Plain Language Summary

Results from a clinical trial called "ALLELE"

Tabelecleucel in relapsed or refractory EBV-positive PTLD after blood stem cell transplant or solid organ transplant

About this summary

This summary focuses on the results from the ALLELE clinical trial. These results were published in *The Lancet Oncology* journal in 2024, by Mahadeo and collaborators. These results are based on the 43 patients from around the world who entered the trial between June 2018 and November 2021. At the time these results were published, the trial was still ongoing.

Sections

Key terms

ALLELE is pronounced *uh-LEEL*

Tabelecleucel is pronounced *tab-el-uh-KLOO-sel*

Relapsed: disease that responded to treatment but returned after the treatment was complete

Refractory: disease that didn't respond to treatment

EBV-positive: involves the Epstein-Barr virus

PTLD: post-transplant lymphoproliferative disease or disorder

Blood (hematopoietic) **stem cell transplant** is also called **HSCT**

Solid organ transplant is also called **SOT**

ALLELE is a **global**, **multicentre**, **single-arm**, **open-label**, **phase 3** trial, meaning:

- The trial is conducted at multiple sites in different countries.
- All patients in the trial receive tabelecleucel. There is no comparison treatment or placebo.
- All patients and researchers involved in the trial know that the drug being studied is tabelecleucel.

The goal of ALLELE is to determine **how well tabelecleucel works** and **its safety profile** in patients with EBV-positive PTLD that didn't go away or came back after treatment.

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What is the ALLELE clinical trial?

The ALLELE clinical trial is studying a drug called **tabelecleucel** as a potential treatment for certain types of post-transplant lymphoproliferative disease (PTLD). Specifically, the trial studies PTLD that:

- is positive for Epstein-Barr virus (EBV-positive), and
- didn't go away or came back after treatment.

Doctors also call this condition **relapsed or refractory (R/R) EBV-positive PTLD**.

Lympho refers to lymphocytes, a type of white blood cell. **Proliferative** means growing or multiplying quickly.

Epstein-Barr virus (EBV) is one of the most common viruses that people can get. Nearly everyone will pick up an EBV infection in their lifetime. Most adults carry EBV without any symptoms, but EBV may cause symptoms in people with a weakened immune system.

Relapsed means disease that responded to treatment but returned after the treatment was complete.

Refractory means disease that didn't respond to treatment.

To respond or have a response means to see an improvement related to treatment.

Initial treatment is the first treatment a patient gets for a disease. It is sometimes called "first line" treatment.

Why is this clinical trial being done?

The standard treatments for PTLD include:

- reduction in immunosuppression
- anti-CD20 monoclonal antibody therapy (rituximab)
- surgery
- radiotherapy
- chemotherapy

In EBV-positive PTLD after HSCT, up to 50% of patients respond to initial treatment. After SOT, over 60% of patients respond.

The prognosis for patients who don't respond to initial treatment or who relapse is poor, and effective therapies are urgently needed. ALLELE is studying how well tabelecleucel works and its safety profile in this group of patients.

What is tabelecleucel?

Tabelecleucel is an investigational drug made of immune cells that fight EBV, called EBV-cytotoxic T lymphocytes (EBV-CTLs). These cells are collected from healthy donors who have immunity against EBV and then used to create a bank of cells. From this bank, tabelecleucel is appropriately matched to patients needing treatment.

Tabelecleucel is not genetically modified. Tabelecleucel is an immunotherapy, and not a chemotherapy.

What is EBV-positive PTLD?

EBV-positive PTLD is an ultra-rare and sometimes deadly condition. PTLD is when lymphocytes grow out of control after transplant. PTLD can develop in anyone taking immunosuppressants after allogeneic HSCT or SOT.

