PLAIN LANGUAGE SUMMARY OF CLINICAL STUDY RESULTS

Study Sponsor: Gilead Sciences

Gilead Study Number: GS-US-548-5916

Date of Study: September 2021 to October 2024 (the study closed per Sponsor's decision)

Short Study Title: A Study of Magrolimab Combination Therapy in People With Head and Neck Squamous Cell Carcinoma (HNSCC)

Study Nickname: ELEVATE HNSCC

Date of this Plain Language Summary: March 2025

The information in this summary does not include any information available after this date.

Thank you

Thank you to the participants who contributed to the clinical study for **magrolimab**, also known as **GS-4721** or **Hu5F9-G4**.

Gilead Sciences sponsored this study. We believe it is important to share the results with study participants and the general public.

If you participated in the study and have questions about the results, please speak with a doctor or staff member at the study site.

Always talk to a doctor or a healthcare provider before making any treatment changes.

This document is a short summary of this study written for a general audience. Links to scientific summaries of this study can be found at the end of this document.

General information about the study

Head and Neck Cancer

What is HNSCC?

Head and neck squamous cell carcinoma (HNSCC) refer to cancers that start in the lining of the moist surfaces inside the head and neck area. This includes cancers of the mouth, throat, voice box, nasal cavity, and salivary glands. These cancers often begin as a growth or sore in the mouth, throat, or neck that doesn't go away. If not caught early, HNSCC can become locally advanced (grow deep) or metastasize (spread to other parts of the body), become unresectable (cannot be removed by surgery), and recurrent (keeps coming back). Early detection of HNSCC is crucial, as it is often curable if treated promptly.

There are treatments available for HNSCC. However, these treatments may not always work or lose their effectiveness over time or cause side effects. Therefore, there is a need for new combination treatments to treat HNSCC.

Magrolimab is a monoclonal antibody (MAb). MAbs are proteins made in a lab to help the body fight diseases like cancer. Immunotherapy and chemotherapy are the medicines that are commonly used by the doctors to treat cancers. In this study, the researchers investigated If adding magrolimab to other HNSCC **standard treatments** could help people with unresectable, recurrent, locally advanced or metastatic HNSCC (mHNSCC).

The **standard treatments** given in this study included combination of immunotherapy and chemotherapy medicines:

- **Pembrolizumab + Platinum (a platinum-based chemotherapy drug including cisplatin or carboplatin) + 5-Fluorouracil (5-FU)**
- **Docetaxel**

Other treatment combination included:

- ***Zimberelimab + Platinum +5-FU**

*Note: Zimberelimab is an investigational drug that is still being tested. It works in a similar way to pembrolizumab.

What was the purpose of the study?

The purpose of the study was to first check if the recommended dose of magrolimab was safe and tolerable to use with the standard HNSCC treatments. It then assessed the safety and effectiveness of the combination of magrolimab and the standard HNSCC treatments.

The main questions the researchers wanted to answer in this study were:

For the effectiveness of the drug:

- Did participants in Group A (magrolimab with standard treatment) have better **progression-free survival (PFS)** than Group B (only standard treatment)?
  - **PFS** was the length of time from when the participant joined the study until their cancer worsened, or the participant died from any cause until the last study follow-up.
- How many participants who received magrolimab + docetaxel achieved a **complete or partial response**?
  - **Complete response** means all tumors went away. **Partial response** means there was a shrink in the tumors and no new tumors appeared. **Objective response** includes both complete and partial responses, meaning the treatment is working to reduce the cancer.

For the safety of the drug:

- How safe and well-tolerated was the recommended dose of magrolimab in combination with standard treatments (pembrolizumab + platinum + 5-FU or docetaxel)?
- What side effects did participants have during the study, if any?

Who took part in the study?

- **192** participants with HNSCC around the world took part in the study.

People could take part in the study if they:

Were 18 years or older	Had confirmed recurrent, unresectable, locally advanced or mHNSCC	Either did not take any treatment for HNSCC or took treatment before, but it failed

The study participants were between the ages of **30** and **83** years.

The participants from each country are shown below (Number (%) of participants).

