

# Lapatinib Plus Capecitabine Versus Capecitabine Alone for ErbB2-Positive Metastatic Breast Cancer: Quality-of-Life Assessment



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## BACKGROUND

### Study Design

- A phase 3, randomized, open-label, multicenter study.

### Patient Population

- Women with ErbB2+ refractory metastatic breast cancer (MBC) who had received prior therapy, including anthracycline, a taxane, and trastuzumab

### Study Treatment

| L+C Arm  | C Arm  |
|--|--|
| Lapatinib: 1,250 mg/day, daily, continuously<br>Capecitabine: 2,000 mg/m <sup>2</sup> /day, days 1-14, every 21 days | Capecitabine: 2,500 mg/m <sup>2</sup> /day, days 1-14, every 21 days |

- Treatment was administered until disease progression or withdrawal due to unacceptable toxicity or other reasons (e.g., consent withdrawn, noncompliance).

## OBJECTIVE

- To evaluate and compare the efficacy and tolerability of lapatinib + capecitabine (L+C) versus capecitabine (C) alone. This analysis focuses on the impact of treatments on quality of life (QOL).

## METHODS

- QOL was assessed using the Functional Assessment of Cancer Therapy-Breast (FACT-B) (Version 4)<sup>1</sup> and EuroQOL (EQ-5D) questionnaires.<sup>2</sup>
- Outcome measures included the FACT-B total score, FACT-General (FACT-G) score, Trial Outcome Index (TOI) score, EQ-5D utility score, and EQ-5D visual analog scale (VAS) score.

### FACT-B

- A 37-item (27 general questions and 10 breast-cancer-specific questions), self-reporting instrument with a recall period of 7 days.
- Produces 5 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

### EQ-5D

- A five-domain (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) health status measure along with a VAS (feeling thermometer)
- Each domain assessed by a 3-point scale (level 1 = no problem; level 2 = some or moderate problem[s]; and level 3 = unable, or extreme problem[s]).
- High scores indicate better health status.

EQ-5D utility score: calculated from the 5 domain scores using United Kingdom tariffs  
 EQ-5D VAS score: collected as a continuous measure ranging from 0 to 100

- Both questionnaires were completed at the screening visit (baseline), every 6 weeks for the first 24 weeks, every 12 weeks thereafter, and at study withdrawal.
- Analysis included changes from baseline scores using analysis of covariance, with baseline value as a covariate.
- Missing postbaseline data were imputed using the last observation carried forward (LOCF) method that used only assessments at scheduled visits.

## CONCLUSIONS

- Overall, subjects' QOL was improved after treatment with both combination therapy (L+C) and monotherapy (C alone). Point estimates for all QOL scores were generally higher for the L+C arm versus the C arm.
- The two treatment groups appear to be similar in QOL scores over a 24-week follow-up, suggesting that there was no detriment to QOL in patients receiving combination therapy (L+C) compared with those receiving monotherapy (C) in this heavily pretreated patient population.
- The addition of lapatinib to capecitabine significantly prolonged time to progression without any loss of QOL, providing overall clinical benefit to patients.

## RESULTS

- Study was closed to new enrollment early when the primary endpoint of the trial (time to progression) was achieved at an interim analysis, and patients receiving C alone were given the option to cross-over and receive L+C.
- At study closure (April 3, 2006), 399 subjects were randomly assigned to treatment (198 subjects to L+C and 201 subjects to C).
- Of the total number, 171 subjects on L+C and 168 subjects on C completed a baseline health outcome questionnaire (FACT-B or EQ-5D).
- Because subjects were enrolled over 2 years and the period of treatment for any subject was dependent on both efficacy and toxicity, the duration of follow-up varied among subjects.
- Table 1 presents the questionnaire completion rates at various scheduled visits.
- To deal with the large amount of missing QOL data (due to high attrition rate), an LOCF analysis was used. An analysis using observed data without imputation and an analysis using a random effect pattern mixture model (data not shown) reached the same conclusion.

### FACT-B

- On average, subjects in the two treatment arms had similar baseline values in all the FACT-B scores (Table 2).

