# Lapatinib Plus Paclitaxel Versus Paclitaxel Alone for First-Line Metastatic Breast Cancer in ErbB2-Positive Patients: Quality-of-Life Results

GlaxoSmithKline Oncology

RTI(h)(s)

**Yun Wu[1], Anthony Segreti[1], David Cella[2], Angelo DiLeo[3], Mayur Amonkar[4], Maria Koehler[4], Michael Arbushites[4], Mel Walker[5]**

*[1]RTI Health Solutions, Research Triangle Park, NC, United States; [2]CORE, Evanston Northwestern Healthcare, Evanston, IL, United States; [3]Sandro Pitigliani Medical Oncology Unit, Prato, Italy; [4]GlaxoSmithKline, Collegeville, PA, United States; [5]GlaxoSmithKline, London, United Kingdom*

## BACKGROUND

- A phase 3, randomized, multicenter, double-blind, placebo-controlled study compared first-line treatment with lapatinib plus paclitaxel (L+P) versus paclitacxel alone (P) in adult women with metastatic breast cancer (MBC).
- The study randomized 579 subjects: 291 to receive oral lapatinib (1,500 mg once daily) plus IV paclitaxel (175 mg/m$^2$ over 3 hours every 3 weeks) and 288 subjects to receive IV paclitaxel plus placebo.
- Treatment was administered until disease progression or patient withdrawal due to unacceptable toxicity or other reasons (i.e., consent withdrawal, noncompliance).
- In a subgroup analysis of 86 ErbB2-positive patients (n = 49 L+P, n = 37 P), time to tumor progression for L+P was significantly improved, with an emerging trend for survival benefit.[1]

## OBJECTIVE

- This analysis focuses on the impact of treatments on quality of life (QOL) in the subset of the randomized intent-to-treat (ITT) population that overexpressed ErbB2.

## METHODS

- QOL was assessed using the Functional Assessment of Cancer Therapy-Breast (FACT-B) questionnaire (version 4),[2] which measures multidimensional QOL in patients with breast cancer.
- It is a 37-item (27 general questions and 10 breast-cancer-specific questions), self-reporting instrument with a recall period of 7 days.
- Outcome measures include the FACT-B total score, FACT-General (FACT-G) score, and Trial Outcome Index (TOI) score.
- The FACT-B produces five subscale scores - physical well-being (PWB), social/family well-being (SWB), emotional well-being (EWB), functional well-being (FWB), and breast cancer subscale (BCS).
- High scores indicate a better QOL.

**FACT-B total score = PWB + SWB + EWB + FWB + BCS**
**FACT-G score = PWB + SWB + EWB + FWB**
**TOI score = PWB + FWB + BCS**

- A clinically meaningful change has been estimated from previous studies (2-3 points for BSC, 7-8 points for FACT-B total score, 5-6 points for FACT-G and the TOI scores).[3]
- The questionnaire was completed at the screening visit, week 9, every 12 weeks thereafter, and at discontinuation of therapy.
- All withdrawals were included in analyses up to the time of withdrawal. Missing FACT-B data were imputed using the LOCF method for scheduled visits (no imputation applied to the data at discontinuation).
- Baseline scores were summarized by treatment group for each of five subscales and for the FACT-B total score, FACT-G score, and TOI score.
- Changes from baseline in the FACT-B total score, FACT-G score, and TOI score were analyzed by parametric analysis of covariance (using baseline value as a covariate).

## RESULTS

- The number of subjects who completed the FACT-B questionnaire at each visit is summarized in Table 1.

**Table 1. Number of Subjects Completing[a] FACT-B Questionnaire at Scheduled Visits**

| | Lapatinib 1,500 mg + Paclitaxel 175 mg/m$^2$ | Paclitaxel 175 mg/m$^2$ + Placebo |
|---|---|---|
| **Visit** | **ErbB 2-positive (n = 49)** | **ErbB 2-positive (n = 37)** |
| Day 1, baseline | 48 (98%) | 37 (100%) |
| Week 9 | 42 (86%) | 32 (86%) |
| Week 21 | 34 (69%) | 19 (51%) |
| Week 33 | 23 (47%) | 10 (27%) |
| Week 45 | 14 (29%) | 3 (8%) |
| Week 57 | 3 (6%) | 1 (3%) |
| Week 69 | 2 (4%) | 1 (3%) |
| Week 81 | 1 (2%) | 0 (0%) |
| Week 93 | 1 (2%) | 0 (0%) |
| Week 105 | 1 (2%) | 0 (0%) |
| Conclusion/withdrawal | 35 (71%) | 30 (81%) |

[a]Complete was defined as completing at least one question in the FACT-B questionnaire.

- Compared to the P arm, subjects in the L+P arm had slightly lower values for all scores suggesting that patients receiving L+P had lower QOL at the beginning of treatment than patients who received P alone (Table 2).

