# Summary of Results for Laypersons

## What was the Study Called?

A Phase 1 Dose Escalation Study of Continuous Oral OSI-906 Dosing in Patients With Advanced Solid Tumors

## 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. Patients took linsitinib once or twice a day. The main question the study helped answer was what the highest dose of linsitinib was that patients could tolerate. The study also looked at finding the recommended dose for once a day linsitinib and twice a day linsitinib. It was also important to find out what unwanted effects the patients had from linsitinib.

The study started in June 2007 and ended in July 2011. 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/or had spread to other places in the body. And were not controlled 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.
- They had recovered from any previous therapies or surgery before the study started. Patients with prostate cancer that had gotten worse and had started hormone therapy that suppresses the function of the testicles, 3 months earlier, were allowed to continue to take it.
- 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.
- In the past, they had serious heart disease that was poorly controlled.
- They were currently taking other cancer treatments (other than hormone therapy).
- They had a history of stroke (stoppage of blood flow to the brain), convulsions or seizures.
- Their cancer had spread to the brain.

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

At the first visit, patients were checked to see if they could be in the study. Patients who could be in the study were assigned to receive 1 of 8 treatments (tablets or capsules) of linsitinib once a day for at least 7 days:

- Group 1: The linsitinib starting dose was 10 mg once a day.
- Group 2: The linsitinib starting dose was 20 mg once a day.
- Group 3: The linsitinib starting dose was 40 mg once a day.
- Group 4: The linsitinib starting dose was 75 mg once a day.
- Group 5: The linsitinib starting dose was 150 mg once a day.
- Group 6: The linsitinib starting dose was 300 mg once a day.
- Group 7: The linsitinib starting dose was 400 mg once a day.
- Group 8: The linsitinib starting dose was 450 mg once a day.

Starting with the lowest dose, the amount of linsitinib was “escalated” (increased) for the next group of patients. During the treatment, the study doctor checked the patients for unwanted effects. After 21 days, the patients returned to the clinic for a check-up. If no safety issues were seen, then the next group of patients could take an increased dose. The dose of linsitinib could be increased until the study doctor determined the patients could no longer tolerate the unwanted effects.

If the study doctor determined the patients could no longer tolerate the unwanted effects, then the patient was assigned to receive the last dose level of linsitinib (the dose before the unwanted effect occurred), but taken 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 2 clinics, 1 clinic in the United States and 1 clinic in the United Kingdom. A total of 86 patients took at least 1 dose of study medicine. 33 patients took linsitinib once a day. 53 patients took linsitinib twice a day.

| | **Number of Patients** | |
|---|---|---|
| | **Once a Day Linsitinib (out of 38 Enrolled Patients)** | **Twice a Day Linsitinib (out of 57 Enrolled Patients)** |
| **Age Group** | | |
| Younger than 65 years | 30 | 37 |
| 65 years or older | 8 | 20 |
| **Sex** | | |
| Men | 23 | 37 |
| Women | 15 | 20 |
| **Clinic Location** | | |
| European Union Countries (*at the time of the study*) | | |
| UK | 25 | 14 |
| Outside European Union | | |
| US | 13 | 43 |

**What Were the Study Results?**

The main question this study helped answer was what the highest dose of linsitinib was that patients with advanced solid tumors could tolerate once a day and twice a day. The results showed that the highest dose of linsitinib that patients with advanced solid tumors could tolerate was 400 mg once a day and 150 mg twice a day.

**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 approximately 10% or more of the patients who took at least 1 dose of study medicine in the study. This means that those adverse reactions were experienced by at least 4 out of 33 patients who took linsitinib once a day and at least 7 out of 53 patients who took linsitinib twice a day.

| Adverse Reaction | Once a Day Linsitinib (out of 33 Patients) | Twice a Day Linsitinib (out of 53 Patients) |
|---|---|---|
| Any adverse reaction | 25 (76%) | 45 (85%) |
| Vomiting | 9 (27%) | 7 (13%) |
| Nausea or the urge to vomit | 8 (24%) | 14 (26%) |
| Fatigue or tiredness | 7 (21%) | 13 (25%) |
| Abnormal drowsiness or sluggishness, an unusual lack of energy | 5 (15%) | 10 (19%) |
| Increased blood sugar level | 4 (12%) | 11 (21%) |
| Skin drug rash | 4 (12%) | 1 (2%) |

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

2 patients who took linsitinib once a day experienced serious adverse reactions. 4 patients who took linsitinib twice a day experienced serious adverse reactions. The table below shows these serious adverse reactions.

| Serious Adverse Reaction | Once a Day Linsitinib (out of 33 Patients) | Twice a Day Linsitinib (out of 53 Patients) |
|---|---|---|
| Any serious adverse reaction | 2 (6%) | 4 (8%) |
| Increased blood level of creatinine (a substance normally eliminated by the kidneys into the urine) | 1 (3%) | 2 (4%) |
| Acute kidney failure | 1 (3%) | 1 (2%) |
| Changes in mental health | 1 (3%) | 0 |
| Kidney failure | 1 (3%) | 0 |
| Vomiting | 0 | 2 (4%) |
| Decreased blood level of sodium | 0 | 1 (2%) |
| Increased blood level of a liver enzyme (alanine aminotransferase) | 0 | 1 (2%) |
| Increased blood level of a liver enzyme (aspartate aminotransferase) | 0 | 1 (2%) |
| Loss of appetite | 0 | 1 (2%) |

**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 November 2012. 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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