



# CLINICAL TRIAL 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 medicine 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

**Protocol Number:** D4280C00015 (C3591004)

**Dates of Trial:** 01 August 2015 to 01 June 2017

**Title of this Trial:** A Single Blind, Randomised, Multi-centre, Active Controlled, Trial to Evaluate Safety, Tolerability, Pharmacokinetics and Efficacy of Ceftazidime and Avibactam When Given in Combination With Metronidazole, Compared With Meropenem, in Children From 3 Months to Less Than 18 Years of Age With Complicated Intra-Abdominal Infections (cIAIs)

**Date of this Report:** 24 January 2019

– *Thank You* –

Pfizer, the Sponsor, would like to thank you and your child for participating in this clinical trial and provide you a summary of results representing everyone who participated. If you have any questions about the study or results please contact the doctor or staff at your child's study site.

## WHY WAS THIS STUDY DONE?

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An intraabdominal infection, or “IAI”, is the name for a type of infection in the abdomen (stomach area). Children with an IAI may have symptoms such as stomach area pain or fever. Some IAIs are serious, and can require someone to be in the hospital to be treated with intravenous (IV) antibiotics and sometimes surgery. This type of serious IAI is known as a “complicated IAI”.

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. This study was designed to learn more about using CAZ-AVI to treat complicated IAI in children, when used together with another antibiotic medicine called metronidazole. CAZ-AVI has not been approved for use in children, as it is still being studied. The ceftazidime half of CAZ-AVI has previously been approved for use in children.

The main purpose of this study was to learn more about the use of CAZ-AVI in children with complicated IAI, when given together with metronidazole, compared to another antibiotic medicine called meropenem. The researchers wanted to answer this main question:

- For children treated with CAZ-AVI, how well was it tolerated, and were there any new medical problems different from those can happen when using ceftazadime alone?

In addition, the researchers also wanted to see how many children in this study were cured or had an improvement in complicated IAI.

## WHAT HAPPENED DURING THE STUDY?

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This study compared 2 groups of children to learn more about the safety and effectiveness of CAZ-AVI when given together with metronidazole, compared to another antibiotic medicine called meropenem. Meropenem is commonly used to treat complicated IAI in children.

This study was for children who were diagnosed with complicated IAI. The children in this study were at least 3 months old, but younger than 18 years old when they started the study.

First, the children were checked by the study doctor to make sure they were a good fit for the study. This was called “screening”.

The children were grouped by age:

- Group 1 (30 children): At least 12 years old, but younger than 18 years old
- Group 2 (43 children): At least 6 years old, but younger than 12 years old
- Group 3 (9 children): At least 2 years old, but younger than 6 years old
- Group 4 (1 child): At least 3 months old, but younger than 2 years old

The children were assigned to join 1 of 2 treatment groups. Children in the first treatment group received CAZ-AVI plus another antibiotic called metronidazole. Children in the second treatment group received an antibiotic called meropenem. These medicines were given into a vein with a small tube, and the doses were based on each child’s weight. The children were picked to receive either treatment by chance alone.

Children received either CAZ-AVI plus metronidazole or meropenem for at least 3 days. Depending on what the study doctor thought was best for each child, after 3 days of either CAZ-AVI plus metronidazole or meropenem given into a vein, some children may have switched to an antibiotic medicine you can take by mouth. Some children could have received either CAZ-AVI plus metronidazole or meropenem for up to 15 days.

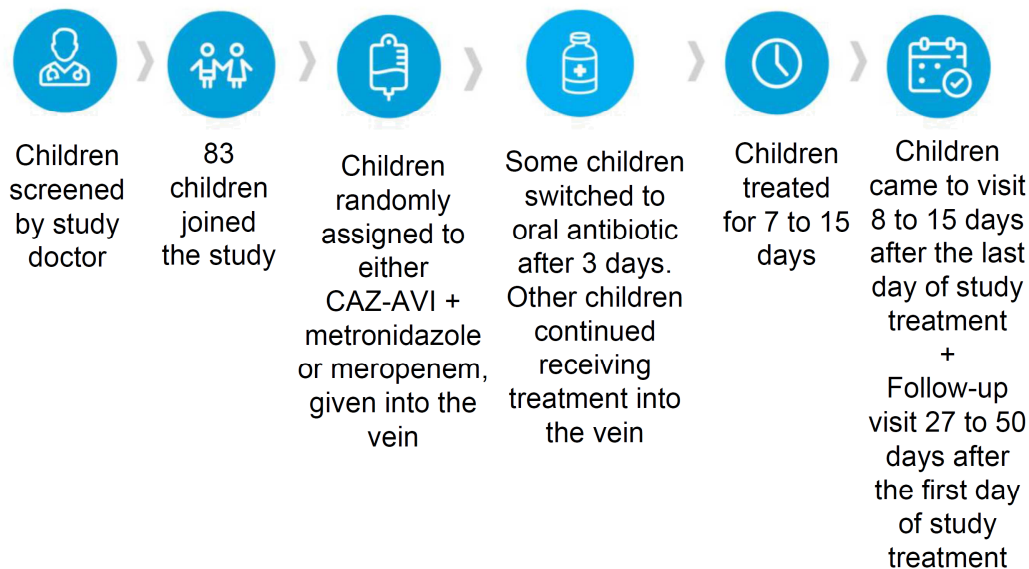
This was a “single-blind” study, which means that the children, their study doctor, pharmacist, parents/caregivers, and most of the researchers knew which medicine they received. However, one study doctor who examined the children did not know which medicine they were given.

