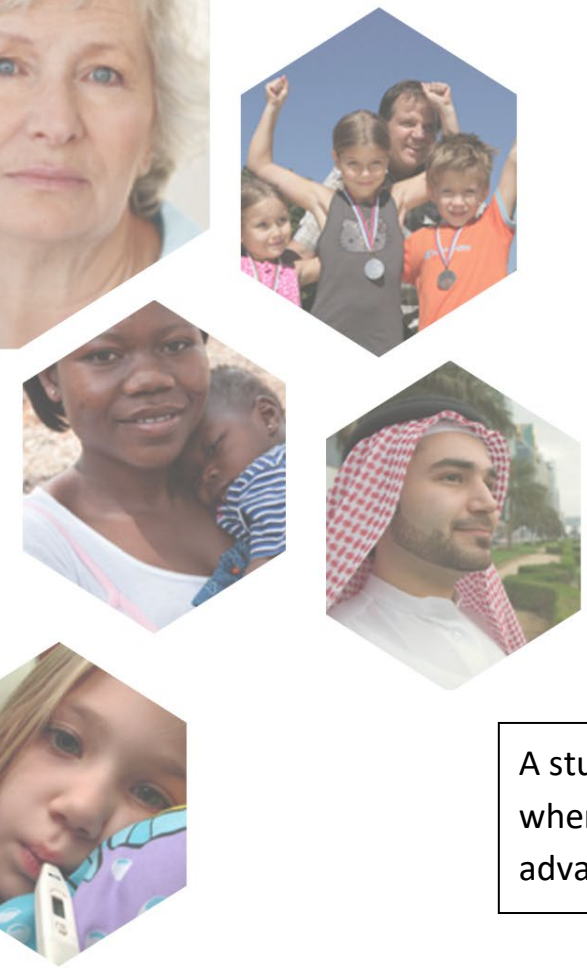

Who sponsored this study?

GSK

Clinical Support Help Desk

- http://www.clinicalsupporthd.gsk.com
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- Telephone: +1-438-899-8201

A study to compare the effect of feladilimab or placebo when given along with pembrolizumab in participants with advanced head and neck cancers

GSK would like to thank all those who took part in this clinical study. We think it is important that you know the study results. We hope it helps you understand and feel proud about your important role in medical research.

General information about the clinical study

When was this study done?

The study started in November 2019 and is still ongoing. In April 2021, it was decided by GSK that no further participants will enter the study and the existing participants will stop receiving the study medicine, feladilimab. This is referred to as data cut-off in the summary. However, participants could continue on the study and receive pembrolizumab. This summary provides details only up to the data cut-off.

Which medicines were studied?

In this study, participants received one of the following two study medicines along with pembrolizumab.

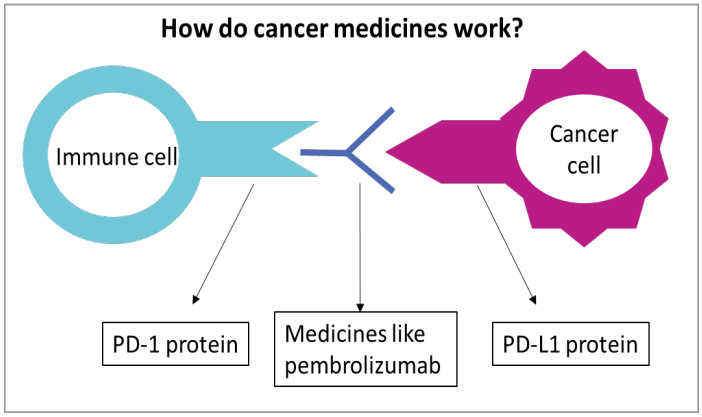
1. **Feladilimab**: It is a medicine that boosts the immune system's reaction and helps immune cells attack cancer cells. This may slow down the growth or return of the cancer. It is not yet approved to treat any disease.
2. **Placebo**: has no active study medicine.

Pembrolizumab is a medicine that helps the body to use its own immune system to treat cancer. It is approved in several countries to treat many types of cancer.

What was the main reason for this study?

Head and neck cancer is a type of cancer that starts in the head and neck region. When the cancer spreads to the sites away from the head and neck region, it is considered metastatic. Cancer that returns or keeps growing even with treatment is considered recurrent. Cancers that are recurrent or metastatic are called advanced cancers.

