CERPASS: A randomized, controlled, open-label, phase 2 study of cemiplimab ± RP1 in patients with advanced cutaneous squamous cell carcinoma

Andrew Haydon[1], Muhammad Alamgeer[2], Daniel Brungs[3], Frances Collichio[4], Nikhil I. Khushalani[5], Dimitrios Colevas[6], Danny Rischin[7], Ragini Kudchadkar[8], Wanxing Chai-Ho[9], Gregory Daniels[10], Jose Lutzky[11], Jenny Lee[12], Samantha Bowyer[13], Michael Migden[14], Ann W. Silk[15], Céleste Lebbé[16], Jean-Jacques Grob[17], Ignacio Melero[18], Piyush Sheladia[19], Praveen K. Bommareddy[19], Shui He[19], Claudia Andreu-Vieyra[19], Matthew G. Fury[20], Andrew Hill[21]

[1]The Alfred Hospital, Melbourne, Australia; [2]Monash Medical Centre, Clayton, Australia; [3]Southern Medical Day Care Centre, Wollongong, Australia; [4]Lineberger Comprehensive Cancer Center, University Of North Carolina, Chapel Hill, NC, USA; [5]Moffitt Cancer Center, Tampa, FL, USA; [6]Stanford University School of Medicine, Stanford, CA, USA; [7]Peter MacCallum Cancer Center and University of Melbourne, Melbourne, Australia; [8]Winship Cancer Institute of Emory University, Atlanta, GA, USA; [9]UCLA David Geffen School of Medicine, Los Angeles, CA, USA; [10]UC San Diego Moores Cancer Center, La Jolla, CA, USA; [11]University of Miami Sylvester Comprehensive Center, Miami, FL, USA; [12]Chris O'Brien Lifehouse, Camperdown, Australia; [13]Sir Charles Gairdner Hospital, Nedlands, Australia; [14]MD Anderson Cancer Center, Houston, TX, USA; [15]Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA, USA; [16]Université de Paris, Department of Dermatology, CIC AP-HP Hôpital Saint Louis, Paris, France; [17]Hôpital de la Timone Service de Dermatologie et Cancérologie Cutanée, Marseille, France; [18]Departamento de Inmunologia and Inmunoterapia, Centro de Investigación Medica Aplicada, Universidad de Navarra, Pamplona, Spain, [19]Replimune Inc, Woburn, MA, USA; [20]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [21]Tasman Oncology Research, Southport, Australia.

Background

- Cutaneous squamous cell carcinoma (CSCC) is the second most common type of skin cancer with an approximate worldwide incidence of ~1.7M cases per year; including 0.18M - 0.42M cases per year in the United States [1,2].
- Although most CSCC patients have a favorable prognosis, the disease has a greater propensity for aggressive recurrences and the prognosis of locally advanced and/or nodal and distant metastatic disease remains poor [3].
- Cemiplimab-rwlc is a the programmed death receptor-1 (PD-1) blocking antibody approved in USA and EU for the treatment of patients with metastatic or locally advanced CSCC who are not candidates for curative surgery or radiation therapy [4, 5].
- RP1 is an enhanced potency oncolytic HSV-1 which expresses a fusogenic glycoprotein (GALV-GP R-) and granulocyte macrophage colony stimulating factor (GM-CSF) [6].
- In pre-clinical studies, RP1 monotherapy induces tumor regression in both injected and distant/un-injected tumors which is further enhanced by combining with anti-PD-1 antibody; thus the combination of RP1 and cemiplimab is expected to provide a synergistic effect.
- RP1 + nivolumab (a PD-1 inhibitor) has shown compelling response rates and a good safety profile in patients with melanoma and other non-melanoma skin cancers (NMSC) including anti-PD-1 failed disease [7].