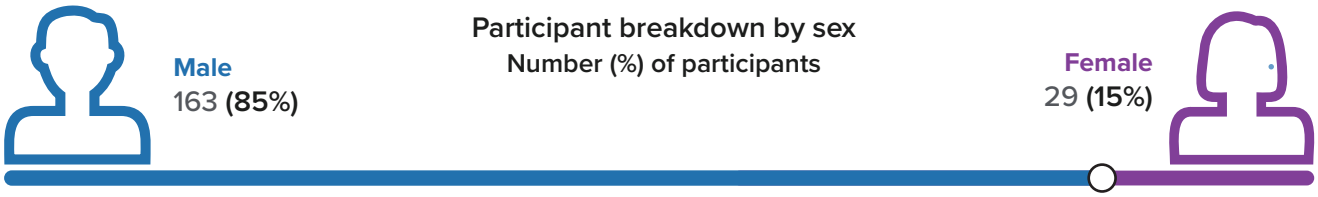
United States	42 **(22%)**	Belgium	15 **(8%)**
France	34 **(18%)**	Spain	12 **(6%)**
Poland	29 **(15%)**	Germany	7 **(4%)**
Portugal	27 **(14%)**	United Kingdom	5 **(3%)**
Australia	19 **(10%)**	Italy	2 **(1%)**

The race of participants is shown below (Number (%) of participants).

White	158 **(82%)**	Other or More Than One Race	7 **(4%)**
Not collected	23 **(12%)**	Asian	4 **(2%)**

The ethnicity of participants is shown below (Number (%) of participants).

Not Hispanic or Latino	153 **(80%)**	Hispanic or Latino	7 **(4%)**
Not collected	32 **(17%)**		



What happened during the study?

This was an **open-label**, **Phase 2** study with 2 parts: **Safety Run-in** and **Expansion Phase**.

The study was planned to first check the safety and then the effectiveness of the drug. **However, this study was closed earlier than planned because the sponsor decided to stop developing magrolimab as a cancer treatment.**

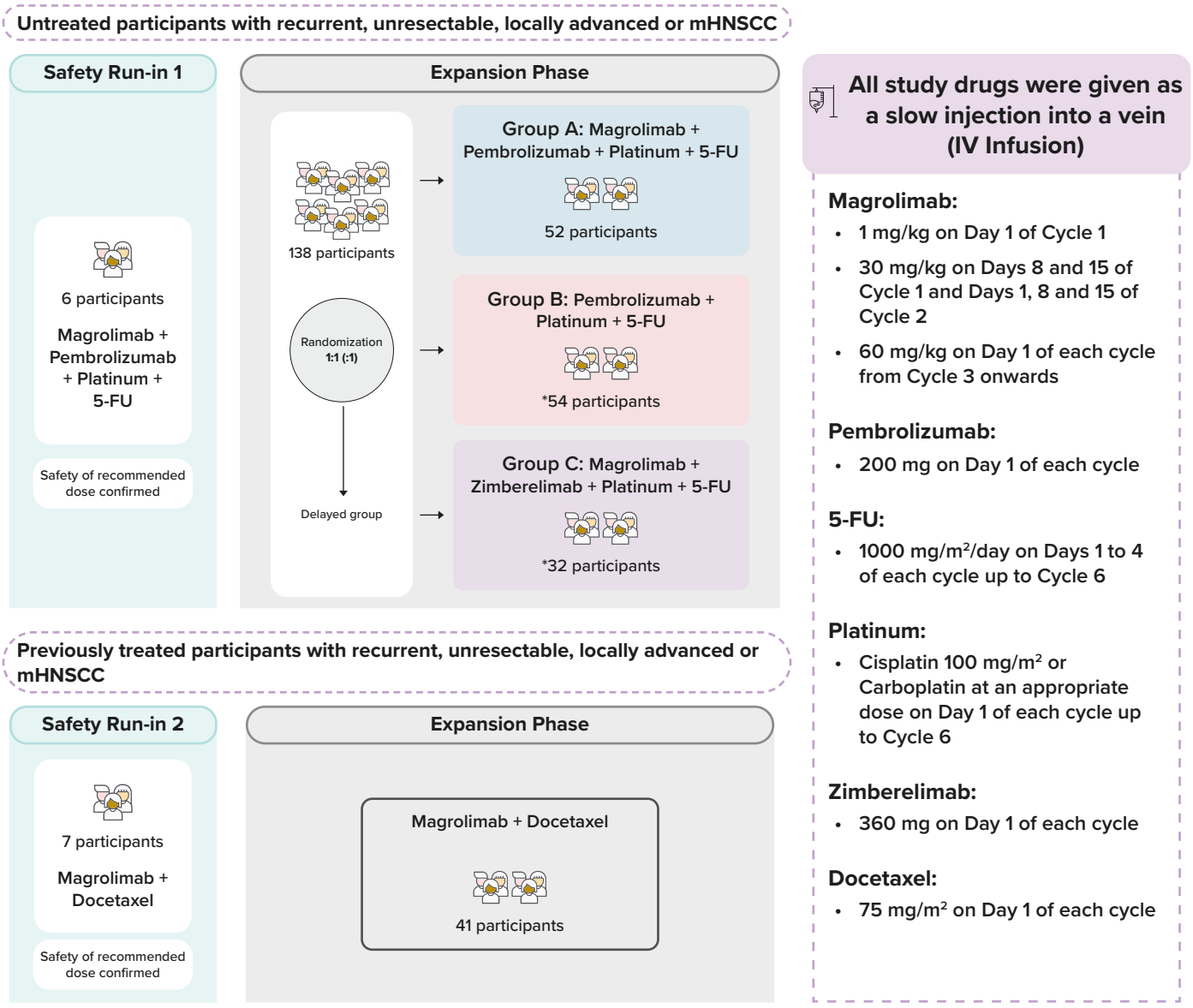
- **Phase 2** studies test an investigational drug in a small number of people to assess its safety and effectiveness.
- **Open-label** means the participants, the study doctors, and the study staff knew what treatment the participants received in each part.

