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Breaking News from ASCO

BY STAFF REPORTS

Updates from the 2008 annual meeting of the American Society of Clinical Oncology includes news on lung, breast, colorectal, and kidney cancers.

The annual meeting of the American Society of Clinical Oncology was held in Chicago from May 30 to June 3. The gathering attracted more than 32,000 cancer researchers, physicians, and representatives from pharmaceutical and biotechnology industries to learn the latest in cancer care, treatment, and prevention. Details can be found at www.asco.org or ASCO's patient website, Cancer.Net.

Erbitux Extends Lung Cancer Survival

One of the highlighted studies at this year's meeting, the FLEX trial, showed Erbitux (cetuximab) extends overall survival by five weeks in non-small cell lung cancer—considered a success in this hard-to-treat cancer.

The international phase III study involved 1,125 newly diagnosed patients with late-stage disease who were given either Erbitux plus chemotherapy (cisplatin and vinorelbine) or chemotherapy alone. While progression-free survival remained unchanged between the two arms at 4.8 months, overall survival in the group receiving Erbitux and chemotherapy reached 11.3 months compared with 10.1 months in patients receiving only chemotherapy. One-year survival improved from 42 percent to 47 percent—a 5 percent absolute gain in survival. “To put it into perspective, that’s half the gain of adding chemotherapy to no treatment in the disease,” said Robert Pirker, MD, lead author of the study, at a press conference.

Dr. Pirker, of the Medical University of Vienna in Austria, suggested the study results could signal a change in the standard of care for metastatic lung cancer patients, possibly those ineligible for the targeted therapy Avastin (bevacizumab). Presented last year, Avastin combined with carboplatin and Taxol (paclitaxel) improved survival from 10.3 months with chemotherapy alone to 12.3 months. However, Dr. Pirker stressed that a direct comparison cannot be made from the

two studies.

Side effects of Erbitux include neutropenia, anemia, and rash—a common effect in therapies that target the epidermal growth factor receptor, or EGFR. Studies have shown many lung cancer patients—as many as 80 percent—carry a mutated version of the EGFR gene. Erbitux is approved for colorectal cancer and head and neck cancer, and is expected to be submitted later this year for approval for newly diagnosed advanced lung cancer.—*Elizabeth Whittington*

Zometa Cuts Recurrence Risk in Breast Cancer

In addition to preventing bone loss, Zometa (zoledronic acid) may also reduce the risk of recurrence in some breast cancer patients. A phase III study showed that for premenopausal early-stage breast cancer patients receiving ovarian suppression and hormone therapy (tamoxifen or Arimidex [anastrozole]) after surgery, adding Zometa reduced the risk of relapse by 35 percent. Patients have been followed for five years, and about 6 percent of patients taking Zometa suffered a relapse compared with 9 percent of women not taking the drug. The combination appears to be well tolerated.

Michael Gnant, MD, of the Medical University of Vienna and the study's lead author, said Zometa, a bisphosphonate drug, should now be further studied in this patient setting to determine the optimal dose, schedule, and treatment duration. He also clarified that findings from the study aren't sweeping. "To say this applies to all breast cancer patients would be exaggerating I couldn't see a good reason why [the benefit] would not be present [in other patient groups], but as scientists we deal with what we have," Dr. Gnant said in an interview at the meeting.

Bisphosphonates, particularly Zometa, have been found to inhibit tumor cell growth, says Dr. Gnant. Larger trials are currently under way to confirm the clinical impact of these anti-tumor effects. "If we can create an environment so hostile [to tumor cells] ... then that keeps our patients healthy," he said.

Although generally well tolerated, side effects of bisphosphonates can include stomach or esophagus irritation and nausea. Rare cases of damage to the kidney and jaw bone have also been reported.—*Melissa Weber*

KRAS Status Predicts Treatment Response

The first molecular marker to determine targeted treatment in newly diagnosed metastatic colorectal cancer patients has been validated in a study presented at ASCO. Results from the CRYSTAL study were presented at last year's annual meeting, showing that adding Erbitux (cetuximab) to chemotherapy decreased the risk of progression by 15 percent in colorectal cancer patients. Moreover, it appeared a subset of patients responded better to the Erbitux combination—an observation that led to a retrospective study of tumor samples from about half of the approximately 1,200 patients involved in the original study to analyze the gene KRAS.

Earlier studies have suggested patients with cancer expressing the wildtype (normal) gene respond better to Erbitux plus chemotherapy than patients with mutant KRAS. About 64 percent of patients in the study carried a normal copy of the KRAS gene (wild-type), while 36 percent carried a mutated version of the gene. For patients with mutated KRAS, no difference in response rates was observed between patients receiving Erbitux plus chemotherapy compared with chemotherapy alone.

Patients with wild-type KRAS, on the other hand, saw one-year progression-free survival improve from 25 percent with chemotherapy alone to 43 percent when Erbitux was added to chemotherapy; the risk of progression decreased by 32 percent. In addition, 59 percent of these patients had their tumors shrink by more than half on the Erbitux regimen compared with 43 percent of patients receiving chemotherapy alone.

The findings could spare a third of metastatic colorectal cancer patients from the side effects of an ineffective treatment and give patients and doctors the knowledge to explore other options. It is likely doctors will begin identifying KRAS status in colorectal cancer patients before determining treatment, said Eric Van Cutsem, MD, PhD, of the University Hospital Gasthuisberg in Belgium and lead author of the study, during a press conference. Lab assays are now becoming available to test tumors for KRAS, although their use in making routine treatment decisions remains controversial. —*EW*

Everolimus Delays Progression of Kidney Cancer

Patients with metastatic renal cell carcinoma who have progressed on other targeted therapies, namely Sutent (sunitinib) and/or Nexavar (sorafenib), may soon have a new option to keep their disease in check.

