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: Anidulafungin (PF-03910960)

Protocol Number: A8851008

Dates of Trial: 27 February 2009 to 14 February 2018

Title of this Trial: A Prospective, Open-Label Study to Assess the Pharmacokinetics, Safety and Efficacy of Anidulafungin when used to Treat Children with Invasive Candidiasis, including Candidemia

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?

Candida is a type of fungus that is normally found in small amounts in the human body. Sometimes, too much *Candida* can grow in the body and cause health problems. This is known as a *Candida* infection.

The name "invasive *Candida* infection" is used when the infection has spread to other parts of the body through the bloodstream. Certain medicines or diseases, like cancer, may make a child more likely to develop an invasive *Candida* infection.

Anidulafungin is a medicine that is currently used to treat *Candida* infections in adults. This study was designed to learn more about using anidulafungin to treat *Candida* infections in children. Anidulafungin has not been approved for use in children, as it is still being studied.

The main purpose of this study was to learn more about the safety of anidulafungin in children with invasive *Candida* infection. The researchers wanted to answer this question:

- Did the children in this study have any new or worsening medical problems? If so, what new or worsening medical problems did the children have?

The researchers also wanted to learn more about how anidulafungin works to treat invasive *Candida* infection in children. The researchers wanted to answer this question:

- How many children were cured or had an improvement in *Candida* infection?

WHAT HAPPENED DURING THE STUDY?

This study was for children who were diagnosed with invasive *Candida* infection, or who were at high risk for getting an invasive *Candida* infection. The children in this study were at least 1 month old, but younger than 18 years old when the study started.

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 1 month old, but younger than 2 years old
- Group 2 (19 children): At least 2 years old, but younger than 5 years old
- Group 3 (30 children): At least 5 years old, but younger than 18 years old

All the children in this study were given anidulafungin by IV (a needle in the vein), and the doses were based on each child's weight. On the first day of treatment, children were given 3 milligrams (mg) of anidulafungin per kilogram (kg) of weight. From the second day of treatment onwards, children were given 1.5 mg of anidulafungin per kg of weight. Children were supposed to receive anidulafungin for at least 10 days if they had a *Candida* infection and at least 5 days if they were at high risk of getting a *Candida* infection.

After the anidulafungin treatment, the study doctor may have decided to switch some of the children to another antifungal medicine called fluconazole, given by mouth, to continue treatment of the *Candida* infection. All children could receive up to 35 days of anidulafungin and up to 49 days of total treatment (anidulafungin + fluconazole).

This was an "open-label" study, which means that the researchers, the children, and the children's parents/caregivers knew which medicines were being given.

Safety was carefully considered throughout the study. The study doctors examined each child, did blood/urine tests, and watched for any medical problems. The study doctors also followed up with the children for 6 weeks after their last dose of study treatment.

The figure on the following page shows what happened during this study.

While children were only in the study for up to 13 weeks (treatment plus follow-up), the entire study took about 9 years to complete. Children joined the study at 1 of 26 locations in 10 countries (Brazil, Canada, Greece, Italy, Republic of Korea, Russia, Spain, Taiwan, United Kingdom, and United States). The first child joined the study on 27 February 2009 and the last child finished the study on 14 February 2018. A total of 30 girls and 38 boys joined the study.

Patients were supposed to receive study treatment for up to 35 days and come to 2 follow-up visits at week 2 and week 6 of the study. Of the 68 children who started the study, 58 children (85%) completed it. Ten (10) children (15%) did not finish the study by their choice or because they passed away. The study doctors determined that none of these deaths were related to the study treatment.

When the study ended in February 2018, 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 children were cured or had an improvement in *Candida* infection?

For the 64 patients who had a *Candida* infection in this study, study doctors examined how well the study treatment worked on the last day the child received study treatment (anidulafungin alone and anidulafungin + fluconazole) and at the follow-up visits.

On the last day that all study treatment was received, *Candida* infection was either cured or improving in 46 (72%) children. At the last follow-up visit, *Candida* infection was cured in 43 (67%) children. The percentage of children who were cured in this study was similar to the percentage of cured patients in previous adult studies with anidulafungin.

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 PATIENTS 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 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.

Out of 68 children in this study, 66 children (97%) had at least 1 medical problem. The most common medical problems reported in children in this study are listed below.

Most Common Medical Problems (Reported in More than 5% of Children)

Medical Problem	Group 1 (19 children)	Group 2 (19 children)	Group 3 (30 children)	Total (68 children)
Vomiting	4 (21%)	7 (37%)	5 (17%)	16 (24%)
Diarrhea	3 (16%)	2 (11%)	9 (30%)	14 (21%)
Fever	4 (21%)	3 (16%)	6 (20%)	13 (19%)

Most Common Medical Problems (Reported in More than 5% of Children)				
Medical Problem	Group 1 (19 children)	Group 2 (19 children)	Group 3 (30 children)	Total (68 children)
Anemia	5 (26%)	3 (16%)	1 (3%)	9 (13%)
Nosebleed	1 (5%)	3 (16%)	5 (17%)	9 (13%)
Headache	0 (0%)	1 (5%)	6 (20%)	7 (10%)
High liver enzyme test that may indicate liver damage (alanine aminotransferase)	2 (11%)	2 (11%)	3 (10%)	7 (10%)
Stomach pain	0 (0%)	3 (16%)	3 (10%)	6 (9%)
Skin rash	2 (11%)	2 (11%)	2 (7%)	6 (9%)
Low number of platelets in blood	2 (11%)	1 (5%)	2 (7%)	5 (7%)
Low blood pressure	0 (0%)	2 (11%)	3 (10%)	5 (7%)
High liver enzyme test that may indicate liver damage (aspartate aminotransferase)	2 (11%)	1 (5%)	2 (7%)	5 (7%)
Low count of white blood cells	1 (5%)	0 (0%)	3 (10%)	4 (6%)
Bloating	0 (0%)	1 (5%)	3 (10%)	4 (6%)
Nausea	0 (0%)	1 (5%)	3 (10%)	4 (6%)
Upper respiratory tract infection	1 (5%)	2 (11%)	1 (3%)	4 (6%)

Most Common Medical Problems (Reported in More than 5% of Children)				
Medical Problem	Group 1 (19 children)	Group 2 (19 children)	Group 3 (30 children)	Total (68 children)
Low calcium in blood	1 (5%)	1 (5%)	2 (7%)	4 (6%)
Low blood sugar	1 (5%)	2 (11%)	1 (3%)	4 (6%)
Low sodium in blood	0 (0%)	0 (0%)	4 (13%)	4 (6%)
Agitation	0 (0%)	3 (16%)	1 (3%)	4 (6%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

Out of 68 children in this study, 30 children (44%) had a serious medical problem. For 3 children, study doctors determined that 1 medical problem for each child (diarrhea, bleeding of the stomach/intestines, high liver enzyme tests that may indicate liver damage) may have been related to the study treatment. Eight (8) children (12%) passed away during the study. The study doctors determined that none of these deaths (0%) were related to the study treatment.

Overall, the medical problems reported in this study were similar to the medical problems reported in past studies with adults and are in line with medical problems expected in children with *Candida* infection. No new issues related to the safety of the study treatment 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 **NCT00761267**
www.clinicaltrialsregister.eu	Use the study identifier **2008-004150-32**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients. No additional studies with anidulafungin 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!