TPS5114 **Poster Session**

Precision diagnostics in prostate cancer treatment (PREDICT): A phase 2 multi-arm biomarker based study (Alliance A032102).

Rana R. McKay, Glenn Heller, Shuang Zhao, Elizabeth Marie Wulff-Burchfield, Dhaval Shah, Alan Tan, Matthew D. Galsky, Jonathan E. Rosenberg, Himisha Beltran; Moores Cancer Center, University of California San Diego, La Jolla, CA; Memorial Sloan Kettering Cancer Center, New York, NY; University of Wisconsin Carbone Cancer Center, Madison, WI; University of Kansas Medical Center, Kansas City, KS; Medical Oncology Hematology Consultants, Newark, DE; Vanderbilt University Medical Center, Nashville, TN; Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, Department of Medical Oncology, New York, NY; Dana-Farber Cancer Institute, Boston, MA

Background: Advances in genomic sequencing have allowed for a deeper understanding of the molecular complexity of metastatic castration-resistant prostate cancer (mCRPC) with several actionable alterations now identified, fueling new biomarker-based treatment strategies. For this reason, it is recommended that all patients with mCRPC undergo germline and somatic tumor profiling. In addition to DNA aberrations, gene expression changes can capture actionable targets and activated pathways. The phase 2 PREDICT trial is using both DNA and RNA aberrations to select patients with mCRPC for rationally designed biomarker-based therapeutic strategies. **Methods:** This is a multi-center, multi-arm, biomarker-driven phase 2 umbrella study with a primary objective of objective response rate for patients with mCRPC and measurable disease. Secondary objectives include radiographic progression-free survival, PSA response, time to first symptomatic skeletal event, overall survival, safety, and correlative studies. Eligible patients must have progressive mCRPC of any histology, received a prior androgen receptor pathway inhibitor (ARPI), and received or refused taxane chemotherapy. Patients with measurable and non-measurable disease are eligible. Patients must have standard of care next generation DNA sequencing via any CLIA-certified tissue or circulating tumor DNA assay for initial trial enrollment. For arm allocation based on RNA alterations, testing will be via the CLIA-certified Caris MI Tumor Seek assay, which includes whole exome and whole transcriptome sequencing, derived from tissue obtained within 12 months of enrollment. A real-time molecular tumor board will convene to review genomic reports and confirm arm allocation on a rolling basis as biomarker results become available. Patients with Rb loss (DNA), Rb functional loss signature (RNA), NEPC signature (RNA) will be allocated to treatment with the EZH1/2 inhibitor valemetostat. Patients with at least 2 of 3 tumor suppressor gene DNA alterations (TP53, RB1, PTEN), FANC alteration (DNA), or SLFN11 overexpression (RNA) will be allocated to cabazitaxel plus carboplatin. Patients without any study-defined alterations will be allocated to physician choice treatment with either cabazitaxel, ARPI, or ^{177}Lu-PSMA-617. The study is designed to accommodate future biomarker arms. A maximum of 64 patients with measurable disease and 94 patients with non-measurable disease for a total of 158 patients will be accrued to each treatment arm. A Simon two-stage minimax design per arm was used to determine whether the response rate for measurable disease patients was greater than 0.20. This design has a type 1 error equal to 0.05 and has power equal to 0.90 if the probability of response is 0.37. Clinical trial information: NCT06632977. Research Sponsor: https://acknowledgments.alliancefound.org; Daiichi Sankyo; U10CA180882.