# PBTC-010 Abstract for Health Professionals

**Study Title:** A Phase II Study of Oxaliplatin in Children with Recurrent or Refractory Medulloblastoma, Supratentorial Primitive Neuroectodermal Tumors and Atypical Teratoid Rhabdoid Tumors

**Description:** This is an open-label, single-agent phase II study of oxaliplatin in pediatric patients with recurrent or refractory embryonal CNS tumors. Such patients will be stratified according to histology and prior recurrences. ***Stratum IA*** will include medulloblastoma patients with measurable disease after failure of initial therapy; ***Stratum IB*** will include recurrent or refractory medulloblastoma patients with only positive CSF cytology or with linear leptomeningeal disease; ***Stratum 1C*** will include medulloblastoma patients with measurable residual disease at second or later relapse; ***Stratum II*** will include patients with recurrent or refractory supratentorial primitive neuroectodermal tumor (S-PNET) including pineoblastomas, and ependymoblastomas; ***Stratum III*** will include patients with recurrent or refractory atypical teratoid rhabdoid tumors (ATRT). Oxaliplatin, 130 mg/m$^2$, will be administered intravenously, over 2 hours, every 21 days (one course) and may be continued for one year in the absence of disease progression or unacceptable toxicity.

## Objectives:

1) To estimate the objective response (CR plus PR) rate to oxaliplatin in patients with recurrent or refractory medulloblastoma at first progression.

2) To estimate the objective response (CR plus PR) rate to oxaliplatin in patients with recurrent or refractory medulloblastoma at second or later relapse.

3) To estimate the objective response rate to oxaliplatin in patients with recurrent or refractory supratentorial PNET and ATRT.

4) To test for functional mismatch repair (MMR) system in tumor samples and patients' peripheral white blood cells.

5) To evaluate the pharmacokinetics of oxaliplatin in the serum and CSF using a limited sampling strategy.

## Eligibility Criteria:

- Patients <= 21 years of age at the time of registration on the protocol
- Patients with histologically confirmed medulloblastoma, supratentorial PNET (including pineoblastoma, ependymoblastoma), or ATRT that is recurrent or refractory to therapy.
- Patients with measurable recurrent or refractory disease documented by radiographic or cytologic criteria. Patients with linear leptomeningeal disease or positive CSF cytology are also eligible.
- Karnofsky or Lansky performance status >= 50%
- Patients with adequate bone marrow, renal, hepatic, cardiac, pulmonary and CNS function.

## Rationale:

Oxaliplatin, trans-l-1,2-diaminocyclohexane (DACH) oxalatoplatinum, is a novel platinum agent, with similar potency to cisplatin[17]. Oxaliplatin has demonstrated efficacy in

preclinical and clinical studies against many tumors types, including those that are cisplatin-resistant[18-24]. Unlike cisplatin, oxaliplatin has caused little or no nephrotoxicity or ototoxicity in clinical trials. Oxaliplatin has demonstrated additive and/or synergistic cytotoxic activity in combination with many other chemotherapeutic agents, including CPT-11, carboplatin, cisplatin, cyclophosphamide and 5-FU.

Although significant progress has been made in the treatment of children with intracranial embryonal tumors such as medulloblastomas and PNETs, the prognosis for patients who have recurrent disease following radiotherapy is dismal[1-6]. Cisplatin has proven to be one of the most active agents against embryonal CNS tumors in newly diagnosed patients; however, the high incidence of ototoxicity as well as nephrotoxicity associated with cisplatin are of great concern since up to 50% of children with medulloblastoma treated with cisplatin as part of their primary therapy develop severe (grade 3 and 4) ototoxicity. In addition, approximately 20% develop severe nephrotoxicity. Thus, there is significant interest in new platinating agents with potentially equivalent activity and a more acceptable spectrum of toxicity, such as oxaliplatin, in this group of patients.

The objectives of this phase II study are to estimate the response rate and further assess the toxicity of oxaliplatin in patients with recurrent or refractory embryonal tumors.

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