14. QUESTION 14

Concerning the paediatric suicide-related adverse events occurred during clinical trials, in the paroxetine group it seemed that some cases, including cases where the patient should be taking the study drug according to the protocol, were associated with down-titration or discontinuation of paroxetine (i.e. may be related to discontinuation/withdrawal reactions). Therefore, it is suggested that MAHs should present all paediatric suicide-related adverse events in the paroxetine group according to their actual occurrence: during active treatment without down-titration, during down-titration, or more than 24 hours after discontinuation of paroxetine.

Response

14.1. Study phase at onset of possibly suicide-related events

The study phase at onset of possibly suicide-related events that occurred in paroxetine paediatric placebo-controlled studies is shown in Table 14.1.

Table 14.1 Study Phase at Onset of Possibly Suicide-Related Events by Treatment Group
Paediatric Placebo-Controlled Trials

Study Phase	Paroxetine (N = 738)	Placebo (N = 647)
Total number of patients with event	25	8
Treatment Phase (excluding taper phase)	17 (68.0%)	6 (75.0%)
Taper Phase	1 (4.0%)	1 (12.5%)
Follow-up Phase	7 (28.0%)	1 (12.5%)

In the paroxetine and placebo treatment groups, similar proportions of the total number of possibly suicide-related events reported occurred during the active treatment phase, excluding the down-titration, taper phase (paroxetine 68%, placebo 75%).

Obviously the remainder of such events occurred on discontinuing treatment. In the paroxetine group more events occurred after paroxetine had been stopped completely than during the down-titration, dose tapering phase. However, analyses of the follow-up period should be made with caution as they can be confounded by a number of different factors. New medications may have been started, patients were aware that the study treatment had ended, follow-up was variable and less systematic than on-study treatment assessments, and no accounting was made for the possible return of symptoms that had been suppressed during treatment.

14.2. Conclusion

In the paediatrics programme, a higher rate of adverse events possibly related to suicidality/self harm were seen in patients receiving paroxetine than in those receiving placebo (predominantly in adolescents with Major Depressive Disorder). Most events occurred on treatment, but there appeared to be more on stopping study treatment in patients who had received paroxetinethan placebo. However, analyses of the follow-up phase should be treated with caution due to possible confounding factors specific to that period.