Diffuse Large B-Cell Lymphoma Clinical Trials

The following clinical trials are currently open and accruing for patients with Large B-Cell Lymphoma.

Contact Jillian Foreman (Clinical Research Manager), jillianm_foreman@dfci.harvard.edu, 617-582-8713 to discuss a patient.

FRONTLINE TRIALS – NEWLY-DIAGNOSED PATIENTS

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TRIALS FOR RELAPSED/REFRACTORY PATIENTS

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<td>A phase 1/2a, open-label, dose-escalation, dose-expansion, parallel assignment study to evaluate the safety and clinical activity of PBCAR0191 in patients with relapsed/refractory (r/r) non-Hodgkin lymphoma (NHL) and r/r B-cell acute lymphoblastic leukemia (B-ALL)</td>
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See the following pages for more information about these trials.

These trials are offered through Dana-Farber/Harvard Cancer Center, an NCI-designated Comprehensive Cancer Center.
TRIALS FOR FRONTLINE TRIALS – NEWLY-DIAGNOSED PATIENTS

18-568: A phase 1b/2, open-label, multicenter, randomized, controlled study investigating the safety, tolerability, pharmacokinetics, and efficacy of mosunetuzumab (BTCT4465A) in combination with CHOP or CHP-polatuzumab vedotin in patients with B-cell non-Hodgkin lymphoma

Rationale: This is a phase 1b/2, multicenter study that combines the new CD3-CD20 bispecific antibody mosunetuzumab in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (M-CHOP), and in combination with cyclophosphamide, doxorubicin, and prednisone (CHP) plus polatuzumab vedotin (CHP-pola) in patients with B-cell Non-Hodgkin lymphoma. Mosu has good activity as a single-agent in R/R DLBCL (OR 34% CR 19% median duration of CR not reached after ~1y). The first part of the phase 1b portion of the study has been completed and confirmed the safety of MCHOP. The next part in 1b will be to test the safety of MCHP-Pola in patients with relapsed/refractory disease, who have received < 200mg/m2 adriamycin in the past (so most likely patients with R/R indolent B-NHL who were not previously treated with RCHOP). Group A provided the recommended phase 2 dose (RP2D) of mosunetuzumab in combination with CHOP, which was 30 mg. The phase 2 cohort, which is now actively accruing, evaluates M-CHOP in patients with previously untreated diffuse large B-cell lymphoma (DLBCL), where the Mosu dose level is equal to RP2D. If safety among a run-in cohort is acceptable, M-CHOP (or later possibly M-CHP-Pola) will then be compared with R-CHP-Pola in a randomized phase 2 portion.

Presently, we are prioritizing this study for patients with untreated DLBCL, IPI 2-5. This provides patients the access to mosu in combination with CHOP chemotherapy.

Key Eligibility Criteria for Phase 2 (current phase):

Inclusion:
- Patients must be 18 years old with a previously untreated, histologically confirmed DLBCL (WHO 2016 classification)
- Patients with a diagnosis of high-grade B-cell lymphoma (HGBL) with rearrangements of MYC and BCL2 and/or BCL6 or HGBL, not otherwise specified, are eligible
- At least one bi-dimensionally measurable node lesion (>1.5 cm in longest dimension), or one bi-dimensionally measurable extranodal lesion (>1.0 cm in longest diameter)
- Confirmed availability of archival or freshly collected tumor tissue before study enrollment
- ECOG of 0-2
- IPI score of 2-5
- Adequate hematologic, hepatic and renal function

Exclusion:
- Patient who have had prior therapy for B-cell NHL are not eligible
- Patients with transformed lymphoma are not eligible
- Patients with a diagnosis of primary mediastinal DLBCL are not eligible
- No prior treatment with mosunetuzumab
- No prior allogeneic stem cell transplant
- No past history of CNS lymphoma or disease

Diffuse Large B-Cell Lymphoma Clinical Trials, Dana-Farber/Brigham and Women’s Cancer Center. These trials are conducted through Dana-Farber/Harvard Cancer Center, an NCI-designated Comprehensive Cancer Center.
To discuss a patient, email jillianm_foreman@dfci.harvard.edu

**Treatment Schedule:** Patients receive 6 cycles of MCHOP (in current cohort). There are 2 mandatory hospitalizations for cycle 1 and cycle 2, and frequent visits during cycle 1. Thereafter all drugs (except prednisone) are given only on day 1 of each cycle.

