The first analysis allowed for the effect of center only, the second analysis allowed for both the effect of center and the above covariates (depending on whether the variable of interest was response or relapse). The impact of adjusting for the covariates was assessed by comparing the results obtained from both analyses.

Categorical Variables

Categorical efficacy variables (i.e., proportion of patients relapsing, proportion of patients with ≥25% reduction in CY-BOCS score) were analyzed using logistic regression (using PROC GENMOD in SAS), allowing for center group effects. The effect of adding treatment by center group interaction into the model was assessed.

These data were also analyzed allowing for both center effects and the effects of the covariates (for relapse or response as appropriate) specified previously. The effect of adding treatment by center interaction into the model was assessed with the covariates and center in the model.

Adequacy of the model fit was explored by inspecting plots of the Pearson residuals and deviance residuals.

For each treatment group there was an odds of a patient being classed as a relapser (or responder). The results are presented in terms of odds ratios (i.e. the odds of the relapse (or response) on paroxetine relative to the odds of relapse (or response) on placebo). 95% confidence intervals around the odds ratios are also provided.

Continuous Variables

Providing the underlying assumptions were satisfied, continuous efficacy data (change from randomization baseline in CY-BOCS scores) were analyzed by analysis of variance (using PROC GLM in SAS) allowing for both center group effects and the effects of the prospectively defined covariates (age at onset of OCD, Baseline CY-BOCS score, and Randomization Baseline CY-BOCS score). The effect of adding treatment by center interaction into the model was assessed with the covariates and center in the model.

Results are presented as the point estimate and 95% confidence interval for the difference between-paroxetine and the placebo group.

The assumptions of normality and homogeneity of variance were assessed by inspection of normal probability plots and residual plots. If these assumptions were not met, appropriate non-parametric methods were used.

All efficacy measures over the course of the study are presented and summarized in graphs and tables; continuous data by means, standard errors of the means and numbers of patients and categorical data by counts and proportions.

Time to event Variables

Time to relapse was estimated using survival analysis methodology (PROC LIFETEST in SAS), and differences between treatment groups in distributions of time to relapse were investigated using the log rank test.

Treatment of Missing Data

Childrens YALE Brown Obsessive Compulsive Scale (CY-BOCS), Hamilton Depression Rating Scale (HAMD), and Hamilton Anxiety Rating Scale (HAMA):

If at least 90% of the items making up the score of interest were present at a particular timepoint, the missing values were allowed for by calculating the total score as:

$$\frac{\text{(Sum of scores for items present) x (Total number of Items that should be present)}}{\text{(Number of items present)}}$$

If less than 90% of the items making up the score of interest were available for a patient at a particular timepoint then that patient's data was excluded from the analysis and the summary tables of that variable at that timepoint. All the data was included in the listings.

YALE Global Tic scale:

If no more than 1 item was missing from each of the motor and phonic tic subscales, at a particular timepoint, the missing value was allowed for by assigning it the "worst case" value. This was "0" for the baseline assessment, and "5" for any treatment assessment.

If more than 1 item was missing from each of the motor and phonic tic subscales for a patient at a particular timepoint, then that patient's data was excluded from the analysis and the summary tables at that timepoint.

3.11.7 Safety Evaluations

All patients who received study medication and for whom at least one post-baseline assessment was made were assessed for clinical safety and tolerability.

Adverse experiences were coded using the WHO adverse experience codelist which was then mapped to the ADECS (COSTART based) classification to give a body system and preferred term. Counts and percentages were made of patients with treatment emergent (tabulated separately for Phase I, Phase II, or during taper and also whether non-gender specific or gender specific) adverse experiences in each treatment group overall and by body system, preferred term, and age subgroup (<12 years old, ≥12 years old). Counts and percentages were also produced of patients with serious emergent adverse experiences and adverse experiences leading to withdrawal, again tabulated separately for Phase I, Phase II, or taper phase and also whether non-gender specific or gender specific. An adverse experience was regarded as occurring on-drug if it started within 14 days after the last dose of the study medication.

Information regarding vital signs and laboratory values are presented as listings and tables. Summary statistics (mean, standard deviation, minimum and maximum) for the absolute values and changes from baseline are presented. The number of patients with laboratory values or vital sign values outside sponsor predefined clinical concern ranges were also tabulated, again separately by study phase. The number and percentage of patients who had a positive drug screen was tabulated by study phase. Refer to Data Source Table 15.0, Section 12, for the complete list of predefined clinical concern criteria for vital signs and laboratory data.

3.11.8 Other Evaluations

Demographic data, data pertaining to diagnosis and disease history, prior and concomitant medication data, medical/surgical history, patient disposition data and patient distribution by center data are as listing and tables. No hypothesis testing was performed. Data for all variables at Baseline were checked for homogeneity between the treatment groups. No pharmacoeconomic or quality of life evaluations were performed during the conduct of this study.

3.11.9 Defined Visit Timepoints

The protocol stipulated that patient visits during the study were to occur at specific timepoints (see Section 3.7). However, because of scheduling problems,

patient visits could not always occur on the exact day in question. Therefore, visit days were defined by visit windows for analyses purposes.

Data were slotted into the following time windows depending upon the frequency with which the assessment was recorded as per study protocol. The first day of dosing with open label paroxetine was denoted as Day 0 of Phase I. The first day of dosing with randomised study medication was denoted as Day 0 of Phase II.

Phase I:

Data recorded at each assessment (i.e. CY-BOCS, CGI, body weight, vital signs), not regarded as follow-up, was slotted according to the following time intervals:

Days Relative to First Dose of Open Label Medication:

Screening	= days ≤ -5
Baseline	= days –4 to 0
Week 2	= days 1 to 21
Week 4	= days 22 to 35
Week 6	= days 36 to 49
Week 8	= days 50 to 70
Week 12	= days 71 to 98
Week 16	= days 99 to randomisation date (inclusive) OR day 126 if randomisation does not occur
Post Week 16	= greater than 126 days (for cases when randomization does not occur)

Data recorded at weeks 4, 8, 12, and 16 only (HAMD, HAMA, Yale Global Tic, GAF), not regarded as follow-up, was slotted according to the following time intervals (ECG will also be slotted in this way):

Days Relative to First Dose of Open Label Medication:

Screening	= days ≤ -5
Baseline	= days –4 to 0
Week 4	= days 1 to 42
Week 8	= days 43 to 70
Week 12	= days 71 to 98
Week 16	= days 99 to randomisation date (inclusive) OR day 126 if randomisation does not occur
Post Week 16	= greater than 126 days (for cases when randomisation does not occur)

Phase II:

Data recorded at each assessment (i.e. CY-BOCS, CGI, HAMA, HAMD, Yale Global Tic, GAF, body weight, vital signs), not regarded as follow-up, will be slotted according to the following time intervals (ECG will also be slotted in this way):

Days Relative to First Dose of Randomised Treatment:

Randomisation Baseline	= days ≤ 0
Week 2	= days 1 to 21
Week 4	= days 22 to 35
Week 6	= days 36 to 49
Week 8	= days 50 to 63
Week 10	= days 64 to 77
Week 12	= days 78 to 98
Week 16	= days 99 to 126
Post Week 16	= greater than 126

Efficacy assessments performed more than 7 days after the last dose of open label medication were excluded from the phase I summary tables and analyses, but are presented in the data listings. Similarly, efficacy assessments performed more than 7 days after the last dose of randomised medication were excluded from the phase II summary tables and analyses, but are presented in the data listings.

Safety assessments performed more than 14 days after the last dose of open label medication were excluded from the phase I summary tables and analyses, but are presented in the data listings. Similarly, safety assessments performed more than 14 days after the last dose of randomised medication were excluded from the phase II summary tables and analyses, but are presented in the data listings.

If more than one assessment occurred in the same time window (or at the same visit for non slotted data) then the latest assessment was used in the data summaries and analyses, however, all assessments are displayed in the listings. For the analysis of the relapse data, all assessments were considered regardless of their interval allocation.

4 Study Population

4.1 Study Dates

The study was initiated at the first study center on Jan. 13, 1997, with the first patient enrolled (Phase I, open-label paroxetine) on Jan. 23, 1997. The last study visit for the last patient to complete participation occurred on Dec. 28, 1998.

4.2 Patient Disposition

4.2.1 Number and Distribution of Patients

A total of 423 patients signed the informed consent form and underwent formal screening for study entry. Of these 423 patients, 84 were withdrawn from the Screening Phase prior to enrolling in Phase I, most commonly for not meeting one or more of the entrance criteria (59/84, 70.2%). Data Source Table 13.31, Section 10, summarizes the number of patients withdrawn by reason during the Screening Phase (refer to Appendix B, Listing 13.31, for a list of all patients withdrawn during Screening by PID number). Data Source Table 13.31 actually contains a total of 88 patients, rather than 84, because it also includes four patients who entered the open-label phase but who withdrew from the study shortly after the Baseline Visit and before a single study visit or assessment was conducted. It is uncertain as to whether these four patients took any of the open-label study medication. Because these patients have been excluded from the Open-Label ITT population (from both efficacy and safety analyses since no data are available), for the purposes of this report these four patients have been categorized as Screening Phase Withdrawals, rather than Phase I (open-label phase) withdrawals. The four patients in question are PID nos. 453.001.00332, 453.007.00001, 453.007.00002, and 453.011.00113.

A total of 335 patients therefore comprised the open-label phase ITT population (423 screened less the 88 PIDs included in DST 13.31). Table 5 presents a summary of the number of patients enrolled (Phase I) and randomized (Phase II) at each study center. A total of 26 study centers enrolled at least one patient. The number of patients enrolled into the open-label phase at each center ranged from a single patient at the lowest enrolling center to 32 patients at the highest enrolling center. The majority of centers (17/26, 65%) enrolled at least 10 patients into the open-label phase.

Of the 335 patients entered into the open-label phase, 194 (57.9%) entered the randomization phase. However, one of these patients (PID 453.008.00371) did not return for a single post-randomization Phase II visit, therefore this patient was excluded from the Phase II intention-to-treat population. It is uncertain as to whether this patient took any of the double-blind study medication. Consequently, the Phase II population consisted of 193 patients (95 assigned to the paroxetine group and 98 assigned to placebo). The number of patients randomized to the double-blind phase at each center ranged from a low of zero (at the center which entered only one patient into the open-label phase) to a high of 18 patients.

Table 5 Number of Patients Enrolled and Randomized by Center (ITT)

Center Nos.	Investigator	Open-Label	Double-Blind		
			Paroxetine	Placebo	Totals
001	xxxxxxxxx	10	2	2	4
002	xxxx	18	6	5	11
003	xxxxxxxx	1	0	0	0
004	xxxxx	5	1	0	1
005	xxxxxxxx	8	4	3	7
006	xxxxxx	28	7	7	14
007	xxxxxxxx	10	3	3	6
008	xxxxxxx	14	5	5	10
009	xxxxxxx	2	0	1	1
010	xxxxxxxxx	4	0	1	1
011	xxxxxx	29	7	8	15
012	xxx	5	1	1	2
013	xxxxxx	5	2	2	4
014	xxxxx	Cancelled	---	---	---
015	xxxxxxxxx	15	4	4	8
016	xxxxx	6	2	2	4
017	xxxxxxxxx xxxxxxx	32	8	10	18
018	xxxxx	12	6	4	10
019	xxxxxxxx	12	3	5	8
020	xxxxxx	11	4	6	10
021	xxxxxxxxx	19	5	4	9
022	xxxxxxxx	19	5	5	10
023	xxxxxxx	19	7	7	14
024	xxxxxxxxxx	11	4	2	6
025	xxxxxx	14	4	5	9
026	xxxxxxxx	8	2	2	4
027	xxxxxx	18	3	4	7
028	xxxxxx	0	0	0	0
Total Enrolled		335	95	98	193

Source: Data Source Table 13.2.1, 13.2.2, Section 10.

4.2.2 Number of Patients Present at Each Visit

Table 6 summarizes the number of patients remaining in the study at the conclusion of each visit by study phase. After the first four weeks of the open-label phase, 90.4% of the patients still remained in the study. By month 2 (Week 8), 81.5% still remained in the study and by month 3 (Week 12), 72.8% still remained in the study. A total of 217 patients (64.8%) reached the final open-label phase visit (Week 16), however, only 196 patients (58.5%) still remained in the study at the conclusion of this visit. The overall withdrawal rate in the double-blind phase was greater, as approximately 60% of the patients randomized

were withdrawn before reaching Week 16. The double-blind phase dropouts also tended to occur earlier than in the open-label phase, as more than one-half of those who withdrew in Phase II (approx. 60%) did so by Week 4. In contrast, of those patients withdrawing during the open-label phase, only 9.6% did so by Week 4. By Week 4 of the DB phase, only 56% of the placebo group and 71% of the paroxetine group were still in the study. Only 44% of the paroxetine group and 34% of the placebo group reached Week 16 of the DB Phase.

Table 6 Cumulative Number (%) of Patients Remaining in the Study by Visit Week (ITT)

Open-Label Paroxetine		Double-Blind			
			Paroxetine	Placebo	Totals
	n (%)		n (%)	n (%)	n (%)
Entry	335 (100)	Entry	95 (100)	98 (100)	193 (100)
Week 2	313 (93.4)	Week 2	80 (84.2)	75 (76.5)	155 (80.3)
Week 4	303 (90.4)	Week 4	67 (70.5)	55 (56.1)	122 (63.2)
Week 6	288 (86.0)	Week 6	62 (65.3)	45 (45.9)	107 (55.4)
Week 8	273 (81.5)	Week 8	54 (56.8)	38 (38.8)	92 (47.7)
Week 10	-	Week 10	50 (52.6)	35 (35.7)	85 (44.0)
Week 12	244 (72.8)	Week 12	44 (46.3)	33 (33.7)	77 (39.9)
Week 16[a]	196 (58.5)	Week 16	42 (44.2)	33 (33.7)	75 (38.9)
Post Week 16	194 (57.9)	Post Week 16	42 (44.2)	33 (33.7)	75 (38.9)

a – 217 patients (64.8%) completed the Week 16 visit, of which 21 patients were withdrawn from the study at this visit.
Source: Data Source Tables 13.33.1and 13.33.2, Section 10.

4.2.3 Withdrawal Reasons

Table 7 summarizes the number (%) of patient withdrawals by the reason for withdrawal for each phase of the study. For the purposes of this table, any patient not entering the randomization phase (Phase II) was considered to be an open-label phase withdrawal. A total of 141 patients of the 335 enrolled (42%) did not enter Phase II and were considered Phase I withdrawals. However, only a small number of patients (19, 5.7%) were actually withdrawn by the investigator during Phase I due to lack of efficacy. However, an additional 20 patients (6.0%) who completed Phase I did not meet the protocol defined response criteria for efficacy, therefore they were ineligible to continue. These 20 patients have been included in the total number of patients who were withdrawn from the study due to lack of efficacy (n=39, 11.6%). The primary reason leading to withdrawal during the open-label phase was adverse experience (n=40, 11.9%). Other reasons leading to

withdrawal from the open-label phase were protocol deviation (6.6%, typically non-compliance), "Other" reasons (9.6%, typically withdrawal of consent), and "lost to follow-up"(2.4%).

The primary reason for withdrawal in the double-blind phase in both treatment groups was lack of efficacy (35% in the paroxetine group and 46% in the placebo group). The incidence of withdrawals due to AE was generally comparable between the two groups (8.4% in the paroxetine group and 11.2% in the placebo group).

Table 7 Number (%) of Patient Withdrawals by Reason and Study Phase (ITT)

Reasons For Withdrawal	Open-Label Paroxetine N = 335		Double-Blind Paroxetine N = 95++		Double-Blind Placebo N = 98	
	N	%	N	%	N	%
Adverse Experience	40	11.9	8	8.4	11	11.2
Lack of Efficacy	39*	11.6	33	34.7	45	45.9
Deviation from Protocol **	22	6.6	5	5.3	3	3.1
Lost to Follow-up	8	2.4	3	3.2	0	0.0
Other Reason +	32	9.6	4	4.2	6	6.1
Totals Withdrawn*+	141	42.1	53++	55.8	65	66.3

Source: Data Source tables 13.32.1 and 13.32.2, Section 10; Appendix B, Listings 13.32.1 and 13.32.2.

* includes patients who completed the Open-Label Phase but who did not meet the protocol-defined response criteria (n = 20)

** includes non-compliance

\+ includes patients eligible for entry into the Double-Blind Phase but who chose not to participate (n = 7).

++ Excludes patient 008.00371 who entered Phase II but was not part of the ITT pop as indicated in Section 4.2.1.

Tables 8, 9 and 10 summarize the number and cumulative percentage of patient withdrawals, by the reason for withdrawal, by Visit Week for the open-label and double-blind phases, respectively. In the open-label phase (Table 8), more than one-half of the withdrawals due to AE (21/40) occurred by Week 6. In contrast, the majority of the withdrawals due to lack of efficacy occurred at or after Week 12. Withdrawals due to protocol deviations, lost to follow-up, or "Other" were generally evenly spread throughout the course of the study.

Table 8 Number (%) of Patient Withdrawals by Reason and by Visit Week - Paroxetine Open Label Phase (ITT)

N =335	AE *		LOE **		PV +		Lost F/U ++		Other		TOTALS #	
Week	n	%	n	%	n	%	n	%	n	%	n	%
2	10	3.0	0	0.0	3	0.9	4	1.2	5	1.5	22	6.6
4	5	4.5	0	0.0	4	2.1	0	1.2	1	1.8	10	9.6
6	6	6.3	1	0.3	4	3.3	1	1.5	3	2.7	15	14.0
8	2	6.9	4	1.5	2	3.9	2	2.1	5	4.2	15	18.5
12	11	10.1	10	4.5	4	5.1	1	2.4	3	5.1	29	27.2
16	6	11.9	24	11.6	5	6.6	0	2.4	15	9.6	50	42.1
Totals	40	11.9	39	11.6	22	6.6	8	2.4	32	9.6	141	42.1

* Adverse Event

** Lack of Efficacy (LOE), including 'Does not meet response criteria'

++ Lost to Follow-up

+ Deviation from protocol, included non-compliance

Total reports per week

Source: Data Source Table 13.32.1, Section 10; Appendix B, Listing 13.32.1.

In the DB Phase, patient withdrawals in general tended to occur early, i.e., within the first four weeks after starting randomized study medication. In the paroxetine group, 19/33 (57.6%) patients withdrawing due to lack of efficacy did so by Week 4. In the placebo group, 31/45 (68.9%) of the patients withdrawing due to lack of efficacy did so by Week 4. Five of the eight patients in the paroxetine group withdrawing due to AEs also did so by Week 4, as did 9/11 (82%) patients assigned to placebo group. Three placebo group patients also withdrew by Week 4 for "Other" reasons. Due to the built-in blinded down titration for patients assigned to placebo, the majority of the placebo patients withdrawing early (by Week 4) for reasons other than lack of efficacy did not actually start taking placebo. For example, nine placebo group patients were withdrawn at Week 2 for a reason other than lack of efficacy. Of these nine patients, six were at dosage level 3 or higher (30mg/day or higher) upon conclusion of the open-label phase, therefore because of the 10mg week blinded down-titration schedule these six placebo group patients were withdrawn before they would have started to take placebo. Furthermore, all three of the placebo patients withdrawn at Week 4 for reason other than lack of efficacy were at the 50 or 60mg dose level at the end of Phase I and therefore were also all withdrawn from the study before actually starting placebo.

Table 9 Number (%) of Patient Withdrawals by Reason by Visit Week - Double Blind Phase Paroxetine Group (ITT)

N = 95	AE *		LOE **		PV +		Lost F/U ++		Other		TOTALS #	
Week	n	%	n	%	n	%	n	%	n	%	n	%
2	4	4.2	9	9.5	0	0.0	1	1.1	1	1.1	15	15.8
4	1	5.3	10	20.0	1	1.1	0	1.1	1	2.1	13	29.5
6	1	6.3	3	23.2	0	1.1	0	1.1	1	3.2	5	34.7
8	1	7.4	5	28.4	1	2.1	0	1.1	1	4.2	8	43.2
10	0	7.4	2	30.5	2	4.2	0	1.1	0	4.2	4	47.4
12	1	8.4	2	32.6	1	5.3	2	3.2	0	4.2	6	53.7
16	0	8.4	2	34.7	0	5.3	0	3.2	0	4.2	2	55.8
Totals	8	8.4	33	34.7	5	5.3	3	3.2	4	4.2	53	55.8

* Adverse Event
** Lack of Efficacy
\+ Deviation from protocol, included non-compliance
++ Lost to Follow-up, excludes PID 453.008.00371 who did not undergo any Phase II assessments and therefore is excluded from the ITT population.
\# Total reports per week
Source: Data Source Table 13.32.2, Section 10; Appendix B, Listing 13.32.2.

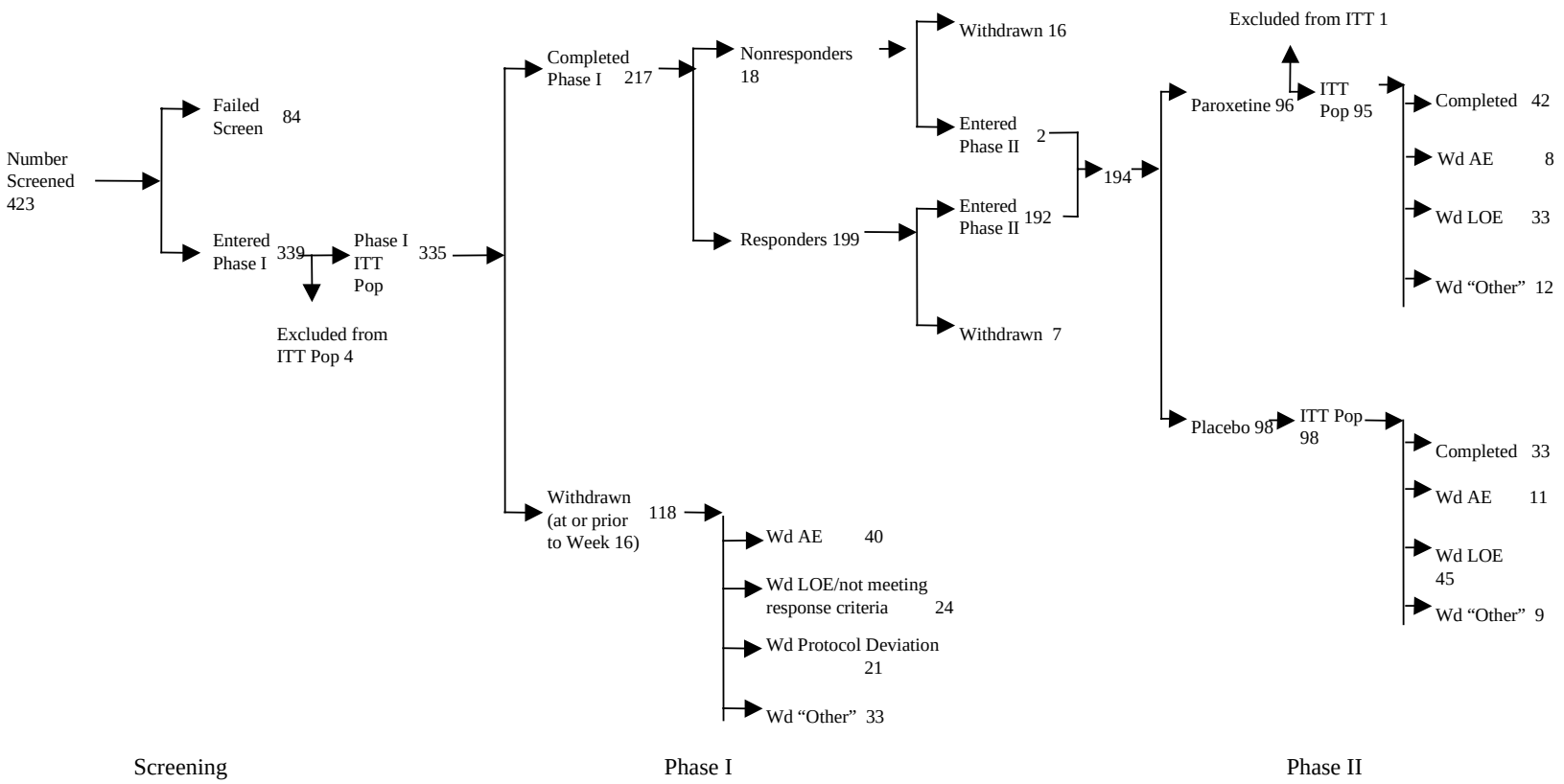
Table 10 Number (%) of Patient Withdrawals by Reason by Visit Week – Double Blind Phase Placebo Group (ITT)

N =98	AE *		LOE **		PV +		Lost F/U ++		Other		TOTALS #	
Week	n	%	n	%	n	%	n	%	n	%	n	%
2	7	7.1	14	14.3	0	0.0	0	0.0	2	2.0	23	23.5
4	2	9.2	17	31.6	0	0.0	0	0.0	1	3.1	20	43.9
6	1	10.2	8	39.8	1	1.0	0	0.0	0	3.1	10	54.1
8	0	10.2	3	42.9	1	2.0	0	0.0	3	6.1	7	61.2
10	1	11.2	1	43.9	1	3.1	0	0.0	0	6.1	3	64.3
12	0	11.2	2	45.9	0	3.1	0	0.0	0	6.1	2	66.3
16	0	11.2	0	45.9	0	3.1	0	0.0	0	6.1	0	66.3
Totals	11	11.2	45	45.9	3	3.1	0	0.0	6	6.1	65	66.3

* Adverse Event
** Lack of Efficacy
\+ Deviation from protocol, included non-compliance
++ Lost to Follow-up
\# Total reports per week
Source: Data Source Table 13.32.2, Section 10; Appendix B, Listing 13.32.2.

Data Source Tables 13.1.1 and 13.1.2, Section 10, present summaries of all patients by population for Phases I and II, respectively, and Figure 2 depicts the overall patient disposition.

Figure 2 Study 453 Overall Patient Disposition



4.3 Protocol Violations

All randomized patients failing to meet one or more of the entrance criteria, and/or who met the non-compliance criteria, were assessed by the sponsor prior to unblinding of the data to determine if the deviation in question was significant enough to classify the patient as a major protocol violator (resulting in exclusion from the Per Protocol Population). Table 11 summarizes the number (%) of patients excluded from the Per Protocol Population by the reason leading to the exclusion. The total number of patients identified as major protocol violotors and warranting exclusion from the Per Protocol Population was 29/193 (15%). The major protocol violators were evenly distributed between the two treatment groups (14.7% in the paroxetine group compared to 15.3% in the placebo group). In both treatment groups, non-compliance (defined as missing more than 5 consecutive days of dosing) was the primary reason for being excluded from the Per Protocol Population. Two patients (453.005.00020 and 453.019.00080) did not meet the protocol defined response criteria upon completion of Phase I but nevertheless were still entered into Phase II by the investigator. In both instances, the patients narrowly missed meeting the response criteria and in the judgement of the investigator had in fact demonstrated significant enough improvement to warrant continuation in the study. As noted in Table 7, Section 4.2.3, a total of 30 patients (9.0%) were withdrawn from the study by the investigator due to a protocol deviation (typically for non-compliance with the dosing regimen).

Table 11 Number (%) of Patients Excluded from Per Protocol Analysis with a Major Violation - Double Blind (Randomization) Phase (ITT)

Major Protocol Violation	Treatment Group					
	Paroxetine N = 95		Placebo N = 98		Total N = 193	
	n	%	n	%	n	%
> 1 year outside of age range	0	0.0	1	1.0	1	0.5
Missed more than 5 consecutive days of study med	10	10.5	6	6.1	16	8.3
Prohibited concomitant med	2	2.1	5	5.1	7	3.6
Prohibited prior med	2	2.1	2	2.0	4	2.1
Entered Ph II, did not meet response criteria at end of Ph I	1	1.1	1	1.0	2	1.0
Total patients with at least one major protocol violation	14	14.7	15	15.3	29	15.0
Total patients with no major protocol violations	81	85.3	83	84.3	164	85.0

Source: Data Source Table 13.2, Section 10; Appendix B, Listing 13.2.

Four patients were excluded from the Per Protocol Population as a result of prohibited prior med use. Two of these patients (453.008.00056 and 453.006.00104) had taken fluoxetine within 42 days of the open-label baseline visit, one patient (453.005.00375) had taken amitriptyline within 14 days prior to the open-label baseline, and one patient (453.022.00395) had stopped taking alprazolam one day prior to the open-label baseline visit. For details regarding "minor" protocol violations not leading to exclusion from the Per Protocol population, most commonly patients outside of the protocol specified age range at entry (but by < 1 year), refer to Appendix B, Listing 13.2.

4.4 Demographic and Baseline Characteristics

4.4.1 Demographic Characteristics

The demographic characteristics of the ITT study population are summarized in Table 12. The mean age was approximately 12 years old and ranged from age 6 up to age 18. The population was evenly split between children (age < 12, 167/335 or 49.9%) and adolescents (age ≥ 12, 168/335 or 50.1%). Most patients were male (198/335, 59.1%), and the vast majority of patients were caucasian (308/335, 92%). In Phase II, the two treatment groups were generally similar with respect to all demographic characteristics, although the placebo group had a higher proportion of males than did the paroxetine group. Data Source Table

13.4.2c, Section 10, summarizes the demographic data for the Phase II Per Protocol Population.

Table 12 Summary of Demographic Data (ITT)

Items		Open-Label N = 335		Double-Blind Paroxetine N = 95		Placebo N = 98	
		n	%	n	%	n	%
Age All (years)		335	100.0	95	100.0	98	100.0
	Median	12		11		12	
	Mean ± SD	11.8 ± 2.72		11.8 ± 2.56		11.6 ± 2.88	
	Range	6 - 18		7 – 17		6 – 18	
Age Band < 12 (years)		167	49.9	49	51.6	47	48.0
	Median	10		10		9	
	Mean ± SD	9.5 ± 1.29		9.8 ±1.20		9.1 ± 1.33	
	Range	6 - 11		7 – 11		6 – 11	
Age Band ≥ 12 (years)		168	50.1	46	48.4	51	52.0
	Median	14		14		13	
	Mean ± SD	14.0 ± 1.71		14.0 ± 1.70		13.9 ± 1.82	
	Range	12 - 18		12 – 17		12 –18	
Gender	Female	137	40.9	48	50.5	40	40.8
	Male	198	59.1	47	49.5	58	59.2
Race	Black	7	2.1	1	1.1	2	2.0
	Caucasian	308	91.9	87	91.6	89	90.8
	Oriental	4	1.2	1	1.1	3	3.1
	Other	16	4.8	6	6.3	4	4.1

Source: Data Source Table 13.4.1b, 13.4.2b, Section 10; Appendix B, Listing 13.4.

4.4.2 Baseline Characteristics

Table 13 summarizes the mean efficacy parameter scores at both the Open-Label and Double-Blind Phase (Randomization) Baselines. At Open-Label Baseline, the CY-BOCS mean Total Score was 26.3, which is consistent with the moderate to severe level of OCD symptomatology reported at Screening by the investigators for the vast majority of patients enrolled. The mean GAF score at Open-Label Baseline was 54.1, also generally consistant with a moderate level of functional impairment. The mean HAM-D and HAM-A scores at Open-Label Baseline were 6.6 and 8.3, respectively, reflective of generally a minimal to mild level of symptomatology. There were no apparent differences between the treatment groups in the double-blind phase with respect to the mean data for any of these parameters.

Table 13 Mean Baseline Efficacy Parameter Scores at Open-Label and Double-Blind (Randomization) Phase Baselines (ITT)

		Open-Label * Paroxetine		Double-Blind **			
				Paroxetine		Placebo	
		N = 335		N = 95		N = 98	
Test Item	N	mean	SE	n / mean	SE	n / mean	SE
HAM-A	316	8.3	0.35	92 / 2.7	0.36	98 / 2.8	0.33
HAM-D	315	6.6	0.29	92 / 2.4	0.32	98 / 2.3	0.26
Yale Global Tic	317	2.5	0.31	93 / 0.7	0.25	98 / 1.4	0.37
CY-BOCS Total Score	329	26.3	0.27	92 / 9.9	0.67	98 / 9.6	0.61
Obsessive Subscale	329	12.9	0.16	91 / 4.7	0.36	98 / 4.4	0.32
Compulsive Subscale	329	13.5	0.15	92 / 5.3	0.38	98 / 5.2	0.34
GAF	335	54.1	0.40	95 / 73.4	1.11	98 /73.5	1.11

* Open-Label Baseline
**Randomization Baseline
Source: Data Source Tables 14.4.1, 14.4.2, 14.5.1, 14.5.2, 14.6.1, 14.6.2, 14.71.1, 14.71.2, 14.21.1, 14.21.2, 14.22.1, 14.22.2, 14.23.1, 14.23.2, Section 11; Appendix C, Listings 14.2.1, 14.2.2, 14.4.1, 14.4.2, 14.5.1, 14.5.2, 14.6.1, 14.6.2, 14.7.1 and 14.7.2.

Table 14 presents a summary of the percentage of patients in each category of the CGI Severity of Illness Item Score at the Open-Label and Double-Blind Phase (randomization) Baselines. At the Open-label Baseline, 98% (229/335) of the patients had a CGI Severity of Illness rating of at least "Moderately Ill", with more than one-half (181/335, 54%) of the patients rated as "Markedly Ill", "Severely Ill", or among the "Most Severely Ill". There were generally no differences between the treatment groups in the double-blind phase with respect to the proportion of patients in each category of the CGI Severity of Illness Item.

Table 14 Number (%) of Patients in Each Category of the CGI Severity of Illness Item Score at Open-Label and Randomization Phase Baselines (ITT)

	Normal Not Ill		Borderline Ill		Mildly Ill		Moderately Ill		Markedly Ill		Severely Ill		Most Severely Ill	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Open-Label (N= 335)	0	0.0	0	0.0	6	1.8	148	44.2	110	32.8	70	20.9	1	0.3
Double-Blind														
Paroxetine (N= 95)	15	15.8	27	28.4	37	38.9	15	15.8	1	1.1	0	0.0	0	0.0
Placebo (N= 98)	17	17.3	31	31.6	34	34.7	14	14.3	2	2.0	0	0.0	0	0.0

Source: Data Source Tables 14.33.1, 14.33.2, Section 11; Appendix C, Listings 14.3.1 and 14.3.2.

4.5 Presenting Conditions and Medical History

4.5.1 General Medical/Surgical History

The majority (64.2%) of the patients had at least one prior condition reported upon study entry (based on the general medical/surgical history and Screening physical examination results). The most frequently reported (≥ 5%) prior conditions (based on reported medical/surgery history and Screening physical examination data) in the Open-Label population were headache (14.0%), nose/mouth operation (9.0%), allergic rhinitis (8.1%), asthma (7.2%), ear operation (6.3%), otitis media (6.3%), upper respiratory disorder (5.7%), abdominal pain (5.4%) and upper limb fracture (5.1%). These findings were typical for a pediatric population. Refer to Data Source Table 13.51.1b, Section 10, for details. There were no relevant differences between the treatment groups in the double-blind (randomization) phase with respect to the number (%) of patients with prior conditions (see Data Source Table 13.51.2b, Section 10). Data Source Tables 13.51.1c and 13.51.2c present similar data (i.e., summary of prior conditions) for the Per Protocol Population. Complete listings of medical/surgical history data by patient are provided in Appendix B, Listings 13.5.1 and 13.5.2.

The majority of patients (71.0%) also had at least one active condition reported upon study entry (again based on the general medical/surgical history and Screening physical examination results). The most frequently reported (≥ 5%) active conditions at baseline in the Open-Label population were headache (27.8%), allergic rhinitis (16.1%), asthma (10.1%), upper respiratory disorder

(5.4%), obesity (5.4%), adverse effect from antibiotic (5.4%), allergy (5.4%), insomnia (6.0%), skin/subcutaneous disorder (8.1%), and abdominal pain (12.2%). Refer to Data Source Table 13.52.1b, Section 10, for details. There were no relevant differences between the treatment groups in the double-blind (randomization) phase with respect to the number (%) of patients with active conditions (see Data Source Table 13.52.2b, Section 10). Data Source Tables 13.52.1c and 13.52.2c present similar data (i.e., summary of active conditions) for the Per Protocol Population.

4.5.2 Psychiatric History (Other than OCD)

Table 15 summarizes the psychiatric histories of the Open-Label Phase study population. Generalized anxiety disorder (14.6%) and major depressive disorder (10.1%) were the two most frequently reported disorders. A history of these two disorders were also suspected in an additional 8.7% and 3.3% of the population, respectively. Data Source Table 13.7.2, Section 10, presents the psychiatry history data by double-blind phase treatment group (refer to Appendix B, Listing 13.7.2, for details of the psychiatric history data by patient for the Phase II population). There were no relevant treatment group differences apparent.

Table 15 Summary of Psychiatric History at Open-Label Baseline (ITT)

	Yes		No		Suspected		Not Recorded	
Psychiatric History	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Substance Abuse	0	0.0	335	100.0	0	0.0	0	0.0
Substance Dependence	0	0.0	335	100.0	0	0.0	0	0.0
GAD	49	14.6	257	76.7	29	8.7	0	0.0
Personality Disorder	0	0.0	334	99.7	0	0.0	1	0.3
Dysthymia	24	7.2	300	89.6	11	3.3	0	0.0
Panic Disorder	6	1.8	327	97.6	2	0.6	0	0.0
Major Depressive Disorder	34	10.1	290	86.6	11	3.3	0	0.0
Other	161	48.1	143	42.7	57	17.0	0	0.0

Source: Data Source Tables 13.7.1, Section 10; Appendix B, Listing 13.7.1.

The K-SADS-L interview was also conducted at Screening. Summary data are presented in Table 16. Based on this instrument, the most frequently reported past or current (or both) disorders were ADHD (22.4%), GAD (21.2%), specific phobia (20.3%), separation anxiety disorder (18.5%), tic disorders (17.9%), major depressive episode (11.3%), oppositional defiant disorder (9.9%) and dysthymic

disorder (9.3%). Data Source Table 13.10.2, Section 10, presents the K-SADS Summary data by treatment group in the double-blind phase. There were no relevant treatment group differences apparent. Refer to Appendix B, Listing 13.10.2, for details of the KSADS data by patient for the Phase II population.

Table 16 KSADS Summary at Screening Visit (ITT)

	Past		Current		Both		N/A*	
	n	%	n	%	n	%	n	%
Major depressive episide	18	5.4	9	2.7	11	3.3	297	88.7
Dysthymic disorder	3	0.9	9	2.7	19	5.7	304	90.7
Hypomanic episode	1	0.3	0	0.0	0	0.0	334	99.7
Manic episode	0	0.0	0	0.0	0	0.0	335	100.0
Anorexia nervosa	3	0.9	0	0.0	0	0.0	332	99.1
Bulimia nervosa	0	0.0	0	0.0	0	0.0	335	100.0
Specific phobia	14	4.2	20	6.0	34	10.1	267	79.7
Separation anxiety disorder	28	8.4	6	1.8	28	8.4	273	81.5
Panic disorder (without agoraphobia	5	1.5	1	0.3	3	0.9	326	97.3
Panic disorder (with agoraphobia)	1	0.3	0	0.0	1	0.3	333	99.4
Agoraphobia (no panic)	0	0.0	0	0.0	1	0.3	334	99.7
Social phobia	0	0.0	4	1.2	15	4.5	316	94.3
Generalized anxiety disorder (GAD)	4	1.2	6	1.8	61	18.2	264	78.8
Post-traumatic stress disorder (PTSD)	5	1.5	1	0.3	0	0.0	329	98.2
Attention-deficit/hyper. disorder (ADHD)	12	3.6	13	3.9	50	14.9	260	77.6
Conduct disorder	0	0.0	0	0.0	2	0.6	333	99.4
Oppositional defiant disorder	5	1.5	11	3.3	17	5.1	302	90.1
Alcohol dependence	0	0.0	0	0.0	0	0.0	335	100.0
Alcohol abuse	0	0.0	0	0.0	0	0.0	335	100.0
Substance Dependence	0	0.0	0	0.0	0	0.0	335	100.0
Substance abuse	0	0.0	0	0.0	0	0.0	335	100.0
Tic disorders	9	2.7	16	4.8	35	10.4	275	82.1
Schizophrenia	0	0.0	0	0.0	0	0.0	335	100.0
Schizoaffective disorder	0	0.0	0	0.0	0	0.0	335	100.0
Brief psychotic disorder	0	0.0	0	0.0	0	0.0	335	100.0
Delusional disorder	0	0.0	0	0.0	0	0.0	335	100.0

*Not applicable (i.e., no past or current history)
Source: Data Source Table 13.10.1, Section 10; Appendix B, Listing 13.10.1.

4.5.3 OCD History

Table 17 summarizes the OCD history and OCD episode at Screening/Baseline for the study population. The mean age at onset of OCD was 10.1 years, with a range of 2 – 18 years. The severity of the illness was rated as moderate or severe at baseline in greater than 95% of the participants. Very few (1.5%) of the patients had ever required hospitalization for OCD, and approximately one-half (48.2%) of the patients had no family history of OCD. The majority of patients (71.3%) had received no prior therapy (neither pharmacotherapy nor psychotherapy). For the current episode of OCD (i.e., at Screening), pharmacotherapy was reported in 13.4% of the population, psychotherapy in 9.9%, and both psychotherapy plus pharmacotherapy were reported in only 5.4% of the population. All treatment for OCD which was ongoing at Screening (including psychotherapy as well as pharmacotherapy) was discontinued prior to starting open-label paroxetine treatment. There were no relevant differences apparent between the two treatment groups with respect to any of these parameters. For details regarding patients with prior pharmacotherapy which was prohibited by the protocol, refer to Section 4.3 of this report.

Table 17 Summary of OCD History and Current Episode (i.e., at Screening) – Open Label Phase (ITT)

	Open-Label		Double-Blind			
			Paroxetine		Placebo	
	N = 335		N = 95		N = 98	
Age at Onset (years)						
Median	10		10		10	
Mean ± SD	10.1 ± 3.32		10.0 ± 3.02		10.0 ± 3.37	
Range	2 – 18		3 – 18		2 – 16	
Family history of OCD	**n**	**%**	**n**	**%**	**n**	**%**
None	160	48.2	42	44.7	49	50.5
Mother	63	19.0	17	18.1	18	18.6
Father	51	15.4	13	13.8	16	16.5
Sibling	21	6.3	7	7.4	7	7.2
Grandparent	62	18.7	18	19.1	13	13.4
Other	65	19.6	21	22.3	16	16.5
Total Patients Included	332	100.0	94	100.0	97	100.0
Missing data	3	---	1	---	1	---
Number of times hospitalized	**n**	**%**	**n**	**%**	**n**	**%**
Never	330	98.5	93	97.9	98	100.0
1	3	0.9	1	1.1	0	0.0
2	0	0.0	0	0.0	0	0.0
3	2	0.6	1	1.1	0	0.0
4	0	0.0	0	0.0	0	0.0
≥ 5	0	0.0	0	0.0	0	0.0
Total	335	100.0	95	100.0	98	100.0
Missing data	0	0.0	0	0.0	0	0.0
Severity of current OCD episode (at Screening)	**n**	**%**	**n**	**%**	**n**	**%**
Mild	14	4.2	4	4.2	4	4.1
Moderate	174	51.9	52	54.7	50	51.0
Severe	147	43.9	39	41.1	44	44.9
Total	335	100.0	95	100.0	98	100.0
Missing	0	0.0	0	0.0	0	0.0
Type of treatment received for current OCD episode	**n**	**%**	**n**	**%**	**n**	**%**
No therapy	239	71.3	69	72.6	69	70.4
Psychotherapy	33	9.9	8	8.4	13	13.3
Pharmacotherapy	45	13.4	10	10.5	15	15.3
Psychotherapy plus pharmacotherapy	18	5.4	8	8.4	1	1.0
Total	335	100.0	95	100.0	98	100.0
Missing data	0	0.0	0	0.0	0	0.0

Source: Data Source Table 13.81.1, 13.81.2, 13.82.1, 13.82.2, 13.83.1, 13.83.2, 13.84.1, 13.84.2, 13.85.1, 13.85.2, Section 10; Appendix B, Listings 13.8.1, 13.8.2, 13.9.1, and 13.9.2.

4.6 Prior and Concomitant Medications

4.6.1 Previous Pharmacologic Treatment for OCD

Table 18 summarizes the most frequently reported (≥ 3%) prior medications taken for OCD. Approximately 22% of the Open-Label population had a history of pharmacotherapy for OCD. This percentage also held true for both treatment groups in the double-blind phase. Fluoxetine (9.0%), clomipramine (6.9%), and fluvoxamine (6.0%) were the three most commonly reported prior medications for OCD.

Table 18 Frequently Reported (≥ 3%)* Prior Medications for OCD

	Open-Label		Double-Blind			
			Paroxetine		Placebo	
Total Number of Patients	N=335		N=95		N=98	
Total Patients with OCD Prior Medication	**n**	**%**	**n**	**%**	**n**	**%**
	75	22.4	21	22.1	21	21.4
THERAPEUTIC CLASS/MEDICATION						
Central nervous system						
Clomipramine	23	6.9	7	7.4	3	3.1
Fluoxetine	30	9.0	7	7.4	7	7.1
Fluvoxamine	20	6.0	5	5.3	8	8.2
Paroxetine	13	3.9	2	2.1	7	7.1
Sertraline	15	4.5	5	5.3	2	2.0

* At least 3% in Open-label population or either DB treatment group.
Source: Data Source Tables 13.9.1, 13.9.2, Section 10; Appendix B, Listings 13.9.1 and 13.9.2.

4.6.2 Prior Medications (Other than for OCD)

Table 19 presents a summary of the most frequently reported (≥ 5%)prior medications by therapeutic class which were taken for reasons other than OCD. Prior medication intake was reported for almost three-fourths (71.6%) of the Open-Label population. Not surprisingly, analgesic/antipyretic agents were the most commonly reported prior medications in this population, with acetaminophen (paracetamol) and ibuprofen being the two most common (22.4% and 13.1%, respectively). There were no other prior medications taken by more than 10% of the population. Fluoxetine (taken for reasons other than OCD) was the third most commonly reported prior medication (9.9%).

In general, there were no differences between the treatment groups in the double-blind phase with respect to prior medication intake. Because medications taken concomitantly with the study medication during the open-label phase were also included as a prior medication (i.e., in addition to those taken prior to study entry), the percentage of patients with at least one reported prior medication in the two treatment groups in the DB phase is higher than that in the open-label population (approx. 90% vs. 72%). This is particularly apparent, for example, with acetaminophen (paracetamol), which was reported as a prior med in 22% of the open-label population but as a prior med in approx. 50% of the double-blind phase population. Refer to Data Source Tables 13.11.1 and 13.11.2, Section 10, for further details.

Table 19 Frequently Reported (≥ 5%)* Prior Medication by Therapeutic Classes and Drug

	Open-Label		Double-Blind			
			Paroxetine		Placebo	
Total Number of Patients	N= 335		N= 95		N= 98	
Total Patients with a	**n**	**%**	**n**	**%**	**n**	**%**
Prior Medication	240	71.6	82	86.3	89	90.8
THERAPEUTIC CLASS/MEDICATION						
Alimentary tract/metabolic						
Bismuth subsalicylate	8	2.4	7	7.4	7	7.1
Calcium carbonate	14	4.2	3	3.2	11	11.2
Vitamins nonspecific	18	5.4	5	5.3	11	11.2
Anti-Infectives						
Amoxicillin	20	6.0	14	14.7	8	8.2
Central nervous system						
Clomipramine	25	7.5	7	7.4	4	4.1
Fluoxetine	33	9.9	7	7.4	9	9.2
Fluvoxamine	20	6.0	5	5.3	8	8.2
Methylphenidate	26	7.8	5	5.3	5	5.1
Paracetamol	75	22.4	46	48.4	50	51.0
Sertraline	17	5.1	5	5.3	2	2.0
Dermatologicals						
Diphenhydramine	15	4.5	8	8.4	11	11.2
Musculoskeletal						
Ibuprofen	44	13.1	37	38.9	28	28.6
Respiratory						
Beclomethasone	16	4.8	4	4.2	8	8.2
Brompheniramine	8	2.4	8	8.4	3	3.1
Chlorpheniramine	18	5.4	13	13.7	9	9.2
Dextromethorphan	9	2.7	13	13.7	6	6.1
Diphenhydramine	16	4.8	8	8.4	8	8.2
Guaifenesin	8	2.4	7	7.4	5	5.1
Loratadine	21	6.3	6	6.3	7	7.1
Paracetamol	11	3.3	11	11.6	9	9.2
Pseudoephedrine	30	9.0	17	17.9	16	16.3
Phenylpropanolamine	15	4.5	16	16.8	8	8.2
Salbutamol	28	8.4	9	9.5	7	7.1

* At least 5% in either the OL population or the overall DB population.
Source: Data Source Tables 13.11.1, 13.11.2, Section 10; Appendix B, Listings 13.11.1and 13.11.2.

4.6.3 Concomitant Medication

Table 20 presents a summary of the most frequently reported (≥ 5%) concomitant medications by therapeutic class. Approximately 80% of the open-label phase population were reported to have taken at least one concomitant medication.

This percentage also held true for both treatment groups in the DB phase as well. Again, as was the case for the prior medications, the most commonly reported concomitant medications were analgesic/antipyretic agents, with acetaminophen (paracetamol) and ibuprofen taken during the open-label phase by 41.2% and 25.4% of the study population, respectively. Cough/cold/allergy preparations accounted for the next most commonly reported concomitant medications, with pseudoephedrine (12.8%), phenylpropanolamine (9.3%), and diphenhydramine (9.3%) being reported most often. In general, there were no differences between the treatment groups in the double-blind phase with respect to concomitant medication intake. Refer to Data Source Tables 13.12.1 and 13.12.2, Section 10, for further details.

Table 20 Frequently Reported (≥ 5%)* Concomitant Medications by Therapeutic Classes and Drug

	Open-Label		Double-Blind			
			Paroxetine		Placebo	
Total Number of Patients	**N= 335**		**N= 95**		**N= 98**	
Total Patients with a	**n**	**%**	**n**	**%**	**n**	**%**
Concomitant Medication	269	80.3	77	81.1	79	80.6
THERAPEUTIC CLASS/MEDICATION						
Alimentary tract/metabolic						
Bismuth subsalicylate	22	6.6	4	4.2	7	7.1
Calcium carbonate	19	5.7	4	4.2	9	9.2
Vitamins NOS	22	6.6	6	6.3	11	11.2
Anti-infectives, systemic						
Amoxicillin	25	7.5	13	13.7	10	10.2
Central nervous system						
Acetylsalicylic acid	13	3.9	7	7.4	5	5.1
Paracetamol	138	41.2	32	33.7	35	35.7
Dermatologicals						
Diphenhydramine	31	9.3	9	9.5	8	8.1
Musculoskeletal						
Ibuprofen	85	25.4	28	29.5	25	25.5
Respiratory						
Beclomethasone	20	6.0	4	4.2	5	5.1
Chlorpheniramine	24	7.2	11	11.6	7	7.1
Dextromethorphan	25	7.5	9	9.5	3	3.1
Diphenhydramine	31	9.3	9	9.5	7	7.1
Guaifenesin	17	5.1	6	6.3	3	3.1
Loratadine	21	9.3	6	6.3	3	3.1
Paracetamol	17	5.1	10	10.5	7	7.1
Phenylpropanolamine	31	9.3	6	6.3	6	6.1
Psuedoephedrine	40	11.9	15	15.9	10	10.2
Salbutamol	26	7.8	8	8.4	6	6.1

* At least 5% in the OL population or in the overall DB population.
Source: Data Source Tables 13.12.1, 13.12.2, Section 10; Appendix B, Listings 13.11.1 and 13.11.2.

4.7 Treatment Compliance and Titration

4.7.1 Treatment Compliance

Table 21 presents an overall summary of patient compliance with the study medication. In this study, patient non-compliance was predefined as missing more than 5 consecutive days of study medication at any time during the study. Based on this definition of compliance, the percentage of patients who were noncompliant at any time was very low (< 5%). In the double-blind phase, the

percentage of patients who missed more than 5 consecutive days of dosing was slightly greater than was reported during the open-label phase. In the paroxetine group, 8.5% of the patients were noncompliant compared to 5.1% of the placebo group. Patients missing ≥ 5 consecutive days of dosing were to be withdrawn from the study. Of the total of 28 patients reported by the investigator as noncompliant, 12 were withdrawn from the study for that reason.

Theoretically, a patient could therefore have missed numerous daily doses of study medication, but as long as he/she didn't miss 5 days in a row would not have been considered noncompliant. However, study sites were also instructed at study intiation to estimate, based on returned tablet counts, whether patients took at least 80% and not more than 120% of the prescribed number of tablets during that dosing interval. If a patient fell outside of the 80-120% range during any given visit interval, then the study site was to assess the reason for noncompliance and to make a determination as to whether the patient should be withdrawn from the study based on the circumstances.

Table 21 Patient Compliance with Study Medication

Treatment Compliance*	Open-Label		Double-Blind			
			Paroxetine		Placebo	
	N = 335		N = 95		N = 98	
	n	%	n	%	n	%
Compliant	316	95.5	86	91.5	93	94.9
Non-Compliant	15	4.5	8	8.5	5	5.1
All**	331	100.0	94	100.0	98	100.0

*Compliance was defined as no break in study medication dosing of 5 or more consecutive days.
**Data missing for 4 patients in the OL phase and 1 patient in the DB phase (paroxetine group)
Source: Data Source Tables 13.16.1, 13.16.2, Section 10; Appendix B, Listings 13.12.1, 13.12.2, and 13.12.X.

Data Source Tables 13.15.1 and 13.15.2, Section 10, provide compliance data for each study phase by Visit Week.

4.7.2 Titration of Dose

In the open-label phase, dosing was intiated at 10mg/day, and if necessary, the dosage could be titrated upward in 10mg increments at weekly intervals to a maximum daily dose of 60 mg. Dose escalation was to be based on therapeutic response and tolerability of the medication. It was recommended in the protocol that the daily dose of paroxetine not exceed 40mg/day until after Week 6 unless

clinically indicated. Table 22 presents a summary of the number (%) of patients on each paroxetine dose level by Visit, as well as the number of patients for whom that dosage was the maximum daily dosage administered, during the open-label phase.

Although there were several instances of patients being uptitrated more quickly than was recommended in the protocol (e.g., 6 patients were reported to be at the 40mg/day dosage level at the Week 2 Visit and 3 patients were reported to be at the 50mg/day dosage level at the Week 4 Visit), in general the titration schedule recommended in the protocol appears to have been followed. By the Week 2 Visit, approximately 60% of the patients remaining in the study were at the 20mg/day dosage level, while approximately 25% of the patients remained at the initial 10mg/day dose level. By Week 4, approximately 47% of the patients remaining in the study were at the 30mg/day dose level or greater, and by Week 6 approximately 61% of the patients still in the study were at the 30mg/day dosage level or greater. By Week 8, approximately 39% of the patients still in the study were at the 40mg/day, or greater, dosage level, and by Week 12 this figure rose to approximately 48%. There appeared to be little further increases in dosage level between Weeks 12 and 16. Approximately 14% of the patients enrolled reached the maximum allowable daily dosage (60mg/day), and approximately 10% never increased beyond the initial 10mg/day dosage. Thirty (30) mg was the maximum daily dose for the greatest percentage of patients (26.3%).

Table 22 Summary of Number of Patients (%) on Each Paroxetine Dose Level by Visit - Open Label Phase (ITT)

Daily Dose Level	Paroxetine N=335					
	10mg	20mg	30mg	40mg	50mg	60mg
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Week 2	85 (25.4)	198 (59.1)	46 (13.7)	6 (1.8)	0 (0.0)	0 (0.0)
Week 4	36 (11.5)	130 (41.5)	112 (35.8)	32 (10.2)	3 (1.0)	0 (0.0)
Week 6	28 (9.2)	90 (29.7)	97 (32.0)	67 (22.1)	17 (5.6)	4 (1.3)
Week 8	25 (8.7)	64 (22.2)	87 (30.2)	54 (18.8)	35 (12.2)	23 (8.0)
Week 12	23 (8.4)	61 (22.3)	59 (21.6)	49 (17.9)	39 (14.3)	42 (15.4)
Week 16	19 (7.9)	52 (21.5)	60 (24.8)	39 (16.1)	29 (12.0)	43 (17.8)
Maximum *	33 (9.9)	67 (20.0)	88 (26.3)	59 (17.6)	40 (11.9)	48 (14.3)

* The number of patients for whom that dosage was the maximum dosing during Phase I.
Note: For each week, percentages are cumulative across dosage level columns
Source: Data Source Tables 13.13.1, 13.14.1, Section 10.

Throughout the double-blind phase patients were to continue at the same dosage level that they were at when they completed the open-label phase (i.e., dosage level 1, 2, 3, 4, 5, or 6, but with randomization to either paroxetine or placebo). Tables 23 and 24 summarize the number (%) of patients at each dose level by Visit Week for the paroxetine and placebo groups, respectively. The percentages of patients at each dosage level at the start of the double-blind phase were comparable between the two treatment groups. At Week 16 of the DB Phase, the paroxetine dosage level group that had the highest percentage of randomized patients still remaining in the study was the 60mg group (10/14 patients randomized, or 71%). In contrast, only 31% of the patients at dosage level 6 who were assigned to placebo were still remaining in the study at Week 16.

Table 23 Summary of the Number (%) of Patients on Each Dose Level by Treatment and Visit- Phase II Randomized Treatment (ITT)

Daily Dose Level	Paroxetine N = 95					
	10mg	20mg	30mg	40mg	50mg	60mg
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Week 2	9 (9.5)	20 (21.1)	26 (27.4)	16 (16.8)	10 (10.5)	14 (14.7)
Week 4	9 (11.3)	15 (18.8)	21 (26.3)	11 (13.8)	10 (12.5)	14 (17.5)
Week 6	9 (13.4)	11 (16.4)	16 (23.9)	11 (16.4)	7 (10.4)	13 (19.4)
Week 8	9 (14.5)	10 (16.1)	15 (24.2)	8 (12.9)	7 (11.3)	13 (21.0)
Week 10	8 (14.8)	7 (13.0)	15 (27.8)	6 (11.1)	6 (11.1)	12 (22.2)
Week 12	7 (14.0)	7 (14.0)	15 (28.0)	5 (10.0)	6 (12.0)	11 (22.0)
Week 16	5 (11.4)	7 (15.9)	13 (29.5)	4 (9.1)	5 (11.4)	10 (22.7)
Maximum *	9 (9.5)	20 (21.1)	26 (27.4)	16 (16.8)	10 (10.5)	14 (14.7)

*The number of patients for whom that dosage was the maximum dosing during this study phase.
Note: For each week, percentages are cumulateive across dosage level columns
Source: Data Source Tables 13.13.2, 13.14.2, Section 10.

Table 24 Summary of the Number (%) of Patients on Each Dose Level by Treatment and Visit- Phase II Randomized Treatment (ITT)

Daily Dose Level	Placebo N = 98					
	1	2	3	4	5	6
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Week 2	8 (8.2)	25 (25.5)	22 (22.4)	15 (15.3)	12 (12.2)	16.16.3)
Week 4	7 (9.3)	14 (18.7)	16 (21.3)	15 (20.0)	9 (12.0)	14 (18.7)
Week 6	5 (9.1)	12 (21.8)	11 (20.0)	8 (14.5)	9 (16.4)	10 (18.2)
Week 8	5 (11.1)	12 (26.7)	8 (17.8)	5 (11.1)	7 (15.6)	8 (17.8)
Week 10	4 (10.5)	10 (26.3)	5 (13.2)	5 (13.2)	7 (18.4)	7 (18.4)
Week 12	4 (11.4)	9 (25.7)	5 (14.3)	5 (14.3)	6 (17.1)	6 (17.1)
Week 16	4 (12.1)	9 (27.3)	4 (12.1)	5 (15.2)	6 (18.2)	5 (15.2)
Maximum *	8 (8.2)	25 (25.5)	22 (22.4)	15 (15.3)	12 (12.2)	16 (16.3)

*The number of patients for whom that dosage was the maximum dosing during this study phase.
Note: For each week, percentages are cumulative across dosage level columns.
Source: Data Source Tables 13.13.2, 13.14.2, Section 10.

5 Efficacy Results

5.1 Efficacy Evaluation

5.1.1 Data Sets Analysed

Table 25 presents the number of patients comprising the populations for the efficacy analyses in each study phase. The intention-to-treat (ITT) population for the primary analysis of efficacy included all patients who received any double-blind medication and for whom at least one valid post-randomization baseline efficacy evaluation was conducted. As noted in Section 4.2.1, one of the 96 patients assigned to the paroxetine group in Phase II was excluded from the ITT population. In addition, as noted in Section 4.3, 14 patients in the paroxetine group and 15 patients in the placebo group were excluded from the Per Protocol population for the analysis of efficacy.

Table 25 The Number of Patients Comprising the Populations for Analysis of Efficacy in Each Phase

Study Phase	Open-Label Paroxetine (Phase I)	Double-Blind Phase	
		Paroxetine	Placebo
Screening Only[1]	423	---	---
Entered Study Phase[2]	339	96	98
ITT Population[3]	335	95	98
Per Protocol Population[4]	---	81	83

1 –Includes screened patients ineligible to start open-label medication and who are not included in the ITT
2 -Includes all patients enrolled into that Phase of the study
3 -Includes all patients enrolled into that Phase of the study and who received at least one dose of study medication and for whom at least one post-baseline evaluation is available (irrespective of whether entry criteria were fulfilled or the protocol violated).
4 –Consists of the subset of the DB Phase ITT population valid for inclusion in the per-protocol efficacy population (i..e, no major protocol violations exist regarding entry criteria, study procedures and/or compliance).
Source: Data Source Tables 13.1.1 and 13.1.2, Section 10; Appendix B, Listings 13.1.1 and 13.1.2.

5.2 Open-Label Efficacy Results

5.2.1 CGI Global Improvement Item and CY-BOCS Total Score Responders

Table 26 presents a summary of the percentage of patients meeting the CGI Global Improvement Item response criteria during the Open-Label Phase, by Visit Week. A CGI responder was defined as a patient with a CGI Global Improvement Item Score of 1 (very much improved) or 2 (much improved) upon evaluation. Almost three-quarters of the patients enrolled for whom data were available met this response criterion at their final Open-Label Phase Visit (231/315, 73.3%). For those who actually completed the Phase I Week 16 visit, the percentage of responders was even higher (209/239, 87.4%).

Table 26 Percentage (%) of Responders* on the CGI Global Improvement Item - Open Label Phase (ITT)

	n	N	%
ITT Population			
Initial Evaluation			
Week 2	52	328	15.9
Week 4	120	305	39.3
Week 6	144	292	49.3
Week 8	170	277	61.4
Week 12	196	263	74.5
Week 16	209	239	87.4
Week 16 Endpoint	231	315	73.3

* Includes score of 1 (Very Much Improved) and 2 (Much Improved) on the CGI Global Improvement Item
Source: Data Source Tables 14.31.1, Section 11; Appendix C, Listing 14.3.1.

The number and percentage of patients in each specific category of the CGI Global Improvement Item Score by Visit Week are presented in Section 11 (Data Source Table 14.32.1). More than one-third (123/335, 36.7%) of the patients enrolled, and nearly one-half (115/239, 48.1%) of those patients completing the Week 16 Visit, were very much improved from Baseline at their final Phase I Visit. The percentage of patients who completed the Week 16 Visit and who showed any degree of improvement over Baseline (i.e., also includes patients with a rating of 3 [minimally improved]) was extremely high (231/239, 96.7%). At the

Week 16 Endpoint, only 35 of 315 patients for whom data were available (11.1%) had no change from baseline or were worse than at Baseline.

Table 27 presents a summary of the percentage of patients meeting the CY-BOCS Total Score response criteria during the Open-Label Phase, by Visit Week. A responder was defined as a patient with a reduction of at least 25% in the CY-BOCS Total Score from the Open-Label Baseline. Consistent with the CGI Global Improvement Item data, based on the CY-BOCs data the majority of patients responded very well to open-label paroxetine. More than three-quarters of the patients enrolled for whom data were available met this response criterion at their final Open-Label Phase Visit (258/329, 78.4%). For those who actually completed the Phase I Week 16 visit, the percentage of responders was even higher (217/239, 90.8%).

Table 27 Percentage (%) of Responders* Based on the CY-BOCS Total Score - Open Label Phase (ITT)

	n	N	%
ITT Population			
Initial Evaluation			
Week 2	91	328	27.7
Week 4	151	304	49.7
Week 6	187	292	64.0
Week 8	209	277	75.5
Week 12	209	263	79.5
Week 16	217	239	90.8
Week 16 Endpoint	258	329	78.4

* Reduction of ≥ 25% from Open-Label Baseline
Source: Data Source Table 14.24.1, Section 11; Appendix C Listings 14.2.1.

In order to participate in the double-blind randomization phase (Phase II), patients had to meet both the CGI Global Improvement Item and the CY-BOCS Total Score response criteria upon completion of the Open-Label Phase. Table 28 summarizes the number and percentage of patients meeting both criteria at Week 16 of the Open-Label Phase. Of patients with data available, 68.7% (226/329) met both response criteria patients at Endpoint, with 86.2% of the patients who reach Week 16 meeting both response criteria.

Table 28 Percentage (%) of Patients Meeting the Response Criteria - Open Label Phase (ITT)

	N	n	%
CGI Responders[1]			
Week 16	239	209	87.4
Week 16 Endpoint	315	231	73.3
CY-BOCS Responders[2]			
Week 16	239	217	90.8
Week 16 Endpoint	329	258	78.4
Meets Both Response Criteria[3]			
Week 16	239	206	86.2
Week 16 Endpoint	329	226*	68.7

1 Includes patients with score of 1 (Very Much Improved) and 2 (Much Improved) on the CGI Global Improvement Item
2 Reduction of ≥ 25% from Open-Label Baseline
3 Meets both of the above criteria
*See Errata 14.1, Section 14.
Source: Data Source Tables 14.31.1, 14.8.1, 14.8.2, and 14.24.1, Section 11; Appendix C, Listings 14.2.1 and 14.3.1.

5.2.2 Additional Open-Label Phase Efficacy Results

The overall responsiveness to open-label paroxetine was also demonstrated based on the CGI Severity of Illness Item Score (Table 29). At Open-Label Baseline, 98% (329/335) of the patients had a CGI severity of illness rating ≥ 4 (moderately ill or worse [more than half were rated markedly or severely ill]). However, at Week 16, only 28.5% (68/239) of the patients were rated at least moderately ill (40% if based on the Endpoint data, 126/315). Of the 239 patients with Week 16 Visit data, 35 (14.6%) were rated normal (not at all ill) at Week 16, with < 1% rated severely ill. Data Source Table 14.34.1, Section 11, summarizes the Baseline and Change from Baseline in the CGI Severity of Illness Score for the Phase I open-label ITT population.

Table 29 Percentage (%) of Patients in Each Category* of the CGI Severity of Illness Item - Open Label Phase (ITT)

	n	%
Baseline	335	100.0
Severity of Illness Score 1-3*	6	1.8
Severity of Illness Score 4-7**	329	98.2
Week 16	239	100.0
Severity of Illness Score 1-3*	171	71.5
Severity of Illness Score 4-7**	68	28.5
Week 16 Endpoint	315	100.0
Severity of Illness Score 1-3*	189	60.0
Severity of Illness Score 4-7**	126	40.0

* Includes scores of 1 (normal, not at all ill), 2 (borderline mentally ill), and 3 (mildly ill).
**Includes scores of 4 (moderately ill), 5 (markedly ill), 6 (severely ill), and 7 (among the most severely ill patients)
Source: Data Source Tables 14.33.1, Section 11; Appendix C, Listing 14.3.1.

Table 30 presents the mean change from Open-Label Baseline to Open-Label Phase endpoint for the CY-BOCS scores (Total and subscale scores), HAM-A, HAM-D and the GAF. The change from baseline in all parameters favored paroxetine. The mean reductions from baseline for the CY-BOCS Total, HAM-A and HAM-D scores were 13.0, 4.4, and 3.1, respectively. The GAF total score improved by a mean of 13.4 from baseline to endpoint.

Table 30 Mean Efficacy Parameter Changes from Baseline to Open-Label Phase Completion (ITT)

Test	n (N= 335)	Mean Change	SE
CY-BOCS Total Score	329	- 13.0	0.46
Obsessive Subscale	329	- 6.6	0.25
Compulsive Subscale	329	- 6.4	0.25
HAM-A	315	- 4.4	0.36
HAM-D	313	- 3.1	0.31
GAF	318	+ 13.4	0.73

Source: Data Source Tables 14.21.1, 14.22.1, 14.23.1, 14.4.1, 14.5.1, 14.72.1, Section 11; Appendix C, Listings 14.2.1, 14.3.1, 14.4.1, 14.5.1, and 14.7.1.

The mean Yale Global Total Tic Scores by Open-Label Phase Visit Week are presented in Section 11 (Data Source Table 14.6.1). At Open-Label Baseline, the mean Total Tic Score was 2.5 (± 0.31 SE). At Week 16 Endpoint (LOCF), the mean Total Tic Score had decreased to 1.7 (± 0.29 SE), and in patients reaching Week 16 the mean Total Tic Score was 1.0 (±0.19 SE).

5.3 Primary Efficacy Parameter

5.3.1 Proportion of Patients Who Relapse

Table 31 presents a summary of the proportion of patients who relapsed during the double-blind (randomization) phase. Approximately one-third (33/95, 34.7%) of the paroxetine patients met the relapse criteria, compared to 43.9% (43/98) of the patients randomized to placebo (see Figure 3), however, this difference was not statistically significant (p=0.136, Odds Ratio=0.62, associated C.I. was 0.34, 1.16). Similar results were observed in the Per-Protocol population. Therefore, although the odds of relapsing were higher for the placebo group, there was no evidence of a statistically significant difference between paroxetine and placebo. The proportion of relapsers in the placebo group was essentially lower than the expected 60% which was used in the sample size calculation. Data Source Tables 14.12.2b and 14.12.2c, Section 11, summarize the percentage of patients who met the relapse criteria by center grouping for the ITT and Per Protocol Populations, respectively.

Table 31 Percentage (%) of Relapsers* Based on CGI Global Improvement Item

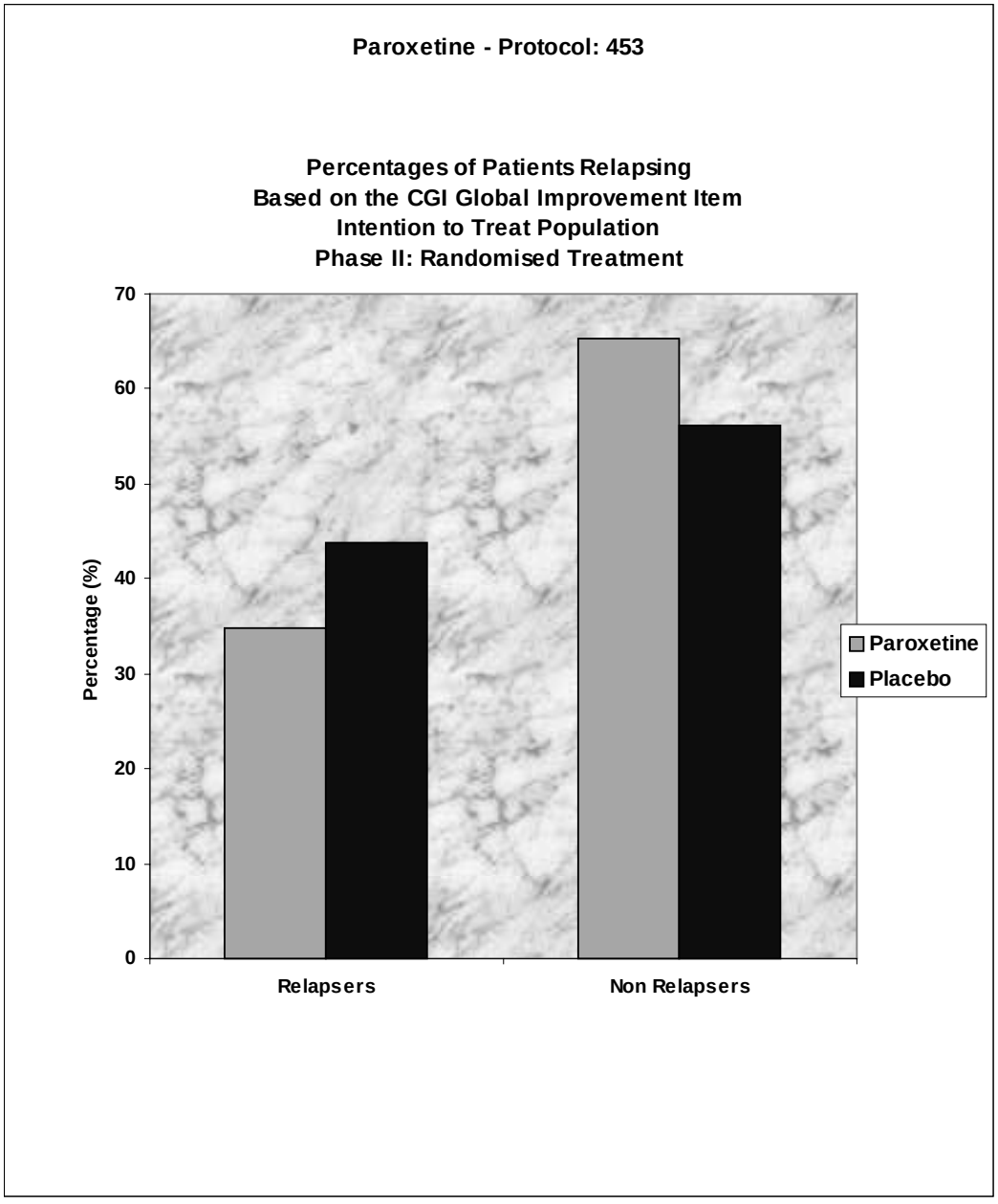
	Double-Blind						
	Paroxetine (N=95)		Placebo (N=98)		Pairwise Comparisons		
Analysis	n	%	n	%	Odds Ratio /CI/ p-value		
ITT	33	34.7	43	43.9	0.62	0.34-1.16	0.136
Per-Protocol**	26	32.1	36	43.4	0.59	0.30-1.17	0.133

* Defined as: a) Increase in CGI Global Improvement score by 1 point for 2 consecutive visits;
b) Increase in CGI Global Improvement score by ≥ 2 points at any single visit;
c) A CGI Global Improvement Score ≥ 5 at any time during the DB Phase.

** For the Per Protocol Population, N=81 for the paroxetine group and 83 for the placebo group.

Source: Data Source Tables 14.11.2b, 14.11.2c, Section 11; Appendix C, Listing 14.3.2.

Figure 3 Percentage (%) of Relapsers (CGI) by Treatment



5.3.2 Dose at Relapse

Data Source Table 14.13.2b (Section 11) presents the mean paroxetine dose at relapse by paroxetine dose level at Randomization Baseline. In both treatment groups, the majority of the patients relapsing (19/33 [58%] paroxetine patients and 25/43 [58%] placebo patients) were receiving one of the three lower dosage levels of study medication (10, 20 or 30mg or corresponding placebo). The 33 patients in the paroxetine group who relapsed consisted of 10 of the 20 patients at the 20 mg dosage level, 8 of the 26 patients at the 30 mg dosage level, 6 of the 14 patients at the 60 mg dosage level, 5 of the 16 patients at the 40 mg dosage level, 3 of the 10 patients at the 50 mg dosage level (3/10), and 1 of the 9 patients at the 10 mg dosage level. The mean dose at relapse by dose at randomization baseline data for the Per Protocol Population (Data Source Table 14.13.2c, Section 11) were very similar.

5.3.3 Proportion of Patients Who Relapse by Age Subgroup

Table 32 presents a summary of the relapse data by age subgroup (age < 12 years, or age ≥ 12 years). As was seen in the overall population, there was essentially no evidence of a statistically significant difference between paroxetine and placebo in either age group. However, although in the paroxetine treatment group the relapse rate in the < 12 years age group (18/95, 36.7%) was only slightly higher than in the ≥ 12 years age group (15/95, 32.6%), in the placebo treatment group the relapse rate in the < 12 years age group (27/98, 55.3%) was substantially larger than in the ≥ 12 years age group (17/98, 33.3%). Therefore, the observed placebo relapse rate in the < 12 years age group approached the assumption of 60% which was used for the sample size estimate and the observed difference between paroxetine and placebo in this subgroup was 18.6%, which is clinically relevant and approached statistical significance (p=0.099).

Table 32 Percentage (%) of Relapsers* Based on CGI Global Improvement Item by Age Subgroup (ITT)

	Double-Blind						
	Paroxetine (N= 95)		Placebo (N= 98)		Pairwise Comparisons** Odds Ratio /CI/ p-value		
Analysis	n	%	n	%			
Age < 12 years	18	36.7	27	55.3	0.45	0.18-1.16	0.099
Age ≥ 12 years	15	32.6	17	33.3	1.07	0.41-2.79	0.883

* Defined as: a) Increase in CGI Global Improvement score by 1 point for 2 consecutive visits;
b) Increase in CGI Global Improvement score by ≥ 2 points at any single visit;
c) A CGI Global Improvement Score ≥ 5 at any time during the DB Phase.

** Odds ratio / 95% C.I. / p-value

Source: Statistical Report, Section 15, Tables 14-17.

5.4 Secondary Efficacy Parameters

5.4.1 Time to Relapse (CGI Global Improvement Item)

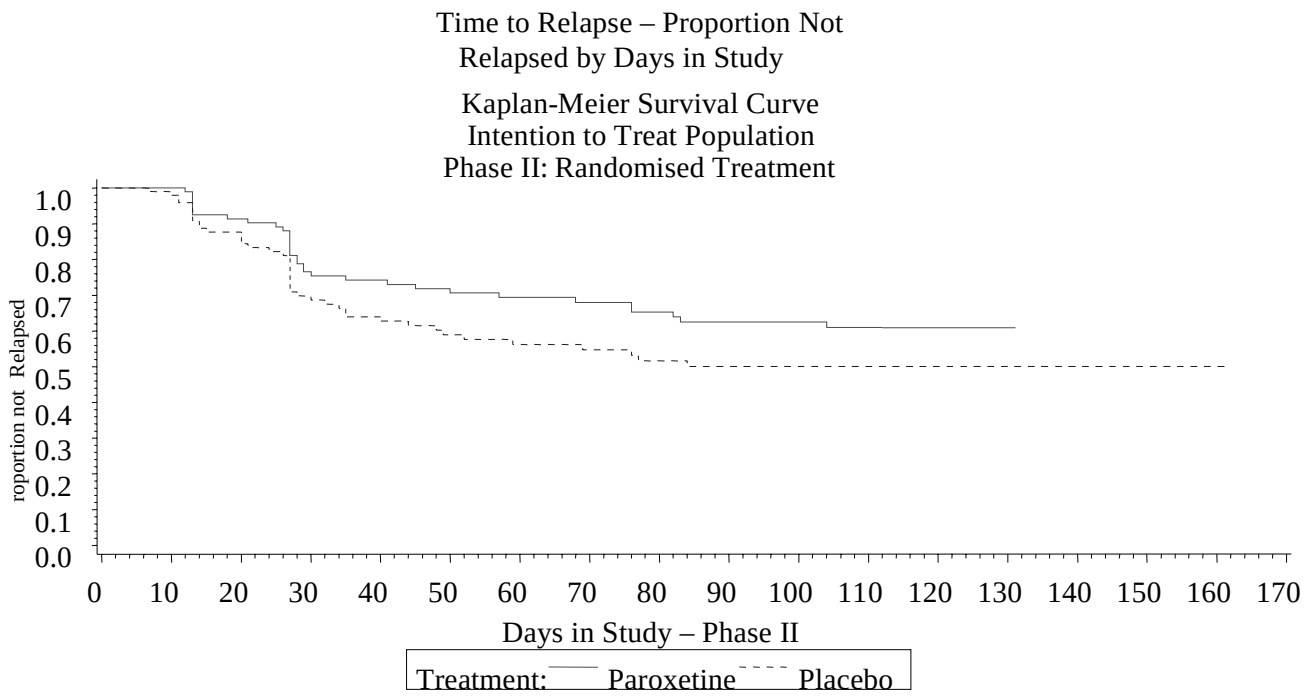
Table 33 presents the results of the time to relapse analyses. There was no evidence of a statistically significant difference between placebo and paroxetine with respect to time to relapse, although the hazard ratio of 1.5 with an associated confidence interval of (0.9, 2.3) indicates that the rate of relapse was greater in the placebo group. The majority of patients in both treatment groups withdrawing from Phase II due to lack of efficacy did so by Week 4 (19/33 patients in the paroxetine group and 31/45 patients in the placebo group, refer to Section 4.2.3 for details). Figure 4 presents the time to relapse data by treatment assignment as a Kaplan-Meier Survival Curve.

Table 33 Time to Relapse* (in days) Based on CGI Global Improvement Item Score

	Double-Blind		
	Paroxetine (N=95)	Placebo (N=98)	Statistical Parameters
Analysis	n	n	
Number of patients relapsing	33	43	---
Q1 (days)	35	27	---
Median (days)	ND	ND	---
Q3 (days)	ND	ND	---
Hazard ratio (paroxetine/placebo)	---	---	1.5
95% C.I.	---	---	0.9, 2.3
p-value (log rank test)	---	---	0.104

*Defined as: Visit date at which relapse was first discovered was used as the closest approximation
ND - Not defined (due to high proportion of observations being censored).
Source: Statistical Report, Section 15, Table 9.

Figure 4 Time to Relapsed (Kaplan-Meier Survival Curve)



5.4.2 CGI Global Improvement Item

Table 34 presents the percentage of patients with a CGI Global Improvement Item Score of 1 (very much improved) or 2 (much improved) by Visit Week during the double-blind randomization phase. In the Week 16 Endpoint dataset, 58.7% of the paroxetine group was rated as much improved or very much improved over baseline, compared to 44.8% of the placebo group. At the 70% endpoint (Week 4), the data also favored paroxetine over placebo (71.0% response rate for paroxetine vs. 59.4% for placebo). In the observed case dataset at Week 16 (i.e., patients with Week 16 data), there was essentially no difference between treatment groups in terms of the percentage of CGI Global Improvement Item responders.

Table 34 Percentage of Patients With a CGI Global Improvement Item Score of 1 (Very Much Improved) or 2 (Much Improved) During the Double-Blind Phase (ITT)

Patients With	Paroxetine			Placebo		
Scores of 1 or 2 *	n	N	%	n	N	%
Randomization Baseline	95	95	100.0	98	98	100.0
Week 2	79	91	86.8	77	97	79.4
Week 4	62	79	78.5	51	74	68.9
Week 6	59	65	90.8	40	51	78.4
Week 8	51	58	87.9	36	42	85.7
Week 10	45	53	84.9	31	36	86.1
Week 12	44	50	88.0	31	35	88.6
Week 16	36	41	87.8	25	30	83.3
70% Endpoint	66	93	71.0	57	96	59.4
Week 16 Endpoint	54	92	58.7	43	96	44.8

* Includes Very Much Improved (1) and Much Improved (2) CGI Global Improvement Item Scores

Source: Data Source Table 14.31.2, Section 1; Appendix C, Listing 14.3.2.

Table 35 presents the percentage of patients in each specific category of the CGI Global Improvement Item Score at Endpoint (Week 16 LOCF). The percentage of patients in the paroxetine group rated as very much improved (41.3%) was almost twice that reported in the placebo group (22.9%). Data Source Table 14.32.2 (Section 11) presents the number (%) of patients in each category of the CGI Global Improvement Item by Visit Week. At the 70% Endpoint (Week 4), the percentage of patients in the paroxetine group rated as very much improved was more than twice than reported in the placebo group (45.2% vs. 20.8%). In

the observed case dataset at Week 16 (i.e., patients with Week 16 data), the percentage of patients rated as very much improved still favored paroxetine vs. placebo (68% vs. 50%), although the difference was not as substantial as was reported in the Week 16 Endpoint and 70% Endpoint datasets.

Table 35 Number (%) of Patients in Each Category of the CGI Global Improvement Item Score at Week 16 Endpoint (ITT)

	Paroxetine (N= 95)		Placebo (N= 98)	
	n	%	n	%
Very Much Improved	38	41.3	22	22.9
Much Improved	16	17.4	21	21.9
Minimally Improved	17	18.5	24	25.0
No Change	6	6.5	15	15.6
Minimally Worse	8	8.7	8	8.3
Much Worse	5	5.4	4	4.2
Very Much Worse	2	2.2	2	2.1
Total	92	96.8	96	98.0
Not Assessed/Missing	3	3.2	2	2.0

Source: Data Source Table 14.32.2, Section 11; Appendix C, Listing 14.3.2.

5.4.3 CY-BOCS

Table 36 presents a summary of the CY-BOCS mean Randomization Baseline Total Score and change from Randomization Baseline Total Score by Visit Week. In both treatment groups, the mean CY-BOCS Total Score increased after randomization baseline, however, the mean increase (indicating a worsening of symptoms) was significantly greater in the placebo group than in the paroxetine group in both the Week 16 Endpoint (LOCF) and 70% Endpoint datasets ($p=0.008$ and $p=0.001$, respectively). In the Week 16 Observed Cases dataset, the mean change from randomization baseline was likewise greater for the placebo group than for the paroxetine group, however, this difference was not statistically significant.

Table 36 CY-BOCS Total Score Mean Change from Randomization Baseline – ITT

	Paroxetine			Placebo			Pairwise Comparisons+
	n	Mean*	SE	n	Mean*	SE	Diff / p-value / (95% CI)
Baseline**	92	9.9	0.67	98	9.6	0.61	-
Week 2	90	0.9	0.59	97	3.7	0.72	-
Week 4	79	1.6	0.86	74	4.9	0.81	-
Week 6	65	- 0.6	0.59	51	2.6	0.81	-
Week 8	58	0.1	0.69	42	1.5	0.86	-1.14 / 0.31 / (-3.35, 1.08)
Week 10	53	0.3	0.82	36	1.1	0.65	-
Week 12	49	- 0.5	0.96	35	1.3	0.77	-
Week 16	41	- 0.4	1.07	30	1.3	0.93	-0.81 / 0.58 / (-3.73, 2.12)
70% Endpoint ++	92	2.3	0.82	98	6.3	0.82	-4.01 / 0.001 / (-6.30, -1.72)
Week 16 Endpoint	92	3.6	0.92	98	6.9	0.86	-3.38 / 0.008 / (-5.88, -0.88)

** Baseline is the last open-label value prior to entering the double-blind phase
* Mean score at Randomization Baseline; Weeks scores are the mean changes from Baseline
+ Adjusted for terms retained in the final model (i.e., center group).
++ Note: The 70% Endpoint Visit is Week 4
Source: Data Source Table 14.21.2, Section 11; Appendix C, Listing 14.2.2.

Tables 37 and 38 present the Randomization Baseline mean data and change from Randomization Baseline mean data for the CY-BOCS Compulsive and Obsessive Subscales. Although these data were not statistically analyzed, the data favored paroxetine over placebo at Week 16, Week 16 Endpoint, and at the 70% Endpoint in both subscales.

Table 37 Table 37 CY-BOCS Obsessive Subscale Score Mean Change from Randomization Baseline – ITT

	Paroxetine			Placebo		
	n	Mean*	SE	n	Mean*	SE
Baseline**	91	4.7	0.36	98	4.4	0.32
Week 2	89	0.3	0.33	97	2.1	0.38
Week 4	78	0.8	0.48	74	2.6	0.45
Week 6	64	-0.0	0.31	51	1.6	0.46
Week 8	58	0.1	0.39	42	1.0	0.45
Week 10	53	0.5	0.47	36	1.0	0.37
Week 12	49	0.2	0.50	35	0.9	0.43
Week 16	41	-0.2	0.57	30	1.1	0.44
70% Endpoint +	91	1.1	0.45	98	3.4	0.43
Week 16 Endpoint	91	1.9	0.50	98	4.0	0.43

** Baseline is the last open-label value prior to entering the double-blind phase
* Mean score at Randomization Baseline; Weeks scores are the mean changes from Baseline
+ Note: The 70% Endpoint Visit is Week 4
Source: Data Source Table 14.23.2, Section 11; Appendix C, Listing 14.2.2.

Table 38 CY-BOCS Compulsive Subscale Score Mean Change from Randomization Baseline – ITT

	Paroxetine			Placebo		
	n	**Mean***	**SE**	**n**	**Mean***	**SE**
Baseline**	92	5.3	0.38	98	5.2	0.34
Week 2	90	0.6	0.31	97	1.6	0.40
Week 4	79	0.8	0.45	74	2.2	0.41
Week 6	65	-0.5	0.34	51	1.1	0.43
Week 8	58	0.0	0.42	42	0.4	0.49
Week 10	53	-0.2	0.49	36	0.1	0.39
Week 12	49	-0.7	0.57	35	0.3	0.46
Week 16	41	-0.2	0.61	30	0.2	0.58
70% Endpoint +	92	1.2	0.42	98	3.0	0.42
Week 16 Endpoint	92	1.7	0.49	98	2.9	0.47

** Baseline is the last open-label value prior to entering the double-blind phase
* Mean score at Randomization Baseline; Weeks scores are the mean changes from Baseline
+ Note: The 70% Endpoint Visit is Week 4
Source: Data Source Table 14.22.2, Section 11; Appendix C, Listing 14.2.2.

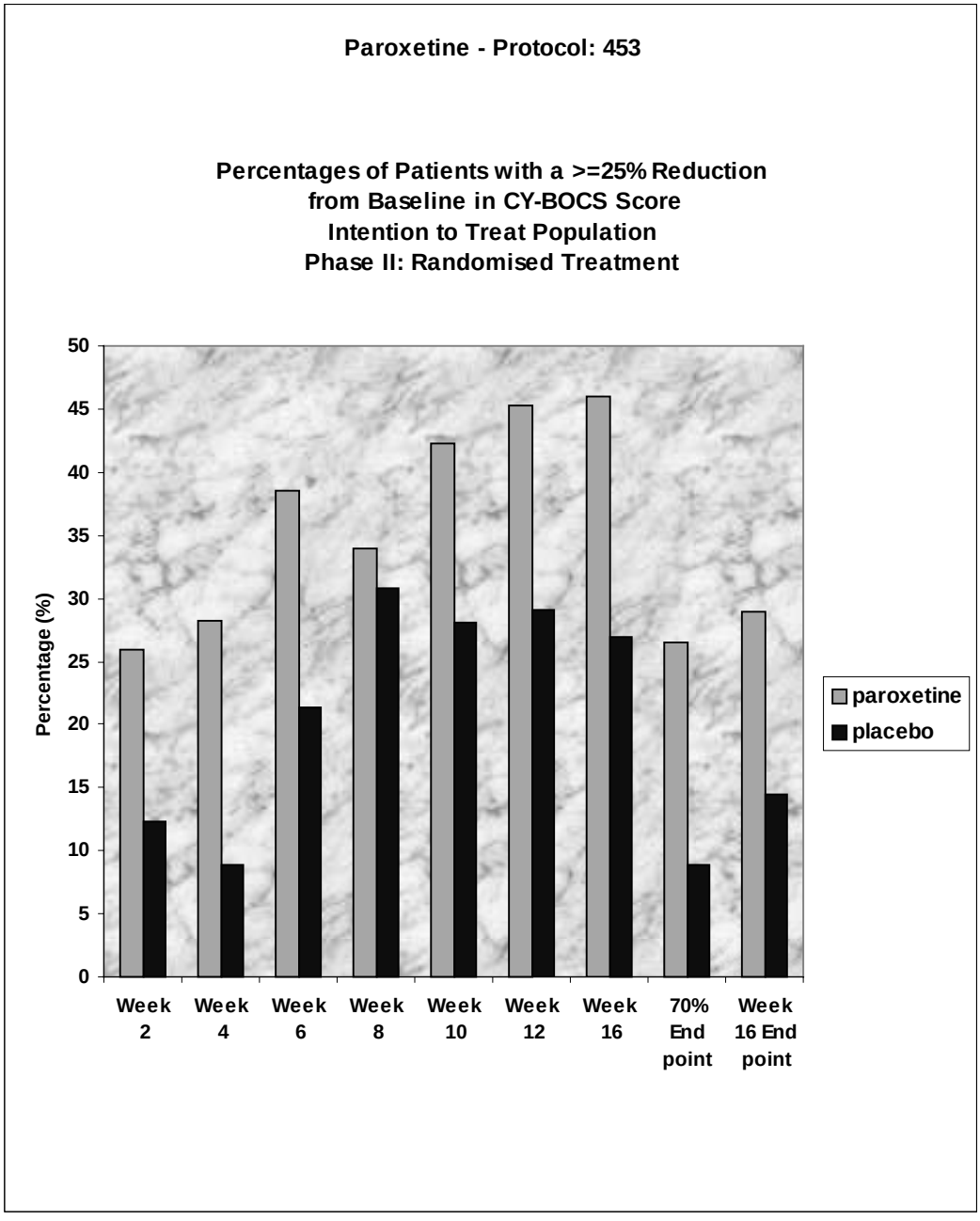
Table 39 and Figure 5 present the percentage of patients with a ≥ 25% reduction in CY-BOCS Total Score from Randomization Baseline. The percentage of patients in the paroxetine group with ≥ 25% reduction in CY-BOCS Total Score was significantly greater than the placebo group at the Week 16 Endpoint and at the 70% Endpoint (p=0.023 [C.I. 1.13, 5.13] and p=0.003 [C.I. 1.54, 8.86], respectively). The 70% Endpoint Visit was at Week 4. Of patients with a Week 16 visit, the percentage of patients in the paroxetine group achieving at least a 25% reduction in CY-BOCS score was also almost twice that of the placebo group, but this difference was not statistically significant.

