

Advances in Pediatric Stem Cell Transplantation and Cellular Therapy



A quarterly newsletter highlighting groundbreaking clinical trials available to pediatric and young adult cancer patients at The University of Texas MD Anderson Children's Cancer Hospital

Now enrolling pediatric patients with lymphoid cancers: umbilical cord-derived CAR-engineered natural killer (NK) cell trial shows complete responses in majority of patients, without significant side effects

Pediatric patients who are at least seven-years-old with certain lymphoid cancers may be eligible for an innovative Phase I/II immunotherapy clinical trial only available at [The University of Texas MD Anderson Cancer Center](#). The regimen, study number [2016-0641](#), uses natural killer (NK) cells taken from umbilical cord blood and engineered by a chimeric antigen receptor (CAR) to better identify and target cancer cells that do a great job of hiding. This research targets the CD19 molecule found on some cancer cells.



In evaluating early results of the trial titled, "Umbilical & Cord Blood-Derived CAR-Engineered NK Cells for B Lymphoid Malignancies," eight out of 11 non-Hodgkin's lymphoma and chronic lymphocytic leukemia (CLL) patients experienced complete remission in 30 days. The treatment requires less wait time than other immunotherapies, such as CAR T cell therapy, and has not triggered the serious complications of cytokine release syndrome, neurotoxicities, nor graft-versus-host disease.

[Katy Rezvani, M.D., Ph.D.](#), professor of Stem Cell Transplantation and Cellular Therapy (SCT-CT) at MD Anderson, was the senior author of early results published in the Feb. 6, 2020 issue of The New England Journal of Medicine. The paper is titled, ["Use of CAR-Transduced Natural Killer Cells in CD19-Positive Lymphoid Tumors."](#) [Loretta Nastoupil, M.D.](#), associate professor of Lymphoma/Myeloma at MD Anderson, is the principal investigator with department colleague, [Chitra Hosing, M.D.](#), professor, serving as co-principal investigator. [Kris Mahadeo, M.D., M.P.H.](#), associate

professor of Pediatrics and section chief at [MD Anderson Children's Cancer Hospital](#), is a collaborator on the study. More clinical trial slots are available.

Eligibility criteria include:

- Patients who are 7 to 80-years-old
- Patients with history of CD19 positive B-lymphoid malignancies, defined as acute lymphoblastic leukemia (ALL), diffuse large B-cell Lymphoma (DLBCL), chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), primary mediastinal large B-cell lymphoma, Richter's transformation of CLL or SLL, follicular lymphoma, marginal zone lymphoma and high grade transformation of follicular or marginal zone lymphoma who have received at least two lines of standard chemoimmunotherapy or targeted therapy and have persistent disease.
- Patients with CD19 positive B-lymphoid malignancies as defined above with relapsed disease following standard therapy or a stem cell transplant.

Patients who have had prior CD19 targeted therapy such as blinatumomab or CAR T cell therapy are excluded from this study.

Setting New Standards of Excellence

The CAR NK trial is one of many options our Pediatrics SCT-CT program is exploring to advance clinical standards of excellence in cell therapy and transplantation services for children and young adults worldwide. Mahadeo and colleagues have published management guidelines for patients receiving CAR T therapy in [Nature Reviews Clinical Oncology](#). In January 2020, their consensus paper on recognizing and responding to sinusoidal obstructive syndrome, also known as veno-occlusive disease, appeared in [Lancet Haematology](#).

Pediatrics co-faculty [Priti Tewari, M.D.](#), associate professor, and [Sajad Khazal, M.B.Ch.B.](#), assistant professor, lead a multi-institutional Pediatrics SCT-CT Case Conference focused on the management of rare and complex cases that do not have established best practice guidelines. Participants include [Demetrios Petropoulos, M.D.](#), professor of Pediatrics and transplantation specialist, and representatives from 20 programs around the world. To participate in this monthly web conference, please email sjkhazal@mdanderson.org.

To find out if your patient is eligible for a novel trial at MD Anderson, please email PediatricCellTherapy@mdanderson.org.

