Protocol Title: A Randomized Double-Blind Phase III Study of Ibrutinib During and Following Autologous Stem Cell Transplantation Versus Placebo in Patients With Relapsed or Refractory Diffuse Large B-Cell Lymphoma of the Activated B-Cell Subtype

Target Population: Relapsed or Refractory Diffuse Large B-Cell Lymphoma of the Activated B-Cell Subtype

Summary: This randomized phase III trial studies ibrutinib to see how well it works compared to placebo when given before and after stem cell transplant in treating patients with diffuse large B-cell lymphoma that has returned after a period of improvement (relapsed) or does not respond to treatment (refractory).

Key Inclusion Criteria:
- Diagnosis of diffuse large B-cell lymphoma, high grade B-cell lymphoma not otherwise specified, or B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma.
- Determination of activated B-cell-like (ABC) subtype by pre-registration central review.
- ECOG Performance Score of ≤ 2.
- Patient must be deemed eligible to proceed with high-dose chemotherapy and autologous stem cell transplantation by local transplant center.
- New York Heart Association class I or less.
- Patient must have progressed or be refractory to prior anthracycline-containing chemotherapy.
- No more than 3 prior regimens for large cell component (e.g. one induction and two salvage therapies); monoclonal antibody alone or involved field/involved site radiotherapy do not count as lines of therapy.
- Prior use of ibrutinib is allowed unless patient has had disease progression while receiving ibrutinib.
- Patient must have chemosensitive disease as defined by at least a partial response to salvage therapy at their latest assessment.
- No major surgery ≤ 7 days prior to registration and no minor surgery ≤ 3 days prior to registration (with the exception of intravenous access placement, e.g. Hickman or peripherally inserted central catheter [PICC]).
- Not pregnant and not nursing; for women of childbearing potential only, a negative serum pregnancy test must be obtained within 14 days prior to registration.
- Patients should not require chronic use of strong CYP3A inhibitors or strong CYP3A inducers.
- Patients should not require concurrent therapeutic doses of steroids.
- HIV infected patients are eligible provided they meet specific criteria and also meet all other eligibility criteria.

Key Exclusion Criteria:
- Active CNS or meningeal involvement by lymphoma.
- Evidence of myelodysplasia or cytogenetic abnormality indicative of myelodysplasia on any bone marrow biopsy prior to initiation of therapy.
- A known bleeding diathesis.
- Requirement for warfarin or similar vitamin K antagonists.
- History of stroke or intracranial hemorrhage ≤ 6 months before treatment.
- Currently active, clinically significant hepatic impairment.
- History of allergic reactions attributed to compounds of similar chemical or biologic composition to ibrutinib or other agents used in study.
- Serologic status reflecting active Hepatitis B or C infection.

Contacts:
- Principal Investigator: Andrew Dalovisio, MD
- Research Nurses (RN): Elise Curry (elisemarie.curry@ochsner.org, ext. 28084)
  Stephanie S Green (stephanie.green2@ochsner.org, ext. 23918)
For additional information: https://clinicaltrials.gov/ct2/show/NCT02443077