Clinical Study Results

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medication works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer Inc.

Medicine Studied: Elranatamab (PF-06863135)

Protocol Number: C1071001 (also known as MagnetisMM-1)

Dates of Study: 29 November 2017 to 19 January 2024

Title of this Study: A Study of Elranatamab Given Alone or in Combination With Other Immunomodulatory Medications in Adults With Multiple Myeloma

[A Phase I, Open Label Study to Evaluate the Safety, Pharmacokinetic, Pharmacodynamic and Clinical Activity of Elranatamab (PF-06863135), a B-Cell Maturation Antigen (BCMA) - CD3 Bispecific Antibody, as a Single Agent and in Combination With Immunomodulatory Agents in Patients With Relapsed/Refractory Advanced Multiple Myeloma (MM)]

Date of this Report: 18 September 2024

– Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

Why was this study done?

What is multiple myeloma?

Cancer occurs when cells in the body divide without control.

Multiple myeloma (MM) is a type of blood cancer. It affects a type of white blood cell called a plasma cell. Plasma cells make antibodies, which are proteins that help the body fight infections and diseases. In people with MM, the body makes too many abnormal plasma cells. These abnormal plasma cells build up in the bone marrow (spongy tissue inside most bones that makes new blood cells) and stop the body from making healthy plasma cells.

Currently, there is no cure for MM but there are available treatments to help control it. Autologous stem cell transplant (ASCT) is one of these treatments. ASCT is a procedure where a patient's own healthy blood-forming cells, called "stem cells", are used to restore the body's ability to produce normal blood cells. Medications that change the body's immune response to diseases (called "immunomodulatory medications") also help with MM.

However, some people's MM may not respond (refractory) to any of these treatments or may come back (relapse) after treatment.

What is elranatamab?

Elranatamab (ehl-RA-na-ta-mab), also known as PF-06863135, is a medicine that is being studied as a possible treatment for people with MM. It is designed to help certain white blood cells called “T cells” to target and destroy MM cells. Elranatamab is given subcutaneously (injection under the skin).

When this study started, elranatamab was an investigational medicine because it was not yet approved for use by the health authorities outside of research studies. But, while the study was ongoing, elranatamab had been approved by health authorities for relapsed or relapsed MM in many countries worldwide.

What was the purpose of this study?

This study had 2 parts: Part 1 and Part 2. The main purpose of each part are as follows:

- **Part 1 (Dose-Finding)**: To learn how safe the different doses of elranatamab were when given alone or in combination with 1 of the following immunomodulatory medications: lenalidomide, pomalidomide, or dexamethasone.

  Researchers monitored the safety of participants and checked if they had any intolerable side effects after treatment with any of the study medications and their doses.

  Intolerable side effects are certain medical problems that researchers believe are related to a study medication and are serious enough to prevent an increase in the dose of that medication.

Checking for side effects helped the researchers find the **recommended dose** (**RD**) of elranatamab to be further studied for safety and effectiveness in Part 2.

In this study, "study medication" refers to elranatamab given alone or in combination with lenalidomide, pomalidomide, or dexamethasone.

- **Part 2 (Dose Expansion)**: To learn how well elranatamab works against MM.

Researchers checked if participants' MM responded to elranatamab by looking at whether participants' MM signs improved after treatment. Researchers measured the following to evaluate response to treatment:

- Proteins released by myeloma cells
- Myeloma cells in the bone marrow
- Destructive lesions in the bones

Researchers wanted to know:

- **How many participants had intolerable side effects after treatment in Part 1?**
- **Did the participants' MM respond to the study medications?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

This study was done in 2 parts. Participants were to take part in 1 of these parts only. The researchers assigned the participants into a part depending on when the participants signed up.

Part 1 (Dose-Finding): Researchers tested different doses of elranatamab given alone or in combination with an immunomodulatory medication in different groups of participants to learn about the safety of these doses and find the **RD**. Researchers also tested 2 ways to give elranatamab: through the vein (also called **intravenously** or **IV**) and through injections under the skin (**subcutaneously** or **SC**).

Part 1 started with giving IV doses of elranatamab. The first group of participants received the lowest dose. If the researchers did not observe any safety concerns, the next group of participants received the next higher dose. This process continued until all planned doses had been tested, or until a dose was identified as unsafe. After IV doses had been tested, SC doses were then tested in a similar way as the IV doses.

