NOVARTIS

Clinical Trial Results Summary

A clinical trial to understand what happens to TIN816 in the body of people admitted to the ICU with acute kidney injury due to sepsis

Thank you!

Thank you to the participants who took part in the clinical trial for **acute kidney injury due to sepsis in people admitted to the intensive care unit (ICU)**. Thank you also to the caregivers, families and friends of the participants who agreed to support this trial**.** Every participant helped the researchers learn more about the trial drug **TIN816**.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public.

We hope this helps the participants understand their important role in medical research.

Trial information

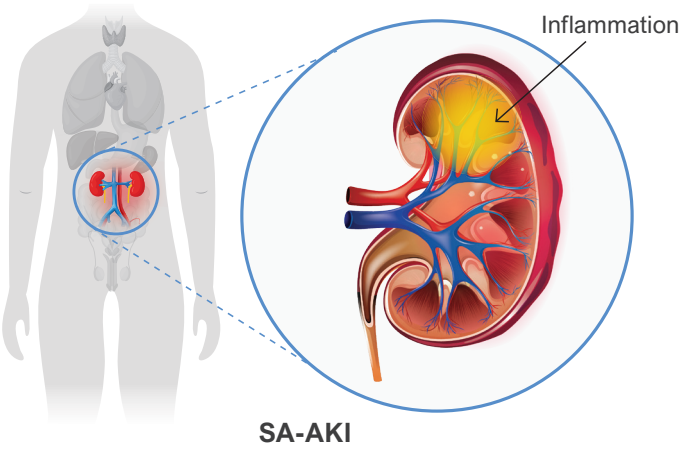
Trial number: CTIN816B12201
Drug studied: TIN816
Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings.

What was the main purpose of this trial?

The main purpose of the trial was to understand what happens to **TIN816** in the body and to monitor the participants' safety. This includes how the drug is absorbed, how it moves through the body, and how it is removed in people admitted to the ICU with **acute kidney injury (AKI)** caused by **sepsis**.



Sepsis is a serious and life-threatening condition caused by the body's extreme response to an infection. Sepsis happens when the immune system releases chemicals into the blood to fight an infection, causing inflammation. This can affect the function of organs and lead to permanent organ damage, or death.

One of the most common complications of sepsis in people who are severely ill is **sepsis-associated acute kidney injury (SA-AKI)**. **SA-AKI** happens when the kidneys stop working as they should. This causes waste and toxins to build up in the body. **SA-AKI** can happen within a few hours or a few days. For most people, AKI develops within 48 hours of sepsis. If left untreated, **SA-AKI** can cause serious complications, including organ failure and death.

Common symptoms of **SA-AKI** are:

- Less need to pass urine
- Shortness of breath
- Confusion or mood changes
- Weakness or loss of appetite

Currently, no specific treatments are approved for **SA-AKI**. So people receive supportive treatment to manage their symptoms, often requiring admission to the ICU.

The trial drug, **TIN816**, is given as a single dose. It breaks down molecules called **adenosine triphosphate (ATP)** and **adenosine diphosphate (ADP)** in the body. These molecules are involved in the body's immune response to sepsis. Thus, **TIN816** can help lower inflammation and may protect the kidneys from further damage.

In this trial, researchers gave participants either **TIN816** or **placebo** after they were admitted to a hospital for sepsis.

A **placebo** looks like the trial drug but does not have any drug in it. Using a **placebo** helps researchers better understand the effect of a trial drug.

The main questions that researchers wanted to answer were:

- How much **TIN816** was present in the blood after a single dose?
- What medical problems, also called adverse events, happened during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial. Adverse events **may** or **may not** be caused by treatments in the trial.

How long was this trial?

The trial began in November 2022 and ended in April 2024. The participants were in the trial for about 3 months.

When the trial ended, researchers created a report of the trial results. This summary is based on that report.

Who was in this trial?

20 participants with **SA-AKI** received treatment in this trial. Participants' ages ranged from 37 to 85 years. Their average age was 67 years.

The number of participants by race is shown below.

Gender

16 Men	4 Women

Race

17 Not Reported	3 White or Caucasian

20 participants from **5 countries** received treatment. The map below shows the number of participants who took part in each country.

