

## **C50303 – Phase III Randomized Study of R-CHOP versus Dose-Adjusted EPOCH-R with Molecular Profiling in Untreated De Novo Diffuse Large B-Cell Lymphomas**

**Primary Objective:** To compare the event-free survival of R-CHOP versus DA-EPOCH-R chemotherapy in untreated CD20+ diffuse large B-cell lymphomas.

### **Eligibility Criteria:**

- Histologically documented de novo CD20+ DLBCL with stage II, III or IV disease. Stage I primary mediastinal (thymic) DLBCL is also eligible. Patients with an underlying low-grade lymphoma, such as a transformed lymphoma or low-grade lymphoma in the bone marrow, are not eligible. Diagnosis should be based on an adequate tissue sample, including open biopsy or core needle biopsy. Needle aspiration for primary diagnosis is unacceptable. Patients must have one of the following WHO [21] classification subtypes:
  - Diffuse large B-cell lymphoma (includes morphological variants: centroblastic; immunoblastic; T-cell/histiocyte rich; and anaplastic).
  - Mediastinal (thymic) large B-cell lymphoma
  - Intravascular large B-cell lymphoma
  - Note: Failure to submit pathology slides within 60 days of patient registration will be considered a major protocol violation (see Section 5.3)

Fresh (frozen) tumor biopsy must be available or attempted (see repeat tissue biopsy guidance below and Section 5.4). A frozen tumor biopsy equivalent to a minimum of four at least 16 gauge needle cores is an important component of this study. Patient without adequate frozen material should have a biopsy performed to obtain material. If a biopsy is performed and does not yield adequate material, the patient is still eligible for the study. If a biopsy cannot be done safely, the patient may still be eligible for the study if permission is granted in writing (e-mail) by the study Chairs (Drs. Wilson or Zelenetz) or their designees.

Drs. Wilson or Zelenetz may be consulted to discuss situations involving invasive biopsy procedures that may pose an increased risk to the patient.

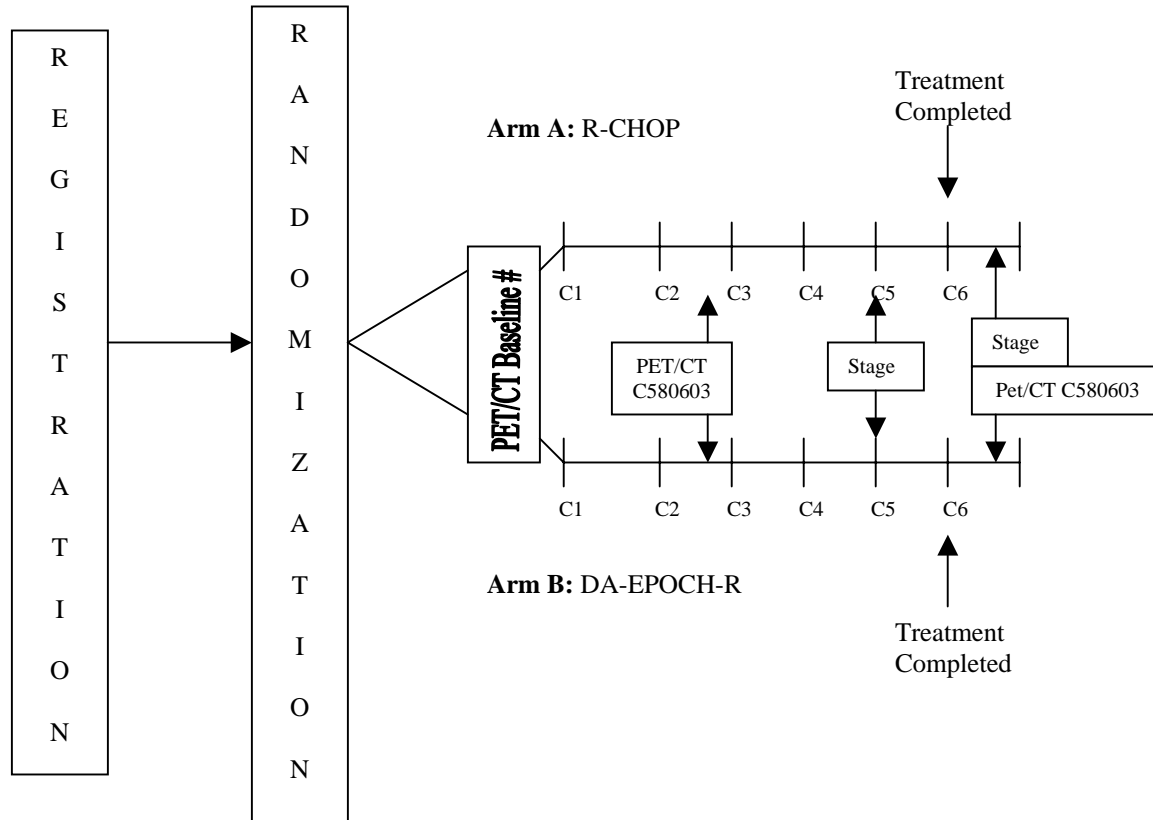
NOTE: This study does not allow concurrent radiation unless a patient has a documented CNS treatment failure with no systemic failure. Please do not enroll a patient you might wish to radiate.

- No prior cytotoxic chemotherapy or rituximab. Patients may be entered if they have received prior limited field radiation therapy or a short course of glucocorticoids (< 10 days) for an urgent local disease complication at diagnosis (e.g. cord compression, SVC syndrome). Patients who have received chemotherapy for prior malignancies are not eligible.
- Age  $\geq$  18 years.
- ECOG performance Status 0-2.
- No active ischemic heart disease or congestive heart failure. If there is suspicion of cardiac disease, a cardiac ejection fraction must show LVEF > 45%, but the study is not required.
- No known lymphomatous involvement of the CNS. A lumbar puncture prior to study is not required in the absence of neurological symptoms.
  - No known HIV disease. Patients with a history of intravenous drug abuse or any other behavior associated with an increased risk of HIV infection should be tested for exposure to the HIV virus. The mechanism of disease in patients with HIV may be different from de novo diffuse large B cell lymphoma. Additionally, the immunocompromised state of patients with HIV infection may result in more extensive dose reductions than intended for the intensive therapeutic regimens used in this study. Therefore, patients who test positive or who are known to be infected are not eligible. An HIV test is not required for entry on protocol, but is required if the patient is perceived to be at risk.
- Non pregnant and non-nursing. Treatment would expose an unborn child to significant risks. Women and men of reproductive potential should agree to use an effective form of contraception.
- Patients with active medical processes (e.g., uncontrolled bacterial or viral infection, bleeding) not related to their lymphoma should be excluded.
- Required Initial Laboratory Values\*:

ANC	$\geq$ 1000/ $\mu$ L
Platelets	$\geq$ 100,000/ $\mu$ L
Creatinine	$\leq$ 1.5 mg/dL or creatinine clearance $\geq$ 50 cc/min.
Total Bilirubin	$\leq$ 2 mg/dL**

  - \* Unless attributable to non-Hodgkin lymphoma
  - \*\* Unless a history of Gilbert's Disease

SCHEMA\*:



# Baseline PET/CT Chest/Abd/Pelvis  
CALGB 580603

C = Cycle = 21 days

