Summary of Results for Laypersons

What was the Study Called?

A Phase 2 Dose-Finding Study with ASP2151 in Subjects with Recurrent Episodes of Genital Herpes

Why was this Study Needed?

Genital herpes is a common sexually transmitted infection caused by the herpes simplex virus (HSV). Sexual contact is the primary way that the virus spreads. After the initial infection, the virus can be in the body, but not be active. However, it can also awaken and become active several times a year. Genital herpes can cause pain, itching and sores in the genital area. A person may have no symptoms of genital herpes. However, if infected, a person can still spread the infection even if that person has no visible sores.

There is no cure for genital herpes, but medicines can ease symptoms and reduce the risk of spreading the infection to others. There are several medicines used to treat genital herpes include acyclovir (also known as Zovirax®), famciclovir (also known as Famvir®) and valacyclovir (also known as Valtrex®). However, these drugs are not very strong; they start working slowly and can possibly produce additional adverse effects when taken with other medicines. It was important to find a treatment for genital herpes that could decrease the risk of spreading the disease, quickly heal lesions (sores) and decrease the number of recurrences in patients. ASP2151 (also known as amenamevir and Amenalief®) is an experimental medicine that was being looked at as a possible treatment for genital herpes. Preclinical data showed that ASP2151 may be more beneficial to patients than the medicines that are currently used to treat genital herpes.

This was the first study to test ASP2151 in patients with genital herpes. The main question this study helped answer was if ASP2151 was better at healing the lesions (sores) in patients with genital herpes than valacyclovir or a placebo. A placebo tablet does not have medicine in it. It was also important to find out what unwanted effects these patients had from the study medicines.

This study took place at 26 clinics in the United States. The study started in June 2007 and ended in August 2008. When the study ended, the sponsor (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 also a “blinded” study. In this study, the patients and the researchers did not know who took which of the study medicines (ASP2151, valacyclovir or placebo). A “placebo” is a dummy treatment such as a tablet or capsule that looks like a medicine, but does not have any medicine in it. Using a placebo helps make study results fair and unbiased, because researchers and patients cannot tell who is taking a placebo, and who is taking the test medicine.

Both men and women aged 18 years or older could take part in the study if:

- They had a history of genital HSV documented by laboratory testing.
- They experienced 4 or more events of genital herpes during the past 12 months.
- Patients who were having sex used reliable birth control methods.

Patients could not take part in this study if:

- They had human immunodeficiency virus (HIV) or had a weak immune system.
- They were taking corticosteroids by mouth within 7 days prior to entering the study.
- They had received HSV treatment or any antiviral therapy within 7 days prior to entering the study.

During the study, the study doctor did a check-up of the patients at several study visits. At visit 1, patients were checked to see if they could be in the study. Blood samples were also collected during this visit.

Patients who could be in the study were assigned to one of 6 treatment groups by chance:

- 100 mg of ASP2151 once a day for 3 days
- 200 mg of ASP2151 once a day for 3 days
- 400 mg of ASP2151 once a day for 3 days
- 1200 mg of ASP2151 once a day for 1 day
- 500 mg of a different medicine called valacyclovir twice a day for 3 days
- Placebo once a day for 3 days

When a patient noticed the first sign or symptom of genital herpes reappearance, the patient was instructed to swab the affected genital area and to take the first dose of study medicine within 6 hours.

Patients went to the clinic daily for a genital exam from day 1 (which was within 24 hours after the patient's first dose of study medicine) through day 6.

After day 1, patients obtained swabs of their affected genital area twice a day (1 self-swab and 1 clinic swab) for each of the 6 days. If their genital herpes sores did not go away by day 6, then they were seen at the clinic on days 8 and 10.

Blood samples were collected on day 1 through day 4 to measure the amount of study medicines absorbed into the body and how long it stayed in the body. Patients completed worksheets throughout their treatment period. The patients recorded the dates and times that they checked their symptoms, took their medicine, ate food and collected their swabs.

A total of 437 patients were in the study and took at least 1 dose of ASP2151, valacyclovir or placebo:

- 84 patients took 100 mg of ASP2151
- 75 patients took 200 mg of ASP2151
- 76 patients took 400 mg of ASP2151
- 64 patients took 1200 mg of ASP2151
- 67 patients took 500 mg of valacyclovir
- 71 patients took placebo

	Number of Patients
Age Group	
Aged between 18 and 44 years	280
Aged between 45 and 64 years	146
Aged 65 years or older	11
Sex	
Men	129
Women	308
Clinic Location	
United States	437

What Were the Study Results?

This study was conducted in patients with genital herpes. The main question this study helped answer was if ASP2151 was better at healing the genital herpes lesions (sores) in patients with genital herpes than valacyclovir or a placebo. As shown in the table below, the time it took the lesions (sores) to heal was shorter in patients taking ASP2151 and valacyclovir than it was in patients taking the placebo. The median time it took the genital herpes lesion to heal in the patients taking ASP2151 and valacyclovir was at least 20 hours shorter than the healing time for patients taking the placebo.

Treatment Group	Number of Patients With Healed Lesions (Sores)	Median Time to Healing (hours)
Placebo	61	139.8
100 mg ASP2151	66	119.6
200 mg ASP2151	54	106.2
400 mg ASP2151	50	115.9
1200 mg ASP2151	47	102.1
500 mg valacyclovir	50	113.9

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.

A total of 70 patients who took at least 1 dose of ASP2151, valacyclovir or placebo each had 1 or more adverse reactions. The most common adverse reactions were nausea or urge to vomit, headache or head pain and diarrhea.

The table below shows the most common adverse reactions experienced by patients who took at least 1 dose of ASP2151, valacyclovir or placebo.

Adverse Reaction	Placebo (out of 71 patients)	ASP2151 100 mg (out of 84 patients)	ASP2151 200 mg (out of 75 patients)	ASP2151 400 mg (out of 76 patients)	ASP2151 1200 mg (out of 64 patients)	Valacyclovir 500 mg (out of 67 patients)
Any adverse reaction	12 (16.9%)	17 (20.2%)	6 (8.0%)	15 (19.7%)	10 (15.6%)	10 (14.9%)
Nausea or urge to vomit	5 (7.0%)	4 (4.8%)	2 (2.7%)	0	1 (1.6%)	2 (3.0%)
Diarrhea	0	5 (6.0%)	1 (1.3%)	3 (3.9%)	0	2 (3.0%)
Dry mouth	0	1 (1.2%)	0	2 (2.6%)	0	0
Vomiting	0	2 (2.4%)	0	1 (1.3%)	0	0
Headache or head pain	3 (4.2%)	4 (4.8%)	1 (1.3%)	1 (1.3%)	1 (1.6%)	3 (4.5%)
Dizziness (or sensation of lightheadedness, unsteadiness, or giddiness)	0	1 (1.2%)	0	0	2 (3.1%)	1 (1.5%)

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care and is judged by the study doctor to be possibly caused by a medicine or treatment used in the study.

One patient experienced serious adverse reactions. The patient experienced rapid heart rate, uncontrolled trembling or shaking movements in one or more parts of the body and fever on day 1 of treatment with 400 mg ASP2151.

One patient died before taking the assigned study medication. This death was not related to the study medicine.

Where Can I Learn More About This Study?

This summary of the clinical study results is available online at http://www.astellasclinicalstudyresults.com.

The information in this document reflects the information available as of November 2017.

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. If you have questions about ASP2151, please discuss these with your doctor.

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