Summary of Results for Laypersons

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

What was the Study Called?

A Phase 1, Single-Blind, Parallel-Group, Pharmacokinetic and Immunogenicity Study with ASP0113 in CMV-Seropositive and CMV-Seronegative Healthy Subjects and CMV-Seronegative Dialysis Patients

Why was this Study Needed?

Human cytomegalovirus (or "CMV" for short) is a type of herpes virus. The immune system is part of the body that fights foreign objects or infections. After a CMV infection, CMV attacks the immune system. When the immune system is weak, it cannot fight a CMV infection well. Patients with organ transplants have a weak immune system. Every day they have to take medicines that reduce the strength of the immune system. Otherwise, their immune system would reject the organ transplants as foreign objects. Because their immune system is weak, they can get very sick from a CMV infection.

Vaccines can help the immune system protect against an infection. They contain pieces of a germ (bacteria or virus) and mimic a natural infection. The immune system recognizes those germ pieces as foreign. The immune response involves defensive white blood cells (B- and T-cells) to fight the imitation infection. The B-cells make antibodies that are specific for the germ pieces. When the antibodies bind to the germ, it can no longer infect cells in the body. The T-cells attack cells in the body that are already infected. When the imitation infection has cleared, some of the B- and T-cells are converted into memory cells. If an infection with the actual germ occurs, the memory cells can quickly divide, make antibodies and stop the infection.

ASP0113 is an experimental vaccine containing man-made substances that are very similar to pieces of CMV. It is given as an injection in the deltoid muscle (muscle on the shoulder). There is not yet enough information on the immune response that ASP0113 produces. Therefore, there was a need to study ASP0113.

This was a phase 1 study. Phase 1 studies often involve healthy volunteers. These studies may also involve patients. Phase 1 studies look at what happens to the study medicine in the body and what the study medicine does to the body.

This study consisted of 2 parts: part 1 and part 2. Part 1 was conducted in healthy volunteers. They received a single ASP0113 injection. Part 2 was conducted in healthy volunteers and patients whose kidneys worked poorly. (The patients were on kidney dialysis.) They received a total of 4 injections of ASP0113 or a placebo solution. (The section below describes what a placebo solution is.)

The study looked at the time it took for ASP0113 to be taken up in the blood and removed from the body. Part 1 of the study measured the time it took after a single injection for

ASP0113 to be removed from the body. Part 2 measured the time it took after the first of 4 injections for ASP0113 to reach its peak blood level. And it measured the time it took for the ASP0113 blood level to decline by half.

Parts 1 and 2 of the study also looked at the immune response. This was done by checking the blood for CMV antibodies and memory T-cells. The blood was checked after a single ASP0113 injection in part 1 of the study and after the third injection in part 2. Further, it was important to find out what unwanted effects the study medicine(s) had on the healthy volunteers in part 1; and on the healthy volunteers and patients in part 2.

Part 1 of the study started in December 2013 and ended in March 2014. Part 2 of the study started in May 2014 and ended in May 2016. When part 2 ended, the sponsor of this study (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?

Part 1 was an "open-label" study. This means that all healthy volunteers and the study doctors knew which study medicine they took (ASP0113).

Part 2 was a "single-blinded" study. That means that the healthy volunteers and patients did not know who took which of the study medicines (ASP0113 or placebo), but the study doctors did. A "placebo" is a dummy treatment that looks like a medicine, but does not have any medicine in it. The placebo solution in this study was saline. Using a placebo helps make study results fair and unbiased, because study doctors and patients cannot tell who is taking a placebo, and who is taking the test medicine.

Parts 1 and 2 of the study included healthy women and men aged between 18 and 65 years, whose kidneys worked normally. Some of these healthy volunteers had a CMV infection in the past. They were CMV-seropositive, which means that their blood contained CMV antibodies. The other healthy volunteers were CMV-seronegative. This means that they never had a CMV infection and their blood did not contain CMV antibodies.

Part 2 of the study also included CMV-seronegative patients aged between 18 and 70 years. Their kidneys worked poorly. They needed a treatment called "dialysis" to filter out waste products and extra salt and fluid from the blood. The kidneys normally do this filtering.

What Happened during the Study?

Part 1:

The study doctor did a check-up of the healthy volunteers in part 1 at several study visits. At the first visit, healthy volunteers were checked to see if they could be in the study. Healthy volunteers who could be in the study received 5 mg of ASP0113 as a single injection in the deltoid muscle.

Part 2:

The study doctor did a check-up of the healthy volunteers and patients in part 2 at several study visits. At the first visit, the healthy volunteers and patients were checked to see if they

could be in the study. Healthy volunteers and patients who could be in the study were picked for a treatment (ASP0113 or placebo) by chance alone. Six times as many healthy volunteers and patients were to be picked for ASP0113 than for placebo.