To learn more PTLD, visit: https://aboutptld.com

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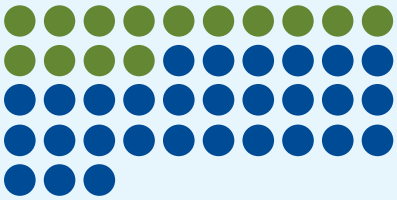
Who are the results based on?

The updated results are based on the 43 patients who enrolled between June 2018 and November 2021 in multiple countries.

Transplant type

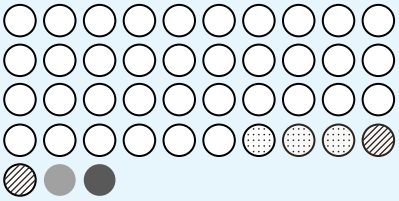
Trial results in section 4 are shown by transplant type.

- 14 patients previously had an HSCT
- 29 patients previously had a SOT



Race

- White: 36 (84%)
- Other: 3 (7%)
- Asian: 2 (5%)
- Black or African American: 1 (2%)
- Native Hawaiian or Other Pacific Islander: 1 (2%)

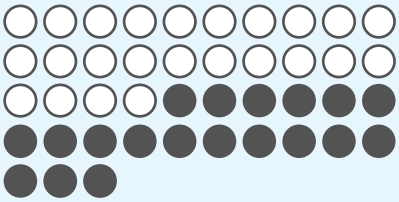


Age and Sex

The median age of patients was 48.5 years.

This means that about half the patients were older than 48.5 and half were younger.

- 24 (56%) were male
- 19 (44%) were female



Patients in the trial met all the inclusion criteria, including:

- Having active EBV-positive PTLD after an HSCT or SOT
- Having EBV-positive PTLD that did not go away or came back after standard treatment
- Having adequate organ function and reasonable performance status[?]
- Being an appropriate HLA[?] match for available cells in the tabelecleucel bank

Patients were not included if they met any of the exclusion criteria, including:

- Having certain medical conditions, including:
  - Burkitt lymphoma
  - classical Hodgkin lymphoma
  - any T-cell lymphoma
  - graft-versus-host disease
  - CNS PTLD that is either untreated or actively being treated
- Having poor performance status
- Being on certain medications
- Being pregnant or breastfeeding

Performance status describes how much a disease affects a patient's ability to function in daily life. It measures a patient's ability to:

- care for themselves
- perform daily tasks
- be physically active

Researchers use standardized tools to assess this. The ECOG and Lansky scales are the tools used for this trial.

HLA (human leukocyte antigens) are genetic markers on most types of cells. HLAs are different from person to person. The immune system uses HLAs to identify and respond to foreign substances.

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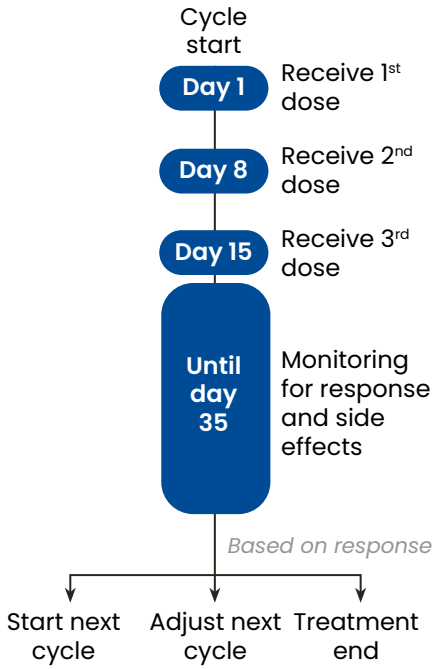
What steps were followed?

Treatment

All patients received tabelecleucel intravenously[?] over 5 to 10 minutes. The dose that each patient received was calculated based on their body weight, at 2 million cells per kilogram.

Patients received tabelecleucel in 35-day cycles. During each cycle, patients received a dose of tabelecleucel on days 1, 8, and 15. Their response[?] and side effects were monitored to the end of the cycle. The number of cycles a patient received depended on how they responded to treatment. If there was no response after one cycle, the following cycle was sometimes adjusted to use tabelecleucel made from a different healthy donor.



