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:	PF-07612577 (Combination ceftibuten and avibactam)
Protocol Number:	C4691001
Dates of Study:	07 October 2022 to 23 June 2023
Title of this Study:	A Study of PF-07612577 in Healthy Adults [A Phase 1, Randomized, Double-Blind, Sponsor-Open, Placebo-Controlled, Single- and Multiple-Dose Study to Evaluate the Safety, Tolerability and Pharmacokinetics of PF-07612577 (PF-06264006 [CTB] and PF-07338233 [AVP]) in Healthy Adult Participants]
Date of this Report:	31 May 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 are complicated urinary tract infections?

There are 2 types of urinary tract infections (UTIs): simple and complicated. Simple UTIs can be treated with antibiotics taken by mouth. Complicated UTIs (cUTIs) are more difficult to treat and can be life-threatening. cUTIs often require treatment with intravenous antibiotics. Intravenous antibiotics are given as a slow injection into a vein. People with cUTIs are often admitted to the hospital to receive treatment.

What are UTIs?

UTIs are infections of the bladder, ureters, and kidneys. UTIs can lead to kidney damage, sepsis, and death.

What is the combination of ceftibuten and avibactam prodrug?

Ceftibuten (CTB) and avibactam prodrug (AVP) are both medications that can be taken by mouth. They work together to form an antibiotic that works against a type of bacteria called Enterobacterales, which is a common cause of cUTIs. CTB+AVP when dosed together are thought to work against the antibiotic-resistant forms of Enterobacterales. "Antibiotic resistance" means that common antibiotics would lose the ability to cure or treat certain bacterial infections.

What is a prodrug?

A prodrug is a substance that the body breaks down into an active drug.

What was the purpose of this study?

The most common cause of UTIs is Enterobacterales bacteria. This bacteria causes about 9100 deaths each year in the United States. Resistant Enterobacterales is considered a serious health threat worldwide. New treatments for cUTIs are needed, especially ones that can be taken by mouth at home.

Studies for new treatments like CTB+AVP are often tested in healthy people first to make sure that the treatment is safe before giving it to people who are sick. As a result, this study did not test if the study drug helps to improve cUTIs.

The purpose of this study was to learn how different doses of CTB alone or with AVP were dealt with by the body. Researchers looked at how much of each dose got into the blood over time. They also checked how quickly it was removed from the body. How participants felt after being given different doses was also studied through laboratory tests, vital signs, and electrocardiogram (ECG).

Researchers wanted to know:

- **How did AVP impact the amount of CTB in the blood when they were taken together as a single dose?**
- **How did CTB impact the amount of AVP in the blood when they were taken together as a single dose?**
- **Did participants have any abnormal laboratory test results, vital signs, or heart ECG results?**
- **What medical problems did participants have during the study that researchers thought were related to the study drugs or placebo?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested different doses of CTB+AVP in a group of healthy participants to learn how much drug got into the blood and how it was removed from the body. The study had 2 parts: Part 1 and Part 2.

In Part 1, each participant took 5 different doses of CTB+AVP, CTB alone, or a placebo. Participants took 1 dose of CTB+AVP, CTB alone, or placebo each week for 5 weeks. Each week, 2 participants took placebo. The participants who took placebo changed every week. Below is a list of the doses of CTB+AVP or CTB alone the other 6 participants took each week.

What is a placebo and why are they used?

A placebo does not have any medicine in it, but it looks just like the study medication. A placebo was used to help researchers understand if the medical problems the participants had during the study could be related to the study medication or related to something else.

- On Week 1, the participants took CTB+ AVP Dose 1.
- On Week 2, the participants took CTB+AVP Dose 2.
- On Week 3, the participants took CTB alone Dose 3.
- On Week 4, the participants took CTB+ AVP Dose 4.
- On Week 5, the participants took CTB alone Dose 5.

In Part 2, participants took the same dose of study medications for 1 week. There were 5 groups of participants in Part 2. Below is a list of the doses of CTB+AVP or placebo each group took during the study. The doses given in Part 2 were different than those given in Part 1.

- In Group 1:
  - 2 participants received placebo.
  - 6 participants received repeated doses of CTB+AVP Dose 1.
- In Group 2:
  - 2 participants received placebo.
  - 6 participants received repeated doses of CTB+AVP Dose 2.
- In Group 3:
  - 2 participants received placebo.
  - 6 participants received repeated doses of CTB+AVP Dose 3.
- In Group 4:
  - 1 participant received placebo.
  - 5 participants received repeated doses of CTB+AVP Dose 4.
- In Group 5:
  - 1 participant received placebo.
  - 3 participants received repeated doses of CTB+AVP Dose 5.

During the study, researchers took samples of blood and urine from participants and measured the amount of drug present. Researchers also checked the participants' health during the study and asked them how they were feeling.

After each dose, researchers recorded each participant's results. They then looked at how blood levels of the drug changed with each dose. They also looked at how much time it took for the drug to leave the body.

The participants and researchers did not know who took different doses of the drug and who took the placebo. This is known as a "blinded" study. Participants were assigned to each group by chance.

Where did this study take place?

The Sponsor ran this study at 1 location in Belgium.

When did this study take place?

It began on 07 October 2022 and ended on 23 June 2023.

Who participated in this study?

The study included healthy participants.

- A total of 39 men participated.
- A total of 3 women participated.
- All participants were between the ages of 19 and 59 years.