Table 39 Proportion (%) of Patients With a >= 25% Reduction in CY-BOCS Total Score from Randomization Baseline - Double Blind Phase (ITT)

	Paroxetine			Placebo			Pairwise Comparisons*
	n	%	N	n	%	N	Odds Ratio /p-value / (95% CI)
Week 2	21	25.9	81	11	12.4	89	-
Week 4	20	28.2	71	6	8.8	68	-
Week 6	22	38.6	57	10	21.3	47	-
Week 8	17	34.0	50	12	30.8	39	1.16 / 0.747 / (0.47, 2.84)
Week 10	19	42.2	45	9	28.1	32	-
Week 12	19	45.2	42	9	29.0	31	-
Week 16	17	45.9	37	7	26.9	26	2.31 / 0.130 / (0.78, 6.80)
70% Endpoint**	22	26.5	83	8	8.9	90	3.70 / 0.003 / (1.54,8.86)
Week 16 Endpoint	24	28.9	83	13	14.4	90	2.41 / 0.023 / (1.13. 5.13)

*Unadjusted due to low numbers of patients per treatment/center group combination
**The 70% Endpoint visit is Week 4
Source: Data Source Table 14.24.2, Section 11; Appendix C, Listing 14.2.2.

Figure 5 CY-BOCS Percentage (%) of Responders as Determined by a >= 25% Reduction From Randomization Baseline Score by Treatment



5.4.4 CGI Severity of Illness Item

Table 40 summarizes the percentage of patients in each treatment group categorized by CGI Severity of Illness Item Score at the Week 16 Endpoint Visit (LOCF). The percentage of patients with either no illness or only borderline illness at Endpoint was greater in the paroxetine group (34/92, 37%) than in the placebo group (24/96, 25%). This difference in the percentage of patients with either no illness or only borderline illness also favored paroxetine at the 70% Endpoint Visit (43% [40/93] vs. 27% [26/96]) and in the Observed Cases dataset at Week 16 (58.5% [24/41] vs. 46.7% [14/30]), see Data Source Table 14.33.2, Section 11.

Table 40 Number (%) of Patients in Each Category of the CGI Severity of Illness Item Score at Week 16 Endpoint (ITT)

	Paroxetine (N= 95)		Placebo (N= 98)	
	n	%	n	%
Normal, not at all ill (1)	15	16.3	11	11.5
Borderline mentally ill (2)	19	20.7	13	13.5
Mildly ill (3)	19	20.7	20	20.8
Moderately ill (4)	23	25.0	36	37.5
Markedly ill (5)	12	13.0	11	11.5
Severely ill (6)	4	4.3	5	5.2
Among the Most extremely ill patients (7)	0	0.0	0	0.0
Total	92	96.8	96	98.0
Not Assessed/Missing	3	3.2	2	2.0

Source: Data Source Table 14.33.2, Section 11; Appendix C, Listing 14.3.2.

Table 41 summarizes the Randomization Baseline and change from Randomization Baseline in the CGI Severity of Illness scores. The paroxetine group had lower median scores than the placebo group at the Week 16 Endpoint and at the 70% Endpoint, although these data were not analyzed statistically.

Table 41 Randomization Baseline and Change from Randomization Baseline in the CGI Severity of Illness Score – Phase II Randomized Treatment (ITT)

	Paroxetine				Placebo			
	n	Median*	Min	Max	n	Median*	Min	Max
Baseline**	95	3	1	5	98	3	1	5
Week 2	91	0	-2	3	97	0	-1	3
Week 4	79	0	-2	4	74	0	-1	3
Week 6	65	0	-2	2	51	0	-1	3
Week 8	58	0	-2	2	42	0	-1	3
Week 10	53	0	-2	2	36	0	-1	2
Week 12	50	0	-2	3	35	0	-1	2
Week 16	41	0	-2	1	30	0	-1	2
70% Endpoint	93	0	-2	4	96	1	-1	3
Week 16 Endpoint	92	0	-2	4	96	1	-1	3

** Baseline is the last open-label value prior to entering the double-blind phase
* Median score at Randomization Baseline; Weeks scores are the median changes from Baseline
Source: Data Source Table 14.34.2, Section 11; Appendix C, Listing 14.3.2.

5.4.5 HAM-A

Table 42 presents the mean change from Randomization Baseline for the HAM-A scale by treatment group. The mean change from baseline was lower in the paroxetine group than in the placebo group at both the Week 16 Endpoint and at the 70% Endpoint. These data were not analyzed statistically.

Table 42 HAM-A Total Score Mean Change from Randomization Baseline (ITT)

	Paroxetine			Placebo		
	n	Mean*	SE	n	Mean*	SE
Baseline**	92	2.7	0.36	98	2.8	0.33
Week 2	90	0.9	0.30	97	1.8	0.53
Week 4	79	1.3	0.51	74	1.3	0.45
Week 6	65	0.2	0.37	51	1.3	0.55
Week 8	57	0.2	0.40	42	0.2	0.53
Week 10	53	0.8	0.46	35	-0.9	0.32
Week 12	48	0.2	0.54	35	-0.5	0.45
Week 16	41	-0.1	0.49	30	0.2	0.52
70% Endpoint	92	1.5	0.46	98	2.4	0.56
Week 16 Endpoint	92	1.8	0.53	98	3.1	0.58

** Baseline is the last open-label value prior to entering the double-blind phase
* Mean score at Randomization Baseline; Weeks scores are the mean changes from Baseline
Source: Data Source Table 14.4.2, Section 11; Appendix C, Listing 14.4.2.

5.4.6 HAM-D

Table 43 presents the mean change from Randomization Baseline for the HAM-D scale by treatment group. Both treatment groups exhibited slight increases in total HAM-D score from Phase II baseline at the Week 16 Endpoint and at the 70% Endpoint, however, the mean increase was less in the paroxetine group than in the placebo group in both instances. These data were not analyzed statistically.

Table 43 HAM-D Total Score Mean Change from Randomization Baseline (ITT)

	Paroxetine			Placebo		
	n	**Mean***	**SE**	**n**	**Mean***	**SE**
Baseline**	92	2.4	0.32	98	2.3	0.26
Week 2	90	1.0	0.38	96	1.7	0.50
Week 4	79	1.1	0.49	74	1.2	0.46
Week 6	65	0.8	0.44	51	1.3	0.51
Week 8	58	0.4	0.38	42	0.3	0.65
Week 10	53	0.7	0.40	35	-0.8	0.47
Week 12	48	0.1	0.51	35	-0.5	0.50
Week 16	41	0.1	0.39	30	0.2	0.58
70% Endpoint	92	1.4	0.47	98	2.3	0.55
Week 16 Endpoint	92	1.9	0.50	98	3.1	0.57

** Baseline is the last open-label value prior to entering the double-blind phase
* Mean score at Randomization Baseline; Weeks scores are the mean changes from Baseline
Source: Data Source Table 14.5.2, Section 11; Appendix C, Listing 14.5.2.

5.4.7 Yale Global Tic Score

Table 44 presents the mean Total Tic Score results (Yale Global Tic Severity Scale). In the paroxetine group, the mean score was essentially half that of the placebo group at the Week 16 Endpoint and at the 70% Endpoint, with little difference noted in the Week 16 Observed Cases dataset. These data were not analyzed statistically.

Table 44 Yale Global Tic Severity Scale - Mean Total Tic Scores (ITT)

	Paroxetine			Placebo		
	n	**Mean***	**SE**	**n**	**Mean***	**SE**
Baseline**	93	0.7	0.25	98	1.4	0.37
Week 2	91	0.6	0.22	97	1.5	0.39
Week 4	79	0.7	0.33	74	1.6	0.46
Week 6	64	0.6	0.29	50	1.3	0.55
Week 8	58	0.6	0.27	42	1.1	0.46
Week 10	53	0.7	0.43	36	1.4	0.72
Week 12	49	0.5	0.28	35	1.1	0.55
Week 16	41	0.7	0.42	30	0.8	0.51
70% Endpoint	93	0.6	0.29	98	1.5	0.40
Week 16 Endpoint	93	0.8	0.32	98	1.6	0.41

** Baseline is the last open-label value prior to entering the double-blind phase
* Mean score at Randomization Baseline; Weeks scores are the mean changes from Baseline
Source: Data Source Table 14.6.2, Section 11; Appendix C, Listing 14.6.2.

5.4.8 Global Assessment of Functioning (GAF) Scale

Table 45 presents the GAF Scale results (mean change from Randomization Baseline in GAF Total Score). The GAF Total mean scores decreased slightly in both groups during Phase II (suggestive of slight increases in functional impairment). The magnitude of the mean decrease was slightly greater in the placebo group than in the paroxetine group, however in general there appeared to be no substantial differences between treatment groups with respect to this parameter. These data were likewise not analyzed statistically.

Table 45 Mean Change from Randomization Baseline in GAF Total Score (ITT)

	Paroxetine			Placebo		
	n	Mean*	SE	n	Mean*	SE
Baseline**	93	73.4	1.13	98	73.5	1.11
Week 2	91	-2.6	0.85	97	-3.6	0.89
Week 4	79	-2.2	0.99	74	-5.7	1.34
Week 6	65	0.4	0.89	51	-2.6	1.19
Week 8	58	-1.5	0.98	42	-1.0	1.22
Week 10	53	-0.8	1.17	36	-1.4	1.12
Week 12	49	-0.2	1.60	35	-1.3	1.20
Week 16	41	-0.6	1.63	30	-0.8	1.81
70% Endpoint	93	-4.0	1.04	98	-7.2	1.18
Week 16 Endpoint	93	-5.8	1.22	98	-8.1	1.26

** Baseline is the last open-label value prior to entering the double-blind phase
* Mean score at Randomization Baseline; Weeks scores are the mean changes from Baseline
Source: Data Source Table 14.72.2, Section 11; Appendix C, Listing 14.7.2.

The mean GAF Total Scores by Visit Week are presented in Data Source Table 14.71.2, Section 11.

6 Safety Results

6.1 Extent of Exposure

Tables 22-24 presented summaries of the number and percentage of patients on each paroxetine dose level by Visit Week for the open-label and double-blind phases. Maximum dose information were also provided as part of those tables. Table 46 below summarizes the number (%) of patients by approximate overall total duration of exposure to paroxetine. Patients who received paroxetine for at least 12 weeks but for not longer than 16 weeks comprised the largest exposure subgroup (43.7%). Approximately 13% of the population received paroxetine for at least 28 weeks and for as long as 32 weeks. Only approx. 10% of the population received paroxetine for 4 weeks or less.

Table 46 The Number (%) of Patients Exposed to Paroxetine by Total Duration of Overall Exposure (i.e., Open-Label plus Double-Blind Exposure)

Overall Paroxetine Exposure **Approximate Duration of Total Exposure:**	**N=339***
Number of Patients with Open-Label Paroxetine Exposure Only (excluding OL Taper Phase dosing upon study withdrawal)*:	**N (%)**
≤ 2 weeks	26 (7.7)
>2 and ≤ 4 weeks	10 (2.9)
> 4 and ≤ 8 weeks	30 (8.8)
> 8 and ≤ 12 weeks	29 (8.6)
> 12 and ≤ 16 weeks	148 (43.7)
Total	243 (71.7)
Number of Patients with Combined Open-Label and Double-Blind Paroxetine Exposure (excluding Taper dosing upon study completion/withdrawal**)**:**	**N (%)**
>16 and ≤ 18 weeks	16 (4.7)
>18 and ≤ 20 weeks	13 (3.8)
>20 and ≤ 24 weeks	13 (3.8)
>24 and ≤ 28 weeks	10 (2.9)
>28 and ≤ 32 weeks	44 (13.0)
Total	96 (28.3)

*includes 4 patients enrolled but excluded from the ITT population.

**also excludes blinded down titration (taper) at the beginning of the double-blind phase for patients randomized to placebo.

Source: Data Source Tables 13.33.1 and 13.33.2, Section 10; Appendix B, Listings 13.12.1 and 13.12.2.

6.2 Adverse Experiences

Table 47 presents the most commonly reported adverse experiences (≥ 5% in either the open-label population or in either treatment group in the double-blind phase). Headache (82/335, 24.5%) was the most commonly reported AE in the open-label phase, followed by asthenia (72/335, 21.5%), and insomnia (71/335, 21.2%). Respiratory disorder (54/335,16.1%), somnolence (49/335,14.6%), nausea (48/335, 14.3%), nervousness (45/335,13.4%), trauma (45/335,13.4%), abdominal pain (40/335,11.9%), hyperkinesia (38/335,11.3%), diarrhea (37/335,11.0%) and weight gain (36/335,10.7%) were also all reported in at least 10% of the open-label population.

Headache was also the most common AE reported in both treatment groups in the double-blind phase (18.9% [18/95] and 26.5% [26/98] in the paroxetine and placebo groups, respectively). In general, the incidence of the AEs in Table 47 in the DB phase was greater in the placebo group than in the paroxetine group. This was clearly apparent for the GI-related AEs, all of which were reported more frequently in the placebo group (most notably nausea and dyspepsia). For some AEs, the increased incidence in the placebo group may have been the result of discontinuation effects (e.g., dizziness, which was reported in 12.2% [12/98] of the placebo patients and 7.4% [7/95] of the paroxetine patients) while in other cases the re-emergence of OCD related-symptoms following the switch to placebo may have been reported as AEs. For instance, anxiety, neurosis, and depression were all reported in the placebo group at substantially greater incidence than in the paroxetine group. Infection and pharyngitis also appeared to have a greater incidence in the placebo group, whereas hyperkinesia, hostility, and dysmenorrhea appeared to have a greater incidence in the paroxetine group.

Table 47 Number and Percentage of Patients with Commonly Reported (>= 5%*) Adverse Experiences by Body System and Preferred Term and by Treatment (ITT Population)

	Open-Label		Double-Blind			
			Paroxetine		Placebo	
	N = 335		N = 95		N = 98	
	n	%	n	%	n	%
Total Patients With AE's	316	94.3	73	76.8	80	81.6
Body as a Whole						
Headache	82	24.5	18	18.9	26	26.5
Asthenia	72	21.5	3	3.2	7	7.1
Trauma	45	13.4	9	9.5	5	5.1
Abdominal pain	40	11.9	6	6.3	9	9.2
Infection	32	9.6	4	4.2	11	11.2
Digestive						
Nausea	48	14.3	5	5.3	15	15.3
Diarrhea	37	11.0	5	5.3	7	7.1
Decreased appetite	30	9.0	2	2.1	3	3.1
Vomiting	24	7.2	0	0.0	4	4.1
Dyspepsia	23	6.9	1	1.1	7	7.1
Metabolic and Nutrional						
Weight gain	36	10.7	6	6.3	7	7.1
Musculoskeletal System						
Myalgia	4	1.2	3	3.2	6	6.1
Nervous System						
Insomnia	71	21.2	9	9.5	7	7.1
Somnolence	49	14.6	4	4.2	3	3.1
Nervousness	45	13.4	6	6.3	6	6.1
Hyperkinesia	38	11.3	3	3.2	0	0.0
Agitation	25	7.5	2	2.1	2	2.0
Hostility	24	7.2	6	6.3	0	0.0
Myoclonus	24	7.2	5	5.3	7	7.1
Dizziness	22	6.6	7	7.4	12	12.2
Neurosis	21	6.3	7	7.4	12	12.2
Tremor	17	5.1	2	2.1	1	1.0
Abnormal dreams	17	5.1	2	2.1	1	1.0
Anxiety	15	4.5	4	4.2	10	10.2
Depression	12	3.6	1	1.1	7	7.1
Respiratory System						
Respiratory disorder	54	16.1	11	11.6	10	10.2
Sinusitis	25	7.5	4	4.2	5	5.1
Rhinitis	22	6.6	4	4.2	4	4.1
Pharyngitis	18	5.4	1	1.1	7	7.1
Skin and Appendage						
Rash	18	5.4	2	2.1	2	2.0
Urogenital						
Dysmenorrhea*	5	3.6	3	6.3	0	0.0

* % corrected for gender

Source: Data Source Tables 15.01.1, 15.01.2, 15.02.1, 15.02.2, 15.03.1, 15.03.2, 15.04.1, 15.04.2, Section 12; App. D, Listings 15.1, 15.1.1, 15.1.2.

6.2.1 Adverse Experiences By Age Subgroup

Table 48 presents the most commonly reported AEs (≥ 10% in either the open-label phase or in either treatment group in the DB phase) by age subgroup (< 12 years, ≥ 12 years). In general, the commonly reported AEs in the open-label phase were reported with similar frequency in the two age groups, although there were a few common AEs which were reported with a greater incidence in one age group vs. another in the open-label phase. For instance, agitation (11.4% vs. 3.6%), hyperkinesia (14.4% vs. 8.3%), trauma (18.6% vs. 8.3%), and infection (12.0% vs. 7.1%) were all reported with greater frequency in the younger group. Others AEs not included in Table 48 (i.e., which did not reach an incidence of at least 10% in the overall open-label population) for which there was also a suggestion of greater incidence in one age group vs. another in the open-label phase included manic reaction (4.2% in the < 12 yr age group vs. 0.6% in the ≥ 12 yr age group), tremor (2.4% in the < 12 yr age group vs. 7.7% in the ≥ 12 yr age group) and myoclonus (9.6% in the < 12 yr age group vs. 4.8% in the ≥ 12 yr age group).

In the double-blind phase, again in general the incidence of the more commonly reported AEs were similar between the two age groups, with a few possible exceptions. Reports of headache were more common in the ≥ 12 yr age group (30-35%) than in the < 12 yr age group (8.2% in the paroxetine subgroup and 17.0% in the placebo subgroup). Somnolence was also more common in the older group (> 5% incidence in both treatment groups, compared to no reports of somnolence in the < 12 yr group). In contrast, agitation and neurosis were more common in the younger (< 12 yr old) age group. Agitation was reported in approx. 4% in each treatment subgroup in the < 12 yr olds, compared to no reports of agitation in the adolescent age group. Neurosis was reported in the < 12 yr old group at essentially twice the incidence reported in the ≥ 12 yr old group (in both treatment subgroups). Data Source Tables 15.01.1X and 15.01.2X, Section 12, summarize AE incidence by Body System and by age subgroup for Phases I and II, respectively.

Table 48 Most Commonly Reported (> 10%) Adverse Experiences by Age Subgroup (< 12 years, >= 12 years), by Study Phase

	Open-Label Phase		Double-Blind Phase			
	Age < 12 years	Age ≥ 12 years	Age < 12 years		Age ≥ 12 years	
			Paroxetine	Placebo	Paroxetine	Placebo
	N=167	N=168	N=49	N=47	N=46	N=51
Patients with AE (%)	**158 (94.6)**	**158 (94.0)**	**33 (67.3)**	**37 (78.7)**	**40 (87.0)**	**43 (84.0)**
AE Preferred Term	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Asthenia	36 (21.6)	36 (21.4)	1 (2.0)	2 (4.3)	2 (4.3)	5 (9.8)
Headache	35 (21.0)	47 (28.0)	4 (8.2)	8 (17.0)	14 (30.4)	18 (35.3)
Insomnia	33 (19.8)	38 (22.6)	6 (12.2)	2 (4.3)	3 (6.5)	5 (9.8)
Trauma	31 (18.6)	14 (8.3)	4 (8.2)	0 (0.0)	5 (10.9)	5 (9.8)
Respiratory Disorder	30 (18.0)	24 (14.3)	7 (14.3)	6 (12.8)	4 (8.7)	4 (7.8)
Somnolence	21 (12.6)	28 (16.7)	0 (0.0)	0 (0.0)	4 (8.7)	3 (5.9)
Abdominal Pain	20 (12.0)	20 (11.9)	1 (2.0)	7 (14.9)	5 (10.9)	2 (3.9)
Infection	20 (12.0)	12 (7.1)	2 (4.1)	4 (8.5)	2 (4.3)	7 (13.7)
Diarrhea	22 (13.2)	15 (8.9)	0 (0.0)	5 (10.6)	5 (10.9)	2 (3.9)
Nausea	20 (12.0)	28 (16.7)	1 (2.0)	7 (14.9)	4 (8.7)	8 (15.7)
Weight Gain	19 (11.4)	17 (10.1)	5 (10.2)	1 (2.1)	1 (2.2)	6 (11.8)
Agitation	19 (11.4)	6 (3.6)	2 (4.1)	2 (4.3)	0 (0.0)	0 (0.0)
Hyperkinesia	24 (14.4)	14 (8.3)	2 (4.1)	0 (0.0)	1 (2.2)	0 (0.0)
Nervousness	23 (13.8)	22 (13.1)	2 (4.1)	2 (4.3)	4 (8.7)	4 (7.8)
Dizziness	9 (5.4)	13 (7.7)	2 (4.1)	5 (10.6)	5 (10.9)	7 (13.7)
Neurosis	12 (7.2)	9 (5.4)	5 (10.2)	8 (17.0)	2 (4.3)	4 (7.8)
Anxiety	7 (4.2)	8 (4.8)	2 (4.1)	3 (6.4)	2 (4.3)	7 (13.7)

Source: Data Source Tables 15.02.1X, 15.02.2X, 15.03.1X, 15.03.2X, 15.04.1X, and 15.04.2X, Section 12; Appendix D, Listings 15.1.1 and 15.1.2.

6.3 Adverse Experiences Leading to Withdrawal of Treatment

Table 49 summarizes the adverse experiences leading to withdrawal by body system, preferred term, and study phase. There were a total of 59 patients withdrawn from the study overall due to AEs (17.6%). A total of 40 patients withdrew during the open-label phase (11.9%) and a total of 19 patients withdrew during the double-blind phase (9.8%). There were two patients (PIDs 453.018.00224 and 453.018.00226) who withdrew during the double-blind phase due to an AE which had an onset during the open-label phase. Therefore, a total of 42 patients (12.5%) withdrew due to an AE which started during open-label treatment and a total of 17 patients (8.8%) withdrew due to an AE which started during double-blind treatment. The majority of the AEs leading to withdrawal in the open-label phase were CNS-related. The AEs leading to withdrawal of more than 1% of the open-label phase population included hostility (2.7%), hyperkinesia (2.1%), agitation (1.8%), concentration impaired (1.5%), nervousness (1.2%) and neurosis (1.2%).

In the double-blind phase, the AE withdrawal rates were not substantially different between the two treatment groups. In fact, the AE withdrawal rate was slightly higher in the placebo group (10.2% vs. 7.4%). In both treatment groups, the majority of the withdrawals due to AE occurred early in Phase II. In the paroxetine group, half (4/8) of the AE withdrawals occurred by Week 2, as did 64% (7/11) of the AE withdrawals in the placebo group (see Tables 9 and 10 in Section 4.2.3). As was the case in the open-label phase, the AEs leading to withdrawal in the DB phase were generally CNS-related, with hostility (3.2% in the paroxetine group, 0.0% in the placebo group), neurosis (3.2% in the paroxetine group, 5.1% in the placebo group), hyperkinesia (2.1% in the paroxetine group, 0.0% in the placebo group) and nervousness (1.1% in the paroxetine group and 2.0% in the placebo group) accounting for the greatest number of withdrawals. Detailed narratives for all patients with an AE leading to withdrawal are included in Section 12, DST 15.09.1a. Data Source Table 15.4, Section 12, provides the location of all safety narratives. Data Source Tables 15.09.1 and 15.09.2, Section 12, presents the incidence of AEs leading to withdrawal by Body System for Phases I and II, respectively.

Table 49 All Adverse Events Leading to Withdrawal for AE

Body System / Preferred Term	Open-Label N=335		Double-Blind			
			Paroxetine N=95		Placebo N=98	
	n	%	n	%	n	%
Patients Withdrawn due to AE	42	12.5	7	7.4	10	10.2
Body as a Whole						
Abdominal Pain	4	1.2	0	0.0	0	0.0
Asthenia	2	0.6	0	0.0	0	0.0
Headache	1	0.3	0	0.0	2	2.0
Cardiovascular System						
Extrasystoles	2	0.6	0	0.0	0	0.0
Migraine	1	0.3	0	0.0	0	0.0
Pallor	1	0.3	0	0.0	0	0.0
Supraventricular extrasystoles	1	0.3	0	0.0	0	0.0
Digestive System						
Decreased Appetite	1	0.3	0	0.0	0	0.0
Diarrhea	1	0.3	0	0.0	0	0.0
Nausea	2	0.6	0	0.0	2	2.0
Nervous System						
Agitation	6	1.8	0	0.0	0	0.0
Anxiety	3	0.9	0	0.0	2	2.0
CNS Disorder (NOS)	1	0.3	0	0.0	0	0.0
Concentration Impaired	5	1.5	0	0.0	0	0.0
Delusions	1	0.3	0	0.0	0	0.0
Depression	2	0.6	0	0.0	1	1.0
Dizziness	0	0.0	0	0.0	1	1.0
Emotional Lability	2	0.6	0	0.0	0	0.0
Euphoria	2	0.6	0	0.0	0	0.0
Hostility	9	2.7	3	3.2	0	0.0
Hyperkinesia	7	2.1	2	2.1	0	0.0
Insomnia	2	0.6	0	0.0	0	0.0
Manic Reaction	3	0.9	1	1.1	0	0.0
Myoclonus	1	0.3	0	0.0	2	2.0
Nervousness	4	1.2	1	1.1	2	2.0
Neurosis	4	1.2	3	3.2	5	5.1
Somnolence	2	0.6	0	0.0	1	1.0
Tremor	2	0.6	0	0.0	1	1.0
Special Senses						
Abnormal Vision	1	0.3	0	0.0	0	0.0
Respiratory System						
Dyspnea	1	0.3	0	0.0	0	0.0
Hyperventilation	0	0.0	0	0.0	1	1.0
Skin and Appendages						
Rash	1	0.3	0	0.0	0	0.0
Skin Disorder	1	0.3	0	0.0	0	0.0

* Percentage corrected for gender

Source: Data Source Tables 15.10.1, 15.10.2, 15.11.1, 15.11.2, 15.12.1, 15.12.2, Section 12; Appendix D, Listings 15.1.1 and 15.1.2.

6.3.1 Adverse Experiences Leading to Discontinuation of Treatment by Age Subgroup

Data Source Tables 15.12.1X and 15.12.2X, Section 12, provide summaries of the number (%) of patients withdrawn due to AEs by age subgroup and study phase. Appendix D, Listings 15.1.1 and 15.1.2, contain all AEs reported by patient and by study phase. Of the 42 patients withdrawn due to an AE with an onset in the open-label phase, 28 (67%) were in the < 12 year old age group and 14 (33%) were in the ≥ 12 year old age group. Of the total 167 children < 12 years old enrolled in the open-label phase, 16.8% (n=28) withdrew due to an AE compared to 8.3% (14/168) of the adolesecent age group. All 5 of the patients withdrawing due to an AE of concentration impaired during the open-label phase were in the < 12 year old age group, as were six of the nine withdrawn due to AEs of hostility, five of the six withdrawn due to AEs of agitation, five of the seven withdrawn due to AEs of hyperkinesia, and both of the patients withdrawn due to AEs of emotional lability. The incidence of the other AEs leading to withdrawal in the open-label phase were generally comparable between the two age subgroups.

In the double-blind phase, the number of patients in each age subgroup withdrawn due to AE were similar (n=9 in the < 12 yr old group and n=8 in the ≥ 12 yr old age group). Neurosis was the only AE leading to withdrawal in the DB phase which was potentially disproportionately represented, as six of the eight Phase II withdrawals due to an AE of neurosis occurred in the younger (< 12 yr old) age group. Five of these six cases of events of "neurosis" leading to withdrawal from the study in the younger age group occurred in patients in the placebo group, and therefore are more than likely a result of a return of the patients' OCD symptoms.

Data Source Tables 15.09.1X and 15.09.2X, Section 12, present the incidence of AEs leading to withdrawal by age subgroup and by body system for Phases I and II, respectively. Data Source Tables 15.10.1X and 15.10.2X, Section 12, present the incidence of male specific AEs leading to withdrawal by age subgroup for Phases I and II, respectively. DSTs 15.11.1X and 15.11.2X present similar data, but for the female specific AEs.

6.4 Taper Phase Emergent Adverse Experiences

Of the 141 patients in the ITT population that did not enter Phase II, only 20.6% underwent down-titration (taper) at the end of Phase I. A greater percentage of the Phase II patients underwent down-titration (taper) upon ending randomized treatment (79/193, 40.9%). Table 50 presents a summary of the most commonly reported (reported in at least two patients) Taper Phase-emergent AEs by study phase. Note that only those AEs which occurred during a taper period at the end of study participation are included (i.e., AEs which occurred at the end of Phase I if not continuing into Phase II, or which occurred at the end of Phase II). Any AEs occurring during Phase II in patients assigned to placebo which had an onset during the time period when the patient was undergoing blinded down-titration (i.e., immediately following randomization to placebo) were not categorized as taper-emergent AEs, but rather were included as placebo group treatment phase-emergent AEs.

In general, the incidence of taper phase emergent AEs was low. Overall (Phase I and Phase II), there were very few taper phase-emergent AEs which were reported in at least two different patients (n=7). Headache (7/71, 9.9%), nausea (5/71, 7.0%), and dizziness (4/71, 5.6%) were the most commonly reported taper-emergent AEs in the combined group of patients tapering off of paroxetine either at the end of open-label or double-blind dosing. In contrast, the incidence of these three events in patients tapering off of placebo at the end of Phase II were 5.4%, 0.0%, and 0.0%, respectively. Data Source Table 15.01.3, Section 12, summarizes all taper phase emergent AEs by body system. There were no Taper Phase emergent AEs leading to withdrawal (see DSTs 15.09.3, 15.09.3X, 15.10.3, 15.10.3X, 15.11.3, 15.11.3X, 15.12.3, and 15.12.3X, Section 12).

Table 50 Summary of Taper Phase Emergent Adverse Experiences Occurring in at Least Two Patients, by Body System and Preferred Term and by Treatment (ITT Population)

	Open-Label		Double-Blind			
			Paroxetine		Placebo	
Body System	N =335		N = 95		N = 98	
Preferred Term	n	%	n	%	n	%
Total Patients Undergoing Taper	29	20.6*	42	44.2	37	37.8
Total Patients With Taper AE's	8	27.6	14	33.3	10	27.0
Body as a Whole						
Headache	2	6.9	5	11.9	2	5.4
Pain	0	0.0	0	0.0	2	5.4
Digestive						
Dyspepsia	1	3.4	1	2.4	0	0.0
Nausea	2	6.9	3	7.1	0	0.0
Nervous System						
Depression	1	3.4	0	0.0	1	2.7
Dizziness	1	3.4	3	7.1	0	0.0
Special Senses						
Otitis Media	0	0.0	1	2.4	1	2.7

* Based on the denominator of 141 patients that did not enter Phase II.
Source: Data Source Tables 15.02.3, 15.03.3, 15.04.3, Section 12; Appendix D, Listings 15.1.1, 15.1.2.

6.4.1 Taper Phase Emergent Adverse Experiences by Age Subgroup

Data Source Table 15.04.3X, Section 12, summarizes the number (%) of patients with Taper Phase emergent AEs by age subgroup and study phase. In general, there did not appear to be any clinically relevant differences in the incidence of taper phase emergent AEs between patients in the two age subgroups, neither in the OL Phase nor between treatment groups in the DB Phase. However, the numbers of patients in age each subgroup undergoing down-titration were small, therefore it is difficult to draw any definitive conclusions, and as such, these data should be interpreted with caution. Of the 29 patients undergoing down-titration at the end of open-label dosing, only nine were in the < 12 year old age group, and there were no taper phase emergent AEs reported for any of these patients. At least one taper phase emergent AE was reported for eight of the 20 (40%) Phase I taper patients who were aged 12 or over. Headache and nausea, each reported in two of these 20 patients (10%), were the most common. In the double-blind phase, 8/19 (42.1%) paroxetine group patients < 12 years old experienced a taper phase emergent AE, compared with 6/23 (26.1%) of the paroxetine group patients ≥ 12 years of age. Data Source Table 15.01.3X

summarizes the Taper Phase AE incidence by body system and age subgroup. Data Source Tables 15.02.3X and 15.03.3X summarize Taper Phase Male Specific and Female Specific AE incidence, respectively, by age subgroup.

6.5 Deaths

There were no deaths reported during the course of the trial, including during a 30 day time period following the last dose of study medication for each patient (Appendix D, Listings 15.5.1 and 15.5.2).

6.6 Serious Adverse Experiences

A serious adverse experience (SAE) was defined as any event which was fatal, life threatening, disabling or incapacitating or resulted in hospitalization, prolonged a hospital stay or was associated with congenital abnormality, cancer or overdose (either accidental or intentional). In addition, any experience which the investigator regarded as serious or which would suggest significant hazard, contraindication or side effect or precautions that may have been associated with theuse of the drug was to be documented as a serious AE.

Table 51 summarizes the number (%) of patients with serious adverse experiences (SAEs) by Preferred Term and study phase. Seventeen patients reported a total of 22 SAEs during the study (17/335, 5.1%). Thirteen patients in the open-label phase (3.9%) reported a total of 17 SAEs and four patients in the double-blind phase (2.1%) reported a total of 5 SAEs. Almost all of the SAEs reported (19/22, 86.4%) were CNS-related. Emotional lability (n=5) and hostility (n=4) were the two most common SAEs reported during open-label treatment, and were the only SAEs reported in more than one patient during the open-label phase. For this reason, these events will be described in more detail below. Detailed patient narratives for all SAEs are included in Section 12, DST 15.05.2a. Data Source Table 15.4, also in Section 12, provides the location for all of the safety narratives by PID no.

For the AE Preferred Term of Emotional Lability, the investigator AE term was either "suicide attempt" (n=2; 453.002.00311 and 453.020.00448) or "suicidal ideation/suicidal thinking/suicidal thoughts" (n=4; 453.017.00335, 453.017.00431, 453.021.00067 and 453.002.00311) in each case. PID 453.002.00311 was a 10 year old female who had an SAE of hostility (oppositional defiant behavior and self-destructive behavior) requiring hospitalization. At that time it was determined that she had also tried to hang or

drown herself. The patient was withdrawn from the study. She had been doing well on the paroxetine up to that point, as her OCD symptoms had improved considerably according to the investigator. PID 453.020.00448 was a 12 year old female who had a prior history of passive suicidal ideation without intention or plan as well as a suspected history of GAD. On study medication she had also shown some improvement in her OCD symptoms. The investigator did not consider this event to be related to the study medication, and the patient was not withdrawn from the study and completed the study as planned. The three instances of suicidal ideation involved a 17 year-old male (453.017.00335), a 10 year-old male (453.017.00431), and a 9 year-old male (453.021.00067). In the case of the 17 year-old, the patient was hospitalized and discharged the next day. The event was considered to be possibly related to the study medication, although the patient, who had a history of conduct disorder, suspected depression and social anxiety disorder, was continued in the study. This patient was eventually withdrawn from the study due to moving out of the state. In the case of the 10 year-old, who had a history of ADHD, tic disorder and dysthymia, increased symptoms of ADHD and aggression were reported shortly after starting the open-label medication (within 2 days after). The patient remained in the study but approx. 2 weeks later was withdrawn from the study due to ongoing increasing ADHD symptoms and aggression. The patient was hospitalized at that time and started on fluvoxamine and clonidine. The patient was discharged approx. one week later. The investigator considered the suicidal ideation possibly related to the study medication. In addition to the suicidal ideation, the 9 year-old also had SAEs of depression and hostility. The investigator withdrew the patient, who had a history of GAD and specific phobia, from the study but continued him on paroxetine off study because the OCD symptoms had been improving. The investigator felt that the events were probably unrelated to the study medication.

Two of the four patients with an SAE of hostility in the OL Phase have been described above (as they also had SAEs of emotional lability). PID 453.024.00180 was a 9 year-old male with a history of ADHD, dysthymia, tic disorders, and depression who became increasingly defiant during the study. The study medication was discontinued and the patient was withdrawn from the study. The investigator considered the event to be possibly related to the study medication. PID 453.026.00287 was a 13 year-old male with a history of ADHD, oppositional defiant disorder, specific phobia, and depression. Approx. one month after starting the study medication, the patient experienced worsening oppositional defiant disorder. The patient was hospitalized and withdrawn from the study because the investigator felt that the study medication may possibly have exacerbated the patient's underlying oppositional defiant disorder. One DB

Phase patient in the paroxetine group had an SAE of hostility (453.021.00129). This patient, an 8 year old male with a history of ADHD, also had an SAE of manic reaction. Both events were considered possibly related to the study medication and the patient was withdrawn from the study.

There was one cardiovascular SAE reported. PID 453.001.00363 was a 15 year-old male with a history of obesity, elevated SGPT, and bilateral erythema. Approx. 2 months after starting the study medication, a routine ECG revealed frequent severe premature ventricular contractions (PVCs). The ECG had been normal at Screening. The patient was asymptomatic for cardiac signs/symptoms. Laboratory findings were also generally unremarkable. The investigator considered the event to be possibly related to the study medication (30mg/day), which was discontinued and the patient withdrawn from the study.

Data Source Tables 15.05.1 and 15.05.2 summarize SAE incidence by Body System for Phases I and II, respectively, and Data Source Table 15.05.3 presents the incidence fo Taper Phase SAEs by body system. Data Source Tables 15.06.3, 15.07.3, and 15.08.3, present Male Specific, Female Specific, and Non-gender specific Taper Phase SAE incidence, respectively.

Table 51 Number and Percentage (%) of Patients with Serious Adverse Experiences

	Open-Label		Double-Blind			
			Paroxetine		Placebo	
Total Patients	N=335		N=95		N=98	
Patients With AEs	13 (3.9%)		2 (2.1%)		2 (2.0%)	
Body System						
Preferred Term	n	%	n	%	n	%
Body as a Whole						
Trauma	1	0.3	0	0.0	0	0.0
Cardiovascular						
Extrasystoles	1	0.3	0	0.0	0	0.0
Nervous System						
Agitation	1	0.3	0	0.0	0	0.0
Anxiety	1	0.3	0	0.0	0	0.0
Delusions	1	0.3	0	0.0	0	0.0
Depression	1	0.3	0	0.0	0	0.0
Drug Dependence	1	0.3	0	0.0	0	0.0
Emotional Lability	5	1.5	0	0.0	0	0.0
Hostility	4	1.2	1	1.1	0	0.0
Neurosis	1	0.3	0	0.0	2	2.0
Manic Reaction	0	0.0	1	1.1	0	0.0
Skin and Appendages						
Skin Hypertrophy	0	0.0	1	1.1	0	0.0

* percentage corrected for gender
Source: Data Source Tables 15.08.1, 15.08.2, 15.06.1, 15.06.2, 15.07.1, 15.07.2, and 15.05.2a, Section 12; Appendix D, Listings 15.1, 15.1.1, and 15.1.2.

6.7 Electrocardiogram (ECG) Results

Table 52 summarizes the number and percentage of patients with significant ECG changes from the Screening Visit assessment by Visit Week (Week 8 and Week 16) and by study phase. A total of eight patients had significant ECG changes noted during the open-label phase (4 at Week 8 only, 3 at Week 16 only, and 1 at both Weeks 8 and 16). In all cases the Screening ECGs were normal and in all cases the ECG changes were reported as an adverse event. For only one patient was the event (extrasystoles at Week 8) considered serious in nature (PID 453.001.00363, see Section 6.6). No significant ECG changes were reported during the double-blind phase. Only two of the 339 patients entered into the open-label phase had an abnormal ECG at Screening. One of these patients exhibited no changes from the Screening ECG at Weeks 8 and 16

(453.004.00086). No post-baseline ECG recordings were obtained for the second patient with an abnormal ECG at Screening (453.021.00067).

Five patients had significant ECG changes reported at Week 8. As noted above, this included one patient with extrasystoles that were considered serious in nature. Two of the other four patients with significant ECG changes at Week 8 had decreases in HR meeting the prefined clinical concern criteria, therefore these two events (bradycardia) are further detailed in patient safety narratives (PIDs 453.013.00248 and 453.021.00068, see Data Source Table 15.4, Section 12). Of the remaining two patients with significant changes at Week 8, one patient (453.024.00038) had extrasystoles and supraventricular extrasystoles reported. The other patient (PID 453.023.00091), in addition to significant ECG changes at Week 8 (reported as "ECG abnormal") also had significant changes at Week 16 of the open-label phase reported as "tachycardia".

Three patients had significant ECG changes reported at Week 16 of the open-label phase only. An AE of "bradycardia" was reported in one case (453.021.00383), an AE of "AV block" was reported in one case (453.026.00136), and the remaining case was reported as an AE of "QT interval prolonged" (453.024.00179). As noted above, none of these events were considered to be serious in nature.

Table 52 Number and Percentage of Patients with ECG Changes from the Screening Assessment (ITT)

	Open-Label		**Double-Blind**			
			Paroxetine		**Placebo**	
	N=335		**N=95**		**N=98**	
Total Patients With Screen ECG	**N=295**		**N=58**		**N=45**	
	n	%	n	%	n	%
Week 8						
Significant Change(s)	5	1.8	0	0.0	0	0.0
No significant change(s)	270	98.2	53	100.0	39	100.0
Total	275	100.0	53	100.0	39	100.0
Missing	20	---	5	---	6	---
Week 16						
Significant Changes(s)	4	1.7	0	0.0	0	0.0
No significant changes(s)	227	98.3	40	100.0	25	100.0
Total	231	100.0	40	100.0	25	100.0
Missing	18	---	4	---	3	---

Source: Data Source Tables 13.6.1 and 13.6.2, Section 10; Appendix B, Listings 13.6.1 and 13.6.2.

6.8 Vital Signs

Table 53 presents a summary of the number and percentage of patients in each phase of study with vital sign(s) measurements meeting sponsor predefined potential clinical concern criteria (described in Data Source Table 15.0, Section 12). This table does not necessarily represent vital sign changes determined to be clinically significant by the investigator. If any vital sign change was considered clinically significant by the investigator, whether or not the value/change met the predefined concern criteria, the event was to be recorded as an AE in the case report form. Patient narratives (see Data Source Table 15.21.2a, Section 12) were prepared for any vital sign value which both exceeded either the high or low cutoff limit and the specified degree of change cutoff, and which was reported as an AE by the investigator.

In the open-label phase the incidence of vital sign values exceeding both the absolute value cutoff and the degree of change cutoff point was generally quite low (< 5% for all parameters except body weight). A total of 29 patients (8.7%) had weight increases in the OL phase meeting both of the concern criteria, however the weight increases were considered clinically significant by the investigator (i.e., reported as an AE) in only 12 of these cases (3.6%). The results were generally similar in the double-blind phase. For only weight gain did the incidence of findings meeting both the absolute and and the degree of change concern criteria exceed 5%. A total of 17 additional patients met both of the clinical concern criteria for weight gain, however in only two of these cases was the weight gain considered clinically significant (i.e., reported as an AE). The instances of weight gain meeting both concern criteria were comparable in the two treatment groups (9.6% vs. 8.2%).

The summary of all treatment emergent AEs by Body System, Preferred Term and study phase (Data Source Tables 15.04.1, 15.04.2, and 15.04.3, Section 12) includes a number of infrequent AEs reflective of vital sign changes, which although not meeting the potential clinical concern criteria, were considered to be clinically significant by the investigator and hence reported as AEs (e.g., hypertension, palpitation, tachycardia, and vasodilatation). However, the nature and incidence of these events were generally similar to those contained in the current product labeling targeting an adult population, and were not suggestive of new concerns specific to a pediatric population.

Table 53 The Number (%) of Patients with Vital Signs Measurements Meeting Sponsor-Defined Potential Clinical Concern Criteria at Any Time During the Study by Treatment Group

Vital Signs of Potential Clinical Concern	Open-Label Paroxetine (N=335)		Double-Blind Phase			
			Paroxetine (N=94)		Placebo (N=98)	
	n	%	n	%	n	%
Blood Pressure						
Systolic (mm Hg)						
< 95	33	9.9	4	4.3	6	6.1
> 145	5	1.5	3	3.2	1	1.0
Decrease ≥ 30	4	1.2	3	3.2	1	1.0
Increase ≥ 40	2	0.6	1	1.1	0	0.0
<95 and decrease ≥ 30	2	0.6	0	0.0	0	0.0
>145 and increase ≥ 40	0	0.0	1	1.1	0	0.0
Diastolic (mm Hg)						
< 50	76	22.7	16	17.0	18	18.4
> 85	39	11.6	8	8.5	4	4.1
Decrease ≥ 20	30	9.1	6	6.4	5	5.1
Increase ≥ 30	1	0.3	1	1.1	1	1.0
<50 and decrease ≥ 20	14	4.2	1	1.1	3	3.1
>85 and increase ≥ 30	1	0.3	1	1.1	0	0.0
Heart Rate (bpm)						
High*:	22	6.6	5	5.3	2	2.0
Low*	99	29.6	18	19.1	18	18.4
Increase ≥ 30	15	4.5	2	2.1	3	3.1
Decrease ≥ 30	18	5.4	3	3.2	3	3.1
High and increase ≥ 30	3	0.9	0	0.0	0	0.0
Low and decrease ≥ 30	4	1.2	1	1.1	3	3.1
Weight (lb)						
High	81	24.2	28	29.8	23	23.5
Low	8	2.4	1	1.1	1	1.0
Increase ≥ 7%	90	27.5	29	30.9	23	23.5
Decrease ≥ 7%	10	3.1	1	1.1	1	1.0
High and increase ≥ 7%	29	8.7	9	9.6	8	8.2
Low and decrease ≥ 7%	0	0.0	0	0.0	0	0.0

*High= >115 bpm (age 8-12), >110 bpm (age 13-17); Low= <65 bpm (age 8-12), < 55 bpm (age 13-17)
Source: Data Source Tables 15.0, 15.21.1, 15.21.2, Section 12; Appendix D, Patient Data Listings 15.2.1, 15.2.2. .

Data Source Tables 15.22.1 and 15.22.2, Section 12, summarize the mean vital sign values (including weight) by Visit Week and study phase. Table 54 summarizes mean (± SD) body weight and vital sign changes from baseline at

each visit for each study phase. The mean changes from baseline for all parameters were generally unremarkable. The mean increases in body weight from OL baseline to OL Week 16 of 4.4 lbs, and from randomization baseline to DB Week 16 of 6.4 lbs and 5.5 lbs, in the paroxetine and placebo groups, respectively, were not unexpected given that that was a pediatric population.

Table 54 Mean (±SD) Weight and Vital Sign Changes From Baseline at Each Visit by Treatment

Vital Sign Measures	Open-Label Paroxetine (N=335)			Double-Blind Phase Paroxetine (N=95)			Placebo (N=98)		
	n	Mean	SD	n	Mean	SD	n	Mean	SD
Weight (lb)									
Baseline*	329	102	37.60	95	109.1	40.61	98	104.2	38.18
Week 2	326	-0.1	2.22	91	1.5	2.39	97	1.4	2.79
Week 4	300	0.2	2.92	81	2.3	3.05	77	2.1	3.48
Week 6	283	0.7	3.43	66	3.0	3.09	52	3.1	4.61
Week 8	271	1.2	3.64	56	3.6	3.42	43	4.0	5.15
Week 10				53	4.4	3.81	35	4.8	5.50
Week 12	256	3.2	4.77	47	5.3	4.39	35	4.9	6.01
Week 16	235	4.4	5.72	41	6.4	5.10	30	5.5	7.04
Systolic BP (mm Hg)									
Baseline*	332	106.3	10.87	95	107.8	12.41	98	106.5	11.30
Week 2	329	-0.1	9.39	91	-1.0	10.07	97	0.4	10.92
Week 4	303	0.5	9.84	81	-1.9	9.85	77	-0.9	10.11
Week 6	288	0.1	10.13	66	-0.7	10.37	52	-1.2	11.93
Week 8	275	0.5	10.62	58	-0.9	10.64	43	1.0	9.95
Week 10				53	-0.7	11.83	35	0.0	10.75
Week 12	260	1.0	10.38	47	-1.1	11.98	35	0.2	9.99
Week 16	237	1.7	11.61	41	1.2	13.97	30	3.9	10.78
Diastolic BP (mmHg)									
Baseline*	332	67.3	8.73	95	66.6	8.56	98	67.3	9.31
Week 2	329	-0.3	9.04	91	0.7	8.46	97	0.6	9.44
Week 4	303	0.6	8.57	81	0.5	9.38	77	-0.5	8.91
Week 6	288	-0.5	9.11	66	0.0	9.55	52	-0.7	10.16
Week 8	275	0.0	9.28	58	1.4	8.93	43	1.4	8.84
Week 10				53	1.1	9.69	35	2.9	8.13
Week 12	260	-0.4	9.07	47	1.7	7.01	35	2.6	10.34
Week 16	237	-0.5	10.04	41	1.4	10.84	30	3.2	9.70
Heart Rate (bpm)									
Baseline*	333	80.3	12.98	95	81.8	13.02	97	81.7	10.59
Week 2	330	-2.0	12.04	91	-0.9	10.79	96	-3.0	13.13
Week 4	303	-0.6	12.25	81	-0.9	11.02	76	-1.7	12.22
Week 6	289	0.6	12.92	66	-0.7	11.16	51	-1.0	10.10
Week 8	275	0.7	11.90	58	0.3	13.83	42	-0.9	11.18
Week 10				53	-2.8	12.77	35	-1.4	11.26
Week 12	261	1.0	13.09	46	-2.6	13.34	34	1.2	10.55
Week 16	236	2.0	13.46	41	-3.3	11.97	29	-2.1	12.44

*Open-label Baseline for open-label results; randomization baseline for double-blind results
Source: Data Source Tables 15.23.1, 15.23.2, Section 12; Appendix D, Listings 15.2.1 and 15.2.2.

6.9 Laboratory Tests

Table 55 summarizes the number and percentage of patients with laboratory values meeting the predefined potential clinical concern criteria by Visit Week and phase of the study (see Data Source Table 15.0, Section 12, for details of the concern criteria). In general, there were very few instances of laboratory results meeting the predefined clinical concern criteria. During the open-label phase, only hematocrit, alkaline phosphatase and mean corpuscular volume (MCV) exhibited greater than a 1% incidence of values meeting the clinical concern criteria. Patient narratives for lab values meeting the concern criteria and which were reported as an AE by the investigator are included in Section 12, DST 15.3.2a (also refer to Data Source Table 15.4, Section 12).

For alkaline phosphatase, five patients had elevated values meeting the concern criteria at Week 8 of the OL Phase. However, for four of these five patients the Screening value also met the concern criteria. At Week 16, only two patients had alkaline phosphatase values meeting the clinical concern criteria and one of these patients also met the concern criteria for this parameter at Screening. There were no alkaline phosphatase results meeting the concern criteria in the double-blind phase of the study. None of these findings were reported as adverse events.

For hematocrit, 16 patients had low values meeting the concern criteria at Week 8 of the OL Phase. For five of these 16 patients the Screening value also met the concern criteria. Similarly, six of the 19 patients with low hematocrit values meeting the concern criteria at Week 16 of the OL Phase also had low values at Screen (which met the concern criteria). An AE of anemia was reported for one of the patients with a low hematocrit meeting the clinical concern criteria Week 16 of the OL Phase (453.017.00195). An AE of anemia was also reported for another patient whose hematocrit level did not meet the concern criteria (453.024.00268). Eleven patients in the DB Phase had hematocrit values which met the clinical concern criteria. Nine of these 11 patients were in the paroxetine group. However, of these nine patients, three had hematocrit values meeting the concern criteria at Screen.

For mean corpuscle volume (MCV), four of the seven patients with a low MCV value which met the concern criteria during the OL and/or DB phases of the study also met the concern criteria for this parameter at Screening.

The summary of all treatment emergent AEs by Body System, Preferred Term and study phase (Data Source Tables 15.04.1, 15.04.2, and 15.04.3, Section 12) includes a number of infrequent AEs reflective of laboratory parameter changes,

which although not meeting the potential clinical concern criteria, were considered to be clinically significant by the investigator and hence reported as AEs (e.g., eosinophilia, leukopenia, thrombocytopenia, hypo/hyperglycemia, SGOT/SGPT increased, LDH increased and abnormal urinalysis findings [hematuria, pyuria, albuminuria, glycosuria]). However, the nature and incidence of these events were similar to those contained in the current product labeling for the adult population, and were not suggestive of any new safety concerns specific to a pediatric population.

Data Source Tables 15.4.1 and 15.4.2, Section 12, present the findings of the urine screens for drugs of abuse. The incidence of positive findings was generally low (2.1% of patients in the OL Phase and 2.8% of the patients in the DB Phase). Refer to Appendix D for listings of drug screen data by patient (15.41.1, 15.41.2) and by parameter (15.42.1, 15.42.2).

Table 55 Number (%) of Patients with Laboratory Values Considered to be of Potential Clinical Concern (F3 Flags) at Any Time During the Study by Treatment Group

Laboratory Test Groupings	Values of Potential Clinical Concern	Open-Label N=335				Double-Blind							
						Paroxetine				Placebo			
		Week 8 N=264*		Week 16 N=227**		Week 8 N=50+		Week 16 N=39		Week 8 N=35		Week 16 N=27	
		n	%	n	%	n	%	n	%	n	%	n	%
Hematology													
Hemoglobin (gm%)	Low	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Hematocrit (vol%)	Low	16	6.1	19	8.5	5	10.0	5	12.8	2	5.7	0	0.0
MCHB	High	2	0.8	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
MCHB concentration	High	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
MCV	Low	5	1.9	3	1.3	3	6.0	2	5.1	0	0.0	0	0.0
	High	1	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
WBC (thou/mel)	≤ 2.8 or ≥ 16	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
RBC	High or Low	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Lymphocytes (%)	≥ 75	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Monocytes (%)	≥ 15	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Basophils (%)	≥ 10	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Eosinophils (%)	≥ 10	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Neutrophils,	≤ 15	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Bands (%)	≥ 10	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Segmented (%)	≤ 15	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Platelets (ths/mm^3)	≤ 75 or ≥ 700	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

(Table continues next page)

Table 55 Number (%) of Patients with Laboratory Values Considered to be of Potential Clinical Concern (F3 Flags) at Any Time During the Study by Treatment Group

Liver Function													
AST (SGOT)	High	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ALT (SGPT)	High	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Alk. Phos.	High	5	1.9	2	0.9	0	0.0	0	0.0	0	0.0	0	0.0
Total Bilirubin	High	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Chemistry													
GGT	High	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Serum Creatinine	High	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
LDH	High	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Glucose (random)	High or Low	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Phosphorous	High	2	0.8	1	0.4	1	2.0	2	5.1	1	2.9	1	3.7
Total Protein	High or Low	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Potassium	High or Low	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Sodium	High or Low	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Chloride	High or Low	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
BUN	High	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

*N=262 in some instances, depending on the laboratory parameter in question
**N=226 in some instances, depending on the laboratory parameter in question
+N=49 in some instances, depending on the laboratory parameter in question
Source: Data Source Tables 15.3.1, 15.3.2, Section 12; Appendix D, Listings 15.31.1, 15.31.2, 15.32.1, 15.32.2.

7 Discussion

Current thinking regarding obsessive-compulsive disorder (OCD) is that it is an illness that has its onset in childhood and which very often continues into adulthood. It is widely believed to be the same condition in both adults and children, both phenomenologically and regarding response to treatment. Paroxetine is a SSRI with proven efficacy in treating adult OCD. The results of this large, two-phase, multicenter, relapse-prevention design study clearly provide supportive evidence that paroxetine is also beneficial in the treatment of children and adolescents with OCD. The administration of open-label paroxetine for 16 weeks in Phase I of the study resulted in substantial and clinically relevant reductions of OCD symptoms in approximately three-fourths of those enrolled, as measured by the CGI Global Improvement Item responder rate and reductions in CY-BOCS Total and subscale scores and CGI Severity of Illness Scores. Only 19 of 335 patients enrolled were withdrawn during Phase I due to lack of efficacy (5.7%). In the absence of a placebo control in the first phase of the study, it is of course impossible to determine the extent to which the patients' improvement could be attributed to paroxetine alone. However, the patients in this study received no psychosocial interventions other than the usual supportive therapy.

Although there was no evidence of a statistically significant difference between paroxetine and placebo with respect to the protocol-defined primary measure of efficacy, that being the proportion of patients meeting relapse criteria during the double-blind phase, there was evidence of statistically significant differences between paroxetine and placebo with respect to the change from randomization baseline in CY-BOCS Total Score and in the proportion of patients with ≥ 25% reduction in CY-BOCS Total Score, both in the Week 16 LOCF dataset and at the 70% endpoint. Based on these data, the proportion of CY-BOCS responders in the double-blind phase was significantly higher in the paroxetine group. Furthermore, although not statistically significant, the relapse data numerically favor paroxetine over placebo, as do the data from all of the other secondary efficacy endpoints which were not statistically analyzed (i.e., CGI Global Improvement Item Responders, change from randomization baseline in the CY-BOCS subscale scores, CGI Severity of Illness Item rating, HAM-A and HAM-D scores, Yale Global Tic Score and GAF Scale).

However, it is important to note that due to the high withdrawal rate in this study, the 70% endpoint occurred relatively early (Week 4), which may have limited clinical relevance. It is also important to note that the Observed Case (OC) datasets generally did not distinguish paroxetine from placebo. The inconsistency

between the OC and endpoint (LOCF) results may have been due to some patients withdrawing early who tended to have a large increase in CY-BOCS Total Score (indicating a worsening), particularly in the placebo group. These values, when carried forward, may tend to inflate the 70% endpoint (Week 4) and Week 16 endpoint point estimates, since they only contribute to the endpoint analyses, leaving the OC analyses with fewer patients and therefore reduced power to detect differences between the treatment groups.

There are several factors which may have contributed to the non-statistically significant finding with respect to the protocol-defined primary endpoint for efficacy (proportion of relapsers). Although the overall proportion of paroxetine patients relapsing (35%) was consistent with that accounted for in the sample size calculations, the overall proportion of placebo patients relapsing (44%) was clearly lower than expected. The early nature of a number of the dropouts in the placebo group for reasons other than lack of efficacy may have contributed to the overall lower than expected relapse rate in this group. Due to the built-in blinded down-titration design which this study employed, a number of these placebo patients withdrawn early in phase II had yet to actually start taking placebo, therefore their final efficacy assessments carried forward were still reflective of the improvement achieved during Phase I of the study. These placebo patients essentially may have been withdrawn from the study before they even had a chance to meet the the relapse criteria.

A second factor which may have contributed to not achieving statistical significance on the primary endpoint was a potential age effect. Although a post-hoc analysis of the relapse data by age subgroup (< 12 years, ≥ 12 years) did not provide evidence of a statistically significant difference between paroxetine and placebo in either age group, the placebo relapse rate in the younger children was much closer to that estimated in the power calculation (55%), resulting in a relapse rate difference between paroxetine and placebo that approached statistical significance ($p=0.09$). The hypothesis that "children" with OCD may respond better to an SSRI than would "adolescents" has been raised previously, for both fluvoxamine and sertraline. However, clearly much more data are needed before a hypothesis that a drug class phenomenon may be occurring can be supported.

The safety and tolerability of paroxetine in the age group studied in this trial (8-17 yr olds) were clearly demonstrated. There were no deaths or unexpected safety findings, and in general the nature and incidence of AEs reported were similar to those reported for adult OCD patients who had received paroxetine in controlled trials. The withdrawal rate due to AEs was relatively low in the open-label phase (approx. 12%), and was comparable to that seen in adult OCD populations.

Suicide attempt/ideation was reported in several patients, but could not be reasonably attributed to paroxetine. Some behavioral activation/hyperactivity type AEs (e.g., agitation, hostility, hyperkinesia, manic reaction and concentration impaired) occurred on open-label therapy with greater frequency than have been reported in adults, and summaries by age group suggest these events were more likely to occur in the younger age group (< 12 years). Some of these particular events were considered serious in a number of patients. One SAE of manic reaction was reported, in a patient who had comorbid ADHD as well as another SAE of hostility. Younger children may be more sensitive to the behavioral activation/disinhibition side effects of SSRIs and therefore should be closely monitored because of the reported risk with antidepressants for hypomanic/manic switch.

Laboratory and vital sign abnormalities of significant clinical concern were few in number and not inconsistent with data generated in adults. Clinically significant weight gain was reported by the investigators in a number of patients, however, in an actively growing and maturing pediatric population such as this, the true clinical relevance of such findings is difficult to establish, without collecting pre- and post- body mass index data, for example. In summary, these safety findings suggest that paroxetine is safe and generally well-tolerated in pediatric patients with OCD when administered over the dosage range studied (10-60mg/day).

8 Conclusions

The results of this two-phase, multicenter, relapse-prevention design study provide supportive evidence that paroxetine is beneficial in the treatment of children and adolescents with OCD. Although there was no statistically significant difference between paroxetine and placebo with respect to the protocol-defined primary measurement of efficacy (the proportion of patients meeting relapse criteria during the double-blind phase), almost three-quarters (69%) of all patients enrolled met the response criteria during the OL phase and the proportion of responders in the double-blind phase (based on CY-BOCS Total Score) was statistically significantly greater in the paroxetine group than in the placebo group. The safety data generated in children and adolescents with OCD in this study did not reveal any adverse findings that were unique to this population nor any that would preclude its use in this population.

9 References

1 Piccinelli M, Pini S, Bellantuono C, Wilkinson G. Efficacy of drug treatment in obsessive-compulsive disorder: a meta-analytic review. Brit. J. Psychiat. 1995; 166:424-443.

2 SB Report MY-1022/BRL-029060/1/CPMS-116; Paroxetine versus placebo in the treatment of obsessive compulsive disorder. August 1994.

3 SB Report MY-1037/BRL-029060/1/CPMS-136; A double-blind study to assess the efficacy and tolerance of a flexible dose of paroxetine compared with a flexible dose of clomipramine and placebo in the treatment of obsessive compulsive disorder. August 1994.

4 SB Report MY-1046/BRL-029060/1/CPMS-126; Long-term treatment with paroxetine of outpatients with obsessive compulsive disorder: an extension of the fixed dose study. November 1994.

5 SB Report MY-1056/BRL-029060/1/CPMS-241; A double-blind study to compare the maintenance of efficacy and relapse rates in patients with obsessive compulsive disorder who responded to paroxetine, clomipramine or placebo in the short-term study 136. Spring 1995.

6 Riddle, MA. Obsessive-compulsive disorder in children and adolescents. *Br J Psychiatry* 1998; 173(Suppl 35): 91-96.

7 Jenike MA. Obsessive compulsive and related disorders - a hidden epidemic. *New Engl. J. Med.* 1989; 321:539-541.

8 Riddle, MA, Scahill, L, King, R., et al. Obsessive-compulsive disorder in children and adolescents. *J Am Acad Child Adolesc Psychiatry* 1990; 29: 766-772.

9 Pauls, DL, Alsobrook, JP, Goodman, W, et al. A family study of obsessive-compulsive disorder. *Am J Psychiatry* 1995; 152: 76-84.

10 Last, CG, Strauss, CC. Obsessive-compulsive disorder in childhood. *J Anxiety Disorders* 1989; 3: 295-302.

11 Hanna, GL. Demographic and clinical features of obsessive-compulsive disorder in children and adolescents. *J Am Acad Child Adolesc Psychiatry* 1995; 34(1): 19-27.

12 Ackerman, DL, Greenland, S, Bystritsky, A, et al. Predictors of treatment response in obsessive-compulsive disorder: multivariate analyses from a multicenter trial of clomipramine. *J Clin Psychopharmacol* 1994; 14: 247-254.

13 Piacentini J, Jaffer M, Gitow A, et al. Psychopharmacologic treatment of child and adolescent obsessive-compulsive disorder. *Ped. Psychopharmacol* 1992; 15: 87-107.

10 Data Source Tables: Study Population

Table 13.1.1

Summary of Patients by Population
All Patients
Phase I: Open Label Treatment

	N
Total Patients Screened	423
Commencing Open Label Treatment	339
Intention to Treat Population	335
Completing Phase I	216
Eligible for Continuation into Phase II	201

Intention to Treat Population is defined as all patients who receive at least one dose of Open Label Medication and for whom at least one Post Baseline evaluation is available

Patients are eligible for continuation to Phase II where there is a >=25% improvement in baseline CY-BOCS Total Score and a CGI Global Improvement Item Score of 1 or 2

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT13_1.SAS (18FEB99 18:12)

Table 13.1.2

Summary of Patients by Population
All Patients
Phase II: Randomised Treatment

	Treatment Groups	
	Paroxetine	Placebo
Total Entering Phase II	96	98
Intention to Treat Population	95	98
Per Protocol Population	81	83
Completing Study	42	33

Table 13.2

Number (%) of Patients Excluded from Per Protocol Analysis with a Major Violation
Intention to Treat Population
Phase II: Randomised Treatment

	Treatment Group					
	Paroxetine		Placebo		Total	
	N	%	N	%	N	%
Out of age range			1	1.0	1	0.5
Missed more than 5 consecutive days of medication	10	10.5	6	6.1	16	8.3
Prohibited Concomitant Medication	2	2.1	5	5.1	7	3.6
Prohibited Prior Medication	2	2.1	2	2.0	4	2.1
Entered Ph II, Did not meet response criteria at end of Ph I	1	1.1	1	1.0	2	1.0
Total Number of Patients with at least one Major Protocol Violation	14	14.7	15	15.3	29	15.0
Total Number of Patients with no Major Protocol Violations	81	85.3	83	84.7	164	85.0
Total Number of Patients	95	100.0	98	100.0	193	100.0

Table 13.2.1

Number (%) of Patients by Centre
Intention to Treat Population
Phase I: Open Label Treatment

		N	%
Centre	Investigator		
001	xxxxxxxxxxxxxxxxx	10	2.99
002	xxxxxxxxxxxxxxxxx	18	5.37
003	xxxxxxxxxxxxxxxxx	1	0.30
004	xxxxxxxxxxxxxxxxx	5	1.49
005	xxxxxxxxxxxxxxxxx	8	2.39
006	xxxxxxxxxxxxxxxxx	28	8.36
007	xxxxxxxxxxxxxxxxx	10	2.99
008	xxxxxxxxxxxxxxxxx	14	4.18
009	xxxxxxxxxxxxxxxxx	2	0.60
010	xxxxxxxxxxxxxxxxx	4	1.19
011	xxxxxxxxxxxxxxxxx	29	8.66
012	xxxxxxxxxxxxxxxxx	5	1.49
013	xxxxxxxxxxxxxxxxx	5	1.49
015	xxxxxxxxxxxxxxxxx	15	4.48
016	xxxxxxxxxxxxxxxxx	6	1.79
017	xxxxxxxxxxxxxxxxx	32	9.55
018	xxxxxxxxxxxxxxxxx	12	3.58

(CONTINUED)

Table 13.2.1

Number (%) of Patients by Centre
Intention to Treat Population
Phase I: Open Label Treatment

		N	%
Centre	Investigator		
019	xxxxxxxx, xxxxxx x.	12	3.58
020	xxxxxx, xxxx	11	3.28
021	xxxxxxxxx, xxxxx x.	19	5.67
022	xxxxxxxx, xxxxx	19	5.67
023	xxxxxxx, xxxxx x.	19	5.67
024	xxxxxxxxxx, xxxxx	11	3.28
025	xxxxxx, xxxxx x.	14	4.18
026	xxxxxxxx, xxxx x.	8	2.39
027	xxxxxx, xxxxxx x.	18	5.37
TOTAL		335	100.00

Table 13.2.2

Number (%) of Patients by Centre
Intention to Treat Population
Phase II: Randomised Treatment

		Treatment Groups			
		Paroxetine		Placebo	
Centre	Investigator	N	%	N	%
001	xxxxxxxxx,xxxx xx.	2	2.11	2	2.04
002	xxxx, xxx x.	6	6.32	5	5.10
003	xxxxxxx, xxxxxxx	0		0	
004	xxxxx, xxxxxxx xx	1	1.05	0	
005	xxxxxxxx, xxxxx x.	4	4.21	3	3.06
006	xxxxxxxxxxxxx	7	7.37	7	7.14
007	xxxxxxxxxxxxxxxx.	3	3.16	3	3.06
008	xxxxxxxxxxxxx	5	5.26	5	5.10
009	xxxxxxxxxxxxxxx.	0		1	1.02
010	xxxxxxxxxxxxxxx	0		1	1.02
011	xxxxxxxxxxxxxxx.	7	7.37	8	8.16
012	xxxxxxxxxxxx	1	1.05	1	1.02
013	xxxxxxxxxxxx	2	2.11	2	2.04
015	xxxxxxxxxxxxxxxx	4	4.21	4	4.08
016	xxxxxxxxxxxxxxxx.	2	2.11	2	2.04

(CONTINUED)

Table 13.2.2

Number (%) of Patients by Centre
Intention to Treat Population
Phase II: Randomised Treatment

		Treatment Groups			
		Paroxetine		Placebo	
Centre	Investigator	N	%	N	%
017	xxxxxxxxxxxxxx	8	8.42	10	10.20
018	xxxxxxxxxxxxxxx	6	6.32	4	4.08
019	xxxxxxxxxxxxxxxxx.	3	3.16	5	5.10
020	xxxxxxxxxxxxxx	4	4.21	6	6.12
021	xxxxxxxxxxxxxxxxx.	5	5.26	4	4.08
022	xxxxxxxxxxxxxx	5	5.26	5	5.10
023	xxxxxxxxxxxxxxx.	7	7.37	7	7.14
024	xxxxxxxxxxxxxxxx	4	4.21	2	2.04
025	xxxxxxxxxxxxxx.	4	4.21	5	5.10
026	xxxxxxxxxxxxxxx.	2	2.11	2	2.04
027	xxxxxxxxxxxxxxx.	3	3.16	4	4.08
TOTAL		95	100.00	98	100.00

Table 13.4.1b

Summary of Demographic Data
Intention to Treat Population
Phase I: Open Label Treatment

Age All (years)	Mean	11.8
	Median	12
	Std Dev	2.72
	Minimum	6
	Maximum	18
	N	335
	Missing	0

Table 13.4.1b

Summary of Demographic Data
Intention to Treat Population
Phase I: Open Label Treatment

Age Band < 12 (years)	Mean	9.5
	Median	10
	Std Dev	1.29
	Minimum	6
	Maximum	11
	N	167
	Missing	0
Age Band >= 12 (years)	Mean	14.0
	Median	14
	Std Dev	1.71
	Minimum	12
	Maximum	18
	N	168
	Missing	0

Table 13.4.1b

Summary of Demographic Data
Intention to Treat Population
Phase I: Open Label Treatment

		N	%
SEX	Male	198	59.1
	Female	137	40.9
	Total	335	100.0
	Missing	0	
RACE	White	308	91.9
	Black	7	2.1
	Oriental	4	1.2
	Other	16	4.8
	Total	335	100.0
	Missing	0	

Table 13.4.2b

Summary of Demographic Data
Intention to Treat Population
Phase II: Randomised Treatment

		Treatment Group	
		Paroxetine	Placebo
Age (years)	Mean	11.8	11.6
	Median	11	12
	Std Dev	2.56	2.88
	Minimum	7	6
	Maximum	17	18
	N	95	98
	Missing	0	0

Table 13.4.2b

Summary of Demographic Data
Intention to Treat Population
Phase II: Randomised Treatment

		Treatment Group	
		Paroxetine	Placebo
Age Band < 12 (years)	Mean	9.8	9.1
	Median	10	9
	Std Dev	1.20	1.33
	Minimum	7	6
	Maximum	11	11
	N	49	47
	Missing	0	0
Age Band >= 12 (years)	Mean	14.0	13.9
	Median	14	13
	Std Dev	1.70	1.82
	Minimum	12	12
	Maximum	17	18
	N	46	51
	Missing	0	0

Table 13.4.2b

Summary of Demographic Data
Intention to Treat Population
Phase II: Randomised Treatment

		Treatment Group			
		Paroxetine		Placebo	
		N	%	N	%
SEX	Male	47	49.5	58	59.2
	Female	48	50.5	40	40.8
	Total	95	100.0	98	100.0
	Missing	0		0	
RACE	White	87	91.6	89	90.8
	Black	1	1.1	2	2.0
	Oriental	1	1.1	3	3.1
	Other	6	6.3	4	4.1
	Total	95	100.0	98	100.0
	Missing	0		0	

Table 13.4.2c

Summary of Demographic Data
Per-Protocol Population
Phase II: Randomised Treatment

		Treatment Group	
		Paroxetine	Placebo
Age (years)	Mean	11.8	11.4
	Median	12	12
	Std Dev	2.50	2.67
	Minimum	7	7
	Maximum	17	17
	N	81	83
	Missing	0	0

Table 13.4.2c

Summary of Demographic Data
Per-Protocol Population
Phase II: Randomised Treatment

		Treatment Group	
		Paroxetine	Placebo
Age Band < 12 (years)	Mean	9.8	9.1
	Median	10	9
	Std Dev	1.22	1.28
	Minimum	7	7
	Maximum	11	11
	N	40	41
	Missing	0	0
Age Band >= 12 (years)	Mean	13.8	13.6
	Median	14	13
	Std Dev	1.67	1.61
	Minimum	12	12
	Maximum	17	17
	N	41	42
	Missing	0	0

Table 13.4.2c

Summary of Demographic Data
Per-Protocol Population
Phase II: Randomised Treatment

		Treatment Group			
		Paroxetine		Placebo	
		N	%	N	%
SEX	Male	40	49.4	49	59.0
	Female	41	50.6	34	41.0
	Total	81	100.0	83	100.0
	Missing	0		0	
RACE	White	75	92.6	74	89.2
	Black	1	1.2	2	2.4
	Oriental	0	0.0	3	3.6
	Other	5	6.2	4	4.8
	Total	81	100.0	83	100.0
	Missing	0		0	

Table 13.6.1

ECG Assessments - Changes from Screening Visit
Intention to Treat population
Phase I: Open Label Treatment

		N	%
Week 8	Significant Changes	5	1.8
	No Significant Changes	270	98.2
	Total	275	100.0
	Missing	20	
Week 16	Significant Changes	4	1.7
	No Significant Changes	227	98.3
	Total	231	100.0
	Missing	18	

Note: This table does not tie in with Table 13.32.1 as different week slottings apply

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT13_6.SAS (01MAR99 16:24)

Table 13.6.2

ECG Assessments - Changes from Screening Visit
Intention to Treat population
Phase II: Randomised Treatment

		Paroxetine		Placebo	
		N	%	N	%
Week 8	Significant Changes				
	No Significant Changes	53	100.0	39	100.0
	Total	53	100.0	39	100.0
	Missing	5		6	
Week 16	Significant Changes				
	No Significant Changes	40	100.0	25	100.0
	Total	40	100.0	25	100.0
	Missing	4		3	

Note: This table does not tie in with Table 13.32.2 as different week slottings apply

Table 13.7.1

Psychiatric History
Intention to Treat Population
Phase I: Open Label Treatment

	Yes		No		Suspected		Not recorded	
	N	%	N	%	N	%	N	%
Substance Abuse			335	100.0				
Substance Dependence			335	100.0				
Generalized Anxiety Disorder	49	14.6	257	76.7	29	8.7		
Personality Disorder			334	99.7			1	0.3
Dysthymia	24	7.2	300	89.6	11	3.3		
Panic Disorder	6	1.8	327	97.6	2	0.6		
Major Depressive Disorder	34	10.1	290	86.6	11	3.3		
Other	161	48.1	143	42.7	57	17.0		

Note: A patient can contribute to both the Yes and Suspected columns of the 'Other' category as more than one 'Other' disorder can occur

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]PSY13_7.SAS (18FEB99 18:19)

Table 13.7.2

Psychiatric History
Intention to Treat Population
Phase II: Randomised Treatment

	Treatment Group															
	Paroxetine								Placebo							
	Yes		No		Suspected		Not recorded		Yes		No		Suspected		Not recorded	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Substance Abuse			95	100.0							98	100.0				
Substance Dependence			95	100.0							98	100.0				
Generalized Anxiety Disorder	17	17.9	71	74.7	7	7.4			13	13.3	72	73.5	13	13.3		
Personality Disorder			94	98.9			1	1.1			98	100.0				
Dysthymia	6	6.3	87	91.6	2	2.1			5	5.1	89	90.8	4	4.1		
Panic Disorder	3	3.2	90	94.7	2	2.1			3	3.1	95	96.9				
Major Depressive Disorder	9	9.5	83	87.4	3	3.2			9	9.2	86	87.8	3	3.1		
Other	46	48.4	40	42.1	17	17.9			33	33.7	55	56.1	16	16.3		

Note: A patient can contribute to both the Yes and Suspected columns of the 'Other' category as more than one 'Other' disorder can occur

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]PSY13_7.SAS (18FEB99 18:19)

TABLE 13.9.1

Summary of History of Pharmacotherapy for Episodes of OCD
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	335	100.0%
PATIENTS WITH MEDICATIONS	75	22.4%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%
CARDIOVASCULAR:	1	0.3
HYPERICUM EXTRACT	1	0.3
CENTRAL NERVOUS SYSTEM:	75	22.4
ALPRAZOLAM	1	0.3
AMPHETAMINE ASPARTATE	1	0.3
AMPHETAMINE SULFATE	1	0.3
BUSPIRONE HYDROCHLORIDE	1	0.3
CLOMIPRAMINE	3	0.9
CLOMIPRAMINE HYDROCHLORIDE	20	6.0
DEXTROAMPHETAMINE SACCHARATE	1	0.3
DEXTROAMPHETAMINE SULFATE	1	0.3
FLUOXETINE	30	9.0
FLUVOXAMINE	2	0.6
FLUVOXAMINE MALEATE	18	5.4
HYPERICUM EXTRACT	1	0.3
IMIPRAMINE	1	0.3
LITHIUM CARBONATE	1	0.3
PAROXETINE	13	3.9
RISPERIDONE	1	0.3
SERTRALINE	2	0.6
SERTRALINE HYDROCHLORIDE	13	3.9
THIORIDAZINE HYDROCHLORIDE	1	0.3
VENLAFAXINE HYDROCHLORIDE{INVESTIGATIONAL DRUG}	2	0.6
VARIOUS:	1	0.3
HYPERICUM EXTRACT	1	0.3

TABLE 13.9.2

Summary of History of Pharmacotherapy for Episodes of OCD
Intention To Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS :	21	22.1%	21	21.4%	42	21.8%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
CARDIOVASCULAR:	0	0.0	1	1.0	1	0.5
HYPERICUM EXTRACT	0	0.0	1	1.0	1	0.5
CENTRAL NERVOUS SYSTEM:	21	22.1	21	21.4	42	21.8
ALPRAZOLAM	0	0.0	1	1.0	1	0.5
AMPHETAMINE ASPARTATE	1	1.1	0	0.0	1	0.5
AMPHETAMINE SULFATE	1	1.1	0	0.0	1	0.5
BUSPIRONE HYDROCHLORIDE	0	0.0	1	1.0	1	0.5
CLOMIPRAMINE	2	2.1	0	0.0	2	1.0
CLOMIPRAMINE HYDROCHLORIDE	5	5.3	3	3.1	8	4.1
DEXTROAMPHETAMINE SACCHARATE	1	1.1	0	0.0	1	0.5
DEXTROAMPHETAMINE SULFATE	1	1.1	0	0.0	1	0.5
FLUOXETINE	7	7.4	7	7.1	14	7.3
FLUVOXAMINE	2	2.1	0	0.0	2	1.0
FLUVOXAMINE MALEATE	3	3.2	8	8.2	11	5.7
HYPERICUM EXTRACT	0	0.0	1	1.0	1	0.5
IMIPRAMINE	0	0.0	1	1.0	1	0.5
LITHIUM CARBONATE	1	1.1	0	0.0	1	0.5
PAROXETINE	2	2.1	7	7.1	9	4.7
RISPERIDONE	1	1.1	0	0.0	1	0.5
SERTRALINE	2	2.1	0	0.0	2	1.0
SERTRALINE HYDROCHLORIDE	3	3.2	2	2.0	5	2.6
THIORIDAZINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
VARIOUS:	0	0.0	1	1.0	1	0.5
HYPERICUM EXTRACT	0	0.0	1	1.0	1	0.5

Table 13.10.1

KSADS Summary at Screening Visit
Intention to Treat Population
Phase I: Open Label Treatment

	Past		Current		Both		N/A	
	N	%	N	%	N	%	N	%
Major Depressive Episode	18	5.4	9	2.7	11	3.3	297	88.7
Dysthymic Disorder	3	0.9	9	2.7	19	5.7	304	90.7
Hypomanic Episode	1	0.3					334	99.7
Manic Episode							335	100.0
Anorexia Nervosa	3	0.9					332	99.1
Bulimia Nervosa							335	100.0
Specific Phobia	14	4.2	20	6.0	34	10.1	267	79.7
Separation Anxiety Disorder	28	8.4	6	1.8	28	8.4	273	81.5
Panic Disorder(without agoraphobia)	5	1.5	1	0.3	3	0.9	326	97.3
Panic Disorder(with agoraphobia)	1	0.3			1	0.3	333	99.4
Agoraphobia (no panic)					1	0.3	334	99.7
Social Phobia			4	1.2	15	4.5	316	94.3
Generalized Anxiety Disorder	4	1.2	6	1.8	61	18.2	264	78.8
Post-Traumatic Stress Disorder	5	1.5	1	0.3			329	98.2
Attention-Deficit/Hyperact. Disorder	12	3.6	13	3.9	50	14.9	260	77.6
Conduct Disorder					2	0.6	333	99.4
Oppositional Defiant Disorder	5	1.5	11	3.3	17	5.1	302	90.1

(CONTINUED)

Table 13.10.1

KSADS Summary at Screening Visit
Intention to Treat Population
Phase I: Open Label Treatment

	Past		Current		Both		N/A	
	N	%	N	%	N	%	N	%
Alcohol Dependence							335	100.0
Alcohol Abuse							335	100.0
Substance Dependence							335	100.0
Substance Abuse							335	100.0
Tic Disorders	9	2.7	16	4.8	35	10.4	275	82.1
Schizophrenia							335	100.0
Schizoaffective Disorder							335	100.0
Brief Psychotic Disorder							335	100.0
Delusional Disorder							335	100.0

Table 13.10.2

KSADS Summary at Screening Visit
Intention to Treat Population
Phase II: Randomised Treatment

	Paroxetine								Placebo							
	Past		Current		Both		N/A		Past		Current		Both		N/A	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Major Depressive Episode	5	5.3	2	2.1	4	4.2	84	88.4	7	7.1	1	1.0	1	1.0	89	90.8
Dysthymic Disorder			3	3.2	5	5.3	87	91.6	2	2.0	1	1.0	3	3.1	92	93.9
Hypomanic Episode							95	100							98	100
Manic Episode							95	100							98	100
Anorexia Nervosa							95	100	1	1.0					97	99.0
Bulimia Nervosa							95	100							98	100
Specific Phobia	5	5.3	6	6.3	11	11.6	73	76.8	2	2.0	4	4.1	3	3.1	89	90.8
Separation Anxiety Disorder	6	6.3	1	1.1	17	17.9	71	74.7	8	8.2	1	1.0	3	3.1	86	87.8
Panic Disorder(without agoraphobia)	1	1.1	1	1.1	2	2.1	91	95.8	2	2.0			1	1.0	95	96.9
Panic Disorder(with agoraphobia)	1	1.1			1	1.1	93	97.9							98	100
Agoraphobia (no panic)					1	1.1	94	98.9							98	100
Social Phobia			1	1.1	5	5.3	89	93.7			1	1.0	4	4.1	93	94.9
Generalized Anxiety Disorder			1	1.1	22	23.2	72	75.8	2	2.0	3	3.1	18	18.4	75	76.5
Post-Traumatic Stress Disorder	1	1.1					94	98.9	1	1.0					97	99.0
Attention-Deficit/Hyperact. Disorder	2	2.1	2	2.1	13	13.7	78	82.1	1	1.0	3	3.1	8	8.2	86	87.8
Conduct Disorder							95	100							98	100

(CONTINUED)

Table 13.10.2

KSADS Summary at Screening Visit
Intention to Treat Population
Phase II: Randomised Treatment

	Paroxetine								Placebo							
	Past		Current		Both		N/A		Past		Current		Both		N/A	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Oppositional Defiant Disorder	1	1.1	2	2.1	2	2.1	90	94.7	3	3.1	2	2.0	1	1.0	92	93.9
Alcohol Dependence							95	100							98	100
Alcohol Abuse							95	100							98	100
Substance Dependence							95	100							98	100
Substance Abuse							95	100							98	100
Tic Disorders	4	4.2	3	3.2	8	8.4	80	84.2	2	2.0	3	3.1	8	8.2	85	86.7
Schizophrenia							95	100							98	100
Schizoaffective Disorder							95	100							98	100
Brief Psychotic Disorder							95	100							98	100
Delusional Disorder							95	100							98	100

Paroxetine - Protocol: 453

TABLE 13.11.1

Summary of Prior Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	240	71.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%
ALIMENTARY TRACT/METAB:	59	17.6
ALUMINIUM HYDROXIDE	2	0.6
ANISE OIL	1	0.3
ANTACID NOS	1	0.3
ASCORBIC ACID	4	1.2
ATROPINE SULFATE	1	0.3
BENZOIC ACID	1	0.3
BISACODYL	1	0.3
BISMUTH SUBSALICYLATE	8	2.4
CALCIUM	1	0.3
CALCIUM CARBONATE	14	4.2
CALCIUM PANTOTHENATE	1	0.3
CALCIUM POLYCARBOPHIL	1	0.3
CAMPHOR	1	0.3
CIMETIDINE	3	0.9
DIMETICONE, ACTIVATED	2	0.6
ETHANOL	2	0.6
FAMOTIDINE	2	0.6
GLYCEROL	1	0.3
HYOSCINE HYDROBROMIDE	1	0.3
HYOSCYAMINE SULFATE	1	0.3
INOSITOL	1	0.3
INVERT SUGAR	1	0.3
IRON	1	0.3
KAOLIN	4	1.2
LACTULOSE	1	0.3
LOPERAMIDE HYDROCHLORIDE	4	1.2
MAGNESIUM HYDROXIDE	5	1.5
MINERALS NOS	1	0.3
NATURAL FIBER LAXATIVE	1	0.3
NICOTINAMIDE	1	0.3
NIZATIDINE	1	0.3

TABLE 13.11.1

Summary of Prior Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	240	71.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%
OPIUM	1	0.3
OPIUM TINCTURE, BENZOATED	1	0.3
PECTIN	4	1.2
PHOSPHORIC ACID	1	0.3
PSYLLIUM HYDROPHILIC MUCILLOID	1	0.3
PYRIDOXINE HYDROCHLORIDE	1	0.3
RANITIDINE HYDROCHLORIDE	3	0.9
RIBOFLAVIN	1	0.3
SODIUM CHLORIDE	1	0.3
THIAMINE HYDROCHLORIDE	1	0.3
TRIAMCINOLONE ACETONIDE	2	0.6
VITAMINS NOS	18	5.4
ZINC	1	0.3
ANTIINFECTIVES,SYSTEMIC:	47	14.0
AMOXICILLIN	16	4.8
AMOXICILLIN TRIHYDRATE	4	1.2
AMPICILLIN	1	0.3
AZITHROMYCIN	1	0.3
CEFACLOR	2	0.6
CEFADROXIL	1	0.3
CEFALEXIN MONOHYDRATE	1	0.3
CEFIXIME	2	0.6
CEFPROZIL MONOHYDRATE	2	0.6
CLARITHROMYCIN	3	0.9
CLAVULANIC ACID	2	0.6
CLINDAMYCIN HYDROCHLORIDE	1	0.3
ERYTHROMYCIN	4	1.2
ERYTHROMYCIN STEARATE	1	0.3
INFLUENZA VIRUS VACCINE POLYVALENT	1	0.3
MINOCYCLINE	4	1.2
MUPIROCIN	2	0.6

TABLE 13.11.1

Summary of Prior Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	240	71.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%
PENICILLIN NOS	1	0.3
PHENOXYMETHYLPENICILLIN POTASSIUM	1	0.3
SULFAMETHOXAZOLE	1	0.3
TETRACYCLINE	1	0.3
TRIMETHOPRIM	1	0.3
ANTINEOPLASTIC & IMMUNOSUP:	4	1.2
TRETINOIN	4	1.2
BLOOD/BLOOD FORM ORGANS:	1	0.3
SODIUM CHLORIDE	1	0.3
CARDIOVASCULAR:	16	4.8
BENZOCAINE	1	0.3
CLONIDINE	9	2.7
HYPERICUM EXTRACT	3	0.9
PHENYLMERCURIC NITRATE	1	0.3
PROPRANOLOL HYDROCHLORIDE	1	0.3
SHARK-LIVER OIL	1	0.3
THEOPHYLLINE	1	0.3
YEAST DRIED	1	0.3
CENTRAL NERVOUS SYSTEM:	156	46.6
ACETYLSALICYLIC ACID	6	1.8
ALPRAZOLAM	3	0.9
AMFEBUTAMONE HYDROCHLORIDE	1	0.3
AMITRIPTYLINE	1	0.3
AMITRIPTYLINE HYDROCHLORIDE	2	0.6
AMPHETAMINE ASPARTATE	6	1.8
AMPHETAMINE SULFATE	6	1.8
BUSPIRONE HYDROCHLORIDE	3	0.9
CAFFEINE	2	0.6

TABLE 13.11.1

Summary of Prior Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	335	100.0%
PATIENTS WITH MEDICATIONS	240	71.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%
CHLORPHENAMINE MALEATE	2	0.6
CITRIC ACID	2	0.6
CLOMIPRAMINE	3	0.9
CLOMIPRAMINE HYDROCHLORIDE	22	6.6
CLONIDINE	9	2.7
CODEINE PHOSPHATE	1	0.3
DESIPRAMINE	1	0.3
DEXAMPHETAMINE SULFATE	4	1.2
DEXTROAMPHETAMINE SACCHARATE	6	1.8
DEXTROAMPHETAMINE SULFATE	6	1.8
DEXTROMETHORPHAN HYDROBROMIDE	2	0.6
DIAZEPAM	1	0.3
DICHLORALPHENAZONE	1	0.3
DIPHENHYDRAMINE HYDROCHLORIDE	2	0.6
FLUOXETINE	33	9.9
FLUVOXAMINE	2	0.6
FLUVOXAMINE MALEATE	18	5.4
HALOPERIDOL	1	0.3
HYDROXYZINE HYDROCHLORIDE	1	0.3
HYPERICUM EXTRACT	3	0.9
IMIPRAMINE	5	1.5
ISOMETHEPTENE	1	0.3
LIDOCAINE	6	1.8
LITHIUM CARBONATE	1	0.3
LORAZEPAM	6	1.8
MEPYRAMINE MALEATE	1	0.3
METHYLPHENIDATE	2	0.6
METHYLPHENIDATE HYDROCHLORIDE	24	7.2
NORTRIPTYLINE	3	0.9
NORTRIPTYLINE HYDROCHLORIDE	1	0.3
PAMABROM	1	0.3
PARACETAMOL	75	22.4

TABLE 13.11.1

Summary of Prior Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	240	71.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%
PAROXETINE	13	3.9
PEMOLINE MAGNESIUM	3	0.9
PRILOCAINE	6	1.8
PSEUDOEPHEDRINE HYDROCHLORIDE	6	1.8
RISPERIDONE	5	1.5
SERTRALINE	2	0.6
SERTRALINE HYDROCHLORIDE	15	4.5
SODIUM BICARBONATE	2	0.6
SUMATRIPTAN	1	0.3
THIORIDAZINE HYDROCHLORIDE	2	0.6
TRAZODONE	1	0.3
VALERIAN ROOT	1	0.3
VENLAFAXINE HYDROCHLORIDE{INVESTIGATIONAL DRUG}	4	1.2
DERMATOLOGICALS:	47	14.0
BACITRACIN	1	0.3
BENZOCAINE	1	0.3
BENZOYL PEROXIDE	2	0.6
BETAMETHASONE DIPROPIONATE	1	0.3
BUDESONIDE	4	1.2
CORTISONE	1	0.3
DIPHENHYDRAMINE HYDROCHLORIDE	15	4.5
ECONAZOLE NITRATE	1	0.3
ERYTHROMYCIN	6	1.8
FLUTICASONE PROPIONATE	1	0.3
HYDROCORTISONE	5	1.5
ISOTRETINOIN	1	0.3
LIDOCAINE	6	1.8
MUPIROCIN	2	0.6
NEOMYCIN SULFATE	1	0.3
NYSTATIN	1	0.3

TABLE 13.11.1

Summary of Prior Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	240	71.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	**N**	**%**
POLYMYXIN B SULFATE	1	0.3
PRILOCAINE	6	1.8
PROMETHAZINE HYDROCHLORIDE	1	0.3
TETRACYCLINE	1	0.3
TRETINOIN	4	1.2
TRIAMCINOLONE ACETONIDE	3	0.9
GU SYSTEM/SEX HORMONES:	3	0.9
ECONAZOLE NITRATE	1	0.3
ETHINYLESTRADIOL	1	0.3
MESTRANOL	1	0.3
NORETHISTERONE	1	0.3
NORETHISTERONE ACETATE	1	0.3
MUSCULO-SKELETAL:	46	13.7
IBUPROFEN	44	13.1
INDOMETACIN	1	0.3
NABUMETONE	1	0.3
NAPROXEN SODIUM	2	0.6
PSEUDOEPHEDRINE HYDROCHLORIDE	1	0.3
RESPIRATORY:	101	30.1
ASTEMIZOLE	1	0.3
BECLOMETASONE	1	0.3
BECLOMETASONE DIPROPIONATE	15	4.5
BENZOCAINE	1	0.3
BENZONATATE	1	0.3
BROMPHENIRAMINE MALEATE	8	2.4
BUDESONIDE	4	1.2
CAMPHOR	1	0.3
CETIRIZINE HYDROCHLORIDE	2	0.6
CHLORPHENAMINE MALEATE	17	5.1

