TPS9607 Poster Session

A phase 1/2 study of vusolimogene oderparepvec (RP1) in primary melanoma (mel) to reduce the risk of sentinel lymph node (SLN) metastasis.

Urvashi Mitbander Joshi, Jabra Zarka, Hong Wang, Yan Zang, Amy Rose, John M. Kirkwood, Jason J. Luke, Hassane M. Zarour, Diwakar Davar, Yana G. Najjar; UPMC Hillman Cancer Center, Pittsburgh, PA; Mayo Clinic, Rochester, MN; University of Pittsburgh, Pittsburgh, PA

Background: The majority of 100,000 annual new U.S. cases of mel consist of localized early-stage disease that undergo wide local excision (WLE) +/- SLN biopsy (SLNB). The tumor draining lymph node is the initial site of immune response including formation of tumor mediated immune suppression and pre-metastatic niches. SLN positivity is a key prognostic factor in early stage mel. Thus, the SLN is a target for local immune intervention to boost the antitumor response. Vusolimogene oderparepvec (RP1) is an intratumorally administered oncolytic immunotherapy with unique potential for neo-adjuvant therapeutic application. RP1 is constructed from a high potency HSV1 strain (RH018A) modified to replicate selectively in tumors (deletion of neurovirulence factors ICP34.5 and ICP47). RP1 encodes GM-CSF and a fusogenic GALV-GP R- protein to maximize oncolytic potency and induce immunogenic cell death. Preclinical and clinical data demonstrate robust antitumor efficacy (including non-injected lesions) of RP1 alone and in combination with checkpoint inhibitors in advanced mel. This trial addresses a crucial gap in understanding the impact of RP1 on SLN dynamics and preventing disease recurrence in high-risk patients (pts). We hypothesize that in pts with high risk, clinically node negative mel (pT3b-T4b), RP1 will reduce rates of SLN positivity as compared to a historic control by favorably reshaping the immune landscape of the primary tumor, SLN, and the peripheral blood. **Methods:** This is an investigator-initiated, single arm phase 1/2 trial (NCT06216938) designed to assess efficacy and safety of neo-adjuvant RP1 in high-risk, clinically node-negative, non-uveal mel. Eligibility criteria: pT3b, T4a, or T4b non-uveal mel with visible residual tumor or positive biopsy margins, ECOG ≤1, and no prior oncolytic virus therapy. Pts receive 3 doses of neo-adjuvant RP1 (10e6 PFU day 1, 10e7 PFU on days 15 and 21), injected at the primary tumor site followed by standard WLE and SLNB within 35 days of dose 1. Biopsy of residual tumor or archival tumor tissue is obtained pre-RP1 and archival tissue from WLE and SLNB is obtained post-RP1. Blood samples are obtained with each RP1 dose and 3 months post-therapy. Pts are followed for 3 years. Primary endpoint: rate of SLN positivity in the overall cohort. Secondary endpoints: treatment related adverse events (per CTCAE), recurrence free survival, and overall survival. Exploratory endpoints: immunophenotype and microenvironment of the primary tumor, SLN and peripheral blood pre- and post-RP1 (via IHC, IF, and flow cytometry). The observed rate of SLN positivity will be compared to the predicted rate (Melanoma Institute of Australia Prediction Tool for SLN metastatic risk) with a one-sided, one-sample proportion test. Kaplan-Meier estimates will be provided for survival endpoints. The trial is active with 13 of 25 pts enrolled in January 2025. Clinical trial information: NCT06216938. Research Sponsor: Replimune.