Summary of Clinical Trial Results

A study to look at how safe different doses of a new medicine called “DSTA4637S” were for patients – and how this medicine was processed through the body

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.
- Patients who took part in the study

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

The study started in July 2017 and finished in January 2020. This summary was written after the study had ended.

No single study can tell us everything about the risks and benefits of a medicine. It takes a lot of people in many studies to find out everything we need to know.

The results from this study may be different from other studies with the same medicine.

- **This means that you should not make decisions based on this one summary.**
- **Always speak to your doctor before making any decisions about your treatment.**

Contents of the summary

Thank you to the people who took part in this study

The patients who took part in this study have helped researchers answer important questions about infections caused by *Staphylococcus aureus* bacteria and a study medicine called “DSTA4637S” which was designed to cure the infections caused by the bacteria.

Key information about this study

- In this study, patients were given different doses of a study medicine called "DSTA4637S", or an intravenous infusion with no medicine known as "placebo".
- Researchers wanted to find out which doses of the study medicine were safe for patients, what the side effects were, and how the medicine was broken down by the body.
- Twenty-five patients received treatment. Nineteen patients received the study medicine and 6 received placebo.
- Two of 19 patients had serious side effects related to the study medicine. None of the 6 patients who received placebo had any serious side effects.
- The main findings in the study were:
    - The study medicine caused fevers, chills, and trouble breathing at the end of being given the medicine – in 5 out of 19 patients.
    - The study medicine was broken down differently in the body in patients with bacterial infections when compared to healthy people.
    - The sponsor decided not to develop the study medicine beyond this study based on the findings in this study.

1. General information about this study

Why was this study done?

People all over the world get infections, especially if you have diabetes or are an older age. One of the most common bacteria to cause infections is called "*Staphylococcus aureus*" or "***S. aureus***" for short.

In severe cases, bacteria can grow in your blood and cause serious complications. These can include blood poisoning (septicemia), infection in the heart valves (infective endocarditis), and infection in the bone (osteomyelitis).

Medicines called "**antibiotics**" are used to treat these infections by killing the bacteria.

Unfortunately, the bacteria are not killed by many antibiotics available today because they can "hide" inside your immune cells. In such cases, patients do not get better following antibiotic treatments.

There is a need for new medicines for treating bacteria where they hide. This study was done to look at a new medicine called "DSTA4637S" which was given to patients with infections caused by *S. aureus* and is designed to kill the bacteria hiding inside your immune cells.

What were the study medicines?

The medicine in this study was called "**DSTA4637S**".

- DSTA4637S is a medicine that is made up of an antibiotic linked to an antibody. This type of medicine is known as an "**antibody-antibiotic conjugate**" or "**AAC**" for short.
- The antibiotic is harmful for bacteria. This is the "active part" of the AAC – it does the intended work.
- The **antibody** is a molecule that recognizes and binds to *S. aureus*. The antibody guides the AAC to the target – the antibody is the "targeting part" of the AAC.
- The medicine works by binding to the surface of *S. aureus* bacteria, which is then taken up into your immune cells where the antibiotic is released, killing the *S. aureus* bacteria hiding in your immune cells.
- The study medicine was given in addition to regular antibiotics your doctor would prescribe for this type of infection.

DSTA4637S was compared to a "**placebo**".

- You say this as "plah – see – bo".
- The placebo did not contain any real medicine. This means it had no medicine-related effect on the body.
- Some patients received DSTA4637S and others received placebo. Researchers wanted to know which benefits or side effects were actually caused by the study medicine compared to treatment without medicine.

What did researchers want to find out?

The main question that researchers wanted to answer was:

1. Does DSTA4637S cause any side-effects in patients?

Other questions that researchers wanted to answer were:

2. What happens to DSTA4637S inside the body?

What kind of study was this?

This was a "**phase 1b, multiple ascending dose study**". Being phase 1b means it was one of the early studies. Patients received several doses of their treatment, described as "multiple doses". Each new group of patients received a higher dose of the treatment, described as "ascending dose".

This was a "**placebo-controlled study**", which means that researchers could compare results for patients who received the study medicine with those who received an infusion without any medicine.

The study was "**randomized**". This means that it was decided by chance who joined the group that got the real medicine and who joined the group that got placebo. Randomly choosing which treatment people get makes it more likely that the types of people in both groups (for example, age, race) will be a similar mix.

This was a "**double-blind study**" because patients and their doctors did not know who was getting the study medicine and who was getting the placebo. Blinding of treatment is a way to reduce any unfairness (bias) when patients and doctors report what happened (such as side-effects) after patients receive their treatments.

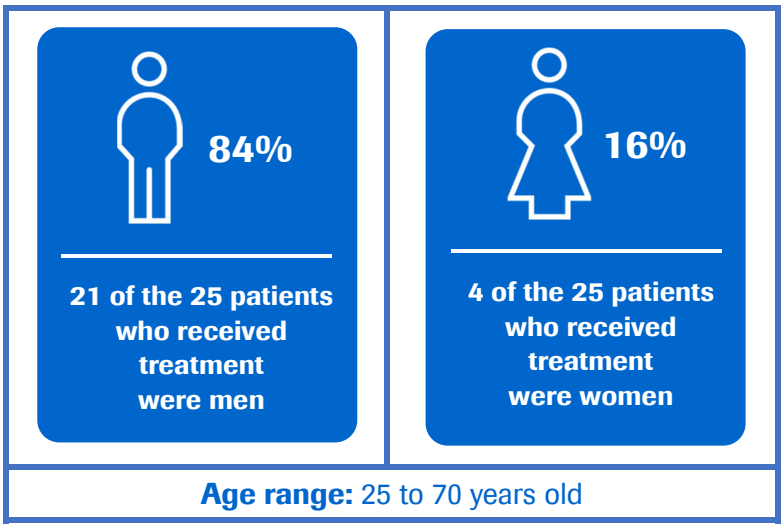
When and where did the study take place?