TABLE 13.11.1

Summary of Prior Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	335	100.0%
PATIENTS WITH MEDICATIONS	240	71.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	**N**	**%**
CHLORPHENAMINE TANNATE	1	0.3
CLEMASTINE FUMARATE	2	0.6
CODEINE PHOSPHATE	1	0.3
COUGH SYRUP/MED	1	0.3
CROMOGLICATE SODIUM	8	2.4
CYPROHEPTADINE HYDROCHLORIDE	1	0.3
DECONGESTANT NOS	1	0.3
DEXBROMPHENIRAMINE MALEATE	1	0.3
DEXTROMETHORPHAN HYDROBROMIDE	9	2.7
DIMENHYDRINATE	1	0.3
DIPHENHYDRAMINE HYDROCHLORIDE	16	4.8
ETHANOL	3	0.9
EUCALYPTUS OIL	1	0.3
FLUTICASONE PROPIONATE	1	0.3
GUAIFENESIN	8	2.4
HYOSCINE METHONITRATE	2	0.6
IBUPROFEN	1	0.3
LODOXAMIDE TROMETAMOL	1	0.3
LORATADINE	21	6.3
MENTHOL	1	0.3
MEPYRAMINE MALEATE	3	0.9
MEPYRAMINE TANNATE	1	0.3
PARACETAMOL	11	3.3
PHENINDAMINE TARTRATE	1	0.3
PHENIRAMINE MALEATE	3	0.9
PHENYLEPHRINE HYDROCHLORIDE	6	1.8
PHENYLEPHRINE TANNATE	1	0.3
PHENYLPROPANOLAMINE HYDROCHLORIDE	15	4.5
PIRBUTEROL ACETATE	2	0.6
PREDNISONE	2	0.6
PROMETHAZINE HYDROCHLORIDE	1	0.3
PSEUDOEPHEDRINE HYDROCHLORIDE	27	8.1

TABLE 13.11.1

Summary of Prior Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	335	100.0%
PATIENTS WITH MEDICATIONS	240	71.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	**N**	**%**
PSEUDOEPHEDRINE SULFATE	3	0.9
SALBUTAMOL	28	8.4
SALMETEROL HYDROXYNAPHTHOATE	1	0.3
SODIUM CHLORIDE	1	0.3
THEOPHYLLINE	1	0.3
TRIAMCINOLONE ACETONIDE	2	0.6
TURPENTINE OIL	1	0.3
SENSORY ORGANS:	29	8.7
BROMPHENIRAMINE MALEATE	3	0.9
CORTISONE	1	0.3
CROMOGLICATE SODIUM	8	2.4
EAR MEDICATION, NOS	1	0.3
ERYTHROMYCIN	4	1.2
HYDROCORTISONE	5	1.5
INDOMETACIN	1	0.3
LODOXAMIDE TROMETAMOL	1	0.3
NEOMYCIN SULFATE	1	0.3
PHENYLPROPANOLAMINE HYDROCHLORIDE	3	0.9
POLYMYXIN B SULFATE	1	0.3
SODIUM CHLORIDE	1	0.3
SULFACETAMIDE	1	0.3
TETRACYCLINE	1	0.3
TRIAMCINOLONE ACETONIDE	2	0.6
SYSTEMIC HORMONAL:	19	5.7
CORTISONE	1	0.3
DESMOPRESSIN	1	0.3
HYDROCORTISONE	5	1.5
LEVOTHYROXINE	1	0.3
LEVOTHYROXINE SODIUM	1	0.3
MELATONIN	3	0.9

TABLE 13.11.1

Summary of Prior Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	240	71.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	**N**	**%**
PREDNISONE	2	0.6
SOMATREM	2	0.6
SOMATROPIN	1	0.3
TRIAMCINOLONE ACETONIDE	2	0.6
UNCLASSIFIABLE:	1	0.3
UNKNOWN MEDICATION	1	0.3
VARIOUS:	9	2.7
ALFALFA	1	0.3
ALLERGENIC EXTRACT, NOS	4	1.2
HYPERICUM EXTRACT	3	0.9
NUTRITIONAL SUPPLEMENT NOS	1	0.3

TABLE 13.11.2

Summary of Prior Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS :	82	86.3%	89	90.8%	171	88.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
ALIMENTARY TRACT/METAB:	26	27.4	30	30.6	56	29.0
ALOES	1	1.1	0	0.0	1	0.5
ALUMINIUM HYDROXIDE	3	3.2	5	5.1	8	4.1
ANISE OIL	0	0.0	1	1.0	1	0.5
ANTACID NOS	1	1.1	0	0.0	1	0.5
ASCORBIC ACID	3	3.2	2	2.0	5	2.6
ATROPINE SULFATE	0	0.0	1	1.0	1	0.5
BENZOIC ACID	0	0.0	1	1.0	1	0.5
BISACODYL	1	1.1	0	0.0	1	0.5
BISMUTH SUBSALICYLATE	7	7.4	7	7.1	14	7.3
CALCIUM	0	0.0	1	1.0	1	0.5
CALCIUM CARBONATE	3	3.2	11	11.2	14	7.3
CALCIUM PANTOTHENATE	1	1.1	0	0.0	1	0.5
CALCIUM POLYCARBOPHIL	1	1.1	1	1.0	2	1.0
CAMPHOR	0	0.0	1	1.0	1	0.5
CASANTHRANOL	1	1.1	0	0.0	1	0.5
CIMETIDINE	2	2.1	0	0.0	2	1.0
CISAPRIDE	1	1.1	0	0.0	1	0.5
DICYCLOVERINE	1	1.1	0	0.0	1	0.5
DIMETICONE, ACTIVATED	3	3.2	5	5.1	8	4.1
DOCUSATE SODIUM	1	1.1	0	0.0	1	0.5
ETHANOL	0	0.0	2	2.0	2	1.0
GLYCEROL	0	0.0	1	1.0	1	0.5
HYOSCINE HYDROBROMIDE	0	0.0	1	1.0	1	0.5
HYOSCYAMINE SULFATE	0	0.0	1	1.0	1	0.5
INVERT SUGAR	1	1.1	0	0.0	1	0.5
IRON	0	0.0	1	1.0	1	0.5
KAOLIN	0	0.0	2	2.0	2	1.0
LACTULOSE	1	1.1	0	0.0	1	0.5
LOPERAMIDE HYDROCHLORIDE	2	2.1	0	0.0	2	1.0

NOTE: Prior medication refers to all those started prior to randomisation baseline

TABLE 13.11.2

Summary of Prior Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS :	82	86.3%	89	90.8%	171	88.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
MAGNESIUM HYDROXIDE	3	3.2	6	6.1	9	4.7
MINERALS NOS	0	0.0	1	1.0	1	0.5
NATURAL FIBER LAXATIVE	0	0.0	1	1.0	1	0.5
NEOMYCIN	1	1.1	0	0.0	1	0.5
NICOTINAMIDE	1	1.1	0	0.0	1	0.5
NIZATIDINE	1	1.1	0	0.0	1	0.5
OPIUM	0	0.0	1	1.0	1	0.5
PANCRELIPASE	1	1.1	0	0.0	1	0.5
PARAFFIN, LIQUID	1	1.1	0	0.0	1	0.5
PECTIN	0	0.0	2	2.0	2	1.0
PHOSPHORIC ACID	1	1.1	0	0.0	1	0.5
PYRIDOXINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
RANITIDINE HYDROCHLORIDE	2	2.1	0	0.0	2	1.0
RIBOFLAVIN	1	1.1	0	0.0	1	0.5
SENNA FRUIT	1	1.1	0	0.0	1	0.5
THIAMINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
TRIAMCINOLONE ACETONIDE	1	1.1	2	2.0	3	1.6
VITAMINS NOS	5	5.3	11	11.2	16	8.3
ZINC	1	1.1	0	0.0	1	0.5
ANTIINFECTIVES,SYSTEMIC:	38	40.0	20	20.4	58	30.1
AMOXICILLIN	8	8.4	6	6.1	14	7.3
AMOXICILLIN TRIHYDRATE	6	6.3	2	2.0	8	4.1
AMPICILLIN	2	2.1	0	0.0	2	1.0
ANTIBIOTIC NOS	1	1.1	0	0.0	1	0.5
AZITHROMYCIN	1	1.1	1	1.0	2	1.0
CEFACLOR	3	3.2	0	0.0	3	1.6
CEFALEXIN	0	0.0	1	1.0	1	0.5
CEFALEXIN MONOHYDRATE	2	2.1	0	0.0	2	1.0
CEFIXIME	1	1.1	1	1.0	2	1.0

NOTE: Prior medication refers to all those started prior to randomisation baseline

TABLE 13.11.2

Summary of Prior Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS :	82	86.3%	89	90.8%	171	88.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
CEFPODOXIME PROXETIL	0	0.0	1	1.0	1	0.5
CEFPROZIL MONOHYDRATE	3	3.2	0	0.0	3	1.6
CEFUROXIME AXETIL	1	1.1	1	1.0	2	1.0
CLARITHROMYCIN	1	1.1	2	2.0	3	1.6
CLAVULANIC ACID	3	3.2	1	1.0	4	2.1
CLINDAMYCIN HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
ERYTHROMYCIN	3	3.2	3	3.1	6	3.1
GENTAMICIN	1	1.1	0	0.0	1	0.5
HEPATITIS B VACCINE	3	3.2	0	0.0	3	1.6
HEPATITIS VACCINE, NOS	1	1.1	2	2.0	3	1.6
INFLUENZA VIRUS VACCINE POLYVALENT	0	0.0	1	1.0	1	0.5
MINOCYCLINE	3	3.2	0	0.0	3	1.6
MUPIROCIN	1	1.1	0	0.0	1	0.5
NEOMYCIN	1	1.1	0	0.0	1	0.5
PENICILLIN NOS	2	2.1	1	1.0	3	1.6
PHENOXYMETHYLPENICILLIN POTASSIUM	2	2.1	0	0.0	2	1.0
SULFAMETHOXAZOLE	3	3.2	2	2.0	5	2.6
TETANUS TOXOID	1	1.1	0	0.0	1	0.5
TETRACYCLINE	0	0.0	1	1.0	1	0.5
TOBRAMYCIN	0	0.0	1	1.0	1	0.5
TRIMETHOPRIM	2	2.1	2	2.0	4	2.1
ANTINEOPLASTIC & IMMUNOSUP:	1	1.1	1	1.0	2	1.0
TRETINOIN	1	1.1	1	1.0	2	1.0
CARDIOVASCULAR:	1	1.1	8	8.2	9	4.7
CLONIDINE	1	1.1	2	2.0	3	1.6
HYPERICUM EXTRACT	0	0.0	2	2.0	2	1.0
LIDOCAINE	0	0.0	1	1.0	1	0.5
PREDNISOLONE SODIUM PHOSPHATE	0	0.0	1	1.0	1	0.5

NOTE: Prior medication refers to all those started prior to randomisation baseline

TABLE 13.11.2

Summary of Prior Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS	82	86.3%	89	90.8%	171	88.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
PROPRANOLOL HYDROCHLORIDE	0	0.0	1	1.0	1	0.5
THEOPHYLLINE	0	0.0	1	1.0	1	0.5
CENTRAL NERVOUS SYSTEM:	62	65.3	67	68.4	129	66.8
ACETYLSALICYLIC ACID	6	6.3	3	3.1	9	4.7
ALPRAZOLAM	1	1.1	2	2.0	3	1.6
AMITRIPTYLINE	0	0.0	2	2.0	2	1.0
AMPHETAMINE ASPARTATE	1	1.1	2	2.0	3	1.6
AMPHETAMINE SULFATE	1	1.1	2	2.0	3	1.6
ANESTHESIA, NOS	1	1.1	0	0.0	1	0.5
BUSPIRONE HYDROCHLORIDE	0	0.0	1	1.0	1	0.5
CAFFEINE	2	2.1	0	0.0	2	1.0
CHLORPHENAMINE MALEATE	2	2.1	1	1.0	3	1.6
CITRIC ACID	0	0.0	2	2.0	2	1.0
CLOMIPRAMINE	2	2.1	0	0.0	2	1.0
CLOMIPRAMINE HYDROCHLORIDE	5	5.3	4	4.1	9	4.7
CLONIDINE	1	1.1	2	2.0	3	1.6
CODEINE PHOSPHATE	1	1.1	3	3.1	4	2.1
DEXAMPHETAMINE SULFATE	0	0.0	1	1.0	1	0.5
DEXTROAMPHETAMINE SACCHARATE	1	1.1	2	2.0	3	1.6
DEXTROAMPHETAMINE SULFATE	1	1.1	2	2.0	3	1.6
DEXTROMETHORPHAN HYDROBROMIDE	2	2.1	1	1.0	3	1.6
DIAZEPAM	1	1.1	1	1.0	2	1.0
DICHLORALPHENAZONE	0	0.0	1	1.0	1	0.5
DIPHENHYDRAMINE HYDROCHLORIDE	0	0.0	1	1.0	1	0.5
FLUOXETINE	7	7.4	9	9.2	16	8.3
FLUVOXAMINE	2	2.1	0	0.0	2	1.0
FLUVOXAMINE MALEATE	3	3.2	8	8.2	11	5.7
HYDROCODONE BITARTRATE	2	2.1	0	0.0	2	1.0
HYDROXYZINE HYDROCHLORIDE	0	0.0	1	1.0	1	0.5

NOTE: Prior medication refers to all those started prior to randomisation baseline

TABLE 13.11.2

Summary of Prior Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS	82	86.3%	89	90.8%	171	88.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
HYPERICUM EXTRACT	0	0.0	2	2.0	2	1.0
IMIPRAMINE	0	0.0	1	1.0	1	0.5
ISOMETHEPTENE	0	0.0	1	1.0	1	0.5
LIDOCAINE	1	1.1	4	4.1	5	2.6
LITHIUM CARBONATE	1	1.1	0	0.0	1	0.5
LORAZEPAM	1	1.1	4	4.1	5	2.6
MAGNESIUM SALICYLATE	0	0.0	1	1.0	1	0.5
METHOHEXITAL SODIUM	0	0.0	1	1.0	1	0.5
METHYLPHENIDATE	0	0.0	1	1.0	1	0.5
METHYLPHENIDATE HYDROCHLORIDE	5	5.3	4	4.1	9	4.7
MORPHINE	1	1.1	0	0.0	1	0.5
NORTRIPTYLINE	0	0.0	1	1.0	1	0.5
PARACETAMOL	46	48.4	50	51.0	96	49.7
PAROXETINE	2	2.1	7	7.1	9	4.7
PEMOLINE MAGNESIUM	1	1.1	0	0.0	1	0.5
PHENACETIN	2	2.1	0	0.0	2	1.0
PHENYLPROPANOLAMINE HYDROCHLORIDE	2	2.1	0	0.0	2	1.0
PHENYLTOLOXAMINE CITRATE	3	3.2	0	0.0	3	1.6
PRILOCAINE	1	1.1	3	3.1	4	2.1
PROCAINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
PSEUDOEPHEDRINE HYDROCHLORIDE	4	4.2	4	4.1	8	4.1
RISPERIDONE	1	1.1	1	1.0	2	1.0
SERTRALINE	2	2.1	0	0.0	2	1.0
SERTRALINE HYDROCHLORIDE	3	3.2	2	2.0	5	2.6
SODIUM BICARBONATE	0	0.0	2	2.0	2	1.0
SUMATRIPTAN	0	0.0	1	1.0	1	0.5
THIORIDAZINE HYDROCHLORIDE	1	1.1	1	1.0	2	1.0
TRAZODONE	0	0.0	2	2.0	2	1.0
DERMATOLOGICALS:	28	29.5	29	29.6	57	29.5

NOTE: Prior medication refers to all those started prior to randomisation baseline

TABLE 13.11.2

Summary of Prior Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS	82	86.3%	89	90.8%	171	88.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
ALOES	1	1.1	1	1.0	2	1.0
BACITRACIN	3	3.2	0	0.0	3	1.6
BENZOCAINE	1	1.1	0	0.0	1	0.5
BENZOIN TINCTURE	1	1.1	0	0.0	1	0.5
BENZOYL PEROXIDE	1	1.1	0	0.0	1	0.5
BUDESONIDE	1	1.1	2	2.0	3	1.6
CALAMINE	0	0.0	1	1.0	1	0.5
CAMPHOR	0	0.0	1	1.0	1	0.5
CERESIN	1	1.1	0	0.0	1	0.5
CETYL ALCOHOL	0	0.0	1	1.0	1	0.5
CETYLPYRIDINIUM CHLORIDE	1	1.1	0	0.0	1	0.5
CLOTRIMAZOLE	1	1.1	0	0.0	1	0.5
CORTISONE	1	1.1	0	0.0	1	0.5
DIPHENHYDRAMINE	1	1.1	0	0.0	1	0.5
DIPHENHYDRAMINE HYDROCHLORIDE	7	7.4	11	11.2	18	9.3
ECONAZOLE NITRATE	0	0.0	1	1.0	1	0.5
ERYTHROMYCIN	4	4.2	3	3.1	7	3.6
FLUTICASONE PROPIONATE	2	2.1	0	0.0	2	1.0
GENTAMICIN	1	1.1	0	0.0	1	0.5
GLYCEROL	0	0.0	1	1.0	1	0.5
GRISEOFULVIN	0	0.0	1	1.0	1	0.5
HYDROCORTISONE	2	2.1	3	3.1	5	2.6
LIDOCAINE	1	1.1	4	4.1	5	2.6
METHYLCHLOROISOTHIAZOLINONE	1	1.1	0	0.0	1	0.5
METHYLISOTHIAZOLINONE	1	1.1	0	0.0	1	0.5
MUPIROCIN	1	1.1	0	0.0	1	0.5
NEOMYCIN	2	2.1	0	0.0	2	1.0
NEOMYCIN SULFATE	3	3.2	0	0.0	3	1.6
PARABENS	0	0.0	1	1.0	1	0.5
PARAFFIN, LIQUID	2	2.1	0	0.0	2	1.0

NOTE: Prior medication refers to all those started prior to randomisation baseline

TABLE 13.11.2

Summary of Prior Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS	82	86.3%	89	90.8%	171	88.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
PARAFFIN, SOFT	1	1.1	0	0.0	1	0.5
POLYMYXIN B	1	1.1	0	0.0	1	0.5
POLYMYXIN B SULFATE	3	3.2	0	0.0	3	1.6
PREDNISOLONE SODIUM PHOSPHATE	0	0.0	1	1.0	1	0.5
PRILOCAINE	1	1.1	3	3.1	4	2.1
PROMETHAZINE HYDROCHLORIDE	0	0.0	1	1.0	1	0.5
SULFACETAMIDE SODIUM	2	2.1	0	0.0	2	1.0
SULFADIAZINE SILVER	1	1.1	0	0.0	1	0.5
TETRACYCLINE	0	0.0	1	1.0	1	0.5
TRETINOIN	1	1.1	1	1.0	2	1.0
TRIAMCINOLONE ACETONIDE	1	1.1	2	2.0	3	1.6
WATER	1	1.1	0	0.0	1	0.5
WOOL ALCOHOLS	1	1.1	0	0.0	1	0.5
ZINC ACETATE	0	0.0	2	2.0	2	1.0
GU SYSTEM/SEX HORMONES:	3	3.2	2	2.0	5	2.6
CLOTRIMAZOLE	1	1.1	0	0.0	1	0.5
ECONAZOLE NITRATE	0	0.0	1	1.0	1	0.5
ETHINYLESTRADIOL	1	1.1	1	1.0	2	1.0
MESTRANOL	1	1.1	0	0.0	1	0.5
NORETHISTERONE	1	1.1	0	0.0	1	0.5
NORETHISTERONE ACETATE	0	0.0	1	1.0	1	0.5
NORGESTIMATE	1	1.1	0	0.0	1	0.5
PHENAZOPYRIDINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
MUSCULO-SKELETAL:	39	41.1	28	28.6	67	34.7
EUCALYPTUS OIL	2	2.1	1	1.0	3	1.6
IBUPROFEN	37	38.9	28	28.6	65	33.7
INDOMETACIN	0	0.0	1	1.0	1	0.5
MENTHOL	2	2.1	1	1.0	3	1.6

NOTE: Prior medication refers to all those started prior to randomisation baseline

TABLE 13.11.2

Summary of Prior Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS	82	86.3%	89	90.8%	171	88.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
NABUMETONE	1	1.1	0	0.0	1	0.5
NAPROXEN	1	1.1	0	0.0	1	0.5
RESPIRATORY:	54	56.8	44	44.9	98	50.8
ACRIVASTINE	1	1.1	0	0.0	1	0.5
AMINOACETIC ACID	1	1.1	1	1.0	2	1.0
BECLOMETASONE	0	0.0	1	1.0	1	0.5
BECLOMETASONE DIPROPIONATE	4	4.2	7	7.1	11	5.7
BENZALKONIUM CHLORIDE	1	1.1	1	1.0	2	1.0
BROMPHENIRAMINE MALEATE	8	8.4	3	3.1	11	5.7
BRONCHODILATORS, NOS	1	1.1	0	0.0	1	0.5
BUDESONIDE	1	1.1	2	2.0	3	1.6
CARBINOXAMINE MALEATE	0	0.0	1	1.0	1	0.5
CETIRIZINE HYDROCHLORIDE	2	2.1	0	0.0	2	1.0
CETYLPYRIDINIUM CHLORIDE	1	1.1	0	0.0	1	0.5
CHLORPHENAMINE	1	1.1	0	0.0	1	0.5
CHLORPHENAMINE MALEATE	12	12.6	8	8.2	20	10.4
CHLORPHENAMINE TANNATE	0	0.0	1	1.0	1	0.5
CLEMASTINE FUMARATE	3	3.2	3	3.1	6	3.1
CODEINE PHOSPHATE	1	1.1	1	1.0	2	1.0
COUGH COLD PREPARATIONS NOS	1	1.1	0	0.0	1	0.5
COUGH SYRUP/MED	1	1.1	0	0.0	1	0.5
CROMOGLICATE SODIUM	0	0.0	2	2.0	2	1.0
CYPROHEPTADINE HYDROCHLORIDE	0	0.0	1	1.0	1	0.5
DECONGESTANT NOS	1	1.1	2	2.0	3	1.6
DEXBROMPHENIRAMINE MALEATE	0	0.0	1	1.0	1	0.5
DEXTROMETHORPHAN	1	1.1	0	0.0	1	0.5
DEXTROMETHORPHAN HYDROBROMIDE	12	12.6	6	6.1	18	9.3
DIMENHYDRINATE	1	1.1	1	1.0	2	1.0
DIPHENHYDRAMINE	1	1.1	0	0.0	1	0.5

NOTE: Prior medication refers to all those started prior to randomisation baseline

TABLE 13.11.2

Summary of Prior Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS	82	86.3%	89	90.8%	171	88.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
DIPHENHYDRAMINE HYDROCHLORIDE	7	7.4	8	8.2	15	7.8
ETHANOL	2	2.1	2	2.0	4	2.1
EUCALYPTUS OIL	2	2.1	1	1.0	3	1.6
FEXOFENADINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
FLUTICASONE PROPIONATE	2	2.1	0	0.0	2	1.0
GUAIFENESIN	7	7.4	5	5.1	12	6.2
HEXYLRESORCINOL	0	0.0	1	1.0	1	0.5
HYDROCODONE	0	0.0	1	1.0	1	0.5
HYDROCODONE BITARTRATE	2	2.1	0	0.0	2	1.0
HYOSCINE METHONITRATE	2	2.1	0	0.0	2	1.0
LIDOCAINE	0	0.0	1	1.0	1	0.5
LORATADINE	6	6.3	7	7.1	13	6.7
MENTHOL	2	2.1	1	1.0	3	1.6
MEPYRAMINE MALEATE	2	2.1	1	1.0	3	1.6
MEPYRAMINE TANNATE	0	0.0	1	1.0	1	0.5
OXYMETAZOLINE HYDROCHLORIDE	1	1.1	1	1.0	2	1.0
PARACETAMOL	11	11.6	9	9.2	20	10.4
PHENIRAMINE MALEATE	2	2.1	1	1.0	3	1.6
PHENYLEPHRINE HYDROCHLORIDE	4	4.2	3	3.1	7	3.6
PHENYLEPHRINE TANNATE	0	0.0	1	1.0	1	0.5
PHENYLMERCURIC ACETATE	1	1.1	1	1.0	2	1.0
PHENYLPROPANOLAMINE HYDROCHLORIDE	16	16.8	8	8.2	24	12.4
PHENYLTOLOXAMINE CITRATE	1	1.1	1	1.0	2	1.0
PIRBUTEROL ACETATE	0	0.0	1	1.0	1	0.5
PREDNISONE	0	0.0	2	2.0	2	1.0
PROMETHAZINE HYDROCHLORIDE	0	0.0	1	1.0	1	0.5
PSEUDOEPHEDRINE	1	1.1	0	0.0	1	0.5
PSEUDOEPHEDRINE HYDROCHLORIDE	15	15.8	15	15.3	30	15.5
PSEUDOEPHEDRINE SULFATE	1	1.1	2	2.0	3	1.6
SALBUTAMOL	8	8.4	7	7.1	15	7.8

NOTE: Prior medication refers to all those started prior to randomisation baseline

TABLE 13.11.2

Summary of Prior Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS	82	86.3%	89	90.8%	171	88.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
SALBUTAMOL SULFATE	1	1.1	0	0.0	1	0.5
SORBITOL	1	1.1	1	1.0	2	1.0
THEOPHYLLINE	0	0.0	1	1.0	1	0.5
TRIAMCINOLONE ACETONIDE	1	1.1	2	2.0	3	1.6
SENSORY ORGANS:	17	17.9	18	18.4	35	18.1
BROMPHENIRAMINE MALEATE	4	4.2	2	2.0	6	3.1
CORTISONE	1	1.1	0	0.0	1	0.5
CROMOGLICATE SODIUM	0	0.0	2	2.0	2	1.0
EAR MEDICATION, NOS	1	1.1	0	0.0	1	0.5
ERYTHROMYCIN	3	3.2	3	3.1	6	3.1
FLUORESCEIN SODIUM	0	0.0	1	1.0	1	0.5
GENTAMICIN	1	1.1	0	0.0	1	0.5
HYDROCORTISONE	2	2.1	3	3.1	5	2.6
INDOMETACIN	0	0.0	1	1.0	1	0.5
LIDOCAINE	0	0.0	1	1.0	1	0.5
NEOMYCIN	2	2.1	0	0.0	2	1.0
OXYBUPROCAINE HYDROCHLORIDE	0	0.0	1	1.0	1	0.5
PHENYLPROPANOLAMINE HYDROCHLORIDE	4	4.2	2	2.0	6	3.1
POLYMYXIN B	1	1.1	0	0.0	1	0.5
POLYMYXIN B SULFATE	1	1.1	0	0.0	1	0.5
PREDNISOLONE SODIUM PHOSPHATE	0	0.0	1	1.0	1	0.5
SULFACETAMIDE	1	1.1	0	0.0	1	0.5
SULFACETAMIDE SODIUM	2	2.1	0	0.0	2	1.0
TETRACYCLINE	0	0.0	1	1.0	1	0.5
TOBRAMYCIN	0	0.0	1	1.0	1	0.5
TRIAMCINOLONE ACETONIDE	1	1.1	2	2.0	3	1.6
TRIMETHOPRIM SULFATE	1	1.1	0	0.0	1	0.5
TROPICAMIDE	0	0.0	1	1.0	1	0.5

NOTE: Prior medication refers to all those started prior to randomisation baseline

TABLE 13.11.2

Summary of Prior Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS	82	86.3%	89	90.8%	171	88.6%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
SYSTEMIC HORMONAL:	4	4.2	12	12.2	16	8.3
CORTISONE	1	1.1	0	0.0	1	0.5
HYDROCORTISONE	2	2.1	3	3.1	5	2.6
LEVOTHYROXINE	0	0.0	1	1.0	1	0.5
LEVOTHYROXINE SODIUM	0	0.0	1	1.0	1	0.5
MELATONIN	1	1.1	0	0.0	1	0.5
PREDNISOLONE SODIUM PHOSPHATE	0	0.0	1	1.0	1	0.5
PREDNISONE	0	0.0	2	2.0	2	1.0
SOMATREM	1	1.1	1	1.0	2	1.0
SOMATROPIN	0	0.0	1	1.0	1	0.5
TRIAMCINOLONE ACETONIDE	1	1.1	2	2.0	3	1.6
UNCLASSIFIABLE:	2	2.1	1	1.0	3	1.6
UNKNOWN MEDICATION	2	2.1	1	1.0	3	1.6
VARIOUS:	1	1.1	7	7.1	8	4.1
ALFALFA	0	0.0	1	1.0	1	0.5
ECHINACEA EXTRACT	0	0.0	2	2.0	2	1.0
HYDRASTIS CANADENSIS	0	0.0	1	1.0	1	0.5
HYPERICUM EXTRACT	0	0.0	2	2.0	2	1.0
NICOTINE	0	0.0	1	1.0	1	0.5
NUTRITIONAL SUPPLEMENT NOS	1	1.1	0	0.0	1	0.5

NOTE: Prior medication refers to all those started prior to randomisation baseline

TABLE 13.12.1

Summary of Concomitant Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	335	100.0%
PATIENTS WITH MEDICATIONS	269	80.3%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	**N**	**%**
ALIMENTARY TRACT/METAB:	92	27.5
ALOES	1	0.3
ALUMINIUM HYDROXIDE	10	3.0
ANISE OIL	1	0.3
ANTACID NOS	1	0.3
ASCORBIC ACID	6	1.8
ATROPINE SULFATE	2	0.6
BENZOIC ACID	1	0.3
BISACODYL	1	0.3
BISMUTH SUBSALICYLATE	22	6.6
CALCIUM	2	0.6
CALCIUM CARBONATE	19	5.7
CALCIUM PANTOTHENATE	1	0.3
CALCIUM POLYCARBOPHIL	2	0.6
CAMPHOR	1	0.3
CASANTHRANOL	1	0.3
CIMETIDINE	2	0.6
CISAPRIDE	1	0.3
DICYCLOVERINE	1	0.3
DIMETICONE, ACTIVATED	10	3.0
DIPHENOXYLATE HYDROCHLORIDE	1	0.3
DOCUSATE SODIUM	2	0.6
ETHANOL	2	0.6
FAMOTIDINE	2	0.6
GLYCEROL	1	0.3
HYOSCINE HYDROBROMIDE	1	0.3
HYOSCYAMINE SULFATE	1	0.3
INOSITOL	1	0.3
INVERT SUGAR	2	0.6

NOTE: Concomitant medications refer to all those started on or after baseline
or are on-going at baseline and who started before the last date of study medication

TABLE 13.12.1

Summary of Concomitant Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	269	80.3%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%
IRON	1	0.3
KAOLIN	3	0.9
LACTULOSE	1	0.3
LOPERAMIDE	1	0.3
LOPERAMIDE HYDROCHLORIDE	8	2.4
MAGNESIUM HYDROXIDE	12	3.6
MAGNESIUM NOS	1	0.3
METHYLCELLULOSE	1	0.3
MINERALS NOS	1	0.3
NATURAL FIBER LAXATIVE	1	0.3
NEOMYCIN	1	0.3
NICOTINAMIDE	1	0.3
NIZATIDINE	1	0.3
OPIUM	1	0.3
OPIUM TINCTURE, BENZOATED	1	0.3
PANCRELIPASE	1	0.3
PARAFFIN, LIQUID	1	0.3
PECTIN	3	0.9
PHOSPHORIC ACID	2	0.6
PSYLLIUM HYDROPHILIC MUCILLOID	1	0.3
PYRIDOXINE HYDROCHLORIDE	1	0.3
RANITIDINE HYDROCHLORIDE	3	0.9
RIBOFLAVIN	1	0.3
SENNA FRUIT	1	0.3
THIAMINE HYDROCHLORIDE	1	0.3
TILACTASE	1	0.3
TRIAMCINOLONE ACETONIDE	3	0.9
VITAMINS NOS	22	6.6
ZINC	2	0.6

NOTE: Concomitant medications refer to all those started on or after baseline
or are on-going at baseline and who started before the last date of study medication

TABLE 13.12.1

Summary of Concomitant Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	269	80.3%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%
ZINC GLUCONATE	2	0.6
ANTIINFECTIVES,SYSTEMIC:	77	23.0
AMOXICILLIN	14	4.2
AMOXICILLIN TRIHYDRATE	11	3.3
AMPICILLIN	2	0.6
ANTIBIOTIC NOS	2	0.6
AZITHROMYCIN	3	0.9
CEFACLOR	4	1.2
CEFALEXIN	2	0.6
CEFALEXIN MONOHYDRATE	3	0.9
CEFIXIME	3	0.9
CEFPODOXIME PROXETIL	1	0.3
CEFPROZIL MONOHYDRATE	3	0.9
CEFUROXIME AXETIL	2	0.6
CIPROFLOXACIN	1	0.3
CLARITHROMYCIN	3	0.9
CLAVULANIC ACID	6	1.8
CLINDAMYCIN HYDROCHLORIDE	1	0.3
DOXYCYCLINE	1	0.3
ERYTHROMYCIN	6	1.8
ERYTHROMYCIN STEARATE	1	0.3
GENTAMICIN	1	0.3
HEPATITIS B VACCINE	3	0.9
HEPATITIS VACCINE, NOS	3	0.9
INFLUENZA VIRUS VACCINE POLYVALENT	1	0.3
LORACARBEF	1	0.3
MINOCYCLINE	4	1.2
MUPIROCIN	2	0.6

NOTE: Concomitant medications refer to all those started on or after baseline
or are on-going at baseline and who started before the last date of study medication

TABLE 13.12.1

Summary of Concomitant Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	269	80.3%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	**N**	**%**
NEOMYCIN	1	0.3
PENICILLIN NOS	4	1.2
PHENOXYMETHYLPENICILLIN POTASSIUM	2	0.6
SULFAMETHOXAZOLE	6	1.8
TETANUS TOXOID	1	0.3
TETRACYCLINE	1	0.3
TOBRAMYCIN	1	0.3
TRIMETHOPRIM	5	1.5
ANTINEOPLASTIC & IMMUNOSUP:	4	1.2
TRETINOIN	4	1.2
BLOOD/BLOOD FORM ORGANS:	1	0.3
FRUCTOSE	1	0.3
CARDIOVASCULAR:	6	1.8
CLONIDINE	3	0.9
LIDOCAINE	1	0.3
PREDNISOLONE SODIUM PHOSPHATE	1	0.3
THEOPHYLLINE	1	0.3
CENTRAL NERVOUS SYSTEM:	163	48.7
ACETYLSALICYLIC ACID	13	3.9
ALPRAZOLAM	1	0.3
AMITRIPTYLINE	1	0.3
AMPHETAMINE ASPARTATE	2	0.6
AMPHETAMINE SULFATE	2	0.6
ANESTHESIA, NOS	1	0.3
ANTI-MIGRAINE PREPARATIONS NOS	1	0.3

NOTE: Concomitant medications refer to all those started on or after baseline
or are on-going at baseline and who started before the last date of study medication

TABLE 13.12.1

Summary of Concomitant Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	269	80.3%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%
BUTALBITAL	1	0.3
CAFFEINE	4	1.2
CANNABIS	1	0.3
CHLORPHENAMINE MALEATE	3	0.9
CINNAMEDRINE HYDROCHLORIDE	1	0.3
CITRIC ACID	3	0.9
CLOMIPRAMINE HYDROCHLORIDE	1	0.3
CLONIDINE	3	0.9
CODEINE PHOSPHATE	3	0.9
DEXAMPHETAMINE SULFATE	2	0.6
DEXTROAMPHETAMINE SACCHARATE	2	0.6
DEXTROAMPHETAMINE SULFATE	2	0.6
DEXTROMETHORPHAN HYDROBROMIDE	3	0.9
DIAZEPAM	1	0.3
DICHLORALPHENAZONE	1	0.3
DIPHENHYDRAMINE HYDROCHLORIDE	2	0.6
FLUVOXAMINE MALEATE	1	0.3
HYDROCODONE BITARTRATE	2	0.6
HYDROXYZINE HYDROCHLORIDE	1	0.3
ISOMETHEPTENE	1	0.3
LIDOCAINE	10	3.0
LORAZEPAM	15	4.5
MAGNESIUM SALICYLATE	1	0.3
MEPYRAMINE MALEATE	1	0.3
METHOHEXITAL SODIUM	1	0.3
METHYLPHENIDATE HYDROCHLORIDE	2	0.6
MORPHINE	1	0.3
PAMABROM	1	0.3
PARACETAMOL	138	41.2

NOTE: Concomitant medications refer to all those started on or after baseline
or are on-going at baseline and who started before the last date of study medication

TABLE 13.12.1

Summary of Concomitant Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	269	80.3%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	**N**	**%**
PAROXETINE	2	0.6
PETHIDINE HYDROCHLORIDE	1	0.3
PHENACETIN	2	0.6
PHENYLPROPANOLAMINE HYDROCHLORIDE	2	0.6
PHENYLTOLOXAMINE CITRATE	3	0.9
PRILOCAINE	9	2.7
PROCAINE HYDROCHLORIDE	1	0.3
PSEUDOEPHEDRINE HYDROCHLORIDE	7	2.1
RISPERIDONE	1	0.3
SODIUM BICARBONATE	3	0.9
SUMATRIPTAN	2	0.6
THIORIDAZINE HYDROCHLORIDE	1	0.3
TRAZODONE	1	0.3
VALERIAN ROOT	1	0.3
DERMATOLOGICALS:	86	25.7
ALOES	2	0.6
BACITRACIN	5	1.5
BENZOCAINE	1	0.3
BENZOIN TINCTURE	1	0.3
BENZOYL PEROXIDE	2	0.6
BETAMETHASONE DIPROPIONATE	1	0.3
BUDESONIDE	4	1.2
CALAMINE	1	0.3
CAMPHOR	1	0.3
CERESIN	1	0.3
CETYL ALCOHOL	1	0.3
CETYLPYRIDINIUM CHLORIDE	1	0.3
CLOTRIMAZOLE	1	0.3

NOTE: Concomitant medications refer to all those started on or after baseline
or are on-going at baseline and who started before the last date of study medication

TABLE 13.12.1

Summary of Concomitant Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	269	80.3%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%
DIPHENHYDRAMINE	1	0.3
DIPHENHYDRAMINE HYDROCHLORIDE	31	9.3
ECONAZOLE NITRATE	1	0.3
ERYTHROMYCIN	8	2.4
FLUTICASONE PROPIONATE	2	0.6
GENTAMICIN	1	0.3
GLYCEROL	1	0.3
GRISEOFULVIN	1	0.3
HYDROCORTISONE	8	2.4
LIDOCAINE	10	3.0
METHYLCHLOROISOTHIAZOLINONE	1	0.3
METHYLISOTHIAZOLINONE	1	0.3
METHYLPREDNISOLONE	1	0.3
MUPIROCIN	2	0.6
NEOMYCIN	2	0.6
NEOMYCIN SULFATE	5	1.5
PARABENS	1	0.3
PARAFFIN, LIQUID	2	0.6
PARAFFIN, SOFT	1	0.3
PHENOL	1	0.3
POLYMYXIN B	1	0.3
POLYMYXIN B SULFATE	5	1.5
PREDNISOLONE SODIUM PHOSPHATE	1	0.3
PRILOCAINE	9	2.7
PROMETHAZINE HYDROCHLORIDE	1	0.3
SULFACETAMIDE SODIUM	2	0.6
SULFADIAZINE SILVER	1	0.3
TETRACYCLINE	1	0.3
TRETINOIN	4	1.2

NOTE: Concomitant medications refer to all those started on or after baseline
or are on-going at baseline and who started before the last date of study medication

TABLE 13.12.1

Summary of Concomitant Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	269	80.3%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	**N**	**%**
TRIAMCINOLONE ACETONIDE	3	0.9
WATER	1	0.3
WOOL ALCOHOLS	1	0.3
ZINC ACETATE	2	0.6
ZINC GLUCONATE	2	0.6
GU SYSTEM/SEX HORMONES:	7	2.1
CIPROFLOXACIN	1	0.3
CLOTRIMAZOLE	1	0.3
ECONAZOLE NITRATE	1	0.3
ETHINYLESTRADIOL	2	0.6
MESTRANOL	1	0.3
NORETHISTERONE	1	0.3
NORETHISTERONE ACETATE	1	0.3
NORGESTIMATE	1	0.3
PHENAZOPYRIDINE HYDROCHLORIDE	1	0.3
SULFABENZAMIDE	1	0.3
SULFACETAMIDE	1	0.3
SULFATHIAZOLE	1	0.3
UREA	1	0.3
MUSCULO-SKELETAL:	90	26.9
EUCALYPTUS OIL	4	1.2
IBUPROFEN	85	25.4
KETOPROFEN	1	0.3
MENTHOL	4	1.2
NAPROXEN	2	0.6
NAPROXEN SODIUM	3	0.9

NOTE: Concomitant medications refer to all those started on or after baseline
or are on-going at baseline and who started before the last date of study medication

TABLE 13.12.1

Summary of Concomitant Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	269	80.3%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%
PARASITOLOGY:	1	0.3
MEBENDAZOLE	1	0.3
RESPIRATORY:	146	43.6
ACRIVASTINE	1	0.3
AMINOACETIC ACID	2	0.6
AMMONIUM CHLORIDE	1	0.3
ASTEMIZOLE	1	0.3
BECLOMETASONE DIPROPIONATE	20	6.0
BENZALKONIUM CHLORIDE	2	0.6
BENZONATATE	1	0.3
BROMPHENIRAMINE MALEATE	16	4.8
BRONCHODILATORS, NOS	1	0.3
BUDESONIDE	4	1.2
CAMPHOR	1	0.3
CARBINOXAMINE MALEATE	1	0.3
CETIRIZINE HYDROCHLORIDE	4	1.2
CETYLPYRIDINIUM CHLORIDE	1	0.3
CHLORPHENAMINE	1	0.3
CHLORPHENAMINE MALEATE	21	6.3
CHLORPHENAMINE TANNATE	2	0.6
CLEMASTINE FUMARATE	5	1.5
CODEINE PHOSPHATE	1	0.3
COUGH COLD PREPARATIONS NOS	1	0.3
COUGH SYRUP/MED	2	0.6
CROMOGLICATE SODIUM	8	2.4
CYPROHEPTADINE	1	0.3
DECONGESTANT NOS	2	0.6
DEXBROMPHENIRAMINE MALEATE	3	0.9

NOTE: Concomitant medications refer to all those started on or after baseline
or are on-going at baseline and who started before the last date of study medication

TABLE 13.12.1

Summary of Concomitant Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	269	80.3%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%
DEXTROMETHORPHAN	1	0.3
DEXTROMETHORPHAN HYDROBROMIDE	24	7.2
DIMENHYDRINATE	3	0.9
DIPHENHYDRAMINE	1	0.3
DIPHENHYDRAMINE HYDROCHLORIDE	30	9.0
DOXYLAMINE SUCCINATE	1	0.3
ETHANOL	6	1.8
EUCALYPTUS OIL	5	1.5
FEXOFENADINE HYDROCHLORIDE	1	0.3
FLUTICASONE PROPIONATE	2	0.6
GUAIFENESIN	17	5.1
HEXYLRESORCINOL	1	0.3
HYDROCODONE	2	0.6
HYDROCODONE BITARTRATE	2	0.6
HYOSCINE METHONITRATE	2	0.6
LIDOCAINE	1	0.3
LODOXAMIDE TROMETAMOL	1	0.3
LORATADINE	21	6.3
MENTHOL	5	1.5
MEPYRAMINE MALEATE	4	1.2
MEPYRAMINE TANNATE	2	0.6
OXYMETAZOLINE HYDROCHLORIDE	2	0.6
PARACETAMOL	17	5.1
PHENINDAMINE TARTRATE	1	0.3
PHENIRAMINE MALEATE	4	1.2
PHENYLEPHRINE HYDROCHLORIDE	13	3.9
PHENYLEPHRINE TANNATE	2	0.6
PHENYLMERCURIC ACETATE	2	0.6
PHENYLPROPANOLAMINE HYDROCHLORIDE	31	9.3

NOTE: Concomitant medications refer to all those started on or after baseline
or are on-going at baseline and who started before the last date of study medication

TABLE 13.12.1

Summary of Concomitant Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	269	80.3%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%
PHENYLTOLOXAMINE	1	0.3
PHENYLTOLOXAMINE CITRATE	2	0.6
PIRBUTEROL ACETATE	2	0.6
PREDNISONE	3	0.9
PROMETHAZINE HYDROCHLORIDE	1	0.3
PSEUDOEPHEDRINE	1	0.3
PSEUDOEPHEDRINE HYDROCHLORIDE	36	10.7
PSEUDOEPHEDRINE SULFATE	6	1.8
SALBUTAMOL	25	7.5
SALBUTAMOL SULFATE	1	0.3
SALMETEROL HYDROXYNAPHTHOATE	1	0.3
SODIUM CITRATE	1	0.3
SORBITOL	2	0.6
THEOPHYLLINE	1	0.3
TRIAMCINOLONE ACETONIDE	3	0.9
TURPENTINE OIL	1	0.3
SENSORY ORGANS:	47	14.0
BROMPHENIRAMINE MALEATE	6	1.8
CIPROFLOXACIN	1	0.3
CROMOGLICATE SODIUM	8	2.4
ERYTHROMYCIN	6	1.8
FLUORESCEIN SODIUM	1	0.3
GENTAMICIN	1	0.3
HYDROCORTISONE	8	2.4
LIDOCAINE	1	0.3
LODOXAMIDE TROMETAMOL	1	0.3
METHYLCELLULOSE	1	0.3
METHYLPREDNISOLONE	1	0.3

NOTE: Concomitant medications refer to all those started on or after baseline
or are on-going at baseline and who started before the last date of study medication

TABLE 13.12.1

Summary of Concomitant Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	269	80.3%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	**N**	**%**
NEOMYCIN	2	0.6
NEOMYCIN SULFATE	1	0.3
OXYBUPROCAINE HYDROCHLORIDE	1	0.3
PHENYLPROPANOLAMINE HYDROCHLORIDE	6	1.8
POLYMYXIN B	1	0.3
POLYMYXIN B SULFATE	2	0.6
PREDNISOLONE SODIUM PHOSPHATE	1	0.3
SULFACETAMIDE	1	0.3
SULFACETAMIDE SODIUM	2	0.6
TETRACYCLINE	1	0.3
TOBRAMYCIN	1	0.3
TRIAMCINOLONE ACETONIDE	3	0.9
TRIMETHOPRIM SULFATE	1	0.3
TROPICAMIDE	1	0.3
SYSTEMIC HORMONAL:	23	6.9
DESMOPRESSIN	1	0.3
HYDROCORTISONE	8	2.4
LEVOTHYROXINE	1	0.3
LEVOTHYROXINE SODIUM	1	0.3
MELATONIN	2	0.6
METHYLPREDNISOLONE	1	0.3
PREDNISOLONE SODIUM PHOSPHATE	1	0.3
PREDNISONE	3	0.9
SOMATREM	2	0.6
SOMATROPIN	1	0.3
TRIAMCINOLONE ACETONIDE	3	0.9
UNCLASSIFIABLE:	3	0.9

NOTE: Concomitant medications refer to all those started on or after baseline
or are on-going at baseline and who started before the last date of study medication

TABLE 13.12.1

Summary of Concomitant Medication
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH MEDICATIONS :	269	80.3%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	**N**	**%**
UNKNOWN MEDICATION	3	0.9
VARIOUS:	7	2.1
ALLERGENIC EXTRACT, NOS	2	0.6
ECHINACEA EXTRACT	3	0.9
HYDRASTIS CANADENSIS	1	0.3
NICOTINE	1	0.3

NOTE: Concomitant medications refer to all those started on or after baseline
or are on-going at baseline and who started before the last date of study medication

TABLE 13.12.2

Summary of Concomitant Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS	77	81.1%	79	80.6%	156	80.8%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
ALIMENTARY TRACT/METAB:	25	26.3	35	35.7	60	31.1
ALUMINIUM HYDROXIDE	3	3.2	1	1.0	4	2.1
ANISE OIL	0	0.0	1	1.0	1	0.5
ANTACID NOS	1	1.1	0	0.0	1	0.5
ASCORBIC ACID	4	4.2	3	3.1	7	3.6
ATROPINE SULFATE	0	0.0	1	1.0	1	0.5
BENZOIC ACID	0	0.0	1	1.0	1	0.5
BISMUTH SUBSALICYLATE	4	4.2	7	7.1	11	5.7
CALCIUM	0	0.0	1	1.0	1	0.5
CALCIUM CARBONATE	4	4.2	9	9.2	13	6.7
CALCIUM PANTOTHENATE	1	1.1	0	0.0	1	0.5
CALCIUM POLYCARBOPHIL	1	1.1	1	1.0	2	1.0
CAMPHOR	0	0.0	1	1.0	1	0.5
CASANTHRANOL	1	1.1	0	0.0	1	0.5
CIMETIDINE	1	1.1	0	0.0	1	0.5
DICYCLOVERINE	1	1.1	0	0.0	1	0.5
DIMETICONE, ACTIVATED	1	1.1	1	1.0	2	1.0
DOCUSATE SODIUM	1	1.1	0	0.0	1	0.5
ERGOCALCIFEROL	1	1.1	0	0.0	1	0.5
ETHANOL	0	0.0	2	2.0	2	1.0
GLYCEROL	0	0.0	1	1.0	1	0.5
HYOSCINE HYDROBROMIDE	0	0.0	1	1.0	1	0.5
HYOSCYAMINE SULFATE	0	0.0	1	1.0	1	0.5
IRON	0	0.0	1	1.0	1	0.5
KAOLIN	0	0.0	2	2.0	2	1.0
LOPERAMIDE HYDROCHLORIDE	3	3.2	2	2.0	5	2.6
MAGNESIUM HYDROXIDE	3	3.2	3	3.1	6	3.1
MINERALS NOS	0	0.0	1	1.0	1	0.5
NATURAL FIBER LAXATIVE	0	0.0	1	1.0	1	0.5

NOTE: Concomitant medications refer to all those started on or after randomisation baseline
or are on-going at randomisation baseline and who started before the last date of study medication

TABLE 13.12.2

Summary of Concomitant Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS	77	81.1%	79	80.6%	156	80.8%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
NICOTINAMIDE	1	1.1	0	0.0	1	0.5
NIZATIDINE	1	1.1	0	0.0	1	0.5
OPIUM	0	0.0	1	1.0	1	0.5
PECTIN	0	0.0	2	2.0	2	1.0
PYRIDOXINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
RANITIDINE HYDROCHLORIDE	0	0.0	1	1.0	1	0.5
RETINOL	1	1.1	0	0.0	1	0.5
RIBOFLAVIN	1	1.1	0	0.0	1	0.5
SENNA FRUIT	1	1.1	0	0.0	1	0.5
THIAMINE	1	1.1	0	0.0	1	0.5
THIAMINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
TOCOPHEROL	0	0.0	1	1.0	1	0.5
TRIAMCINOLONE ACETONIDE	0	0.0	3	3.1	3	1.6
VITAMINS NOS	6	6.3	11	11.2	17	8.8
ANTIINFECTIVES,SYSTEMIC:	26	27.4	19	19.4	45	23.3
AMOXICILLIN	10	10.5	7	7.1	17	8.8
AMOXICILLIN TRIHYDRATE	3	3.2	3	3.1	6	3.1
AMPICILLIN	2	2.1	0	0.0	2	1.0
AZITHROMYCIN	1	1.1	0	0.0	1	0.5
CEFACLOR	1	1.1	0	0.0	1	0.5
CEFALEXIN	1	1.1	1	1.0	2	1.0
CEFALEXIN MONOHYDRATE	1	1.1	0	0.0	1	0.5
CEFPROZIL MONOHYDRATE	1	1.1	0	0.0	1	0.5
CEFUROXIME AXETIL	0	0.0	1	1.0	1	0.5
CIPROFLOXACIN HYDROCHLORIDE	0	0.0	1	1.0	1	0.5
CLARITHROMYCIN	1	1.1	2	2.0	3	1.6
CLAVULANIC ACID	2	2.1	2	2.0	4	2.1
CLINDAMYCIN HYDROCHLORIDE	1	1.1	0	0.0	1	0.5

NOTE: Concomitant medications refer to all those started on or after randomisation baseline
or are on-going at randomisation baseline and who started before the last date of study medication

TABLE 13.12.2

Summary of Concomitant Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS :	77	81.1%	79	80.6%	156	80.8%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
ERYTHROMYCIN	1	1.1	2	2.0	3	1.6
GENTAMICIN SULFATE	0	0.0	1	1.0	1	0.5
HEPATITIS VACCINE, NOS	1	1.1	1	1.0	2	1.0
HYDROCORTISONE ACETATE	1	1.1	0	0.0	1	0.5
MINOCYCLINE	3	3.2	0	0.0	3	1.6
MUPIROCIN	1	1.1	0	0.0	1	0.5
OFLOXACIN	1	1.1	0	0.0	1	0.5
PHENOXYMETHYLPENICILLIN POTASSIUM	2	2.1	0	0.0	2	1.0
SULFAMETHOXAZOLE	1	1.1	2	2.0	3	1.6
TETRACYCLINE	0	0.0	2	2.0	2	1.0
TETRACYCLINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
TRIMETHOPRIM	0	0.0	2	2.0	2	1.0
ANTINEOPLASTIC & IMMUNOSUP:	2	2.1	0	0.0	2	1.0
TRETINOIN	2	2.1	0	0.0	2	1.0
CARDIOVASCULAR:	3	3.2	3	3.1	6	3.1
BENZOCAINE	1	1.1	0	0.0	1	0.5
CLONIDINE	0	0.0	1	1.0	1	0.5
HYDROCORTISONE ACETATE	1	1.1	0	0.0	1	0.5
LIDOCAINE	1	1.1	0	0.0	1	0.5
THEOPHYLLINE	0	0.0	1	1.0	1	0.5
XIPAMIDE	0	0.0	1	1.0	1	0.5
CENTRAL NERVOUS SYSTEM:	41	43.2	42	42.9	83	43.0
ACETYLSALICYLIC ACID	7	7.4	5	5.1	12	6.2
CAFFEINE	3	3.2	2	2.0	5	2.6
CANNABIS	1	1.1	0	0.0	1	0.5
CHLORPHENAMINE MALEATE	4	4.2	0	0.0	4	2.1

NOTE: Concomitant medications refer to all those started on or after randomisation baseline
or are on-going at randomisation baseline and who started before the last date of study medication

TABLE 13.12.2

Summary of Concomitant Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS :	77	81.1%	79	80.6%	156	80.8%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
CINNAMEDRINE HYDROCHLORIDE	2	2.1	0	0.0	2	1.0
CITRIC ACID	0	0.0	2	2.0	2	1.0
CLONIDINE	0	0.0	1	1.0	1	0.5
CODEINE PHOSPHATE	0	0.0	1	1.0	1	0.5
DEXTROMETHORPHAN HYDROBROMIDE	4	4.2	0	0.0	4	2.1
DICHLORALPHENAZONE	0	0.0	2	2.0	2	1.0
DIPHENHYDRAMINE CITRATE	0	0.0	1	1.0	1	0.5
DIPHENHYDRAMINE HYDROCHLORIDE	0	0.0	1	1.0	1	0.5
FLUVOXAMINE MALEATE	1	1.1	1	1.0	2	1.0
HYDROCODONE BITARTRATE	1	1.1	0	0.0	1	0.5
ISOMETHEPTENE	0	0.0	2	2.0	2	1.0
LIDOCAINE	2	2.1	1	1.0	3	1.6
LORAZEPAM	1	1.1	4	4.1	5	2.6
MEPYRAMINE MALEATE	1	1.1	0	0.0	1	0.5
MORPHINE	1	1.1	0	0.0	1	0.5
PAMABROM	2	2.1	0	0.0	2	1.0
PARACETAMOL	32	33.7	35	35.7	67	34.7
PAROXETINE	0	0.0	5	5.1	5	2.6
PETHIDINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
PHENACETIN	1	1.1	0	0.0	1	0.5
PHENYLPROPANOLAMINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
PHENYLTOLOXAMINE CITRATE	1	1.1	0	0.0	1	0.5
PRILOCAINE	1	1.1	1	1.0	2	1.0
PSEUDOEPHEDRINE HYDROCHLORIDE	6	6.3	3	3.1	9	4.7
SODIUM BICARBONATE	0	0.0	2	2.0	2	1.0
SUMATRIPTAN	0	0.0	1	1.0	1	0.5
TRAZODONE	0	0.0	1	1.0	1	0.5
DERMATOLOGICALS:	27	28.4	22	22.4	49	25.4

NOTE: Concomitant medications refer to all those started on or after randomisation baseline
or are on-going at randomisation baseline and who started before the last date of study medication

TABLE 13.12.2

Summary of Concomitant Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS :	77	81.1%	79	80.6%	156	80.8%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
ALOES	0	0.0	1	1.0	1	0.5
BACITRACIN	2	2.1	0	0.0	2	1.0
BENTONITE	1	1.1	0	0.0	1	0.5
BENZOCAINE	2	2.1	0	0.0	2	1.0
BENZOIN TINCTURE	1	1.1	0	0.0	1	0.5
BENZOYL PEROXIDE	2	2.1	0	0.0	2	1.0
BETAMETHASONE DIPROPIONATE	0	0.0	1	1.0	1	0.5
BUDESONIDE	1	1.1	2	2.0	3	1.6
CALAMINE	1	1.1	0	0.0	1	0.5
CETYL ALCOHOL	0	0.0	1	1.0	1	0.5
CETYLPYRIDINIUM CHLORIDE	1	1.1	0	0.0	1	0.5
CORTISONE	1	1.1	1	1.0	2	1.0
DESONIDE	0	0.0	1	1.0	1	0.5
DIPHENHYDRAMINE	1	1.1	0	0.0	1	0.5
DIPHENHYDRAMINE CITRATE	0	0.0	1	1.0	1	0.5
DIPHENHYDRAMINE HYDROCHLORIDE	8	8.4	7	7.1	15	7.8
ECONAZOLE NITRATE	0	0.0	1	1.0	1	0.5
ERGOCALCIFEROL	1	1.1	0	0.0	1	0.5
ERYTHROMYCIN	3	3.2	2	2.0	5	2.6
FLUTICASONE PROPIONATE	3	3.2	1	1.0	4	2.1
GENTAMICIN SULFATE	0	0.0	1	1.0	1	0.5
GLYCEROL	1	1.1	0	0.0	1	0.5
GRISEOFULVIN	0	0.0	1	1.0	1	0.5
HYDROCORTISONE	2	2.1	2	2.0	4	2.1
HYDROCORTISONE ACETATE	1	1.1	0	0.0	1	0.5
HYDROCORTISONE VALERATE	0	0.0	1	1.0	1	0.5
LIDOCAINE	2	2.1	1	1.0	3	1.6
MOMETASONE FUROATE	1	1.1	0	0.0	1	0.5
MUPIROCIN	1	1.1	0	0.0	1	0.5

NOTE: Concomitant medications refer to all those started on or after randomisation baseline
or are on-going at randomisation baseline and who started before the last date of study medication

TABLE 13.12.2

Summary of Concomitant Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS :	77	81.1%	79	80.6%	156	80.8%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
NEOMYCIN SULFATE	2	2.1	0	0.0	2	1.0
PARABENS	0	0.0	1	1.0	1	0.5
PARACETAMOL	0	0.0	1	1.0	1	0.5
PHENOL, LIQUEFIED	1	1.1	0	0.0	1	0.5
POLYMYXIN B SULFATE	2	2.1	0	0.0	2	1.0
PRILOCAINE	1	1.1	1	1.0	2	1.0
PROMETHAZINE	0	0.0	1	1.0	1	0.5
RETINOL	1	1.1	0	0.0	1	0.5
SALICYLIC ACID	1	1.1	0	0.0	1	0.5
SODIUM CITRATE	1	1.1	0	0.0	1	0.5
SULFACETAMIDE SODIUM	1	1.1	0	0.0	1	0.5
TETRACYCLINE	0	0.0	2	2.0	2	1.0
TETRACYCLINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
TOCOPHEROL	0	0.0	1	1.0	1	0.5
TRETINOIN	2	2.1	0	0.0	2	1.0
TRIAMCINOLONE ACETONIDE	0	0.0	3	3.1	3	1.6
ZINC ACETATE	0	0.0	1	1.0	1	0.5
ZINC OXIDE	1	1.1	0	0.0	1	0.5
GU SYSTEM/SEX HORMONES:	3	3.2	4	4.1	7	3.6
CIPROFLOXACIN HYDROCHLORIDE	0	0.0	1	1.0	1	0.5
ECONAZOLE NITRATE	0	0.0	1	1.0	1	0.5
ETHINYLESTRADIOL	1	1.1	2	2.0	3	1.6
MESTRANOL	1	1.1	0	0.0	1	0.5
NORETHISTERONE	1	1.1	1	1.0	2	1.0
NORETHISTERONE ACETATE	0	0.0	1	1.0	1	0.5
NORGESTIMATE	1	1.1	0	0.0	1	0.5
OFLOXACIN	1	1.1	0	0.0	1	0.5

NOTE: Concomitant medications refer to all those started on or after randomisation baseline
or are on-going at randomisation baseline and who started before the last date of study medication

TABLE 13.12.2

Summary of Concomitant Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS	77	81.1%	79	80.6%	156	80.8%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
MUSCULO-SKELETAL:	28	29.5	28	28.6	56	29.0
EUCALYPTUS OIL	0	0.0	1	1.0	1	0.5
IBUPROFEN	28	29.5	25	25.5	53	27.5
INDOMETACIN	1	1.1	0	0.0	1	0.5
MENTHOL	1	1.1	2	2.0	3	1.6
NAPROXEN	0	0.0	1	1.0	1	0.5
NAPROXEN SODIUM	1	1.1	1	1.0	2	1.0
SALICYLIC ACID	1	1.1	0	0.0	1	0.5
RESPIRATORY:	42	44.2	32	32.7	74	38.3
ACETYLSALICYLIC ACID	0	0.0	1	1.0	1	0.5
AMINOACETIC ACID	1	1.1	0	0.0	1	0.5
BECLOMETASONE DIPROPIONATE	4	4.2	5	5.1	9	4.7
BENZALKONIUM CHLORIDE	1	1.1	0	0.0	1	0.5
BENZOCAINE	1	1.1	0	0.0	1	0.5
BROMPHENIRAMINE MALEATE	3	3.2	1	1.0	4	2.1
BUDESONIDE	1	1.1	2	2.0	3	1.6
CAFFEINE	0	0.0	1	1.0	1	0.5
CARBINOXAMINE MALEATE	0	0.0	1	1.0	1	0.5
CETIRIZINE HYDROCHLORIDE	2	2.1	0	0.0	2	1.0
CETYLPYRIDINIUM CHLORIDE	1	1.1	0	0.0	1	0.5
CHLORPHENAMINE MALEATE	10	10.5	6	6.1	16	8.3
CHLORPHENAMINE TANNATE	1	1.1	1	1.0	2	1.0
CLEMASTINE FUMARATE	1	1.1	1	1.0	2	1.0
CODEINE	1	1.1	0	0.0	1	0.5
COUGH COLD PREPARATIONS NOS	2	2.1	0	0.0	2	1.0
CROMOGLICATE SODIUM	0	0.0	2	2.0	2	1.0
DEXBROMPHENIRAMINE MALEATE	1	1.1	0	0.0	1	0.5
DEXTROMETHORPHAN	1	1.1	0	0.0	1	0.5

NOTE: Concomitant medications refer to all those started on or after randomisation baseline
or are on-going at randomisation baseline and who started before the last date of study medication

TABLE 13.12.2

Summary of Concomitant Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS	77	81.1%	79	80.6%	156	80.8%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
DEXTROMETHORPHAN HYDROBROMIDE	8	8.4	3	3.1	11	5.7
DIMENHYDRINATE	0	0.0	2	2.0	2	1.0
DIPHENHYDRAMINE	1	1.1	0	0.0	1	0.5
DIPHENHYDRAMINE CITRATE	0	0.0	1	1.0	1	0.5
DIPHENHYDRAMINE HYDROCHLORIDE	8	8.4	6	6.1	14	7.3
DOXYLAMINE SUCCINATE	0	0.0	2	2.0	2	1.0
ETHANOL	2	2.1	2	2.0	4	2.1
EUCALYPTUS OIL	0	0.0	1	1.0	1	0.5
FEXOFENADINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
FLUTICASONE PROPIONATE	3	3.2	1	1.0	4	2.1
GUAIFENESIN	6	6.3	3	3.1	9	4.7
HEXYLRESORCINOL	0	0.0	1	1.0	1	0.5
HYDROCODONE BITARTRATE	1	1.1	0	0.0	1	0.5
HYOSCINE METHONITRATE	2	2.1	0	0.0	2	1.0
LIDOCAINE	1	1.1	0	0.0	1	0.5
LORATADINE	6	6.3	3	3.1	9	4.7
MENTHOL	1	1.1	2	2.0	3	1.6
MEPYRAMINE MALEATE	1	1.1	1	1.0	2	1.0
MEPYRAMINE TANNATE	1	1.1	1	1.0	2	1.0
MOMETASONE FUROATE	1	1.1	0	0.0	1	0.5
OXYMETAZOLINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
PARACETAMOL	10	10.5	7	7.1	17	8.8
PHENIRAMINE MALEATE	1	1.1	1	1.0	2	1.0
PHENYLEPHRINE HYDROCHLORIDE	5	5.3	2	2.0	7	3.6
PHENYLEPHRINE TANNATE	1	1.1	1	1.0	2	1.0
PHENYLMERCURIC ACETATE	1	1.1	0	0.0	1	0.5
PHENYLPROPANOLAMINE HYDROCHLORIDE	6	6.3	6	6.1	12	6.2
PHENYLTOLOXAMINE CITRATE	0	0.0	1	1.0	1	0.5
PIRBUTEROL ACETATE	0	0.0	1	1.0	1	0.5

NOTE: Concomitant medications refer to all those started on or after randomisation baseline
or are on-going at randomisation baseline and who started before the last date of study medication

TABLE 13.12.2

Summary of Concomitant Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS :	77	81.1%	79	80.6%	156	80.8%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
PROMETHAZINE	0	0.0	1	1.0	1	0.5
PROMETHAZINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
PSEUDOEPHEDRINE	1	1.1	0	0.0	1	0.5
PSEUDOEPHEDRINE HYDROCHLORIDE	11	11.6	9	9.2	20	10.4
PSEUDOEPHEDRINE SULFATE	3	3.2	1	1.0	4	2.1
SALBUTAMOL	8	8.4	6	6.1	14	7.3
SORBITOL	1	1.1	0	0.0	1	0.5
THEOPHYLLINE	0	0.0	1	1.0	1	0.5
TRIAMCINOLONE ACETONIDE	0	0.0	3	3.1	3	1.6
SENSORY ORGANS:	13	13.7	12	12.2	25	13.0
ANTIBIOTIC EYE MEDICATION, NOS	1	1.1	0	0.0	1	0.5
BROMPHENIRAMINE MALEATE	1	1.1	1	1.0	2	1.0
CITRATE	1	1.1	0	0.0	1	0.5
CORTISONE	1	1.1	1	1.0	2	1.0
CROMOGLICATE SODIUM	0	0.0	2	2.0	2	1.0
EDETIC ACID	1	1.1	0	0.0	1	0.5
ERYTHROMYCIN	1	1.1	2	2.0	3	1.6
GENTAMICIN SULFATE	0	0.0	1	1.0	1	0.5
HYDROCORTISONE	2	2.1	2	2.0	4	2.1
HYDROCORTISONE ACETATE	1	1.1	0	0.0	1	0.5
INDOMETACIN	1	1.1	0	0.0	1	0.5
LIDOCAINE	1	1.1	0	0.0	1	0.5
OFLOXACIN	1	1.1	0	0.0	1	0.5
PHENYLPROPANOLAMINE HYDROCHLORIDE	1	1.1	1	1.0	2	1.0
POLYQUATERNIUM-1	1	1.1	0	0.0	1	0.5
SODIUM CHLORIDE	1	1.1	0	0.0	1	0.5
SULFACETAMIDE SODIUM	1	1.1	0	0.0	1	0.5
TETRACYCLINE	0	0.0	2	2.0	2	1.0

NOTE: Concomitant medications refer to all those started on or after randomisation baseline
or are on-going at randomisation baseline and who started before the last date of study medication

TABLE 13.12.2

Summary of Concomitant Medication
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH MEDICATIONS	77	81.1%	79	80.6%	156	80.8%
ATC CLASSIFICATION LEVEL 1 : GENERIC TERM	N	%	N	%	N	%
TETRACYCLINE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5
TRIAMCINOLONE ACETONIDE	0	0.0	3	3.1	3	1.6
SYSTEMIC HORMONAL:	7	7.4	10	10.2	17	8.8
CORTISONE	1	1.1	1	1.0	2	1.0
CORTISONE INJECTION	0	0.0	1	1.0	1	0.5
DESMOPRESSIN ACETATE	1	1.1	0	0.0	1	0.5
HYDROCORTISONE	2	2.1	2	2.0	4	2.1
HYDROCORTISONE ACETATE	1	1.1	0	0.0	1	0.5
HYDROCORTISONE VALERATE	0	0.0	1	1.0	1	0.5
LEVOTHYROXINE	0	0.0	1	1.0	1	0.5
LEVOTHYROXINE SODIUM	0	0.0	1	1.0	1	0.5
MELATONIN	1	1.1	0	0.0	1	0.5
SOMATREM	1	1.1	1	1.0	2	1.0
SOMATROPIN	0	0.0	1	1.0	1	0.5
TRIAMCINOLONE ACETONIDE	0	0.0	3	3.1	3	1.6
UNCLASSIFIABLE:	1	1.1	0	0.0	1	0.5
UNKNOWN MEDICATION	1	1.1	0	0.0	1	0.5
VARIOUS:	2	2.1	3	3.1	5	2.6
ECHINACEA EXTRACT	1	1.1	2	2.0	3	1.6
HYDRASTIS CANADENSIS	1	1.1	1	1.0	2	1.0
NALOXONE HYDROCHLORIDE	1	1.1	0	0.0	1	0.5

NOTE: Concomitant medications refer to all those started on or after randomisation baseline
or are on-going at randomisation baseline and who started before the last date of study medication

Table 13.13.1

Number of Patients (%) on Each Dose Level by Visit
Intention to Treat Population
Phase I: Open Label Treatment

	Daily Dose Level															
	10mg		20mg		30mg		40mg		50mg		60mg		Total	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Week 2	85	25.4	198	59.1	46	13.7	6	1.8					335	100.0
Week 4	36	11.5	130	41.5	112	35.8	32	10.2	3	1.0			313	100.0
Week 6	28	9.2	90	29.7	97	32.0	67	22.1	17	5.6	4	1.3	303	100.0
Week 8	25	8.7	64	22.2	87	30.2	54	18.8	35	12.2	23	8.0	288	100.0
Week 12	23	8.4	61	22.3	59	21.6	49	17.9	39	14.3	42	15.4	273	100.0
Week 16	19	7.9	52	21.5	60	24.8	39	16.1	29	12.0	43	17.8	242	100.0

Table 13.13.2

Number of Patients (%) on Each Dose Level by Treatment and Visit
Intention to Treat Population
Phase II: Randomised Treatment

Treatment Group: Paroxetine

	Daily Dose Level													
	10mg		20mg		30mg		40mg		50mg		60mg		Total Number of Pts	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Week 2	9	9.5	20	21.1	26	27.4	16	16.8	10	10.5	14	14.7	95	100.0
Week 4	9	11.3	15	18.8	21	26.3	11	13.8	10	12.5	14	17.5	80	100.0
Week 6	9	13.4	11	16.4	16	23.9	11	16.4	7	10.4	13	19.4	67	100.0
Week 8	9	14.5	10	16.1	15	24.2	8	12.9	7	11.3	13	21.0	62	100.0
Week 10	8	14.8	7	13.0	15	27.8	6	11.1	6	11.1	12	22.2	54	100.0
Week 12	7	14.0	7	14.0	14	28.0	5	10.0	6	12.0	11	22.0	50	100.0
Week 16	5	11.4	7	15.9	13	29.5	4	9.1	5	11.4	10	22.7	44	100.0

Table 13.13.2

Number of Patients (%) on Each Dose Level by Treatment and Visit
Intention to Treat Population
Phase II: Randomised Treatment

Treatment Group: Placebo

	Daily Dose Level													
	1		2		3		4		5		6		Total Number of Pts	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Week 2	8	8.2	25	25.5	22	22.4	15	15.3	12	12.2	16	16.3	98	100.0
Week 4	7	9.3	14	18.7	16	21.3	15	20.0	9	12.0	14	18.7	75	100.0
Week 6	5	9.1	12	21.8	11	20.0	8	14.5	9	16.4	10	18.2	55	100.0
Week 8	5	11.1	12	26.7	8	17.8	5	11.1	7	15.6	8	17.8	45	100.0
Week 10	4	10.5	10	26.3	5	13.2	5	13.2	7	18.4	7	18.4	38	100.0
Week 12	4	11.4	9	25.7	5	14.3	5	14.3	6	17.1	6	17.1	35	100.0
Week 16	4	12.1	9	27.3	4	12.1	5	15.2	6	18.2	5	15.2	33	100.0

Table 13.14.1

Summary of Maximum Dose Level (At any Point During Study)
Intention to Treat Population
Phase I: Open Label Treatment

		Maximum Daily Dose Level						
	Total Number of Patients	10mg	20mg	30mg	40mg	50mg	60mg
Number	335	33	67	88	59	40	48
%	100.0	9.9	20.0	26.3	17.6	11.9	14.3

Table 13.14.2

Summary of Maximum Dose Level by Treatment (At any Point During Study)
Intention to Treat Population
Phase II: Randomised Treatment

	Paroxetine							Placebo						
	Maximum Daily Dose Level							Maximum Daily Dose Level						
	Total Number of Pts	10mg	20mg	30mg	40mg	50mg	60mg	Total Number of Pts	1	2	3	4	5	6
Number	95	9	20	26	16	10	14	98	8	25	22	15	12	16
%	100.0	9.5	21.1	27.4	16.8	10.5	14.7	100.0	8.2	25.5	22.4	15.3	12.2	16.3

Table 13.15.1

Number (%) of Compliant* Patients during the Open Label Phase of the Study by Visit
Intention to Treat Population
Phase I: Open Label Treatment

	Compliant					
	Yes		No		All	
	N	%	N	%	N	%
Week 2	328	99.4	2	0.6	330	100.0
Week 4	305	99.3	2	0.7	307	100.0
Week 6	290	99.3	2	0.7	292	100.0
Week 8	275	99.3	2	0.7	277	100.0
Week 12	262	99.2	2	0.8	264	100.0
Week 16	232	97.9	5	2.1	237	100.0

* Compliant = no break in study medication of >= 5 consecutive days

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]CMP13A.SAS (03MAR99 13:47)

Table 13.15.2

Number (%) of Compliant* Patients during the Treatment Phase of the Study by Visit
Intention to Treat Population
Phase II: Randomised Treatment

	Compliant																	
	Paroxetine						Placebo						Total					
	Yes		No		All		Yes		No		All		Yes		No		All	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Week 2	91	98.9	1	1.1	92	100.0	96	99.0	1	1.0	97	100.0	187	98.9	2	1.1	189	100.0
Week 4	76	96.2	3	3.8	79	100.0	74	98.7	1	1.3	75	100.0	150	97.4	4	2.6	154	100.0
Week 6	66	100.0			66	100.0	49	96.1	2	3.9	51	100.0	115	98.3	2	1.7	117	100.0
Week 8	58	100.0			58	100.0	42	100.0			42	100.0	100	100.0			100	100.0
Week 10	49	94.2	3	5.8	52	100.0	35	97.2	1	2.8	36	100.0	84	95.5	4	4.5	88	100.0
Week 12	49	100.0			49	100.0	35	100.0			35	100.0	84	100.0			84	100.0
Week 16	40	97.6	1	2.4	41	100.0	30	100.0			30	100.0	70	98.6	1	1.4	71	100.0

* Compliant = no break in study medication of >= 5 consecutive days

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]CMP13B.SAS (18FEB99 17:49)

Table 13.16.1

Number (%) of Compliant Patients during the Open Label Phase of the Study
Intention to Treat Population
Phase I: Open Label Treatment

	N	%
Compliant	316	95.5
Non-Compliant	15	4.5
All	331	100.0

Compliant = no break in study medication of >= 5 consecutive days

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]CMP13A.SAS (03MAR99 13:47)

Table 13.16.2

Number (%) of Compliant Patients during the Treatment Phase of the Study
Intention to Treat Population
Phase II: Randomised Treatment

	Paroxetine		Placebo		Total	
	N	%	N	%	N	%
Compliant	86	91.5	93	94.9	179	93.2
Non-Compliant	8	8.5	5	5.1	13	6.8
All	94	100.0	98	100.0	192	100.0

Compliant = no break in study medication of >= 5 consecutive days

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]CMP13B.SAS (18FEB99 17:49)

Table 13.31

Number of Patient Withdrawals by Reason for Concluding Study During the Screening Phase
Screening Population Only

	N
Number of Patients	88
REASON	
Baseline adverse experience	1
Does not meet inclusion/exclusion criteria	59
Protocol Deviation, including Non-Compliance	7
Lost to Follow-up	4
Other Reason	17
Number of Withdrawals	88

Table 13.32.1

Number of Patient Withdrawals by Reason During Treatment Phase
Intention to Treat Population
Phase I: Open Label Treatment

	Week 2	Week 4	Week 6	Week 8	Week 12	Week 16	Post Week 16	Total
Number of Patients	335	313	303	288	273	244	196	194
REASON								
Does not Meet Response Criteria						19	1	20
Adverse Experience	10	5	6	2	11	6		40
Lack of Efficacy			1	4	10	4		19
Deviation from Protocol	3	4	4	2	4	5		22
Lost to Follow-up	4		1	2	1			8
Other Reason	5	1	3	5	3	14	1	32
Number of Withdrawals	22	10	15	15	29	48	2	141

4 patients who entered the Open Label Treatment phase had screening and baseline assessments only therefore are excluded from the Intention to Treat population

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]WITH13_3.SAS (15MAR99 15:05)

Table 13.32.2

Number of Patient Withdrawals by Reason During Treatment Phase
Intention to Treat Population
Phase II: Randomised Treatment

Treatment Group: Paroxetine

	Week 2	Week 4	Week 6	Week 8	Week 10	Week 12	Week 16	Total
Number of Patients	95	80	67	62	54	50	44	42
REASON								
Adverse Experience	4	1	1	1		1		8
Lack of Efficacy	9	10	3	5	2	2	2	33
Deviation from Protocol		1		1	2	1		5
Lost to Follow-up	1					2		3
Other Reason	1	1	1	1				4
Number of Withdrawals	15	13	5	8	4	6	2	53

Table 13.32.2

Number of Patient Withdrawals by Reason During Treatment Phase
Intention to Treat Population
Phase II: Randomised Treatment

Treatment Group: Placebo

	Week 2	Week 4	Week 6	Week 8	Week 10	Week 12	Week 16	Total
Number of Patients	98	75	55	45	38	35	33	33
REASON								
Adverse Experience	7	2	1		1			11
Lack of Efficacy	14	17	8	3	1	2		45
Deviation from Protocol			1	1	1			3
Lost to Follow-up								
Other Reason	2	1		3				6
Number of Withdrawals	23	20	10	7	3	2		65

Table 13.33.1

Cumulative Number (%) of Patients Remaining and Withdrawing from the Study by Week
Intention to Treat Population
Phase I: Open Label Treatment

		N	%
Week 2	Still in Study	313	93.4
	Withdrawn	22	6.6
	Total	335	100.0
Week 4	Still in Study	303	96.8
	Withdrawn	10	3.2
	Total	313	100.0
Week 6	Still in Study	288	95.0
	Withdrawn	15	5.0
	Total	303	100.0
Week 8	Still in Study	273	94.8
	Withdrawn	15	5.2
	Total	288	100.0
Week 12	Still in Study	244	89.4
	Withdrawn	29	10.6
	Total	273	100.0
Week 16	Still in Study	196	80.3
	Withdrawn	48	19.7

(CONTINUED)

4 patients who entered the Open Label Treatment phase had screening and baseline assessments only therefore are excluded from the Intention to Treat population

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]WITH13_3.SAS (15MAR99 15:05)

Table 13.33.1

Cumulative Number (%) of Patients Remaining and Withdrawing from the Study by Week
Intention to Treat Population
Phase I: Open Label Treatment

		N	%
Week 16	Total	244	100.0
Post Week 16	Still in Study	194	99.0
	Withdrawn	2	1.0
	Total	196	100.0

4 patients who entered the Open Label Treatment phase had screening and baseline assessments only therefore are excluded from the Intention to Treat population

Table 13.33.2

Cumulative Number (%) of Patients Remaining and Withdrawing from the Study by Week
Intention to Treat Population
Phase II: Randomised Treatment

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 2	Still in Study	80	84.2	75	76.5	155	80.3
	Withdrawn	15	15.8	23	23.5	38	19.7
	Total	95	100.0	98	100.0	193	100.0
Week 4	Still in Study	67	83.8	55	73.3	122	78.7
	Withdrawn	13	16.3	20	26.7	33	21.3
	Total	80	100.0	75	100.0	155	100.0
Week 6	Still in Study	62	92.5	45	81.8	107	87.7
	Withdrawn	5	7.5	10	18.2	15	12.3
	Total	67	100.0	55	100.0	122	100.0
Week 8	Still in Study	54	87.1	38	84.4	92	86.0
	Withdrawn	8	12.9	7	15.6	15	14.0
	Total	62	100.0	45	100.0	107	100.0
Week 10	Still in Study	50	92.6	35	92.1	85	92.4
	Withdrawn	4	7.4	3	7.9	7	7.6
	Total	54	100.0	38	100.0	92	100.0
Week 12	Still in Study	44	88.0	33	94.3	77	90.6

(CONTINUED)

Table 13.33.2

Cumulative Number (%) of Patients Remaining and Withdrawing from the Study by Week
Intention to Treat Population
Phase II: Randomised Treatment

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 12	Withdrawn	6	12.0	2	5.7	8	9.4
	Total	50	100.0	35	100.0	85	100.0
Week 16	Still in Study	42	95.5	33	100.0	75	97.4
	Withdrawn	2	4.5			2	2.6
	Total	44	100.0	33	100.0	77	100.0
Post Week 16	Still in Study	42	100.0	33	100.0	75	100.0
	Withdrawn						
	Total	42	100.0	33	100.0	75	100.0

Paroxetine - Protocol: 453

TABLE 13.51.1b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH CONDITIONS :	215	64.2%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
ANOMALIES:	11	3.3
CONG ANOM, CIRC SYST	1	0.3
CONG ANOM, GI	2	0.6
CONG ANOM, GU	5	1.5
CONG ANOM, HEART	1	0.3
CONG ANOM, INTEGUMENT	1	0.3
CONGEN ANOM, HEAD/NECK	1	0.3
BLOOD/BLOOD FORMING ORGAN DIS:	2	0.6
ANEMIA, OTHER	1	0.3
LEUKOPENIA	1	0.3
CIRCULATORY SYST:	7	2.1
ARREST, CARDIAC	1	0.3
ARRHYTHMIA	1	0.3
BRADYCARDIA	1	0.3
HEMORRHAGE, INTRACRANIAL	1	0.3
MITRAL VALVE DISORD	2	0.6
RHEUMATIC FEVER	1	0.3
DIGESTIVE SYST:	29	8.7
BILIARY DISORD, OTHER	1	0.3
CONSTIPATION	11	3.3
DENTOFACIAL ANOM	1	0.3
DYSPEPSIA	2	0.6
ESOPHAGITIS	2	0.6
ESOPHAGUS DIS	1	0.3
HERNIA, ABDOMINAL	7	2.1
STOMACH/DUODENUM DISORD	1	0.3
TEETH DISORD	2	0.6
ULCER, GASTRIC	1	0.3

TABLE 13.51.1b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH CONDITIONS :	215	64.2%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
ENDOCR/METAB/IMMUNITY DISORD:	15	4.5
CHOLEST/TRIGLYCERIDE, ELEVATED	1	0.3
HYPOGLYCEMIA	1	0.3
HYPOTHYROIDISM	1	0.3
IMMUNE MECH DISORD	1	0.3
OBESITY	11	3.3
EXT CAUSES OF INJURY/POISONING:	21	6.3
ACCIDENT/ENVIRON CAUSE	1	0.3
ACCIDENT/FALL	3	0.9
ACCIDENT/MOTOR VEHICLE	1	0.3
ACCIDENT/PEDAL CYCLE	1	0.3
ADVERSE EFF/ANTI-INFECT	2	0.6
ADVERSE EFF/ANTIBIOTIC	13	3.9
ADVERSE EFF/PSYCHOTROPICS	1	0.3
ADVERSE EFF/RESP AGENT	1	0.3
ADVERSE EFF/VACCINE	1	0.3
FAMILY/PERSONAL HISTORY:	1	0.3
DEVELOPMENT, CHILD	1	0.3
GENITOURINARY SYST DIS:	10	3.0
CYSTITIS	1	0.3
GENITAL FEMALE DISORD, OTHER	1	0.3
GENITAL MALE DISORD, OTHER	3	0.9
INFLAM PELVIC DIS	1	0.3
RENAL FAILURE	1	0.3
URINARY TRACT INFECTION	3	0.9
INFECTIOUS/PARASITIC DIS:	17	5.1
BACT DIS, OTHER	4	1.2
INFECTION, BACTERIAL	4	1.2

TABLE 13.51.1b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	335	100.0%
PATIENTS WITH CONDITIONS	215	64.2%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
INTEST INFECT DIS	2	0.6
POLIO AND CNS DIS, VIRAL	1	0.3
VIRAL DIS/EXANTHEM	4	1.2
VIRUS/CHLAMYD DIS, OTHER	3	0.9
INJURY/POISONING:	44	13.1
ADVERSE EFF/OTHER	1	0.3
ALLERGIC REACTION, FOOD	2	0.6
ALLERGY, NEC	9	2.7
FRACTURE, BONE UNSPEC	1	0.3
FRACTURE, LOWER LIMB	3	0.9
FRACTURE, NECK/TRUNK	3	0.9
FRACTURE, SKULL	1	0.3
FRACTURE, UPPER LIMB	17	5.1
INJURY, INTRACRANIAL	5	1.5
INJURY, SUPERFICIAL	1	0.3
OPEN WOUND	3	0.9
SPRAINS/STRAINS	2	0.6
TRAUMA/INJURIES, UNSPEC	1	0.3
MENTAL DISORD:	15	4.5
DEPRESSION	2	0.6
DRUG DEPEND	1	0.3
MENTAL DEVELOP DISORD	4	1.2
NEUROSES	1	0.3
POSTCONCUSSION SYNDROME	1	0.3
PSYCHOGENIC PHYSIOL DYSFUNC	4	1.2
PSYCHOSES, DRUG INDUCED	1	0.3
PSYCHOSES, PARANOID	1	0.3
STRESS REACTION	1	0.3
TICS	2	0.6

TABLE 13.51.1b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH CONDITIONS :	215	64.2%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
MUSCULOSKEL/CONNECT TISSUE DIS:	18	5.4
ARTHRITIS, PYOGENIC	1	0.3
ARTHRITIS, RHEUMATOID	1	0.3
ARTHROPATHY	1	0.3
BONE/CARTIL DISORD, OTHER	1	0.3
CRAMP, LIMB	1	0.3
DEFORMITY, ACQUIRED	2	0.6
JOINT DISORD, OTHER	1	0.3
MYALGIA	7	2.1
PAIN, JOINT	1	0.3
PAIN, LIMB	3	0.9
SPASM, MUSCLE	3	0.9
NEOPLASMS:	7	2.1
NEOPLASM, UNSPEC	1	0.3
NEOPLASMS BENIGN	6	1.8
NERVOUS SYST/SENSE ORGAN DIS:	46	13.7
AUT NERV SYST DISORD	1	0.3
CONJUNCTIVAL DISORD	1	0.3
EAR/MASTOID DISORD	5	1.5
EPILEPSY	1	0.3
EYE DISORD, OTHER	4	1.2
HEARING LOSS	1	0.3
HEMIPARESIS	1	0.3
MENINGITIS	4	1.2
MIGRAINE	4	1.2
OTITIS MEDIA	21	6.3
VISUAL DISTURB	6	1.8
OPERATIONS:	72	21.5
OPERATION, APPENDIX	4	1.2

TABLE 13.51.1b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	335	100.0%
PATIENTS WITH CONDITIONS	215	64.2%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
OPERATION, BONE/JOINT	8	2.4
OPERATION, EAR	21	6.3
OPERATION, EYE	7	2.1
OPERATION, HERNIA REPAIR	4	1.2
OPERATION, INTEST	2	0.6
OPERATION, MALE GENITAL	6	1.8
OPERATION, NOSE/MOUTH	30	9.0
OPERATION, OTHER MUSCULOSKEL	1	0.3
OPERATION, OTHER URINARY	3	0.9
OPERATION, OTHER VESSELS	1	0.3
OPERATION, SKIN/SUBCUT	7	2.1
PERINATAL COND:	3	0.9
CONDITIONS, PERINATAL	3	0.9
PROCEDURES:	4	1.2
EVALUATION, DX EXAM	1	0.3
PROCEDURE, EYE/EAR	2	0.6
RADIOLOGY, DIAGNOSTIC	1	0.3
THERAPY, REHAB	1	0.3
RESPIRATORY SYST DIS:	83	24.8
ASTHMA	24	7.2
BRONCHITIS, OTHER	1	0.3
INFECTION, RESP	2	0.6
LARYNGITIS/TRACH, ACUTE	2	0.6
NASAL SEPTUM DEVIATED	1	0.3
NASOPHARYNGITIS, ACUTE	6	1.8
PHARYNGITIS, ACUTE	4	1.2
PHARYNGITIS, CHRONIC	1	0.3
PNEUMONIA, OTHER	7	2.1
RESP DIS, OTHER	1	0.3

TABLE 13.51.1b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	335	100.0%
PATIENTS WITH CONDITIONS	215	64.2%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
RHINITIS, ALLERGIC	27	8.1
RHINITIS,NOS	1	0.3
SINUSITIS, OTHER	1	0.3
SINUSITIS,NOS	9	2.7
TONSILLITIS, ACUTE	2	0.6
UPPER RESP DISORD, OTHER	19	5.7
UPPER RESP INFECT, ACUTE	2	0.6
SIGNS,SYMPTOMS,ILL-DEFINED CON:	83	24.8
ANOREXIA	2	0.6
APNEA	2	0.6
CARDIAC MURMURS	2	0.6
CONVULSIONS	4	1.2
COUGH	3	0.9
DEVELOPMENT, ABN	4	1.2
DIARRHEA	2	0.6
DISTURBANCE, SPEECH	1	0.3
DIZZINESS AND GIDDINESS	2	0.6
DYSPNEA, OTHER	3	0.9
EPISTAXIS	2	0.6
FLATULENCE	1	0.3
FLUSHING	2	0.6
HEADACHE	47	14.0
HYPERHIDROSIS	2	0.6
HYPOESTHESIA	1	0.3
INCONTINENCE, URINARY	8	2.4
INSOMNIA	7	2.1
JAUNDICE, UNSPEC	3	0.9
LYMPHADENOPATHY	1	0.3
MALAISE AND FATIGUE	3	0.9
MENTAL STATUS, IMPAIRED	1	0.3
NAUSEA	4	1.2

TABLE 13.51.1b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH CONDITIONS :	215	64.2%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
NUTRIT, METAB SYMPTOMS	1	0.3
PAIN UNSP, CHEST	4	1.2
PAIN, ABDOMINO-PELVIC	18	5.4
PAIN, GENERAL	1	0.3
POLYURIA	1	0.3
RASH/OTHER SKIN ERUPTION	3	0.9
RBC'S, ABN	1	0.3
SYNCOPE AND COLLAPSE	2	0.6
THYROID FUNCTION, ABN	1	0.3
SKIN/SUBCUTANEOUS TISSUE DIS:	29	8.7
CELLULITIS/ABSCESS	2	0.6
IMPETIGO	1	0.3
INFLAM SKIN/SUBCUT	8	2.4
PRURITUS DISORD, UNSPEC	1	0.3
SCARRING	3	0.9
SKIN INFECT, LOCAL, OTHER	2	0.6
SKIN/SUBCUT DISORD, OTHER	12	3.6

TABLE 13.51.1c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Per Protocol Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	164	100.0%
PATIENTS WITH CONDITIONS :	106	64.6%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
ANOMALIES:	10	6.1
CONG ANOM, CIRC SYST	1	0.6
CONG ANOM, GI	2	1.2
CONG ANOM, GU	4	2.4
CONG ANOM, HEART	1	0.6
CONG ANOM, INTEGUMENT	1	0.6
CONGEN ANOM, HEAD/NECK	1	0.6
BLOOD/BLOOD FORMING ORGAN DIS:	1	0.6
LEUKOPENIA	1	0.6
CIRCULATORY SYST:	5	3.0
ARRHYTHMIA	1	0.6
BRADYCARDIA	1	0.6
HEMORRHAGE, INTRACRANIAL	1	0.6
MITRAL VALVE DISORD	2	1.2
DIGESTIVE SYST:	14	8.5
CONSTIPATION	6	3.7
DYSPEPSIA	1	0.6
ESOPHAGITIS	1	0.6
ESOPHAGUS DIS	1	0.6
HERNIA, ABDOMINAL	4	2.4
TEETH DISORD	1	0.6
ENDOCR/METAB/IMMUNITY DISORD:	7	4.3
CHOLEST/TRIGLYCERIDE, ELEVATED	1	0.6
HYPOTHYROIDISM	1	0.6
OBESITY	5	3.0
EXT CAUSES OF INJURY/POISONING:	11	6.7
ACCIDENT/ENVIRON CAUSE	1	0.6

