TPS5118 **Poster Session**

Trial in progress (XALute): Phase 3 study of xaluritamig vs investigator's choice of cabazitaxel or second androgen receptor directed therapy (ARDT) in post-taxane metastatic castration-resistant prostate cancer (mCRPC).

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Background: The median overall survival of patients with mCRPC remains under 2 years even with newer therapies. Xaluritamig, an XmAb 2+1 T-cell engager that targets the six-transmembrane epithelial antigen of prostate 1 (STEAP1), facilitates lysis of STEAP1-expressing cancer cells, such as those in advanced prostate cancer. In a first-in-human study, xaluritamig demonstrated encouraging efficacy and a manageable safety profile for patients with mCRPC refractory to standard of care therapies (Kelly WK, et al. Cancer Discov. 2024;14(1): 76-89). **Methods:** XALute is a randomized, multicenter, open-label, phase 3 study to evaluate the efficacy and safety of xaluritamig vs cabazitaxel or second ARDT in men with mCRPC previously treated with taxane chemotherapy. Enrollment in the control arm treatments will be split evenly between cabazitaxel and second ARDT. Stratification factors include LDH $\leq$ or $>$ 260 IU/L, liver metastases (Y/N), prior prostate-specific membrane antigen radioligand therapy (PSMA-RLT) (Y/N) and the intention to treat with cabazitaxel or ARDT switch. Approximately 675 patients will be enrolled. Participants will be randomly assigned in a 2:1 ratio to xaluritamig monotherapy or standard care. Participants will receive treatment until radiographic disease progression per Prostate Cancer Clinical Trials Working Group 3 (PCWG3), unacceptable toxicity, initiation of other anticancer therapy, withdrawal of consent, death, or end of study as determined by the sponsor. The primary efficacy endpoint is overall survival. The key secondary efficacy endpoint is radiographic progression-free survival per PCWG3 by blinded independent central review. Key inclusion criteria are pathological/cytological confirmation of prostate adenocarcinoma; mCRPC with at least one metastatic lesion; evidence of progressive disease; prior treatment with at least one ARDT; one taxane therapy in the mCRPC setting, and ongoing androgen deprivation with serum testosterone levels ($<$50 ng/dL or $<$1.7 nmol/L). Prior treatment with PSMA-RLT, poly ADP-ribosylation inhibitors, and immune checkpoint inhibitors are permitted. Exclusion criteria include prior STEAP1-targeted therapy, any anticancer therapy within 4 weeks prior to first dose of study treatment (not including androgen deprivation therapy), prior PSMA-RLT within 2 months of first dose of study treatment unless less than 2 cycles received, and prior radionuclide therapy (radium-223) within 2 months of first dose of study treatment To mitigate risk of cytokine release syndrome, xaluritamig will be administered with step dosing. Cabazitaxel or second ARDT will be administered according to regional prescribing information. Funded by Amgen Inc. Clinical trial information: NCT06691984. Research Sponsor: Amgen Inc.