Learn more about our current immune effector cell therapy trials for children and young adults

Other chimeric antigen receptor (CAR) therapy and natural killer (NK) cell trials

- Phase I/II multi-center study evaluating the safety and efficacy of KTE-X19 in pediatric and adolescent subjects with relapsed/refractory bs-precursor acute lymphoblastic leukemia or relapsed/refractory b-cell non-Hodgkin lymphoma (ZUMA-4). [2016-0316](#)
- Managed access program (MAP) to provide access to CTL019, for acute lymphoblastic leukemia (ALL) or diffuse large b-cell lymphoma (DLBCL) patients with out of specification leukapheresis product and/or manufactured tisagenlecleucel out of specification for commercial release. [2018-0744](#)

Cytotoxic lymphocytes (CTLs)

- Expanded access protocol for tacecleucel for patients with Epstein-Barr virus-associated viremia or malignancies for whom there are no appropriate alternative therapies. [2019-0079](#)
- Phase III multicenter, open-label, trial of ATA129 for allogeneic hematopoietic cell transplant subjects with Epstein-Barr Virus-associated post-transplant lymphoproliferative disease after failure of rituximab [MATCH Study] (Atara 301). [2017-0769](#)
- Phase III multicenter, open label trial of ATA129 for solid organ transplant subjects with Epstein-Barr Virus-associated post-transplant lymphoproliferative disease after failure of rituximab or rituximab and chemotherapy (ALLELE Study) (Atara 302). [2017-0771](#)
- Phase II study of most closely HLA-matched allogeneic cytomegalovirus (CMV) specific cytotoxic T-lymphocytes (CTL) to treat CMV infection after hematopoietic stem cell transplantation (HSCT). [2013-0657](#)
- Phase II study assessing the effect of BK specific CTL lines generated by ex vivo expansion in patients with BK virus infection and JC virus infection. [2014-0279](#)
- Phase I study of the administration of off-the-shelf, expanded, most closely HLA matched, third party adenovirus specific T cells for therapy of adenovirus related disease in immunocompromised patients. [2017-0350](#)
- Phase I/II trial for which cord blood transplantation patients can be considered to determine the optimal dose of intravenous injection of donor-derived cytotoxic T lymphocytes (CTLs) specific for cytomegalovirus, EBV, BKV, and adenovirus. Pediatric and adult patients (with malignant or nonmalignant diseases who are candidates for cord blood transplant) are eligible to participate. Known as the CHEERS trial. [2018-0664](#)

Regenerative medicine

- Expanded access protocol: umbilical cord blood infusions for children with brain Injuries. [2019-0481](#)
- Phase I trial studying any side effects and best method of delivery of bone marrow derived mesenchymal stem cells (MSCs) in improving heart function in patients with heart failure caused by anthracyclines. [2014-0519](#)

Other immune effector cell therapies

- Phase I/II study of ex-vivo expanded allogeneic NK cells for the treatment of pediatric solid tumors. [2017-0085](#)
- Phase II clinical study to assess efficacy and safety of LN-145 (autologous centrally manufactured tumor infiltrating lymphocytes) across multiple tumor types. [2017-0672](#)
- Phase I/II study of anti-viral central memory CD8 veto cells in haploidentical hematopoietic stem cell transplantation. [2018-0221](#)

Training Future Stem Cell Transplantation Experts

Our Pediatric Stem Cell Transplantation and Cellular Therapy Clinical Fellowship provides one year of training to pediatric hematology/oncology or pediatric allergy/immunology for specialists who want to further develop clinical and research expertise in the field under the direction of a faculty mentor.

Core rotations will include inpatient and outpatient patient care, apheresis unit, core stem cell and Human Leukocyte Antigen (HLA) Laboratory, radiation oncology and immunotherapy. This clinical fellowship is approved by the Texas Medical Board. Interested applicants may contact the program director, [Sajad Khazal, M.B.Ch.B.](#), assistant professor of Pediatrics, at sjkhazal@mdanderson.org.



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