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: Emblaveo® (aztreonam-avibactam, also called ATM-AVI)

Protocol Number: C3601009

Dates of Study: 25 December 2020 to 23 January 2023

Title of this Study: A Study to Learn How Well ATM-AVI With or Without Metronidazole Works Compared to Best Available Therapy in Treating Serious Infections Caused by Gram-Negative Bacteria that Produce a Protein Called Metallo-β-Lactamase (MBL)

[A Prospective, Randomized, Open-Label, Comparative Study to Assess the Efficacy, Safety and Tolerability of Aztreonam-Avibactam (ATM-AVI) and Best Available Therapy for the Treatment of Serious Infections due to Multi-Drug Resistant Gram-Negative Bacteria Producing Metallo-β-Lactamase (MBL)]

Date of this Report: 17 November 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 are Gram-negative bacterial infections?

Infections happen when bacteria grow in places in the body where they should not grow. When an infection becomes severe, patients may need treatment with antibiotics, surgery, or both, depending on the type and severity of infection

"**Gram-negative bacteria**" are a type of bacteria that can cause serious infections. Gram-negative bacteria are often linked to infections caught while being hospitalized.

These bacteria can cause infections in many parts of the body, such as the abdomen, lungs, urinary tract, and bloodstream.

Gram-negative bacterial infections can be hard to treat. This is because Gram-negative bacteria can have high resistance to many antibiotics. For example, the bacteria can produce proteins like "metallo-β-lactamase" or **MBL,** which stop antibiotics from killing them.

What is aztreonam-avibactam (ATM-AVI)?

- Aztreonam is also called **ATM**. ATM is an antibiotic that has been approved in many countries to treat certain bacterial infections.
- Avibactam is also called **AVI**. It is an investigational drug that is designed to help certain antibiotics to work better against infections. AVI may help ATM by preventing the proteins in the bacteria from breaking apart ATM.

ATM-AVI is a combination of aztreonam and avibactam. It is being studied for the possible treatment of Gram-negative bacterial infections. In this study, participants received ATM-AVI through a needle into a vein, also called an intravenous (IV) infusion.

The use of ATM-AVI in this study is investigational because this combination of antibiotics is not approved for use by health authorities at this time.

What was the purpose of this study?

The main purpose of this study was to learn how well ATM-AVI (with or without metronidazole) and best available therapy treat serious Gram-negative bacteria that produce MBL.

- **Metronidazole**, also called **MTZ**, is an antibiotic. Study doctors gave MTZ in addition to ATM-AVI to some participants to treat bacteria not targeted by ATM-AVI.
- **Best available therapy**, also referred to in this summary as **BAT**, is the recommended antibiotics available in the hospital at the time of this study for treatment of a certain infection. BAT could include just one antibiotic or a combination of antibiotics.

  ATM-AVI was compared to BAT because BAT is the standard antibiotics used for treatment of certain infections.

Researchers wanted to know:

- **How many participants who were assigned to receive ATM-AVI with or without MTZ and who were assigned to receive BAT were treated successfully at the end of treatment period?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Study doctors checked adults with the following serious infections caused by Gram-negative bacteria that produce MBL to make sure they met the study requirements:

Complicated abdominal infection that needs to be treated with surgery. Abdominal means around the abdomen or belly area.

Hospital-acquired or ventilator-associated lung infection, which means a lung infection that started after being admitted to the hospital or is due to use of a ventilator, a machine that helps with breathing.

Complicated urinary tract infection, also called UTI, is an infection of the urinary tract that is more severe and harder to treat**.**
The urinary tract gets rid of the body's waste in the form of urine. The urinary tract is made up of the kidneys, ureters, bladder, and urethra.

Blood stream infection.

Then, participants were assigned to 1 of 2 treatment groups by chance.

ATM-AVI with or without MTZ	BAT
All participants assigned to this group received ATM-AVI. Only participants with complicated abdominal infection received MTZ in addition to ATM-AVI.	All participants assigned to this group received BAT, the recommended antibiotic or combination of antibiotics for their infection available in the hospital at the time of study.

Participants had

- a 2 in 3 chances of receiving ATM-AVI with or without MTZ.
- a 1 in 3 chances of receiving BAT.

