

CONTENTS**Breaking News from ASCO**

BY STAFF REPORTS

Updates from the 2006 annual meeting of the American Society of Clinical Oncology.

The annual meeting of the American Society of Clinical Oncology was held in Atlanta in early June. The gathering of more than 25,000 cancer researchers, physicians, and representatives from pharmaceutical and biotechnology industries reported more than 3,700 cancer research studies on cancer care, treatment, and prevention. Details can be found at www.asco.org or on ASCO's consumer website, People Living With Cancer (www.plwc.org).

Tykerb Offers Hope to Patients Whose Breast Cancers Progress after Herceptin

Breast cancers that overexpress the HER2 protein tend to be more aggressive. Herceptin (trastuzumab), an antibody that targets the HER2 protein, reduces recurrence in patients with early-stage breast cancer and extends survival in patients with metastatic breast cancer. Metastatic breast cancer eventually progresses, even if the patient is taking Herceptin. But there may be new hope for these patients based on results from an international phase III study that showed Tykerb (lapatinib), an oral drug that targets both HER2 and HER1 (also known as the epidermal growth factor receptor), slows cancer growth or spread when given in combination with Xeloda (capecitabine). Early analysis of the study included 321 patients, all of whom had HER2-positive metastatic breast cancer, and whose tumors continued to grow despite prior Herceptin-containing therapy. The Tykerb/Xeloda combination nearly doubled the time to progression—36.9 weeks (8.5 months) compared with 19.7 weeks (4.5 months) with Xeloda alone. In addition, unlike Herceptin, Tykerb can penetrate into the brain, which resulted in fewer cases of brain metastases. (Another study found Tykerb may be effective in treating brain metastasis in breast cancer patients.) These results suggest Tykerb may be an option for HER2-positive breast cancer patients who no longer respond to Herceptin. Side effects associated with Tykerb include mild to moderate diarrhea, fatigue and rash. Ongoing trials will also investigate Tykerb in combination with other hormonal or chemotherapy drugs. GlaxoSmithKline, the

drug's maker, plans to submit Tykerb to the Food and Drug Administration for approval later this year.

Approval Expected Soon for Leukemia Drug

In June, the Oncologic Drugs Advisory Committee recommended accelerated approval by the Food and Drug Administration of Sprycel (dasatinib) for the treatment of patients with chronic myelogenous leukemia (CML) and Philadelphia chromosome-positive acute lymphocytic leukemia who have not responded to previous therapy with Gleevec (imatinib), an FDA-approved targeted drug. Sprycel is a pill that has demonstrated significant activity in patients with CML, both in the early and late stages of the disease. The accelerated approval recommendation for Sprycel is based on several phase II trials that showed up to half of Gleevec-resistant or refractory CML patients responded to Sprycel. In a trial comparing high doses of Gleevec with Sprycel in CML patients resistant to lower doses of Gleevec, more patients responded (and for a longer period of time) to Sprycel than high-dose Gleevec. A decision is expected from the FDA on the accelerated approval of Sprycel by the end of June.

New Approach to Target Bone Metastases

Bone metastasis (cancer cells that break off a main tumor and start to grow in bones) is a common complication associated with a number of cancers, including breast cancer. Breast cancer patients with bone metastases often receive treatment with intravenous bisphosphonates, but new agents are on the horizon. Denosumab (AMG 162), a human monoclonal antibody that specifically targets a key mediator of bone remodeling, called RANK ligand protein, might have a useful role in the treatment of bone metastases. Data were presented from a phase II trial investigating different doses of denosumab in patients with metastatic breast cancer with bone involvement who had not previously received bisphosphonates. The study demonstrated that denosumab reduced levels of a marker of bone turnover called urinary N-telopeptide, with decreases ranging from 63 to 82 percent. In addition, denosumab appeared to prevent skeletal-related events as effectively as bisphosphonates. The most frequent side effects associated with denosumab were nausea, vomiting, weakness and diarrhea, compared with fever, bone and joint pain and weakness with bisphosphonate therapy. Phase III trials are planned to directly compare therapy with denosumab to bisphosphonates in this patient population.

Drug for Kidney Cancer May Offer Patients New Option

Patients with advanced renal cell carcinoma (RCC), the most common type of kidney cancer, often face limited therapeutic options. The current treatments for kidney cancer include Nexavar (sorafenib) and Sutent (sunitinib), both of which are oral agents that have just been approved by the FDA (see *CURE*, Spring 2006), do not provide long-lasting remissions. Torisel (temsirolimus) is a new agent that targets a different pathway than Sutent and Nexavar, and results of a phase III

study with the drug provide hope for kidney cancer patients. Torisel curbs tumor cell growth by inhibiting an important signaling pathway known as mTOR (mammalian target of rapamycin). The study included 626 untreated advanced RCC patients who were treated with Torisel alone, interferon alone or Torisel plus interferon. Results showed that patients treated with Torisel alone had longer overall survival (10.9 months) compared with patients who received interferon alone (7.3 months), which translates into a 49 percent increase in median overall survival. Side effects associated with Torisel include anemia, fatigue and shortness of breath. Wyeth, the maker of Torisel, plans to submit the drug for approval by the end of 2006.

Taxotere Improves Survival in Head and Neck Cancer

Data from a phase III study show that adding Taxotere (docetaxel) to chemotherapy increases survival in patients with locally advanced head and neck cancer. Patients received the current standard chemotherapy combination of cisplatin and 5-FU with or without Taxotere. All patients were then treated with carboplatin and radiation therapy (chemoradiotherapy) at the same time. Three years after treatment, 62 percent of patients receiving the Taxotere regimen were alive compared with 48 percent of patients who received only chemotherapy. Side effects of Taxotere include nausea, mouth sores and low blood count. The use of initial, or induction, chemotherapy followed by chemoradiotherapy is known as “sequential therapy” and aims to control cancer at the local site as well as distant metastasis. These latest results provide another option for patients with locally advanced head and neck cancer, but still unknown is if this approach will be better than current treatments. Ongoing studies should answer this important question.

Zolinza Effective Against Lymphoma of the Skin

Cutaneous T-cell lymphoma (CTCL) is a type of non-Hodgkin lymphoma that becomes localized in the skin and causes lesions and tumors in advanced cases. Several treatments exist for CTCL, but a targeted agent called Zolinza (vorinostat) has demonstrated activity against advanced CTCL in early clinical studies. A study of 74 advanced CTCL patients whose cancer did not respond to prior therapy showed that 30 percent responded to the new drug. In addition, 43 percent of patients experienced relief of severe itching, a common complication with CTCL. Side effects with Zolinza include diarrhea, fatigue and nausea. Zolinza was given priority review by the FDA and a decision is expected by October 2006.