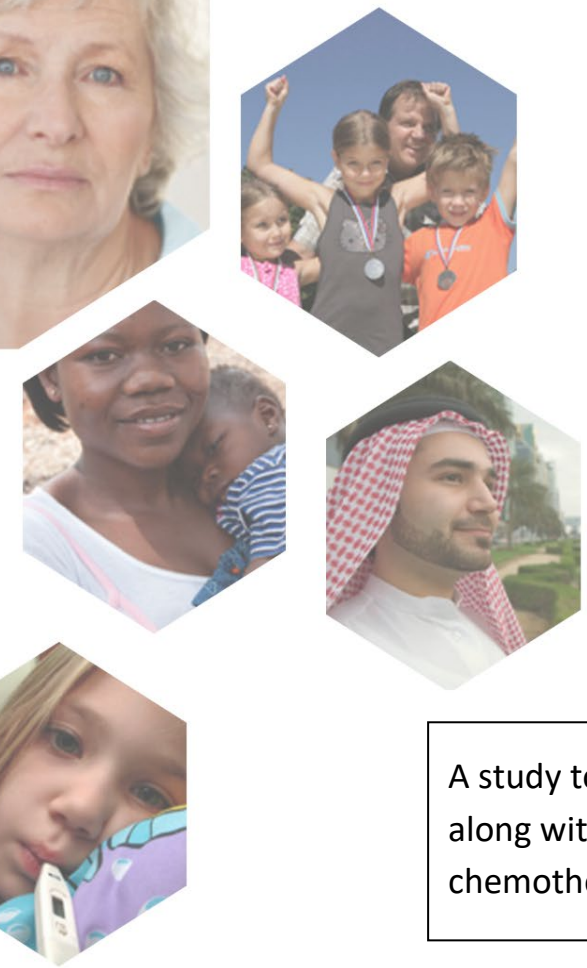


Who sponsored this study?

GSK

Clinical Support Help Desk

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

A study to compare the effects of feladilimab or placebo when given along with the combination of pembrolizumab and platinum chemotherapy in participants with advanced head and neck cancer.

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 August 2020 and is still ongoing. In April 2021, GSK decided that no further participants will enter this study and the existing participants will stop receiving one of the study medicines, feladilimab. This is referred to as data cut-off in the summary. This is because in a different study, the researchers found that fewer participants than expected responded to feladilimab. However, participants could continue on in this study and receive the combination of pembrolizumab and chemotherapy. This summary provides details only up to the data cut-off.

Which medicines were studied?

In this study, participants received feladilimab or placebo in combination with pembrolizumab and chemotherapy.

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.

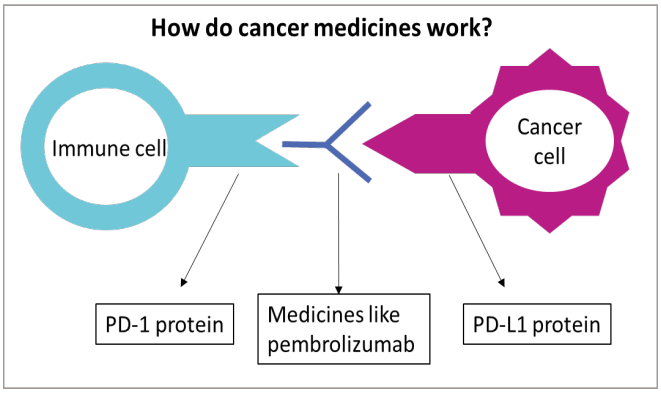
Pembrolizumab is a medicine that helps the body to use its own immune system to treat cancer. It is approved in several countries to treat many types of cancer.

Chemotherapy in this study consisted of cisplatin or carboplatin plus 5-fluorouracil. These medicines are used to treat 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 worsens after being successfully treated 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 protein 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 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. 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 or without PD-L1 protein on their cancer cells took part in the study. Researchers wanted to know if feladilimab along with pembrolizumab and chemotherapy improved survival and delayed the growth or return of cancer. Researchers also studied the safety of these medicines.

Who took part in this study?

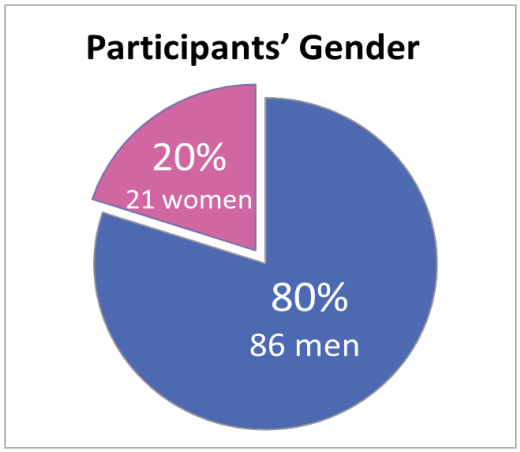
Studies have a list of requirements for participants who can enter (inclusion criteria) and those who cannot enter (exclusion criteria). For this study, the main inclusion and exclusion criteria are listed below.