After finding the RD of elranatamab, its safety was to be further tested in the following treatment conditions:

- **Part 1.1 ("step-up" dosing)**: Elranatamab RD only.
  Step-up dosing means a lower dose (also called "priming dose") of elranatamab was given first before the full dose was given in a regular schedule of either once every week or once every 2 weeks (also called "maintenance dose").

  A step-up dosing is sometimes needed to help the body's immune system to adjust to the full dose of a medication.

- **Part 1C**: Elranatamab RD plus lenalidomide.
- **Part 1D**: Elranatamab RD plus pomalidomide.
- **Part 1E**: Elranatamab RD plus dexamethasone.

Part 2 (Dose Expansion): Researchers were to study elranatamab RD further to learn more about how safe the RD was when given alone or in combination with an immunomodulatory medication. Part 2 also checked whether elranatamab RD worked on MM. The following treatment conditions were to be further studied in Part 2:

- **Part 2A**: Elranatamab RD only.
- **Part 2C**: Elranatamab RD plus lenalidomide.
- **Part 2D**: Elranatamab RD plus pomalidomide.
- **Part 2E**: Elranatamab RD plus dexamethasone.

Researchers did not enroll any participants in **Part 1E** and **Parts 2C**, **2D**, and **2E** due to strategic reasons. Future studies will further assess combination treatment with elranatamab, therefore, no data were collected from these planned parts in this study.

Participants took their assigned study medications for as long as they were responding to treatment and their MM was not worsening, or until they had an intolerable side effect, they decided to stop taking part in the study, or the study ended, whichever came first.

The participants and researchers knew which study medications each participant received. This is known as an “open-label” study.

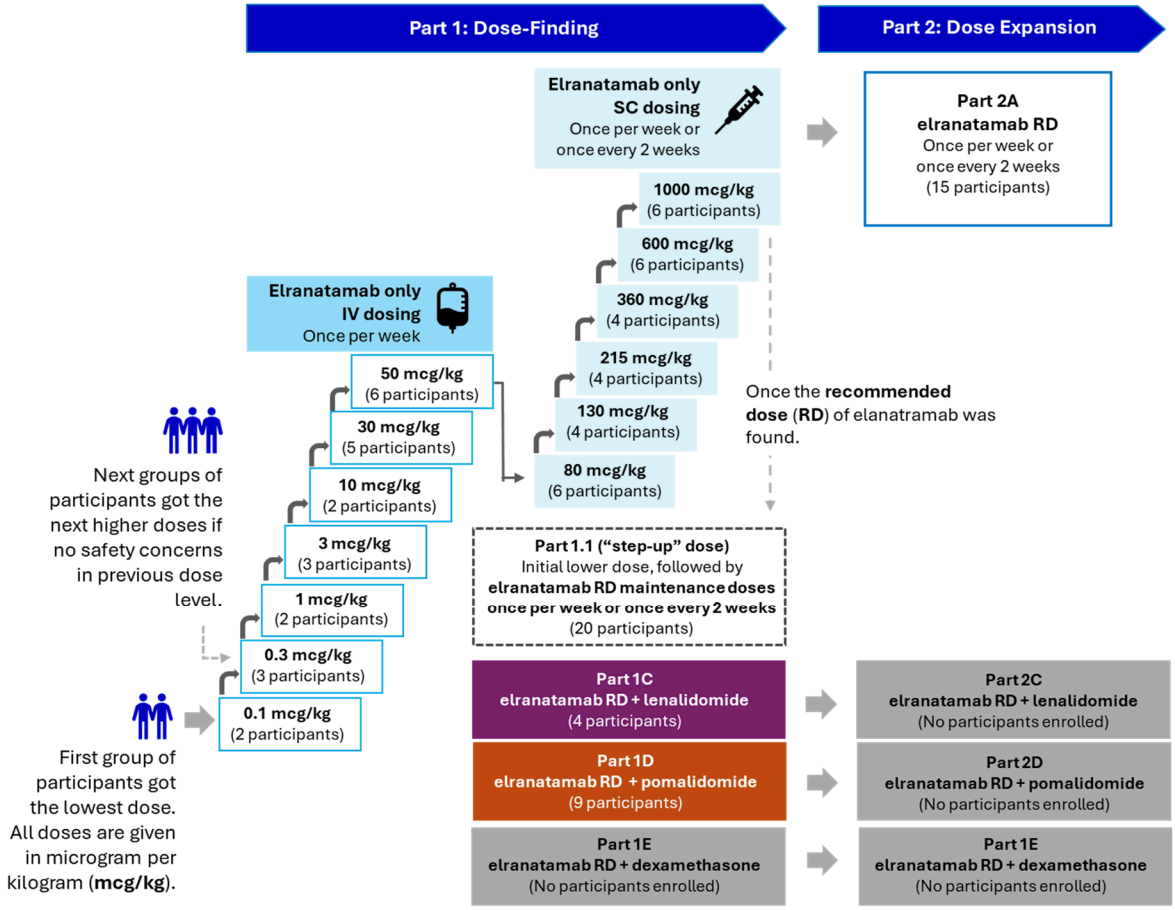
Researchers checked the participants’ health throughout the study and asked them how they were feeling. They also took samples of blood, urine, and bone marrow from participants to monitor their MM and overall health.

