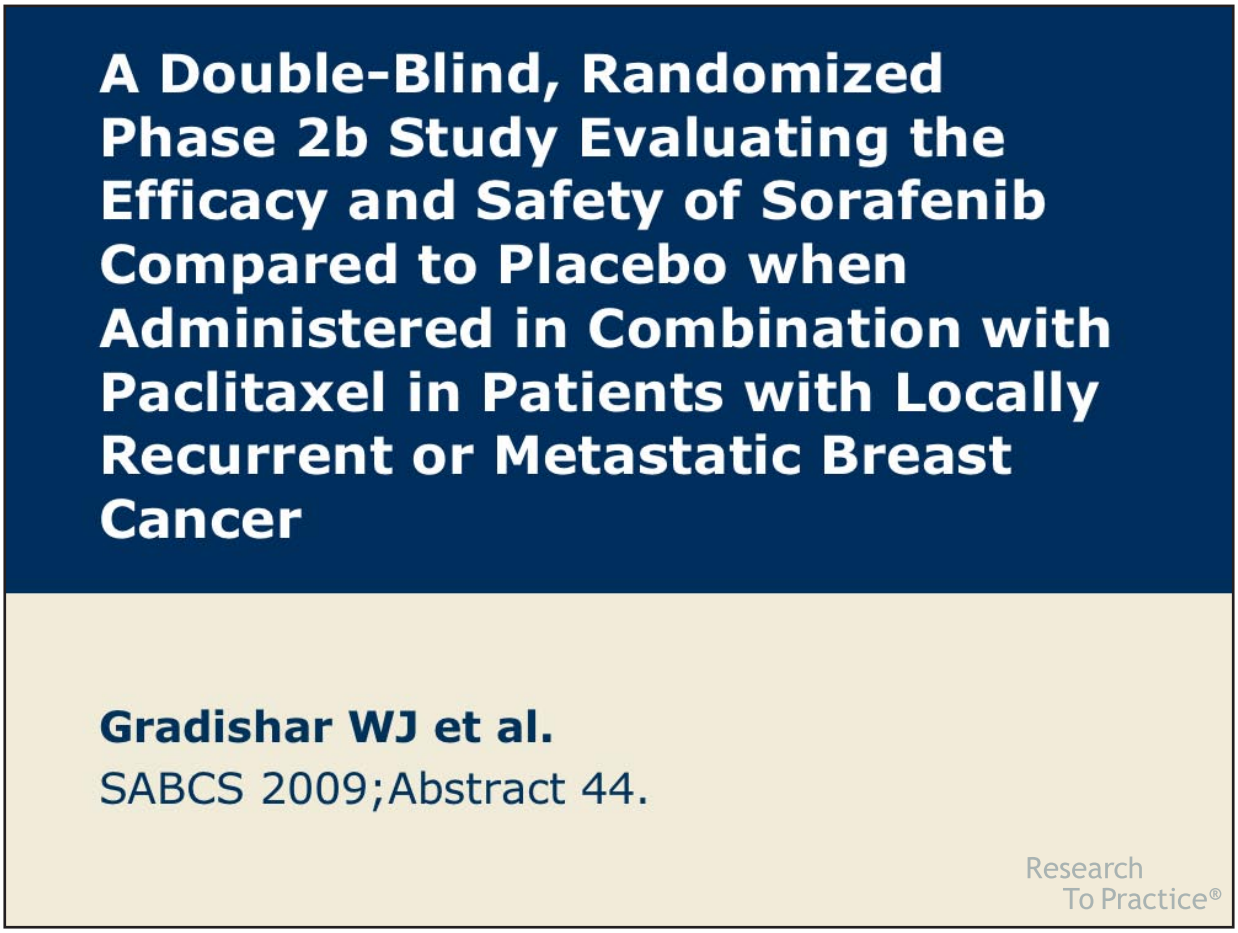
# Double-Blind, Randomized Phase IIb Study of Paclitaxel with or without Sorafenib for Patients with HER2-Negative Advanced Breast Cancer

## Presentation discussed in this issue:

Gradishar WJ et al. **A double-blind, randomized Phase IIb study evaluating the efficacy and safety of sorafenib compared to placebo when administered in combination with paclitaxel in patients with locally recurrent or metastatic breast cancer.** San Antonio Breast Cancer Symposium 2009;**Abstract 44**.

