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:	Ceftazidime-Avibactam (PF-06947386)
Protocol Number:	C3591036
Dates of Study:	01 October 2021 to 15 September 2022
Title of this Study:	A study to assess the efficacy and safety of ceftazidime-avibactam plus metronidazole in Japanese patients with complicated intra-abdominal infections. [A Phase 3, Multicenter, Open-Label, Single-Arm Study to Assess the Efficacy and Safety of Ceftazidime-Avibactam (PF-06947386) Plus Metronidazole in Japanese Adult Patients With Complicated Intra-Abdominal Infection Requiring Hospitalization]
Date(s) of this Report:	09 August 2023

– 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 is complicated intra-abdominal infection?

An intra-abdominal infection, or “IAI”, is the name for a type of infection; in which bacteria invade and damage the tissues in the abdomen (stomach area). People with an IAI may have symptoms such as stomach area pain, swelling or fever. Some IAIs are serious and can require people to be in the hospital for treatment with intravenous (IV) antibiotics and sometimes surgery. This type of serious IAI when bacteria invade and damage areas beyond the organ is known as a “complicated IAI”.

What is Ceftazidime-avibactam (CAZ-AVI)?

Ceftazidime-avibactam (CAZ-AVI) is an antibiotic medicine which is used to treat a number of infections caused by certain types of bacteria. CAZ-AVI is currently used to treat serious infections, such as complicated IAI, in adults. CAZ-AVI is a combination drug that contains ceftazidime and avibactam. Ceftazidime is an antibiotic that is used worldwide including Japan for the treatment of infections. Avibactam protects antibiotics from enzymes produced by bacteria which make the bacteria resistant. Avibactam is not yet being used in Japan. The combination of ceftazidime with avibactam is expected to be effective against most bacteria for which ceftazidime is not effective when used alone. Metronidazole (MTZ) is an antibiotic that is used worldwide including Japan for the treatment of infections caused by certain bacteria.

What was the purpose of this study?

- The main purpose of this study was to learn more about the possible effectiveness of CAZ-AVI when given in combination with MTZ by putting drug into the blood stream through a small tube or needle, in Japanese people with complicated IAIs. The researchers wanted to

see how many people in the study were cured or had an improvement in their infection.

- Additionally, the researchers wanted to see what medical problems participants had during the study.

Researchers wanted to know:

- **How many participants taking CAZ-AVI in combination with metronidazole had clinical cure?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested CAZ-AVI plus MTZ on a group of study participants to find out how many study participants taking CAZ-AVI plus MTZ had improvement in infection/symptoms at the test of cure (TOC) visit (visit at which improvement in infection will be measured).

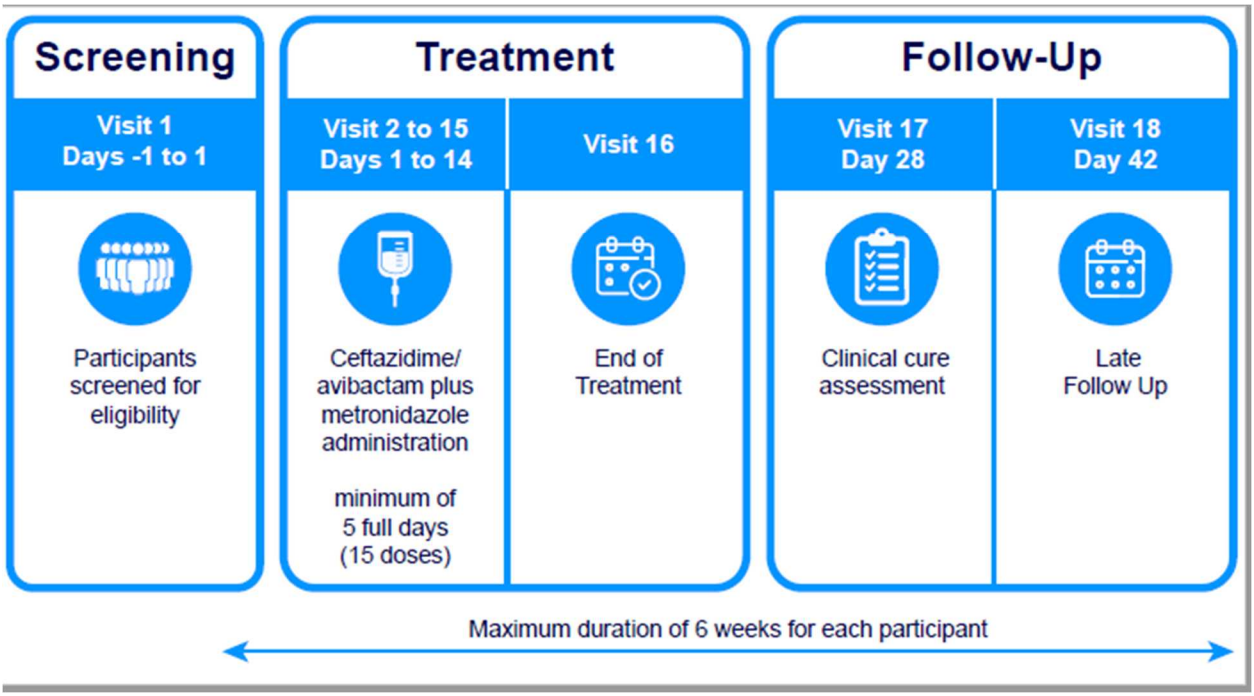
Participants remained in this study for a maximum of about 50 days. During the study drug treatment period in hospital, all participants received study drug combination containing 2.0 g of ceftazidime and 0.5 g of avibactam (CAZ-AVI) and 0.5 g of MTZ for a minimum of 5 days to a maximum of 14 days depending upon their conditions. Participants received CAZ-AVI as an infusion (putting drug into the blood stream through a small tube or needle), over 2 hours every 8 hours. Then, participants received MTZ as an infusion over 1 hour immediately after CAZ-AVI dosing was completed. The study doctor or staff prepared the

