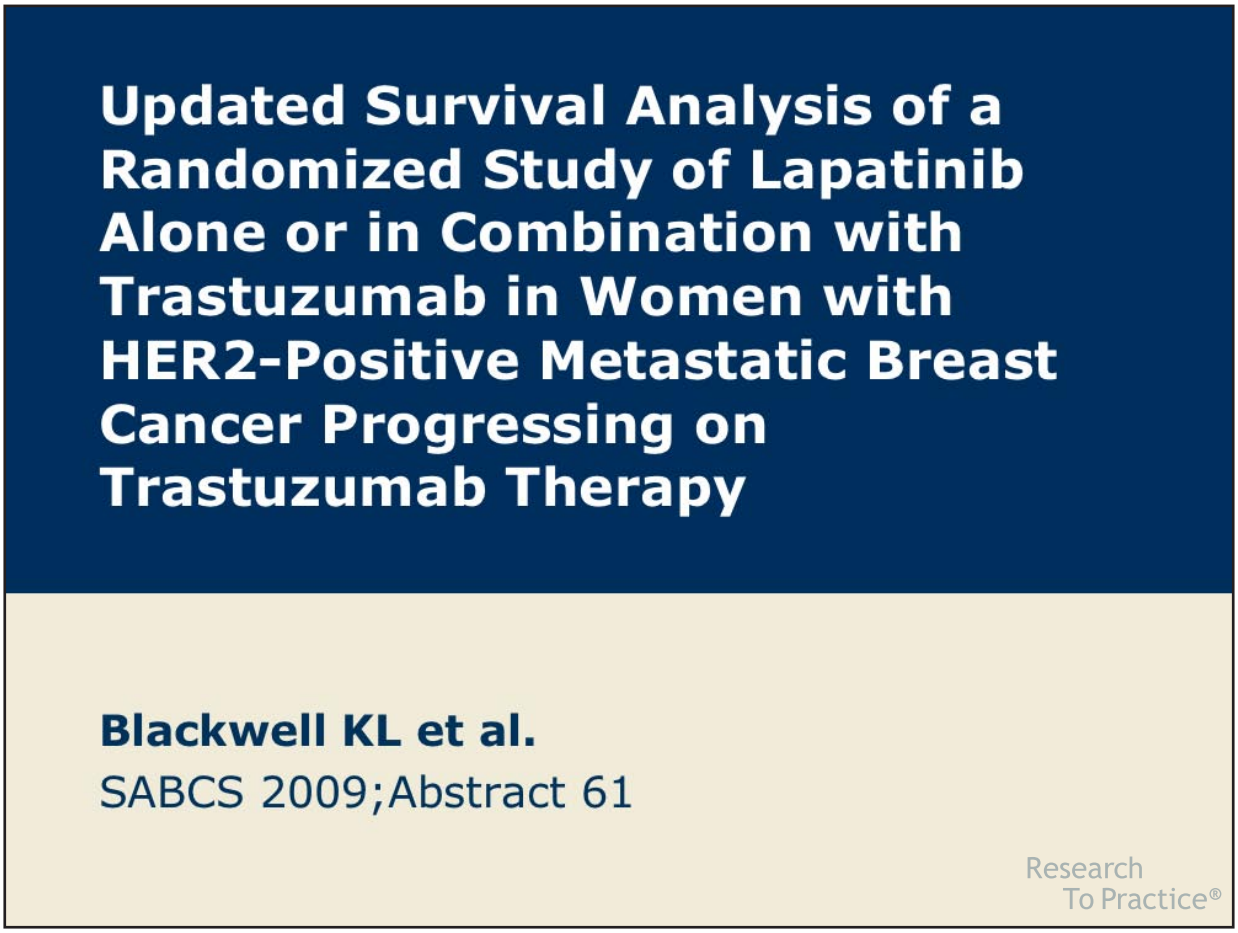
# Updated Survival Analysis of the EGF104900 Randomized Study of Lapatinib Alone or Combined with Trastuzumab for HER2-Positive Breast Cancer Progressing on Trastuzumab

## Presentation discussed in this issue:

Blackwell KL et al. **Updated survival analysis of a randomized study of lapatinib alone or in combination with trastuzumab in women with HER2-positive metastatic breast cancer progressing on trastuzumab therapy.** San Antonio Breast Cancer Symposium 2009;**Abstract 61**.

## Slides from a presentation at SABCS 2009



# Introduction

- Synergy between lapatinib (L) and trastuzumab (T) has been established in preclinical models (*Cancer Res* 2006;66:1630).
- Phase III trial EGF104900 compared L + T versus L alone in patients with HER2+ metastatic breast cancer (mBC) who progressed on multiple lines of trastuzumab-based therapy (ASCO 2008;Abstract 1015).
  - Significant improvement in progression-free survival (PFS) at 6 months and in the clinical benefit rate (CBR) were demonstrated:
    - PFS: 28% (L+T) vs 13% (L)
    - CBR: 24.7% (L+T) vs 12.4% (L)
  - Trend toward overall survival (OS) favoring L+T was shown.
- **Current Study Objectives**
  - Provide updated EGF104900 study results with final intent-to-treat OS analysis and cardiac and safety event data.

Blackwell KL et al. SABCS 2009;Abstract 61.