Objective

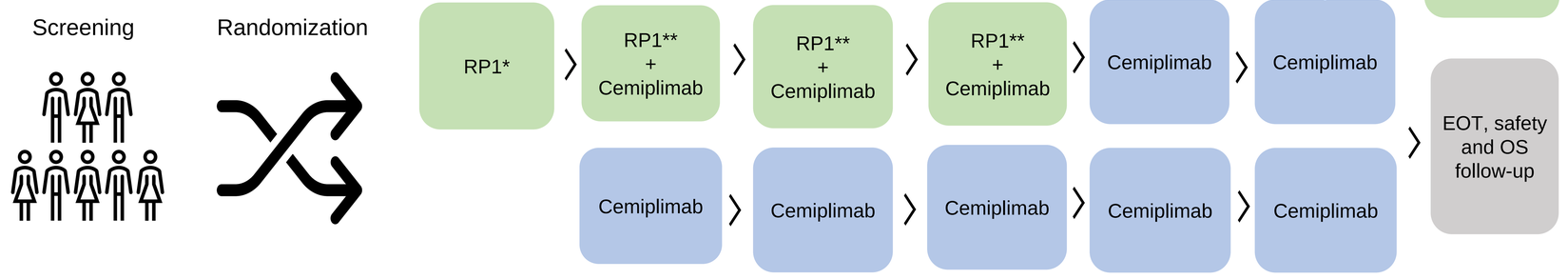
The primary objective of this study is to assess the safety and efficacy of cemiplimab monotherapy vs. RP1 + cemiplimab combination in patients with locally advanced or nodal or distant metastatic cutaneous squamous cell carcinoma (CSCC).

Methods

Phase 2 | Open-label | Randomized | Global

Trial Design

- Target enrollment = 180
- 2:1 randomization favoring combination arm



*First dose = 1 x 10^6 PFU/ml
**Subsequent doses = 1 x 10^7 PFU/ml
†1 Cycle = 63 days
‡RP1 re-initiation (up to 8 additional doses of RP1) can occur at any time during the 108 week treatment period after a 12-week RP1 dosing holiday, during which patients will receive cemiplimab alone. If no reinitiation occurs, patients may receive cemiplimab only from Cycle 3 D22 up to Cycle 12 D43.

Treatment period = 108 weeks

RP1 will be administered via direct intratumoral injection into superficial or subcutaneous lesions or into deep/visceral lesions using image guidance (e.g., ultrasound or CT imaging).

Cemiplimab 350 mg intravenous over 30 minutes every 21 days for up to 108 weeks.

Key Eligibility Criteria

Inclusion

- Histologically confirmed diagnosis of locally advanced or metastatic CSCC that was previously treated, not suitable candidates for radiotherapy, chemotherapy or surgery or have refused those treatments.
- At least 1 measurable lesion by study criteria and lesion(s) that are injectable, which individually or in aggregate are ≥ 1 cm longest in diameter.
- ECOG ≤1; ECOG 2 allowed if due to CSCC.
- Anticipated life expectancy > 12 weeks.
- Provide archival (within 6-12 months of screening date) or new biopsy (FFPE block or unstained slides) for central pathology review and biomarkers.

Exclusion

- Prior treatment with oncolytic therapy or PD-1/PD-L1 inhibitors or with other immune modulating agents.
- Active significant herpetic infections or prior complications of HSV-1.
- Untreated brain metastasis(es).
- SCC of the dry red lip (vermillion) or anogenital area and mixed histology is excluded unless predominantly CSCC.
- Ongoing or recent auto-immune disease requiring systemic immunosuppressive treatments, a diagnosis of immunodeficiency disorders, organ transplantation or hematologic malignancies linked with immune suppression.

Key Endpoints

- **Primary**
  Objective response rate and complete response rate by independent review per RECIST v1.1 and clinical and composite response criteria.
- **Secondary**
  Safety by CTCAE V5.0, PFS and OS.
- **Exploratory**
  Comprehensive biomarker analysis using tumor biopsies and peripheral blood, including the assessment of RP1 biodistribution and shedding.

CERPASS is now recruiting patients. To learn more about enrolling your patient contact: clinicaltrials@replimune.com or +1 (781) 222 9570.

Additional information could be obtained by visiting ClinicalTrials.Gov (NCT04050436).

References:
1.Urban K, et al. *JAAD International.*2021;2: 98–108.
2.Rogers HW, et al. *Arch Dermatol.*2010;146(3):283-7.
3.Rees JR, et al. *Int J Cancer*. 2015;137(4):878-884.
4.Migden MR, et al. *Lancet Oncol.* 2020;21(2):294-305.
5.Migden MR, et al. *N Engl J Med*. 2018;379(4):341-351.
6.Thomas S, et al. *J Immunother Cancer*. 2019;7(1):214.
7.Middleton M, et al. *J Immunother Cancer.*2020;8.

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