study drug infusion and provided it. If the kidney was not functioning normally, during the treatment period, the dose was adjusted.

The doctor asked participants to make a visit (Day 28) for the assessment of clinical cure (test of cure [TOC]). The doctor also asked participants to make a visit for late follow-up (Day 42).

Safety was carefully monitored throughout the study. The study doctors examined each participant, did blood tests, tested samples from site of infection in the abdomen, and watched for any medical problems.

The figure below shows what happened during the study.



Where did this study take place?

The Sponsor conducted this study at 27 locations in Japan.

When did this study take place?

It began 01 October 2021 and ended 15 September 2022.

Who participated in this study?

Participants included in the study:

- Were examined by a study doctor and determined to be appropriate to participate.
- Were 20 years of age or older.
- Were diagnosed with complicated IAI.
- Participants who underwent surgery or procedures for complicated IAI, those who were undergoing, and those who will be undergoing surgery.

The study included 60 participants out of which 59 (98.3%) completed the study treatment.

- A total of 34 (57.6%) men participated.
- A total of 25 (42.4%) women participated.
- All participants were between the ages of 20 and 90.

Participants were to be treated until end of treatment visit. Of the 60 participants who started the study, 57 (95.0%) participants finished the TOC visit and 56 (93.3%) finished the study including coming back for the last visit.

4 (6.7%) participants left before the study was over by their choice or a doctor decided it was best for a participant to stop being in the study. One participant stopped participating in the study because of death due to serious medical condition which was not related to the study treatment.

How long did the study last?

Study participants were in the study for 6 weeks. The entire study took 12 months to complete. The study was completed as planned.

When the study ended in September 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?

Did ceftazidime-avibactam plus metronidazole help to cure and improve complicated intra-abdominal infections?

To answer this question, the researchers looked at how many participants with a certain type of bacteria had improved or resolved symptoms of infection. 40 out of the 60 participants who took CAZ-AVI plus MTZ [66.7%] were eligible for testing of improvement in infection/ symptoms at the TOC visit on Day 28. 36 out of the 40 participants [90.0%] were cured and had improved or resolved symptoms of infection at the TOC visit, compared to 78.0% clinical cure which was the pre-defined threshold before study start.

Based on these results, the researchers decided that the study medication may help achieve clinical cure in Japanese patients.

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

42 out of 60 participants [70.0%] in this study had at least 1 medical problem. A total of 2 participants left the study because of medical problems. The most common medical problems – those reported by at least 3 participants – are described 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 reported during the study. All medical problems reported by at least 3 participants are listed.
- The **2nd** column tells how many of the 60 participants taking the study medication reported each medical problem. Next to this number is the percentage of the 60 participants taking the study medication who reported the medical problem.
- Using these instructions, you can see that 7 out of the 60 (11.7%) participants taking the study medication reported medical problems of constipation and diarrhoea.

Table 1. Commonly reported medical problems by study participants	
Medical Problem	**CAZ-AVI plus MTZ (60 Participants)**
Hard and dry stool (constipation)	7 out of 60 participants (11.7%)
Loose and watery stools (diarrhoea)	7 out of 60 participants (11.7%)
Difficulty falling asleep (insomnia)	6 out of 60 participants (10.0%)
Feeling of sickness or discomfort in the stomach (nausea)	4 out of 60 participants (6.7%)
Wound complication	4 out of 60 participants (6.7%)
Pain in the stomach/belly (abdominal pain)	3 out of 60 participants (5.0%)

Itchy skin (pruritus)	3 out of 60 participants (5.0%)
Raised blood pressure (hypertension)	3 out of 60 participants (5.0%)

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.

3 out of 60 participants had serious medical problems.

One (1) participant died during the study but was not related to the study medication. Researchers do not believe any of the serious medical problems reported by participants were related to study medications.

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 C3591036

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

www.clinicaltrials.gov	Use the study identifier **NCT04927312**

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!