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Targeted drug found effective in patients who have lung cancer with certain mutations

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A targeted therapy called capmatinib can provide significant benefits to patients who have advanced lung cancer with specific gene mutations, according to recently published results from a phase two clinical trial.

The trial, which is published in the *New England Journal of Medicine*, was conducted by an international team led by investigators at Massachusetts General Hospital (MGH).

A protein called MET affects a wide range of processes within cells, and alterations that activate the MET gene, which codes for this protein, have been implicated in many cancers. MET can be activated by a variety of mechanisms. Multiples copies of the MET gene, called MET amplification, occurs in one-to-six percent of patients with non-small-cell lung cancer (NSCLC). MET exon 14 skipping mutations, which cause deletion of a region called exon 14 in the expressed protein, occur in approximately three-to-four percent of patients with NSCLC and are associated with a poor prognosis.

The drug capmatinib is a highly potent and selective inhibitor of MET. Now researchers report results from the phase 2 GEOMETRY mono-1 study, which investigated the activity of capmatinib in 364 patients with advanced NSCLC with MET exon 14 skipping mutations or MET amplification. Results from this study were the basis for the US Food and Drug Administration's May 2020 approval of capmatinib for the treatment of NSCLC patients with MET exon 14 skipping.

In patients with MET exon 14 skipping mutations, capmatinib had a very high response rate (68 percent) when used as the first line of treatment, and an excellent response rate (41 percent) when used after patients had been treated with other therapies such as chemotherapy and immunotherapy. Among patients with MET amplification with at least 10 copies of the gene, capmatinib had a response rate of 40 percent when used as a first-line treatment and a response rate of 29 percent when used after other treatments. The drug had limited effectiveness in patients with a lower level of MET amplification.

The results indicate that capmatinib may be an especially effective

treatment for patients who have NSCLC with MET exon 14 skipping mutations and who have not been treated previously.

"There are many advances in NSCLC treatment that are helping people live longer and better with their disease, and it is really important that all newly diagnosed patients with NSCLC get broad molecular profiling to determine what their optimal first-line therapy should be," said senior author Rebecca Suk Heist, MD, investigator in the MGH Cancer Center and assocoiate professor of Medicne at Harvard Medical School. "If we don't test, we don't know." Heist noted that MET exon 14 skipping and amplification join a number of other drivers of NSCLC for which researchers have developed targeted therapies. "It is critically important that all patients have their lung cancers tested for these to know whether there is a targeted treatment option or not," she said.

More information: Jürgen Wolf et al, Capmatinib in MET Exon 14–Mutated or MET-Amplified Non–Small-Cell Lung Cancer, *New England Journal of Medicine* (2020). DOI: 10.1056/NEJMoa2002787

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