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Introduction & Objectives: The cell surface glycoprotein prostate-specific membrane antigen (PSMA) has proven to be an ideal therapeutic target in prostate cancer (PC) as it is highly expressed by malignant prostate cells.¹,² ¹⁷⁷Lu-DOTA-HuJ591-CHO (TLX591) is a radioimmunoconjugate comprised of the humanized IgG1 mAb rosopatamab, linked to the low energy beta-emitting radioisotope lutetium-177 (¹⁷⁷Lu) via the bifunctional chelating agent DOTA-NHS ester. Chinese Hamster Ovary (CHO) cell line has been selected for the manufacture of the recombinant mAb. There is a strong rationale for investigation of TLX591 as a potential radioligand therapy for the treatment of PC, supported by previous clinical evidence of the safety of the antibody, as unconjugated and as a DOTA conjugate, and of the specificity of the antibody for PC tumors.³,⁴,⁵,⁶ This multicenter Phase 1 study (ClinicalTrials.gov Identifier: NCT04786847) is designed to evaluate the safety, tolerability, biodistribution and dosimetry of TLX591 administered with best SoC to patients with PSMA-expressing, metastatic castration-resistant prostate cancer (mCRPC) progressing despite prior treatment with a novel androgen axis drug (NAAD). At the time of this abstract the study has commenced recruitment in Australia.

Materials & Methods: The study will consist of 2 cohorts:

Cohort 1: Five patients will be recruited for evaluation of biodistribution of TLX591 administered in combination with SoC. These patients will receive a single tracer (27 mCi) intravenous (IV) infusion of TLX591, and SPECT images and pharmacokinetic blood samples acquired at several time points until Day 13. A qualitative comparison of biodistribution of tracer level TLX591, as demonstrated by SPECT, with ⁶⁸Ga-PSMA-11 on PET imaging will be performed to ensure equivalent (or improved) radiopharmaceutical tumour targeting. Dosimetry analysis will also be performed. If safety is confirmed by independent DSMB review, each individual patient in Cohort 1 will proceed 14 days following the initial tracer dose to a second administration of TLX591. SoC therapy will continue according to standard practice.

Cohort 2: All further enrolled patients will receive two administrations of 76 mCi TLX591 for further evaluation of safety, tolerability and biodistribution, and efficacy in combination with SoC.

2. Dorff TB et al., 2019
3. Tagawa, Milowsky et al., 2013
4. Tagawa et al., 2019
5. Tagawa, Whang et al., 2014
6. Niaz et al., 20...