After treatment: About 4 weeks after the participants' last dose, they had 1 follow-up visit at the study site. Some participants may have had additional follow-up checks at the study site depending on how they were feeling.

All participants had follow-up phone calls with the study staff every 3 months after they stopped treatment. The follow-up phone calls might have lasted until about 2 and a half years after the last dose of the last participant enrolled in the study.

Figure 1 shows what happened during the study and the study medication doses that participants received.

Figure 1. How was the study done?



Where did this study take place?

The Sponsor ran this study at 14 locations in Canada and the United States.

When did this study take place?

It began on 29 November 2017 and ended on 19 January 2024.

Who participated in this study?

The study included participants who met the study requirements, including the following:

- At least 18 years of age.
- Have MM that had relapsed or is refractory to standard anticancer medications for MM.
- Had no other types of cancer.

A total of 101 participants with MM joined the study and received a study medication.

- A total of 54 men and 47 women participated.
- Participants were between the ages of 32 and 86 years.

The most common reason for not finishing treatment in this study was worsening of participants' MM.

How long did the study last?

The length of each participant's participation in the study depended on the response of their MM to treatment. The entire study took about 6 years to complete.

When the study ended in January 2024, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

How many participants had intolerable side effects after treatment in Part 1?

This section includes results from **Part 1 (Dose-Finding)**. This section will focus on the results of participants who received elranatamab only (also called “monotherapy”).

Overall, 3 participants who received eltranatamab as monotherapy had intolerable side effects during the study. These participants were from the following groups:

Part 1 Elranatamab IV Groups:

- 1 out of 5 participants (20%) in the IV 30 mcg/kg group.
- 1 out of 6 participants (17%) in the IV 50 mcg/kg group.

Part 1.1 Elranatamab Step-up Dosing Groups:

- 1 out of 13 participants (8%) in the once every 2 weeks maintenance dose (SC 1000 mcg/kg) group.

Based on these results, the researchers determined that elranatamab SC doses up to 1000 mcg/kg were tolerable. Because of this, elranatamab SC 1000 mcg/kg was determined to be the RD in this study.

Did the participants' MM respond to study medications?

To answer this question, researchers looked at the laboratory test results of participants who received 1 of the doses in the efficacious dose range in the study.

> **Efficacious dose range** refers to the doses that may give clinical benefit to patients. In this study, the efficacy dose range was elranatamab SC 215 to 1000 mcg/kg once per week or once every 2 weeks.
>
> The group of participants who received 1 of these doses is called the **Efficacious Dose Range Group** in this summary.
>
> Because of limited data, participants who received combination treatments in this study were not counted in this group.

Researchers then calculated the percentage of participants whose MM responded to elranatamab based on the results of their laboratory tests. Researchers also measured how long the participants' MM continued responding to elranatamab.

After receiving elranatamab:

- Overall, 35 out of 55 participants (**64%**) in the Efficacious Dose Range Group had MM that **responded to elranatamab**.
- Half of the participants whose MM responded to elranatamab **continued responding to treatment** for about **17 months**.

Based on these results, the researchers determined that elranatamab SC 1000 mcg/kg may help people with relapsed or refractory MM.

This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study. Other studies may have different results.

What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medication might have on a participant.

This section will focus on the results for the **Efficacious Dose Range Group**.

