PLAIN LANGUAGE SUMMARY OF CLINICAL STUDY RESULTS

Study Sponsor: Gilead Sciences

Gilead Protocol Number: GS-US-546-5857

Dates of Trial: July 2021 – March 2024 (the study closed earlier than planned)

Short Study Title: A Study of Magrolimab plus Azacitidine versus Physician's Choice of Venetoclax plus Azacitidine or Intensive Chemotherapy in Previously Untreated Participants with Acute Myeloid Leukemia with TP53 Mutation

Study Nickname: ENHANCE-2

Date of this Report: September 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.

What was the purpose of the study?

The purpose of this clinical study is to find out how magrolimab plus azacitidine works in participants with acute myeloid leukemia (AML) with TP53 mutation.

What is AML?

In healthy people, the blood forming cells (known as stem cells) in the bone marrow make 3 main types of blood cells: red blood cells (RBCs), white blood cells (WBCs), and platelets. The bone marrow is a spongy material in the middle of a bone.

AML is a cancer of blood in which the bone marrow makes too many defective blood cells (called blast cells) that do not function as normal cells do. In AML one or all types of these blood cells may get affected. If left untreated, AML leads to death.

Some patients with AML may have developed faulty (mutated) **genes**. In AML with TP53 mutation, the TP53 gene becomes faulty due to the changes in the DNA of the stem cells. The TP53 gene is responsible for controlling cell growth. In order to treat AML with TP53 mutation, standard treatment like **chemotherapy** is used. The doctors check whether to give intensive or non-intensive therapies based on the patient's condition.

A **gene** is a part of **DNA** that directs the body to make specific proteins for normal functioning. **DNA** stands for deoxyribonucleic acid. It is an essential building block in all living organisms.

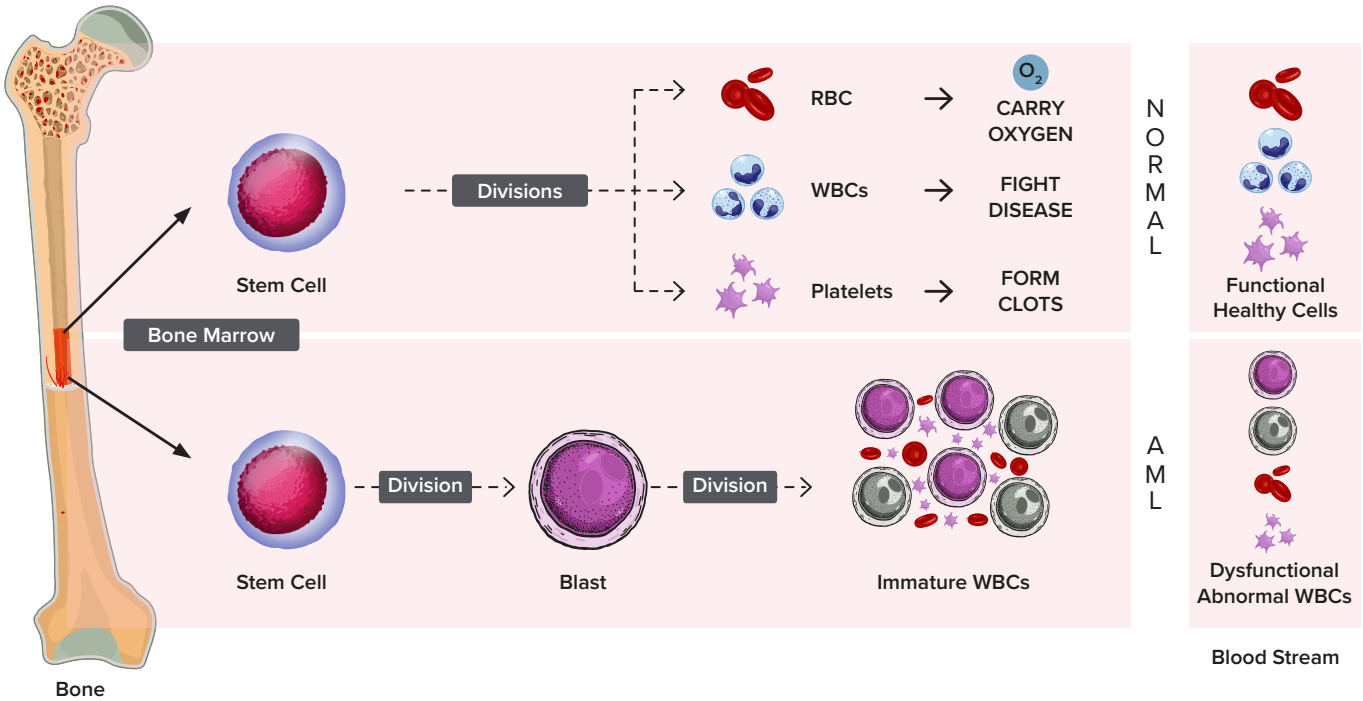
Chemotherapy is a combination of medicines that kill cancer cells.

