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TAZNI: A PHASE I/II COMBINATION TRIAL OF TAZEMETOSTAT WITH NIVOLUMAB AND IPILIMUMAB FOR CHILDREN WITH INI1-NEGATIVE OR SMARCA4-DEFICIENT TUMORS (NCT03213665)

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BACKGROUND: Recent pediatric trials with EZH2 inhibitor tazemetostat monotherapy have demonstrated efficacy and disease stabilization in children with relapsed INI1/SMARCA4-deficient tumors; overall response rate (ORR) 14% in all patients (dose expansion cohort), and 24%, 33% and 22% response rates in ATRT, chordoma and epithelioid sarcoma, respectively (NCT02601937); and prolonged disease stabilization >6 months (NCT03213665). Leveraging the role of EZH2 in tumor immunity and increased immune signaling by tazemetostat, we hypothesized that combining this EZH2 inhibitor with checkpoint inhibitors may benefit pediatric patients with these rare cancers.

METHODS: “TAZNI” is a phase 1/2, multi-center trial of tazemetostat, nivolumab and ipilimumab for children with INI1- or SMARCA4-deficient tumors, administered either after standard upfront therapy or in the relapsed setting. All patients will receive standard nivolumab and ipilimumab doses/dosing schedule, with continuous tazemetostat dosing determined by disease strata: Stratum A- subjects with ATRT; Stratum B- all other (non-ATRT) tumors. Each stratum is subdivided by disease status: A1/B1- refractory disease; A2/B2- relapsed disease; and A3/B3- no evidence of disease. Part 1 of the study consists of two concurrent “rolling six” phase 1 studies to identify the recommended phase 2 dose (RP2D) by disease stratum. Two dose levels are planned, with one dose de-escalation. Part 2 will consist of two phase 2 studies to estimate...
Six patients (4M:2F, 5-12 years) in 2 cohorts received 22 SDT-treatments 30-days apart; the others receiving entire pons treatment. Single-treatment Each cohort involves three subjects: the first receiving half-pons treatment (PpIX), inducing tumor cell death and extending survival in glioma models. reveal that sonodynamic therapy (SDT) via MR-guided focused ultrasound...

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**BACKGROUND:** Children with DIPG have limited treatment options...