

TYKERB at ASCO 2006

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GlaxoSmithKline

100151 Study Design

HER2+ LABC or
MBC with prior
exposure to an
anthracycline, a
taxane and
trastuzumab*
N=528

Stratification:

- Disease sites
- Stage of disease

R
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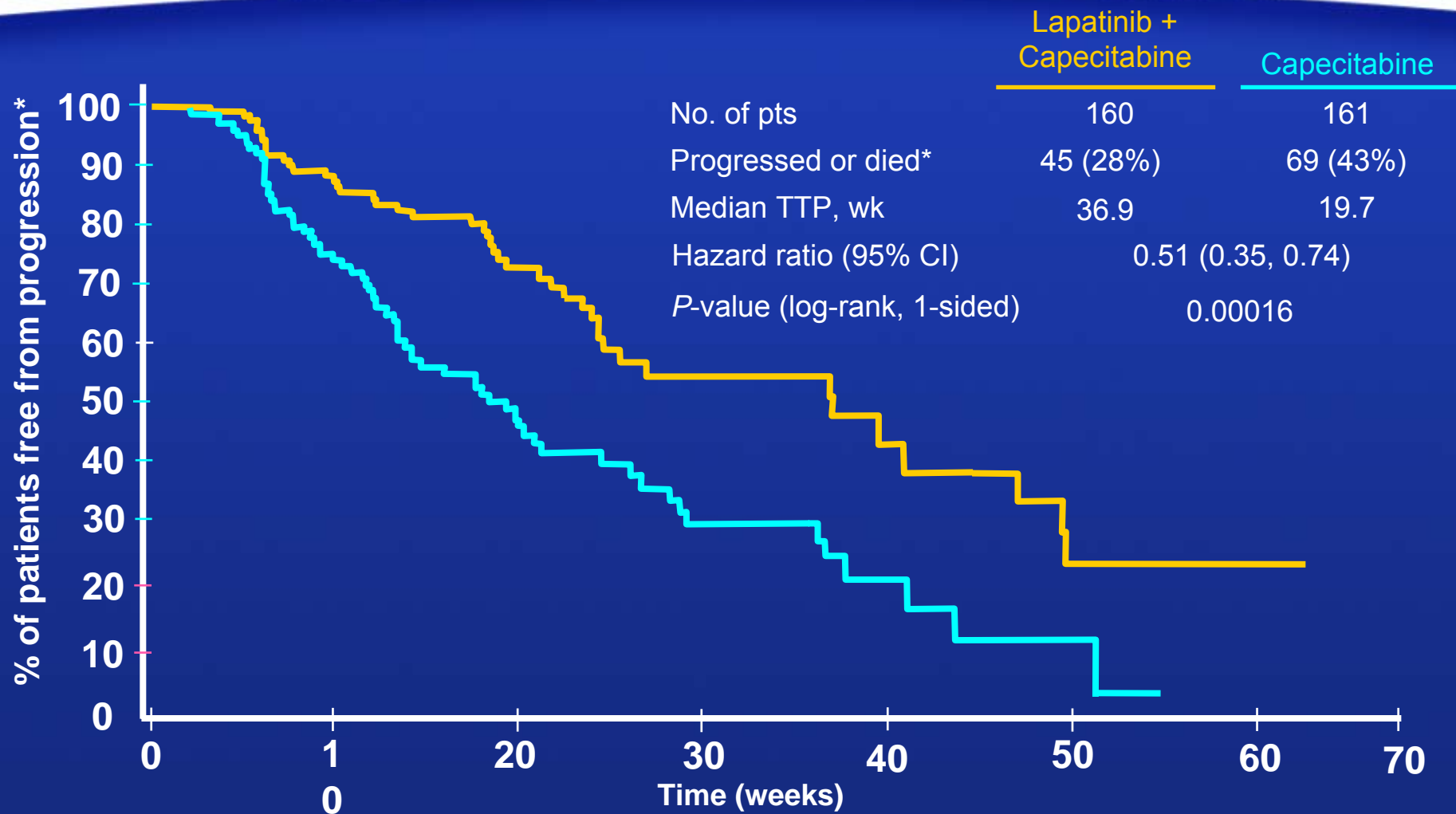
Lapatinib 1250 mg po qd
continuously +
Capecitabine 2000 mg/m²/d
po days 1-14 q 3 wk

Capecitabine 2500 mg/m²/d
po days 1-14 q 3 wk

Patients on treatment until
progression or unacceptable
toxicity, then followed for survival

