Summary of Results for Laypersons

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

What was the Study Called?

A Phase 3, Multicenter, Investigator-blind, Randomized, Parallel Group Study to Investigate the Safety and Efficacy of Fidaxomicin Oral Suspension or Tablets Taken q12h, and Vancomycin Oral Liquid or Capsules Taken q6h, for 10 Days in Pediatric Subjects with *Clostridium difficile*-associated Diarrhea. This is also known as the SUNSHINE study.

Why was this Study Needed?

Clostridium difficile bacteria can overgrow in the colon or large bowel and cause an infection. Patients with *Clostridium difficile* infections can have watery diarrhea. This is called *Clostridium difficile*-associated diarrhea (or CDAD for short). Fidaxomicin and vancomycin are oral (taken by mouth) prescription medicines used to treat adults with CDAD. Vancomycin may not work well in all patients. Treatment with it may result in a type of bacteria that is resistant to medicine. Or it may result in the *Clostridium difficile*-associated diarrhea coming back after treatment stops. When a child develops this, the adult form of medicine such as a tablet or capsule may pose a problem. Tablets and capsules are difficult for young children to swallow. Therefore, there was a need to make a new fidaxomicin solution that was easier for young children to swallow. Vancomycin is available in a liquid form.

This study was conducted in children who were diagnosed with *Clostridium difficile*-associated diarrhea (CDAD). They took either fidaxomicin or vancomycin. Older children took their medicine as tablets or capsules. Younger children took their medicine as a solution or a liquid. This study looked at whether the children's diarrhea stopped after 10 days of treatment and did not return 2 days later. The study compared fidaxomicin and vancomycin in stopping diarrhea in all of the children. And the study looked at how the new fidaxomicin solution worked compared to the vancomycin liquid, in younger children. It was also important to find out what unwanted effects these children had from the study medicines.

The study started in January 2015 and ended in March 2018. When the study ended, the sponsor of this study (Astellas) reviewed all the study information and created a report of the results. This is a summary of that report.

What Kind of Study was This and Who Took Part in it?

This was an "investigator-blinded" study. That means that the study doctors did not know who took which of the study medicines (fidaxomicin or vancomycin). Each child and its parents knew which of the study medicines that child took.

The study included children from birth up to 18 years of age in Europe and Canada. And it included children from 6 months up to 18 years of age in the USA. The children had been diagnosed with *Clostridium difficile*-associated diarrhea (CDAD). Either *Clostridium difficile* or toxins from it were found in the child's stool. If the children were 2 years of age

or under, they had watery diarrhea. And if they were over 2 years of age, they had 3 loose (unformed) stools. They either had no treatment or not more than 24 hours of treatment for their diarrhea before joining the study.

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 be in the study. Children who could be in the study were picked for treatment (fidaxomicin or vancomycin) by chance alone (randomization). Children took their assigned medicine for 10 days. If an older child was unable to swallow the tablet or capsule they were assigned to, they took the solution or liquid forms of that medicine. After the children stopped taking study medicine, the study doctor followed up with them for 30 days.

Age of Child	**Fidaxomicin (solution or tablets)**	**Vancomycin (liquid or capsules)**
Birth up to 6 years	32 mg of fidaxomicin solution for every square meter of body surface, divided in 2 doses per day	40 mg of liquid vancomycin for every square meter of body surface, divided in 4 doses per day
6 years up to 18 years	200 mg fidaxomicin tablets 2 times a day	125 mg vancomycin capsules 4 times a day

This study took place at 74 clinics in several countries. 148 children were in the study. Out of these children, 142 children took at least 1 dose of study medicine.

	Number of Children (out of 142)
Age Group	
Birth to less than 2 years	30
Aged 2 years to less than 6 years	48
Aged 6 years to less than 12 years	36
Aged 12 years to less than 18 years	28
Sex	
Boys	82
Girls	60
Clinic Location	
European Union Countries (*at the time of the study*)	86
Belgium	6
France	11
Germany	5
Hungary	17
Italy	7
Poland	14
Romania	9
Spain	17
Outside European Union	56
Canada	1
The US	55

What Were the Study Results?

This study was in children diagnosed with CDAD. It looked to see if a child's diarrhea stopped after 10 days of treatment with fidaxomicin or vancomycin and did not return 2 days later. Adult forms of the 2 medicines (tablets or capsules) were taken by children 6 years and older. Child forms (solution or liquid) were taken by children under 6 years.

The proportions of children whose diarrhea stopped after treatment without returning later are in the table below. That is the number of children whose diarrhea stopped compared to the total number of treated children.

	Children Whose Diarrhea Stopped After Treatment	
Age Groups	**Fidaxomicin**	**Vancomycin**
(Birth to less than 18 years)	77.6% (76 out of 98 children)	70.5% (31 out of 44 children)
Birth to less than 2 years	65.0% (13 out of 20 children)	90.0% (9 out of 10 children)
2 years to less than 6 years	78.1% (25 out of 32 children)	75% (12 out of 16 children)
6 years to less than 12 years	88.5% (23 out of 26 children)	50.0% (5 out of 10 children)
12 years to less than 18 years	75.0% (15 out of 20 children)	62.5% (5 out of 8 children)

In children 6 years to less than 12 years, statistical testing showed that the difference between fidaxomicin (88.5%) and vancomycin (50.0%) was not likely to be due to chance. It is considered to be an effect of the study medicine, fidaxomicin. Statistical testing in the other age groups showed that the difference between the 2 medicines was likely to be due to chance.

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.

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	Fidaxomicin (out of 98 children)	Vancomycin (out of 44 children)
Any adverse reaction	7 (7.1%)	5 (11.4%)
Belly pain	0	1 (2.3%)
Constipation	2 (2.0%)	0
Infection caused by an overgrowth of *Candida* yeast in the mouth or throat	1 (1.0%)	1 (2.3%)
Low blood pressure	0	1 (2.3%)
Vomiting	0	1 (2.3%)
Fungal infection of the vulva (external female genitalia) and vagina	0	1 (2.3%)

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

None of the children experienced a serious adverse reaction in this study.

Three of the children died during the study (between day 1 and day 40). None died because of the study medicine. After the study ended, the deaths of 2 additional children were reported. Neither child died because of the study medicine.

Where Can I Learn More About This Study?

This document is a short summary of the main results from this study and reflects the information available as of August 2018. 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 doctor may help you understand more about the results of this study.

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