TABLE 13.51.1c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Per Protocol Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	164	100.0%
PATIENTS WITH CONDITIONS :	106	64.6%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
ACCIDENT/FALL	2	1.2
ACCIDENT/MOTOR VEHICLE	1	0.6
ADVERSE EFF/ANTI-INFECT	1	0.6
ADVERSE EFF/ANTIBIOTIC	6	3.7
ADVERSE EFF/PSYCHOTROPICS	1	0.6
FAMILY/PERSONAL HISTORY:	1	0.6
DEVELOPMENT, CHILD	1	0.6
GENITOURINARY SYST DIS:	6	3.7
CYSTITIS	1	0.6
GENITAL FEMALE DISORD, OTHER	1	0.6
GENITAL MALE DISORD, OTHER	2	1.2
RENAL FAILURE	1	0.6
URINARY TRACT INFECTION	1	0.6
INFECTIOUS/PARASITIC DIS:	6	3.7
INFECTION, BACTERIAL	3	1.8
POLIO AND CNS DIS, VIRAL	1	0.6
VIRAL DIS/EXANTHEM	1	0.6
VIRUS/CHLAMYD DIS, OTHER	1	0.6
INJURY/POISONING:	21	12.8
ADVERSE EFF/OTHER	1	0.6
ALLERGIC REACTION, FOOD	1	0.6
ALLERGY, NEC	5	3.0
FRACTURE, BONE UNSPEC	1	0.6
FRACTURE, NECK/TRUNK	1	0.6
FRACTURE, UPPER LIMB	9	5.5
INJURY, INTRACRANIAL	2	1.2
OPEN WOUND	1	0.6
TRAUMA/INJURIES, UNSPEC	1	0.6

TABLE 13.51.1c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Per Protocol Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	164	100.0%
PATIENTS WITH CONDITIONS	106	64.6%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
MENTAL DISORD:	10	6.1
DEPRESSION	1	0.6
DRUG DEPEND	1	0.6
MENTAL DEVELOP DISORD	3	1.8
NEUROSES	1	0.6
PSYCHOGENIC PHYSIOL DYSFUNC	3	1.8
PSYCHOSES, DRUG INDUCED	1	0.6
PSYCHOSES, PARANOID	1	0.6
STRESS REACTION	1	0.6
TICS	1	0.6
MUSCULOSKEL/CONNECT TISSUE DIS:	11	6.7
ARTHRITIS, PYOGENIC	1	0.6
ARTHROPATHY	1	0.6
BONE/CARTIL DISORD, OTHER	1	0.6
DEFORMITY, ACQUIRED	2	1.2
JOINT DISORD, OTHER	1	0.6
MYALGIA	3	1.8
PAIN, JOINT	1	0.6
PAIN, LIMB	3	1.8
SPASM, MUSCLE	2	1.2
NEOPLASMS:	3	1.8
NEOPLASMS BENIGN	3	1.8
NERVOUS SYST/SENSE ORGAN DIS:	23	14.0
CONJUNCTIVAL DISORD	1	0.6
EAR/MASTOID DISORD	3	1.8
EYE DISORD, OTHER	2	1.2
HEMIPARESIS	1	0.6
MENINGITIS	4	2.4
MIGRAINE	2	1.2

TABLE 13.51.1c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Per Protocol Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	164	100.0%
PATIENTS WITH CONDITIONS :	106	64.6%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
OTITIS MEDIA	8	4.9
VISUAL DISTURB	4	2.4
OPERATIONS:	35	21.3
OPERATION, APPENDIX	2	1.2
OPERATION, BONE/JOINT	4	2.4
OPERATION, EAR	9	5.5
OPERATION, EYE	2	1.2
OPERATION, HERNIA REPAIR	3	1.8
OPERATION, INTEST	1	0.6
OPERATION, MALE GENITAL	6	3.7
OPERATION, NOSE/MOUTH	14	8.5
OPERATION, OTHER MUSCULOSKEL	1	0.6
OPERATION, OTHER VESSELS	1	0.6
OPERATION, SKIN/SUBCUT	4	2.4
PERINATAL COND:	1	0.6
CONDITIONS, PERINATAL	1	0.6
PROCEDURES:	2	1.2
PROCEDURE, EYE/EAR	1	0.6
RADIOLOGY, DIAGNOSTIC	1	0.6
THERAPY, REHAB	1	0.6
RESPIRATORY SYST DIS:	41	25.0
ASTHMA	10	6.1
INFECTION, RESP	1	0.6
NASOPHARYNGITIS, ACUTE	2	1.2
PHARYNGITIS, ACUTE	2	1.2
PNEUMONIA, OTHER	2	1.2
RESP DIS, OTHER	1	0.6
RHINITIS, ALLERGIC	17	10.4

TABLE 13.51.1c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Per Protocol Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	164	100.0%
PATIENTS WITH CONDITIONS :	106	64.6%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
RHINITIS,NOS	1	0.6
SINUSITIS, OTHER	1	0.6
SINUSITIS,NOS	6	3.7
TONSILLITIS, ACUTE	1	0.6
UPPER RESP DISORD, OTHER	11	6.7
SIGNS,SYMPTOMS,ILL-DEFINED CON:	44	26.8
ANOREXIA	1	0.6
APNEA	1	0.6
CARDIAC MURMURS	2	1.2
CONVULSIONS	2	1.2
COUGH	1	0.6
DEVELOPMENT, ABN	2	1.2
DIARRHEA	1	0.6
DISTURBANCE, SPEECH	1	0.6
DIZZINESS AND GIDDINESS	2	1.2
DYSPNEA, OTHER	3	1.8
FLATULENCE	1	0.6
FLUSHING	2	1.2
HEADACHE	28	17.1
HYPERHIDROSIS	2	1.2
HYPOESTHESIA	1	0.6
INCONTINENCE, URINARY	4	2.4
INSOMNIA	1	0.6
JAUNDICE, UNSPEC	1	0.6
MALAISE AND FATIGUE	2	1.2
NAUSEA	3	1.8
PAIN UNSP, CHEST	2	1.2
PAIN, ABDOMINO-PELVIC	12	7.3
PAIN, GENERAL	1	0.6
RASH/OTHER SKIN ERUPTION	2	1.2
SYNCOPE AND COLLAPSE	2	1.2

TABLE 13.51.1c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Per Protocol Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	164	100.0%
PATIENTS WITH CONDITIONS :	106	64.6%
DISEASE CODE LEVEL 1 : PREFERRED TERM	**N**	**%**
THYROID FUNCTION, ABN	1	0.6
SKIN/SUBCUTANEOUS TISSUE DIS:	16	9.8
CELLULITIS/ABSCESS	2	1.2
IMPETIGO	1	0.6
INFLAM SKIN/SUBCUT	4	2.4
PRURITUS DISORD, UNSPEC	1	0.6
SCARRING	2	1.2
SKIN/SUBCUT DISORD, OTHER	6	3.7

TABLE 13.51.2b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH CONDITIONS :	60	63.2%	64	65.3%	124	64.2%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
ANOMALIES:	3	3.2	7	7.1	10	5.2
CONG ANOM, CIRC SYST	0	0.0	1	1.0	1	0.5
CONG ANOM, GI	1	1.1	1	1.0	2	1.0
CONG ANOM, GU	0	0.0	4	4.1	4	2.1
CONG ANOM, HEART	1	1.1	0	0.0	1	0.5
CONG ANOM, INTEGUMENT	1	1.1	0	0.0	1	0.5
CONGEN ANOM, HEAD/NECK	0	0.0	1	1.0	1	0.5
BLOOD/BLOOD FORMING ORGAN DIS:	2	2.1	0	0.0	2	1.0
ANEMIA, OTHER	1	1.1	0	0.0	1	0.5
LEUKOPENIA	1	1.1	0	0.0	1	0.5
CIRCULATORY SYST:	2	2.1	3	3.1	5	2.6
ARRHYTHMIA	1	1.1	0	0.0	1	0.5
BRADYCARDIA	0	0.0	1	1.0	1	0.5
HEMORRHAGE, INTRACRANIAL	0	0.0	1	1.0	1	0.5
MITRAL VALVE DISORD	1	1.1	1	1.0	2	1.0
DIGESTIVE SYST:	9	9.5	9	9.2	18	9.3
CONSTIPATION	3	3.2	4	4.1	7	3.6
DYSPEPSIA	0	0.0	1	1.0	1	0.5
ESOPHAGITIS	1	1.1	0	0.0	1	0.5
ESOPHAGUS DIS	1	1.1	0	0.0	1	0.5
HERNIA, ABDOMINAL	3	3.2	2	2.0	5	2.6
STOMACH/DUODENUM DISORD	0	0.0	1	1.0	1	0.5
TEETH DISORD	1	1.1	1	1.0	2	1.0
ENDOCR/METAB/IMMUNITY DISORD:	6	6.3	3	3.1	9	4.7
CHOLEST/TRIGLYCERIDE, ELEVATED	0	0.0	1	1.0	1	0.5
HYPOTHYROIDISM	1	1.1	0	0.0	1	0.5
IMMUNE MECH DISORD	1	1.1	0	0.0	1	0.5
OBESITY	4	4.2	2	2.0	6	3.1

TABLE 13.51.2b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH CONDITIONS	60	63.2%	64	65.3%	124	64.2%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
EXT CAUSES OF INJURY/POISONING:	1	1.1	11	11.2	12	6.2
ACCIDENT/ENVIRON CAUSE	0	0.0	1	1.0	1	0.5
ACCIDENT/FALL	0	0.0	2	2.0	2	1.0
ACCIDENT/MOTOR VEHICLE	0	0.0	1	1.0	1	0.5
ADVERSE EFF/ANTI-INFECT	0	0.0	1	1.0	1	0.5
ADVERSE EFF/ANTIBIOTIC	1	1.1	6	6.1	7	3.6
ADVERSE EFF/PSYCHOTROPICS	0	0.0	1	1.0	1	0.5
FAMILY/PERSONAL HISTORY:	1	1.1	0	0.0	1	0.5
DEVELOPMENT, CHILD	1	1.1	0	0.0	1	0.5
GENITOURINARY SYST DIS:	4	4.2	3	3.1	7	3.6
CYSTITIS	0	0.0	1	1.0	1	0.5
GENITAL FEMALE DISORD, OTHER	0	0.0	1	1.0	1	0.5
GENITAL MALE DISORD, OTHER	2	2.1	0	0.0	2	1.0
RENAL FAILURE	1	1.1	0	0.0	1	0.5
URINARY TRACT INFECTION	1	1.1	1	1.0	2	1.0
INFECTIOUS/PARASITIC DIS:	3	3.2	5	5.1	8	4.1
BACT DIS, OTHER	1	1.1	0	0.0	1	0.5
INFECTION, BACTERIAL	1	1.1	3	3.1	4	2.1
POLIO AND CNS DIS, VIRAL	1	1.1	0	0.0	1	0.5
VIRAL DIS/EXANTHEM	0	0.0	1	1.0	1	0.5
VIRUS/CHLAMYD DIS, OTHER	0	0.0	2	2.0	2	1.0
INJURY/POISONING:	17	17.9	9	9.2	26	13.5
ADVERSE EFF/OTHER	1	1.1	0	0.0	1	0.5
ALLERGIC REACTION, FOOD	1	1.1	0	0.0	1	0.5
ALLERGY, NEC	4	4.2	2	2.0	6	3.1
FRACTURE, BONE UNSPEC	0	0.0	1	1.0	1	0.5
FRACTURE, LOWER LIMB	1	1.1	0	0.0	1	0.5
FRACTURE, NECK/TRUNK	1	1.1	1	1.0	2	1.0

TABLE 13.51.2b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH CONDITIONS :	60	63.2%	64	65.3%	124	64.2%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
FRACTURE, SKULL	1	1.1	0	0.0	1	0.5
FRACTURE, UPPER LIMB	7	7.4	5	5.1	12	6.2
INJURY, INTRACRANIAL	1	1.1	1	1.0	2	1.0
OPEN WOUND	2	2.1	0	0.0	2	1.0
TRAUMA/INJURIES, UNSPEC	1	1.1	0	0.0	1	0.5
MENTAL DISORD:	3	3.2	7	7.1	10	5.2
DEPRESSION	0	0.0	1	1.0	1	0.5
DRUG DEPEND	0	0.0	1	1.0	1	0.5
MENTAL DEVELOP DISORD	1	1.1	2	2.0	3	1.6
NEUROSES	0	0.0	1	1.0	1	0.5
PSYCHOGENIC PHYSIOL DYSFUNC	2	2.1	1	1.0	3	1.6
PSYCHOSES, DRUG INDUCED	0	0.0	1	1.0	1	0.5
PSYCHOSES, PARANOID	1	1.1	0	0.0	1	0.5
STRESS REACTION	0	0.0	1	1.0	1	0.5
TICS	1	1.1	0	0.0	1	0.5
MUSCULOSKEL/CONNECT TISSUE DIS:	6	6.3	5	5.1	11	5.7
ARTHRITIS, PYOGENIC	1	1.1	0	0.0	1	0.5
ARTHROPATHY	1	1.1	0	0.0	1	0.5
BONE/CARTIL DISORD, OTHER	1	1.1	0	0.0	1	0.5
DEFORMITY, ACQUIRED	1	1.1	1	1.0	2	1.0
JOINT DISORD, OTHER	1	1.1	0	0.0	1	0.5
MYALGIA	1	1.1	2	2.0	3	1.6
PAIN, JOINT	1	1.1	0	0.0	1	0.5
PAIN, LIMB	2	2.1	1	1.0	3	1.6
SPASM, MUSCLE	0	0.0	2	2.0	2	1.0
NEOPLASMS:	4	4.2	0	0.0	4	2.1
NEOPLASM, UNSPEC	1	1.1	0	0.0	1	0.5
NEOPLASMS BENIGN	3	3.2	0	0.0	3	1.6

TABLE 13.51.2b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH CONDITIONS	60	63.2%	64	65.3%	124	64.2%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
NERVOUS SYST/SENSE ORGAN DIS:	14	14.7	16	16.3	30	15.5
AUT NERV SYST DISORD	1	1.1	0	0.0	1	0.5
CONJUNCTIVAL DISORD	0	0.0	1	1.0	1	0.5
EAR/MASTOID DISORD	2	2.1	1	1.0	3	1.6
EPILEPSY	1	1.1	0	0.0	1	0.5
EYE DISORD, OTHER	0	0.0	2	2.0	2	1.0
HEMIPARESIS	0	0.0	1	1.0	1	0.5
MENINGITIS	3	3.2	1	1.0	4	2.1
MIGRAINE	0	0.0	2	2.0	2	1.0
OTITIS MEDIA	6	6.3	6	6.1	12	6.2
VISUAL DISTURB	2	2.1	3	3.1	5	2.6
OPERATIONS:	25	26.3	18	18.4	43	22.3
OPERATION, APPENDIX	0	0.0	2	2.0	2	1.0
OPERATION, BONE/JOINT	4	4.2	1	1.0	5	2.6
OPERATION, EAR	8	8.4	3	3.1	11	5.7
OPERATION, EYE	0	0.0	3	3.1	3	1.6
OPERATION, HERNIA REPAIR	2	2.1	2	2.0	4	2.1
OPERATION, INTEST	1	1.1	0	0.0	1	0.5
OPERATION, MALE GENITAL	2	2.1	4	4.1	6	3.1
OPERATION, NOSE/MOUTH	10	10.5	9	9.2	19	9.8
OPERATION, OTHER MUSCULOSKEL	0	0.0	1	1.0	1	0.5
OPERATION, OTHER URINARY	1	1.1	0	0.0	1	0.5
OPERATION, OTHER VESSELS	0	0.0	1	1.0	1	0.5
OPERATION, SKIN/SUBCUT	4	4.2	1	1.0	5	2.6
PERINATAL COND:	1	1.1	0	0.0	1	0.5
CONDITIONS, PERINATAL	1	1.1	0	0.0	1	0.5
PROCEDURES:	1	1.1	1	1.0	2	1.0
PROCEDURE, EYE/EAR	1	1.1	0	0.0	1	0.5
RADIOLOGY, DIAGNOSTIC	0	0.0	1	1.0	1	0.5

TABLE 13.51.2b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH CONDITIONS	60	63.2%	64	65.3%	124	64.2%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
THERAPY, REHAB	0	0.0	1	1.0	1	0.5
RESPIRATORY SYST DIS:	19	20.0	26	26.5	45	23.3
ASTHMA	5	5.3	7	7.1	12	6.2
INFECTION, RESP	1	1.1	0	0.0	1	0.5
NASOPHARYNGITIS, ACUTE	0	0.0	2	2.0	2	1.0
PHARYNGITIS, ACUTE	0	0.0	2	2.0	2	1.0
PNEUMONIA, OTHER	1	1.1	2	2.0	3	1.6
RESP DIS, OTHER	0	0.0	1	1.0	1	0.5
RHINITIS, ALLERGIC	7	7.4	11	11.2	18	9.3
RHINITIS,NOS	1	1.1	0	0.0	1	0.5
SINUSITIS, OTHER	0	0.0	1	1.0	1	0.5
SINUSITIS,NOS	3	3.2	3	3.1	6	3.1
TONSILLITIS, ACUTE	1	1.1	0	0.0	1	0.5
UPPER RESP DISORD, OTHER	7	7.4	5	5.1	12	6.2
SIGNS,SYMPTOMS,ILL-DEFINED CON:	21	22.1	30	30.6	51	26.4
ANOREXIA	0	0.0	1	1.0	1	0.5
APNEA	0	0.0	1	1.0	1	0.5
CARDIAC MURMURS	1	1.1	1	1.0	2	1.0
CONVULSIONS	3	3.2	0	0.0	3	1.6
COUGH	1	1.1	0	0.0	1	0.5
DEVELOPMENT, ABN	3	3.2	1	1.0	4	2.1
DIARRHEA	1	1.1	0	0.0	1	0.5
DISTURBANCE, SPEECH	0	0.0	1	1.0	1	0.5
DIZZINESS AND GIDDINESS	1	1.1	1	1.0	2	1.0
DYSPNEA, OTHER	3	3.2	0	0.0	3	1.6
FLATULENCE	0	0.0	1	1.0	1	0.5
FLUSHING	1	1.1	1	1.0	2	1.0
HEADACHE	14	14.7	17	17.3	31	16.1
HYPERHIDROSIS	1	1.1	1	1.0	2	1.0
HYPOESTHESIA	0	0.0	1	1.0	1	0.5

TABLE 13.51.2b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH CONDITIONS	60	63.2%	64	65.3%	124	64.2%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
INCONTINENCE, URINARY	1	1.1	3	3.1	4	2.1
INSOMNIA	0	0.0	1	1.0	1	0.5
JAUNDICE, UNSPEC	0	0.0	1	1.0	1	0.5
MALAISE AND FATIGUE	0	0.0	2	2.0	2	1.0
NAUSEA	0	0.0	3	3.1	3	1.6
NUTRIT, METAB SYMPTOMS	0	0.0	1	1.0	1	0.5
PAIN UNSP, CHEST	0	0.0	2	2.0	2	1.0
PAIN, ABDOMINO-PELVIC	4	4.2	8	8.2	12	6.2
PAIN, GENERAL	0	0.0	1	1.0	1	0.5
RASH/OTHER SKIN ERUPTION	0	0.0	3	3.1	3	1.6
RBC'S, ABN	1	1.1	0	0.0	1	0.5
SYNCOPE AND COLLAPSE	0	0.0	2	2.0	2	1.0
THYROID FUNCTION, ABN	0	0.0	1	1.0	1	0.5
SKIN/SUBCUTANEOUS TISSUE DIS:	8	8.4	12	12.2	20	10.4
CELLULITIS/ABSCESS	0	0.0	2	2.0	2	1.0
IMPETIGO	0	0.0	1	1.0	1	0.5
INFLAM SKIN/SUBCUT	2	2.1	2	2.0	4	2.1
PRURITUS DISORD, UNSPEC	1	1.1	0	0.0	1	0.5
SCARRING	1	1.1	2	2.0	3	1.6
SKIN/SUBCUT DISORD, OTHER	4	4.2	5	5.1	9	4.7

TABLE 13.51.2c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Per Protocol Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	81	100.0%	83	100.0%	164	100.0%
PATIENTS WITH CONDITIONS :	50	61.7%	56	67.5%	106	64.6%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
ANOMALIES:	3	3.7	7	8.4	10	6.1
CONG ANOM, CIRC SYST	0	0.0	1	1.2	1	0.6
CONG ANOM, GI	1	1.2	1	1.2	2	1.2
CONG ANOM, GU	0	0.0	4	4.8	4	2.4
CONG ANOM, HEART	1	1.2	0	0.0	1	0.6
CONG ANOM, INTEGUMENT	1	1.2	0	0.0	1	0.6
CONGEN ANOM, HEAD/NECK	0	0.0	1	1.2	1	0.6
BLOOD/BLOOD FORMING ORGAN DIS:	1	1.2	0	0.0	1	0.6
LEUKOPENIA	1	1.2	0	0.0	1	0.6
CIRCULATORY SYST:	2	2.5	3	3.6	5	3.0
ARRHYTHMIA	1	1.2	0	0.0	1	0.6
BRADYCARDIA	0	0.0	1	1.2	1	0.6
HEMORRHAGE, INTRACRANIAL	0	0.0	1	1.2	1	0.6
MITRAL VALVE DISORD	1	1.2	1	1.2	2	1.2
DIGESTIVE SYST:	7	8.6	7	8.4	14	8.5
CONSTIPATION	2	2.5	4	4.8	6	3.7
DYSPEPSIA	0	0.0	1	1.2	1	0.6
ESOPHAGITIS	1	1.2	0	0.0	1	0.6
ESOPHAGUS DIS	1	1.2	0	0.0	1	0.6
HERNIA, ABDOMINAL	2	2.5	2	2.4	4	2.4
TEETH DISORD	1	1.2	0	0.0	1	0.6
ENDOCR/METAB/IMMUNITY DISORD:	4	4.9	3	3.6	7	4.3
CHOLEST/TRIGLYCERIDE, ELEVATED	0	0.0	1	1.2	1	0.6
HYPOTHYROIDISM	1	1.2	0	0.0	1	0.6
OBESITY	3	3.7	2	2.4	5	3.0
EXT CAUSES OF INJURY/POISONING:	1	1.2	10	12.0	11	6.7
ACCIDENT/ENVIRON CAUSE	0	0.0	1	1.2	1	0.6

TABLE 13.51.2c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Per Protocol Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	81	100.0%	83	100.0%	164	100.0%
PATIENTS WITH CONDITIONS :	50	61.7%	56	67.5%	106	64.6%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
ACCIDENT/FALL	0	0.0	2	2.4	2	1.2
ACCIDENT/MOTOR VEHICLE	0	0.0	1	1.2	1	0.6
ADVERSE EFF/ANTI-INFECT	0	0.0	1	1.2	1	0.6
ADVERSE EFF/ANTIBIOTIC	1	1.2	5	6.0	6	3.7
ADVERSE EFF/PSYCHOTROPICS	0	0.0	1	1.2	1	0.6
FAMILY/PERSONAL HISTORY:	1	1.2	0	0.0	1	0.6
DEVELOPMENT, CHILD	1	1.2	0	0.0	1	0.6
GENITOURINARY SYST DIS:	3	3.7	3	3.6	6	3.7
CYSTITIS	0	0.0	1	1.2	1	0.6
GENITAL FEMALE DISORD, OTHER	0	0.0	1	1.2	1	0.6
GENITAL MALE DISORD, OTHER	2	2.5	0	0.0	2	1.2
RENAL FAILURE	1	1.2	0	0.0	1	0.6
URINARY TRACT INFECTION	0	0.0	1	1.2	1	0.6
INFECTIOUS/PARASITIC DIS:	2	2.5	4	4.8	6	3.7
INFECTION, BACTERIAL	1	1.2	2	2.4	3	1.8
POLIO AND CNS DIS, VIRAL	1	1.2	0	0.0	1	0.6
VIRAL DIS/EXANTHEM	0	0.0	1	1.2	1	0.6
VIRUS/CHLAMYD DIS, OTHER	0	0.0	1	1.2	1	0.6
INJURY/POISONING:	13	16.0	8	9.6	21	12.8
ADVERSE EFF/OTHER	1	1.2	0	0.0	1	0.6
ALLERGIC REACTION, FOOD	1	1.2	0	0.0	1	0.6
ALLERGY, NEC	3	3.7	2	2.4	5	3.0
FRACTURE, BONE UNSPEC	0	0.0	1	1.2	1	0.6
FRACTURE, NECK/TRUNK	0	0.0	1	1.2	1	0.6
FRACTURE, UPPER LIMB	5	6.2	4	4.8	9	5.5
INJURY, INTRACRANIAL	1	1.2	1	1.2	2	1.2
OPEN WOUND	1	1.2	0	0.0	1	0.6
TRAUMA/INJURIES, UNSPEC	1	1.2	0	0.0	1	0.6

TABLE 13.51.2c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Per Protocol Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	81	100.0%	83	100.0%	164	100.0%
PATIENTS WITH CONDITIONS	50	61.7%	56	67.5%	106	64.6%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
MENTAL DISORD:	3	3.7	7	8.4	10	6.1
DEPRESSION	0	0.0	1	1.2	1	0.6
DRUG DEPEND	0	0.0	1	1.2	1	0.6
MENTAL DEVELOP DISORD	1	1.2	2	2.4	3	1.8
NEUROSES	0	0.0	1	1.2	1	0.6
PSYCHOGENIC PHYSIOL DYSFUNC	2	2.5	1	1.2	3	1.8
PSYCHOSES, DRUG INDUCED	0	0.0	1	1.2	1	0.6
PSYCHOSES, PARANOID	1	1.2	0	0.0	1	0.6
STRESS REACTION	0	0.0	1	1.2	1	0.6
TICS	1	1.2	0	0.0	1	0.6
MUSCULOSKEL/CONNECT TISSUE DIS:	6	7.4	5	6.0	11	6.7
ARTHRITIS, PYOGENIC	1	1.2	0	0.0	1	0.6
ARTHROPATHY	1	1.2	0	0.0	1	0.6
BONE/CARTIL DISORD, OTHER	1	1.2	0	0.0	1	0.6
DEFORMITY, ACQUIRED	1	1.2	1	1.2	2	1.2
JOINT DISORD, OTHER	1	1.2	0	0.0	1	0.6
MYALGIA	1	1.2	2	2.4	3	1.8
PAIN, JOINT	1	1.2	0	0.0	1	0.6
PAIN, LIMB	2	2.5	1	1.2	3	1.8
SPASM, MUSCLE	0	0.0	2	2.4	2	1.2
NEOPLASMS:	3	3.7	0	0.0	3	1.8
NEOPLASMS BENIGN	3	3.7	0	0.0	3	1.8
NERVOUS SYST/SENSE ORGAN DIS:	10	12.3	13	15.7	23	14.0
CONJUNCTIVAL DISORD	0	0.0	1	1.2	1	0.6
EAR/MASTOID DISORD	2	2.5	1	1.2	3	1.8
EYE DISORD, OTHER	0	0.0	2	2.4	2	1.2
HEMIPARESIS	0	0.0	1	1.2	1	0.6
MENINGITIS	3	3.7	1	1.2	4	2.4
MIGRAINE	0	0.0	2	2.4	2	1.2

TABLE 13.51.2c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Per Protocol Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	81	100.0%	83	100.0%	164	100.0%
PATIENTS WITH CONDITIONS	50	61.7%	56	67.5%	106	64.6%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
OTITIS MEDIA	4	4.9	4	4.8	8	4.9
VISUAL DISTURB	2	2.5	2	2.4	4	2.4
OPERATIONS:	19	23.5	16	19.3	35	21.3
OPERATION, APPENDIX	0	0.0	2	2.4	2	1.2
OPERATION, BONE/JOINT	3	3.7	1	1.2	4	2.4
OPERATION, EAR	6	7.4	3	3.6	9	5.5
OPERATION, EYE	0	0.0	2	2.4	2	1.2
OPERATION, HERNIA REPAIR	1	1.2	2	2.4	3	1.8
OPERATION, INTEST	1	1.2	0	0.0	1	0.6
OPERATION, MALE GENITAL	2	2.5	4	4.8	6	3.7
OPERATION, NOSE/MOUTH	6	7.4	8	9.6	14	8.5
OPERATION, OTHER MUSCULOSKEL	0	0.0	1	1.2	1	0.6
OPERATION, OTHER VESSELS	0	0.0	1	1.2	1	0.6
OPERATION, SKIN/SUBCUT	3	3.7	1	1.2	4	2.4
PERINATAL COND:	1	1.2	0	0.0	1	0.6
CONDITIONS, PERINATAL	1	1.2	0	0.0	1	0.6
PROCEDURES:	1	1.2	1	1.2	2	1.2
PROCEDURE, EYE/EAR	1	1.2	0	0.0	1	0.6
RADIOLOGY, DIAGNOSTIC	0	0.0	1	1.2	1	0.6
THERAPY, REHAB	0	0.0	1	1.2	1	0.6
RESPIRATORY SYST DIS:	16	19.8	25	30.1	41	25.0
ASTHMA	4	4.9	6	7.2	10	6.1
INFECTION, RESP	1	1.2	0	0.0	1	0.6
NASOPHARYNGITIS, ACUTE	0	0.0	2	2.4	2	1.2
PHARYNGITIS, ACUTE	0	0.0	2	2.4	2	1.2
PNEUMONIA, OTHER	0	0.0	2	2.4	2	1.2
RESP DIS, OTHER	0	0.0	1	1.2	1	0.6
RHINITIS, ALLERGIC	6	7.4	11	13.3	17	10.4

TABLE 13.51.2c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Per Protocol Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	81	100.0%	83	100.0%	164	100.0%
PATIENTS WITH CONDITIONS	50	61.7%	56	67.5%	106	64.6%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
RHINITIS,NOS	1	1.2	0	0.0	1	0.6
SINUSITIS, OTHER	0	0.0	1	1.2	1	0.6
SINUSITIS,NOS	3	3.7	3	3.6	6	3.7
TONSILLITIS, ACUTE	1	1.2	0	0.0	1	0.6
UPPER RESP DISORD, OTHER	6	7.4	5	6.0	11	6.7
SIGNS,SYMPTOMS,ILL-DEFINED CON:	17	21.0	27	32.5	44	26.8
ANOREXIA	0	0.0	1	1.2	1	0.6
APNEA	0	0.0	1	1.2	1	0.6
CARDIAC MURMURS	1	1.2	1	1.2	2	1.2
CONVULSIONS	2	2.5	0	0.0	2	1.2
COUGH	1	1.2	0	0.0	1	0.6
DEVELOPMENT, ABN	1	1.2	1	1.2	2	1.2
DIARRHEA	1	1.2	0	0.0	1	0.6
DISTURBANCE, SPEECH	0	0.0	1	1.2	1	0.6
DIZZINESS AND GIDDINESS	1	1.2	1	1.2	2	1.2
DYSPNEA, OTHER	3	3.7	0	0.0	3	1.8
FLATULENCE	0	0.0	1	1.2	1	0.6
FLUSHING	1	1.2	1	1.2	2	1.2
HEADACHE	12	14.8	16	19.3	28	17.1
HYPERHIDROSIS	1	1.2	1	1.2	2	1.2
HYPOESTHESIA	0	0.0	1	1.2	1	0.6
INCONTINENCE, URINARY	1	1.2	3	3.6	4	2.4
INSOMNIA	0	0.0	1	1.2	1	0.6
JAUNDICE, UNSPEC	0	0.0	1	1.2	1	0.6
MALAISE AND FATIGUE	0	0.0	2	2.4	2	1.2
NAUSEA	0	0.0	3	3.6	3	1.8
PAIN UNSP, CHEST	0	0.0	2	2.4	2	1.2
PAIN, ABDOMINO-PELVIC	4	4.9	8	9.6	12	7.3
PAIN, GENERAL	0	0.0	1	1.2	1	0.6
RASH/OTHER SKIN ERUPTION	0	0.0	2	2.4	2	1.2
SYNCOPE AND COLLAPSE	0	0.0	2	2.4	2	1.2

TABLE 13.51.2c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Prior Conditions
Per Protocol Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	81	100.0%	83	100.0%	164	100.0%
PATIENTS WITH CONDITIONS	50	61.7%	56	67.5%	106	64.6%
DISEASE CODE LEVEL 1 : PREFERRED TERM	**N**	**%**	**N**	**%**	**N**	**%**
THYROID FUNCTION, ABN	0	0.0	1	1.2	1	0.6
SKIN/SUBCUTANEOUS TISSUE DIS:	6	7.4	10	12.0	16	9.8
CELLULITIS/ABSCESS	0	0.0	2	2.4	2	1.2
IMPETIGO	0	0.0	1	1.2	1	0.6
INFLAM SKIN/SUBCUT	2	2.5	2	2.4	4	2.4
PRURITUS DISORD, UNSPEC	1	1.2	0	0.0	1	0.6
SCARRING	1	1.2	1	1.2	2	1.2
SKIN/SUBCUT DISORD, OTHER	2	2.5	4	4.8	6	3.7

Paroxetine - Protocol: 453

TABLE 13.52.1b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH CONDITIONS :	238	71.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
ANOMALIES:	5	1.5
CONG ANOM, GU	3	0.9
CONG ANOM, MUSCULOSKEL	1	0.3
CONGEN ANOM, HEAD/NECK	1	0.3
BLOOD/BLOOD FORMING ORGAN DIS:	5	1.5
ANEMIA, OTHER	1	0.3
BLOOD DIS, OTHER	1	0.3
EOSINOPHILIA	1	0.3
LEUKOPENIA	2	0.6
LYMPHOCYTOSIS	1	0.3
THROMBOCYTHEMIA	1	0.3
CIRCULATORY SYST:	4	1.2
BRADYCARDIA	2	0.6
MITRAL VALVE DISORD	1	0.3
TACHYCARDIA SUPRAVENTRICULAR	1	0.3
DIGESTIVE SYST:	31	9.3
CONSTIPATION	15	4.5
DIGESTIVE DISORD, OTHER	3	0.9
DYSPEPSIA	6	1.8
ESOPHAGITIS	1	0.3
INTEST MALABSORPTION	1	0.3
ORAL SOFT TISSUE DIS	2	0.6
PERIODONTAL DIS	1	0.3
TEETH DISORD	3	0.9
ENDOCR/METAB/IMMUNITY DISORD:	24	7.2
AMINO-ACID DISORD	1	0.3
CARBOHYDRATE DISORD	2	0.6
HYPOGLYCEMIA	1	0.3

TABLE 13.52.1b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH CONDITIONS :	238	71.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	**N**	**%**
HYPOTHYROIDISM	1	0.3
IMMUNE MECH DISORD	1	0.3
OBESITY	18	5.4
PITUITARY DISORD	1	0.3
EXT CAUSES OF INJURY/POISONING:	27	8.1
ACCIDENT/MOTOR VEHICLE	1	0.3
ADVERSE EFF/ANALGESIC	1	0.3
ADVERSE EFF/ANTI-INFECT	6	1.8
ADVERSE EFF/ANTIBIOTIC	18	5.4
ADVERSE EFF/GI AGENT	1	0.3
ADVERSE EFF/PSYCHOTROPICS	1	0.3
ADVERSE EFF/RESP AGENT	2	0.6
ADVERSE EFF/VACCINE	2	0.6
GENITOURINARY SYST DIS:	11	3.3
CYSTITIS	1	0.3
GENITAL FEMALE DISORD, OTHER	6	1.8
KIDNEY DISORD	1	0.3
KIDNEY INFECT	1	0.3
URINARY TRACT INFECTION	2	0.6
INFECTIOUS/PARASITIC DIS:	3	0.9
MYCOSES	1	0.3
VIRAL INFECTION	1	0.3
VIRUS/CHLAMYD DIS, OTHER	1	0.3
INJURY/POISONING:	28	8.4
ADVERSE EFF/OTHER	1	0.3
ALLERGIC REACTION, FOOD	5	1.5
ALLERGY, NEC	18	5.4
CONTUSION	1	0.3

TABLE 13.52.1b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH CONDITIONS :	238	71.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	**N**	**%**
FRACTURE, UPPER LIMB	1	0.3
MOTION SICKNESS	1	0.3
TRAUMA/INJURIES, UNSPEC	2	0.6
MENTAL DISORD:	14	4.2
ANXIETY	1	0.3
DEPRESSION	2	0.6
DRUG DEPEND	1	0.3
MENTAL DEVELOP DISORD	3	0.9
NEUROSES	1	0.3
POSTCONCUSSION SYNDROME	1	0.3
PSYCHOGENIC PHYSIOL DYSFUNC	4	1.2
STRESS REACTION	1	0.3
TICS	1	0.3
TOBACCO USE	1	0.3
MUSCULOSKEL/CONNECT TISSUE DIS:	31	9.3
ARTHRITIS, PYOGENIC	1	0.3
ARTHRITIS, RHEUMATOID	1	0.3
ARTHROPATHY	1	0.3
BACK PAIN	3	0.9
BONE/CARTIL DISORD, OTHER	1	0.3
CRAMP, LIMB	1	0.3
DEFORMITY, ACQUIRED	5	1.5
JOINT DISORD, OTHER	1	0.3
MYALGIA	9	2.7
OSTEOCHONDROPATHIES	1	0.3
PAIN, JOINT	2	0.6
PAIN, LIMB	5	1.5
RHEUMATIC DISORD	1	0.3
SPASM, MUSCLE	3	0.9

Paroxetine - Protocol: 453

TABLE 13.52.1b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH CONDITIONS :	238	71.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
NEOPLASMS:	5	1.5
NEOPLASMS BENIGN	4	1.2
NEOPLASMS, UNCERT BEHAV	1	0.3
NERVOUS SYST/SENSE ORGAN DIS:	30	9.0
CEREBRAL PALSY	1	0.3
CNS DISORD, OTHER	1	0.3
CONJUNCTIVAL DISORD	1	0.3
EAR/MASTOID DISORD	5	1.5
EYE DISORD, OTHER	2	0.6
HEARING LOSS	3	0.9
MIGRAINE	4	1.2
OTITIS MEDIA	3	0.9
VESTIBULAR DISORD	1	0.3
VISION ABNORMAL	1	0.3
VISUAL DISTURB	10	3.0
OPERATIONS:	6	1.8
OPERATION, BONE/JOINT	1	0.3
OPERATION, CNS	1	0.3
OPERATION, EAR	1	0.3
OPERATION, FEM GENITAL	1	0.3
OPERATION, INTEST	1	0.3
OPERATION, NOSE/MOUTH	1	0.3
PROCEDURES:	6	1.8
EVALUATION, DX EXAM	1	0.3
PROCEDURE, EYE/EAR	5	1.5
RESPIRATORY SYST DIS:	112	33.4
ASTHMA	34	10.1
INFECTION, RESP	1	0.3

TABLE 13.52.1b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH CONDITIONS :	238	71.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
NASAL SEPTUM DEVIATED	1	0.3
NASOPHARYNGITIS, ACUTE	1	0.3
PHARYNGITIS, ACUTE	1	0.3
RESP DIS, OTHER	1	0.3
RHINITIS, ALLERGIC	54	16.1
RHINITIS,NOS	1	0.3
SINUSITIS, OTHER	1	0.3
SINUSITIS,NOS	15	4.5
TONSILS/ADENOIDS DIS	2	0.6
UPPER RESP DISORD, OTHER	18	5.4
UPPER RESP INFECT, ACUTE	5	1.5
SIGNS,SYMPTOMS,ILL-DEFINED CON:	144	43.0
ANOREXIA	1	0.3
CARDIAC MURMURS	1	0.3
CARDIOVAS FUNCTIONS/ECG, ABN	1	0.3
COUGH	3	0.9
DEVELOPMENT, ABN	2	0.6
DIARRHEA	6	1.8
DISTURBANCE, SLEEP, UNSPEC	1	0.3
DISTURBANCES, SLEEP	1	0.3
DIZZINESS AND GIDDINESS	4	1.2
DYSFUNCTION, SYMBOLIC	1	0.3
DYSPNEA, OTHER	2	0.6
EPISTAXIS	5	1.5
FLATULENCE	1	0.3
FLUSHING	3	0.9
GASTROINTEST PROB, NEC	3	0.9
HEAD AND NECK SYMPTOMS, OTHER	1	0.3
HEADACHE	93	27.8
HYPERACTIVITY	1	0.3
HYPERHIDROSIS	3	0.9

TABLE 13.52.1b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH CONDITIONS :	238	71.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
HYPOESTHESIA	1	0.3
INCONTINENCE, URINARY	5	1.5
INSOMNIA	20	6.0
LYMPHADENOPATHY	4	1.2
MALAISE AND FATIGUE	5	1.5
MENTAL STATUS, IMPAIRED	1	0.3
NAUSEA	5	1.5
NERVOUSNESS	1	0.3
NUTRIT, METAB SYMPTOMS	1	0.3
PAIN UNSP, CHEST	3	0.9
PAIN, ABDOMINO-PELVIC	41	12.2
PAIN, GENERAL	3	0.9
PAIN, RESP	1	0.3
PARESTHESIA	1	0.3
POLYURIA	1	0.3
RASH/OTHER SKIN ERUPTION	7	2.1
TACHYCARDIA, UNSPEC	1	0.3
TRANSAMINASE/LDH, ELEVATION	1	0.3
URINATION, ABN, OTHER	1	0.3
VOMITING	2	0.6
SKIN/SUBCUTANEOUS TISSUE DIS:	44	13.1
DYSCHROMIA	1	0.3
INFLAM SKIN/SUBCUT	14	4.2
PRURITUS DISORD, UNSPEC	1	0.3
SKIN INFECT, LOCAL, OTHER	1	0.3
SKIN/SUBCUT DISORD, OTHER	27	8.1
URTICARIA	1	0.3

Paroxetine - Protocol: 453

TABLE 13.52.1c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Per Protocol Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	164	100.0%
PATIENTS WITH CONDITIONS :	123	75.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
ANOMALIES:	4	2.4
CONG ANOM, GU	3	1.8
CONG ANOM, MUSCULOSKEL	1	0.6
BLOOD/BLOOD FORMING ORGAN DIS:	1	0.6
LEUKOPENIA	1	0.6
CIRCULATORY SYST:	3	1.8
BRADYCARDIA	2	1.2
MITRAL VALVE DISORD	1	0.6
DIGESTIVE SYST:	17	10.4
CONSTIPATION	9	5.5
DIGESTIVE DISORD, OTHER	2	1.2
DYSPEPSIA	2	1.2
ESOPHAGITIS	1	0.6
ORAL SOFT TISSUE DIS	1	0.6
PERIODONTAL DIS	1	0.6
TEETH DISORD	2	1.2
ENDOCR/METAB/IMMUNITY DISORD:	11	6.7
CARBOHYDRATE DISORD	1	0.6
HYPOTHYROIDISM	1	0.6
OBESITY	9	5.5
PITUITARY DISORD	1	0.6
EXT CAUSES OF INJURY/POISONING:	12	7.3
ACCIDENT/MOTOR VEHICLE	1	0.6
ADVERSE EFF/ANTI-INFECT	4	2.4
ADVERSE EFF/ANTIBIOTIC	8	4.9
ADVERSE EFF/RESP AGENT	1	0.6

TABLE 13.52.1c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Per Protocol Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	164	100.0%
PATIENTS WITH CONDITIONS :	123	75.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
GENITOURINARY SYST DIS:	7	4.3
CYSTITIS	1	0.6
GENITAL FEMALE DISORD, OTHER	5	3.0
KIDNEY DISORD	1	0.6
INFECTIOUS/PARASITIC DIS:	2	1.2
MYCOSES	1	0.6
VIRAL INFECTION	1	0.6
INJURY/POISONING:	13	7.9
ADVERSE EFF/OTHER	1	0.6
ALLERGIC REACTION, FOOD	1	0.6
ALLERGY, NEC	8	4.9
FRACTURE, UPPER LIMB	1	0.6
TRAUMA/INJURIES, UNSPEC	2	1.2
MENTAL DISORD:	6	3.7
ANXIETY	1	0.6
DRUG DEPEND	1	0.6
MENTAL DEVELOP DISORD	2	1.2
PSYCHOGENIC PHYSIOL DYSFUNC	3	1.8
STRESS REACTION	1	0.6
MUSCULOSKEL/CONNECT TISSUE DIS:	19	11.6
ARTHRITIS, PYOGENIC	1	0.6
ARTHROPATHY	1	0.6
BONE/CARTIL DISORD, OTHER	1	0.6
DEFORMITY, ACQUIRED	4	2.4
JOINT DISORD, OTHER	1	0.6
MYALGIA	5	3.0
OSTEOCHONDROPATHIES	1	0.6
PAIN, JOINT	1	0.6

TABLE 13.52.1c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Per Protocol Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	164	100.0%
PATIENTS WITH CONDITIONS :	123	75.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
PAIN, LIMB	5	3.0
RHEUMATIC DISORD	1	0.6
SPASM, MUSCLE	2	1.2
NEOPLASMS:	3	1.8
NEOPLASMS BENIGN	2	1.2
NEOPLASMS, UNCERT BEHAV	1	0.6
NERVOUS SYST/SENSE ORGAN DIS:	13	7.9
CONJUNCTIVAL DISORD	1	0.6
EAR/MASTOID DISORD	2	1.2
HEARING LOSS	1	0.6
MIGRAINE	1	0.6
OTITIS MEDIA	1	0.6
VISION ABNORMAL	1	0.6
VISUAL DISTURB	6	3.7
OPERATIONS:	4	2.4
OPERATION, CNS	1	0.6
OPERATION, EAR	1	0.6
OPERATION, FEM GENITAL	1	0.6
OPERATION, NOSE/MOUTH	1	0.6
PROCEDURES:	5	3.0
EVALUATION, DX EXAM	1	0.6
PROCEDURE, EYE/EAR	4	2.4
RESPIRATORY SYST DIS:	60	36.6
ASTHMA	14	8.5
INFECTION, RESP	1	0.6
NASOPHARYNGITIS, ACUTE	1	0.6
PHARYNGITIS, ACUTE	1	0.6

TABLE 13.52.1c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Per Protocol Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	164	100.0%
PATIENTS WITH CONDITIONS :	123	75.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
RESP DIS, OTHER	1	0.6
RHINITIS, ALLERGIC	35	21.3
RHINITIS,NOS	1	0.6
SINUSITIS, OTHER	1	0.6
SINUSITIS,NOS	7	4.3
UPPER RESP DISORD, OTHER	9	5.5
UPPER RESP INFECT, ACUTE	2	1.2
SIGNS,SYMPTOMS,ILL-DEFINED CON:	73	44.5
ANOREXIA	1	0.6
DEVELOPMENT, ABN	2	1.2
DIARRHEA	5	3.0
DISTURBANCE, SLEEP, UNSPEC	1	0.6
DIZZINESS AND GIDDINESS	2	1.2
DYSPNEA, OTHER	2	1.2
EPISTAXIS	1	0.6
FLATULENCE	1	0.6
FLUSHING	2	1.2
GASTROINTEST PROB, NEC	2	1.2
HEADACHE	52	31.7
HYPERHIDROSIS	2	1.2
HYPOESTHESIA	1	0.6
INCONTINENCE, URINARY	1	0.6
INSOMNIA	5	3.0
LYMPHADENOPATHY	2	1.2
MALAISE AND FATIGUE	3	1.8
NAUSEA	3	1.8
NERVOUSNESS	1	0.6
PAIN UNSP, CHEST	2	1.2
PAIN, ABDOMINO-PELVIC	25	15.2
PAIN, GENERAL	2	1.2
PARESTHESIA	1	0.6

TABLE 13.52.1c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Per Protocol Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	164	100.0%
PATIENTS WITH CONDITIONS :	123	75.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%
RASH/OTHER SKIN ERUPTION	2	1.2
SKIN/SUBCUTANEOUS TISSUE DIS:	24	14.6
DYSCHROMIA	1	0.6
INFLAM SKIN/SUBCUT	6	3.7
PRURITUS DISORD, UNSPEC	1	0.6
SKIN/SUBCUT DISORD, OTHER	16	9.8

TABLE 13.52.2b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH CONDITIONS :	69	72.6%	74	75.5%	143	74.1%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
ANOMALIES:	2	2.1	3	3.1	5	2.6
CONG ANOM, GU	1	1.1	2	2.0	3	1.6
CONG ANOM, MUSCULOSKEL	0	0.0	1	1.0	1	0.5
CONGEN ANOM, HEAD/NECK	1	1.1	0	0.0	1	0.5
BLOOD/BLOOD FORMING ORGAN DIS:	0	0.0	2	2.0	2	1.0
BLOOD DIS, OTHER	0	0.0	1	1.0	1	0.5
LEUKOPENIA	0	0.0	1	1.0	1	0.5
CIRCULATORY SYST:	2	2.1	1	1.0	3	1.6
BRADYCARDIA	1	1.1	1	1.0	2	1.0
MITRAL VALVE DISORD	1	1.1	0	0.0	1	0.5
DIGESTIVE SYST:	8	8.4	10	10.2	18	9.3
CONSTIPATION	3	3.2	7	7.1	10	5.2
DIGESTIVE DISORD, OTHER	1	1.1	1	1.0	2	1.0
DYSPEPSIA	1	1.1	1	1.0	2	1.0
ESOPHAGITIS	1	1.1	0	0.0	1	0.5
ORAL SOFT TISSUE DIS	0	0.0	1	1.0	1	0.5
PERIODONTAL DIS	1	1.1	0	0.0	1	0.5
TEETH DISORD	2	2.1	0	0.0	2	1.0
ENDOCR/METAB/IMMUNITY DISORD:	8	8.4	6	6.1	14	7.3
AMINO-ACID DISORD	1	1.1	0	0.0	1	0.5
CARBOHYDRATE DISORD	0	0.0	1	1.0	1	0.5
HYPOTHYROIDISM	0	0.0	1	1.0	1	0.5
IMMUNE MECH DISORD	1	1.1	0	0.0	1	0.5
OBESITY	6	6.3	4	4.1	10	5.2
PITUITARY DISORD	0	0.0	1	1.0	1	0.5
EXT CAUSES OF INJURY/POISONING:	5	5.3	9	9.2	14	7.3
ACCIDENT/MOTOR VEHICLE	1	1.1	0	0.0	1	0.5

TABLE 13.52.2b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH CONDITIONS	69	72.6%	74	75.5%	143	74.1%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
ADVERSE EFF/ANTI-INFECT	0	0.0	4	4.1	4	2.1
ADVERSE EFF/ANTIBIOTIC	3	3.2	6	6.1	9	4.7
ADVERSE EFF/RESP AGENT	0	0.0	1	1.0	1	0.5
ADVERSE EFF/VACCINE	1	1.1	0	0.0	1	0.5
GENITOURINARY SYST DIS:	4	4.2	3	3.1	7	3.6
CYSTITIS	0	0.0	1	1.0	1	0.5
GENITAL FEMALE DISORD, OTHER	3	3.2	2	2.0	5	2.6
KIDNEY DISORD	1	1.1	0	0.0	1	0.5
INFECTIOUS/PARASITIC DIS:	0	0.0	2	2.0	2	1.0
MYCOSES	0	0.0	1	1.0	1	0.5
VIRAL INFECTION	0	0.0	1	1.0	1	0.5
INJURY/POISONING:	12	12.6	3	3.1	15	7.8
ADVERSE EFF/OTHER	1	1.1	0	0.0	1	0.5
ALLERGIC REACTION, FOOD	1	1.1	0	0.0	1	0.5
ALLERGY, NEC	7	7.4	3	3.1	10	5.2
FRACTURE, UPPER LIMB	1	1.1	0	0.0	1	0.5
TRAUMA/INJURIES, UNSPEC	2	2.1	0	0.0	2	1.0
MENTAL DISORD:	2	2.1	5	5.1	7	3.6
ANXIETY	1	1.1	0	0.0	1	0.5
DRUG DEPEND	0	0.0	1	1.0	1	0.5
MENTAL DEVELOP DISORD	1	1.1	1	1.0	2	1.0
PSYCHOGENIC PHYSIOL DYSFUNC	1	1.1	2	2.0	3	1.6
STRESS REACTION	0	0.0	1	1.0	1	0.5
TOBACCO USE	0	0.0	1	1.0	1	0.5
MUSCULOSKEL/CONNECT TISSUE DIS:	12	12.6	8	8.2	20	10.4
ARTHRITIS, PYOGENIC	1	1.1	0	0.0	1	0.5
ARTHROPATHY	1	1.1	0	0.0	1	0.5

TABLE 13.52.2b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH CONDITIONS	69	72.6%	74	75.5%	143	74.1%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
BONE/CARTIL DISORD, OTHER	1	1.1	0	0.0	1	0.5
DEFORMITY, ACQUIRED	4	4.2	1	1.0	5	2.6
JOINT DISORD, OTHER	1	1.1	0	0.0	1	0.5
MYALGIA	3	3.2	2	2.0	5	2.6
OSTEOCHONDROPATHIES	0	0.0	1	1.0	1	0.5
PAIN, JOINT	1	1.1	0	0.0	1	0.5
PAIN, LIMB	2	2.1	3	3.1	5	2.6
RHEUMATIC DISORD	1	1.1	0	0.0	1	0.5
SPASM, MUSCLE	0	0.0	2	2.0	2	1.0
NEOPLASMS:	2	2.1	1	1.0	3	1.6
NEOPLASMS BENIGN	1	1.1	1	1.0	2	1.0
NEOPLASMS, UNCERT BEHAV	1	1.1	0	0.0	1	0.5
NERVOUS SYST/SENSE ORGAN DIS:	12	12.6	5	5.1	17	8.8
CNS DISORD, OTHER	0	0.0	1	1.0	1	0.5
CONJUNCTIVAL DISORD	1	1.1	0	0.0	1	0.5
EAR/MASTOID DISORD	1	1.1	1	1.0	2	1.0
HEARING LOSS	2	2.1	0	0.0	2	1.0
MIGRAINE	1	1.1	0	0.0	1	0.5
OTITIS MEDIA	1	1.1	0	0.0	1	0.5
VISION ABNORMAL	1	1.1	0	0.0	1	0.5
VISUAL DISTURB	5	5.3	3	3.1	8	4.1
OPERATIONS:	2	2.1	2	2.0	4	2.1
OPERATION, CNS	1	1.1	0	0.0	1	0.5
OPERATION, EAR	0	0.0	1	1.0	1	0.5
OPERATION, FEM GENITAL	0	0.0	1	1.0	1	0.5
OPERATION, NOSE/MOUTH	1	1.1	0	0.0	1	0.5
PROCEDURES:	3	3.2	2	2.0	5	2.6
EVALUATION, DX EXAM	0	0.0	1	1.0	1	0.5

TABLE 13.52.2b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH CONDITIONS	69	72.6%	74	75.5%	143	74.1%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
PROCEDURE, EYE/EAR	3	3.2	1	1.0	4	2.1
RESPIRATORY SYST DIS:	31	32.6	37	37.8	68	35.2
ASTHMA	8	8.4	8	8.2	16	8.3
INFECTION, RESP	0	0.0	1	1.0	1	0.5
NASOPHARYNGITIS, ACUTE	1	1.1	0	0.0	1	0.5
PHARYNGITIS, ACUTE	1	1.1	0	0.0	1	0.5
RESP DIS, OTHER	0	0.0	1	1.0	1	0.5
RHINITIS, ALLERGIC	16	16.8	22	22.4	38	19.7
RHINITIS,NOS	1	1.1	0	0.0	1	0.5
SINUSITIS, OTHER	0	0.0	1	1.0	1	0.5
SINUSITIS,NOS	4	4.2	3	3.1	7	3.6
TONSILS/ADENOIDS DIS	0	0.0	1	1.0	1	0.5
UPPER RESP DISORD, OTHER	5	5.3	5	5.1	10	5.2
UPPER RESP INFECT, ACUTE	1	1.1	2	2.0	3	1.6
SIGNS,SYMPTOMS,ILL-DEFINED CON:	41	43.2	44	44.9	85	44.0
ANOREXIA	0	0.0	1	1.0	1	0.5
DEVELOPMENT, ABN	1	1.1	1	1.0	2	1.0
DIARRHEA	4	4.2	1	1.0	5	2.6
DISTURBANCE, SLEEP, UNSPEC	0	0.0	1	1.0	1	0.5
DIZZINESS AND GIDDINESS	3	3.2	1	1.0	4	2.1
DYSPNEA, OTHER	2	2.1	0	0.0	2	1.0
EPISTAXIS	1	1.1	0	0.0	1	0.5
FLATULENCE	0	0.0	1	1.0	1	0.5
FLUSHING	1	1.1	1	1.0	2	1.0
GASTROINTEST PROB, NEC	2	2.1	0	0.0	2	1.0
HEADACHE	30	31.6	31	31.6	61	31.6
HYPERACTIVITY	0	0.0	1	1.0	1	0.5
HYPERHIDROSIS	1	1.1	1	1.0	2	1.0
HYPOESTHESIA	0	0.0	1	1.0	1	0.5
INCONTINENCE, URINARY	0	0.0	1	1.0	1	0.5

TABLE 13.52.2b

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH CONDITIONS :	69	72.6%	74	75.5%	143	74.1%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
INSOMNIA	1	1.1	5	5.1	6	3.1
LYMPHADENOPATHY	2	2.1	1	1.0	3	1.6
MALAISE AND FATIGUE	1	1.1	2	2.0	3	1.6
NAUSEA	1	1.1	3	3.1	4	2.1
NERVOUSNESS	0	0.0	1	1.0	1	0.5
NUTRIT, METAB SYMPTOMS	0	0.0	1	1.0	1	0.5
PAIN UNSP, CHEST	1	1.1	1	1.0	2	1.0
PAIN, ABDOMINO-PELVIC	12	12.6	17	17.3	29	15.0
PAIN, GENERAL	1	1.1	2	2.0	3	1.6
PARESTHESIA	1	1.1	0	0.0	1	0.5
RASH/OTHER SKIN ERUPTION	1	1.1	2	2.0	3	1.6
SKIN/SUBCUTANEOUS TISSUE DIS:	16	16.8	11	11.2	27	14.0
DYSCHROMIA	1	1.1	0	0.0	1	0.5
INFLAM SKIN/SUBCUT	4	4.2	2	2.0	6	3.1
PRURITUS DISORD, UNSPEC	1	1.1	0	0.0	1	0.5
SKIN/SUBCUT DISORD, OTHER	10	10.5	9	9.2	19	9.8

TABLE 13.52.2c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Per Protocol Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	81	100.0%	83	100.0%	164	100.0%
PATIENTS WITH CONDITIONS :	57	70.4%	66	79.5%	123	75.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
ANOMALIES:	1	1.2	3	3.6	4	2.4
CONG ANOM, GU	1	1.2	2	2.4	3	1.8
CONG ANOM, MUSCULOSKEL	0	0.0	1	1.2	1	0.6
BLOOD/BLOOD FORMING ORGAN DIS:	0	0.0	1	1.2	1	0.6
LEUKOPENIA	0	0.0	1	1.2	1	0.6
CIRCULATORY SYST:	2	2.5	1	1.2	3	1.8
BRADYCARDIA	1	1.2	1	1.2	2	1.2
MITRAL VALVE DISORD	1	1.2	0	0.0	1	0.6
DIGESTIVE SYST:	7	8.6	10	12.0	17	10.4
CONSTIPATION	2	2.5	7	8.4	9	5.5
DIGESTIVE DISORD, OTHER	1	1.2	1	1.2	2	1.2
DYSPEPSIA	1	1.2	1	1.2	2	1.2
ESOPHAGITIS	1	1.2	0	0.0	1	0.6
ORAL SOFT TISSUE DIS	0	0.0	1	1.2	1	0.6
PERIODONTAL DIS	1	1.2	0	0.0	1	0.6
TEETH DISORD	2	2.5	0	0.0	2	1.2
ENDOCR/METAB/IMMUNITY DISORD:	5	6.2	6	7.2	11	6.7
CARBOHYDRATE DISORD	0	0.0	1	1.2	1	0.6
HYPOTHYROIDISM	0	0.0	1	1.2	1	0.6
OBESITY	5	6.2	4	4.8	9	5.5
PITUITARY DISORD	0	0.0	1	1.2	1	0.6
EXT CAUSES OF INJURY/POISONING:	4	4.9	8	9.6	12	7.3
ACCIDENT/MOTOR VEHICLE	1	1.2	0	0.0	1	0.6
ADVERSE EFF/ANTI-INFECT	0	0.0	4	4.8	4	2.4
ADVERSE EFF/ANTIBIOTIC	3	3.7	5	6.0	8	4.9
ADVERSE EFF/RESP AGENT	0	0.0	1	1.2	1	0.6

TABLE 13.52.2c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Per Protocol Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	81	100.0%	83	100.0%	164	100.0%
PATIENTS WITH CONDITIONS :	57	70.4%	66	79.5%	123	75.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
GENITOURINARY SYST DIS:	4	4.9	3	3.6	7	4.3
CYSTITIS	0	0.0	1	1.2	1	0.6
GENITAL FEMALE DISORD, OTHER	3	3.7	2	2.4	5	3.0
KIDNEY DISORD	1	1.2	0	0.0	1	0.6
INFECTIOUS/PARASITIC DIS:	0	0.0	2	2.4	2	1.2
MYCOSES	0	0.0	1	1.2	1	0.6
VIRAL INFECTION	0	0.0	1	1.2	1	0.6
INJURY/POISONING:	10	12.3	3	3.6	13	7.9
ADVERSE EFF/OTHER	1	1.2	0	0.0	1	0.6
ALLERGIC REACTION, FOOD	1	1.2	0	0.0	1	0.6
ALLERGY, NEC	5	6.2	3	3.6	8	4.9
FRACTURE, UPPER LIMB	1	1.2	0	0.0	1	0.6
TRAUMA/INJURIES, UNSPEC	2	2.5	0	0.0	2	1.2
MENTAL DISORD:	2	2.5	4	4.8	6	3.7
ANXIETY	1	1.2	0	0.0	1	0.6
DRUG DEPEND	0	0.0	1	1.2	1	0.6
MENTAL DEVELOP DISORD	1	1.2	1	1.2	2	1.2
PSYCHOGENIC PHYSIOL DYSFUNC	1	1.2	2	2.4	3	1.8
STRESS REACTION	0	0.0	1	1.2	1	0.6
MUSCULOSKEL/CONNECT TISSUE DIS:	11	13.6	8	9.6	19	11.6
ARTHRITIS, PYOGENIC	1	1.2	0	0.0	1	0.6
ARTHROPATHY	1	1.2	0	0.0	1	0.6
BONE/CARTIL DISORD, OTHER	1	1.2	0	0.0	1	0.6
DEFORMITY, ACQUIRED	3	3.7	1	1.2	4	2.4
JOINT DISORD, OTHER	1	1.2	0	0.0	1	0.6
MYALGIA	3	3.7	2	2.4	5	3.0
OSTEOCHONDROPATHIES	0	0.0	1	1.2	1	0.6
PAIN, JOINT	1	1.2	0	0.0	1	0.6

TABLE 13.52.2c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Per Protocol Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	81	100.0%	83	100.0%	164	100.0%
PATIENTS WITH CONDITIONS	57	70.4%	66	79.5%	123	75.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
PAIN, LIMB	2	2.5	3	3.6	5	3.0
RHEUMATIC DISORD	1	1.2	0	0.0	1	0.6
SPASM, MUSCLE	0	0.0	2	2.4	2	1.2
NEOPLASMS:	2	2.5	1	1.2	3	1.8
NEOPLASMS BENIGN	1	1.2	1	1.2	2	1.2
NEOPLASMS, UNCERT BEHAV	1	1.2	0	0.0	1	0.6
NERVOUS SYST/SENSE ORGAN DIS:	10	12.3	3	3.6	13	7.9
CONJUNCTIVAL DISORD	1	1.2	0	0.0	1	0.6
EAR/MASTOID DISORD	1	1.2	1	1.2	2	1.2
HEARING LOSS	1	1.2	0	0.0	1	0.6
MIGRAINE	1	1.2	0	0.0	1	0.6
OTITIS MEDIA	1	1.2	0	0.0	1	0.6
VISION ABNORMAL	1	1.2	0	0.0	1	0.6
VISUAL DISTURB	4	4.9	2	2.4	6	3.7
OPERATIONS:	2	2.5	2	2.4	4	2.4
OPERATION, CNS	1	1.2	0	0.0	1	0.6
OPERATION, EAR	0	0.0	1	1.2	1	0.6
OPERATION, FEM GENITAL	0	0.0	1	1.2	1	0.6
OPERATION, NOSE/MOUTH	1	1.2	0	0.0	1	0.6
PROCEDURES:	3	3.7	2	2.4	5	3.0
EVALUATION, DX EXAM	0	0.0	1	1.2	1	0.6
PROCEDURE, EYE/EAR	3	3.7	1	1.2	4	2.4
RESPIRATORY SYST DIS:	24	29.6	36	43.4	60	36.6
ASTHMA	6	7.4	8	9.6	14	8.5
INFECTION, RESP	0	0.0	1	1.2	1	0.6
NASOPHARYNGITIS, ACUTE	1	1.2	0	0.0	1	0.6
PHARYNGITIS, ACUTE	1	1.2	0	0.0	1	0.6

TABLE 13.52.2c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Per Protocol Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	81	100.0%	83	100.0%	164	100.0%
PATIENTS WITH CONDITIONS	57	70.4%	66	79.5%	123	75.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
RESP DIS, OTHER	0	0.0	1	1.2	1	0.6
RHINITIS, ALLERGIC	13	16.0	22	26.5	35	21.3
RHINITIS,NOS	1	1.2	0	0.0	1	0.6
SINUSITIS, OTHER	0	0.0	1	1.2	1	0.6
SINUSITIS,NOS	4	4.9	3	3.6	7	4.3
UPPER RESP DISORD, OTHER	4	4.9	5	6.0	9	5.5
UPPER RESP INFECT, ACUTE	0	0.0	2	2.4	2	1.2
SIGNS,SYMPTOMS,ILL-DEFINED CON:	36	44.4	37	44.6	73	44.5
ANOREXIA	0	0.0	1	1.2	1	0.6
DEVELOPMENT, ABN	1	1.2	1	1.2	2	1.2
DIARRHEA	4	4.9	1	1.2	5	3.0
DISTURBANCE, SLEEP, UNSPEC	0	0.0	1	1.2	1	0.6
DIZZINESS AND GIDDINESS	1	1.2	1	1.2	2	1.2
DYSPNEA, OTHER	2	2.5	0	0.0	2	1.2
EPISTAXIS	1	1.2	0	0.0	1	0.6
FLATULENCE	0	0.0	1	1.2	1	0.6
FLUSHING	1	1.2	1	1.2	2	1.2
GASTROINTEST PROB, NEC	2	2.5	0	0.0	2	1.2
HEADACHE	26	32.1	26	31.3	52	31.7
HYPERHIDROSIS	1	1.2	1	1.2	2	1.2
HYPOESTHESIA	0	0.0	1	1.2	1	0.6
INCONTINENCE, URINARY	0	0.0	1	1.2	1	0.6
INSOMNIA	0	0.0	5	6.0	5	3.0
LYMPHADENOPATHY	1	1.2	1	1.2	2	1.2
MALAISE AND FATIGUE	1	1.2	2	2.4	3	1.8
NAUSEA	0	0.0	3	3.6	3	1.8
NERVOUSNESS	0	0.0	1	1.2	1	0.6
PAIN UNSP, CHEST	1	1.2	1	1.2	2	1.2
PAIN, ABDOMINO-PELVIC	11	13.6	14	16.9	25	15.2
PAIN, GENERAL	0	0.0	2	2.4	2	1.2
PARESTHESIA	1	1.2	0	0.0	1	0.6

TABLE 13.52.2c

Medical/Surgical History and Physical Examination - Number (%) of Patients with Active Conditions
Per Protocol Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	81	100.0%	83	100.0%	164	100.0%
PATIENTS WITH CONDITIONS	57	70.4%	66	79.5%	123	75.0%
DISEASE CODE LEVEL 1 : PREFERRED TERM	N	%	N	%	N	%
RASH/OTHER SKIN ERUPTION	0	0.0	2	2.4	2	1.2
SKIN/SUBCUTANEOUS TISSUE DIS:	14	17.3	10	12.0	24	14.6
DYSCHROMIA	1	1.2	0	0.0	1	0.6
INFLAM SKIN/SUBCUT	4	4.9	2	2.4	6	3.7
PRURITUS DISORD, UNSPEC	1	1.2	0	0.0	1	0.6
SKIN/SUBCUT DISORD, OTHER	8	9.9	8	9.6	16	9.8

Table 13.81.1

History and Current Episode of OCD
Intention to Treat Population
Phase I: Open Label Treatment

Age at Onset (years)	Mean	10.1
	Median	10
	Std Dev	3.32
	Minimum	2
	Maximum	18
	N	335
	Missing	0

Table 13.81.2

History and Current Episode of OCD
Intention to Treat Population
Phase II: Randomised Treatment

		Treatment Group	
		Paroxetine	Placebo
Age at Onset (years)	Mean	10.0	10.0
	Median	10	10
	Std Dev	3.02	3.37
	Minimum	3	2
	Maximum	18	16
	N	95	98
	Missing	0	0

Table 13.82.1

History and Current Episode of OCD
Family History of OCD
Intention to Treat Population
Phase I: Open Label Treatment

	N	%
None	160	48.2
Mother	63	19.0
Father	51	15.4
Sibling	21	6.3
Grandparent	62	18.7
Other	65	19.6
No. of Non-Missing Patients in Group	332	100.0
Missing	3	

Table 13.82.2

History and Current Episode of OCD
Family History of OCD
Intention to Treat Population
Phase II: Randomised Treatment phase

	Paroxetine		Placebo	
	N	%	N	%
None	42	44.7	49	50.5
Mother	17	18.1	18	18.6
Father	13	13.8	16	16.5
Sibling	7	7.4	7	7.2
Grandparent	18	19.1	13	13.4
Other	21	22.3	16	16.5
No. of Non-Missing Patients in Group	94	100.0	97	100.0
Missing	1		1	

Table 13.83.1

History and Current Episode of OCD
Number of Times Hospitalised
Intention to Treat Population
Phase I: Open Label Treatment

	N	%
Never	330	98.5
1	3	0.9
2		
3	2	0.6
4		
>=5		
Total	335	100.0
Missing		

Table 13.83.2

History and Current Episode of OCD
Number of Times Hospitalised
Intention to Treat Population
Phase II: Randomised Treatment

	Paroxetine		Placebo	
	N	%	N	%
Never	93	97.9	98	100.0
1	1	1.1		
2				
3	1	1.1		
4				
>=5				
Total	95	100.0	98	100.0
Missing				

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]T13_8_3.SAS (18FEB99 18:22)

Table 13.84.1

History and Current Episode of OCD
Severity of Current Episode as at Screening
Intention to Treat Population
Phase I: Open Label Treatment

	N	%
Mild	14	4.2
Moderate	174	51.9
Severe	147	43.9
Total	335	100.0
Missing		

Table 13.84.2

History and Current Episode of OCD
Severity of Current Episode as at Screening
Intention to Treat Population
Phase II: Randomised Treatment

	Paroxetine		Placebo	
	N	%	N	%
Mild	4	4.2	4	4.1
Moderate	52	54.7	50	51.0
Severe	39	41.1	44	44.9
Total	95	100.0	98	100.0
Missing				

Table 13.85.1

History and Current Episode of OCD
Type of Treatment Received for Current Episode
Intention to Treat Population
Phase I: Open Label Treatment

	N	%
No Therapy	239	71.3
Psychotherapy	33	9.9
Pharmacotherapy	45	13.4
Psychotherapy + Pharmacotherapy	18	5.4
Total	335	100.0
Missing		

Table 13.85.2

History and Current Episode of OCD
Type of Treatment Received for Current Episode
Intention to Treat Population
Phase II: Randomised Treatment

	Paroxetine		Placebo	
	N	%	N	%
No Therapy	69	72.6	69	70.4
Psychotherapy	8	8.4	13	13.3
Pharmacotherapy	10	10.5	15	15.3
Psychotherapy + Pharmacotherapy	8	8.4	1	1.0
Total	95	100.0	98	100.0
Missing				

11 Data Source Tables: Efficacy Tables

Table 14.4.1

Baseline and Change from Baseline in HAMA Total Score
Intention to Treat Population
Phase I: Open Label Treatment

	Mean (Std Err) N
Baseline	8.3 (0.35) 316
Week 4	-3.0 (0.32) 313
Week 8	-4.0 (0.36) 287
Week 12	-4.4 (0.37) 262
Week 16	-4.9 (0.39) 237
Week 16 End point	-4.4 (0.36) 315

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

Table 14.4.2

Randomisation Baseline and Change from Randomisation Baseline in HAMA Total Score
Intention to Treat Population
Phase II: Randomised Treatment

	Treatment Group			
	Paroxetine		Placebo	
	Mean (Std Err)	N	Mean (Std Err)	N
Randomisation Baseline	2.7 (0.36)	92	2.8 (0.33)	98
Week 2	0.9 (0.30)	90	1.8 (0.53)	97
Week 4	1.3 (0.51)	79	1.3 (0.45)	74
Week 6	0.2 (0.37)	65	1.3 (0.55)	51
Week 8	0.2 (0.40)	57	0.2 (0.53)	42
Week 10	0.8 (0.46)	53	-0.9 (0.32)	35
Week 12	0.2 (0.54)	48	-0.5 (0.45)	35
Week 16	-0.1 (0.49)	41	0.2 (0.52)	30
70% End point	1.5 (0.46)	92	2.4 (0.56)	98
Week 16 End point	1.8 (0.53)	92	3.1 (0.58)	98

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_4.SAS (18FEB99 17:51)

Table 14.5.1

Baseline and Change from Baseline in HAMD Total Score
Intention to Treat Population
Phase I: Open Label Treatment

	Mean (Std Err) N
Baseline	6.6 (0.29) 315
Week 4	-2.3 (0.25) 309
Week 8	-2.7 (0.31) 286
Week 12	-3.1 (0.32) 261
Week 16	-3.7 (0.34) 237
Week 16 End point	-3.1 (0.31) 313

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_5.SAS (18FEB99 17:51)

Table 14.5.2

Randomisation Baseline and Change from Randomisation Baseline in HAMD Total Score
Intention to Treat Population
Phase II: Randomised Treatment

	Treatment Group			
	Paroxetine		Placebo	
	Mean (Std Err)	N	Mean (Std Err)	N
Randomisation Baseline	2.4 (0.32)	92	2.3 (0.26)	98
Week 2	1.0 (0.38)	90	1.7 (0.50)	96
Week 4	1.1 (0.49)	79	1.2 (0.46)	74
Week 6	0.8 (0.44)	65	1.3 (0.51)	51
Week 8	0.4 (0.38)	58	0.3 (0.65)	42
Week 10	0.7 (0.40)	53	-0.8 (0.47)	35
Week 12	0.1 (0.51)	48	-0.5 (0.50)	35
Week 16	0.1 (0.39)	41	0.2 (0.58)	30
70% End point	1.4 (0.47)	92	2.3 (0.55)	98
Week 16 End point	1.9 (0.50)	92	3.1 (0.57)	98

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_5.SAS (18FEB99 17:51)

Table 14.6.1

Yale Global Tic Severity Scale
Total Tic Scores
Intention to Treat Population
Phase I: Open Label Treatment

	Mean (Std Err) N
Baseline	2.5 (0.31) 317
Week 4	2.0 (0.28) 313
Week 8	1.6 (0.24) 285
Week 12	1.4 (0.25) 263
Week 16	1.0 (0.19) 239
Week 16 End point	1.7 (0.29) 317

Total Tic Score = Number (0-5) + Frequency (0-5) + Intensity (0-5) +
Complexity (0-5) + Interference (0-5)

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_6.SAS (02MAR99 11:29)

Table 14.6.2

Yale Global Tic Severity Scale
Total Tic Scores
Intention to Treat Population
Phase II: Randomised Treatment

	Treatment Group			
	Paroxetine		Placebo	
	Mean (Std Err)	N	Mean (Std Err)	N
Randomisation Baseline	0.7 (0.25)	93	1.4 (0.37)	98
Week 2	0.6 (0.22)	91	1.5 (0.39)	97
Week 4	0.7 (0.33)	79	1.6 (0.46)	74
Week 6	0.6 (0.29)	64	1.3 (0.55)	50
Week 8	0.6 (0.27)	58	1.1 (0.46)	42
Week 10	0.7 (0.43)	53	1.4 (0.72)	36
Week 12	0.5 (0.28)	49	1.1 (0.55)	35
Week 16	0.7 (0.42)	41	0.8 (0.51)	30
70% End point	0.6 (0.29)	93	1.5 (0.40)	98
Week 16 End point	0.8 (0.32)	93	1.6 (0.41)	98

Total Tic Score = Number (0-5) + Frequency (0-5) + Intensity (0-5) +
Complexity (0-5) + Interference (0-5)

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_6.SAS (02MAR99 11:29)

Table 14.8.1

Number (%) of Responders at Week 16
Intention to Treat Population
Phase I: Open Label Treatment

	N	%
Responders	206	86.2
Non-Responders	33	13.8

Note: A responder is defined as a patient with a >= 25% reduction from baseline in CY-BOCS score and a CGI improvement item of 1 (very much improved) or 2 (much improved)

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_8.SAS (18FEB99 17:58)

Table 14.8.2

Number (%) of Responders at Week 16 Endpoint
Intention to Treat Population
Phase I: Open Label Treatment

	N	%
Responders	232	70.5
Non-Responders	97	29.5

Note: A responder is defined as a patient with a >= 25% reduction from baseline in CY-BOCS score and a CGI improvement item of 1 (very much improved) or 2 (much improved)

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_8.SAS (18FEB99 17:58)

Table 14.11.2b

Number (%) of Relapsers
Intention to Treat Population
Phase II: Randomised Treatment

	Paroxetine			Placebo			Pairwise Comparisons *			
	n	%	N	n	%	N	Odds Ratio	Lower 95% CI Limit	Upper 95% CI Limit	p-value
Relapsers	33	34.7	95	43	43.9	98	0.62	0.34	1.16	0.136
Non-relapsers	62	65.3	95	55	56.1	98				

Definition of Relapsers is based on the CGI Global Improvement Score

* = Adjusted for terms retained in the final model (i.e. centre group)

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1411.SAS (05MAR99 12:53)

Table 14.11.2c

Number (%) of Relapsers
Per Protocol Population
Phase II: Randomised Treatment

	Paroxetine			Placebo			Pairwise Comparisons *			
	n	%	N	n	%	N	Odds Ratio	Lower 95% CI Limit	Upper 95% CI Limit	p-value
Relapsers	26	32.1	81	36	43.4	83	0.59	0.30	1.17	0.133
Non-relapsers	55	67.9	81	47	56.6	83				

Definition of Relapsers is based on the CGI Global Improvement Score

* = Adjusted for terms retained in the final model (i.e. centre group)

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1411.SAS (05MAR99 12:53)

Table 14.12.2b

Number (%) of Relapsers by Centre Grouping
Intention to Treat Population
Phase II: Randomised Treatment

Centre Group=001/002

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	3	37.5	8	3	42.9	7
Non-relapsers	5	62.5	8	4	57.1	7

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2b

Number (%) of Relapsers by Centre Grouping
Intention to Treat Population
Phase II: Randomised Treatment

Centre Group=004/017

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	4	44.4	9	7	70.0	10
Non-relapsers	5	55.6	9	3	30.0	10

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2b

Number (%) of Relapsers by Centre Grouping
Intention to Treat Population
Phase II: Randomised Treatment

Centre Group=005/021

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	7	77.8	9	4	57.1	7
Non-relapsers	2	22.2	9	3	42.9	7

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2b

Number (%) of Relapsers by Centre Grouping
Intention to Treat Population
Phase II: Randomised Treatment

Centre Group=006/012

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	2	25.0	8	3	37.5	8
Non-relapsers	6	75.0	8	5	62.5	8

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2b

Number (%) of Relapsers by Centre Grouping
Intention to Treat Population
Phase II: Randomised Treatment

Centre Group=007/008

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	3	37.5	8	1	12.5	8
Non-relapsers	5	62.5	8	7	87.5	8

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2b

Number (%) of Relapsers by Centre Grouping
Intention to Treat Population
Phase II: Randomised Treatment

Centre Group=009/011

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	2	28.6	7	3	33.3	9
Non-relapsers	5	71.4	7	6	66.7	9

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2b

Number (%) of Relapsers by Centre Grouping
Intention to Treat Population
Phase II: Randomised Treatment

Centre Group=010/023

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	1	14.3	7	1	12.5	8
Non-relapsers	6	85.7	7	7	87.5	8

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2b

Number (%) of Relapsers by Centre Grouping
Intention to Treat Population
Phase II: Randomised Treatment

Centre Group=013/022

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	1	14.3	7	2	28.6	7
Non-relapsers	6	85.7	7	5	71.4	7

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2b

Number (%) of Relapsers by Centre Grouping
Intention to Treat Population
Phase II: Randomised Treatment

Centre Group=015

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	0	0.0	4	3	75.0	4
Non-relapsers	4	100.0	4	1	25.0	4

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2b

Number (%) of Relapsers by Centre Grouping
Intention to Treat Population
Phase II: Randomised Treatment

Centre Group=016/020

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	2	33.3	6	6	75.0	8
Non-relapsers	4	66.7	6	2	25.0	8

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2b

Number (%) of Relapsers by Centre Grouping
Intention to Treat Population
Phase II: Randomised Treatment

Centre Group=018/026

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	4	50.0	8	1	16.7	6
Non-relapsers	4	50.0	8	5	83.3	6

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2b

Number (%) of Relapsers by Centre Grouping
Intention to Treat Population
Phase II: Randomised Treatment

Centre Group=019/027

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	1	16.7	6	4	44.4	9
Non-relapsers	5	83.3	6	5	55.6	9

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2b

Number (%) of Relapsers by Centre Grouping
Intention to Treat Population
Phase II: Randomised Treatment

Centre Group=024/025

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	3	37.5	8	5	71.4	7
Non-relapsers	5	62.5	8	2	28.6	7

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2c

Number (%) of Relapsers by Centre Grouping
Per Protocol Population
Phase II: Randomised Treatment

Centre Group=001/002

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	3	42.9	7	2	33.3	6
Non-relapsers	4	57.1	7	4	66.7	6

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2c

Number (%) of Relapsers by Centre Grouping
Per Protocol Population
Phase II: Randomised Treatment

Centre Group=004/017

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	4	50.0	8	7	70.0	10
Non-relapsers	4	50.0	8	3	30.0	10

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2c

Number (%) of Relapsers by Centre Grouping
Per Protocol Population
Phase II: Randomised Treatment

Centre Group=005/021

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	6	85.7	7	2	40.0	5
Non-relapsers	1	14.3	7	3	60.0	5

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2c

Number (%) of Relapsers by Centre Grouping
Per Protocol Population
Phase II: Randomised Treatment

Centre Group=006/012

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	2	28.6	7	2	28.6	7
Non-relapsers	5	71.4	7	5	71.4	7

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2c

Number (%) of Relapsers by Centre Grouping
Per Protocol Population
Phase II: Randomised Treatment

Centre Group=007/008

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	2	28.6	7	1	16.7	6
Non-relapsers	5	71.4	7	5	83.3	6

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2c

Number (%) of Relapsers by Centre Grouping
Per Protocol Population
Phase II: Randomised Treatment

Centre Group=009/011

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	2	28.6	7	2	28.6	7
Non-relapsers	5	71.4	7	5	71.4	7

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2c

Number (%) of Relapsers by Centre Grouping
Per Protocol Population
Phase II: Randomised Treatment

Centre Group=010/023

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	1	14.3	7	1	12.5	8
Non-relapsers	6	85.7	7	7	87.5	8

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2c

Number (%) of Relapsers by Centre Grouping
Per Protocol Population
Phase II: Randomised Treatment

Centre Group=013/022

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	0	0.0	5	2	40.0	5
Non-relapsers	5	100.0	5	3	60.0	5

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2c

Number (%) of Relapsers by Centre Grouping
Per Protocol Population
Phase II: Randomised Treatment

Centre Group=015

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	0	0.0	4	3	75.0	4
Non-relapsers	4	100.0	4	1	25.0	4

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

Table 14.12.2c

Number (%) of Relapsers by Centre Grouping
Per Protocol Population
Phase II: Randomised Treatment

Centre Group=016/020

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	1	25.0	4	6	85.7	7
Non-relapsers	3	75.0	4	1	14.3	7

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2c

Number (%) of Relapsers by Centre Grouping
Per Protocol Population
Phase II: Randomised Treatment

Centre Group=018/026

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	3	50.0	6	1	16.7	6
Non-relapsers	3	50.0	6	5	83.3	6

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2c

Number (%) of Relapsers by Centre Grouping
Per Protocol Population
Phase II: Randomised Treatment

Centre Group=019/027

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	0	0.0	5	2	40.0	5
Non-relapsers	5	100.0	5	3	60.0	5

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.12.2c

Number (%) of Relapsers by Centre Grouping
Per Protocol Population
Phase II: Randomised Treatment

Centre Group=024/025

	Paroxetine			Placebo		
	n	%	N	n	%	N
Relapsers	2	28.6	7	5	71.4	7
Non-relapsers	5	71.4	7	2	28.6	7

Definition of Relapsers is based on the CGI Global Improvement Score

Note: Centres have been grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients has been ranked one. Centres with equal numbers of patients have been ranked depending on centre number, the lowest centre number has been allocated the lowest rank. The centre with the lowest rank was then combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1412.SAS (05MAR99 11:32)

Table 14.13.2b

Dose at Relapse by Dose at Randomisation Baseline
Intention to Treat Population
Phase II: Randomised Treatment

	Dose at Relapse																			
	Relapser														Non-relapser		Total No of Patients in Group	
	Placebo		10 mg		20 mg		30 mg		40 mg		50 mg		60 mg		-			
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Dose at Randomisation Baseline																		
10 mg	3	75.0	1	25.0											13	100.0	17	100.0
20 mg	11	52.4			10	47.6									25	100.0	46	100.0
30 mg	11	57.9					8	42.1							27	100.0	46	100.0
40 mg	8	61.5							5	38.5					19	100.0	32	100.0
50 mg	3	50.0									3	50.0			17	100.0	23	100.0
60 mg	7	53.8											6	46.2	16	100.0	29	100.0

Table 14.13.2c

Dose at Relapse by Dose at Randomisation Baseline
Per Protocol Population
Phase II: Randomised Treatment

	Dose at Relapse																	
	Relapser												Non-relapser		Total No of Patients in Group	
	Placebo		20 mg		30 mg		40 mg		50 mg		60 mg		-			
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Dose at Randomisation Baseline																
10 mg	2	100.0											12	100.0	14	100.0
20 mg	10	58.8	7	41.2									22	100.0	39	100.0
30 mg	9	52.9			8	47.1							21	100.0	38	100.0
40 mg	8	66.7					4	33.3					17	100.0	29	100.0
50 mg	3	60.0							2	40.0			16	100.0	21	100.0
60 mg	4	44.4									5	55.6	14	100.0	23	100.0

Table 14.21.1

Baseline and Change from Baseline in CY-BOCS Total Scores
Intention to Treat Population
Phase I: Open Label Treatment

	Mean	Std Err	N
Baseline	26.3	0.27	329
Week 2	-4.1	0.33	328
Week 4	-7.4	0.40	304
Week 6	-9.6	0.42	292
Week 8	-11.1	0.44	277
Week 12	-13.0	0.48	263
Week 16	-15.2	0.47	239
Week 16 End point	-13.0	0.46	329

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1421A.SAS (22FEB99 16:32)

Table 14.21.2

Randomisation Baseline and Change from Randomisation Baseline in CY-BOCS Total Scores
Intention to Treat Population
Phase II: Randomised Treatment

	Paroxetine			Placebo			Pairwise Comparisons *			
	Mean	Std Err	N	Mean	Std Err	N	Diff	Lower 95% CI Limit	Upper 95% CI Limit	p-value
Randomisation Baseline	9.9	0.67	92	9.6	0.61	98				
Week 2	0.9	0.59	90	3.7	0.72	97				
Week 4	1.6	0.86	79	4.9	0.81	74				
Week 6	-0.6	0.59	65	2.6	0.81	51				
Week 8	0.1	0.69	58	1.5	0.86	42	-1.14	-3.35	1.08	0.310
Week 10	0.3	0.82	53	1.1	0.65	36				
Week 12	-0.5	0.96	49	1.3	0.77	35				
Week 16	-0.4	1.07	41	1.3	0.93	30	-0.81	-3.73	2.12	0.583
70% End point	2.3	0.82	92	6.3	0.82	98	-4.01	-6.30	-1.72	0.001
Week 16 End point	3.6	0.92	92	6.9	0.86	98	-3.38	-5.88	-0.88	0.008

* = Adjusted for terms retained in the final model (i.e. centre group)

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1421B.SAS (26FEB99 11:57)

Table 14.22.1

Baseline and Change from Baseline in CY-BOCS Total Scores
Compulsive Subscale
Intention to Treat Population
Phase I: Open Label Treatment

	Mean	Std Err	N
Baseline	13.5	0.15	329
Week 2	-1.9	0.18	328
Week 4	-3.5	0.22	304
Week 6	-4.7	0.24	292
Week 8	-5.4	0.24	277
Week 12	-6.5	0.27	263
Week 16	-7.6	0.27	239
Week 16 End point	-6.4	0.25	329

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1421A.SAS (22FEB99 16:32)

Table 14.22.2

Randomisation Baseline and Change from Randomisation Baseline in CY-BOCS Total Scores
Compulsive Subscale
Intention to Treat Population
Phase II: Randomised Treatment

	Paroxetine			Placebo		
	Mean	Std Err	N	Mean	Std Err	N
Randomisation Baseline	5.3	0.38	92	5.2	0.34	98
Week 2	0.6	0.31	90	1.6	0.40	97
Week 4	0.8	0.45	79	2.2	0.41	74
Week 6	-0.5	0.34	65	1.1	0.43	51
Week 8	0.0	0.42	58	0.4	0.49	42
Week 10	-0.2	0.49	53	0.1	0.39	36
Week 12	-0.7	0.57	49	0.3	0.46	35
Week 16	-0.2	0.61	41	0.2	0.58	30
70% End point	1.2	0.42	92	3.0	0.42	98
Week 16 End point	1.7	0.49	92	2.9	0.47	98

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1421B.SAS (26FEB99 11:57)

Table 14.23.1

Baseline and Change from Baseline in CY-BOCS Total Scores
Obsessive Subscale
Intention to Treat Population
Phase I: Open Label Treatment

	Mean	Std Err	N
Baseline	12.9	0.16	329
Week 2	-2.2	0.19	328
Week 4	-3.9	0.22	304
Week 6	-5.0	0.23	292
Week 8	-5.7	0.25	277
Week 12	-6.6	0.27	263
Week 16	-7.6	0.26	238
Week 16 End point	-6.6	0.25	329

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1421A.SAS (22FEB99 16:32)

Table 14.23.2

Randomisation Baseline and Change from Randomisation Baseline in CY-BOCS Total Scores
Obsessive Subscale
Intention to Treat Population
Phase II: Randomised Treatment

	Paroxetine			Placebo		
	Mean	Std Err	N	Mean	Std Err	N
Randomisation Baseline	4.7	0.36	91	4.4	0.32	98
Week 2	0.3	0.33	89	2.1	0.38	97
Week 4	0.8	0.48	78	2.6	0.45	74
Week 6	-0.0	0.31	64	1.6	0.46	51
Week 8	0.1	0.39	58	1.0	0.45	42
Week 10	0.5	0.47	53	1.0	0.37	36
Week 12	0.2	0.50	49	0.9	0.43	35
Week 16	-0.2	0.57	41	1.1	0.44	30
70% End point	1.1	0.45	91	3.4	0.43	98
Week 16 End point	1.9	0.50	91	4.0	0.43	98

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1421B.SAS (26FEB99 11:57)

Table 14.24.1

Number (%) of Patients with a >= 25% Reduction from Baseline In CY-BOCS Total Score
Intention to Treat Population
Phase I: Open Label Treatment

	n	%	N
Week 2	91	27.7	328
Week 4	151	49.7	304
Week 6	187	64.0	292
Week 8	209	75.5	277
Week 12	209	79.5	263
Week 16	217	90.8	239
Week 16 End point	258	78.4	329

Table 14.24.2

Number (%) of Patients with a >= 25% Reduction in CY-BOCS Score
Intention to Treat Population
Phase II: Randomised Treatment

	Paroxetine			Placebo			Pairwise Comparisons *			
	n	%	N	n	%	N	Odds Ratio	Lower 95% CI Limit	Upper 95% CI Limit	p-value
Week 2	21	25.9	81	11	12.4	89				
Week 4	20	28.2	71	6	8.8	68				
Week 6	22	38.6	57	10	21.3	47				
Week 8	17	34.0	50	12	30.8	39	1.16	0.47	2.84	0.747
Week 10	19	42.2	45	9	28.1	32				
Week 12	19	45.2	42	9	29.0	31				
Week 16	17	45.9	37	7	26.9	26	2.31	0.78	6.80	0.130
70% End point	22	26.5	83	8	8.9	90	3.70	1.54	8.86	0.003
Week 16 End point	24	28.9	83	13	14.4	90	2.41	1.13	5.13	0.023

* = Unadjusted due to low numbers of patients per treatment/centre group combination

Note: Only patients with a non-zero baseline and at least one post baseline assessment have been summarised

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]LT1421B.SAS (26FEB99 11:57)

Table 14.31.1

Number (%) of Patients with a CGI Global Improvement Score of 1 (Very Much Improved) or 2 (Much Improved)
Intention to Treat Population
Phase I: Open Label Treatment

	n N (%)
Week 2	52 328 (15.9%)
Week 4	120 305 (39.3%)
Week 6	144 292 (49.3%)
Week 8	170 277 (61.4%)
Week 12	196 263 (74.5%)
Week 16	209 239 (87.4%)
Week 16 End point	231 315 (73.3%)

Table 14.31.2

Number (%) of Patients with a CGI Global Improvement Score of 1 (Very Much Improved) or 2 (Much Improved)
Intention to Treat Population
Phase II: Randomised Treatment

