Summary of Results for Laypersons

What was the Study Called?

A Randomized, Double-blind, Placebo-controlled, Phase 2 Study to Assess the Efficacy, Safety, and Dose-Response Relationship of ASP1707 in Subjects with Endometriosis Associated Pelvic Pain for 12 Weeks, Followed by a 12-Week Double-blind Extension without Placebo Control, Including a 24-Week Open-label Leuprorelin Acetate Treatment Group for Bone Mineral Density Assessment. This is also known as the TERRA study.

Why was this Study Needed?

The "endometrium" is tissue on the inside of the "uterus" (womb). Growth of tissue similar to the endometrium outside the uterus is called "endometriosis". Endometrial growths outside the uterus cause pain when they shed blood and tissue.

Medicine for endometriosis is already available but the medicine may cause bones to lose calcium and other minerals. Bones then become less solid and weaker: the "bone density" decreases. Less bone density makes the bones easier to break. Endometriosis medicine may also cause symptoms of menopause, for example hot flashes. "Leuprorelin" is a medicine for endometriosis that makes bones weaker and causes hot flashes.

ASP1707 is a medicine that affects the levels of sex hormones in the body. The effect of ASP1707 could be to keep the level of sex hormones low. This could make the endometriosis pain less strong.

This study helped answer how well ASP1707 treats endometriosis pain and which dose of ASP1707 works best. It was also important to find out what unwanted effects patients had from ASP1707. And the study compared the effects of ASP1707 and leuprorelin on bone density.

Patients in this study had 3 kinds of endometriosis pain:

1. "Overall pelvic pain" was the average pain over the whole menstrual cycle (days with and without a period).
2. "Dysmenorrhea" was the average pain over the days with a period.
3. "Nonmenstrual pelvic pain" was the average pain over the days without a period.

This study for ASP1707 took place at 97 clinics. Of the 97 clinics, 86 clinics in Belgium, Bulgaria, Germany, Hungary, Poland, Romania, Ukraine, the UK and Japan enrolled patients in the study. The study took place from December 2012 to July 2015. 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 a "blinded" study. The patients and the researchers did not know who took ASP1707 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.

Some patients in the study took "open-label" leuprorelin. Open-label means that these patients knew that they took leuprorelin.

Part 1 of the study was 12 weeks long. The study patients were picked for 1 of the following treatments by chance alone:

- 3 mg of ASP1707
- 5 mg of ASP1707
- 10 mg of ASP1707
- 15 mg of ASP1707
- Placebo
- Leuprorelin

Part 2 of the study was also 12 weeks long. Patients who took ASP1707 in part 1 took the same medicine in part 2. Patients who took leuprorelin in part 1 took the same medicine in part 2. Patients who took placebo in part 1 were switched to 1 of the 4 ASP1707 treatments.

At visit 1 patients were checked to see if they could be in the study. The patients then started an "observation phase". The observation phase lasted for at least 1 complete menstrual cycle. Patients did not take any study medicine during this time. Patients recorded their level of endometriosis pain every day. A scale to measure pain called the "NRS" was used. The scale goes from 0 ("no pain") to 10 ("worst pain imaginable"). The patients entered the pain scores in an electronic diary.

Visit 2 was after the observation phase on days 1 to 4 of the menstrual cycle. Day 1 was the first day of having a period. Day 4 was the fourth day of having a period. The pain scores in the diary were checked to see if patients could be in the study. The study doctor also checked how long the menstrual cycle lasted. Patients who could be in the study were picked for 1 of the study treatments by chance alone. These treatments were ASP1707, placebo or leuprorelin. Each day during the study patients entered a score for endometriosis pain in the diary.

Only women took part in the study. They were all aged from 18 (20 in Japan) to 45 years old. Their endometriosis was diagnosed during surgery in the last 5 years. They all had a menstrual cycle that lasted between 24 and 35 days. Their pain scores before visit 2 showed that they had at least 1 of the following:

- Moderate to severe dysmenorrhea (average pain score over all the days with a period was at least 4 points on the pain scale),
- Moderate nonmenstrual pelvic pain (average pain score on at least 7 days without a period was at least 4 points on the pain scale) and/or
- Severe nonmenstrual pelvic pain (average pain score on at least 3 days without a period was at least 7 points on the pain scale).

The days without a period did not need to be back to back.

A patient was not in the study if she:

- Was breastfeeding, was pregnant within 24 weeks before starting the study or wanted to become pregnant during the study,
- Had surgery for endometriosis within 4 weeks before starting the study,
- Had a tumor in the uterus that was larger than 3 cm,
- Had abnormal bleeding from the vagina or
- Had surgery to remove the uterus or had a surgery to remove both ovaries.

A total of 540 patients were in this study. Eight patients did not take study medicine. A total of 532 patients took at least 1 dose of study medicine.

	Number of Patients (out of 532 patients)
Age Group	
Aged between 18 and 45 years	532
Clinic Location	
EU Countries	301
Belgium	7
Bulgaria	15
Germany	3
Hungary	28
Poland	134
Romania	111
The UK	3
Outside EU	231

What Were the Study Results?

The study showed that patients who took ASP1707 to treat endometriosis pain did not have a lot of unwanted effects.

Statistical testing showed that:

- Higher doses of ASP1707 worked better for overall pelvic pain, for dysmenorrhea and for nonmenstrual pelvic pain.
- 10 mg of ASP1707 gave more relief of overall pelvic pain than did placebo.
- Any dose of ASP1707 gave more relief of dysmenorrhea than did placebo.
- ASP1707 caused less decrease in bone density compared to leuprorelin.

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 number of patients who had headache was similar for the placebo and ASP1707 groups. More patients in the ASP1707 groups than in the placebo group had hot flashes ("feeling hot for a brief time"). The table below shows the most common adverse reactions experienced by patients who took at least 1 dose of study medicine during part 1 of the study.

Adverse Reaction	Placebo (out of 88 patients)	Number of ASP1707 Patients					Leuprorelin (out of 89 patients)
		3 mg (out of 86 patients)	5 mg (out of 91 patients)	10 mg (out of 90 patients)	15 mg (out of 88 patients)	Total (out of 355 patients)	
Headache or head pain	10 (11.4%)	9 (10.5%)	5 (5.5%)	10 (11.1%)	11 (12.5%)	35 (9.9%)	13 (14.6%)
Feeling hot for a brief time	4 (4.5%)	4 (4.7%)	12 (13.2%)	9 (10.0%)	17 (19.3%)	42 (11.8%)	25 (28.1%)

The table below shows the most common adverse reactions experienced by patients who took the same dose of ASP1707 or leuprorelin during parts 1 and 2 of the study.

Adverse Reaction	Number of ASP1707 Patients					Leuprorelin (out of 89 patients)
	3 mg (out of 86 patients)	5 mg (out of 91 patients)	10 mg (out of 90 patients)	15 mg (out of 88 patients)	Total (out of 355 patients)	
Headache or head pain	10 (11.6%)	8 (8.8%)	11 (12.2%)	14 (15.9%)	43 (12.1%)	16 (18.0%)
Feeling hot for a brief time	6 (7.0%)	15 (16.5%)	10 (11.1%)	17 (19.3%)	48 (13.5%)	25 (28.1%)

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care. Two patients experienced a serious adverse reaction. One of the 2 patients had taken 3 mg ASP1707. The second patient had taken 5 mg ASP1707.

None of the patients died during the study.

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 March 2016. 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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