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 Multicenter, Two-arm, Randomized, Open-label Clinical Study Investigating Renal Function in an Advagraf®-based Immunosuppressive Regimen with or without Sirolimus in Kidney Transplant Patients. This study was also known as the ADHERE study.

Why was this Study Needed?

The immune system is part of the body that fights foreign objects or infections. After organ transplant surgery, the immune system recognizes the new organ as a foreign object. Advagraf (also known as tacrolimus prolonged-release, tacrolimus extended release or tacrolimus modified-release) is a prescription medicine that reduces the strength of the immune system (this is called an immunosuppressant medicine). It helps to prevent the body from rejecting the new organ.

Standard treatment for patients with kidney transplants is to take a combination of immunosuppressant medicines and corticosteroids (steroids) every day as prescribed by their doctors. Sometimes these medicines can damage the new kidney over time. The prescription medicine sirolimus is an immunosuppressant. It may have fewer damaging effects to the kidney compared with other medicines. A study was needed to find out what effect Advagraf and sirolimus have on transplanted kidneys after a year.

This study was conducted in patients who needed a kidney transplant. All patients took Advagraf, Mycophenolate Mofetil (MMF) and steroids for up to 28 days after surgery. Starting at day 28, patients either took Advagraf plus MMF for a year. Or they took Advagraf plus sirolimus for a year. This study looked at the effect of these 2 treatments on the patient's kidney function.

It was also important to find out what unwanted effects these patients had from their medicines.

The study started in March 2011 and ended in September 2013. When the study ended, the sponsor of the 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?

This was an "open-label" study. This means that each patient and the study doctors knew which study medicines the patients took.

This study included women and men 18 years or older. They had advanced kidney disease. These patients needed a kidney transplant or re-transplant.

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. If they could, they took Advagraf, MMF and steroids for 28 days after their transplant surgery. Patients could

discontinue from the study at any time for any reason. Or their doctor could remove them from the study. At day 28, patients who had not discontinued from the study were picked for a treatment in 1 of 2 treatment groups by chance alone ("randomization"). This assigned treatment was continued for 1 year after surgery.

- Group 1: Patients took Advagraf plus MMF plus steroids. Patients took Advagraf capsules once a day. And they took MMF capsules twice a day. The dose of steroids was gradually reduced.
- Group 2: Patients took Advagraf plus sirolimus plus steroids. Patients took Advagraf capsules once a day. At day 42, the dose was reduced so it was lower than the dose in treatment group 1. And they took sirolimus tablets once a day. The dose of steroids was gradually reduced.

This study took place at 58 clinics in the following countries: Australia, Austria, Belarus, Belgium, Czech Republic, France, Germany, Hong Kong, Hungary, Italy, Poland, Republic of Korea, Russia, South Korea, Spain, Taiwan, The Netherlands and Turkey.

853 patients were in the study. Out of these patients, 730 patients remained in the study at day 28 to be picked for 1 of 2 treatment groups. 362 patients were in group 1 (Advagraf plus MMF) and 368 patients were in group 2 (Advagraf plus sirolimus).

	Number of Patients (out of 730 patients)
Age Group	
Aged less than 50 years	334
Aged 50 to 65 years	323
Aged 66 to 75 years	71
Aged older than 75 years	2
Sex	
Men	481
Women	249

What Were the Study Results?

28 days after kidney transplant surgery, patients in group 1 took Advagraf plus MMF. And patients in group 2 took Advagraf plus sirolimus. Patients took their assigned treatment for 1 year after their kidney surgery. This study looked at the effect of these 2 treatments on the patient's kidney function. Glomerular filtration rate (GFR) is a blood test that looks at how well the kidneys are working. GFR was measured a year after kidney surgery in both treatment groups.

There was little difference between group 1 and group 2 in GFR a year after surgery. The average GFR for patients in group 1 was 40.73. The average GFR for patients in group 2 was 41.75. Statistical testing showed that this difference was likely to be due to chance.

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 were picked for 1 of the 2 treatments in the study.

Most Common Adverse Reactions	**Group 1 Advagraf + MMF (out of 362 patients)**	**Group 2 Advagraf + Sirolimus (out of 368 patient)**
Any adverse reaction	212 (58.6%)	215 (58.4%)
Low white blood cell count	38 (10.5%)	3 (0.8%)
Diarrhea	29 (8.0%)	13 (3.5%)
Infection with cytomegalovirus (a type of herpes virus)	27 (7.5%)	6 (1.6%)
Uncontrolled trembling or shaking movements in one or more parts of the body	26 (7.2%)	24 (6.5%)

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

159 patients who were picked for 1 of 2 treatments (21.8%, or 159 out of 730 patients) experienced serious adverse reactions in this study. 82 patients in group 1 and 77 patients in group 2.

16 patients died during the study. Two of these deaths (1 patient in group 1 and 1 patient in group 2) could have been related to Advagraf.

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 July 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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