Participants **could take part** in this trial if they:

- Were between 18 and 85 years old
- Were admitted to the ICU or high dependency unit (HDU) at a hospital
- Had confirmed **SA-AKI**
- Did not have a history of chronic kidney disease or other kidney disease
- Were not receiving kidney dialysis or needed it urgently after being admitted

What treatments did the participants receive?

All participants received standard-of-care treatment for their condition as decided by their trial doctor. Standard-of-care treatments are the widely accepted treatments for a particular disease or disorder. They are the treatments usually recommended by doctors.

The treatments in this trial were given as a single intravenous (IV) infusion over 2 hours on Day 1. An IV infusion is a slow drip through a tube directly into the vein.

TIN816: The dose given was **2 milligrams per kilogram of body weight (mg/kg)**.

Placebo: Looks like the trial drug but does not have any drug in it. Using a **placebo** helps researchers better understand and confirm the effect of the trial drug.

Researchers used a computer to randomly assign participants to their treatment. Participants were 3 times more likely to receive **TIN816** than **placebo**.

The participants, researchers, and trial staff did not know what treatment the participants were receiving. Some trials are done this way because knowing what treatment the participants receive can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness across all treatments.

What happened during this trial?

Before treatment

Up to 48 hours

The trial staff checked to make sure the participants could be in this trial. Participants were included if they were admitted to the ICU and their **SA-AKI** was confirmed during the ICU stay before they received treatment.

During treatment

Day 1

A total of **20 participants** received either **TIN816** or **placebo**. They were randomly assigned to 1 of 2 treatment groups.

TIN816	Placebo
16 participants	4 participants

All the participants received a single dose of **TIN816** or **placebo**. Trial doctors performed regular blood and urine tests before and after treatment to check how **TIN816** moved through the body. They also recorded any adverse events participants had.

After treatment

Up to 3 months after treatment

Trial staff checked participants' general health and for any adverse events for up to 3 months after the treatment was given.

Trial doctors checked participants for their overall health throughout the trial.

What were the main results of this trial?

How much TIN816 was present in the blood after a single dose?

Researchers found that the blood levels of **TIN816** in people in the ICU with **SA-AKI** were similar to previous **TIN816** trials.

Researchers wanted to understand what happens to **TIN816** in the body after a single dose. To study this, doctors collected blood samples from participants to measure the amount of **TIN816** in the blood over time.

They looked at:

- The highest amount of the drug found in the blood after a single dose.
- How long it took for the drug to reach its highest level in the blood.
- How long it takes for the level of the drug in the body to drop by half. This is also called the half-life.

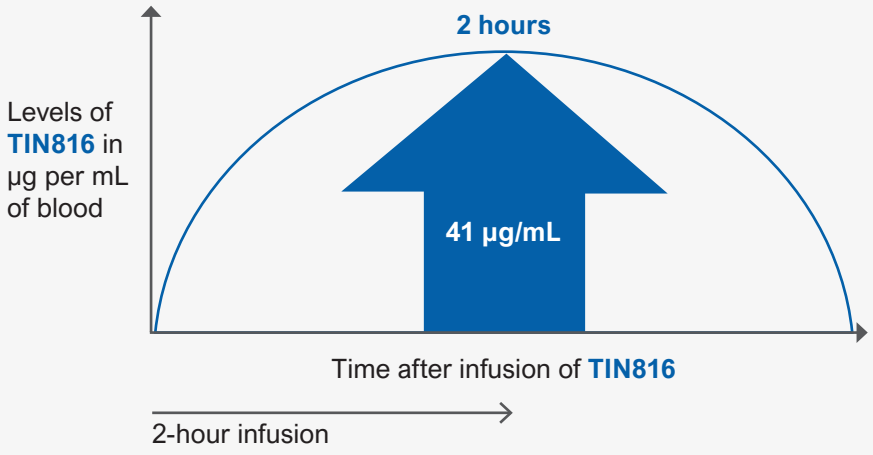
These measurements help researchers understand how the drug is absorbed and how long it stays in the body. This information can guide how the drug might be taken in future trials.

