507 A PHASE 1 CLINICAL TRIAL OF RP2, AN ENHANCED POTENCY ONCOLYTIC HSV EXPRESSING AN ANTI-CTLA-4 ANTIBODY, AS A SINGLE AGENT AND COMBINED WITH NIVOLUMAB IN PATIENTS WITH ADVANCED SOLID TUMORS

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Background RP2 is a first-in-class, enhanced potency oncolytic herpes simplex virus (HSV) -1 expressing GM-CSF, a fusogenic protein (GALV-GP R-), and an anti-CTLA-4 antibody-like molecule that is being tested in an open-label, multicenter, phase 1 study alone and combined with nivolumab (nivo). Preliminary data with RP2 as monotherapy has been presented previously [1–2]. We present updated safety, tolerability, and clinical activity data of RP2 alone and initial data in combination with nivolumab.

Methods Using a 3+3 dose escalation, patients (pts) received intratumoral injections of up to 10 mL RP2 to superficial and/or visceral tumors Q2W up to 5 times at two dose levels (Dose level 1: 10^5 PFU/mL then 4 doses of 10^6 PFU/mL; dose level 2: 10^6 PFU/mL then 4 doses of 10^7 PFU/mL). Following determination of the RP2D (10^6 PFU/mL, followed by subsequent doses of 10^7 PFU/mL, Q2W X 7), a combination cohort of 30 pts were dosed with RP2 up to 8 times combined with nivo (240 mg Q2W for 4 mos from the second RP2 dose, then 480 mg Q4W for 20 mos). Re-initiation of up to 8 additional RP2 doses is permitted in prespecified circumstances.

Results Nine pts were enrolled into the RP2 monotherapy phase (6 seropositive and 3 seronegative for HSV). Objective responses were observed in 3 pts, 1 ongoing CR for ≥15 months in mucoepidermoid carcinoma, 1 ongoing PR for ≥18 months in esophageal cancer with liver metastases, 1 PR in uveal melanoma with liver metastases that progressed at 15 months. As of June 3rd 2021, 27 patients had been enrolled and ongoing partial responses had been observed in 4/9 anti-PD-1 failed cutaneous melanoma, 1/3 uveal melanoma and 1/3 SCCHN pts. A further 8 patients remained on study with the opportunity for response. Biomarker analyses indicate T cell infiltration, increase in tumor inflammation signature, expansion of existing T cell clones and emergence of new T cell clones, together indicative of local and systemic anti-tumor activity. The combination was well tolerated and no new safety signals were identified.

Conclusions RP2 ± nivo demonstrated good tolerability and durable systemic responses in pts with difficult-to-treat, heavily pretreated and anti-PD-1 failed advanced cancers. These data continue to support the hypothesis that oncolytic delivery of anti-CTLA-4 into tumors, with accompanying antigen release, presentation and immune activation, can provide potent systemic anti-tumor effects. Updated data from the full 30 patient cohort will be presented.

Trial Registration NCT04336241

REFERENCES

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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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