

EMERGING TAXANE THERAPY

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Nab-paclitaxel (Abraxane®) is indicated for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant therapy. Prior therapy should have included an anthracycline unless clinically contraindicated. The recommended regimen for Abraxane is 260 mg/m² administered intravenously over 30 minutes every three weeks. Black box warning cautions that an albumin form of paclitaxel may substantially affect a drug's functional properties relative to those of drug in solution and cautions not to substitute Abraxane for or with other paclitaxel formulations (*Prescribing Information*, Abraxis Bioscience, January 2007).

Nab-paclitaxel is a novel anti-neoplastic drug using nanoparticle technology to combine human albumin with water-insoluble paclitaxel. An albumin receptor-mediated transport (gp60, alondin) is present in many human breast tumors and results in higher concentrations of nab-paclitaxel into tumor tissue compared with healthy cells. Drug bioavailability is improved by avoidance of solvent micelles. Dose-dependant activity is predicated by linear pharmacokinetics as compared with solvent-based taxanes. Furthermore, the solvent-free delivery platform of nab-paclitaxel results in an improved safety profile. Intrinsic toxicities of castor oil-derived solvent and polysorbate 80 include acute hypersensitivity reactions necessitating corticosteroid and anti-histamine premedication, prolonged neutropenia, slowly resolving neuropathy, and fluid retention. Administration of nab-paclitaxel does not require routine premedication for hypersensitivity reactions and edema. Infusion time is reduced to 30 minutes.

See below for several notable presentations from the 2007 Annual Meeting of the American Society of Clinical Oncology:

- > Gradishar, et al. reported a randomized trial of weekly or every 3 week nab-paclitaxel vs. every 3 week docetaxel as 1st line therapy for metastatic breast cancer. Nab-paclitaxel 150 mg/m² weekly for 3 of 4 weeks and nab-paclitaxel 300 mg/m² every 3 weeks improved progression-free survival compared to docetaxel with an improved safety profile. Nab-paclitaxel 100 mg/m² weekly for 3 of 4 weeks was extremely well tolerated and resulted in improved progression-free survival compared with docetaxel. In an unplanned, preliminary analysis, peripheral neuropathy improved more rapidly with nab-paclitaxel than with peripheral neuropathy following docetaxel.
- > Burstein, et al. from Dana Farber Cancer Center reported a feasibility study of nab-paclitaxel as adjuvant therapy in early breast cancer. They concluded that nab-paclitaxel at 260 mg/m² for 4 cycles can be administered in a dose-dense schedule after 4 cycles of doxorubicin plus cyclophosphamide with G-CSF support. Tolerability and feasibility were comparable to doxorubicin plus cyclophosphamide followed by paclitaxel at 175 mg/m².
- > Guan, et al. reported a randomized study of nab-paclitaxel vs. solvent-based paclitaxel in Chinese women with metastatic breast cancer and demonstrated respective overall response rates of 54% and 24% with p<0.001.
- > Conlin, et al from Memorial Sloan Kettering Cancer Center, Gulf Coast

Oncology Center and Palm Beach Institute of Hematology & Oncology reported a phase II study of 3 dosing regimens of nab-paclitaxel with bevacizumab as 1st line therapy of HER2-negative metastatic breast cancer. All 3 regimens were well tolerated and no unexpected toxicities were observed. Anti-tumor activity was seen in all 3 regimens.

- > Dickler, et al. from Memorial Cancer Center and the University of San Francisco Comprehensive Cancer Center reported preliminary cardiac safety data with adjuvant bevacizumab plus dose-dense doxorubicin with cyclophosphamide followed by nab-paclitaxel in early stage breast cancer. At the time of the report there was no symptomatic left ventricular dysfunction observed. Link et al reported a retrospective analysis of bevacizumab and nab-paclitaxel in 40 women with metastatic breast cancer. Two patients had possible central nervous system hemorrhage into suspected brain metastases.
- > Mehta, et al. from the University of California at Irvine described pathologic complete responses in women with inflammatory breast cancer treated with weekly paclitaxel (solvent-based or albumin-bound) plus carboplatin +/- trastuzumab +/-bevacizumab.
- > Roy, et al. for the North Central Cancer Treatment Group reported the feasibility and tolerability of weekly nab-paclitaxel with gemcitabine in metastatic breast cancer.
- > Somer, et al. reported a Phase II trial of nab-paclitaxel with capecitabine in metastatic breast cancer. ★