A phase III trial randomly assigned patients to receive everolimus (an mTOR inhibitor) or placebo plus best supportive care. After six months, 26 percent of 272 patients in the everolimus group were progression-free compared with 2 percent of 138 patients in the placebo group. Median progression-free survival (the average time before disease progression) was four months for patients in the everolimus arm compared with 1.9 months for patients on placebo. (Patients in the placebo arm were offered everolimus once their disease progressed.) Side effects of everolimus included mouth ulcers and anemia.

Robert Motzer, MD, of Memorial Sloan-Kettering Cancer Center and lead author of the study, said everolimus is the first agent to help RCC patients whose disease has progressed on other targeted therapies and should therefore be considered standard of care for this group of patients. “It’s more like treating a chronic disease where people respond to one for a time period and then when they stop, now we have something where we didn’t have anything before,” Dr. Motzer said in an interview at the meeting. “For years we’ve had nothing and now there are multiple different therapies. It’s made a dramatic difference for our patients.” Dr. Motzer said his team is currently recruiting patients for a phase I study combining Sutent and everolimus.

Novartis plans to file everolimus for approval in renal cell carcinoma, the most

common form of kidney cancer, later this year. —*MW*

Breast Cancer Prognosis Linked to Vitamin D Deficiency

Researchers have found that women who have a vitamin D deficiency at the time of breast cancer diagnosis were 94 percent more likely to have metastasis of their cancer and 73 percent more likely to die within 10 years compared with women with adequate vitamin D levels. In the study of more than 500 newly diagnosed women, researchers also found that only 24 percent of the women had adequate vitamin D levels.

However, lead author Pamela Goodwin, MD, of the University of Toronto, cautioned physicians on applying the study's results to patients. "I believe it is premature to advise breast cancer patients to use vitamin D supplementation in doses higher than what is recommended for normal health in the hopes of precluding their breast cancer outcomes based on our data," Dr. Goodwin told colleagues during her presentation. This finding, however, does not prove the deficiency actually contributes to recurrence.

If doctors wish to recommend vitamin D to their patients, Dr. Goodwin recommended a dosage of 400 to 800 IU per day. The recommended daily allowance is 400 IU for women ages 51 to 70 and 600 IU for women over 70. Dr. Goodwin said vitamin D comes from two sources: sun exposure and food or supplements. —*Lena Huang*

Avastin Plus Taxotere Slows Newly Diagnosed Advanced Breast Cancer

For women newly diagnosed with locally recurrent or metastatic breast cancer, new research shows either taxane chemotherapy—Taxol (paclitaxel) or Taxotere (docetaxel)—combined with Avastin (bevacizumab) is more effective than chemotherapy alone. (The Food and Drug Administration granted accelerated approval to Avastin in combination with Taxol in February. Find details in *CURE's* Spring 2008 "Drugs in the News".)

A phase III trial, called the AVADO trial, randomly assigned 736 patients to receive Taxotere plus placebo, low-dose Avastin plus Taxotere, or high-dose Avastin plus Taxotere. After a median follow-up of 11 months, the low-dose group was 21 percent less likely to have their disease progress compared with Taxotere alone, and the high-dose group was 28 percent less likely to have disease progression compared with the Taxotere-only arm. Tumors shrank by at least half in 44.4 percent in the Taxotere-alone group, 55.2 percent in the low-dose group, and 63.1 percent in the high-dose group. Overall survival data are not yet mature.

David Miles, MD, of the Mount Vernon Cancer Centre in London and the study's lead author, said the message of the trial is that use of Avastin increases the response rate, but the option of combining the targeted agent with Taxol or Taxotere—both effective chemotherapies—may have more to do with tolerability of side effects. "[Taxotere is] a treatment that we kind of give on six occasions, and after that, patients are saying, 'I need a rest,' " Dr. Miles said in an interview at

the meeting. “[Avastin plus Taxol is a] more tolerable regimen that you can probably use for longer.”

Side effects of Taxotere include anemia, neutropenia, peripheral neuropathy, and fatigue. Side effects of Avastin include high blood pressure, diarrhea, and, rarely, hemorrhage and gastrointestinal perforation. —*MW*

Maintenance Therapy Delays Lung Cancer Growth

Alimta (pemetrexed) given as maintenance therapy for non-small cell lung cancer has been shown to delay progression-free survival by 50 percent in patients with advanced or metastatic disease. The phase III study involved 663 lung cancer patients who had received prior platinum chemotherapy, with 441 taking Alimta and 222 taking placebo. All patients received best supportive care, which included vitamin B12, folic acid, and the steroid dexamethasone.

Alimta delayed progression for four months compared with two months in patients receiving placebo, a 40 percent reduction in risk of progression. Preliminary findings also showed overall survival increased from 10.2 months to 13 months with Alimta, which was not statistically significant. Tudor-Eliade Ciuleanu, MD, PhD, from the University of Medicine and Pharmacy Iuliu Hatieganu in Romania and lead author of the study, noted the data are not mature and final overall survival data are expected in six to 12 months.

Alimta was approved as second-line therapy for NSCLC in 2004, but not as maintenance therapy. It is also approved for pleural mesothelioma. This is the first study to show maintenance therapy is beneficial in lung cancer patients after prior chemotherapy. Severe anemia appeared in 4.5 percent of patients receiving Alimta. Other common side effects include fatigue, nausea, and constipation.—*EW*