

February 23, 2018

National Cancer Institute
CCR Clinical Trials at NIH

Dear USCLC Members:

I propose a collaboration between your group and those of us on the Clinical Trials Team of NCI's Center for Cancer Research (CCR) Lymphoid Malignancies Branch (LYMB) in Bethesda, Maryland. We would ask you to refer patients for a study we are conducting with patients who have chronic and acute subtypes HTLV-1 associated adult T-cell leukemia (ATL), cutaneous T-cell lymphoma (CTCL) stage III or IV with leukemic involvement or erythroderma, or peripheral T-cell lymphoma who have failed standard treatments and for whom there are no standard treatments associated with survival advantage. Protocol Title 16-C-0062 "A Phase I Study of Subcutaneous Recombinant Human IL-15 (s.c.) rhIL-15 and Alemtuzumab for Patients with Refractory or Relapsed Chronic and Acute Adult T-Cell Leukemia (ATL)". Clinical Trials Identifier: NCT02689453. The objective of the study is to determine the safety and maximum tolerated dose (MTD) of s.c. rhIL-15 in combination with standard 3 x per week i.v. alemtuzumab treatment.

Previously we reported that administering alemtuzumab (CAMPATH-1) to patients with chronic, acute and lymphomatous subtypes HTLV-1 associated ATL yielded an overall response rate of 52% in 29 patients, with 12 of 15 patients with acute ATL responding. However, the median duration of response was only 3.4 months and median overall survival 5.9 months.

The administration of recombinant human IL-15 by continuous intravenous infusion to adult cancer patients produced a 30-fold expansion in the number of circulating NK cells and an over 350-increase in the number of CD56bright NK cells. In preclinical murine malignancy models the administration of IL-15 with anticancer monoclonal antibodies increased their antibody dependent cellular cytotoxicity and efficacy. For example, a syngeneic model of immunocompetent mice bearing an EL4 cell line, transfected with human CD20 manifested a dramatic increase in ADCC and improved survival for mice treated with IL-15 and rituximab compared to mice treated with either agent alone or to controls. It is hoped that the administration of IL-15 with alemtuzumab to patients with ATL and CTCL will increase the antibody ADCC and the magnitude and duration of responses.

Key Eligibility Criteria:

- Diagnosis of relapsed/refractory adult T-cell leukemia (HTLV-1 associated chronic or acute), cutaneous T-cell lymphoma (stage III or IV, with leukemic involvement or erythroderma), or peripheral T-cell lymphoma (NOS, angioimmunoblastic, and hepatosplenic).
- ≥ 18 years of age.
- Measurable or evaluable disease.
- Adequate organ (heart, lungs, liver, kidneys and bone marrow) function.
- ECOG performance status ≤ 1 .
- Patients with treated brain metastases demonstrating stable radiographic involvement (≥ 3 months post treatment) are potentially eligible.
- Patients with history of allogeneic stem cell transplant are eligible in the absence of chronic graft-versus-host disease requiring treatment in the last 6 weeks.
- Absence of any significant medical conditions that would preclude safe treatment.

Design

- This is a single institution, nonrandomized phase I dose-escalation study evaluating increasing doses of s.c. rhIL-15 in combination with alemtuzumab using a standard 3 + 3 dose escalation.
- Treatment schedule:
 - rhIL-15 weeks 1 and 2 (s.c. Monday through Friday) all doses in cohorts.
 - Alemtuzumab initiation dosing week 3 (day 1 \rightarrow 3 mg., day 2 \rightarrow 10 mg., day 3 \rightarrow 30 mg., and day 5 \rightarrow 30 mg. i.v. over 2 hours).
 - Standard alemtuzumab weeks 4, 5 and 6 (30 mg. Monday, Wednesday and Friday).
 - rhIL-15 dose levels
 - Cohort 1 \rightarrow 0.5 mg/kg/dose
 - Cohort 2 \rightarrow 1 mg/kg/dose
 - Cohort 3 \rightarrow 2 mg/kg/dose
 - Cohort 4 \rightarrow 3 mg/kg/dose

We hope that you would be interested in collaborating with us in this trial by your referral of patients that are vital to our efforts to find new and better ways to treat patients with cancer. The NCI is an institution of the National Institutes of Health (NIH), which provides medical care at no cost for both U.S. citizens and non-U.S. citizens.

Send patient referrals to:

NCI Clinical Trials Referral Office
National Institutes of Health, Clinical Center (CC)
10 Center Drive, Building 10, Room 12N226
Bethesda, Maryland 20892
Phone: 1-888-NCI-1937
E-mail: NCIMO_Referrals@mail.nih.gov

If you would join us in this study and refer patients, we would include you among the coauthors of any manuscript describing this trial.

Best wishes,

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