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Pediatric Brain Tumor Consortium phase 1 study of CD40 agonist sotigalimab in pediatric and young adult patients with recurrent CNS tumors and newly-diagnosed DIPG

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Abstract

Purpose: The PBTC-051 study is the first pediatric evaluation of a CD40 agonist and assessed the safety, pharmacokinetics, and preliminary efficacy of sotigalimab in children and young adults with recurrent or progressive malignant central nervous system (CNS) tumors (stratum 1) and post-radiation pre-progression diffuse intrinsic pontine glioma (DIPG) (stratum 2).

Patients and methods: This prospective phase 1 study conducted by the Pediatric Brain Tumor Consortium evaluated sotigalimab using a 3+3 design for dose escalation. Immune pharmacodynamics were assessed with RNA transcript analysis, T cell receptor sequencing, and cytokine profiling.

Results: 31 eligible patients were enrolled (stratum 1: 20, stratum 2: 11). The stratum 1 recommended phase 2 dose was 0.6 mg/kg every 3 weeks; the stratum 2 maximum tolerated dose was 0.3 mg/kg every 3 weeks. Five patients had dose-limiting toxicities. No patients had an objective response. For stratum 1, 6-month and 12-month progression-free survivals (PFS) were 13.3% (standard error [SE], 8.1%) and 6.7% (SE, 6.2%), respectively; for stratum 2, 6-month PFS and overall survival were 31.2% (SE, 14.8%) and 44.4% (SE, 16.6%), respectively. At all dose levels, the maximum serum concentration was reached at the end of infusion; no drug accumulation was detected. More than 40% of patients developed anti-drug antibodies. Signaling pathways associated with activated antigen presenting cells and T cells were enriched in patients with higher PFS, while increased loss of heterozygosity was noted in patients with lower PFS.

Conclusions: Sotigalimab was well-tolerated in pediatric patients with recurrent or progressive CNS tumors and post-radiation pre-progression DIPG.