

Letetresgene autoleucl is not approved to treat the condition discussed in this summary

Final Results of a Pilot Study Investigating the Effects of Letetresgene Autoleucl (Lete-Cel) in Patients With Advanced Synovial Sarcoma

This document provides a short summary of information about this Phase 1 synovial sarcoma clinical study presented at the Society for Immunotherapy of Cancer (SITC) and Connective Tissue Oncology Society (CTOS) Annual Meetings 2020 (virtual format). At the end of this document there are links to websites where you can find more information about this study.

Full title of presentation:	Final analysis of the Phase 1 trial of NY-ESO-1–specific T-cell receptor (TCR) T-cell therapy (letetresgene autoleucl; GSK3377794) in patients with advanced synovial sarcoma (SS)
Study number:	208466; NCT01343043
Who sponsored the study:	GlaxoSmithKline (GSK) and Adaptimmune

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Why was the study carried out?

To find out:



How effective is letetresgene autoleucel (lete-cel), a personalized, genetically modified immune cell therapy, at treating patients with advanced synovial sarcoma whose tumors express NY-ESO-1?

Whether lete-cel is effective in patients with high or low NY-ESO-1 tumor expression and which type of immune cell depletion chemotherapy enhances lete-cel treatment?

Which side effects occur as a result of lete-cel therapy?

About the study



Patients could join the study if they had synovial sarcoma that was recurrent, which had spread throughout the body and/or could not be surgically removed. Patients must have already received certain standard treatments for synovial sarcoma. Patients also had to express a marker called human leukocyte antigen A*02.

Everyone in the study received the same lete-cel treatment, but first they were split into four groups depending on their NY-ESO-1 tumor expression. Before lete-cel treatment, patients had to receive immune cell depletion chemotherapy, this was different between the four groups.

Group 1

High NY-ESO-1 expression

Patients received a **high dose*** of chemotherapy before lete-cel treatment

*Fludarabine (30 mg/m²/day for 4 days) and cyclophosphamide (1800 mg/m²/day for 2 days).

Group 2

Low NY-ESO-1 expression

Patients received a **high dose*** of chemotherapy before lete-cel treatment

*Fludarabine (30 mg/m²/day for 4 days) and cyclophosphamide (1800 mg/m²/day for 2 days).

Group 3

High NY-ESO-1 expression

Patients received a **high dose*** of a single chemotherapy before lete-cel treatment

*Cyclophosphamide (1800 mg/m²/day for 2 days).

Group 4

High NY-ESO-1 expression

Patients received a **low dose*** of chemotherapy before lete-cel treatment

*Fludarabine (30 mg/m²/day for 3 days) and cyclophosphamide (600 mg/m²/day for 3 days).



The investigators recorded how well each patient responded clinically to the treatment, and the impact on outcomes. They monitored any side effects and other signs relating to drug safety.

