## 742 A MULTICOHORT PHASE 1B STUDY (STELLAR-002) OF XL092 IN COMBINATION WITH IMMUNOTHERAPY IN PATIENTS WITH ADVANCED SOLID TUMORS

[1]Bradley Mcgregor*, [1]Toni Choueiri, [2]Neil Shah, [3]Aung Bajaj, [4]Jad Chahoud, [5]Bert O'Neil, [6]Joel Michalski, [7]Benjamin Garmezy, [8]Lixian Jin, [9]Usman Aziz, [9]Fiona Xu, [2]Robert Motzer. *[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]Arizona Oncology, Tucson, AZ, USA; [4]Moffitt Cancer Center, Tampa, FL, USA; [5]Indiana University, Indianapolis, IN, USA; [6]Nebraska Cancer Specialists, Omaha, NE, USA; [7]Sarah Cannon Research Institute, Nashville, TN, USA; [8]Bristol Myers Squibb, Lawrenceville, NY, USA; [9]Exelixis, Inc., Alameda, CA, USA*

**Background** XL092 is a novel, oral inhibitor of multiple receptor tyrosine kinases including MET, VEGFR2, AXL, and MER, which are implicated in tumor growth, metastasis, angiogenesis, and immune modulation. XL092 has a half-life of ~21h, convenient for daily dosing and managing tolerability. Preclinical studies of XL092 plus an immune checkpoint inhibitor (ICI) showed antitumor activity in tumor models. STELLAR-002 will evaluate the safety and clinical activity of XL092 alone and in combination with nivolumab ± ipilimumab in patients with advanced solid tumors. Presented here is the study design which includes a dose-escalation stage in solid tumors and a cohort-expansion stage in genitourinary cancers.

**Methods** This multicenter phase 1b, open-label study (NCT05176483) will enroll patients with unresectable advanced or metastatic solid tumors. The dose-escalation stage will determine recommended doses of XL092 (orally) in combination with nivolumab ± ipilimumab (intravenously) for the cohort-expansion stage. Dose escalation will enroll a total of ~24 patients into two cohorts using a rolling 6 design: Cohort A, XL092 + nivolumab (360 mg Q3W); Cohort B, XL092 + nivolumab (3 mg/kg Q3W × 4, then 480 mg Q4W) + ipilimumab (1 mg/kg Q3W × 4). The cohort-expansion stage will include six tumor-specific cohorts: clear cell renal cell carcinoma (ccRCC), first-line therapy; ccRCC, second-line therapy after one prior ICI regimen; metastatic castration-resistant prostate cancer (mCRPC), second-line therapy after one prior novel hormonal therapy; urothelial carcinoma (UC), second-line therapy after prior platinum-based regimen and ICI-naïve; UC, ICI-experienced, up to 2 prior lines of systemic therapy with prior platinum-based regimens allowed; non-clear cell RCC, first-line therapy. Cohort-specific randomization will include XL092 alone or in combination with nivolumab ± ipilimumab to evaluate the contribution of the individual agents to the combination regimens. Thirty patients will be enrolled in each XL092 alone arm and 40 patients in each combination arm. Preliminary efficacy, safety, and pharmacokinetics of XL092 alone or in combination with ICI will be assessed in each cohort. Primary endpoints include objective response rate per RECIST v1.1 by investigator, progression-free survival per Prostate Working Group 3 criteria by blinded review (mCRPC cohort only), and safety. The study is enrolling patients.

**Trial Registration** Trial registry is ClinicalTrials.gov NCT05176483

**Ethics Approval** The study will adhere to the principles outlined in "Guideline for Good Clinical Practice" (GCP) and remain consistent with the most recent version of the Declaration of Helsinki.

**Consent** Patients will be required to provide written informed consent.

http://dx.doi.org/10.1136/jitc-2022-SITC2022.0742