IARB1:A Pilot Study of Intra-Ophthalmic Artery Topotecan Infusion for the Treatment of Retinoblastoma

Purpose

This study will test if giving Topotecan directly into the blood vessel of the eye will improve the treatment of retinoblastoma. This method is referred to as "selective intra-ophthalmic artery chemotherapy" (SIOAC).

Study Type: Interventional

Study Design: Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

GOALS

The goals of this study are:

- To find out if Topotecan is an effective treatment for retinoblastoma when delivered directly to the ophthalmic artery (SIOAC delivery)
- To find out what kind of effects (good and bad) can be expected when Topotecan is given by SIOAC
- To assess visual pathway function before and after the study therapy
- To learn more about the pharmacology (how your body handles the drug) of Topotecan when delivered directly to the ophthalmic artery

ELIGIBILITY

Up to 15 Years

INCLUSION CRITERIA

1. Age: 15 years of age or younger
2. Diagnosis: Patients with untreated Group C/D/E unilateral Retinoblastoma at presentation without an indication for immediate enucleation (neovascular glaucoma or orbital pain) (Stratum A), or patients with a history of bilateral retinoblastoma and recurrent and/or refractory intraocular retinoblastoma where chemotherapy, external beam radiation and/or enucleation remain the only known option for disease control (Stratum B).
3. Therapeutic Options: Chemotherapy, External Beam Radiation therapy and/or Enucleation
4. Lansky 50 for patients ≤ 10 years of age; Karnofsky ≥ 50 for patients > 10 years of age. Patients who are unable to walk because of paralysis, but who are up in a wheelchair, will be considered ambulatory for the purpose of assessing the performance score.
5. Prior Therapy: Stratum A: No prior therapy is allowed. Stratum B: Patients must have local relapsed/refractory disease after receiving standard upfront therapy involving at least one chemotherapeutic regimen. There is no limit to prior chemotherapeutic regimens permitted. Prior radiation therapy is permitted.
6. Patients must have recovered from the acute toxic effects of all prior chemotherapy, immunotherapy, or radiotherapy prior to entering this study, as described below:
    - Myelosuppressive chemotherapy: patients must not have received myelosuppressive chemotherapy within 3 weeks of study enrollment.
    - Biologic therapies: Patients must not have received biologic anti-cancer agents within one week of study enrollment.
    - Radiation therapy: Four weeks must have elapsed since external beam radiation therapy, if given.
7. Adequate Bone Marrow Function Defined as:

- Peripheral absolute neutrophil count (ANC) greater than or equal to 750/uL
- Platelet count greater than or equal to 75,000/uL (transfusion independent, defined as not receiving platelet transfusions within a 7-day period prior to enrollment)
- Hemoglobin greater than or equal to 8.0 gm/dL (may receive RBC transfusions)

8. Adequate Renal Function Defined as:

   -Maximum serum creatinine based on age as follows: 1 to < 2 years-08 mg/dL; 6 to < 10 years-1 mg/dL; 10 to < 13 years-1.2 mg/dL; 13 to 15 years-1.5 mg/dL for boys and 1.4 mg/dL for girls.

   OR

   Creatinine clearance or radioisotope GFR greater than or equal to 70ml/min/1.73 m^2

9. Adequate Liver Function Defined As:
   - Bilirubin (sum of conjugated + unconjugated) less than or equal to 1.5 x upper limit of normal (ULN) for age
   - SGPT (ALT) less than or equal to 5 x upper limit of normal (ULN) for age
   - Serum albumin greater than or equal to 2 g/dL
10. Informed Consent: All patients and/or their parents or legal guardians must sign a written informed consent. Assent, when appropriate, will be obtained according to institutional guidelines.
11. Target eye ophthalmic artery diameter > 0.7 mm based on pre-operative imaging
12. Patients of child-bearing potential must have a negative pregnancy test and agree to use an effective birth control method (abstinence is an acceptable form of birth control).

Exclusion Criteria:

1. Extra-ocular retinoblastoma or retinoblastoma involving the anterior chamber
2. Retinoblastoma that could otherwise be treated with laser therapy, cryotherapy, or plaque therapy only
3. Structural brain abnormality
4. Uncontrolled infection, defined as requiring intravenous antibiotics at the time of enrollment
5. Concomitant Medications
   - Growth factors that support platelet or white cell number or function must not have been administered within 3 days prior to enrollment.
   - Patients who are currently receiving non-FDA approved drugs, or who have received a non-FDA approved drug within 7 days prior to enrollment, are ineligible.
   - Patients who are currently receiving other anti-cancer agents are ineligible.
6. Patients who in the opinion of the investigator may not be able to comply with the safety monitoring requirements of the study are not eligible.

Who should I contact for more information?

For more information contact:

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