Summary of Clinical Trial Results

A study to look at the side effects of a study medicine (efmarodocokin alfa) in patients undergoing hematopoietic stem cell transplantation (HSCT)

See the end of the summary for the full title of the study.

About this summary

This is a summary of the results of a clinical trial (called a "study" in this document).

This summary is written for:

- Members of the public
- People who took part in the study

This summary is based on information known at the time of writing.

The study started in November 2020 and finished in February 2023. This summary was written after the study had ended.

A single study cannot tell us all there is to know about the risks and benefits of a medicine. It takes many people in several studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

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Contents of the summary

Thank you to the people who took part in this study

The people who took part have helped researchers answer important questions about hematopoietic stem cell transplantation (HSCT) and the medicine studied – "efmarodocokin alfa."

Key information about this study

- This study was done to look at the side effects from a study medicine (efmarodocokin alfa) when given to patients undergoing hematopoietic stem cell transplantation (HSCT).
- Patients were given the study medicine in addition to the regular care and treatments that doctors had prescribed for their medical procedure.
- This study included 18 patients at 6 study centers in one country – the USA.
- The main finding was that researchers thought the study medicine could be tolerated by patients who were undergoing HSCT.
- While patients had serious side effects, study doctors did not think any of those were caused by efmarodocokin alfa. Patients also experienced several side effects that were non-serious. Among those, study doctors thought some were caused by efmarodocokin alfa (9 patients with 48 non-serious side effects).
- At the time of writing this summary, the study sponsor decided not to conduct further clinical trials of efmarodocokin alfa for patients undergoing HSCT.

1. General information about this study

Why was this study done?

Hematopoietic stem cell transplantation (HSCT) is a medical procedure where special blood cells (stem cells) from a healthy person (the donor) are transplanted into the patient (the recipient). The donor can be a blood relative (like a brother or sister), or someone else who is a good match.

HSCT treatment is used primarily for patients with certain cancers of the blood or bone marrow. Following HSCT, healthy stem cells from the donor can develop into many different types of blood cells in the recipient.

Graft Versus Host Disease (GVHD) is a complication that can occur after HSCT. In GVHD, blood cells that arise from the donor's stem cells recognize the recipient's body as different or "foreign." Then, the donor's blood cells (the graft) start an immune response and attack the recipient's cells (the host). GVHD typically shows up in the patient in the skin (rash), liver (hepatitis), and gut (diarrhea).

GVHD is a serious condition that can lead to death. Choosing a donor who is a close match reduces the risk of GVHD – but does not eliminate it.

Significant advancements have been made in the prevention and treatment of GVHD. But unfortunately, GVHD remains a risk factor for sickness and death (morbidity and mortality). There is a need for new treatments with fewer side effects and better outcomes for patients.

Efmarodocokin alfa is a study medicine that researchers believe could help patients undergoing HSCT. It is a medicine that may prevent or reduce the immune response from the donor cells without further suppressing the patient's immune system. Before researchers find out if it is effective, they need to find out about dose levels and side effects.

This study was done to test efmarodocokin alfa treatments in patients undergoing HSCT to learn about side effects at different doses.

What was the study medicines?

A medicine called “efmarodocokin alfa” was the focus of this study. This medicine is also known as “UTTR1147A.”

Efmarodocokin alfa is a medicine made by connecting (fusing) two different proteins. One of the proteins is a called “IL-22” which is naturally made by the human body.

IL-22 that is naturally made in the body, is involved in immune responses and tissue repair processes, particularly in the gut. The man-made medicine based on IL-22 could help prevent and treat GVHD in patients who have undergone HSCT – by focusing on the gut region of the disease.

IL-22 also appears to reduce inflammation in the body. The man-made medicine based on IL-22 could possibly help reduce the unwanted immune response seen in GVHD.

What did researchers want to find out?

The main question that researchers wanted to answer was:

1. Was efmarodocokin alfa safe enough to be given to patients undergoing HSCT – could it be tolerated based on the side effects seen at the doses tested?

What kind of study was this?