Safety Run-in

The Safety Run-in had 2 assessments: **Safety Run-in 1** checked if magrolimab was safe with pembrolizumab + platinum + 5-FU. **Safety Run-in 2** checked if magrolimab was safe with docetaxel, in a small group before giving to rest of the participants in the Expansion Phase.

Expansion Phase

After confirming the recommended dose of magrolimab in the Safety Run-in parts, additional participants were enrolled in the Expansion Phase groups to receive the treatment as shown below:



All study drugs were given as a slow injection into a vein (IV Infusion)

Magrolimab:

- 1 mg/kg on Day 1 of Cycle 1
- 30 mg/kg on Days 8 and 15 of Cycle 1 and Days 1, 8 and 15 of Cycle 2
- 60 mg/kg on Day 1 of each cycle from Cycle 3 onwards

Pembrolizumab:

- 200 mg on Day 1 of each cycle

5-FU:

- 1000 mg/m^2/day on Days 1 to 4 of each cycle up to Cycle 6

Platinum:

- Cisplatin 100 mg/m^2 or Carboplatin at an appropriate dose on Day 1 of each cycle up to Cycle 6

Zimberelimab:

- 360 mg on Day 1 of each cycle

Docetaxel:

- 75 mg/m^2 on Day 1 of each cycle

***4 out of 192 participants (1 participant from Group B and 3 participants from Group C) did not take any study treatment.**

The participants received treatment in 21-day cycles. A cycle is the time between one round of treatment and the start of the next. Magrolimab doses were based on the participant's weight (mg/kg), while other standard treatments doses followed the standard clinical practice.

Participants were to continue the treatment until the end of the study. The treatment was stopped if their cancer got worse, they had unacceptable side effects, they decided to leave this study, they died, or the study was closed by the sponsor.

What were the results of the study?

This is a summary of the main results from this study. The individual results of each participant might be different and are not in this summary. A detailed presentation of the results can be found on the websites listed at the end of this summary.

The researchers assessed the status of cancer in participants through blood tests and scans. Study doctors reviewed the results of these tests and scans to determine the effectiveness of the drug in the Expansion Phase groups. They checked PFS in previously untreated participants and participants with complete or partial response in previously treated participants.

Did participants in Group A (magrolimab with standard treatment) have better PFS than Group B (only standard treatment)?

The researchers found that both Groups A and B had similar PFS of **6 months**. Group C (magrolimab with zimberelimab + platinum + 5-FU) was not part of this comparison.

How many participants who received magrolimab + docetaxel achieved a complete or partial response?

The researchers found that **5 out of 41 (12%)** participants who received magrolimab + docetaxel achieved a complete or partial response.

As Gilead decided to close the study, data was not sufficient for researchers to conclude if the combination of magrolimab and standard treatments (pembrolizumab + platinum + 5-FU or docetaxel) were effective.

What were the safety results of the study?

How safe and well-tolerated was the recommended dose of magrolimab in combination with standard treatments (pembrolizumab + platinum + 5-FU or docetaxel)?