The study started in July 2017 and finished in January 2020. This summary was written after the study had ended.

The study included patients from 17 study centers in 3 countries:

- South Korea (4 study centers).
- Spain (8 study centers).
- United States (5 study centers).

2. Who took part in this study?



Patients with *S. aureus* infection could take part in the study. Patients had *S. aureus* that was either resistant or sensitive to a certain antibiotic (methicillin), called "methicillin-resistant *S. aureus*" (**MRSA**), or "methicillin-sensitive *S. aureus*" (**MSSA**).

Patients with MRSA or MSSA could take part in the study if they met the following criteria:

- Be 18 to 80 years old.
- Body mass index between 18 and 40 kg/m^2.
- Tested positive for *S. aureus* infection in the blood within 5 days of enrolling in the study.
- Doctors thought these patients needed at least 4 weeks of standard antibiotic treatment to get better.

Patients could not take part in the study if:

- They had *S. aureus* infection that was associated with an implanted medical device (artificial material inserted in the body via surgery) or prosthetic (artificial body part).
- The patient was to receive a certain antibiotic (rifampin) while on the study
- The patient's condition suggested there would be a need for heart surgery early in the study.
- The patient was infected with more than one type (species) of bacteria.
- The patient had an unhealthy liver or heart.
- The patient had other medical conditions (immune suppression).
- The patient's doctor thought they were too sick to participate.

3. What happened during the study?

During the study, patients were selected by chance to get one of 2 treatments. The treatments were selected at random by a computer.

- **6 patients received placebo.**
- **19 patients received DSTA4637S.**

DSTA4637S treatment dose levels were:

- 15 mg/kg for 6 patients.
- 45 mg/kg for 6 patients.
- 100 mg/kg for 7 patients.

All patients continued to receive their regular antibiotic treatment for their *S. aureus* infection in addition to getting the treatment on this study. The regular antibiotic treatment was called "**standard of care**" or "SOC" for short.

Patients on the study could receive up to **6 treatments** (DSTA4637S or placebo) – **once every 7 days**. They were examined and got medical tests throughout the study. Side effects were treated as needed.

4. What were the results of the study?

Question 1: Does DSTA4637S cause any side-effects in patients?

Researchers found that side effects were not balanced (not the same %). There were more side effects in the group that received DSTA4637S and fewer in the group that received placebo.

Reactions to the treatment at the time of dosing or shortly thereafter – called "infusion-related reactions" or "**IRR**" for short – were the most common side effects.

- These were seen in 5 out of 19 patients after the first or second dose of DSTA4637S and they all stopped the study treatment early.
- The reaction consisted of fevers, chills, changes in blood pressure, and trouble breathing.
- The reaction got better over 2 days with standard care you would receive in a hospital.

Question 2: What happens to DSTA4637S inside the body?

In a previous study, DSTA4637S was given to healthy people. Researchers found that the amount of DSTA4637S in the body of patients infected with *S. aureus* in this study was lower than what was found in the body of healthy people. Researchers are still exploring the cause for this. No cause has been identified to date.

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 happen during the study.

- They are described in this summary because the study doctor believes the side effects were related to the treatments in the study.
- Not all of the patients in this study had all of the side effects.
- 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.
- Side effects can vary from mild to very serious and may vary from person to person.
- Serious and common side effects are 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.

During this study, 2 of 19 patients (11%) who received DSTA4637S had serious side effects that the study doctor thought were related to the study medicine. None of the 6 patients who got the placebo had any serious side effects that the study doctor thought were related to the study medicine.

There was one death on this study due to not enough oxygen in the blood (respiratory failure) in a patient who already had lung disease. Researchers decided that the death was not related to the study medicine.

Most common side effects

During this study, 10 of 19 patients (53%) who received DSTA4637S had a side effect considered related to study treatment that was not considered serious.

The most common side effects that were considered related to study treatment in patients who received DSTA4637S were:

- IRR in 5 of 19 patients (26%)
- Abnormal serum color in 5 of 19 patients (26%)
- Skin discoloration in 3 of 19 patients (16%)

Four patients (16%) stopped the study treatment due to side effects related to the treatment.

One of the 6 patients who got the placebo (17%) had a side effect that the study doctor thought was related to the study treatment that was not considered serious. None of the 6 patients who got the placebo stopped the study treatment due to side effects related to the treatment.

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 25 patients with infections caused by *S. aureus*. These results helped researchers learn more about bacterial infections and DSTA4637S.

Based on the results of this study, the sponsor decided not to develop the study medicine beyond this study.

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7. Are there plans for other studies?

At the time of writing this summary, no more studies looking at DSTA4637S were planned.

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/NCT03162250
- https://forpatients.roche.com/en/trials/infectious-diseases/bacterial-infection/study-to-investigate-the-safety--tolerability--and-pharmacokinet.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, randomized, double-blind, placebo-controlled, multiple-ascending dose study to investigate the safety, tolerability, and pharmacokinetics of DSTA4637S in patients with *Staphylococcus aureus* bacteremia receiving standard of care antibiotics"

- The protocol number for this study is **GV39131**.
- The ClinicalTrials.gov identifier for this study is **NCT03162250**.
- The EudraCT number for this study is **2016-001880-35**.