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(s) Studied: Zavicefta® (ceftazidime-avibactam, also known as PF-06947386)

Protocol Number: C3591024

Dates of Study: 14 January 2020 to 30 December 2022

Title of this Study: A Study of Ceftazidime-Avibactam in Newborns and Infants Less Than 3 Months Old With Suspected or Confirmed Infections Due to Gram-Negative Bacteria That Needed Intravenous Antibiotic Treatment

[A Phase 2a, 2-Part, Open-Label, Non-Randomized, Multicenter, Single and Multiple Dose Trial to Evaluate Pharmacokinetics, Safety and Tolerability of Ceftazidime and Avibactam in Neonates and Infants From Birth to Less Than 3 Months of Age With Suspected or Confirmed Infections due to Gram-Negative Pathogens Requiring Intravenous Antibiotic Treatment]

Date(s) of this Report: 22 June 2023

– Thank You –

If you and your child participated in this study, Pfizer, the Sponsor, would like to thank you and your child 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 are bacterial infections?

Bacterial infections happen when bacteria (or germs) grow in numbers more than normal and cause a reaction in the body.

There are different types of bacteria. A type of bacteria called “Gram-negative bacteria” can be harder to kill by any drug. These bacteria can cause severe infections in different parts of the body, such as the lungs, bloodstream, or digestive tract.

Currently, antibiotics are available to treat some, but not all, of these bacterial infections.

What is ceftazidime-avibactam (CAZ-AVI)?

The study medication (CAZ-AVI, also called Zavicefta) consisted of investigational drugs called ceftazidime (CAZ) and avibactam (AVI). CAZ-AVI:

- is used to treat Gram-negative bacterial infections in children older than 3 months and in adults .
- is an investigational study medication not approved for use in infants less than 3 months old.
- was given as an intravenous (IV) injection (a needle through the vein).

What was the purpose of this study?

The main purpose of this study was to learn about the effects of CAZ-AVI in infants less than 3 months old with bacterial infections.

Researchers wanted to know:

1. **How did CAZ-AVI act in the body of participants?**
2. **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested CAZ-AVI on a group of study participants to learn about:

- how CAZ-AVI acted in the body.
- any medical problems during the study.

This was an open-label study. This means that the participants' parents/caregivers and the researchers knew the treatment being given. All participants received CAZ-AVI through an IV line. The doses of CAZ-AVI were given based on the participants' age and weight.

The study had 2 parts:

- **Part A**: Infants received 1 dose of CAZ-AVI on Day 1. All infants continued receiving other IV antibiotics to treat their bacterial infection.
- **Part B**: Infants received CAZ-AVI every 8 hours up to 14 days. Some infants were allowed to switch over to receive other antibiotics given by mouth starting on Day 3.

Figure 1 shows what happened in Parts A and B.

Figure 1: Overall study design

What happened in Part A?

Screening	Treatment	Follow-up	Long-Term Follow-up
27 hospitalized infants with bacterial infections and were receiving other IV antibiotics joined **Part A**.	**Day 1** **25 infants** received 1 dose of **CAZ-AVI** through an IV line.	**Days 2 to 3** The study doctor or team checked on the infants' health at the hospital.	**28 to 35 days after the last dose of CAZ-AVI** At the study site or by a phone call: The study doctor or team asked parents/caregivers how the infants have been feeling.

All infants continued receiving their other IV antibiotics to treat their bacterial infection.

What happened in Part B?

Screening	Treatment	Follow-up	Long-Term Follow-up
21 hospitalized infants with Gram-negative bacterial infections that need treatment with IV antibiotics joined **Part B**	**Day 1 to 14** From **Day 1 to 2**, **all infants** received **CAZ-AVI** through an IV line every 8 hours. From **Day 3 to 14**, some infants continued receiving **CAZ-AVI** through an IV line every 8 hours, while other infants were allowed to switch over to receive **other antibiotics** given by mouth. From **Day 1 to 14**, some infants may have also received **additional antibiotics** to treat other bacterial infections they had that were not covered by CAZ-AVI.	**7 to 14 days after the last dose of CAZ-AVI** The study doctor or team checked on the infants' health at the hospital.	**28 to 35 days after the last dose of CAZ-AVI** At the study site or by a phone call: The study doctor or team asked parents/caregivers how the infants have been feeling.

Where did this study take place?

This study took place at 39 locations in 9 countries around the world.

When did this study take place?

It began 14 January 2020 and ended 30 December 2022.

Who participated in this study?

The study included hospitalized infants less than 3 months old with suspected or confirmed bacterial infections that needed IV antibiotics.

- A total of 21 boys and 25 girls participated.
- All participants were between the ages of 2 and 89 days.

In total, 48 infants participated in the study. Of these infants, 46 received at least 1 dose of CAZ-AVI.

- Part A: 25 infants
- Part B: 21 infants

In Part A, 2 infants left the study before receiving CAZ-AVI by their parents'/caregivers' choice.

How long did the study last?

Participants were in the study up to 35 days after the last dose of CAZ-AVI. The entire study took about 35 months to complete.

The Sponsor stopped signing up infants in December 2022 and ended the study earlier than planned. This was because enrollment was slow, and the Sponsor had collected enough data. It was not because of safety concerns with CAZ-AVI.

When the study ended in December 2022, 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 did CAZ-AVI act in the body of participants?

To answer this question, blood samples were taken from participants after receiving CAZ-AVI. The levels of CAZ and AVI in the blood were checked at different timepoints.

In participants less than 3 months old, the levels of CAZ and AVI in the blood were as expected after 1 dose of CAZ-AVI in Part A and after multiple doses of CAZ-AVI in Part B.

- CAZ and AVI levels were the highest at the end of the dose (within 15 minutes after stopping CAZ-AVI).
- Then, CAZ and AVI levels slowly dropped over time (within 5 hours of completing the CAZ-AVI infusion).

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, researchers try to understand what effects a study medication might have on a participant.

In Parts A and B, 23 out of 46 infants (50%) had medical problems. One (1) infant left the study because of medical problems.

The most common medical problems – those seen in at least 3 infants – are described 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 seen in the study. All medical problems seen in at least 3 infants taking CAZ-AVI are listed.
- The **2nd** column tells how many of the 46 infants had each medical problem. Next to this number is the percentage of the 46 infants who had the medical problem.
- Using these instructions, you can see that 5 out of 46 infants (11%) had generalized infection.

Table 1: Most common medical problems seen in study participants (Parts A and B)	
Medical Problem	**CAZ-AVI (46 Participants)**
Generalized infection	5 out of 46 infants (11%)
Vomiting	3 out of 46 infants (7%)
Low red blood cell count	3 out of 46 infants (7%)

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.

In Parts A and B, 8 out of 46 infants (17%) had serious medical problems.

- Researchers do not believe any serious medical problems were related to CAZ-AVI.
- The serious medical problem seen in 2 infants was necrotizing enterocolitis, a severe disease of the gut (“intestine”) seen in premature babies that can cause death of gut tissue. Other serious medical problems were seen in 1 infant each.

Overall, 2 infants died: 1 during the study and 1 after the study ended. Researchers do not believe either death was related to CAZ-AVI.

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 **C3591024**

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

www.clinicaltrials.gov	Use the study identifier **NCT04126031**
www.clinicaltrialsregister.eu	Use the study identifier **2018-002800-16**

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 and your child 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!