Treatment ended for the patient when they:

- reached maximal response[?] to treatment; or
- reacted badly to the treatment and had to stop because of severe side effects; or
- started another therapy that was not being investigated in this trial; or
- didn't respond to treatment after trying tabelecleucel made from:
  - up to 4 different healthy donors (for HSCT)
  - up to 2 different healthy donors (for SOT)

Intravenously (IV) means through a vein, usually with a needle.

To respond or have a response means to see an improvement related to treatment.

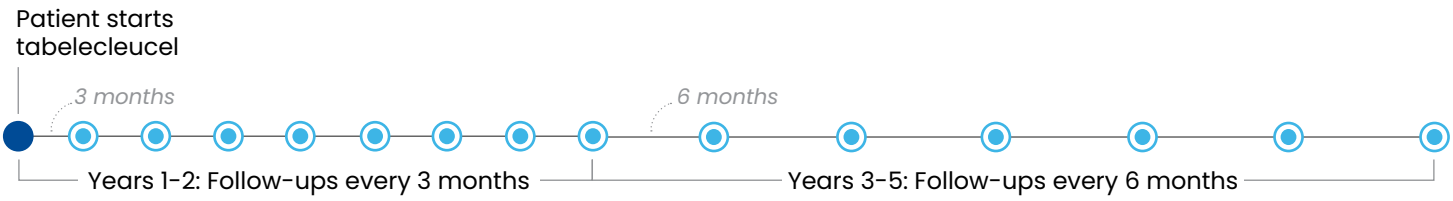
Maximal response is the most improvement possible with a treatment. No further improvements are seen with additional treatment.

Medical imaging is using technology to see structures inside the body. The types of imaging used in this trial included PET/CT scans.

Follow-up

Patients had up to 5 years of follow-up after starting tabelecleucel. Patients were regularly assessed every 3 months for up to 24 months, and every 6 months thereafter. Follow-up included medical imaging[?] at specific points and regular tracking of side effects.

Patients were able to leave the trial at any time.



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What are the results so far?

What is the high-level takeaway?

According to the authors of the article, the results showed that treatment with tabelecleucel was linked to clinically meaningful outcomes for people with relapsed or refractory EBV-positive PTLD after treatment with current options.

- Roughly half of participants responded to tabelecleucel.
- Patients who responded also had improved survival rates.
- There was no evidence of immune-related adverse events typically seen in other therapies involving immune cells.

This represents a major step forward in the treatment of this ultra-rare and sometimes deadly condition.

How many treatment cycles and doses did patients end up receiving?

Patients with an HSCT went through a median of **3 cycles**

This means roughly half of these patients went through fewer than 3 cycles, and half went through more than 3 cycles.

Patients with an SOT went through a median of **2 cycles**

This means roughly half of these patients went through fewer than 2 cycles, and half went through more than 2 cycles.

Patients with an HSCT received a median of **9 doses**

This means roughly half of these patients received fewer than 9 doses, and half had more than 9 doses.

Patients with an SOT received a median of **6 doses**

This means roughly half of these patients received fewer than 6 doses, and half had more than 6 doses.

How long were patients on treatment?

Patients with an HSCT were on treatment for a median of **2.8 months**

This means roughly half of these patients were on treatment for less than 2.8 months, and half were on treatment for more than 2.8 months.

Patients with an SOT were on treatment for a median of **1.9 months**

This means roughly half of these patients were on treatment for less than 1.9 months, and half were on treatment for more than 1.9 months.

Main Measurement

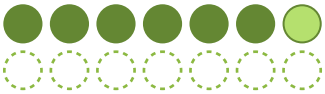
The **main measurement** of this trial is the **objective response rate**. This is the percentage of patients who saw any improvement after treatment with tabelecleucel. This number is calculated based on the number of patients who had a **complete response** or **partial response**.

