Medical Xpress

Iressa proves just as effective as chemotherapy for lung cancer

November 21 2008

Gefitinib, also known as Iressa, the once-promising targeted therapy for the treatment of non-small cell lung cancer, has proven as effective as chemotherapy as a second-line therapy for the disease with far fewer side effects, according to an international Phase III clinical trial, led by researchers at The University of Texas M. D. Anderson Cancer Center.

However, in contrast to earlier Iressa findings, the study showed that there was no additional survival benefit for patients who expressed an elevated level of the epidermal growth factor receptor (EGFR) mutation.

The Iressa in Non-small cell lung cancer Trial Evaluating REsponse and Survival versus Taxotere (INTERST) study, published today in The Lancet, represents a paradigm shift for the treatment of the disease, according to lead author Edward S. Kim, M.D., assistant professor in M. D. Anderson's Department of Thoracic Head and Neck Medical Oncology. It marks the first time in lung cancer that an oral pill has proven as effective as chemotherapy in a head-to-head trial.

"This is the largest study in lung cancer comparing an oral biologic therapy to chemotherapy, and shows, for the first time, that an oral biologic therapy is just as effective as chemotherapy," said Kim, the study's corresponding author. "Based on our findings, I'm hopeful that Iressa can return as a treatment for lung cancer in the United States, offering this some patients a therapy with far fewer side effects."

The study also should offer both physicians and patients some

confidence in another biological oral therapy, erlotinib, commercially known as Tarceva, that hits similar targets as Iressa and is commercially available for the treatment of lung cancer in the second line setting, explained Kim.

To best appreciate these findings, it's important to remember Iressa's history, said Kim. Iressa, a once-daily, oral tablet, was the first in a new class of anti-cancer drugs known as EGFR tyrosine kinase inhibitors (TKI) to become commercially available after two Phase II trials found the drug to be efficacious. Iressa was fast-tracked to the FDA and received approval May 5, 2003 as a single agent treatment for patients whose advanced lung cancer had continued to progress despite treatment with platinum-based and docetaxel chemotherapy.

However, in 2005, a large randomized lung cancer study reported that Iressa failed to significantly improve survival in patients with non-small cell lung cancer when compared to placebo. Ultimately, the drug's labeling was altered by the FDA; only cancer patients who had already taken the medicine and whose physicians believed it was helping them were allowed to receive the drug. No new lung cancer patients in the United States were given the drug after this time. However, Iressa remained an available therapy in other countries around the world.

Just prior to these negative findings, the INTEREST study began to enroll patients in 2004. Because of the negative data, INTEREST, an FDA-mandated study, was halted in the United States but continued in other parts of the world.

The Phase III international study enrolled 1,466 lung cancer patients from 149 centers in 24 countries. Of those enrolled, 1,433 were evaluable. All had either locally advanced or metastatic disease and had been previously treated for their cancer. Patients were randomized to receive either Iressa (250 milligrams daily) or docetaxel (75 mg/m2)

every three weeks. The study had two primary survival endpoints: in all treated patients and in those whose tumors had high EGFR gene copy number, explained Kim.

When comparing all treated patients, median overall survival for those receiving Iressa was 7.6 months and one-year survival was 32 percent, compared to 8 months and a 34 percent one-year survival for those taking chemotherapy. In an assessment of quality of life, Iressa patients experienced far fewer side effects, with the most common being a rash and diarrhea. In contrast, patients taking docetaxel experienced low blood count, infection, and hair loss.

In the subgroup of 174 patients with a high EGFR gene copy number, median overall survival in the Iressa arm was 8.4 months and one-year survival was 32 percent, versus 7.5 months overall survival and a one-year survival rate of 35 percent for those taking chemotherapy.

Tissue samples were evaluable for at least one biomarker in 453 patients. In an additional analysis of the biomarkers EGFR and K-ras mutations, the study indicates that both mutations are overall prognostic survival markers for lung cancer, but not predictive to treatment with either therapy.

"Our study found that patients who received Iressa and whose tumors had EGFR mutations will have an improved response rate and progression-free survival compared to docetaxel, but overall survival was similar in both treatment groups. In contrast, the K-ras gene mutation proved to be an overall poor prognostic marker, with both treatment arms doing poorly," said Kim.

"As lung cancer researchers, our mandate is to focus on finding appropriate biomarkers for the disease so ultimately, we can begin to tailor therapies for lung cancer patients based on their individual tumor

characteristics."

Source: University of Texas M. D. Anderson Cancer Center