Here are a few ways to describe this study.

Phase 1b study: This is an early study that usually follows other Phase 1 studies. While Phase 1 studies may involve healthy volunteers, Phase 1b studies typically involve patients with the disease or condition that is a target for the treatment under investigation.

Open-label study: This is a type of clinical trial in which both the researchers and the patients participating in the study are aware of the treatment being administered. Everyone in this study received the study medicine. No one received a placebo. (A placebo looks like the real medicine but does not have any active medicinal ingredient.)

Dose-escalation study: In a dose-escalation study, each new group of patients gets a higher dose of medicine than what was given to the previous group. It starts with the smallest dose given to the first group. When a dose is found to be safe based on the side effects seen for that dose, the next group gets a higher dose. The goal is to find the highest dose that can be given to patients without causing unacceptable side effects.

Safety study: A safety study is designed to look at the side effects – to decide if a new medicine is safe to give to patients at the doses tested in the study.

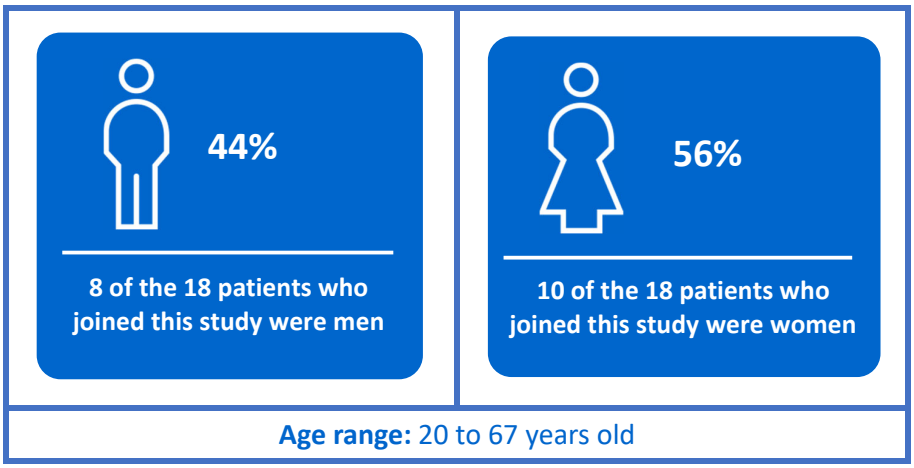
When and where did the study take place?

The study started in November 2020 and finished in February 2023. This summary was written after the study had ended.

The study took place at six study centers in one country – the USA.

2. Who took part in this study?

Eighteen patients who were undergoing HSCT were allowed to join this study.



Patients could take part in the study if they met all of the following conditions:

- Males and females at least 18 years old
- Met the criteria for undergoing HSCT according to the hospital rules
- Sufficient kidney and liver function
- Patients and their donors were a good match for the procedure
- Agreed to use birth control methods; males agreed to not donate sperm

Patients could not take part in the study if they met any one of the following conditions:

- Undergone HSCT previously – in addition to the current one
- Plan to undergo HSCT using a procedure that was not allowed (T-cell depleted donor graft)
- History or current diagnosis of health conditions not allowed in this study
- Use of medicines not allowed in this study

3. What happened during the study?

Screening: Patients who were waiting to undergo HSCT treatment could join the study. Study doctors asked questions to find out if those interested met the conditions for the study.

Standard-of-care: Patients received their usual care and treatment for undergoing HSCT procedure. This was "the standard-of-care" and was given in addition to receiving the study medicine.

Study treatment: Efmarodocokin alfa was given through a vein (intravenously). It was an "IV" dose. The day of HSCT was numbered "Day 0." The first efmarodocokin alfa dose was given on Day -1 (one day before HSCT), and up to a day after HSCT (Day 1).

Dose groups: Patients joined one of three study groups.

