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, or ATM-AVI)

Protocol Number: C3601002

Dates of Study: 05 April 2018 to 23 February 2023

Title of this Study: A Study to Learn How Well ATM-AVI With or Without Metronidazole Works Compared to Meropenem With or Without Colistin in Treating Serious Infections Caused by Gram-Negative Bacteria

[A Phase 3 Prospective, Randomized, Multicenter, Open-Label, Central Assessor Blinded, Parallel Group, Comparative Study to Determine the Efficacy, Safety and Tolerability of Aztreonam Avibactam (ATM-AVI) ± Metronidazole (MTZ) Versus Meropenem ± Colistin (MER ± COL) for the Treatment of Serious Infections due to Gram-Negative Bacteria, Including Metallo β-Lactamase (MBL) Producing Multidrug Resistant Pathogens, for

Which There are Limited or No Treatment Options]

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. This is called an intravenous (IV) infusion.

The use of ATM-AVI in this study was investigational because health authorities have not approved the use of this combination of antibiotics 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 meropenem (with or without colistin) treat serious Gram-negative bacterial infections. This study focused on serious abdominal and lung infections.

Metronidazole, also called **MTZ**, is an antibiotic. Study doctors gave MTZ in addition to ATM-AVI to some participants to treat bacteria that are not targeted by ATM-AVI.

Meropenem, also called **MER**, is the antibiotic that ATM-AVI was compared to in the study. MER was chosen because it is an antibiotic approved for the treatment of abdominal and lung infections.

Colistin, also called **COL**, is an antibiotic used to treat Gram-negative bacterial infections that are resistant to other antibiotics. Study doctors gave COL with MER to some participants to treat bacteria that are not targeted by MER.

Researchers wanted to know:

- **How many participants who were assigned to receive ATM-AVI with or without MTZ and who were assigned to receive MER with or without COL 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 Gram-negative bacterial infections 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 the use of a ventilator, a machine that helps with breathing.

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

ATM-AVI with or without MTZ	MER with or without COL
All participants assigned to this group received ATM-AVI.	All participants assigned to this group received MER.
Only participants with complicated abdominal infection received MTZ in addition to ATM-AVI.	Participants received COL in addition to MER only if the study doctor thought they needed it.

Participants had

- a 2 in 3 chance of receiving ATM-AVI with or without MTZ.
- a 1 in 3 chance of receiving MER with or without COL.

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

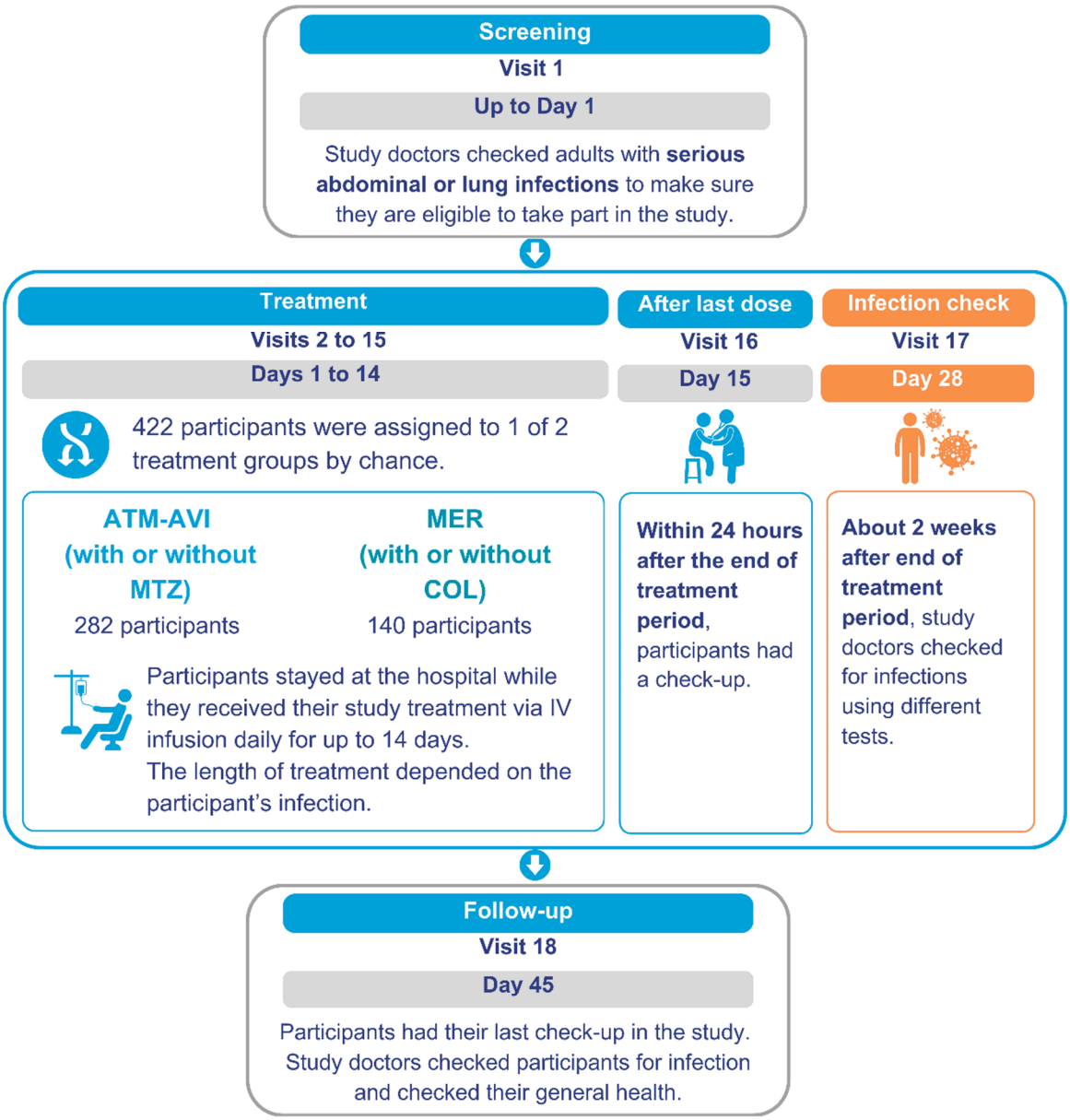
After the treatment period, researchers checked how many participants in each treatment group were treated successfully.