Men and women were included in the study if they:

- Were 18 years or older.
- Had advanced head and neck cancer.
- Had their main cancer around the 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.

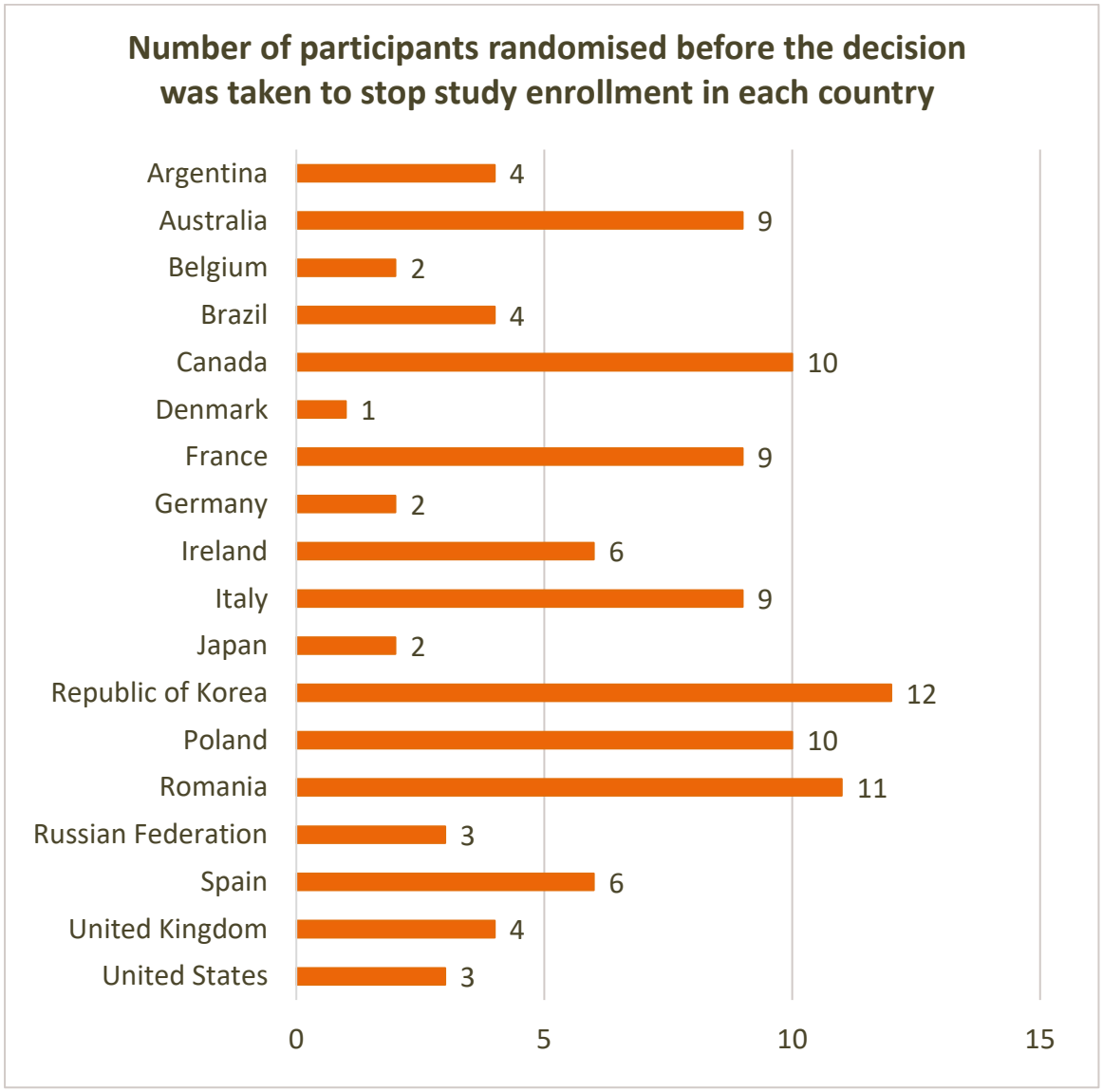


Overall, 107 participants were assigned to one of the two study group by chance (randomisation) before the decision was taken to stop study medicines.

The average age was 60 years. The youngest participant was 19 years old and the eldest participant was 82 years old.

Where was this study done?

