INTRATUMORAL ONCOLYTIC VIRUS V937 PLUS IPILIMUMAB IN PATIENTS WITH ADVANCED MELANOMA: THE PHASE 1B MITC1 STUDY

Brendan Curti1, Jon Richards3, GregoryDaniels4, Mark Faries3, Lynn Feun5, Kim Margolin6, SigrunHallmeyer7, Mark Grose8, Yiwei Zhang9, Anlong Li9, RobertHAndtbacka10
1 Providence Cancer Institute, Earle A. Chiles Research Institute, Portland, OR, USA; 2 AdvocateAurora Health, Park Ridge, IL, USA; 3 Huntsman Cancer Institute, Salt Lake City, UT, USA; 4 Moores Cancer Center, UCSD, La Jolla, CA, USA; 5 Cedars-Sinai Medical Center, Angeles Clinic and Research Institute, Santa Monica, CA, USA; 6 Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, USA; 7 City of Hope, Duarte, CA, USA; 8 Viralytics, Viralytics Limited, Sydney, Australia; 9 Merck and Co., Inc., Kenilworth, NJ, USA; 10 Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA

Background Intratumoral administration of V937, a bioselected genetically unmodified Coxackievirus A21, has shown antitumor activity both as a monotherapy and in combination with the anti-PD-1 antibody pembrolizumab.1–3 V937 induces lytic tumor cell infection and upregulation of members of immune checkpoint pathways.2 We present the results from the phase 1b MITC1 study that evaluated V937 plus ipilimumab for advanced melanoma.

Methods Eligible patients had unresectable or metastatic stage IIIb/C or IV melanoma amenable to intratumoral injection. Patients received intratumoral V937 3×10⁸ TCID₅₀ on days 1, 3, 5, 8, and 22, then Q3W for 14 more injections plus intravenous ipilimumab 3 mg/kg Q3W administered 4 times starting on day 22. Imaging was done Q6W beginning at day 106; response was assessed per immune-related response criteria (irRC). The primary endpoints were safety and ORR in the overall population and in patients whose disease progressed on prior anti-PD-1 therapy.

Results 50 patients were enrolled and received ≥1 dose of study treatment. At data cutoff (February 21, 2020), all had discontinued the study and study therapy. Median (range) age was 64.5 (28–88) years. Fourteen patients (28%) had stage III disease. Forty patients (80%) had received prior systemic treatment, 33 of whom had received prior anti-PD-1 therapy. The median number of cycles of ipilimumab was 4 (range, 1–4), and the number of intratumoral injections of V937 was 9 (range, 5–19). Among the 94% of patients who had ≥1 treatment-related AE, 14% had grade 3/4 treatment-related AEs, none of which were considered related to V937. The most common grade 3/4 treatment-related AEs were dehydration, diarrhea, and hepatotoxicity (4% each). No grade 5 treatment-related AEs occurred. The most common treatment-related AEs were pruritus (50%), fatigue (44%), diarrhea (32%), and nausea (22%). Efficacy outcomes for the overall population and by prior anti-PD-1 therapy use are presented in table 1. Tumor regression was observed in injected and noninjected lesions.

Conclusions V937 plus ipilimumab was safe and the toxicities were manageable and consistent with that anticipated for the individual treatment components. ORR was robust and significantly higher than anticipated with ipilimumab monotherapy, including in patients who had received prior anti-PD-1 therapy. Most responses were durable (>26 weeks), and responses seen in noninjected metastases provided evidence of probable systemic immune activation. The combination of V937 plus ipilimumab warrants further investigation in a larger trial in patients with advanced melanoma.

Acknowledgements Medical writing assistance was provided by Kathleen Estes, PhD, of ICON plc (North Wales, PA, USA), funded by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Trial Registration NCT02307149

REFERENCES

Ethics Approval An independent institutional review board or ethics committee approved the protocol at each study site, and the trial was conducted in compliance with Good Clinical Practice guidelines and the Declaration of Helsinki. All patients provided informed consent.

http://dx.doi.org/10.1136/jitc-2021-SITC2021.381