PLAIN LANGUAGE SUMMARY OF CLINICAL STUDY RESULTS

Study Sponsor: Gilead Sciences

Gilead Study Number: GS-US-587-6156

Date of Study: July 2022 to June 2024 (the study closed per Sponsor's decision)

Short Study Title: Study of Magrolimab Given Together With BEV + FOLFIRI in People With Previously Treated Advanced Inoperable Metastatic Colorectal Cancer (mCRC)

Study Nickname: ELEVATE CRC

Date of this Plain Language Summary: January 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.

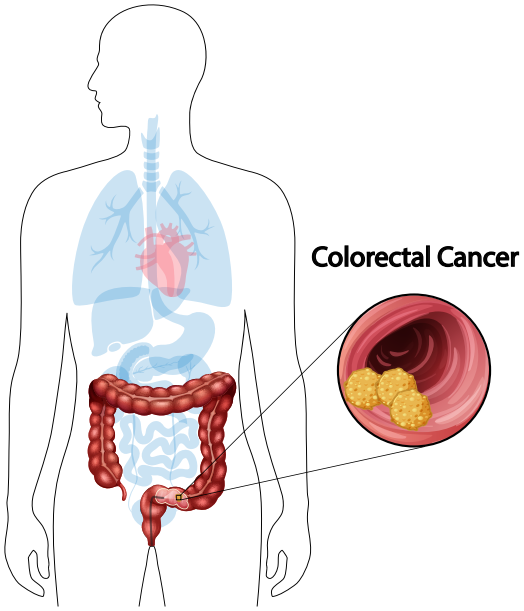
General information about the study

What is Colorectal Cancer?

Colorectal cancer is a type of cancer that occurs when the cells in the colon or rectum grow out of control. The colon is the large intestine, and the rectum is the passageway that connects the colon to the anus. The exact cause of this cancer isn't clear, but it often starts from small growths called polyps that may develop into cancer over time.

Some risk factors include older age, family history of the disease, diet, lifestyle, and certain inherited conditions. Common symptoms include changes in bowel habits like diarrhea or constipation, blood in the stool, stomach pain, unexplained weight loss, and feeling tired or weak.

There are therapies available for colorectal cancer. However, these therapies may not work or stop working after some time, or cause side effects. Often, they are not suitable for people with advanced, inoperable, and metastatic colorectal cancer (mCRC), where the cancer is spread throughout the colorectal part or other parts of the body and cannot be surgically removed.



In this study, the researchers wanted to see if adding magrolimab to the standard treatment can help people with advanced inoperable mCRC, compared to the standard treatment.

Magrolimab is an investigational drug. It is a monoclonal antibody (MAb). MAbs are proteins made in a lab to help the body fight diseases like cancer.

The standard treatment is bevacizumab (BEV) + FOLFIRI. BEV is an MAb and FOLFIRI is a combination of 3 **chemotherapy** medicines - irinotecan, leucovorin, and fluorouracil. **Chemotherapy medicines are used to treat cancers**.

BEV + FOLFIRI was selected for comparison with magrolimab in combination with BEV + FOLFIRI because it is a commonly used treatment for patients with mCRC.

What was the purpose of the study?

The purpose of the study was to first check if the recommended dose of magrolimab can be safely given with BEV + FOLFIRI in the initial safety run-in part. Then, in the next part, the study looked at how effective this combination (magrolimab and BEV + FOLFIRI) treatment was in participants in the randomized part.

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

For the effectiveness of drug:

- Did participants who took magrolimab with BEV+ FOLFIRI have better **progression-free survival** than those who took BEV + FOLFIRI?
  - **Progression-free survival** 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.

For the safety of drug:

- How safe and well-tolerated the recommended dose of the magrolimab was in combination with BEV + FOLFIRI?
- What side effects did participants have during the study, if any?

Who took part in the study?

- **77** participants living with mCRC around the world took part.
- **2** out of **77** participants left the study before taking the treatment.

People could take part in the study if they:

Were at least 18 years of age

Had confirmed advanced inoperable mCRC

Took treatment for mCRC before, but it failed

The participants enrolled in the study were between the ages of **31** and **81** years.

