Albumin-Bound Paclitaxel Improves Response Rate vs Docetaxel in Metastatic Breast Cancer

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Abraxis BioScience, Inc, presented data at the 29th Annual San Antonio Breast Cancer Symposium (SABCS) from an interim analysis of a randomized, head-to-head phase II trial of albumin-bound paclitaxel (Abraxane) vs docetaxel (Taxotere), in the first-line treatment of metastatic breast cancer. The interim analysis showed that first-line treatment with weekly albumin-bound paclitaxel (100 and 150 mg/m²) increased tumor response rate by greater than 60% with less toxicity vs docetaxel (100 mg/m²) given every 3 weeks in patients with metastatic breast cancer. The analysis also showed that weekly paclitaxel protein-bound particles nearly doubled the response rate with less toxicity compared to albumin-bound paclitaxel at 300 mg/m² dosed every 3 weeks. Although the data are not fully mature, the interim analysis showed that all three paclitaxel regimens currently have longer progression-free survivals than docetaxel dosed every 3 weeks. A blinded, independent radiologic review of the response data is in process, and the company intends to submit the final analysis of the data to the American Society of Clinical Oncology (ASCO) in 2007.

Phase III Trial Planned
Based on these encouraging data, Abraxis plans to initiate a worldwide head-to-head phase III registration trial comparing weekly albumin-bound paclitaxel to every-3-week docetaxel for the treatment of first-line metastatic breast cancer. The phase III registration trial is expected to begin in the first half of 2007 in multiple sites throughout North America, Eastern and Western Europe, and Asia.

"These interim data show that weekly Abraxane, when used in the first-line treatment of patients with metastatic breast cancer, increased the response rate by over 60% with less toxicity than the FDA-approved dose of Taxotere given every 3 weeks," said William Gradishar, MD, FACP, director, breast medical oncology at Robert H. Lurie Comprehensive Cancer Center Northwestern University, a lead investigator in the study. "These data are consistent with previous study results of both Abraxane and Taxotere, and are very encouraging for both physicians and patients." In the randomized phase II study more than 300 patients with stage IV metastatic breast cancer and no prior chemotherapy treatments received one of four treatment regimens: albumin-bound paclitaxel, 300 mg/m² (n = 76) dosed every 3 weeks, albumin-bound paclitaxel, 100 mg/m² (n = 76) or 150 mg/m² (n = 74) dosed weekly for 3 weeks out of 4, and docetaxel, 100 mg/m² (n = 76) dosed every 3 weeks. The purpose of the study was to obtain comparative toxicity and preliminary antitumor response data addressing three issues: (1) albumin-bound paclitaxel vs docetaxel, (2) weekly vs every-3-week dosing of albumin-bound paclitaxel, and (3) a high and low dose of albumin-bound paclitaxel. The secondary endpoint of the study was progression-free survival.

Study Results
The prospectively planned interim analysis demonstrated that first-line treatment with albumin-bound paclitaxel, 100 or 150 mg/m² weekly, compared to docetaxel resulted in a statistically significant increase in response rates of 61% (58% vs 36%, \( P = .004 \)) and 72% (62% vs 36%, \( P = .0016 \)), respectively. Both weekly dose regimens of albumin-bound paclitaxel also increased the response rate compared to every-3-week paclitaxel (58% and 62% vs 33%; \( P < .001 \)). Although these data are not mature with only 33% of potential events having occurred, in the current analysis, all three paclitaxel treatment arms have longer progression-free survivals compared to docetaxel (by log rank).

Compared to docetaxel, all three paclitaxel treatment arms demonstrated less frequent adverse events with regard to neutropenia (grade 4, 74% with docetaxel vs 4%, 3%, and 7% with paclitaxel); febrile neutropenia (7% vs 1%, 1%, and 1%); and mucositis/stomatitis (grade 1/2, 20% vs 3%, 1%, and 0%). No grade 4 peripheral neuropathy was reported in any of the treatment arms, and there
was no statistical difference in arthralgias between paclitaxel at 100 mg/m\(^2\) compared to docetaxel. Fatigue was significantly lower with paclitaxel at 100 mg/m\(^2\) compared to docetaxel (21% vs 46%, \(P < .001\)).

The only adverse event occurring at a greater frequency with albumin-bound paclitaxel (300 mg/m\(^2\) every 3 weeks and 150 mg/m\(^2\) weekly) compared to docetaxel was arthralgia (33% and 35% vs 16%, respectively, \(P \leq .03\)). Compared to the other two paclitaxel treatment arms (300 mg/m\(^2\) every 3 weeks, 150 mg/m\(^2\) weekly), the 100 mg/m\(^2\) weekly regimen resulted in less peripheral neuropathy (51% and 47% vs 37%, respectively), arthralgias (33% and 35% vs 16%, respectively), and fatigue (33% and 39% vs 21%, respectively).

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