Intensive therapy means one or more medicines are given together for better control of the disease. They are given at a high dose and can result in more frequent side effects. Non-intensive therapy is a combination of medicines that are given in lower doses, are easier to take, and may cause fewer side effects. This type of therapy may be better for older patients or patients with a lot of medical problems.

Magrolimab is an investigational monoclonal antibody, and researchers think it can help immune cells of the body recognize and kill cancer cells.

Venetoclax plus azacitidine or intensive chemotherapy is a common therapy used by doctors to treat people with AML with TP53 mutation. In this study, researchers compared magrolimab plus azacitidine with venetoclax plus azacitidine or intensive chemotherapy.

The below graphic shows stem cells function in healthy people versus people with AML with TP53 mutation



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

- How long did participants live for after joining the study, in the group of participants appropriate for non-intensive therapy?
- What side effects did participants have during the study, if any?

Who took part in the study?

In total, **257 participants** living with AML with TP53 mutation, around the world, took part in this study.

People could take part in the study if they:

- Were at least 18 years of age
- Had confirmed AML with presence of at least one TP53 gene mutation that can cause cancer
- Did not receive any prior treatment for AML with TP53 mutation

The participants enrolled in the study were between the ages of **27** to **88** years.

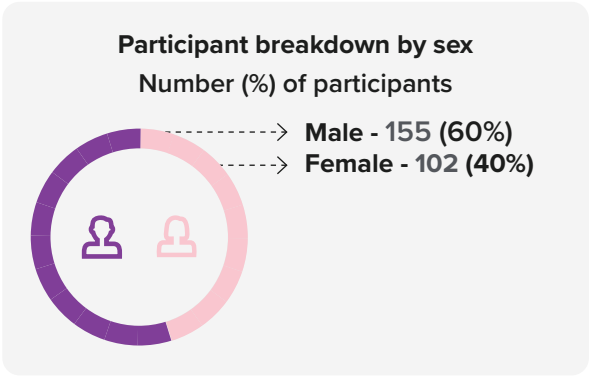
The table below shows how many study participants were from each country.

	Percentage of participants	Number of participants
United States	25%	65
Spain	14%	35
France	12%	32
United Kingdom	10%	26
Japan	8%	21
Australia	8%	20
Italy	7%	18
Germany	6%	16
Switzerland	3%	8
Hong Kong	2%	5
Belgium	less than 2%	4
Canada	less than 2%	4
Austria	less than 1%	2
Sweden	less than 1%	1

Race of participants who took part are shown below.

	Percentage of participants	Number of participants
White	68%	174
Unknown or Not Reported	14%	37
Asian	12%	30
Other or more than one race	less than 4%	9
Black or African American	2%	6
Native Hawaiian Or Other Pacific Islander	less than 1%	1

Sex of participants who took part are shown below.



Ethnicity of participants who took part are shown below.

	Percentage of participants	Number of participants
Not Hispanic Or Latino	76%	195
Unknown or Not Reported	14%	37
Hispanic Or Latino	10%	25

What happened during the study?

The study was **randomized** and **open-label**.

Randomized: This means, researchers used a computer program to randomly choose the treatment each participant took. This helped make sure the treatments were chosen fairly. In this study participants had an equal chance of receiving any of the study treatments.

