Summary of Results for Laypersons

What was the Study Called?

A Randomized, Double-blind, Placebo-controlled, Phase 3 Study of OSI-906 in Patients with Locally Advanced or Metastatic Adrenocortical Carcinoma (OSI-906-301)

Why was this Study Needed?

The adrenal glands are located on top of the kidneys. They produce hormones that give instructions to almost every organ and tissue in our body. Adrenocortical carcinoma (or ACC for short) is a cancer of the adrenal glands. Mitotane is a prescription medicine for the treatment of ACC. But ACC in some patients may not respond to treatment with mitotane. Therefore, there was a need to study new treatments for ACC.

Linsitinib (also known as OSI-906 and ASP7487) is an experimental medicine taken by mouth. It works by blocking 2 proteins (called IGF-1R and IR) that can be active in ACC. When these proteins are blocked, they can no longer help cancer cells grow or survive.

This study was conducted in patients who had ACC. Patients took linsitinib or placebo. (The section below describes what placebo is.) The main question this study helped answer was which study medicine (linsitinib or placebo) was better at improving overall survival. That is the length of time from the start of study medicine up until the time half of the patients in each treatment group were still alive. It was also important to find out what unwanted effects these patients had from the study medicines.

The study started in December 2009. The sponsor of this study (Astellas) did a review of the study results in November 2011. The review showed that overall survival was not better with linsitinib. Astellas then informed patients which medicine they were taking. Patients who took linsitinib and were in this study on 19 March 2012 could continue taking linsitinib. Some of these patients continued treatment in Study OSI-906-209. Patients who were taking placebo could not stay in the study. The study ended in October 2012. When the study ended, 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. That means that the patients and the researchers did not know who took which of the study medicines (linsitinib 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.

Clinical studies have a list of requirements for patients who can be in a study (“inclusion” criteria) and patients who cannot take part in a study (“exclusion” criteria). The requirements for this study are listed below.

Women and men aged 18 years or older could be in the study if:

- Their doctor had confirmed that they had ACC that was in an advanced stage or that had spread from the adrenal glands to other places in the body. And their ACC could not be removed via surgery.
- The size of their tumor could be accurately measured.
- Within 6 months before their first dose of study medicine, X-rays showed that their ACC was getting worse.
- They were active or they could perform light daily activities. Or they were ambulatory and capable of all self-care, but unable to carry out any work activities. And they were up and about more than 50% of waking hours. They were expected to live for at least 3 months.
- They had taken 1 or 2 drug treatments for ACC in the past. They had taken mitotane as a treatment for ACC. There were at least 3 weeks between the last day of their earlier ACC treatment and their first dose of study medicine in this study.

Patients could not take part in this study if:

- Within the past 3 years, they had another cancer besides ACC. It was acceptable if they were cured of a cancer that had stayed on the surface (skin). It was also acceptable if they were cured of a cancer that had not spread outside the organ where it started (breast, cervix and bladder). (The cervix is the lower end of the uterus [womb].)
- They had diabetes and were taking insulin. Or they were taking a medication that enhanced the production of insulin.
- In the past, they had serious heart disease that was poorly controlled.

During the study, the study doctor did a check-up of the patients at several study visits. At the first visit, patients were checked to see if they could be in the study. Patients who could be in the study were picked for 1 of 2 treatments (linsitinib or placebo) by chance alone. Twice as many patients were picked for linsitinib than for placebo.

- Linsitinib: Patients took linsitinib tablets (150 mg) twice a day.
- Placebo: Patients took placebo tablets twice a day.

The patients could take study medicine until their cancer got worse, they had unwanted effects they could not tolerate, they asked to stop treatment or they died.

This study took place at 35 clinics in several countries. 139 patients were in the study. Out of these patients, 138 patients took at least 1 dose of study medicine.

	Number of Patients
Age Group	
Aged less than 60 years	104
Aged 60 years or older	34
Sex	
Men	48
Women	90
Clinic Location	
European Union Countries (*at the time of the study*)	70
France	19
Germany	22
Italy	15
The Netherlands	8
Poland	1
The UK	5
Outside European Union	68
Australia	2
Canada	6
The US	60

What Were the Study Results?

This study in patients with ACC looked at the length of time from the start of study medicine up until the time half of the patients in each treatment group were still alive (overall survival). The results showed that from the start of study medicine, half of the patients were still alive:

- After 323 days in the linsitinib group.
- After 356 days in the placebo group.

The difference was due to chance. Compared to placebo, linsitinib did not improve the overall survival.

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 adverse reactions experienced by approximately 10% or more of patients who took at least 1 dose of study medicine in this study. This means that those adverse reactions were experienced by at least 9 out of 90 patients in the linsitinib group and/or at least 5 out of 48 patients in the placebo group.

Adverse Reaction	Linsitinib (out of 90 patients)	Placebo (out of 48 patients)
Any adverse reaction	50 (55.6%)	21 (43.8%)
Fatigue or tiredness	30 (33.3%)	11 (22.9%)
Nausea or the urge to vomit	24 (26.7%)	15 (31.3%)
Vomiting	19 (21.1%)	10 (20.8%)
Abnormal electrical conduction within the heart	18 (20.0%)	3 (6.3%)
Belly pain	18 (20.0%)	10 (20.8%)
Back pain	17 (18.9%)	6 (12.5%)
Constipation	13 (14.4%)	9 (18.8%)
Diarrhea	13 (14.4%)	4 (8.3%)
Fever	12 (13.3%)	5 (10.4%)
Shortness of breath	12 (13.3%)	6 (12.5%)
Swelling of the arms and/or legs	11 (12.2%)	5 (10.4%)
Decreased blood level of potassium	10 (11.1%)	3 (6.3%)
Increased blood sugar level	10 (11.1%)	5 (10.4%)
Cough	9 (10.0%)	5 (10.4%)
Headache or head pain	9 (10.0%)	9 (18.8%)
High blood pressure	7 (7.8%)	5 (10.4%)

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

Seven patients experienced serious adverse reactions. The table below shows these serious adverse reactions.

Serious Adverse Reaction	Linsitinib (out of 90 patients)	Placebo (out of 48 patients)
Any serious adverse reaction	6 (6.7%)	1 (2.1%)
Abnormal drowsiness or sluggishness, an unusual lack of energy	1 (1.1%)	0
Abnormally fast irregular heartbeat involving the upper chambers of the heart (atria)	1 (1.1%)	0
Agitation or restlessness	1 (1.1%)	0
Confusion	1 (1.1%)	0
Feeling of spinning or whirling	1 (1.1%)	0
Fever	1 (1.1%)	0
Increased blood sugar level	1 (1.1%)	0
Loss of appetite	1 (1.1%)	0
Nausea or the urge to vomit	1 (1.1%)	0
Vomiting	1 (1.1%)	0
Abnormal dilation of the colon	0	1 (2.1%)
Belly pain	0	1 (2.1%)
Severe illness in which the bloodstream is overwhelmed by bacteria	0	1 (2.1%)

Ten patients died during the study: 5 patients who took linsitinib and 5 patients who took placebo. None of the patients who took linsitinib died because of the study medicine. The

death of 1 of the patients who took placebo could have been related to this patient's study medicine. This patient experienced serious adverse reactions of abnormal dilation of the colon and severe illness in which the bloodstream is overwhelmed by bacteria.

Between July 2012 and October 2012, 4 patients remained in the study and took linsitinib. During this period, 1 patient experienced a serious adverse reaction (inflammation [swelling and pain] of the pancreas).

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 October 2014. 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.

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