**Principal Investigator:** Philippe Armand, MD, PhD

**Slots Available at Last Update:** Please email us for the latest slot availability

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TRIALS FOR PATIENTS WITH RELAPSED/REFRACTORY DISEASE

17-313: A phase 1b/2 trial of Hu5F9-G4 in combination with rituximab in patients with relapsed/refractory B-cell non-Hodgkin lymphoma. Hu5F9-G4 is a monoclonal antibody which is designed to block a protein called CD47, which is widely expressed on human cancer cells.

Rationale: This is a phase 1b/2 for relapsed/refractory DLBCL and indolent lymphomas (marginal zone and follicular lymphoma). This study uses rituximab in combination with Hu5F9-G4 an anti–CD47 drug. We are currently open with the combination arm with chemotherapy (RGemOx) + HuF59-G4 arm as well.

Key Eligibility Criteria:
- Patients must have had their last treatment either 2 weeks prior, or 5 half-lives whichever is longer in order to start treatment
- Patients with DLBCL must be Rituximab refractory and ineligible to receive CAR-T cell therapy based upon the treating physician’s clinical judgement
- Patients cannot have received CAR-T cells or an allogenic stem cell transplant
- Patients cannot be transfusion dependent (receiving more than 2 units of RBC transfusions during the 4-week period prior to screening)

Treatment Schedule:
Patients will be required to have intensive treatment schedules during the first two months of treatment. The first cycle of treatment includes 8 visit dates. They will be coming in for treatment visits on 7 of those 8 dates this includes infusion of rituximab, Hu5F9-G4, gemcitabine and oxaliplatin. After the completion of the first cycle, the number of visits will decrease to 5 visits during cycle 2 and then three visits per month for 4 cycles. After the completion of cycle 4 patients will then transfer over to only receiving rituximab + Hu5F9-G4. Rituximab will be administered every other cycle from cycle 5 on. Also, patients will be receiving their first scan at the beginning of cycle 3 and their further treatment will be based upon that. As of note patients must also be willing to have the optional tumor biopsy done at pre-treatment and while on treatment.

Principal Investigator: Ann LaCasce, MD, MMSc

Slots Available at Last Update: Slots will vary. Please email us for the latest slot availability.

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17-448: A phase 2 study of pembrolizumab in patients with histiocyte/dendritic cell neoplasms and biologically selected subtypes of relapsed/refractory aggressive lymphomas

Rationale: The primary goal of this investigator-initiated study is to examine the efficacy of pembrolizumab in patients with histiocyte/dendritic cell neoplasms or relapsed/refractory biologically selected subtypes of aggressive lymphoma. Pembrolizumab is a potent and highly selective humanized monoclonal antibody designed to directly block the interaction between PD-1 and its ligands. Patients will receive pembrolizumab 200 mg IV every 3 weeks for up to 35 cycles. Treatment past disease progression is allowed at the discretion of the overall PI. Patients must have a confirmed diagnosis of histiocyte/dendritic cell neoplasm or R/R aggressive lymphoma with at least one of the following features: EBV+ DLBCL, DLBCL leg type, plasmablastic lymphoma, T-cell/histiocyte rich DLBCL, EBV+ T cell lymphoma of any histology, histiocytic sarcoma, follicular dendritic cell sarcoma, or interdigitating dendritic cell sarcoma. Sarcoma patients must have disease that is not amenable to surgical resection or radiation while lymphoma patients must have had at least one prior systemic chemotherapy and must have relapsed after ASCT (or been ineligible for or declined ASCT). Exclusion criteria includes previous treatment with a PD-1, PD-L1, or PD-L2 inhibitor, prior anti-cancer monoclonal antibody w/in 4 weeks prior to C1D1, and chemotherapy/targeted small molecule therapy/radiotherapy w/in 2 weeks prior to C1D1.

