

Lauren Harris MSA – Abstract

Phase 1 Trial of Selinexor in Pediatric Recurrent/Refractory Solid and CNS tumors (ADV1414): A Children's Oncology Group Phase 1 Consortium Trial

Adam L. Green, Charles G. Minard, Xiaowei Liu, Stephanie L. Safgren, Kerice Pinkney, Lauren Harris, Gabrielle Link, John DeSisto, Stephan Voss, Marvin D. Nelson, Joel M. Reid, Elizabeth Fox, Brenda J. Weigel, Julia Glade Bender

Background: Selinexor is a first-in-class, central nervous system (CNS)-penetrant, oral inhibitor of exportin 1 (XPO1), the main nuclear exporter of many key tumor suppressors. We report a phase 1 trial of selinexor in children and adolescents with recurrent CNS and solid tumors (NCT02323880).

Methods: A rolling-six design was used to evaluate the maximum tolerated dose (MTD) and first dose pharmacokinetics (PK) of selinexor administered once (QW, 35-45 mg/m²) or twice (BIW, 20-35 mg/m²) weekly during a 28-day cycle (Part A). Ten additional patients with high-grade glioma (HGG) were treated at the QW MTD (Part B).

Results: In Part A, 49 patients were enrolled. Continuous BIW dosing was limited by extended hematologic toxicity. The MTD on a BIW schedule for three weeks on/one-week off (BIW 3/1) was 20 mg/m²/dose. Dose-limiting toxicities (DLTs) on this schedule included fatigue, acute reversible neurologic changes, neutropenia, thrombocytopenia, and AST/ALT increase. On a continuous QW schedule, the MTD was 35 mg/m²/dose, DLTs included seizure and thrombocytopenia. In Part B (HGG expansion), there were no additional DLTs observed. Non-dose-limiting toxicity included lymphopenia, leukopenia, neutropenia, thrombocytopenia, anorexia, fatigue, hypophosphatemia, nausea, and vomiting. There were no objective responses. The median number of cycles received was 1 (range 1-9); Eight of 59 patients (13.5%) received 5-9 cycles, five of whom had HGG.

Conclusions: Selinexor-related toxicities were primarily hematologic and neurologic requiring dose or dose-frequency reduction. The MTD and recommended initial phase 2 dose of selinexor in children and adolescents with recurrent solid and CNS tumors is 35 mg/m²/dose QW.