705 **BIODISTRIBUTION AND SHEDDING ANALYSIS FOLLOWING RP1 ONCOLYTIC IMMUNOTHERAPY DOSING IN PATIENTS FROM THE IGNYTE CLINICAL TRIAL**

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Background RP1 is an HSV-1-based oncolytic immunotherapy expressing GM-CSF and the fusogenic GALV-GP-R- protein. We present biodistribution and shedding data from 87 patients enrolled in the phase 1 dose expansion (n=14) and phase 2 (n=73) cohorts from the ongoing IGNYTE clinical trial (NCT03767348).

Methods Patients received RP1 via intratumoral injection into superficial or deep, including visceral, lesions. Nivolumab was given at 240mg Q2W for 4 months, then 480mg Q4W for 20 months from the second dose of RP1. Blood, urine, oral mucosa/saliva, swab samples, and injection-site dressings were collected at various timepoints on the study. Samples were assessed for the presence of RP1 DNA by an RP1-specific qPCR assay; any swab samples positive for RP1 DNA were further tested for the presence of live virus (TCID50 assay).

Results RP1 DNA was detected in blood of 37/87 (42.5%) patients and 134/791 (16.9%) samples during treatment cycles 1–8. The highest levels of RP1 DNA were in blood 6h post-injection and diminished thereafter. RP1 DNA detection in urine was minimal, with 5/86 (5.8%) patients and 8/894 (0.9%) samples testing positive. Most patients (50/87 [57.5%]) and 260/914 (28.4%) samples had RP1 DNA on the surface of injected lesions sometime during treatment. The incidence of RP1 DNA from dressings was lower than that from the injection site (18/68 [26.5%] patients; 43/525 [8.2%] samples), indicating that dressings act as a barrier to RP1 DNA. We found no live virus, per TCID50, from RP1 DNA-positive injection sites and injection-site dressings. RP1 DNA was rarely detected in oral mucosa, and mostly at low levels (15/87 [17.2%] patients; 18/931 [1.9%] samples). During follow-ups, RP1 DNA was only detected on the surface of injected lesions, with 4/56 (7.1%) and 3/42 (7.1%) patients testing positive for RP1 DNA at 30 and 60 days, respectively, after the last RP1 injection. To date, no RP1 DNA has been detected in swab samples from lesions that may be of potentially herpetic origin. There have been no reports of herpetic infection in patients' caregivers or study staff.

Conclusions RP1 DNA was primarily detected on the surface of injected lesions, with dressings appearing to serve as a protective barrier against potential RP1 DNA dissemination. Importantly, there was no evidence of live virus following culture of qPCR-positive samples, and no reported cases of transmission or confirmed herpetic infection. These findings suggest that the risk of infection and transmission of RP1 to patients and caregivers is minimal.

Trial Registration Clinicaltrials.gov; NCT03767348

Ethics Approval The study was conducted in accordance with the ethical principles originating from the Declaration of Helsinki and was approved by the Institutional Review Board/Ethics Committee at each participating site. Written informed consent was obtained from all patients prior to the conduct of any study-related procedures.

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