Vandetanib shows clinical benefit when combined with docetaxel for lung cancer

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When combined with standard chemotherapy, an international Phase III trial has shown that the oral targeted therapy vandetanib improves progression-free survival for patients with advanced non-small cell lung cancer, according to research from The University of Texas M. D. Anderson Cancer Center.

The findings, presented today at the American Society of Clinical Oncology's annual meeting, mark the first clinical benefit of a small molecule targeted agent and standard chemotherapy in combination for lung cancer. Roy Herbst, M.D., Ph.D., professor and chief of the section of M. D. Anderson's Department of Thoracic/Head and Neck Medical Oncology, presented the findings on ASCO's press program.

"This study shows that an oral tyrosine kinase inhibitor can be combined with chemotherapy safely and effectively to provide systematic benefit to patients with this life-threatening disease," said Herbst. "This study will have immediate clinical implications. Still, we need to build on this research and turn our focus toward better identifying molecular markers involved, with the ultimate goal of personalizing our patient's care."

The therapy is unique in that it's a dual inhibitor and targets the epidermal growth factor receptor (EGFR) and vascular endothelial growth factor receptor (VEGFR). It is the first single agent in lung cancer to target both receptors, said Herbst, the study's international principal investigator.

"Both receptors are active in lung cancer. EGFR targets the tumor cell and VEGF targets the blood vessels, so, with vandetanib, we're really targeting the entire tumor environment at the same time," explained Herbst. "As a dual inhibitor, it also may provide cost-savings to patients in that they can now potentially take one therapy instead of two."

According to the American Cancer Society, lung cancer accounts for the most cancer-related deaths. In 2009, 219,440 are expected to be diagnosed and 159,390 will likely die from the disease.

The ZODIAC, (Zactima in cOmbination with Docetaxel In non-smAll cell lung Cancer) study enrolled 1,391 patients with non-small cell lung cancer from 198 centers between May 2006 and April 2008; all had received chemotherapy previously. Participants were randomized to receive either docetaxel and placebo, or docetaxel and vandetanib. The median follow-up was 12.8 months and the study's primary endpoint was progression-free survival.

Patients in the combination arm had a 21 percent reduction in disease progression, compared to those who received docetaxel alone (hazard ratio, .79), and their median progression-free survival was 17.3 weeks. In contrast, the median progression-free survival in the control arm was 14 weeks. While it trended positive, however, there was no statistical difference in overall survival in the two groups. There was a statistically significant improvement in the time to worsening of symptoms (hazard ratio, .77).

"Obviously, our ultimate goal is to always improve survival for our patients, however the improved time to progression with less of a number of significant effects is important," said Herbst. "This is certainly a drug, where, if we could identify molecular parameters that predict response, we could some day take a group that's receiving docetaxel and vandetanib and see them do even better. We're not there

yet, but hopefully this study will serve as the foundation for the merger of personalization and discovery with the now-proven safety and efficacy."

In terms of side effects, patients who received vandetanib experienced more diarrhea, rash and neutropenia. However, they experienced less of the significant side effects - nausea, vomiting, and anemia - than those who received docetaxel alone. The lack of significant side effects is quite striking, said Herbst, because other agents that target VEGF are associated with increased toxicity, including pulmonary bleeding.

As follow up, Herbst plans to update the survival data later this year. Other studies with vandetanib in lung cancer as a single agent, as well as in thyroid cancer, are currently ongoing.

Source: University of Texas M. D. Anderson Cancer Center (news : web)