

INITIAL RESULTS FROM AN OPEN-LABEL PHASE 1B/2 STUDY OF RP1 ONCOLYTIC IMMUNOTHERAPY IN SOLID ORGAN AND HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS WITH ADVANCED CUTANEOUS MALIGNANCIES (ARTACUS)

¹Michael R Migden*, ²Wanxing Chai-Ho, ³Gregory A Daniels, ⁴Trisha M Wise-Draper, ⁵Meenal Kheterpal, ⁶Jennifer C Tang, ⁷Diana Bolotin, ⁸Claire Verschraegen, ⁹Andrew S Poklepovic, ¹⁰Shaheer A Khan, ¹¹Sherrif F Ibrahim, ¹²Nathalie C Zeitouni, ¹³Theresa Medina, ¹⁴Katy K Tsai, ¹⁵Chris Tucci, ¹⁵Susan Navia, ¹⁵Laxminarasimha Donthireddy, ¹⁵Praveen K Bommareddy, ¹⁵Jeannie W Hou, ¹⁶Diwakar Davar. ¹MD Anderson Cancer Center, Houston, TX, USA; ²UCLA David Geffen School of Medicine, Los Angeles, CA, USA; ³University of California San Diego, San Diego, CA, USA; ⁴Division of Hematology-Oncology, University of Cincinnati, Cincinnati, OH, USA; ⁵Department of Dermatology, Duke University Medical Center, Durham, NC, USA; ⁶University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA; ⁷University of Chicago, Department of Medicine, Section of Dermatology, Chicago, IL, USA; ⁸Division of Medical Oncology, Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; ⁹Department of Biochemistry and Molecular Biology, Medicine, Virginia Commonwealth University, Richmond, VA, USA; ¹⁰Columbia University Irving Medical Center, New York, NY, USA; ¹¹Rochester Dermatologic Surgery, Victor, NY, USA; ¹²University of Arizona College of Medicine and US Dermatology Partners, Phoenix, AZ, USA; ¹³University of Colorado, Aurora, CO, USA; ¹⁴University of California, San Francisco, San Francisco, CA, USA; ¹⁵Replimune, Inc., Woburn, MA, USA; ¹⁶UPMC Hillman Cancer Center, Pittsburgh, PA, USA

Background Skin cancers are common post-transplant malignancies in stem cell transplant (SCT) and solid organ transplant (SOT) recipients. The use of immune checkpoint inhibitors has improved outcomes in the general patient population but is associated with a high risk of allograft rejection in transplant recipients. RP1 is an oncolytic immunotherapy that expresses a fusogenic glycoprotein (GALV-GP-R-) and granulocyte-macrophage colony-stimulating factor (GM-CSF). The purpose of this study is to assess the safety and efficacy of single-agent RP1 in SCT/SOT recipients with skin cancer.

Methods The trial will enroll up to 65 transplant recipients with histologically confirmed recurrent and/or locally advanced cutaneous squamous cell carcinoma (CSCC) and up to 10 patients with non-CSCC skin cancer in two parts. Part A will enroll kidney and liver transplant recipients until safety is established, and Part B will also enroll other transplant types. Patients must have stable allograft function, and ECOG performance status ≤ 1 . Patients with visceral metastases are excluded. Patients receive an initial RP1 dose at 1×10^6 plaque-forming units (PFU)/mL followed by 1×10^7 PFU/mL after 2 weeks and continuing every 2 weeks until prespecified study endpoints are met. Tumor biopsies are collected for biomarker analyses and HSV-1 serostatus is monitored.

Results Part A of the trial enrolled 13 kidney transplant patients (median age: 68 [range 57–81] years). The most common (>20%) treatment-emergent adverse events (TEAEs) were fatigue (46%); pyrexia (38%); chills (31%); and injection site pain, nausea, urinary tract infection, and vomiting (23% each). No immune-mediated adverse events (irAEs) or evidence of allograft rejection were observed. One patient died of COVID-19-related pneumonia, 1 from progressive disease, and 1 from cerebrovascular accident. The preliminary objective response rate (ORR) for the 11 evaluable patients was 27% (3/11; all confirmed complete response [CR]). One patient (9%) had stable disease. Immunohistochemistry from tumor biopsies indicated influx of CD8+ T cells and upregulation of PD-L1 expression upon RP1 post-treatment. Additional biomarker data from gene expression analysis will be presented.

Conclusions This is the first trial assessing single-agent RP1 activity in SCT/SOT patients. RP1 monotherapy showed

compelling antitumor activity (ORR 27%; all CR) in evaluable patients from Part A of the study. No irAEs and/or evidence of allograft rejection were observed. RP1 monotherapy was well tolerated, and the safety profile was similar to non-immunocompromised patients with advanced skin cancers (IGNYTE study). Enrollment has now been expanded to include patients with non-kidney/liver transplants.

Trial Registration Clinicaltrials.gov; NCT04349436

Ethics Approval The study was conducted in accordance with the ethical principles originating from the Declaration of Helsinki and was approved by the Institutional Review Board/Ethics Committee at each participating site. Written informed consent was obtained from all patients prior to the conduct of any study-related procedures.

<http://dx.doi.org/10.1136/jitc-2023-SITC2023.0777>