PLAIN LANGUAGE SUMMARY OF CLINICAL STUDY RESULTS

Study Sponsor: Gilead Sciences

Gilead Study Number: GS-US-590-6154

Date of Study: July 2022 to April 2024 (the study closed earlier than planned)

Short Study Title: Study of Magrolimab Versus Placebo in Combination With Venetoclax and Azacitidine in Newly Diagnosed Previously Untreated Participants With Acute Myeloid Leukemia

Study Nickname: ENHANCE-3

Date of this Plain Language Summary: October 2024

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.

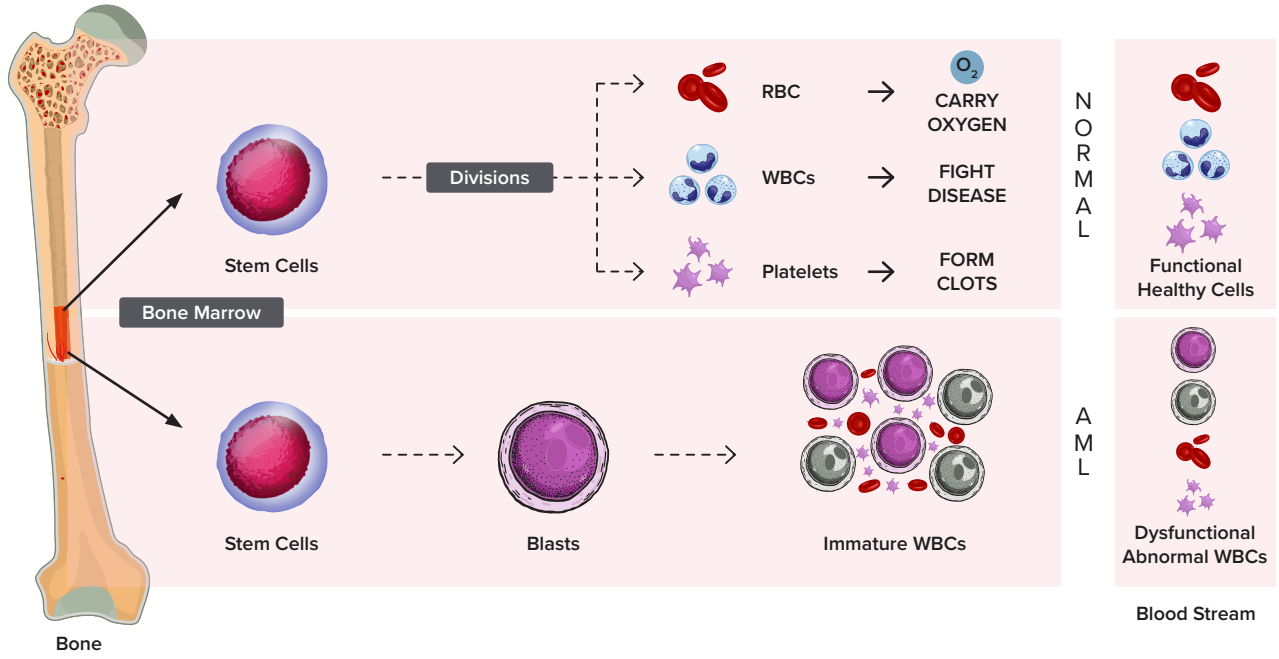
This document is a short summary of this study written for a general audience. Links to scientific summaries of this study can be found at the end of this document.

General information about the study

What is acute myeloid leukemia (AML)?

The bone marrow is a spongy material in the middle of a bone. Bone marrow has blood-forming cells known as stem cells. In a healthy body, these stem cells make 3 main types of blood cells, red blood cells (RBCs), white blood cells (WBCs), and platelets. AML is a cancer of the blood where the bone marrow makes too many defective blood cells called blast cells. These blast cells do not work as normal blood cells do. In AML one or all types of blood cells may be affected. If left untreated, AML can lead to death.