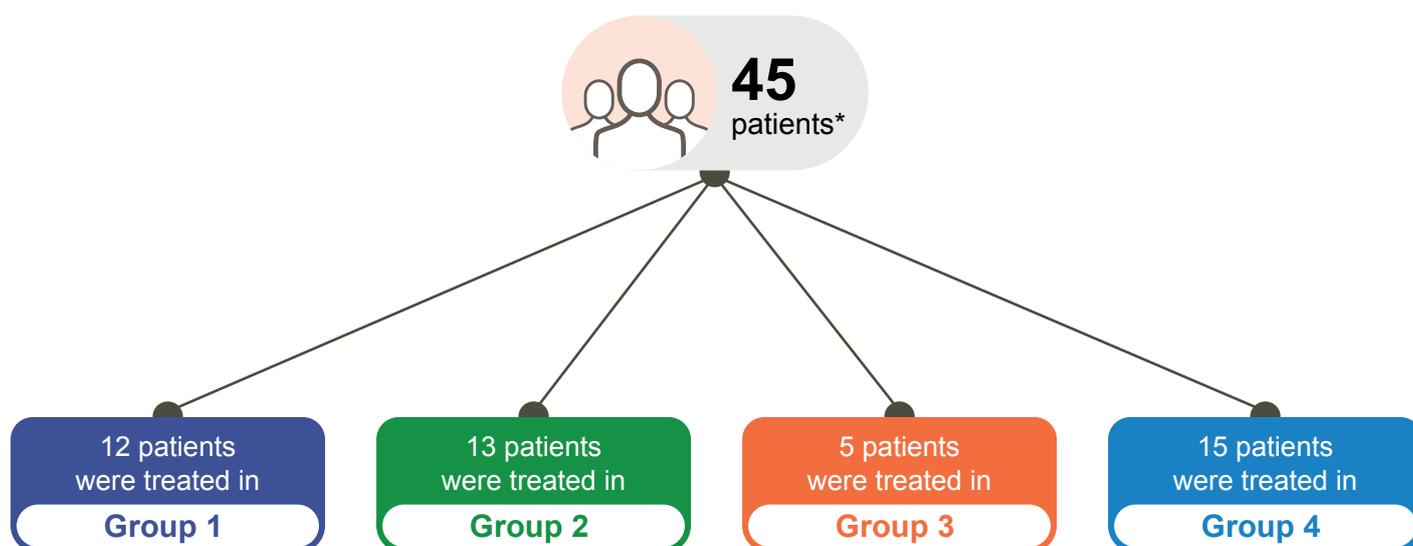
Timeline: Patients were monitored for up to 5 years after lete-cel treatment or until their disease progressed. After 5 years, eligible patients could enter a long-term follow-up study.

About this analysis

Some of the data from this trial has been **published previously**.¹⁻³

The current analysis shows the **final results** from the study, including how effective lete-cel is at treating synovial sarcoma, and which side effects occur.

