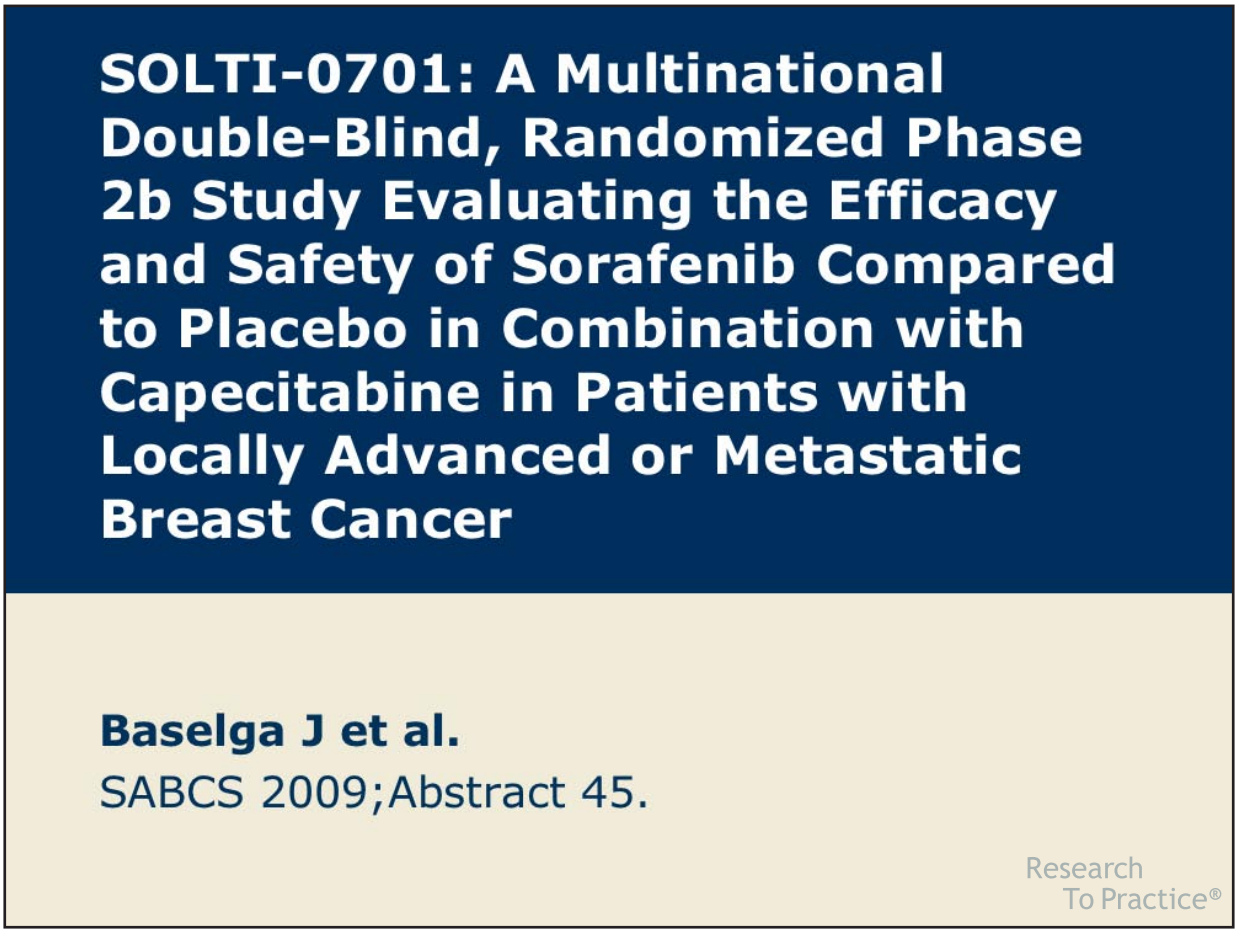
SOLTI-0701 — A Double-Blind, Randomized Phase IIb Study of Capecitabine with or without Sorafenib in Advanced Breast Cancer

Presentation discussed in this issue:

Baselga J et al. **SOLTI-0701: A multinational double-blind, randomized Phase IIb study evaluating the efficacy and safety of sorafenib compared to placebo when administered in combination with capecitabine in patients with locally recurrent or metastatic breast cancer.** San Antonio Breast Cancer Symposium 2009;**Abstract 45**.

