Leukemia insights

APRIL 2025

MONTHLY EDITION

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Making Cancer History®

In this month's Leukemia Insights newsletter, written by Nicholas Short, M.D., we describe clinical trials available at MD Anderson Cancer Center for patients with relapsed or refractory acute lymphoblastic leukemia. Learn more about our Leukemia program.

Clinical trials for relapsed/refractory acute lymphoblastic leukemia (ALL)

The outcomes of adults with acute lymphoblastic leukemia (ALL) have significantly improved recently with the development of novel agents such as inotuzumab ozogamicin (INO), blinatumomab, CD19 CAR T-cells and more potent BCR::ABL1 tyrosine kinase inhibitors (TKIs) such as ponatinib. These agents are being increasingly used in the frontline setting, leading to more durable responses and higher rates of cure in newly diagnosed patients. However, many patients still relapse, and the outcomes with currently available salvage therapies remain poor. For example, patients with B-cell ALL who have previously received both INO and blinatumomab have a median overall survival of <6 months, highlighting the need for novel agents in this population. Effective salvage options are also very limited in patients with T-cell ALL. At MD Anderson Cancer Center, we have several clinical trials of novel drugs and combinations for patients with relapsed or refractory ALL, as outlined below.

1. Ph-negative B-cell ALL

- **AZD0486 (CD19 bispecific antibody) –** AZD0486 is a new CD19-CD3 bispecific antibody that is administered as a weekly IV infusion. This trial allows patients with either Ph-negative or Ph-positive B-cell ALL, including patients with prior exposure to CD19-targeted therapies.
- **VNX-101 (CD19 gene therapy)** – VNX-101 is a novel gene therapy that transduces cells of the liver to cause continuous *in vivo* production of blinatumomab-like (CD19-CD3) bispecific antibody. This trial requires only a one-time infusion of the gene therapy product. Patients are eligible regardless of whether they have received prior CD19- or CD22-targeted therapies. This study will soon allow inclusion of any patient with a CD19-positive leukemia or lymphoma.

ABOUT MyMDAnderson

myMDAnderson is a secure, personalized web site helping community physicians expedite patient referrals, as well as improve continuity of care through information access and streamlined communications.

Physicians who have referred patients to MD Anderson or plan to do so, can utilize the HIPAA-compliant features of myMDAnderson to:

- Refer a patient
- View your patient's appointments Access patient reports
- Send and receive secure messages

JOIN THE COVERSATION

Connect with us.

JOIN OUR MAILING LIST

If you would like to receive an electronic issue of the MD Anderson Leukemia Insights e-Newsletter on a monthly basis, please email us at Leukemia@mdanderson.org.

It's the easiest way to stay current with information on the latest leukemia news, research, and resources. View archived issues.

CONTACT OUR STAFF

Mary Alma Welch - Editor
Lisa Palacios - Publishing Editor
Leukemia@mdanderson.org

- **Subcutaneous blinatumomab –** This novel product is administered subcutaneously three times a week, allowing for more convenient administration than standard, continuous-infusion blinatumomab. In a phase Ib study in relapsed/refractory B-cell ALL, 12 of 13 patients (92%) treated at the highest dose level responded, with responses seen even in patients with prior blinatumomab exposure. This study is open for relapsed/refractory ALL, and a cohort for patients with MRD-positive B-cell ALL will open soon.
- **Mini-hyper-CVD + INO + blinatumomab –** In this ongoing phase II study of the combination of mini-hyper-CVD + INO + blinatumomab, the response rate in patients' treatment in first salvage was 89%, and the 3-year overall survival was 49%. These results are superior to historical expectations with either of these agents given as monotherapy, where the median survival is only 7-8 months. INO and blinatumomab are provided free of charge through the study. It is also open for adults ≥60 years of age with newly diagnosed Ph-negative B-cell ALL.
- **Brexu-cel (Tecartus) consolidation study –** CD19 CAR T-cells can result in durable remissions in patients with relapsed/refractory ALL, even without need for allogeneic stem cell transplant. This phase II study evaluates brexu-cel (Tecartus), an approved CD19 CAR T-cell therapy, as consolidation therapy after response to salvage therapy. The goal of this study is to reduce the need for allogeneic stem cell transplant for patients with relapsed/refractory B-cell ALL, thus reducing the potential for treatment-related mortality in these patients.
- **ADCT-602 (CD22 antibody-drug conjugate) –** ADCT-602 is a novel antibody-drug conjugate directed against CD22. In this ongoing phase I/II study, the rate of MRD-negative CR at the recommended phase II dose is 33%, including responses in heavily pretreated patients. Patients with prior INO exposure are still eligible.
- **UCART-22 (CD22 CAR T-cells) –** UCART-22 is an allogeneic, "off-the-shelf" CAR T-cell product targeting CD22. In the ongoing phase I study, a response rate of 67% was observed with the current UCART-22 product, with responses observed even in patients with prior INO and/or CD19 CAR T-cell exposure. This agent has been delivered safely without any high-grade cytokine release syndrome observed.

2. Ph-positive B-cell ALL

- **Blinatumomab + asciminib –** Asciminib is a newer, highly effective BCR::ABL1 TKI that is approved for patients with CML and has shown activity in patients with prior ponatinib exposure and in T315I mutations. This study is enrolling patients with relapsed/refractory Ph-positive B-cell ALL or CML in lymphoid blast phase; a frontline cohort will open soon. Asciminib is provided free or charge on the study.
- **Blinatumomab + olverembatinib –** Olverembatinib is a novel BCR::ABL1 TKI that is currently in clinical development for Ph-positive leukemias. It has shown activity in patients highly resistant CML, including those with prior ponatinib exposure and *ABL1* resistance mutations. Olverembatinib is provided free of charge on the study. A second study combining olverembatinib with subcutaneous blinatumomab will open soon.

3. T-cell ALL

- **WU-CART-007 (CD7 allogeneic CAR T-cells) –** WU-CART-007 is a CD7-targeted allogeneic, “off-the-shelf” CAR T-cell product for patients with relapsed/refractory CD7-positive T-cell ALL. This CAR T-cell product has been shown to be safe and effective in an ongoing phase I/II study, where 11 of 13 patients (82%) who received the recommended phase 2 dose achieved CR. This study is enrolling patients with relapsed/refractory CD7-positive T-cell ALL, regardless of prior therapies.
- **LP-118 (oral Bcl-2/Bcl-xL inhibitor)** – LP-118 is a novel, oral Bcl-2/Bcl-xL inhibitor that is being evaluated in both ALL and CLL. Patients with either B-cell or T-cell ALL are eligible. Bcl-2/Bcl-xL inhibition may be particularly effective for patients with early T-cell precursor ALL, a high-risk subtype of T-cell ALL.

The Leukemia Department welcomes referrals and is committed to collaborating with you to provide access to novel therapies for your patients. To refer a patient, please contact any of the Leukemia faculty listed.