PLAIN LANGUAGE SUMMARY OF CLINICAL STUDY RESULTS

Study Sponsor: Gilead Sciences

Gilead Protocol Number: 5F9009

Dates of Trial: September 2020 to September 2023

Short Study Title: Magrolimab plus Azacitidine versus Azacitidine plus Placebo in Untreated Participants with Myelodysplastic Syndromes

Study Nickname: ENHANCE

Date of this Report: February 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 untreated participants with higher risk myelodysplastic syndromes (MDS) by **IPSS-R**. This is compared to the treatment of **placebo** plus azacitidine.

IPSS-R: It stands for Revised International Prognostic Scoring System. The prognostic scoring system helps to find out the prognosis (likely outcome) of MDS. The score is based on various factors and categorize people with MDS in 5 risk categories: very low, low, intermediate, high or very high risk MDS.

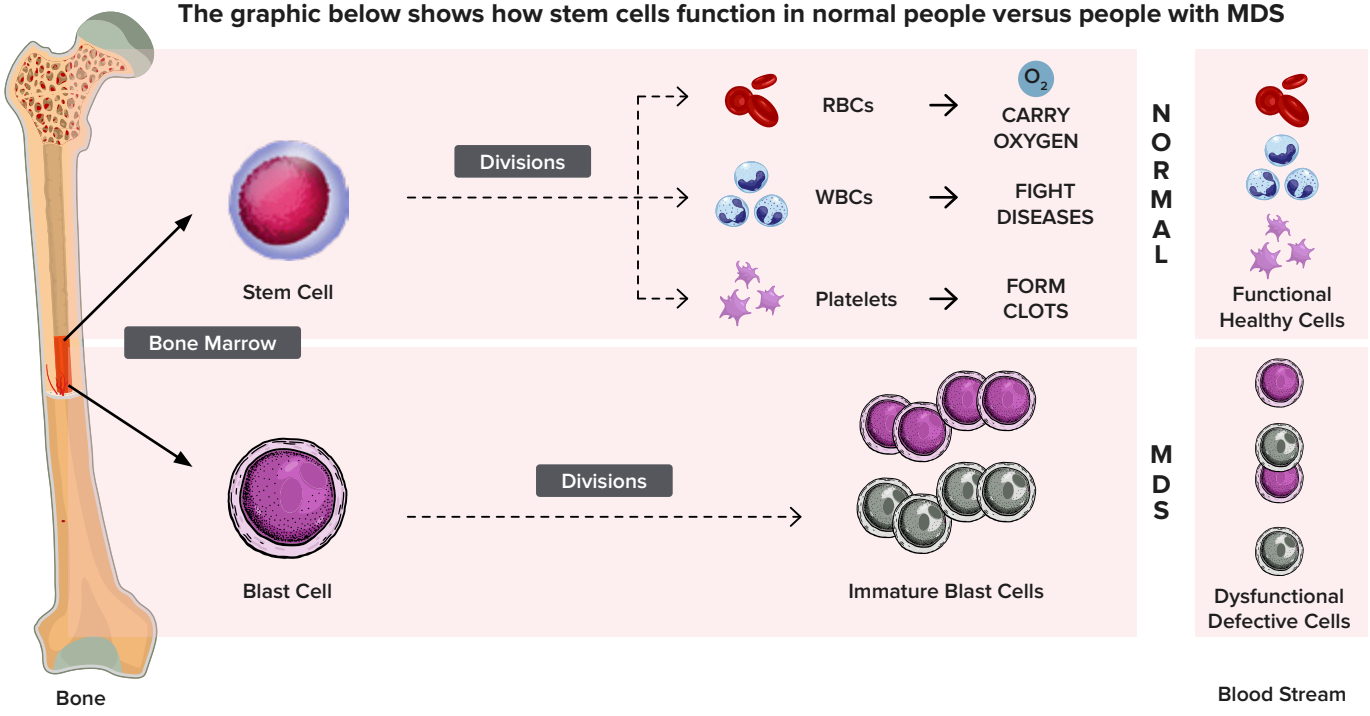
Placebo: A placebo looks like a treatment but does not have any active ingredient drug in it.

The researchers added placebo to azacitidine so that the participants would not know which treatment they were receiving. The placebo looked like magrolimab.

What is MDS?

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. In MDS condition, the stem cells in the bone marrow becomes defective (dysplastic) and have problems making new blood cells, in which one or all types of the blood cells may get affected. Many of the blood cells formed by these bone marrow cells are defective. Defective cells (also called blast cells) often die earlier than normal cells. The body also destroys some of these defective blood cells, leaving a person without enough normal blood cells.