	Treatment Group	
	Paroxetine	Placebo
	n N (%)	n N (%)
Randomisation Baseline	95 95 (100.0%)	98 98 (100.0%)
Week 2	79 91 (86.8 %)	77 97 (79.4 %)
Week 4	62 79 (78.5 %)	51 74 (68.9 %)
Week 6	59 65 (90.8 %)	40 51 (78.4 %)
Week 8	51 58 (87.9 %)	36 42 (85.7 %)
Week 10	45 53 (84.9 %)	31 36 (86.1 %)
Week 12	44 50 (88.0 %)	31 35 (88.6 %)
Week 16	36 41 (87.8 %)	25 30 (83.3 %)
70% End point	66 93 (71.0 %)	57 96 (59.4 %)
Week 16 End point	54 92 (58.7 %)	43 96 (44.8 %)

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_3.SAS (18FEB99 17:49)

Table 14.32.1

Number (%) of Patients in Each Category of the CGI Global Improvement Score
Intention to Treat Population
Phase I: Open Label Treatment

	Very Much Improved		Much Improved		Minimally Improved		No Change		Minimally Worse		Much Worse		Very Much Worse			Not Assessed-/Missing
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	Total	
Week 2	6	1.8	46	14.0	129	39.3	131	39.9	15	4.6	1	0.3			328	2
Week 4	23	7.5	97	31.8	119	39.0	59	19.3	5	1.6	2	0.7			305	2
Week 6	48	16.4	96	32.9	111	38.0	27	9.2	6	2.1	2	0.7	2	0.7	292	0
Week 8	67	24.2	103	37.2	82	29.6	18	6.5	7	2.5					277	0
Week 12	86	32.7	110	41.8	48	18.3	8	3.0	6	2.3	4	1.5	1	0.4	263	0
Week 16	115	48.1	94	39.3	22	9.2	5	2.1	2	0.8	1	0.4			239	0
Week 16 End point	123	39.0	108	34.3	49	15.6	16	5.1	10	3.2	6	1.9	3	1.0	315	2

Table 14.32.2

Number (%) of Patients in Each Category of the CGI Global Improvement Score
Intention to Treat Population
Phase II: Randomised Treatment

Treatment Group: Paroxetine

	Very Much Improved		Much Improved		Minimally Improved		No Change		Minimally Worse		Much Worse		Very Much Worse			
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	Total	Not Assessed-/Missing
Randomisation Baseline	53	55.8	42	44.2											95	0
Week 2	43	47.3	36	39.6	6	6.6	4	4.4	1	1.1	1	1.1			91	1
Week 4	40	50.6	22	27.8	6	7.6	1	1.3	4	5.1	5	6.3	1	1.3	79	0
Week 6	37	56.9	22	33.8	6	9.2									65	0
Week 8	33	56.9	18	31.0	4	6.9	2	3.4	1	1.7					58	0
Week 10	30	56.6	15	28.3	7	13.2			1	1.9					53	0
Week 12	30	60.0	14	28.0	4	8.0			1	2.0			1	2.0	50	0
Week 16	28	68.3	8	19.5	4	9.8			1	2.4					41	0
70% End point	42	45.2	24	25.8	10	10.8	5	5.4	5	5.4	6	6.5	1	1.1	93	1
Week 16 End point	38	41.3	16	17.4	17	18.5	6	6.5	8	8.7	5	5.4	2	2.2	92	1

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_3.SAS (18FEB99 17:49)

Table 14.32.2

Number (%) of Patients in Each Category of the CGI Global Improvement Score
Intention to Treat Population
Phase II: Randomised Treatment

Treatment Group: Placebo

	Very Much Improved		Much Improved		Minimally Improved		No Change		Minimally Worse		Much Worse		Very Much Worse			Not Assessed-/Missing
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	Total	
Randomisation Baseline	51	52.0	47	48.0											98	0
Week 2	28	28.9	49	50.5	10	10.3	5	5.2	3	3.1	1	1.0	1	1.0	97	0
Week 4	19	25.7	32	43.2	12	16.2	7	9.5	1	1.4	2	2.7	1	1.4	74	0
Week 6	18	35.3	22	43.1	7	13.7	1	2.0	3	5.9					51	0
Week 8	20	47.6	16	38.1	4	9.5			2	4.8					42	0
Week 10	18	50.0	13	36.1	2	5.6	1	2.8	1	2.8	1	2.8			36	0
Week 12	17	48.6	14	40.0	1	2.9	3	8.6							35	0
Week 16	15	50.0	10	33.3	4	13.3	1	3.3							30	0
70% End point	20	20.8	37	38.5	19	19.8	11	11.5	4	4.2	3	3.1	2	2.1	96	0
Week 16 End point	22	22.9	21	21.9	24	25.0	15	15.6	8	8.3	4	4.2	2	2.1	96	0

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_3.SAS (18FEB99 17:49)

Table 14.33.1

Number (%) of Patients in Each Category of the CGI Severity of Illness Score
Intention to Treat Population
Phase I: Open Label Treatment

	Normal, not at all ill		Borderline mentally ill		Mildly ill		Moderately ill		Markedly ill		Severely ill		Among the most severely ill patients			Not Assessed-/Missing
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	Total	
Baseline					6	1.8	148	44.2	110	32.8	70	20.9	1	0.3	335	0
Week 2			3	0.9	29	8.8	165	50.3	86	26.2	45	13.7			328	2
Week 4	3	1.0	13	4.3	70	23.0	137	44.9	58	19.0	24	7.9			305	2
Week 6	9	3.1	21	7.2	81	27.7	129	44.2	39	13.4	12	4.1	1	0.3	292	0
Week 8	10	3.6	44	15.9	75	27.1	114	41.2	30	10.8	4	1.4			277	0
Week 12	21	8.0	50	19.0	84	31.9	87	33.1	13	4.9	7	2.7	1	0.4	263	0
Week 16	35	14.6	63	26.4	73	30.5	58	24.3	8	3.3	2	0.8			239	0
Week 16 End point	36	11.4	68	21.6	85	27.0	92	29.2	22	7.0	10	3.2	2	0.6	315	2

Table 14.33.2

Number (%) of Patients in Each Category of the CGI Severity of Illness Score
Intention to Treat Population
Phase II: Randomised Treatment

Treatment Group: Paroxetine

	Normal, not at all ill		Borderline mentally ill		Mildly ill		Moderately ill		Markedly ill		Severely ill		Among the most severely ill patients			Not Assessed-/Missing
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	Total	
Randomisation Baseline	15	15.8	27	28.4	37	38.9	15	15.8	1	1.1					95	0
Week 2	13	14.3	25	27.5	31	34.1	17	18.7	5	5.5					91	1
Week 4	14	17.7	24	30.4	23	29.1	11	13.9	3	3.8	4	5.1			79	0
Week 6	15	23.1	18	27.7	22	33.8	9	13.8	1	1.5					65	0
Week 8	13	22.4	13	22.4	23	39.7	9	15.5							58	0
Week 10	12	22.6	12	22.6	21	39.6	7	13.2	1	1.9					53	0
Week 12	15	30.0	12	24.0	16	32.0	4	8.0	2	4.0	1	2.0			50	0
Week 16	12	29.3	12	29.3	8	19.5	8	19.5	1	2.4					41	0
70% End point	14	15.1	26	28.0	26	28.0	15	16.1	8	8.6	4	4.3			93	1
Week 16 End point	15	16.3	19	20.7	19	20.7	23	25.0	12	13.0	4	4.3			92	1

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_3.SAS (18FEB99 17:49)

Table 14.33.2

Number (%) of Patients in Each Category of the CGI Severity of Illness Score
Intention to Treat Population
Phase II: Randomised Treatment

Treatment Group: Placebo

	Normal, not at all ill		Borderline mentally ill		Mildly ill		Moderately ill		Markedly ill		Severely ill		Among the most severely ill patients			
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	Total	Not Assessed-/Missing
Randomisation Baseline	17	17.3	31	31.6	34	34.7	14	14.3	2	2.0					98	0
Week 2	11	11.3	21	21.6	37	38.1	22	22.7	3	3.1	3	3.1			97	0
Week 4	9	12.2	15	20.3	18	24.3	22	29.7	8	10.8	2	2.7			74	0
Week 6	8	15.7	13	25.5	16	31.4	13	25.5	1	2.0					51	0
Week 8	12	28.6	9	21.4	11	26.2	10	23.8							42	0
Week 10	11	30.6	7	19.4	9	25.0	9	25.0							36	0
Week 12	10	28.6	9	25.7	8	22.9	8	22.9							35	0
Week 16	8	26.7	6	20.0	9	30.0	7	23.3							30	0
70% End point	9	9.4	17	17.7	25	26.0	30	31.3	10	10.4	5	5.2			96	0
Week 16 End point	11	11.5	13	13.5	20	20.8	36	37.5	11	11.5	5	5.2			96	0

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_3.SAS (18FEB99 17:49)

Table 14.34.1

Baseline and Change from Baseline in the CGI Severity of Illness Score
Intention to Treat Population
Phase I: Open Label Treatment

	Median	Minimum	Maximum	N
Baseline	5	3	7	331
Week 2	0	-3	1	328
Week 4	-1	-5	1	305
Week 6	-1	-4	1	292
Week 8	-1	-5	1	277
Week 12	-1	-5	1	263
Week 16	-2	-5	1	239
Week 16 End point	-2	-5	1	315

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_3.SAS (18FEB99 17:49)

Table 14.34.2

Randomisation Baseline and Change from Randomisation Baseline in the CGI Severity of Illness Score
Intention to Treat Population
Phase II: Randomised Treatment

	Treatment Group							
	Paroxetine				Placebo			
	Median	Minimum	Maximum	N	Median	Minimum	Maximum	N
Randomisation Baseline	3	1	5	95	3	1	5	98
Week 2	0	-2	3	91	0	-1	3	97
Week 4	0	-2	4	79	0	-1	3	74
Week 6	0	-2	2	65	0	-1	3	51
Week 8	0	-2	2	58	0	-1	3	42
Week 10	0	-2	2	53	0	-1	2	36
Week 12	0	-2	3	50	0	-1	2	35
Week 16	0	-2	1	41	0	-1	2	30
70% End point	0	-2	4	93	1	-1	3	96
Week 16 End point	0	-2	4	92	1	-1	3	96

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_3.SAS (18FEB99 17:49)

Table 14.71.1

GAF Total Scores
Intention to Treat Population
Phase I: Open Label Treatment

	Mean (Std Err) N
Baseline	54.1 (0.40) 335
Week 4	60.3 (0.56) 315
Week 8	64.7 (0.63) 287
Week 12	67.3 (0.70) 263
Week 16	71.1 (0.76) 239
Week 16 End point	67.4 (0.75) 318

Table 14.71.2

GAF Total Scores
Intention to Treat Population
Phase II: Randomised Treatment

	Treatment Group			
	Paroxetine		Placebo	
	Mean (Std Err)	N	Mean (Std Err)	N
Randomisation Baseline	73.4 (1.11)	95	73.5 (1.11)	98
Week 2	70.7 (1.29)	91	69.9 (1.19)	97
Week 4	71.3 (1.45)	79	67.9 (1.67)	74
Week 6	74.3 (1.55)	65	72.4 (1.69)	51
Week 8	72.7 (1.83)	58	75.2 (1.87)	42
Week 10	73.7 (1.73)	53	74.7 (2.16)	36
Week 12	74.7 (2.14)	49	75.4 (2.18)	35
Week 16	74.2 (2.31)	41	76.3 (2.36)	30
70% End point	69.3 (1.36)	93	66.3 (1.37)	98
Week 16 End point	67.6 (1.55)	93	65.4 (1.43)	98

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_7.SAS (19FEB99 15:09)

Table 14.72.1

Baseline and Change from Baseline in GAF Total Scores
Intention to Treat Population
Phase I: Open Label Treatment

	Mean (Std Err) N
Baseline	54.0 (0.41) 318
Week 4	6.2 (0.49) 315
Week 8	10.7 (0.59) 287
Week 12	13.1 (0.70) 263
Week 16	16.7 (0.77) 239
Week 16 End point	13.4 (0.73) 318

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_7.SAS (19FEB99 15:09)

Table 14.72.2

Randomisation Baseline and Change from Randomisation Baseline in GAF Total Scores
Intention to Treat Population
Phase II: Randomised Treatment

	Treatment Group			
	Paroxetine		Placebo	
	Mean (Std Err)	N	Mean (Std Err)	N
Randomisation Baseline	73.4 (1.13)	93	73.5 (1.11)	98
Week 2	-2.6 (0.85)	91	-3.6 (0.89)	97
Week 4	-2.2 (0.99)	79	-5.7 (1.34)	74
Week 6	0.4 (0.89)	65	-2.6 (1.19)	51
Week 8	-1.5 (0.98)	58	-1.0 (1.22)	42
Week 10	-0.8 (1.17)	53	-1.4 (1.12)	36
Week 12	-0.2 (1.60)	49	-1.3 (1.20)	35
Week 16	-0.6 (1.63)	41	-0.8 (1.81)	30
70% End point	-4.0 (1.04)	93	-7.2 (1.18)	98
Week 16 End point	-5.8 (1.22)	93	-8.1 (1.26)	98

Note: Only patients with a baseline and at least one post baseline assessment have been summarised

Note: The 70% End point visit is Week 4

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]EFF14_7.SAS (19FEB99 15:09)

12 Data Source Tables: Safety Results

Confidential

SmithKline Beecham

Paroxetine

BRL-029060

Predefined Clinical Concern Limits for the Vital Signs and Laboratory Data

453

Table 15.0

SB Document Number: BRL-029060/RSD-100W8B/1

A. Vital Signs Data:

Systolic Blood Pressure (mmHg):

Normal Range: 95-145 mmHg

Significant Increase: Increase of >= 40 mmHg from baseline

Significant Decrease: Decrease of >= 30 mmHg from baseline

Diastolic Blood Pressure (mmHg):

Normal Range: 50-85 mmHg

Significant Increase: Increase of >= 30 mmHg from baseline

Significant Decrease: Decrease of >= 20 mmHg from baseline

Heart Rate (bpm):

Normal Range:

Ages 8 to 12: 65 - 115 bpm

Ages 13 to 17: 55-110 bpm

Significant Increase: Increase of >= 30 bpm from baseline

Significant Decrease: Decrease of >= 30 bpm from baseline

Weight (LB):

Boys: Normal Range for Age

8:	<40 or >81
9:	<44 or >92
10:	<48 or >104
11:	<54 or >118
12:	<60 or > 133
13:	<69 or >148
14:	<79 or > 164
15:	<90 or >179
16:	<100 or >198
17:	<108 or >206

Girls: Normal Range for Age

8:	<38 or >81
9:	<43 or >94
10:	<48 or >109
11:	<55 or >124
12:	<62 or >139
13:	<70 or >153
14:	<78 or >166
15:	<85 or >176
16:	<90 or >183
17:	<93 or >186

Significant Increase: Increase of >= 7% from baseline

Significant Decrease: Decrease of >=7% from baseline

B. Laboratory Parameters

Criteria for Defining Clinically Significant Abnormalities for Laboratory Parameters (Extended Ranges)

Variable	Flagged values
Haematology	
Haemoglobin - Male	< 115 g/l
Haemoglobin - Female	< 95 g/l
Hematocrit	6-11 yrs: <35% 12-17yrs: <36% F: 18-64 yrs: <35% M:18-64 yrs: <41%
Mean Cell Volume	6-11 yrs: < 77 or > 95 FL 12-17yrs: <78 or >102 FL 18-64yrs: < 80 or >100 FL
Mean Cell Haemoglobin	6-11 yrs: < 22 or > 33 pg 12-18 yrs: < 22 or >35 pg
Mean Cell Haemoglobin Concentration	No flagging
WBC	< 2.8 or > 16.0 $x10^9$/l
Neutrophils	<=15%
Lymphocytes	>=75%
Monocytes	>= 15%
Basophils	>= 10%
Eosinophils	>= 10%
Platelets	< 75 or > 700 $x10^9$/l
Bands	> 10%
Segmented Neutrophils	<= 15%
RBC - Male	> 8 $x10^{12}$/l
RBC - Female	> 10 $x10^{12}$/l
Clinical Chemistry	
BUN	> 10.71 mmol/l
Serum creatinine	> 176.8 mcmol/l
Total bilirubin	> 34.2 mcmol/1
SGOT (AST)	> 150 U/l
SGPT (ALT)	> 165 U/l
Alkaline phosphatase	3-12 yrs: > 415 U/l F: 13-15 yrs: > 350 U/l F: 16-19 yrs: > 165 U/l M:13-15 yrs: > 500 U/l M:16-19 yrs: > 225 U/l

Total protein	< 45 or > 100 g/l
T3 (Total)	< 1.3 > 2.84 nmol/l
T4 (Total)	< 57.91 > 160.87 nmol/l
Chloride	< 90 >118 mmol/l
Potassium	< 3 > 6 mmol/l
Phosphorous	3-12 yrs: < 0.646 or > 2.261 mmol/l 13 - 18 yrs: < 0.4845 or > 1.938 mmol/l
Sodium	< 126 > 156 mmol/l
Glucose (random)	< 3 or > 7 mmol/l
Gamma Glutamyl Transferase	3-12 yrs: > 98 u/l Males: 13-18 yrs: > 98 u/l Females: 13-18 yrs: > 68 u/l
Lactate Dehydrogenase	> 375 u/l

Confidential

SmithKline Beecham

Paoxetine

BRL-029060

Location of Report Narratives

453

Table 15.4

SB Document Number: BRL-029060/RSD-100W8H/1

The Narrative for the PID can be found in the table indicated. An x denotes an additional category in which the patient was also included

PID	NARRATIVE				
	Deaths *	Serious AEs (nonfatal)	AE leading to withdrawal	Vital signs of potential clinical concern	Laboratory values of potential clinical concern
	Table	Table	Table	Table	
453.001.00360			15.09.1a		
453.001.00361				15.21.2a	
453.001.00363		15.05.2a	X		
453.002.00259					15.3.2a
453.002.00260			15.09.1a		
453.002.00307			15.09.1a		
453.002.00311		15.05.2a	X		
453.003.00011			15.09.1a		
453.004.00088			15.09.1a		
453.005.00016			15.09.1a		
453.005.00376			15.09.1a		
453.006.00102			15.09.1a		
453.006.00105		15.05.2a **			
453.006.00170			15.09.1a		
453.006.00347			15.09.1a		
453.006.00391			15.09.1a		
453.006.00463			15.09.1a		
453.007.00003				15.21.2a	
453.008.00456			15.09.1a		
453.008.00460			15.09.1a		
453.010.00049			15.09.1a		
453.011.00014			15.09.1a		
453.011.00015			15.09.1a		
453.011.00142			15.09.1a		
453.011.00143			15.09.1a		
453.011.00148			15.09.1a		
453.011.00150			15.09.1a		
453.011.00199			15.09.1a		
453.011.00425			15.09.1a		
453.012.00065		15.05.2a			
453.013.00055			15.09.1a		
453.013.00248				15.21.2a	
453.015.00353		15.05.2a			
453.015.00488			15.09.1a		
453.016.00164			15.09.1a		
453.016.00344			15.09.1a	X	
453.017.00009			15.09.1a	X	
453.017.00192			15.09.1a		
453.017.00195				15.21.2a	X
453.017.00197				15.21.2a	
453.017.00211		15.05.2a	X	X	
453.017.00212		15.05.2a	X		
453.017.00243			15.09.1a		
453.017.00247			15.09.1a		
453.017.00335		15.05.2a			

The Narrative for the PID can be found in the table indicated. An x denotes an additional category in which the patient was also included

PID	NARRATIVE				
	Deaths *	Serious AEs (nonfatal)	AE leading to withdrawal	Vital signs of potential clinical concern	Laboratory values of potential clinical concern
	Table	Table	Table	Table	
453.017.00339			15.09.1a		
453.017.00431		15.05.2a	X		
453.017.00453			15.09.1a		
453.017.00455			15.09.1a		
453.018.00027			15.09.1a		
453.018.00223				15.21.2a	
453.018.00224			15.09.1a		
453.018.00226			15.09.1a		
453.018.00420		15.05.2a			
453.019.00301				15.21.2a	
453.019.00302				15.21.2a	
453.020.00448		15.05.2a			
453.021.00067		15.05.2a	X		
453.021.00068				15.21.2a	
453.021.00126		15.05.2a	X		
453.021.00127		15.05.2a	X		
453.021.00129		15.05.2a	X		
453.022.00096			15.09.1a		
453.022.00097			15.09.1a		
453.022.00099			15.09.1a		
453.022.00116			15.09.1a		
453.022.00367			15.09.1a		
453.022.00397			15.09.1a		
453.023.00091				15.21.2a	
453.023.00092				15.21.2a	
453.023.00157			15.09.1a		
453.023.00400				15.21.2a	
453.023.00401				15.21.2a	
453.024.00038			15.09.1a	X	
453.024.00180		15.05.2a	X		
453.025.00021				15.21.2a	
453.025.00023			15.09.1a		
453.025.00295			15.09.1a		
453.025.00297		15.05.2a			
453.026.00137				15.21.2a	
453.026.00140		15.05.2a			
453.026.00285				15.21.2a	
453.026.00287		15.05.2a	X		
453.027.00172			15.09.1a		

* No deaths were reported to date in this study

** SAE occurred post-therapy and does not appear in Data Source Tables 15.08.1 or 15.08.2

Paroxetine - Protocol: 453

TABLE 15.01.1

Number (%) of Patients with Emergent Adverse Experiences - Displayed by Body System
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	316	94.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Body as a Whole	199	59.4
Cardiovascular System	24	7.2
Digestive System	163	48.7
Endocrine System	1	0.3
Hemic and Lymphatic System	18	5.4
Metabolic and Nutritional Disorders	48	14.3
Musculoskeletal System	10	3.0
Nervous System	232	69.3
Respiratory System	119	35.5
Skin and Appendages	53	15.8
Special Searches	1	0.3
Special Senses	35	10.4
Urogenital System	47	14.0

Paroxetine - Protocol: 453

TABLE 15.01.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category - Displayed by Body System
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: <12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	167	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	158	94.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Body as a Whole	101	60.5
Cardiovascular System	9	5.4
Digestive System	83	49.7
Endocrine System	1	0.6
Hemic and Lymphatic System	7	4.2
Metabolic and Nutritional Disorders	23	13.8
Musculoskeletal System	4	2.4
Nervous System	119	71.3
Respiratory System	64	38.3
Skin and Appendages	28	16.8
Special Searches	1	0.6
Special Senses	17	10.2
Urogenital System	23	13.8

Paroxetine - Protocol: 453

TABLE 15.01.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category - Displayed by Body System
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: >=12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	168	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	158	94.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Body as a Whole	98	58.3
Cardiovascular System	15	8.9
Digestive System	80	47.6
Hemic and Lymphatic System	11	6.5
Metabolic and Nutritional Disorders	25	14.9
Musculoskeletal System	6	3.6
Nervous System	113	67.3
Respiratory System	55	32.7
Skin and Appendages	25	14.9
Special Senses	18	10.7
Urogenital System	24	14.3

Paroxetine - Protocol: 453

TABLE 15.01.2

Number (%) of Patients with Emergent Adverse Experiences - Displayed by Body System
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	73	76.8%	80	81.6%	153	79.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Body as a Whole	36	37.9	46	46.9	82	42.5
Cardiovascular System	1	1.1	5	5.1	6	3.1
Digestive System	18	18.9	32	32.7	50	25.9
Hemic and Lymphatic System	3	3.2	3	3.1	6	3.1
Metabolic and Nutritional Disorders	8	8.4	11	11.2	19	9.8
Musculoskeletal System	4	4.2	8	8.2	12	6.2
Nervous System	44	46.3	43	43.9	87	45.1
Respiratory System	19	20.0	27	27.6	46	23.8
Skin and Appendages	11	11.6	6	6.1	17	8.8
Special Senses	5	5.3	4	4.1	9	4.7
Urogenital System	6	6.3	3	3.1	9	4.7

Paroxetine - Protocol: 453

TABLE 15.01.2X

Number (%) of Patients with Emergent Adverse Experiences by Age Category - Displayed by Body System
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: <12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	49	100.0%	47	100.0%	96	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	33	67.3%	37	78.7%	70	72.9%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Body as a Whole	13	26.5	18	38.3	31	32.3
Cardiovascular System	1	2.0	2	4.3	3	3.1
Digestive System	6	12.2	15	31.9	21	21.9
Metabolic and Nutritional Disorders	6	12.2	1	2.1	7	7.3
Musculoskeletal System	1	2.0	3	6.4	4	4.2
Nervous System	23	46.9	18	38.3	41	42.7
Respiratory System	9	18.4	11	23.4	20	20.8
Skin and Appendages	5	10.2	2	4.3	7	7.3
Special Senses	2	4.1	0	0.0	2	2.1
Urogenital System	2	4.1	0	0.0	2	2.1

TABLE 15.01.2X

Number (%) of Patients with Emergent Adverse Experiences by Age Category - Displayed by Body System
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: >=12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	46	100.0%	51	100.0%	97	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	40	87.0%	43	84.3%	83	85.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Body as a Whole	23	50.0	28	54.9	51	52.6
Cardiovascular System	0	0.0	3	5.9	3	3.1
Digestive System	12	26.1	17	33.3	29	29.9
Hemic and Lymphatic System	3	6.5	3	5.9	6	6.2
Metabolic and Nutritional Disorders	2	4.3	10	19.6	12	12.4
Musculoskeletal System	3	6.5	5	9.8	8	8.2
Nervous System	21	45.7	25	49.0	46	47.4
Respiratory System	10	21.7	16	31.4	26	26.8
Skin and Appendages	6	13.0	4	7.8	10	10.3
Special Senses	3	6.5	4	7.8	7	7.2
Urogenital System	4	8.7	3	5.9	7	7.2

Paroxetine - Protocol: 453

TABLE 15.01.3

Number (%) of Patients with Emergent Adverse Experiences - Displayed by Body System
Intention to Treat Population
Taper Phase

TREATMENT GROUP	TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	29	100.0%	42	100.0%	37	100.0%	108	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	8	27.6%	14	33.3%	10	27.0%	32	29.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%	N	%
Body as a Whole	2	6.9	5	11.9	6	16.2	13	12.0
Cardiovascular System	2	6.9	0	0.0	0	0.0	2	1.9
Digestive System	2	6.9	4	9.5	0	0.0	6	5.6
Hemic and Lymphatic System	0	0.0	0	0.0	1	2.7	1	0.9
Metabolic and Nutritional Disorders	2	6.9	0	0.0	0	0.0	2	1.9
Musculoskeletal System	0	0.0	1	2.4	0	0.0	1	0.9
Nervous System	5	17.2	5	11.9	2	5.4	12	11.1
Respiratory System	0	0.0	3	7.1	0	0.0	3	2.8
Special Senses	0	0.0	1	2.4	1	2.7	2	1.9
Urogenital System	0	0.0	1	2.4	1	2.7	2	1.9

Paroxetine - Protocol: 453

TABLE 15.01.3X

Number (%) of Patients with Emergent Adverse Experiences by Age Category - Displayed by Body System
Intention to Treat Population
Taper Phase

Age Group: <12 YEARS

TREATMENT GROUP	TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	9	100.0%	19	100.0%	15	100.0%	43	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	0	0.0%	8	42.1%	3	20.0%	11	25.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%	N	%
Body as a Whole	0	0.0	2	10.5	2	13.3	4	9.3
Digestive System	0	0.0	2	10.5	0	0.0	2	4.7
Hemic and Lymphatic System	0	0.0	0	0.0	1	6.7	1	2.3
Nervous System	0	0.0	3	15.8	1	6.7	4	9.3
Respiratory System	0	0.0	2	10.5	0	0.0	2	4.7
Special Senses	0	0.0	1	5.3	0	0.0	1	2.3

TABLE 15.01.3X

Number (%) of Patients with Emergent Adverse Experiences by Age Category - Displayed by Body System
Intention to Treat Population
Taper Phase

Age Group: >=12 YEARS

TREATMENT GROUP	TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	20	100.0%	23	100.0%	22	100.0%	65	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	8	40.0%	6	26.1%	7	31.8%	21	32.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%	N	%
Body as a Whole	2	10.0	3	13.0	4	18.2	9	13.8
Cardiovascular System	2	10.0	0	0.0	0	0.0	2	3.1
Digestive System	2	10.0	2	8.7	0	0.0	4	6.2
Metabolic and Nutritional Disorders	2	10.0	0	0.0	0	0.0	2	3.1
Musculoskeletal System	0	0.0	1	4.3	0	0.0	1	1.5
Nervous System	5	25.0	2	8.7	1	4.5	8	12.3
Respiratory System	0	0.0	1	4.3	0	0.0	1	1.5
Special Senses	0	0.0	0	0.0	1	4.5	1	1.5
Urogenital System	0	0.0	1	4.3	1	4.5	2	3.1

Paroxetine - Protocol: 453

TABLE 15.02.1

Number (%) of Patients with Emergent Adverse Experiences (Male Specific)
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	198	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	6	3.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Endocrine System	1	0.5
TESTES DISORDER	1	0.5
Urogenital System	5	2.5
ABNORMAL EJACULATION	3	1.5
IMPOTENCE	2	1.0

Paroxetine - Protocol: 453

TABLE 15.02.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Male Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: <12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS	106	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	1	0.9%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Endocrine System	1	0.9
TESTES DISORDER	1	0.9

Paroxetine - Protocol: 453

TABLE 15.02.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Male Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: >=12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS	92	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	5	5.4%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Urogenital System	5	5.4
ABNORMAL EJACULATION	3	3.3
IMPOTENCE	2	2.2

Paroxetine - Protocol: 453

TABLE 15.02.2

Number (%) of Patients with Emergent Adverse Experiences (Male Specific)
Intention to Treat Population
Phase II: Randomised Treatment

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.02.2X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Male Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: <12 YEARS

TREATMENT GROUP		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	:	28	100.0%	33	100.0%	61	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	:	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM		N	%	N	%	N	%

Paroxetine - Protocol: 453

TABLE 15.02.2X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Male Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: >=12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	19	100.0%	25	100.0%	44	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%

Paroxetine - Protocol: 453

TABLE 15.02.3

Number (%) of Patients with Emergent Adverse Experiences (Male Specific)
Intention to Treat Population
Taper Phase

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.02.3X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Male Specific)
Intention to Treat Population
Taper Phase

Age Group: <12 YEARS

TREATMENT GROUP	PHASE I TAPER		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	6	100.0%	7	100.0%	11	100.0%	24	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	0	0.0%	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%	N	%

TABLE 15.02.3X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Male Specific)
Intention to Treat Population
Taper Phase

Age Group: >=12 YEARS

TREATMENT GROUP		PHASE I TAPER		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	:	15	100.0%	10	100.0%	11	100.0%	36	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	:	0	0.0%	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM		N	%	N	%	N	%	N	%

Paroxetine - Protocol: 453

TABLE 15.03.1

Number (%) of Patients with Emergent Adverse Experiences (Female Specific)
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	137	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	8	5.8%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Urogenital System	8	5.8
DYSMENORRHEA	5	3.6
FEMALE GENITAL DISORDERS	1	0.7
MENSTRUAL DISORDER	1	0.7
VAGINAL HEMORRHAGE	1	0.7
VAGINITIS	1	0.7

Paroxetine - Protocol: 453

TABLE 15.03.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Female Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: <12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	61	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	2	3.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Urogenital System	2	3.3
VAGINAL HEMORRHAGE	1	1.6
VAGINITIS	1	1.6

TABLE 15.03.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Female Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: >=12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS	76	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	6	7.9%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Urogenital System	6	7.9
DYSMENORRHEA	5	6.6
FEMALE GENITAL DISORDERS	1	1.3
MENSTRUAL DISORDER	1	1.3

Paroxetine - Protocol: 453

TABLE 15.03.2

Number (%) of Patients with Emergent Adverse Experiences (Female Specific)
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	48	100.0%	40	100.0%	88	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	3	6.3%	0	0.0%	3	3.4%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Urogenital System	3	6.3	0	0.0	3	3.4
DYSMENORRHEA	3	6.3	0	0.0	3	3.4

Paroxetine - Protocol: 453

TABLE 15.03.2X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Female Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: <12 YEARS

TREATMENT GROUP		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	:	21	100.0%	14	100.0%	35	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	:	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM		N	%	N	%	N	%

TABLE 15.03.2X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Female Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: >=12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	27	100.0%	26	100.0%	53	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	3	11.1%	0	0.0%	3	5.7%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Urogenital System	3	11.1	0	0.0	3	5.7
DYSMENORRHEA	3	11.1	0	0.0	3	5.7

Paroxetine - Protocol: 453

TABLE 15.03.3

Number (%) of Patients with Emergent Adverse Experiences (Female Specific)
Intention to Treat Population
Taper Phase

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.03.3X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Female Specific)
Intention to Treat Population
Taper Phase

Age Group: <12 YEARS

TREATMENT GROUP		TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	:	3	100.0%	12	100.0%	4	100.0%	19	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	:	0	0.0%	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM		N	%	N	%	N	%	N	%

TABLE 15.03.3X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Female Specific)
Intention to Treat Population
Taper Phase

Age Group: >=12 YEARS

TREATMENT GROUP		TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	:	5	100.0%	13	100.0%	11	100.0%	29	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	:	0	0.0%	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM		N	%	N	%	N	%	N	%

Paroxetine - Protocol: 453

TABLE 15.04.1

Number (%) of Patients with Emergent Adverse Experiences (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	316	94.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Body as a Whole	199	59.4
ABDOMINAL PAIN	40	11.9
ABNORMAL LABORATORY VALUE	1	0.3
ALLERGIC REACTION	12	3.6
ASTHENIA	72	21.5
BACK PAIN	3	0.9
CHEST PAIN	3	0.9
CHILLS	5	1.5
FEVER	12	3.6
FLU SYNDROME	1	0.3
HEADACHE	82	24.5
INFECTION	32	9.6
MALAISE	1	0.3
PAIN	4	1.2
TRAUMA	45	13.4
Cardiovascular System	24	7.2
AV BLOCK	1	0.3
BRADYCARDIA	1	0.3
ELECTROCARDIOGRAM ABNORMAL	3	0.9
EXTRASYSTOLES	2	0.6
HYPERTENSION	5	1.5
MIGRAINE	2	0.6
PALLOR	2	0.6
PALPITATION	3	0.9
QT INTERVAL PROLONGED	1	0.3
SUPRAVENTRICULAR EXTRASYSTOLES	1	0.3
TACHYCARDIA	4	1.2
VASODILATATION	4	1.2
Digestive System	163	48.7
BRUXISM	2	0.6

TABLE 15.04.1

Number (%) of Patients with Emergent Adverse Experiences (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	316	94.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
CONSTIPATION	15	4.5
DECREASED APPETITE	30	9.0
DIARRHEA	37	11.0
DRY MOUTH	15	4.5
DYSPEPSIA	23	6.9
ERUCTATION	1	0.3
FECAL INCONTINENCE	2	0.6
FLATULENCE	7	2.1
GASTRITIS	1	0.3
GASTROENTERITIS	2	0.6
GASTROINTESTINAL DISORDER	2	0.6
GINGIVITIS	2	0.6
INCREASED APPETITE	13	3.9
NAUSEA	48	14.3
STOMATITIS	4	1.2
TOOTH DISORDER	12	3.6
ULCERATIVE STOMATITIS	2	0.6
VOMITING	24	7.2
Hemic and Lymphatic System	18	5.4
ANEMIA	1	0.3
EOSINOPHILIA	4	1.2
LEUKOCYTOSIS	1	0.3
LEUKOPENIA	3	0.9
LYMPHADENOPATHY	4	1.2
LYMPHOCYTOSIS	1	0.3
PURPURA	5	1.5
THROMBOCYTOPENIA	1	0.3
Metabolic and Nutritional Disorders	48	14.3
HYPERGLYCEMIA	1	0.3
LACTIC DEHYDROGENASE INCREASED	1	0.3

TABLE 15.04.1

Number (%) of Patients with Emergent Adverse Experiences (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	316	94.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
THIRST	6	1.8
WEIGHT GAIN	36	10.7
WEIGHT LOSS	7	2.1
Musculoskeletal System	10	3.0
ARTHRALGIA	5	1.5
ARTHRITIS	1	0.3
MYALGIA	4	1.2
Nervous System	232	69.3
ABNORMAL DREAMS	17	5.1
AGITATION	25	7.5
ANXIETY	15	4.5
CENTRAL NERVOUS SYSTEM DISORDE	1	0.3
CONCENTRATION IMPAIRED	14	4.2
CONFUSION	2	0.6
DELUSIONS	1	0.3
DEPERSONALIZATION	1	0.3
DEPRESSION	12	3.6
DIPLOPIA	1	0.3
DIZZINESS	22	6.6
DRUG DEPENDENCE	3	0.9
DYSKINESIA	1	0.3
EMOTIONAL LABILITY	15	4.5
EUPHORIA	11	3.3
HOSTILITY	24	7.2
HYPERKINESIA	38	11.3
HYPERTONIA	4	1.2
HYPESTHESIA	2	0.6
HYPOKINESIA	1	0.3
INSOMNIA	71	21.2
LACK OF EMOTION	1	0.3

TABLE 15.04.1

Number (%) of Patients with Emergent Adverse Experiences (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	316	94.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
LIBIDO INCREASED	1	0.3
MANIC REACTION	8	2.4
MYOCLONUS	24	7.2
NERVOUSNESS	45	13.4
NEUROSIS	21	6.3
PARESTHESIA	1	0.3
SOMNOLENCE	49	14.6
SPEECH DISORDER	1	0.3
TREMOR	17	5.1
Respiratory System	119	35.5
ASTHMA	3	0.9
BRONCHITIS	4	1.2
COUGH INCREASED	15	4.5
DYSPNEA	3	0.9
EPISTAXIS	7	2.1
HYPERVENTILATION	1	0.3
PHARYNGITIS	18	5.4
RESPIRATORY DISORDER	54	16.1
RHINITIS	22	6.6
SINUSITIS	25	7.5
YAWN	4	1.2
Skin and Appendages	53	15.8
ACNE	1	0.3
ALOPECIA	1	0.3
CONTACT DERMATITIS	10	3.0
DRY SKIN	3	0.9
ECZEMA	1	0.3
HERPES SIMPLEX	1	0.3
HERPES ZOSTER	1	0.3
LEUKODERMA	1	0.3

TABLE 15.04.1

Number (%) of Patients with Emergent Adverse Experiences (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	335	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	316	94.3%
ADECS BODY SYSTEM : PREFERRED TERM	**N**	**%**
MACULOPAPULAR RASH	1	0.3
NAIL DISORDER	1	0.3
PRURITUS	1	0.3
RASH	18	5.4
SKIN BENIGN NEOPLASM	2	0.6
SKIN DISCOLORATION	1	0.3
SKIN DISORDER	2	0.6
SKIN HYPERTROPHY	1	0.3
SWEATING	10	3.0
URTICARIA	2	0.6
Special Searches	1	0.3
PUNCTURE SITE REACTION	1	0.3
Special Senses	35	10.4
ABNORMAL VISION	7	2.1
BLEPHARITIS	1	0.3
CONJUNCTIVITIS	6	1.8
EAR PAIN	3	0.9
EYE APPENDAGE DISORDER	1	0.3
EYE DISORDER	1	0.3
EYE PAIN	1	0.3
MIOSIS	1	0.3
MYDRIASIS	3	0.9
OTITIS EXTERNA	1	0.3
OTITIS MEDIA	9	2.7
STRABISMUS	2	0.6
TASTE PERVERSION	1	0.3
TINNITUS	1	0.3
Urogenital System	38	11.3
ALBUMINURIA	5	1.5

TABLE 15.04.1

Number (%) of Patients with Emergent Adverse Experiences (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	316	94.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
CYSTITIS	1	0.3
DYSURIA	4	1.2
HAEMATURIA	3	0.9
PYURIA	1	0.3
URINARY FREQUENCY	7	2.1
URINARY INCONTINENCE	14	4.2
URINARY TRACT INFECTION	4	1.2
URINATION IMPAIRED	6	1.8
URINE ABNORMALITY	2	0.6

Paroxetine - Protocol: 453

TABLE 15.04.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: <12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	167	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	158	94.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Body as a Whole	101	60.5
ABDOMINAL PAIN	20	12.0
ALLERGIC REACTION	2	1.2
ASTHENIA	36	21.6
BACK PAIN	1	0.6
CHEST PAIN	2	1.2
CHILLS	2	1.2
FEVER	8	4.8
HEADACHE	35	21.0
INFECTION	20	12.0
MALAISE	1	0.6
PAIN	2	1.2
TRAUMA	31	18.6
Cardiovascular System	9	5.4
ELECTROCARDIOGRAM ABNORMAL	1	0.6
EXTRASYSTOLES	1	0.6
HYPERTENSION	2	1.2
MIGRAINE	1	0.6
PALLOR	2	1.2
PALPITATION	1	0.6
QT INTERVAL PROLONGED	1	0.6
SUPRAVENTRICULAR EXTRASYSTOLES	1	0.6
TACHYCARDIA	1	0.6
Digestive System	83	49.7
BRUXISM	2	1.2
CONSTIPATION	11	6.6
DECREASED APPETITE	15	9.0
DIARRHEA	22	13.2
DRY MOUTH	6	3.6
DYSPEPSIA	11	6.6

TABLE 15.04.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: <12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	167	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	158	94.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
ERUCTATION	1	0.6
FECAL INCONTINENCE	1	0.6
FLATULENCE	4	2.4
GASTROENTERITIS	2	1.2
GASTROINTESTINAL DISORDER	1	0.6
INCREASED APPETITE	11	6.6
NAUSEA	20	12.0
STOMATITIS	2	1.2
TOOTH DISORDER	8	4.8
ULCERATIVE STOMATITIS	1	0.6
VOMITING	15	9.0
Hemic and Lymphatic System	7	4.2
EOSINOPHILIA	2	1.2
LYMPHADENOPATHY	2	1.2
PURPURA	3	1.8
Metabolic and Nutritional Disorders	23	13.8
THIRST	4	2.4
WEIGHT GAIN	19	11.4
WEIGHT LOSS	2	1.2
Musculoskeletal System	4	2.4
ARTHRALGIA	2	1.2
MYALGIA	2	1.2
Nervous System	119	71.3
ABNORMAL DREAMS	8	4.8
AGITATION	19	11.4
ANXIETY	7	4.2
CENTRAL NERVOUS SYSTEM DISORDE	1	0.6
CONCENTRATION IMPAIRED	11	6.6

TABLE 15.04.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: <12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	167	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	158	94.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
CONFUSION	1	0.6
DEPERSONALIZATION	1	0.6
DEPRESSION	5	3.0
DIPLOPIA	1	0.6
DIZZINESS	9	5.4
EMOTIONAL LABILITY	9	5.4
EUPHORIA	7	4.2
HOSTILITY	13	7.8
HYPERKINESIA	24	14.4
HYPERTONIA	2	1.2
HYPESTHESIA	1	0.6
HYPOKINESIA	1	0.6
INSOMNIA	33	19.8
LIBIDO INCREASED	1	0.6
MANIC REACTION	7	4.2
MYOCLONUS	16	9.6
NERVOUSNESS	23	13.8
NEUROSIS	12	7.2
SOMNOLENCE	21	12.6
SPEECH DISORDER	1	0.6
TREMOR	4	2.4
Respiratory System	64	38.3
ASTHMA	3	1.8
BRONCHITIS	4	2.4
COUGH INCREASED	7	4.2
DYSPNEA	2	1.2
EPISTAXIS	4	2.4
HYPERVENTILATION	1	0.6
PHARYNGITIS	8	4.8
RESPIRATORY DISORDER	30	18.0
RHINITIS	9	5.4

TABLE 15.04.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: <12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	167	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	158	94.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
SINUSITIS	13	7.8
YAWN	2	1.2
Skin and Appendages	28	16.8
ALOPECIA	1	0.6
CONTACT DERMATITIS	4	2.4
DRY SKIN	1	0.6
ECZEMA	1	0.6
HERPES SIMPLEX	1	0.6
MACULOPAPULAR RASH	1	0.6
NAIL DISORDER	1	0.6
RASH	11	6.6
SKIN BENIGN NEOPLASM	1	0.6
SKIN DISCOLORATION	1	0.6
SKIN DISORDER	2	1.2
SKIN HYPERTROPHY	1	0.6
SWEATING	5	3.0
URTICARIA	1	0.6
Special Searches	1	0.6
PUNCTURE SITE REACTION	1	0.6
Special Senses	17	10.2
ABNORMAL VISION	3	1.8
BLEPHARITIS	1	0.6
CONJUNCTIVITIS	2	1.2
EAR PAIN	1	0.6
EYE DISORDER	1	0.6
MIOSIS	1	0.6
MYDRIASIS	2	1.2
OTITIS EXTERNA	1	0.6
OTITIS MEDIA	3	1.8

TABLE 15.04.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: <12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	167	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	158	94.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
STRABISMUS	1	0.6
TASTE PERVERSION	1	0.6
TINNITUS	1	0.6
Urogenital System	21	12.6
ALBUMINURIA	3	1.8
DYSURIA	2	1.2
URINARY FREQUENCY	5	3.0
URINARY INCONTINENCE	9	5.4
URINARY TRACT INFECTION	1	0.6
URINATION IMPAIRED	2	1.2

TABLE 15.04.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: >=12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	168	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	158	94.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Body as a Whole	98	58.3
ABDOMINAL PAIN	20	11.9
ABNORMAL LABORATORY VALUE	1	0.6
ALLERGIC REACTION	10	6.0
ASTHENIA	36	21.4
BACK PAIN	2	1.2
CHEST PAIN	1	0.6
CHILLS	3	1.8
FEVER	4	2.4
FLU SYNDROME	1	0.6
HEADACHE	47	28.0
INFECTION	12	7.1
PAIN	2	1.2
TRAUMA	14	8.3
Cardiovascular System	15	8.9
AV BLOCK	1	0.6
BRADYCARDIA	1	0.6
ELECTROCARDIOGRAM ABNORMAL	2	1.2
EXTRASYSTOLES	1	0.6
HYPERTENSION	3	1.8
MIGRAINE	1	0.6
PALPITATION	2	1.2
TACHYCARDIA	3	1.8
VASODILATATION	4	2.4
Digestive System	80	47.6
CONSTIPATION	4	2.4
DECREASED APPETITE	15	8.9
DIARRHEA	15	8.9
DRY MOUTH	9	5.4
DYSPEPSIA	12	7.1

TABLE 15.04.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: >=12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	168	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	158	94.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
FECAL INCONTINENCE	1	0.6
FLATULENCE	3	1.8
GASTRITIS	1	0.6
GASTROINTESTINAL DISORDER	1	0.6
GINGIVITIS	2	1.2
INCREASED APPETITE	2	1.2
NAUSEA	28	16.7
STOMATITIS	2	1.2
TOOTH DISORDER	4	2.4
ULCERATIVE STOMATITIS	1	0.6
VOMITING	9	5.4
Hemic and Lymphatic System	11	6.5
ANEMIA	1	0.6
EOSINOPHILIA	2	1.2
LEUKOCYTOSIS	1	0.6
LEUKOPENIA	3	1.8
LYMPHADENOPATHY	2	1.2
LYMPHOCYTOSIS	1	0.6
PURPURA	2	1.2
THROMBOCYTOPENIA	1	0.6
Metabolic and Nutritional Disorders	25	14.9
HYPERGLYCEMIA	1	0.6
LACTIC DEHYDROGENASE INCREASED	1	0.6
THIRST	2	1.2
WEIGHT GAIN	17	10.1
WEIGHT LOSS	5	3.0
Musculoskeletal System	6	3.6
ARTHRALGIA	3	1.8
ARTHRITIS	1	0.6

TABLE 15.04.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: >=12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	168	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	158	94.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
MYALGIA	2	1.2
Nervous System	113	67.3
ABNORMAL DREAMS	9	5.4
AGITATION	6	3.6
ANXIETY	8	4.8
CONCENTRATION IMPAIRED	3	1.8
CONFUSION	1	0.6
DELUSIONS	1	0.6
DEPRESSION	7	4.2
DIZZINESS	13	7.7
DRUG DEPENDENCE	3	1.8
DYSKINESIA	1	0.6
EMOTIONAL LABILITY	6	3.6
EUPHORIA	4	2.4
HOSTILITY	11	6.5
HYPERKINESIA	14	8.3
HYPERTONIA	2	1.2
HYPESTHESIA	1	0.6
INSOMNIA	38	22.6
LACK OF EMOTION	1	0.6
MANIC REACTION	1	0.6
MYOCLONUS	8	4.8
NERVOUSNESS	22	13.1
NEUROSIS	9	5.4
PARESTHESIA	1	0.6
SOMNOLENCE	28	16.7
TREMOR	13	7.7
Respiratory System	55	32.7
COUGH INCREASED	8	4.8
DYSPNEA	1	0.6

TABLE 15.04.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: >=12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	168	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	158	94.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
EPISTAXIS	3	1.8
PHARYNGITIS	10	6.0
RESPIRATORY DISORDER	24	14.3
RHINITIS	13	7.7
SINUSITIS	12	7.1
YAWN	2	1.2
Skin and Appendages	25	14.9
ACNE	1	0.6
CONTACT DERMATITIS	6	3.6
DRY SKIN	2	1.2
HERPES ZOSTER	1	0.6
LEUKODERMA	1	0.6
PRURITUS	1	0.6
RASH	7	4.2
SKIN BENIGN NEOPLASM	1	0.6
SWEATING	5	3.0
URTICARIA	1	0.6
Special Senses	18	10.7
ABNORMAL VISION	4	2.4
CONJUNCTIVITIS	4	2.4
EAR PAIN	2	1.2
EYE APPENDAGE DISORDER	1	0.6
EYE PAIN	1	0.6
MYDRIASIS	1	0.6
OTITIS MEDIA	6	3.6
STRABISMUS	1	0.6
Urogenital System	17	10.1
ALBUMINURIA	2	1.2
CYSTITIS	1	0.6

Paroxetine - Protocol: 453

TABLE 15.04.1X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: >=12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	168	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	158	94.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
DYSURIA	2	1.2
HAEMATURIA	3	1.8
PYURIA	1	0.6
URINARY FREQUENCY	2	1.2
URINARY INCONTINENCE	5	3.0
URINARY TRACT INFECTION	3	1.8
URINATION IMPAIRED	4	2.4
URINE ABNORMALITY	2	1.2

Paroxetine - Protocol: 453

TABLE 15.04.2

Number (%) of Patients with Emergent Adverse Experiences (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	73	76.8%	80	81.6%	153	79.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Body as a Whole	36	37.9	46	46.9	82	42.5
ABDOMINAL PAIN	6	6.3	9	9.2	15	7.8
ALLERGIC REACTION	1	1.1	4	4.1	5	2.6
ASTHENIA	3	3.2	7	7.1	10	5.2
BACK PAIN	2	2.1	2	2.0	4	2.1
CELLULITIS	0	0.0	1	1.0	1	0.5
CHEST PAIN	1	1.1	0	0.0	1	0.5
CHILLS	0	0.0	2	2.0	2	1.0
FEVER	3	3.2	3	3.1	6	3.1
HEADACHE	18	18.9	26	26.5	44	22.8
INFECTION	4	4.2	11	11.2	15	7.8
PAIN	2	2.1	3	3.1	5	2.6
TRAUMA	9	9.5	5	5.1	14	7.3
Cardiovascular System	1	1.1	5	5.1	6	3.1
BRADYCARDIA	0	0.0	2	2.0	2	1.0
HYPERTENSION	0	0.0	1	1.0	1	0.5
PALPITATION	0	0.0	1	1.0	1	0.5
VASODILATATION	1	1.1	1	1.0	2	1.0
Digestive System	18	18.9	32	32.7	50	25.9
CONSTIPATION	2	2.1	0	0.0	2	1.0
DECREASED APPETITE	2	2.1	3	3.1	5	2.6
DIARRHEA	5	5.3	7	7.1	12	6.2
DRY MOUTH	2	2.1	2	2.0	4	2.1
DYSPEPSIA	1	1.1	7	7.1	8	4.1
FECAL INCONTINENCE	0	0.0	1	1.0	1	0.5
FLATULENCE	1	1.1	1	1.0	2	1.0
GASTROINTESTINAL DISORDER	1	1.1	0	0.0	1	0.5
INCREASED APPETITE	2	2.1	1	1.0	3	1.6
NAUSEA	5	5.3	15	15.3	20	10.4
STOMATITIS	1	1.1	1	1.0	2	1.0

TABLE 15.04.2

Number (%) of Patients with Emergent Adverse Experiences (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	73	76.8%	80	81.6%	153	79.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
TOOTH DISORDER	4	4.2	0	0.0	4	2.1
ULCERATIVE STOMATITIS	1	1.1	0	0.0	1	0.5
VOMITING	0	0.0	4	4.1	4	2.1
Hemic and Lymphatic System	3	3.2	3	3.1	6	3.1
ANEMIA	0	0.0	1	1.0	1	0.5
LEUKOPENIA	0	0.0	1	1.0	1	0.5
LYMPHADENOPATHY	2	2.1	0	0.0	2	1.0
LYMPHANGITIS	0	0.0	1	1.0	1	0.5
PURPURA	1	1.1	0	0.0	1	0.5
Metabolic and Nutritional Disorders	8	8.4	11	11.2	19	9.8
HYPERGLYCEMIA	0	0.0	1	1.0	1	0.5
HYPERPHOSPHATEMIA	0	0.0	1	1.0	1	0.5
HYPOGLYCEMIA	2	2.1	1	1.0	3	1.6
WEIGHT GAIN	6	6.3	7	7.1	13	6.7
WEIGHT LOSS	1	1.1	2	2.0	3	1.6
Musculoskeletal System	4	4.2	8	8.2	12	6.2
ARTHRALGIA	1	1.1	0	0.0	1	0.5
ARTHROSIS	0	0.0	1	1.0	1	0.5
MYALGIA	3	3.2	6	6.1	9	4.7
MYASTHENIA	0	0.0	1	1.0	1	0.5
Nervous System	44	46.3	43	43.9	87	45.1
ABNORMAL DREAMS	2	2.1	1	1.0	3	1.6
AGITATION	2	2.1	2	2.0	4	2.1
ALCOHOL ABUSE	1	1.1	0	0.0	1	0.5
AMNESIA	1	1.1	0	0.0	1	0.5
ANXIETY	4	4.2	10	10.2	14	7.3
CONCENTRATION IMPAIRED	0	0.0	3	3.1	3	1.6
DEPRESSION	1	1.1	7	7.1	8	4.1

TABLE 15.04.2

Number (%) of Patients with Emergent Adverse Experiences (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	73	76.8%	80	81.6%	153	79.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
DIZZINESS	7	7.4	12	12.2	19	9.8
EMOTIONAL LABILITY	1	1.1	1	1.0	2	1.0
HOSTILITY	6	6.3	0	0.0	6	3.1
HYPERKINESIA	3	3.2	0	0.0	3	1.6
HYPERTONIA	1	1.1	1	1.0	2	1.0
HYPESTHESIA	1	1.1	0	0.0	1	0.5
INSOMNIA	9	9.5	7	7.1	16	8.3
MANIC REACTION	1	1.1	0	0.0	1	0.5
MYOCLONUS	5	5.3	7	7.1	12	6.2
NERVOUSNESS	6	6.3	6	6.1	12	6.2
NEUROSIS	7	7.4	12	12.2	19	9.8
SOMNOLENCE	4	4.2	3	3.1	7	3.6
TREMOR	2	2.1	1	1.0	3	1.6
Respiratory System	19	20.0	27	27.6	46	23.8
ASTHMA	0	0.0	1	1.0	1	0.5
BRONCHITIS	0	0.0	1	1.0	1	0.5
COUGH INCREASED	3	3.2	4	4.1	7	3.6
DYSPNEA	0	0.0	2	2.0	2	1.0
HYPERVENTILATION	0	0.0	2	2.0	2	1.0
PHARYNGITIS	1	1.1	7	7.1	8	4.1
RESPIRATORY DISORDER	11	11.6	10	10.2	21	10.9
RHINITIS	4	4.2	4	4.1	8	4.1
SINUSITIS	4	4.2	5	5.1	9	4.7
Skin and Appendages	11	11.6	6	6.1	17	8.8
ACNE	1	1.1	1	1.0	2	1.0
CONTACT DERMATITIS	1	1.1	0	0.0	1	0.5
FUNGAL DERMATITIS	1	1.1	0	0.0	1	0.5
HERPES ZOSTER	1	1.1	0	0.0	1	0.5
MACULOPAPULAR RASH	1	1.1	0	0.0	1	0.5
PRURITUS	1	1.1	0	0.0	1	0.5

TABLE 15.04.2

Number (%) of Patients with Emergent Adverse Experiences (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	73	76.8%	80	81.6%	153	79.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
PUSTULAR RASH	1	1.1	0	0.0	1	0.5
RASH	2	2.1	2	2.0	4	2.1
SKIN BENIGN NEOPLASM	0	0.0	1	1.0	1	0.5
SKIN DISCOLORATION	0	0.0	1	1.0	1	0.5
SKIN HYPERTROPHY	1	1.1	0	0.0	1	0.5
SWEATING	1	1.1	2	2.0	3	1.6
Special Senses	5	5.3	4	4.1	9	4.7
ABNORMAL VISION	0	0.0	2	2.0	2	1.0
BLEPHARITIS	1	1.1	0	0.0	1	0.5
EAR DISORDER	1	1.1	1	1.0	2	1.0
OTITIS MEDIA	3	3.2	1	1.0	4	2.1
TINNITUS	1	1.1	0	0.0	1	0.5
Urogenital System	3	3.2	3	3.1	6	3.1
ALBUMINURIA	1	1.1	0	0.0	1	0.5
GLYCOSURIA	0	0.0	1	1.0	1	0.5
HAEMATURIA	0	0.0	1	1.0	1	0.5
URINARY INCONTINENCE	2	2.1	1	1.0	3	1.6
URINE ABNORMALITY	1	1.1	0	0.0	1	0.5

Paroxetine - Protocol: 453

TABLE 15.04.2X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: <12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	49	100.0%	47	100.0%	96	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	33	67.3%	37	78.7%	70	72.9%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Body as a Whole	13	26.5	18	38.3	31	32.3
ABDOMINAL PAIN	1	2.0	7	14.9	8	8.3
ALLERGIC REACTION	1	2.0	1	2.1	2	2.1
ASTHENIA	1	2.0	2	4.3	3	3.1
CHILLS	0	0.0	1	2.1	1	1.0
FEVER	2	4.1	2	4.3	4	4.2
HEADACHE	4	8.2	8	17.0	12	12.5
INFECTION	2	4.1	4	8.5	6	6.3
PAIN	0	0.0	1	2.1	1	1.0
TRAUMA	4	8.2	0	0.0	4	4.2
Cardiovascular System	1	2.0	2	4.3	3	3.1
HYPERTENSION	0	0.0	1	2.1	1	1.0
VASODILATATION	1	2.0	1	2.1	2	2.1
Digestive System	6	12.2	15	31.9	21	21.9
DECREASED APPETITE	2	4.1	0	0.0	2	2.1
DIARRHEA	0	0.0	5	10.6	5	5.2
DYSPEPSIA	1	2.0	3	6.4	4	4.2
GASTROINTESTINAL DISORDER	1	2.0	0	0.0	1	1.0
INCREASED APPETITE	0	0.0	1	2.1	1	1.0
NAUSEA	1	2.0	7	14.9	8	8.3
TOOTH DISORDER	2	4.1	0	0.0	2	2.1
VOMITING	0	0.0	2	4.3	2	2.1
Metabolic and Nutritional Disorders	6	12.2	1	2.1	7	7.3
HYPOGLYCEMIA	1	2.0	0	0.0	1	1.0
WEIGHT GAIN	5	10.2	1	2.1	6	6.3
WEIGHT LOSS	0	0.0	1	2.1	1	1.0
Musculoskeletal System	1	2.0	3	6.4	4	4.2
MYALGIA	1	2.0	2	4.3	3	3.1

TABLE 15.04.2X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: <12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	49	100.0%	47	100.0%	96	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	33	67.3%	37	78.7%	70	72.9%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
MYASTHENIA	0	0.0	1	2.1	1	1.0
Nervous System	23	46.9	18	38.3	41	42.7
ABNORMAL DREAMS	1	2.0	0	0.0	1	1.0
AGITATION	2	4.1	2	4.3	4	4.2
ANXIETY	2	4.1	3	6.4	5	5.2
DEPRESSION	1	2.0	2	4.3	3	3.1
DIZZINESS	2	4.1	5	10.6	7	7.3
EMOTIONAL LABILITY	1	2.0	0	0.0	1	1.0
HOSTILITY	4	8.2	0	0.0	4	4.2
HYPERKINESIA	2	4.1	0	0.0	2	2.1
INSOMNIA	6	12.2	2	4.3	8	8.3
MANIC REACTION	1	2.0	0	0.0	1	1.0
MYOCLONUS	4	8.2	2	4.3	6	6.3
NERVOUSNESS	2	4.1	2	4.3	4	4.2
NEUROSIS	5	10.2	8	17.0	13	13.5
Respiratory System	9	18.4	11	23.4	20	20.8
COUGH INCREASED	2	4.1	1	2.1	3	3.1
DYSPNEA	0	0.0	1	2.1	1	1.0
HYPERVENTILATION	0	0.0	1	2.1	1	1.0
PHARYNGITIS	0	0.0	2	4.3	2	2.1
RESPIRATORY DISORDER	7	14.3	6	12.8	13	13.5
RHINITIS	1	2.0	1	2.1	2	2.1
SINUSITIS	1	2.0	2	4.3	3	3.1
Skin and Appendages	5	10.2	2	4.3	7	7.3
HERPES ZOSTER	1	2.0	0	0.0	1	1.0
MACULOPAPULAR RASH	1	2.0	0	0.0	1	1.0
PUSTULAR RASH	1	2.0	0	0.0	1	1.0
RASH	1	2.0	1	2.1	2	2.1
SKIN HYPERTROPHY	1	2.0	0	0.0	1	1.0

TABLE 15.04.2X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: <12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	49	100.0%	47	100.0%	96	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	33	67.3%	37	78.7%	70	72.9%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
SWEATING	0	0.0	1	2.1	1	1.0
Special Senses	2	4.1	0	0.0	2	2.1
OTITIS MEDIA	1	2.0	0	0.0	1	1.0
TINNITUS	1	2.0	0	0.0	1	1.0
Urogenital System	2	4.1	0	0.0	2	2.1
ALBUMINURIA	1	2.0	0	0.0	1	1.0
URINARY INCONTINENCE	1	2.0	0	0.0	1	1.0
URINE ABNORMALITY	1	2.0	0	0.0	1	1.0

TABLE 15.04.2X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: >=12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	46	100.0%	51	100.0%	97	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	40	87.0%	43	84.3%	83	85.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Body as a Whole	23	50.0	28	54.9	51	52.6
ABDOMINAL PAIN	5	10.9	2	3.9	7	7.2
ALLERGIC REACTION	0	0.0	3	5.9	3	3.1
ASTHENIA	2	4.3	5	9.8	7	7.2
BACK PAIN	2	4.3	2	3.9	4	4.1
CELLULITIS	0	0.0	1	2.0	1	1.0
CHEST PAIN	1	2.2	0	0.0	1	1.0
CHILLS	0	0.0	1	2.0	1	1.0
FEVER	1	2.2	1	2.0	2	2.1
HEADACHE	14	30.4	18	35.3	32	33.0
INFECTION	2	4.3	7	13.7	9	9.3
PAIN	2	4.3	2	3.9	4	4.1
TRAUMA	5	10.9	5	9.8	10	10.3
Cardiovascular System	0	0.0	3	5.9	3	3.1
BRADYCARDIA	0	0.0	2	3.9	2	2.1
PALPITATION	0	0.0	1	2.0	1	1.0
Digestive System	12	26.1	17	33.3	29	29.9
CONSTIPATION	2	4.3	0	0.0	2	2.1
DECREASED APPETITE	0	0.0	3	5.9	3	3.1
DIARRHEA	5	10.9	2	3.9	7	7.2
DRY MOUTH	2	4.3	2	3.9	4	4.1
DYSPEPSIA	0	0.0	4	7.8	4	4.1
FECAL INCONTINENCE	0	0.0	1	2.0	1	1.0
FLATULENCE	1	2.2	1	2.0	2	2.1
INCREASED APPETITE	2	4.3	0	0.0	2	2.1
NAUSEA	4	8.7	8	15.7	12	12.4
STOMATITIS	1	2.2	1	2.0	2	2.1
TOOTH DISORDER	2	4.3	0	0.0	2	2.1
ULCERATIVE STOMATITIS	1	2.2	0	0.0	1	1.0
VOMITING	0	0.0	2	3.9	2	2.1

TABLE 15.04.2X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: >=12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	46	100.0%	51	100.0%	97	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	40	87.0%	43	84.3%	83	85.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Hemic and Lymphatic System	3	6.5	3	5.9	6	6.2
ANEMIA	0	0.0	1	2.0	1	1.0
LEUKOPENIA	0	0.0	1	2.0	1	1.0
LYMPHADENOPATHY	2	4.3	0	0.0	2	2.1
LYMPHANGITIS	0	0.0	1	2.0	1	1.0
PURPURA	1	2.2	0	0.0	1	1.0
Metabolic and Nutritional Disorders	2	4.3	10	19.6	12	12.4
HYPERGLYCEMIA	0	0.0	1	2.0	1	1.0
HYPERPHOSPHATEMIA	0	0.0	1	2.0	1	1.0
HYPOGLYCEMIA	1	2.2	1	2.0	2	2.1
WEIGHT GAIN	1	2.2	6	11.8	7	7.2
WEIGHT LOSS	1	2.2	1	2.0	2	2.1
Musculoskeletal System	3	6.5	5	9.8	8	8.2
ARTHRALGIA	1	2.2	0	0.0	1	1.0
ARTHROSIS	0	0.0	1	2.0	1	1.0
MYALGIA	2	4.3	4	7.8	6	6.2
Nervous System	21	45.7	25	49.0	46	47.4
ABNORMAL DREAMS	1	2.2	1	2.0	2	2.1
ALCOHOL ABUSE	1	2.2	0	0.0	1	1.0
AMNESIA	1	2.2	0	0.0	1	1.0
ANXIETY	2	4.3	7	13.7	9	9.3
CONCENTRATION IMPAIRED	0	0.0	3	5.9	3	3.1
DEPRESSION	0	0.0	5	9.8	5	5.2
DIZZINESS	5	10.9	7	13.7	12	12.4
EMOTIONAL LABILITY	0	0.0	1	2.0	1	1.0
HOSTILITY	2	4.3	0	0.0	2	2.1
HYPERKINESIA	1	2.2	0	0.0	1	1.0
HYPERTONIA	1	2.2	1	2.0	2	2.1
HYPESTHESIA	1	2.2	0	0.0	1	1.0

TABLE 15.04.2X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: >=12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	46	100.0%	51	100.0%	97	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	40	87.0%	43	84.3%	83	85.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
INSOMNIA	3	6.5	5	9.8	8	8.2
MYOCLONUS	1	2.2	5	9.8	6	6.2
NERVOUSNESS	4	8.7	4	7.8	8	8.2
NEUROSIS	2	4.3	4	7.8	6	6.2
SOMNOLENCE	4	8.7	3	5.9	7	7.2
TREMOR	2	4.3	1	2.0	3	3.1
Respiratory System	10	21.7	16	31.4	26	26.8
ASTHMA	0	0.0	1	2.0	1	1.0
BRONCHITIS	0	0.0	1	2.0	1	1.0
COUGH INCREASED	1	2.2	3	5.9	4	4.1
DYSPNEA	0	0.0	1	2.0	1	1.0
HYPERVENTILATION	0	0.0	1	2.0	1	1.0
PHARYNGITIS	1	2.2	5	9.8	6	6.2
RESPIRATORY DISORDER	4	8.7	4	7.8	8	8.2
RHINITIS	3	6.5	3	5.9	6	6.2
SINUSITIS	3	6.5	3	5.9	6	6.2
Skin and Appendages	6	13.0	4	7.8	10	10.3
ACNE	1	2.2	1	2.0	2	2.1
CONTACT DERMATITIS	1	2.2	0	0.0	1	1.0
FUNGAL DERMATITIS	1	2.2	0	0.0	1	1.0
PRURITUS	1	2.2	0	0.0	1	1.0
RASH	1	2.2	1	2.0	2	2.1
SKIN BENIGN NEOPLASM	0	0.0	1	2.0	1	1.0
SKIN DISCOLORATION	0	0.0	1	2.0	1	1.0
SWEATING	1	2.2	1	2.0	2	2.1
Special Senses	3	6.5	4	7.8	7	7.2
ABNORMAL VISION	0	0.0	2	3.9	2	2.1
BLEPHARITIS	1	2.2	0	0.0	1	1.0
EAR DISORDER	1	2.2	1	2.0	2	2.1

TABLE 15.04.2X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: >=12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	46	100.0%	51	100.0%	97	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	40	87.0%	43	84.3%	83	85.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
OTITIS MEDIA	2	4.3	1	2.0	3	3.1
Urogenital System	1	2.2	3	5.9	4	4.1
GLYCOSURIA	0	0.0	1	2.0	1	1.0
HAEMATURIA	0	0.0	1	2.0	1	1.0
URINARY INCONTINENCE	1	2.2	1	2.0	2	2.1

TABLE 15.04.3

Number (%) of Patients with Emergent Adverse Experiences (Non-gender Specific)
Intention to Treat Population
Taper Phase

TREATMENT GROUP	TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	29	100.0%	42	100.0%	37	100.0%	108	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	8	27.6%	14	33.3%	10	27.0%	32	29.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%	N	%
Body as a Whole	2	6.9	5	11.9	6	16.2	13	12.0
ABDOMINAL PAIN	0	0.0	0	0.0	1	2.7	1	0.9
ALLERGIC REACTION	0	0.0	0	0.0	1	2.7	1	0.9
FEVER	0	0.0	1	2.4	0	0.0	1	0.9
HEADACHE	2	6.9	5	11.9	2	5.4	9	8.3
INFECTION	0	0.0	1	2.4	0	0.0	1	0.9
PAIN	0	0.0	0	0.0	2	5.4	2	1.9
Cardiovascular System	2	6.9	0	0.0	0	0.0	2	1.9
QT INTERVAL PROLONGED	1	3.4	0	0.0	0	0.0	1	0.9
VASODILATATION	1	3.4	0	0.0	0	0.0	1	0.9
Digestive System	2	6.9	4	9.5	0	0.0	6	5.6
DIARRHEA	1	3.4	0	0.0	0	0.0	1	0.9
DYSPEPSIA	1	3.4	1	2.4	0	0.0	2	1.9
NAUSEA	2	6.9	3	7.1	0	0.0	5	4.6
TOOTH DISORDER	0	0.0	1	2.4	0	0.0	1	0.9
VOMITING	1	3.4	0	0.0	0	0.0	1	0.9
Hemic and Lymphatic System	0	0.0	0	0.0	1	2.7	1	0.9
EOSINOPHILIA	0	0.0	0	0.0	1	2.7	1	0.9
Metabolic and Nutritional Disorders	2	6.9	0	0.0	0	0.0	2	1.9
SGOT INCREASED	1	3.4	0	0.0	0	0.0	1	0.9
SGPT INCREASED	1	3.4	0	0.0	0	0.0	1	0.9
WEIGHT LOSS	1	3.4	0	0.0	0	0.0	1	0.9
Musculoskeletal System	0	0.0	1	2.4	0	0.0	1	0.9
MYALGIA	0	0.0	1	2.4	0	0.0	1	0.9
Nervous System	5	17.2	5	11.9	2	5.4	12	11.1
ABNORMAL DREAMS	0	0.0	0	0.0	1	2.7	1	0.9

TABLE 15.04.3

Number (%) of Patients with Emergent Adverse Experiences (Non-gender Specific)
Intention to Treat Population
Taper Phase

TREATMENT GROUP	TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	29	100.0%	42	100.0%	37	100.0%	108	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	8	27.6%	14	33.3%	10	27.0%	32	29.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%	N	%
CONFUSION	1	3.4	0	0.0	0	0.0	1	0.9
DEPRESSION	1	3.4	0	0.0	1	2.7	2	1.9
DIZZINESS	1	3.4	3	7.1	0	0.0	4	3.7
DYSTONIA	0	0.0	1	2.4	0	0.0	1	0.9
EMOTIONAL LABILITY	0	0.0	1	2.4	0	0.0	1	0.9
INSOMNIA	0	0.0	0	0.0	1	2.7	1	0.9
MYOCLONUS	1	3.4	0	0.0	0	0.0	1	0.9
NERVOUSNESS	1	3.4	0	0.0	0	0.0	1	0.9
PARESTHESIA	1	3.4	0	0.0	0	0.0	1	0.9
WITHDRAWAL SYNDROME	1	3.4	0	0.0	0	0.0	1	0.9
Respiratory System	0	0.0	3	7.1	0	0.0	3	2.8
PHARYNGITIS	0	0.0	1	2.4	0	0.0	1	0.9
RESPIRATORY DISORDER	0	0.0	1	2.4	0	0.0	1	0.9
SINUSITIS	0	0.0	1	2.4	0	0.0	1	0.9
Special Senses	0	0.0	1	2.4	1	2.7	2	1.9
OTITIS MEDIA	0	0.0	1	2.4	1	2.7	2	1.9
Urogenital System	0	0.0	1	2.4	1	2.7	2	1.9
HAEMATURIA	0	0.0	0	0.0	1	2.7	1	0.9
URINARY INCONTINENCE	0	0.0	1	2.4	0	0.0	1	0.9

Paroxetine - Protocol: 453

TABLE 15.04.3X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-gender Specific)
Intention to Treat Population
Taper Phase

Age Group: <12 YEARS

TREATMENT GROUP	TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	9	100.0%	19	100.0%	15	100.0%	43	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	0	0.0%	8	42.1%	3	20.0%	11	25.6%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%	N	%
Body as a Whole	0	0.0	2	10.5	2	13.3	4	9.3
ABDOMINAL PAIN	0	0.0	0	0.0	1	6.7	1	2.3
FEVER	0	0.0	1	5.3	0	0.0	1	2.3
HEADACHE	0	0.0	2	10.5	0	0.0	2	4.7
INFECTION	0	0.0	1	5.3	0	0.0	1	2.3
PAIN	0	0.0	0	0.0	1	6.7	1	2.3
Digestive System	0	0.0	2	10.5	0	0.0	2	4.7
NAUSEA	0	0.0	2	10.5	0	0.0	2	4.7
Hemic and Lymphatic System	0	0.0	0	0.0	1	6.7	1	2.3
EOSINOPHILIA	0	0.0	0	0.0	1	6.7	1	2.3
Nervous System	0	0.0	3	15.8	1	6.7	4	9.3
DEPRESSION	0	0.0	0	0.0	1	6.7	1	2.3
DIZZINESS	0	0.0	2	10.5	0	0.0	2	4.7
EMOTIONAL LABILITY	0	0.0	1	5.3	0	0.0	1	2.3
Respiratory System	0	0.0	2	10.5	0	0.0	2	4.7
PHARYNGITIS	0	0.0	1	5.3	0	0.0	1	2.3
SINUSITIS	0	0.0	1	5.3	0	0.0	1	2.3
Special Senses	0	0.0	1	5.3	0	0.0	1	2.3
OTITIS MEDIA	0	0.0	1	5.3	0	0.0	1	2.3

TABLE 15.04.3X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-gender Specific)
Intention to Treat Population
Taper Phase

Age Group: >=12 YEARS

TREATMENT GROUP	TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	20	100.0%	23	100.0%	22	100.0%	65	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	8	40.0%	6	26.1%	7	31.8%	21	32.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%	N	%
Body as a Whole	2	10.0	3	13.0	4	18.2	9	13.8
ALLERGIC REACTION	0	0.0	0	0.0	1	4.5	1	1.5
HEADACHE	2	10.0	3	13.0	2	9.1	7	10.8
PAIN	0	0.0	0	0.0	1	4.5	1	1.5
Cardiovascular System	2	10.0	0	0.0	0	0.0	2	3.1
QT INTERVAL PROLONGED	1	5.0	0	0.0	0	0.0	1	1.5
VASODILATATION	1	5.0	0	0.0	0	0.0	1	1.5
Digestive System	2	10.0	2	8.7	0	0.0	4	6.2
DIARRHEA	1	5.0	0	0.0	0	0.0	1	1.5
DYSPEPSIA	1	5.0	1	4.3	0	0.0	2	3.1
NAUSEA	2	10.0	1	4.3	0	0.0	3	4.6
TOOTH DISORDER	0	0.0	1	4.3	0	0.0	1	1.5
VOMITING	1	5.0	0	0.0	0	0.0	1	1.5
Metabolic and Nutritional Disorders	2	10.0	0	0.0	0	0.0	2	3.1
SGOT INCREASED	1	5.0	0	0.0	0	0.0	1	1.5
SGPT INCREASED	1	5.0	0	0.0	0	0.0	1	1.5
WEIGHT LOSS	1	5.0	0	0.0	0	0.0	1	1.5
Musculoskeletal System	0	0.0	1	4.3	0	0.0	1	1.5
MYALGIA	0	0.0	1	4.3	0	0.0	1	1.5
Nervous System	5	25.0	2	8.7	1	4.5	8	12.3
ABNORMAL DREAMS	0	0.0	0	0.0	1	4.5	1	1.5
CONFUSION	1	5.0	0	0.0	0	0.0	1	1.5
DEPRESSION	1	5.0	0	0.0	0	0.0	1	1.5
DIZZINESS	1	5.0	1	4.3	0	0.0	2	3.1
DYSTONIA	0	0.0	1	4.3	0	0.0	1	1.5
INSOMNIA	0	0.0	0	0.0	1	4.5	1	1.5
MYOCLONUS	1	5.0	0	0.0	0	0.0	1	1.5

TABLE 15.04.3X

Number (%) of Patients with Emergent Adverse Experiences by Age Category (Non-gender Specific)
Intention to Treat Population
Taper Phase

Age Group: >=12 YEARS

TREATMENT GROUP	TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	20	100.0%	23	100.0%	22	100.0%	65	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	8	40.0%	6	26.1%	7	31.8%	21	32.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%	N	%
NERVOUSNESS	1	5.0	0	0.0	0	0.0	1	1.5
PARESTHESIA	1	5.0	0	0.0	0	0.0	1	1.5
WITHDRAWAL SYNDROME	1	5.0	0	0.0	0	0.0	1	1.5
Respiratory System	0	0.0	1	4.3	0	0.0	1	1.5
RESPIRATORY DISORDER	0	0.0	1	4.3	0	0.0	1	1.5
Special Senses	0	0.0	0	0.0	1	4.5	1	1.5
OTITIS MEDIA	0	0.0	0	0.0	1	4.5	1	1.5
Urogenital System	0	0.0	1	4.3	1	4.5	2	3.1
HAEMATURIA	0	0.0	0	0.0	1	4.5	1	1.5
URINARY INCONTINENCE	0	0.0	1	4.3	0	0.0	1	1.5

Paroxetine - Protocol: 453

TABLE 15.05.1

Number (%) of Patients with Serious Emergent Adverse Experiences - Displayed by Body System
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS :	335	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	13	3.9%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Body as a Whole	1	0.3
Cardiovascular System	1	0.3
Nervous System	11	3.3

Paroxetine - Protocol: 453

TABLE 15.05.2

Number (%) of Patients with Serious Emergent Adverse Experiences - Displayed by Body System
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	2	2.1%	2	2.0%	4	2.1%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Nervous System	1	1.1	2	2.0	3	1.6
Skin and Appendages	1	1.1	0	0.0	1	0.5

Confidential

Paroxetine

BRL-029060

Table 15.05.2a. Patient Narratives: Serious Adverse Experiences

453

xxxxx x. xxxxxxxxx, R.Ph., M.S.*
xxxxxx x. xxxxx, Ph.D.

*CNS, PMTU

SB Document Number: BRL-029060/RSD-100W8D/1

Study 29060/453
PID 453.001.00363 (1998005799-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience and Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Extrasystoles (Ventricular Bigeminy/ Trigeminy Pulse Beats)

Screening Demography:
Age: 15 years
Date of birth: 10 Oct 82
Sex: Male
Weight: 175.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Bilateral Erythema (Fingertips to Mid-Upper Arms)
Elevated ALAT (SGPT)
Obesity
Otitis Externa
Tonsillectomy

Psychiatric History:
Oppositional Defiant Disorder
Post-Traumatic Stress Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally

Start: 30 Dec 97 **Stop:** 12 Jan 98

Study Drug: Open-Label Paroxetine 20 mg Given Orally

Start: 13 Jan 98 **Stop:** 26 Jan 98

Study Drug: Open-Label Paroxetine 30 mg Given Orally

Start: 27 Jan 98 **Stop:** 23 Feb 98

Study Drug: Open-Label Paroxetine Down Titration Given Orally

Start: 24 Feb 98 **Stop:** 24 Feb 98

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Mild Headache	08 Jan 98	11 Jan 98
Moderate Stuffy Nose	19 Jan 98	25 Jan 98
Moderate Cough	19 Jan 98	25 Jan 98
Mild Dry Mouth	09 Feb 98	20 Feb 98
Mild Weight Gain	10 Feb 98	Ongoing

AE Remarks:

This patient started open-label study medication, 10 mg per day paroxetine, on 30 Dec 97, increased to 20 mg per day on 13 Jan 98, and increased to 30 mg per day on 27 Jan 98. On 23 Feb 98, 55 days after the first dose of study medication, a routine ECG performed at the week 8 visit revealed frequent severe premature ventricular contractions (PVCs). The PVCs were unifocal, isolated (in most part), and in bigeminal fashion frequently. There were occasional couplets but no triplets or runs. A serious adverse experience of ventricular bigeminy/trigeminy pulse beats was reported. The ECG was normal for the patient's age in other respects and had been normal at screening. The patient was asymptomatic for cardiac signs or symptoms. Vital signs were BP 124/86 supine, 126/88 sitting; pulse 74 bpm. The patient reported only mild dry mouth. The patient's sister was born with a ventricular septal defect, his mother has mitral valve prolapse, and both grandfathers have atherosclerotic heart disease. Study medication was tapered to 10 mg per day the following day and the patient was discontinued from the study a day later, after 57 days on study medication.

The next day, follow-up ECG revealed trigeminal PVCs. Laboratory values were normal except for slight elevation of total bilirubin (1.5 mg/dL; reference range 0.0-1.3 mg/dL). The investigator considered the adverse experience possibly related to study medication. ECGs performed on 03 Mar 98 and 10 Mar 98 revealed unifocal PVCs, isolated and in couplets. The sponsor agreed with the ECG interpretations and added that the patient exhibits sinus arrhythmia (normal variant) with R-R intervals differing by 1.60 milliseconds at times. No further follow-up information is available.

Concomitant Drugs	Onset	Stopped
None		

Study 29060/453
PID 453.002.00311 (1998007622-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience and Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Emotional Lability (Suicide Attempts)

Other Adverse Experiences: Hostility (Oppositional Defiant Behavior)
Hostility (Self-Destructive Behavior [Impulsivity])
Emotional Lability (Suicidal Ideation)

Screening Demography: Age: 10 years
Date of birth: 21 Jul 87
Sex: Female
Weight: 60.0 lbs.
Race: Caucasian

Country: United States

Medical History: Bruises Bilateral Legs
Environmental Allergies
Exercise-Induced Asthma
Gastrointestinal Upset
Headache

Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Paroxetine 10 mg Given Orally

Start: 29 Jan 98 **Stop:** 15 Mar 98

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Moderate Dry Mouth	02 Feb 98	01 Mar 98
Moderate Agitation	30 Jan 98	07 Feb 98

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 29 Jan 98, and symptoms of obsessive-compulsive disorder (OCD) improved,

with her Children's Yale Brown Obsessive Compulsive Score (CYBOCS) decreasing from 37 at screening to 14 (date unknown). There was no reported history of oppositional or conduct disorder or suicidal behavior. Evidence of behavioral problems was first noted on 19 Feb 98, when the patient's mother reported that the patient was lying, defiant, "brazen and bold." The patient was also failing to do her homework, and her teachers were reporting these difficulties to the patient's mother. She was preoccupied with fire and had probably set one. The site was notified on 11 Mar 98 and agreed to continue the study with close monitoring as the OCD symptoms remained very much improved. Severe oppositional defiant behavior was noted as an adverse experience on 01 Mar 98.

On 14 Mar 98, the patient displayed severe self-destructive behavior and severe suicidal ideation. The patient was withdrawn from the study on 15 Mar 98, after 47 days of study medication, due to the oppositional defiant behavior. On 17 Mar 98, it was discovered that the patient had made suicide attempts by attempting to hang and drown herself. The patient was hospitalized at a children's hospital for treatment of her behavioral difficulties.

The investigator considered these events possibly related to study medication, or that they could be related to the OCD or another unspecified condition. The sponsor considered that the response of the patient's OCD symptomology to paroxetine makes any causal relationship between these events and study medication unlikely.

Concomitant Drugs	**Onset**	**Stopped**
Acetaminophen	01 Jan 96	Ongoing
Calcium Carbonate/Magnesium Hydroxide	01 Dec 97	Ongoing

Study 29060/453
PID 453.006.00105 (1997016729-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience

Primary Adverse Experience (Verbatim Term): Neurosis (Worsening of Obsessive-Compulsive Disorder)
Other Adverse Experience: Agitation (Agitation)

Screening Demography:
Age: 11 years
Date of birth: 01 Oct 85
Sex: Male
Weight: 62.0 lbs.
Race: Caucasian

Country: United States

Medical History: Migraine Headaches
Psychiatric History: Major Depressive Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-label Paroxetine 10 mg Given Orally

Start: 26 Mar 97 **Stop:** 01 Apr 97
Study Drug: Open-label Paroxetine 20 mg Given Orally

Start: 02 Apr 97 **Stop:** 08 Apr 9797
Study Drug: Open-label Paroxetine 30 mg Given Orally

Start: 09 Apr 97 **Stop:** 22 Apr 97
Study Drug: Open-label Paroxetine 40 mg Given Orally

Start: 23 Apr 97 **Stop:** 06 May 97
Study Drug: Open-label Paroxetine 30 mg Given Orally

Start: 07 May 97 **Stop:** 20 May 97

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Moderate Increased Agitation	22 Apr 97	10 Jun 97
Moderate Vivid Dreaming	23 Apr 97	Ongoing
Severe Hypomania	23 Apr 97	Ongoing

AE Remarks:

This patient started open-label study medication, 10 mg per day paroxetine, on 26 Mar 97. The dosage was gradually increased to 40 mg per day by 23 Apr 97. On 22 and 23 Apr 97, the patient experienced moderate increased agitation, moderate vivid dreaming, and severe hypomania. The adverse experiences were ongoing, and the dose was decreased to 30 mg per day on 07 May 97. The patient withdrew his consent and was withdrawn from the study on 20 May 97, after 55 days of study medication, and he was given paroxetine 20 mg per day off study.

On 03 Jun 97, off-study paroxetine was discontinued and the patient was to receive fluvoxamine 20 mg bid po. On 10 Jun 97, the increased agitation became severe and was accompanied by severe worsening of obsessive-compulsive disorder. The patient was admitted to the psychiatric unit via emergency room. The report indicates the treatment with fluvoxamine was started at this time, as well as diphenhydramine 25-50 mg prn po/IM for sleep/agitation and risperidone 1.5 mg qd po for agitation. At last report, the adverse experiences were ongoing. The investigator considered the events probably unrelated to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Acetaminophen	04 May 97	Ongoing
Fluvoxamine	10 Jun 97	Ongoing
Diphenhydramine	10Jun 97	Ongoing
Risperidone	10 Jun 97	Ongoing

Study 29060/453
PID 453.012.00065 (1998007233-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience

Primary Adverse Experience (Verbatim Term): Skin Hypertrophy (Closure of Stoma [Failure of Old Gastric Tube Site to Heal])

Screening Demography:
Age: 9 years
Date of birth: 17 May 88
Sex: Female
Weight: 64.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Reactive Airway Disease
Short Stature
Rhinitis
Sinusitis
Stenosis of Gastroesophageal Sphincter

Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-label: Paroxetine 10 mg Given Orally

Start: 11 Jul 97 **Stop:** 21 Jul 97
Study Drug: Open-label Paroxetine 20 mg Given Orally

Start: 22 Jul 97 **Stop:** 13 Aug 97
Study Drug: Open-label Paroxetine 30 mg Given Orally

Start: 14 Aug 97 **Stop:** 07 Nov 97
Study Drug: Double-blind Paroxetine 30 mg Given Orally

Start: 08 Nov 97 **Stop:** 06 Apr 98

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Mild Increased Dreaming	05 Sep 97	17 Jun 98
Mild Decreased Concentration	07 Oct 97	17 Jun 98
Mild Decreased Appetite	08 Oct 97	17 Jun 98
Mild Rhinitis	07 Nov 97	09 Nov 97
Mild Flu with Fatigue	13 Feb 98	28 Feb 98

AE Remarks:

This patient started open-label study medication, 10 mg per day paroxetine, on 11 Jul 97. The dosage was gradually increased to 30 mg per day by 14 Aug 97. The patient completed 16 weeks of open-label study medication and was randomized to active paroxetine. She began double-blind study medication 30 mg per day on 08 Nov 97. On 25 Nov 97, the patient had surgery to close a gastric tube stoma that did not close when the tube was pulled. The investigator considered the event unrelated to study medication and the patient continued in the study.

Concomitant Drugs	Onset	Stopped
Somatrem	01 Jan 89	Ongoing
Beclomethasone Inhaled	01 Jan 95	Ongoing
Salbutamol Inhaled	01 Jan 95	Ongoing
Chlorphenamine/Hycosin/Phenylephrine	01 Jan 96	Ongoing
Cimetidine	01 Jan 97	05 Dec 97
Antacids NOS	01 Jan 97	Ongoing
Morphine	26 Nov 97	26 Nov 97
Meperidine	26 Nov 97	26 Nov 97

Study 29060/453
PID 453.015.00353 (1998002987-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience

Primary Adverse Experiences (Verbatim Term): Agitation (Agitation)
Neurosis (Self-Injurious Behavior [Compulsivity])

Screening Demography:
Age: 10 years
Date of birth: 20 Jan 87
Sex: Female
Weight: 119.0 lbs.
Race: Caucasian

Country: United States

Medical History: None
Psychiatric History: Major Depressive Disorder
Separation Anxiety Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-label Paroxetine 10 mg Given Orally

Start: 04 Dec 97 **Stop:** 06 Dec 97

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
None		

AE Remarks:

This patient started open-label study medication, 10 mg per day paroxetine, on 04 Dec 97. At the time the patient started taking study medication, she had been experiencing an escalation of obsessive-compulsive disorder symptoms, including the urge to hurt herself. This urge included biting her lips and tongue, bending back her fingers, and gagging herself. These behaviors were only superficially harmful but caused distress to the patient and her family. Adverse experiences of moderate agitation and mild self-injurious behavior were reported.

The patient and her mother called the study coordinator several times during the 3 days the patient was taking study medication to discuss their frustration and

sadness. On 06 Dec 97, the patient requested that she be admitted to the psychiatric unit at UCLA, with the expectation of receiving help to control her compulsions. Diphenhydramine was administered 25 mg 1-3 times per day and thioridazine 25 mg 1-3 times per day. The patient was withdrawn from the study on 06 Dec 97 because consent was withdrawn. On 10 Dec 97, paroxetine 30 mg per day was initiated to the patient in the hospital. The events resolved on 20 Dec 97. The investigator considered the events unrelated to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Diphenhydramine	06 Dec 97	20 Dec 97
Thioridazine	06 Dec 97	20 Dec 97

Study 29060/453
PID 453.017.00211 (1997020787-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience and Adverse Experience Leading to Withdrawal and Vital Sign of Potential Clinical Concern

Primary Adverse Experience (Verbatim Term): Delusions (Delusional Thinking)
Weight Loss (Weight Loss)
Vital Sign of Potential Clinical Concern: Significant Weight Loss

Screening Demography:
Age: 15 years
Date of birth: 21 Aug 81
Sex: Male
Weight: 130.0 lbs.
Race: Caucasian

Country: United States

Medical History: Allergies to Pollen, Dust, and Molds
Tonsillectomy Age 11
Psychiatric History: Generalized Anxiety Disorder
Specific Phobias, NOS

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-label Paroxetine 10 mg Given Orally

Start: 10 Jun 97 **Stop:** 23 Jun 97
Study Drug: Open-label Paroxetine 20 mg Given Orally

Start: 24 Jun 97 **Stop:** 08 Jul 97
Study Drug: Open-label Paroxetine 30 mg Given Orally

Start: 09 Jul 97 **Stop:** 22 Jul 97
Study Drug: Open-label Paroxetine 40 mg Given Orally

Start: 23 Jul 97 **Stop:** 05 Aug 97
Study Drug: Open-label Paroxetine 50 mg Given Orally

Start: 06 Aug 97 **Stop:** 12 Aug 97

Study Drug: Open-label Paroxetine 60 mg Given Orally

Start: 13 Aug 97 **Stop:** 20 Aug 97
Study Drug: Open-label Paroxetine 40 mg Given Orally

Start: 21 Aug 97 **Stop:** 24 Aug 97
Study Drug: Open-label Paroxetine 30 mg Given Orally

Start: 25 Aug 97 **Stop:** 25 Aug 97

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Mild Nausea/Vomiting	13 Jun 97	13 Jun 97
Mild Daytime Tiredness	25 Jun 97	Ongoing
Mild Nausea	08 Jul 97	08 Jul 97
Moderate Increased Obsessions	04 Aug 97	16 Aug 97
Moderate Increased Anxiety	06 Aug 97	16 Aug 97
Moderate Increased Insomnia	16 Aug 97	02 Sep 97
Moderate Physical Threat to Peer	25 Aug 97	25 Aug 97
Severe Significant Increased Anxiety	17 Aug 97	02 Sep 97
Moderate Worsened Depression	07 Aug 97	02 Sep 97
Severe Significant Worsened Obsession	17 Aug 97	02 Sep 97

AE Remarks:

This patient began open-label study medication, paroxetine 10 mg per day, on 10 Jun 97. Paroxetine dosage was increased by 10 mg every 2 weeks; at week 6, the patient displayed minimal improvement. At week 8, the patient's Children's Yale Brown Obsessive Compulsive Score (CYBOCS) increased from 24 at baseline to 28; the increase was attributed to the patient's verbalizing more, and more openly discussing OCD symptoms.

