Detection of targetable kinase fusions in 7260 patients in an integrated cancer system

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Background: Kinase fusions (KF), such as those involving ALK, are eminently targetable genomic alterations (GA) in lung and other cancers, the latter suggested by early clinical evidence (PMID: 29079636). We undertook a review of 7260 patient samples from a tertiary cancer care–focused network of five hospitals assayed with comprehensive genomic profiling (CGP).

Methods: Hybrid capture based CGP was performed on 7260 advanced cancer cases (12/2012-2/2018), with assessment of at least 186 genes (intronic baiting for at least 14) in tissue, and 62 genes (intronic baiting for 6) in circulating tumor DNA samples. Tumor mutational burden (TMB) was determined up to 1.2 Mbp of sequenced DNA.

Results: 77/7260 (1%) samples in this series harbored KF. Patients (pts) with KF+ tumors had a median age of 53 years vs. 56 years in the overall population. The TMB in KF+ cases was 3.51 mut/Mb vs. 4.39 mut/Mb for all cases. KF were found in 55 lung (71%) and 22 (29%) non-lung samples. Of KF+ cases, 71% were non-small cell lung cancer, and the remainder were sarcoma (5%), breast cancer (4%), thyroid (4%), cancer of unknown primary (4%), pancreatic (3%), colorectal (3%) and others (1% each).
Of KF+ non-lung cases, 39% had BRAF fusions, 30% had ALK fusions, 26% had RET fusions, and 4% had ROS1 fusions. One KF+ sarcoma pt received matched targeted therapy with ALK inhibitors including ceritinib and crizotinib. More recently, in 2017 samples alone, 42% (10/24) of KF+ cases were non-lung.

**Conclusions:** Greater access to CGP has led to increased detection of advanced cancer patients with tumors harboring KF, particularly those with non-lung cancers. The low frequency of the latter is a challenge for clinical investigation. As such, innovative solutions such as basket trial for kinase inhibitors are needed, which may be feasible in an integrated cancer care system with high patient volume.

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