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 Study of the Safety and Pharmacokinetics of Escalating Doses of AGS-22M6E or ASG-22CE Given as Monotherapy Followed by Expansion Cohorts in Subjects With Malignant Solid Tumors that Express Nectin-4

Why was this Study Needed?

A solid tumor is an abnormal mass of tissue that usually does not contain cysts or liquid. The most commonly used treatments for solid tumors include some combination of surgery, radiation therapy and chemotherapy. But some solid tumors are resistant to standard treatments. When that happens the disease becomes worse. Or the tumor spreads to other areas in the body. These are called malignant solid tumors. There was a need to study new medicines for malignant solid tumors.

AGS-22M6E and ASG-22CE are experimental medicines for malignant solid tumors given through a vein (intravenous or IV for short). It is thought they are attracted to tumors which have nectin 4 on their surface. AGS-22M6E and ASG-22CE come from 2 different sources (cell lines) when they are made.

This was a phase 1 study. These studies look at what the body does to the study medicine and what the study medicine does to the body. Patients received gradually increasing dose levels of AGS-22M6E or ASG-22CE in this study. The main question this study helped answer was how these study medicines were taken up, broken down, distributed through the body and removed from the body. And what was the highest dose that patients could tolerate. It was also important to find out what unwanted effects the patients had from the study medicines.

The study started in July 2011. The sponsor (Astellas) stopped the study earlier than planned in April 2015. The study was stopped because the medicine level in the blood declined too quickly for dosing every 3 weeks. It was necessary to focus on having a shorter time between doses. When the study stopped, 34 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 an “open-label” study. That means that each patient and the study doctors knew which of the study medicines that patient took.

This study was conducted in adult patients 18 years of age or older. They had been diagnosed with malignant solid tumors that had nectin-4 on the surface. The patients had received prior standard treatments for their tumor but their disease had continued to progress. The patients were active or they could perform light daily activities.

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 take part in the study. The early patients received AGS-22M6E at gradually increasing doses through a vein in the arm. Planned dose levels ranged from 0.3 milligrams (mg) of medicine per kilogram (kg) of body weight (mg/kg) to 3.0 mg/kg. The dose increased in a stepwise fashion until the highest dose that patients could tolerate was reached. After this dose level was known, patients began to be treated with ASG-22CE. The dosing was once every 3 weeks through a vein in the arm. The starting dose level for this medicine was selected by using what was learned with AGS-22M6E.

Patients could take the study medicines until their disease got worse, they had unwanted effects they could not tolerate or they asked to stop treatment. Or the study doctor decided that continuing treatment was no longer in the patients' best interest.

This study took place at 9 clinics in the United States and Canada. 34 patients were in the study and took at least 1 dose of study medicine.

	Number of Patients
Age Group	
Aged less than 65 years	19
Aged 65 years up to and including 74 years	11
Aged 75 years or older	4
Sex	
Men	12
Women	22
Clinic Location	
The United States	24
Canada	10

What Were the Study Results?

The main questions this study helped answer was how the study medicines were taken up, broken down, distributed through the body and removed from the body. To do that, the study measured the peak level of the study medicine in the patient's blood after a single dose (called Cmax). And it looked at the time it takes for the medicine level in the blood to decline by half (called half-life). Also, the study looked at the highest dose of the medicine that patients could tolerate.

The peak level of medicine in the blood after a 1.2 mg/kg dose was similar for AGS-22M6E and ASG-22CE. It was an average of approximately 32 micrograms per milliliter (µg/mL).

The highest dose of AGS-22M6E that patients could tolerate was 1.2 mg/kg. Some patients received 1.2 mg/kg of ASG-22CE and tolerated that dose.

The time it took for the medicine levels in the blood to decline by half (half-life) was also similar. It ranged from approximately 1 to 6 days for AGS-22M6E and approximately 1 to 4 days for ASG-22CE. This amount of time was too short when giving a dose of medicine

every 3 weeks. The level of medicine in the blood would fall too low before the next dose. Because of the short half-life, the study was stopped earlier than planned.

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.

18 patients (72.0%, or 18 out of 25 patients) who took AGS-22M6E experienced adverse reactions. 7 patients (77.8%, or 7 out of 9 patients) who took ASG-22CE experienced adverse reactions.

The table below shows the most common adverse reactions experienced by patients who took at least 1 dose of either study medicine in this study.

Adverse Reaction	AGS-22M6E (out of 25 patients)	ASG-22CE (out of 9 patients)
Condition in which the number of white bloods cells called neutrophils is abnormally low	3 (12.0%)	0
Nausea or the urge to vomit	5 (20.0%)	1 (11.1%)
Fatigue or tiredness	9 (36.0%)	4 (44.4%)
Increased blood level of a liver enzyme (AST/SGOT)	3 (12.0%)	0
Decreased appetite	3 (12.0%)	2 (22.2%)
Hair loss	3 (12.0%)	2 (22.2%)

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

5 patients (14.7%, or 5 out of 34 patients) experienced a serious adverse reaction in this study.

4 patients died during the study. The deaths of 2 of the patients could have been related to AGS-22M6E.

Where Can I Learn More About This Study?

This document is a short summary of the main results from this study. 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.

Sponsor contact details:

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