Table 2. Summary of Baseline FACT-B Subscale Scores, Total Scores, FACT-G Scores, and TOI Scores\*

| Score (Range)                            | Lapatinib 1,250 mg + Capecitabine 2,000 mg/m <sup>2</sup> |              | Capecitabine 2,500 mg/m <sup>2</sup> |              |
|--|---|--------------|--------------------------------------|--------------|
|  | n   | Mean (SD)    | n                                    | Mean (SD)    |
| Physical well-being subscale (0-28)      | 167   | 20.3 (5.62)  | 168                                  | 20.5 (5.68)  |
| Social/family well-being subscale (0-28) | 167   | 21.6 (5.08)  | 167                                  | 22.3 (5.00)  |
| Emotional well-being subscale (0-24)     | 166   | 15.0 (4.85)  | 167                                  | 15.1 (5.00)  |
| Functional well-being subscale (0-28)    | 167   | 17.6 (5.71)  | 167                                  | 17.2 (6.34)  |
| Breast cancer subscale (0-36)            | 167   | 21.2 (6.54)  | 167                                  | 21.5 (6.19)  |
| FACT-B total (0-144)                     | 163   | 95.7 (19.50) | 166                                  | 96.4 (19.88) |
| FACT-G (0-108)                           | 164   | 74.4 (15.45) | 166                                  | 74.9 (16.35) |
| TOI (0-92)                               | 164   | 59.0 (13.72) | 165                                  | 59.1 (14.67) |

SD = standard deviation.  
 \*This summary is based on observed data. No imputation was made for missing data.

- In both arms, the unadjusted breast cancer subscale scores increased approximately 2 to 3 points after treatment, which indicated clinically meaningful symptom improvement (minimally important difference [MID] = 2-3)<sup>3</sup> with slightly higher point estimates for L+C.
- Group differences in adjusted mean change from baseline were consistently in favor of the L+C arm and ranged from 0.7 to 2.2 (FACT-B), 0.9 to 1.5 (FACT-G), and 0.2 to 1.5 (TOI) over a 24-week follow-up (Figure 1). No treatment differences were statistically significant ( $P > 0.05$ ) or reached clinical MIDs (MID: FACT-B = 7-8; FACT G = 5-6; TOI = 5-6).<sup>3</sup>

### EQ-5D

- On average, subjects in the two treatment arms had similar baseline EQ-5D utility and VAS scores (Table 3).

Table 3. Summary of Baseline EQ-5D Health Domain, Utility, and VAS Scores\*

| Health Domain      | Lapatinib 1,250 mg + Capecitabine 2,000 mg/m <sup>2</sup> |                          | Capecitabine 2,500 mg/m <sup>2</sup> |                          |
|--------------------|---|--------------------------|--------------------------------------|--------------------------|
|                    | n   | % Level = 1 <sup>b</sup> | n                                    | % Level = 1 <sup>b</sup> |
| Mobility           | 169   | 61%                      | 166                                  | 63%                      |
| Self-care          | 169   | 79%                      | 165                                  | 80%                      |
| Usual activities   | 169   | 49%                      | 166                                  | 39%                      |
| Pain/discomfort    | 169   | 23%                      | 167                                  | 30%                      |
| Anxiety/depression | 170   | 32%                      | 166                                  | 36%                      |

| Score (Range)            | Lapatinib 1,250 mg + Capecitabine 2,000 mg/m <sup>2</sup> |              | Capecitabine 2,500 mg/m <sup>2</sup> |              |
|--------------------------|---|--------------|--------------------------------------|--------------|
|                          | n   | Mean (SD)    | n                                    | Mean (SD)    |
| EQ-5D utility (-0.594-1) | 168   | 0.64 (0.258) | 163                                  | 0.66 (0.240) |
| EQ-5D VAS (0-100)        | 163   | 65.3 (18.68) | 163                                  | 67.5 (20.10) |

SD = standard deviation.  
 \*This summary is based on observed data. No imputation was made for missing data.  
<sup>b</sup>Level = 1 indicates no problem in the health domain.

- There was little change in the EQ-5D utility scores in either arm after treatment (Figure 2) (MID = 0.074).<sup>4</sup>
- The point estimates for the VAS score were generally higher for the L+C arm versus the C arm. Group difference in adjusted mean change from baseline was in favor of the L+C arm and ranged from 0.3 to 1.8 points, although not statistically significant ( $P > 0.05$ ) (Figure 2).

