Abstract: TPS9593

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

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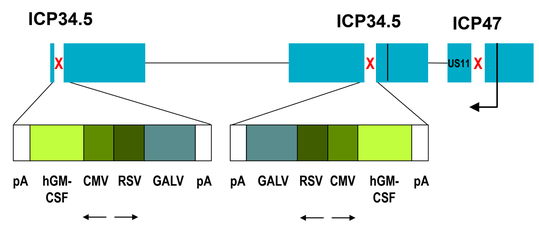
Background

- Cutaneous squamous cell carcinoma (CSCC) is the second most common type of skin cancer with an approximate worldwide incidence of ~1,700,000 cases per year; including 180,000–420,000 cases per year in the US [1,2]
- Most patients with CSCC have a favorable prognosis; however, for a subset of patients, the disease has a propensity for aggressive recurrences and the prognosis of locally advanced and/or nodal and distant metastatic disease remains poor [3]
- Cemiplimab-rwlc (cemiplimab) is a programmed death receptor-1 (PD-1)–blocking antibody approved in US 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 herpes simplex virus 1 (HSV-1) that expresses a fusogenic glycoprotein (GALV-GP-R−) and granulocyte-macrophage colony-stimulating factor [6]
  - GALV-GP-R− expression leads to cell-to-cell fusion formation in infected tumor cells through binding to the constitutively expressed phosphate transporter 1 receptor for GALV. This results in the death of the cells by membrane fusion and is also intended to enhance the spread of the virus through the tumor [7]
- In preclinical studies, RP1 monotherapy induces tumor regression in both injected and distant/uninjected tumors, which is further enhanced by combining with an anti–PD-1 antibody; thus, the combination of RP1 and cemiplimab is expected to produce a synergistic effect [6]
- In the IGNYTE study, RP1 + nivolumab (an anti–PD-1 inhibitor) demonstrated compelling response rates and a good safety profile in patients with melanoma and nonmelanoma skin cancers, including in CSCC and in anti–PD-1–failed disease [8]

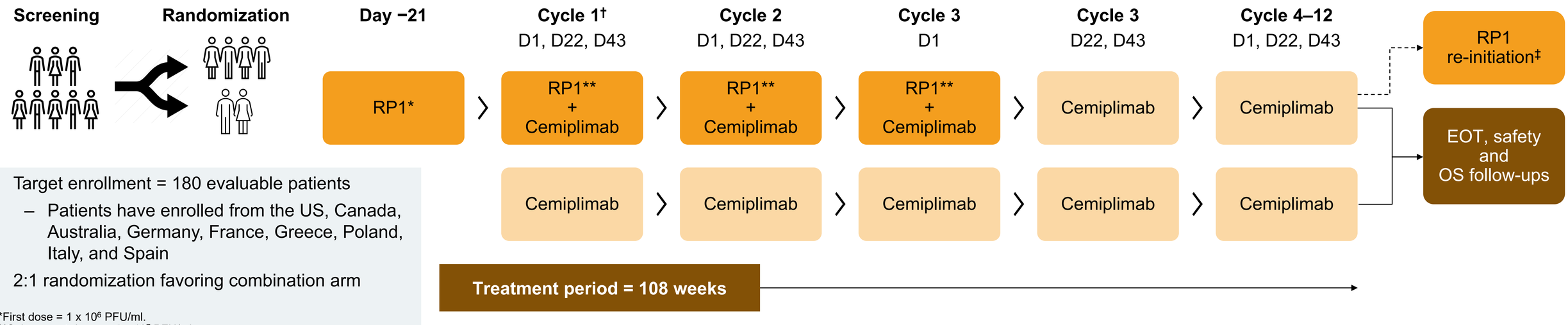
Objective

To assess the safety and efficacy of cemiplimab monotherapy vs RP1 + cemiplimab combination in patients with locally advanced, nodal, or distant metastatic CSCC.

RP1



Trial Design



- Target enrollment = 180 evaluable patients
  - Patients have enrolled from the US, Canada, Australia, Germany, France, Greece, Poland, Italy, and Spain
- 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 re-initiation occurs, patients may receive cemiplimab only from Cycle 3 D22 up to Cycle 12 D43.
CT, computed tomography; D, day; EOT, end of treatment; OS, overall survival.

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

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

Key Eligibility Criteria

Inclusion

- Histologically confirmed locally advanced or metastatic CSCC: must not be a suitable candidate for radiotherapy or surgery, or patient has refused those treatments
- At least 1 measurable, injectable lesion, which individually or in aggregate must be ≥1 cm in the longest diameter
- Eastern Cooperative Oncology Group (ECOG) score ≤1; ECOG score of 2 allowed if attributed to CSCC
- Anticipated life expectancy >12 weeks
- Provide archival (within 6–12 months of screening date) or new biopsy (formalin-fixed paraffin-embedded block or unstained slides) for central pathology review and biomarkers

Exclusion

- Prior treatment with oncolytic viral therapy, PD-1/programmed death-ligand 1 (PD-L1) inhibitors, or other immune-modulating agents
- Active significant herpetic infections or prior complications of HSV-1
- Untreated brain metastasis(es)
- Ongoing or recent autoimmune disease requiring systemic immunosuppressive treatments, a diagnosis of human immunodeficiency virus, organ transplantation, or hematologic malignancies linked with immune suppression

Key Endpoints

Primary

- Objective response rate and complete response rate by blinded independent review

Secondary

- Duration of response, safety, progression-free survival, and overall survival

Exploratory

- Biomarker analysis including tumor-infiltrating lymphocytes, PD-L1 expression, tumor mutation burden, and anti–HSV-1 antibodies
- 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 can be obtained by visiting ClinicalTrials.gov (NCT04050436).

Acknowledgments

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Study Sponsor

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