NCI National Clinical Trials Network

EA4231

ECOG-ACRIN cancer research group

For Patients with Aggressive B-Cell Lymphoma

Please Enroll Your Eligible Patients!

EA4231 Available Through ECOG-ACRIN Cancer Research Group

A Phase II Study of Venetoclax, Ibrutinib, Prednisone, Obinutuzumab, and Revlimid (ViPOR) in Relapsed or Refractory CD10-Negative Diffuse-Large B-Cell Lymphoma (DLBCL) and High-Grade B-Cell Lymphoma with MYC and BCL2 rearrangements (HGBCL-DH-BCL2)

Patient Population

See protocol Section 3 for complete eligibility criteria

- Age ≥ 18, ECOG PS 0-2, with adequate lab values ≤ 7 days prior to registration
- Must have measurable disease, per Section 6.1
- Must have histologically or cytologically confirmed aggressive B-cell lymphoma as follows (see protocol for details):
  - ◊ CD10-negative DLBCL *or*
  - ◊ CD10-positive or negative HGBCL with MYC and BCL2 rearrangements (with or without BCL6 rearrangement)
- Must have relapsed and/or refractory disease after ≥ 1 prior anthracycline and anti-CD20 antibody-containing regimen
- Must not have confirmed/suspected primary:
  - ◊ Mediastinal large B-cell lymphoma
  - ◊ DLBCL of the CNS
- Patients with history of secondary CNS lymphoma are eligible if follow-up brain imaging after CNS-directed therapy shows no evidence of progression
- Must not have taken or require warfarin or other strong CYP3A inhibitors or inducers within 7 days prior to registration
- Must not have evidence of an active infection at the time of registration
- Must not have received current or prior anti-cancer treatment per protocol criterion 3.1.21
- Patients with known history/current symptoms of cardiac disease, or history of treatment with cardiotoxic agents should be NYHA class 2B or better
- Must have adequate formalin fixed paraffin embedded (FFPE) tumor tissue specimen from the initial diagnostic biopsy or on-study repeat tumor tissue biopsy for molecular analysis, per protocol criterion 3.1.23

Treatment Plan

See protocol Section 5 for complete treatment details

At the time of registration, sites will be asked to identify which of the following cohorts the patient belongs:

- Cohort 1: Relapsed/refractory CD10-negative diffuse-large B-cell lymphoma after 1 prior treatment regimen) [80 patients]
- Cohort 2: Relapsed/refractory high-grade B-cell lymphoma with MYC and BCL2 rearrangements after 1 prior treatment regimen [40 patients]

Both cohorts will receive **Arm A (ViPOR) treatment** (1 cycle = 21 days, maximum of 6 cycles):

- Venetoclax 800 mg PO QD on Days 2-14
- Ibrutinib 560 mg PO QD on Days 1-14
- Prednisone 100 mg PO QD on Days 1-7
- Obinutuzumab 1000 mg IV Days 1 and 2
- Lenalidomide 15 mg PO QD on Days 1-14
- G-CSF (preferred agent/dose): Pegfilgrastim 6 mg SQ on Day 8 (filgrastim or equivalent biosimilar are allowed for neutropenia prophylaxis if pegfilgrastim or equivalent biosimilar unavailable)

Notes:

- *Treatment should be given primarily on an outpatient basis; however, inpatient treatment should be initiated in patients at high-risk of tumor lysis syndrome (TLS) (or other reasons documented in the medical record) as defined per protocol*
- *Patients with CrCl 30–60 mL/min at the time of registration will initiate therapy with Lenalidomide 10 mg PO QD on Days 1-14*
- *Supplementation of long-acting G-CSF with short-acting G-CSF is permitted for severe or prolonged neutropenia*
- *Patients will be restaged after cycles 2 and 6, and assessed by clinical evaluation and imaging to monitor status every 6 months during post-treatment years 1 and 2*

Study Chair:
Christopher Melani, MD

EA Study Co-Chair:
Craig Portell, MD

NCI Study Co-Chair:
Wyndham H. Wilson, MD, PhD

Patient Enrollment (Oncology Patient Enrollment Network [OPEN])

https://open.ctsu.org/open 1-888-823-5923

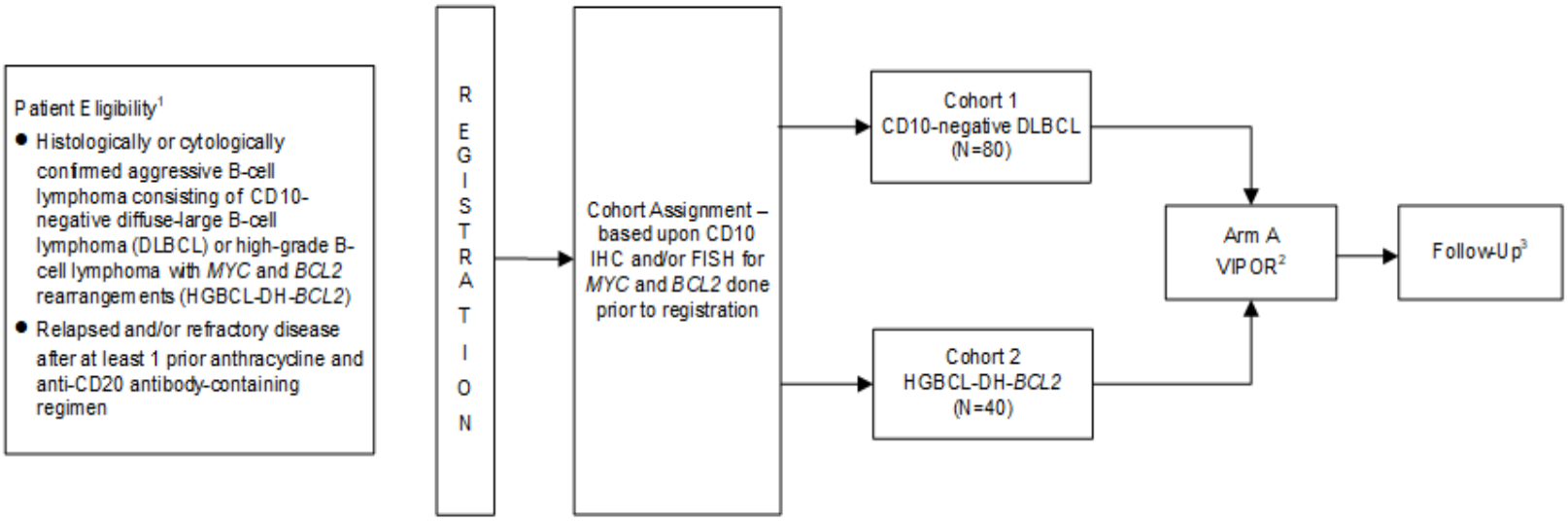
Protocol Information (ECOG-ACRIN Operations – Boston)

http://ecog-acrin.org (Member Login) 1-857-504-2900

v.05/20/25

EA4231

Schema



N=120

1. Patients will undergo testing for CD10 immunohistochemistry (IHC) and/or FISH for *MYC* and *BCL2* rearrangements prior to registration in order to confirm eligibility and be assigned to one of the following two patient cohorts:
   - CD10-negative DLBCL
   - HGBCL-DH-*BCL2*
2. Patients in both Cohort 1 and 2 will receive the same treatment as described in Section 5.1. Please see Section 5.1 for detailed dosing information.
3. Patients will undergo surveillance followup for 5 years after end of treatment. See study parameters Section 7.1.