TPS4229 **Poster Session**

A phase 1b/2 trial of onvansertib in combination with NALIRIFOX for first line treatment of advanced pancreatic cancer (PANCONVA trial).

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Background: Pancreatic cancer is a highly lethal disease. Despite research and drug development efforts focused on KRAS, no effective RAS inhibitors have been approved for the treatment of pancreatic cancer with KRAS mutation. PLK1 inhibition is a potential target in KRAS-mutated pancreatic cancer and may provide a new first-line treatment option. Onvansertib (also known as PCM-075 and NMS-1286937) is the first PLK1-specific adenosine triphosphate competitive inhibitor administered by oral route to enter clinical trials with proven antitumor activity in different preclinical models. **Methods:** This is a phase 1b/II, non-randomized, open label single arm study being conducted at the University of Kansas Cancer Center and its affiliated sites. The study is open for enrollment. Eligibility: Key inclusion includes pts with locally advanced, unresectable, or metastatic pancreatic adenocarcinoma who are treatment naïve, have adequate archival tissue for biomarker evaluation or are willing to undergo a biopsy, and have an ECOG of 0-1. Key Exclusion: Planned concomitant use of medications known to prolong the QT/QTc interval, use of strong CYP3A4 or CYP2C19 inhibitors or strong CYP3A4 inducers. Treatment Plan: The phase 1b (safety lead-in) will follow a dose de-escalation phase in which up to 2 different Onvansertib dose levels will be tested in combination with standard NALIRIFOX. Onvansertib starting dose level is 30mg orally once daily. The Phase II portion of the study will be a single-arm open-label enrollment with dosing based on the starting dose determination in the Phase Ib portion of the study (30mg or 20mg). NALIRIFOX (Nano-liposomal Irinotecan 50 mg/m2, Oxaliplatin 60 mg/m2, Leucovorin 400 mg/m2, 5-FU 2400 mg/m2) will be administered intravenously on D1 of the 14-day cycle. Onvansertib will be dosed orally on D1-5 of each 14-day cycle. Imaging will be performed at baseline and after every 4 cycles. Objectives: The primary objective of this study is to determine anti-tumor activity by measuring Overall Response Rate (ORR). The secondary objectives are to determine treatment safety based on toxicities in participants who have received at least one dose of onvansertib, to determine anti-tumor activity by Progression Free Survival (PFS), to determine anti-tumor activity by Disease Control Rate (DCR), to determine Overall Survival (OS). Statistical Plan: Simon's two-stage Optimum design will be used. The null hypothesis that the true response rate is 41% will be tested against a one-sided alternative that the true response rate is 65%. In the first stage, 10 evaluable pts will be enrolled. If there are 4 or fewer responses in these 10 pts, the study will be stopped. Otherwise, 11 additional evaluable pts will be accrued for a total of 21 evaluable pts. The null hypothesis will be rejected if 12 or more responses are observed in 21 evaluable pts. Clinical trial information: NCT06736717. Research Sponsor: Cardiff Oncology.