In patients with metastatic breast cancer, the roles of the taxanes — docetaxel, paclitaxel, and nab-paclitaxel — are evolving. Recent Phase III trials have demonstrated that every-three-week regimens of docetaxel or nab-paclitaxel have better efficacy than every-three-week paclitaxel. Nab-paclitaxel presents the advantage of not requiring premedication, which avoids side effects, particularly of steroid premedication. Another advantage of nab-paclitaxel is that it can be administered over 30 minutes. Nab-paclitaxel has also been evaluated in two Phase II trials on a weekly schedule, which seems to retain efficacy with less toxicity. A Phase II trial found weekly docetaxel comparable to every-three-week docetaxel in terms of efficacy, but weekly docetaxel appeared to have a more favorable toxicity profile. Clinical trials will continue to delineate the role of the taxanes in the metastatic setting.

### PHASE III TRIAL COMPARING DOCETAXEL VERSUS PACLITAXEL IN PATIENTS WHO HAD PROGRESSION AFTER AN ANTHRACYCLINE-CONTAINING REGIMEN

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Docetaxel (n = 225)</th>
<th>Paclitaxel (n = 225)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response rate</td>
<td>32.0%</td>
<td>25.0%</td>
<td>0.10</td>
</tr>
<tr>
<td>Time to tumor progression</td>
<td>5.7 months</td>
<td>3.6 months</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of response</td>
<td>15.6 months</td>
<td>4.6 months</td>
<td>0.01</td>
</tr>
<tr>
<td>Overall survival</td>
<td>15.4 months</td>
<td>12.7 months</td>
<td>0.03</td>
</tr>
</tbody>
</table>

**NEUROTOXICITY EVENTS**

- Grade 3/4 neutropenia: 13.3% vs. 14.5%, p = 0.10
- Grade 3/4 anemia: 19.4% vs. 16.3%, p = 0.31
- Grade 3/4 thrombocytopenia: 6.5% vs. 8.8%, p = 0.31

**Median survival**

- Overall: 15.4 months vs. 12.7 months, p = 0.03

**Source:** J Clin Oncol 2005;23(24):5542-51.

### PHASE II STUDY OF WEEKLY VERSUS EVERY THREE-WEEK DOCETAXEL

**Eligibility**

- Metastatic breast cancer

**Study Details**

- **ARM 1**
  - Docetaxel 33 mg/m² q3wk
  - 6 cycles

- **ARM 2**
  - Docetaxel 100 mg/m² q3wk
  - 6 cycles

**Proportion of patients receiving docetaxel as final-line treatment:** 83.7% vs. 10.8%, p < 0.001

**EFFICACY DATA**

- **Response rates**
  - Overall: 33.0% vs. 25.0%, p = 0.03
  - First-line: 42% vs. 27%, p = 0.029
  - Second-line or greater: 35% vs. 25.0%, p = 0.006

- **Time to tumor progression**
  - Overall: 23.5 vs. 18.9 weeks, p = 0.006

**Median survival**

- Overall: 85.3 weeks vs. 56.4 weeks, p = 0.024

**Safety data**

- Grade 3 or 4 neutropenia: 9% vs. 22%, p < 0.001
- Grade 3 or 4 sensory neuropathy: 10% vs. 2%, p < 0.001
- Growth factors used: 3% vs. 4%, NR

**Source:** J Clin Oncol 2005;23(24):5542-51 (abstract ahead of print).

### ANTHERCYCLINES WITH OR WITHOUT TAXANES AS FIRST-LINE CHEMOTHERAPY: POOLED META-ANALYSIS OF 2850 PATIENTS

**Parameter**

- Number of patients: 2850
- Number of studies: 28
- Number of comparisons: 56

**Risk ratio**

- All patients: 1.10 (95% CI 1.00-1.21, p = 0.05)
- First-line: 1.13 (95% CI 1.04-1.22, p = 0.001)
- Second-line or greater: 1.06 (95% CI 1.00-1.12, p = 0.04)

**Median survival**

- Overall: 23.0 weeks vs. 16.9 weeks, p = 0.006

**Source:** J Clin Oncol 2004;22(14):2953-64.

### SELECT PUBLICATIONS


### PHASE III TRIAL COMPARING NAB PACLITAXEL VERSUS STANDARD PACLITAXEL

**Efficacy data**

- Nab-paclitaxel vs. docetaxel
  - Number of patients: 229
  - Median time to progression: 5.2 months vs. 5.8 months, p < 0.001
  - Incidence of Grade III/IV hematologic toxicity: 4.6% vs. 8.8%, p = 0.31
  - Incidence of Grade III/IV non-hematologic toxicity: 8.7% vs. 12.9%, p = 0.31

**Safety data**

- Grade III sensory neuropathy: 10% vs. 2%, p < 0.001
- Grade IV neutropenia: 14.9% vs. 1.8%, p < 0.001

**Equivalence**

- Risk ratio of anthracycline + taxane vs anthracycline + nontaxane

**Source:** J Clin Oncol 2005;23(24):5542-51 (abstract ahead of print).

**NAPARCITAXEL VERSUS STANDARD PACLITAXEL**

The superior efficacy, favorable safety profile, and greater patient convenience of ABI-007 (nab-paclitaxel) make this novel albumin-bound paclitaxel an important advance in the treatment of patients with MBC (metastatic breast cancer). ABI-007 warrants further investigation, using additional dosing regiments (eg, weekly) and in combination with other treatment modalities, as front-line treatment of breast cancer and other solid tumors.


**NAPARCITAXEL COMPARISON TO OTHER TAXANES**

I believe nanoparticle paclitaxel is more active than paclitaxel based on the randomized trials. In cross-study comparisons of nanoparticle paclitaxel versus docetaxel, each given every three weeks, the response rates were similar in the 30 percent range. However, docetaxel in the metastatic setting, whether given weekly or every three weeks, is toxic because of side effects like arthralgia, fluid retention, and neuropathy, and it’s difficult to administer for long periods of time.

I can give docetaxel in the adjuvant setting where treatment is short term, but I believe nanoparticle paclitaxel is better tolerated. I don’t single-agent docetaxel in the metastatic setting, and I would use nanoparticle paclitaxel in lieu of weekly paclitaxel.

I would like to see more data on combinations with nanoparticle paclitaxel from more nanoparticle taxane toxicity profiles before using it in a combination off protocol.

— Joanne L. Blum, MD, PhD. Breast Cancer Update 2005 (1)

### CHOICE OF TAXANES IN THE METASTATIC SETTING

A weekly regimen of the original paclitaxel formulation would have been my choice in the past. Now that we have data with nab-paclitaxel, I think that’s a reasonable option also. From the data, nab-paclitaxel may be preferable. It outperformed the original paclitaxel formulation when administered every three weeks. A weekly regimen allows us to outperform an every three-week regimen of the original paclitaxel formulation, and I’m left wondering which is the best drug to use. For patients who prefer an every-three-week schedule, I believe nab-paclitaxel is the way to go. Otherwise, it’s a toss-up between every-three-week nab-paclitaxel and a weekly regimen of the original paclitaxel formulation. I don’t believe there’s a way to compare the two.

CALGB is planning to conduct a head-to-head trial comparing weekly regimens of nab-paclitaxel and the original paclitaxel formulation.

— Debbi Tripathy, MD. Breast Cancer Update 2005 (3)