The below graphic shows how stem cells function in healthy people versus people with AML



There are therapies available for AML. However, these therapies sometimes do not work, stop working after some time, or cause side effects. Often, they are not suitable for people with multiple conditions. Doctors use venetoclax and azacitidine as a standard treatment for people with newly diagnosed AML who cannot use **chemotherapy**.

Chemotherapy: It is a combination of medicines that kill cancer cells.

Magrolimab is an investigational drug. In this study, researchers examined whether magrolimab combined with standard treatment (venetoclax + azacitidine) could be a good treatment option for AML. They compared the combination medication (magrolimab + venetoclax + azacitidine) with the standard treatment (venetoclax + azacitidine).

This was a Phase 3 study. This means that researchers looked at how magrolimab and the standard treatment combination worked in a large group of people with AML.

What was the purpose of the study?

The purpose of this study was to find out if magrolimab in combination with the standard treatment of venetoclax and azacitidine can help people with previously untreated AML live longer. This was compared to **placebo** plus standard treatment.

Placebo: A placebo looks like a treatment but does not have active drug in it.

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

- How long did participants live (known as **overall survival time**) after joining the study?
- What side effects did participants have during the study, if any?

Who took part in the study?

- **378** people newly diagnosed with AML in **20** countries around the world took part in the study.
- **5** out of 378 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 AML
- Did not receive any prior treatment for AML
- Could not use **intensive chemotherapy**. **Intensive chemotherapy** means one or more high dose medicines given together for better control of the disease.

The participants enrolled in the study were between the ages of **28** to **91** years.

The table below shows how many study participants were from each country.

United States	93 **(25%)**	Italy	10 **(3%)**
Spain	50 **(13%)**	Hong Kong	9 **(2%)**
France	40 **(11%)**	Israel	8 **(2%)**
Czech Republic	26 **(7%)**	Poland	6 **(2%)**
Germany	22 **(6%)**	United Kingdom	6 **(2%)**
Taiwan	22 **(6%)**	Austria	5 **(1%)**
Netherlands	21 **(6%)**	Hungary	4 **(1%)**
Australia	18 **(5%)**	Norway	4 **(1%)**
Belgium	17 **(4%)**	Switzerland	2 **(less than 1%)**
South Korea	12 **(3%)**	Canada	1 **(less than 1%)**

Race of participants is shown below (Number (%) of participants).

White	260 **(69%)**	Asian	51 **(13%)**
Not Collected	56 **(15%)**	Other or more than one race	6 **(2%)**
		Black or African American	5 **(1%)**

Ethnicity of participants is shown below (Number (%) of participants).

Not Hispanic Or Latino	298 **(79%)**	Not Collected	50 **(13%)**
		Hispanic Or Latino	30 **(8%)**

Participant breakdown by sex
Number (%) of participants

Male
222 **(59%)**

Female
156 **(41%)**

What happened during the study?

The study was a **randomized**, **double-blind**, and **placebo-controlled** study.

Randomized: This means the researchers used a computer program to put participants into treatment groups by chance. This helped make sure the treatments were chosen fairly. In this study, participants had an equal chance of getting magrolimab plus venetoclax and azacitidine or placebo plus venetoclax and azacitidine. This is called 1:1 randomization.

Double-blind: This means none of the participants, doctors or other study staff, and the sponsor personnel directly involved in conducting the study knew what treatment each participant took. This was done to ensure the study results were not influenced in any way. Participants were monitored closely for any side effects, and the safety measures were in place to address any safety concerns.

Placebo-controlled: This means the researchers added placebo to venetoclax plus azacitidine so that the participants would not know which treatment they were receiving. The placebo looked like magrolimab.

