therapies) were enrolled. There was no limit on the number of prior lines of therapy. At least one accessible lesion was electroprolated with plasmid IL-12 (pIL-12-EP) on days 1, 5 and 8 every 6 weeks and pembrolizumab was administered every 3 weeks. Tumor response in treated and untreated lesions was assessed by RECIST v1.1 every 12 weeks. Endpoints include ORR, safety, PFS, OS, and DOR.

**Results**

The first 56 patients treated of 100 planned were included in this interim analysis. Of these, 84% had Stage IV disease, 30% had M1c or M1d disease, and 27% had prior exposure to ipilimumab. In 54 efficacy evaluable patients the investigator-assessed ORR was 30% (3 CR/13 PR), 5 patients had 100% reduction of target lesions. All responses have been confirmed, only two responding patient progressed while on study, 2 patients completed the study with ongoing responses confirmed, only two responding patient progressed while on study, 2 patients completed the study with ongoing responses.

The median overall survival (mOS) and duration of response (mDOR) has not been reached, with a median follow-up time of 13 months. Grade 3 treatment-related adverse events (TRAEs) were seen in 5.4% of patients, and there were no grade 4/5 TRAEs. The rate of grade 3 treatment-emergent (TEAEs) regardless of cause was 23.2%. The median time for pIL-12-EP treatment was 10 minutes (range 2,46). Consistent with prior studies of single-agent pIL-12-EP, tumor IHC, and transcriptomic assessments revealed hallmarks of antigen-specific antitumor immunity in this study. Additional analyses including microbiome, TCR clonality, and peripheral blood biomarker assays will be presented.

**Conclusions**

In this rigorously defined PD-1 antibody refractory patient population, the addition of pIL-12-EP to PD-1 antibody therapy induced deep, durable, systemic response in local treated and distant visceral metastatic untreated lesions with nominal systemic toxicity.

**Trial Registration**

Trial Registration: NCT#03132675

**Ethics Approval**

The study was approved by a central IRB and/or local institutional IRBs/Ethics Committees as required for each participating institution.

**Consent**

Written informed consent was obtained from the patients participating within the trial, the current abstract does not contain sensitive or identifiable information requiring an additional consent from patients.

**REFERENCES**


http://dx.doi.org/10.1136/jitc-2020-SITC2020.0799
PRIME™ IL-15 (RPTR-147): PRELIMINARY CLINICAL RESULTS AND BIOMARKER ANALYSIS FROM A FIRST-IN-HUMAN PHASE 1 STUDY OF IL-15 LOADED PERIPHERALLY-DERIVED AUTOLOGOUS T CELL THERAPY IN SOLID TUMOR PATIENTS

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Background RPTTR-147 is a novel autologous non-genetically modified multi-clonal T cell product loaded with an IL-15-Fc nanogel. The product was derived from rare peripherally-derived anti-tumor T cell clones that were primed against a multi-antigen cassette containing tumor associated antigens (TAA), known to be over-expressed in specific tumor types.

We describe preliminary results from the ongoing first-in-human Phase 1 trial.

Methods Autologous anti-TAA T cells are generated with a proprietary dendritic cell priming process and then loaded with an IL-15-Fc nanogel. TAs used in cassette: PRAME, NY-ESO-1, SSX2, Survivin and WT1. Thawed RPTTR-147 is delivered by infusion. Pre- and post-treatment biopsies were collected for biomarker analysis by immunohistochemistry (IHC) and transcriptome sequencing. Serial blood collections were obtained for measuring IL-15 pharmacokinetics and pharmacodynamic parameters including plasma cytokine levels and immunophenotyping by flow cytometry. T cell receptor sequencing (TCRSeq) was used to characterize the T cell repertoire from manufactured T cell product and the patient’s blood.

Results Interim clinical and biomarker data from 17 patients with advanced metastatic disease refractory to SOC who received monthly infusions of 20-360 million cells/m², were reviewed (table 1). There were no dose-limiting toxicities and no evidence of cytokine-release syndrome. The 360M/m² dose contained 3X more IL15-Fc than the MTD of systemically administered IL15-Fc, but produced less than a tenth of the systemic exposure to free IL15-Fc. Currently, 360M/m² is considered safe and well-tolerated. Further dose escalation is planned.

Matched evaluable biopsies were obtained in 7 patients. Tumor-infiltrating T cell lymphocytes was observed in 5 cases for CD8 T cells and 4 cases for CD4 T cells. A dose dependent CD8 and CD4 T cells was observed, consistent with expected MOA and PK. TCRSeq analysis demonstrated that product specific T cell clones could be tracked in both patient’s blood and tumor over time. Further analysis to decode the specificity of those cells and demonstrate that tumor antigen specific T cells can be found in patient’s blood and tumor biopsies is ongoing.

Of the 17 patients who received RPTTR-147 infusions 10 were noted to have stable disease (SD) and in 4 patients SD lasted > 6 months.

Conclusions Interim results with RPTTR-147 have shown it to be well-tolerated and have a favorable safety profile. Dose-escalation is proceeding. Ongoing biomarker analysis will inform future clinical strategies in matching patients to an optimized PRIME IL-15 T cell product.

Trial Registration NCT03815682

Ethics Approval The study was approved by local institutional IRBs after acceptance of the IND by the FDA.