TPS4232 **Poster Session**

Adaptive organoid-based precision therapy study in pancreatic cancer (ADOPT): A phase II single-arm study to evaluate the efficacy of patient-derived organoid (PDO)-directed therapy in advanced pancreatic ductal adenocarcinoma (PDAC).

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Background: PDAC is a devastating malignancy. High-throughput genomic technologies have yielded insights regarding the molecular underpinnings and heterogeneity of PDAC. Systemic treatment options are limited to cytotoxic chemotherapies, except for approx. 10%, who receive targeted treatment based on genomic profiling. PDO's are three-dimensional *ex vivo* experimental models grown directly from tumor tissue and can provide a direct assessment of drug response. By directly exposing cancer cells to potential drug therapies, functional profiling provides a dynamic measurement of response that is more informative than static gene panels. PDOs can theoretically be used to direct therapeutic decisions, offering an opportunity to expand the reach of precision therapies for PDAC beyond genomics. To date, PDO testing has been limited by small sample sizes, few drugs included in the screens, and retrospective studies. To expand the impact of precision therapy, we developed a rapid high-throughput screening (HTS) platform where over 3,000 drugs can be tested in PDOs within 8-10 weeks of diagnosis. In ADOPT, we aim to formally investigate the efficacy of PDO-directed therapy in a prospective phase II study, leveraging our existing platforms using real-time HTS of PDOs. This study represents one of the first formal trials of PDO-directed therapy in solid tumors. Our novel approach will enroll pts with advanced PDAC who do not have alternative treatment options.
Methods: This is an actively recruiting prospective, single-arm phase II trial. Patients (pts) with advanced epithelial PDAC are eligible if they either: 1) progressed on, were intolerant to, or refused first-line or subsequent therapies (Cohort A), or 2) have stable disease after $\geq$8 cycles of FOLFIRINOX ("Maintenance" Cohort B) and have a PDO showing sensitivity to an approved HC drug. Pts will be recruited, from multiple ongoing studies including PROSPER-PANC where we have successfully generated and tested a PDO. PDO-directed treatment will be selected based on drug sensitivity as tested through our validated HTS platform. Each case will be discussed at our PDO dedicated tumor board. All pts must meet the inclusion/exclusion and drug-specific eligibility criteria. The primary endpoint is disease control rate. A Simon's two-stage optimal design will be used to test the hypothesis: H0: $P \leq 0.05$ versus H1: $P \geq 0.25$. In the first stage, 9 pts will be evaluated. The trial will be discontinued if no disease control response is observed in this stage. If at least one response is observed, then the trial will continue to the second stage and an additional 17 pts will be evaluated for a total of 26 evaluable. This design has a one-sided alpha of 0.05 and power of 80%. We will reject the null hypothesis after 26 if 3 or more responses are observed. Clinical trial information: awaited. Research Sponsor: Ontario Institute for Cancer Research and Princess Margaret Cancer Foundation; Terry Fox Research Institute - Marathon of Hope Cancer Centres Network Funding; Sinai Health Foundation; The MNitz Pancreatic Cancer Research Fund (Michelle Reisman); The MNitz Pancreatic Cancer Research Fund (Veroli Cultural Society); The MNitz Pancreatic Cancer Research Fund (Elyse Graff).