



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: D4280C00016 (C3591005)

Dates of Trial: 24 September 2015 to 15 September 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 Compared with Cefepime in Children From 3 Months to Less Than 18 Years of Age With Complicated Urinary Tract Infections (cUTIs)

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?

A urinary tract infection, or “UTI”, is the name for an infection in part of the urinary system, such as the bladder or urethra. Children with a UTI may have symptoms such as needing to urinate more often, pain when urinating, or blood in the urine. UTIs are usually caused by bacteria, and they are usually simple to treat. However, sometimes UTIs can be harder to treat and may require someone to be in the hospital to be treated with intravenous (IV) antibiotics. When this happens, it is known as a “complicated UTI.”

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 UTI, in adults. This study was designed to learn more about using CAZ-AVI to treat complicated UTI in children. 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 UTI, compared to another antibiotic medicine called cefepime. 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 that can happen when using ceftazidime alone?

In addition, the researchers also wanted to see how many children in the study were cured or had an improvement in their infection (complicated UTI).

WHAT HAPPENED DURING THE STUDY?

This study compared 2 groups of children to learn more about the safety and effectiveness of CAZ-AVI, compared to another antibiotic medicine called cefepime. Cefepime is commonly used to treat complicated UTI in children.

This study was for children who were diagnosed with complicated UTI. 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 (19 children): At least 12 years old, but younger than 18 years old
- Group 2 (22 children): At least 6 years old, but younger than 12 years old
- Group 3 (18 children): At least 2 years old, but younger than 6 years old
- Group 4 (38 children): At least 3 months old, but younger than 2 years old

The children were assigned to receive either CAZ-AVI or cefepime. Both medicines were given into a vein through 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 or cefepime for at least 3 days. Depending on what the study doctor thought was best for each child, after 3 days of receiving either CAZ-AVI or cefepime 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 or cefepime into a vein for up to 14 days.

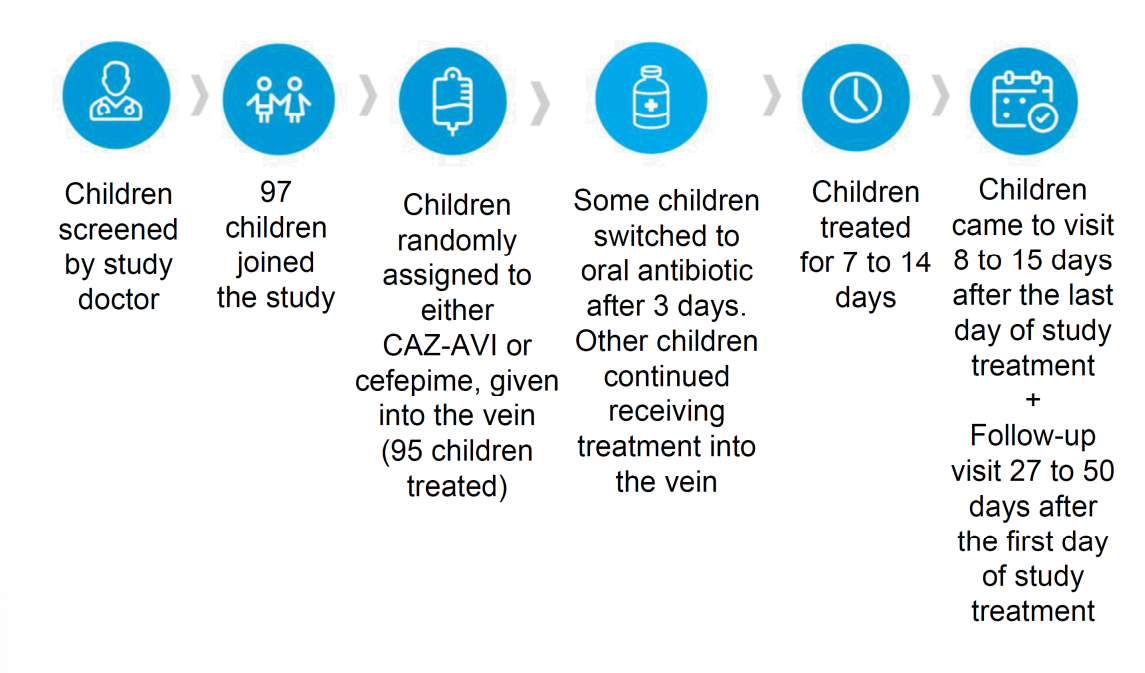
This was a “single-blind” study, which means that the children, their parents/caregivers, their study doctor, pharmacist, and most of the researchers knew which medicine they received. However, one study doctor who examined the children did not know which medicine they were given.