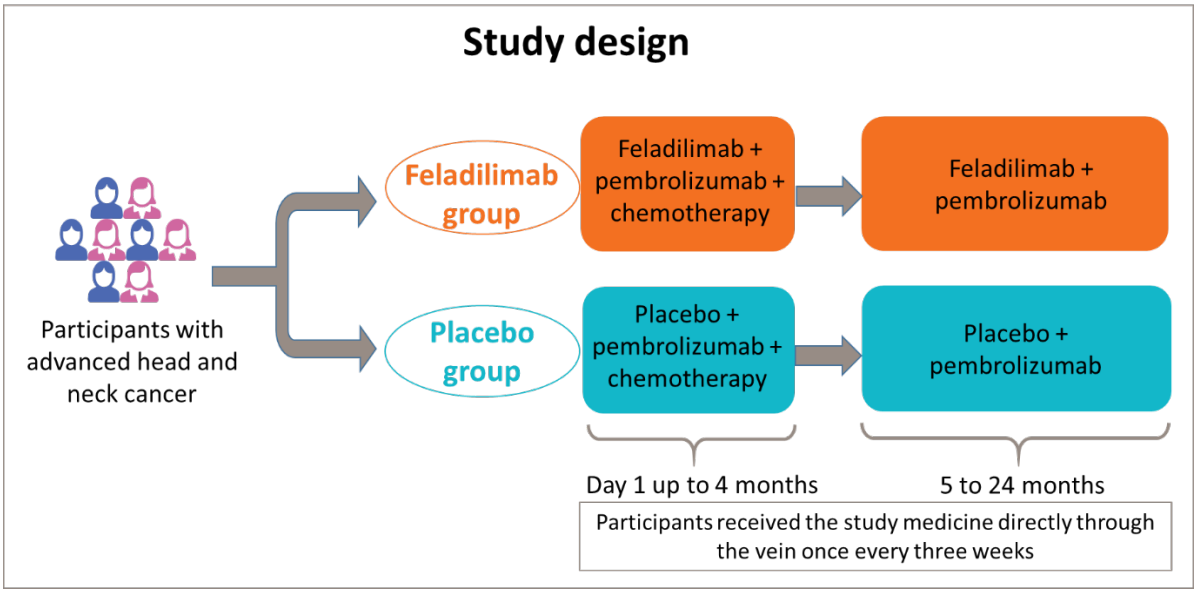
Study sites were in 18 countries.



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 combination.

At the start of the study, participants were randomised into one of the study groups as shown in the figure below. Participants were divided in a way that each treatment group had similar numbers of participants with PD-L1 positive and negative cancers. This allowed a similar mix of participants within each treatment group.



What were the main results of the study?

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

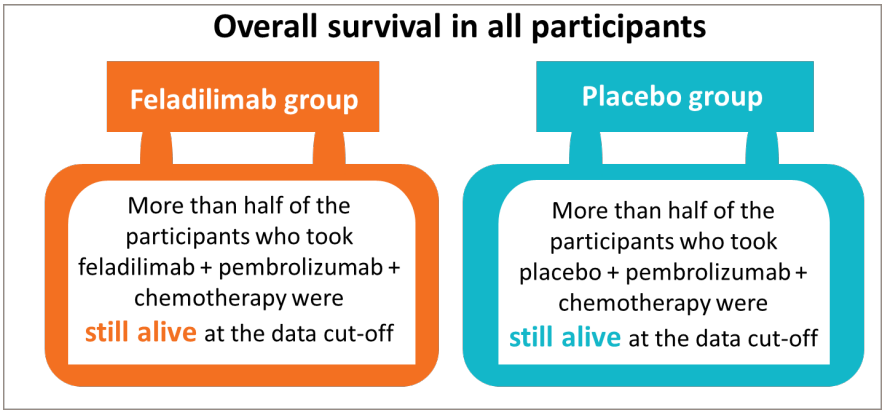
How long did the participants live after randomisation to treatment?

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

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

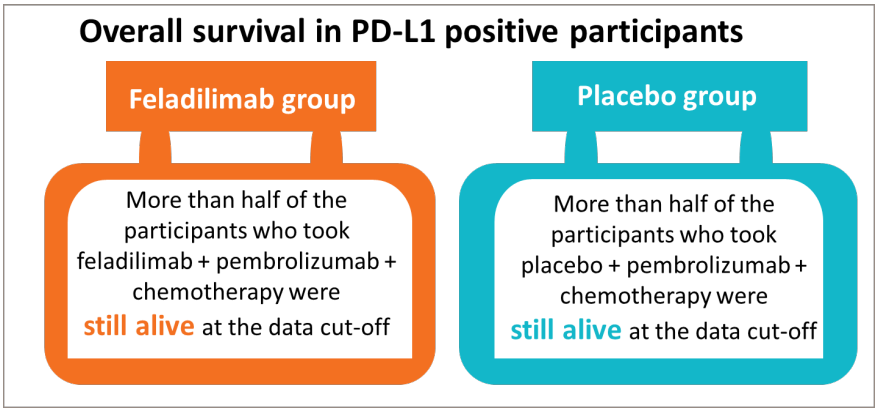
<u>All participants</u>:

The results were available for 52 participants in the feladilimab group and 55 participants in the placebo group.