- **Complete response** is when all signs of PTLD go away after treatment. This does not always mean the disease is cured.
- **Partial response** is when PTLD improves but hasn't disappeared after treatment.

Objective Response Rate

What percentage of patients saw any improvement after treatment with tabelecleucel?

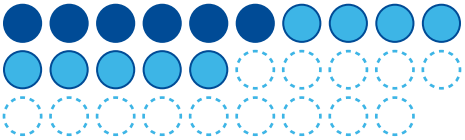
For patients with an HSCT, the objective response rate was 50%



A total of 7 of the 14 patients with an HSCT saw a response after treatment with tabelecleucel:

- 6 patients (43%) had a complete response.
- 1 patient (7%) had a partial response.
- 7 patients (50%) didn't respond.

For patients with an SOT, the objective response rate was 52%



A total of 15 of the 29 patients with an SOT saw a response after treatment with tabelecleucel:

- 6 patients (21%) had a complete response.
- 9 patients (31%) had a partial response.
- 14 patients (48%) didn't respond.

Objective response rates were similar between patients of different age, sex, and race.

Other Measurements

Overall Survival

How long did patients live between the first dose of tabelecleucel and death from any cause?

Not yet reached

Among patients with an HSCT, **more than half were still alive** at the time of reporting.

In other words, the median overall survival was not reached.

Among patients who responded to treatment, more than half were still alive at the time or reporting.

Among patients who didn't respond, the median overall survival was 11 months. This means that about half of these patients lived longer than 11 months, and half lived a shorter time.

16.4 months

Among patients with an SOT, the **median overall survival was 16.4 months**.

This means that about half of the patients lived longer than 16.4 months, and half lived for a shorter time.

Among patients who responded to treatment, more than half were still alive at the time of reporting.

Among patients who didn't respond, the median overall survival was 5 months. This means that about half these patients lived longer than 5 months, and half lived a shorter time.

Overall, patients who responded to treatment had a longer survival than those who didn't.

Time to Response

How long did it take for patients who responded to see an improvement?

1 month

It took patients with an HSCT a **median of 1 month** to see an improvement

This means about half of these patients saw an improvement in less than 1 month, and half saw an improvement in more than 1 month.

1.1 months

It took patients with an SOT a **median of 1.1 months** to see an improvement

This means about half of these patients saw an improvement in less than 1.1 months, and half saw an improvement in more than 1.1 months.

Duration of Response

How long did the response last for these patients?

23 months

For patients with an HSCT, the response lasted a **median of 23 months**

This means the response lasted less than 23 months in about half of these patients, and more than 23 months in the other half.

15.2 months

For patients with an SOT, the response lasted a **median of 15.2 months**

This means the response lasted less than 15.2 months in about half of these patients, and more than 15.2 months in the other half.

Other Measurements: Safety

The trial studied and tracked adverse events to understand the safety profile of tabelecleucel. Adverse events are unwanted symptoms or medical issues that happened during the trial. Adverse events include side effects. They are not always related to treatment.

Researchers have divided adverse events into two categories:

- **Adverse events related to treatment**: These are adverse events that are reported as related to tabelecleucel.
- **Adverse events during treatment**: These are adverse events that happen in a specific time frame: from the first dose of tabelecleucel until 30 days after the last dose. Despite the timing, they are not always related to tabelecleucel. Researchers also call these "treatment-emergent adverse events."

Adverse events related to treatment

Serious treatment-related adverse events were reported in 4 of 43 patients. They were:

- red and swollen rash
- low blood pressure
- low oxygen levels in tissues
- fever
- diarrhea

The serious treatment-related adverse events didn't lead to treatment being stopped.