An independent group of experts checked the participants’ responses to the study medications. They decided whether participants were successfully or unsuccessfully treated at the end of 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 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 81 locations in 20 countries in Europe, North and South America, and Asia.

When did this study take place?

It began on 05 April 2018 and ended on 23 February 2023.

Who participated in this study?

The study included participants at least 18 years old who were in the hospital due to

- complicated abdominal infections, or
- hospital-acquired/ventilator-associated lung infections.

Out of the 461 participants that joined this study, 422 were assigned to receive 1 of the 2 study medications.

- 38 participants did not meet study requirements, so they did not receive a study medication.
- 1 met study requirements but did not receive a study medication.

Out of 422 participants who were assigned to a treatment group:

- 287 were men and 135 were women.
- All were between the ages of 18 and 87 years old.

Overall, 363 out of 422 participants (86.0%) finished the treatment period of the study. A total of 59 out of 422 participants (14.0%) did not finish the treatment period of the study, mostly because:

- They made the decision to stop treatment before the treatment period was over.
- They were not feeling better.
- Of a medical problem they had during the study.

How long did the study last?

Study participants were in the study for up to 49 days. The entire study took about 5 years to complete.

When the study ended in February 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 MER with or without COL 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.

This section describes the results of the following participants:

- **Overall Group**: 422 participants who were assigned to receive 1 of the 2 study medications.
- **Evaluable Group**: 318 participants from the Overall Group who met certain study conditions. These conditions include at least 2 days of treatment with study medication and having a clear treatment outcome (treatment succeeded or failed), among others. Researchers looked at the results of this subgroup to further assess the effect of study medications.

The number of participants who were treated successfully at the end of the treatment period was similar between the 2 treatment groups.

In the Overall Group, the percentage of participants who were treated successfully after the end of the treatment period was:

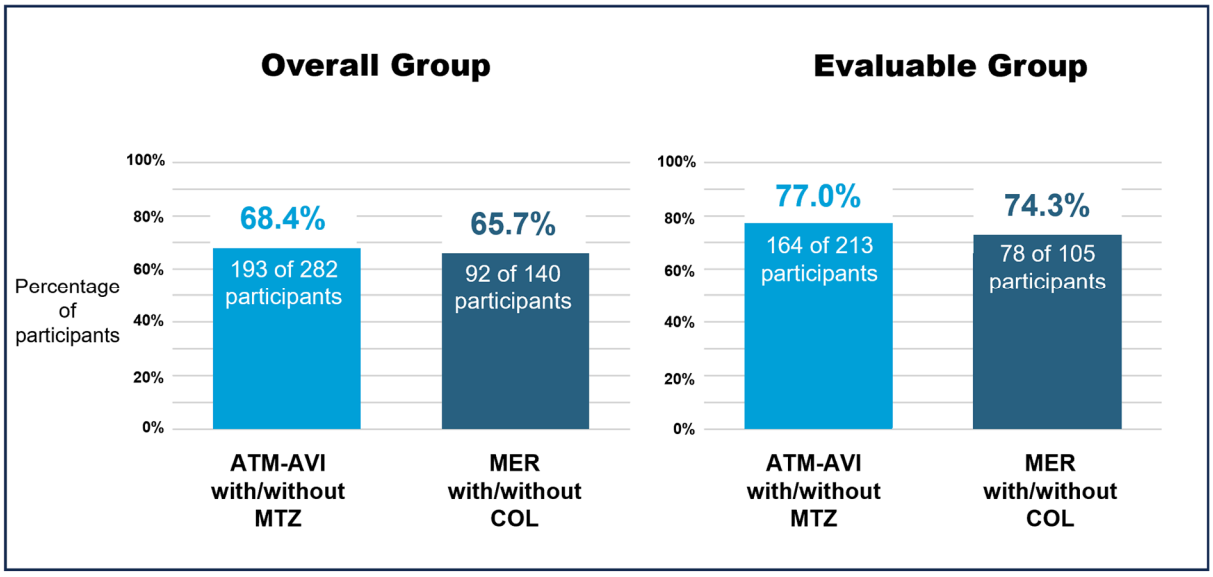
- **68.4%** of participants who were assigned to receive ATM-AVI with or without MTZ.
- **65.7%** of participants who were assigned to receive MER with or without COL.

