Abstract #4136

Background: Pancreatic adenocarcinoma (PDAC) is a challenging disease with overall 5-year survival rate below 10%. As highlighted through recent advances in molecular profiling of PDAC, new targeted agents are desperately needed. The vast majority of PDAC cases are driven by activating mutations in KRAS and TP53. The use of molecular profiling in PDAC allowed assessment of the presence of other actionable driver mutations.

Methods: 2400 cases referred internationally to Caris Life Sciences were evaluated using a combination of sequencing, IHC or ISH, and overexpression of drug resistance. 48 biomarkers were assessed using various technologies: Sanger sequencing (Sanger or next generation sequencing (NGS)), protein expression (immunohistochemistry), and/or in situ hybridization (ISH). 44 genes belonging to 11 pathways (the RAS/MAPK pathway, Wnt/β-catenin pathway, KRAS signaling, PI3K/AKT/mTOR pathway, DNA damage response, PDGF receptor signaling, Bcl-2 family apoptosis, hedgehog signaling, tumor suppressor genes, and cell cycle) were analyzed. Biomarkers that were studied included PEPT1, SMO, GNA11, GNAS, IDH1, and RB1).

Results: The overall distribution of AR, ER, and HER2 in the KRAS WT cases is shown in Figure 1. The figure on the right shows hormonal biomarkers and HER2. As shown, HER2 FISH tumors drive the need for specific HER2-targeted therapy.

Conclusions: Mutations in BRAF, EGFR, HER2, FLT3, HRAS, PDGFRA and PTEN were identified exclusively in KRAS WT cases. The numbers vary as technologies and test menu options changed over time. Percentages in red indicate Sanger) in 2400 pancreatic adenocarcinomas. The tables below show the overall distribution. and total cases tested. The numbers vary as technologies and test menu options changed over time. Percentages in red indicate

Figure 2. Differences in Sequence Analysis Between KRAS mutated and wild type pancreatic cancer. Testing was performed using Sanger and/or NGS. KRAS WT cases with results for KRAS and TP53. Not all cases were tested for KRAS (insufficient tissue or other reason). Only genes where differences showed were significant.

KRAS WT versus MT Comparison of Selection Biomarkers

Figure 3. Distribution of AR, ER, PR, and HER2 in the KRAS type versus KRAS mutated pancreatic cancer.

Figure 4. Differences in Sequence Analysis Between KRAS mutated and wild type pancreatic cancer. Testing was performed using Sanger and/or NGS. KRAS WT cases with results for KRAS and TP53. Not all cases were tested for KRAS (insufficient tissue or other reason). Only genes where differences showed were significant.

Figure 5. Potential actionable targets identified using a multiparameter approach. Drug associations are determined using Caris Molecular Intelligence™ recommendations based on biomarker status and published evidence, which includes gene reweighted literature and/or NGS findings, but independent of cancer type. KRAS WT cases (A) are not treated with conventional primary therapy and gene mutations have increased potential for targeted therapy as well as traditional therapeutic options. DRGs (Based on the Caris Molecular Intelligence® platform with Caris Molecular Intelligence recommendations). Multidisciplinary Research. New York, NY

References


