TPS5126 **Poster Session**

A phase 3 study of 177Lu-rosptamab plus standard of care vs. standard of care alone in patients with metastatic castration-resistant prostate cancer (ProstACT Global).

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Background: The treatment of advanced prostate cancer (PC) is challenging, with undesirable side effects that impact patient quality of life. Radioimmunotherapy (RIT) can localize therapy to specific tumor cells in multiple organs to reduce or eliminate damage to normal tissue. The cell surface glycoprotein prostate-specific membrane antigen (PSMA) is an ideal therapeutic target as it is highly expressed by malignant prostate cells. There is a strong rationale for further investigation of the ^{177}Lu-labeled, chelator-conjugated antibody, ^{177}Lu-rosopatamab, as a potential first-line RIT candidate for the treatment of PC. **Methods:** This multinational, multicenter, prospective, randomized, open label phase 3 study will have 2 parts: a dosimetry and safety lead-in (n=30) and a randomized treatment expansion (n=490). In Part 1, patients will be divided into 3 groups (n=10 each) to receive 2 single intravenous (IV) injections of 76 millicuries (mCi) each, 14 days apart, of ^{177}Lu-rosopatamab with best standard of care (SoC) combinations with abiraterone, enzalutamide, or docetaxel to fully characterize biodistribution and safety profiles of ^{177}Lu-DOTA-rosopatamab + SoC. SoC received will be determined prior to treatment with ^{177}Lu-rosopatamab. In Part 2, patients will be enrolled in a 2:1 ratio to receive either the best SoC or 2 single IV injections of 76 mCi each of ^{177}Lu-rosopatamab, given 14 days apart, plus best SoC. SoC will be determined prior to randomization. Eligible patients must have PSMA-expressing metastatic castration-resistant PC (mCRPC) that have progressed despite prior therapy with either enzalutamide or abiraterone plus prednisone, and 1 line of prior taxane therapy or have refused or are ineligible for taxanes. Patients must have adequate organ function including at least 150x10^9/L platelets, hemoglobin 10 g/dL, and have PSMA-positive disease on ^{68}Ga-PSMA-11 PET/CT imaging as confirmed by a central reader. Key exclusion criteria include small cell histology, increased risk of hemorrhage or bleeding, known brain or hepatic metastases, or history of stroke, seizure, or treatment with radioisotopes within 6 months prior to randomization. The primary endpoint is radiographic progression-free survival (rPFS). Key secondary endpoint is OS. Additional secondary endpoints include 5-year overall survival, tumor objective response rate, time to symptomatic skeletal event, and health-related quality of life. An alpha control and 95% confidence intervals will be used; patients will be substratified between TLX591 + 2nd ARPI or TLX591 + docetaxel. This study is currently enrolling. Clinical trial information: NCT06520345. Research Sponsor: Telix Pharmaceuticals.