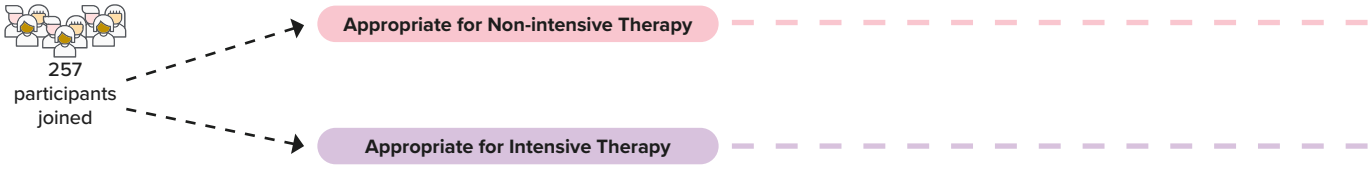
Open-label: This means, the participants or caregiver, and doctors knew the treatment the participants took.

The participants were randomized into 4 groups under 2 umbrellas to receive the following treatment in cycles. A cycle is the time between one round of treatment until the start of the next. Each cycle consisted of 28 days.

The 2 umbrellas were: **Appropriate for Non-intensive Therapy** and **Appropriate for Intensive Therapy**.

The study doctors decided which umbrella the participants were best fit for. Both umbrellas had 2 groups each. Participants had equal chance (1:1 randomization) of getting assigned to any one of the 2 groups:

The graphic below shows what treatments the participants took:



Appropriate for Non-intensive Therapy

Group 1: Magrolimab + Azacitidine

1:1 Randomization

Group 2: Venetoclax + Azacitidine

101 participants
***Group 1**

104 participants
****Group 2**

Magrolimab - Through a needle into a vein

Azacitidine - Through a needle into a vein or an injection under the skin

Drug	Dose	Cycle 1	Cycle 2	Cycle 3 onwards
Dosing Schedule				
Magrolimab	1 mg/kg	Days 1 and 4		
	15 mg/kg	Day 8		
	30 mg/kg	Days 11 and 15, and then every week for 5 weeks		
	30 mg/kg	Every 2 weeks beginning 1 week after the 5 weekly 30 mg/kg dose		
Dosing Schedule				
Azacitidine	75 mg/m²	Days 1-7 or Days 1-5, 8 and 9		

Venetoclax - Tablet taken by mouth

Azacitidine - Through a needle into a vein or an injection under the skin

Drug	Dose	Cycle 1	Cycle 2	Cycle 3 onwards
Dosing Schedule				
Venetoclax	100 mg	Day 1	-	-
	200 mg	Day 2	-	-
	400 mg	Day 3 and daily thereafter	Daily	Daily
Dosing Schedule				
Azacitidine	75 mg/m²	Days 1-7 or Days 1-5, 8 and 9		

*Out of 101 participants, 5 participants did not receive treatment; **Out of 104 participants, 6 participants did not receive treatment

Appropriate for Intensive Therapy

Group 1: Magrolimab + Azacitidine

1:1 Randomization

Group 2: Chemotherapy (In 2 stages)

27 participants
Group 1

Magrolimab - Through a needle into a vein

Azacitidine - Through a needle into a vein or an injection under the skin

Drug	Dose	Cycle 1	Cycle 2	Cycle 3 onwards
Dosing Schedule				
Magrolimab	1 mg/kg	Days 1 and 4		
	15 mg/kg	Day 8		
	30 mg/kg	Days 11 and 15, and then every week for 5 weeks		
	30 mg/kg	Every 2 weeks beginning 1 week after the 5 weekly 30 mg/kg dose		
Dosing Schedule				
Azacitidine	75 mg/m²	Days 1-7 or Days 1-5, 8 and 9		

25 participants
***Group 2**

All Chemotherapy Medicines - Through a needle into a vein

Steroidal Eye Drops

Stages	Drug/Dose	Stage 1 Taken for 7+3 days	Stage 1 Taken for 5+2 days
Dosing Schedule			
Stage 1	Daunorubicin 60 mg/m² or Idarubicin 12 mg/m²	Days 1–3	Days 1–2
	Cytarabine 100 or 200 mg/m²	Days 1–7	Days 1–5
Dosing Schedule			
Stage 2	High dose Cytarabine 1500 or 3000 mg/m²	Every 12 hours on Days 1, 3, and 5 (up to 4 cycles)	
	Steroidal Eye Drops	As per hospital standard	

*Out of 25 participants, 2 participants did not receive treatment

Magrolimab doses were based on participant's weight (milligram/kilogram; mg/kg).

