Summary of Results for Laypersons

What was the Study Called?

An open-label, single-arm, phase 4 study to assess the safety and efficacy of a tacrolimus in active rheumatoid arthritis patients shown unsuccessful response against DMARDs. This is also known as the TREASURE study.

Why was this Study Needed?

The immune system is part of the body that fights foreign objects or infections. Patients with rheumatoid arthritis have a faulty immune system that attacks the body's own tissues. As a result, these patients have inflammation (swelling and redness) in joints (arthritis). There are several antirheumatic medicines that slow down the progress of joint damage (disease modifying antirheumatic drugs or DMARDs for short). These medicines may cause unwanted effects or may not work in all patients. There was a need to study new medicines.

Tacrolimus is a medicine that reduces the strength of the immune system. Tacrolimus (also known as Prograf, FK506, immediate-release tacrolimus, Adoport, Capexion, Vivadex, Tacni, Tacniteva and Tacni-transplant) blocks the release of substances in the body that promote the inflammation of rheumatoid arthritis.

This study was conducted in patients with rheumatoid arthritis who did not get relief from their usual antirheumatic medicines. They took tacrolimus for 6 months. The main question this study helped answer was how many patients improved at least 20% in their rheumatoid arthritis symptoms. It was also important to find out what unwanted effects these patients had from the study medicine.

This study took place at 6 clinics in South Korea. The study took place from December 2011 to May 2015. 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, which means that all patients knew that they took tacrolimus.

Patients could take part in the study if:

- They were older than 20 years and younger than 75 years.
- A doctor had determined that they had rheumatoid arthritis for more than 6 months.
- They had been taking an antirheumatic medication for more than 6 months.
- At study visit 1, they had a protocol-specified blood level of a particular protein.
- At study start, at least 3 of the 66 joints that were checked for swollenness were swollen.
- At study start, at least 6 of the 68 joints that were checked for tenderness were tender.

Patients could not take part in the study if:

- They were pregnant or were breastfeeding. Or they were planning to become pregnant within 6 months.

- They had taken tacrolimus in the past.
- Their kidneys were in poor working condition.
- They had disorder of the liver caused by a virus. They had scar tissue in their liver. Or they had increased blood levels of a liver enzyme (alanine aminotransferase/serum glutamic pyruvic transaminase or aspartate aminotransferase/serum glutamic oxaloacetic transaminase) more than 2 times the normal level. Increased blood levels of these liver enzymes indicate that liver cells are damaged.
- They had inflammation (swelling and redness) of the pancreas. They had, or used to have, poor control of their blood sugar levels. Or their average level of blood sugar over the past 3 months was above a protocol-specified limit. This meant that their diabetes was controlled poorly.
- They had an increased blood level of potassium. Or at study start, their serum level of potassium was above a protocol-specified limit.
- They had a history of heart disease: repeated chest pain or discomfort that was the result of a part of the heart not receiving enough blood; irregular heartbeat that required treatment; or inability of the heart to adequately pump blood to supply oxygen to the body.

During this study, the study doctor did a check-up of the patients at 5 study visits. At visit 1, patients were checked to see if they could be in the study. Patients who could be in the study stopped taking any medications that they were using. After those medications were expected to no longer be in their body, the patients returned to the clinic for visit 2. