Summary of Results for Laypersons

What was the Study Called?

A Phase 1, Open-label Study to Investigate the Absorption, Metabolism, and Excretion of ^{14}C-OSI-906 in Subjects with Advanced Solid Tumors with an Optional Treatment Phase

Why was this Study Needed?

A solid tumor is an abnormal mass of tissue that usually does not contain cysts or liquid areas. Solid tumors may be benign (not cancer), or malignant (cancer). Different types of solid tumors are named for the type of cells that form them. Examples of solid tumors are sarcomas (cancers of the connective or supporting tissues, such as bone or muscle), carcinomas (cancers of the cells in the skin or in the tissues that line or cover organs in the body), and lymphomas (cancers of the organs that make and store cells that fight infection). The most commonly used treatments for solid tumors include some combination of surgery, radiation therapy and chemotherapy. However, some advanced solid tumors cannot be cured or controlled with these treatments. Therefore, there was a need to study new treatments for advanced solid tumors.

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 solid tumors. When these proteins are blocked, they can no longer help cancer cells grow or survive.

This study was conducted in patients with any type of advanced cancer that forms solid tumors. During part A of the study, patients took linsitinib that was radiolabeled (a technique used to track the reaction or pathway of a substance) and unlabeled once a day. During part B of the study, patients took linsitinib twice a day. The main question part A helped answer was how linsitinib was taken up, broken down, distributed through the body and removed from the body. During both parts of the study, it was also important to find out what unwanted effects the patients had from linsitinib.

The study started in October 2011. Part A of the study ended in December 2012 and part B of the study ended in February 2013. When this 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 an "open-label" study. This means that all patients knew that they took linsitinib once or twice a day.

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.

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

- They had solid tumors that were in an advanced stage and not cured by established therapies.
- 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.
- Their fasting glucose (or sugar) level was ≤ 125 mg/dL at the start of the study.
- Their liver and kidney worked sufficiently and their production of blood cells was sufficient.

Patients could not take part in this study if:

- They had diabetes (a disease in which the blood sugar level is too high) and were taking insulin or they were taking a medication that enhanced the production of insulin.
- They had surgery, radiation or chemotherapy within 3 weeks before starting the study medicine.
- They had a history of a poorly controlled gastrointestinal disorder (such as diarrhea or Crohn's disease), hepatocellular carcinoma (a type of liver cancer), stroke (stoppage of blood flow to the brain), or convulsions or seizures.
- They had a history of prior insulin-like growth receptor (IGFR) inhibitor therapy within the last 6 months.
- In the past, they had serious heart disease that was poorly controlled.
- They participated in a radiolabeled study within the last 12 months.

During the study, the study doctor did a check-up of the patients at all study visits.

Part A

At the first visit, patients were checked to see if they could be in part A of the study. Patients who could be in the study received a single dose of an oral solution containing radiolabeled and unlabeled linsitinib (150 mg). After 30 days, the patients returned to the clinic for a check-up. Patients were allowed to continue to part B of the study within 10 days of completing part A.

Part B

At the first visit, patients were checked to see if they could be in part B of the study. Patients who could be in the study were assigned to receive linsitinib (150 mg) tablets twice a day. After 21 days, the patients returned to the clinic for a check-up.

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 1 clinic in the United States. 5 patients took at least 1 dose of study medicine.

	Number of Patients	
	Part A (out of 5 Patients)	**Part B (out of 5 Patients)**
Age Group		
Aged 65 years or younger	2	2
Aged older than 65 years	3	3
Sex		
Men	3	3
Women	2	2
Clinic Location		
US	5	5

What Were the Study Results?

The main question part A helped answer was how linsitinib was taken up, broken down, distributed through the body and removed from the body. Blood is the main bodily fluid that is responsible for moving nutrients and oxygen to the organs and tissues. Blood is made of plasma, red blood cells, white blood cells and platelets. The greatest amount of radiolabeled linsitinib in the blood was seen 3 hours after the last dose and was between 821 to 2680 nanograms (ng). A nanogram (ng) is a unit that is used to measure the amount of drug. Plasma is the liquid part of blood. It is made of water, sugar, fat, protein and salts. The greatest amount of radiolabeled linsitinib in the plasma was seen 1 to 4 hours after the last dose and was between 959 to 3640 ng.

During both parts of the study, it was also important to find out what unwanted effects the patients had from linsitinib. The unwanted effects that happened in this study that the study doctor judged as being related to linsitinib are presented below.

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 the patients who took at least 1 dose of study medicine in the study.

Adverse Reaction	Part A (out of 5 Patients)	Part B (out of 5 Patients)
Any adverse reaction	0	4 (80%)
Fatigue or tiredness	0	3 (60%)
Lack of enough red blood cells (anemia)	0	1 (20%)
Decreased number of lymphocytes, a type of white blood cell, in the peripheral blood	0	1 (20%)
Clogged ears	0	1 (20%)
Diarrhea	0	1 (20%)
Nausea or the urge to vomit	0	2 (40%)
Abnormal blood level of a liver enzyme	0	1 (20%)
Decreased weight	0	1 (20%)
Loss of appetite	0	2 (40%)
Dehydration (when your body does not have as much water and fluid as it should)	0	1 (20%)
A decline in general condition including weight loss, decreased appetite and lack of activity	0	1 (20%)
Dizziness (or sensation of lightheadedness, unsteadiness or giddiness)	0	1 (20%)
Taste changes	0	1 (20%)
Headache or head pain	0	1 (20%)
Abnormal drowsiness or sluggishness, an unusual lack of energy	0	1 (20%)
Shortness of breath on exertion	0	1 (20%)
Itchy skin	0	1 (20%)

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

1 patient in part B experienced serious adverse reactions of fatigue or tiredness, dehydration (when your body does not have as much water and fluid as it should) and a decline in general condition including weight loss, decreased appetite and lack of activity.

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 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.

Sponsor contact details:

Astellas Pharma Global Development, Inc.
1 Astellas Way
Northbrook, IL 60062
USA