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?

Investigating New Onset Diabetes Mellitus in Kidney Transplant Recipients Receiving an Advagraf-Based Immunosuppressive Regimen With or Without Corticosteroids – A Multicenter, Two Arm, Randomized, Open Label Clinical Study. This study was also known as the ADVANCE 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 immunosuppressant medicines and corticosteroids (steroids) together every day, as prescribed by their doctors. Patients who take Advagraf along with the usual dose of steroids may develop diabetes. Diabetes is a disease in which the blood sugar level is too high. A study was needed to look at the effect of eliminating steroids after transplant surgery.

This study was conducted in patients who needed a kidney transplant. One group of patients received Advagraf, other medicines and steroids after surgery. The other group of patients received Advagraf, other medicines but no steroids. The study looked at how many patients in each treatment group developed diabetes during the 24 weeks after surgery.

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

This study started in January 2011 and ended in May 2013. When the study 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?

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. Patients who could be in the study were picked for one of the 2 treatment groups by chance alone (randomization). During kidney transplant surgery all patients received a single dose of steroids.

- Group 1: After their kidney transplant surgery, patients took Advagraf once every day and were followed in the study for 24 weeks. And they took steroids every day for 10 days. The dose of steroids was gradually reduced over the 10 days. Patients also received 1 dose of Basiliximab after surgery and took Mycophenolate Mofetil (MMF) twice a day for 24 weeks.

- Group 2: After their kidney transplant surgery, patients took a dose of Advagraf once every day and were followed in the study for 24 weeks. Patients did not take steroids. Steroids could only be taken for a short time if they were needed for a rejection episode. Patients also received 1 dose of Basiliximab after surgery and took MMF twice a day for 24 weeks.

This study took place at 99 clinics in 24 countries.

A total of 1166 patients were in the study. Out of these patients, 1138 patients took at least 1 dose of study medicines. Out of these patients, 1081 had transplant surgery and had information collected at least once (528 patients in group 1 and 553 patients in group 2).

	Number of Patients (Out of 1138 patients)
Age Group	
Aged less than 50 years	533
Aged 50 to 65 years	470
Aged 66 to 75 years	122
Aged older than 75 years	13
Sex	
Men	757
Women	381
Clinic Location	
European Union Countries (*at the time of the study*)	
Belgium	69
Czech Republic	75
Estonia	31
Finland	16
France	242
Germany	124
Hungary	22
Italy	120
Latvia	5
Lithuania	15
The Netherlands	15
Norway	9
Poland	68
Portugal	6
Romania	8
Russia	70
Slovak Republic	25
Spain	99
Sweden	75
Switzerland	9
Outside European Union	
Australia	8
Republic of Korea	19
Mexico	8

What Were the Study Results?

All patients took Advagraf and other medicines for up to 24 weeks after surgery. In group 1, patients took steroids in addition to their study medicines. And in group 2, patients did not take steroids with their study medicines. This study looked at how many patients in each treatment group developed diabetes during the 24 weeks after surgery.

There was little difference between the 2 groups in diabetes in this study. 77 patients (17.4%, or 77 out of 528 patients) in group 1 had diabetes during the 24 weeks after surgery. And 74

patients (16.6%, or 74 out of 553 patients) in group 2 had diabetes. 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 in this study.

Most Common Adverse Reaction	Group 1 Advagraf+Steroids (out of 561 patients)	Group 2 Advagraf (out of 577 patients)
Any adverse reaction	322 (57.4%)	342 (59.3%)
Increased blood sugar level	53 (9.4%)	55 (9.5%)
Uncontrolled trembling or shaking movements in one or more parts of the body	38 (6.8%)	47 (8.1%)
Diabetes (a disease in which the blood sugar is too high)	34 (6.1%)	31 (5.4%)
Urinary tract infection	31 (5.5%)	30 (5.2%)
Kidney transplant rejection (patient's body attacked the new kidney)	18 (3.2%)	36 (6.2%)

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

213 patients (18.7%, or 213 out of 1138 patients) experienced serious adverse reactions in this study: 106 patients in group 1 and 107 patients in group 2.

13 patients died during the study, 8 patients in group 1 and 5 patients in group 2. Four of these deaths (2 patients in each group) could have been related to Advagraf or the other immunosuppressant medications that patients were taking as part 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 December 2013. 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 Europe Ltd
2000 Hillswood Drive
Chertsey KT16 ORS
United Kingdom