Study suggests patients with lung cancer who carry specific HER2 mutations may benefit from certain anti-HER2 treatments

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New results from a retrospective study conducted in Europe suggest that anti-HER2 treatments, like the widely used breast cancer agent trastuzumab (Herceptin), have anti-cancer effects in a small subset of patients with advanced non-small cell lung cancer (NSCLC) harboring specific HER2 protein mutations. Although genetic changes cause tumor cells to make too much of the HER2 protein in up to 20% of lung cancers, mutations in the HER2 gene occur in only 1-2% of lung cancers. Such mutations in the HER2 gene lead to continuous activation of the protein, which keeps tumor cells alive and stimulates their growth. This is the largest study to date to explore the effect of anti-HER2 drugs among patients with these rare mutations who had already completed standard initial chemotherapy. The findings, published April 22 in the in the *Journal of Clinical Oncology*, suggest that HER2 testing to identify patients who might benefit from such treatments may be worthwhile.

"Our study suggests that many patients with HER2 mutations may benefit from anti-HER2 drugs," said lead study author Julien Mazières, MD, PhD, professor of pulmonology at Larrey Hospital in Toulouse, France. "While this benefit still needs to be confirmed in a prospective clinical trial, we hope that, based on this and other studies, HER2 status will be taken into account when making treatment decisions."

Lung cancer is the leading cause of cancer-related death worldwide, with only one in seven patients surviving for five years after diagnosis. In

recent years, growing knowledge about the molecular basis of lung cancer has launched an era of personalized medicine, which offers the promise of better patient outcomes by tailoring treatments to key genetic mutations in each patient's tumor. These key mutations are known as "driver mutations," because they trigger and fuel tumor growth.

HER2 is a promising treatment target because a number of anti-HER2 drugs (e.g., trastuzumab, pertuzumab, lapatinib) are already approved to treat other types of cancer. Early studies in patients with lung tumors that make abnormal amounts of HER2 (due to extra copies of the HER2 gene) showed minimal benefit from anti-HER2 treatment. But there has been little research on the benefit of such treatments in patients with the HER2 mutations, or mutations, explored in this study. In this study, HER2 mutations were detected in 65 out of 3,800 (1.7 percent) patients with NSCLC diagnosed in France, Spain, and Switzerland. All 65 patients with the mutations had the adenocarcinoma form of lung cancer, most (45 out of 65) were women, and roughly half were never-smokers (34 out of 65). About 50 percent of those patients had stage IV disease.

Sixteen patients (all with stage IV lung cancer and prior therapy consisting of platinum-based doublet with or without bevacizumab) were treated with one or more anti-HER2 drugs – afatinib, trastuzumab, lapatinib (Tykerb), and masatinib. Trastuzumab was always used in combination with chemotherapy (carboplatin, paclitaxel, vinorelbin, or docetaxel), whereas the other three anti-HER2 agents were given as monotherapy.

Overall, nine out of 16 patients experienced some tumor shrinkage after one round of treatment with trastuzumab and an additional two patients experienced shrinkage after a second round of treatment (one with trastuzumab, one with afatinib). Three additional patients experienced disease stabilization (tumor growth suspended). Among those patients that benefited from anti-HER2 treatments, disease worsening was

delayed by an average of 5.1 months (progression-free survival), about twice as much as typically seen in patients who undergo two or three rounds of conventional chemotherapy. Two patients received lapatinib and one masatinib, but those treatments did not prevent disease worsening. FDA has not yet approved afatanib and masatinib. In January afatinib was granted priority review for treatment of patients with advanced NSCLC harboring mutations EGFR (HER1), a protein related to HER2.

Dr. Mazières projects that in about one or two years data from more patients will be available to validate the use of anti-HER2 drugs in this patient population.

In ASCO Perspective, Jyoti Patel, MD, ASCO Cancer Communications Committee member and lung cancer expert says, "Although HER2 mutations occur in only 2 percent of cases, this still equates to several thousand U.S. lung cancer patients annually. We are finding more and more important mutations that drive lung cancer and matching them to targeted drugs. While confirmatory data are certainly needed, it appears that HER2 mutations represent another 'druggable' target, and drugs such as trastuzumab that are already available may be a reasonable treatment option for patients who harbor these mutations."

Provided by American Society of Clinical Oncology

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