Plain Language Summary of Clinical Study Results

Bristol Myers Squibb™

Short Study Title:	A Study to Evaluate the Safety and Efficacy of JCAR017 in Pediatric Subjects with Relapsed/Refractory (r/r) B-cell Acute Lymphoblastic Leukemia (B-ALL) and B-cell Non-Hodgkin Lymphoma (B-NHL)
Study Medicine:	Liso-cel, also called lisocabtagene maraleucel, Breyanzi®, JCAR017, BMS-986387
Date of Summary:	26 Jul 2024

Thank You!

Celgene (a Bristol Myers Squibb Company) the sponsor, would like to thank you and your child for taking part in this clinical study for a medicine called liso-cel.

With you and your child's help, we learned more about liso-cel and what effect it has on relapsed/refractory B-cell acute lymphoblastic leukemia (r/r B-ALL) in children and teenagers.

Overview

In this study, researchers wanted to answer the following questions in two study phases.

1. **Phase 1: What is the best dose of liso-cel to treat relapsed/refractory B-cell acute lymphoblastic leukemia (r/r B-ALL)?**

   Relapsed disease means a cancer has come back. Refractory disease means a cancer has stopped responding to treatment.

   - Researchers could not find the best dose of liso-cel to treat children and teenagers with r/r B-ALL. This is because the liso-cel doses tested in this study did not work well enough and there were side effects.
   - Because of this, it was thought that liso-cel was not better than other treatments already available.
   - The study was stopped in Phase 1, and did not reach Phase 2.

2. **Phase 2: How many participants with B-ALL and B-NHL showed improvement in their disease in response to the study treatment?**
   - Researchers were not able to measure the disease response of participants because the study ended before any participants enrolled in Phase 2.

3. **Phase 1 and Phase 2: What side effects did participants have during the study?**
   - Researchers found that the dose levels of liso-cel tested in the Phase 1 portion of the study had unwanted side effects. The most common side effects were decreased blood cell counts and immune system overreaction, also called Cytokine Release Syndrome. Other side effects were also reported in a small number of participants and are described later in the summary. No participants were enrolled or treated in the Phase 2 portion of the study.

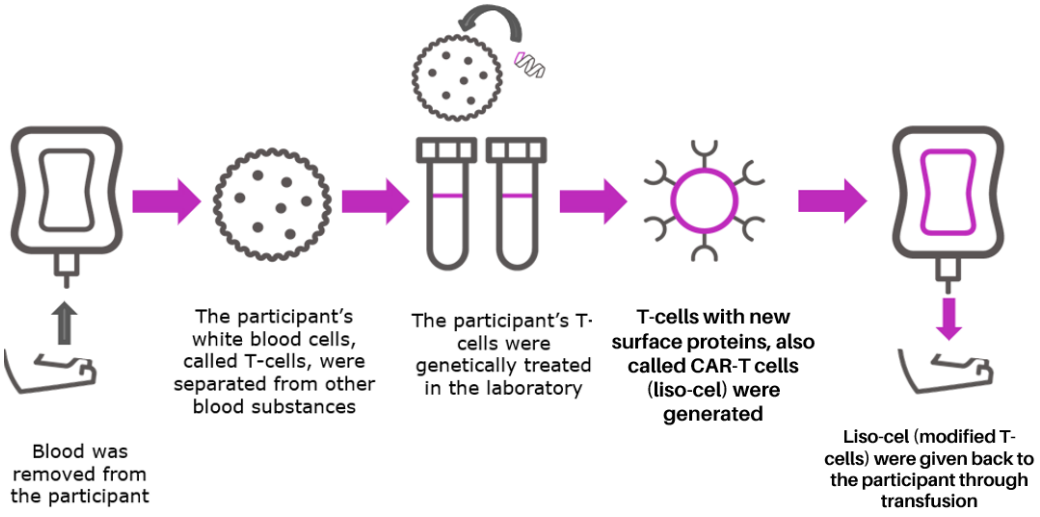
Why was the study done?

The aim of this study was to look at the effects of liso-cel on children and teenagers with B-ALL in Phase 1 and those with B-ALL and B-NHL in Phase 2.