## Slides from a presentation at SABCS 2009



# Introduction

- Phase III trial of first-line paclitaxel and bevacizumab (bev) in patients with metastatic breast cancer (mBC) has demonstrated improved efficacy when compared to paclitaxel alone (*NEJM* 2007;357:2666).
  - Median progression free survival (PFS) = 11.8 mos vs 5.9 mos
  - Objective response rate (ORR) = 36.9% vs 21.2%
- Phase II trials have demonstrated modest single-agent activity with sorafenib in patients with heavily pre-treated mBC (*JCO* 2009;27:11, *AntiCancer Drugs* 2009;20:616).
- Phase I trial of combined paclitaxel, carboplatin and sorafenib therapy has shown regimen to be well tolerated in patients with advanced solid tumors (*Clin Cancer Res* 2008;14:4836).
- **Current Study Objectives:**
  - Assess the safety and efficacy of paclitaxel combined with sorafenib compared to paclitaxel and placebo for locally recurrent or metastatic BC (mBC).

Gradishar W et al. SABCS 2009;Abstract 44.

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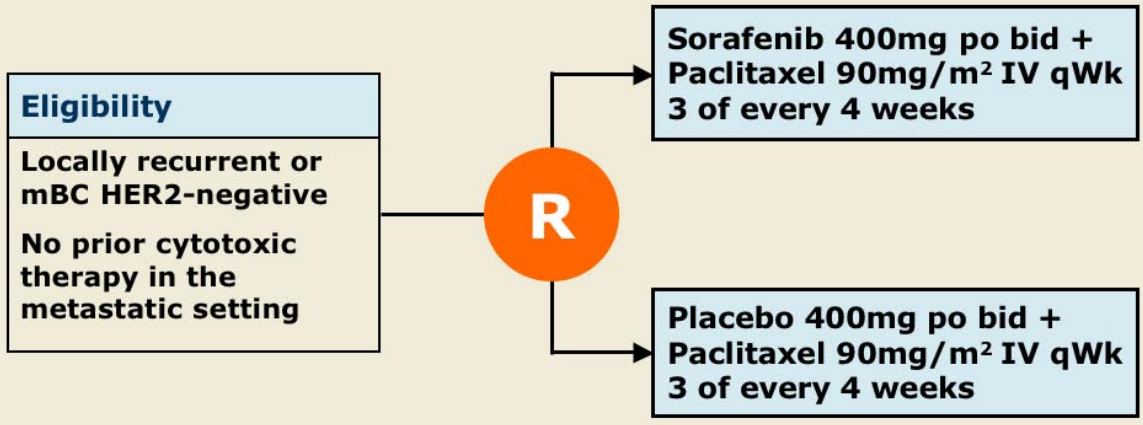
# Phase IIb Double-Blind Study of Sorafenib Compared to Placebo When Combined with Paclitaxel

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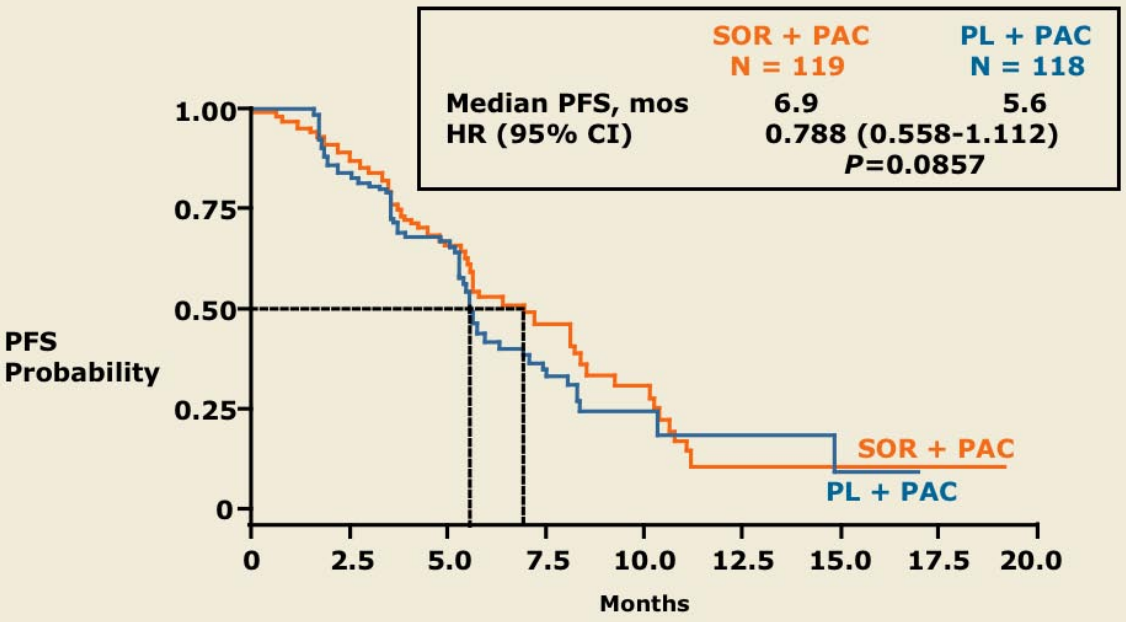
# Primary Endpoint: PFS (Intent-to-Treat Population)