Immune cells have a type of protein on their surface called programmed cell death 1 (PD-1). Cancer cells make a protein called programmed cell death ligand protein (PD-L1) that can attach to the PD-1 protein and turn off the immune cell. Cancer medicines can attach to the PD-1 protein and block the PD-L1 protein. This blocking activity may help the immune system



attack and destroy the cancer cells. Some head and neck cancer cells have the PD-L1 protein on their surface. These are called PD-L1 positive cancers.

People with PD-L1 positive cancers may have different amounts of the protein on their surface. Cancer cells with more PD-L1 protein are called PD-L1 highly positive cancers. The effectiveness of the PD-1 blocking medicine can depend on the amount of PD-L1 protein on the cancer cells.

Participants with advanced head and neck cancer with different amounts of PD-L1 protein on their cancer cells took part in the study. Researchers wanted to know if feladilimab along with pembrolizumab improved survival and delayed the growth or return of cancer. Researchers also studied the safety of these medicines.

Who took part in this study?

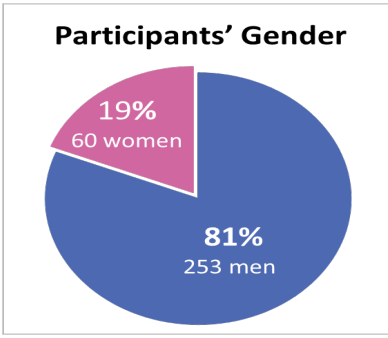
Studies have a list of requirements for participants who can enter (inclusion criteria) and those who cannot enter (exclusion criteria). For this study, the main inclusion and exclusion criteria are listed below.

Men and women were included in the study if they:

- Were 18 years or older.
- Had advanced PD-L1 positive head and neck cancer.
- Had the main cancer around their mouth and throat.
- Were expected to live for at least three months.
- Had the PD-L1 status of their main cancer available.

Men and women were excluded from the study if they had:

- A high risk of bleeding from their cancer.
- Any major surgery within four weeks before starting the study.
- Any other serious medical problems apart from cancer.