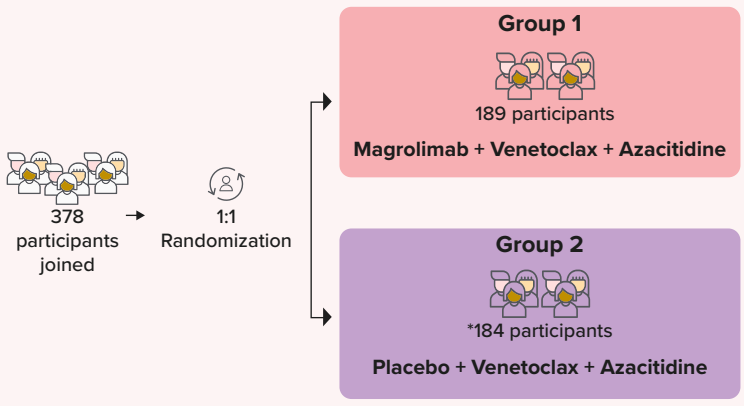
The participants were assigned into 2 groups to receive treatment in cycles. A cycle is the time between one round of treatment and the start of the next. Each cycle consisted of 28 days.

Group 1: Participants received magrolimab + venetoclax + azacitidine.

Group 2: Participants received placebo + venetoclax + azacitidine.

Magrolimab was given in increasing doses. After the first few doses, a fixed dose was given for the rest of the treatment days called the **maintenance dose**. Magrolimab doses were based on the participant's weight (milligram/kilogram; mg/kg). Participants in Group 2 received a placebo that mimicked magrolimab dosing.

The graphic below shows the treatment plan.



*Out of 189 participants in Group 2, 5 participants left the study without taking any treatment.

Magrolimab (or placebo) dosing:

As slow injection into a vein (IV infusion)

Initial Dose:
1 mg/kg on Days 1 and 4
15 mg/kg on Day 8
30 mg/kg on Days 11 and 15
30 mg/kg weekly for 5 doses (Days 22, 29, 36, 43, and 50)

Maintenance Dose:
30 mg/kg on Day 57 and 30 mg/kg every 2 weeks thereafter

Azacitidine Dosing: OR

75 mg/m^2 as a slow injection into a vein or injection under the skin on Days 1-7 (or Days 1-5 and Days 8-9) every 28-day cycle

Venetoclax Dosing:

Tablets given by mouth, 100 mg on Cycle 1 Day 1, 200 mg on Cycle 1 Day 2, and 400 mg on Cycle 1 Day 3 and then daily thereafter.

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.

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 included here. A detailed presentation of the results can be found on the websites listed at the end of this summary.

How long did participants live (known as overall survival time) after joining the study?

Overall survival time was the length of time from the date participants joined the study until their death or the last known alive date. It was reported as **median overall survival time**.

Median overall survival time: In this study, median overall survival time was calculated using a statistical model. The model measured the median number of months the participants lived. The model used the 'number of already occurred deaths' and the 'participants at risk' to find the survival chance of the remaining participants. Measuring the median survival is one way to see how well a treatment works.

The below graphic shows the median overall survival time in both groups:

Group 1: Magrolimab + Venetoclax + Azacitidine (out of 189 participants)

Median overall survival time: 11 months

Group 2: Placebo + Venetoclax + Azacitidine (out of 189 participants)

Median overall survival time: 14 months

The results showed that the participants who took magrolimab plus venetoclax and azacitidine (Group 1) had shorter survival time than participants who took placebo plus venetoclax and azacitidine (Group 2).

Researchers did not see any benefit of combining magrolimab to the standard treatment in participants with AML.

The Sponsor stopped the study earlier than planned as the treatment of magrolimab plus venetoclax and azacitidine did not work as expected.

The other ongoing studies of magrolimab with AML also did not show any treatment benefits. The Sponsor also noted safety concerns in different ongoing magrolimab studies in other types of cancers.

What side effects did participants have during the study?

Unwanted medical events can happen to the study participants when they take study treatments. In this summary, "**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. The results of this study are based on 189 participants in Group 1 and 184 participants in Group 2. Group 2 started with 189 participants but 5 participants left the study before taking any 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

	Group 1 Magrolimab + Venetoclax + Azacitidine (out of 189 participants)	**Group 2** Placebo + Venetoclax + Azacitidine (out of 184 participants)	**Total** (out of 373 participants)
Overall side effects	Number of participants (%)		
How many participants had any side effects?	177 (94%)	162 (88%)	339 (91%)
How many participants had any serious side effects?	87 (46%)	72 (39%)	159 (43%)
How many participants died from side effects?	10 (5%)	4 (2%)	14 (4%)
How many participants stopped taking the study treatment because of side effects?	23 (12%)	13 (7%)	36 (10%)

What were the serious side effects?