The graphic below shows how stem cells function in normal people versus people with MDS



General symptoms associated with MDS include extreme tiredness, sensation of spinning around and loosing one's balance (dizziness), weakness, bruising and bleeding, frequent infections, and headaches. The exact cause of MDS is unknown but genetics, certain toxic exposures in the environment, and previous treatment with other cancer drugs may play a part.

In some affected individuals, MDS may progress to life-threatening failure of the bone marrow or develop into acute myeloid leukemia (AML, a type of blood cancer). In order to improve bone marrow function and to stop progress of MDS to AML, there is a need of novel drug therapies.

Magrolimab is an investigational monoclonal antibody, and researchers think it can help immune cells of the body recognize and kill cancer cells. Azacitidine was chosen for comparison because it is a common therapy used by doctors to treat people with intermediate, high or very high risk MDS. However, MDS patients treated with azacitidine have been noted to have low survival chances. Therefore, there is a need for a better therapy.

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

- How many participants achieved **complete remission**?
- How long did participants live for after joining the study?
- What side effects did participants have during the study, if any?

Complete remission: Complete remission is defined as decrease in blast cells (immature cells) and rise in healthy blood forming cells or blood cells.

Who took part in the study?

In total, **539 participants** living with MDS around the world took part in this study.

People could take part in the study if they:

- Were 18 years of age or older
- Had MDS that was of either intermediate, high or very high risk
- Did not take any prior treatment for MDS

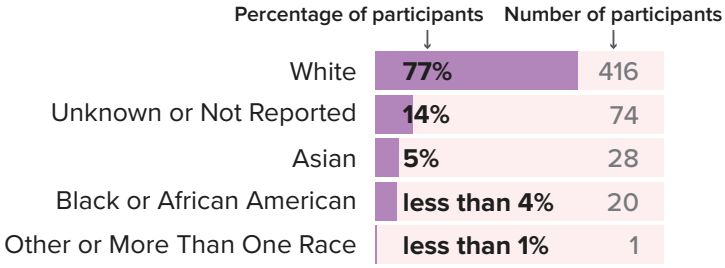
The participants enrolled in the study were between the ages of **19** to **88** years.

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

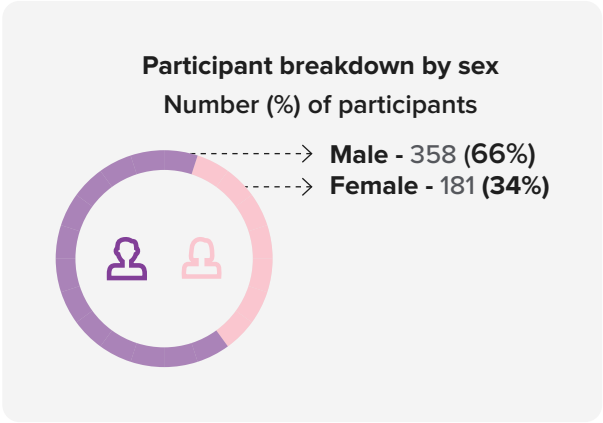
	Percentage of participants	Number of participants
United States	**65%**	352
Australia	**14%**	75
Spain	**5%**	27
France	**4%**	21
Italy	**2%**	13
Poland	**2%**	10
United Kingdom	**2%**	9
Hong Kong	**less than 2%**	8
New Zealand	**1%**	6

	Percentage of participants	Number of participants
Germany	**less than 1%**	4
Portugal	**less than 1%**	3
Canada	**less than 1%**	2
Finland	**less than 1%**	2
Switzerland	**less than 1%**	2
Turkey	**less than 1%**	2
Belgium	**less than 1%**	1
Hungary	**less than 1%**	1
Norway	**less than 1%**	1

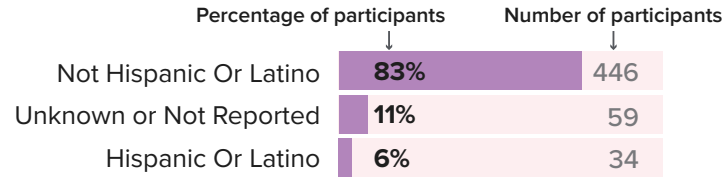
Race of participants who took part are shown below.



Sex of participants who took part are shown below.



Ethnicity of participants who took part are shown below.



What happened during the study?

The study was **randomized** and **double-blind**.

Randomized: This means, that the 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 taking magrolimab plus azacitidine or placebo plus azacitidine.