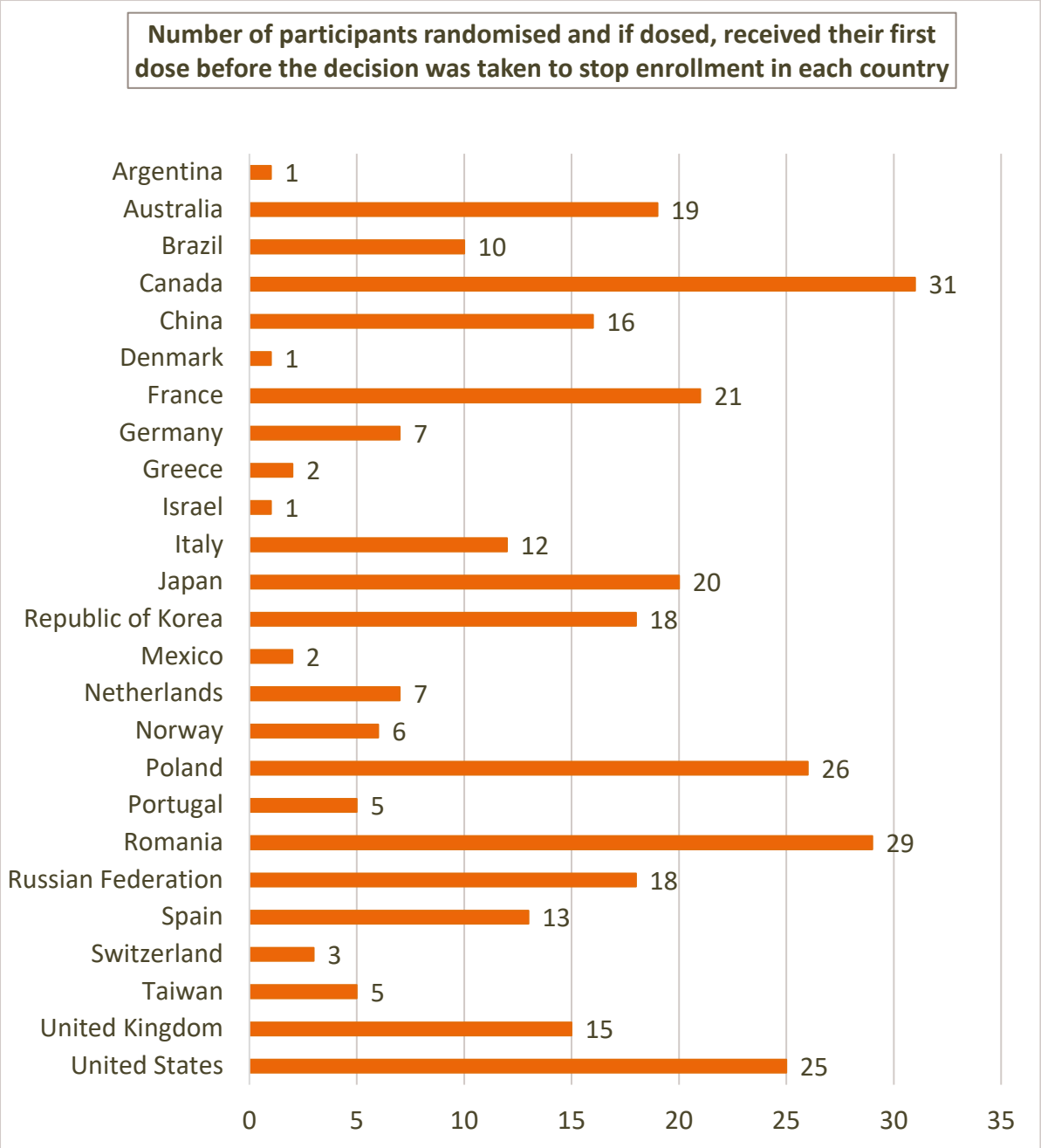


Overall, 313 participants were assigned to one of the two study groups by chance (randomisation) and if dosed, received their first dose before the decision was taken to stop study medicines.

The average age was 63 years. The youngest participant was 25 years old and the eldest participant was 88 years old.

Where was this study done?

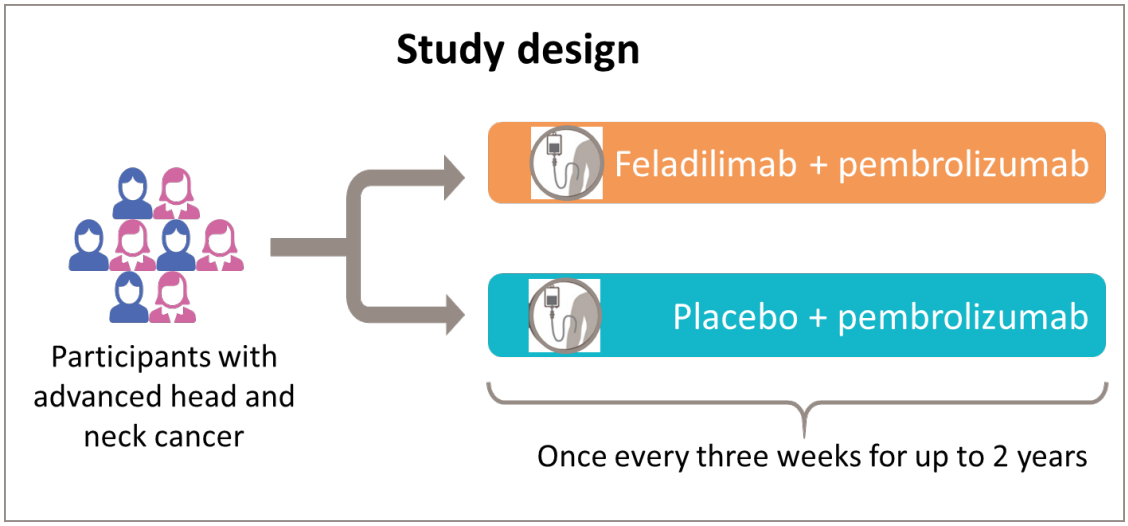
Study sites were in 25 countries.



How was the study done?

This was a double-blind study which means neither participants nor study doctors knew who was receiving which study medicine.

At the start of the study, participants were randomised into one of the treatment groups as shown in the study design figure below. Participants were divided in a way that each treatment group had similar numbers of participants with PD-L1 highly positive and low positive cancers. This allowed a similar mix of participants within each treatment group. However, GSK decided to stop feladilimab treatment in April 2021 based on an early look at the data while the study was ongoing.



What were the main results of the study?

Study doctors assessed each participants' cancer using physical examinations, scans, and blood tests.