Key Eligibility Criteria:
- At least 18 years of age
- ECOG performance status of 0 or 1
- Normal organ and marrow function (ANC at least 500/mcL, PLT at least 75,000/mcL OR at least 30,000 if marrow is involved, creatinine less 1.5 x ULN)

Treatment Schedule:
Patients will receive pembrolizumab 200 mg IV every 3 weeks for up to 35 cycles. All study therapy will occur in the outpatient setting and there are no dose reductions allowed. A bone marrow biopsy is required at screening only if patients have unexplained cytopenias of grade 2 or above or if PET/CT is suggestive of bone marrow involvement. Newly obtained lymph node biopsy (within 90 days of C1D1 or longer at discretion of PI) will be required at screening.

Principal Investigator: Eric Jacobsen, MD

Slots Available at Last Update: Slots will vary. Please email us for the latest slot availability.
18-509: A phase 1/2 multicenter study evaluating the safety and efficacy of axicabtagene ciloleucel in combination with utomilumab in patients with refractory large B-cell lymphoma

Rationale: Addition of utomilumab to FDA approved Yescarta to test increased efficacy

Key Eligibility Criteria:

- Chemotherapy-refractory disease, defined as one or more of the following:
  - No response to second or greater lines of therapy or PD as best response to most recent therapy regimen SD as best response after at least 2 cycles of last line of therapy with SD duration no longer than 6 months from last dose of therapy

  - OR

  - Refractory post-ASCT or disease progression or relapsed ≤ 12 months after ASCT (must have biopsy proven recurrence in relapsed patients) if salvage therapy is given post-ASCT, the patient must have had no response to or relapsed after the last line of therapy.

- No prior treatment with PD-L1 inhibitor, PD-1 inhibitor, anti-CTLA4, anti-CD137 (4-1BB), anti-OX40 or another immune checkpoint blockade or activator therapy

- No evidence, suspicion and/or history of central nervous system (CNS) involvement of lymphoma

- No prior CAR T-cell therapy

Treatment Schedule:
Patients will have a single leukapheresis for collection of T cells. After successful manufacturing of CAR T cells, patients will receive 3 days of conditioning chemotherapy in the clinic followed by a single infusion of axicabtagene ciloleucel in the hospital, where they will remain for a minimum of 7 days or until CAR T-cell related toxicities resolve to grade 1 or better. Utomilumab will be administered as an IV infusion once every four weeks (± 2 days) starting on either Day 1 or Day 21 (depending on Cohort). Then given every 28 days for up to 6 infusions. Protocol visits and restage at every 1-6 months until month 60, then yearly through year 15.

Principal Investigator: Caron Jacobson, MD

Slots Available at Last Update: Slots will vary. Please email us for the latest slot availability.
18-608: A phase 1/2a, open-label, dose-escalation, dose-expansion, parallel assignment study to evaluate the safety and clinical activity of PBCAR0191 in patients with relapsed/refractory (r/r) non-Hodgkin lymphoma (NHL) and r/r B-cell acute lymphoblastic leukemia (B-ALL)

Rationale: Allogeneic CAR-T product. No manufacturing required and 14-day consent to cells window

Key Eligibility Criteria:
The following types of lymphoma are included and must be confirmed CD19+ (biopsy can be within 6 months if no CD19 directed therapy was administered):
- Diffuse large B cell lymphoma (DLBCL) including Richter’s transformation
- Primary mediastinal B-cell lymphoma (PMBL)
- Follicular Lymphoma (FL) including grade 3B or transformed FL (TFL)
- High-grade B-cell lymphoma
- Small lymphocytic lymphoma (SLL)
- Mantle cell lymphoma (MCL)

- Patient must have received at least 2 prior chemotherapy-containing regimens, one of which have contained an anthracycline and an anti-CD20 monoclonal antibody (unless the investigator determines that the subject’s tumor is CD20 negative
- Adequate bone marrow, renal, pulmonary and cardiac (creatinine clearance >60 mL/min) (Platelet count ≥30,000) (AST and ALT ≤3 times upper limit of normal)
- Cannot have received stem cell transplant within 90 days before screening

Treatment Schedule:
Patients sign consent on Day -14, undergo conditioning chemotherapy on Days -5 to Day -3 and receive PBCAR0191 on Day 0. They are then seen in clinic for follow-up on Day 14, 28, 42, 60, 120, 150, 180, 270, and 360, where they will then be asked to sign-up for a long-term follow-up study.

Principal Investigator: Caron Jacobson, MD

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