Study participants and researchers knew what study medication the participants received. This is known as an "open-label" study.

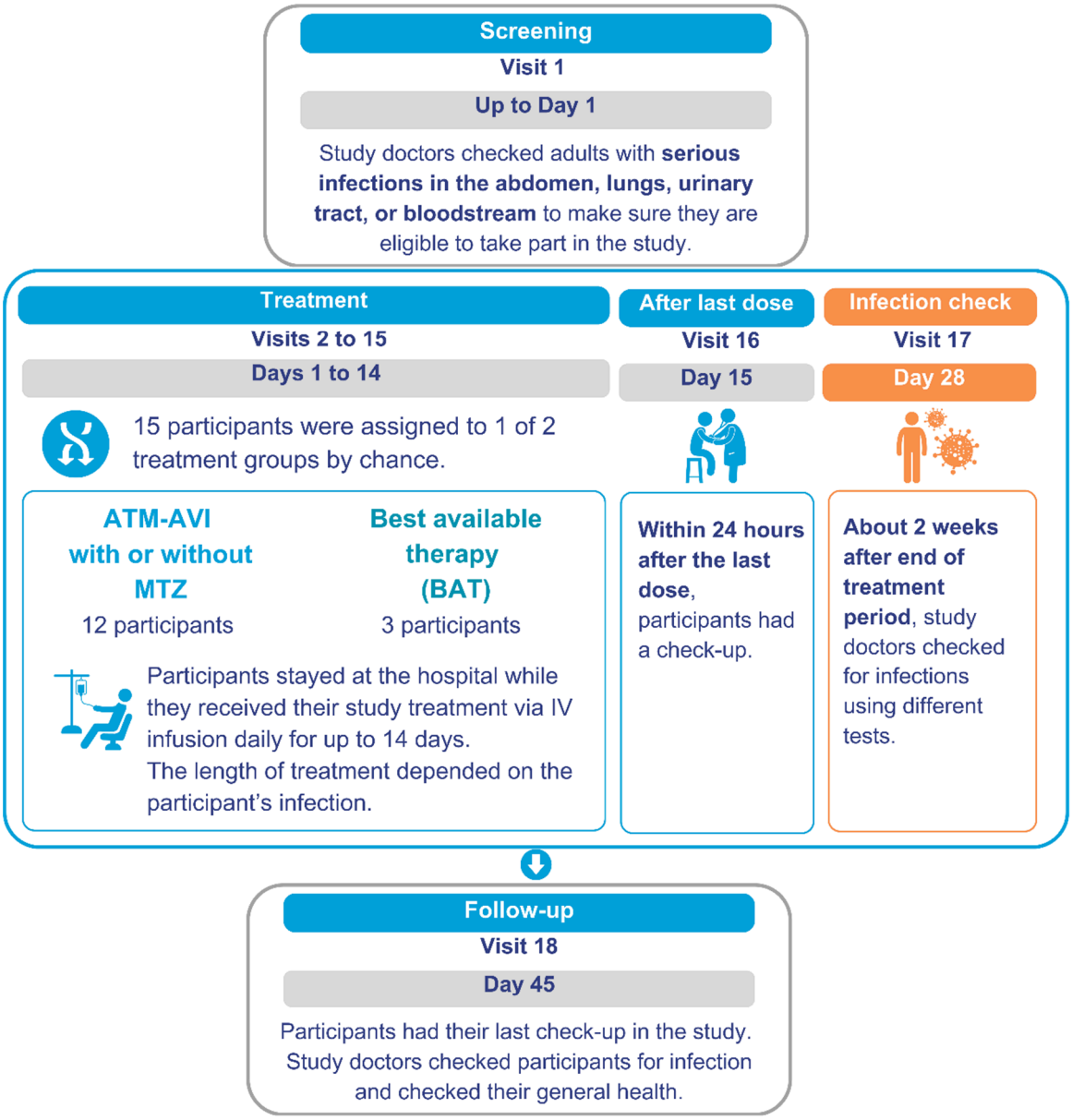
After the treatment period, researchers checked how many study participants in each treatment group were treated successfully.

An independent group of experts checked the participants' responses to study medications. They decided whether participants were successfully or unsuccessfully treated after the treatment period.