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

United States	32 **(42%)**	Puerto Rico	5 **(7%)**
Australia	11 **(14%)**	Canada	3 **(4%)**
Spain	11 **(14%)**	France	3 **(4%)**
Belgium	5 **(7%)**	Germany	1 **(1%)**
Italy	5 **(7%)**	Hong Kong	1 **(1%)**

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

White	59 **(77%)**	Black or African American	6 **(8%)**
Asian	7 **(9%)**	Other or more than one race	3 **(4%)**
Not collected	2 **(3%)**		

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

Not Hispanic Or Latino	65 **(84%)**	Hispanic Or Latino	9 **(12%)**
Not collected	3 **(4%)**		

Participant breakdown by sex
Number (%) of participants

Male
45 **(58%)**

Female
32 **(42%)**

What happened during the study?

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

Phase 2 means the researchers tested magrolimab with BEV + FOLFIRI in a small number of people with mCRC. **Open-label** means the participants, the study doctors, and the study staff knew what treatment the participants received.

Safety Run-in Part

Safety Run-in part checked if the recommended dose of magrolimab was safe to be given with BEV + FOLFIRI, in a small group of participants before giving it to the rest of the participants in the randomized part.

Randomized Part

Randomized means the researchers used a computer program to randomly choose the treatment each participant received. This helped make sure the treatments were chosen fairly.

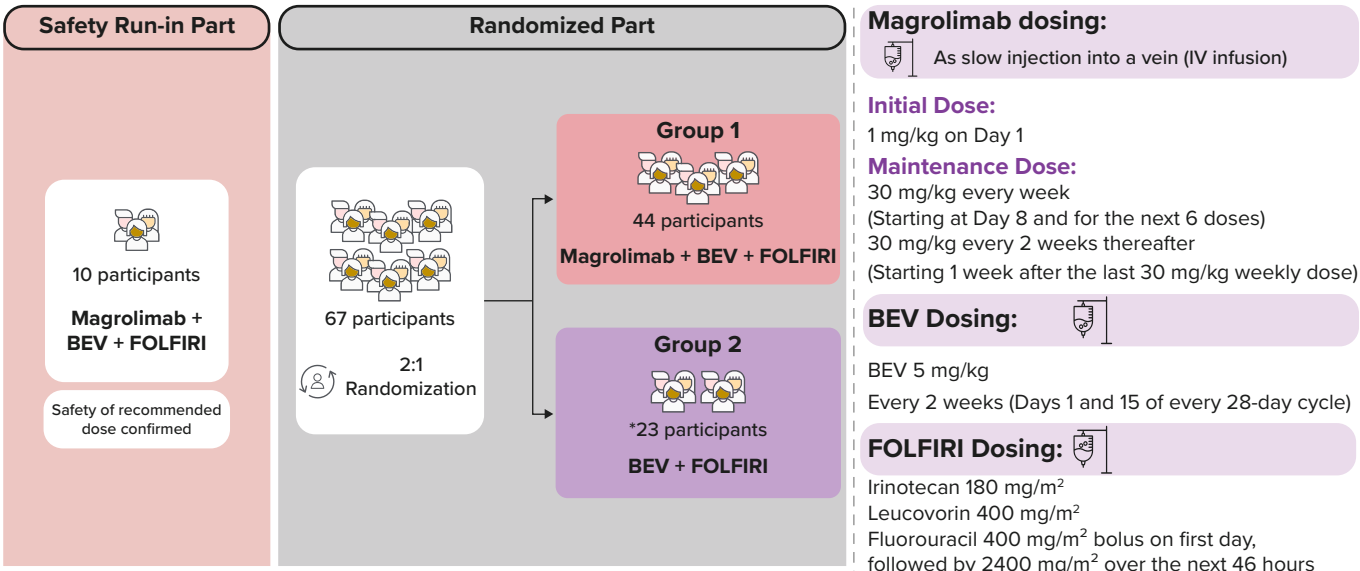
After confirming the recommended dose of magrolimab in the safety run-in part, additional participants were enrolled in the randomized part. They were randomly assigned to 2 groups, with twice as many participants receiving magrolimab with BEV + FOLFIRI as those receiving only BEV + FOLFIRI. This was called 2:1 randomization.

Group 1: Magrolimab + BEV + FOLFIRI

Group 2: BEV + FOLFIRI

The participants received treatment in 28-day cycles. A cycle is the time between one round of treatment and the start of the next. After the initial dose, a fixed dose was given for the rest of the treatment days called the maintenance dose. Magrolimab and BEV doses were based on the participant's weight (mg/kg), while FOLFIRI doses followed standard clinical practice.

The graphic below shows the treatment plan.



*2 out of 23 participants in group 2 of the randomized part did not take any treatment.

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

The study was closed because the sponsor decided to stop developing magrolimab, both alone and in combination, as a treatment for cancer.

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.

Did participants who took magrolimab with BEV+ FOLFIRI have better progression-free survival than those who took BEV + FOLFIRI?