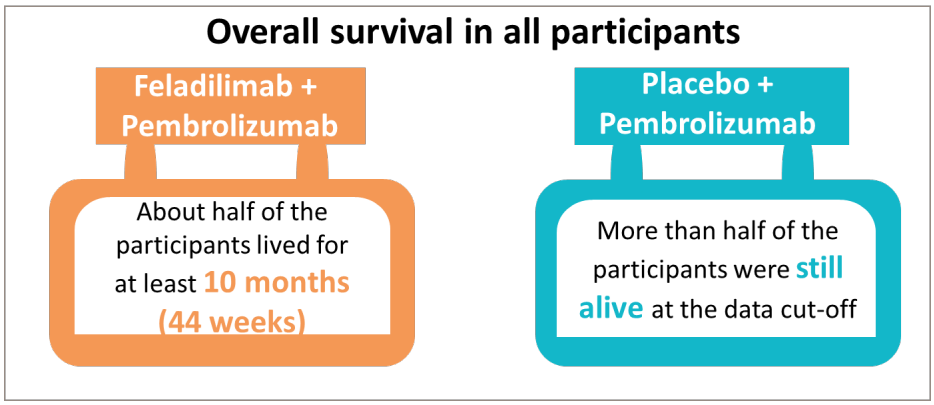
How long did the participants live after randomisation to treatment?

Overall survival (OS) is measured from the time of randomisation to treatment until participants' death.

The median OS was calculated in weeks for all participants and PD-L1 highly positive participants. This was calculated at the time of data cut-off, 17 months after starting the study. Median is the number in the middle of the ordered list, with equal values above and below this number.

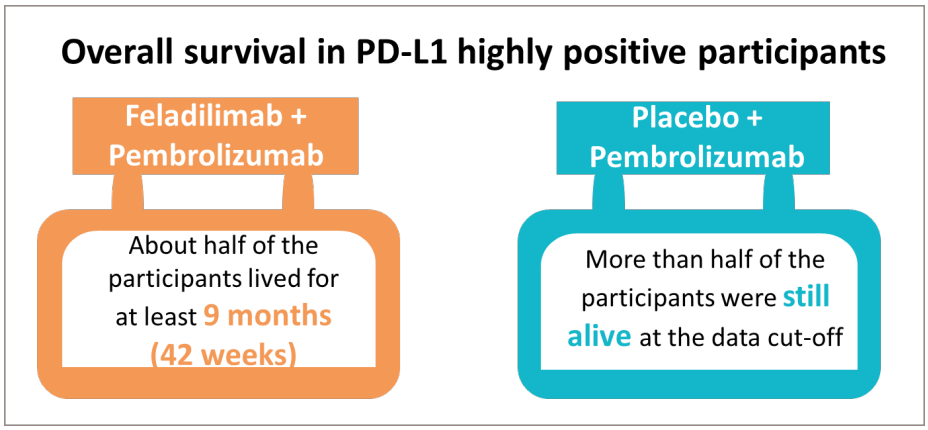
<u>All participants:</u>

The results were available for 157 participants in the feladilimab + pembrolizumab group and 156 participants in the placebo + pembrolizumab group.



PD-L1 highly positive participants:

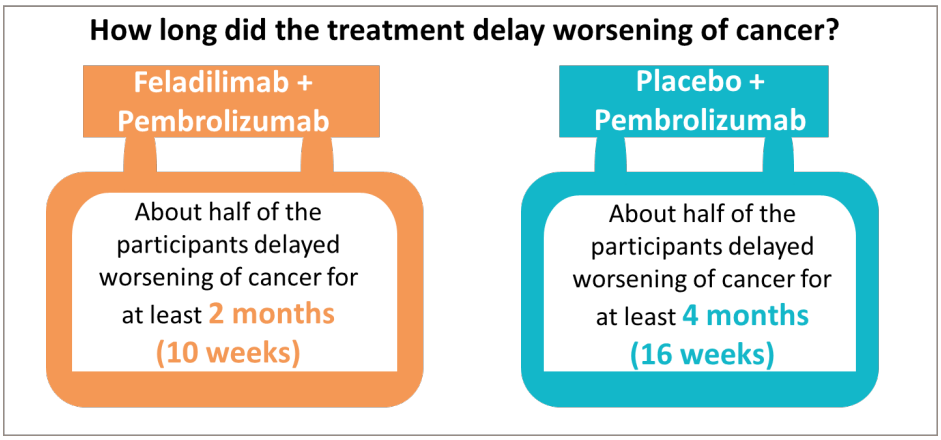
The results were available for 70 participants in the feladilimab + pembrolizumab group and 69 participants in the placebo + pembrolizumab group.



How long did the treatment delay the growth or return of the cancer?