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 in this summary.

How long did participants live for after joining the study, in the group of participants appropriate for non-intensive therapy?

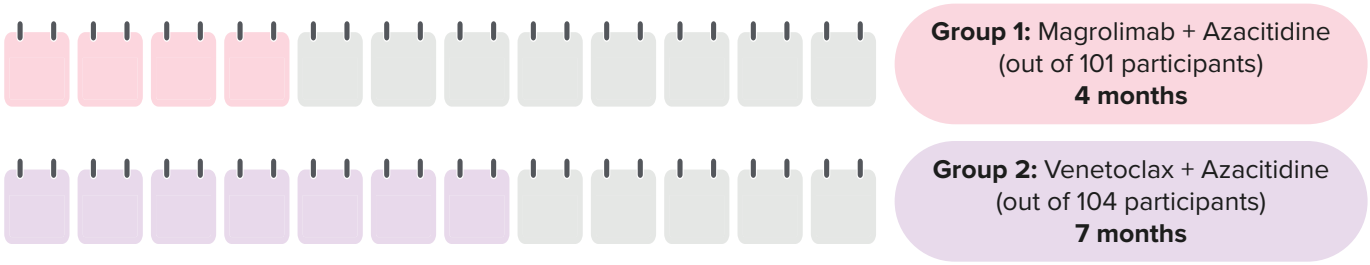
Researchers wanted to find out how long participants lived (**overall survival time**), after joining the study.

The results are presented for the non-intensive therapy groups, Group 1 (magrolimab plus azacitidine) versus Group 2 (venetoclax plus azacitidine).

Overall survival time was measured as the length of time the participants joined the study until the death of the participant due to any reason. This was measured for each participant and the **median** number of months the participants lived for was calculated for all participants in each group.

Median is defined as the middle value of a list of values ordered from smallest to largest. In this analysis, the median survival time was calculated using a statistical model. It uses the 'already occurred deaths' and the 'participants at risk' to find the survival chance of participants.

The below graphic shows the median overall survival time in the non-intensive therapy groups.



The results showed that the participants who took magrolimab plus azacitidine had lesser survival time than participants who took venetoclax plus azacitidine.

Researchers did not see any benefit of magrolimab plus azacitidine treatment in participants with AML with TP53 mutation.

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

What side effects did the participants have during the study?

For the purpose of this summary, "**side effects**" are defined as unwanted medical events reported by the participants that the study doctors thought might be related to 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 results from several studies are usually needed to help decide if a treatment actually causes a side effect.

Out of 257 participants, 244 participants received treatment. Therefore, these results are available only for 244 participants. This includes 96 participants in magrolimab+azacitidine group and 98 participants in venetoclax plus azacitidine group in appropriate for non-intensive therapy. For appropriate for intensive therapy, there were 27 participants in magrolimab plus azacitidine group and 23 participants in chemotherapy group. The table below shows how many participants had side effects during the study.

Overall Side Effects

	Appropriate for Non-intensive Therapy		Appropriate for Intensive Therapy		Total (out of 244 participants)
	Magrolimab + Azacitidine (Out of 96 participants)	Venetoclax + Azacitidine (Out of 98 participants)	Magrolimab + Azacitidine (Out of 27 participants)	Chemotherapy (Out of 23 participants)	
	Number of participants (%)				
Serious side effects	34 (35%)	30 (31%)	6 (22%)	4 (17%)	74 (30%)
Side effects	78 (81%)	80 (82%)	22 (81%)	16 (70%)	196 (80%)
Side effects that caused death	2 (2%)	5 (5%)	2 (7%)	0	9 (4%)
Side effects that caused participants to stop treatment	4 (4%)	3 (3%)	3 (11%)	0	10 (4%)

What were the serious side effects?

The most common **serious side effect** was fever with a low number of white blood cells called neutrophils (febrile neutropenia).

The table below shows the **serious side effects** that occurred in at least 5 out of 244 (2%) participants during the study.

