Background: Pancreatic adenocarcinoma (PAC) is a challenging disease with overall single digit 5-year survival. BRCA1 and BRCA2 germline mutations are associated with increased risk of PC. Recent retrospective studies have described response of BRCA patients to platinum agents and PARP inhibitors. Additionally, immune therapies targeting the programmed cell death pathway in other cancers have shown promise; evaluating the incidence of alterations of these markers in PAC impact therapeutic decisions.

Methods: 450 PAC’s were evaluated at a commercial CxIA laboratory using a combination of sequencing (Sanger or next generation sequencing (NGS)) and protein expression (immunohistochemistry). BRCA1/2 mutations that could be germline or somatic, co-incidence with other mutations identified in the tissue, and expression levels of PD-L1 and PD-1 tumor infiltrating lymphocytes (TILs) were evaluated.

Results: Mutations (MT) in BRCA1 and BRCA2 were identified in 5 and 17 percent of tumors, respectively. BRCA1 and BRCA2 MT had different rates of concurrence with other gene alterations, which was also different from the general PC population (table). Overexpression of PD-L1 and PD-1 TILs were also identified in 7% and 37% of PAC cases, respectively. BRCA2 MT cases had a higher incidence of PD-L1+ TIL’s, while BRAF V600E cases had a higher incidence of PD-L1 status with therapeutic implications.

Conclusions: The different frequencies of KRAS, TP53, PIK3CA and SMAD4 MT between the overall PAC population and BRCA MT populations may inform driver differences and may help select drugs and refine treatment decision making for certain patients. Evaluating the profiles of the BRCA MT populations with clinical outcomes will provide valuable insight into the clinical behavior in genomically defined subsets and may facilitate in developing rational combinations of targeted agents in PAC.

Abstract (No. 11108)
Please note, below is a revised version of the abstract

Methods
An additional 188 patients were identified to be included in the analysis since the submission of the abstract

Results
All 556 pancreatic cancer cases underwent molecular profiling at Caris Life Sciences between 2014 - 2015. From this original cohort, three subgroups were formed: wildtype BRCA1 and BRCA2 (+) (n=26), wildtype BRCA status or BRCA1/2 (–) (n=165) and compared to BRCA1 + (n=8) and BRCA2 + (n=25) and wildtype BRCA status or BRCA1/2 (-) (n=165). No statistically significant differences exist among the subgroups.

Conclusions
• The different frequencies of KRAS, TP53, PIK3CA and SMAD4 MT between the overall PAC population and BRCA MT populations may inform driver differences and may help select drugs and refine treatment decision making for certain patients.
• Evaluating the profiles of the BRCA MT populations with clinical outcomes will provide valuable insight into the clinical behavior in genomically defined subsets and may facilitate in developing rational combinations of targeted agents in PAC.

References