Background RP1 is an enhanced potency oncolytic HSV-1 which expresses a fusogenic glycoprotein (GALV-GP R-) and granulocyte macrophage colony stimulating factor (GM-CSF).

In pre-clinical studies, RP1 demonstrated potent GALV-GP R-enhanced anti-tumor activity and immunogenic cell death. This Phase 1/2 (Ph 1/2) study was designed to evaluate the safety and efficacy of RP1 ± nivolumab (nivo) in patients (pts) with advanced solid tumors, including pts whose disease failed prior anti-PD-1/PD-L1 therapy and has reported promising interim data in a number of tumor types including cutaneous squamous cell carcinoma (CSCC) and anti-PD1 failed melanoma to date.

Methods This is a multi-center, first-in-human, open label, multi-cohort, non-randomized Ph1 study of RP1 alone and combined with nivo followed by Ph2 in combination with nivo in pts with recurrent advanced solid tumors including those that progressed after prior anti-PD-1/PD-L1 therapy. The Ph 1 monotherapy dose escalation (n=14) and RP-1 combination expansion (n=22) cohorts are fully enrolled. Approximately 260 pts are expected to be enrolled in the ongoing Ph 2 portion across five cohorts; melanoma (n=30, enrollment complete), non-melanoma skin cancer (n=45, to include 15 pts with anti-PD-1/PD-L1 failed disease), anti-PD-1 failed MSI-H/dMMR tumors (n=30), anti-PD-1/PD-L1-failed non-small-cell lung cancer (n=30) and a registration-directed cohort in anti-PD-1 failed cutaneous melanoma (n=125). Pts in the Ph 2 portion receive up to 10 mL of RP1 intratumorally into one or more superficial or deep seated/visceral lesions at the recommended Ph 2 dose (1x10^5 - 6 PFU/mL × 1 followed by 1x10^7 PFU/mL × 7, Q2W). Following the first dose of RP1, nivo (240 mg IV Q2W for 4 months then 480 mg IV Q4W for up to 2 years) is subsequently administered in combination. Pts may receive up to 8 additional doses of RP1 if they meet protocol-specified criteria. Tumor assessments are performed Q8W. The primary objectives of the Ph 2 part of the study are to assess the safety, tolerability, and overall response rate (ORR) of RP1 in combination with nivo, by independent review for the anti-PD1 failed melanoma cohort. Secondary objectives include duration of response, complete response rate, disease control rate, PFS, 1-year and 2-year survival rates. Exploratory objectives include biodistribution and shedding analysis of RP1 and biomarker studies, including analyses of tumor biopsies and blood samples. Enrollment is currently ongoing in the UK and US, with additional sites in the EU (including France and Spain) are expected to open in 2021.

Trial Registration NCT03767348

REFERENCES


Ethics Approval The study was approved by institutional review board or the local ethics committee at each site. Informed consent was obtained from patients prior to enrollment.

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