The researchers found that:

- **TIN816** levels in the blood peaked right after the 2-hour infusion was finished. On average, the highest amount of **TIN816** measured per dose was **41 microgram per milliliter of blood (µg/mL).**
- The average time it took for **TIN816** levels to drop by half in the body was about **6 days.**

The graph below shows the highest level of **TIN816** in the blood after the infusion.

Highest level of TIN816 in the blood after the infusion



What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all medical problems, also called **adverse events**, that happen in trials. They track adverse events even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

An **adverse event** is:

- Any **sign or symptom** that the participants have during a trial
- Considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death

Adverse events **may** or **may not** be caused by treatments in the trial.

This clinical trial includes critically ill participants being cared for in the ICU. As a result, researchers expect to see signs or symptoms that need to be recorded as adverse events. This section is a summary of the adverse events that happened in participants from the time they agreed to join the trial until 3 months after the treatment was given.

A total of **18 out of 20 participants (90%)** had adverse events, including serious adverse events.

- 12 participants had adverse events that were considered serious.
- None of the participants left the trial due to an adverse event.
- 3 participants died due to any cause, including participants who died from their health condition.

No new, unexpected safety concerns were seen with **TIN816**. The adverse events that happened in this trial reflect those expected in people with **SA-AKI** in the ICU.

How many participants had adverse events?

Adverse events are reported for participants who received at least 1 dose of **TIN816** or **placebo**.

Summary of adverse events

Participants who:	TIN816 16 participants	Placebo 4 participants
Had at least **1 serious adverse event**	11 of 16 **(69%)**	1 of 4 **(25%)**
Had at least **1 other (not including serious) adverse event**	14 of 16 **(88%)**	4 of 4 **(100%)**
Died	3 of 16 **(19%)**	0 of 4 **(0%)**

What serious adverse events did the participants have?

The table below shows the most common serious adverse events that happened during the trial.

Serious adverse events	TIN816 16 participants	Placebo 4 participants
Worsening of AKI Acute kidney injury	2 of 16 **(13%)**	0 of 4 **(0%)**
Lung infection Pneumonia	2 of 16 **(13%)**	0 of 4 **(0%)**
Dangerous drop in blood pressure due to serious complication of an infection Septic shock	2 of 16 **(13%)**	0 of 4 **(0%)**

What other (not including serious) events did the participants have?

The table below shows the most common other (not including serious) events that happened during the trial.

Other (not including serious) events	TIN816 16 participants	Placebo 4 participants
Low red blood cell count Anemia	3 of 16 **(19%)**	2 of 4 **(50%)**
High blood sodium levels Hypernatremia	3 of 16 **(19%)**	1 of 4 **(25%)**
Low blood levels of phosphates Hypophosphatemia	3 of 16 **(19%)**	1 of 4 **(25%)**

What was learned from this trial?

This trial helped researchers learn how **TIN816** was absorbed, how it moved through the body, and how it was removed in people with **SA-AKI**.

The researchers concluded that:

- Blood levels of **TIN816** were similar to those seen in earlier **TIN816** trials.
- There were no new, unexpected safety concerns with **TIN816**. The adverse events that happened in this trial reflect those expected in people with **SA-AKI** in the ICU.

Further research into the safety and effects of **TIN816** in **SA-AKI** is ongoing. When this summary was written, there were 2 ongoing studies of **TIN816** for **sepsis** and other types of **AKI**.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website, www.novctrd.com.

Follow these steps to find the scientific summary:

Go to www.novctrd.com → Click **Clinical Trial Results** → Accept the terms ☑ **I accept** → Search for **CTIN816B12201**

For more information about this trial go to any of the following websites:

- clinicaltrials.gov – search using the number **NCT05507437**
- clinicaltrialsregister.eu – search using the number **2022-000887-23**

Other trials with **TIN816** appear on the public websites above. When there, search for **TIN816**.

Full clinical trial title: A Multicenter, Participant and Investigator-Blinded, Randomized, Placebo-Controlled Phase 2a Study to Investigate the Pharmacokinetics, Pharmacodynamics, Safety and Tolerability of TIN816 in the Treatment of Patients With Sepsis-Associated Acute Kidney Injury

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