Leukemia insights

OCTOBER 2020

MONTHLY EDITION

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Making Cancer History®

In this month's Leukemia Insights newsletter, written by Elias Jabbour, M.D., and Nitin Jain, M.D., and sponsored in part by the Charif Souki Cancer Research Fund, we describe clinical trials with CAR T-cell therapies available at our institution for patients with R/R B-ALL. Learn more about our Leukemia Program.

Chimeric Antigen Receptor (CAR) Therapies for Patients with Acute Lymphoblastic Leukemia (ALL)

The development of chimeric antigen receptor-modified T-cells, better known as CAR T-cells, is one of the most exciting recent developments in cancer research and treatment. Autologous CAR-T cell therapy is approved for pediatric patients with B-cell acute lymphoblastic leukemia (ALL) (up to the age of 25 years) and adults with several types of non-Hodgkin's lymphoma (NHL). With this approach, T-cells are collected from the patient by leukopheresis and engineered in the laboratory to express a receptor directed at a cancer antigen such as CD19. The cells are then infused back into the patient after administration of a lymphodepletion regimen, most commonly a combination of fludarabine and cyclophosphamide. Durable remissions have been observed in pediatric patients with B-ALL and adults with NHL.

The ELIANA trial led to the approval of tisagenlecleucel (Kymriah) in patients with relapsed/refractory (R/R) B-ALL up to the age of 25 years. The complete remission (CR) rate at 3 months was 82% with 2-year relapse-free survival and overall survival of 62% and 66%, respectively. No CAR-T product is yet approved for adult patients with B-ALL who are 26 years or older.

In this newsletter, we describe clinical trials with CAR T-cell therapies available at our institution for patients with R/R B-ALL. A brief overview is provided in the table below.

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 complete the **Subscription Request Form.**

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

	Trial	Class	Target	Source of Cells	Sponsor
	UCART22	Allogeneic	CD22	Healthy donor	Cellectis
	UCART19	Allogeneic	CD19	Healthy donor	Servier
	PBCAR0191	Allogeneic	CD19	Healthy donor	Precision Biosciences
	TCR2-19	Autologous	CD19	Patient	TCR2 Therapeutics
	AUTO1	Autologous	CD19	Patient	Autolus
	FT819	Allogeneic	CD19	Induced pluripotent stem cells (iPSCs)	Fate Therapeutics
	CAR-NK	Allogeneic	CD19	Cord blood	MD Anderson

UCART22 CD22

The UCART platform provides an "off-the-shelf" approach in which the cells are derived from healthy-volunteer donor T-cells. These cells undergo genetic engineering to remove the T-cell receptor to prevent graft-versus-host disease. As they are premade and available for infusion, there is no requirement to leukopheresis or wait for the cells to be manufactured. This strategy also will benefit patients who are cytopenic (not an uncommon scenario for leukemia patients) and from whom autologous T-cell collection is not possible.

UCART22 is such a therapy targeting CD22. Preclinical data supporting this concept was presented by our group (Marina Konopleva, M.D., Ph.D.) previously at the American Society of Hematology (ASH) meeting. Patients receive lymphodepletion with fludarabine and cyclophosphamide with or without alemtuzumab, followed by UCART22 infusion. This trial is enrolling patients. Patients who have already received CD19 CAR T-cells are still eligible.

UCART19 CD19

UCART19, similar to the UCART22, is an off-the-shelf product targeting CD19. Patients receive lymphodepletion with fludarabine and cyclophosphamide with alemtuzumab, followed by UCART19 infusion. Adults patients with R/R B-ALL are eligible. This trial is open.

Preliminary results of this trial were presented at the 2018 ASH meeting. A total of 21 adult and pediatric patients were treated. The median age was 22 years (range, 0.8-62 years) and the median number of prior therapies was 4 (range, 1-6). Sixty-two percent of the patients (13/21) had a prior allogeneic stem cell transplant. Eighty-two percent of patients (14/17) who received lymphodepletion with fludarabine/cyclophosphamide/alemtuzumab achieved CR/CRi, and 59% of them (10/17) achieved MRD-negative remission.