PD-L1 positive participants:

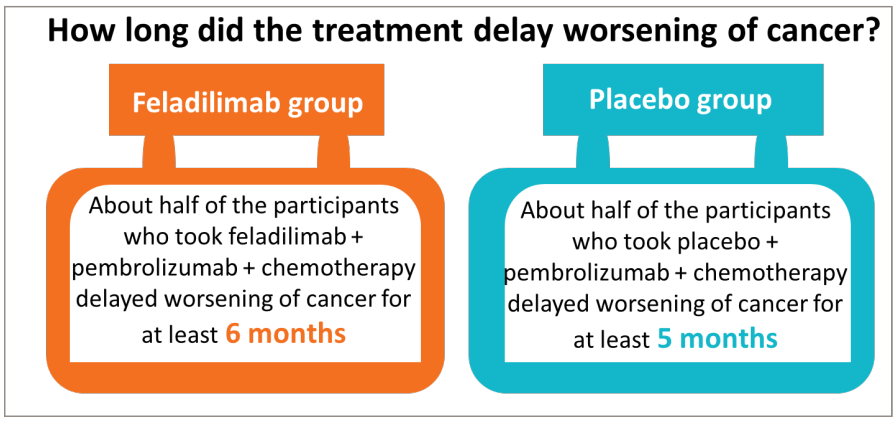
The results were available for 49 participants in the feladilimab group and 52 participants in the placebo group.



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

The 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 months for each group at the data cut-off.

The results were available for 52 participants in the feladilimab group and 55 participants in the placebo 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 115 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. There were nine participants who were randomised after GSK took the decision to stop study medicines. These participants were included in the placebo group for presentation of safety results in this section. Side effects were reported for these participants up to the time of data cut-off (April 2021). One participant who was randomised into the study did not receive any study medicine and was not included in the safety results.

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 group 50 participants	**Placebo group 65 participants**
How many participants had side effects?	47 (94%)	56 (86%)
How many participants had serious side effects?	7 (14%)	14 (22%)
How many participants stopped treatment due to side effects?	7 (14%)	2 (3%)

The most common side effects reported by 10% or more participants in either treatment group is shown in the table below.

Number (percent) of participants with side effects		
	Feladilimab group 50 participants	**Placebo group 65 participants**
Feeling sick	20 (40%)	25 (38%)

Very low levels of the oxygen carrying protein in blood (anaemia)	19 (38%)	15 (23%)
Tiredness	9 (18%)	14 (22%)
Inflammation or swelling of the mouth	9 (18%)	12 (18%)
Very low levels of neutrophils (a type of white blood cell that helps fight some diseases) (neutropenia)	8 (16%)	10 (15%)
Lower than normal levels of neutrophils (a type of white blood cell that helps fight some diseases)*	8 (16%)	8 (12%)
Constipation	6 (12%)	6 (9%)
Vomiting	6 (12%)	8 (12%)
Weakness	5 (10%)	4 (6%)
Inflammation or swelling in the inner lining of the nose, mouth, and/or stomach	4 (8%)	16 (25%)
Diarrhea	2 (4%)	10 (15%)
*Levels of neutrophils were low, but not low enough to be considered as neutropenia.		

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.

Serious side effects were reported by 7 participants (14%) in the feladilimab group and 14 participants (22%) in the placebo group. The non-fatal serious side effects reported by 3% or more of participants in either treatment group is shown below.

Number (percent) of participants with non-fatal serious side effects		
	Feladilimab group 50 participants	**Placebo group 65 participants**
Kidney failure	2 (4%)	0
Inflammation in the inner lining of the oral cavity	1 (2%)	2 (3%)
Feeling sick	1 (2%)	2 (3%)
Vomiting	1 (2%)	2 (3%)

No serious side effects that resulted in death (fatal) were reported for participants in neither group.

How has this study helped participants and researchers?

At the time of data cut-off, the study medicine group had stopped too early for accurate conclusions to be made. The study results provided a better understanding of the effects of feladilimab in combination with pembrolizumab and chemotherapy on cancer cells. The side effects reported were as expected for the type 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 in combination with pembrolizumab and 5FU-platinum chemotherapy versus placebo in combination with pembrolizumab plus 5FU-platinum chemotherapy for first-line treatment of 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)	2019-003981-42[1]
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	NCT04428333[2]

The scientific summaries include 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.

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.

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=2019-003981-42
[2] https://clinicaltrials.gov/ct2/show/NCT04428333