Approximately one week later, starting between 04 and 07 Aug 97, the patient experienced increased anxiety, increased frequency of obsessions, and worsened depression; these events were attributed to the fact that school was starting soon and the patient had been teased by peers the previous year. On 13 Aug 97, the paroxetine dose was increased to 60 mg per day. Four days later the patient became more preoccupied with his obsessions. They developed a delusional quality, which was reported as a serious adverse experience. Paroxetine was decreased to 40 mg per day. On 25 Aug 97, the patient placed his hands around a peer's neck in the restroom. At a scheduled visit the next day, the patient was withdrawn from the study after 77 days on study medication. He was hospitalized

due to the adverse experiences of delusional thinking, anxiety and obsession, which the investigator considered probably unrelated to study medication, and depression, which the investigator considered possibly related to study medication. Olanzapine 5 mg po qd was started on 29 Aug 97.

At follow-up on 02 Sep 997, it was reported that the delusional thinking, anxiety, depression, and obsession were resolved. Paroxetine was restarted off study the following day at 30 mg per day.

Vital Signs of Potential Clinical Concern:

Date	Visit	Week	Weight (lbs.)
03 Jun 97	1	Screening	130.0
10 Jun 97	2	Baseline	129.0
24 Jun 97	3	Week 2	116.5 *
09 Jul 97	4	Week 4	112.0 *
23 Jul 97	5	Week 6	115.5 *
06 Aug 97	6	Week 8	119.0 *
26 Aug 97		Early Discontinuation	122.0
03 Sep 97		Follow-up	122.0

* Value of potential clinical concern

Vital Sign Remarks:

The patient's baseline weight was 129.0 lbs. On 24 Jun 97, 14 days after start of study medication, the patient's weight decreased to 116.5, which was a decrease from baseline of potential clinical concern but not out of range for the patient's age. Weight loss was reported as a moderate adverse experience on 24 Jun 97 continuing to 09 Jul 97, when the patient weighed 112.0 lbs. The investigator did not considered that the weight loss was serious and the patient continued in the study. After that date the patient's weight started to increase until it was 122.0 at the early discontinuation visit on 26 Aug 97, 78 days after the start of study medication. The investigator considered that the weight loss was probably unrelated to study medication.

Concomitant Drugs	Onset	Stopped
Allergy Injections	01 Feb 96	Ongoing

Study 29060/453
PID 453.017.00212 (1997022592-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience and Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Anxiety (Severe Persistent Anxiety)

Screening Demography:
Age: 9 years
Date of birth: 04 Sep 87
Sex: Female
Weight: 62.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Chest Pain
Enuresis
Lower Leg Cramping
Skin Mole/Nevi (Neck)

Psychiatric History:
Generalized Anxiety Disorder
Specific Phobia, NOS
Oppositional Defiant Disorder
Tourette's Disorder
Attention Deficit/Hyperactivity Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Paroxetine 10 mg Given Orally

Start: 28 Jun 97 **Stop:** 09 Jul 97

Study Drug: Paroxetine 20 mg Given Orally

Start: 10 Jul 97 **Stop:** 30 Jul 97

Study Drug: Paroxetine 30 mg Given Orally

Start: 31 Jul 97 **Stop:** 06 Aug 97

Study Drug: Paroxetine 20 mg Given Orally

Start: 07 Aug 97 **Stop:** 15 Aug 97

Study Drug: Paroxetine 10 mg Given Orally

Start: 16 Aug 97 **Stop:** 28 Aug 97

Study Drug: Paroxetine 20 mg Given Orally

Start: 29 Aug 97 **Stop:** 21 Sep 97

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Moderate Libido Increased	15 Jul 97	14 Aug 97
Moderate Increased Anxiety	15 Jul 97	14 Aug 97
Moderate Worsened Tics	15 Jul 97	14 Aug 97
Moderate Increased Obsessive-Compulsive Disorder	15 Jul 97	14 Aug 97
Moderate Worsened Tics	23 Aug 97	25 Aug 97
Mild Worsened Anxiety	23 Aug 97	10 Sep 97
Moderate Worsened Obsessions	23 Aug 97	10 Sep 97
Mild Restlessness	23 Aug 97	20 Sep 97
Moderate Weight Gain	29 Aug 97	Ongoing
Mild Insomnia	01 Sep 97	20 Sep 97
Moderate Increased Blood Pressure	18 Sep 97	22 Sep 97
Moderate Increased Depression	20 Sep 97	24 Sep 97
Moderate Increased Obsessive-Compulsive Disorder	20 Sep 97	26 Sep 97
Severe Panic Attacks	21 Sep 97	23 Sep 97
Moderate Worsened Insomnia	21 Sep 97	24 Sep 97

AE Remarks:

This patient started open-label study medication, paroxetine 10 mg per day, on 28 Jun 97. The dose was gradually increased and then decreased to 10 mg, then increased to 20 mg on 29 Aug 97 after the patient experienced restlessness and worsened tics, anxiety, and obsessions. On 21 Sep 97, the patient had a severe panic attack and was unable to sleep. The patient had no history of panic attacks. The parent was directed to give the patient 1 mg lorazepam prn for insomnia, but 4 hours later the parent reported persistent anxiety, which the investigator considered a serious adverse experience, and continuing panic. The patient was able to sleep after another dose of lorazepam. The patient was withdrawn from the study the same day, after 86 days of study medication. When the patient awoke, she again experienced severe anxiety and panic and was hospitalized. The events resolved on 23 Sep 97. The investigator considered these events probably unrelated to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Lorazepam	21 Sep 97	23 Sep 97

Study 29060/453
PID 453.017.00335 (1997028393-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience

Primary Adverse Experience (Verbatim Term): Emotional Lability (Suicidal Thinking)

Screening Demography:
Age: 17 years
Date of birth: 27 Nov 79
Sex: Male
Weight: 147.5 lbs.
Race: Caucasian

Country: United States

Medical History:
Muscle Aches
Environmental Allergies
Fatigue
Headaches
Hypoglycemia

Psychiatric History:
Conduct Disorder
Major Depressive Disorder, Suspected
Social Phobia

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Paroxetine 10 mg Given Orally

Start: 24 Oct 97 **Stop:** 06 Nov 97

Study Drug: Paroxetine 20 mg Given Orally

Start: 07 Nov 97 **Stop:** 19 Nov 97

Study Drug: Paroxetine 30 mg Given Orally

Start: 20 Nov 97 **Stop:** 09 Dec 97

Study Drug: Paroxetine 40 mg Given Orally

Start: 10 Dec 97 **Stop:** 02 Jan 98

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Moderate Worsened Fatigue	13 Oct 97	02 Dec 97
Mild Muscle Aches	13 Oct 97	02 Dec 97
Mild Dyspepsia	24 Oct 97	02 Nov 97
Mild Weight Loss	07 Nov 97	Ongoing
Severe Increased Major Depressive Disorder	19 Nov 97	26 Nov 97
Moderate Dry Mouth	20 Nov 97	02 Dec 97
Mild Urinary Frequency	20 Nov 97	12 Dec 97
Mild Difficulty Initiating Urination	20 Nov 97	12 Dec 97
Mild Increased Cough	13 Dec 97	31 Dec 97

AE Remarks:

This patient started taking study medication, open-label paroxetine 10 mg per day, on 24 Oct 97. The dose was increased to 20 mg per day 2 weeks later, and to 30 mg per day after 2 more weeks, on 20 Nov 97, following worsening of major depressive disorder. On 25 Nov 97, the patient's Children's Yale Brown Obsessive Compulsive Score (CYBOCS) was 33 and the patient complained of worsening depressive disorder and suicidal thought. The patient was hospitalized that evening but discharged the next day with decreased suicidal thoughts. The investigator initially considered that the suicidal thinking was not related to study medication but later changed his assessment to possibly related.

Study medication was not interrupted. The patient continued in the study and the paroxetine dosage was increased to 40 mg per day on 10 Dec 97. On 02 Jan 98, she withdrew from the study because she moved out of state. She was prescribed off-study paroxetine 40 mg per day at that time.

Concomitant Drugs	Onset	Stopped
Menthol Cough Drops	13 Dec 97	Ongoing

Study 29060/453
PID 453.017.00431 (1998005534-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience and Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Emotional Lability(Worsened Suicidal Thoughts)

Other Adverse Experiences: Concentration Impaired (Worsened Attention Deficit/Hyperactivity Disorder)
Hostility (Verbal Aggression)

Screening Demography:
Age: 10 years
Date of birth: 25 Sep 87
Sex: Male
Weight: 100.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Penicillin Allergy
Constipation
Overweight
Dust Allergy
Headaches
Insomnia
Nasal Congestion

Psychiatric History:
Attention Deficit/Hyperactivity Disorder, Suspected
Tic Disorder
Dysthymia

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open Label Paroxetine 10 mg Given Orally

Start: 03 Feb 98 **Stop:** 16 Feb 98

Study Drug: Open Label Paroxetine 15 mg Given Orally

Start: 17 Feb 98 **Stop:** 18 Feb 98

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Moderate Weight Gain	18 Feb 98	27 Feb 98
Moderate Worsened Anxiety	18 Feb 98	Ongoing

AE Remarks:

This patient began taking open-label study medication, 10 mg paroxetine per day, on 03 Feb 98. Two days later, the family reported an increase in attention deficit/hyperactivity disorder and verbal aggression. The patient was given PO lorazepam 0.5 mg per day on 05 and 06 Feb 98. On 10 Feb 98, dextroamphetamine was given for attention deficit/hyperactivity disorder. The patient's paroxetine was increased to 15 mg per day by the family on 17 Feb 98 without site consent. On 18 Feb 98, the family reported increased anxiety and the patient was withdrawn from the study after 16 days on study medication. Upon completion of the visit the patient was given PO lorazepam 0.75 mg.

The following day, 19 Feb 98, the family reported ongoing increasing anxiety, attention deficit/hyperactivity disorder, verbal aggression, and increasing intensity and frequency of suicidal comments. Under the advisement of the investigator, the patient was admitted to a mental health inpatient unit on the evening of 19 Feb 98. PO paroxetine 15 mg was administered and dextroamphetamine was discontinued. On 20 Feb 98 fluvoxamine and clonidine were started. The suicidal thinking resolved the same day and discharge was planned for 26 Feb 98. As of 24 Mar 98, the patient was continuing on fluvoxamine and clonidine. The investigator considered the worsened suicidal thinking possibly related to paroxetine and possibly associated with depression.

Concomitant Drugs	Onset	Stopped
Pseudophedrine	01 Jan 97	Ongoing
Paracetamol	01 Aug 97	Ongoing
Lorazepam	05 Feb 98	06 Feb 98
Dextroamphetamine	10 Feb 98	19 Feb 98
Lidocaine/Prilocaine	18 Feb 98	18 Feb 98
Lorazepam	18 Feb 98	19 Feb 98

Study 29060/453
PID 453.018.00420 (1998011760-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience

Primary Adverse Experience (Verbatim Term): Drug Dependence (Inpatient Psychiatric Hospitalization due to Chemical Dependency)

Screening Demography:
Age: 17 years
Date of birth: 17 Dec 80
Sex: Female
Weight: 142.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Nasal Congestion
TMJ Surgery Age 15
Wisdom Teeth (All 4) Removed Approx. 1 Month Ago
Allergy to Penicillin
Allergy to Codeine

Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-label Paroxetine 10 mg Given Orally

Start: 17 Feb 98 Stop: 02 Mar 98

Study Drug: Open-label Paroxetine 20 mg Given Orally

Start: 03 Mar 98 **Stop:** 19 Mar 98

Study Drug: Open-label Paroxetine 30 mg Given Orally

Start: 20 Mar 98 **Stop:** 17 Apr 98

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Mild Headache	19 Feb 98	20 Feb 98
Mild Nausea	19 Feb 98	20 Feb 98
Mild Headache	04 Mar 98	04 Mar 98
Mild Diarrhea	23 Mar 98	25 Mar 98
Mild Abdominal Pain, Left Lower Quadrant	01 Apr 98	Ongoing
Mild Diarrhea	03 Apr 98	13 Apr 98
Mild Human Bites, Nose and Right Ear	04 Apr 98	04 Apr 98

AE Remarks:

This patient started open-label study medication, 10 mg per day paroxetine, on 17 Feb 98. The dosage was gradually increased to 30 mg per day by 20 Mar 98. On 29 Apr 98, 51 days after the start of study medication, the patient's mother brought the patient to the emergency room after she exhibited "bizarre and erratic behavior." The patient was subsequently admitted to a short-term inpatient evaluation unit for chemical dependency evaluation. The patient had been missing from 26 Apr 98 through 28 Apr 98. According to a contact at the hospital where the patient was admitted, the primary drug of abuse is crack/amphetamines. A urine drug screen was positive for amphetamines and THC. The most recent information received reports the outcome of the event to be resolved as of 04 May 1998. The investigator considered the drug use unrelated to study medication and possibly associated with the primary condition and a chemical deficiency.

The patient was not withdrawn from the study but was subsequently lost to follow-up.

Concomitant Drugs	Onset	Stopped
Methylcellulose	13 Apr 98	Ongoing
Ibuprofen	04 Mar 98	04 Mar 98
Penicillin	04 Apr 98	14 Apr 98

Study 29060/453
PID 453.020.00448 (1998007308-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience

Primary Adverse Experience (Verbatim Term): Emotional Lability (Suicide Attempt)

Screening Demography:
Age: 12 years
Date of birth: 16 Apr 85
Sex: Female
Weight: 119.0 lbs.
Race: Caucasian

Country: United States

Medical History: None
Psychiatric History: Generalized Anxiety Disorder , Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally

Start: 27 Jan 98 **Stop:** 09 Feb 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally

Start: 10 Feb 98 **Stop:** 23 Feb 98
Study Drug: Open-Label Paroxetine 30 mg Given Orally

Start: 24 Feb 98 **Stop:** 09 Feb 98
Study Drug: Open-Label Paroxetine 40 mg Given Orally

Start: 10 Mar 98 **Stop:** 23 Mar 98
Study Drug: Open-Label Paroxetine 50 mg Given Orally

Start: 24 Mar 98 **Stop:** 15 May 98
Study Drug: Double-Blind Paroxetine 50 mg Given Orally

Start: 16 May 98 **Stop:** 08 Sep 98
Study Drug: Double-Blind Paroxetine Down Titration Given Orally (Per Protocol)
Start: 09 Sep 98 **Stop:** 01 Oct 98

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Mild Stomach Pain	27 Jan 98	30 Jan 98
Mild Nausea	27 Jan 98	30 Jan 98
Moderate Vomiting	30 Jan 98	30 Jan 98
Mild Fatigue	04 Mar 98	01 May 98
Mild Headache	07 Mar 98	08 Mar 98
Mild Stomach Pain	07 Mar 98	08 Mar 98
Mild Enuresis	20 Mar 98	23 Mar 98
Moderate Cloudy Urine	23 Mar 98	15 May 98
Moderate Amorphous Sediment in Urine	23 Mar 98	15 May 98
Moderate Elevated WBC (Urine)	20 Apr 98	Ongoing
Moderate Bacteria in Urine	20 Apr 98	15 May 98
Moderate Pruritus	22 Apr 98	22 Apr 98
Mild Headache	23 Apr 98	23 Apr 98
Mild Pruritus	20 May 98	22 May 98
Mild Stomach Pain	09 Jun 98	09 Jun 98
Mild Pruritus	09 Jun 98	09 Jun 98
Mild Stomach Ache	15 Jul 98	15 Jul 98
Mild Pruritus	15 Jul 98	15 Jul 98

AE Remarks:

This patient started open-label study medication, 10 mg per day paroxetine, on 27 Jan 98. The dosage was gradually increased to 40 mg per day by 10 Mar 98. On 16 Mar 98, 48 days from the start of study medication, the patient “tried to commit suicide.” The patient had a prior history of passive suicidal ideation without intention or plan. On study medication, the patient had shown improvement in attitude towards school work and attendance; however, the patient felt she still procrastinated with school work. On the morning of the incident, the patient was very anxious as she had not completed a major assignment due that day. She did not work on it all weekend, but had a pleasant time with the family. The patient's mother set limits over the patient's being upset and the patient complained of being embarrassed, angry and tired of OCD symptoms. She showed her mother a knife and asked if it was sharp. The patient stated she imagined stabbing herself in the heart, but was fearful it might hurt. The patient wanted her mother to take her more seriously and went to a room where she used a drawstring from sweat pants to tighten around her neck. The patient was not trying to kill herself, by her report, and was frightened by her behavior. The mother saw the resulting red ring on her neck and reported the incident.

When seen in the office, the patient was anxious and forthcoming, and had no suicidal ideation; she was still upset over incomplete school work. The plan was to send the patient home with parents, continuing study medication; phone contact was to occur the next day, with a visit in two days to reassess. The investigator considered the suicide attempt unrelated to study medication, and possibly associated with the primary condition. The investigator considered this event a serious adverse experience.

The dosage of paroxetine was increased to 50 mg per day on 24 Mar 98. The patient completed 16 weeks of open-label study medication and was randomized to active paroxetine. She completed the study as planned.

Concomitant Drugs	**Onset**	**Stopped**
Diphenhydramine	22 Apr 98	22 Apr 98
Paracetamol	23 Apr 98	23 Apr 98
Sulfamethoxazole/Trimethoprim	24 Apr 98	28 Apr 98
Pseudophedrine/Ibuprofen	20 May 98	22 May 98
Diphenhydramine	20 May 98	21 May 98
Diphenhydramine	09 Jun 98	09 Jun 98

Study 29060/453
PID 453.021.00067 (1997009461-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience and Adverse Experience Leading to Withdrawal

Primary Adverse Experiences (Verbatim Term): Depression (Depressive Episode)
Hostility (Acting Out Behavior [Aggression])
Emotional Lability (Suicidal Ideation)

Screening Demography: Age: 9 years
Date of birth: 20 Aug 87
Sex: Male
Weight: 57.0 lbs.
Race: Caucasian

Country: United States

Medical History: Questionable Prolonged QT Wave Interval/Repeat EKG Ordered
Asthma
EKG Repeated—Result within Normal Limits

Psychiatric History: Separation Anxiety, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-label Paroxetine 10 mg Given Orally

Start: 29 Jan 97 Stop: 12 Feb 97

Study Drug: Open-label Paroxetine 20 mg Given Orally

Start: 13 Feb 97 Stop: 26 Feb 97

Study Drug: Open-label Paroxetine 30 mg Given Orally

Start: 27 Feb 97 Stop: 11 Mar 97

Study Drug: Open-label Paroxetine 40 mg Given Orally

Start: 12 Mar 97 Stop: 19 Mar 97

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
None		

AE Remarks:

This patient started open-label study medication, 10 mg per day paroxetine, on 29 Jan 97. The dosage was gradually increased to 40 mg per day by 12 Mar 97. On 19 Mar 97, 49 days after the first dose of study medication, the patient had a severe depressive episode with suicidal ideation and acting-out behaviors. The mother of the patient stated, "He has become more aggressive, has frightened the two-year-old twins, has locked himself in the garage refusing to come out, and has literally taken control of the household and family on a daily basis. Directions are not followed; punishment does not work. He has gotten progressively worse in his behavior; these things occurred on a weekly basis before, but occurred daily now." The patient had acting-out behaviors (aggressive behavior) since June 1995; a full medical work-up had been negative. The depression was identified in March 1997. The child had had major conflict with the mother, which was worsening since prior to the start of the study. The patient withdrew from the study on 19 Mar 97 due to lack of efficacy, after 50 days of study medication.

The investigator assessed the patient as severely ill and recommended hospitalization. The parents refused and the patient was managed as an outpatient. The patient was started on off-study paroxetine 10 mg q am along with other medications. The paroxetine was titrated up slowly because the obsessions had been decreasing on the study. The patient was seen twice weekly by the investigator and received extensive family and behavioral therapy. As of 31 Mar 97, the patient was still doing poorly with obsessive-compulsive disorder and depression. He locked himself in the bathroom and still had outbursts. He was free of additional suicidal ideations. Per report on 23 Apr 97, the patient is improving with the paroxetine and his regimen.

Initially the investigator reported that the depression and hostility were possibly related to study medication. The investigator later considered that the events were probably unrelated to study medication.

Concomitant Drugs	Onset	Stopped
None		

Study 29060/453
PID 453.021.00126 (1997029657-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience and Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Neurosis (Acute Exacerbation of Severe Obsessive-Compulsive Disorder Symptoms)

Screening Demography:
Age: 8 years
Date of birth: 28 Mar 89
Sex: Female
Weight: 60.0 lbs.
Race: Caucasian

Country: United States

Medical History: None
Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-label Paroxetine 10 mg Given Orally

Start: 24 May 97 **Stop:** 20 Jun 97
Study Drug: Open-label Paroxetine 20 mg Given Orally

Start: 21 Jun 97 **Stop:** 11 Jul 97
Study Drug: Open-label Paroxetine 30 mg Given Orally

Start: 12 Jul 97 **Stop:** 25 Jul 97
Study Drug: Open-label Paroxetine 40 mg Given Orally

Start: 26 Jul 97 **Stop:** 10 Aug 97
Study Drug: Open-label Paroxetine 50 mg Given Orally

Start: 11 Aug 97 **Stop:** 19 Aug 97
Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 20 Sep 97 **Stop:** 20 Oct 97

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Moderate Reaction to Hepatitis Vaccine, Temperature 102°	05 Aug 97	05 Aug 97

AE Remarks:

This patient started open-label study medication, 10 mg per day paroxetine, on 24 May 97. The dosage was gradually increased to 50 mg per day by 11 Aug 97. The patient completed 16 weeks of open-label study medication and was randomized to placebo. She began double-blind down titration on 20 Sep 97. On 09 Oct 97, the patient experienced an acute exacerbation of obsessive-compulsive disorder symptoms. The patient was withdrawn from the study the following day after 139 days of study medication. Paroxetine was restarted off study on 11 Oct 97 at 10 mg per day.

At last report, the exacerbation of obsessive-compulsive disorder symptoms was ongoing. The investigator considered the adverse experience related to study medication.

Concomitant Drugs	Onset	Stopped
Hepatitis Vaccine	05 Aug 97	05 Aug 97

Study 29060/453
PID 453.021.00127 (1997029641-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience and Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Neurosis (Major Increase in Obsessive-Compulsive Disorder Symptoms)

Screening Demography:
Age: 11 years
Date of birth: 29 Jan 86
Sex: Male
Weight: 88.0 lbs.
Race: Caucasian

Country: United States

Medical History: Hernia (Groin)
Surgery for Hernia (Groin)
Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally

Start: 03 May 97 **Stop:** 12 May 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally

Start: 13 May 97 **Stop:** 30 May 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally

Start: 31 May 97 **Stop:** 11 Jun 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally

Start: 12 Jun 97 **Stop:** 25 Jun 97
Study Drug: Open-Label Paroxetine 50 mg Given Orally

Start: 26 Jun 97 **Stop:** 11 Jul 97
Study Drug: Open-Label Paroxetine 60 mg Given Orally

Start: 12 Jul 97 **Stop:** 25 Aug 97

Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 26 Aug 97 **Stop:** 22 Sep 97

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Mild Bumped Right Wrist, Possible Broken Finger	30 May 97	15 Jun 97
Mild Wart Removed Right Shin	05 Aug 97	05 Aug 97

AE Remarks:

This patient started open-label study medication, 10 mg per day paroxetine, on 03 May 97. The dosage was gradually increased to 60 mg per day by 12 Jul 97. The patient completed 16 weeks of open-label study medication and was randomized to placebo. He began double-blind down titration on 26 Aug 97. On 05 Sep 97, the patient experienced a severe major increase in obsessive-compulsive disorder symptoms. Study medication was increased and then subsequently stopped on 22 Sep 97. The patient was withdrawn from the study after 143 days of study medication. On 23 Sep 97, paroxetine 10 mg po qd was started off study. Risperidone was given from 23 Sep 97 to 25 Sep 97 for angry outbursts and increased impulsivity.

The increase in obsessive-compulsive disorder symptoms resolved on 22 Sep 97. The investigator considered the adverse experience related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
None		

Study 29060/453
PID 453.021.00129 (1997030185-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience and Adverse Experience Leading to Withdrawal

Primary Adverse Experiences (Verbatim Term): Manic Reaction (Severe Manic Behavior)
Hostility (Increased Aggression)

Other Adverse Experiences:

Screening Demography:
Age: 8 years
Date of birth: 02 Feb 89
Sex: Male
Weight: 57.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Allergic—Seasonal and Dust and Mold
Asthma—Infrequent Problems
Cyst on Kidney
Sore Throat Cold/Cough
Ileoatresia (Three Surgeries Birth to 1 to Correct)
Kidney Problems—Renal Failure (Post Op Age 1)

Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally

Start: 07 Apr 97 **Stop:** 05 May 97

Study Drug: Open Label Paroxetine 20 mg Given Orally

Start: 06 May 97 **Stop:** 11 Aug 97

Study Drug: Double-Blind Paroxetine 20 mg Given Orally

Start: 12 Aug 97 **Stop:** 10 Oct 97

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Moderate Sinus Infection	11 May 97	28 May 97
Moderate Asthma	11 May 97	28 May 97
Mild Electric Shock	12 Jun 97	12 Jun 97

AE Remarks:

This patient started open-label study medication, 10 mg per day paroxetine, on 07 Apr 97. The dosage was increased to 20 mg per day on 06 May 97. The patient completed 16 weeks of open-label study medication and was randomized to active paroxetine. He began double-blind study medication 20 mg per day on 12 Aug 97. On 09 Oct 97, the patient experienced severe manic behavior and severe increased aggression. Study medication was stopped on 10 Oct 97 and the patient was withdrawn from the study due to the serious adverse experiences after 177 days on study medication. Subsequently, the blind was broken by the investigator and it was discovered that the patient had been randomized to active paroxetine.

At last report, the adverse experience was ongoing. The investigator considered the severe manic behavior and increased aggression possibly related to study medication.

Concomitant Drugs	Onset	Stopped
Cefprozil	02 May 97	12 May 97
Salbutamol	12 May 97	28 May 97
Loratadine	17 Jun 97	Ongoing
Beclomethasone	17 Jun 97	Ongoing

Study 29060/453
PID 453.024.00180 (1997026527-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience and Adverse Experience Leading to Withdrawal

Primary Adverse Experiences (Verbatim Term): Hostility (Oppositional Defiant Behavior [Aggression])

Screening Demography:
Age: 9 years
Date of birth: 20 May 88
Sex: Male
Weight: 84.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Epistaxis
Jaundice: Newborn
Recurrent Ear Infections

Psychiatric History:
Dysthymia
Attention Deficit/Hyperactivity Disorder
Tic Disorders
Major Depressive Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-label Paroxetine 10 mg Given Orally

Start: 29 Jul 97 **Stop:** 11 Aug 97

Study Drug: Open-label Paroxetine 20 mg Given Orally

Start: 12 Aug 97 **Stop:** 13 Oct 97

Study Drug: Open-label Paroxetine 30 mg Given Orally

Start: 14 Oct 97 **Stop:** 03 Nov 97

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Mild Peri-Nasal Rash	28 Jul 97	13 Aug 97
Moderate Nausea	30 Jul 97	30 Jul 97
Moderate Vomiting	30 Jul 97	30 Jul 97
Moderate Head Cold	08 Aug 97	11 Aug 97
Mild Tiredness	12 Aug 97	Ongoing
Moderate Sunburn	18 Aug 97	20 Aug 97
Mild Sprained Right Fifth Digit Finger	24 Aug 97	26 Aug 97
Moderate Diarrhea	03 Sep 97	06 Sep 97
Mild Left Sprained Wrist	19 Sep 97	25 Sep 97

AE Remarks:

This patient started open-label study medication, 10 mg per day paroxetine, on 29 Jul 97. The dosage was gradually increased to 30 mg per day by 14 Oct 97. The psychiatrist indicated the parents became frustrated to a point, and that on 01 Nov 1997 they left their son by himself for a short time at a restaurant when he refused to get into the car. On 03 Nov 1997, the patient exhibited oppositional and defiant behavior; he climbed onto the roof of his house, refused to get down, and verbally threatened to jump off the roof. He jumped off the roof, but did not hurt himself. Later in the day he refused all direction from his parents, e.g., refused to exit the car. His parents took him to the family therapist, and due to the lack of improvement in mood and behavior the patient was taken to a local hospital, then transferred to another facility. According to the patient's attending psychiatrist, the patient's parents "are quite well meaning and not malicious in any way, but have had a very difficult time in setting limits" with him. Paroxetine was discontinued on 03 Nov 1997 and the patient was withdrawn from the study after 98 days on study medication. The patient was treated with clonidine 0.05 mg/day from 03 Nov 97 to discharge on 09 Nov 97 for treatment of attention deficit/ hyperactivity disorder symptoms. During the patient's hospitalization, his parents were very motivated to learn how to deal with the patient's behavior, and at discharge on 09-Nov-1997 the patient was much improved with respect to decreased depression, dysphoria and acting-out behaviors. The primary diagnoses per the discharge summary were depressive disorder NOS and anxiety disorder NOS. The patient's physical examination and laboratory tests at the early termination visit were normal.

The investigator initially considered the adverse experience unrelated to study medication; she later changed her causality assessment to possibly related.

Concomitant Drugs	Onset	Stopped
Hydrocortisone Cream	28 Jul 97	13 Aug 97
Pseudophedrine/Ibuprofen	08 Aug 97	11 Aug 97
Paracetamol	18 Aug 97	20 Aug 97
Bismuth Subsalicylate	03 Sep 97	06 Sep 97

Study 29060/453
PID 453.025.00297 (1998009486-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience

Primary Adverse Experience (Verbatim Term): Trauma (Broken Left Femur)

Screening Demography:
Age: 9 years
Date of birth: 30 Jun 88
Sex: Male
Weight: 82.0 lbs.
Race: Other (Hispanic)

Country: United States

Medical History:
Left Femur Tumor—Broken Femur
3 Surgeries (Age 4)—Tumor Removal and Femur Repair
Broke Right Wrist Age 9
Fractured Rib (Age 3-10)
Seasonal Allergies
Severe Chronic Ear Infections

Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-label Paroxetine 10 mg Given Orally

Start: 24 Jan 98 **Stop:** 24 Feb 98

Study Drug: Open-label Paroxetine 20 mg Given Orally

Start: 25 Feb 98 **Stop:** 04 Jun 98

Study Drug: Double-Blind Paroxetine 20 mg Given Orally

Start: 05 Jun 98 **Stop:** 05 Aug 98

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Mild Headache	22 Jan 98	26 Jan 98
Mild Stomach Ache	22 Jan 98	27 Jan 98
Mild Stomach Ache	02 Feb 98	04 Feb 98
Mild Vomiting	12 Feb 98	12 Feb 98
Severe Broken Left Femur (Rebroken)	29 May 98	Ongoing
Moderate Abdominal Pain	18 Jun 98	18 Jun 98

AE Remarks:

This patient started open-label study medication, 10 mg per day paroxetine, on 24 Jan 98. The dosage was increased to 20 mg per day on 25 Feb 98. The patient had a history of a bone cyst of the left femur and a broken left femur in 1993, with three surgeries for tumor removal and femur repair. On 27 Mar 98, 63 days after the start of study medication, the patient was jumping on a trampoline when another child landed on the patient's leg. The patient was placed in traction and transported to the emergency room. X-rays revealed a broken left femur. Surgery was performed to place an external fixator and repeat a biopsy on the area of the cyst. The patient received hydrocodone/paracetamol and morphine for pain. Study medication was not interrupted. The patient was discharged on 31 Mar 98. The investigator considered the broken left femur unrelated to study medication, but associated with a prior history of broken left femur.

The patient completed 16 weeks of open-label study medication and was randomized to active paroxetine. He began double-blind study medication 20 mg per day on 05 Jun 98. The patient again rebroke his left femur on 29 May 98. This adverse experience was not considered serious. The patient continued in the study until 05 Aug 98, when he withdrew due to lack of efficacy. He was prescribed paroxetine off study on 08 Aug 98.

Concomitant Drugs	Onset	Stopped
Calcium Carbonate/Magnesium Hydroxide	02 Feb 98	02 Feb 98
Calcium Carbonate/Magnesium Hydroxide	12 Feb 98	12 Feb 98
Calcium Carbonate/Magnesium Hydroxide	18 Jun 98	18 Jun 98

Study 29060/453
PID 453.026.00140 (1997023988-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience

Primary Adverse Experiences (Verbatim Term):
Emotional Lability (Ideas of Self Harm [Suicidal Ideation])
Agitation (Agitation)
Depression (Depression)
Hostility (Physically Abusive Behavior [Aggression])

Screening Demography:
Age: 15 years
Date of birth: 29 May 82
Sex: Male
Weight: 115.0 lbs.
Race: Other (Caucasian, Egyptian)

Country: United States

Medical History: Deaf
Post-Concussion Syndrome

Psychiatric History: Attention Deficit/Hyperactivity Disorder
Post-Traumatic Stress Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-label Paroxetine 10 mg Given Orally
Start: 21 Jul 97 **Stop:** 27 Jul 97
Study Drug: Open-label Paroxetine 20 mg Given Orally
Start: 28 Jul 97 **Stop:** 03 Aug 97
Study Drug: Open-label Paroxetine 30 mg Given Orally
Start: 04 Aug 97 **Stop:** 18 Aug 97
Study Drug: Open-label Paroxetine 40 mg Given Orally
Start: 19 Aug 97 **Stop:** 31 Aug 97

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Moderate Sexual Dysfunction	04 Aug 97	Unknown
Severe Behavioral Uncontrol (Self Abusive Behavior [Impulsivity])	31 Aug 97	Unknown

AE Remarks:

This patient started open-label study medication, 10 mg per day paroxetine, on 21 Jul 97. The dosage was gradually increased to 40 mg per day by 19 Aug 97. After enrolling in the study, the patient apparently began demonstrating aggressive behavior, which escalated. His parents became frustrated and discontinued study medication on 31 Aug 97 without consulting the investigator. The patient was hospitalized on 24 Sep 97 in the Adolescent Acute Unit for treatment of his agitation, abusive behavior to his brother and mother, depression and suicidal ideations. The patient is severely hearing impaired and has limited writing skills and limited communication abilities. He has a long-standing history of depression coupled with behavioral problems. The patient had been physically aggressive to his younger brother and mother. He was developing suicidal ideations and reported thoughts of wanting to get a gun to kill himself. The patient had also been repeatedly washing his hands in the sink with soap and water. These behaviors had intensified prior to admission. He was treated in the hospital with paroxetine 30 mg per day and fluvoxamine 50 mg per day. After one-on-one and group therapies, the patient demonstrated improved coping abilities and increased affective stability, and was discharged. He was not suicidal or homicidal and demonstrated no psychotic symptomatology. The patient continued to wash his hands but seemed to be better able to control this. His final diagnosis included major depression, recurrent, severe, without psychotic features. The serious adverse experience was considered resolved on 29 Sep 97.

The investigator learned about this situation when the patient did not show up for his scheduled study visit, and withdrew the patient because of deviation from protocol. Repeated attempts by the site to get the patient to come in for follow-up were unsuccessful. The investigator considered that the events were not related to study medication, but could be associated with the primary condition.

Concomitant Drugs	**Onset**	**Stopped**
None		

Study 29060/453
PID 453.026.00287 (1998005367-1)

Reason for Narrative: Serious Non-Fatal Adverse Experience and Adverse Experience Leading to Withdrawal

Primary Adverse Experiences (Verbatim Term): Hostility (Worsened Oppositional Defiant Disorder Symptoms [Aggressive Reaction])

Screening Demography:
Age: 13 years
Date of birth: 20 Jul 84
Sex: Male
Weight: 91.0 lbs.
Race: Caucasian

Country: United States

Medical History: Allergic Asthma
Psychiatric History: Attention Deficit/Hyperactivity Disorder
Oppositional Defiant Disorder
Specific Phobia NOS
Major Depressive Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-label Paroxetine 10 mg Given Orally

Start: 21 Jan 98 **Stop:** 27 Jan 98
Study Drug: Open-label Paroxetine 20 mg Given Orally

Start: 28 Jan 98 **Stop:** 10 Feb 98
Study Drug: Open-label Paroxetine 30 mg Given Orally

Start: 11 Feb 98 **Stop:** 27 Feb 98

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Mild Headache	14 Jan 98	20 Jan 98
Mild Headache	20 Jan 98	20 Jan 98
Mild Insomnia	05 Feb 98	12 Feb 98

AE Remarks:
This patient started open-label study medication, 10 mg per day paroxetine, on 21 Jan 98. The dosage was gradually increased to 30 mg per day by 11 Feb 98. On 21 Feb 98, the patient experienced worsening of oppositional defiant disorder. He had been arguing with his father and became physically and verbally abusive. When his parents could not calm him down and get the situation under control, they called the police. When the police arrived, the patient was still beating his father. The police took him into custody and drove him to a hospital, where he stayed until the following day. The hospital did not run any tests or prescribe medication, and study medication was taken as prescribed. The patient was terminated from the study on 27 Feb 98, after 38 days on study medication. The investigator considered the worsening of oppositional defiant behavior possibly related to study medication. He feels that the study medication may possibly have exacerbated the patient's underlying oppositional defiant disorder.

Concomitant Drugs	**Onset**	**Stopped**
Loratadine	01 Dec 97	31 Jan 98
Lorazepam	05 Feb 98	05 Feb 98
Marijuana (Recreational)	12 Feb 98	12 Feb 98
Lorazepam	12 Feb 98	12 Feb 98

Paroxetine - Protocol: 453

TABLE 15.05.3

Number (%) of Patients with Serious Emergent Adverse Experiences - Displayed by Body System
Intention to Treat Population
Taper Phase

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.06.1

Number (%) of Patients with Serious Emergent Adverse Experiences (Male Specific)
Intention to Treat Population
Phase I: Open Label Treatment

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.06.2

Number (%) of Patients with Serious Emergent Adverse Experiences (Male Specific)
Intention to Treat Population
Phase II: Randomised Treatment

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.06.3

Number (%) of Patients with Serious Emergent Adverse Experiences (Male Specific)
Intention to Treat Population
Taper Phase

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.07.1

Number (%) of Patients with Serious Emergent Adverse Experiences (Female Specific)
Intention to Treat Population
Phase I: Open Label Treatment

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.07.2

Number (%) of Patients with Serious Emergent Adverse Experiences (Female Specific)
Intention to Treat Population
Phase II: Randomised Treatment

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.07.3

Number (%) of Patients with Serious Emergent Adverse Experiences (Female Specific)
Intention to Treat Population
Taper Phase

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.08.1

Number (%) of Patients with Serious Emergent Adverse Experiences (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	335	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	13	3.9%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Body as a Whole	1	0.3
TRAUMA	1	0.3
Cardiovascular System	1	0.3
EXTRASYSTOLES	1	0.3
Nervous System	11	3.3
AGITATION	1	0.3
ANXIETY	1	0.3
DELUSIONS	1	0.3
DEPRESSION	1	0.3
DRUG DEPENDENCE	1	0.3
EMOTIONAL LABILITY	5	1.5
HOSTILITY	4	1.2
NEUROSIS	1	0.3

Paroxetine - Protocol: 453

TABLE 15.08.2

Number (%) of Patients with Serious Emergent Adverse Experiences (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	2	2.1%	2	2.0%	4	2.1%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Nervous System	1	1.1	2	2.0	3	1.6
HOSTILITY	1	1.1	0	0.0	1	0.5
MANIC REACTION	1	1.1	0	0.0	1	0.5
NEUROSIS	0	0.0	2	2.0	2	1.0
Skin and Appendages	1	1.1	0	0.0	1	0.5
SKIN HYPERTROPHY	1	1.1	0	0.0	1	0.5

Paroxetine - Protocol: 453

TABLE 15.08.3

Number (%) of Patients with Serious Emergent Adverse Experiences (Non-gender Specific)
Intention to Treat Population
Taper Phase

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.09.1

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal - Displayed by Body System
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	335	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	42	12.5%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Body as a Whole	4	1.2
Cardiovascular System	4	1.2
Digestive System	3	0.9
Nervous System	37	11.0
Respiratory System	1	0.3
Skin and Appendages	2	0.6
Special Senses	1	0.3

Confidential

SmithKline Beecham

Paroxetine

BRL-029060

Table 15.09.1A. Patient Narratives for Study 453: Adverse Experiences Leading to Withdrawal

453

xxxxx x. xxxxxxxxx, R.Ph., M.S.*
xxxxxx x. xxxxx, Ph.D.

*CNS, PMTU

SB Document Number: BRL-029060/RSD-100W89/1

Study 29060/453
PID 453.001.00360

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Pallor (Pale [Decreased Color to Cheeks/Face])

Other: Somnolence (Lethargy [Tired])

Screening Demography:
Age: 9 years
Date of birth: 04 Jul 88
Sex: Male
Weight: 69.0 lbs.
Race: Caucasian

Country: United States

Medical History: None
Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 05 Nov 97 **Stop:** 18 Nov 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 19 Nov 97 **Stop:** 21 Jan 98
Study Drug: Open-Label Paroxetine Down Titration Given Orally
Start: 22 Jan 98 **Stop:** 23 Jan 98

Adverse Experiences (Verbatim Term):	Onset	Stopped
Moderate Anorexia	05 Nov 97	26 Jan 98
Moderate Headache	21 Nov 97	21 Nov 97
Mild Dry Mouth	23 Nov 97	Ongoing
Mild Thirsty	23 Nov 97	24 Jan 98
Mild Headache	24 Nov 97	24 Nov 97
Moderate Weight Loss (Approx. 5 lbs.)	07 Dec 97	24 Jan 98
Moderate Flatus	16 Dec 97	15 Jan 98
Mild Black Spots in Front of Eyes	19 Jan 98	23 Jan 98
Mild Nausea	27 Jan 98	28 Jan 98

AE Remarks:

This patient started open-label paroxetine 10 mg per day on 05 Nov 97, which was increased to 20 mg per day on 19 Nov 97. The patient had mild AEs of thirst and dry mouth that began 4 days after the dose increase and lasted until after withdrawal from study medication. The patient also experienced weight loss of 5 lbs. and flatus. On 22 Jan 98, 79 days after the first dose of study medication, the mother decided on her own to taper the dose to 10 mg per day and then withdraw the patient from the study due to unspecified adverse experiences. The AEs that were the most recent were mild pallor and mild somnolence, both starting on 20 Jan 98. The patient took the last dose of study medication on 23 Jan 98, after 80 days of dosing. Both AEs resolved 3 days after the patient began tapering the dosage and both were considered by the investigator to be probably unrelated to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Paracetamol	21 Nov 97	21 Nov 97
Paracetamol	24 Nov 97	24 Nov 97

Study 29060/453
PID 453.002.00260

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Neurosis (Increase in Obsessive-Compulsive Disorder Symptoms)

Screening Demography:
Age: 9 years
Date of birth: 11 Oct 87
Sex: Female
Weight: 82.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Abdomen Tender Right Lower Quadrant
Enlarged Tonsil
Headache
Right Submaxillary Node Tender (Lymph)
Stomach Ache
Ear Infection
Fracture Left Wrist
Infectious Mononucleosis
Scarring Left Ear Canal
Streptococcus Throat

Psychiatric History: Specific Phobia—Needles

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 16 Jul 97 **Stop:** 31 Jul 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 01 Aug 97 **Stop:** 27 Aug 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 28 Aug 97 **Stop:** 05 Nov 97
Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 06 Nov 97 **Stop:** 19 Nov 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Severe Fracture Forearm Refracture	26 Jul 97	01 Sep 97
Moderate Insomnia	31 Jul 97	03 Aug 97
Moderate Leg Twitching (Bilateral)	31 Jul 97	27 Aug 97
Severe Insomnia	04 Aug 97	11 Sep 97
Moderate Moodiness	10 Aug 97	28 Aug 97
Moderate Insomnia	12 Sep 97	Ongoing

AE Remarks:

This patient started open-label Paroxetine at 10 mg per day on 16 Jul 97 and was gradually increased to 30 mg per day by 28 Aug 97. The patient completed the open-label phase of the study and was randomized to placebo on 06 Nov 97. During the down titration period, the patient experienced an increase of severe obsessive-compulsive disorder symptoms. After 12 days, the patient was withdrawn from the study at the parents' request and started on active paroxetine. The patient took study medication a total of 127 days. At last report, the increase in obsessive-compulsive disorder symptoms was ongoing. The investigator considered the increase of symptoms related to the study medication.

Concomitant Drugs	Onset	Stopped
Ibuprofen	26 Jul 97	Ongoing
Lorazepam	06 Sep 97	Ongoing

Study 29060/453
PID 453.002.00307

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Neurosis (Increase in Obsessive-Compulsive Disorder Symptoms)

Screening Demography:
Age: 10 years
Date of birth: 17 Jun 87
Sex: Male
Weight: 69.5 lbs.
Race: Caucasian

Country: United States

Medical History: Ankle Pain
Headache
Psychiatric History: Dysthymia

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 23 Oct 97 **Stop:** 19 Nov 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 20 Nov 97 **Stop:** 11 Feb 98
Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 12 Feb 98 **Stop:** 19 Feb 98
Study Drug: Double-Blind Placebo Given Orally
Start: 20 Feb 98 **Stop:** 04 Mar 98

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Mild Sleep Talking	12 Nov 97	20 Nov 97
Moderate Fractured Right Wrist	28 Nov 97	28 Dec 97
Moderate Upper Respiratory Infection	20 Feb 98	03 Mar 98
Mild GI Distress	28 Feb 98	28 Feb 98

AE Remarks:

This patient started open-label study medication, 10 mg per day, on 23 Oct 97. Study medication was increased on Day 29 to 20 mg, and the patient completed the open-label phase. She was randomized to placebo and began the down titration of paroxetine on 12 Feb 98. On 19 Feb 98, she experienced a moderate increase in obsessive-compulsive disorder symptoms. On 26 Feb 98, the patient started taking double-blind placebo. The symptoms continued, and on 04 Mar 98 the patient was withdrawn from the study and started on active paroxetine. Her obsessive-compulsive disorder symptoms resolved on 24 Mar 98. The patient took paroxetine a total of 126 days. The investigator considered the adverse experience related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Paracetamol	01 Jan 94	Ongoing
Ibuprofen	01 Jan 94	Ongoing

Study 29060/453
PID 453.003.00011

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Rash (Truncal Rash)
Nausea (Nausea)

Screening Demography:
Age: 16 years
Date of birth: 16 Nov 80
Sex: Male
Weight: 169.0 lbs.
Race: Caucasian

Country: United States

Medical History: Allergies—Airborne
Allergies—Food
Asthma
Psychiatric History: Generalized Anxiety Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 15 Mar 97 **Stop:** 27 Mar 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 28 Mar 97 **Stop:** 01 Apr 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Mild Diarrhea	24 Mar 97	24 Mar 97

AE Remarks:

This patient, who had a history of airborne and food allergies and asthma, started study medication, 10 mg paroxetine, on 15 Mar 97, which was increased to 20 mg on 28 Mar 97. On 28 Mar 97, the patient experienced a mild truncal rash that persisted until 18 Apr 97. On 31 Mar 97 she experienced moderate nausea, which lasted <1 day. On 29 Apr 97, a phone conversation with the mother revealed that she had withdrawn the patient from study medication on 01 Apr 97, after 19 days of dosing. The mother refused a follow-up visit because she lived at some

distance from the clinic. The investigator considered the rash related to study medication and the nausea possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Allergenic Extract	01 Apr 94	Ongoing
Loperamide	24 Mar 97	24 Mar 97

Study 29060/453
PID 453.004.00088

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Hostility (Disruptive Behavior)

Screening Demography:
Age: 13 years
Date of birth: 11 Nov 83
Sex: Female
Weight: 113.0 lbs.
Race: Caucasian

Country: United States

Medical History: None
Psychiatric History: Dysthymia, Suspected
Specific Phobia, NOS
Attention Deficit/Hyperactivity Disorder
Separation Anxiety Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 08 Oct 97 **Stop:** 12 Oct 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 13 Oct 97 **Stop:** 17 Nov 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 18 Nov 97 **Stop:** 19 Nov 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 20 Nov 97 **Stop:** 20 Nov 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Moderate Disinhibition	24 Oct 97	Ongoing
Mild Cold Symptom	30 Oct 97	31 Oct 97
Mild Cold Symptom	05 Nov 97	Ongoing
Mild Stomach Ache	17 Nov 97	17 Nov 97

AE Remarks:

This patient started taking open-label study medication, 10 mg paroxetine, on 08 Oct 97, which was increased to 20 mg on 13 Oct 97. On 24 Oct 97, she started showing signs of moderate disinhibition, which remained ongoing. On 07 Nov 97, her behavior became disruptive. The behavior continued and the patient was withdrawn from the study on 20 Nov 97, after 44 days of study medication. The investigator considered the disruptive behavior possibly related to study medication. At last report, the adverse experience was ongoing.

Concomitant Drugs	**Onset**	**Stopped**
Zinc Gluconate	30 Oct 97	31 Oct 97
Zinc Gluconate	05 Nov 97	06 Nov 97

Study 29060/453
PID 453.005.00016

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Neurosis (Worsening Obsessive-Compulsive Disorder)

Screening Demography:
Age: 14 years
Date of birth: 21 Mar 82
Sex: Female
Weight: 118.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Sinus Bradycardia
Sore Throat
Allergy to Sulfites
Asthma, Mild

Psychiatric History: Panic Disorder (without Agoraphobia), Suspected
Post-traumatic Stress Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 25 Feb 97 **Stop:** 20 Mar 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 21 Mar 97 **Stop:** 28 Mar 97
Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 29 Mar 97 **Stop:** 21 Apr 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 22 Apr 97 **Stop:** 12 May 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 13 May 97 **Stop:** 30 Jun 97
Study Drug: Double-Blind Paroxetine 30 mg Given Orally
Start: 01 Jul 97 **Stop:** 28 Jul 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Mild Flu	01 Mar 97	15 Mar 97
Mild Anxiety Related to School-Based Conflict	28 Mar 97	29 Mar 97
Mild Injured Left Arm Related to Incident at School	14 Apr 97	30 Jun 97
Mild Headache	12 Jul 97	12 Jul 97
Mild Insect Bite	Unknown	14 Jul 97
Mild Headache	26 Jul 97	26 Jul 97

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 25 Feb 97. When she completed the open-label phase on 30 Jun 97, she was taking 30 mg paroxetine per day. She entered the double-blind phase the following day and continued on the same dosage. On 28 Jul 97, the patient experienced severe worsening of her obsessive-compulsive disorder symptoms and she was withdrawn from the study the same day, after 154 days of study medication. The symptoms continued until 25 Aug 97. The investigator considered the experience related to study medication.

Concomitant Drugs	Onset	Stopped
Salbutamol	01 Jan 95	Ongoing
Azithromycin	01 Mar 97	15 Mar 97
Paracetamol	14 Apr 97	30 Jun 97
Paracetamol	12 Jul 97	12 Jul 97
Bentonite/Calamine/Glycerol/Phenol/Sodium Citrate/Zinc Oxide	Unknown	14 Jul 97
Ibuprofen	26 Jul 97	26 Jul 97

Study 29060/453
PID 453.005.00376

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Hyperkinesia (Akathisia)

Screening Demography:
Age: 7 years
Date of birth: 13 Apr 90
Sex: Male
Weight: 60.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Allergy to Amoxicillin
Asthma
Atopic Dermatitis (Hand Eczema)

Psychiatric History:
Specific Phobia—Needles/Injections

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 09 Feb 98 **Stop:** 17 Feb 98

Adverse Experiences (Verbatim Term):	Onset	Stopped
None		

AE Remarks:

This patient received his first dose of open-label study medication, 10 mg paroxetine, on 09 Feb 98. On 16 Feb 98, he experienced moderate akathisia. He was withdrawn from the study the following day after 9 days of study medication. The akathisia continued until 26 Feb 98. The investigator considered the akathisia related to study medication.

Concomitant Drugs	Onset	Stopped
Salbutamol	01 Nov 97	Ongoing
Beclomethasone	01 Nov 97	Ongoing

Study 29060/453
PID 453.006.00102

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Manic Reaction (Hypomania)

Screening Demography:
Age: 10 years
Date of birth: 27 Sep 86
Sex: Female
Weight: 75.2 lbs.
Race: Caucasian

Country: United States

Medical History:
Chronic Stomach Aches
Cyclic Vomiting
Depressive Symptoms
Difficulty Voiding
Furoxone Allergy
Insomnia
Sulfa-Based Medication Allergy
Cough
Kidney Reflux
Ear Infection
Nausea

Psychiatric History:
Generalized Anxiety Disorder, Suspected
Major Depressive Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 01 Mar 97 **Stop:** 13 Mar 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Mild Cough	21 Mar 97	Ongoing
Mild Sinus Congestion	31 Mar 97	08 Apr 97
Mild Diarrhea	31 Mar 97	08 Apr 97
Mild Vaginal Itching	31 Mar 97	08 Apr 97

AE Remarks:

This patient started study medication, 10 mg paroxetine per day, on 01 Mar 97. On 11 Mar 97, he experienced hypomania. He was withdrawn from the study on 13 Mar 97, after 13 days of study medication. The hypomania continued until 18 Mar 97. The investigator considered the experience possibly related to study medication.

Concomitant Drugs	Onset	Stopped
Melatonin	01 Nov 96	Ongoing
Phenylpropanolamine	31 Mar 97	08 Apr 97
Guaifenesin	31 Mar 97	08 Apr 97

Study 29060/453
PID 453.006.00170

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Hyperkinesia (Hyperactivity)

Screening Demography:
Age: 9 years
Date of birth: 07 Mar 88
Sex: Female
Weight: 58.9 lbs.
Race: Caucasian

Country: United States

Medical History: None
Psychiatric History: Attention Deficit/Hyperactivity Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 21 May 97 **Stop:** 03 Jun 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 04 Jun 97 **Stop:** 09 Jul 97
Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 10 Jul 97 **Stop:** 12 Aug 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Moderate Insomnia	13 Jun 97	Ongoing
Severe Hyperactivity	17 Jun 97	15 Jul 97
Mild Somnolence	15 Jul 97	26 Aug 97

AE Remarks:

This patient started study medication, 10 mg open-label paroxetine, on 21 May 97. He had a history of attention deficit/hyperactivity disorder (suspected) along with obsessive-compulsive disorder. His dosage was increased to 20 mg per day on 04 Jun 97. He experienced severe hyperactivity starting on 17 Jun 97. The dosage was decreased to 10 mg per day on 10 Jul 97, and the

hyperactivity was reported as moderate starting 15 Jul 97. The hyperactivity continued, and the patient was withdrawn from the study on 12 Aug 97, after 84 days of study medication. The hyperactivity was ongoing at study end. The investigator considered the AE reported as severe hyperactivity to be related to study medication, and the AE of moderate severity to be possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Diphenhydramine	13 Jun 97	15 Jul 97
Methylphenidate	13 Aug 97	Ongoing

Study 29060/453
PID 453.006.00347

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Agitation (Psychomotor Agitation)

Screening Demography:
Age: 9 years
Date of birth: 15 Jul 88
Sex: Male
Weight: 54.0 lbs.
Race: Other (Hispanic)

Country: United States

Medical History:
Allergy-Induced Asthma
Headache (Occasional)
Insomnia
Seasonal Sinus Allergies
Stomach Ache (Occasional)
Ear Infections
Sleep Apnea
Tonsillectomy/Adenoidectomy
Tubes in Ears

Psychiatric History:
Major Depressive Disorder
Attention Deficit/Hyperactivity Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 10 Sep 97 **Stop:** 21 Oct 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 22 Oct 97 **Stop:** 04 Nov 97
Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 05 Nov 97 **Stop:** 02 Dec 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Severe Hypomania	04 Nov 97	Ongoing

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 10 Sep 97. On 22 Oct 97, the dosage was increased to 20 mg per day. On 04 Nov 97, the patient experienced severe hypomania The dosage was decreased to 10 mg per day but the hypomania continued. On 02 Dec 97 the patient also experienced moderate psychomotor agitation and was withdrawn from the study after 84 days of study medication. At last report, the adverse experience was ongoing. The investigator considered that the psychomotor agitation was possibly related to study medication.

Concomitant Drugs	Onset	Stopped
Cromoglycate	01 Jan 94	Ongoing
Salbutamol	01 Jan 94	Ongoing
Ibuprofen	01 Oct 96	Ongoing
Calcium Carbonate	01 Jan 97	Ongoing
Diphenhydramine	04 Oct 97	Ongoing

Study 29060/453
PID 453.006.00391

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Agitation (Psychomotor Agitation)

Screening Demography:
Age: 7 years
Date of birth: 12 Feb 90
Sex: Male
Weight: 49.5 lbs.
Race: Caucasian

Country: United States

Medical History:
Cold Syndrome
Left Tear Duct Repair (Surgical)
Pneumonia
Environmental Allergies

Psychiatric History:
Generalized Anxiety Disorder
Attention Deficit/Hyperactivity Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 29 Oct 97 **Stop:** 25 Nov 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Mild Nausea	30 Oct 97	31 Oct 97

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 29 Oct 97. On 12 Nov 97, the patient experienced moderate psychomotor agitation. The agitation continued and the patient was withdrawn from the study on 25 Nov 97 after 28 days of study medication. The agitation resolved on 16 Dec 97. The investigator considered that the agitation was related to study medication.

Concomitant Drugs	Onset	Stopped
Paracetamol/Dextromethorphan/Ethanol	01 Jan 90	Ongoing
Guaifenesin	01 Jan 90	Ongoing
Ibuprofen	01 Jan 92	Ongoing
Salbutamol	01 Mar 97	Ongoing

Study 29060/453
PID 453.006.00463

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Manic Reaction (Hypomania)

Screening Demography:
Age: 9 years
Date of birth: 09 Dec 88
Sex: Male
Weight: 59.4 lbs.
Race: Caucasian

Country: United States

Medical History: Sutures Under Left Eye
Psychiatric History: Dysthymia

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 11 Feb 98 **Stop:** 10 Mar 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 11 Mar 98 **Stop:** 27 Mar 98
Study Drug: Open-Label Paroxetine Down Titration Given Orally
Start: 28 Mar 98 **Stop:** 07 Apr 98

Adverse Experiences (Verbatim Term):	Onset	Stopped
Mild Daytime Fatigue	11 Feb 98	25 Feb 98
Mild Nausea	11 Feb 98	25 Feb 98
Moderate Decreased Appetite	11 Feb 98	03 Mar 98
Moderate Vomiting	27 Feb 98	02 Mar 98
Moderate Diarrhea	27 Feb 98	02 Mar 98
Mild Cut on Legs Right and Left	03 Apr 98	21 Apr 98

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 11 Feb 98. On 11 Mar 98, the dosage was increased to 20 mg per day. On

23 Mar 98, the patient experienced moderate hypomania. Study medication was titrated down until 07 Apr 98 and the patient was withdrawn from the study. The patient received a total of 56 days of study medication. The hypomania resolved on 21 Apr 98. The investigator considered that the hypomania was related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
None		Ongoing

Study 29060/453
PID 453.008.00456

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Myoclonus (Increased Tics)

Screening Demography:
Age: 14 years
Date of birth: 12 May 83
Sex: Male
Weight: 161.0 lbs.
Race: Caucasian

Country: United States

Medical History: None
Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 05 Feb 98 **Stop:** 11 Feb 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 12 Feb 98 **Stop:** 24 Feb 98
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 25 Feb 98 **Stop:** 05 Mar 98
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 06 Mar 98 **Stop:** 17 Mar 98
Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 18 Mar 98 **Stop:** 02 Apr 98
Study Drug: Open-Label Paroxetine 60 mg Given Orally
Start: 03 Apr 98 **Stop:** 04 Jun 98
Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 05 Jun 98 **Stop:** 11 Jul 98
Study Drug: Double-Blind Placebo Given Orally
Start: 12 Jul 98 **Stop:** 11 Aug 98

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Mild Nausea	06 Feb 98	09 Feb 98
Moderate Headache	30 Mar 98	30 Mar 98
Moderate Indigestion	25 Apr 98	25 Apr 98
Moderate Indigestion	01 May 98	Ongoing

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 05 Feb 98. The dosage was increased gradually in 10-mg increments until 03 Apr 98, when the patient was receiving 60 mg per day. On 05 Jun 98, the patient was randomized to placebo and double-blind down titration of paroxetine was started. The patient began placebo approximately 22 Jul 98. On 25 Jul 98, the patient experienced severe increased tics, of which there was no reported history. The patient was withdrawn from the study on 11 Aug 98 after approximately 167 days of study medication. The tics decreased to moderate on 16 Sep 98. At last report, the adverse experience was ongoing. The investigator considered that the adverse experience was possibly related to study medication.

Concomitant Drugs	Onset	Stopped
Paracetamol	30 Mar 98	30 Mar 98
Paracetamol	25 Apr 98	25 Apr 98

Study 29060/453
PID 453.008.00460

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Headache (Headache)

Other:
Nausea (Nausea)
Myoclonus (Twitching)
Hyperventilation (Hyperventilation)
Tremor (Shaking)

Screening Demography:
Age: 15 years
Date of birth: 26 Jul 82
Sex: Female
Weight: 132.0 lbs.
Race: Caucasian

Country: United States

Medical History: Acne—Treated with Retin A Cream
Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 20 Mar 98 **Stop:** 26 Mar 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 27 Mar 98 **Stop:** 02 Apr 98
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 03 Apr 98 **Stop:** 16 Apr 98
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 17 Apr 98 **Stop:** 12 May 98
Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 13 May 98 **Stop:** 27 May 98
Study Drug: Open-Label Paroxetine 60 mg Given Orally
Start: 28 May 98 **Stop:** 17 Jul 98
Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 18 Jul 98 **Stop:** 28 Aug 98

Adverse Experiences (Verbatim Term):	Onset	Stopped
Severe Anxiety	15 May 98	15 May 98
Mild Diarrhea	10 Jun 98	13 Jun 98
Mild Decreased Weight	18 Jun 98	29 Jun 98
Moderate Increased Weight	26 Jul 98	02 Sep 98
Moderate Acne	26 Jul 98	Ongoing

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 20 Mar 98. The dosage was increased gradually in 10-mg increments until 28 May 98, when the patient was receiving 60 mg per day. On 17 Jul 98, the patient was randomized to placebo and double-blind down titration of paroxetine was started. On 26 Aug 98, the patient experienced severe headache, nausea, twitching, shaking, and hyperventilation. The down titration continued and the patient was withdrawn from the study on 28 Aug 98 after 162 days of study medication. The patient was started on active paroxetine the same day. The adverse experiences leading to the withdrawal resolved on 31 Aug 98. The investigator considered that the adverse experiences were related to study medication.

Concomitant Drugs	Onset	Stopped
Tretinoin	01 Jan 96	30 Mar 98
Ethinylestradiol/Norethisterone	26 Jul 98	Ongoing

Study 29060/453
PID 453.010.00049

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Asthenia (Tiredness)
Other: Insomnia (Initial Insomnia)

Screening Demography:
Age: 15 years
Date of birth: 07 Jul 81
Sex: Female
Weight: 182.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Rash
Allergic Rhinitis
Headaches
Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 01 May 97 **Stop:** 14 May 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 15 May 97 **Stop:** 28 May 97
Study Drug: Open-Label Paroxetine Down Titration Given Orally
Start: 29 May 97 **Stop:** 04 Jun 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Moderate Upper Respiratory Infection	02 May 97	16 May 97
Moderate Bilateral Otitis Media	08 May 97	28 May 97
Moderate Nightmare	17 May 97	17 May 97
Mild Depressed Mood	01 Jun 97	09 Jun 97

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 01 May 97. On 15 May 97, the dosage was increased to 20 mg per day. The

same day, the patient experienced moderate tiredness and moderate initial insomnia. Both adverse experiences continued, and the patient was put on taper medication until 04 Jun 97, when she was withdrawn from the study after 35 days of study medication. The insomnia resolved on 01 Jun 97, and the tiredness resolved on 11 Jun 97. The investigator considered that both adverse experiences were possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Dextromethorphan/Paracetamol/Pseudophedrine	02 May 97	02 May 97
Paracetamol	03 May 97	04 May 97
Paracetamol	08 May 97	13 May 97
Amoxicillin	08 May 97	18 May 97
Azithromycin	23 May 97	28 May 97

Study 29060/453
PID 453.011.00014

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Headache (Headache)

Other: Nausea (Nausea)
Dizziness (Dizziness)

Screening Demography: Age: 17 years
Date of birth: 08 Nov 80
Sex: Female
Weight: 114.0 lbs.
Race: Caucasian

Country: United States

Medical History: Frequent Stomach Aches
Gum Surgery
Psychiatric History: Possible Past Anorexia Nervosa, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 21 Feb 98 **Stop:** 09 Mar 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 10 Mar 98 **Stop:** 07 Apr 98
Study Drug: Open-Label Paroxetine 10 mg Orally
Start: 08 Apr 98 **Stop:** 22 May 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 23 May 98 **Stop:** 23 Jun 98
Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 24 Jun 98 **Stop:** 10 Jul 98

Adverse Experiences (Verbatim Term):	Onset	Stopped
Mild Lightheaded	21 Feb 98	23 Feb 98
Mild Nausea	23 Feb 98	23 Feb 98
Moderate Quivering Mouth	23 Feb 98	Ongoing
Mild Cold Symptoms	21 Mar 98	28 Mar 98
Mild Restless Feeling During Day	01 Apr 98	Ongoing
Mild Eye and Mouth Tic	07 Apr 98	21 Apr 98
Mild Root Canal Surgery (Abscessed Tooth)	30 Apr 98	30 Apr 98
Moderate Increased Anxiety	15 May 98	30 May 98
Mild Insomnia	15 May 98	30 May 98

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 21 Feb 98 and took 10 mg or 20 mg per day throughout the open-label phase of the study. On 23 Jun 98, the patient was randomized to placebo and started double-blind down titration of paroxetine. On 03 Jul 98, the patient experienced moderate headache, nausea, and dizziness and was started on taper medication. The experiences resolved on 08 Jul 98; the patient was withdrawn from the study 2 days later and put on active paroxetine. The patient received a total of 140 days of study medication. The investigator considered that the experiences were all possibly related to study medication.

Concomitant Drugs	Onset	Stopped
Bismuth Subsalicylate	23 Feb 98	23 Feb 98
Penicillin NOS	23 Apr 98	05 May 98
Dimenhydrinate	03 Jul 98	03 Jul 98

Study 29060/453
PID 453.011.00015

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Hostility (Aggressiveness)

Other: Hyperkinesia (Hyperactivity)

Screening Demography:
Age: 7 years
Date of birth: 06 Oct 90
Sex: Female
Weight: 54.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Asthma, Stabilized
Nasal Congestion
Respiratory Virus (Hospitalized)

Psychiatric History:
Possible Past Transient Tic Disorders
Specific Phobias—Dark, Thunderstorms, Flying

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 27 Feb 98 **Stop:** 22 Jun 98
Study Drug: Double-Blind Paroxetine 10 mg Given Orally
Start: 23 Jun 98 **Stop:** 15 Sep 98

Adverse Experiences (Verbatim Term):	Onset	Stopped
Mild Daytime Sleepiness	27 Feb 98	21 Apr 98
Mild Upper Respiratory Infection	07 Mar 98	11 Mar 98
Mild Inattentiveness	03 Apr 98	03 Apr 98
Mild Abrasion on Chin Secondary to Bike Fall	11 Apr 98	14 Apr 98
Mild Constipation	28 Apr 98	26 May 98
Mild Allergies (Seasonal)	22 Jun 98	22 Jun 98
Mild Increased Eosinophils	22 Jun 98	Ongoing
Moderate Chicken Pox	11 Jul 98	17 Jul 98

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 27 Feb 98. On 23 Jun 98, the patient completed the open-label phase of the study and was randomized to double-blind paroxetine. On 27 Jun 98, the patient experienced moderate hyperactivity. The experience was not resolved but the patient continued in the study. On 01 Sep 98, the patient experienced mild aggressiveness, which also continued, and was withdrawn from the study on 15 Sep 98, after 201 days of study medication. The patient was put on active paroxetine the following day. At last report, both adverse experience were ongoing. The investigator considered that both experiences were possibly related to study medication.

Concomitant Drugs	Onset	Stopped
Brompheniramine/Phenylpropanolamine	09 Mar 98	10 Mar 98
Paracetamol/Aluminum Hydroxide/Magnesium Hydroxide	12 Jul 98	13 Jul 98
Salbutamol	12 Jul 98	13 Jul 98
Paracetamol	12 Jul 98	16 Jul 98
Diphenhydramine	12 Jul 98	17 Jul 98

Study 29060/453
PID 453.011.00142

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Hyperkinesia (Increased Hyperactivity and Disruptiveness)

Screening Demography:
Age: 12 years
Date of birth: 25 Oct 84
Sex: Male
Weight: 107.8 lbs.
Race: Caucasian

Country: United States

Medical History:
Headaches
Nasal Congestion
Sore Throat

Psychiatric History:
Longstanding History of "Behavior Problems"
Tic Disorders

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 25 Mar 97 **Stop:** 06 Apr 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Mild Daily Headaches	28 Mar 97	07 Apr 97
Mild Decreased Appetite	28 Mar 97	08 Apr 97
Mild Arm and Hand Tic (New Tic)	28 Mar 97	08 Apr 97

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 25 Mar 97. On 28 Mar 97, the patient experienced mild increased hyperactivity and disruptiveness. The experience continued and the patient was withdrawn from the study on 06 Apr 97, after 13 days of study medication. The

hyperkinesia resolved on 08 Apr 97. The investigator considered that the hyperkinesia was possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Paracetamol	01 Jan 91	Ongoing
Turpentine Oil/Camphor/Eucalyptus Oil/Menthol	01 Jan 88	Ongoing

Study 29060/453
PID 453.011.00143

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Hyperkinesia (Increased Hyperactivity)

Other: Nervousness (Increased Irritability)
Neurosis (Increased Obsessive-Compulsive Disorder Symptoms)

Screening Demography: Age: 7 years
Date of birth: 29 Mar 89
Sex: Male
Weight: 80.0 lbs. (measured at Visit 2)
Race: Caucasian

Country: United States

Medical History: Eczema
Warts on Both Hands
Staphylococcal Infection

Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 01 Apr 97 **Stop:** 07 Apr 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
None		

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 01 Apr 97. On 05 Apr 97, the patient experienced moderate increased hyperactivity, moderate increased irritability, and moderate increased obsessive-compulsive disorder symptoms. The events continued and the patient was withdrawn from the study on 07 Apr 97, after 7 days of study medication. The

adverse experiences resolved on 09 Apr 97. The investigator considered that all the events were possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
None		

Study 29060/453
PID 453.011.00148

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Neurosis (Increased Trichotillomania)

Screening Demography:
Age: 11 years
Date of birth: 07 Mar 86
Sex: Female
Weight: 75.0 lbs.
Race: Caucasian

Country: United States

Medical History: Initial Insomnia
Psychiatric History: Specific Phobia, NOS
Trichotillomania

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 02 May 97 **Stop:** 02 Jun97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 03 Jun 97 **Stop:** 16 Jun 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 17 Jun 97 **Stop:** 30 Jun 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 01 Jul 97 **Stop:** 10 Jul 97
Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 11 Jul 97 **Stop:** 28 Jul 97
Study Drug: Open-Label Paroxetine 60 mg Given Orally
Start: 29 Jul 97 **Stop:** 22 Aug 97
Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 23 Aug 97 **Stop:** 29 Sep 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Mild Occasional Headaches	24 Apr 97	03 Sep 97
Mild Urinary Frequency, Urinary Burning	26 Apr 97	26 Apr 97
Mild Anal Itching and Burning	30 Apr 97	30 Apr 97
Mild Constipation	30 Apr 97	30 Apr 97
Moderate Sore Throat	07 Jun 97	09 Jun 97
Mild Sinus Drainage and Nasal Congestion	08 Jun 97	15 Jun 97
Moderate Pinworms	21 Jun 97	22 Jun 97
Moderate Sore Throat	22 Jun 97	27 Jun 97

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 02 May 97. The dosage was gradually increased to 30 mg per day by 17 Jun 97. On 30 Jun 97, the patient experienced moderate increased trichotillomania. The dosage was increased gradually to 60 mg per day by 29 Jul 97 but the adverse experience continued. The dosage was down titrated starting 22 Aug 97 until 29 Sep 97, when the patient was withdrawn from the study after 151 days of study medication. The event was ongoing at study termination. The patient was subsequently prescribed 20 mg paroxetine. The investigator considered that the trichotillomania was possibly related to study medication.

Concomitant Drugs	Onset	Stopped
Paracetamol	24 Apr 97	Ongoing
Diphenhydramine	13 Jun 97	13 Jun 97
Mebendazole	22 Jun 97	22 Jun 97

Study 29060/453
PID 453.011.00150

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Tremor (Shaking [Trembling])

Other:
Skin Disorder (Clammy Feeling)
Headache (Headache)
Hyperkinesia (Increased Hyperactivity)
Abnormal Vision (Difficulty Focusing Eyes)

Screening Demography:
Age: 11 years
Date of birth: 03 Mar 86
Sex: Male
Weight: 96.5 lbs.
Race: Caucasian

Country: United States

Medical History:
Asthma
Seasonal Allergies
Adenoidectomy
Fall
Nosebleeds
Ruptured Ear Drum
Sutures—Chin
Tympanoplasty
Indigestion

Psychiatric History:
Attention Deficit/Hyperactivity Disorder
Oppositional Defiant Disorder
Specific Phobias, NOS
Night Terrors/Somnambulism

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 10 May 97 **Stop:** 13 May 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
None		

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 10 May 97. On the same day, the patient experienced moderate shaking and moderate clammy feeling. The clammy feeling resolved the same day but the shaking continued. Two days later the patient experienced a moderate headache, which also continued. The following day, 13 May 97, the patient experienced moderate increased hyperactivity and moderate difficulty focusing eyes. The patient was withdrawn from the study the same day, after 4 days of study medication. The hyperactivity and focus difficulty resolved the same day. The shaking and headache resolved on 19 May 98. The investigator considered that all the adverse experiences were possibly related to study medication.

Concomitant Drugs	Onset	Stopped
Calcium Carbonate	01 Jan 96	Ongoing
Pirbuterol Acetate	01 Jan 96	Ongoing
Cromoglycate	26 Feb 90	Ongoing
Astemizole	26 Feb 90	Ongoing
Vitamins NOS	01 Jan 89	Ongoing
Beclomethasone	01 Jan 88	Ongoing

Study 29060/453
PID 453.011.00199

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Abdominal Pain (Stomach Pain)

Other: Diarrhea (Diarrhea)

Screening Demography:
Age: 12 years
Date of birth: 17 Jan 88
Sex: Male
Weight: 137.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Seasonal Allergies
Asthma

Psychiatric History:
Attention Deficit/Hyperactivity Disorder
Post-traumatic Stress Disorder
Separation Anxiety Disorder
Social Phobia
Specific Phobia, NOS
Tic Disorders

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 04 Jun 97 **Stop:** 17 Jun 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 18 Jun 97 **Stop:** 01 Jul 97

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 02 Jul 97 **Stop:** 08 Jul 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Mild Lower Respiratory Infection	30 May 97	08 Jun 97
Moderate Stomach Ache	05 Jun 97	15 Jun 97
Mild Decreased Appetite	05 Jun 97	15 Jun 97
Moderate Lethargy	18 Jun 97	09 Jul 97
Moderate Vomiting	29 Jun 97	29 Jun 97
Mild Nausea	29 Jun 97	02 Jul 97

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 04 Jun 97. On 18 Jun 97, the dosage was increased to 20 mg per day. On the same day, the patient experienced moderate stomach pain and diarrhea. The dosage was decreased to 10 mg per day but the adverse experiences continued. On 08 Jul 97, the patient was withdrawn from the study after 35 days of study medication. The investigator considered that the adverse experiences were possibly related to study medication. The events resolved on 09 Jul 97.

Concomitant Drugs	Onset	Stopped
Diphenhydramine	01 Jan 91	Ongoing
Chlorphenamine	01 Jan 91	Ongoing
Brompheniramine/Phenylephrine/ Phenylpropanolamine	01 Jan 91	Ongoing
Salbutamol	01 Jan 91	Ongoing
Amoxicillin	30 May 97	08 Jun 97
Loratadine	30 May 97	08 Jun 97
Loperamide	30 Jun 97	30 Jun 97

Study 29060/453
PID 453.011.00425

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Hostility (Increased Oppositionality)
Other: Hyperkinesia (Increased Hyperactivity)

Screening Demography:
Age: 13 years
Date of birth: 06 Jan 85
Sex: Male
Weight: 154.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Allergic to Dogs
Allergic to Eggs
Appendectomy

Psychiatric History:
Attention Deficit/Hyperactivity Disorder
Mild Depressive Symptoms (Past)
Separation Anxiety Disorder
Simple Phobias

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 06 Feb 98 **Stop:** 20 Feb 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 21 Feb 98 **Stop:** 05 Mar 98
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 06 Mar 98 **Stop:** 30 Apr 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 01 May 98 **Stop:** 06 May 98
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 07 May 98 **Stop:** 21 May 98

Adverse Experiences (Verbatim Term):	Onset	Stopped
Mild Stomach Ache	02 Mar 98	02 Mar 98
Mild Lightheaded	05 Mar 98	03 Apr 98
Mild Rash on Face	05 Mar 98	07 Mar 98
Mild Upper Respiratory Infection	17 Mar 98	20 Mar 98
Mild Vomiting	28 Apr 98	28 Apr 98

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 06 Feb 98. The dosage was gradually increased to 30 mg per day by 06 Mar 98. On 09 Apr 98, the patient experienced moderate increased oppositionality and moderate increased hyperactivity. The adverse experiences continued and the patient was withdrawn from the study on 21 May 98, with no down titration, after 105 days of study medication. The events remained ongoing. The patient was restarted on paroxetine on 22 May 98. The investigator considered that the events were possibly related to study medication.

Concomitant Drugs	Onset	Stopped
Pseudophedrine	18 Mar 98	18 Mar 98

Study 29060/453
PID 453.013.00055

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Neurosis (Worsening of Obsessive-Compulsive Disorder Symptoms)

Other: Anxiety (Anxious)
Nervousness (Irritable)

Screening Demography: Age: 7 years
Date of birth: 02 Jun 89
Sex: Male
Weight: 56.0 lbs.
Race: Other (Hispanic)

Country: United States

Medical History: Constipation
Central Nervous System Hemorrhage
Depressed Mood
Head Injury, Loss of Consciousness
Magnetic Resonance Imaging
Migraine Headache
Right Hemiparesis
Speech and Language Problems
Speech Therapy
Stitches
Trauma—Fall
Undescended Testes
Undescended Testes as a Toddler, Restored

Psychiatric History: Attention Deficit/Hyperactivity Disorder
Tic Disorders, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 21 Mar 97 **Stop:** 27 Mar 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 28 Mar 97 **Stop**: 03 Apr 97

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 04 Apr 97 **Stop**: 12 Apr 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 13 Apr 97 **Stop**: 17 Apr 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 18 Apr 97 **Stop**: 08 May 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 09 May 97 **Stop**: 14 May 97
Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 15 May 97 **Stop**: 11 Jun 97
Study Drug: Open-Label Paroxetine 60 mg Given Orally
Start: 12 Jun 97 **Stop**: 11 Jul 97
Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 12 Jul 97 **Stop**: 31 Jul 97

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Mild Falling Asleep Earlier	24 Mar 97	08 Apr 97
Mild Waking Earlier	28 Mar 97	05 Apr 97
Mild Stomach Ache	02 Apr 97	02 Apr 97
Mild Loose Stools	02 Apr 97	02 Apr 97
Moderate Swallowed 1” Diameter Plug from Salt Shaker	10 Apr 97	10 Apr 97
Moderate No Bowel Movements	10 Apr 97	19 Apr 97
Mild Tired	22 Apr 97	25 Apr 97
Mild Trouble Falling Asleep	30 Apr 97	08 May 97
Mild Dry Mouth	22 May 97	Ongoing
Moderate Increase in Vocal Tic	22 May 97	Ongoing
Mild Trouble Falling Asleep If Alone	29 May 97	Ongoing
Moderate Irritable	13 Jul 97	30 Jul 97
Moderate Anxious	14 Jul 97	30 Jul 97
Mild Headache	29 Jul 97	30 Jul 97

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 21 Mar 97. The dosage was gradually increased to 60 mg per day by 12 Jun 97. The patient completed the open-label phase of the study and on 12 Jul 97 was randomized to placebo. The dose was down titrated and on 13 Jul 97 he experience moderate irritability, with moderate anxiety the following day. Both adverse experiences continued and on 24 Jul 97 he experienced moderate worsening of obsessive-compulsive disorder symptoms. On 30 Jul 97, the patient

also experienced severe anxiety and irritability and was withdrawn from the study the following day, after 133 days of study medication. On 01 Aug 97, the patient was started on 40 mg per day paroxetine. The anxiety and irritability decreased to moderate on 03 Aug 97, and both were considered resolved on 06 Aug 97. The investigator considered that the worsening of obsessive-compulsive disorder symptoms was related to study medication. The severe anxiety and irritability were considered possibly related to study medication, but the investigator considered the moderate anxiety and irritability that started on 03 Aug to be unrelated to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Natural Fiber Laxative	01 Jan 96	Ongoing

Study 29060/453
PID 453.015.00488

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Euphoria (Disinhibition)

Screening Demography: Age: 13 years
Date of birth: 10 May 84
Sex: Male
Weight: 166.0 lbs.
Race: Caucasian

Country: United States

Medical History: Hay Fever
Ingrown Toenails
Facial Acne
Mild Chronic Motor Tic Disorder

Psychiatric History: Tic Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 10 Mar 98 **Stop**: 16 Mar 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 17 Mar 98 **Stop**: 23 Mar 98
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 24 Mar 98 **Stop**: 16 Apr 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 17 Apr 98 **Stop**: 26 Apr 98
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 27 Apr 98 **Stop**: 04 May 98
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 05 May 98 **Stop**: 11 Jun 98
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 12 Jun 98 **Stop**: 12 Jun 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 15 Jun 98 **Stop**: 21 Jun 98

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 22 Jun 98 **Stop**: 28 Jun 98

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Moderate Irritability	04 Apr 98	Ongoing
Moderate Hyperactivity	10 Apr 98	01 May 98

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 10 Mar 98. The dosage was increased to 20 mg per day on 17 Mar and to 30 mg per day on 24 Mar 1998. On 04 Apr 98 the patient experienced moderate irritability and on 10 Apr 98 he experienced moderate hyperactivity. The dose was decreased from 17 Apr to 26 Apr 98 and then increased to 40 mg by 05 May 98. The hyperactivity resolved but the irritability remained ongoing. On 08 Jun 98, the patient experienced moderate disinhibition. The dosage was gradually decreased to 20 mg per day but the disinhibition continued. The dosage was decreased to 10 mg on 22 Jun 98 and the disinhibition resolved the following day. The patient was withdrawn from the study due to this adverse experience on 28 Jun 98, after 111 days of study medication. The investigator considered that the disinhibition was possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Chlorphenamine	01 Jan 98	31 Mar 98
Pseudophedrine	01 Jan 98	31 Mar 98

Study 29060/453
PID 453.016.00164

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Manic Reaction (Hypomania)

Screening Demography:
Age: 10 years
Date of birth: 10 Apr 87
Sex: Male
Weight: 56.0 lbs.
Race: Other (Asian)

Country: United States

Medical History: Insomnia
Psychiatric History: Attention Deficit/Hyperactivity Disorder, Suspected
Tic Disorders, Suspected
Dysthymia Disorder
Major Depressive Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 5 mg Given Orally
Start: 30 Jul 97 **Stop**: 25 Aug 97
Study Drug: Open-Label Paroxetine 15 mg Given Orally
Start: 26 Aug 97 **Stop**: 14 Oct 97
Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 15 Oct 97 **Stop**: 31 Oct 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Mild Stomach Ache Two Times a Week	07 Jul 97	Ongoing
Moderate Headache Intermittent Week 4 and Week 6	01 Aug 97	30 Sep 97
Mild Nasal Congestion (Chronic but Increased) Week 4 and Week 6	01 Aug 97	Ongoing

AE Remarks:

This patient started open-label study medication, 5 mg paroxetine per day, on 30 Jul 97. On 26 Aug 97, the dosage was increased to 15 mg per day. On

14 Oct 97, the patient experienced moderate hypomania. The dosage was decreased to 10 mg per day but the hypomania continued. The patient was withdrawn from the study by his mother on 31 Oct 97 after 94 days of study medication because he was “out of control.” The hypomania remained ongoing. The investigator considered that the hypomania was possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
None		

Study 29060/453

PID 453.016.00344

Reason for Narrative: Adverse Experience Leading to Withdrawal and Vital Sign of Potential Clinical Concern

Primary Adverse Experience (Verbatim Term): Migraine (Migraine)

Vital Sign of Potential Clinical Concern: Significant Decrease in Systolic Blood Pressure

Screening Demography:
Age: 13 years
Date of birth: 11 Dec 84
Sex: Male
Weight: 88.5 lbs.
Race: Caucasian

Country: United States

Medical History:
Back Pain
Cluster Headaches
Migraines
Sinus Congestion
Asthma

Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 05 Mar 98 **Stop**: 17 Apr 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 18 Apr 98 **Stop**: 01 Jun 98
Study Drug: Open-Label Paroxetine Down Titration Given Orally
Start: 06 Jun 98 **Stop**: 14 Jun 98

Adverse Experiences (Verbatim Term):	Onset	Stopped
Moderate Seasonal Allergies	08 Mar 98	Ongoing
Moderate Migraine	01 May 98	02 May 98

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 05 Mar 98. On 18 Apr 98, the dosage was increased to 20 mg per day. On 17 May 98, the patient experienced severe migraine; the patient had a history of migraines and cluster headache. The migraine continued and on 06 Jun 98 the patient was started on down titration dosage of study medication and was withdrawn from the study on 14 Jun 98 after a total of 102 days of study medication. The investigator considered that the migraine was probably unrelated to study medication. At last report the migraine was ongoing.

Vital Signs of Potential Clinical Concern:

Date	Visit	Week	Systolic BP (mm Hg)	Diastolic BP (mm Hg)
20 Feb 98	1	Screening	122	81
04 Mar 98	2	Baseline	84 *	57
19 Mar 98	3	Week 2	100	70
02 Apr 98	4	Week 4	108	62
17 Apr 98	5	Week 6	115	66
05 May 98	6	Week 8	95	78
16 Jun 98		Early Discontinuation	124	70

* Value of potential clinical concern

Vital Sign Remarks:

This patient's blood pressure at screening was 122/81. At baseline 12 days later, it had decreased to 84/57; the systolic pressure out of range for his age. At the next visit 15 days later, his blood pressure had increased to within reference range but lower than it had been at screening. It remained within reference range for the remainder of the study.

Concomitant Drugs	Onset	Stopped
Salbutamol	01 Nov 96	Ongoing
Cromoglycate	01 Nov 97	Ongoing
Pseudophedrine	28 Feb 98	Ongoing
Ibuprofen	28 Feb 98	Ongoing
Dexbrompheniramine/Pseudophedrine	10 Mar 98	10 Mar 98
Dexbrompheniramine/Pseudophedrine	30 Mar 98	Ongoing
Diphenhydramine	06 Apr 98	Ongoing
Ketoprofen	01 May 98	01 May 98
Imitrex	02 Jun 98	02 Jun 98
Sumatriptan	04 Jun 98	04 Jun 98
Pethidine	04 Jun 98	04 Jun 98
Butalbital	07 Jun 98	07 Jun 98
Cyproheptadine	08 Jun 98	Ongoing
Naproxen	08 Jun 98	Ongoing

Study 29060/453

PID 453.017.00009

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Agitation (Increased Agitation)
Weight Gain (Weight Gain)

Vital Sign of Potential Clinical Concern: Significant Weight Increase

Screening Demography: Age: 10 years
Date of birth: 15 Sep 86
Sex: Female
Weight: 121.0 lbs.
Race: Caucasian

Country: United States

Medical History: Asthma
Bed Wetting (Enuresis)
Eczema on Ankles, Legs, Knees, Elbows
Expressive and Math Processing Difficulties
Headaches
Insomnia
Muscle Cramps
Nasal Congestion
Stomach Aches

Psychiatric History: Generalized Anxiety Disorder, Suspected
Attention Deficit Disorder Without Hyperactivity
Separation Anxiety Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 17 Apr 97 **Stop**: 30 Apr 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 01 May 97 **Stop**: 14 May 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 15 May 97 **Stop**: 30 May 97

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Mild Increased Appetite	17 Apr 97	Ongoing
Moderate Exacerbated Asthma	12 May 97	01 Jun 97

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 17 Apr 97. On 01 May 97, the dosage was increased to 20 mg per day. Five days later, the patient experienced moderate increased agitation. On 15 May 97, the dosage was increased to 30 mg per day. The agitation continued and on 30 May 97 the patient's mother stopped the patient's study medication without site direction. The patient received a total of 44 days of study medication. The investigator considered that the agitation was possibly related to study medication. The agitation resolved on 04 Jun 97.

Vital Signs of Potential Clinical Concern:

Date	**Visit**	**Week**	**Weight (lbs.)**
09 Apr 97	1	Screening	121.0
16 Apr 97	2	Baseline	121.5
30 Apr 97	3	Week 2	124.5
14 May 97	4	Week 4	124.5
28 May 97	5	Week 6	133.5 *
25 Jun 97		Follow-up	136.0 *

* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 17 Apr 97. The patient's baseline weight was 121.5 lbs. On 28 May 97, after 42 days of study medication, the patient's weight was 133.5 lbs., considered out of range for her age and a significant increase from baseline. It was reported as an adverse experience of moderate intensity. The investigator did not consider that the weight gain was serious and the patient continued in the study until her mother stopped the patient's study medication without site direction on 30 May 97. Her weight remained elevated and on 25 Jun 97, her weight was 136.0 lbs. At last report, the weight gain was ongoing. The investigator considered that the adverse experience was possibly related to study medication.

Concomitant Drugs	Onset	Stopped
Hydrocortisone Cream	01 Oct 95	Ongoing
Paracetamol	01 Jan 96	Ongoing
Diphenhydramine	01 Feb 96	Ongoing
Albuterol	01 Oct 96	Ongoing
Lorazepam	06 Apr 97	06 Apr 97
Pseudophedrine	16 Apr 97	Ongoing
Lorazepam	16 Apr 97	16 Apr 97
Lorazepam	22 Apr 97	22 Apr 97
Lorazepam	30 Apr 97	30 Apr 97

Study 29060/453
PID 453.017.00192

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Concentration Impaired (Worsened Attention Deficit/Hyperactivity Disorder Symptoms)

Screening Demography:
Age: 11 years
Date of birth: 26 Nov 85
Sex: Male
Weight: 80.2 lbs.
Race: Caucasian

Country: United States

Medical History:
Removal of Adenoid
Respiratory Infections
Allergy to Diphtheria, Pertussis, Tetanus Shots
Allergy to Pertussin
Asthma
Headaches
Nasal Congestion
Stomach Aches

Psychiatric History:
Generalized Anxiety Disorder
Dysthymia, Suspected
Attention Deficit Disorder Without Hyperactivity
Separation Anxiety Disorder
Oppositional Defiant Disorder
Tic Disorders, Suspected
Major Depressive Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 01 May 97 **Stop**: 13 May 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 14 May 97 **Stop**: 15 May 97

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
None		

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 01 May 97. On 14 May 97, the dosage was increased to 20 mg per day. The following day, the patient experienced moderate worsening of attention deficit/hyperactivity disorder symptoms. His mother stopped study medication that day without site direction. The patient received a total of 15 days of study medication. The worsening attention deficit/hyperactivity disorder symptoms resolved on 19 May 97. The investigator considered that the adverse experience was not related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Diphenhydramine/Paracetamol/Pseudophedrine	01 Mar 96	Ongoing
Ascorbic Acid	01 Jan 97	Ongoing
Chlorphenamine/Paracetamol/Pseudophedrine	01 Apr 97	Ongoing

Study 29060/453
PID 453.017.00243

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Neurosis (Increased Obsessive-Compulsive Disorder Symptoms)

Other:
Nervousness (Increased Restlessness in Late PM)
Insomnia (Increased Insomnia)
Anxiety (Increased Anxiety)

Screening Demography:
Age: 15 years
Date of birth: 22 Oct 81
Sex: Male
Weight: 140.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Chest Pain
Groin Infection at Age 14
Myringotomy at Age 3
Testicular Infection at Age 14
Allergy to Eggs
Allergy to Penicillin
Asthma
Insomnia

Psychiatric History:
Generalized Anxiety Disorder
Attention Deficit/Hyperactivity Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 28 Jun 97 **Stop**: 02 Jul 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 03 Jul 97 **Stop**: 22 Jul 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 23 Jul 97 **Stop**: 03 Aug 97

Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 04 Aug 97 **Stop**: 09 Aug 97
Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 10 Aug 97 **Stop**: 11 Aug 97

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Mild Tired During Day	29 Jun 97	12 Aug 97
Mild Nasal Congestion	20 Jul 97	26 Jul 97

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 28 Jun 97. The dosage was gradually increased to 30 mg per day by 23 Jul 98. Two days later, the patient experienced mild increased anxiety and moderate increased insomnia and increased restlessness in the late PM. On 01 Aug 97, the patient also experienced moderate increased obsessive-compulsive disorder symptoms. The dosage was decreased to 20 mg per day on 04 Aug 97 but the adverse experiences continued. Study medication was down titrated and the patient withdrew himself from study medication without site consent on 11 Aug 97, after 45 days of study medication. The investigator considered that the adverse experiences were possibly related to study medication. The restlessness and insomnia resolved on 13 Aug 97; the increased obsessive-compulsive disorder symptoms resolved on 14 Aug 97; and the anxiety resolved on 25 Aug 97.