Due to Gilead's decision to stop the study, the data were not sufficient for researchers to make any conclusions for the **progression-free survival** results.

What were the safety results of the study?

How safe and well-tolerated the recommended dose of the magrolimab was in combination with BEV + FOLFIRI?

To answer this question, the researchers first reviewed the safety of the treatment combinations of magrolimab with BEV + FOLFIRI in participants in the safety run-in part. They kept track of any **unwanted medical events** that the participants had during the safety run-in part. They also did laboratory tests and measurements of participants before and after taking the treatment. They checked if the changes in laboratory test values were abnormal, meaning they were out of normal reference range. They assessed if the unwanted medical events or laboratory test abnormalities were dose-limiting toxicities (**DLTs**).

They found that:

- **All of the 10 (100%) participants in the safety run-in part had some unwanted medical events and abnormalities in their laboratory test results.**
- **However, none of the 10 participants in the safety run-in part had any 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 BEV + FOLFIRI. In case DLTs were observed, a lower dose of magrolimab would be studied in combination with BEV + FOLFIRI.

The researchers confirmed that the recommended dose of magrolimab was safe and well-tolerated to be given in combination with BEV + FOLFIRI, in the randomized part.

The recommended dose of magrolimab was an initial dose of 1 mg/kg followed by 30 mg/kg administered weekly and later every 2 weeks.

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 BEV + FOLFIRI during the entire study.

The results from several studies are usually needed to help conclude if a treatment actually causes a **side effect**.

2 out of 23 participants who received BEV + FOLFIRI (Group 2) did not take study treatment. So, the results in this section only include 75 participants.

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

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 shows how many participants had side effects during the study.

Overall Side Effects

	Safety Run-in Part	Randomized Part		Total (out of 75 participants)
		Group 1	Group 2	
	Magrolimab + BEV + FOLFIRI (out of 10 participants)	Magrolimab + BEV + FOLFIRI (out of 44 participants)	BEV + FOLFIRI (out of 21 participants)	
	Number of participants (%)			
How many participants had any side effects?	10 (100%)	44 (100%)	18 (86%)	72 (96%)
How many participants had any serious side effects?	2 (20%)	11 (25%)	2 (10%)	15 (20%)
How many participants stopped taking the study treatment because of side effects?	1 (10%)	5 (11%)	2 (10%)	8 (11%)

None of the participants died due to any side effects in the study.

What were the serious side effects?

The **most common serious side effects** that occurred during the study were loose watery stools (**diarrhea**) and fever with low number of white blood cells called neutrophils (**febrile neutropenia**). Each of these two serious side effects occurred in 2 (3%) of the study participants who received magrolimab with BEV + FOLFIRI (Group 1).

None of the serious side effects occurred in the Safety run-in part or in Group 1.

What were the non-serious side effects?

The table below shows the **most common non-serious side effects** that occurred in more than 30% 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.
These occurred in more number of participants who received magrolimab with BEV + FOLFIRI (Group 1) than participants who received BEV + FOLFIRI (Group 2).

Non-Serious Side Effects

	Safety Run-in Part	Randomized Part		
		Group 1	Group 2	Total
	Magrolimab + BEV + FOLFIRI (out of 10 participants)	**Magrolimab + BEV + FOLFIRI** (out of 44 participants)	**BEV + FOLFIRI** (out of 21 participants)	(out of 75 participants)
Non-serious side effects	Number of participants (%)			
Loose watery stools (Diarrhea)	4 (40%)	25 (57%)	11 (52%)	40 (53%)
Feeling sick to the stomach (Nausea)	9 (90%)	20 (45%)	9 (43%)	38 (51%)
Extreme tiredness (Fatigue)	7 (70%)	18 (41%)	6 (29%)	31 (41%)
Low number of red blood cells (Anemia)	6 (60%)	19 (43%)	4 (19%)	29 (39%)

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 of magrolimab with BEV + FOLFIRI combination and how it works in people living with advanced, inoperable, metastatic mCRC.

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.euclinicaltrials.eu)	EU CT number: 2022-500177-13-00
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	ClinicalTrials.gov ID: NCT05330429
www.gileadclinicaltrials.com	GS-US-587-6156

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

Full Study Title: A Phase 2, Randomized, Open-Label Study Evaluating the Safety and Efficacy of Magrolimab in Combination With Bevacizumab and FOLFIRI Versus Bevacizumab and FOLFIRI in Previously Treated Advanced Inoperable Metastatic Colorectal Cancer (mCRC)

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