Researchers conducted this study to find a safe and effective treatment for two types of blood cancer, B-cell acute lymphoblastic leukemia (B-ALL) and B-cell non-Hodgkin lymphoma (B-NHL). The researchers wanted to see if a new type of therapy, called liso-cel, could help children and teenagers with these cancers who have not gotten better with other treatments. The researchers planned to look at how safe this new therapy was and how well it worked in treating B-ALL and B-NHL.

Liso-cel is made using a participant's own white blood cells.

- A type of white blood cells, called T-cells, are collected from the participants when they are connected to a machine that collects the cells from their blood. This process is called leukapheresis.
- After the white blood cells are removed from the blood, they are genetically treated in the laboratory. This treatment makes them produce special proteins on their surface.
- T-cells with the new surface proteins, also called CAR-T cells can recognize the cancer cell and kill them.



What happened during the study?

The study started in October 2018 and ended in January 2024. The participants were in the study for up to approximately 26 months, until:

- their B-ALL got worse,
- until they left the study early because of their choice,
- or until the study ended.

Researchers found that liso-cel did not work well enough and there were side effects. A best dose was not found. The study ended before any participants enrolled in Phase 2, therefore researchers could not answer the study questions intended for Phase 2 of the study.

Who took part in the study?

This study included 21 participants with B-ALL who underwent leukapheresis:

- In total, 10 male and 11 female participants underwent leukapheresis.
- They were between 1 and 17 years old.

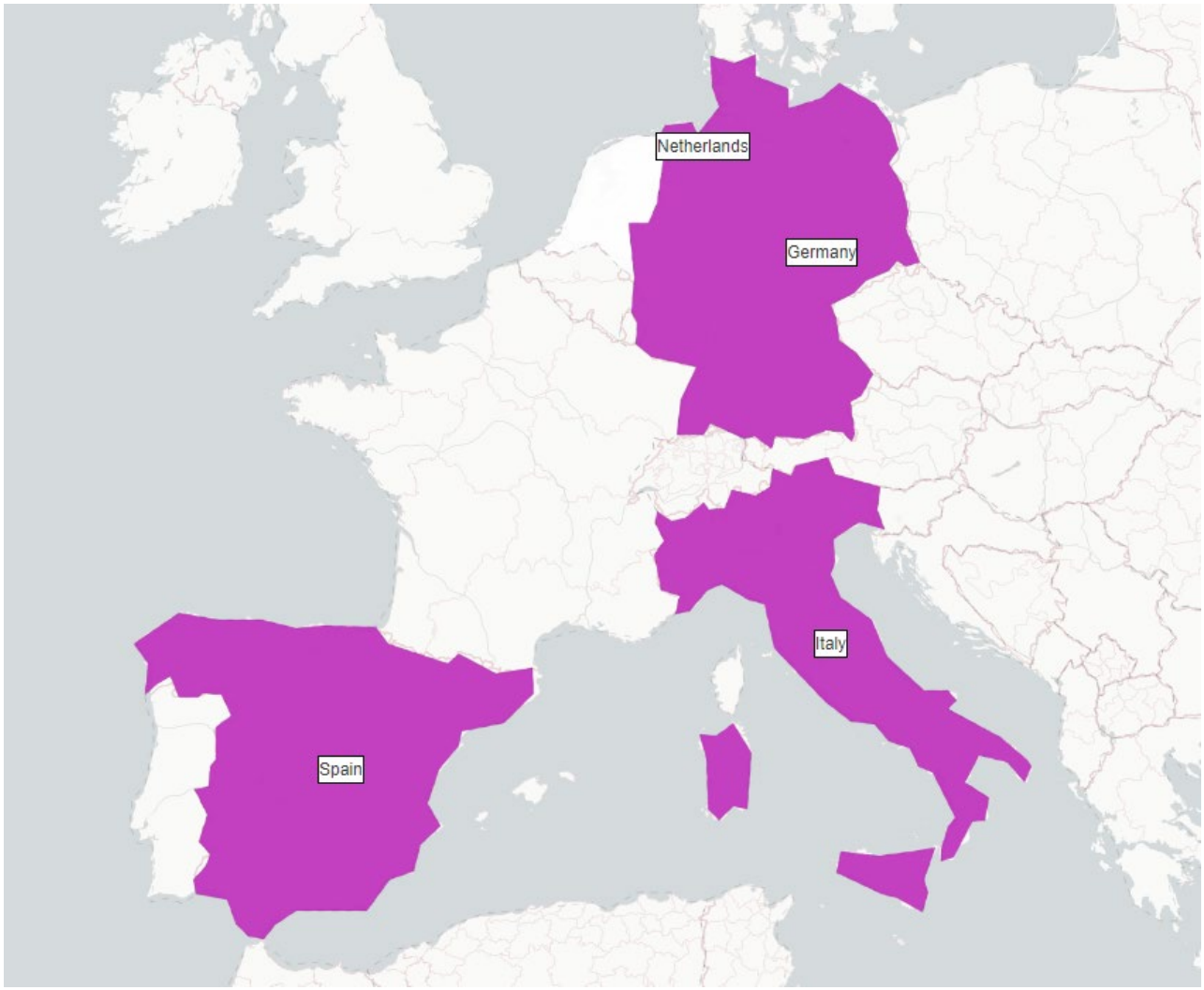
Of the 21 participants who underwent leukapheresis:

- 5 participants did not receive any treatment after leukapheresis.
- 16 participants received lymphodepleting chemotherapy (LDC) after leukapheresis.
- 14 participants received liso-cel after completing the LDC.

Lymphodepleting Chemotherapy (LDC)

LDC is a type of anticancer medicine given to lower the number of white blood cells in the body to prepare the body for CAR-T treatment. Participants received LDC before liso-cel, so their white blood cells did not attack the CAR-T cells that were introduced during the study drug infusion.

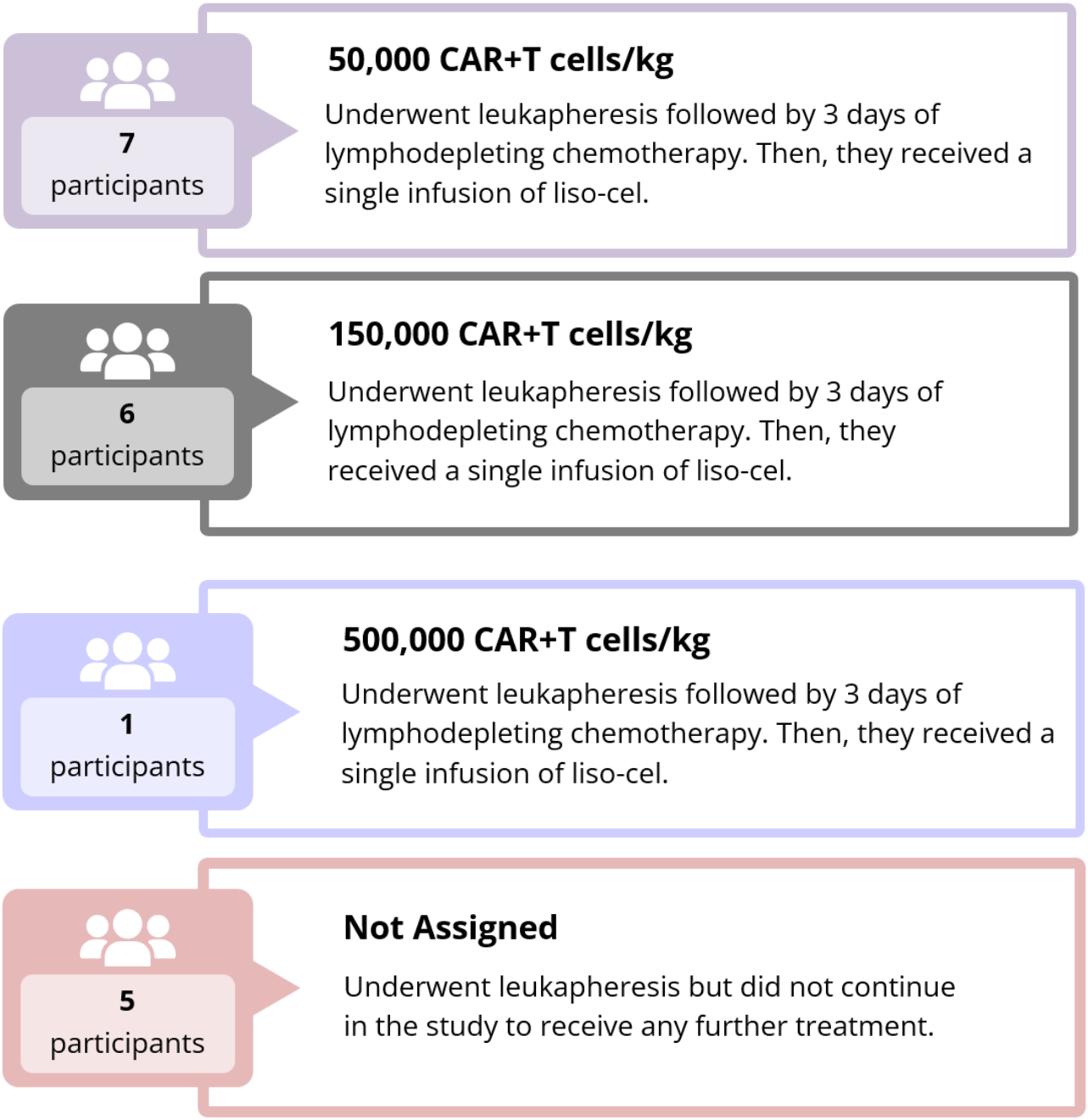
The map below shows which country the study participants were from:



What treatments were studied?

Participants were assigned to receive liso-cel in one of the doses shown below. Each dose is defined by the number of cells the participants received based on their body weight.

Participants underwent leukapheresis to create liso-cel product. Next, the participants received lymphodepleting chemotherapy over 3 days to prepare them for the CAR-T cell infusion, after which they received a single infusion of liso-cel.


7
participants
50,000 CAR+T cells/kg
Underwent leukapheresis followed by 3 days of lymphodepleting chemotherapy. Then, they received a single infusion of liso-cel.
6
participants
150,000 CAR+T cells/kg
Underwent leukapheresis followed by 3 days of lymphodepleting chemotherapy. Then, they received a single infusion of liso-cel.
1
participants
500,000 CAR+T cells/kg
Underwent leukapheresis followed by 3 days of lymphodepleting chemotherapy. Then, they received a single infusion of liso-cel.
5
participants
Not Assigned
Underwent leukapheresis but did not continue in the study to receive any further treatment.

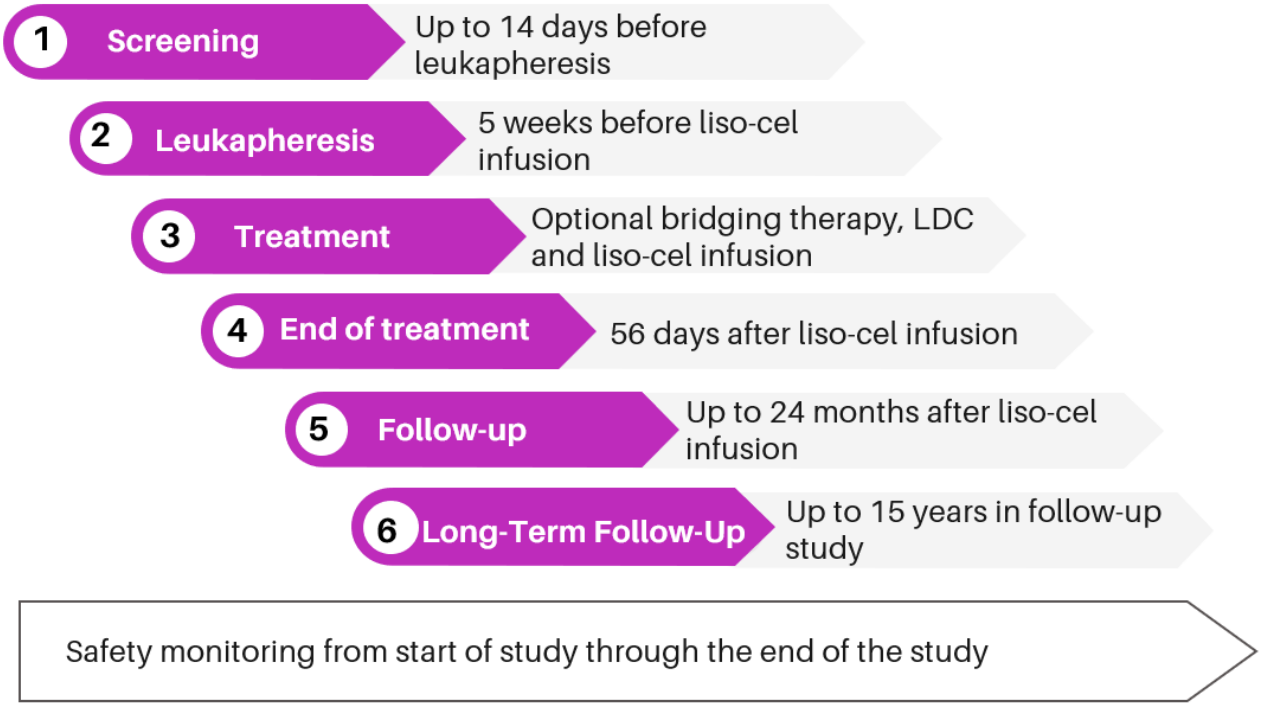
How was the study done?