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 about 2 years to complete. Children joined the study at 1 of 25 locations in 9 countries (Czech Republic, Greece, Hungary, Poland, Romania, Russian Federation, Taiwan, Turkey, and United States). The first child joined the study on 24 September 2015 and the last child finished the study on 15 September 2017. A total of 77 girls and 18 boys joined the study.

Children could receive study treatment for a total of 7 to 14 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. Of the 97 children who started the study, 90 children (93%) completed it, including coming back for the last visit. A total of 7 children (7%) did not finish the study by 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 the study.



When the study ended in September 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?

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

To answer this question, the researchers looked at how many children with a certain type of bacteria in their urine had improved or resolved symptoms of infection. This included 54 children in the CAZ-AVI group and 23 children in the cefepime group. They also looked at samples of the children's urine, to find out if bacteria present in the urine before treatment would no longer be present after treatment. 8 to 15 days after they last got study treatment, 39 out of 54 children (72%) in the CAZ-AVI group were cured or had an improvement in complicated UTI, and had no bacteria present in urine. 14 out of 23 children (61%) in the cefepime group were cured or had an improvement in complicated UTI, and had no bacteria present in urine.

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 cefepime.

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?

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 their disease or by chance). Or, medical problems could have been caused by a study procedure, 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.

A total of 97 children started the study, but 2 children (1 child in the CAZ-AVI group and 1 child in the cefepime group) left the study before receiving treatment. So, there were 95 children who received study treatment. To learn more about the safety of CAZ-AVI, the researchers looked at the medical problems that happened in these 95 children. In this study, 51 children (54%) had at least 1 medical problem, including 36 out of 67 children (54%) in the CAZ-AVI group and 15 out of 28 children (54%) in the cefepime group.

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

Most Common Medical Problems (Reported in 2 or More Children Taking the Same Medicine)		
Medical Problem	CAZ-AVI (67 children treated)	Cefepime (28 children treated)
Diarrhea	5 (8%)	3 (11%)
Urinary tract infection	5 (8%)	0 (0%)
Stuffy or runny nose	4 (6%)	2 (7%)
Cough or cold that didn't go to the lungs	3 (5%)	0 (0%)
Rash	3 (5%)	2 (7%)
Stomach ache	2 (3%)	0 (0%)
Feeling sick (nausea)	2 (3%)	1 (4%)
Vomiting	2 (3%)	2 (7%)
Fever	2 (3%)	1 (4%)
Gut infection that usually causes diarrhea and vomiting	2 (3%)	0 (0%)
Common cold	2 (3%)	0 (0%)

Kidney infection	2 (3%)	1 (4%)
Cough or cold caused by virus	2 (3%)	0 (0%)
Irritation, redness, or itching in the female genital region	2 (3%)	0 (0%)
Cough	2 (3%)	1 (4%)
Rash caused by thrush or yeast infection between folds of skin	1 (2%)	2 (7%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

10 children (11%) of the 95 who had study medicine had a serious medical problem. This included 8 children (12%) in the CAZ-AVI group and 2 children (7%) in the cefepime group. 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?

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

Use the study identifier **NCT02497781**

www.clinicaltrialsregister.eu

Use the study identifier **2014-003244-13**

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!