*Trastuzumab must have been administered for metastatic disease

Time to Progression – ITT Population



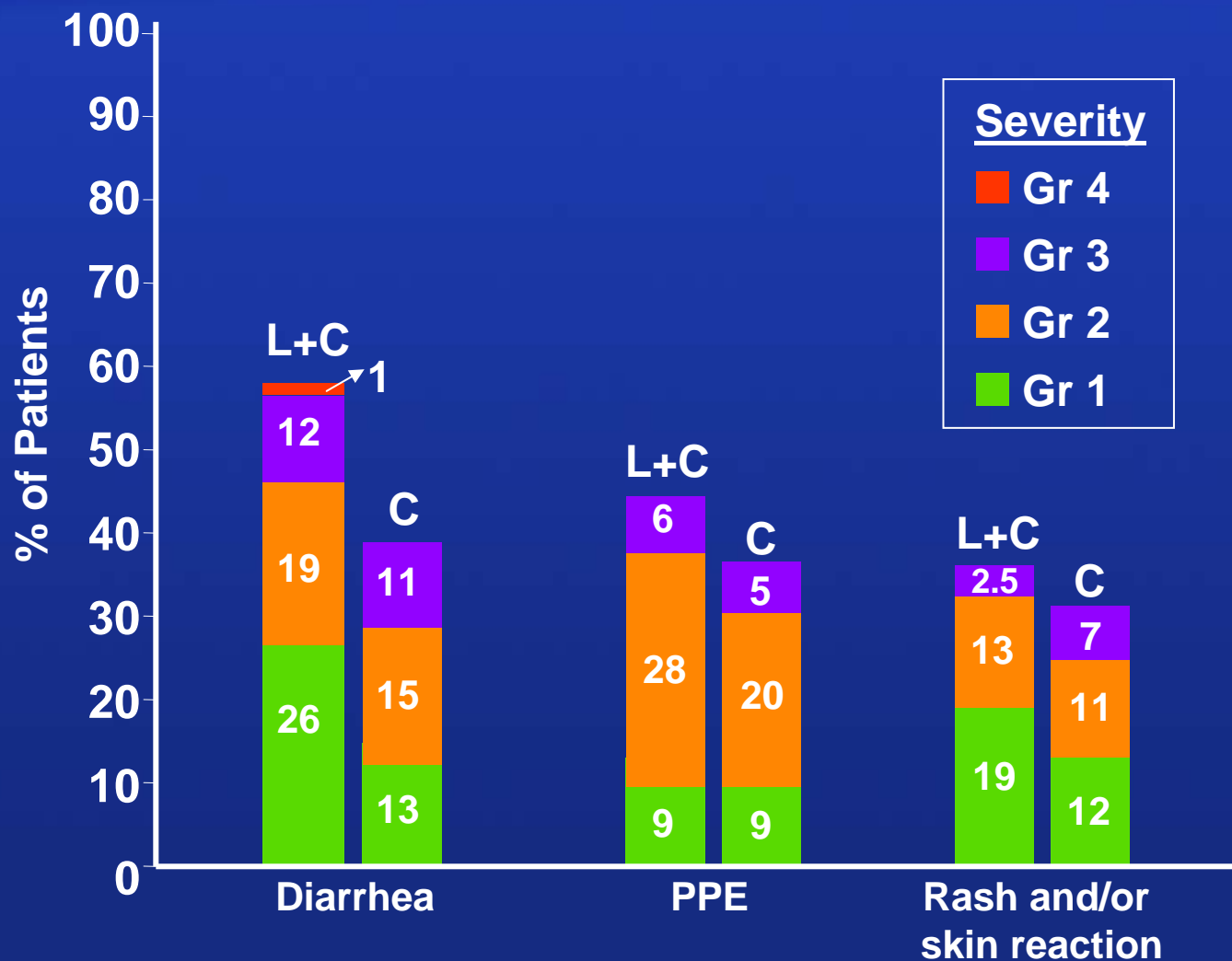
* Censors 4 patients who died due to causes other than breast cancer

Brain Metastases by IRC Review

	Lapatinib + Capecitabine (n=160)	Capecitabine (n=161)
Patients with CNS metastases at baseline	2	2
Patients with CNS relapse*	4	11
Patients with CNS as only site of relapse	3	10

**P*-value (Fisher's exact, 2-sided) = 0.110

Key Adverse Events – All Grades



Effects of Lapatinib on LV Function

- 5 cardiac events reported
 - All considered asymptomatic (\leq Grade 2)
 - 4 with lapatinib + capecitabine
(all treatment-related; all recovered)
 - 1 with capecitabine monotherapy
(unrelated to treatment; unresolved)
- No withdrawals due to decrease in LVEF