Slides from a presentation at SABCS 2009



Introduction

- Phase III trial of capecitabine (CAP) combined with anti-VEGF agent bevacizumab demonstrated an improved objective response rate (ORR) in patients with metastatic breast cancer, though progression-free survival (PFS) was not prolonged (*JCO* 2005;23:792).
  - ORR: 19.8% (combination) vs 9.1% (CAP alone)
  - PFS: 4.86 mos vs 4.17 mos
- Sorafenib (SOR), a multi-targeted tyrosine kinase inhibitor (TKI), targets VEGF receptors VEGFR1 and VEGFR2.
- Phase I studies have found combination therapies containing SOR and CAP to be safe and feasible (*Ann Oncol* 2007;18:Abstract 402, *ASCO* 2008;Abstract 369).
- **Current Study Objectives:**
  - Assess the efficacy and safety of combination therapy with sorafenib and capecitabine in patients with advanced breast cancer.

Baselga J et al. SABCS 2009;Abstract 45.

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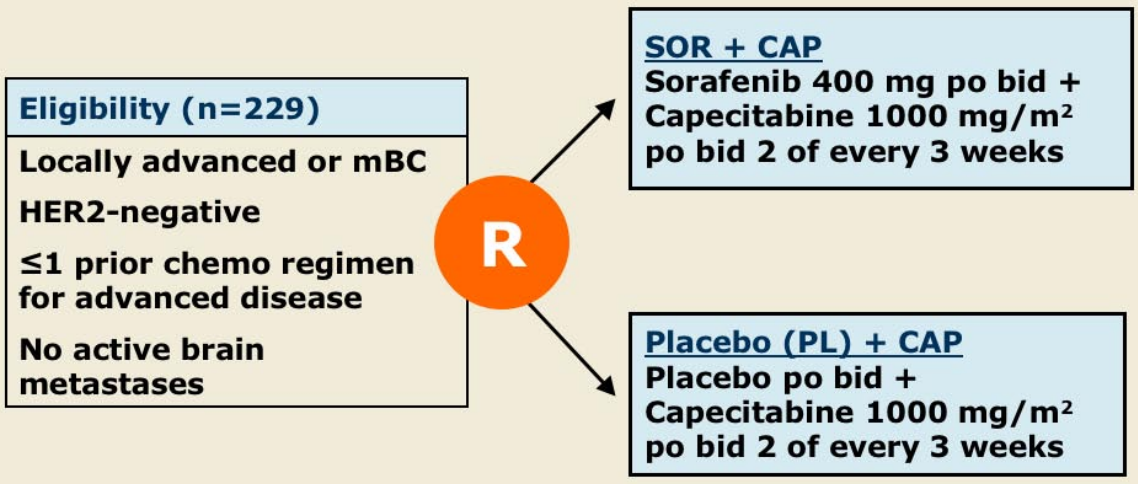
SOLTI-0701: Phase IIb, Double-blind, Placebo-Controlled Study of Sorafenib Combined with Capecitabine



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Efficacy Results

Efficacy Parameter	SOR + CAP	PL + CAP	Hazard Ratio	*p*-value
Progression-free survival (PFS)				
Intent-to-treat (n=115, 114)	6.4 mos	4.1 mos	0.576	0.0006
1st-line patients (n=50, 62)	7.6 mos	4.1 mos	0.498	0.0022
2nd-line patients (n=65, 51)	5.7 mos	4.1 mos	0.652	0.0339
ORR (n=115, 114)	38.3%	30.7%	—	0.1229
Complete response	1.7%	0.9%		
Partial response	36.5%	29.8%		
Stable disease	43.5%	37.7%		
Progressive disease	10.4%	23.7%		

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Select Adverse Events - Grade 3/4 (Safety Population)

Adverse Events	SOR + CAP (N=112)	PL + CAP (N=112)
Hand-foot syndrome	**45%**	**13%**
Diarrhea	5%	5%
Dyspnea	5%	4%
Neutropenia	5%	3%

Most common adverse events related to treatment discontinuation in sorafenib and placebo arms:

- **Hand-foot skin reaction: 8 vs 2 patients**
- **Diarrhea: 1 vs 3 patients**

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Conclusions

- Sorafenib combined with capecitabine demonstrated a significant PFS benefit over capecitabine alone in patients with advanced BC.
  - PFS: 6.4 vs 4.1 mos (p=0.0006)
- Subgroup analyses demonstrated robustness of PFS benefit across all exploratory subgroups (data not shown) and in both lines of advanced BC:
  - PFS 1st-line: 7.6 vs 4.1 mos (p=0.0022)
  - PFS 2nd-line: 5.7 mos vs 4.1 mos (p=0.0339)
- No new toxicities were observed in the combination arm and adverse events were manageable.
- A Phase III registration trial will begin in 2010 examining sorafenib combined with capecitabine as treatment for advanced BC.

Baselga J et al. SABCS 2009;Abstract 45.

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