This section describes what kind of study it was and what happened in the study.

Open-label

This was a single-arm **open-label** study. This means that the participants, their caregivers, the study doctors, and the other study staff knew which treatments the participants got during the study. All participants received the same medicine but at different dose levels.

In this study, participants received liso-cel, but at different dose levels. The figure below shows the timeline of what happened in the study.



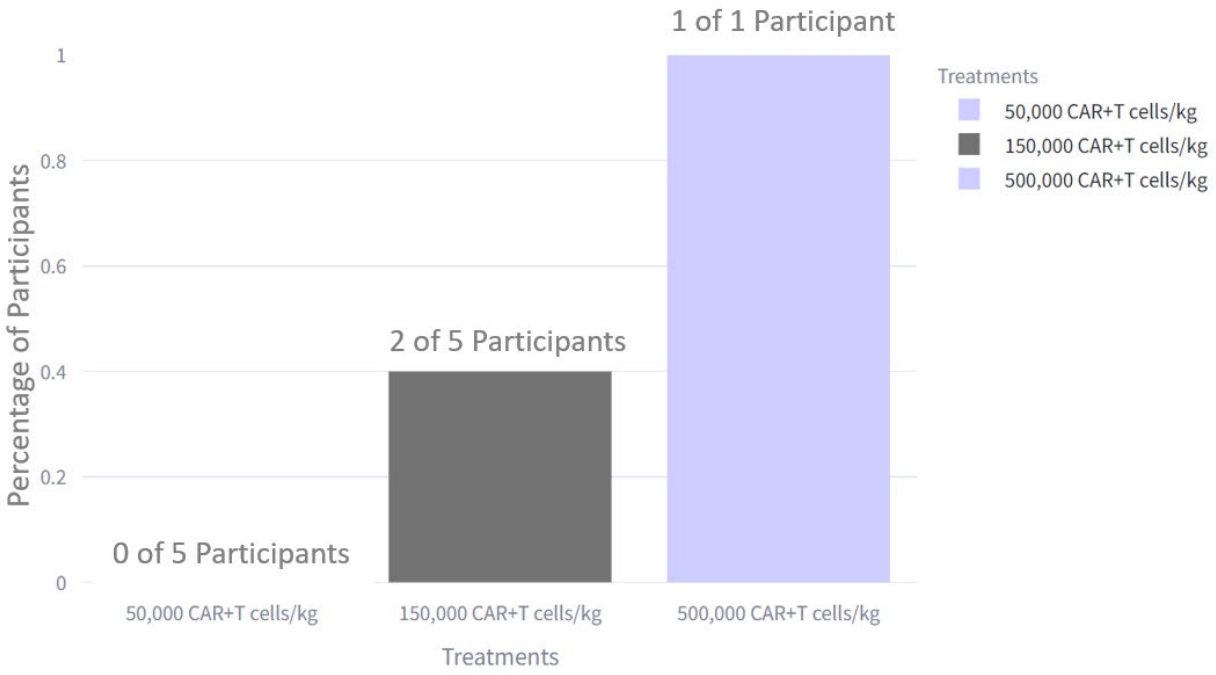
What were the main results of the study?

What is the best dose of liso-cel to treat r/r B-ALL?

Researchers find the best dose levels by monitoring for and measuring the number of side effects that prevent increasing the dose of treatment, also known as Dose-Limiting Toxicities (DLTs). DLTs are effects of a treatment that are severe enough to prevent an increase in dose of that treatment, as decided by the study team.

