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Breaking News from ASH and SABCS

BY STAFF REPORTS

The annual meetings of the American Society of Hematology and the San Antonio Breast Cancer Symposium were held in December. Each gathering brought together thousands of cancer researchers, physicians and others to report on critical issues in each respective field of cancer. Details can be found at www.hematology.org and www.sabcs.org.

AMERICAN SOCIETY OF HEMATOLOGY

Next-Generation CML Agent Active Against Resistant Mutation

Chronic myeloid leukemia (CML) and 25 percent of acute lymphoblastic leukemia cases are characterized by a chromosomal abnormality called the Philadelphia chromosome, which results in an abnormal gene called bcr-abl. This gene has been the focus of CML targeted agents, but in some patients, leukemia cells become resistant because of new mutations, including T315I. CML with this mutation is resistant to first-generation tyrosine kinase inhibitor Gleevec® (imatinib) as well as second-generation tyrosine kinase inhibitors Sprycel® (dasatinib) and Tassigna® (nilotinib). Tyrosine kinase inhibitors have difficulty binding to the T315I mutation, but a new class of drugs called aurora kinase inhibitors may be able to overcome the resistance caused by the mutation. A third-generation CML drug called MK-0457, an aurora kinase inhibitor, has shown activity against leukemia cells that have the difficult-to-treat mutation. A phase I study of 15 CML patients included 11 patients whose leukemia cells had the T315I mutation. Nine out of the 11 patients, all of whom had Gleevec-resistant CML and had progressed on other therapies, had a response to MK-0457, including one complete cytogenetic response (a decrease in the number of Philadelphia chromosome-positive cells). Although these are very early results, MK-0457 offers new hope to patients with CML and may lead to finding a cure for the disease. Researchers plan to continue studying the agent, particularly in combination with other kinase inhibitors.

—Elizabeth Whittington

New Velcade Data for Myeloma Coincides with Mantle Cell Lymphoma Approval

Velcade® (bortezomib) and Revlimid® (lenalidomide), both targeted agents approved for multiple myeloma, showed benefit when researchers used them in combination at various doses. In the phase I trial of 36 multiple myeloma

patients, more than half had a response that lasted a median of six months regardless if they progressed on previous therapies, including Velcade or Revlimid alone. In 14 patients whose multiple myeloma did progress while on the combination therapy, adding the steroid Decadron® (dexamethasone) resulted in a response in nearly three-quarters of these patients. A few days before these data were presented in early December, Velcade was approved for treatment of mantle cell lymphoma that progressed on earlier treatment. The approval was based on a phase II trial that proved Velcade's ability to delay progression of mantle cell lymphoma, a rare and aggressive type of non-Hodgkin's lymphoma, for a median of six months, with a 31 percent overall response.

—Elizabeth Whittington

Promacta Boosts Platelets and Reduces Bleeding

Thrombocytopenia is a side effect of cancer therapy that results in a decrease in the number of circulating platelets—irregularly shaped blood cells that initiate blood clotting. Without enough platelets to help the blood to clot, even minor cuts or bruises can result in significant bleeding. A new oral drug called Promacta™ (eltrombopag) is designed to increase the number of platelets in patients who have reduced platelet production. Some cases of thrombocytopenia result from idiopathic thrombocytopenic purpura, an autoimmune condition associated with chronic lymphocytic leukemia and certain lymphomas. Results from a phase II trial found that Promacta led to a decrease in bleeding events and significantly increased the number of platelets in adult patients with idiopathic thrombocytopenic purpura. Promacta was well tolerated with no major side effects reported. An ongoing phase III study will provide further details of the effectiveness of the drug, which is expected to lead to the drug's approval in 2007. Researchers are also testing Promacta in patients undergoing aggressive chemotherapy.

—Chris Schwab, PhD

SAN ANTONIO BREAST CANCER SYMPOSIUM

Tykerb Nears Approval for HER2-Positive Breast Cancer

Herceptin® (trastuzumab) is an antibody that targets HER2, a protein present in normal breast cells that is overly abundant in some malignant cells. Herceptin prolongs survival in patients with HER2-positive metastatic breast cancer, but the disease eventually progresses in most cases. Results from a phase III study show that Tykerb® (lapatinib), an oral drug that targets both HER2 and HER1 (also known as the epidermal growth factor receptor), slows cancer growth when given in combination with Xeloda® (capecitabine) in patients whose tumors progressed despite prior therapy that included Herceptin. The drug combination nearly doubled the time to progression—8.4 months compared with 4.4 months with Xeloda alone. A second study evaluated the combination of Tykerb plus Taxol® (paclitaxel) in 35 patients with newly diagnosed inflammatory breast cancer, 30

of whom had HER2-positive disease. The combination was active, producing complete responses in 10 percent of patients, and partial responses in 67 percent of HER2-positive patients. Side effects associated with Tykerb include mild to moderate diarrhea, rash and fatigue. Ongoing trials will investigate Tykerb in combination with other hormonal or chemotherapy drugs, and a global trial launched in December to investigate Tykerb in the adjuvant setting, known as TEACH (Tykerb Evaluation After CHEmotherapy), will assess its impact in early-stage disease. GlaxoSmithKline submitted Tykerb in combination with Xeloda to the Food and Drug Administration for approval in metastatic breast cancer, and a decision is expected by early 2007.

—Susan Peck, PhD

Fewer Breast Cancer Cases Linked to Decline in HRT Use

By 2003, millions of women had stopped taking hormone replacement therapy following results from the Women's Health Initiative study that connected estrogen and progestin hormone therapy use to an increased risk of invasive breast cancer. That same year, breast cancer incidence dropped 7 percent—translating into 14,000 fewer women diagnosed in 2003 than in 2002. A new analysis says the dramatic reduction in HRT use is the reason. The analysis also revealed that for the type of breast cancer that is hormone sensitive, known as estrogen receptor-positive breast cancer, the decline was 12 percent for women ages 50 to 69, while estrogen receptor-negative tumors declined only 4 percent for the same age group. Researchers did stress, however, that since these data are based on population statistics, causation cannot be proven. Experts say other possible effects could include improvements in breast cancer screening that are detecting more noninvasive breast cancers, or changes in the use of selective estrogen receptor modulators, such as Evista® (raloxifene) for osteoporosis—a drug recently proven to lower the risk of invasive breast cancer in postmenopausal women that was submitted for approval in this setting in early December. National cancer incidence data for 2004 will be available in spring 2007, at which time researchers can determine if the drop was a single event or a new trend.

—Melissa Weber

Zometa Reduces Aromatase Inhibitor-Associated Bone Loss

Aromatase inhibitors can significantly reduce the risk of recurrence in postmenopausal women with early breast cancer. But because these drugs block the production of estrogen, they can also cause an increased rate of bone loss, which may put some women at a higher risk for fractures. Two phase III studies found that adding the bisphosphonate Zometa® (zoledronic acid) effectively prevents bone loss associated with aromatase inhibitors. More than 1,600 early-stage breast cancer patients in both the American Z-FAST trial and the international ZO-FAST trial received Zometa either when starting treatment with Femara® (letrozole) or just after the emergence of clinically measurable bone loss. After one year, upfront Zometa resulted in a 5.1 percent improvement in bone

density in the spine, and a 3.4 percent improvement in the hip compared with women who didn't receive Zometa until bone loss occurred. Interestingly, women in both groups had a similar incidence of bone fractures (about 2 percent). Zometa was safe and well-tolerated, with no serious side effects.

—Zach Moore, PhD