Serious Side Effects

	Appropriate for Non-intensive Therapy		Appropriate for Intensive Therapy		Total (out of 244 participants)
	Magrolimab + Azacitidine (Out of 96 participants)	Venetoclax + Azacitidine (Out of 98 participants)	Magrolimab + Azacitidine (Out of 27 participants)	Chemotherapy (Out of 23 participants)	
Serious Side Effects	**Number of participants (%)**				
Fever with a low number of white blood cells called neutrophils (Febrile neutropenia)	9 (9%)	19 (19%)	2 (7%)	0	30 (12%)
Low number of red blood cells (Anaemia)	6 (6%)	0	0	0	6 (2%)
Infection in the bloodstream due to low level of white blood cells called neutrophils (Neutropenic sepsis)	2 (2%)	2 (2%)	2 (7%)	0	6 (2%)
Lung infection; an infection of one or both of the lungs caused by bacteria, viruses, or fungi (Pneumonia)	1 (1%)	4 (4%)	1 (4%)	0	6 (2%)
Reaction during or following infusion of a drug (Infusion related reaction)	5 (5%)	0	0	0	5 (2%)
Fever (Pyrexia)	4 (4%)	1 (1%)	0	0	5 (2%)

What were the non-serious side effects?

The table below shows the **top 10 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. The most common side effects were feeling sick to the stomach (nausea), and low number of red blood cells (anaemia).

Non-Serious Side Effects

	Appropriate for Non-intensive Therapy		Appropriate for Intensive Therapy		Total (out of 244 participants)
	Magrolimab + Azacitidine (Out of 96 participants)	Venetoclax + Azacitidine (Out of 98 participants)	Magrolimab + Azacitidine (Out of 27 participants)	Chemotherapy (Out of 23 participants)	
Non-serious Side Effects	**Number of participants (%)**				
Feeling sick to the stomach (Nausea)	20 (21%)	16 (16%)	10 (37%)	4 (17%)	50 (20%)
Low number of red blood cells (Anaemia)	23 (24%)	17 (17%)	6 (22%)	3 (13%)	49 (20%)
Decrease in part of blood that causes clots (Platelet count decreased)	12 (13%)	18 (18%)	2 (7%)	1 (4%)	33 (14%)
Frequent, loose watery stools (Diarrhea)	9 (9%)	13 (13%)	2 (7%)	7 (30%)	31 (13%)
Fever with a low number of white blood cells called neutrophils (Febrile neutropenia)	10 (10%)	12 (12%)	5 (19%)	4 (17%)	31 (13%)
Fever (Pyrexia)	15 (16%)	5 (5%)	6 (22%)	3 (13%)	29 (12%)
Low number of white blood cells called neutrophils (Neutropenia)	6 (6%)	18 (18%)	0	3 (13%)	27 (11%)
Decreased level of white blood cells called neutrophils (Neutrophil count decreased)	7 (7%)	18 (18%)	1 (4%)	0	26 (11%)
Infrequent bowel movements; difficult passage of stools (Constipation)	12 (13%)	9 (9%)	2 (7%)	1 (4%)	24 (10%)
Vomiting	9 (9%)	12 (12%)	3 (11%)	0	24 (10%)

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 plus azacitidine and if it works in people living with AML with TP53 mutation.

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. Always talk to a doctor before making any treatment changes.

Gilead Sciences does not plan to have further clinical studies with magrolimab in participants with AML with TP53 mutation.

Where can I learn more about this study?

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

www.clinicaltrials.gov

Once you are on this website, type **NCT04778397** into the search box and click **"Search"**

www.clinicaltrialsregister.eu

Once you are on the website, click “Home and Search”, then type **2020-003949-11** into the search box and click **"Search"**

Company Website: www.gileadclinicaltrials.com
National Clinical Trials Number: NCT04778397
EU Clinical Trials Number: 2020-003949-11

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

Full Study Title: A Phase 3, Randomized, Open-Label Study Evaluating the Safety and Efficacy of Magrolimab in Combination with Azacitidine versus Physician’s Choice of Venetoclax in Combination with Azacitidine or Intensive Chemotherapy in Previously Untreated Patients with TP53 Mutant Acute Myeloid Leukemia

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

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Thank you

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