therapies) were enrolled. There was no limit on the number of prior lines of therapy. At least one accessible lesion was electroporated 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.

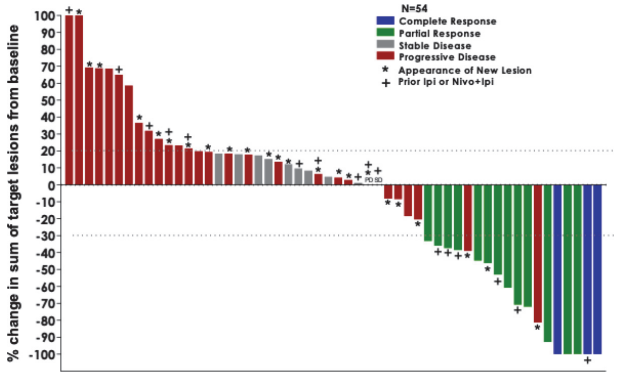
Results The first 56 patients treated of 100 planned were included in this interim analysis. Of these, 84% had Stage IV disease, 30% had M1c or M1d disease, and 27% had prior exposure to ipilimumab. In 54 efficacy evaluable patients the investigator-assessed ORR was 30% (3 CR/13 PR), 5 patients had 100% 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 (figures 1 and 2). In patients with M1c/M1d disease, the ORR was 35.2% (n=6/17). Tumor reduction was observed in untreated lesions in 12 of 12 patients who had unaccessible lesions or accessible untreated lesions. 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.

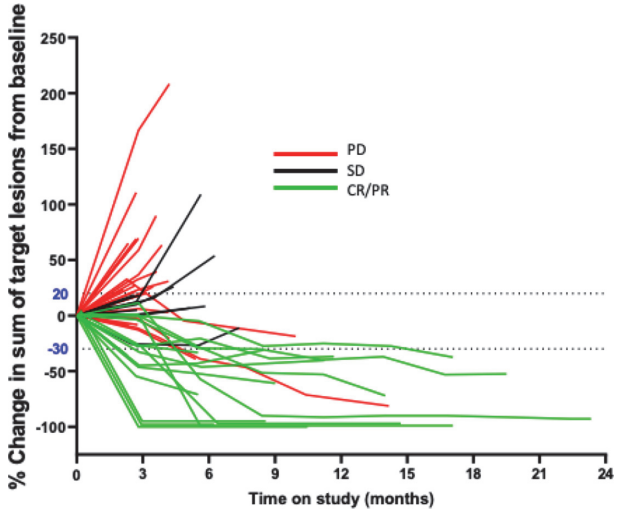
Trial Registration Trial Registration: NCT#03132675

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.



Abstract 799 Figure 1
Best confirmed overall response by RECIST v1.1 after confirmed progression on anti PD-1



Abstract 799 Figure 2
Percent change in sum of target lesions over time

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800 A PHASE I DOSE ESCALATION AND EXPANSION STUDY OF INTRATUMORALLY ADMINISTERED CV8102 AS A SINGLE-AGENT OR IN COMBINATION WITH ANTI-PD-1 ANTIBODIES IN PATIENTS WITH ADVANCED SOLID TUMORS

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Background CV8102 is a non-coding, non-capped RNA complexed with a carrier peptide activating the innate (via TLR7/8, RIG-I) and adaptive immune system.[1 2] An ongoing phase I trial is investigating i.t. CV8102 either as a single agent or in combination with systemic anti-PD-1 antibodies in patients with advanced melanoma (MEL), squamous cell carcinoma of the skin (cSCC) or head and neck (hnSCC) and adenoid cystic carcinoma (ACC).

Methods An open-label, cohort-based, dose escalation and expansion study in patients with advanced cutaneous melanoma (cMEL), cutaneous squamous cell carcinoma (cSCC), head and neck squamous cell carcinoma (hnSCC) or adenoid cystic carcinoma (ACC) is ongoing investigating i.t. CV8102 as single agent and in combination with anti-PD-1 antibodies.

8 intratumoral injections of CV8102 are being administered initially over a 12 week period, while patients benefiting from the single agent therapy may receive further treatment. In an initial dose escalation part the maximum tolerated dose and recommended phase 2 dose for subsequent cohort expansion will be defined.

Results As of September 16, 2020, 29 patients have been treated with CV8102 as a single agent (25-900 µg) and 21 patients have received CV8102 (25-900 µg) in combination with anti-PD-1 antibodies. Most frequent treatment related adverse events were mild to moderate fever, fatigue, chills and headache. One patient treated at the 900 µg single agent experienced a dose limiting toxicity (G3 transaminase increase in the context of G2 cytokine release syndrome).

Regression of injected and distant noninjected lesions was observed in several patients in the single agent and the anti-PD-1 combination cohorts. Updated safety and efficacy results will be presented.

Conclusions CV8102 showed an acceptable tolerability and preliminary evidence of clinical efficacy as single agent and in combination with anti-PD-1- antibodies.

Trial Registration NCT03291002

Ethics Approval The study was approved by the Central Ethics Committees in Tuebingen, Germany under 785/2016AMG1, in France under 19.05.17.64111, in Barcelona, Spain under the EudraCT number.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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http://dx.doi.org/10.1136/jitc-2020-SITC2020.0800

801 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 RPTR-147 is a novel autologous non-genetically modified multi-clonal T cell product loaded with an IL15-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 IL15-Fc nanogel. TAAs used in cassette: PRAME, NY-ESO-1, SSX2, Survivin and WT1. Thawed RPTR-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,[1] but produced less than a tenth of the systemic exposure to free IL15-Fc. Currently, 360M cells/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 increase in both inflammatory cytokines and NK & CD8 + 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 RPTR-147 infusions 10 were noted to have stable disease (SD) and in 4 patients SD lasted > 6 months.

Conclusions Interim results with RPTR-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.

Abstract 801 Table 1 Summary of Patients

Tumor Type	Number of Patients
Melanoma	6
Non-Small Cell Lung Carcinoma	4
Renal Cell Carcinoma	2
Head & Neck	2
Appendiceal Carcinoma	1
Ovarian Carcinoma	1
Synovial Carcinoma	1

Tumor types for the 17 patients with advanced metastatic disease included in this clinical trial (NCT0381568)