FGFR2: A Pan-Genomic Target

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RESULTS

Mutations Across Tumor Types

Alterations by Tumor Type

Frequency of specific classes of genomic alterations (GA) have been described in a variety of solid tumors and emerged as biomarkers for investigational ongoing clinical trials.

Results: FGFR2-GAs were detected in 2,993 (1.5%) cases featuring short variant (SV) mutations (42%), copy number changes (37%), rearrangements (28%), and multiple GA (2%). The most frequent SV GA were S252L, N549K, C382R, and P533R, P755C, H588E and N964K. A small cohort (5%) of tumors featured the V564I and V564L GA that are associated with resistance to TKI drugs. The FGFR2-alt altered cases were 63% female/37% male with median age of 61 yrs. Most frequent GA in FGFR2 altered cancers: TP53 (47%), PIK3CA (22%), PTEN (20%), ARID1A (18%), CDKN2A/2B (18-16%) and MYC (12%). FGFR2 ALK is most common in endometrial, breast cancers (ca) and CUP, ALK amplification most common in breast, gastrointestinal and lung ca. FGFR2 rearrangement/fusions most common in cholangio (37% of rearrangement positive cases), CUP (15%), pancreatic (12%) and breast (9%). The FGFR2-BICC1 was the most frequent fusion followed by fusions with TACC2, AHCYL1, CCDC6, VCL, and H441/27T. MSI-high status present in 6.8% of evaluable FGFR2 altered cases (63% in endometrial ca). Median TMB was 3.5 mut/Mb with 21% featuring ≥ 10 mut/Mb and 12.5% featuring ≥ 20 mut/Mb. Only 63% of MSI-high FGFR2 altered tumors had TMB ≥ 20 mut/Mb, 12.5% FGFR2 altered tumors had TMB ≥ 10 mut/Mb, 3.4%-5% TMB ≥ 100 mut/Mb. 29% of PD-L1 IHC+ cases in NSCLC. FGFR2 altered ca’s responding to anti-FGFR drugs were presented.

Conclusions: FGFR2-GAs are most frequent in cholangio, breast, GI tract, lung and CUP, with enrichment of FGFR-2 fusions in bilary tract ca. Cases with FGFR2-GA typically do not feature other kinase driver GA and are associated with mutations in the MYC/PIK3CA/AKT pathways. Finally, in contrast with RTK driver GA in EGFR (5.7%) and ERBB2 (7.5%), at 12.5% across all tumor types, FGFR2 mut cancers may have higher frequency of TMB ≥ 20 mut/Mb suggesting potential immunotherapy responsiveness.

MATERIALS AND METHODS

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