All 55 participants (100%) in this group reported at least 1 medical problem during the study. A total of 10 out of 55 participants (18%) left the study because of medical problems they had in the study.

The most common medical problems – those reported by more than 50% of participants– are listed in Table 1 below.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported in the Efficacious Dose Range Group during the study. All medical problems reported by more than 50% of participants are listed.
- The **2nd** column tells how many of the 55 participants in the Efficacious Dose Range Group reported each medical problem. Next to this number is the percentage of these 55 participants who reported the medical problem.
- For example, using these instructions, you can see that 48 out of the 55 participants (87%) in this group reported CRS.

Table 1. Commonly reported medical problems by study participants in the Efficacy Dose Range Group (elranatamab SC 215 to 1000 mcg/kg once per week or once every 2 weeks)

Medical Problem	Efficacy Dose Range Group (55 Participants)
Cytokine release syndrome or **CRS** (a serious immune reaction with symptoms such as fever, low blood pressure, or shortness of breath)	48 out of 55 participants (87%)

Table 1. Commonly reported medical problems by study participants in the Efficacy Dose Range Group (elranatamab SC 215 to 1000 mcg/kg once per week or once every 2 weeks)

Medical Problem	Efficacy Dose Range Group (55 Participants)
Neutropenia (low levels of neutrophils, a type of white blood cell that helps fight infections)	41 out of 55 participants (75%)
Anemia (low levels of red blood cells that carry oxygen around the body)	37 out of 55 participants (67%)
Reaction of the skin at the site where elranatamab was injected	31 out of 55 participants (56%)
Lymphopenia (low levels of lymphocytes, a type of white blood cell that helps to fight infections)	29 out of 55 participants (53%)
Thrombocytopenia (low levels of platelets, blood cells that help form clots to stop bleeding)	28 out of 55 participants (51%)

Did study participants have any serious medical problems?

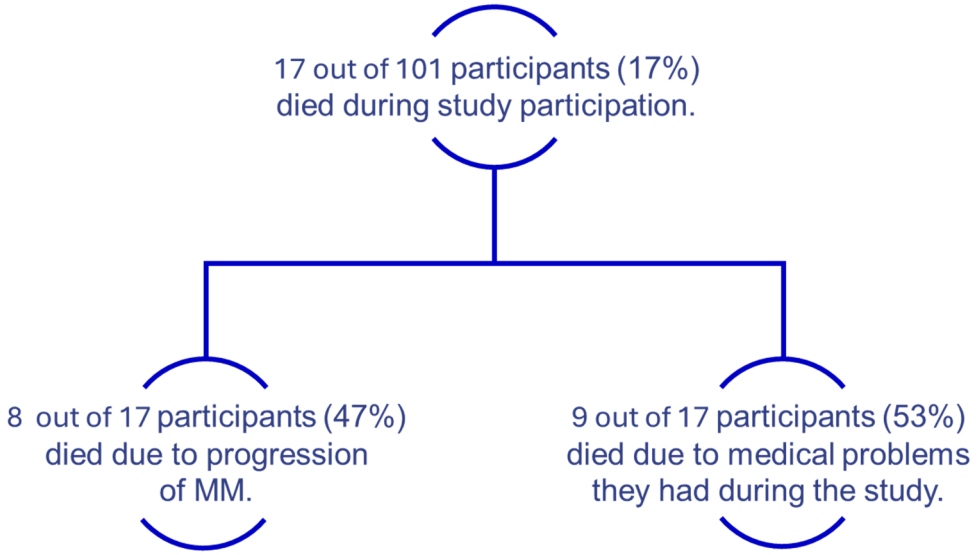
A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems.

There were 42 out of 55 participants (76%) in the Efficacious Dose Range Group who reported at least 1 serious medical problem.

The most common serious medical problem – those reported by more than 50% of participants – in this group was CRS. CRS was reported by 15 out of 55 participants (27%). Researchers believe that CRS might be related to elranatamab.

Figure 2 shows that overall, 17 out of 101 participants (17%) who joined the study died during study participation:

Figure 2. How many participants died during the study?



Where can I learn more about this study?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on your study protocol, please visit:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **C1071001**

The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier **NCT03269136**
www.clinicaltrialsregister.eu	Use the study identifier **2019-000822-24**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you participated in this study, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!