In the Evaluable Group, the percentage of participants who were treated successfully at the end of treatment period was:

- **77.0%** of participants who were assigned to receive ATM-AVI with or without MTZ.
- **74.3%** of participants who were assigned to receive MER with or without COL.

Figure 2 below shows these results.

Figure 2. How many participants were treated successfully 2 weeks after the end of treatment period?



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 412 participants who received at least 1 dose of study medication in the study.

Overall, 264 out of 412 participants (64.1%) had at least 1 medical problem:

- 177 out of 275 participants (64.4%) who received ATM-AVI with or without MTZ.
- 87 out of 137 participants (63.5%) who received MER with or without COL.

A total of 31 out of 412 participants (7.5%) left the study early because of medical problems they had during the study.

Table 1 below lists the most common medical problems – those reported by at least 5% of participants in either of the 2 treatment groups – in the study.

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 5% of participants in any of the treatment groups are listed.
- The **2nd** column tells how many of the 275 participants who received ATM-AVI with or without MTZ reported each medical problem. Next to this number is the percentage of the

275 participants in this group who reported the medical problem.

- The **3rd** column tells how many of the 137 participants who received MER with or without COL reported each medical problem. Next to this number is the percentage of the 137 participants in this group who reported the medical problem.
- Using these instructions, you can see that 20 out of the 275 participants (7.3%) who received ATM-AVI with or without MTZ reported low level of red blood cell. A total of 7 out of the 137 participants (5.1%) who received MER with or without COL reported the same medical problem.

Table 1. Commonly reported medical problems by study participants

Medical Problem	ATM-AVI with or without MTZ (275 Participants)	MER with or without COL (137 Participants)
Low level of red blood cell	20 out of 275 participants (7.3%)	7 out of 137 participants (5.1%)
High level of alanine aminotransferase	18 out of 275 participants (6.5%)	7 out of 137 participants (5.1%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**ATM-AVI with or without MTZ (275 Participants)**	**MER with or without COL (137 Participants)**
(a protein mainly found in the liver)		
Loose stools	16 out of 275 participants (5.8%)	5 out of 137 participants (3.6%)
Low level of potassium in blood	16 out of 275 participants (5.8%)	4 out of 137 participants (2.9%)
High level of aspartate aminotransferase (a protein mainly found in the liver)	15 out of 275 participants (5.5%)	5 out of 137 participants (3.6%)
Fever	14 out of 275 participants (5.1%)	6 out of 137 participants (4.4%)

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, 78 out of 412 participants (18.9%) had a serious medical problem:

- 53 out of 275 participants (19.3%) who received ATM-AVI with or without MTZ.
- 25 out of 137 participants (18.2%) who received MER with or without COL.

Table 2 below lists the most common serious medical problems in the study. These serious medical problems are reported in more than 2 participants in either of the treatment groups.

Instructions on how to read Table 2 are the same as those of Table 1.

Table 2. Commonly reported serious medical problems by study participants

Medical Problem	ATM-AVI with or without MTZ (275 Participants)	MER with or without COL (137 Participants)
Pocket of pus inside the abdomen	4 out of 275 participants (1.5%)	2 out of 137 participants (1.5%)

Table 2. Commonly reported serious medical problems by study participants		
Medical Problem	**ATM-AVI with or without MTZ (275 Participants)**	**MER with or without COL (137 Participants)**
COVID-19 infection	3 out of 275 participants (1.1%)	0 out of 137 participants (0%)
Lung infection	4 out of 275 participants (1.5%)	1 out of 137 participants (0.7%)
Life-threatening complication of an infection	2 out of 275 participants (0.7%)	3 out of 137 participants (2.2%)
Blockage of a blood vessel in the lung	4 out of 275 participants (1.5%)	0 out of 137 participants (0%)
Failure of lungs to deliver enough oxygen to blood	3 out of 275 participants (1.1%)	2 out of 137 participants (1.5%)

Study doctors did not think that the serious medical problems were related to any of the study medications, except for one:

One (1) participant who received MER with or without COL had a serious medical problem of abnormal liver test result that was thought by the study doctors to be likely related to MER.

Overall, 30 out of 412 participants (7.3%) died because of a medical problem they had after joining the study. Three (3) of these participants died after the end of their study participation. Study doctors did not think that any of the fatal serious medical problems 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 **C3601002**

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

www.clinicaltrials.gov	Use the study identifier **NCT03329092**
www.clinicaltrialsregister.eu	Use the study identifier **2017-002742-68**

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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!