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Measles oncolytic virus as an immunotherapy for recurrent/refractory pediatric medulloblastoma and atypical teratoid rhabdoid tumor: results from PNOC005

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Abstract

Purpose: Pediatric recurrent medulloblastoma (MB) and atypical teratoid rhabdoid tumor (ATRT) are largely incurable and warrant novel therapies. PNOC005 is a phase 1 clinical trial investigating the safety and tolerability of intratumoral or intrathecal administration of oncolytic measles virus (MV-NIS) in children and young adults with recurrent medulloblastoma (MB) or atypical teratoid/rhabdoid tumor (ATRT).

Experimental design: We investigated a) the safety of a measles virus variant, MV-NIS, in a pediatric phase 1 study and b) the mechanisms of MV-NIS and potential benefit of combination with immune checkpoint inhibition (ICI). Pediatric patients with recurrent MB or ATRT were treated with intratumoral injections for local recurrence or via lumbar puncture for disseminated recurrence. We evaluated local immune responses to MV-NIS with and without ICI via single-cell and bulk RNA sequencing in an intracranial, immunocompetent, syngeneic murine model.

Results: MV-NIS given intratumorally or via repeat intrathecal dosing was safe.MV-NIS prolonged survival in murine models but did not demonstrate additive benefit with ICI. No changes in tumor-infiltrating immune-cell composition or activation were observed in response to MV-NIS treatment; however, MV-NIS induced local expression of neutralizing antibodies, complement cascade, and phagocytosis-related genes.

Conclusion: This is the first trial investigating intratumoral as well as repeated intrathecal delivery of MV-NIS in children with MB and ATRT. We show that therapy is safe and well-tolerated with minimal adverse effects. Immune markers and biologic correlates preliminarily indicate anti-viral effects in tumors.