Concomitant Drugs	**Onset**	**Stopped**
Salbutamol	01 Jan 95	Ongoing
Lorazepam	07 Aug 97	10 Aug 97

Study 29060/453
PID 453.017.00247

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Concentration Impaired (Worsened Attention Deficit/Hyperactivity Disorder Symptoms)

Screening Demography:
Age: 11 years
Date of birth: 25 Jul 86
Sex: Male
Weight: 78.5 lbs.
Race: Caucasian

Country: United States

Medical History:
Upper Right Molar Partially Decayed
Adenoidectomy
Asthma
Cardiac Arrest X 2 (at 3 months of age)
Double Inguinal Hernias
Tonsillectomy
Headaches

Psychiatric History:
Separation Anxiety Disorder
Specific Phobia, NOS
Attention Deficit with Hyperactivity, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 22 Aug 97 **Stop**: 02 Sep 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 03 Sep 97 **Stop**: 11 Sep 97
Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 12 Sep 97 **Stop**: 09 Oct 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 10 Oct 97 **Stop**: 13 Nov 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 14 Nov 97 **Stop**: 04 Dec 97
Study Drug: Open-Label Paroxetine Down Titration Given Orally
Start: 05 Dec 97 **Stop**: 12 Dec 97

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Mild Worsened Irritability	02 Sep 97	10 Sep 97
Mild Bedwetting	02 Sep 97	29 Sep 97
Mild Oppositional Behaviors	02 Sep 97	10 Nov 97
Moderate Weight Gain	03 Sep 97	09 Oct 97
Mild Increased Anxiety	20 Oct 97	10 Nov 97
Mild Vomiting	26 Oct 97	27 Oct 97
Mild Enuresis	01 Nov 97	Ongoing
Mild Insomnia	10 Nov 97	Ongoing

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 22 Aug 97. The dosage remained at 10 mg to 20 mg per day until 14 Nov 97, when it was increased to 30 mg per day. On 01 Dec 97, the patient experienced worsened attention deficit/hyperactivity disorder. The dosage was decreased to 20 mg per day and then titrated down until the patient was withdrawn from the study on 12 Dec 97, after 113 days of study medication. At last report the worsened attention deficit/hyperactivity disorder was ongoing. The investigator considered that the adverse experience was possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Paracetamol	26 Aug 97	26 Aug 97
Acetylsalicylic Acid/Citric Acid/ Sodium Bicarbonate	26 Oct 97	26 Oct 97

Study 29060/453
PID 453.017.00339

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Concentration Impaired (Worsened Attention Deficit/Hyperactivity Disorder Symptoms)

Screening Demography:
Age: 10 years
Date of birth: 06 Oct 87
Sex: Male
Weight: 78.5 lbs.
Race: Caucasian

Country: United States

Medical History:
Ear Infection
Myringectomy, Age 3
Allergies to Vantin
Allergies, Environmental
Headaches
Muscle Aches
Stomach Aches

Psychiatric History:
Oppositional Defiant Disorder
Attention Deficit/Hyperactivity Disorder, Suspected
Dysthymia
Specific Phobia, NOS

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 20 Nov 97 **Stop**: 03 Dec 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 04 Dec 97 **Stop**: 17 Dec 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
None		

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 20 Nov 97. On 04 Dec 97, the dosage was increased to 20 mg per day. One week later, the patient experienced moderate worsening of attention deficit/ hyperactivity disorder. The adverse experience continued and the patient was withdrawn from the study on 17 Dec 97, after 28 days of study medication. At last report the adverse experience was ongoing. The investigator considered that the adverse experience was possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Paracetamol	01 Jan 97	Ongoing
Lidocaine/Prilocaine	17 Dec 97	17 Dec 97

Study 29060/453
PID 453.017.00453

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Concentration Impaired (Worsened Attention Deficit/Hyperactivity Disorder Symptoms)

Other: Hostility (Verbal Aggression)

Screening Demography:
Age: 11 years
Date of birth: 30 Nov 86
Sex: Male
Weight: 103.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Enuresis
Headaches
Insomnia
Learning Disorder
Stomach Ache

Psychiatric History:
Dysthymia
Attention Deficit/Hyperactivity Disorder
Separation Anxiety Disorder
Tic Disorder
Oppositional Defiant Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 19 Feb 98 **Stop**: 26 Feb 98

Adverse Experiences (Verbatim Term):	Onset	Stopped
Moderate Increased Attention Deficit/ Hyperactivity Disorder Symptoms	15 Feb 98	22 Feb 98
Moderate Increased Anxiety	20 Feb 98	10 Mar 98

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 19 Feb 98. Four days later, the patient experienced severe worsening of attention deficit/hyperactivity disorder and moderate verbal aggression. The patient was withdrawn from the study on 26 Feb 98, after 8 days of study medication. The adverse experiences resolved on 10 Mar 98. The investigator considered that the adverse experiences were probably unrelated to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Paracetamol	01 Jan 97	Ongoing
Lorazepam	19 Feb 98	19 Feb 98
Lidocaine/Prilocaine	26 Feb 98	26 Feb 98

Study 29060/453
PID 453.017.00455

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Depression (Increased Depression)

Screening Demography: Age: 9 years
Date of birth: 29 Sep 88
Sex: Male
Weight: 53.0 lbs.
Race: Caucasian

Country: United States

Medical History: Pneumonia
Speech Disorder
Restrictive Airway Disease with Seasonal Changes
Psychiatric History: Generalized Anxiety Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 05 Mar 98 **Stop**: 18 Mar 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 19 Mar 98 **Stop**: 15 Apr 98
Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 16 Apr 98 **Stop**: 10 May 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 11 May 98 **Stop**: 24 Jun 98
Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 25 Jun 98 **Stop**: 10 Jul 98

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Mild Fatigue	15 Mar 98	19 Mar 98
Mild Increased Obsessive-Compulsive Disorder	24 Mar 98	30 Mar 98
Mild Upper Respiratory Infection	27 Mar 98	29 Mar 98
Moderate Worsened Obsessive-Compulsive Disorder	08 Apr 98	18 Apr 98
Mild Leg Pain	27 Apr 98	28 Apr 98
Mild Upper Respiratory Infection	01 Jun 98	05 Jun 98
Mild Fatigue	15 Jun 98	19 Jun 98
Moderate Dizziness	04 Jul 98	11 Jul 98
Moderate Increased Sweating	04 Jul 98	11 Jul 98
Moderate Increased Fatigue	04 Jul 98	22 Jul 98

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 05 Mar 98. The dosage ranged from 10 to 20 mg per day and was 20 mg per day when the patient completed the open-label phase of the study. On 25 Jun 98, the patient was randomized to placebo and started double-blind down titration of paroxetine. On 04 Jul 98, he experience moderate increased depression. He was withdrawn from the study on 10 Jul 98, after 128 days of study medication. The depression resolved on 13 Jul 98. The investigator considered that the increased depression was possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Pirbuterol	01 Jan 97	Ongoing
Dextromethorphan/Phenylpropanolamine	27 Mar 98	27 Mar 98
Ibuprofen	27 Mar 98	28 Mar 98
Ibuprofen	27 Apr 98	27 Apr 98
Paracetamol	01 Jun 98	01 Jun 98
Ibuprofen	01 Jun 98	05 Jun 98
Lidocaine/Prilocaine	24 Jun 98	24 Jun 98

Study 29060/453
PID 453.018.00027

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Hostility (Aggressive Outburst)

Screening Demography: Age: 13 years
Date of birth: 24 Feb 84
Sex: Male
Weight: 92.0 lbs.
Race: Caucasian

Country: United States

Medical History: Bilateral Lymphadenopathy
Pressure Equalization Tubes, Age 2-3
Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 09 Apr 97 **Stop**: 24 Apr 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 25 Apr 97 **Stop**: 08 May 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 09 May 97 **Stop**: 21 May 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 22 May 97 **Stop**: 28 May 97
Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 29 May 97 **Stop**: 05 Jun 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 06 Jun 97 **Stop**: 31 Jul 97
Study Drug: Double-Blind Paroxetine 20 mg Given Orally
Start: 01 Aug 97 **Stop**: 22 Aug 97
Study Drug: Double-Blind Paroxetine, Down Titration, Given Orally
Start: 23 Aug 97 **Stop**: 29 Aug 97

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Mild Headache	09 Apr 97	10 Apr 97
Mild Stomach Ache	09 Apr 97	10 Apr 97
Mild Upset Stomach	15 Apr 97	22 May 97
Mild Suture Due to Dog Bite (Wrist)	24 Apr 97	24 Apr 97
Mild Fatigue	30 Apr 97	30 Aug 97
Moderate Dizziness	02 May 97	06 May 97
Mild Difficulty Focusing vision	04 May 97	05 May 97
Moderate Headache	05 May 97	06 May 97
Mild Flatulence	05 May 97	01 Aug 97
Mild Nausea	05 May 97	05 May 97
Mild Akathisia	09 May 97	11 Sep 97
Moderate Aggressive Outbursts	16 May 97	31 May 97
Mild Heart Palpitations	10 Jun 97	10 Jun 97
Mild Dizziness	10 Jun 97	10 Jun 97
Mild Sweating	10 Jun 97	10 Jun 97
Mild Pulled Left Thumb Playing Hockey	27 Jun 97	27 Jun 97
Mild Common Cold Symptoms	30 Jun 97	19 Jul 97
Moderate Aggressive Outbursts	14 Jul 97	16 Jul 97
Mild Streptococcus Throat	20 Jul 97	25 Jul 97
Moderate Aggressive Outburst	31 Jul 97	31 Jul 97
Mild Poison Ivy	01 Aug 97	16 Aug 97
Mild Seasonal Rhinitis	20 Aug 97	24 Aug 97
Mild Enuresis, Nocturnal	25 Aug 97	Ongoing

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 09 Apr 97. The dosage was gradually increased to 30 mg per day and then decreased; the patient completed the open-label phase of the study at a dosage of 20 mg paroxetine per day. The patient was randomized to receive double-blind paroxetine on 01 Aug 97. On 19 Aug 97, the patient experienced severe aggressive outbursts, which resolved the same day. He had experienced the same event on three prior occasions (one of which had lasted for 2 weeks) while on study medication. Study medication was down titrated starting on 23 Aug 97 and the patient was withdrawn from the study on 29 Aug 97, after 143 days of study medication. The investigator considered that the aggressive outbursts were probably unrelated to study medication.

Concomitant Drugs	Onset	Stopped
Vitamins NOS	01 Jan 97	Ongoing
Bacitracin/Neomycin/Polymyxin B	24 Apr 97	28 May 97
Procaine	24 Apr 97	24 Apr 97
Ibuprofen	05 May 97	05 May 97
Calcium Carbonate	19 May 97	19 May 97
Paracetamol	20 Jul 97	21 Jul 97
Phenoxymethylpenicillin Potassium	22 Jul 97	01 Aug 97
Hydrocortisone Cream	01 Aug 97	23 Aug 97
Diphenhydramine	03 Aug 97	03 Aug 97
Diphenhydramine	21 Aug 97	23 Aug 97
Fluvoxamine	23 Aug 97	Ongoing

Study 29060/453
PID 453.018.00224

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Hostility (Increase in Oppositional Defiant Behavior)

Screening Demography:
Age: 9 years
Date of birth: 28 Aug 88
Sex: Male
Weight: 100.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Current Complaint, Daily, of "Sore Feet" Times One Month
Weight Is Above SKB Normal Range of 49-88 Pounds for His Age
Chronic "Body Aches" (Three Times a Week)
Chronic Headaches (Three Times a Week)
Chronic Stomach Aches (Four Times a Week)

Psychiatric History:
Attention Deficit/Hyperactivity Disorder
Oppositional Defiant Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 21 Oct 97 **Stop**: 07 Nov 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 08 Nov 97 **Stop**: 18 Nov 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 19 Nov 97 **Stop**: 03 Dec 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 04 Dec 97 **Stop**: 13 Jan 98
Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 14 Jan 98 **Stop**: 03 Feb 98
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 04 Feb 98 **Stop**: 10 Feb 98

Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally
Start: 11 Feb 98 **Stop**: 09 Mar 98
Study Drug: Double-Blind Placebo Down Titration Given Orally
Start: 10 Mar 98 **Stop**: 30 Mar 98

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Mild Stomach Ache	22 Oct 97	23 Oct 97
Moderate Influenza	07 Nov 97	08 Nov 97
Mild Stomach Ache	11 Nov 97	11 Nov 97
Mild Stomach Ache	30 Nov 97	05 Dec 97
Mild Sore Throat	30 Nov 97	07 Dec 97
Mild Cough	30 Nov 97	10 Dec 97
Mild Headache	01 Dec 97	03 Dec 97
Moderate Akathisia	19 Jan 98	06 Feb 98
Mild Stomach Ache	02 Feb 98	06 Feb 98
Mild Vomiting	05 Feb 98	06 Feb 98
Mild Akathisia	07 Feb 98	Ongoing
Moderate Cough	16 Feb 98	24 Feb 98
Moderate Sore Throat	16 Feb 98	24 Feb 98
Mild Diarrhea	17 Feb 98	17 Feb 98
Mild Diarrhea	20 Feb 98	20 Feb 98
Mild Initial Insomnia	02 Mar 98	08 Mar 98

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 21 Oct 97. The dosage was gradually increased to 50 mg per day by 14 Jan 98. On 26 Jan 98, the patient experienced a moderate increased in oppositional-defiant behavior. The dosage was decreased to 40 mg per day but the behavior continued. The patient completed the open-label phase of the study and was randomized to double-blind placebo on 11 Feb 98. The oppositional-defiant behavior continued and down titration was started on 10 Mar 98. The patient was withdrawn from the study on 30 Mar 98, after 113 days of study medication, and started on active paroxetine. At last report the behavior was ongoing. The investigator considered that the behavior was possibly related to study medication.

Concomitant Drugs	Onset	Stopped
Ascorbic Acid	01 Jan 96	12 Nov 97
Vitamins NOS	01 Nov 96	Ongoing
Paracetamol	07 Nov 97	07 Nov 97
Dextromethorphan/Ethanol/Guaifenesin	01 Dec 97	06 Dec 97
Ibuprofen	02 Dec 97	02 Dec 97
Echinacea	02 Dec 97	02 Dec 97
Amoxicillin	06 Dec 97	15 Dec 97
Dextromethorphan/Ethanol/Guaifenesin	19 Feb 98	21 Feb 98
Paracetamol	20 Feb 98	21 Feb 98
Dextromethorphan/Doxylamine Succinate/ Paracetamol	24 Feb 98	24 Feb 98

Study 29060/453
PID 453.018.00226

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Hyperkinesia (Akathisia)

Screening Demography:
Age: 8 years
Date of birth: 23 Aug 89
Sex: Male
Weight: 64.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Allergy to Augmentin
Chronic Nasal Congestion
Slight Hearing Loss, Both Ears
Chronic Ear Infections, Infancy Through Age 7
Pressure Equalization Tubes, Both Ears, Three Times from Age 1-4

Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 21 Nov 97 **Stop**: 04 Dec 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 05 Dec 97 **Stop**: 10 Mar 98
Study Drug: Double-Blind Paroxetine 20 mg Given Orally
Start: 11 Mar 98 **Stop**: 26 Mar 98
Study Drug: Double-Blind Paroxetine Down Titration Given Orally
Start: 27 Mar 98 **Stop**: 02 Apr 98

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Mild Akathisia	21 Nov 97	17 Feb 98
Mild Bruised Forehead (Injury Related)	02 Dec 97	02 Dec 97
Mild Headache	05 Dec 97	05 Dec 97
Mild Decreased Appetite	10 Dec 97	03 Jan 98
Mild Common Cold Symptoms	12 Dec 97	20 Dec 97
Mild Headache	13 Dec 97	13 Dec 97
Mild Rash	14 Dec 97	15 Dec 97
Mild Fatigue	21 Dec 97	09 Apr 98
Mild Myoclonic Jerking When Waking and When Falling Asleep	26 Dec 97	15 Apr 98
Mild Skin Discoloration (Yellow) Palms and Feet	31 Dec 97	15 Apr 98
Mild Dizziness	01 Feb 98	07 Feb 98
Mild Blurred Vision	05 Mar 98	Ongoing
Moderate Headache	08 Mar 98	08 Mar 98
Mild Stomach Ache	08 Mar 98	08 Mar 98
Mild Vomiting	09 Mar 98	09 Mar 98

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 21 Nov 97. The same day, the patient experienced mild akathisia, which did not resolve. The dosage was increased to 20 mg per day and the patient completed the open-label phase of the study. On 18 Feb 98 the akathisia worsened and was reported as being of moderate intensity. The patient was randomized to active paroxetine and started double-blind study medication on 11 Mar 98. The akathisia again did not resolve and down titration of paroxetine began on 27 Mar 98. The patient was withdrawn from the study on 02 Apr 98, after a total of 133 days of study medication. The akathisia resolved on 05 Apr 98. The investigator considered that the akathisia was possibly related to study medication.

Concomitant Drugs	Onset	Stopped
Ascorbic Acid	01 Nov 97	Ongoing
Ibuprofen	02 Dec 97	03 Dec 97
Paracetamol	05 Dec 97	05 Dec 97
Dextromethorphan/Guaifenesin/Paracetamol /Pseudophedrine	12 Dec 97	16 Dec 97
Paracetamol	13 Dec 97	13 Dec 97
Diphenhydramine	14 Dec 97	14 Dec 97
Acetylsalicylic Acid/Caffeine/Paracetamol	15 Dec 97	15 Dec 97
Dimenhydrinate	01 Feb 98	01 Feb 98
Bismuth Subsalicylate	08 Mar 98	08 Mar 98
Naproxen	08 Mar 98	08 Mar 98
Paracetamol	08 Mar 98	08 Mar 98

Study 29060/453
PID 453.022.00096

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Neurosis (Increase in Obsessive-Compulsive Disorder Symptoms)

Screening Demography:
Age: 10 years
Date of birth: 11 Oct 86
Sex: Male
Weight: 77.5 lbs.
Race: Caucasian

Country: United States

Medical History:
Allergic Reaction to Pertussis Immunization
Phenylketonuria
Upper Respiratory Infection

Psychiatric History:
Attention Deficit/Hyperactivity Disorder
Separation Anxiety Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 28 Jan 97 **Stop**: 11 Feb 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 12 Feb 97 **Stop**: 25 Mar 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 26 Mar 97 **Stop**: 25 Apr 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 26 Apr 97 **Stop**: 20 May 97
Study Drug: Double-Blind Paroxetine 40 mg Given Orally
Start: 21 May 97 **Stop**: 25 May 97

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Moderate Nausea	29 Jan 97	29 Jan 97
Moderate Headache	07 Feb 97	07 Feb 97
Moderate Cough	19 Feb 97	22 Feb 97
Mild Headache Related to Cold	21 Mar 97	22 Mar 97
Mild Streptococcus Throat	12 Apr 97	22 Apr 97

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 28 Jan 97. The dosage was gradually increased to 40 mg per day and the patient completed the open-label phase of the study. On 21 May 97, the patient was randomized to double-blind paroxetine and continued on 40 mg per day. On 25 May, the patient experienced a moderate increase in obsessive-compulsive disorder symptoms and the patient was withdrawn from the study after 118 days of study medication. The investigator considered that the increase in obsessive-compulsive disorder symptoms was possibly related to study medication. There was no down titration because the patient was started the following day on 40 mg paroxetine. At last report, the increased obsessive-compulsive disorder symptoms were ongoing.

Concomitant Drugs	**Onset**	**Stopped**
Ibuprofen	07 Feb 97	07 Feb 97
Cough Syrup/Med NOS	19 Feb 97	22 Feb 97
Ibuprofen	21 Mar 97	22 Mar 97
Amoxicillin	12 Apr 97	22 Apr 97

Study 29060/453
PID 453.022.00097

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Euphoria (Severe Disinhibition, Psychosocial)
Nervousness (Severe Fidgetiness)

Screening Demography:
Age: 9 years
Date of birth: 21 Aug 87
Sex: Male
Weight: 81.0 lbs.
Race: Caucasian

Country: United States

Medical History: Bloody Nose
Psychiatric History: Tic Disorder, Suspected
Specific Phobia—Dark, Seeing Others Vomit
Generalized Anxiety Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 13 Feb 97 **Stop:** 18 Feb 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 19 Feb 97 **Stop:** 03 Mar 97
Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 04 Mar 97 **Stop:** 04 Mar 97
Study Drug: Open-Label Paroxetine 00 mg Given Orally
Start: 05 Mar 97 **Stop:** 07 Mar 97
Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 08 Mar 97 **Stop:** 01 Apr 97
Study Drug: Open-Label Paroxetine 15 mg Given Orally
Start: 02 Apr 97 **Stop:** 09 Apr 97
Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 10 Apr 97 **Stop:** 28 Apr 97
Study Drug: Open-Label Paroxetine 5 mg Given Orally
Start: 29 Apr 97 **Stop:** 03 May 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Mild Drowsiness	16 Feb 97	10 Mar 97
Mild Dry Mouth	18 Feb 97	29 Feb 97
Moderate Sore Throat	26 Feb 97	26 Feb 97
Mild Headache	26 Feb 97	26 Feb 97
Severe Strep Throat	20 Mar 97	30 Mar 97
Moderate Diarrhea	03 Apr 97	07 Apr 97

This patient started open-label study medication, 10 mg paroxetine per day, on 13 Feb 97. The dosage was increased to 20 mg per day, decreased to 0 mg per day, and increased to 5 mg per day on 29 Apr 97. On 17 Apr 97, the patient experienced severe disinhibition and fidgetiness. The adverse experience continued and the patient was withdrawn from the study on 03 May 97, after 80 days of study medication. The adverse experiences were considered resolved on 04 May 97. The investigator considered that the adverse experiences were related to study medication.

Concomitant Drugs	Onset	Stopped
Ibuprofen	26 Feb 97	26 Feb 97
Amoxicillin	20 Mar 97	30 Mar 97

Study 29060/453
PID 453.022.00099

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Neurosis (Increase in Obsessive-Compulsive Disorder Symptoms)

Screening Demography:
Age: 13 years
Date of birth: 01 Oct 83
Sex: Male
Weight: 110.0 lbs.
Race: Caucasian

Country: United States

Medical History: Acne
Environmental Allergies
Psychiatric History: Generalized Anxiety Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 04 Mar 97 **Stop**: 17 Mar 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 18 Mar 97 **Stop**: 30 Mar 97
Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 31 Mar 97 **Stop**: 02 Apr 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 03 Apr 97 **Stop**: 30 Apr 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 01 May 97 **Stop**: 14 May 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 15 May 97 **Stop**: 02 Jun 97
Study Drug: Double-Blind Paroxetine 40 mg Given Orally
Start: 02 Jun 97 **Stop**: 18 Jun 97

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Moderate Fatigue	18 Mar 97	25 Apr 97

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 04 Mar 97. The dosage was gradually increased to 40 mg per day and the patient completed the open-label phase of the study. The patient was randomized to double-blind paroxetine on 02 Jun 97. Four days later, the patient experienced a moderate increase in obsessive-compulsive disorder symptoms. The adverse experience continued and the patient was withdrawn from the study on 18 Jun 97, after 107 days of study medication. The investigator considered that the increase in obsessive-compulsive disorder symptoms was possibly related to study medication. There was no down titration because the patient started on 40 mg paroxetine on 19 Jun 97. At last report the increase in obsessive-compulsive disorder symptoms was ongoing.

Concomitant Drugs	**Onset**	**Stopped**
Erythromycin, Topical	15 Feb 97	Ongoing
Tretinoin	15 Feb 97	Ongoing

Study 29060/453
PID 453.022.00116

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Agitation (Agitation)

Other: Nervousness (Fidgetiness)

Screening Demography:
Age: 11 years
Date of birth: 17 Dec 85
Sex: Male
Weight: 85.0 lbs.
Race: Caucasian

Country: United States

Medical History: None
Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 08 May 97 **Stop**: 22 May 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 23 May 97 **Stop**: 30 Jul 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 31 Jul 97 **Stop**: 08 Aug 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 09 Aug 97 **Stop**: 28 Aug 97
Study Drug: Open-Label Paroxetine Down Titration Given Orally
Start: 29 Aug 97 **Stop**: 02 Sep 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Moderate Sleepiness	25 May 97	04 Jun 97
Moderate Mouth Ulcers	18 Jun 97	14 Jul 97

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 08 May 97. The dosage was gradually increased to 30 mg per day by 31 Jul 97. The following day, the patient experienced moderate agitated disinhibition and moderate fidgetiness. The dosage was decreased to 20 mg per day but the adverse experiences continued. The patient started on down titration on 29 Aug 97 and was withdrawn from the study on 02 Sep 97, after a total of 118 days of study medication. The adverse experiences resolved on 28 Aug 97. The investigator considered that the agitated disinhibition and fidgetiness were related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
None		

Study 29060/453
PID 453.022.00367

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Agitation (Agitated Disinhibition)

Screening Demography: Age: 12 years
Date of birth: 08 Aug 85
Sex: Male
Weight: 94.2 lbs.
Race: Caucasian

Country: United States

Medical History: Non-specific Allergies
Seasonal Allergies
Psychiatric History: Separation Anxiety Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 20 Nov 97 **Stop**: 04 Dec 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 05 Dec 97 **Stop**: 02 Jan 98
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 03 Jan 98 **Stop**: 11 Jan 98
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 12 Jan 98 **Stop**: 27 Jan 98
Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 28 Jan 98 **Stop**: 10 Feb 98
Study Drug: Open-Label Paroxetine Down Titration Given Orally
Start: 11 Feb 98 **Stop**: 24 Feb 98

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Moderate GI Upset	02 Dec 97	02 Dec 97
Mild Daytime Sleepiness	08 Dec 97	21 Dec 97
Severe Injured Finger Under Rocking Chair	01 Jan 98	01 Jan 98
Moderate Face, Ears and Cheeks Are Red and Swollen—Nonspecific Allergy	01 Jan 98	03 Jan 98
Mild GI Upset	08 Jan 98	08 Jan 98
Moderate Streptococcus Throat	03 Feb 98	13 Feb 98
Mild GI Upset	11 Feb 98	11 Feb 98
Moderate Tingling Sensation in Fingers and Toes	14 Feb 98	Ongoing
Moderate Nausea Accompanied with Hot Flashes and Disorientation	14 Feb 98	27 Feb 98
Mild Fidgety	14 Feb 98	27 Feb 98
Mild Electric Shocks Going Through Body	14 Feb 98	27 Feb 98

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 20 Nov 97. The dosage was gradually increased to 50 mg per day by 28 Jan 98. On 09 Feb 98, the patient experienced severe agitated disinhibition. The adverse experience continued and down titration started on 11 Feb 98. The patient was withdrawn from the study on 24 Feb 98, after 97 days of study medication. The adverse experience resolved on 12 Feb 98. The investigator considered that the agitated disinhibition was related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Beclomethasone	01 Sep 95	14 Dec 97
Bismuth Subsalicylate	02 Dec 97	02 Dec 97
Diphenhydramine	01 Jan 98	01 Jan 98
Ibuprofen	01 Jan 98	01 Jan 98
Beclomethasone	08 Jan 98	08 Jan 98
Penicillin	03 Feb 98	13 Feb 98
Loperamide	01 Mar 98	03 Mar 98
Bismuth Subsalicylate	08 Jan 98	08 Jan 98

Study 29060/453
PID 453.022.00397

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Anxiety (Anxiety)

Other: Nervousness (Irritability)
Somnolence (Lethargy)

Screening Demography: Age: 12 years
Date of birth: 04 Dec 85
Sex: Male
Weight: 102.2 lbs.
Race: Caucasian

Country: United States

Medical History: Chipped Right Front Tooth
Otitis Media
Psychiatric History: Generalized Anxiety Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 13 Feb 98 **Stop**: 26 Feb 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 27 Feb 98 **Stop**: 26 Mar 98
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 27 Mar 98 **Stop**: 24 Jun 98
Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 25 Jun 98 **Stop**: 10 Jul 98

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Moderate Mouth Pain from Braces to Teeth	25 Feb 98	04 Mar 98
Moderate Restlessness	08 Mar 98	16 Mar 98
Severe Poison Oak/Sumac	07 Jun 98	23 Jun 98

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 13 Feb 98. The dosage was gradually increased to 30 mg per day. The patient completed the open-label phase of the study and was randomized to placebo starting on 25 Jun 98. On 08 Jul 98, the patient experienced severe irritability, lethargy, and symptoms of anxiety. The adverse experiences continued and the patient was withdrawn from the study on 10 Jul 98. The patient received a total of 148 days of study medication. The adverse experiences resolved on 14 Jul 98. The investigator considered that the irritability, lethargy, and anxiety were related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Paracetamol	25 Feb 98	04 Mar 98
Ibuprofen	26 Feb 98	28 Feb 98
Prednisone	09 Jun 98	16 Jun 98

Study 29060/453
PID 453.023.00157

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Asthenia (Decreased Energy)

Other:
Nausea (Nausea)
Decreased Appetite (Loss of Appetite)
Somnolence (Sleepiness)
Tremor (Feeling "Shaky")
Dyspnea (Shortness of Breath)

Screening Demography:
Age: 16 years
Date of birth: 10 Jul 80
Sex: Female
Weight: 93.0 lbs.
Race: Caucasian

Country: United States

Medical History: None
Psychiatric History: Social Phobia
Specific Phobia, NOS
Separation Anxiety Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 14 Jun 97 **Stop**: 15 Jun 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
None		

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 14 Jun 97. On the same day, the patient experienced moderate decreased energy, nausea, loss of appetite, sleepiness, feeling "shaky," and shortness of breath. The patient was withdrawn from the study the following day after 2 days of study

medication. The adverse experiences resolved on 15 Jul 98. The investigator considered that the adverse experiences were possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
None		

Study 29060/453
PID 453.024.00038

Reason for Narrative: Adverse Experience Leading to Withdrawal and Vital Sign of Potential Clinical Concern

Primary Adverse Experience (Verbatim Term): Extrasystoles/Supraventricular Extrasystoles (Premature Fascicular Beats on ECGs and Holter Monitor)

Vital Sign of Potential Clinical Concern: Significant Increase in Heart Rate

Screening Demography:
Age: 10 years
Date of birth: 08 May 96
Sex: Male
Weight: 76.3 lbs.
Race: Caucasian

Country: United States

Medical History: Intermittent Headaches
Recurrent Epistaxis

Psychiatric History: Dysthymia
Specific Phobia—Bee
Episodes of Mild Hypomania
Separation Anxiety Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 01 Apr 97 **Stop**: 28 Apr 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 29 Apr 97 **Stop**: 12 Jun 97
Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 13 Jun 97 **Stop**: 28 Jun 97

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Mild Decreased Energy	28 Apr 97	05 May 97

Vital Signs of Potential Clinical Concern:

Date	Visit	Week	Heart Rate (bpm)
14 Mar 97	1	Screening	60
31 Mar 97	2	Baseline	60
16 Apr 97	3	Week 2	60
28 Apr 97	4	Week 4	60
12 May 97	5	Week 6	90 *
27 May 97	6	Week 8	66
24 Jun 97	7	Week 12	72
14 Jul 97	8	Week 16	72

* Value of potential clinical concern

AE and Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 01 Apr 97. On 29 Apr 97, the dosage was increased to 20 mg per day. The patient's heart rate had been 60 bpm at baseline but increased to 90 bpm on 12 May 97. which was an increase from baseline of potential clinical concern. . On 28 May 97, the patient experienced moderate premature fascicular beats on ECG and Holter monitor. The dosage was decreased to 10 mg per day on 13 Jun 97 but the adverse experience of premature fascicular beats continued. The patient's heart rate decreased but on 24 Jun 97 increased to 72 BPM. The patient was withdrawn from the study on 28 Jun 97 after 89 days of study medication. At last report the adverse experience of premature fascicular beats had not resolved. The investigator considered that the adverse experience of extrasystoles was possibly related to study medication and that the increased heart rate was associated with the ECG findings.

Concomitant Drugs	Onset	Stopped
Ibuprofen	01 Sep 96	01 May 97
Paracetamol	26 Apr 97	01 May 97

Study 29060/453
PID 453.025.00023

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Nervousness (Irritability)

Other: Hyperkinesia (Akathisia)

Screening Demography:
Age: 12 years
Date of birth: 11 Mar 85
Sex: Male
Weight: 119.0 lbs.
Race: Caucasian

Country: United States

Medical History: Bilateral Tube Placement, Eustachian
Psychiatric History: Pervasive Developmental Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-label Paroxetine 10 mg Given Orally
Start: 11 Apr 97 **Stop**: 08 May 97
Study Drug: Open-label Paroxetine 20 mg Given Orally
Start: 09 May 97 **Stop**: 10 Jul 97
Study Drug: Open-label Paroxetine 30 mg Given Orally
Start: 11 Jul 97 **Stop**: 07 Aug 97
Study Drug: Double-Blind Paroxetine 40 mg Given Orally
Start: 08 Aug 97 **Stop**: 17 Sep 97
Study Drug: Double-Blind Paroxetine Down Titration Given Orally
Start: 18 Sep 97 **Stop**: 09 Oct 97

Adverse Experiences (Verbatim Term):	**Onset**	**Stopped**
Mild Increased Motor Activity	18 Apr 97	21 Apr 97
Moderate Sunburn (Injury)	27 Jun 97	30 Jun 97
Moderate Nausea (Secondary to Sunburn)	28 Jun 97	28 Jun 97
Mild Dizziness	25 Aug 97	05 Sep 97
Moderate Congestion, Nasal	10 Sep 97	20 Sep 97
Severe Sore Throat	10 Sep 97	17 Sep 97

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 11 Apr 97. The dosage was gradually increased to 30 mg per day by 11 Jul 97. The patient completed the open-label phase of the study and was randomized to receive double-blind paroxetine. He received his first dose of 40 mg double-blind study medication on 08 Aug 97, which represented an increase over the dose the patient received in the open-label phase. On 14 Aug 97, the patient experienced severe irritability, and on 25 Aug 97 he experienced severe akathisia. The adverse experiences continued and on 17 Sep 97 it was decided to withdrew the patient from the study, since decreasing the dose in the double-blind phase was not permitted by protocol. The patient's dose was down titrated and he took his final dose on 09 Oct 97, after 182 days of study medication. The adverse experiences resolved on 20 Sep 97. The investigator considered that the irritability was possibly related and the akathisia was related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Sulfadiazine Silver	28 Jun 97	29 Jun 97
Ibuprofen	28 Jun 97	28 Jun 97
Bismuth Subsalicylate	28 Jun 97	28 Jun 97
Aloe Lotion	30 Jun 97	30 Jun 97
Ofloxacin	10 Sep 97	16 Sep 97
Loratadine	10 Sep 97	20 Sep 97

Study 29060/453
PID 453.025.00295

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Myoclonus (Tic Disorder)

Screening Demography: Age: 10 years
Date of birth: 06 Apr 97
Sex: Male
Weight: 68.0 lbs.
Race: Caucasian

Country: United States

Medical History: Excoriated Crusted Lesions Around Mouth and Lips
Seasonal Allergies
Broken Left Arm
Psychiatric History: Specific Phobia, NOS

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 24 Oct 97 **Stop**: 14 Jan 98

Adverse Experiences (Verbatim Term):	Onset	Stopped
Moderate Cough	07 Nov 97	08 Nov 97
Moderate Sinusitis	25 Nov 97	25 Nov 97
Moderate Behavioral Agitation	26 Nov 97	12 Jan 98
Moderate Akathisia	26 Nov 97	12 Jan 98
Moderate Broken Right Rib (Back)	18 Dec 97	16 Jan 98

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 24 Oct 97. On 05 Jan 98, the patient experienced severe tic disorder. The adverse experience resolved on10 Jan 98. The patient was withdrawn from the study on 14 Jan 98, after 83 days of study medication. The investigator considered that the tic disorder was unrelated to study medication.

Concomitant Drugs	Onset	Stopped
Bacitracin/Neomycin/Polymyxin B Topical	01 Sep 97	Ongoing
Pseudophedrine	01 May 97	Ongoing
Cromoglycate	01 May 97	Ongoing
Loratadine	01 May 97	Ongoing
Guaifenesin	07 Nov 98	08 Nov 98
Mepyramine/Pheniramine/Phenylpropanolamine	14 Dec 97	14 Dec 97
Chlorphenamine/Dextromethorphan/ Pseudophedrine	16 Dec 97	16 Dec 97

Study 29060/453
PID 453.027.00172

Reason for Narrative: Adverse Experience Leading to Withdrawal

Primary Adverse Experience (Verbatim Term): Central Nervous System Disorder (Tourette's Syndrome with Increased Severity of Tics)

Screening Demography:
Age: 10 years
Date of birth: 04 Sep 86
Sex: Male
Weight: 75.3 lbs.
Race: Caucasian

Country: United States

Medical History:
Allergic to Erythromycin
Allergic to Penicillin
Initial Insomnia
Bacterial Gastroenteritis
Tonsillectomy and Adenoidectomy

Psychiatric History:
Attention Deficit/Hyperactivity Disorder
Tics
Oppositional Defiant Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 20 Jun 97 **Stop**: 03 Jul 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 04 Jul 97 **Stop**: 17 Jul 97

Adverse Experiences (Verbatim Term):	Onset	Stopped
Mild Diarrhea	24 Jun 97	26 Jun 97
Mild Diarrhea	01 Jul 97	01 Jul 97

AE Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 20 Jun 97. On 04 Jul 97, the dosage was increased to 20 mg per day. On

10 Jul 97, the patient had a severe adverse experience of Tourette's syndrome with increased severity of tics. The patient had previously received medication (haloperidol and clonidine) for Tourette's syndrome but the disease was not included in his medical or psychiatric history. The adverse experience continued and the patient was withdrawn from the study on 17 Jul 97, after 28 days of study medication. There was no down titration period because the patient was put on active paroxetine 20 mg per day the day following withdrawal from the study At last report the adverse experience was ongoing. The investigator considered that the adverse experience was probably unrelated to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Bismuth Subsalicylate	01 Jul 97	01 Jul 97

Paroxetine - Protocol: 453

TABLE 15.09.1X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category - Displayed by Body System
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: <12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	167	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	28	16.8%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Body as a Whole	1	0.6
Cardiovascular System	2	1.2
Nervous System	27	16.2
Skin and Appendages	1	0.6
Special Senses	1	0.6

Paroxetine - Protocol: 453

TABLE 15.09.1X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category - Displayed by Body System
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: >=12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	168	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	14	8.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Body as a Whole	3	1.8
Cardiovascular System	2	1.2
Digestive System	3	1.8
Nervous System	10	6.0
Respiratory System	1	0.6
Skin and Appendages	1	0.6

Paroxetine - Protocol: 453

TABLE 15.09.2

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal - Displayed by Body System
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	7	7.4%	10	10.2%	17	8.8%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Body as a Whole	0	0.0	2	2.0	2	1.0
Digestive System	0	0.0	2	2.0	2	1.0
Nervous System	7	7.4	10	10.2	17	8.8
Respiratory System	0	0.0	1	1.0	1	0.5

Paroxetine - Protocol: 453

TABLE 15.09.2X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category - Displayed by Body System
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: <12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	49	100.0%	47	100.0%	96	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	3	6.1%	6	12.8%	9	9.4%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Nervous System	3	6.1	6	12.8	9	9.4

TABLE 15.09.2X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category - Displayed by Body System
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: >=12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	46	100.0%	51	100.0%	97	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	4	8.7%	4	7.8%	8	8.2%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Body as a Whole	0	0.0	2	3.9	2	2.1
Digestive System	0	0.0	2	3.9	2	2.1
Nervous System	4	8.7	4	7.8	8	8.2
Respiratory System	0	0.0	1	2.0	1	1.0

Paroxetine - Protocol: 453

TABLE 15.09.3

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal - Displayed by Body System
Intention to Treat Population
Taper Phase

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.09.3X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category - Displayed by Body System
Intention to Treat Population
Taper Phase

Age Group: <12 YEARS

TREATMENT GROUP		TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	:	9	100.0%	19	100.0%	15	100.0%	43	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	:	0	0.0%	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM		N	%	N	%	N	%	N	%

TABLE 15.09.3X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category - Displayed by Body System
Intention to Treat Population
Taper Phase

Age Group: >=12 YEARS

TREATMENT GROUP	TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	20	100.0%	23	100.0%	22	100.0%	65	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	0	0.0%	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%	N	%

Paroxetine - Protocol: 453

TABLE 15.10.1

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal (Male Specific)
Intention to Treat Population
Phase I: Open Label Treatment

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.10.1X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Male Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: <12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS	106	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%

Paroxetine - Protocol: 453

TABLE 15.10.1X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Male Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: >=12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS	92	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%

Paroxetine - Protocol: 453

TABLE 15.10.2

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal (Male Specific)
Intention to Treat Population
Phase II: Randomised Treatment

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.10.2X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Male Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: <12 YEARS

TREATMENT GROUP		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	:	28	100.0%	33	100.0%	61	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	:	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM		N	%	N	%	N	%

TABLE 15.10.2X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Male Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: >=12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	19	100.0%	25	100.0%	44	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%

Paroxetine - Protocol: 453

TABLE 15.10.3

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal (Male Specific)
Intention to Treat Population
Taper Phase

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.10.3X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Male Specific)
Intention to Treat Population
Taper Phase

Age Group: <12 YEARS

TREATMENT GROUP	TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	6	100.0%	7	100.0%	11	100.0%	24	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	0	0.0%	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%	N	%

TABLE 15.10.3X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Male Specific)
Intention to Treat Population
Taper Phase

Age Group: >=12 YEARS

TREATMENT GROUP		TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	:	15	100.0%	10	100.0%	11	100.0%	36	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	:	0	0.0%	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM		N	%	N	%	N	%	N	%

Paroxetine - Protocol: 453

TABLE 15.11.1

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal (Female Specific)
Intention to Treat Population
Phase I: Open Label Treatment

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.11.1X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Female Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: <12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS	61	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%

TABLE 15.11.1X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Female Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: >=12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS	76	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%

Paroxetine - Protocol: 453

TABLE 15.11.2

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal (Female Specific)
Intention to Treat Population
Phase II: Randomised Treatment

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.11.2X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Female Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: <12 YEARS

TREATMENT GROUP		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	:	21	100.0%	14	100.0%	35	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	:	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM		N	%	N	%	N	%

TABLE 15.11.2X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Female Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: >=12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	27	100.0%	26	100.0%	53	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%

Paroxetine - Protocol: 453

TABLE 15.11.3

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal (Female Specific)
Intention to Treat Population
Taper Phase

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.11.3X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Female Specific)
Intention to Treat Population
Taper Phase

Age Group: <12 YEARS

TREATMENT GROUP		TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	:	3	100.0%	12	100.0%	4	100.0%	19	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	:	0	0.0%	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM		N	%	N	%	N	%	N	%

Paroxetine - Protocol: 453

TABLE 15.11.3X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Female Specific)
Intention to Treat Population
Taper Phase

Age Group: >=12 YEARS

TREATMENT GROUP		TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	:	5	100.0%	13	100.0%	11	100.0%	29	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	:	0	0.0%	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM		N	%	N	%	N	%	N	%

Paroxetine - Protocol: 453

TABLE 15.12.1

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	335	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	42	12.5%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Body as a Whole	4	1.2
ABDOMINAL PAIN	1	0.3
ASTHENIA	2	0.6
HEADACHE	1	0.3
Cardiovascular System	4	1.2
EXTRASYSTOLES	2	0.6
MIGRAINE	1	0.3
PALLOR	1	0.3
SUPRAVENTRICULAR EXTRASYSTOLES	1	0.3
Digestive System	3	0.9
DECREASED APPETITE	1	0.3
DIARRHEA	1	0.3
NAUSEA	2	0.6
Nervous System	37	11.0
AGITATION	6	1.8
ANXIETY	3	0.9
CENTRAL NERVOUS SYSTEM DISORDE	1	0.3
CONCENTRATION IMPAIRED	5	1.5
DELUSIONS	1	0.3
DEPRESSION	2	0.6
EMOTIONAL LABILITY	2	0.6
EUPHORIA	2	0.6
HOSTILITY	9	2.7
HYPERKINESIA	7	2.1
INSOMNIA	2	0.6
MANIC REACTION	3	0.9
MYOCLONUS	1	0.3
NERVOUSNESS	4	1.2
NEUROSIS	4	1.2

TABLE 15.12.1

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

	TOTAL	
TOTAL NUMBER OF PATIENTS	335	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	42	12.5%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
SOMNOLENCE	2	0.6
TREMOR	2	0.6
Respiratory System	1	0.3
DYSPNEA	1	0.3
Skin and Appendages	2	0.6
RASH	1	0.3
SKIN DISORDER	1	0.3
Special Senses	1	0.3
ABNORMAL VISION	1	0.3

Paroxetine - Protocol: 453

TABLE 15.12.1X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: <12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	167	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	28	16.8%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Body as a Whole	1	0.6
HEADACHE	1	0.6
Cardiovascular System	2	1.2
EXTRASYSTOLES	1	0.6
PALLOR	1	0.6
SUPRAVENTRICULAR EXTRASYSTOLES	1	0.6
Nervous System	27	16.2
AGITATION	5	3.0
ANXIETY	1	0.6
CENTRAL NERVOUS SYSTEM DISORDE	1	0.6
CONCENTRATION IMPAIRED	5	3.0
DEPRESSION	1	0.6
EMOTIONAL LABILITY	2	1.2
EUPHORIA	1	0.6
HOSTILITY	6	3.6
HYPERKINESIA	5	3.0
MANIC REACTION	3	1.8
MYOCLONUS	1	0.6
NERVOUSNESS	3	1.8
NEUROSIS	2	1.2
SOMNOLENCE	1	0.6
TREMOR	1	0.6
Skin and Appendages	1	0.6
SKIN DISORDER	1	0.6
Special Senses	1	0.6
ABNORMAL VISION	1	0.6

TABLE 15.12.1X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Non-Gender Specific)
Intention to Treat Population
Phase I: Open Label Treatment

Age Group: >=12 YEARS

	TOTAL	
TOTAL NUMBER OF PATIENTS :	168	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	14	8.3%
ADECS BODY SYSTEM : PREFERRED TERM	N	%
Body as a Whole	3	1.8
ABDOMINAL PAIN	1	0.6
ASTHENIA	2	1.2
Cardiovascular System	2	1.2
EXTRASYSTOLES	1	0.6
MIGRAINE	1	0.6
Digestive System	3	1.8
DECREASED APPETITE	1	0.6
DIARRHEA	1	0.6
NAUSEA	2	1.2
Nervous System	10	6.0
AGITATION	1	0.6
ANXIETY	2	1.2
DELUSIONS	1	0.6
DEPRESSION	1	0.6
EUPHORIA	1	0.6
HOSTILITY	3	1.8
HYPERKINESIA	2	1.2
INSOMNIA	2	1.2
NERVOUSNESS	1	0.6
NEUROSIS	2	1.2
SOMNOLENCE	1	0.6
TREMOR	1	0.6
Respiratory System	1	0.6
DYSPNEA	1	0.6
Skin and Appendages	1	0.6
RASH	1	0.6

Paroxetine - Protocol: 453

TABLE 15.12.2

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS :	95	100.0%	98	100.0%	193	100.0%
PATIENTS WITH ADVERSE EXPERIENCES :	7	7.4%	10	10.2%	17	8.8%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Body as a Whole	0	0.0	2	2.0	2	1.0
HEADACHE	0	0.0	2	2.0	2	1.0
Digestive System	0	0.0	2	2.0	2	1.0
NAUSEA	0	0.0	2	2.0	2	1.0
Nervous System	7	7.4	10	10.2	17	8.8
ANXIETY	0	0.0	2	2.0	2	1.0
DEPRESSION	0	0.0	1	1.0	1	0.5
DIZZINESS	0	0.0	1	1.0	1	0.5
HOSTILITY	3	3.2	0	0.0	3	1.6
HYPERKINESIA	2	2.1	0	0.0	2	1.0
MANIC REACTION	1	1.1	0	0.0	1	0.5
MYOCLONUS	0	0.0	2	2.0	2	1.0
NERVOUSNESS	1	1.1	2	2.0	3	1.6
NEUROSIS	3	3.2	5	5.1	8	4.1
SOMNOLENCE	0	0.0	1	1.0	1	0.5
TREMOR	0	0.0	1	1.0	1	0.5
Respiratory System	0	0.0	1	1.0	1	0.5
HYPERVENTILATION	0	0.0	1	1.0	1	0.5

Paroxetine - Protocol: 453

TABLE 15.12.2X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: <12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	49	100.0%	47	100.0%	96	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	3	6.1%	6	12.8%	9	9.4%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Nervous System	3	6.1	6	12.8	9	9.4
ANXIETY	0	0.0	1	2.1	1	1.0
DEPRESSION	0	0.0	1	2.1	1	1.0
HOSTILITY	2	4.1	0	0.0	2	2.1
HYPERKINESIA	1	2.0	0	0.0	1	1.0
MANIC REACTION	1	2.0	0	0.0	1	1.0
NERVOUSNESS	0	0.0	1	2.1	1	1.0
NEUROSIS	1	2.0	5	10.6	6	6.3

TABLE 15.12.2X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Non-gender Specific)
Intention to Treat Population
Phase II: Randomised Treatment

Age Group: >=12 YEARS

TREATMENT GROUP	PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	46	100.0%	51	100.0%	97	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	4	8.7%	4	7.8%	8	8.2%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%
Body as a Whole	0	0.0	2	3.9	2	2.1
HEADACHE	0	0.0	2	3.9	2	2.1
Digestive System	0	0.0	2	3.9	2	2.1
NAUSEA	0	0.0	2	3.9	2	2.1
Nervous System	4	8.7	4	7.8	8	8.2
ANXIETY	0	0.0	1	2.0	1	1.0
DIZZINESS	0	0.0	1	2.0	1	1.0
HOSTILITY	1	2.2	0	0.0	1	1.0
HYPERKINESIA	1	2.2	0	0.0	1	1.0
MYOCLONUS	0	0.0	2	3.9	2	2.1
NERVOUSNESS	1	2.2	1	2.0	2	2.1
NEUROSIS	2	4.3	0	0.0	2	2.1
SOMNOLENCE	0	0.0	1	2.0	1	1.0
TREMOR	0	0.0	1	2.0	1	1.0
Respiratory System	0	0.0	1	2.0	1	1.0
HYPERVENTILATION	0	0.0	1	2.0	1	1.0

Paroxetine - Protocol: 453

TABLE 15.12.3

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal (Non-gender Specific)
Intention to Treat Population
Taper Phase

NO DATA AVAILABLE FOR THIS REPORT

Paroxetine - Protocol: 453

TABLE 15.12.3X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Non-gender Specific)
Intention to Treat Population
Taper Phase

Age Group: <12 YEARS

TREATMENT GROUP	TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	9	100.0%	19	100.0%	15	100.0%	43	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	0	0.0%	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM	N	%	N	%	N	%	N	%

TABLE 15.12.3X

Number (%) of Patients with Emergent Adverse Experiences Leading to Withdrawal by Age Category (Non-gender Specific)
Intention to Treat Population
Taper Phase

Age Group: >=12 YEARS

TREATMENT GROUP		TAPER PHASE I		PAROXETINE		PLACEBO		TOTAL	
TOTAL NUMBER OF PATIENTS	:	20	100.0%	23	100.0%	22	100.0%	65	100.0%
PATIENTS WITH ADVERSE EXPERIENCES	:	0	0.0%	0	0.0%	0	0.0%	0	0.0%
ADECS BODY SYSTEM : PREFERRED TERM		N	%	N	%	N	%	N	%

Table 15.21.1

Summary of Flagged Vital Signs by Parameter
Intention to Treat Population
Phase I: Open Label Treatment

Sitting Systolic Blood Pressure (mmHg)

	N	%
High	5	1.5
Low	33	9.9
Significant Increase	2	0.6
Significant Decrease	4	1.2
Number with Assessment	335	100.0
Number with Base and Post-base Assessment	330	100.0

High = >145 mmHg
Low = <95 mmHg
Increase = Increase of >=40 mmHg from Baseline
Decrease = Decrease of >=30 mmHg from Baseline

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]VIT15_2.SAS (02MAR99 16:18)

Table 15.21.1

Summary of Flagged Vital Signs by Parameter
Intention to Treat Population
Phase I: Open Label Treatment

Sitting Diastolic Blood Pressure (mmHg)

	N	%
High	39	11.6
Low	76	22.7
Significant Increase	1	0.3
Significant Decrease	30	9.1
Number with Assessment	335	100.0
Number with Base and Post-base Assessment	330	100.0

High = >85 mmHg
Low = <50 mmHg
Increase = Increase of >=30 mmHg from Baseline
Decrease = Decrease of >=20 mmHg from Baseline

Table 15.21.1

Summary of Flagged Vital Signs by Parameter
Intention to Treat Population
Phase I: Open Label Treatment

Sitting Heart Rate (bpm)

	N	%
High	22	6.6
Low	99	29.6
Significant Increase	15	4.5
Significant Decrease	18	5.4
Number with Assessment	335	100.0
Number with Base and Post-base Assessment	331	100.0

High = >115 bpm (Ages 8 to 12), >110 bpm (Ages 13 to 17)
Low = <65 bpm (Ages 8 to 12), <55 bpm (Ages 13 to 17)
Increase = Increase of >=30 bpm from Baseline
Decrease = Decrease of >=30 bpm from Baseline

Table 15.21.1

Summary of Flagged Vital Signs by Parameter
Intention to Treat Population
Phase I: Open Label Treatment

Weight (LB)

	N	%
High	81	24.2
Low	8	2.4
Significant Increase	90	27.5
Significant Decrease	10	3.1
Number with Assessment	335	100.0
Number with Base and Post-base Assessment	327	100.0

High:Low Flags - (Weight in LB's)

Age 8:	Boys = >81:<40	Girls = >81:<38	Age 13: Boys = >148:<69 Girls = >153:<70
Age 9:	Boys = >92:<44	Girls = >94:<43	Age 14: Boys = >164:<79 Girls = >166:<78
Age 10:	Boys = >104:<48	Girls = >109:<48	Age 15: Boys = >179:<90 Girls = >176:<85
Age 11:	Boys = >118:<54	Girls = >124:<55	Age 16: Boys = >198:<100 Girls = >183:<90
Age 12:	Boys = >133:<60	Girls = >139:<62	Age 17: Boys = >206:<108 Girls = >186:<93

Increase = Increase of >=7% from Baseline
Decrease = Decrease of >=7% from Baseline

Table 15.21.2

Summary of Flagged Vital Signs by Parameter
Intention to Treat Population
Phase II: Randomised Treatment

Sitting Systolic Blood Pressure (mmHg)

	Treatment Group			
	Paroxetine		Placebo	
	N	%	N	%
High	3	3.2	1	1.0
Low	4	4.3	6	6.1
Significant Increase	1	1.1	0	0.0
Significant Decrease	3	3.2	1	1.0
Number with Assessment	94	100.0	98	100.0
Number with Base and Post-base Assessment	94	100.0	98	100.0

High = >145 mmHg Low = <95 mmHg
Highs and Lows are counted at post randomisation baseline visits
Increase = Increase of >=40 mmHg from Baseline
Decrease = Decrease of >=30 mmHg from Baseline

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]VIT15_2.SAS (02MAR99 16:18)

Table 15.21.2

Summary of Flagged Vital Signs by Parameter
Intention to Treat Population
Phase II: Randomised Treatment

Sitting Diastolic Blood Pressure (mmHg)

	Treatment Group			
	Paroxetine		Placebo	
	N	%	N	%
High	8	8.5	4	4.1
Low	16	17.0	18	18.4
Significant Increase	1	1.1	1	1.0
Significant Decrease	6	6.4	5	5.1
Number with Assessment	94	100.0	98	100.0
Number with Base and Post-base Assessment	94	100.0	98	100.0

High = >85 mmHg Low = <50 mmHg
Highs and Lows are counted at post randomisation baseline visits
Increase = Increase of >=30 mmHg from Baseline
Decrease = Decrease of >=20 mmHg from Baseline

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]VIT15_2.SAS (02MAR99 16:18)

Table 15.21.2

Summary of Flagged Vital Signs by Parameter
Intention to Treat Population
Phase II: Randomised Treatment

Sitting Heart Rate (bpm)

	Treatment Group			
	Paroxetine		Placebo	
	N	%	N	%
High	5	5.3	2	2.0
Low	18	19.1	18	18.4
Significant Increase	2	2.1	3	3.1
Significant Decrease	3	3.2	3	3.1
Number with Assessment	94	100.0	98	100.0
Number with Base and Post-base Assessment	94	100.0	97	100.0

High = >115 bpm (Ages 8 to 12), >110 bpm (Ages 13 to 17)
Low = <65 bpm (Ages 8 to 12), <55 bpm (Ages 13 to 17)
Highs and Lows are counted at post randomisation baseline visits
Increase = Increase of >=30 bpm from Baseline
Decrease = Decrease of >=30 bpm from Baseline

DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]VIT15_2.SAS (02MAR99 16:18)

Table 15.21.2

Summary of Flagged Vital Signs by Parameter
Intention to Treat Population
Phase II: Randomised Treatment

Weight (LB)

	Treatment Group			
	Paroxetine		Placebo	
	N	%	N	%
High	28	29.8	23	23.5
Low	1	1.1	1	1.0
Significant Increase	29	30.9	23	23.5
Significant Decrease	1	1.1	1	1.0
Number with Assessment	94	100.0	98	100.0
Number with Base and Post-base Assessment	94	100.0	98	100.0

High:Low Flags - counted at post-randomisation baseline visits (Weight in LB's)

Age 8:	Boys = >81:<40 Girls = >81:<38	Age 13: Boys = >148:<69 Girls = >153:<70
Age 9:	Boys = >92:<44 Girls = >94:<43	Age 14: Boys = >164:<79 Girls = >166:<78
Age 10:	Boys = >104:<48 Girls = >109:<48	Age 15: Boys = >179:<90 Girls = >176:<85
Age 11:	Boys = >118:<54 Girls = >124:<55	Age 16: Boys = >198:<100 Girls = >183:<90
Age 12:	Boys = >133:<60 Girls = >139:<62	Age 17: Boys = >206:<108 Girls = >186:<93

Increase = Increase of >=7% from Baseline
Decrease = Decrease of >=7% from Baseline

Confidential

SmithKline Beecham

Paroxetine

BRL-029060

Table 15.21.2a. Patient Narratives: Vital Sign Changes of Potential Clinical Concern

453

xxxxxx x. xxxxxxxxx, R.Ph., M.S.*
xxxxxx x. xxxxx, Ph.D.

*CNS, PMTU

SB Document Number: BRL-029060/RSD-100W8F/1

Study 29060/453
PID 453.001.00361

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Weight Increase

Adverse Experience (Verbatim): Weight Gain (Weight Gain)

Screening Demography:
Age: 7 years
Date of birth: 31 Mar 90
Sex: Female
Weight: 56.0 lbs.
Race: Caucasian

Country: United States

Medical History: Ankle Fracture Age 6
Car Sickness (Nausea and Vomiting)
Headaches

Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 11 Nov 97 **Stop:** 02 Mar 98

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Mild Difficulty with Sleep Onset	11 Nov 97	12 Dec 97
Mild Hyperactive	11 Nov 97	Ongoing
Mild Upset Stomach (Nauseous)	11 Nov 97	Ongoing
Moderate Increased Appetite	26 Nov 97	Ongoing
Mild Cold Symptoms (Nasal Congestion)	15 Dec 97	16 Dec 97
Mild Pain in Left Ankle	20 Dec 97	20 Dec 97
Mild Common Cold	28 Dec 97	04 Jan 98
Mild Nasal Congestion	05 Feb 98	06 Feb 98

Vital Signs of Potential Clinical Concern:

Date	Visit	Week	Weight (lbs.)
03 Nov 97	1	Screening	56.0
10 Nov 97	2	Baseline	56.0
24 Nov 97	3	Week 2	58.0
08 Dec 97	4	Week 4	65.0 *
22 Dec 97	5	Week 6	65.0 *
05 Jan 98	6	Week 8	65.5 *
02 Feb 98	7	Week 12	65.0 *
02 Mar 98	8	Week 16	68.5 *

* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 11 Nov 97. The dosage was not increased during the course of the study. The patient's baseline weight was 56.0 lbs. On 08 Dec 97, after 28 days of study medication, the patient's weight was 65.0 lbs., considered out of range for her age and a significant increase from baseline. It was reported as an adverse experience of moderate intensity. The investigator did not consider that the weight gain was serious and the patient continued in the study. Her weight remained elevated and on 02 Mar 98, her weight was 68.5 lbs.

The patient completed the open-label phase of the study on 02 Mar 98 and was to be randomized to double-blind study medication. Her parents withdrew her from the study because they were pleased with her response to study medication and did not want to subject her to the possibility of receiving placebo in Phase 2. She was then prescribed paroxetine off study. At last report, the weight gain was

ongoing. The investigator considered that the adverse experience was possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Dimenhydrinate	01 Jan 95	Ongoing
Glucose/Fructose/Phosphoric Acid	11 Nov 97	Ongoing
Fructose	08 Dec 97	08 Dec 97
Diphenhydramine	15 Dec 97	15 Dec 97
Phenylpropanolamine/Diphenhydramine	05 Feb 98	05 Feb 98
Paracetamol	05 Feb 98	05 Feb 98
Paracetamol	03 Apr 98	03 Apr 98

Study 29060/453
PID 453.007.00003

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Weight Increase

Adverse Experience (Verbatim): Weight Gain (Weight Gain 6.5 lbs. over 1 Month)

Screening Demography:
Age: 10 years
Date of birth: 16 Jun 86
Sex: Female
Weight: 101.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Eczema (Hands)
Fractured Right Wrist
Sensitive to Some Soaps (Dry Hands)
Short of Breath without Exertion

Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 02 May 97 **Stop:** 16 May 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 17 May 97 **Stop:** 26 Jun 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 27 Jun 97 **Stop:** 21 Aug 97
Study Drug: Double-Blind Paroxetine 30 mg Given Orally
Start: 22 Aug 97 **Stop:** 10 Dec 97
Study Drug: Double-Blind Taper End Medication Given Orally
Start: 11 Dec 97 **Stop:** 22 Dec 97

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Moderate Infection Left Great Toe	10 May 97	17 May 97
Moderate Foot Surgery Left Great Toe (Ingrown Toenail)	13 May 97	13 May 97
Mild Fatigue	17 May 97	Ongoing
Mild Yawning	17 May 97	15 Aug 97
Mild Restless Legs	20 May 97	03 Jan 98
Moderate Depression	01 Jul 97	01 Aug 97
Moderate Torn Ligaments Right Ankle	10 Jul 97	15 Dec 97
Moderate Increased Mid-Nocturnal Wakenings	24 Aug 97	22 Sep 97

Vital Signs of Potential Clinical Concern:

Date	**Visit**	**Week**	**Weight (lbs.)**
25 Apr 97	1	Screening	101.0
02 May 97	2	Baseline	101.0
16 May 97	3	Week 2	103.0
30 May 97	4	Week 4	100.0
16 Jun 97	5	Week 6	101.0
27 Jun 97	6	Week 8	101.0
21 Jul 97	7	Week 12	103.5
22 Aug 97	8	Week 16	110.0 *
03 Sep 97	9	Week 2 DB	113.5 *
17 Sep 97	10	Week 4 DB	117.0 *
01 Oct 97	11	Week 6 DB	120.0 *
15 Oct 97	12	Week 8 DB	123.0 *
29 Oct 97	13	Week 10 DB	123.5 *
14 Nov 97	14	Week 12 DB	127.0 *
11 Dec 97	15	Week 16 DB	128.0 *
23 Dec 97	16	Taper End	127.0 *
23 Jan 98		Follow-up	131.0 *

DB = Double-Blind Phase (Phase 2)
* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 02 May 97. The patient's baseline weight was 101.0 lbs. The dosage was gradually increased to 30 mg per day by 27 Jun 97 and the patient completed the open-label phase of the study. On 22 Aug 97, the patient was randomized to

double-blind paroxetine and continued on 30 mg per day. The patient's weight had been gradually increasing and at that same visit, after 113 days of study medication, the patient's weight was 110.0 lbs., which was out of range for her age and an increase from baseline of potential clinical concern. It was reported as a moderate adverse experience of weight gain of 6.5 lbs. over a 1-month period. The investigator did not consider that the weight gain was serious and the patient continued in the study. At study end, after 235 days of study medication, the patient weighed 128.0 lbs. At follow-up on 23 Jan 98, 32 days after the last dose of study medication, the patient's weight was 131.0 lbs. At last report, the adverse experience was ongoing. The investigator considered that the adverse experience was possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Melatonin	14 Mar 97	23 Aug 97
Vitamin B Complex	10 Apr 97	Ongoing
Cefuroxime	12 May 97	16 May 97
Amoxicillin	06 Jan 98	16 Jan 98

Study 29060/453
PID 453.013.00248

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Decreased Heart Rate
Significant Weight Increase

Adverse Experience (Verbatim): Bradycardia (Decreased Heart Rate)
ECG Abnormal (Flattened T-Wave on ECG)
Weight Gain (Weight Gain)

Screening Demography: Age: 12 years
Date of birth: 22 May 85
Sex: Male
Weight: 164.0 lbs.
Race: Caucasian

Country: United States

Medical History: Strep Throat
Conjunctivitis
Allergic to Dust and Grass
Cavernous Hemangioma (No Symptoms or Signs)
Rash
Dry Skin—Small Non-blanching Papules
Psychiatric History: Tic Disorders (Tourette's Disorder)

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 06 Jun 97 **Stop:** 19 Jun 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 20 Jun 97 **Stop:** 26 Jun 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 27 Jun 97 **Stop:** 03 Jul 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 04 Jul 97 **Stop:** 17 Jul 97
Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 18 Jul 97 **Stop:** 24 Jul 97

Study Drug: Open-Label Paroxetine 60 mg Given Orally
Start: 25 Jul 97 **Stop:** 02 Aug 97
Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 03 Aug 97 **Stop:** 28 Aug 97
Study Drug: Open-Label Paroxetine 60 mg Given Orally
Start: 29 Aug 97 **Stop:** 08 Oct 97
Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 09 Oct 97 **Stop:** 12 Nov 97
Study Drug: Double-Blind Placebo Given Orally
Start: 13 Nov 97 **Stop:** 10 Dec 97

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Mild Dry Mouth	17 Jun 97	07 Jul 97
Moderate Irritable	05 Jul 97	14 Jul 97
Moderate Restless	05 Jul 97	14 Jul 97
Moderate Depressed Mood	11 Jul 97	11 Jul 97
Moderate Shaking Involuntarily (Arms and Legs)	11 Jul 97	11 Jul 97
Moderate Sinus Infection	24 Oct 97	29 Oct 97
Moderate Diarrhea	04 Dec 97	05 Dec 97
Mild Head Cold (Viral)	11 Dec 97	12 Dec 97

Vital Signs of Potential Clinical Concern:

Date	**Visit**	**Week**	**Systolic BP (mm Hg)**	**Diastolic BP (mm Hg)**	**Heart Rate (bpm)**	**Weight (lbs.)**
29 May 97	1	Screening	125	60	82	164.0
05 Jun 97	2	Baseline	117	79	98	164.0
19 Jun 97	3	Week 2	115	85	82	165.0
03 Jul 97	4	Week 4	115	56	111	162.0
17 Jul 97	5	Week 6	107	83	110	162.0
31 Jul 97	6	Week 8	138	73	95	162.0
28 Aug 97	7	Week 12	132	75	91	170.0
07 Oct 97	8	Week 16	121	78	102	177.0
23 Oct 97	9	Week 2 DB	109	55	66 *	174.0
06 Nov 97	10	Week 4 DB	116	77	81	175.0
20 Nov 97	11	Week 6 DB	118	73	100	178.0 *
13 Dec 97		Early Disc.	117	78	102	183.0 *

DB = Double-Blind Phase (Phase 2)
* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 06 Jun 97. The patient's baseline weight was 164 lbs.; blood pressure was 117/79; and heart rate was 98 bpm. The dosage was gradually increased to 60 mg per day by 25 Jul 98, decreased to 50 mg per day by the patient's mother without site consent, and increased again to 60 mg per day. A routine electrocardiogram showed a flattened T-wave, which was reported as a mild adverse experience from 14 Aug 97 to 02 Oct 97. The patient completed the open-label phase of the study. On 09 Oct 97, the patient was randomized to double-blind placebo and was down titrated over 5 weeks to 0 mg paroxetine per day. On 23 Oct 97, after 140 days of study medication, the patient's heart rate was 66 bpm, which was reported as a mild adverse experience. It was considered out of range for his age and a decrease from baseline of potential clinical concern. Blood pressure was

within reference range throughout the study. The investigator did not consider that the decreased heart rate was serious and the patient continued in the study. The decreased heart rate was considered resolved on 06 Nov 97, when it was 81 bpm. On 20 Nov 97, after 168 days on study medication, the patient's weight was 178.0 lbs., which was reported as a moderate adverse experience. It was out of range for his age and an increase from baseline of potential clinical concern. The investigator did not consider that the increased weight was serious and the patient continued in the study. The patient discontinued from the study on 10 Dec 97 because of deviation from protocol (the mother was noncompliant). The weight gain was considered resolved on 13 Dec 97; at that time the patient's weight was 183.0 lbs. The investigator considered that the weight gain and the bradycardia were possibly related to study medication, and that the abnormal ECG was probably unrelated to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Citric Acid/Dextromethorphan/Glucose/Glycerol/ Guaifenesin/High Fructose Corn Syrup/Saccharin	25 Jul 97	25 Jul 97
Tropicamide	25 Jul 97	25 Jul 97
Amoxicillin	26 Oct 97	07 Nov 97
Loperamide	04 Dec 97	05 Dec 97
Paracetamol	11 Dec 97	12 Dec 97
Guaifenesin/Dextromethorphan Hydrobromide	11 Dec 97	12 Dec 97

Study 29060/453

PID 453.017.00195

Reason for Narrative: Patient with Vital Sign and Laboratory Values of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Weight Increase

Laboratory Value of Potential Clinical Concern: Low (Extended) Mean Corpuscular Volume
Low (Extended) Hematocrit

Adverse Experience (Verbatim): Weight Gain (Weight Gain)
Anemia (Abnormal CBC)

Screening Demography:
Age: 12 years
Date of birth: 10 Jun 84
Sex: Male
Weight: 121.0 lbs.
Race: Caucasian

Country: United States

Medical History: Chronic Sinusitis
Encopresis/Constipation
Stomach Aches
Headaches
Allergies to Pollen

Psychiatric History: Attention Deficit/Hyperactivity Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 01 May 97 **Stop:** 04 May 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 05 May 97 **Stop:** 11 May 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 12 May 97 **Stop:** 18 May 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 19 May 97 **Stop:** 03 Jun 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 04 Jun 97 **Stop:** 29 Jun 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 30 Jun 97 **Stop:** 29 Jul 97

Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 30 Jul 97 **Stop:** 21 Aug 97
Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 22 Aug 97 **Stop:** 01 Sep 97

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Moderate Agitation	04 Jun 97	07 Jun 97
Moderate Worsened Encopresis	01 Jul 97	30 Jul 97
Mild Daytime Tiredness	01 Jul 97	01 Aug 97
Moderate Worsened OCD Symptoms	15 Jul 97	30 Jul 97
Mild Increased Blood Pressure	30 Jul 97	11 Sep 97
Moderate Worsened OCD Symptoms	26 Aug 97	Ongoing
Moderate Worsened Attention Deficit/ Hyperactivity Disorder Symptoms	26 Aug 97	Ongoing
Moderate Worsened Depressive Symptoms	26 Aug 97	Ongoing
Moderate Worsened Anxiety Symptoms	26 Aug 97	Ongoing

Vital Signs of Potential Clinical Concern:

Date	**Visit**	**Week**	**Weight (lbs.)**
25 Apr 97	1	Screening	121.0
30 Apr 97	2	Baseline	121.0
16 May 97	3	Week 2	121.5
28 May 97	4	Week 4	124.0
11 Jun 97	5	Week 6	128.0
25 Jun 97	6	Week 8	126.5
30 Jul 97	7	Week 12	130.5
22 Aug 97	8	Week 16	133.0 *
02 Sep 97	9	Week 2 DB	136.5 *
11 Sep 97		Follow-up	136.5 *

DB = Double-Blind Phase (Phase 2)
* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 01 May 97. The patient's baseline weight was 121.0 lbs. Weight gain was reported as a mild adverse experience from 23 May to 25 Jun 97, and again starting on 30 Jul 97. The dosage was gradually increased to 50 mg per day and the patient completed the open-label phase of the study. On 22 Aug 97, the patient was randomized to double-blind placebo. At the same visit, after 114 days of study medication, the patient's weight was 133.0 lbs., which was out of range for his age and an increase from baseline of potential clinical concern. The investigator did not consider that the weight gain was serious and the patient

continued in the study. He withdrew on 02 Sep 97 due to lack of efficacy and was subsequently prescribed paroxetine. At last report, the adverse experience was ongoing. The investigator considered that the adverse experience was possibly related to study medication.

Laboratory Values of Potential Clinical Concern:

Date	Visit	Week	MCV Reference range: 78-102 fl	MCH Reference range: 25.0-35.0 pg	Hgb Reference range: 12.0-16.0 g/dL	Hct Reference range: 36.0-49.0%
25 Apr 97	1	Screening	77 *	26.0	12.4	36.7
25 Jun 97	6	Week 8	77 *	25.0	11.7	36.2
22 Aug 97	8	Week 16	75 *	25.1	11.6	34.6 *
02 Sep 97	9	Week 2 DB	75 *	24.8	11.3	34.2
11 Sep 97		Follow-up	75 *	24.5	11.0	33.4

DB = Double-Blind Phase (Phase 2)
* Value of potential clinical concern

Laboratory Values Remarks:

At screening, this patient's baseline hematology values were at the lower end of the reference range for MCH (mean corpuscular hemoglobin), Hgb (hemoglobin), and Hct (hematocrit), and below reference range for MCV (mean corpuscular volume). Values tended to decrease over time and MCV values were flagged as being of potential clinical concern, but they were considered by the investigator to have no clinical significance until week 16 of the open-label phase, when abnormal CBC was reported as a mild adverse experience. The patient was randomized to placebo and withdrew two weeks later. At follow-up on 11 Sep 97, his hematology values were still decreasing or remaining the same, and the investigator considered the adverse experience ongoing. The investigator considered the decreased values probably unrelated to study medication.

Concomitant Drugs	Onset	Stopped
Magnesium Hydroxide	01 Jan 94	Ongoing
Ibuprofen	11 Nov 96	Ongoing
Amoxicillin	27 May 97	05 Jun 97

Study 29060/453
PID 453.017.00197

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Weight Increase

Adverse Experience (Verbatim): Weight Gain (Weight Gain)

Screening Demography:
Age: 7 years
Date of birth: 07 Oct 89
Sex: Male
Weight: 88.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Allergy to Penicillin, Sulfa, Amoxicillin, K-Flex
Headaches
Stomach Aches
Chest Pain
Hay Fever
Tonsillectomy Age 2-1/2
Ear Infections
Nasal Congestion

Psychiatric History:
Generalized Anxiety Disorder
Dysthymia
Separation Anxiety
Specific Phobia NOS

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 13 May 97 **Stop:** 26 May 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 27 May 97 **Stop:** 09 Jun 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 10 Jun 97 **Stop:** 07 Jul 97

Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 08 Jul 97 **Stop:** 13 Jul 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 14 Jul 97 **Stop:** 04 Aug 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 05 Aug 97 **Stop:** 18 Aug 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 19 Aug 97 **Stop:** 01 Sep 97
Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 02 Sep 97 **Stop:** 16 Sep 97
Study Drug: Double-Blind Placebo Given Orally
Start: 17 Sep 97 **Stop:** 22 Sep 97

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Moderate Daytime Tiredness	15 May 97	05 Jun 97
Mild Increased Aggression	10 Jul 97	08 Aug 97
Moderate Increased Obsessive-Compulsive Disorder Symptoms	20 Jul 97	19 Aug 97
Moderate Increased Activity Level	01 Aug 97	24 Aug 97
Moderate Increased Irritability	01 Aug 97	24 Aug 97
Moderate Increased Oppositional Behaviors	01 Aug 97	24 Aug 97
Moderate Late Evening Restlessness	01 Aug 97	26 Aug 97
Moderate Insomnia	01 Aug 97	26 Aug 97
Mild Shortness of Breath	01 Aug 97	10 Sep 97
Moderate Increased Appetite	20 Aug 97	26 Aug 97
Moderate Increased Blood Pressure	02 Sep 97	17 Sep 97
Mild Weight Loss	17 Sep 97	01 Oct 97
Moderate Worsened Obsessive-Compulsive Disorder	18 Sep 97	20 Sep 97
Severe Worsened Obsessive-Compulsive Disorder	21 Sep 97	28 Sep 97
Moderate Worsened Anxiety	21 Sep 97	28 Sep 97
Severe Worsened Depression Symptoms	21 Sep 97	01 Oct 97
Moderate Insomnia	21 Sep 97	03 Oct 97

Vital Signs of Potential Clinical Concern:

Date	**Visit**	**Week**	**Weight (lbs.)**
06 May 97	1	Screening	88.0
13 May 97	2	Baseline	90.0
27 May 97	3	Week 2	95.0
10 Jun 97	4	Week 4	99.0 *
24 Jun 97	5	Week 6	100.0 *
08 Jul 97	6	Week 8	105.0 *
05 Aug 97	7	Week 12	114.0 *
02 Sep 97	8	Week 16	113.0 *
17 Sep 97	9	Week 2 DB	124.0 *
23 Sep 97	Early Discontinuation		120.5 *
21 Oct 97	Follow-up		124.0

DB = Double-Blind Phase (Phase 2)
* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 13 May 97. The dosage was gradually increased to 30 mg per day. The patient's baseline weight was 90.0 lbs., and his weight increased gradually until it was 99.0 on 10 Jun 97, after 29 days on study medication. It was reported as a moderate adverse experience starting on 27 May 97, when the value was out of range for his age and an increase from baseline of potential clinical concern. The investigator did not consider that the weight gain was serious. The patient completed the open-label phase of the study and on 02 Sep 97 was randomized to double-blind placebo and down titration of paroxetine was started. The weight gain was considered resolved on 17 Sep 97, when the patient's weight was 124.0 lbs. The patient discontinued from the study on 22 Sep 97 due to lack of efficacy and started 30 mg paroxetine off study. The investigator considered that the weight gain was possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Calcium Carbonate	12 Feb 95	Ongoing
Paracetamol	01 Aug 96	Ongoing
Lidocaine/Prilocaine Cream	08 Jul 97	08 Jul 97
Lorazepam	12 Aug 97	14 Aug 97
Lorazepam	16 Aug 97	17 Aug 97
Lorazepam	21 Sep 97	22 Sep 97
Lidocaine/Prilocaine Cream	23 Sep 97	23 Sep 97

Study 29060/453
PID 453.018.00223

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Weight Increase

Adverse Experience (Verbatim): Weight Gain (Weight Gain)

Screening Demography:
Age: 8 years
Date of birth: 12 Nov 88
Sex: Female
Weight: 84.0 lbs.
Race: Caucasian

Country: United States

Medical History: Mild Constipation, Approximately 1 x per Week
Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 20 Aug 97 **Stop:** 04 Sep 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 05 Sep 97 **Stop:** 09 Dec 97
Study Drug: Double-Blind Paroxetine 20 mg Given Orally
Start: 10 Dec 97 **Stop:** 03 Apr 98
Study Drug: Double-Blind Taper End Medication Given Orally
Start: 04 Apr 98 **Stop:** 13 Apr 98

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Mild Sore Throat	31 Aug 97	31 Aug 97
Mild Headache	12 Sep 97	12 Sep 97
Mild Swollen Cervical Lymph Node	15 Sep 97	24 Sep 97
Mild Proteinuria	14 Oct 97	28 Oct 97
Moderate Influenza	07 Nov 97	08 Nov 97
Mild Stomach Ache	11 Nov 97	11 Nov 97
Mild Fever	02 Feb 98	02 Feb 98
Mild Common Cold Symptoms	02 Feb 98	20 Feb 98
Mild Dizziness	11 Apr 98	18 Apr 98
Mild Nausea	11 Apr 98	18 Apr 98

Vital Signs of Potential Clinical Concern:

Date	**Visit**	**Week**	**Weight (lbs.)**
12 Aug 97	1	Screening	84.0
19 Aug 97	2	Baseline	82.0
04 Sep 97	3	Week 2	83.5
17 Sep 97	4	Week 4	89.5 *
01 Oct 97	5	Week 6	85.0
14 Oct 97	6	Week 8	88.0 *
11 Nov 97	7	Week 12	83.0
09 Dec 97	8	Week 16	85.0
19 Dec 97	9	Week 2 DB	84.0
06 Jan 98	10	Week 4 DB	85.0
20 Jan 98	11	Week 6 DB	87.0
04 Feb 98	12	Week 8 DB	87.0
17 Feb 98	13	Week 10 DB	88.0 *
03 Mar 98	14	Week 12 DB	88.0 *
03 Apr 98	15	Week 16 DB	90.0 *
17 Apr 98	16	Taper End	91.0 *
05 May 98		Follow-up	88.0 *

DB = Double-Blind Phase (Phase 2)
* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 20 Aug 97. The patient's baseline weight was 82.0 lbs. The dosage was increased to 20 mg per day on 05 Sep 97. On 17 Sep 97, after 29 days of study

medication, the patient's weight was 89.5 lbs., which was reported as a mild adverse experience of weight gain. The weight was out of range for the patient's age and an increase from baseline of potential clinical concern. The investigator did not consider that the adverse experience was serious and the patient continued in the study at the same dosage. The adverse experience was considered resolved on 11 Nov 97, when the patient's weight was 83.0 lbs. The patient completed the open-label phase of the study was randomized on 10 Dec 97 to double-blind paroxetine at 20 mg per day. The patient completed the study as planned. At the final study visit on 17 Apr 98, the patient weighed 91.0 lbs., after a total of 241 days on study medication; it was 88.0 lbs. at the follow-up visit 19 days later. The investigator considered that the adverse experience was possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Vitamin C	01 Jan 96	Ongoing
Menthol	31 Aug 97	31 Aug 97
Paracetamol	12 Sep 97	12 Sep 97
Paracetamol	07 Nov 97	07 Nov 97
Paracetamol	03 Feb 98	04 Feb 98

Study 29060/453
PID 453.019.00301

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Weight Increase

Adverse Experience (Verbatim): Weight Gain (Weight Gain)
Increased Appetite (Increased Appetite)

Screening Demography: Age: 8 years
Date of birth: 25 Apr 89
Sex: Male
Weight: 84.2 lbs.
Race: Caucasian

Country: United States

Medical History: Decreased WBC (2.8 on 26 Jul 97)
Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 31 Jul 97 **Stop:** 06 Aug 27
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 07 Aug 97 **Stop:** 27 Aug 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 28 Aug 97 **Stop:** 24 Sep 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 25 Sep 97 **Stop:** 19 Nov 97
Study Drug: Double-Blind Paroxetine 20 mg Given Orally
Start: 20 Nov 97 **Stop:** 11 Mar 98
Study Drug: Double-Blind Taper End Medication Given Orally
Start: 12 Mar 98 **Stop:** 22 Mar 98

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Mild Daytime Drowsiness	19 Aug 97	19 Nov 97
Mild Fatigue and Chills	19 Aug 97	19 Nov 97
Mild Restlessness	25 Aug 97	19 Nov 97
Mild Facial Rash	30 Nov 97	10 Dec 97
Mild Rash—Side of Face	04 Dec 97	10 Dec 97
Mild Concussion with Brief Loss of Memory	13 Dec 97	17 Dec 97
Mild Dizziness	13 Dec 97	16 Jan 98
Mild URI Pulmonary	14 Dec 97	20 Dec 97
Mild Restlessness	14 Jan 98	28 Jan 98

Vital Signs of Potential Clinical Concern:

Date	Visit	Week	Weight (lbs.)
23 Jul 97	1	Screening	84.2
30 Jul 97	2	Baseline	82.3
14 Aug 97	3	Week 2	81.8
28 Aug 97	4	Week 4	81.4
10 Sep 97	5	Week 6	81.5
24 Sep 97	6	Week 8	82.2
22 Oct 97	7	Week 12	85.6
19 Nov 97	8	Week 16	87.8
03 Dec 97	9	Week 2 DB	89.2 *
17 Dec 97	10	Week 4 DB	89.6 *
07 Jan 98	11	Week 6 DB	93.0 *
14 Jan 98	12	Week 8 DB	91.3 *
28 Jan 98	13	Week 10 DB	94.6 *
11 Feb 98	14	Week 12 DB	94.2 *
11 Mar 98	15	Week 16 DB	94.2 *
22 Mar 98	16	Taper End	94.4 *
27 Apr 98		Follow-up	94.2 *

DB = Double-Blind Phase (Phase 2)
* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 31 Jul 97. The dosage was stabilized at 20 mg per day. The patient's baseline weight was 82.3 lbs. and increased gradually throughout the study. Weight gain with increased appetite was reported as a mild adverse experience on 22 Oct 97. The patient completed the open-label phase of the study and on 20 Nov 97 was

randomized to double-blind paroxetine 20 mg per day. At the Week 2 visit of the double-blind phase on 03 Dec 98, after 126 days of study medication, the patient's weight was 89.2, which was out of range for his age and an increase from baseline of potential clinical concern. The investigator did not consider that the adverse experience was serious and the patient completed the study as planned. At last report, the increased appetite and weight gain were ongoing. The investigator considered that both the increased appetite and the weight gain were possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
None		

Study 29060/453
PID 453.019.00302

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Weight Increase

Adverse Experience (Verbatim): Weight Gain (Weight Gain)

Screening Demography:
Age: 16 years
Date of birth: 25 Sep 80
Sex: Male
Weight: 171.7 lbs.
Race: Caucasian

Country: United States

Medical History: None
Psychiatric History: Mild Depressive Symptoms, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 07 Aug 97 **Stop:** 13 Aug 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 14 Aug 97 **Stop:** 21 Aug 97
Study Drug: Open-Label Paroxetine 30g Given Orally
Start: 22 Aug 97 **Stop:** 27 Aug 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 28 Aug 97 **Stop:** 02 Oct 97
Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 03 Oct 97 **Stop:** 26 Nov 97
Study Drug: Double-Blind Paroxetine 50 mg Given Orally
Start: 27 Nov 97 **Stop:** 05 Feb 98

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Mild Daytime Fatigue	17 Aug 97	Ongoing
Mild Upper Respiratory Infection	21 Nov 97	22 Nov 97
Mild Increased Obsessive-Compulsive Disorder Symptoms	24 Dec 97	24 Dec 97
Moderate Sinusitis	31 Dec 97	09 Jan 98
Mild Sleep Disturbance	07 Jan 98	Ongoing
Mild Irritability	07 Jan 98	Ongoing
Mild Increased Anxiety	07 Jan 98	04 Feb 98
Moderate Bronchitis	01 Feb 98	10 Feb 98

Vital Signs of Potential Clinical Concern:

Date	**Visit**	**Week**	**Weight (lbs.)**
01 Aug 97	1	Screening	171.7
06 Aug 97	2	Baseline	170.8
21 Aug 97	3	Week 2	167.0
04 Sep 97	4	Week 4	173.1
17 Sep 97	5	Week 6	177.0
02 Oct 97	6	Week 8	180.1
29 Oct 97	7	Week 12	184.1
26 Nov 97	8	Week 16	193.6 *
10 Dec 97	9	Week 2 DB	198.5 *
24 Dec 97	10	Week 4 DB	192.0 *
07 Jan 98	11	Week 6 DB	202.4 *
21 Jan 98	12	Week 8 DB	202.0 *
04 Feb 98	13	Week 10 DB	206.8 *
11 Feb 98	14	Week 12 DB	204.2 *

* Value of potential clinical concern
DB = Double-Blind Phase (Phase 2)

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 07 Aug 97. The patient's baseline weight was 170.8 lbs. The dosage was gradually increased to 50 mg per day. On 10 Dec 97, the patient's weight was 198.5, which was out of range for his age and an increase from baseline of potential clinical concern. No adverse experience was reported and the patient completed the open-label phase of the study. On 27 Nov 97, the patient was randomized to double-blind paroxetine and continued on 50 mg per day. On

07 Jan 98, after 154 days of study medication, the patient's weight was 202.4 lbs., which was reported as a mild adverse experience. The investigator did not consider that the adverse experience was serious and the patient continued in the study until 05 Feb 98, when he withdrew due to deviation from protocol (non-compliance). The adverse experience was considered resolved on 07 Jan 98. The investigator considered that the adverse experience was probably unrelated to study medication; he reported that the patient was large for his age and that the weight gain was probably a normal growth spurt and an increase in muscle mass from power weight lifting.

Concomitant Drugs	**Onset**	**Stopped**
Oxymetazoline (Nasal)	21 Nov 97	23 Nov 97
Cefuroxime	31 Dec 97	09 Jan98
Ciprofloxacin	01 Feb 98	10 Feb 98

Study 29060/453
PID 453.021.00068

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Decrease in Heart Rate

Adverse Experience (Verbatim): ECG Abnormal (EKG—Normal Sinus Rhythm/Voltage Criteria for Left Ventricular Hypertrophy)

Screening Demography:
Age: 9 years
Date of birth: 28 Nov 87
Sex: Male
Weight: 68.0 lbs.
Race: Caucasian

Country: United States

Medical History: None
Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 07 Feb 97 **Stop:** 21 Feb 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 22 Feb 97 **Stop:** 02 May 97

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Severe Belligerent Behavior	25 Feb 97	26 Feb 97

Vital Signs of Potential Clinical Concern:

Date	Visit	Week	Systolic BP (mm Hg)	Diastolic BP (mm Hg)	Heart Rate (bpm)
31 Jan 97	1	Screening	110	64	100
07 Feb 97	2	Baseline	100	64	96
21 Feb 97	3	Week 2	90	60	80
07 Mar 97	4	Week 4	114	62	80
21 Mar 97	5	Week 6	105	78	60 *
04 Apr 97	6	Week 8	98	60	102
02 May 97	7	Week 12	114	67	97

* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 07 Feb 97. The patient's baseline blood pressure was 100/64 and heart rate was 96 bpm. The dosage was increased to 20 mg per day. On 21 Mar 97, after 43 days of study medication, the patient's heart rate was 60 bpm, which was out of range for his age and a decrease from baseline of potential clinical concern. A routine electrocardiogram on 04 Apr 97 revealed voltage criteria for left ventricular hypertrophy, which was asymptomatic. An adverse experience of mild intensity was reported, with no cardiomegaly. The investigator did not consider that either event was serious and that the electrocardiogram findings were probably unrelated to study medication. The investigator felt that the decreased heart rate was due to the fact that the patient was calmer and that the family showed less anxiety at that visit. The patient's heart rate was 102 bpm at the next visit, within reference range. The electrocardiogram findings were considered resolved on 10 Apr 98. The patient continued in the study until 02 May 97, when he was withdrawn because of an increased need for family therapy.

