N.N. Alexandrov National Cancer Centre of Belarus

Clinical Trial

Official Title:
Treatment Method of Patients with Refractory and Relapsed CD-19 Positive Leukemia and Lymphoma Using Academic Anti-CD19 CAR-T Human Cells (001-0123).

Brief Title
Real World Practice with Academic Anti CD19 CAR-T Cell Therapy in Relapse/Refractory B-cell Lymphoma.

Keywords:
Academic CAR-T cell products, r/r large B-cell lymphomas, efficacy, safety.

Brief Summary
Chimeric antigen receptor (CAR) T-cell therapy has been the standard of care for relapsed/refractory large B-cell lymphomas (R/R LBCLs) since 2018. However, high cost of commercial products limits their application in real-world clinical practice. Academic approach to manufacturing CAR-T cell products can reduce the costs and improve availability and affordability of this therapy option. The aim of the present study is assess the efficacy and safety of the use of academic CAR-T cell products in r/r LBCL patients. This prospective observational study with r/r LBCL patients treated in the NN Alexandrov National Cancer Centre of Belarus. The CAR-T cell product was manufactured using lentiviral vector encoding anti-CD19 CAR.

Name of the Sponsor:
N.N. Alexandrov National Cancer Centre.

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February 9, 2024

INFORMED CONSENT

Protocol Title: "Anti-CD19 CAR-T Cell Therapy for Patients with Relapsed/Refractory B-Cell Lymphoma."

Name of Treatment Facility: N.N. Alexandrov National Cancer Center.

Introduction: Dear patient, you are being offered anti-CD19 CAR-T cell therapy. The term "relapsed" means that the tumor has returned after a period of remission. The term "refractory" means that the tumor is resistant and does not respond to treatment.

Basic information about antigens and T cells:

About antigens:

Antigens are substances that activate (turn on) the immune system. The immune system helps the body fight infections and other diseases.

About T-cells:

T-cells are used by the immune system to recognize antigens that do not belong to the body. T-cells are a type of lymphocyte. T-cells have receptors that they use to bind to specific antigens. When a T-cell binds to an antigen, it sends messages to other cells of the immune system. These cells help destroy the antigen and remove it from the body.

About chimeric antigen receptor (CAR) T-cells:

CAR-T cells are T-cells that have been genetically modified in the laboratory to bind to antigens on cancer cells. When a CAR-T cell binds to a cancer cell, the immune system sends other types of immune cells to destroy the cancer cell and remove it from the body. In autologous CAR-T cell therapy, some T-cells are taken (extracted) from your blood. They are sent to a laboratory, where a new gene is added to them. This process is called genetic modification. The new gene helps them find and destroy cancer cells. After this new gene is added, the T-cells are called CAR-T cells.

Once the CAR-T cells are ready, you'll receive low-dose chemotherapy. This will help prepare your body to maximize the effectiveness of the CAR-T cells. Chemotherapy isn't intended to kill cancer cells. Once your body is ready, the CAR-T cells will be injected into your bloodstream.

CAR-T cell therapy stages:

CAR T-cell therapy consists of six stages. The table below provides an overview and more detailed information about each stage.

Stage	Description
Step 1: T-cell collection (lymphocytapheresis)	Extraction of lymphocytes from the patient's blood. During the procedure, the patient is connected to a device that filters their venous blood, "selects" lymphocytes, and returns the remaining components to the bloodstream. The procedure lasts two to four hours, during

	which at least 100 million cells are extracted. The collected biomaterial is then frozen or sent directly to a lab for genetic modification.
Step 2: T cell modification	Certain types of lymphocytes are modified using a special technology so that a synthetic receptor appears on their surface, which can detect cancer cells and signal the body to destroy them. After modification, CAR-T lymphocytes are multiplied to the required number. While your T-cells are being genetically modified to become CAR-T cells, you will undergo pre-treatment testing and analysis. During this time, you may undergo other treatments (chemotherapy, radiation therapy, targeted therapy) to reduce the tumor burden before CAR-T cell therapy begins. T-cell modification lasts approximately 10-14 days.
Stage 3: lymphodepleting chemotherapy	Lymphodepleting chemotherapy is administered approximately 3-5 days before the CAR-T cell infusion. After a comprehensive preliminary evaluation, the patient undergoes a course of chemotherapy. The goal of the chemotherapy is not to kill the tumor, but to minimize the patient's own white blood cell count. This helps prevent rejection of the new cells transplanted into the bloodstream and promotes their survival and proliferation. The CAR-T cell therapy team will inform you of the duration of the treatment.
Step 4: CAR T cell infusion	Ready-to-use modified T-lymphocytes (CAR-T cells) will be injected into your bloodstream intravenously in a hospital setting. The CAR-T cell infusion lasts approximately 30 minutes.

Stage 5: Early Recovery Period	The CAR T-cell therapy team will monitor your well-being and manage any side effects that arise. You will remain in the hospital. The early phase lasts approximately four weeks.
Stage 6: Long-term recovery	Long-term recovery lasts approximately 100 days from the time of infusion or longer.

After the CAR-T cell infusion, you will be closely monitored for side effects.

The most common side effects of CAR-T cell infusions include cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), and hematologic toxicity (ICAHT).

Cytokine release syndrome (CRS) is a group of symptoms that occur when T-cells attack cancer cells.

Common symptoms of CRS include:

- fever of 38°C or higher;
- flu-like symptoms, such as: muscle aches; headache; chills; unusually tired;
- nausea or vomiting;
- faster heartbeat than usual;
- dizziness or lightheadedness;
- in more severe cases - hypotension and decreased oxygen saturation, sometimes requiring vasopressor therapy and/or artificial ventilation.

Immune effector cell-associated neurotoxicity syndrome (ICANS):

• confusion;
• difficulty finding words;
• tremors;
• longer than usual sleep;
• extreme drowsiness and slower than usual reaction times;
• in severe cases, prolonged seizures, confusion, stupor, coma, sometimes requiring mechanical ventilation.

Hematologic toxicity (ICAHT) includes leukopenia and thrombocytopenia, which may occur and persist for a considerable period after CAR-T cell infusion. During this period, you may be susceptible to various infectious episodes.

These side effects are not permanent. Your healthcare team will closely monitor you for them. Specialists will manage any side effects that occur. It is very important that you or your caregiver report any of these side effects to your healthcare team.

According to publicly available literature, this method of therapy is highly effective; however, in some cases, achieving remission is not possible.

TREATMENT CONSENT

If you have any questions, please ask your treating physician at the Center before signing this document.

• I confirm that I have read and understand this informed consent form. This information was explained to me. I have had the opportunity to ask questions. I have received answers to all my questions.

• I confirm that I have been informed of possible side effects.

• I agree that I am obligated to inform the medical team of any changes in my condition, allergic reactions, or individual intolerance to medications.

• I consent to treatment with anti-CD19 CAR-T cell therapy.

Approved at the Ethics Committee meeting
on February 9, 2024

For any questions, please contact your treating physician by phone:
_____

Patient	_____	_____	_____
	(surname)	(date)	(signature)
Doctor	_____	_____	_____
	(surname)	(date)	(signature)