A Study of the Clinical Utility of NTRKs Only vs Comprehensive Gene Fusion Panel Testing from a Single Assay Platform

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Overview:

- Gene fusion events involving 1100+ genes occur in 30% of patients across 33 cancer classifications.
- Fusions in druggable pathways occur in 5% of patients, while NRTKs are only detected in 1.2% of the patients.
- The 5 most frequent druggable fusions account for 52% of all detected actionable gene rearrangements.
- Testing for a comprehensive set of actionable fusions results in a therapeutic opportunity given to 4 times more patients than testing for any single gene family.

Background: Gene fusions have important implications for therapeutic selection and patient quality of care, and though they have a low prevalence individually, many fusions are targeted effectively, agnostic of any tumor type. Unfortunately, patients in the community oncology setting are most often only tested for NTRK fusions, which have a prevalence of around 1%. Here, we compared side by side the actual clinical actionability differences using real-world testing data between broad vs. NTRK fusion only panels offered by our clinical laboratory, both with identical assay performance characteristics, reimbursement, and cost levels.

Methods: Clinical samples (n=8307) from 33 tumor types were tested for known and novel RNA fusions using our hybridization capture RNA-seq based solid tumor fusion panels in our clinical laboratory, which targets RNA breakpoints at 1104 genes. Deidentified results were analyzed before or after filtering for fusions based on either a 19 gene fusions panel (16 drug targetable genes) or only NTRKs fusions panel. Deidentified patient data presented was analyzed according to an IRB-approved protocol.

Results: The prevalence of fusions in the cohort was 30.5% involving any of the 1104 targeted genes by the assay (27% in frame, 20% out of frame, and 41% others). Druggable fusions were present in 5.1% (422) of patients, where 53% were female with a median age of 68 years old, and 47% were male with a median age of 70. However, when filtering only for NTRK fusions, only 104 patients had an NTRK fusion (38 NTRK1, 10 NTRK2, 56 NTRK3), while an additional 318 patients had detected fusions from the 19 genes targeted panel. These druggable fusions had the following prevalences; ALK 0.6 %, BRAF 0.3%, FGFR1 0.2%, FGFR2 0.3%, FGFR3 0.4%, FGFR4 0.0% n=4, MET 0.4%, NOTCH1 0.0% n=1, NOTCH2 0.2%, NRG1 0.2%, PDGFB 0.0% n=3, PDGFRA 0.1%, PDGFRB 0.0% n=0, RAF1 0.2%, RET 0.5%, ROS1 0.2%, excluding NTRK positive cases. The incidence of NTRK 1/2/3 fusions was 1.25%, while 3.8% of patients have other fusions included on the targeted panel in the absence of an NTRK fusion. Two patients (0.02%) had both an NTRK fusion and an additional fusion covered on one of the other 16 genes in the targeted fusion panel.

Conclusions: Actionable fusions showed a combined prevalence in the clinical setting of 5.1%. This study demonstrates that when fusion testing is performed, four times more patients can benefit from a therapeutic option when testing for these 19 genes compared to the widespread panel of the current clinicians’ favorite choice composed of only NTRK fusions. More data and education are needed to change the testing paradigm of treating physicians to test broader sets of fusions, specially when assay performance and financial considerations are equal, to increase cancer care access.