Progression free survival (PFS) is measured from the time of randomisation to treatment until the cancer grows or returns or the participant dies. The median PFS was calculated in weeks for each treatment group at the data cut-off.

The results were available for 157 participants in the feladilimab + pembrolizumab group and 156 participants in the placebo + pembrolizumab group.



What were the side effects?

Unwanted medical problems (adverse events) can happen to people when they receive a medicine. Study doctors record these events. In this summary, **side effects** refer to those events that the study doctor thinks may have been caused by the study medicine.

The side effects in this summary may be different to those of other documents related to the study medicine. A summary of all events reported in this study may be found in the links to clinical results summaries provided at the end of this document.

A total of 315 participants received at least one dose of study medicine. Participants were included in the feladilimab group if they had received at least one dose of feladilimab. Otherwise, they were included in the placebo group. Two participants were randomised after GSK took the decision to stop study medicines. These participants only received pembrolizumab. Side effects were reported for these participants up to the time of data cut-off (April 2021).

The table below shows the number of participants who had side effects, based on the study medicine received.

Number (percent) of participants with side effects		
	Feladilimab + Pembrolizumab 159 participants	**Placebo + Pembrolizumab 156 participants**
How many participants had side effects?	76 (48%)	89 (57%)
How many participants had serious side effects?	12 (8%)	13 (8%)
How many participants stopped treatment due to side effects?	1 (less than 1%)	7 (4%)

The most common side effects reported by 5% or more participants in either treatment group is shown in the table below.

Number (percent) of participants with side effects		
	Feladilimab + Pembrolizumab 159 participants	**Placebo + Pembrolizumab 156 participants**
Feeling tired	12 (8%)	16 (10%)
Lesser than normal levels of hormone made by the thyroid gland	10 (6%)	12 (8%)
No interest in eating	8 (5%)	14 (9%)
Rash	7 (4%)	16 (10%)
Itchiness	6 (4%)	11 (7%)

What were the serious side effects?

The side effects were considered "serious" if they caused death (fatal), were life threatening, caused lasting problems, or required hospital care.

Fatal serious side effects:

Two participants in the feladilimab + pembrolizumab group had fatal side effects of a hole in the small intestines and failure of the lungs. One participant in the placebo + pembrolizumab group died due to bleeding from the mouth.

Non-fatal serious side effects:

Non-fatal serious side effects were reported by 11 participants (7%) in the feladilimab + pembrolizumab group and 13 participants (8%) in the placebo + pembrolizumab group. The non-fatal serious side effects reported by two participants or more in either treatment group is shown below.

Number (percent) of participants with non-fatal serious side effects		
	Feladilimab + Pembrolizumab 159 participants	**Placebo + Pembrolizumab 156 participants**
Low blood potassium levels	2 (1%)	1 (less than 1%)
Diarrhea	0	2 (1%)

How has this study helped participants and researchers?

Researchers concluded that giving feladilimab along with pembrolizumab did not increase the participants' OS and PFS compared with pembrolizumab alone. Researchers recommended to stop treating participants with feladilimab. The study results provided a better understanding of the effects of feladilimab in combination with pembrolizumab on cancer cells. The side effects reported were as expected for the types of treatments in this study.

Are there any plans for further studies?

Some studies of feladilimab in participants with head and neck cancer have been completed and some are still ongoing. No further studies of feladilimab are currently planned.

Where can I find more information about this study?

Full title of this study: A randomized, double-blind, adaptive, phase II/III study of GSK3359609 or placebo in combination with pembrolizumab for first-line treatment of PD-L1 positive recurrent/metastatic head and neck squamous cell carcinoma.

Clinical studies have unique study numbers. The unique study numbers associated with this study are shown below with internet links to scientific summaries.

Organisation (Website)	Study Identifier
European Medicines Agency (www.clinicaltrialsregister.eu)	2019-002263-99[1]
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	NCT04128696[2]

The scientific summaries of this study includes more details about the requirements for study enrolment, the study visit schedule, results from other endpoints, and more detailed information about adverse events.

Your doctor can help you understand more about this study and the results. You should not make changes to your care based on the results of this or any single study.

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=2019-002263-99
[2] https://clinicaltrials.gov/ct2/show/NCT04128696

We would like to **thank the participants** who contributed to this study. The results of this study will help answer scientific questions about treating participants with head and neck cancer.

The content for this document was finalised by GSK on 08 September 2022. The information in this summary does not include additional information available after this date.