There were 3 participants who left before the study was over by their choice or because a doctor decided it was best for the participant to stop being in the study. These 3 participants were in Part 2 of the study.

How long did the study last?

Study participants were in the study for up to 12 weeks. The entire study took 8 months to complete.

When the study ended in June 2023, the Sponsor created a report of the results. This is a summary of that report.

What were the results of the study?

How did AVP impact the amount of CTB in the blood when they were taken together as a single dose?

- CTB took longer to reach its peak level in the blood when taken with AVP. The higher the dose of AVP, the longer it took CTB to reach its highest blood levels.
- After CTB reached its peak blood levels, it was removed from the body at about the same rate across all dose combinations.
- The amount of CTB that the body was exposed to when taken alone was about the same as when it was taken with AVP.

How did CTB impact the amount of AVP in the blood when they were taken together as a single dose?

- AVP took about the same time to reach its peak level in the blood when taken with all doses of CTB.
- After AVP reached its peak blood levels, it was removed from the body at about the same rate across all dose combinations.
- The amount of AVP that the body was exposed to was higher when taken together with CTB than when taking AVP alone. The amount of AVP in the body increased with the dose of CTB.

Did participants have any abnormal laboratory test results, vital signs, or heart ECG results?

- Researchers did not find any clinically meaningful changes in the participants' laboratory tests results, vital signs, or heart ECG results.

What medical problems did participants have during the study that researchers thought were related to the drug or placebo?

Researchers record all medical problems that participants have during the study. These medical problems may or may not be caused by the study treatment. However, researchers make a list of all medical problems that they think are related to the study drug.

In Part 1 of this study:

- 5 out of 8 participants (63%) had medical problems they thought were related to the study drugs.
- None of the participants had a serious medical problem thought to be related to CTB+AVP. A medical problem is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems.
- None of the participants left Part 1 of the study due to a serious medical problem thought to be related to the study drugs.
- None of the participants died during Part 1.

Table 1 shows the common related medical problems that were reported by 2 or more participants in Part 1.

Table 1. Commonly reported related medical problems by study participants in Part 1

Medical Problem	Study Medication (8 Participants)	Placebo (8 Participants)
Nausea	2 out of 8 participants (25%)	0 out of 8 participants (0%)

In Part 2 of this study:

- 19 out of 34 participants (60%) had medical problems they thought were related to CTB+AVP.
- None of the participants had a serious medical problem thought to be related to CTB+AVP. A medical problem is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems.
- 2 out of 34 participants (6%) left the study due to a serious medical problem thought to be related to CTB+AVP or placebo.
- None of the participants died during Part 2.

Table 2 shows the common related medical problems that were reported by 10% or more of participants in Part 2.

Table 2. Commonly reported related medical problems by study participants in Part 2		
Medical Problem	**Study Medication (26 Participants)**	**Placebo (8 Participants)**
Diarrhea	6 out of 26 participants (23%)	2 out of 8 participants (25%)
Headache	5 out of 26 participants (19%)	1 out of 8 participants (13%)
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 unknown 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.

In Part 1, 6 out of 8 participants (75%) had at least 1 medical problem. None of the participants left the study because of medical problems. The most common medical problems – those reported by 25% or more of participants in Part 1 – are described in Table 3.

Below are instructions on how to read Table 3.

Instructions for Understanding Table 3.

- The **1st** column of Table 3 lists medical problems that were commonly reported during the study. All medical problems reported by 25% or more of participants are listed.
- The **2nd** column tells how many of the 8 participants taking the study medication reported each medical problem. Next to this number is the percentage of the 8 participants taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 8 participants taking placebo reported each medical problem. Next to this number is the percentage of the 8 participants taking placebo who reported the medical problem.

Table 3. Commonly reported medical problems by study participants		
Medical Problem	**Study Medication (8 Participants)**	**Placebo (8 Participants)**
Fatigue	2 out of 8 participants (25%)	0 out of 8 participants (0%)
Nausea	2 out of 8 participants (25%)	0 out of 8 participants (0%)
Bruise from drawing blood	4 out of 8 participants (50%)	0 out of 8 participants (0%)

In Part 2, 24 out of 34 participants (71%) had at least 1 medical problem. A total of 4 participants left the study because of medical problems. The most common medical problems – those reported by 10% or more of participants in Part 2 – are described in Table 4.

Below are instructions on how to read Table 4.

Instructions for Understanding Table 4.

- The **1st** column of Table 4 lists medical problems that were commonly reported during the study. All medical problems reported by 10% or more of participants are listed.

- The **2nd** column tells how many of the 26 participants taking the study medication reported each medical problem. Next to this number is the percentage of the 26 participants taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 8 participants taking placebo reported each medical problem. Next to this number is the percentage of the 8 participants taking placebo who reported the medical problem.

Table 4. Commonly reported medical problems by study participants

Medical Problem	Study Medication (26 Participants)	Placebo (8 Participants)
Diarrhea	6 out of 26 participants (23%)	2 out of 8 participants (25%)
Headache	4 out of 26 participants (15%)	1 out of 8 participants (13%)

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.

None of the participants had serious medical problems.

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 C4691001

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

www.clinicaltrials.gov	Use the study identifier **NCT05554237**
www.clinicaltrialsregister.eu	Use the study identifier **2021-005428-39**

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!