Summary of Results for Laypersons

What was the Study Called?

Open-Label, Randomized, Comparative, Multi-Center Clinical Trial on the Therapeutic Effect of Tacrolimus (Prograf Cap.®) in Combination with Low-Dose Corticosteroid Compared with High-Dose Corticosteroid alone in Patients with Minimal-Change Nephrotic Syndrome (MCNS). This is also known as the T-OPTIMUM study.

Why was this Study Needed?

The glomeruli are the tiny units within your kidneys where blood is filtered. In minimal-change nephrotic syndrome (or MCNS for short), the glomeruli get damaged but that damage can only be seen under a very powerful microscope. The damage to the glomeruli may cause protein from the blood to leak into the urine. MCNS in adults is treated with high-dose corticosteroid (1 mg/kg per day). This treatment may cause unwanted effects and may not work in all adult patients. Therefore, there was a need to study new treatments for MCNS. Tacrolimus (also known as Prograf, FK506, immediate-release tacrolimus, Adoport, Capexion, Vivadex, Tacni, Tacniteva and Tacni-transplant) is a medicine that reduces the strength of the immune system.

This study was conducted in patients with MCNS. They took either high-dose corticosteroid or tacrolimus together with low-dose corticosteroid (tacrolimus/low-dose corticosteroid). The main question this study helped answer was if tacrolimus/low-dose corticosteroid was not worse than high-dose corticosteroid at increasing the percentage of patients without signs of MCNS based on a urine test score. It was also important to find out what unwanted effects these patients had from the study medicine(s).

The study took place from July 2012 to August 2017. When the study ended, the sponsor (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 knew which study medicine(s) they took (high-dose corticosteroid or tacrolimus/low-dose corticosteroid).

Clinical studies have a list of requirements for patients who can be in a study ("inclusion" criteria) and patients who cannot take part in a study ("exclusion" criteria). The requirements for this study are listed below.

Men and women could take part in the study if:

- They were between 16 and 79 years old.
- A doctor had determined that they had MCNS that was not caused by another disease or a medication. It was the first time they had MCNS or the MCNS had come back.

Patients could not take part in the study if:

- Their kidneys were in poor working condition.

- Within 2 weeks before study start, they had taken a medication that reduces the strength of the immune system.
- Within 2 weeks before study start, they had taken more than 10 mg prednisolone or a similar dose of steroid each day.

During this study, the study doctor did a check-up of the patients at 10 study visits; the last visit was at 6 months. At visit 1, patients were checked to see if they could be in the study. Patients who could be in the study were picked for 1 of 2 treatments by chance alone:

- High-dose corticosteroid: Patients took prednisolone tablets 1 mg/kg once a day by mouth. The maximum dose was 80 mg per day.
- Tacrolimus/low-dose corticosteroid: Patients took prednisolone tablets 0.5 mg/kg once a day and tacrolimus capsules 0.05 mg/kg twice a day by mouth. The study doctor checked that the blood level of tacrolimus was between 5 and 10 ng/mL and adjusted the dose as needed. ("ng/mL" is the unit that measures the amount of the medicine in blood. For example, a tacrolimus blood level of 5 ng/mL means that there is 5 ng of tacrolimus in 1 mL of blood.)

The study doctor tested a sample of the patients' urine at each visit. Three weeks after the test results showed that patients no longer had signs of MCNS, the study doctor adjusted their doses as follows:

- High-dose corticosteroid: The study doctor lowered the prednisolone dose by 5 mg per week to 7.5 mg per day for patients weighing more than 80 kg; and to 5 mg per day for patients weighing less than 80 kg.
- Tacrolimus/low-dose corticosteroid: The study doctor lowered the prednisolone dose by 5 mg per week to 7.5 mg per day for patients weighing more than 80 kg; and to 5 mg per day for patients weighing less than 80 kg. The study doctor checked that the blood level of tacrolimus was between 3 and 8 ng/mL and adjusted the dose as needed.

This study took place at 15 clinics in South Korea. 144 patients were in the study. Out of these patients, 136 patients took at least 1 dose of study medicine.

	Number of Patients (out of 136 patients)
Age Group	
Aged 12 to 17 years	2
Aged 18 to 64 years	121
Aged 65 to 84 years	13
Sex	
Men	85
Women	51
Clinic Location	
South Korea	136

What Were the Study Results?

This study in patients with MCNS looked at the percentage of patients with a urine test score of 0.2 or less after they took study medicine for 8 weeks. A urine test score of 0.2 or less means that patients no longer have signs of MCNS.

For patients who took at least 1 dose of study medicine, the percentage of patients with a urine test score of 0.2 or less was 76.81% (53 out of 69 patients) in the high-dose corticosteroid group. That percentage was 79.1% (53 out of 67 patients) in the tacrolimus/low-dose corticosteroid group. Statistical testing showed that tacrolimus/low-dose corticosteroid was not worse than high-dose corticosteroid in treating MCNS.

Of the 136 patients who took at least 1 dose of study medicine, 44 patients in the high-dose corticosteroid group and 39 patients in the tacrolimus/low-dose corticosteroid group fulfilled all study requirements. For these patients, the percentages were 86.36% (38 out of 44 patients) in the high-dose corticosteroid group and 84.62% (33 out of 39 patients) in the tacrolimus/low-dose corticosteroid group. Statistical testing showed that tacrolimus/low-dose corticosteroid was not worse than high-dose corticosteroid in treating MCNS.

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 adverse reactions experienced by approximately 3% or more of patients who took at least 1 dose of study medicine in this study. This means that those adverse reactions were experienced by at least 2 out of 69 patients in the high-dose corticosteroid group and by at least 2 out of 67 patients in the tacrolimus/low-dose corticosteroid group.

Adverse Reaction	High-dose Corticosteroid (out of 69 patients)	Tacrolimus Together With Low-dose Corticosteroid (out of 67 patients)
Any adverse reaction	19 (27.54%)	26 (38.81%)
Heartburn	5 (7.25%)	2 (2.99%)
Increased blood sugar level	3 (4.35%)	1 (1.49%)
Swelling of the face	3 (4.35%)	0
Muscle pain	2 (2.9%)	1 (1.49%)
Swelling of the arms and/or legs	2 (2.9%)	0
Hair loss	1 (1.45%)	2 (2.99%)
Joint pain	1 (1.45%)	2 (2.99%)
Muscle spasms	1 (1.45%)	2 (2.99%)
Abnormal buildup of fluid that affects the whole body	0	2 (2.99%)
Belly pain	0	2 (2.99%)
Diarrhea	0	5 (7.46%)
Pain in the upper belly (just below the breastbone)	0	3 (4.48%)

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

Four patients experienced a serious adverse reaction. The table below shows those serious adverse reactions.

Serious Adverse Reaction	High-dose Corticosteroid (out of 69 patients)	Tacrolimus Together With Low-dose Corticosteroid (out of 67 patients)
Any serious adverse reaction	1 (1.45%)	3 (4.48%)
Shingles	1 (1.45%)	0
Disease involving the digestive tract	0	1 (1.49%)
Disease usually of the lungs caused by bacteria (*Mycobacterium tuberculosis*)	0	1 (1.49%)
Pneumonia	0	1 (1.49%)

Where Can I Learn More About This Study?

Astellas may perform additional studies to better understand tacrolimus.

This document is a short summary of the main results from this study and reflects the information available as of March 2018. 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. If you have questions about tacrolimus, please discuss these with your doctor.

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