Genomic landscape in small intestine cancer from real-world data (RWD) of clinical genomic testing.

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Background: Panel-based comprehensive genomic profiling (CGP) is used in clinical practice worldwide, however, large aggregated RWD of patients with advanced small intestine cancer have not been characterized. In particular, there has been limited data regarding examining CGP in pediatric/Adolescent and Young Adult (AYA) small intestine cancer. For patient subgroups, it is unclear what clinically relevant alterations co-occur. Here, we investigated the genomic landscape of small intestine cancer patients, stratified by sub-group to help refine and discover new targets for improved cancer therapies in advanced small intestine cancer. Methods: This is a collaborative biomarker study using RWD paired with CGP testing (Foundation Medicine, Inc.). Hybrid capture was carried out on up to 395 cancer-related genes and select introns from up to 31 genes frequently rearranged in cancer. One thousand three hundred sixty-four patients were available for analyses and were stratified by age (≥40/ < 40), MSI status, tumor mutational burden (TMB) status (High ≥10/Low < 10Muts/Mb), and select gene alterations. Using a chi-square test with Yate’s correction, frequencies of alterations were analyzed according to clinical or genomic background.

Results: Genes with frequent alterations including mutation, amplification, and rearrangement/fusion were TP53 (59.8%), KRAS (54.8%), APC (27.7%), CDKN2A (22.4%), and SMAD4 (20.2%). Genomic profiling according to age, MSI, and TMB status is shown in the following table. In pediatric/AYA patients, frequency of APC alterations was significantly low (P < 0.001). In KRAS mutated tumors, codon 12 most abundant mutations were G12D (31.1%) followed by G12V (22.3%), G12C (6.2%), and G12R (5.1%), while G13D (13.8%) was the predominant mutation in codon 13. In TMB-High tumors, which were detected in 12% of patients, the mutation rate of KRAS was modestly lower compared to TMB-Low tumors (42.3% vs. 53.3%). Frequent genes with amplification were MYC (6.7%), MDM2 (5.9%), GATA6 (5.5%), CCND1 (3.4%), GFG19 (3.3%), and ERBB2 (2.3%). The number of any gene amplification was lower in MSI-High compared to TMB-High population.

Conclusions: RWD from clinical panel testing revealed the genomic landscape in small intestine cancer and differences in CGP according to clinical or genomic background. These findings would provide insight on the direction of the future development of the treatment in advanced small intestine cancer. Research Sponsor: None.