This helps the researchers choose which dose of liso-cel is the safest and most effective. Examples of DLTs experienced by participants during this study include infusion reaction and neurotoxicity, which is an adverse effect on the structure or function of the central or peripheral nervous system. Some cases of neurotoxicity included an increase in the water content of brain tissue, also called a brain edema.

Eleven participants were included in the DLT evaluation. The graph below shows the **number of participants who experienced Dose-Limiting Toxicities** per dose level.



This study ended early, so not all planned dose levels were tested. More research was planned for Phase 2 of the study. However, since the study ended before any participants started Phase 2, no data is available.

What side effects did participants have during the study?

The safety of every participant is important throughout the development and testing of study medicines. The study doctors keep a record of all symptoms the participants have during the study.

Symptoms or abnormal findings that study doctors think may or may not be related to treatment are called **"side effects."**

A side effect that is life-threatening, needs hospital care, or is considered by the study doctor as medically important is called a **"serious side effect."**

This section includes the safety results of 14 participants who received the liso-cel infusion.

The table below shows the number of participants who had side effects during this study which may or may not be related to the study drug:

Overall side effects	**50,000 CAR+T cells/kg** 7 participants	**150,000 CAR+T cells/kg** 6 participants	**500,000 CAR+T cells/kg** 1 participant
	Number of participants (%)		
How many participants had any side effects related to liso-cel?	5 (71%)	5 (83%)	1 (100%)
How many participants had serious side effects related to liso-cel?	1 (14%)	3 (50%)	1 (100%)
How many participants stopped taking the study medicine because of side effects?	0 (0%)	0 (0%)	0 (0%)
How many participants died from side effects?	0 (0%)	0 (0%)	0 (0%)

What were the side effects?

The list below shows the 5 most common side effects reported during this study which may or may not have been related to the study drug:

- Lower-than-normal number of healthy red blood cells, also called Anemia (11 participants [79%])
- Lower-than-normal number of platelets, also called Thrombocytopenia (8 participants [57%])
- Lower-than-normal number of white blood cells, also called Leukopenia (6 participants [43%])
- Lower-than-normal number of neutrophils, also called Neutropenia. A neutrophil is a type of white blood cell that your bone marrow makes. (6 participants [43%])
- Immune system overreaction, also called Cytokine Release Syndrome (9 participants [64%])

What were the serious side effects?

The list below shows all the serious side effects reported during this study which may or may not have been related to the study drug:

- Immune system overreaction, also called Cytokine Release Syndrome (3 participants [21%])
- Lung infection, also called Pneumonia (1 participant [7%])
- Abnormal function of organs due to the body responding to an infection known as sepsis (1 participant [7%])
- Virus in the bloodstream, also called Viremia (1 participant [7%])
- Damage to the brain or nervous system caused by toxic substances, also called neurotoxicity. In two cases, the neurotoxicity was with an increase in water content of the brain tissue, also called brain edema (3 participants [21%])
- Brain Edema (1 participant [7%])
- Blood collecting in space between skull and outermost membrane, also called Extradural Hematoma (1 participant [7%])

- Infusion related reaction (1 participant [7%])

How has this study helped participants and researchers?

You and your child have helped us learn more about the safety of liso-cel and how it works in participants with relapsed/refractory (r/r) B-cell acute lymphoblastic leukemia (B-ALL) in children and teenagers.

Researchers must look at the results of many studies to decide which treatments work and are safe.

This summary includes only the main results from this one study. Other studies may show new information or different results.

Other studies of liso-cel are ongoing. If you have questions about the study results or liso-cel, please speak with a doctor or staff member at the study site.

Always talk to a doctor before making any treatment decisions.

Where can I learn more about this study?

You can find more information about this study on the websites listed below.

https://www.clinicaltrials.gov/study/NCT03743246?term=LISO-CEL-BCM-004&rank=1

https://www.clinicaltrialsregister.eu/ctr-search/trial/2018-001246-34/BE

Full Study Title: A Phase 1/2, Open-Label, Single Arm, Multicohort, Multicenter Trial to Evaluate the Safety And Efficacy Of JCAR017 In Pediatric Subjects With Relapsed/Refractory B-ALL And B-NHL

Study Identification: JCAR017-BCM-004

Celgene (a Bristol Myers Squibb Company) is the sponsor of this study.

For general contact information, go to the link below:

www.globalbmsmedinfo.com