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Proceedings Paper:

Milhem, M, VanderWalde, A, Bowles, T et al. (20 more authors) (2022) 611 Biodistribution and shedding analysis following treatment with RP1 oncolytic immunotherapy in the skin cancer patients from the IGENCYTE clinical trial. In: Journal for ImmunoTherapy of Cancer. SITC 37th Annual Meeting (SITC 2022), 08-12 Nov 2022, Boston, USA. BMJ , A643-A643.

<https://doi.org/10.1136/jitc-2022-sitc2022.0611>

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BIODISTRIBUTION AND SHEDDING ANALYSIS FOLLOWING TREATMENT WITH RP1 ONCOLYTIC IMMUNOTHERAPY IN THE SKIN CANCER PATIENTS FROM THE IGNYTE CLINICAL TRIAL

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Background RP1 is HSV1-based oncolytic immunotherapy expressing GM-CSF and the fusogenic GALV-GP R- protein. We present biodistribution and shedding data from the melanoma (n=30) and NMSC patients (n=31) of an ongoing clinical trial of RP1 + nivolumab (nivo).

Methods RP1 was injected into lesions (10⁶ PFU/mL, then 10⁷ PFU/mL Q2W) for up to 8 cycles. Injected lesions were covered with occlusive dressings. Blood, urine and swabs from dressing exteriors, tumor surface, oral mucosa, and areas of suspected herpetic origin were collected. RP1 DNA presence was assessed using qPCR and infectivity by TCID50.

Results RP1 DNA was detected in blood from 32.1% patients and 11.0% of blood samples. Highest levels were detected at 6 hrs. A sub-set of patients showed continued DNA until the next injection, with kinetics indicating RP1 replication. RP1 DNA was undetectable in all urine samples. Additionally, 50.9% of patients and 22.7% of swabs were positive from injection sites, with approximately 20% of patients positive at the next injection, also indicating RP1 replication. 20.5% of patients and 6.2% of samples tested positive for RP1 DNA on the dressing exterior between 24 hrs and the next dose, at low levels compared to injection sites. RP1 DNA was detected at low levels on the oral mucosa (15.1% of patients or 1.9% of samples). During the safety follow-up period, RP1 DNA was only detected on the injected lesion surface and not other sites, with 5.5% and 3.8% of patients positive at 30 and 60 days after the last RP1 dose respectively. Swabs positive for RP1 DNA were assessed for infectious virus by TCID50, and all were negative. No RP1 DNA was detected in swabs from potentially herpetic lesions, with no reports of herpetic infection in patient's caregivers.

Conclusions All positive samples showed only residual RP1 DNA rather than RP1 itself. RP1 DNA was detected on injected tumor surfaces at higher levels compared to other sites for up to 15 days (time of next dose), and then at diminishing levels up to 60 days from last dose. DNA levels at other sites were much lower and transient. In blood, RP1 DNA was detected in a quantity and with kinetics indicative of virus replication in a sub-set of patients, as expected based on the mechanism of action of RP1. Overall, the data suggest that the possibility of RP1 transmission to contacts is minimal, with no evidence of transmission reported.

Trial Registration NCT03767348

Ethics Approval The study was approved by the institutional review board or the local ethics committee at each participating site. Informed consent was obtained from patients before participating in the trial.

<http://dx.doi.org/10.1136/jitc-2022-SITC2022.0611>