Double-blind: This means, none of the participants, doctors, nor the sponsor, i.e., Gilead personnel knew what treatment each participant took. This was done to make sure that the trial results were not influenced in any way.

The participants were assigned into 2 groups to receive treatment in cycles. Participants had equal chance (1:1 random selection) of getting assigned to any one of the 2 groups. A cycle is the time between one round of treatment until the start of the next. Each cycle consisted of 28 days.

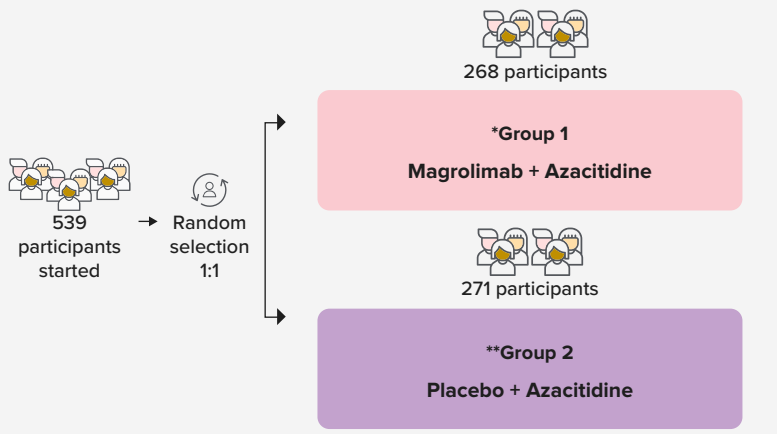
Group 1: Participants received magrolimab + azacitidine.

Group 2: Participants received placebo + azacitidine.

Magrolimab was given in increasing doses called **priming dose**. After the first few doses, a fixed dose was given for the rest of the treatment days called **maintenance dose**. Both priming and maintenance doses were based on participant's weight (milligram/kilogram; mg/kg).

Participants received treatment until their disease got worse, they had unacceptable side effects, they decided to leave the study, or they died.

The graphic below shows the treatment participants took.



*Out of 268 participants, 5 participants left the study without taking any drug in Group 1

**Out of 271 participants, 7 participants left the study without taking any drug in Group 2

As slow injection into a vein (IV infusion)

Magrolimab (or placebo) dosing:

Priming 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:
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

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 present in this summary.

How many participants achieved complete remission?
The researchers wanted to find out how many participants achieved complete remission after taking the study treatment. The participants had blood tests and bone marrow tests done during the study. The doctors checked the results of these tests. If test results showed that there was a rise in healthy blood cells and if the blast cells almost disappeared, the participants were said to have achieved complete remission.

The graphic below shows percentage of participants with complete remission in each group.

Group 1: Magrolimab + Azacitidine
21% (Out of 268 participants)

Group 2: Placebo + Azacitidine
24% (Out of 271 participants)

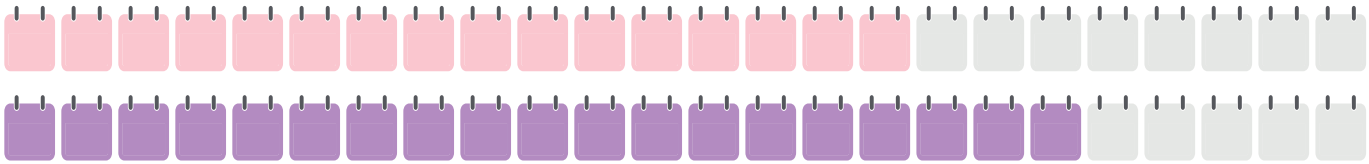
The percentage of participants with complete remission was less in participants who received magrolimab plus azacitidine compared with participants who received placebo plus azacitidine.

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

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 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 graphic below shows median overall survival time in each group.



Group 1: Magrolimab + Azacitidine
(Out of 268 participants)
16 months

Group 2: Placebo + Azacitidine
(Out of 271 participants)
19 months

The participants who took magrolimab plus azacitidine had lesser survival time than participants who took placebo plus azacitidine.

Researchers did not see any benefit of magrolimab plus azacitidine treatment in participants with MDS.

The Sponsor decided to stop the study earlier than planned as the treatment of magrolimab plus azacitidine did not work and there were too many side effects.

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

The results from several studies are usually needed to help decide if a treatment actually causes a side effect. Out of 539 participants, 12 participants did not take any study treatment. So, the results in this section only include 527 participants.

