Diffuse Large B-Cell Lymphoma Clinical Trials

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

Contact Kalin Morrell (Assistant Clinical Research Manager), kalin_morrell@dfci.harvard.edu, 617-582-8713 to discuss a patient.

FRONTLINE TRIALS – NEWLY-DIAGNOSED PATIENTS

| 18-205 p. 2 | A phase 3, randomized, double-blind, placebo-controlled study comparing the efficacy, safety, and pharmacokinetics of polatuzumab vedotin plus R-CHP versus R-CHOP in patients with previously-untreated diffuse large B-cell lymphoma (DLBCL) |

TRIALS FOR RELAPSED/REFRACTORY PATIENTS

| 17-541 p. 3 | A phase 3, randomized, open label study evaluating the efficacy of axicabtagene ciloleucel versus standard of care therapy in patients with relapsed/refractory diffuse large B cell lymphoma |

| 17-313 p. 4 | 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. |

| 17-448 p. 5 | A phase 2 study of pembrolizumab in patients with histiocyte/dendritic cell neoplasms and biologically selected subtypes of relapsed/refractory aggressive lymphomas |

| 16-712 p. 6 | A phase 2 trial of the heat shock protein-90 (Hsp90) inhibitor AT13387 (onalespib) in patients with relapsed/refractory ALK+ ALCL, mantle cell lymphoma, and BCL6+ DLBCL |

| 18-509 p. 7 | 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 |

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.
FRONTLINE TRIALS FOR NEWLY-DIAGNOSED PATIENTS

18-205: A phase 3, randomized, double-blind, placebo-controlled study comparing polatuzumab vedotin plus R-CHP versus R-CHOP in participants with previously-untreated diffuse large B-cell lymphoma (DLBCL).

**Rationale:** This is a phase 3 randomized double blinded study testing the efficacy of standard of care RCHOP therapy compared to R-CHP + Pola. Patients will be randomized to either arm and the study team will be blinded to what arm they have been randomized. Patients must be newly-diagnosed with DLBCL with no prior treatments. Patients can receive steroids in the interim between screening and enrollment if they are experiencing symptoms.

**Key Eligibility Criteria:**
- Must have available biopsy tissue to make 15 slides
- Must have an IPI score greater than or equal to 2
- Must have an ECOG from 0-2

**Treatment Schedule:***
Patients will be required to come in every 3 weeks for 6 cycles of RCHOP/R-CHP+Pola and 2 cycles of rituximab alone after the completion of the combination therapy. Patients will be required to come in to clinic 4-8 weeks after the completion of their therapy for an EOT visit; then, every 3 months for follow up.

**Principal Investigator:** Austin Kim, MD

**Slots Available at Last Update:** 25. Slots will vary. Please email us for the latest slot availability.

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TRIALS FOR PATIENTS WITH RELAPSED/REFRACTORY DISEASE


Rationale: Yescarta is FDA approved in this population.

Key Eligibility Criteria:

- Relapsed or refractory disease after first-line chemoimmunotherapy
  - Refractory disease defined as no complete remission to first-line therapy; patients who are intolerant to first-line therapy are excluded
    - Progressive disease (PD) as best response to first-line therapy
    - Stable disease (SD) as best response after at least 4 cycles of first-line therapy (e.g., 4 cycles of R-CHOP)
    - Partial response (PR) as best response after at least 6 cycles, and biopsy-proven residual disease or disease progression ≤ 12 months from initiation of therapy
- Prior chimeric antigen receptor therapy or other genetically modified T-cell therapy, or prior randomization into ZUMA-7
- Intent to proceed to HDT and ASCT if response to second-line therapy (PR is considered response and must go to transplant)

Treatment Schedule:
Patients are randomized 1:1 to axicabtagene ciloleucel vs. SOC. SOC can be given as RICE, R-GDP, R-ESHAP, R-DHAP as second line salvage regimen. Patients with SD or PD to salvage come off study. Patients with a PR or CR to salvage proceed to auto transplant and then will come in for SOC visits and protocol visits with restaging every 2-3 months until month 30. Patients randomized to axicabtagene ciloleucel 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. Protocol visits and restage at day 50, 100, 150 and month 9; then every 3 months until month 30. Patients are then followed by phone up to 15 years.

Principal Investigator: Caron Jacobson, MD

Slots Available at Last Update: Slots will vary. Please email us for the latest slot availability.
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 and will be opening with a chemotherapy + 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 come to clinic for treatment once a week for the first four weeks. After the first cycle, patients will come to clinic twice a month for their treatments. Day 1 will be a combination of Rituximab + Hu5F9-G4 and day 15 will be a single of infusion of Hu5F9-G4. Patients will also be required to have a screening biopsy performed along with one done at day 22 unless a biopsy is deemed not clinically feasible by the treating physician. Treatment can continue indefinitely at this time with a continued combination of rituximab + HuF59-G4 until cycle 7 at which time they will continue to get HuF59-G4 and rituximab every other cycle. Patients must have had their last treatment either 2 weeks prior or 5 half-lives whichever is longer. They must also be deemed ineligible for CAR T-cell treatment per their treating physician.

**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:** 5. Please email us for the latest information.

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16-712: A phase 2 trial of the heat shock protein-90 (Hsp90) inhibitor AT13387 (onalespib) in patients with relapsed/refractory ALK+ ALCL, mantle cell lymphoma, and BCL6+ DLBCL

**Rationale:** The primary goal of this CTEP study is to investigate the overall response rate of patients with relapsed/refractory ALK + ALCL, DLBCL, and MCL to single agent AT13387 (onalespib). The secondary objectives include assessing the progression free survival, overall survival, and duration of response for patients as well as the safety and tolerability of the treatment. Onalespib is a small molecule inhibitor of HSP90. Inhibition of HSP90 leads to the degradation of many oncogenes, and it is therefore felt that targeting HSP90 can inhibit multiple oncogenic pathways simultaneously. Patients are ineligible if they have known leptomeningeal or brain metastases, uncontrolled intercurrent illness, consistent QTc> 450 msec for men and >470 msec for, and LVEF < 50%.

**Key Eligibility Criteria:**
- Histology of ALK+ ALCL, MCL, or BCL6+ DLBCL
- Patients with measurable disease by PET/CT that has not been previously irradiated (if previous irradiation has occurred then must be evidence of progression since radiation)
- At least 18 years of age, ECOG performance status of 2 or below, as well as normal organ and marrow function

**Treatment Schedule:**
A pre-treatment bone marrow biopsy, followed by a pre-treatment lymph node biopsy if marrow is negative, as well as an on-treatment biopsy (C1D17) and biopsy at the time of progression are required. The treatment schedule includes IV infusion over 1 hour of 160 mg/m2 onalespib on Days 1, 2, 8, 9, 15, and 16 in 28-day cycles.

**Principal Investigator:** Caron Jacobson, MD

**Slots Available at Last Update:** 13. Please email us for the latest information.

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*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 kalin_morrell@dfci.harvard.edu.

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
  - 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.
- 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.

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