Plain Language Summary of Study Results

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

What was the Study Called?

A Phase 3, Randomized, Open, Parallel-Controlled, Multi-center Study to Compare the Efficacy and Safety of Tacrolimus Capsules and Cyclophosphamide Injection in Treatment of Lupus Nephritis.

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, also known as "lupus", the immune system attacks the body's own cells and organs. Lupus that causes inflammation in the kidneys is called lupus nephritis. This leads to the kidneys not working properly. This means they are unable to remove waste properly from the blood or control the amount of fluids in the body. That results in blood cells and protein leaking into the urine. It also leads to swelling in body parts such as the legs, ankles and around the eyes. It can also cause high blood pressure.

Patients with lupus nephritis are treated with medicines such as cyclophosphamide with steroids. Patients receive cyclophosphamide through a vein (injection). Cyclophosphamide might cause unwanted effects in some patients.

There was a need to find a new treatment for patients with lupus nephritis. Research has shown that a medicine called Tacrolimus (also known as Prograf) reduces the strength of the immune system. Tacrolimus is taken by mouth as a capsule.

In this study, patients with lupus nephritis either took tacrolimus capsules or received cyclophosphamide injections.

The researchers wanted to know the following:

- Was the number of patients in remission lower for those who took tacrolimus capsules compared to those who received cyclophosphamide injections by a medically important amount?

  In this study, remission means the patients' kidney function stayed stable and some specific proteins in their blood and urine returned to normal or close to normal amounts.

- Did these patients have any unwanted effects from the study medicines (tacrolimus capsules or cyclophosphamide injections)?

The study started in March 2015 and ended in September 2018. 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. That means that each patient and the study doctors knew which study medicine that patient took (tacrolimus capsules or cyclophosphamide injections).

This study included Chinese men and women from 18 to 60 years old with severe lupus nephritis. Severe means patients with Stage III to V lupus nephritis.

What happened during the study?

During the study, the study doctor did a check-up of the patients at several study visits. At the first visit the study doctor checked if patients could take part in the study. Patients who could take part were picked for treatment with 1 of 2 study medicines by chance alone.

All patients received 1 steroid injection (shot) each day for 3 days.

Then patients received 1 of the following 2 study medicines for 24 weeks:

- Tacrolimus - Patients took tacrolimus capsules twice a day. They started on a dose of 4 milligrams (mg) each day. After 14 days the study doctor decided the dose for each patient.
- Cyclophosphamide - Patients received cyclophosphamide as an injection. The starting dose was 0.75 grams (g) for every square meter of each patient's body surface area (BSA). This is also known as 0.75 g/m^2 BSA. The study doctor decided the next doses for each patient. Patients received a cyclophosphamide injection every 4 weeks for a total of 6 doses.

All patients in this study also took steroids every day for 24 weeks.

This study took place at 35 clinics in the Republic of China. 314 patients were in the study. Out of these patients, 299 patients took at least 1 dose of study medicine.

	Number of Patients
Age Group Aged 18 to 58 years	 299
Sex Men Women	 37 262

What Were the Study Results?

A total of 157 patients took tacrolimus capsules and 142 patients received cyclophosphamide injections. Of these, 141 patients who took tacrolimus capsules and 124 patients who received cyclophosphamide injections had information for the study results at 24 weeks.

Was the number of patients in remission lower for those who took tacrolimus capsules compared to those who received cyclophosphamide injections by a medically important amount?

In this study, remission means the patient's kidney function stayed stable and some specific

proteins in their blood and urine returned to normal or close to normal amounts.

- 117 out of 141 patients (83%) who took tacrolimus capsules went into remission
- 93 out of 124 patients (75%) who received cyclophosphamide injections went into remission

Although these percentages look different, some differences can be due to chance.

A statistical test showed that the percentage of tacrolimus-treated patients in remission was not lower than those treated with cyclophosphamide injections by a medically important amount.

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 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.

238 patients (79.6%, or 238 out of 299 patients) had adverse reactions in this 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	Tacrolimus Capsules (out of 157 patients)	Cyclophosphamide Injections (out of 142 patients)
Infection of the upper respiratory tract (nose, sinuses, throat, wind pipe and voice box)	37 (23.6%)	40 (28.2%)
Diarrhea	16 (10.2%)	2 (1.4%)
Uncontrolled trembling or shaking movements in one or more parts of the body	15 (9.6%)	2 (1.4%)
Increased blood level of uric acid, a waste material from food digestion	13 (8.3%)	5 (3.5%)
Cough	11 (7.0%)	7 (4.9%)
Urinary tract infection	9 (5.7%)	6 (4.2%)
Lung infection	8 (5.1%)	11 (7.7%)
Increased blood levels of liver enzymes	8 (5.1%)	10 (7.0%)
Inflammation of the lining of the bronchial tubes, which carry air to and from the lungs	8 (5.1%)	10 (7.0%)

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

48 patients (16.1%, or 48 out of 299 patients) had serious adverse reactions.

Of these, 18 patients (11.5%, or 18 out of 157 patients) had taken tacrolimus capsules and 30 patients (21.1%, or 30 out of 142 patients) had received cyclophosphamide injections.

The most common serious adverse reaction was lung infection. This happened in 5 patients (3.2%, or 5 out of 157 patients) who took tacrolimus capsules and 10 patients (7.0%, or 10 out of 142 patients) who received cyclophosphamide injections.

2 patients died during the study. Of these, 1 had taken tacrolimus capsules and 1 had received cyclophosphamide injections. The deaths of the 2 patients could have been related to the study medicines.

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.

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