## REFERENCES

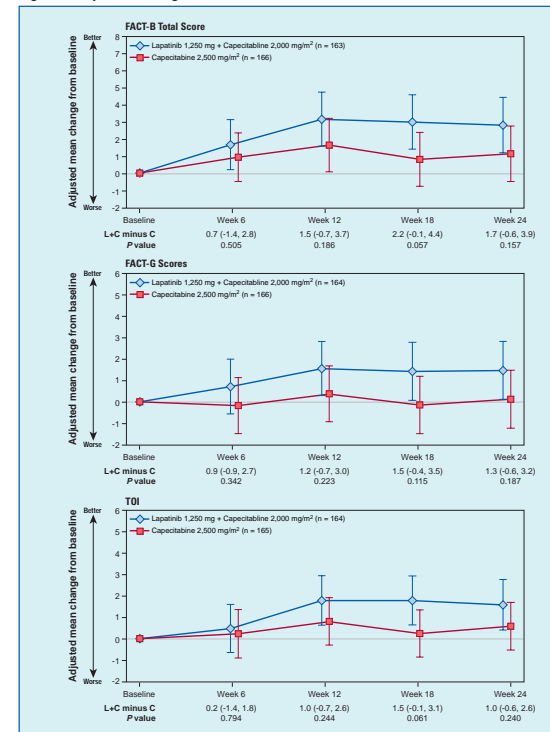
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Table 1. Number of Subjects Completing Questionnaire\* at Scheduled Visits

| Visit    | Lapatinib 1,250 mg + Capecitabine 2,000 mg/m <sup>2</sup> | Capecitabine 2,500 mg/m <sup>2</sup> |
|----------|---|--------------------------------------|
| Baseline | 171 (100%)  | 168 (100%)                           |
| Week 6   | 118 (69%)   | 107 (64%)                            |
| Week 12  | 88 (51%)  | 68 (40%)                             |
| Week 18  | 71 (42%)  | 46 (27%)                             |
| Week 24  | 47 (27%)  | 30 (18%)                             |
| Week 36  | 21 (12%)  | 12 (7%)                              |
| Week 48  | 10 (6%)   | 2 (1%)                               |
| Week 60  | 3 (2%)  | 1 (1%)                               |
| Week 72  | 4 (2%)  | 0 (0%)                               |
| Week 84  | 1 (1%)  | 0 (0%)                               |

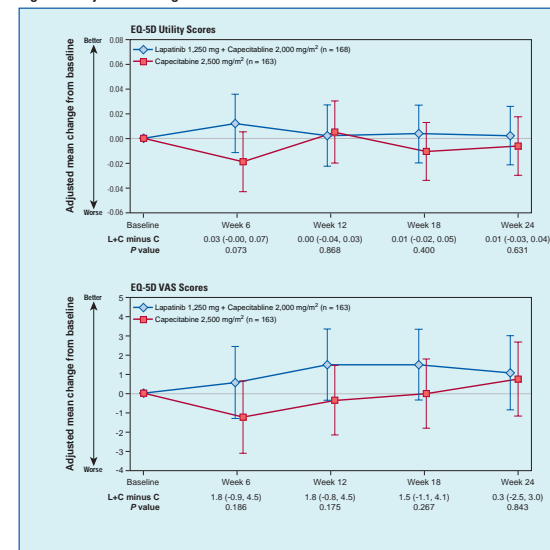
\*Completing at least one question in the FACT-B or EQ-5D questionnaire.  
 Note: percentage is of those who completed baseline questionnaire.

Figure 1. Adjusted\* Changes From Baseline for FACT-B Scores<sup>b,c</sup>



L+C = lapatinib plus capecitabine; C = capecitabine alone.  
 \*Adjusted for baseline score.  
<sup>b</sup>The bars indicate  $\pm 1.96$  standard errors.  
<sup>c</sup>Missing postbaseline data were imputed using the last observation carried forward method. Higher scores indicate a better QOL.

Figure 2. Adjusted\* Changes From Baseline for EQ-5D Scores<sup>b,c</sup>



L+C = lapatinib plus capecitabine; C = capecitabine alone.  
 \*Adjusted for baseline score.  
<sup>b</sup>The bars indicate  $\pm 1.96$  standard errors.  
<sup>c</sup>Missing postbaseline data were imputed using the last observation carried forward method. Higher scores indicate better health status.

## CONTACT INFORMATION

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