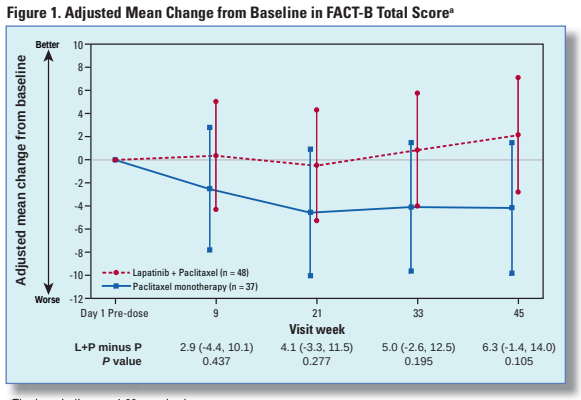
**Table 2. Summary of Baseline Scores by Treatment**

| | Lapatinib 1,500 mg + Paclitaxel 175 mg/m$^2$ n = 48 | Paclitaxel 175 mg/m$^2$ + Placebo n = 37 |
|---|---|---|
| **Score** | **Mean (SD)** | **Mean (SD)** |
| Physical well-being | 19.2 (6.63) | 20.5 (5.84) |
| Social/family well-being | 19.1 (5.82) | 19.3 (5.64) |
| Emotional well-being | 15.7 (4.32) | 16.6 (4.17) |
| Functional well-being | 15.8 (6.49) | 17.6 (5.36) |
| Breast cancer subscale | 21.1 (5.30) | 23.4 (6.06) |
| FACT-B total score | 90.8 (19.67) | 97.3 (18.74) |
| FACT-G score | 69.8 (16.59) | 74.0 (14.88) |
| TOI | 56.1 (15.60) | 61.5 (13.28) |

FACT-B = Functional Assessment of Cancer Therapy-Breast; FACT-G = FACT-General; SD = standard deviation; TOI = Trial Outcome Index.

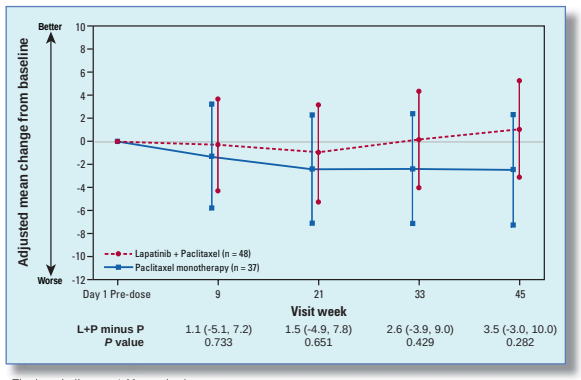
- Overall, the L+P arm showed improvement compared to the P arm for FACT-B total scores, FACT-G scores, and TOI scores at all scheduled postbaseline visits. The group difference in mean change from baseline, although not statistically significant, increased over time in favor of L+P, from 2.9 to 6.3 (FACT-B), 1.1 to 3.5 (FACT-G), and 1.8 to 5.3 (TOI) from week 9 to week 45, respectively (Figures 1–3).

**Figure 1. Adjusted Mean Change from Baseline in FACT-B Total Score[a]**



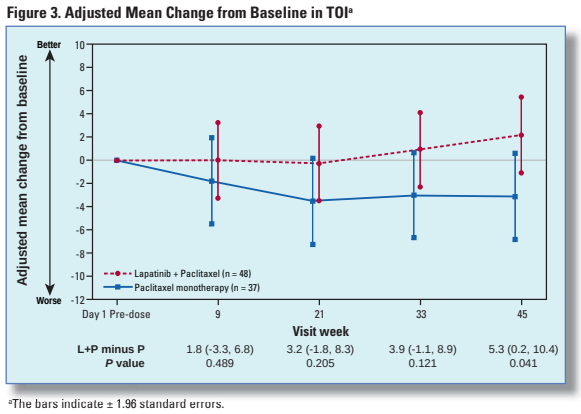

[a]The bars indicate ± 1.96 standard errors.

**Figure 2. Adjusted Mean Change from Baseline in FACT-G Score[a]**




[a]The bars indicate ± 1.96 standard errors.

**Figure 3. Adjusted Mean Change from Baseline in TOI[a]**




[a]The bars indicate ± 1.96 standard errors.

- For the assessment at discontinuation, treatment differences were statistically significant for the FACT-B total score ($P = 0.039$) and the TOI score ($P = 0.032$), and it approached statistical significance for the FACT-G score ($P = 0.066$) (Table 3).

**Table 3. Adjusted Changes from Baseline for FACT-B Total Scores, FACT-G Scores, and TOI Scores, for the Assessment at Discontinuation**

| | Lapatinib 1,500 mg + Paclitaxel 175 mg/m$^2$ | | Paclitaxel 175 mg/m$^2$ + Placebo | | Treatment Difference | |
|---|---|---|---|---|---|---|
| | n | Adjusted Mean | n | Adjusted Mean | Mean (95% CI) | *P* Value |
| FACT-B total score | 33 | 0.3 | 29 | -10.2 | 10.6 (0.5, 20.6) | 0.039 |
| FACT-G score | 34 | -0.5 | 29 | -8.2 | 7.7 (-0.5, 16.0) | 0.066 |
| TOI score | 33 | 0.8 | 29 | -6.6 | 7.4 (0.6, 14.2) | 0.032 |

FACT-B = Functional Assessment of Cancer Therapy-Breast; FACT-G = FACT-General; TOI = Trial Outcome Index.

## CONCLUSIONS

- On average, health-related QOL was stable for subjects in the L+P arm and decreased for subjects in the P arm after treatment.
- While not all differences were statistically significant, ErbB2-positive subjects treated with L+P demonstrated consistently better QOL compared to subjects treated with P alone.
- **The addition of lapatinib to paclitaxel significantly prolonged time to progression without any detriment to QOL, giving overall clinical benefit to ErbB2-positive patients in a first-line MBC setting.**

## REFERENCES

1. Di Leo et al. ASCO. 2007.
2. Brady MJ, et al. J Clin Oncol 1997 Mar;15(3):974-86.
3. Eton DT, et al. J Clin Epidemiol 2004;57(9):898-910.

## CONTACT INFORMATION

**Yun Wu, MAS**
RTI Health Solutions
Phone: 919-637-6976
E-mail: ywu@rti.org