Concomitant Drugs	Onset	Stopped
None		

Study 29060/453
PID 453.023.00091

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Increase in Blood Pressure

Adverse Experience (Verbatim): ECG Abnormal (Sinus Tachycardia and T-Wave Abnormality)

Screening Demography:
Age: 15 years
Date of birth: 01 May 81
Sex: Male
Weight: 126.25 lbs.
Race: Black

Country: United States

Medical History:
Asthma
Ear Infection
Heart Murmur
Febrile Seizures
Allergies to Mold, Ragweed
Allergy to Penicillin
Eczema
Nearsighted–Wears Glasses

Psychiatric History: Attention Deficit/Hyperactivity Disorder, Inattentive Type

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 02 Apr 97 **Stop:** 07 Apr 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 08 Apr 97 **Stop:** 20 Apr 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 21 Apr 97 **Stop:** 12 May 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 13 May 97 **Stop:** 23 May 97

Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 24 May 97 **Stop:** 23 Jun 97
Study Drug: Open-Label Paroxetine 60 mg Given Orally
Start: 24 Jun 97 **Stop:** 25 Jul 97
Study Drug: Double-Blind Paroxetine 60 mg Given Orally
Start: 26 Jul 97 **Stop:** 14 Nov 97
Study Drug: Double-Blind Taper End Medication Given Orally
Start: 15 Nov 97 **Stop:** 19 Dec 97

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Mild Nausea	02 Apr 97	08 Apr 97
Moderate Nervousness	08 Apr 97	27 Apr 97
Moderate Sleepiness	15 Apr 97	27 Apr 97
Mild Body Jerks	28 Apr 97	13 Dec 97
Mild Eye Irritation	30 Apr 97	04 May 97
Mild Root Canal—Tooth Pain	28 Sep 97	03 Oct 97

Vital Signs of Potential Clinical Concern:

Date	Visit	Week	Systolic BP (mm Hg)	Diastolic BP (mm Hg)	Heart Rate (bpm)
05 Mar 97	1	Screening	120	88 *	84
01 Apr 97	2	Baseline	120	70	90
14 Apr 97	3	Week 2	120	70	70
20 Apr 97	4	Week 4	120	80	90
29 Apr 97	5	Week 6	120	80	90
13 May 97	6	Week 8	120	70	100
23 Jun 97	7	Week 12	128	80	108
25 Jul 97	8	Week 16	120	70	104
07 Aug 97	9	Week 2 DB	120	80	96
20 Aug 97	10	Week 4 DB	120	80	110
05 Sep 97	11	Week 6 DB	120	80	104
19 Sep 97	12	Week 8 DB	120	80	108
03 Oct 97	13	Week 10 DB	120	90 *	104
17 Oct 97	14	Week 12 DB	114	71	90
14 Nov 97	15	Week 16 DB	125	107 *	86
22 Dec 97	16	Taper End	110	64	90

DB = Double-Blind Phase (Phase 2)
* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 02 Apr 97. The dosage was gradually increased to 40 mg per day by 23 May 97. The patient's baseline blood pressure was 120/70 and heart rate was 90 bpm; his screening diastolic blood pressure had been 88mg Hg, which was out of range for his age. A routine electrocardiogram on 23 May 97, after 52 days of study medication, revealed sinus tachycardia and T-wave abnormalities, reported as moderate adverse experiences. At the previous visit, 13 May 97, the patient's blood pressure had been 120/70 and his heart rate had been 100 bpm. The dose

was increased to 50 mg open-label paroxetine per day. On 23 Jun 97, the patient's blood pressure was 128/80, which was within reference range for his age. The investigator did not consider the electrocardiogram findings serious and increased the dose of paroxetine to 60 mg per day. The patient completed the open-label phase of the study and was randomized to double-blind paroxetine 60 mg per day. The electrocardiogram abnormalities were considered resolved on 19 Sep 97. The patient's blood pressure remained at approximately the same level until study end, after 227 days on study medication, when his diastolic blood pressure was 107, which was out of range for his age and an increase from baseline of potential clinical concern. At taper end on 22 Dec 97, after 265 days on study medication, his blood pressure decreased to 110/64, considered a decrease of potential clinical concern. There was no associated adverse experience. The investigator considered the adverse experience of abnormal ECG probably unrelated to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Loratadine	01 Mar 96	12 May 96
Neomycin Drops	30 Apr 97	04 May 97
Loratadine/Pseudophedrine	13 May 97	18 Jun 97
Loratadine	19 Jun 97	11 Aug 97
Loratadine/ Pseudophedrine	12 Aug 97	Ongoing
Salbutamol	20 Aug 97	Ongoing
Budesonide	10 Oct 97	Ongoing

Study 29060/453
PID 453.023.00092

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Weight Increase

Adverse Experience (Verbatim): Weight Gain (Weight Gain)

Screening Demography:
Age: 14 years
Date of birth: 21 Sep 82
Sex: Female
Weight: 166.5 lbs.
Race: Caucasian

Country: United States

Medical History: Asthma
Allergies—Molds, Pollen

Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 15 Mar 97 **Stop:** 21 Mar 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 22 Mar 97 **Stop:** 26 Mar 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 27 Mar 97 **Stop:** 02 Apr 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 03 Apr 97 **Stop:** 23 Apr 97
Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 24 Apr 97 **Stop:** 30 Apr 97
Study Drug: Open-Label Paroxetine 60 mg Given Orally
Start: 01 May 97 **Stop:** 02 Jul 97
Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 03 Jul 97 **Stop:** 07 Aug 97

Study Drug: Double-Blind Placebo Given Orally
Start: 08 Aug 97 **Stop:** 22 Oct 97
Study Drug: Double-Blind Taper End Medication Given Orally
Start: 23 Oct 97 **Stop:** 26 Nov 97

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Moderate Increased Appetite	27 Mar 97	10 Sep 97
Mild Jaw Pain	28 Mar 97	05 Apr 97
Mild Jaw Pain	10 Apr 97	15 Apr 97
Mild Headache	24 Apr 97	01 May 97
Mild Jaw Pain	06 May 97	06 May 97
Mild Jaw Pain	04 Jun 97	04 Jun 97
Mild Bad Dreams at Night	15 Jun 97	21 Nov 97
Mild Rash on Arm	17 Jun 97	10 Sep 97
Mild Sunburn	21 Jun 97	21 Jun 97
Mild Sunburn	23 Aug 97	23 Aug 97
Mild Jaw Pain	27 Aug 97	27 Aug 97
Mild Jaw Pain	30 Aug 97	09 Sep 97
Mild Jaw Pain	11 Sep 97	20 Oct 97
Mild Stomach Ache	20 Oct 97	20 Oct 97
Mild Jaw Pain	30 Oct 97	30 Oct 97
Mild Jaw Pain	06 Nov 97	06 Nov 97

Vital Signs of Potential Clinical Concern:

Date	**Visit**	**Week**	**Weight (lbs.)**
07 Mar 97	1	Screening	166.5
14 Mar 97	2	Baseline	167.5
26 Mar 97	3	Week 2	173.3
09 Apr 97	4	Week 4	175.0
23 Apr 97	5	Week 6	171.0
07 May 97	6	Week 8	170.5
04 Jun 97	7	Week 12	179.0
02 Jul 97	8	Week 16	184.0 *
17 Jul97	9	Week 2 DB	190.5 *
31 Jul 97	10	Week 4 DB	192.5 *
14 Aug 97	11	Week 6 DB	193.5 *
28 Aug 97	12	Week 8 DB	198.0 *
10 Sep 97	13	Week 10 DB	197.5 *
25 Sep 97	14	Week 12 DB	202.0 *
22 Oct 97	15	Week 16 DB	208.0 *
03 Dec 97	16	Taper End	208.0 *
17 Dec 97		Follow-up	207.0 *

DB = Double-Blind Phase (Phase 2)
* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 15 Mar 97. The patient's baseline weight was 167.5 lbs., which was out of range for her age. The dosage was gradually increased to 60 mg per day by 01 May 97. the patient's weight had increased gradually and was reported as a moderate adverse experience of weight gain when it was 179.0 on 04 Jun 97, after 82 days of study medication. On 02 Jul 97, the increased weight (184.0 lbs.) was also considered an increase from baseline of potential clinical concern. The investigator did not consider that the weight gain was serious and the patient continued in the study. She completed the open-label phase of the study and on 03 Jul 97 was randomized to double-blind placebo. Her weight continued to increase and at taper end, on 03 Dec 97, 7 days after the last dose of study medication, it was 208.0 lbs.; it decreased to 207.0 lbs. at follow-up 15 days later. At last report, the weight gain was ongoing. The investigator considered that the adverse experience was related to study medication. After the patient completed the study, she was prescribed paroxetine.

Concomitant Drugs	**Onset**	**Stopped**
Theophylline	21 Sep 93	Ongoing
Clemastine/Phenylpropanolamine	21 Sep 93	Ongoing
Salbutamol	21 Sep 93	Ongoing
Paracetamol	21 Sep 93	Ongoing
Paracetamol	28 Mar 97	05 Apr 97
Paracetamol	10 Apr 97	15 Apr 97
Paracetamol	24 Apr 97	01 May 97
Paracetamol	06 May 97	06 May 97
Paracetamol	21 Jun 97	21 Jun 97
Cortisone Cream	17 Aug 97	10 Sep 97
Paracetamol	23 Aug 97	23 Aug 97
Paracetamol	27 Aug 97	27 Aug 97
Paracetamol	30 Aug 97	30 Aug 97
Paracetamol	04 Sep 97	04 Sep 97
Paracetamol	08 Sep 97	09 Sep 97
Paracetamol	11 Sep 97	25 Sep 97
Paracetamol	26 Sep 97	20 Oct 97
Magnesium Hydroxide	20 Oct 97	20 Oct 97
Paracetamol	30 Oct 97	30 Oct 97
Paracetamol	06 Nov 97	06 Nov 97

Study 29060/453
PID 453.023.00400

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Weight Increase

Adverse Experience (Verbatim): Weight Gain (Weight Gain)

Screening Demography:
Age: 13 years
Date of birth: 25 Oct 84
Sex: Male
Weight: 127.0 lbs.
Race: Caucasian

Country: United States

Medical History: Headaches
Flushing
Sweating
Nausea

Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 23 Nov 97 **Stop:** 28 Nov 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 29 Nov 97 **Stop:** 05 Dec 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 06 Dec 97 **Stop:** 19 Dec 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 20 Dec 97 **Stop:** 26 Dec 97
Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 27 Dec 97 **Stop:** 20 Feb 98
Study Drug: Open-Label Paroxetine 60 mg Given Orally
Start: 21 Feb 98 **Stop:** 01 Mar 98
Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 02 Mar 98 **Stop:** 20 Mar 98

Study Drug: Double-Blind Placebo (Paroxetine Down Titration) Given Orally (Per Protocol)
Start: 21 Mar 98 **Stop:** 17 Apr 98
Study Drug: Double-Blind Placebo Given Orally
Start: 18 Apr 98 **Stop:** 10 Jul 98
Study Drug: Double-Blind Taper End Medication Given Orally
Start: 11 Jul 98 **Stop:** 03 Aug 98

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Mild Fatigue	23 Feb 98	01 Mar 98
Mild Weighty Forearms	22 Feb 98	23 Feb 98
Mild 3-D Vision	22 Feb 98	23 Feb 98
Mild Weighty Forearms	28 Feb 98	28 Feb 98
Mild Tremor	28 Nov 97	02 Mar 98
Mild Ear Infection	10 Dec 97	17 Dec 97
Mild Fever	15 Dec 97	16 Dec 97
Mild Diarrhea	17 Dec 97	18 Dec 97
Mild Headache	15 Jan 98	15 Jan 98
Mild Headache	24 Jan 98	19 Feb 98
Mild Headache	03 Mar 98	03 Mar 98
Mild Headache	22 Apr 98	24 Apr 98
Mild Headache	30 Apr 98	30 Apr 98
Mild Headache	14 Jun 98	14 Jun 98
Mild Headache	09 Jul 98	09 Jul 98

Vital Signs of Potential Clinical Concern:

Date	**Visit**	**Week**	**Weight (lbs.)**
21 Nov 97	1	Screening	127.0
23 Nov 97	2	Baseline	127.0
05 Dec 97	3	Week 2	127.0
19 Dec 97	4	Week 4	126.0
06 Jan 98	5	Week 6	125.0
23 Jan 98	6	Week 8	131.8
20 Feb 98	7	Week 12	133.9
20 Mar 98	8	Week 16	133.5
08 Apr 98	9	Week 2 DB	137.3
17 Apr 98	10	Week 4 DB	136.0
01 May 98	11	Week 6 DB	140.8
15 May 98	12	Week 8 DB	139.9
03 Jun 98	13	Week 10 DB	145.8 *
12 Jun 98	14	Week 12 DB	146.9 *
10 Jul 98	15	Week 16 DB	147.8 *
11 Aug 98	16	Taper End	147.4 *

DB = Double-Blind Phase (Phase 2)

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 23 Nov 97. The patient's baseline weight was 127.0 lbs. The dosage was gradually increased to 50 mg per day and the patient completed the open-label phase of the study. The patient had been gaining weight and weight gain was reported as a mild adverse experience starting on 23 Jan 98, when his weight was 131.8 lbs. On 21 Mar 98, the patient was randomized to double-blind placebo. On 10 Jul 98, after 230 days of study medication, the patient's weight was 147.8 lbs., which was reported as a value of potential clinical concern. The investigator did not consider that the weight gain was serious and reported it resolved on 11 Aug 98. The investigator considered that the weight gain was possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Cefixime	10 Dec 97	17 Dec 97
Ibuprofen	15 Dec 97	16 Dec 97
Paracetamol	15 Jan 98	15 Jan 98
Paracetamol	24 Jan 98	24 Jan 98
Paracetamol	30 Jan 98	30 Jan 98
Paracetamol	03 Feb 98	03 Feb 98
Paracetamol	06 Feb 98	06 Feb 98
Paracetamol	19 Feb 98	19 Feb 98
Paracetamol	03 Mar 98	03 Mar 98
Paracetamol	22 Apr 98	24 Apr 98
Paracetamol	30 Apr 98	30 Apr 98
Paracetamol	14 Jun 98	14 Jun 98
Paracetamol	09 Jul 98	09 Jul 98

Study 29060/453
PID 453.023.00401

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Weight Increase

Adverse Experience (Verbatim): Weight Gain (Weight Gain)
Increased Appetite

Screening Demography: Age: 8 years
Date of birth: 11 Mar 89
Sex: Female
Weight: 72.0 lbs.
Race: Caucasian

Country: United States

Medical History: Abdominal Pain
Red, Dry Chapped Hands
Otitis Media

Psychiatric History: Attention Deficit/Hyperactivity Disorder
Oppositional Defiant Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 19 Dec 97 **Stop:** 25 Dec 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 26 Dec 97 **Stop:** 06 Jan 98
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 07 Jan 98 **Stop:** 21 Jan 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 22 Jan 98 **Stop:** 04 Feb 98
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 05 Feb 98 **Stop:** 17 Feb 98
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 18 Feb 98 **Stop:** 05 Mar 98
Study Drug: Open-Label Paroxetine 50 mg Given Orally
Start: 06 Mar 98 **Stop:** 17 Mar 98

Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 18 Mar 98 **Stop:** 01 Apr 98
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 02 Apr 98 **Stop:** 14 Apr 98
Study Drug: Double-Blind Paroxetine 20 mg Given Orally
Start: 15 Apr 98 **Stop:** 09 Aug 98
Study Drug: Double-Blind Taper End Medication Given Orally
Start: 10 Aug 98 **Stop:** 18 Aug 98

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Mild Otitis Media	15 Dec 97	25 Dec 97
Mild Diarrhea	19 Dec 97	19 Dec 97
Mild Neck Pain	19 Dec 97	22 Dec 97
Mild Impulsivity	22 Dec 97	23 Jan 98
Mild Inattentiveness	22 Dec 97	31 Jan 98
Mild Somnolence	27 Dec 97	31 Jan 98
Mild Sore Throat	13 Jan 98	21 Jan 98
Mild Cough	13 Jan 98	21 Jan 98
Mild Headache	15 Jan 98	15 Jan 98
Mild Fever	17 Jan 98	19 Jan 98
Mild Stomach Ache	21 Jan 98	13 May 98
Mild Urinary Frequency	23 Jan 98	Ongoing
Mild Headache	26 Jan 98	26 Jan 98
Mild Headache	08 Feb 98	10 Feb 98
Mild Headache	19 Feb 98	19 Feb 98
Moderate Fidgety	24 Feb 98	Ongoing
Moderate Distractible	24 Feb 98	Ongoing
Mild Grinding Teeth	10 Mar 98	07 Aug 98
Mild Vomiting	02 Apr 98	02 Apr 98
Mild Allergic Reaction to Bee Sting	17 Jun 98	17 Jun 98

Vital Signs of Potential Clinical Concern:

Date	Visit	Week	Weight (lbs.)
08 Dec 97	1	Screening	72.0
18 Dec 97	2	Baseline	72.0
06 Jan 98	3	Week 2	71.0
21 Jan 98	4	Week 4	70.6
04 Feb 98	5	Week 6	73.0
17 Feb 98	6	Week 8	75.0
17 Mar 98	7	Week 12	79.2
15 Apr 98	8	Week 16	82.1 *
28 Apr 98	9	Week 2 DB	87.3
11 May 98	10	Week 4 DB	86.2
27 May 98	11	Week 6 DB	86.7
10 Jun 98	12	Week 8 DB	85.1
29 Jun 98	13	Week 10 DB	87.8 *
13 Jul 98	14	Week 12 DB	86.7
10 Aug 98	15	Week 16 DB	88.2 *
19 Aug 98	16	Taper End	88.7 *

DB = Double-Blind Phase (Phase 2)
* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 19 Dec 97. The patient's baseline weight was 72.0 lbs. The dosage was gradually increased to 30 mg per day but decreased to 20 mg per day on 22 Jan 98. The patient's weight had increased gradually and at the visit on 04 Feb 98, after 48 days of study medication, her weight was 73.0 lbs., reported as a moderate adverse experience. The weight gain continued, and on 05 Mar 98, a moderate adverse experience of increased appetite, related to the weight gain, was reported. The investigator did not consider either event serious and the patient continued in the study. The dosage was increased gradually to 50 mg per day by 06 Mar 98, and then decreased to 20 mg per day by 02 Apr 98. On 15 Apr 98, after 118 days of study medication, the patient's weight was 82.1 lbs., which was out of range for her age and an increase from baseline of potential clinical concern. The patient completed the open-label phase of the study and on 15 Apr 98 was randomized to double-blind paroxetine 20 mg per day. When she completed the study on 10 Aug 98, her weight was 88.2 lbs.; at follow-up 7 days later it was 88.7 lbs. At last report, the increased appetite was ongoing and the weight gain resolved on 28 Apr 98. The investigator considered that the increased appetite was related to study medication and that the weight gain was possibly related.

Concomitant Drugs	Onset	Stopped
Amoxicillin	15 Dec 97	Ongoing
Loperamide	19 Dec 97	19 Dec 97
Ibuprofen	19 Dec 97	22 Dec 97
Ibuprofen	15 Jan 98	15 Jan 98
Guaifenesin	15 Jan 98	15 Jan 98
Dextromethorphan	16 Jan 98	16 Jan 98
Phenylpropanolamine/Brompheniramine/ Pseudophedrine	17 Jan 98	17 Jan 98
Ibuprofen	17 Jan 98	18 Jan 98
Dextromethorphan/Ibuprofen/Chlorphenamine	17 Jan 98	20 Jan 98
Paracetamol	08 Feb 98	10 Feb 98
Paracetamol	19 Feb 98	19 Feb 98
Diphenhydramine	17 Jun 98	17 Jun 98

Study 29060/453
PID 453.025.00021

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Weight Increase

Adverse Experience (Verbatim): Weight Gain (Weight Gain)

Screening Demography:
Age: 13 years
Date of birth: 30 Jan 84
Sex: Male
Weight: 178.0 lbs.
Race: Caucasian

Country: United States

Medical History: Juvenile Polyps, Colonic
Broken Left Middle Finger

Psychiatric History: Attention Deficit/Hyperactivity Disorder

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 28 Feb 97 **Stop:** 13 Mar 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 14 Mar 97 **Stop:** 10 Apr 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 11 Apr 97 **Stop:** 24 Apr 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 25 Apr 97 **Stop:** 21 May 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 22 May 97 **Stop:** 18 Jun 97
Study Drug: Double-Blind Paroxetine 30 mg Given Orally
Start: 19 Jun 97 **Stop:** 24 Oct 97
Study Drug: Double-Blind Taper End Medication Given Orally
Start: 25 Oct 97 **Stop:** 06 Nov 97

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Mild Fidgety	10 Mar 97	01 Apr 97
Mild Increased Motor Activity	24 Apr 97	29 May 97
Moderate Drowsiness	25 Apr 97	15 May 97
Moderate Sinus Congestion	10 Jun 97	14 Jun 97
Moderate Foot Swelling—Football Injury	18 Aug 97	21 Aug 97
Moderate Neck Pain	09 Sep 97	13 Sep 97
Moderate Shoulder Pain	16 Sep 97	18 Sep 97
Moderate Bruise on Thumb	07 Oct 97	14 Oct 97
Moderate Increased Appetite	10 Oct 97	17 Oct 97
Moderate Shakiness	10 Oct 97	17 Oct 97
Moderate Headache	08 Nov 97	08 Nov 97

Vital Signs of Potential Clinical Concern:

Date	**Visit**	**Week**	**Weight (lbs.)**
14 Feb 97	1	Screening	178.0
27 Feb 97	2	Baseline	177.0
13 Mar 97	3	Week 2	184.0
28 Mar 97	4	Week 4	189.0 *
10 Apr 97	5	Week 6	180.0
24 Apr 97	6	Week 8	180.0
22 May 97	7	Week 12	194.0 *
19 Jun 97	8	Week 16	197.0 *
07 Jul 97	9	Week 2 DB	202.0
21 Jul 97	10	Week 4 DB	206.0
04 Aug 97	11	Week 6 DB	210.0 *
22 Aug 97	12	Week 8 DB	213.0 *
10 Sep 97	13	Week 10 DB	213.0 *
08 Oct 97	14	Week 12 DB	211.0 *
24 Oct 97	15	Week 16 DB	215.0 *
10 Nov 97	16	Taper End	216.0 *

DB = Double-Blind Phase (Phase 2)
* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 28 Feb 97. The patient's baseline weight was 177.0 lbs., which was out of range for his age. The dosage was gradually increased to 30 mg per day by 24 Apr 97.

On 28 Mar 97, after 29 days on study medication, the patient's weight was 189.0 lbs., which was not only out of range for his age but also an increase from baseline of potential clinical concern. Weight gain was reported as a moderate adverse experience on 24 Apr 97, after 56 days of study medication, when the patient weighed 180.0 lbs. The investigator did not consider that the adverse experience was serious and the patient continued in the study. The patient completed the open-label phase of the study and on 19 Jun 97 was randomized to double-blind paroxetine 30 mg per day. The adverse experience was considered resolved on 22 Aug 97, when the patient weighed 213.0 lbs.; his weight stabilized thereafter. The patient completed the study as planned on 24 Oct 97; at follow-up 17 days after the last dose of study medication, his weight was 216.0 lbs. The investigator considered that the weight increase was probably unrelated to study medication.

Concomitant Drugs	**Onset**	**Stopped**
Acetaminophen/Dextromethorphan/ Guaifenesin/Pseudophedrine	10 Jun 97	14 Jun 97
Multivitamin	01 Jul 97	Ongoing
Ibuprofen	14 Aug 97	18 Aug 97
Ibuprofen	16 Sep 97	18 Sep 97
Ibuprofen	08 Nov 97	08 Nov 97
Ibuprofen	13 Nov 97	14 Nov 97

Study 29060/453
PID 453.026.00137

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Weight Increase

Adverse Experience (Verbatim): Weight Gain (Weight Gain)

Screening Demography:
Age: 11 years
Date of birth: 04 Feb 86
Sex: Male
Weight: 120.0 lbs.
Race: Caucasian

Country: United States

Medical History: Questionable Arrhythmia on EKG 2-1/2 Years Ago, Asymptomatic

Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 12 Jun 97 **Stop:** 26 Jun 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 27 Jun 97 **Stop:** 23 Jul 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 24 Jul 97 **Stop:** 08 Aug 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 09 Aug 97 **Stop:** 08 Oct 97
Study Drug: Double-Blind Paroxetine 40 mg Given Orally
Start: 09 Oct 97 **Stop:** 22 Oct 97

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Mild Incontinence of Urine	02 Jul 97	08 Aug 97
Mild Tic: Exaggerated Grin and Grimace	02 Jul 97	24 Aug 97

Vital Signs of Potential Clinical Concern:

Date	**Visit**	**Week**	**Weight (lbs.)**
05 Jun 97	1	Screening	120.0
12 Jun 97	2	Baseline	122.0
26 Jun 97	3	Week 2	123.5
10 Jul 97	4	Week 4	122.5
24 Jul 97	5	Week 6	124.2
08 Aug 97	6	Week 8	122.0
05 Sep 97	7	Week 12	126.5
08 Oct 97	8	Week 16	133.8 *
21 Oct 97		Early Discontinuation	134.0 *

* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 12 Jun 97. The patient's baseline weight was 122.0 lbs., which was out of range for his age. The dosage was gradually increased to 40 mg per day and the patient completed the open-label phase of the study. On 09 Oct 97, the patient was randomized to double-blind paroxetine and continued on 40 mg per day. The patient's weight had been increasing and on 08 Oct 97, after 119 days of study medication, when the patient weighed 133.8 lbs., weight gain was reported as a mild adverse experience. This increased weight was not only out of range for his age but also an increase from baseline of potential clinical concern. The investigator did not consider that the weight gain was serious and the patient continued in the study. The adverse experience was considered resolved on 21 Oct 97. The patient withdrew from the study on 22 Oct 97, after 133 days of study medication, due to lack of efficacy. There was no taper period as the patient was continued on paroxetine. The investigator considered that the weight gain was possibly related to study medication.

Concomitant Drugs	**Onset**	**Stopped**
None		

Study 29060/453
PID 453.026.00285

Reason for Narrative: Patient with Vital Signs of Potential Clinical Concern

Vital Sign of Potential Clinical Concern: Significant Weight Increase

Adverse Experience (Verbatim): Weight Gain (Weight Gain)

Screening Demography:
Age: 8 years
Date of birth: 19 Jul 89
Sex: Female
Weight: 79.0 lbs.
Race: Caucasian

Country: United States

Medical History: Frequent UTIs
Out of Control Anxiety at Bedtime

Psychiatric History: None

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 04 Aug 97 **Stop:** 10 Aug 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 11 Aug 97 **Stop:** 18 Aug 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 19 Aug 97 **Stop:** 08 Sep 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 09 Sep 97 **Stop:** 16 Sep 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 17 Sep 97 **Stop:** 21 Sep 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 22 Sep 97 **Stop:** 30 Sep 97
Study Drug: Open-Label Paroxetine 30 mg Given Orally
Start: 01 Oct 97 **Stop:** 18 Oct 97
Study Drug: Open-Label Paroxetine 40 mg Given Orally
Start: 19 Oct 97 **Stop:** 05 Nov 97

Study Drug: Open-Label Taper End Medication Given Orally
Start: 06 Nov 97 **Stop:** 11 Nov 97

Adverse Experiences (Verbatim Term):	Onset:	Stopped:
Mild Allergies	25 Aug 97	06 Oct 97
Moderate Picking Scabs Constantly	31 Aug 97	08 Sep 97
Mild Irritable, Argumentative	04 Sep 97	08 Sep 97
Mild Insomnia	08 Sep 97	20 Sep 97
Moderate Irritable, Argumentative	08 Sep 97	Ongoing
Severe Picking at Scabs	09 Sep 97	15 Sep 97
Moderate Picking Scabs	15 Sep 97	30 Sep 97
Moderate Insomnia	01 Oct 97	Ongoing
Moderate Sinusitis	06 Oct 97	16 Oct 97

Vital Signs of Potential Clinical Concern:

Date	Visit	Week	Weight (lbs.)
31 Jul 97	1	Screening	79.0
04 Aug 97	2	Baseline	80.5
18 Aug 97	3	Week 2	80.5
02 Sep 97	4	Week 4	83.5
16 Sep 97	5	Week 6	82.0
30 Sep 97	6	Week 8	89.2 *
28 Oct 97	7	Week 12	90.5 *
11 Nov 97		Taper End	87.0 *

* Value of potential clinical concern

Vital Sign Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 04 Aug 97. The patient's baseline weight was 80.5 lbs., which was out of range for her age. The dosage was gradually increased to 30 mg per day by 19 Aug 97. The patient's weight had been increasing and was reported as a mild adverse experience starting on 02 Sep 97, when her weight was 83.5 lbs., after 30 days of study medication. The investigator did not consider that the weight gain was serious and the patient continued in the study. Her dosage was increased to 40 mg per day on 19 Oct 97. On 30 Sep 97, her weight was 89.2 lbs., which was not only out of range for her age but also an increase from baseline of potential clinical concern. She discontinued from the study on 11 Nov 97 due to lack of efficacy. The weight gain was considered resolved at the final visit on 11 Nov 97, when her weight was 87.0 lbs. The investigator considered that the weight gain was possibly related to study medication.

Concomitant Drugs	Onset	Stopped
Loratadine	25 Aug 97	31 Aug 97
Loratadine	02 Oct 97	06 Oct 97
Cefaclor	10 Oct 97	19 Oct 97

Table 15.22.1

Summary of Group Mean Vital Signs
Intention to Treat Population
Phase I: Open Label Treatment

Sitting Systolic Blood Pressure (mmHg)

	Mean	Median	Std Dev	Minimum	Maximum	N
Screening	107.4	108.0	12.24	72	149	328
Baseline	106.3	106.0	10.87	78	140	332
Week 2	106.4	106.0	11.48	78	152	332
Week 4	107.0	106.0	10.91	80	151	306
Week 6	106.8	106.0	11.53	80	154	291
Week 8	106.8	106.0	12.25	71	148	278
Week 12	107.2	107.0	11.31	80	145	263
Week 16	107.9	108.0	12.11	80	140	240

Table 15.22.1

Summary of Group Mean Vital Signs
Intention to Treat Population
Phase I: Open Label Treatment

Sitting Diastolic Blood Pressure (mmHg)

	Mean	Median	Std Dev	Minimum	Maximum	N
Screening	67.5	68.0	9.24	38	90	328
Baseline	67.3	68.0	8.73	46	90	332
Week 2	67.0	68.0	8.98	42	90	332
Week 4	67.8	68.0	8.58	49	95	306
Week 6	67.0	68.0	9.27	35	95	291
Week 8	67.5	68.0	9.82	40	102	278
Week 12	67.3	68.0	8.64	42	90	263
Week 16	67.4	68.0	9.01	43	90	240

Table 15.22.1

Summary of Group Mean Vital Signs
Intention to Treat Population
Phase I: Open Label Treatment

Sitting Heart Rate (bpm)

	Mean	Median	Std Dev	Minimum	Maximum	N
Screening	80.5	80.0	12.40	55	120	327
Baseline	80.3	80.0	12.98	55	124	333
Week 2	78.5	80.0	11.03	47	114	332
Week 4	79.5	80.0	10.93	54	111	305
Week 6	80.7	80.0	11.25	56	112	291
Week 8	80.9	80.0	11.59	56	118	277
Week 12	81.0	80.0	11.19	54	120	263
Week 16	81.8	80.0	11.89	52	117	238

Table 15.22.1

Summary of Group Mean Vital Signs
Intention to Treat Population
Phase I: Open Label Treatment

Weight (LB)

	Mean	Median	Std Dev	Minimum	Maximum	N
Screening	101.6	94.2	37.80	44	262	327
Baseline	102.0	95.7	37.60	44	264	329
Week 2	102.1	94.6	37.56	44	257	331
Week 4	103.0	95.0	37.77	45	258	306
Week 6	103.3	95.5	38.08	44	258	288
Week 8	102.6	95.0	36.72	45	257	276
Week 12	105.6	96.8	38.27	45	260	261
Week 16	107.4	100.0	38.43	45	259	240

Table 15.22.2

Summary of Group Mean Vital Signs
Intention to Treat Population
Phase II: Randomised Treatment

Sitting Systolic Blood Pressure (mmHg)

	Treatment Group											
	Paroxetine						Placebo					
	Mean	Median	Std Dev	Minimum	Maximum	N	Mean	Median	Std Dev	Minimum	Maximum	N
Randomisation Baseline	107.8	108.0	12.41	80	140	95	106.5	108.0	11.30	80	140	98
Week 2	106.5	104.0	13.52	70	153	91	106.7	108.0	11.79	82	145	97
Week 4	106.5	108.0	10.94	70	134	81	106.4	108.0	12.69	70	138	77
Week 6	107.1	108.0	10.64	85	135	66	107.0	105.5	12.64	78	142	52
Week 8	107.4	108.0	11.97	88	157	58	107.4	108.0	14.28	80	152	43
Week 10	107.3	108.0	12.98	78	141	53	106.5	105.0	12.03	82	136	35
Week 12	108.0	108.0	12.83	80	152	47	105.5	108.0	10.99	82	129	35
Week 16	110.1	110.0	11.61	94	156	41	108.4	110.0	10.96	78	135	30

Table 15.22.2

Summary of Group Mean Vital Signs
Intention to Treat Population
Phase II: Randomised Treatment

Sitting Diastolic Blood Pressure (mmHg)

	Treatment Group											
	Paroxetine						Placebo					
	Mean	Median	Std Dev	Minimum	Maximum	N	Mean	Median	Std Dev	Minimum	Maximum	N
Randomisation Baseline	66.6	66.0	8.56	43	88	95	67.3	68.0	9.31	48	90	98
Week 2	67.3	68.0	8.61	48	94	91	67.9	70.0	9.55	46	88	97
Week 4	66.9	68.0	9.02	49	85	81	66.5	68.0	8.29	40	82	77
Week 6	66.4	67.0	9.31	44	90	66	66.9	68.0	8.08	45	88	52
Week 8	68.2	67.0	9.30	49	87	58	68.6	68.0	8.59	48	94	43
Week 10	67.7	68.0	9.72	48	90	53	69.7	70.0	7.01	52	86	35
Week 12	68.4	70.0	8.53	53	85	47	68.4	70.0	9.67	48	90	35
Week 16	67.8	67.0	9.85	53	107	41	69.3	69.5	7.24	54	82	30

Table 15.22.2

Summary of Group Mean Vital Signs
Intention to Treat Population
Phase II: Randomised Treatment

Sitting Heart Rate (bpm)

	Treatment Group											
	Paroxetine						Placebo					
	Mean	Median	Std Dev	Minimum	Maximum	N	Mean	Median	Std Dev	Minimum	Maximum	N
Randomisation Baseline	81.8	80.0	13.02	58	117	95	81.7	80.0	10.59	53	106	97
Week 2	80.9	80.0	11.37	55	114	91	79.1	79.0	11.05	49	111	97
Week 4	81.5	80.0	10.43	64	110	81	79.7	80.0	10.77	56	101	77
Week 6	81.3	80.0	11.49	56	112	66	81.2	82.5	9.82	56	100	52
Week 8	82.9	84.0	11.59	60	108	58	79.5	79.0	10.86	56	108	43
Week 10	80.3	80.0	12.18	51	110	53	79.9	79.0	13.02	52	110	36
Week 12	81.2	81.5	11.33	60	108	46	82.2	84.0	10.88	58	104	35
Week 16	79.4	78.0	9.62	56	100	41	78.2	80.0	10.91	56	106	30

Table 15.22.2

Summary of Group Mean Vital Signs
Intention to Treat Population
Phase II: Randomised Treatment

Weight (LB)

	Treatment Group											
	Paroxetine						Placebo					
	Mean	Median	Std Dev	Minimum	Maximum	N	Mean	Median	Std Dev	Minimum	Maximum	N
Randomisation Baseline	109.1	101.0	40.61	45	259	95	104.2	97.5	38.18	53	254	98
Week 2	109.5	102.0	39.41	46	264	91	104.9	99.0	38.74	54	253	97
Week 4	110.7	101.2	39.86	46	267	81	107.2	100.8	37.14	56	203	77
Week 6	109.9	102.3	39.38	46	245	66	114.6	105.8	39.86	60	205	52
Week 8	110.6	101.7	39.01	46	244	56	113.9	107.1	40.16	63	202	43
Week 10	112.6	108.0	42.00	46	249	53	118.6	109.3	43.63	64	204	35
Week 12	115.0	110.0	42.18	50	248	47	114.1	109.2	37.22	65	202	35
Week 16	116.9	111.5	41.43	50	250	41	113.2	110.3	37.58	64	208	30

Table 15.23.1

Summary of Group Mean Vital Signs Baseline and Changes from Baseline
Intention to Treat Population
Phase I: Open Label Treatment

Sitting Systolic Blood Pressure (mmHg)

	Mean	Median	Std Dev	Minimum	Maximum	N
Baseline	106.3	106.0	10.87	78	140	332
Week 2	-0.1	0.0	9.39	-34	26	329
Week 4	0.5	0.0	9.84	-29	32	303
Week 6	0.1	0.0	10.13	-34	36	288
Week 8	0.5	0.0	10.62	-39	33	275
Week 12	1.0	0.0	10.38	-33	30	260
Week 16	1.7	0.0	11.61	-32	40	237

Table 15.23.1

Summary of Group Mean Vital Signs Baseline and Changes from Baseline
Intention to Treat Population
Phase I: Open Label Treatment

Sitting Diastolic Blood Pressure (mmHg)

	Mean	Median	Std Dev	Minimum	Maximum	N
Baseline	67.3	68.0	8.73	46	90	332
Week 2	-0.3	0.0	9.04	-32	28	329
Week 4	0.6	0.0	8.57	-26	23	303
Week 6	-0.5	0.0	9.11	-31	30	288
Week 8	-0.0	0.0	9.28	-36	25	275
Week 12	-0.4	0.0	9.07	-27	22	260
Week 16	-0.5	0.0	10.04	-33	24	237

Table 15.23.1

Summary of Group Mean Vital Signs Baseline and Changes from Baseline
Intention to Treat Population
Phase I: Open Label Treatment

Sitting Heart Rate (bpm)

	Mean	Median	Std Dev	Minimum	Maximum	N
Baseline	80.3	80.0	12.98	55	124	333
Week 2	-2.0	0.0	12.04	-46	40	330
Week 4	-0.6	0.0	12.25	-50	42	303
Week 6	0.6	0.0	12.92	-48	44	289
Week 8	0.7	0.0	11.90	-41	39	275
Week 12	1.0	0.0	13.09	-42	32	261
Week 16	2.0	0.0	13.46	-36	48	236

Table 15.23.1

Summary of Group Mean Vital Signs Baseline and Changes from Baseline
Intention to Treat Population
Phase I: Open Label Treatment

Weight (LB)

	Mean	Median	Std Dev	Minimum	Maximum	N
Baseline	102.0	95.7	37.60	44	264	329
Week 2	-0.1	0.0	2.22	-13	8	326
Week 4	0.2	0.0	2.92	-17	12	300
Week 6	0.7	1.0	3.43	-14	13	283
Week 8	1.2	1.0	3.64	-10	16	271
Week 12	3.2	3.0	4.77	-13	24	256
Week 16	4.4	4.0	5.72	-10	25	235

Table 15.23.2

Summary of Group Mean Vital Signs Baseline and Changes from Baseline
Intention to Treat Population
Phase II: Randomised Treatment

Sitting Systolic Blood Pressure (mmHg)

	Treatment Group											
	Paroxetine						Placebo					
	Mean	Median	Std Dev	Minimum	Maximum	N	Mean	Median	Std Dev	Minimum	Maximum	N
Randomisation Baseline	107.8	108.0	12.41	80	140	95	106.5	108.0	11.30	80	140	98
Week 2	-1.0	0.0	10.07	-26	25	91	0.4	0.0	10.92	-36	37	97
Week 4	-1.9	0.0	9.85	-31	18	81	-0.9	0.0	10.11	-25	30	77
Week 6	-0.7	0.0	10.37	-30	28	66	-1.2	-2.0	11.93	-26	33	52
Week 8	-0.9	-2.0	10.64	-25	29	58	1.0	0.0	9.95	-18	28	43
Week 10	-0.7	0.0	11.83	-30	23	53	0.0	0.0	10.75	-19	32	35
Week 12	-1.1	-2.0	11.98	-28	25	47	0.2	-1.0	9.99	-17	32	35
Week 16	1.2	1.0	13.97	-30	46	41	3.9	0.0	10.78	-22	30	30

Table 15.23.2

Summary of Group Mean Vital Signs Baseline and Changes from Baseline
Intention to Treat Population
Phase II: Randomised Treatment

Sitting Diastolic Blood Pressure (mmHg)

	Treatment Group											
	Paroxetine						Placebo					
	Mean	Median	Std Dev	Minimum	Maximum	N	Mean	Median	Std Dev	Minimum	Maximum	N
Randomisation Baseline	66.6	66.0	8.56	43	88	95	67.3	68.0	9.31	48	90	98
Week 2	0.7	0.0	8.46	-20	28	91	0.6	0.0	9.44	-23	30	97
Week 4	0.5	0.0	9.38	-20	28	81	-0.5	0.0	8.91	-22	22	77
Week 6	0.0	0.0	9.55	-22	27	66	-0.7	0.0	10.16	-22	22	52
Week 8	1.4	2.0	8.93	-20	24	58	1.4	2.0	8.84	-16	20	43
Week 10	1.1	0.0	9.69	-18	20	53	2.9	0.0	8.13	-14	25	35
Week 12	1.7	1.0	7.01	-14	18	47	2.6	2.0	10.34	-18	22	35
Week 16	1.4	0.0	10.84	-20	37	41	3.2	0.0	9.70	-21	20	30

Table 15.23.2

Summary of Group Mean Vital Signs Baseline and Changes from Baseline
Intention to Treat Population
Phase II: Randomised Treatment

Sitting Heart Rate (bpm)

	Treatment Group											
	Paroxetine						Placebo					
	Mean	Median	Std Dev	Minimum	Maximum	N	Mean	Median	Std Dev	Minimum	Maximum	N
Randomisation Baseline	81.8	80.0	13.02	58	117	95	81.7	80.0	10.59	53	106	97
Week 2	-0.9	0.0	10.79	-32	28	91	-3.0	-2.0	13.13	-36	34	96
Week 4	-0.9	0.0	11.02	-28	25	81	-1.7	-3.0	12.22	-28	34	76
Week 6	-0.7	0.0	11.16	-35	25	66	-1.0	0.0	10.10	-24	20	51
Week 8	0.3	0.0	13.83	-32	36	58	-0.9	-1.5	11.18	-26	27	42
Week 10	-2.8	-4.0	12.77	-29	25	53	-1.4	-2.0	11.26	-28	24	35
Week 12	-2.6	-1.0	13.34	-37	32	46	1.2	0.0	10.55	-24	20	34
Week 16	-3.3	-3.0	11.97	-34	24	41	-2.1	0.0	12.44	-29	18	29

Table 15.23.2

Summary of Group Mean Vital Signs Baseline and Changes from Baseline
Intention to Treat Population
Phase II: Randomised Treatment

Weight (LB)

	Treatment Group											
	Paroxetine						Placebo					
	Mean	Median	Std Dev	Minimum	Maximum	N	Mean	Median	Std Dev	Minimum	Maximum	N
Randomisation Baseline	109.1	101.0	40.61	45	259	95	104.2	97.5	38.18	53	254	98
Week 2	1.5	1.1	2.39	-6	10	91	1.4	1.0	2.79	-11	11	97
Week 4	2.3	2.4	3.05	-7	9	81	2.1	2.0	3.48	-10	11	77
Week 6	3.0	2.5	3.09	-5	13	66	3.1	2.3	4.61	-9	15	52
Week 8	3.6	3.0	3.42	-6	13	56	4.0	3.0	5.15	-7	19	43
Week 10	4.4	4.0	3.81	-5	16	53	4.8	5.1	5.50	-7	19	35
Week 12	5.3	4.8	4.39	-4	17	47	4.9	5.0	6.01	-8	18	35
Week 16	6.4	7.0	5.10	-4	18	41	5.5	4.2	7.04	-9	24	30

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Alanine Aminotransferase

		N	%
Screening	Low (Normal)	0	0
	High (Normal)	4	1.2
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	325	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	4	1.5
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	262	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	4	1.8
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	226	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Alkaline Phosphatase

		N	%
Screening	Low (Normal)	1	0.3
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	11	3.4
	Number of Patients with Assessment	325	100.0
Week 8	Low (Normal)	1	0.4
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	5	1.9
	Number of Patients with Assessment	262	100.0
Week 16	Low (Normal)	1	0.4
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	2	0.9
	Number of Patients with Assessment	226	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Aspartate Aminotransferase

		N	%
Screening	Low (Normal)	0	0
	High (Normal)	3	0.9
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	325	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	3	1.1
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	262	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	4	1.8
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	226	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Basophils

		N	%
Screening	Low (Normal)	0	0
	High (Normal)	3	0.9
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	322	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	3	1.1
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	264	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	227	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Blood Urea Nitrogen

		N	%
Screening	Low (Normal)	8	2.5
	High (Normal)	1	0.3
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	325	100.0
Week 8	Low (Normal)	4	1.5
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	262	100.0
Week 16	Low (Normal)	5	2.2
	High (Normal)	1	0.4
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	226	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Chloride

		N	%
Screening	Low (Normal)	1	0.3
	High (Normal)	4	1.2
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	325	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	6	2.3
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	262	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	226	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Creatinine

		N	%
Screening	Low (Normal)	10	3.1
	High (Normal)	2	0.6
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	325	100.0
Week 8	Low (Normal)	8	3.1
	High (Normal)	2	0.8
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	262	100.0
Week 16	Low (Normal)	6	2.7
	High (Normal)	1	0.4
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	226	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Eosinophils

		N	%
Screening	Low (Normal)	0	0
	High (Normal)	76	23.6
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	322	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	78	29.5
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	264	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	67	29.5
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	227	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Gamma Glutamyl Transferase

		N	%
Screening	Low (Normal)	0	0
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	323	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	262	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	226	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Glucose - Random

		N	%
Screening	Low (Normal)	14	4.3
	High (Normal)	28	8.6
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	325	100.0
Week 8	Low (Normal)	10	3.8
	High (Normal)	23	8.8
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	262	100.0
Week 16	Low (Normal)	2	0.9
	High (Normal)	17	7.5
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	226	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Hematocrit

		N	%
Screening	Low (Normal)	0	0
	High (Normal)	7	2.2
	Low (Extended)	16	5.0
	High (Extended)	0	0
	Number of Patients with Assessment	321	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	2	0.8
	Low (Extended)	16	6.1
	High (Extended)	0	0
	Number of Patients with Assessment	264	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	3	1.3
	Low (Extended)	19	8.5
	High (Extended)	0	0
	Number of Patients with Assessment	224	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Hemoglobin

		N	%
Screening	Low (Normal)	7	2.2
	High (Normal)	10	3.1
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	321	100.0
Week 8	Low (Normal)	9	3.4
	High (Normal)	3	1.1
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	264	100.0
Week 16	Low (Normal)	6	2.7
	High (Normal)	1	0.4
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	224	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Lactate Dehydrogenase

		N	%
Screening	Low (Normal)	0	0
	High (Normal)	10	3.1
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	323	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	18	6.9
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	262	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	11	4.9
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	226	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Lymphocytes

		N	%
Screening	Low (Normal)	14	4.3
	High (Normal)	12	3.7
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	322	100.0
Week 8	Low (Normal)	10	3.8
	High (Normal)	6	2.3
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	264	100.0
Week 16	Low (Normal)	10	4.4
	High (Normal)	10	4.4
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	227	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Mean Corpuscle Hemoglobin

		N	%
Screening	Low (Normal)	1	0.3
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	320	100.0
Week 8	Low (Normal)	2	0.8
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	2	0.8
	Number of Patients with Assessment	264	100.0
Week 16	Low (Normal)	1	0.4
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	224	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Mean Corpuscle Hemoglobin Concentration

		N	%
Screening	Low (Normal)	0	0
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	320	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	264	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	224	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Mean Corpuscle Volume

		N	%
Screening	Low (Normal)	0	0
	High (Normal)	0	0
	Low (Extended)	4	1.3
	High (Extended)	0	0
	Number of Patients with Assessment	320	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	0	0
	Low (Extended)	5	1.9
	High (Extended)	1	0.4
	Number of Patients with Assessment	264	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	0	0
	Low (Extended)	3	1.3
	High (Extended)	0	0
	Number of Patients with Assessment	224	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Monocytes

		N	%
Screening	Low (Normal)	0	0
	High (Normal)	29	9.0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	322	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	17	6.4
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	264	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	20	8.8
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	227	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Neutrophil Bands

		N	%
Screening	Low (Normal)	2	66.7
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	3	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	2	100.0
Week 16	Low (Normal)	4	80.0
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	5	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Phosphorus

		N	%
Screening	Low (Normal)	1	0.3
	High (Normal)	53	16.4
	Low (Extended)	0	0
	High (Extended)	1	0.3
	Number of Patients with Assessment	324	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	55	21.0
	Low (Extended)	0	0
	High (Extended)	2	0.8
	Number of Patients with Assessment	262	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	47	20.8
	Low (Extended)	0	0
	High (Extended)	1	0.4
	Number of Patients with Assessment	226	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Platelets

		N	%
Screening	Low (Normal)	3	0.9
	High (Normal)	3	0.9
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	321	100.0
Week 8	Low (Normal)	2	0.8
	High (Normal)	3	1.1
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	264	100.0
Week 16	Low (Normal)	2	0.9
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	224	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Potassium

		N	%
Screening	Low (Normal)	0	0
	High (Normal)	2	0.6
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	325	100.0
Week 8	Low (Normal)	1	0.4
	High (Normal)	2	0.8
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	262	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	226	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Red Blood Cell Count

		N	%
Screening	Low (Normal)	8	2.5
	High (Normal)	14	4.4
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	320	100.0
Week 8	Low (Normal)	9	3.4
	High (Normal)	5	1.9
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	264	100.0
Week 16	Low (Normal)	9	4.0
	High (Normal)	8	3.6
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	224	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Segmented Neutrophils

		N	%
Screening	Low (Normal)	3	0.9
	High (Normal)	22	6.8
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	322	100.0
Week 8	Low (Normal)	3	1.1
	High (Normal)	15	5.7
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	264	100.0
Week 16	Low (Normal)	2	0.9
	High (Normal)	15	6.6
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	227	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Sodium

		N	%
Screening	Low (Normal)	1	0.3
	High (Normal)	1	0.3
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	325	100.0
Week 8	Low (Normal)	1	0.4
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	262	100.0
Week 16	Low (Normal)	1	0.4
	High (Normal)	2	0.9
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	226	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Total Bilirubin

		N	%
Screening	Low (Normal)	0	0
	High (Normal)	2	0.6
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	325	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	1	0.4
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	262	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	226	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Total Neutrophils

		N	%
Screening	Low (Normal)	3	0.9
	High (Normal)	22	6.8
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	322	100.0
Week 8	Low (Normal)	3	1.1
	High (Normal)	15	5.7
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	264	100.0
Week 16	Low (Normal)	2	0.9
	High (Normal)	15	6.6
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	227	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = Total Protein

		N	%
Screening	Low (Normal)	0	0
	High (Normal)	21	6.5
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	324	100.0
Week 8	Low (Normal)	0	0
	High (Normal)	10	3.8
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	262	100.0
Week 16	Low (Normal)	0	0
	High (Normal)	7	3.1
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	226	100.0

Table 15.3.1

Number (%) of Patients with Abnormal Laboratory Results.
Intention to Treat Population
Phase I: Open Label Treatment

Parameter = White Blood Cell Count

		N	%
Screening	Low (Normal)	19	5.9
	High (Normal)	2	0.6
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	321	100.0
Week 8	Low (Normal)	20	7.6
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	264	100.0
Week 16	Low (Normal)	22	9.8
	High (Normal)	0	0
	Low (Extended)	0	0
	High (Extended)	0	0
	Number of Patients with Assessment	224	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Alanine Aminotransferase

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	2	4.1	0	0	2	2.4
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	49	100.0	35	100.0	84	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Alkaline Phosphatase

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	49	100.0	35	100.0	84	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Aspartate Aminotransferase

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	49	100.0	35	100.0	84	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	1	2.6	1	3.7	2	3.0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Basophils

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	50	100.0	35	100.0	85	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Blood Urea Nitrogen

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	2	4.1	0	0	2	2.4
	High (Normal)	1	2.0	0	0	1	1.2
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	49	100.0	35	100.0	84	100.0
Week 16	Low (Normal)	2	5.1	0	0	2	3.0
	High (Normal)	1	2.6	0	0	1	1.5
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Chloride

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	2	4.1	1	2.9	3	3.6
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	49	100.0	35	100.0	84	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	2	5.1	1	3.7	3	4.5
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Creatinine

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	3	6.1	3	8.6	6	7.1
	High (Normal)	1	2.0	0	0	1	1.2
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	49	100.0	35	100.0	84	100.0
Week 16	Low (Normal)	2	5.1	1	3.8	3	4.6
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	26	100.0	65	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Eosinophils

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	17	34.0	10	28.6	27	31.8
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	50	100.0	35	100.0	85	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	7	17.9	8	29.6	15	22.7
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Gamma Glutamyl Transferase

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	49	100.0	35	100.0	84	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	26	100.0	65	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Glucose - Random

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	2	4.1	1	2.9	3	3.6
	High (Normal)	10	20.4	3	8.6	13	15.5
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	49	100.0	35	100.0	84	100.0
Week 16	Low (Normal)	1	2.6	3	11.1	4	6.1
	High (Normal)	6	15.4	2	7.4	8	12.1
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Hematocrit

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	1	2.0	0	0	1	1.2
	Low (Extended)	5	10.0	2	5.7	7	8.2
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	50	100.0	35	100.0	85	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	5	12.8	0	0	5	7.6
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Hemoglobin

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	3	6.0	1	2.9	4	4.7
	High (Normal)	3	6.0	0	0	3	3.5
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	50	100.0	35	100.0	85	100.0
Week 16	Low (Normal)	3	7.7	0	0	3	4.5
	High (Normal)	1	2.6	0	0	1	1.5
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Lactate Dehydrogenase

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	3	6.1	1	2.9	4	4.8
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	49	100.0	35	100.0	84	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	3	7.7	2	7.4	5	7.6
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Lymphocytes

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	5	10.0	2	5.7	7	8.2
	High (Normal)	1	2.0	2	5.7	3	3.5
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	50	100.0	35	100.0	85	100.0
Week 16	Low (Normal)	1	2.6	0	0	1	1.5
	High (Normal)	2	5.1	1	3.7	3	4.5
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Mean Corpuscle Hemoglobin

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	1	2.0	0	0	1	1.2
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	50	100.0	35	100.0	85	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Mean Corpuscle Hemoglobin Concentration

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	50	100.0	35	100.0	85	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Mean Corpuscle Volume

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	3	6.0	0	0	3	3.5
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	50	100.0	35	100.0	85	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	2	5.1	0	0	2	3.0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Monocytes

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	4	8.0	1	2.9	5	5.9
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	50	100.0	35	100.0	85	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	1	2.6	2	7.4	3	4.5
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Neutrophil Bands

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	0	0	1	100.0	1	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	0	0	0	0	0	0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Phosphorus

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	1	2.0	0	0	1	1.2
	High (Normal)	8	16.3	7	20.0	15	17.9
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	1	2.0	1	2.9	2	2.4
	Number of Patients with Assessment	49	100.0	35	100.0	84	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	4	10.3	6	22.2	10	15.2
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	2	5.1	1	3.7	3	4.5
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Platelets

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	2	4.0	0	0	2	2.4
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	50	100.0	35	100.0	85	100.0
Week 16	Low (Normal)	2	5.1	0	0	2	3.0
	High (Normal)	1	2.6	0	0	1	1.5
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Potassium

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	49	100.0	35	100.0	84	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	1	3.7	1	1.5
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Red Blood Cell Count

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	2	4.0	2	5.7	4	4.7
	High (Normal)	3	6.0	1	2.9	4	4.7
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	50	100.0	35	100.0	85	100.0
Week 16	Low (Normal)	3	7.7	1	3.7	4	6.1
	High (Normal)	1	2.6	1	3.7	2	3.0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Segmented Neutrophils

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	3	6.0	2	5.7	5	5.9
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	50	100.0	35	100.0	85	100.0
Week 16	Low (Normal)	1	2.6	0	0	1	1.5
	High (Normal)	3	7.7	1	3.7	4	6.1
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Sodium

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	49	100.0	35	100.0	84	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Total Bilirubin

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	1	2.9	1	1.2
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	49	100.0	35	100.0	84	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	26	100.0	65	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Total Neutrophils

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	3	6.0	2	5.7	5	5.9
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	50	100.0	35	100.0	85	100.0
Week 16	Low (Normal)	1	2.6	0	0	1	1.5
	High (Normal)	3	7.7	1	3.7	4	6.1
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = Total Protein

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	0	0	0	0	0	0
	High (Normal)	2	4.1	0	0	2	2.4
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	49	100.0	35	100.0	84	100.0
Week 16	Low (Normal)	0	0	0	0	0	0
	High (Normal)	1	2.6	0	0	1	1.5
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Table 15.3.2

Number (%) of Patients with Abnormal Laboratory Results
Intention to Treat Population
Phase II: Randomised Treatment

Parameter = White Blood Cell Count

		Treatment Group					
		Paroxetine		Placebo		Total	
		N	%	N	%	N	%
Week 8	Low (Normal)	4	8.0	3	8.6	7	8.2
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	50	100.0	35	100.0	85	100.0
Week 16	Low (Normal)	1	2.6	1	3.7	2	3.0
	High (Normal)	0	0	0	0	0	0
	Low (Extended)	0	0	0	0	0	0
	High (Extended)	0	0	0	0	0	0
	Number of Patients with Assessment	39	100.0	27	100.0	66	100.0

Confidential

SmithKline Beecham

Paroxetine

BRL-029060

Table 15.3.2a. Patient Narratives: Laboratory Results of Potential Clinical Concern

453

xxxxx x. xxxxxxxxx, R.Ph., M.S.*
xxxxxx x. xxxxx, Ph.D.

*CNS, PMTU

SB Document Number: BRL-029060/RSD-100W8C/1

Study 29060/453
PID 453.002.00259

Reason for Narrative: Patient with Laboratory Value of Potential Clinical Concern

Laboratory Value of Potential Clinical Concern: High (Extended) Phosphorus, Inorganic

Adverse Experience (Verbatim): Hyperphosphatemia (Elevated Phosphorus Inorganic Level)

Screening Demography:
Age: 13 years
Date of birth: 28 Feb 84
Sex: Male
Weight: 108.0 lbs.
Race: Caucasian

Country: United States

Medical History:
Exercise-Induced Asthma
Headache Once a Week
Mouth Pain Due to Orthodontia
Sulfa Drug Allergy
Fractured Wrist

Psychiatric History: Attention Deficit/Hyperactivity Disorder, Suspected

Study Diagnosis: Obsessive-Compulsive Disorder

Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 02 Oct 97 **Stop:** 07 Nov 97
Study Drug: Open-Label Paroxetine 00 mg Given Orally
Start: 08 Nov 97 **Stop:** 11 Nov 97
Study Drug: Open-Label Paroxetine 10 mg Given Orally
Start: 12 Nov 97 **Stop:** 26 Nov 97
Study Drug: Open-Label Paroxetine 20 mg Given Orally
Start: 27 Nov 97 **Stop:** 21 Jan 98
Study Drug: Double-Blind Placebo (Down Titration) Given Orally (Per Protocol)
Start: 22 Jan 98 **Stop:** 28 Jan 98
Study Drug: Double-Blind Placebo Given Orally
Start: 29 Jan 98 **Stop:** 03 Jun 98

Study Drug: Double-Blind Taper End Medication Given Orally
Start: 20 May 98 **Stop:** 03 Jun 98

Adverse Experiences (Verbatim Term):	**Onset:**	**Stopped:**
Severe Rash	08 Oct 97	09 Oct 97
Severe Urticaria	08 Oct 97	09 Oct 97
Mild Exercise-Induced Wheezing (Respiratory)	02 Apr 98	02 Apr 98

Laboratory Value of Potential Clinical Concern:

Date	**Visit**	**Week**	**Phosphorus Inorganic** Reference range: 2.5–4.5 mg/dL
24 Sep 97	1	Screening	5.8
26 Nov 97	6	Week 8	5.7
21 Jan 98	8	Week 16	5.2
23 Mar 98	12	Week 8 DB	5.3
19 May 98	15	Week 16 DB	8.0 *
01 Jun 98		Follow-up	5.5

DB = Double-Blind Phase (Phase 2)
* Value of potential clinical concern

Laboratory Value Remarks:

This patient started open-label study medication, 10 mg paroxetine per day, on 02 Oct 97. The patient's phosphorus level at screening was 5.8 mg/dL (reference range 2.5–4.5 mg/dL). The dosage was gradually increased to 20 mg per day and the patient completed the open-label phase of the study. On 22 Jan 98, the patient was randomized to double-blind placebo and completed the study as planned. At the final visit of the double-blind period, on 19 May 98, 118 days after the last dose of study medication, hyperphosphatemia was reported as a moderate adverse experience. The value at that time was 8.0 mg/dL, which was flagged as being of potential clinical concern and was also an increase from baseline of potential clinical concern. The investigator did not consider that the hyperphosphatemia was serious and the patient completed the study as planned. At study end, the patient was prescribed paroxetine. At follow-up on 01 Jul 98, the patient's phosphorus value was 5.5 mg/dL, still elevated above the reference range but considered by the investigator to be of no clinical concern. The investigator considered the adverse experience resolved on 04 Jul 98. The investigator considered that the adverse experience was probably unrelated to study medication.

Concomitant Drugs	Onset	Stopped
Paracetamol	01 Jan 95	Ongoing
Salbutamol	22 Apr 98	22 Apr 98

Table 15.4.1

Number (%) of Patients with Positive Drug Screens
Intention to Treat Population
Phase I: Open Label Treatment

	N	%
Amphetamines	1	0.3
Barbiturates		
Benzodiazepines	2	0.6
Cannabinoids	2	0.6
Cocaine		
Ethanol in Urine		
Methadone		
Methaqualone		
Opiates	2	0.6
Phencyclidine		
Propoxyphene		
Overall No. of Patients with Positive Screen	7	2.1
No. of Non Missing Patients in Group	332	100.0
Missing	3	

Table 15.4.2

Number (%) of Patients with Positive Drug Screens
Intention to Treat Population

Phase II: Randomised Treatment

	Treatment Group					
	Paroxetine		Placebo		Total	
	N	%	N	%	N	%
Amphetamines						
Barbiturates						
Benzodiazepines						
Cannabinoids	2	2.7			2	1.4
Cocaine						
Ethanol in Urine						
Methadone						
Methaqualone						
Opiates	2	2.7			2	1.4
Phencyclidine						
Propoxyphene						
Overall No. of Patients with Positive Screen	4	5.4	0	0.0	4	2.8
No. of Non Missing Patients in Group	74	100.0	68	100.0	142	100.0
Missing	21		30		51	

13 Data Source Figures

Confidential

SmithKline Beecham

Paroxetine

BRL-029060

CY-BOCS Score Mean Change from Randomisation Baseline and Standard Errors Intention to Treat Population Phase II: Randomised Treatment

453

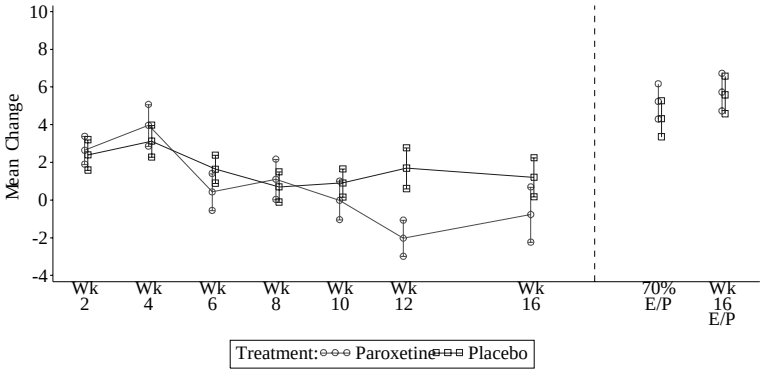
Figure 14.2.1

SB Document Number: BRL-029060/CGR-102C8R/1

Paroxetine - Protocol : 453

Figure 14.2.1

CY-BOCS Score
Mean Change from Randomisation Baseline and Standard Errors
Intention to Treat Population
Phase II: Randomised Treatment



DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]PL_CYBOC.SAS (04DEC98 09:53)

Confidential

SmithKline Beecham

Paroxetine

BRL-029060

Percentages of Patients with a >=25% from Baseline in CY-BOCS Intention to Treat Phase II: Randomised

453

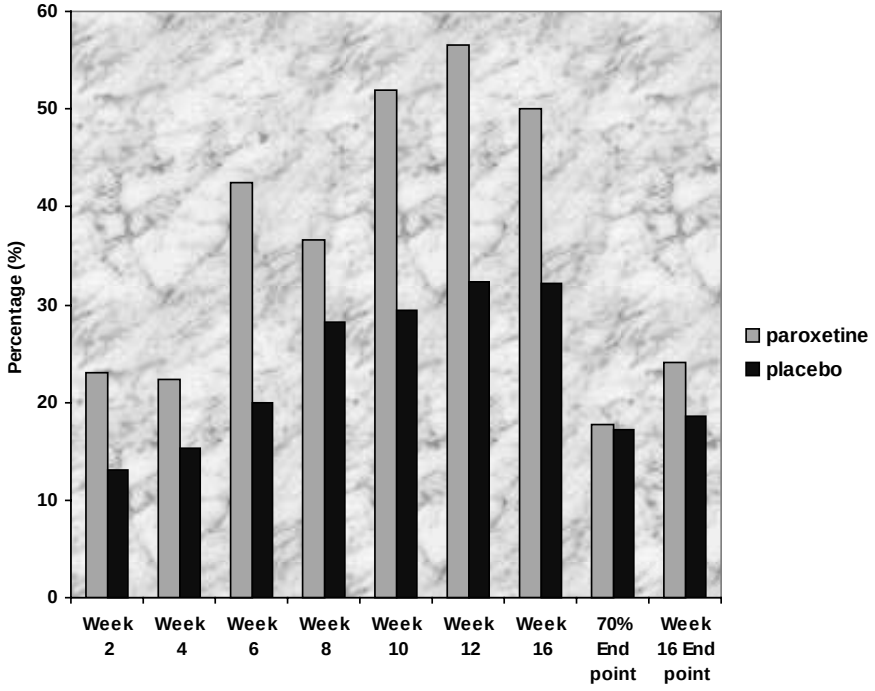
Figure 14.2.4

SB Document Number: BRL-029060/CGR-102C8S/1

Paroxetine - Protocol: 453

Figure 14.2.4

Percentages of Patients with a >=25% Reduction from Baseline in CY-BOCS Score
Intention to Treat Population
Phase II: Randomised Treatment



Confidential

SmithKline Beecham

Paroxetine

BRL-029060

Percentages of Patients Based on the CGI Global Intention to Treat Phase II: Randomised

453

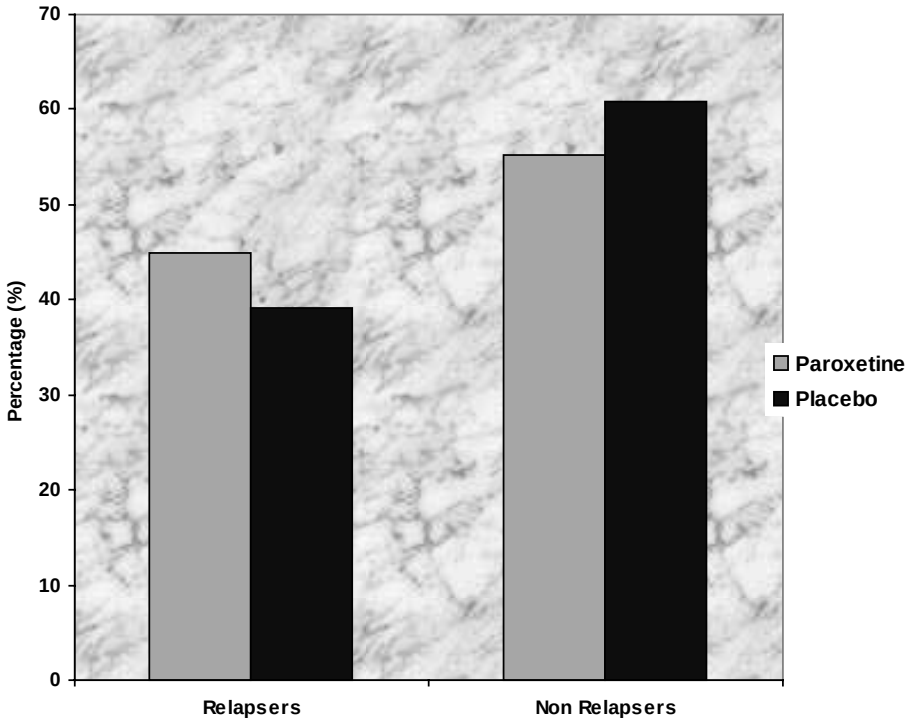
Figure 14.11.2

SB Document Number: BRL-029060/CGR-102C8T/1

Paroxetine - Protocol: 453

Figure 14.11.2

Percentages of Patients Relapsing
Based on the CGI Global Improvement Item
Intention to Treat Population
Phase II: Randomised Treatment



Confidential

SmithKline Beecham

Paroxetine

BRL-029060

Figure 14.12.2

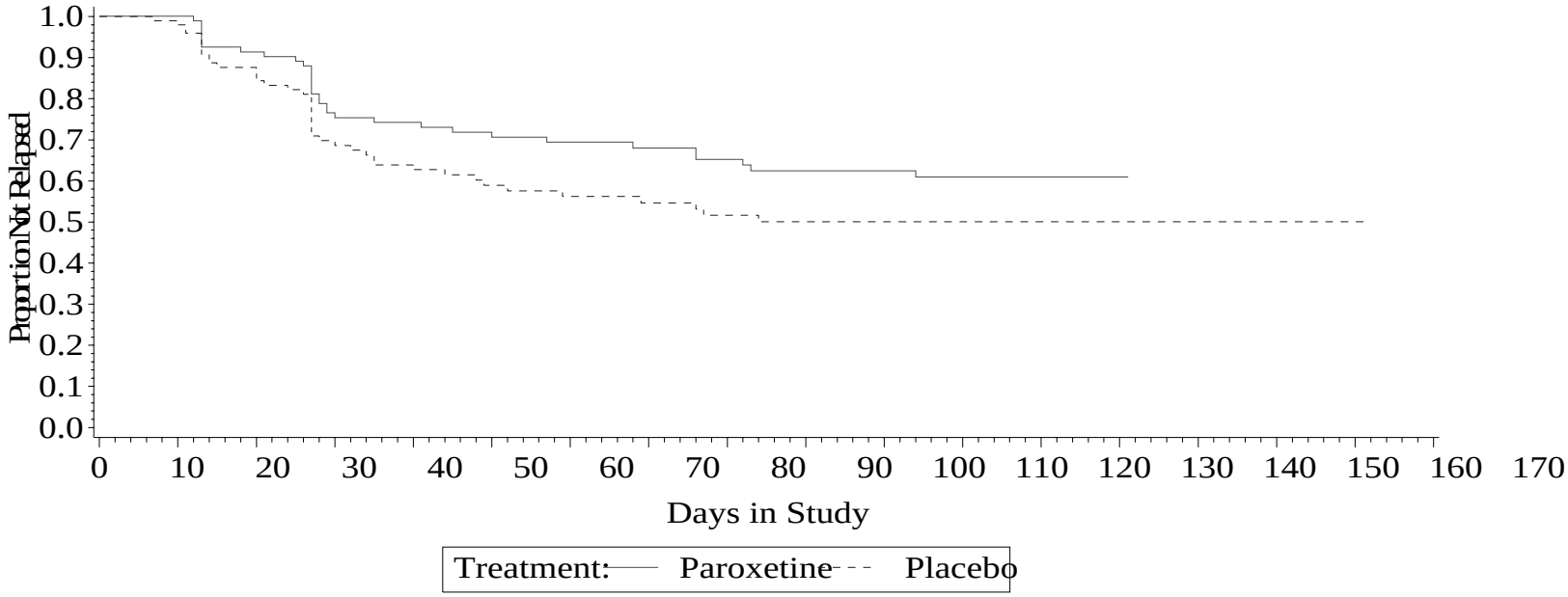
453

SB Document Number: BRL-029060/RSD-101637/1

Paroxetine - Protocol: 453

Figure 14.12.2

Time to Relapse
Kaplan-Meier Survival Curve
Intention to Treat Population
Phase II: Randomised Treatment



DISK$STATS4:[STATS_GROUP.SBBRL29060.453.CODE]SURVIVAL.SAS (05MAR99 14:29)

14 Data Source Tables: Errata

Confidential

SmithKline Beecham

Paroxetine

BRL-029060

Data Source Tables: Errata

453

SB Document Number: BRL-029060/RSD-10162Z/1

Data Source Table: Errata

Data Source Table: Errata 1

DST 14.8.2 shows 232/329 (70.5%) patients were responders at the Week 16 Endpoint. However, 6 of the 232 patients included in the Cell Index for Table 14.8.2 met only one of the response criteria, not both (according to the cell indices for DSTs 14.31.1 [patients with a CGI Global Improvement Item Score of 1 or 2 at Week 16 Endpoint] and 14.24.1 [patients with at least a 25% reduction from baseline in CY-BOCS Total Score]). In each of these 6 cases, the patient in question had at least a 25% reduction in CY-BOCS Total Score but did not have a CGI Global Improvement Item Score of 1 or 2 at Week 16 Endpoint. Therefore the actual number of patients meeting both criteria at Week 16 Endpoint is 226 (68.7%), as indicated in in-text table 28 of this report. The 6 PIDs involved are:

453.011.00202, 453.017.00499, 453.019.00303, 453.022.00119, 453.024.00178, 453.025.00183

All six of these patients did not complete Phase I, and therefore were ineligible for consideration to continue into Phase II anyway, irregardless of whether they met one or both of the protcol defined response criteria. Consequently, the study results and any conclusions drawn therefrom are unaffected by these errors.

Data Source Table: Errata 2

PID 453.022.00099 is incorrectly omitted from DST 14.8.1 (the Number [%] of responders at Week). Therefore, the actual number of responders at Week 16 is 207 instead of 206. This patient met both of the response criteria at his/her Week 16 visit and was enrolled in Phase II by the investigator. However, because the Week 16 visit was conducted early (i.e., outside of the window specified in Section 3.11.9, Defined Visit Timepoints) the patient was programatically excluded from the list of responders.

Final Statistical Appendix

Confidential

SmithKline Beecham

Paroxetine

BRL-029060

Final Statistical Appendix

453

xxx xxxxxxxxx, Pg.D.*

*Biostatistics and Data Sciences

SB Document Number: BRL-029060/RSD-10135B/1

Final Statistical Appendix Table of Contents

Final Statistical Appendix List of Tables

1 Investigation of Data

The following prospectively defined covariates were assumed to be associated with response:

- Age at onset of OCD symptoms (in years)
- CY-BOCS total score at randomisation baseline

To assess the relationship between the covariates above and the response variable (change from randomisation baseline in CY-BOCS total score), both covariates were plotted against response, at week 8, week 16, 70% endpoint (week 4) and week 16 endpoint, using the Phase II intention-to-treat (ITT) population.

The association between the pre-defined covariates and the response variable was investigated for linearity. At most timepoints, both covariates demonstrated evidence of inverse linear trends with the response variable i.e. patients with higher age at onset of OCD symptoms tended to have larger decreases from randomisation baseline as did patients with higher randomisation baseline CY-BOCS total scores. Therefore these terms were fitted as continuous covariates in the model.

The following prospectively defined covariate was assumed to be associated with relapse:

- CY-BOCS total score at randomisation baseline

The association between this pre-defined covariate and relapse was not investigated for linearity, due to the binary nature of the relapse variable.

2 Baseline Testing

Within SB-Biometrics, it is our current policy not to statistically test for treatment differences in baseline parameters. Altman (1985) argues that the use of statistical tests is inappropriate because they only assess the correctness of the randomisation. Using purely statistical tests could therefore be misleading, although it could be argued that performing tests at baseline provides a useful tool for the statistician. 'Significant' differences could highlight potential problems and focus attention on particular parameters which may have been overlooked by eye. Therefore as long as it is remembered that baseline tests can miss important differences and highlight unimportant ones, baseline tests do not pose any great problems.

The similarity (or otherwise) of the two treatment groups at randomisation baseline, with respect to certain demographic characteristics and randomisation baseline CY-BOCS total score, was investigated using formal hypothesis testing. The χ^2 test or Student's t-test (assuming homogeneity of within-group variances) were used, depending on whether the variable was categorical or continuous respectively. Testing was two-tailed and was carried out on the Phase II intention-to-treat (ITT) population.

Variables tested were age in years, age group (<12 or ≥12 years old), sex (male or female), race (white or non-white), age at onset of OCD symptoms in years and randomisation baseline CY-BOCS total score. The following table shows the results of these analyses:

Table 1 Testing of Homogeneity of Treatment Groups at Randomisation Baseline – Continuous Variables, Phase II ITT Population

	Paroxetine			Placebo			P-value
	N	Mean	S.D.	N	Mean	S.D.	
Age (in Years)	95	11.79	2.564	98	11.63	2.880	0.690
Age at Onset of OCD Symptoms (in Years)	95	9.70	2.989	98	9.70	3.294	0.998
Randomisation Baseline CY-BOCS Total Score	92	9.93	6.460	98	9.59	6.061	0.706

Table 2 Testing of Homogeneity of Treatment Groups at Randomisation Baseline – Categorical Variables, Phase II ITT Population

	Paroxetine		Placebo		P-value
	Proportion	%	Proportion	%	
Age Group (≥12 years old)	46/95	48.42	51/98	52.04	0.615
Sex (male)	47/95	49.47	58/98	59.18	0.176
Race (white)	87/95	91.58	89/98	90.82	0.852

No statistically significant differences between treatment groups were observed for any of these variables at randomisation baseline.

3 Centre Groupings

A total of 27 centres recruited patients into Phase I of this study. Of these, 25 centres entered patients into Phase II. The number of Phase II ITT patients available for the primary efficacy parameter (proportion of patients who relapse during Phase II) by centre, are shown in the table below:

Table 3 Number of Patients by Centre, Phase II ITT Population

Centre	Number of patients per centre		
	Paroxetine	Placebo	Total
001	2	2	4
002	6	5	11
004	1	0	1
005	4	3	7
006	7	7	14
007	3	3	6
008	5	5	10
009	0	1	1
010	0	1	1
011	7	8	15
012	1	1	2
013	2	2	4
015	4	4	8
016	2	2	4
017	8	10	18
018	6	4	10
019	3	5	8
020	4	6	10
021	5	4	9
022	5	5	10
023	7	7	14
024	4	2	6
025	4	5	9
026	2	2	4
027	3	4	7
Total	95	98	193

Because some centres had randomised less than 8 patients to study treatment, centres were grouped into centre groups (according to the algorithm given in section 4.3 of the RAP) for the purpose of the efficacy analyses as follows:

Centres were grouped by ranking all centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients being ranked one. Centres with equal numbers of patients were ranked depending on centre number, the lowest centre number being allocated the lowest rank. The centre with the lowest rank was combined with the centre with the highest rank. The centre with the second lowest rank was combined with the centre with the second largest rank and so on. This procedure was repeated until every combined centre consisted of at least 8 patients.

The number of Phase II ITT patients available for the primary efficacy parameter (proportion of patients who relapse during Phase II) by centre group, are shown in the table below:

Table 4 Number of Patients by Centre Group, Phase II ITT Population

Centre group	Number of patients per centre group		
	Paroxetine	Placebo	Total
001/002	8	7	15
004/017	9	10	19
005/021	9	7	16
006/012	8	8	16
007/008	8	8	16
009/011	7	9	16
010/023	7	8	15
013/022	7	7	14
015	4	4	8
016/020	6	8	14
018/026	8	6	14
019/027	6	9	15
024/025	8	7	15
Total	95	98	193

4 Modelling Process

The primary inferences concerning the efficacy of paroxetine were made using the last observation carried forward dataset (LOCF) of the Phase II ITT population, defined as the last on-drug assessment during the randomised treatment phase. Only assessments performed after the randomisation baseline were carried forward.

For the primary efficacy variable, analysis of proportion of patients who relapsed was determined throughout the entire Phase II period.

For the secondary variables, two additional datasets to the study endpoint dataset were considered to ensure the robustness of the results:

1. an LOCF dataset at the latest timepoint (visit) where at least 70% of the patients in each treatment group remained in the study (defined as the 70% endpoint). This dataset was only created if at least 30% of the patients withdrew prior to week 16.

2. an observed cases (OC) dataset at 8 and 16 weeks.

No statistical analyses were performed for the open label treatment phase (Phase I) of the study.

The Phase II ITT population consisted of all patients who were enrolled into the study, who received at least one-dose of randomised treatment and for whom at least one post-randomisation baseline evaluation was available. Patients were included in this population regardless of whether the entry criteria were fulfilled or the protocol was violated. The number of patients available for analysis in the Phase II ITT population varies between parameters and timepoints depending on whether certain assessments were performed.

4.1 Analysis of Binary Response Data

The proportion of patients relapsing (see definition in section 5.1) was analysed using logistic regression (SAS/PROC GENMOD), allowing for centre group effects. The effect of adding treatment by centre group interaction into the model was assessed. If the treatment by centre group interaction was not significant ($p \geq 0.1$), it was dropped from the model and an overall estimate of the treatment differences was calculated. If the treatment by centre group interaction was

significant ($p < 0.1$), the reason for its presence was explored. If one or more reasons could be found, then these were adjusted for in the analysis. If no reason could be found, then the results were presented by centre group.

The data were also analysed allowing for both centre group effects and the effects of the covariate for relapse specified in section 1. The effect of adding the treatment by centre group interaction into the model was assessed with the covariate and the effect of centre group in the model

Odds ratios, associated 95% confidence intervals and p-values, all adjusted for terms in the final model, were presented. A bar chart to show proportion of patients relapsing in each treatment group, was also presented.

To assess the possible effect of observations with a large influence on the model, the following diagnostic plots were produced and examined:

- Change in treatment group β (standardised difference in regression estimates) versus predicted value
- Change in χ^2 goodness-of-fit value versus predicted value
- Change in C (a confidence interval displacement diagnostic) versus predicted value
- Standardised residual versus centre group.

4.2 Analysis of Normally-Distributed Response Data

Provided the underlying assumptions were satisfied, the change from randomisation baseline in total CY-BOCS score was analysed by analysis of variance (SAS/PROC GLM) allowing for centre group effects. The effect of adding treatment by centre group interaction into the model was assessed. If the treatment by centre group interaction was not significant ($p \geq 0.1$), it was dropped from the model and an overall estimate of the treatment difference was calculated. If the treatment by centre group interaction was significant ($p < 0.1$), the reason for its presence was explored. If one or more reasons could be found, then these were adjusted for in the analysis. If no reason could be found, then the results were presented by centre group.

The data were also analysed allowing for both centre group effects and the effects of the covariates specified for response in section 1. The effect of adding treatment by centre group interaction into the model was assessed with the covariates and the effect of centre group in the model.

The results from the analyses were presented as the point estimate and 95% confidence interval (adjusted for terms in the model) for the difference between paroxetine and the placebo group.

The assumptions of normality and homogeneity of variance were assessed using diagnostic plots (studentised residuals versus normal order scores and studentised residuals versus predicted values). If the data differed markedly from a normal distribution, then a non-parametric analysis was performed.

4.3 Other Analyses

Time to relapse was estimated using Kaplan-Meier estimates via the PROC LIFETEST SAS procedure. Differences between treatment groups in distributions of time to relapse were tested using the Log-Rank test. The Log-Rank test compares the observed times of an event on two treatments with the times expected if the two treatments were equivalent.

Kaplan-Meier survival curves for each treatment group were presented.

5 Primary Efficacy Variable

5.1 Proportion of Patients Relapsing During the Randomisation Phase (Phase II)

Relapse was defined as a patient who met any of the following criteria:

1) An increase in CGI Global Improvement score by 1 point for 2 consecutive Phase II visits

2) An increase in CGI Global Improvement score by ≥ 2 points at any single Phase II visit

3) A CGI Global Improvement score of 5 or greater during Phase II.

The proportion of patients relapsing during the randomisation phase, was analysed as described in section 4.1. The table below summarises the results of these analyses for the Phase II ITT dataset:

Table 5 Proportion of Patients Relapsing During the Randomisation Phase, Phase II ITT Population (Model Including Centre Group only)

Paroxetine Proportion of relapsers	Placebo Proportion of relapsers	Adjusted Odds Ratio	95% C.I. (Paroxetine/ Placebo)	P-value
33/95 (34.7%)	**43/98 (43.9%)**	**0.62**	**(0.34, 1.16)**	**0.136**

(An odds ratio <1 implies a lower proportion of relapsers with paroxetine)

Table 6 Proportion of Patients Relapsing During the Randomisation Phase, Phase II ITT Population (Model Including Centre Group and Covariate)

Paroxetine Proportion of relapsers	Placebo Proportion of relapsers	Adjusted Odds Ratio	95% C.I. (Paroxetine/ Placebo)	P-value
33/95 (34.7%)	**43/98 (43.9%)**	**0.60**	**(0.32, 1.13)**	**0.114**

(An odds ratio <1 implies a lower proportion of relapsers with paroxetine)

No statistically significant treatment difference was observed using either model.

The assessment of treatment by centre group interaction could not be performed as model convergence problems were encountered due to the small numbers of patients per treatment group/centre group combination.

Confirmatory Analyses - Per protocol (PP) population

The analysis described in section 4.1 was repeated for the PP dataset and the results can be found in the table below:

Table 7 Proportion of Patients Relapsing During the Randomisation Phase, Phase II PP Population (Model Including Centre Group only)

Paroxetine Proportion of relapsers	Placebo Proportion of relapsers	Adjusted Odds Ratio	95% C.I. (Paroxetine/ Placebo)	P-value
26/81 (32.1%)	**36/83 (43.4%)**	**0.59**	**(0.30, 1.17)**	**0.133**

(An odds ratio <1 implies a lower proportion of relapsers with paroxetine)

Table 8 Proportion of Patients Relapsing During the Randomisation Phase, Phase II PP Population (Model Including Centre Group and Covariate)

Paroxetine Proportion of relapsers	Placebo Proportion of relapsers	Adjusted Odds Ratio	95% C.I. (Paroxetine/ Placebo)	P-value
26/81 (32.1%)	**36/83 (43.4%)**	**0.56**	**(0.28, 1.12)**	**0.103**

(An odds ratio <1 implies a lower proportion of relapsers with paroxetine)

No statistically significant treatment difference was observed using either model.

The assessment of treatment by centre group interaction could not be performed as model convergence problems were encountered due to the small numbers of patients per treatment group/centre group combination.

The confirmatory analyses backed up the results from the Phase II ITT dataset, indicating that there was no evidence of treatment differences between paroxetine and placebo in the proportion of patients relapsing during the randomisation phase.

6 Secondary Efficacy Variables

6.1 Time to Relapse During the Randomisation Phase

Time to relapse was analysed using the methods described in section 4.3. The table below summarises the results of this analysis for the Phase II ITT dataset:

Table 9 Time to Relapse During the Randomisation Phase, Phase II ITT Population

	Paroxetine	Placebo
Number of patients	95	98
Number of patients relapsing	33	43
Q1 (days)	35	27
Median (days)	ND	ND
Q3 (days)	ND	ND
Hazard ratio (paroxetine/placebo)	1.5	
95% C.I.	0.9, 2.3	
p-value	0.104	

ND – Not Defined (due to high proportion of observations being censored)

(A hazard ratio >1 implies a higher risk of relapse on placebo)

No statistically significant treatment difference was observed.

It is worth noting that the time of relapse was not recorded specifically in the CRF. Therefore the visit date at which relapse was first discovered was used as the closest approximation. This has probably lead to an overestimate of the actual time to relapse. However, this problem is likely to occur to an equal extent in both treatment groups, but there is a potential for the treatment difference to be diluted as early benefit may be lost by the time of a later visit.

6.2 Change from Randomisation Baseline in CY-BOCS Total Score

Change from randomisation baseline in the CY-BOCS total score was assessed using the methods described in section 4.2 at week 8, week 16, 70% endpoint

(week 4) and week 16 endpoint. The table below summarises the results of these analyses for the Phase II ITT dataset:

Table 10 Change from Randomisation Baseline in CY-BOCS Total Score, Phase II ITT Population (Model Including Centre Group only)

	Paroxetine adjusted mean	Placebo adjusted mean	Difference in adjusted means	95% C.I. (Paroxetine – Placebo)	P-value
Week 8	0.322	1.459	-1.14	(-3.35, 1.08)	0.310
Week 16	-0.091	0.716	-0.81	(-3.73, 2.12)	0.583
70% Endpoint	2.176	6.189	-4.01	(-6.30, -1.72)	0.001*
Week 16 Endpoint	**3.485**	**6.864**	**-3.38**	**(-5.88, -0.88)**	**0.008***

(A negative difference implies a greater improvement with paroxetine)

* - *significant at the 5% level*

Table 11 Change from Randomisation Baseline in CY-BOCS Total Score, Phase II ITT Population (Model Including Centre Group and Covariates)

	Paroxetine adjusted mean	Placebo adjusted mean	Difference in adjusted means	95% C.I. (Paroxetine – Placebo)	P-value
Week 8	0.431	1.350	-0.92	(-3.02, 1.18)	0.387
Week 16	-0.028	0.727	-0.75	(-3.73, 2.22)	0.613
70% Endpoint	2.270	6.170	-3.90	(-6.11, -1.70)	0.001*
Week 16 Endpoint	**3.546**	**6.867**	**-3.32**	**(-5.76, -0.88)**	**0.008***

(A negative difference implies a greater improvement with paroxetine)

* - *significant at the 5% level*

A statistically significant treatment difference was observed at 70% endpoint (week 4) and at week 16 endpoint using both models. However, this was not the case at the week 8 and week 16 observed case timepoints.

The inconsistency between observed case and endpoint (last observation carried forward) results above are due to patients withdrawing early who tend to have a large positive increase in CY-BOCS total score, particularly in the placebo group (e.g. at week 2, the mean change from randomisation baseline for the observations carried forward to week 4 is 6.7 for the paroxetine group and 10.9 for placebo). These values, when carried forward, inflate the 70% endpoint (week 4) and week 16 endpoint point estimates. These values only contribute to the endpoint

analyses, leaving the observed case analyses with fewer patients and therefore reduced power to detect differences between treatment groups. This is particularly noticeable in this study, due to the high withdrawal rate.

Examining the residual plots exposed an outlier in the placebo group at week 8 (PID = 453.011.00323). The analysis was performed again, but this time excluding this patient from the model. However, this did not alter the conclusions reached above.

The assessment of treatment by centre group interaction was performed both with and without the covariates included in the model. The results are presented in the table below:

Table 12 Interactions for Change from Randomisation Baseline in CY-BOCS Total Score, Phase II ITT Population

	Interaction	P-value
Week 8	Treatment by centre group (without covariates)	0.850
	Treatment by centre group (with covariates)	0.846
Week 16	Treatment by centre group (without covariates)	0.178
	Treatment by centre group (with covariates)	0.210
70% Endpoint	Treatment by centre group (without covariates)	0.068*
	Treatment by centre group (with covariates)	0.113
Week 16 Endpoint	**Treatment by centre group (without covariates)**	**0.260**
	Treatment by centre group (with covariates)	**0.332**

* - *significant at the 10% level*

The significant interaction at 70% endpoint for the first model was not deemed important as it was not confirmed in the second model, nor at any other timepoint tested. Hence results were presented pooled across centre groups.

6.3 Overall Proportion of Responders as Determined by a Reduction of ≥ 25% from Randomisation Baseline in CY-BOCS Total Score

Proportion of responders as determined by a reduction of ≥ 25% from randomisation baseline in CY-BOCS total score was analysed using the methods described in section 4.1 at week 8, week 16, 70% endpoint (week 4) and week 16 endpoint.

The assessment of treatment differences adjusting for centre group could not be performed, as model convergence problems were encountered due to the small numbers of patients per treatment group/centre group combination. Hence unadjusted results have been presented below.

The table below summarises the results of these analyses for the Phase II ITT dataset:

Table 13 Proportion of Responders as Determined by a Reduction of ≥ 25% from Randomisation Baseline in CY-BOCS Total Score, Phase II ITT Population

	Paroxetine Proportion of responders	Placebo Proportion of responders	Odds Ratio	95% C.I. (Paroxetine/ Placebo)	P-value
Week 8	17/50 (34.0%)	12/39 (30.8%)	1.16	(0.47, 2.84)	0.747
Week 16	17/37 (45.9%)	7/26 (26.9%)	2.31	(0.78, 6.80)	0.130
70% Endpoint	22/83 (26.5%)	8/90 (8.9%)	3.70	(1.54, 8.86)	0.003*
Week 16 Endpoint	**24/83 (28.9%)**	**13/90 (14.4%)**	**2.41**	**(1.13, 5.13)**	**0.023***

(An odds ratio >1 implies a higher proportion of responders with paroxetine)

* - *significant at the 5% level*

A statistically significant treatment difference was observed at 70% endpoint (week 4) and at week 16 endpoint. However, this was not the case at the week 8 and week 16 observed case timepoints.

The possible reason for this discrepancy has been explained above in section 6.2.

6.4 Post-Hoc Analysis of Primary Efficacy (ITT) by Age

Post-hoc analyses of the primary efficacy variable by age (<12 years, >=12 years) were performed to investigate efficacy in paediatrics and adolescents in the patient population.

Table 14 Proportion of Patients Relapsing Aged < 12 During the Randomisation Phase, Phase II ITT Population (Model Including Centre Group only)

Paroxetine Proportion of relapsers	Placebo Proportion of relapsers	Adjusted Odds Ratio	95% C.I. (Paroxetine/ Placebo)	P-value
18/49 (36.7%)	**26/47 (55.3%)**	**0.45**	**(0.18, 1.16)**	**0.099**

(An odds ratio <1 implies a lower proportion of relapsers with paroxetine)

Table 15 Proportion of Patients Relapsing Aged < 12 During the Randomisation Phase, Phase II ITT Population (Model Including Centre Group and Covariate)

Paroxetine Proportion of relapsers	Placebo Proportion of relapsers	Adjusted Odds Ratio	95% C.I. (Paroxetine/ Placebo)	P-value
18/49 (36.7%)	**26/47 (55.3%)**	**0.44**	**(0.17, 1.14)**	**0.093**

(An odds ratio <1 implies a lower proportion of relapsers with paroxetine)

Table 16 Proportion of Patients Relapsing Aged >=12 During the Randomisation Phase, Phase II ITT Population (Model Including Centre Group only)

Paroxetine Proportion of relapsers	Placebo Proportion of relapsers	Adjusted Odds Ratio	95% C.I. (Paroxetine/ Placebo)	P-value
15/46 (32.6%)	**17/51 (33.3%)**	**1.07**	**(0.41, 2.79)**	**0.883**

(An odds ratio <1 implies a lower proportion of relapsers with paroxetine)

Table 17 Proportion of Patients Relapsing Aged >=12 During the Randomisation Phase, Phase II ITT Population (Model Including Centre Group and Covariate)				
Paroxetine Proportion of relapsers	Placebo Proportion of relapsers	Adjusted Odds Ratio	95% C.I. (Paroxetine/ Placebo)	P-value
15/46 (32.6%)	**17/51 (33.3%)**	**1.07**	**(0.39, 2.72)**	**0.948**

(An odds ratio <1 implies a lower proportion of relapsers with paroxetine)

There is no evidence of a statistically significant difference between Paroxetine and placebo in either age group in either model. In the >=12 age group the relapse rates are very similar between Paroxetine and placebo (32.6% vs 33.3%) leading to odds ratios close to unity. However, in the <12 age group although the Paroxetine relapse rate is only slightly higher (36.7%) the placebo relapse rate is greatly increased (55.3%). This placebo relapse rate approaches that estimated in the power calculation (60%) and the difference between Paroxetine and Placebo of 18.6% approaches that targeted in the power calculation (25%).