345 PHASE I/II TRIAL OF CABOZANTINIB PLUS DURVALUMAB IN ADVANCED GASTROESOPHAGEAL CANCER AND OTHER GASTROINTESTINAL MALIGNANCIES (CAMILLA): PHASE IB SAFETY AND EFFICACY RESULTS

[1]Anwaar Saeed*, [2]Robin Park, [3]Junqiang Dai, [1]Raed Al-Rajabi, [1]Anup Kasi, [1]Joaquina Baranda, [1]Stephen Williamson, [1]Zachary Collins, [1]Jacob Ripp, [4]Azhar Saeed, [3]Kelly Mulvaney, [3]Vanna Manirad, [3]Rashna Madan, [3]Dharmalingam Subramaniam, [3]Shrikant Anant, [3]Milind Phadnis, [3]Weijing Sun. *[1]Kansas University Cancer Center, Fairway, KS, USA; [2]MetroWest Medical Center, Framingham, MA, USA; [3]Kansas University Medical Center, Kansas City, KS, USA; [4]University of Minnesota Medical Center, Minneapolis, MN, USA*

Background Cabozantinib is a multi-tyrosine kinase inhibitor primarily targeting VEGFR, MET, and AXL. These targets promote a tumor immune permissive microenvironment. Cabozantinib has demonstrated immunomodulatory properties & clinical synergy when paired with PD-L1 inhibitors such as durvalumab. Here, we present final results of phase Ib of the Camilla trial assessing cabozantinib plus durvalumab in advanced GE adenocarcinoma (GEA), colorectal cancer (CRC), and hepatocellular carcinoma (HCC). This is an investigator-initiated trial funded by Exelixis & Astrazeneca.

Methods Patients were administered cabozantinib + durvalumab in a dose escalation (3+3) then expansion to find the Dose Limiting Toxicities (DLTs), Recommended Phase 2 Dose (RP2D), ORR, PFS, and OS. Subgroup analysis was conducted to assess efficacy in patients with PD-L1 Combined Positive Score (CPS) $\geq$ 5. Dosing of cabozantinib was 20mg QD, 40mg QD, and 60mg QD PO in the 1st, 2nd, and 3rd cohorts. Dosing of durvalumab was 1500mg IV Q4W in all cohorts. DLT window was 28 days. Treatment beyond progression was allowed following modified RECIST v1.1 criteria.

Results 35 patients (14F, 21M), median age 53 years (range 27–79) were enrolled. 10 patients had GEA, 20 had CRC, and 5 had HCC; none had MMR deficiency. Median number of prior systemic therapies was 3 (range 0–3). No DLTs were observed during dose escalation. Per mature tolerability data, 11/14 patients receiving cabozantinib 60mg required dose-reduction post cycle 2 to 40mg. RP2D was determined to be cabozantinib 40mg QD plus durvalumab 1500mg Q4W. Of the 247 observed Treatment-Related Adverse Events (TRAEs), 10% (24) were grade$\geq$3. Most common TRAEs were grade 1–2 fatigue (57%), nausea (43%), anorexia (40%), diarrhea (37%), transaminitis (34%), hand-foot syndrome (23%), & weight loss (23%). 2 patients each developed grade$\geq$3 fatigue, weight loss, & abdominal pain. Overall, 30 pts were evaluable for efficacy. ORR 26.7%; DCR 83.3%; median PFS 4.5 months; 6-month PFS 36.7%; and median OS 9.1 months. 12 patients had PD-L1 CPS $\geq$5. In this subgroup, ORR 33.33%; DCR 91.67%; median PFS 6.13 months; 6-month PFS 50%; and median OS was not reached.

Conclusions Cabozantinib plus durvalumab demonstrated promising efficacy and was fairly tolerated without new safety signals. High PD-L1 expression defined as CPS $\geq$ 5 was associated with improved efficacy & survival. The phase II multi-cohort part of the trial is currently ongoing.

Trial Registration NCT03539822

Ethics Approval The study was approved by the participating site's local IRB.

Consent All study participants granted a written informed consent prior to treatment initiation.

http://dx.doi.org/10.1136/jitc-2021-SITC2021.345