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, Non-comparative, Open-labeled, Prospective Study to Evaluate the Efficacy and Safety of Tacrolimus (Prograf®) With Steroid in Korean Lupus Nephritis Patients Who Are Non-responders to Steroid Monotherapy. This is also known as the APPLE study.

Why was this Study Needed?

The immune system is part of the body that fights foreign objects or infections. In patients with systemic lupus erythematosus (or "lupus" for short), the immune system attacks the body's own cells and organs. Lupus that causes inflammation in the kidneys is called lupus nephritis. This makes the kidneys unable to properly remove waste from the blood or control the amount of fluids in the body. That results in blood and protein leaking into the urine. It also leads to swelling in body parts (legs, ankles, around the eyes) and high blood pressure. Lupus nephritis is treated with oral prescription medicines (taken by mouth) such as steroids that reduce the strength of the immune system. Steroids may not work well or may cause unwanted effects in some patients. Therefore, there was a need to study a new treatment for lupus nephritis. Tacrolimus (also known as Prograf) is an experimental oral medicine for lupus nephritis that reduces the strength of the immune system.

This study was conducted in patients who had lupus nephritis. In this study, patients took Prograf. The main question this study meant to answer was what the remission rate was after treatment with Prograf for 24 weeks. That is the number of treated patients whose symptoms improved or disappeared compared to all treated patients. It was also important to find out what unwanted effects these patients had from the study medicine.

The study started in April 2011. The sponsor (Astellas) stopped the study in April 2016. The reason was that not enough patients joined the study. When the study was stopped, 37 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. This means that all patients and the study doctors knew which study medicine the patients took (Prograf).

This study included adult women and men aged 20 years or older. They had lupus nephritis. They had been taking steroids (10 mg or more per day) for more than 10 months. The steroids did not improve their lupus nephritis symptoms. Or they had unwanted effects from the steroids and could not take a higher dose.

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 took Prograf capsules (3 mg) once a day. If the study doctor found no safety

issues, the study doctor could increase the daily dose to up to 5 mg as needed. The patients took study medicine for 24 weeks.

This study took place at 10 clinics in South Korea. 37 patients were in the study and took at least 1 dose of study medicine.

	Number of Patients
Age Group	
Aged less than 20 years	1
Aged between 20 and 29 years	15
Aged between 30 and 39 years	11
Aged between 40 and 49 years	4
Aged between 50 and 59 years	5
Aged between 60 and 69 years	1
Sex	
Men	3
Women	34

What Were the Study Results?

This study was conducted in patients with lupus nephritis. The main question this study meant to answer was what the remission rate was after treatment with Prograf for 24 weeks. That is the number of treated patients whose symptoms improved or disappeared compared to all treated patients.

The study was planned for 56 patients. When this study was stopped, only 37 patients had taken Prograf for 24 weeks. The remission rate was 21.62%. This means that symptoms of lupus nephritis improved or disappeared in 8 out of the 37 treated patients. Because there were not enough patients in the study, these results will need to be confirmed in a study with more patients.

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	Prograf (out of 37 patients)
Any adverse reaction	18 (48.65%)
Headache or head pain	4 (10.81%)
Increased blood level of creatinine (a substance normally eliminated by the kidneys into the urine)	4 (10.81%)
A toxic blood level of tacrolimus	3 (8.11%)
Stomach pain or belly ache	2 (5.41%)
Diarrhea	2 (5.41%)
Increased blood level of urea (a waste product formed in the liver when protein is broken down into its component parts)	2 (5.41%)
Infection of the upper respiratory tract (nose, sinuses, throat, windpipe, and voice box)	2 (5.41%)
Inflammation of the small bowel	2 (5.41%)
Severe pain that continues after a bout of shingles (herpes zoster)	2 (5.41%)
Shingles (herpes zoster)	2 (5.41%)
Upper belly pain	2 (5.41%)

An adverse event is considered “serious” when it is life-threatening, causes lasting problems or needs hospital care.

Six patients (16.22%, or 6 out of 37 patients) experienced a serious adverse event in 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 March 2017. 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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