100151 Conclusions

- The planned interim analysis demonstrated a clinically meaningful and statistically significant improvement in median TTP
 - Lapatinib + capecitabine 8.5 mo vs capecitabine 4.5 mo
- Lapatinib and capecitabine well tolerated; declines in LVEF were infrequent, asymptomatic, reversible
- Fewer patients with brain metastases as first site of progression in the group receiving lapatinib
- Trials evaluating the role of lapatinib in earlier stages of HER2+ breast cancer are clinically warranted

Lapatinib with capecitabine is an effective new regimen for advanced HER2+ breast cancer and should be considered a new standard of care for women meeting eligibility criteria of this trial

Brain Metastases Associated with Breast Cancer

- Phase II NCI-CTEP 6969 trial (n=39)
- Very encouraging results
- Volumetric analysis superior method to RECIST for CNS lesions
- GSK PII study ongoing in 220 patients with volumetric analysis as primary endpoint reports 2Q07

RECIST Criteria (n=38)

2-dimensional tumor measurement

- 2 patients PR
- 1 patient $\geq 30\%$ decrease in LD but not meet RECIST
- 5 patients SD ≥ 16 wks
- Median TTP 3.2 months

Volumetric Analysis (n=20)

More precise three-dimensional measure of tumor volume

- 8/20 patients (40%) response
- 5 patients $\geq 30\%$ volumetric decline
- 3 patients 15-30% volumetric decline

IBC: EGF103900 Study Design



Two Stage Green-Dahlberg Design

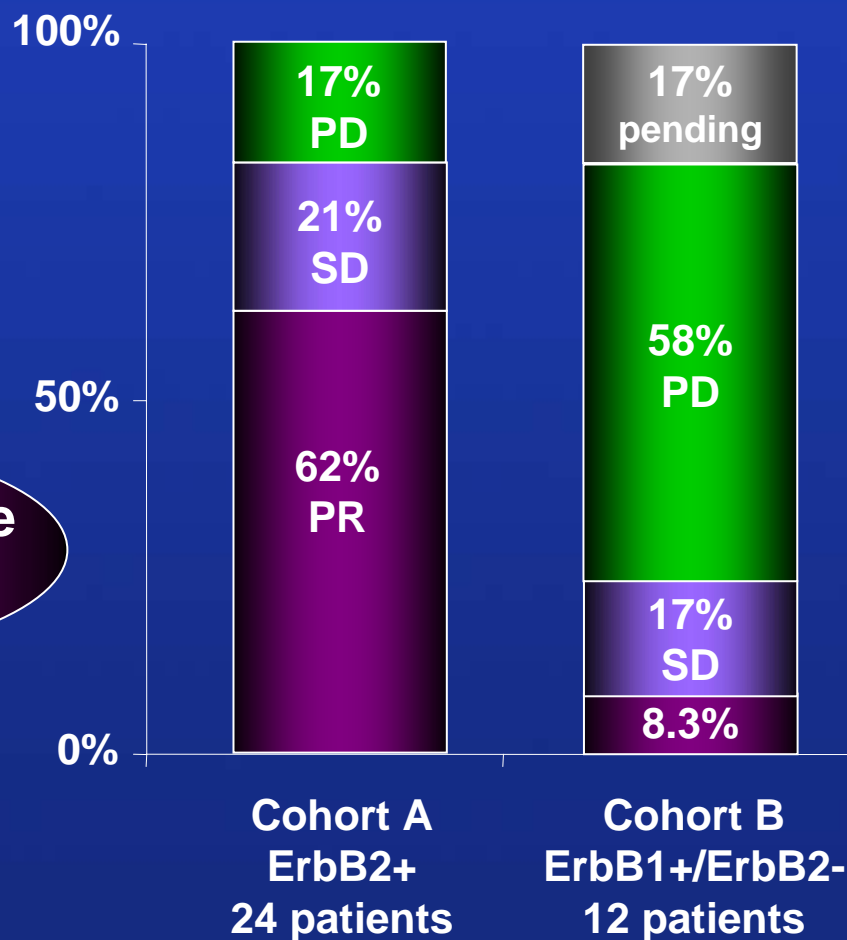
Pre-treatment tumor biopsy

Administer lapatinib (1500 mg/d)

Clinical Evaluation: according to RECIST criteria and *chest wall/skin response documented by Canfield digital photography

*(CR: complete resolution of disease; PR >50% reduction; SD 20-40% reduction)