The table below shows most common serious side effects that occurred in at least 9 (2%) participants during the study.

The serious side effects occurred in more participants taking magrolimab plus venetoclax and azacitidine (Group 1) than those taking placebo plus venetoclax and azacitidine (Group 2).

Serious Side Effects

	Group 1 Magrolimab + Venetoclax + Azacitidine (out of 189 participants)	**Group 2** Placebo + Venetoclax + Azacitidine (out of 184 participants)	**Total** (out of 373 participants)
	Number of participants (%)		
Fever with a low number of white blood cells (Febrile neutropenia)	30 (16%)	35 (19%)	65 (17%)
Low number of white blood cells (Neutropenia)	8 (4%)	7 (4%)	15 (4%)
Inflammation throughout the body caused due to an infection (Sepsis)	9 (5%)	5 (3%)	14 (4%)
Reaction during or following infusion of a drug (Infusion related reaction)	7 (4%)	2 (1%)	9 (2%)
Lung infection (Pneumonia)	7 (4%)	2 (1%)	9 (2%)

14 out of 373 (4%) participants died due to serious side effects during the study.

More number of deaths were noted in participants taking magrolimab plus venetoclax and azacitidine (Group 1) than those taking placebo plus venetoclax and azacitidine (Group 2).

Group 1 (Magrolimab + Venetoclax + Azacitidine): 10 out of 189 (5%) participants died

- 4 deaths were due to inflammation throughout the body caused by an infection (sepsis).
- 2 deaths were due to fever with a low number of WBCs (febrile neutropenia).
- 2 deaths were due to lung infection (pneumonia).
- 1 death was due to multiple organ failure (multiple organ dysfunction syndrome).
- 1 death was due to lungs not working properly, difficulty breathing with low levels of oxygen in blood (respiratory failure).

Group 2 (Placebo + Venetoclax + Azacitidine): 4 out of 184 (2%) participants died

- 2 deaths were due to inflammation throughout the body caused by an infection (sepsis).
- 1 death was due to fever with a low number of WBCs (febrile neutropenia).
- 1 death was due to one or both kidney failure (renal failure).

What were the non-serious side effects?

The table below shows the **top 5 most common non-serious side effects** that occurred during the study. 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 a similar number of participants taking magrolimab plus venetoclax and azacitidine (Group 1) as those taking placebo plus venetoclax and azacitidine (Group 2).

Non-Serious Side Effects

	Group 1 **Magrolimab + Venetoclax + Azacitidine** (out of 189 participants)	**Group 2** **Placebo + Venetoclax + Azacitidine** (out of 184 participants)	**Total** (out of 373 participants)
	Number of participants (%)		
Low number of white blood cells (Neutropenia)	62 (33%)	67 (36%)	129 (35%)
Low number of red blood cells (Anaemia)	74 (39%)	47 (26%)	121 (32%)
Feeling sick to the stomach (Nausea)	56 (30%)	41 (22%)	97 (26%)
Reduced white blood cells count (Neutrophil count decreased)	48 (25%)	31 (17%)	79 (21%)
Low number of platelets in blood (Thrombocytopenia)	35 (19%)	42 (23%)	77 (21%)

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 and how it works in people with newly diagnosed AML. 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.

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: 2021-003434-36
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	ClinicalTrials.gov ID: NCT05079230
www.gileadclinicaltrials.com	GS-US-590-6154

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

Full Study Title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of Magrolimab versus Placebo in Combination with Venetoclax and Azacitidine in Newly Diagnosed, Previously Untreated Patients with Acute Myeloid Leukemia Who Are Ineligible for Intensive Chemotherapy

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