To answer this question, the researchers first reviewed the safety of magrolimab and standard treatment (pembrolizumab + platinum + 5-FU or docetaxel) in participants in the Safety Run-in parts. They kept track of any **unwanted medical events** that the participants had during Safety Run-in parts. They also did laboratory tests and measurements of participants before and after taking the treatment. They checked if the changes in laboratory test results were abnormal, meaning they were out of normal reference range. They assessed if the unwanted medical events or abnormalities in laboratory test results were dose-limiting toxicities (**DLTs**).

Out of 13, 6 participants in Safety Run-in 1 and 6 in Safety Run-in 2 were assessed for DLTs.

- **All of the 12 (100%) participants in the Safety Run-in parts had some unwanted medical events and abnormalities in their laboratory test results.**
- **However, none of the 12 participants had DLTs.**

An **unwanted medical event** is any unwanted sign or symptom that participants may have during the study. This **may or may not be caused by the study treatment**.

DLTs were the medical events that were severe enough to stop the study doctor from giving the recommended dose of magrolimab in combination with pembrolizumab + platinum + 5-FU or docetaxel. In case DLTs were observed, a lower dose of magrolimab would be studied in combination with pembrolizumab + platinum + 5-FU or docetaxel.

The researchers confirmed that the recommended dose of magrolimab was safe and well-tolerated to be given in combination with pembrolizumab + platinum + 5-FU or docetaxel, in the Expansion Phase.

The recommended dose of magrolimab was an initial dose of 1 mg/kg followed by 30 mg/kg administered weekly up to Cycle 2 and 60 mg/kg on Day 1 of each cycle from Cycle 3 onwards.

What side effects did participants have during the study, if any?

The researchers also checked the overall safety (**side effects**) of magrolimab in combination with pembrolizumab + platinum + 5-FU or docetaxel during the entire study.

Side effects are defined as unwanted medical events that the study doctors thought **might be caused by the study treatment**.

The results from several studies are usually needed to help conclude if a treatment actually causes a side effect:
There were 4 participants who did not take any study treatment.
So, the results in this section only include 188 participants.

A side effect is considered "serious" if it:

- results in death
- is life-threatening
- is considered by the study doctor to be medically important
- causes lasting problems
- requires hospital care
- causes a birth defect

The table below lists how many participants had side effects during the study.

Overall Side Effects

	Participants with Previously Untreated HNSCC				Participants with Previously Treated HNSCC	
		Expansion Phase				Expansion Phase
	Safety Run-in 1 (Magrolimab + Pembrolizumab + Platinum + 5-FU) **(out of 6 participants)**	**Group A** (Magrolimab + Pembrolizumab + Platinum + 5-FU) **(out of 52 participants)**	**Group B** (Pembrolizumab + Platinum + 5-FU) **(out of 53 participants)**	**Group C** (Magrolimab + Zimberelimab + Platinum + 5-FU) **(out of 29 participants)**	**Safety Run-in 2** (Magrolimab + Docetaxel) **(out of 7 participants)**	(Magrolimab + Docetaxel) **(out of 41 participants)**
	Number (%) of participants					
Side effects	6 (100%)	50 (96%)	52 (98%)	29 (100%)	7 (100%)	40 (98%)
Serious side effects	3 (50%)	17 (33%)	13 (25%)	10 (34%)	4 (57%)	13 (32%)
Side effects that caused participants to stop treatment	2 (33%)	14 (27%)	12 (23%)	9 (31%)	1 (14%)	5 (12%)

5 out of 188 (3%) participants died due to serious side effects during the study.

- 2 out of 52 (4%) participants died due to side effects in Group A (magrolimab + pembrolizumab + platinum + 5-FU). The deaths were due to:
  - Fever with low number of white blood cells (febrile neutropenia).
  - Body's response to infection and inflammation in large intestine leading to severe illness (septic shock from neutropenic colitis).
- 1 out of 53 (2%) participants died in Group B (pembrolizumab + platinum + 5-FU). The death was due to an infection caused by inhaling something other than air into the lungs (pneumonia aspiration).
- 2 out of 41 (5%) participants died in Group (magrolimab + docetaxel). The deaths were due to:
  - Presence of fluid in the lungs, usually as a result of infection (pneumonia).
  - Fever with low number of white blood cells (febrile neutropenia).