IBC: 103900 Preliminary Results



**62% Partial Response
in erbB2+ patients**

5 enrolled patients were not evaluable (did not express target or died prior to Day 28)
PD = Progressed Disease, SD = Stable Disease, PR = Partial Response

TYKERB Registration Studies in Breast Cancer

Refractory Studies

Study	Treatment Groups	Study Start	Data Analysis	End Points
EGF100151 PIII, n=528	<i>Xeloda + TYKERB</i>	Nov 03	1 st interim Mar 06. Enrollment stopped	<ul style="list-style-type: none"> • Overall Survival • Time To Progression • Response Rate
	<i>Xeloda</i>			
EGF104900 PIII, n=270	<i>Herceptin + TYKERB</i>	Nov 05	2Q07	<ul style="list-style-type: none"> • Progression Free Survival • Response Rate
	<i>TYKERB</i>			
EGF 105084 PII, n=220	<i>TYKERB monotherapy in brain metastases</i>	Nov 05	2Q07	<ul style="list-style-type: none"> • Response Rate

Firstline Studies

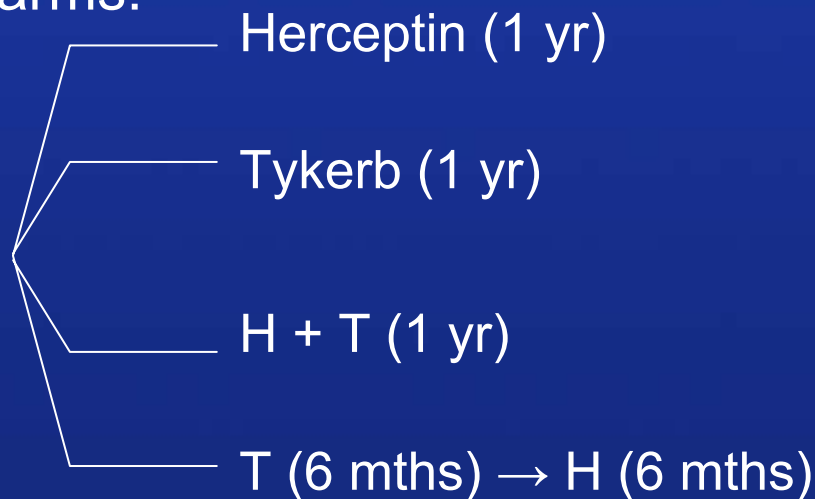
Study	Treatment Groups	ErbB2+ Selected?	Study Start	Data Analysis
EGF30001 n=570	<i>Taxol + TYKERB</i>	No	Dec 03	4Q06
	<i>Taxol + placebo</i>			
EGF30008 n=1280	<i>Femara + TYKERB</i>	No	Nov 03	3Q07
	<i>Femara + placebo</i>			
EGF104383 n=740	<i>Taxol + Herceptin + TYKERB</i>	Yes	Nov 05	2009
	<i>Taxol + Herceptin + placebo</i>			
EGF104535 n=460	<i>Taxol + TYKERB</i>	Yes	Jan 06	2008
	<i>Taxol + placebo</i>			

All refractory studies in ErbB2+. Study Endpoints in Firstline: Time To Progression, Overall Survival, Response Rate Biomarker

TYKERB Adjuvant Trial

Breast Cancer International Group (BIG)
to initiate *TYKERB* adjuvant study

- ~8,000 women
- Study to start late 2006
- Four arms:



Discussions underway for further adjuvant studies

TYKERB in Other Tumors

- **Pancreaticobiliary cancer**
 - Phase I data in combination with gemcitabine, oxaplatin
 - 25% response rate (5 of 20 evaluable patients)
- **Renal cancer**
 - 2nd line metastatic (n=416) open-label monotherapy vs hormone therapy (HT)
 - Primary endpoint: time to progression (TTP)
 - No TTP or survival benefit in full population
 - Preliminary sub-group analysis (n=241) in EGFR overexpressors (IHC 3+)
 - Median TTP: 15.1 weeks Tykerb vs 10.9 weeks HT
 - Median OS: 46.0 weeks Tykerb vs 37.9 weeks HT
 - Promising activity suggests potential to combine with other targeted therapies
- **Head and neck**
 - In combination with chemo and radiation showed promising activity
 - Preliminary phase I showed 9/10 patients with complete response
 - Further positive Phase I data to be presented Monday
 - Phase II initiated 1H06
 - Monotherapy
 - PII CTEP study showed no response (also poster Monday)