This independent group of experts did not know which study medication the participants got. This helped to make sure that their assessments were fair.

Figure 1 below shows what happened during the study.

Figure 1. What happened in this study?



Participants had different health checks throughout the study, such as:

- Blood, urine, and other samples (like phlegm, or fluids from infected part of the abdomen) tests to check for infection.
- Imaging tests of the abdomen or lungs so study doctors can check the condition inside their bodies.
- General check-up about their health, symptoms, and medicines they were taking.

Where did this study take place?

The Sponsor ran this study at 12 locations in 9 countries in Europe, North America, and Asia.

When did this study take place?

It began on 25 December 2020 and ended on 23 January 2023.

Who participated in this study?

The study included participants at least 18 years old who were in the hospital due to complicated abdominal infection, hospital-acquired or ventilator-associated lung infection, complicated urinary tract infection, or blood stream infection.

Overall, 15 participants joined this study. All participants were assigned to 1 of the 2 treatment groups.

- 9 men and 6 women participated.
- All were between the ages of 31 and 83 years old.

Overall, 10 out of 15 participants (66.6%) finished the treatment period of study. Five (5) out of 15 participants (33.3%) did not finish the treatment period of the study because of the following reasons:

- 2 participants died.
- 1 participant had a medical problem during the study.
- 1 participant left the study by their choice before receiving any study medication.
- 1 participant was not feeling better after starting treatment.

How long did the study last?

Study participants were in the study for up to 49 days. The entire study took about 2 years to complete.

The study ended earlier than planned because of difficulty finding participants with certain serious infections required in this study.

When the study ended in January 2023, 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 many participants who were assigned to receive ATM-AVI with or without MTZ and who were assigned to receive BAT were treated successfully at the end of treatment period?

An independent group of experts checked the participants' symptoms and laboratory or imaging test results about 2 weeks after the end of the treatment period to see the status of their infection.

Researchers then checked the number of participants who were treated successfully in each treatment group.

The number of participants who were treated successfully at the end of treatment period was:

- 5 out of 12 participants **(41.7%)** who were assigned to receive ATM-AVI with or without MTZ.
- 0 out of 3 participants **(0%)** who were assigned to receive BAT.

These results are limited because of the small number of participants who joined the study. For this reason, the researchers cannot make a conclusion in this study about how well ATM-AVI with or without MTZ worked in treating serious infections caused by Gram-negative bacteria that produce MBL.

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.

This section describes results from the 14 participants who received at least 1 dose of study medication in the study.

Overall, 13 out of 14 participants (92.9%) had at least 1 medical problem.

- 11 out of 12 participants (91.7%) who received ATM-AVI with or without MTZ.
- 2 out of 2 participants (100%) who received BAT.

A total of 3 out of 14 participants (21.4%) left the study early because of medical problems they had during the study.

The most common medical problems in the study included the following:

Two (2) out of 14 participants experienced failure of several body organs. This medical problem happened to 1 participant in each treatment group.

Two (2) out of 14 participants experienced a low level of potassium in their blood. Both participants received ATM-AVI with or without MTZ in the study.

No other medical problems were experienced by more than 1 participant each.

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.

Overall, 7 out of 14 participants (50.0%) had a serious medical problem:

- 5 out of 12 participants (41.7%) who received ATM-AVI with or without MTZ.
- 2 out of 2 participants (100%) who received BAT.

One (1) serious medical problem was reported by at least 2 participants overall. This serious medical problem was failure of several body organs to function as they should. This happened to 1 participant in each treatment group.

No other serious medical problems happened to more than 2 participants.

One (1) participant who received BAT had a serious medical problem of kidney damage or loss of function. Study doctors thought this serious medical problem was likely related to BAT.

Study doctors did not think that any of the serious medical problems were related to ATM-AVI.

Overall, 3 out of 14 participants (21.4%) died because of a medical problem they had during the study. Study doctors did not believe that any of the fatal medical problems in the study were related to any of the 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 **C3601009**

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

www.clinicaltrials.gov	Use the study identifier **NCT03580044**
www.clinicaltrialsregister.eu	Use the study identifier **2017-004544-38**

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Pfizer and AbbVie developed ATM-AVI.

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!