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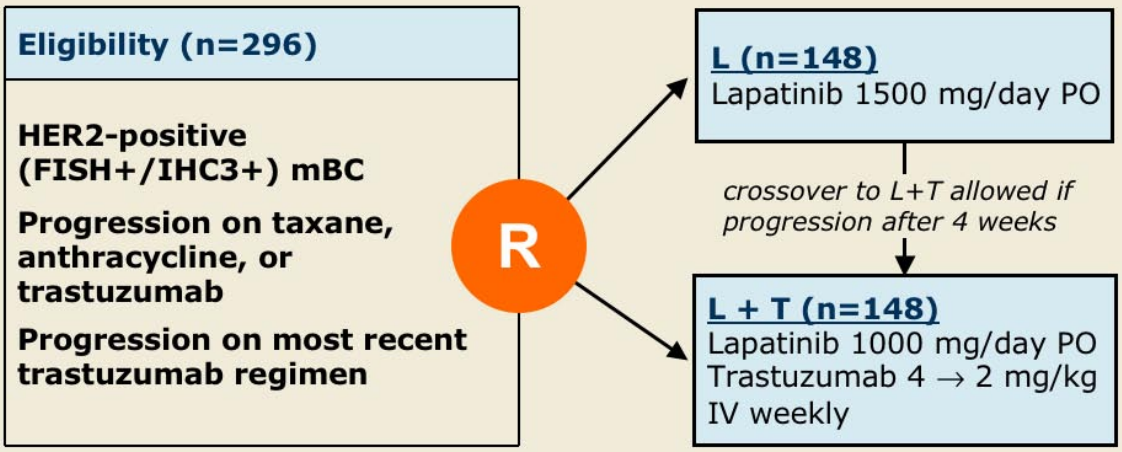
# EGF104900: Phase III Study of Dual HER2 Blockade




*Staging at 4, 8, 12, 16 weeks, then every 8 weeks*
*Steady state of single-agent lapatinib occurs at ~7 days*

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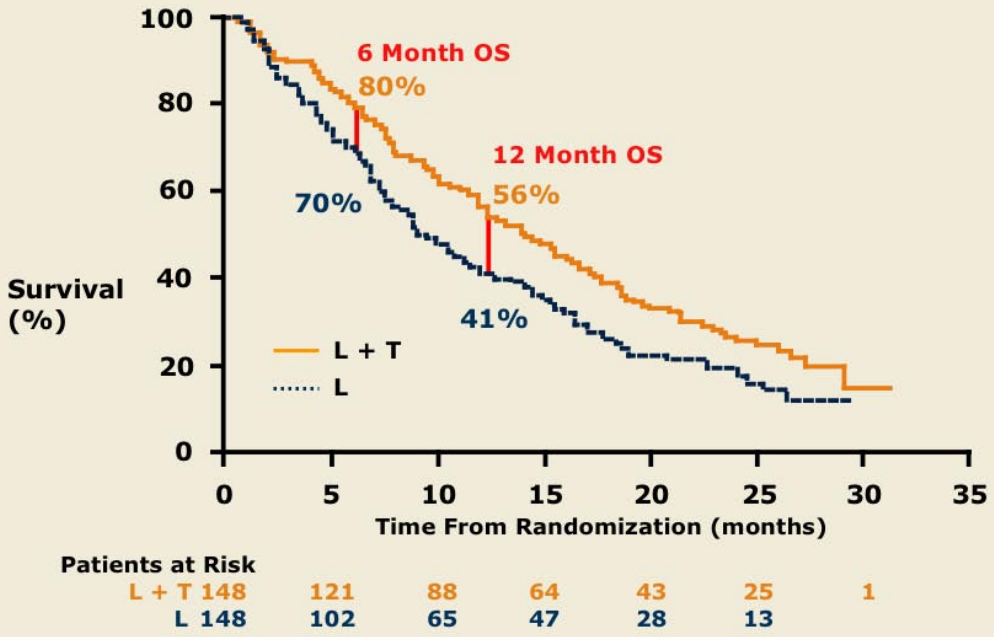
# Updated Overall Survival in ITT

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# EGF104900: Final Survival Analysis

| | L + T (n=146) | L (n=145) |
|---|---|---|
| Events, n (%) | 105 (72) | 113 (78) |
| **Median Survival (months)** | **14** | **9.5** |
| Hazard ratio (95% CI) | 0.74 (0.57, 0.97) | |
| Log-rank *p*-value | 0.026 | |

**Factors influencing overall survival (from COX proportional hazard analysis):**

- **Treatment assignment**
- **ECOG performance status**
- **Disease site**
- **Number of metastatic sites**
- **Time from first or initial diagnosis of BC until randomization**

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# EGF104900: Updated Cardiac and Safety Events

| | L + T (n=149) | L (n=146) |
|---|---|---|
| Total number of patients with event | 11[a] | 3 |
| Grade 3/4 events, n (%) | 3 (2) | 1 (<1) |
| Serious events[b], n | 10 | 3 |
| Events related to study drug(s), n | 10 | 2 |
| Deaths (n)[c] | 1 | 0 |

[a]Two patients experienced 2 events (other event was Grade 1/2)
[b]LV dysfunction ≥ Grade 3 or LVEF decrease ≥ 20% from baseline + < LLN
[c]Cardiac failure; cause of death: pulmonary thromboembolism

- **Majority of AEs with ≥10% incidence were Grade 1/2**
- **Grade 3/4 AEs with ≥5% incidence: Diarrhea (8% L+T; 7% L)**

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# Conclusions

- Treatment with L + T resulted in a 26% reduction in the risk of death ($p$=0.026) for patients with HER2+ mBC with disease progression on trastuzumab.
- Survival benefit was observed despite a 52% crossover of patients from single-agent L to combination therapy at progression (data not shown).
- Tolerability profile of combined L+T was acceptable, with no observed increase in cardiac signal.
- Trial results lend support and evidence for the ongoing Phase III ALTTO trial that will examine adjuvant T and L monotherapy,
  T followed by L, and L+T combination therapy for patients with HER2-amplified BC.

Blackwell KL et al. SABCS 2009;Abstract 61, www.ClinicalTrials.gov (January 2010).