An Open-Label, Multicenter, Phase 1/2 Clinical Trial of RP1 as a Single Agent and in Combination with Nivolumab in Patients with Solid Tumors [IGNYTE]

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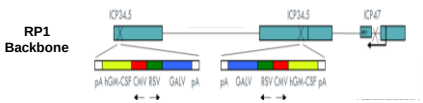
Background

- Oncolytic viruses preferentially replicate in tumors, promote immunogenic cell death & the induction of systemic anti-tumor immunity and may provide the optimum means to generate patient-specific anti-tumor immune responses.
- RP1 is an enhanced potency oncolytic HSV-1 expressing a fusogenic glycoprotein (GALV-GP R-) and granulocyte macrophage colony stimulating factor (GM-CSF). Pre-clinical studies with RP1 demonstrated potent GALV-GP R-enhanced anti-tumor activity and immunogenic cell death [1].



- IGNYTE is an ongoing Phase 1/2 trial that is evaluating RP1 as a single agent and in combination with anti-PD1 inhibitor nivolumab (nivo) in patients with solid tumors.
- The Phase 1 part of the trial is completed. Recommended phase 2 dose (RP2D) of RP1 was determined to be a first dose of 1×10^6 PFU/mL followed by subsequent doses of 1×10^7 PFU/mL [2].
- The Phase 2 part is currently ongoing and recruiting patients. Here we present the Phase 2 updated trial design, key eligibility criteria and endpoints (Amendment 10/Protocol version 11.0).

Objective

The objective of phase 2 part of the trial is to assess safety, tolerability and efficacy of RP1 + nivolumab in solid tumors including anti-PD failed disease.

Methods

Phase 1/2 | Open-label | Multi-cohort | Global

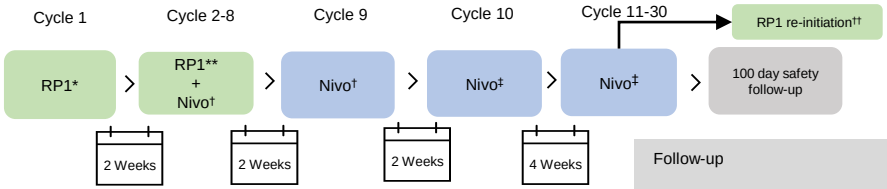
Methods (Phase 2 Trial Design)

Actively Recruiting Cohort*	Target N
Anti-PD1-failed cutaneous melanoma	125
Non-melanoma skin cancer (NMSC) anti-PD1/PD-L1-failed disease	60
Non-small cell lung cancer (NSCLC) anti-PD1/PD-L1-failed	30
Micro Satellite Instability and deficient Mis-match Repair (MSI-H/dMMR) disease	30

*Melanoma cohort (N=30) is fully enrolled and not recruiting. Urothelial bladder cancer cohort was terminated as of protocol amendment 8.

RP1
*First dose = 1 X 10^6 PFU/mL
**Subsequent doses = 1 X 10^7 PFU/mL

Nivo
†240 mg (Q2W) for 8 cycles
‡480 mg (Q4W) for 21 cycles



RP1 Re-initiation††

- The following criteria must be met: (i) injectable disease and lesions that are safe to inject, (ii) stable performance status, (iii) patient did not experience either of the following during the first course of RP1 treatment: a Grade 4 AE, a Grade 3 injection site reaction (e.g. injection site necrosis) lasting > 14 days, a suspected imAE Grade 3 event or Grade 3 infections lasting more > 14 days, unless the AE was deemed not related to RP1.
- The additional course of RP1 may be given for persistent or progressive lesions if persistence or progression is confirmed after at least 4 weeks, or for new lesion(s), at any time within 24 months from treatment initiation with RP1.

Follow-up

- 3 follow-up visits will be completed (30 day post last RP1 dose, 60 days post last RP1 dose, and 100 days past last nivo dose).
- Long term follow up (to include subsequent anti-cancer therapies) will be expected for all patient who discontinue study treatment prior to cycle 30.
- Patients will be followed for tumor response, survival, and other therapy.

Key Eligibility Criteria

Inclusion

- Patients with at least one measurable tumor of ≥1cm in longest diameter and ECOG ≤1.
- Stage IIIb-IV cutaneous melanoma for whom PD1 therapy is indicated or previously received or have exhausted or become intolerant to, or refuse, currently available therapies.
- Anti-PD1-failed cutaneous melanoma who have progressed on anti-PD1 ± anti-CTLA.
- Metastatic MSI-H or dMMR disease who have progressed on prior anti-PD1 therapy.
- Locally advanced or metastatic NMSC that are not considered treatable with surgical excision ± failed to prior PD1/PD-L1 therapy.
- Anti-PD1/PD-L1 failed NSCLC.

Exclusion

- Prior treatment with oncolytic therapy.
- Active significant herpetic infections or prior complications of HSV-1.
- Known history of acute or chronic active hepatitis B and C virus, or HIV infection.
- Systemic anticancer therapies within 4 weeks prior to enrollment (excluding PD1/PD-L1) and systemic infection requiring IV antibiotics or other serious infection within 14 days prior to dosing.
- Patients with uncontrolled, untreated brain or CNS metastasis.

Key Endpoints

- **Primary**
  - Objective response rate (ORR).
  - For anti-PD1-failed cutaneous melanoma cohort, ORR will be assessed by independent review.
  - Safety and tolerability.
- **Secondary**
  - Duration of response (DOR), complete response rate (CRR), disease control rate (DCR), overall survival (OS) and progression-free survival (PFS).
- **Exploratory**
  - Biodistribution and shedding of RP1 and activation of tumor-infiltrating lymphocytes.

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

Additional information could be obtained by visiting ClinicalTrials.Gov (NCT03767348)

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1. Thomas S, et al. J Immunother Cancer. 2019 Aug 10;7(1):214.
2. Aroldi F, et al. Journal for ImmunoTherapy of Cancer 2020;8

Disclosures: Dr. Francesca Aroldi does not have any disclosures.

Acknowledgement: Authors would like to thank Dharmendra Chaudhari, Isabel Bordo, Selda Samakoglu, Jaya Vemuri, Rachael Mills, Taylor Jew, Syed Raza and April Dovholuk for their contribution to the study.

Study Sponsor:
The study is sponsored by Replimune Group Inc, Woburn MA, USA.

Presented at the European Society for Medical Oncology (ESMO) Virtual Congress 2021, 16–21 September, 2021