T-Cell Lymphoma Clinical Trials

The following clinical trials are currently open and accruing for patients with T-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>Page</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-239</td>
<td>2</td>
<td>A multicenter, phase 2, open-label, parallel cohort study of efficacy and safety of duvelisib in patients with relapsed or refractory peripheral T-cell lymphoma (PTCL)</td>
</tr>
<tr>
<td>17-548</td>
<td>3</td>
<td>A phase 2 multicenter study of ruxolitinib in relapsed or refractory T or NK cell lymphoma</td>
</tr>
<tr>
<td>18-322</td>
<td>4</td>
<td>A phase 1b study of TAK-659 in combination with venetoclax for adult patients with previously-treated non-Hodgkin lymphoma</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.
TRIALS FOR PATIENTS WITH RELAPSED/REFRACTORY DISEASE

**18-239**: A multicenter, phase 2, open-label, parallel cohort study of efficacy and safety of duvelisib in patients with relapsed or refractory peripheral T-cell lymphoma (PTCL)

**Rationale**: This sponsor-initiated study has two phases: the dose optimization phase and the dose expansion phase. The primary goal of the dose optimization phase is to determine the optimal dose of duvelisib for utilization in the expansion phase and to determine the efficacy of duvelisib in patients with R/R PTCL. The dose optimization recently reached the accrual goal and the data is currently being reviewed to determine the optimal dose to be used in the dose expansion phase. The dose optimization phase will continue to enroll until the expansion phase is open. Patients receive duvelisib in 28-day cycles on one of two cohorts: Cohort 1 includes duvelisib PO BID at a starting dose of 25 mg, with potential to increase to 50 mg and then 75 mg pending patient’s response and tolerance; Cohort 2 includes a set dose of duvelisib at 75 mg PO BID. Patients are excluded if there is clinical evidence of transformation to a more aggressive subtype of lymphoma, have received prior allogeneic transplant, prior treatment with PI3K inhibitor, major surgery within 4 weeks, and known CNS involvement by PTCL. Thus far, patients have been tolerating treatment well with limited toxicities.

**Key Eligibility Criteria**:
- Diagnosis of PTCL-NOS, AITL, ALCL, or NKTL
- At least 2 cycles of one prior regimen (failed to achieve at least a PR, failed to achieve CR after 6 or more cycles, progressed after initial response)
- Measurable disease as defined by IWG for PTCL
- ECOG performance status of 2 or below, washout of 14 day or 5 half-lives from previous PTCL-directed therapy, and normal organ and marrow function

**Treatment Schedule**:
Patients will come to clinic for in patient dosing for C1D1, C1D8, C1D15, C2D1, C2D15 and C4D1 and then only on the first day of every even number cycle going forward. Either fresh or archival tissue from a tumor biopsy must be provided at screening. Patients are assessed for response by PET/CT after cycle 1, and then every 2 cycles thereafter.

**Principal Investigator**: Eric Jacobsen, MD

**Slots Available at Last Update**: 6. Slots will vary. Please email us for the latest slot availability.

<return to page 1>

_T-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.
17-548: A phase 2 multicenter study of ruxolitinib in relapsed or refractory T or NK cell lymphoma

**Rationale:** The primary goal of this study is to evaluate the efficacy of ruxolitinib as well as to evaluate for markers of sensitivity and characterize the effects of JAK 1/2 inhibition in patients with T-cell lymphoma. The study includes three cohorts: Cohort 1 is for patients with R/R disease with known JAK/STAT activation; Cohort 2 is for patients with R/R disease with functional evidence of JAK/STAT activation (at least 30% Phospho-STAT3 expression by immunohistochemistry) for whom genetic profiling has not been done or has failed to show JAK/STAT mutations; and Cohort 3 is for patients with R/R disease who do not meet criteria for Cohort 1 or 2 (Unknown JAK/STAT status).

**Key Eligibility Criteria:**
- Patients must have pathologically confirmed T or NK cell lymphoma and be relapsed or refractory to at least 1 systemic therapy
- Patients with CTCL must have stage 1B disease or greater to be eligible
- Measurable disease by Lugano classification
- No systemic anti-cancer therapy for T-cell lymphoma within 2 weeks prior to C1D1
- ANC ≥ 1.0/mm³ (or ANC ≥ 0.5/mm³ if baseline neutropenia due to lymphoma), PLT ≥ 100 x 10^9/L (or 50 x 10^9/L if related to lymphoma), HgB ≥ 8g/dL, total bilirubin ≤ 1.5 x ULN, and creatinine clearance ≥ 30 mL/min

**Treatment Schedule:**
Patients will receive ruxolitinib 20 mg PO BID on 28-day cycles. Fresh or archival tissue is required at baseline and research blood will be collected throughout the study and at disease progression. Additional research biopsies may be required depending on the site of disease involvement.

**Principal Investigator:** Eric Jacobsen, MD

**Slots Available at Last Update:** 5; please email us for the latest information.

<return to page 1>
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, 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: 10. Slots will vary. Please email us for the latest slot availability.

<return to page 1>

Rationale: The primary goal of this study is to estimate the 18-month progression-free survival (PFS) rate after ASCT in patients treated with pembrolizumab as an early consolidation post-ASCT. Pembrolizumab binds to the PD-1 receptor and inhibits its interaction with PD-L1 and PD-L2, therefore serving as a PD-1 blockade. A large fraction of the patients with DLBCL, cHL, and PTCL who undergo an ASCT will still relapse. Studies have shown that a subset of PTCL tumors use the PD-1 pathway as a mechanism for tumor escape, and therefore there is a strong rationale for the use of pembrolizumab – an anti-PD1 monoclonal antibody – post-ASCT to inhibit this pathway with the hope of increasing PFS.

Key Eligibility Criteria:
- Patients with PTCL, NOS; AITL; ALK-negative ALC; EATL and MEITL; and extranodal NK/T-cell lymphoma (ENKTL)
- Patients with ALK-positive PTCL and cutaneous T-cell lymphoma will not be eligible
- Patients can have no more than 1 line of anthracycline-containing chemotherapy prior to ASCT, must have had PET/CT restaging after salvage therapy and before ASCT
- ECOG performance status ≤ 1 and have normal organ and marrow function. Patients with CNS involvement or a syndrome that requires systemic steroids or autoimmune agents are excluded.

Treatment Schedule:
Patients will receive the first dose of pembrolizumab no later than 21 days from the post-ASCT discharge. Pembrolizumab 200 mg intravenously every three weeks for up to 8 cycles. Response will be assessed with PET/CT during Cycle 4 and Cycle 8 while on treatment and then at month 12 and month 18 post-ASCT after treatment has ended.

Principal Investigator: Philippe Armand, MD PhD

Slots Available at last update: 5. Please email us for the latest information.