Summary of Results for Laypersons

What was the Study Called?

A Randomized, Placebo-controlled, Double-blind Phase 2 Study of Second-line Treatment with OSI-906 in Patients with Advanced Hepatocellular Carcinoma (HCC) after Failure of First-line Treatment with Sorafenib

Why was this Study Needed?

Hepatocellular carcinoma (or HCC for short) is the most common type of liver cancer. If it cannot be removed by surgery, it can be treated with the prescription medicine sorafenib. But HCC in advanced stage may become resistant to sorafenib, which means that sorafenib can no longer stop its growth or keep the cancer stable. Therefore, there was a need to study a new treatment for advanced HCC.

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 are often found at high levels in HCC. When these proteins are blocked, they can no longer help cancer cells grow or survive.

This study was conducted in patients with advanced HCC. Their cancer was resistant to sorafenib. Or the patients could not tolerate the unwanted effects sorafenib caused. The patients took linsitinib or placebo in this study. (The section below describes what placebo is.) The main question this study was meant to answer was which study medicines (linsitinib or placebo) were better at improving time to progression. That is the length of time from the start of study medicine until the cancer got worse. It was also important to find out what unwanted effects these patients had from the study medicines.

The study started in January 2011. The sponsor (Astellas) stopped the study in November 2011. When the study was stopped, 22 patients had taken study medicine. 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. This 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 take part in the study if:

- Their doctor had confirmed that they had advanced HCC.
- They took their last dose of sorafenib at least 14 days before they were to receive their first dose of study medicine in this study.
- Their cancer had gotten worse while taking sorafenib. Or they had to stop taking sorafenib because they could not tolerate its unwanted effects.
- The size of their tumor could be accurately measured.
- They were active or they could perform light daily activities.

Patients could not take part in this study if:

- Their liver worked poorly.
- Their cancer could potentially be cured by removing it by surgery. Or they were candidates for liver transplantation.
- They had diabetes and were taking insulin. Or they were taking a medication that enhanced the production of insulin.
- They needed treatment with interferon. Interferon is a substance that can improve the body's natural response to infections and other diseases.
- They had abnormal buildup of fluid in the abdomen that was not 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. In July 2011, the sponsor (Astellas) briefly stopped the study after the death of 2 patients. A group of independent safety experts reviewed the information about all of the patients who were in the study at that time. The group recommended continuing the study, with some changes to who could take part in the study. But Astellas decided to stop the study. The last patient stopped taking study medicine in November 2011.

This study took place at 15 clinics in several countries. When this study was stopped, 23 patients were in the study. Out of these patients, 22 patients took at least 1 dose of study medicine.

	Number of Patients
Age Group	
Aged younger than 60 years	7
Aged 60 years or older	15
Sex	
Men	17
Women	5
Clinic Location	
European Union Countries (*at the time of the study*)	13
Belgium	1
France	6
Germany	1
Italy	1
Spain	4
Outside European Union	9
South Korea	6
The US	3

What Were the Study Results?

The main question this study in patients with advanced HCC was meant to answer was which study medicine (linsitinib or placebo) was better at increasing the length of time from the start of study medicine until the cancer got worse. Because the study was stopped, the study's main question could not be answered.

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 adverse reactions experienced by 3 or more patients who took at least 1 dose of study medicine in this study.

Adverse Reaction	**Linsitinib (out of 14 patients)**	**Placebo (out of 8 patients)**
Any adverse reaction	10 (71%)	4 (50%)
Increased blood sugar level	3 (21%)	0
Kidney failure	3 (21%)	1 (12%)
Decreased appetite	3 (21%)	2 (25%)
Weakness; lack of energy and strength	3 (21%)	0

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

7 patients experienced serious adverse reactions. The table below shows the serious adverse reaction experienced by more than 1 patient.

Serious Adverse Reaction	Linsitinib (out of 14 patients)	Placebo (out of 8 patients)
Any serious adverse reaction	6 (43%)	1 (12%)
Kidney failure	3 (21%)	1 (12%)

Six patients died during the study: 4 patients who took linsitinib and 2 patients who took placebo. The deaths of 3 of the 6 patients could have been related to their study medicine. The table below shows the serious adverse reactions experienced by those 3 patients.

Serious Adverse Reaction That Led to Death	Linsitinib (out of 14 patients)	Placebo (out of 8 patients)
Any serious adverse reaction that led to death	2 (14%)	1 (12%)
Kidney failure	1 (7%)	1 (12%)
Late stage scarring (fibrosis) of the liver caused by long-term alcohol abuse	1 (7%)	0
Liver failure	1 (7%)	0

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 January 2013. 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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