AdMeTech24

A Phase 3 Study of ^{177}Lu-TLX591 plus SOC vs SOC alone in patients with mCRPC (ProstACT GLOBAL)

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Introduction: The treatment of advanced prostate cancer (PC) is challenging, with no curative therapy to date and undesirable side effects that may impact patient quality of life. Monoclonal antibodies enable high specificity with low rates of off-target organ exposure, prolonged retention in PSMA+ tumors, and a predictable safety profile. There is a strong rationale for further investigation of the ^{177}Lu-labeled, chelator-conjugated antibody, ^{177}Lu-DOTA-rosopatamab (hereafter, TLX591), with prior studies demonstrating favorable safety and efficacy, particularly with a fractionated (dose-dense) regimen. Phase 1 ProstACT SELECT preliminary results demonstrate consistent uptake between TLX591 and ^{68}Ga-PSMA-11 imaging and reinforces advantages of this first-in-class radio-antibody drug conjugate investigational therapy.

Methods: In this multinational, multicenter, prospective, randomized, open label phase 3 study, patients (N=400) with PSMA-expressing metastatic castration-resistant PC (mCRPC) that have progressed despite prior treatment with an androgen-receptor pathway inhibitor (ARPI) will be enrolled in 1) a safety and dosimetry lead-in (N=30) and 2) a randomized treatment expansion (N=400) in a 2:1 ratio to receive best protocol-defined standard of care (SoC) with or without 2 intravenous injections of 2.8 GBq of TLX591, given 14 days apart. SoC may be an alternative ARPI or docetaxel. Eligible patients must have received 1 prior ARPI in the mCRPC setting. Patients must have 150x10^9 /L platelets and have PSMA-positive disease on ^{68}Ga-PSMA-11 PET/CT imaging.

The primary endpoint is radiographic progression-free survival. Secondary endpoints include 5-year overall survival, tumor objective response rate, time to symptomatic skeletal event, health-related quality of life, and treatment-related adverse events count. An alpha control and 95% confidence intervals will be used; patients will be sub-stratified between TLX591 + 2nd ARPI or TLX591 + docetaxel. This study is currently enrolling.

Results: This study is ongoing; no results are available at the time of abstract submission.

Conclusions: Effective treatment options for mCRPC with favorable safety and tolerability profiles continue to be an unmet need. Combining the advantages of targeted radiotherapy and immunotherapy, along with proven patient selection capabilities of ^{68}Ga-PSMA-11 PET, provides reasonable justification for further evaluation of ^{177}Lu-TLX591 in a large-scale trial.

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