INITIAL RESULTS OF A PHASE 1 STUDY OF INTRATUMORAL ONCR-177, AN ONCOLYTIC HERPES-SIMPLEX VIRUS-1 EXPRESSING FIVE IMMUNOMODULATORY TRANSGENES, IN SUBJECTS WITH ADVANCED INJECTABLE TUMORS

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Background ONCR-177 is a recombinant oncolytic herpes simplex virus (oHSV) that retains $\gamma 34.5$ and is engineered to express five immunomodulatory transgenes (IL-12, FLT3LG ECD, CCL4 and anti-PD-1 and anti-CTLA-4 antibodies) for the intratumoral treatment of solid tumors. Attenuation by miRNA leads to selective replication in tumor cells, and mutations in UL37 act as an orthogonal safety strategy. Transgenes elicit potent systemic stimulation of anti-tumor immunity.¹ ONCR-177 is being tested in an open-label, multicenter, phase 1 study alone and in combination with pembrolizumab (NCT04348916), for surface lesion injection and intrahepatic injection. Here we present the surface lesion escalation data.

Methods The objectives were determination of safety and recommended phase 2 dose (RP2D) of ONCR-177 monotherapy in subjects with advanced and/or refractory injectable surface lesions using a modified toxicity probability interval-2 (mTPI-2) escalation design at four dose levels: (Cohort 1: 1×10^6 PFU in 1 mL, Cohort 2: 1×10^7 PFU in 1 mL, Cohort 3: 1×10^8 PFU in 1 mL and Cohort 4: 4×10^8 PFU in 4 mL). Subjects received ONCR-177 by intratumoral injection once every 2 weeks (up to 10 times) until disease progression or unacceptable toxicity. There was no inpatient dose escalation.

Results As of June 28, 2021, 14 subjects with injectable tumors were enrolled in the dose escalation phase (3 in cohort 1, 4 in cohort 2, 3 in cohort 3 and 4 in cohort 4). Enrolled tumor types included: melanoma (3), breast (3), anal squamous cell (1), lung (1), duodenal (1), basal cell (1), chondrosarcoma (1), thyroid (1), oropharyngeal (1) and papillary renal cell (1). Subject median age was 67 years. Median number of prior lines of therapy was 4 (range 2–11), including 11 of 14 subjects with prior immunotherapy. Nine subjects were HSV-1 seropositive at baseline, 4 were negative, one was unknown. Treatment-related Adverse Events were all Grade 1–2. Most commonly reported were: cytokine release syndrome (2 occurrences in Cohort 4), fatigue, nausea, chills, headache, decreased appetite, hypotension, and injection site pain. There were no dose-limiting toxicities. The RP2D was selected as 4×10^8 PFU in 4 mL every 2 weeks up to 10 doses. Clinical data, including safety, viral shedding and exploratory biomarker data including peripheral payloads, peripheral cytokines and immune infiltration and PD-L1 expression in the tumor microenvironment will be presented.

Conclusions ONCR-177 monotherapy in heavily pretreated subjects with advanced, injectable, solid tumors at the RP2D was safe and tolerable. Enrollment at the RP2D is underway in monotherapy expansion.

Trial Registration NCT04348916

REFERENCES

1. Haines BB, Denslow A, Grzesik P, Lee JS, Farkaly T, Hewett J, Wambua D, Kong L, Behera P, Jacques J, et al. ONCR-177, an Oncolytic HSV-1 Designed to Potently Activate Systemic Antitumor Immunity. *Cancer Immunol Res* 2021;**9**: 291–308

Ethics Approval This study was approved by the following institutional Ethics Boards:-University Health Network Research Ethics Board (ID Number: 20-5069)-Integreview IRB (ID Number RM 694) -WCG IRB (ID Number: 20200150)-Advarra (ID Number: 00000971)-Roswell Park IRB (ID Number: STUDY00001189/P-553719)-The Ohio State University Cancer IRB (ID Number: 2020C0139) -Dana Farber Cancer Institute IRB (ID Number 354020)All participants gave informed consent before taking part in this clinical trial.

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