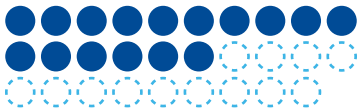
Adverse events during treatment

The **most common adverse events during treatment** were:

PTLD progression (getting worse)

5 of 14 (36%) of patients with an HSCT experienced PTLD progression

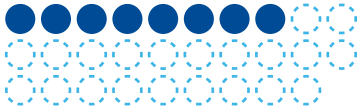
16 of 29 (55%) of patients with an SOT experienced PTLD progression



Fever

5 of 14 (36%) of patients with an HSCT experienced fever

8 of 29 (28%) of patients with an SOT experienced fever

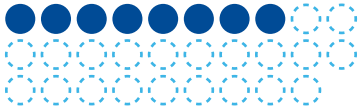


The **most common adverse events during treatment** (continued):

Diarrhea

4 of 14 (29%) of patients with an HSCT experienced diarrhea

8 of 29 (28%) of patients with an SOT experienced diarrhea



Serious adverse events during treatment were reported in **23 of 43 (53%)** patients.

Immune-related adverse events

Because tabelecleucel is made with human cells, researchers were interested in any immune-related adverse events.

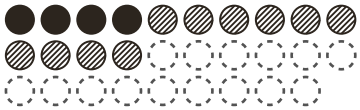
- There were **no reports** of tumor flare reaction, cytokine release syndrome, neurotoxicity syndrome, transmission of infectious diseases, marrow rejection, or infusion-related reactions
- **Chronic graft-versus-host disease (GvHD)** was reported as **non-serious and unrelated to tabelecleucel** in **one** patient with an HSCT. Treatment was not changed or interrupted.
- **Potential risk of rejection** was reported as **non-serious and unrelated to tabelecleucel** in **one** patient with a history of SOT and transplant rejection before starting tabelecleucel. Treatment was not changed or interrupted.

What other events happened?

- During the trial, a total of 4 (29%) of 14 patients in the HSCT group and 14 (48%) of 29 in the SOT group died
  - ● 5 patients (1 HSCT, 4 SOT) died from adverse events unrelated to tabelecleucel
  - ▨ 13 patients (3 HSCT, 10 SOT) died from other causes:
    - disease progression (6 patients)
    - adverse events that happened more than 30 days after the last dose (2 patients)
    - unknown (5 patients died after the end of the study)
- Some patients left the trial. The reasons for leaving included voluntarily withdrawing consent and losing contact with the trial.

Patients with an HSCT

Patients with an SOT



Overall, the reported adverse events were consistent with the high disease burden and transplant complications in this trial's patient population.

This is the end of the summary

About Plain Language Summaries

Clinical trials are only possible because of the participants who volunteer to receive investigational treatments and be monitored over extended periods. Historically, the results of clinical trials are published in medical journals for a specialized, expert audience. Because of this, it can be difficult for clinical trial participants to understand these results of the research they helped make possible. Plain Language Summaries try to fill that gap by translating the results of clinical research into something that is more easily understood without specialized medical training.

Original Article

Tabelecleucel for allogeneic haematopoietic stem-cell or solid organ transplant recipients with Epstein–Barr virus-positive post-transplant lymphoproliferative disease after failure of rituximab or rituximab and chemotherapy (ALLELE): a phase 3, multicentre, open-label trial

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Link to the article

https://www.sciencedirect.com/science/article/abs/pii/S1470204523006496?via%3Dihub

The ALLELE trial is ongoing. The data reported in this summary was collected while the trial was funded by Atara Biotherapeutics. The trial is now being funded by Pierre Fabre Medicament.

Where else can I find information?

As of October 2025, the ALLELE trial is still ongoing and looking for participants. For information about the trial in the US, visit: https://PTLDclinicaltrial.com

For information about the trial in other countries, visit: https://clinicaltrials.gov/study/NCT03394365

Tabelecleucel is also being studied in other EBV-related diseases. For more information, visit: https://www.clinicaltrials.gov/study/NCT04554914

Pierre Fabre

Electronic Certificate

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