Safety was carefully monitored throughout the study. The study doctors examined each child, did blood or urine tests, and watched for any medical problems. The study doctors also followed up with the children for 27 to 50 days after they started study treatment.

While children were only in the study for up to 50 days (treatment plus follow-up), the entire study took almost 2 years to complete. Children joined the study at 1 of 29 locations in 10 countries (Czech Republic, Greece, Hungary, Poland, Romania, Russian Federation, Spain, Taiwan, Turkey, and United States). The first child joined the study on 01 August 2015, and the last child finished the study on 01 June 2017. A total of 30 girls and 53 boys joined the study.

Children could receive study treatment for a total of 7 to 15 days, and come to a visit 8 to 15 days after the last day they got the study treatment. The children could come to a follow-up visit 27 to 50 days after the first day they got the study treatment. In total, 83 children started the study and 81 children (98%) completed it, including coming back for the last visit. There were 2 children (2%) who did not finish the study because of parent/guardian choice, or because a doctor decided it was best for the child not to continue in the study.

The figure below shows what happened during this study.



When the study ended in June 2017, the Sponsor reviewed 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?

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### How many children in this study were cured or had an improvement in complicated IAI?

To answer this question, the researchers looked at how many children with a certain type of bacteria had improved or resolved symptoms of infection. 8 to 15 days after they last got study treatment, 45 out of 50 children (90%) in the CAZ-AVI plus metronidazole group were cured or had an improvement in complicated IAI. 18 out of 19 children (95%) in the meropenem group were cured or had an improvement in complicated IAI.

It is important to know that there were not enough children enrolled in the study to make any conclusions about the effectiveness of CAZ-AVI compared to meropenem.

This does not mean that everyone in this study had these results. Other studies may produce different results, as well. These are just some of the main findings of the study, and more information may be available at the websites listed at the end of this summary.

## WHAT MEDICAL PROBLEMS DID CHILDREN HAVE DURING THE STUDY?

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The researchers recorded any medical problems the children had during the study. Children 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 have been caused by a study treatment, or by another medicine the child 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 the side effects of an experimental drug might be.

In this study, 45 children (54%) who received study medication had at least 1 medical problem, including 32 out of 61 children (53%) in the CAZ-AVI plus metronidazole group and 13 out of 22 children (59%) in the meropenem group.

The most common medical problems reported in children in this study are listed below.

<b>Most Common Medical Problems</b> <b>(Reported in 2 or More Children Taking the Same Medicine)</b>		
Medical Problem	CAZ-AVI + metronidazole (61 children treated)	Meropenem (22 children treated)
Stomach ache	0 (0%)	2 (9%)
Vomiting	9 (15%)	2 (9%)
Redness and swelling at place where the medicine goes into the vein	4 (7%)	0 (0%)
Fever	2 (3%)	0 (0%)
Cold	2 (3%)	0 (0%)
Fluid in the skin around a wound	3 (5%)	0 (0%)
Low level of potassium in the blood	2 (3%)	0 (0%)
Cough	1 (2%)	2 (9%)

## WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems.

In this study, 6 children (7%) of the 83 who had study treatment had a serious medical problem. This included 5 children (8%) in the CAZ-AVI plus metronidazole group



and 1 child (5%) in the meropenem group. None of these serious medical problems were considered to be related to study treatment. No children died during the study.

Overall, the medical problems reported in this study are similar to the medical problems reported in past studies with adults. No new issues related to the safety of CAZ-AVI were found.

## **WHERE CAN I LEARN MORE ABOUT THIS STUDY?**

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If you have questions about the results of your child's study, please speak with the doctor or staff at your child's study site.

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

[www.clinicaltrials.gov](http://www.clinicaltrials.gov)

Use the study identifier **NCT02475733**

[www.clinicaltrialsregister.eu](http://www.clinicaltrialsregister.eu)

Use the study identifier **2014-003242-28**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients. Additional studies with CAZ-AVI in children are planned.

**Again, thank you for volunteering.**  
**We do research to try to find the**  
**best ways to help patients, and you**  
**helped us to do that!**