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.

**TRIALS FOR RELAPSED/REFRACTORY PATIENTS**

<table>
<thead>
<tr>
<th>Trial Code</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-541 p. 2</td>
<td>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</td>
</tr>
<tr>
<td>17-313 p. 3</td>
<td>A phase 1b/2 trial of Hu5F9-G4 in combination with rituximab plus rituximab, gemcitabine and oxaliplatin in patients with relapsed/refractory diffuse large B-cell lymphoma. Hu5F9-G4 is a monoclonal antibody which is designed to block a protein called CD47, which is widely expressed on human cancer cells.</td>
</tr>
<tr>
<td>17-448 p. 4</td>
<td>A phase 2 study of pembrolizumab in patients with histiocyte/dendritic cell neoplasms and biologically selected subtypes of relapsed/refractory aggressive lymphomas</td>
</tr>
<tr>
<td>18-509 p. 5</td>
<td>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</td>
</tr>
<tr>
<td>18-322 p. 6</td>
<td>A phase 1b study of TAK-659 in combination with venetoclax for adult patients with previously-treated non-Hodgkin lymphoma</td>
</tr>
<tr>
<td>15-212 p. 7</td>
<td>An open-label, multicenter phase I study to investigate the safety and tolerability of REGN1979, an anti-CD20 X anti-CD3 bispecific monoclonal antibody, in patients with CD20+ B-cell malignancies previously treated with CD20-directed antibody therapy</td>
</tr>
<tr>
<td>18-608 p. 8</td>
<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 and r/r B-cell acute lymphoblastic leukemia</td>
</tr>
</tbody>
</table>

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.
To discuss a patient, email kalin_morrell@dfci.harvard.edu.

TRIALS FOR PATIENTS WITH RELAPSED/REFRACTORY DISEASE

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

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 the end 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.

<return to page 1>

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.
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. Patients will receive their first scan at the beginning of cycle 3 and further treatment will be based upon that. Note: Patients must 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.
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.

<return to page 1>
18-509: A phase 1/2 multicenter study evaluating the safety and efficacy of axicabtagene ciloleucel (Yescarta™) 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.
- 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.
18-322: A phase 1b study of TAK-659 in combination with venetoclax for adult patients with previously treated non-Hodgkin lymphoma

**Rationale:** This is a phase 1B, dose escalation study of TAK-659 in combination with venetoclax in adult patients with advanced non-Hodgkin lymphoma (NHL) after at least 1 prior line of therapy. The study’s primary objective is to determine the maximum tolerated dose (MTD) and/or the recommended phase 2 dose (RP2D) of TAK-659 and venetoclax when administered in combination. The study also looks to evaluate the safety and tolerability of TAK-659 and venetoclax when administered in combination. The TAK-659/venetoclax MTD/RP2D will be determined after consideration of safety data, preliminary pharmacokinetic (PK) data, and any early antitumor activity observed.

**Key Eligibility Criteria:**
- Patients must be aged 18 years or older with a confirmed diagnosis of advanced NHL of any histology (except CLL or MCL), including radiographically or clinically measurable disease
- Patients must be refractory or relapsed after 1 prior line of therapy, have no available effective standard therapy per investigator’s assessment; and be either treatment naïve to, relapsed/refractory to, or experienced treatment failure of ibrutinib, idelalisib or any other investigational B-cell receptor pathway inhibitor
- Patients must have an ECOG score of 0 or 1, adequate organ and coagulation function and life expectancy of greater than 3 months

**Treatment Schedule:**
Patients present to clinic following one of three TAK-659 dosing schemas, each seeking to dose escalate per patient’s response: Continuous daily dosing, 7 days on/7 days off, or 14 days on/7 days off. Please reach out to the study contact to confirm which TAK dosing schema has slot availability.

**Principal Investigator:** Matthew Davids, MD, MMSc

**Slots Available at Last Update:** Slots will vary. Please email us for the latest slot availability.
15-212: An open-label, multicenter phase I study to investigate the safety and tolerability of REGN1979, an anti-CD20 X anti-CD3 bispecific monoclonal antibody, in patients with CD20+ B-cell malignancies previously treated with CD20-directed antibody therapy

**Rationale:** REGN1979 is a human bispecific antibody based on an IgG4 isotype modified to further reduce Fc binding (designated anti-CD20 x anti-CD3). REGN1979 is designed to bind to CD20-expressing target cells and to cross-link them to CD3-expressing T-cells, resulting in local T-cell activation and generation of an antigen-nonspecific polyclonal cytotoxic T-cell response. The cytotoxic T-cell response seen with the anti-CD20 x anti-CD3 bispecific antibody is thus independent of the typical requirements for specific T-cell receptor recognition of a target cell. This novel mechanism of action is distinct from that of anti-CD20 antibodies and as such may also provide a therapeutic benefit in patients who have relapsed following anti-CD20 mAb therapy.

**Key Eligibility Criteria:**
- Have documented CD20+ B-cell malignancy, with active disease not responsive to prior therapy, for whom no standard of care options exist, and for whom treatment with an anti-CD20 antibody may be appropriate
- NHL must have prior anti CD 20 antibody therapy
- For follicular—must have received at least 2 therapies including anti CD 20 anti-body and an alkylating agent

**Treatment Schedule:**
During the induction period (4 weeks), patients will be treated with a split dose of REGN during days 1 and 2 of weeks 1, 2 and 3. During these weeks patients will be admitted and will receive additional blood draws on days 3 and 4 for CRP and TLS monitoring. The patients will then receive the full dose of REGN on day 1 of week 4 and will return on days 2 and 3 for additional lab monitoring. From week 6-12, patients will enter the QW dosing phase. After QW dosing, the patients will enter the maintenance period and will be treated with full dose REGN on even weeks up to week 36.

**Principal Investigator:** Jennifer Brown, MD, PhD

**Slots Available at Last Update:** Currently accruing for the expansion cohorts—follicular, indolent NHL, and aggressive NHL (for post CAR-T). 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 and r/r B-cell acute lymphoblastic leukemia

**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 patient’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

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

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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.