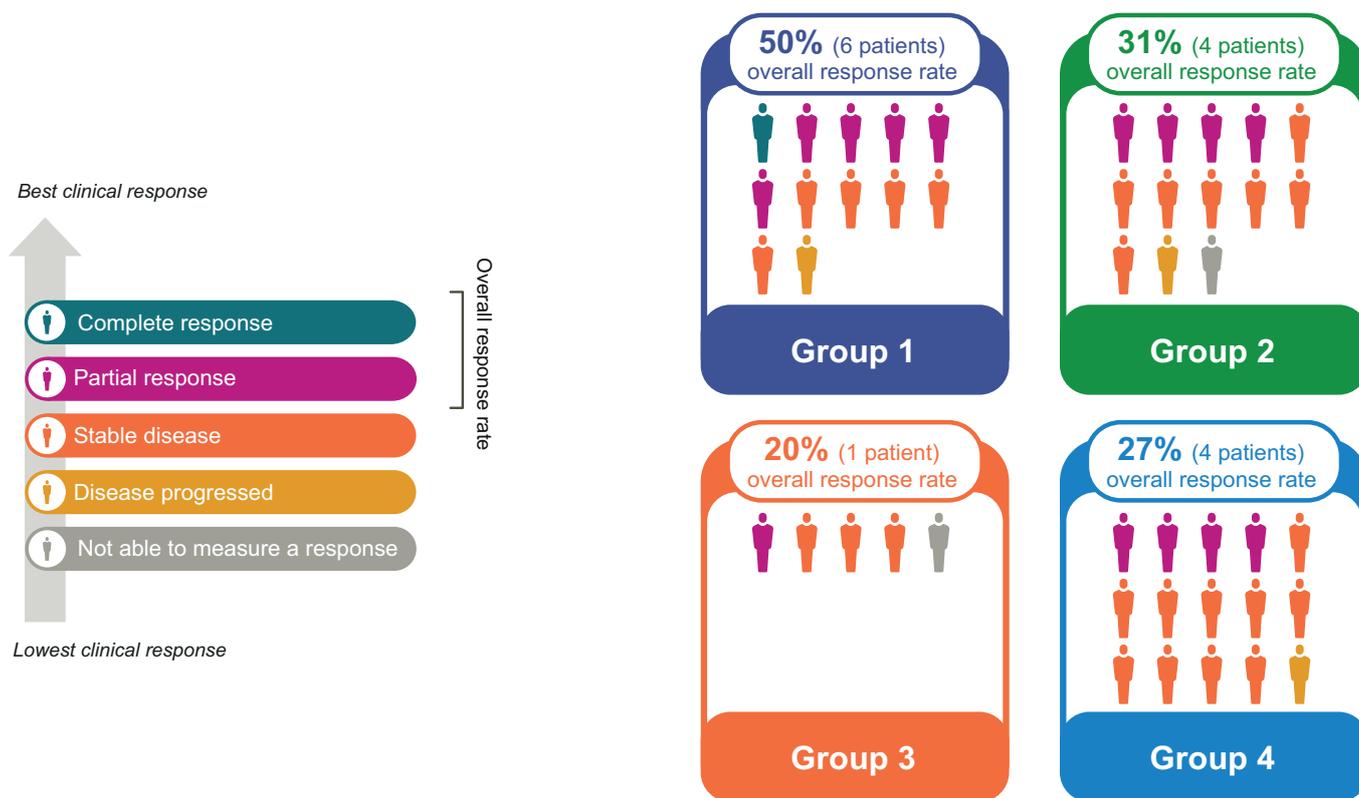
Study patients



*Five more patients joined the study but did not receive lete-cel therapy.

What were the results of the study?

Across all groups, one third of patients responded to lete-cel treatment. In Group 1, half the patients had a clinical response to lete-cel.



Response Criteria

Results

How did the treatment impact outcomes?

The median* length of time that patients showed a clinical response was:



Median* time that patients remained free from synovial sarcoma worsening (in weeks):

Group 1	15.4
Group 2	13.1
Group 3	8.6
Group 4	22.4

Median* time that patients survived (in months)[†]:

Group 1	24.3
Group 2	9.9
Group 3	19.9
Group 4	Not yet available

*The median is the middle value when all values are sorted from lowest to highest, so half of all values fall above the median and half fall below.

[†]Some patients are still being followed, these results are from January 27, 2020.

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What side effects occurred during the study?

Most patients experienced at least one side effect.

Group 1

50% (6 of 12 patients) Reported a serious side effect

Group 2

54% (7 of 13 patients) Reported a serious side effect

Group 3

80% (4 of 5 patients) Reported a serious side effect

Group 4

40% (6 of 15 patients) Reported a serious side effect



The most common side effects of moderate or severe intensity were:

- A drop in white blood cells (all types and specific kinds of white blood cells), red blood cells, and platelets, which is common following chemotherapy.

Side effects of special interest included:

- Cytokine Release Syndrome, in which a large number of immune cells release proteins to trigger further immune cell activation. This occurred in 20 of 45 (44%) patients and was mild in 80% of affected patients.
- Guillain-Barre Syndrome, an immune disorder affecting the nervous system. This occurred in 2 of 45 (4%) patients, who both recovered. It is not yet clear whether this side effect was due to lete-cel treatment.



Guidance on where to find further information is available at the bottom of this summary.

What were the main conclusions reported by the researchers?



- The final results of this study show that lete-cel has anti-tumor properties with acceptable side effects in patients with advanced synovial sarcoma who have already received standard treatment.
- Patients in all four groups showed a response. The highest effect was seen in Group 1, in which patients had tumors with high NY-ESO-1 expression and received a high dose of immune cell depletion chemotherapy.
- Lete-cel is being studied further to understand how effective it is and which side effects occur in patients with synovial sarcoma, including those who have already received standard treatments or who have never been treated. This study (NCT03967223) is currently enrolling.

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Where can I find more information?

Clinical studies have unique study numbers that are included in publications and other information about the study. The unique study numbers associated with this study are shown below with internet links to other information.

Organization	Website	Study Number
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT01343043
GlaxoSmithKline (GSK)	www.gsk-clinicalstudyregister.com	208466

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References

1. D'Angelo SP, et al. Presented at the Society for Immunotherapy of Cancer Congress 2019, National Harbor, MD; November 6–10, 2019.
2. D'Angelo SP, et al. *Cancer Discov* 2018;8(8):944–57.
3. Ramachandran I, et al. *J Immunother Cancer* 2019;7:276.