PBCAR0191 CD19

PBCAR0191 is an off-the-shelf CAR T-cell product targeting CD19. This trial is also exploring some novel lymphodepletion strategies in addition to fludarabine and cyclophosphamide. Patients with R/R ALL, R/R CLL, R/R Richter transformation, and R/R NHL are eligible. Patients with MRD+ B-ALL are eligible as well. This trial is enrolling patients.

TCR2-19 CD19

In this clinical trial, autologous T-cells are collected by leukopheresis and undergo genetic engineering to create 'TRuC-T' cells targeting CD19. This strategy combines the best features of CAR T-cells and the native T-cell receptor. It is open for R/R NHL and R/R B-ALL.

AUTO1 CD19

This is an autologous CD19 CAR that uses a single-chain variable fragment (scFv) called CAT with a lower affinity for CD19 and a faster off-rate compared to the FMC63 scFv used in other approved CD19 CAR T-cell therapies. The altered binding kinetics may allow an opportunity for physiological T-cell activation, reduced toxicity, improved engraftment and potential for long-term persistence leading to a sustained response. Adult patients with R/R B-ALL will be eligible. The protocol should open in the next few weeks.

FT819 CD19

FT819 is an off-the-shelf CAR T targeting CD19. The T-cells are derived from induced pluripotent stem cells (iPSCs).

Patients will receive lymphodepletion with fludarabine and cyclophosphamide; some patients will also receive IL-2. Patients with R/R ALL, R/R CLL, R/R Richter transformation, and R/R NHL are eligible. Patients with MRD+ B-ALL are eligible as well. The protocol should open in the next few weeks.

CAR-NK CD19

Allogeneic cord blood-derived NK cells are another off-the-shelf product that does not require the collection of cells from each patient. Unlike T-cells, NK-cells do not cause GVHD and can be given safely in the allogeneic setting. Dr. Rezvani laboratory here has developed a novel cord blood-derived NK-CAR product that expresses a CAR against CD19; ectopically produces IL-15 to support NK-cell proliferation and persistence in vivo; and expresses a suicide gene, inducible caspase 9, to address any potential safety concerns. The results of this trial were reported in NEJM (Liu et al. N Engl J Med 2020; 382:545-553). This study is open for R/R B-ALL, including MRD+ disease.

Announcements

SOHO Highlights Invitation | Society of Hematologic Oncology

"The "**SOHO Highlights**" meeting is designed to provide participants with an overview of the latest advances in hematologic malignancies and a preview of where the field is going next. Investigators from around the world will join the meeting for a day of learning and interactive, virtual discussion with the speakers. Each presentation is 25 minutes followed by a 10-minute, **live Questions & Answer session** with the audience. Note that the **Zoom platform** will be utilized to facilitate interaction with attendees. For more information and registration, go https://www.sohohighlights.com/."

Leukemia Insights Newsletter

Our Leukemia Insights e-newsletter is now available online. Started in 2007 by Hagop Kantarjian, M.D., Leukemia Insights focuses on our various therapy options at MD Anderson Cancer Center. Click here to visit our new website.

Emil J Freireich Hematology Grand Rounds

The MD Anderson Cancer Center Emil J Freireich Hematology Grand Rounds now has a virtual format. This series highlights the incredible research taking place at MD Anderson Cancer Center while showcasing leaders from our research community, in an effort to remain engaged and inspired during the COVID-19 pandemic. Hosted by the Department of Leukemia in collaboration with the Department of Lymphoma/Myeloma, and Department of Stem Cell Transplantation and Cellular Therapy, we aim to strengthen the connections between the scientific and medical community at MD Anderson Cancer Center, our colleagues, patients and friends from around the world. Click here to visit our new website.

Leukemia Faculty Contacts

Completing these studies in a timely manner will allow us to move quickly on positive leads. We appreciate referrals and will make every effort, once a patient is enrolled on a study, to continue as much of the care as possible through the referring oncologist. We also will keep you apprised of the patient's progress. View our faculty roster.

