Summary of Results for Laypersons

Astellas is grateful to parents and children who took part in this clinical study. Thank you.

What was the Study Called?

A Multicenter, Double-Blind, Comparative, Randomized Study to Evaluate the Efficacy and Safety of Micafungin (FK463) versus Liposomal Amphotericin B (AmBisome®) in the Treatment of Invasive Candidiasis and Candidemia

Why was this Study Needed?

When children are in the hospital they are at risk for getting fungal infections. One reason for this risk is the use of antibiotics. Another is when doctors puncture, open or cut the skin for a procedure. There is also a risk of getting a fungal infection if the child's immune system is not working well. Fungal infections can be caused by yeast called *Candida*. If the infection with *Candida* has spread throughout the body it is called systemic candidiasis. When it is in the blood it is called candidemia. Children can become seriously ill with these infections. There are some medicines available for candidiasis and candidemia. However, these medicines do not work well in all children. Also, these medicines can cause unwanted side effects in some children. New medicines for candidiasis and candidemia were needed for use in children.

This study was conducted in patients with *Candida* infection that had spread throughout their body (candidiasis). Or it was in their blood (candidemia). The study included adults and children. This report is on the children who took part in the study.

The children in this study received micafungin or liposomal amphotericin B. Questions this study wanted to answer were how well did micafungin work against candidiasis and candidemia in children. And how much micafungin stayed in the blood of these children over time. This helped researchers work out the best dose and how often the study medicine should be given. This study also wanted to learn how safe micafungin is in children. It was important to find out what unwanted effects these children had from the study medicines.

The study started in January 2003 and ended in September 2006. The sponsor of this study (Astellas) reviewed all the study information and created a report of the results. This is a summary of the report on children.

What Kind of Study was this and Who Took Part in It?

This study included children from birth to 15 years of age. They had been diagnosed with candidemia or invasive candidiasis. And the infection was confirmed with blood tests. Some of these children may have had dangerously low levels of a type of white blood cell (called neutrophils).

This study had 2 parts: a "double-blinded" part, followed by an "open-label" part.

Double-blinded part: Double-blinded means that the parents of the children, the children and the study doctors did not know who received which of the 2 study medicines. This helps make study results fair and unbiased.

During the study, the study doctor did a check-up of the children at several study visits. At the first visit, children were checked to see if they could take part in the study. Children who could take part in the study received one of the 2 following study medicines by chance alone.

Both medicines were given slowly through a tube inserted into a vein. This is called an infusion.

- Children who weighed 40 kilogram (kg), approximately 88 pounds, or less were given 2.0 milligrams (mg) up to 4.0 mg of micafungin for every kg of body weight each day. This is called mg/kg. Children who weighed more than 40 kg were given 100 mg up to 200 mg of micafungin each day. The dose each day was slowly given over 1 hour.
- Children were given 3.0 mg (up to 5 mg) of liposomal amphotericin B for every kg of body weight each day. This is called mg/kg.

Children were treated for at least 14 days. And up to 8 weeks, if necessary.

After the double-blinded part of the study ended, additional children could enter the open-label part of the study.

Open-label part: Open-label means that the parents of each child and the study doctors knew that the child received micafungin.

Children in this part received micafungin at the same dose levels as children in part 1.

- Children who weighed 40 kg, approximately 88 pounds, or less were given 2.0 mg (up to 4.0 mg) of micafungin for every kg of body weight each day. Children who weighed more than 40 kg were given 100 mg up to 200 mg of micafungin each day. The dose each day was slowly given over 1 hour

This study took place at 27 clinics in 11 countries. 109 children were in the study. Out of these children, 106 children received at least 1 dose of a study medicine.

	Number of Children
Age Group	
0 up to 4 weeks	17
4 weeks up to 2 years	44
2 to 11 years	35
12 to 15 years	10

Sex	
Boys	65
Girls	41
Clinic Location	
European Union Countries (at the time of the study)	
Belgium	1
France	7
Poland	1
Portugal	1
Outside European Union	
Australia	2
Brazil	40
Croatia	6
India	12
South Africa	12
Thailand	12
United States	12

What Were the Study Results?

The questions this study helped answer were:

How well did micafungin work against candidiasis and candidemia in children?

This study showed that micafungin was similar to amphotericin B in successfully treating *Candida* infections in children. Success in treating *Candida* infections meant that the child's symptoms went away. And *Candida* was not found in the child anymore.

36 children (69.2%, or 36 out of 52 children) on micafungin were treated successfully.
40 children (74.1%, or 40 out of 54 children) on amphotericin B were treated successfully.

How much micafungin stayed in the blood of children over time?

The answer to this question helped researchers work out the best dose for children. And it helped them find out how often micafungin should be given. Researchers checked the blood samples taken from children after they were given micafungin.

12 children provided blood samples.

7 of the children were between 3 weeks and 4 years of age. 5 of the children were 11 years to 15 years of age.

The researchers discovered that the average time it takes for the micafungin blood level to decline by half was 10 – 20 hours. And this did not vary over the time of the study. This means the level of micafungin in the body did not build up over time.

They also discovered that the amount of micafungin that left the child's body did not vary over the time of the study.

These results were similar for children under 5 years of age and children over 5 years of age.

What Adverse Reactions did Patients Have?

A lot of research is needed to know whether a medicine causes a medical problem. So when new medicines are being studied researchers keep track of all medical problems that patients have while they are in the study. These medical problems are called "adverse events" and are recorded whether or not they might be caused by the treatment taken. An "adverse reaction" is any medical problem or "adverse event" that is judged by the study doctor to be possibly caused by a medicine or treatment used in the study.

19 children (36.5%, or 19 out of 52 children) treated with micafungin had adverse reactions in this study. 23 children (42.6%, or 23 out of 54 children) treated with amphotericin B had adverse reactions in this study.

The table below shows the most common adverse reactions experienced by children who took at least 1 dose of study medicine in this study.

Adverse Reaction	Micafungin (out of 52 children)	Amphotericin B (out of 54 children)
Fever	2 (3.8%)	6 (11.1%)
Decreased blood level of potassium	3 (5.8%)	6 (11.1%)
Vomiting	1 (1.9%)	4 (7.4%)
Increased blood levels of liver enzymes	1 (1.9%)	3 (5.6%)
Increased number of a type of blood cell that helps to clot blood (platelet)	0	3 (5.6%)
Chills	0	2 (3.7%)
Nausea or the urge to vomit	0	2 (3.7%)

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care.

2 children (3.8%, or 2 out of 52 children) treated with micafungin had serious adverse reactions in this study. 5 children (9.3%, or 5 out of 54 children) treated with amphotericin B had serious adverse reactions in this study.

13 children treated with micafungin died in this study. 13 children treated with amphotericin B also died in this study. None of the deaths were caused by the study medicines.

Where Can I Learn More About This Study?

This document is a short summary of the main results from children who participated in this study. You can find this summary and more information about this study online at http://www.astellasclinicalstudyresults.com.

Please remember that researchers look at the results of many studies to find out how well medicines work and which adverse reactions they might cause. This summary only shows the results of this 1 study. Your child's doctor may help you understand more about the results of this study.

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