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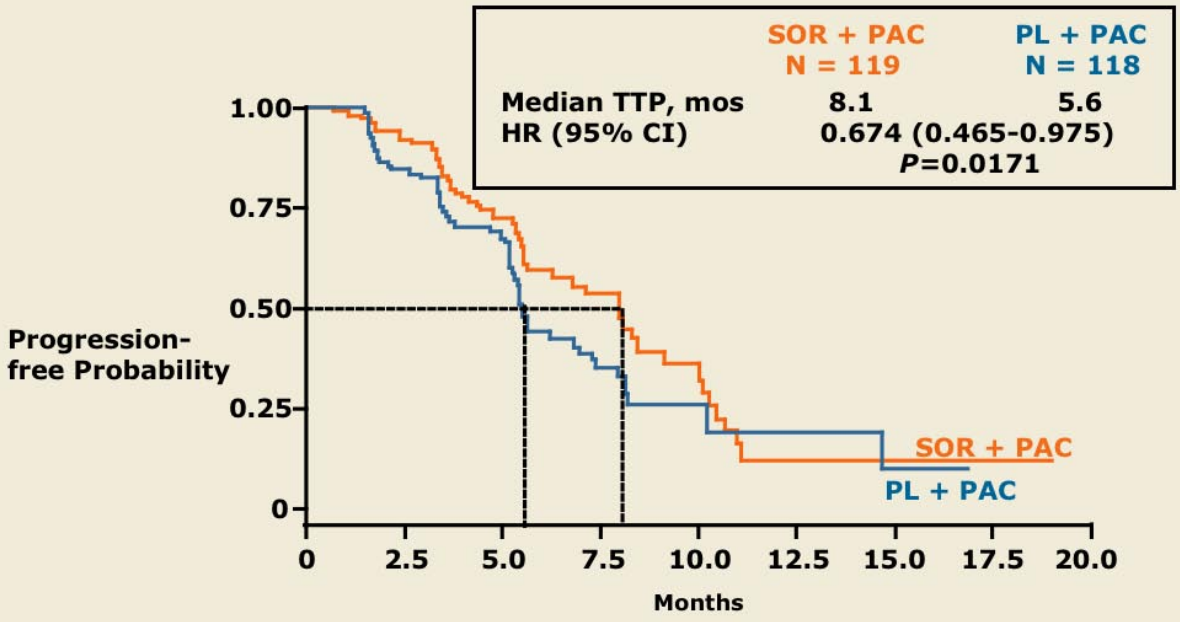
# Secondary Endpoint: Time to Progression (Intent-to-Treat Population)

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# Response Rate

| Clinical Response, n (%) | Sorafenib + Paclitaxel (n=119) | Placebo + Paclitaxel (n=118) | *p*-value |
|---|---|---|---|
| Overall response rate<br>Complete response<br>Partial response | 80 (67%)<br>8 (7%)<br>72 (61%) | 64 (54%)<br>5 (4%)<br>59 (50%) | 0.0234 |
| Stable disease | 16 (13%) | 32 (27%) | — |
| Progressive disease | 9 (8%) | 17 (14%) | — |
| Median duration of response* | 5.6 mos | 3.7 mos | 0.0079 |

**Calculated for responders only. Nonresponders were assigned a value of zero.*

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

| Adverse Events | Sorafenib + Placebo (n=115) | Placebo + Paclitaxel (n=118) |
|---|---|---|
| **Hand-foot syndrome** | **30%** | **3%** |
| Asthenia | 7% | 3% |
| Peripheral neuropathy | 6% | 7% |
| Neuropathy | 5% | 1% |
| Neutropenia | 13% | 7% |
| Anemia | 10% | 6% |
| Vomiting | 3% | 0% |
| Stomatitis | 3% | 0% |

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# Conclusions

- Results demonstrated a trend favoring sorafenib + paclitaxel over placebo + paclitaxel as first-line treatment for patients with HER2-negative, locally recurrent or mBC.
  - PFS: 6.9 mos vs 5.6 mos ($p$=0.0857)
  - TTP = 8.1 vs 5.6 mos ($p$=0.0171)
  - ORR = 67% vs 54% ($p$=0.0234)
- Sub-group analyses did not demonstrate a significant difference in PFS between the two study arms (data not shown).
- No new toxicities were observed in the combination arm and adverse events were manageable.
- Sorafenib combined with paclitaxel may provide additional benefit compared to paclitaxel alone in the first-line setting of advanced breast cancer.

Gradishar W et al. SABCS 2009;Abstract 44.

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