Not all EGFR mutations are the same when it comes to therapy for non-small cell lung cancer

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Certain rare epidermal growth factor receptor (EGFR) mutations are associated with tobacco smoking, worse prognosis and poor response to EGFR tyrosine kinase inhibitor (TKI) therapy compared to the more common "classical" EGFR mutations. However, as not all rare mutations are the same, testing and therapy may need to be evaluated for each individual mutation.

Lung cancer is the leading cause of cancer mortality in the world with nearly 1.4 million deaths each year. Mutations within the EGFR gene lead to an oncogenic EGFR protein which can be turned off with EGFR TKIs. These alterations with EGFR are the most frequently therapeutically-targeted genomic alterations in NSCLC. Deletions within Exon 19 or a point mutation in Exon 21 are the common mutations predictive of response to EGFR TKI therapy and the ones most often and sometimes exclusively tested for. However, less common EGFR mutations exist and some, for example G719x and L861Q, appear sensitive to TKI therapy.

As lung cancer is a pressing health care problem in Central Europe, researchers in Austria and Hungary examined the EGFR mutation status on 814 Hungarian patients with pathologically confirmed adenocarcinoma, a histological subtype of NSCLC, and compared the epidemiology and clinical consequence of rare and classic EGFR mutations. Clinical and pathological data were available for 645 of those

examined and disease outcome data were available for 419.

The results published in the *Journal of Thoracic Oncology*, the official Journal of the International Association for the Study of Lung Cancer (IASLC), show that the 5% had classic (Exon 19 or 21) mutations, 6% rare mutations, and 3% with synonymous (non-protein altering) mutations. Of note, 10% of patients with rare mutations carried alterations known to be sensitive to EGFR TKIs. As expected the classic mutations were associated with never smokers (p