Clinical Faculty

Kantarjian, Hagop	*Department Chair*	(713) 792-7026
Garcia-Manero, Guillermo	*Deputy Chair, Chief, Section of Translational Research, Chief, Section of Myelodysplastic Syndromes (MDS), and Director, Leukemia Clinical Fellowship Program*	(713) 745-3428
Wierda, William	*Deputy Chair, Chief, Section of Chronic Lymphocytic Leukemia (CLL), and Leukemia Center Medical Director*	(713) 745-0428
Andreeff, Michael	*Chief, Section of Molecular Hematology and Therapy,* Center Medical Director, Bone Marrow Aspiration Clinic	(713) 792-7261
Borthakur, Gautam	*Chief, Section of Developmental Therapeutics*	(713) 563-1586
Daver, Naval	*Director, Leukemia Research Alliance Program*	(713) 794-4392
DiNardo, Courtney D.	*Co-Leader, Section of Acute Myeloid Leukemia (AML), Co-Leader, Section of Developmental Therapeutics Leader, Hereditary Hematologic Malignancy Clinic*	(734) 358-1053
Ferrajoli, Alessandra	*Leukemia Center Associate Medical Director*	(713) 792-2063
Issa, Ghayas “Gus"	*Co-Leader, Section of Chronic Myeloid Leukemia (CML)*	(713) 745-8432
Jabbour, Elias	*Chief, Section of Acute Lymphoblastic Leukemia (ALL)*	(713) 792-4764
Kadia, Tapan	*Co-Leader, Section of Acute Myeloid Leukemia (AML), Co-Leader, Section of Developmental Therapeutics, Co-Leader, Leukemia Clinical Fellowship Program*	(713) 563-3534
Montalban Bravo, Guillermo	*Director, Chronic Myelomonocytic Leukemia (CMML) Program*	*(713) 792-4956*
Pemmaraju, Naveen	*Director, Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) Program*	*(713) 794-3604*
Ravandi, Farhad	*Chief, Section of Acute Myeloid Leukemia (AML)*	(281) 216-7806
Sasaki, Koji	*Co-Leader, Section of Chronic Myeloid Leukemia (CML)*	(713) 745-2882
Verstovsek, Srdan	*Chief, Section of Myeloproliferative Neoplasms (MPNs), Director, Clinical Research Center for MPNs*	*(713) 745-3429*

Leukemia Faculty Contacts

(Continued)

Clinical Faculty

Alvarado, Yesid	(713) 794-4364
Bose, Prithviraj	(713) 792-7747
Burger, Jan	(713) 563-1487
Chien, Kelly	(713) 745-7584
Estrov, Zeev	(713) 794-1675
Jain, Nitin	(713) 745-6080
Kornblau, Steven	(713) 794-1568
Masarova, Lucia	(832) 750-4211
Montalban Bravo, Guillermo	(713) 794-3604
Ohanian, Maro	(713) 792-0091
Pemmaraju, Naveen	(713) 792-4956
Short, Nicholas	(713) 563-4485
Takahashi, Koichi	(713) 745-4613
Thompson, Philip	(713) 792-7430
Yilmaz, Musa	(713) 745-9945

Research Faculty

Battula, Venkata	(713) 563-2227
Bhalla, Kapil N.	(713) 563-8619
Burks, Jared K.	(713) 792-7640
Carter, Bing Z.	(713) 794-4014
Chang, Kyung Hee	(713) 792-4694
Colla, Simona	(713) 794-5223
Fiskus, Warren	(713) 563-5901
Freireich, Emil	(713) 792-2660
Gandhi, Varsha V.	(713) 792-2989
Han, Lina	(713) 792-7640
Ishizawa, Jo	(713) 792-7640
Keating, Michael	(713) 745-2376
Piya, Sujan	(713) 792-7305
Plunkett, William	(713) 792-3335
Post, Sean	(713) 794-1458
Pourebrahimabadi, Rasoul	(713) 792-7305
Rytting, Michael E.	(713) 792-4855
Ruvolo, Peter	(713) 745-9211
Wei, Yue	(713) 792-9854
Yang, Hui	(713) 792-2558
Zhang, Weiguo	(713) 794-4085