MedicalXpress

High concordance between EGFR mutations from circulating-free tumor DNA and tumor tissue in non-small cell lung cancer

August 22 2014

Epidermal growth factor receptor (EGFR) mutations found in the circulating free tumor DNA (ctDNA) from the plasma of advanced non-small cell lung cancer (NSCLC) patients correlates well with the EGFR mutations from patient-matched tumor tissue DNA.

EGFR tyrosine kinase inhibitor (TKI) therapy is approved for EGFR activating mutation positive patients with advanced NSCLC, but the standard for determining mutation status is with DNA derived directly from tumor tissue, which can be limited or not available. A more abundant and less invasive source of tumor DNA may be cell free tumor DNA found circulating in the blood.

International researchers prospectively analyzed and compared tumor and matched plasma DNA for EGFR mutations from 1060 patients that were screened as part of a phase IV, open-label, single-arm, first-line gefitinib in EGFR mutation positive Caucasian patients. Also, when two plasma samples from the same patient were available the mutation status of each was compared.

The September issue of the *Journal of Thoracic Oncology*, the official journal of the International Association for the Study of Lung Cancer (IASLC), reports that the mutation status concordance between tumor and matched plasma for 652 patients that had results for both was 94% (95% CI 92-96) with a sensitivity of 66% (CI 56-75) and specificity of

100% (CI 99-100). The reproducibility between two plasma specimens from the same patient was also high with a mutation concordance of 97% (CI 94-99) for 224 matched specimens. Post-hoc analysis of the efficacy of first-line gefitinib revealed there was similar progression-free survival (PFS) for those with EGFR mutation positive tissue (9.7 months [CI 8.5-11.0]) versus both mutation positive tissue and plasma (10.2 months [CI 8.5-12.5]).

The authors acknowledge that "tumor tissue should be considered the preferred sample type when available, however, our encouraging results suggest that a single plasma-derived ctDNA sample may be considered appropriate for assessment of EGFR mutation status when tumor tissue is unavailable or exhausted". "As there are no published guidelines for the use of ctDNA for EGFR mutation analysis in the absence of tumor tissue, these results may help address this current unmet need." Dr. Douillard, lead author of the study, says his next steps are to "look for resistance mutations, like T790M, during treatment to better understand mechanisms of resistance and anticipate later line treatment at progression". For future research he also suggests "searching for other resistance mutations along the EGFR pathway, as well as other related pathways, and improving the sensitivity by using more powerful testing methods, like next generation sequencers".

Provided by International Association for the Study of Lung Cancer