# Summary of Results for Laypersons

Astellas is grateful to the patients who took part in this clinical study. Thank you.

## What was the Study Called?

A Phase 1, Multicenter, Open-label, Dose Escalation Study of ASP9853 in Combination with Either Docetaxel or Paclitaxel in Subjects with Advanced Non-hematologic Malignancies.

## Why was this Study Needed?

A nonhematologic malignancy is a cancer that does not begin in the blood or bone marrow. Bone marrow is the soft tissue inside bones that helps form blood cells. Cancer can be treated with surgery, radiation and/or chemotherapy. Not all cancers can be cured or controlled with these treatments and they continue to grow and advance. Therefore, there was a need to study new treatments. ASP9853 is an experimental medicine taken by mouth that blocks or dampens an enzyme. This results in a decreased nitric oxide level in the body. Nitric oxide works against a type of drug commonly used in chemotherapy (taxane). It makes that type of drug less successful against the cancer. Docetaxel and paclitaxel are 2 taxane drugs used for chemotherapy. Treatment with ASP9853 together with docetaxel or paclitaxel may slow down the growth of cancer.

This study was planned to consist of 2 parts: part 1 and part 2.

The study was conducted in patients whose advanced cancer did not begin in the blood or bone marrow. In part 1, patients took increasing doses of ASP9853 together with the chemotherapy drug docetaxel. Part 2 was planned to study ASP9853 taken together with the chemotherapy drug paclitaxel. The main question this study helped answer was whether there were unwanted effects from increasing doses of ASP9853 taken together with docetaxel.

The study started in August 2012. The sponsor of this study (Astellas) did a review of the part 1 study results in June 2014. The review showed that ASP9853 and docetaxel taken together had unwanted effects. And the cancer was not controlled by treatment with the 2 drugs. The study was stopped in June 2014. Part 2 of the study was not started. When the study was stopped, 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 each patient and the study doctor knew what study medicines that patient took.

This study included adult women and men who had cancer that did not begin in the blood or bone marrow. Their cancer had advanced or failed to respond to prior standard cancer treatments. They were expected to live at least 12 weeks. Their bone marrow, liver and kidneys worked sufficiently.

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.

Prior to the start of part 1, patients took a low dose of ASP9853 for 7 days. For part 1, patients who could be in the study were assigned to 1 of 4 treatments. The patient took a dose of ASP9853 once a day and received an injection of docetaxel once every 3 weeks:

- Group 1: ASP9853 25 mg + docetaxel 60 mg/m$^2$ injection (a dose of 60 mg/m$^2$ means that patients received 60 mg docetaxel for every square meter of body surface )
- Group 2: ASP9853 25 mg + docetaxel 75 mg/m$^2$ injection
- Group 3: ASP9853 37.5 mg + docetaxel 60 mg/m$^2$ injection
- Group 4: ASP9853 50 mg + docetaxel 60 mg/m$^2$ injection

The first group of patients received the lowest dose. 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 unwanted effects were seen in Group 1, the dose of docetaxel was increased in Group 2. If no unwanted effects were seen in Group 2, the dose of ASP9853 was increased for Group 3. The dose of ASP9853 was 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 a lower dose of ASP9853 once a day.

Patients could take study medicine until their cancer got worse, they could no longer tolerate the unwanted effects, they asked to stop treatment at any time for any reason, or the doctor decided that continuing the treatment was no longer in the patients best interest.

This study took place at 4 clinics in the US. 21 patients were in the study. Out of these patients, 20 patients took at least 1 dose of study medicine.

| | **Number of Patients** |
|---|---|
| **Age Group**<br>Aged between 36 and 87 years | <br>20 |
| **Sex**<br>Men<br>Women | <br>14<br>6 |

**What Were the Study Results?**

The study was done in patients with advanced cancer that did not start in the blood or bone marrow. The main question this study helped answer was whether there were unwanted effects from increasing doses of ASP9853 taken together with docetaxel.

In part 1, ASP9853 appeared to make the unwanted effect of low white blood cells worse than it would have been with docetaxel treatment alone. The standard dose of docetaxel (the

dose usually given as a standard of therapy) is 75 mg/m$^2$. But in this study, the study doctor reduced the dose to 60 mg/m$^2$ due to increased unwanted effects caused by the 2 drugs together. This dose of docetaxel was too low to control the cancer. Part 2 of the study was cancelled because of these unwanted effects.

**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 most common adverse reactions experienced by patients who took at least 1 dose of study medicine in this study.

| **Adverse Reaction** | **Number of Patients (out of 20 patients)** |
|---|---|
| Any adverse reaction | 18 (90.0%) |
| Fatigue or tiredness | 9 (45.0%) |
| Decrease in the total number of white blood cells (leukocyte) | 5 (25.0%) |
| Condition in which the number of white bloods cells called neutrophils is abnormally low | 4 (20.0%) |
| Diarrhea | 4 (20.0%) |
| Nausea or the urge to vomit | 4 (20.0%) |
| Vomiting | 4 (20.0%) |
| Constipation | 3 (15.0%) |
| Lack of enough red blood cells (anemia) | 3 (15.0%) |
| Dizziness (or sensation of lightheadedness, unsteadiness, or giddiness) | 3 (15.0%) |
| Decreased appetite | 2 (10.0%) |
| Weakness; lack of energy and strength | 2 (10.0%) |
| Decreased number of a type of white blood cell (neutrophil) | 2 (10.0%) |
| Fever associated with dangerously low levels of a type of white blood cell (neutrophils) | 2 (10.0%) |

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

Three patients (15%, 3 out of 20) had serious adverse reactions.

Two patients died during the study. Neither patient died because of the study medicines.

**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 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. Your doctor may help you understand more about the results of this study.

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