

02-C-0193: A Phase II Study of Pegylated Interferon Alfa-2b (Peg-Intron®) in Children with Diffuse Pontine Gliomas

Interferon-alpha is a cytokine that has been studied in patients with gliomas and has demonstrated some activity in prior clinical trials. Recent in vitro data suggest that the most significant inhibition of tumor growth, tumor vascularization, and maximal inhibition of angiogenesis-regulating genes may be demonstrated when there is continuous low-dose exposure to interferon-alpha. PEG-Intron® is a covalent conjugate of recombinant interferon alfa-2b with monomethoxy-polyethylene glycol (PEG). Pegylation increases the biologic half-life of the compound, enabling it to be administered once weekly, and also reduces the peaks and troughs in blood levels. In this study, we plan to administer pegylated interferon alfa-2b (PEG-Intron®) subcutaneously once a week to pediatric patients with diffuse pontine gliomas who have completed radiation therapy. The endpoint of the trial will be 2-year survival compared to historical controls.

ELIGIBILITY CRITERIA:

Age: ≤21 years of age at the time of initial diagnosis.

Diagnosis: Histologic confirmation is not required for this study. Patients must have a diffuse pontine glioma as diagnosed by MRI, with the epicenter presumed to be in the pons, and the T-2 weighted sequence must reveal a diffuse signal abnormality involving at least 50% of the pons.

Prior therapy: The patient must have received adequate radiation therapy. Radiation must be completed between 2-10 weeks prior to the start of treatment with Peg-Intron®.

Performance Status: Patients should have an ECOG performance score of 0, 1, 2 or 3 (see below). Patients who are wheelchair bound because of paralysis should be considered “ambulatory” when they are up in their wheel chair.

ECOG Performance Status

Score	Clinical Status
0	Asymptomatic
1	Symptomatic, fully ambulatory
2	Symptomatic, in bed < 50% of the day
3	Symptomatic, in bed > 50% of the day but not bedridden
4	Bedridden

Hepatic Function: Patients must have adequate liver function, defined as total bilirubin ≤2.0x the upper limit of normal, direct bilirubin within normal limits, and SGPT ≤2.0 x the upper limit of normal.

Renal Function: Patients must have an age-adjusted normal serum creatinine (see Table below) OR a creatinine clearance ≥60 mL/min/1.73 m².

Age (Years)	Maximum Serum Creatinine (mg/dl)
< 5	0.8
5 ≤ age <10	1.0
10 ≤ age <15	1.2
≥15	1.5

Hematologic Function: Patients must have an absolute granulocyte count ≥1,000/mm³, a hemoglobin ≥ 8.0 gm/dl, and a platelet count ≥100,000/mm³ at study entry. Packed red blood cell and platelet transfusions are allowed to meet these criteria.

Steroids: Patients on steroids must be on a stable or decreasing dose of steroids for ≥1 week prior to study entry.

Informed Consent: All patients or their legal guardians (if the patient is <18 years of age) must sign an IRB-approved informed consent indicating their awareness of the investigational nature and the risks of this study. When appropriate, minor patients will be included in all discussions in order to obtain verbal assent.

Durable Power of Attorney (DPA): All patients ≥ 18 years of age will be offered the opportunity to assign DPA so that another person can make decisions about their medical care if they become incapacitated or cognitively impaired.

EXCLUSION CRITERIA:

- Patients with known or suspected neurofibromatosis-1
- Patients who have received prior chemotherapy, including radiosensitizers, or who are currently receiving other investigational chemotherapeutic agents
- Patients with a known hypersensitivity to interferon-alpha.
- Pregnant or breast-feeding females
- Patients with clinically significant unrelated systemic illness

PRETREATMENT EVALUATION: (within 72 hours prior to receiving study drugs unless otherwise stated)

- History and physical examination, including neurological exam and weight.
- Laboratory work to assess blood counts, organ function and metabolic status within 72 hours prior to enrollment
- MRI of brain must be performed at the NCI within 2 weeks prior to entering this study. (If MRI is contraindicated, patients may be imaged by CT.) $^1\text{H-MRSI}$ will also be done at this time if possible.
- Spine MRI: Patients with a history of known spinal disease will have baseline imaging of their spine within 2 weeks prior to entering study
- Quality of Life assessment: Questionnaires for patients 6-18 years of age and their parents at study entry
- Research Labs: serum and urine for bFGF and VEGF levels
- Neuropsychologic testing: To be performed within 1 week of study entry.

GENERAL TREATMENT PLAN:

Treatment with pegylated interferon alfa-2b (PEG-Intron \square) must begin within 72 hours of patient registration. Patients will be premedicated with acetaminophen 10-15 mg/kg (maximum 650 mg per dose) or ibuprofen 10 mg/kg within 1 hour of receiving PEG-Intron. The patients will continue on either acetaminophen or ibuprofen for up to 48 hours after PEG-Intron injection. Each cycle of therapy will consist of pegylated interferon alfa-2b (PEG-Intron \square) administered subcutaneously once weekly for 4 weeks. Each dose should be administered on the same day each week. There will be no breaks between cycles. Each dose is 0.3 \square g/kg subcutaneously. Nursing staff will instruct the patients or their caregivers regarding sites of injection and injection technique.

ACCRUAL:

This study is open to accrual. 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.