

IN EVERY ISSUE

Breast Cancer, Liver Cancer & Leukemia

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New Chemotherapy Class Heads to Market

The latest approval for metastatic breast cancer is the first in a new class of chemotherapy agents called epothilones. In October, the Food and Drug Administration approved Ixempra (ixabepilone) in combination with Xeloda (capecitabine), another chemotherapy used to treat metastatic breast cancer, for patients whose tumors have stopped responding to other therapies, specifically taxanes and anthracyclines. It was also approved for use as a single agent in patients whose tumors are resistant to taxanes, anthracyclines, and Xeloda.

Epothilones interfere with cell division in the same fashion as taxanes, such as Taxol (paclitaxel), but epothilone agents work on cancer cells that have become resistant to taxanes because of their specific molecular makeup.

When investigators added Ixempra to Xeloda in clinical trials, patients with advanced breast cancer had their tumors regress or stabilize for an average of 5.8 months compared with 4.2 months in patients taking only Xeloda. Results expected in late 2008 from two Ixempra trials will provide data on the drug's survival impact. If survival does improve in the metastatic setting, doctors say Ixempra may also be effective in early-stage breast cancer, possibly following the path of breast cancer drugs Herceptin (trastuzumab) and Tykerb (lapatinib).

Side effects of Ixempra include peripheral neuropathy, constipation, nausea, and fatigue. For more information on Ixempra, go to www.ixempra.com.

First Drug Approved for Liver Cancer

Before November, surgery was the only option for effective treatment of hepatocellular carcinoma, the most common type of liver cancer—a disease that affects about 19,000 Americans each year. If not removed completely, patients usually succumb to the cancer within six months. But on November 19, the Food and Drug Administration approved Nexavar (sorafenib) for inoperable cases, making Nexavar the first drug to be approved for this difficult-to-treat tumor.

The FDA based its decision on a phase III clinical trial, known as the SHARP trial, which showed liver cancer patients taking Nexavar survived nearly 11 months compared with eight months for patients taking a placebo. Study results also showed the drug extended time to tumor progression from 2.8 months to 5.5

months. The study was stopped early following positive results from an early analysis, and patients were allowed to switch to the Nexavar arm of the trial. Side effects of Nexavar may include diarrhea, rash, and fatigue.

Approved for advanced kidney cancer in 2005, Nexavar is an oral drug that blocks molecules believed to contribute to a tumor's blood supply and, thus, cancer cell growth. Researchers are examining genes that may help identify which patients would benefit from the drug. For more information on Nexavar, go to www.nexavar.com.

Osteoporosis Drug Gets OK for Preventing Breast Cancer

Since its approval nearly 10 years ago, tamoxifen has dominated as the sole chemoprevention agent to reduce the risk of breast cancer. But now, Evista (raloxifene) joins the chemoprevention ranks following its approval in September.

Like tamoxifen, Evista is a selective estrogen receptor modulator, or SERM, a drug that blocks the effects of estrogen on cell growth by mimicking the hormone and binding to its receptor. Because SERMs mimic estrogen in postmenopausal patients who have low levels of estrogen, these drugs can also strengthen bone tissue and lower cholesterol.

Originally approved in 1997 for the prevention of osteoporosis in postmenopausal women followed by an approval in 1999 for treating osteoporosis, the Food and Drug Administration has now approved Evista for reducing the risk of invasive breast cancer in postmenopausal women with osteoporosis and postmenopausal women at high risk for breast cancer. Approval was based on results from the STAR (Study of Tamoxifen And Raloxifene) trial, comparing the effectiveness and safety of tamoxifen to Evista in nearly 20,000 women at high risk for breast cancer.

The results showed Evista was just as beneficial as tamoxifen—lowering the risk of invasive breast cancer by about half—but Evista carried a lower risk of side effects, including 36 percent fewer uterine cancers and 29 percent fewer blood clots. However, Evista didn't appear to be as good as tamoxifen in reducing the risk of noninvasive breast cancer (ductal carcinoma in situ and lobular carcinoma in situ).

Common side effects of Evista include hot flashes, leg cramps, and peripheral edema (abnormal buildup of fluid in the legs, feet, and ankles). For more information on Evista, go to www.evista.com.

Good News for Patients With Gleevec-Resistant CML

Although 95 percent of patients with chronic myeloid leukemia are still alive after five years of treatment with Gleevec (imatinib), some cancers either don't respond or eventually recur. In late October, the Food and Drug Administration made Tasigna (nilotinib) the second drug to be approved for treatment of Gleevec-resistant CML. The FDA approved Sprycel (dasatinib) in June 2006. Tasigna works similarly to Gleevec, which targets a protein created by the

mutated Philadelphia chromosome—the result of the long arms of chromosomes 9 and 22 switching places (translocation). When the segments switch, a fusion protein called bcr-abl is created and becomes the driving force of CML, a slow-progressing cancer that causes the body to produce too many cancerous myeloid white blood cells.

While most CML cases have a specific mutation that can be blocked by Gleevec, there are other mutations that are unaffected. Tasigna and Sprycel are more potent than Gleevec, inhibiting 32 of the 33 most common mutations.

In a phase II study of patients with Gleevec-resistant chronic phase CML (considered early-stage leukemia), Tasigna decreased white blood cell counts in 137 (74 percent) of 185 patients. The drug also reduced or eliminated the number of cells carrying the abnormal Philadelphia chromosome in 145 of 279 patients, or 52 percent. Of 64 patients in the trial with accelerated phase CML, 38 patients (59 percent) experienced decreased white blood cell counts, and 23 patients (36 percent) saw a reduction or elimination of Philadelphia chromosome-containing cells.

About 4,600 people are diagnosed with CML each year. Side effects of Tasigna include rash, headache, and low blood counts. For more information on Tasigna, go to www.tasigna.com.