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

Overall Side Effects

	Magrolimab + Azacitidine (out of 263 participants)	**Placebo + Azacitidine** (out of 264 participants)	**Total** (out of 527 participants)
	Number of participants (%)		
How many participants had serious side effects?	114 (43%)	52 (20%)	166 (31%)
How many participants had any side effects?	252 (96%)	229 (87%)	481 (91%)
How many participants died from side effects?	6 (2%)	1 (less than 1%)	7 (1%)
How many participants stopped taking study treatment because of side effects?	29 (11%)	9 (3%)	38 (7%)

The most common **serious side effects** were fever with a low number of white blood cells called neutrophils (febrile neutropenia), reaction during or following infusion of a drug (infusion related reaction), and low number of red blood cells (anaemia).

The table below shows **serious side effects** that occurred in at least 5 participants during the study.

Serious Side Effects

Serious Side Effects	Magrolimab + Azacitidine (out of 263 participants)	Placebo + Azacitidine (out of 264 participants)	Total (out of 527 participants)
	Number of participants (%)		
Fever with a low number of white blood cells called neutrophils (Febrile neutropenia)	31 (12%)	20 (8%)	51 (10%)
Reaction during or following infusion of a drug (Infusion related reaction)	31 (12%)	1 (less than 1%)	32 (6%)
Low number of red blood cells (Anaemia)	19 (7%)	3 (1%)	22 (4%)
Lung infection; an infection of one or both of the lungs caused by bacteria, viruses, or fungi (Pneumonia)	9 (3%)	3 (1%)	12 (2%)
Widespread inflammation throughout the body caused by a strong immune response to an infection (Sepsis)	6 (2%)	4 (2%)	10 (2%)
Breakdown in red blood cells (Haemolysis)	9 (3%)	0	9 (2%)
Fever (Pyrexia)	4 (2%)	5 (2%)	9 (2%)
A life-threatening condition that happens when the blood pressure drops to a dangerously low level after an infection (Septic shock)	3 (1%)	2 (less than 1%)	5 (less than 1%)
Vomiting	4 (2%)	1 (less than 1%)	5 (less than 1%)

The table below shows the **top 10 most common side effects** that occurred during the study. There were other side effects, but those occurred in fewer participants. Some participants may have had more than one side effect.

The **most common side effects** were feeling sick to the stomach (nausea), low number of red blood cells (anaemia), infrequent bowel movements; difficult passage of stools (constipation).

Most Common Side Effects

Most Common Side Effects	Magrolimab + Azacitidine (out of 263 participants)	Placebo + Azacitidine (out of 264 participants)	Total (out of 527 participants)
	Number of participants (%)		
Feeling sick to the stomach (Nausea)	108 (41%)	92 (35%)	200 (38%)
Low number of red blood cells (Anaemia)	101 (38%)	57 (22%)	158 (30%)
Infrequent bowel movements; difficult passage of stools (Constipation)	79 (30%)	76 (29%)	155 (29%)
Extreme tiredness (Fatigue)	73 (28%)	63 (24%)	136 (26%)
Reaction during or following infusion of a drug (Infusion related reaction)	90 (34%)	37 (14%)	127 (24%)
Decreased level of white blood cells called neutrophils (Neutrophil count decreased)	60 (23%)	49 (19%)	109 (21%)
Decrease in part of blood that causes clots (Platelet count decreased)	58 (22%)	51 (19%)	109 (21%)
Low number of white blood cells called neutrophils (Neutropenia)	48 (18%)	49 (19%)	97 (18%)
Frequent, loose watery stools (Diarrhea)	48 (18%)	47 (18%)	95 (18%)
Vomiting	37 (14%)	39 (15%)	76 (14%)
White blood cells count decreased	39 (15%)	37 (14%)	76 (14%)

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 MDS.

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 MDS.

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 "**NCT04313881**" into the search box and click "**Search**"

www.clinicaltrialsregister.eu

Once you are on the website, click "Home and Search", then type "**2020-004287-26**" into the search box and click "**Search**"

Company Website: www.gileadclinicaltrials.com
National Clinical Trials Number: NCT04313881
EU Clinical Trials Number: 2020-004287-26

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

Full Study Title: ENHANCE: A Randomized, Double-blind, Multicenter Study Comparing Magrolimab in Combination with Azacitidine versus Azacitidine Plus Placebo in Treatment-naïve Patients with Higher Risk Myelodysplastic Syndrome

For more information about clinical trials, click here.

Gilead Sciences
333 Lakeside Drive, Foster City, CA 94404, USA
GileadClinicalTrials@gilead.com

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