

## **01-C-0030: Short-Course EPOCH-Rituximab for Untreated CD-20+ HIV-Associated Lymphomas**

This is a study to investigate short course chemotherapy to patients with HIV-associated non-Hodgkin's lymphoma (HIV-NHL). A recent NCI trial demonstrated efficacy of the infusional chemotherapy regimen, EPOCH (etoposide, vincristine, doxorubicin, prednisone, cytoxan) in adults with HIV-associated non-Hodgkin's lymphoma. In this follow-up trial, children and adults with CD20+ HIV-associated non-Hodgkin's lymphoma will be treated with a combination of EPOCH and rituximab. Therapy will be administered every three weeks for one cycle beyond complete resolution of all detectable tumors for a minimum of three and maximum of six cycles. This study will investigate if treatment can be reduced from a standard of 6 cycles to one cycle beyond complete remission with 6 total allowable cycles. Anti-HIV therapy will be suspended prior to initiation of the chemotherapy and optimum therapy (HAART) will be reinitiated after all the cycles have been administered. The primary objective of the study is to assess the progression free survival rate at one year after short-course EPOCH-R. The secondary objectives are to assess toxicity; to assess response rate, and response duration; to assess the utility of PET scans to predict freedom from relapse; to assess effects on CD4 cell depletion and recovery; and to assess response to antiretroviral therapy following treatment with EPOCH-R for patients with HIV-associated non-Hodgkin's lymphoma. To study the effects of treatment approach on parameters of HIV disease, measurements of CD4 cells and viral loads will be made at baseline and at the completion of therapy, and then for 2 years following chemotherapy.

### **Eligibility Criteria**

#### **Inclusion Criteria**

- Aggressive CD20 positive NHL.
  - HIV+ serology.
  - All stages (I-IV) of disease.
  - ECOG Performance status 0-4
  - NHL previously untreated with cytotoxic chemotherapy.
  - Age  $\geq$  4 years
  - Laboratory tests (unless impairment due to respective organ involvement by tumor):
  - Creatinine  $\leq$  1.5 mg/dl or creatinine clearance  $\geq$  50 ml/min
- Pediatric patients: Age-adjusted normal serum creatinine according to the following table or a creatinine clearance  $>$  60 ml/min/1.73 m<sup>2</sup>.

Age (years)	Maximum serum creatinine (mg/dl)
$\leq$ 5	0.8
$>$ 5, $\leq$ 10	1.0
$>$ 10, $\leq$ 15	1.2
$>$ 15	1.5

- Bilirubin < 2.0 mg/dl, or total bilirubin ≤ 4.5 mg/dl with direct fraction ≤ 0.3 mg/dl in patients for whom these abnormalities are felt to be due to protease inhibitor therapy
- AST and ALT ≤ 3x ULN (AST and ALT ≤ 6x ULN for patients on hyperalimentation for whom these abnormalities are felt to be due to the hyperalimentation)
- ANC ≥ 1000/mm<sup>3</sup>
- Platelet ≥ 75,000/mm<sup>3</sup> (unless impairment due to ITP)
- Ability of patient or parent/guardian to provide informed consent.

### **Exclusion Criteria**

- Previous rituximab
- Pregnancy or nursing.
- Current clinical heart failure or symptomatic ischemic heart disease.
- Serious underlying medical condition or infection other than HIV that would contraindicate EPOCH-R.
- Primary CNS lymphoma.
- Adolescents who do not freely assent to treatment.

### **General Treatment Plan:**

**Initial evaluation:** Patient will be screened for eligibility.

**Lymphoma Treatment:** 3-6 cycles of EPOCH-R chemotherapy [Etoposide/Doxorubicin/Vincristine continuous IV infusion on days 1 to 4, Prednisone days 1 to 5, Cyclophosphamide day 5, and Rituximab days 1 and 5] followed by Filgrastim daily from day 6 until neutrophil recovery.

**CNS Prophylaxis:** All patients will receive CNS prophylaxis with intrathecal chemotherapy.

**Antiretroviral therapy:** Antiretrovirals will be discontinued prior to starting chemotherapy and will resume after the final cycle of chemotherapy

**Accrual:** Open to accrual. Patients can be referred to the NIH, NCI, and Pediatric Oncology Branch for evaluation and treatment.