- Group 1: Efmarodocokin alfa, 30 µg/kg IV dose every 4 weeks for 3 treatments
- Group 2: Efmarodocokin alfa, 30 µg/kg IV dose every 2 weeks for 6 treatments
- Group 3: Efmarodocokin alfa, 60 µg/kg IV dose every 2 weeks for 6 treatments

What happened during the study: Study staff collected blood samples, did physical exams and medical tests, photographed the skin, and asked questions. This happened before, during, and after treatments.

Study completion: Patients returned to the clinic for "study completion visits" one year after HSCT.

4. What were the results of the study?

Question 1: Was efmarodocokin alfa safe enough to be given to patients undergoing HSCT – could it be tolerated based on the side effects seen at the doses tested?

Researchers looked at the results for blood tests, physical exams, medical tests, pictures of the skin, and notes about how patients were feeling. They looked at the kinds of side effects, how often they happened, and how severe they were. Side effects were reported in this study and are discussed in Section 5. Based on the data collected in this study, researchers decided that efmarodocokin alfa could be tolerated at the doses tested – it was "adequately tolerated" by patients undergoing HSCT.

This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see Section 8).

5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happened during the study.

- If they were seen in this study, they are described in this summary because the study doctor believes the side effects were related to the treatments in the study.
- Not everyone participating in a study will have all the side effects.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflet.
- If serious and common side effects were seen in this study, they will be listed in the following sections.

Serious side effects

A side effect is considered "serious" if it is life-threatening, needs hospital care, or causes lasting problems.

Study doctors did not believe that any of the serious side effects seen in this study were caused by efmarodocokin alfa.

Four patients in this study died due to different reasons. The study doctors did not believe that any of the deaths were caused by efmarodocokin alfa.

- Two patients died due from a disease that came back, the disease that HSCT was supposed to treat. It was a disease caused by abnormal blood-forming cells, "myelodysplastic relapse."
- One patient died due to pneumonia.
- One patient died due to bleeding into the lungs (pulmonary hemorrhage) following a car crash.

During the study, three patients decided to stop taking their medicine (withdraw from treatment) because of side effects. Study doctors believed that two of these three patients had side effects that were caused by efmarodocokin alfa.

Most common side effects

Nine of the 18 patients in this study (50%) had 48 side effects that were not serious, but study doctors thought they may be caused by efmarodocokin alfa. The most common of these – those that happened in two or more patients – are listed in the table below.

Common side effect	**How many of the 18 patients in the study had this side effect that was thought to be caused by efmarodocokin alfa?**
Rash	4 patients (22%)
Itching (pruritus)	3 patients (17%)
Abnormal blood test result (alanine aminotransferase increased)	3 patients (17%)
Abnormal blood test result (aspartate aminotransferase increased)	3 patients (17%)
Abnormal blood test result (blood alkaline phosphatase increased)	2 patients (11%)
Abnormal blood test result (blood lactate dehydrogenase increased)	2 patients (11%)
Dry skin	2 patients (11%)

Other side effects

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see section 8.

6. How has this study helped research?

The information presented here is from a single study of 18 patients who underwent HSCT. These results helped researchers learn more about HSCT and efmarodocokin alfa.

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7. Are there plans for other studies?

At the time of writing this summary, the study sponsor no longer wishes to develop efmarodocokin alfa as a therapy (single agent) for use in patients undergoing HSCT.

8. Where can I find more information?

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

- https://clinicaltrials.gov/ct2/show/results/NCT04539470
- https://forpatients.roche.com/en/trials/cancer/leukemia/study-to-evaluate-the-safety-and-pharmacokinetics-of-ut-83821.html

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – https://forpatients.roche.com/en/About.html
- Contact a representative at your local Roche office.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

Who organized and paid for this study?

This study was organized and paid for by Genentech, Inc., South San Francisco, CA, USA. Genentech is part of F. Hoffmann-La Roche Ltd., with headquarters in Basel, Switzerland.

Full title of the study and other identifying information

- The full title of this study is:
  A Phase 1b, open-label, dose-escalation study to evaluate the safety and pharmacokinetics of efmarodocokin alfa in combination with standard-of-care in patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT).
- The protocol number for this study is GA41825.
- The ClinicalTrials.gov identifier for this study is NCT04539470.