ABSTRACT

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Vorinostat and isotretinoin with chemotherapy in young children with embryonal brain tumors: A report from the Pediatric Brain Tumor Consortium (PBTC-026).

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BACKGROUND: Embryonal tumors of the CNS are the most common malignant tumors occurring in the first years of life. This study evaluated the feasibility and safety of incorporating novel non-cytotoxic therapy with vorinostat and isotretinoin to an intensive cytotoxic chemotherapy backbone.

METHODS: PBTC-026 was a prospective multi-institutional clinical trial for children < 48 months of age with newly diagnosed embryonal tumors of the CNS. Treatment included three 21-day cycles of induction therapy with vorinostat and isotretinoin, cisplatin, vincristine, cyclophosphamide, and etoposide; three 28-day cycles of consolidation therapy with carboplatin and thiotepa followed by stem cell rescue; and twelve 28-day cycles of maintenance therapy with vorinostat and isotretinoin. Patients with M0 medulloblastoma received focal radiation following consolidation therapy. Molecular classification was by DNA methylation.

RESULTS: Thirty-one patients with median age 26 months (range 6-46) received treatment on study; 19 (61%) were male. Diagnosis was medulloblastoma (MB) in 20 and supratentorial CNS embryonal tumor in 11. 24/31 patients completed induction therapy within a pre-specified feasibility window of 98 days. Five-year progression free (PFS) and overall survival (OS) for all 31 patients was 55 + 15 and 61 + 13, respectively. Five-year PFS was 42 + 13 for Group 3 MB (n=12); 80 + 25 for SHH MB (n=5); 33 + 19 for Embryonal Tumor with Multilayered Rosettes (ETMR, n=6).

CONCLUSION: It was safe and feasible to incorporate vorinostat and isotretinoin into an intensive chemotherapy regimen. Further study to define efficacy in this high-risk group of patients is warranted.

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