

PHASE II PROTOCOLS

Protocol #98-C-0074: Pediatric Phase II Trial of Intravenous Cereport(®) (RMP-7 or Lobradimil) and Carboplatin in Childhood Brain Tumors

Cereport(®) is a synthetic bradykinin analog which specifically binds to the B₂ receptors expressed on the brain capillary endothelial cells and preferentially increases capillary permeability within the CNS Tumors. Carboplatin is an anticancer agent with preclinical antitumor activity against a variety of tumors. A pediatric phase II trial of the combination of Cereport(®) and carboplatin will be conducted to determine the objective response rate and assess the toxicities of the combination of Cereport(®) and carboplatin in children with refractory or recurrent brain tumors, stratified by histology.

Eligibility Criteria:

- Age ≤ 21 at time of initial diagnosis.
- Histologically confirmed high grade glioma (anaplastic astrocytoma or glioblastoma multiforme), low grade glioma, medulloblastoma/PNET, or ependymoma. Patients with radiographic evidence of brainstem tumor or optic glioma are also eligible but are not required to have histologic confirmation.
- Measurable Disease: must have measurable tumor by MRI that has not received radiation within 6 weeks prior to study entry. Must have evidence of recurrent or PD after front-line therapy as documented by an increase in tumor size or presence of new lesions on MRI
- Performance status: ECOG of 0, 1, or 2. Life expectancy of at least 8 weeks.
- Prior Therapy: Eligible at the time of first recurrence. Patients who did not receive radiation therapy as front-line therapy are eligible at second recurrence, if the first recurrence was treated with radiation alone. Patients who have tumors for which there is no standard effective chemotherapy may be treated without having received prior chemotherapy.
- Recovery from toxic effects of prior therapy: Must be off all myelosuppressive chemotherapy for 2 weeks prior to entry to protocol (a minimum of 4 weeks for prior nitrosureas unless the patient received stem cell/bone marrow rescue, then the treatment free interval will be 2 weeks). Patients who received G-CSF after the prior cycle of chemotherapy must be off G-CSF for at least 72 hours prior to starting Cereport(r) and carboplatin.
- Patients must not have received radiation therapy for at least 6 weeks prior to study entry.
- Patients who are on corticosteroids for management of tumor related edema are eligible
- Hematologic function: Must have absolute granulocyte count of ≥1,000/μL, hemoglobin ≥8 gm/dl (pts can be transfused to bring the hemoglobin above 8.0 gm/dl), platelet count ≥100,000/μL).
- Adequate liver function (bilirubin <1.5 X upper limit of normal and SGPT ≤2.5 X the upper limit of normal).
- Normal serum creatinine for age

Exclusion Criteria:

- Women of childbearing age who are pregnant or lactating.
- Prior treatment with Cereport(®), carboplatin or >1 prior chemotherapy regimen for the treatment of the brain tumor.
- Patients with significant systemic illness.
- Patients who have disease limited to the meninges and patients with metastases outside the CNS.
- A history of severe reaction to platinum-containing compounds.
- Use of vasodilating agents, ACE inhibitors, calcium channel blockers, β-blockers, within 24hrs prior to Cereport(®) infusion.

Pretreatment Evaluation:

- History and physical including height, weight, ideal body weight, BSA and neuro exam.
- Laboratory studies (see protocol) and Quality of Life Assessment.
- MRI within two weeks of the first administration of Cereport(r) and carboplatin. Patients with medulloblastoma should also have an MRI of the spine within 4 weeks of the start of therapy.
- GFR: ^{99m}Tc DTPA estimation of the glomerular filtration rate.
- Patients should bring to NIH summaries of previous treatment, most recent laboratory work, copies of most recent radiologic studies including 2 scans that document disease progression from last treatment, and the original pathology slides and report.

General Treatment Plan:

- A combination of Cereport(®) and carboplatin will be given for two consecutive days every 28 days for 12 Cycles. The carboplatin will be given as a fifteen minute infusion. The dose will be calculated using an adaptive formula applying the patient's glomerular filtration rate and a target AUC of 3.5. Cereport(®) will be given as a 10 minute infusion beginning 10 minutes after the start of the 15 minute carboplatin infusion. The Cereport(®) dose will be 600 nanograms/kg IDW (Ideal Body Weight)/day. B/P will be monitored q15min for one hour prior to and one hour after treatment.

Toxicity/Accrual:

- Brain Stem Glioma strata is closed. Open to all other strata (high/low grade glioma, medulloblastoma/PNET, ependymoma).
- Patients meeting the eligibility criteria can be referred to the Neuro-Oncology Branch, NCI (Dr. Kathy Warren at 301-402-6298) for evaluation and treatment on this trial. Select CCG Institutions are also participating in this trial.