- ASP0113: Healthy volunteers and patients received 5 mg of ASP0113 as an injection in the deltoid muscle. They received a total of 4 injections. The first 3 injections were given 1 month apart. The last injection was given 6 months after the first injection.
- Placebo: Healthy volunteers and patients received an injection of a placebo solution. They received a total of 4 injections in the deltoid muscle. The timing was the same as for the ASP0113 injections.

This study took place at 4 clinics in the USA. Four healthy volunteers were in part 1 of the study and received 1 dose of study medicine. 44 healthy volunteers and patients were in part 2 of the study and received at least 1 dose of study medicine.

	Number of Healthy Volunteers/Patients	
	Part 1 of the Study (out of 4 healthy volunteers)	**Part 2 of the Study (out of 44 healthy volunteers and patients)**
Age Group Aged between 22 and 63 years	4	44
Sex Men Women	 2 2	 32 12

What Were the Study Results?

Part 1:

In part 1 of this study, healthy volunteers received a single ASP0113 injection. Part 1 measured the time it took for ASP0113 to be removed from the body. The study results showed that 1 week after the single injection, the body had removed ASP0113.

Part 1 also looked at the immune response after a single ASP0113 injection. This was done by checking the blood for CMV antibodies and memory T-cells. The study results showed that there was no immune response after the single ASP0113 injection.

Part 2:

In part 2 of this study, healthy volunteers and patients on kidney dialysis received 4 injections of ASP0113 or a placebo solution over 6 months. Part 2 measured the time it took after the first of 4 injections for the ASP0113 blood level to peak and to decline by half. The study results showed that the peak level of ASP0113 in the blood happened at 10 hours after the injection and between 24 to 48 hours after the injection. The average number of hours it took for the ASP0113 amount in the blood to decline by half was approximately 7 hours.

Part 2 also looked at the immune response 2 weeks after the third ASP0113 or placebo injection. This was done by checking the blood for CMV antibodies and memory T-cells.

The study results showed that there was no immune response 2 weeks after the third placebo injection.

The table below shows that CMV-seronegative healthy volunteers and patients did not start to make CMV antibodies during the study. Memory T-cells were present in the blood of some CMV-seronegative healthy volunteers; and in the blood of 1 CMV-seronegative patient. (Test 2 was more sensitive than test 1.)

Study results 2 weeks after the third ASP0113 injection	**Number of CMV-seronegative Healthy Volunteers (out of 12 healthy volunteers)**	**Number of CMV-seronegative Patients on Dialysis (out of 12 patients)**
CMV antibodies in the blood	0	0
Memory T-cells in the blood		
Test 1 results	1 (8.3%)	1 (8.3%)
Test 2 results	6 (50.0%)	1 (8.3%)

The table below shows that compared to study start, CMV-seropositive healthy volunteers did not make more CMV antibodies. Their memory T-cells did not increase.

Study results 2 weeks after the third ASP0113 injection	**Number of CMV-seropositive Healthy Volunteers (out of 13 healthy volunteers)**
More CMV antibodies in the blood compared to study start	0
More memory T-cells in the blood compared to study start	
Test 1 results	0
Test 2 results	*Test 2 was not done*

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.

Part 1:

The table below shows adverse reactions experienced by healthy volunteers who took at least 1 dose of study medicine in part 1 of this study.

Adverse Reaction	**ASP0113 (out of 4 healthy volunteers)**
Any adverse reaction	3 (75.0)
Fatigue or tiredness	2 (50.0)
Pain at the injection site	2 (50.0)
Muscle pain	1 (25.0)

Part 2:

None of the healthy volunteers or patients who received at least 1 dose of placebo in part 2 experienced adverse reactions. The table below shows adverse reactions experienced by healthy volunteers and patients who took at least 1 dose of ASP0113 in part 2 of this study.

	ASP0113		
Adverse Reaction	**CMV-seronegative Healthy Volunteers (out of 12 healthy volunteers)**	**CMV-seropositive Healthy Volunteers (out of 13 healthy volunteers)**	**CMV-seronegative Patients on Dialysis (out of 12 patients)**
Any adverse reaction	9 (75.0%)	9 (69.2%)	9 (75.0%)
Pain at the injection site	9 (75.0%)	8 (61.5%)	7 (58.3%)
Fatigue or tiredness	2 (16.7%)	4 (30.8%)	0
Muscle pain	0	1 (7.7%)	3 (25.0%)
Redness of the skin at the injection site	0	0	1 (8.3%)

Parts 1 and 2:

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

None of the healthy volunteers or patients experienced serious adverse reactions in part 1 or part 2 of this study.

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 October 2016. 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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