What were the serious side effects?

The table below lists serious side effects that occurred in more than 2 participants in study population during the study.

Serious Side Effects

Serious side effects	Participants with Previously Untreated HNSCC				Participants with Previously Treated HNSCC	
		Expansion Phase				Expansion Phase
	Safety Run-in 1 (Magrolimab + Pembrolizumab + Platinum + 5-FU) (out of 6 participants)	Group A (Magrolimab + Pembrolizumab + Platinum + 5-FU) (out of 52 participants)	Group B (Pembrolizumab + Platinum + 5-FU) (out of 53 participants)	Group C (Magrolimab + Zimberelimab + Platinum + 5-FU) (out of 29 participants)	Safety Run-in 2 (Magrolimab + Docetaxel) (out of 7 participants)	(Magrolimab + Docetaxel) (out of 41 participants)
	Number (%) of participants					
Fever with low number of white blood cells (Febrile neutropenia)	1 (17%)	2 (4%)	5 (9%)	1 (3%)	3 (43%)	8 (20%)
Low number of red blood cells (Anemia)	1 (17%)	3 (6%)	0	0	2 (29%)	4 (10%)
Presence of fluid in the lungs, usually as a result of infection (Pneumonia)	2 (33%)	1 (2%)	1 (2%)	1 (3%)	0	2 (5%)
Sudden episode of kidney injury (Acute kidney injury)	0	4 (8%)	1 (2%)	1 (3%)	0	0
Fever (Pyrexia)	0	2 (4%)	0	2 (7%)	0	0
Loose watery stools (Diarrhea)	1 (17%)	1 (2%)	0	0	1 (14%)	0

What were the non-serious side effects?

The table below lists the **most common non-serious side effects** that occurred in at least 25% of the study participants. These side effects were not serious in nature and did not meet the definition of 'serious side effects' mentioned in the section above in this summary.

Non-Serious Side Effects

Non-serious side effects	Participants with Previously Untreated HNSCC				Participants with Previously Treated HNSCC	
		Expansion Phase				Expansion Phase
	Safety Run-in 1 (Magrolimab + Pembrolizumab + Platinum + 5-FU) (out of 6 participants)	Group A (Magrolimab + Pembrolizumab + Platinum + 5-FU) (out of 52 participants)	Group B (Pembrolizumab + Platinum + 5-FU) (out of 53 participants)	Group C (Magrolimab + Zimberelimab + Platinum + 5-FU) (out of 29 participants)	Safety Run-in 2 (Magrolimab + Docetaxel) (out of 7 participants)	(Magrolimab + Docetaxel) (out of 41 participants)
	Number (%) of participants					
Low number of red blood cells (Anemia)	5 (83%)	40 (77%)	32 (60%)	19 (66%)	4 (57%)	27 (66%)
Feeling sick to the stomach (Nausea)	4 (67%)	16 (31%)	19 (36%)	11 (38%)	2 (29%)	12 (29%)
Extreme tiredness (Fatigue)	4 (67%)	11 (21%)	10 (19%)	8 (28%)	4 (57%)	14 (34%)
An inflamed and sore mouth (Stomatitis)	5 (83%)	7 (13%)	17 (32%)	9 (31%)	2 (29%)	8 (20%)

There were other serious and non-serious side effects, but those occurred in fewer participants. Some participants may have had more than 1 serious or non-serious side effect.

How has this study helped researchers?

The researchers learned more about the safety and effectiveness of magrolimab and standard HNSCC treatments. They also learned how these combination treatments work in people who were either previously untreated or treated for HNSCC.

The results from several studies are needed to help decide which treatments work and are safe. This summary shows only the main results from this one study. Other studies may provide new information or different results.

Gilead Sciences does not plan to have further clinical studies with magrolimab alone or in combination.

Where can I learn more about this study?

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

Organization (Website)	Study Identifier
European Medicines Agency (www.clinicaltrialsregister.eu)	EudraCT number: 2020-005708-20
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	ClinicalTrials.gov ID: NCT04854499
www.gileadclinicaltrials.com	GS-US-548-5916

Please note that information on these websites may be presented in a different way from this summary.

Full Study Title: A Phase 2 Study of Magrolimab Combination Therapy in Patients with Head and Neck Squamous Cell Carcinoma

To learn more about clinical trials in general,
please visit this page on www.clinicaltrials.gov website

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Clinical study participants belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

GILEAD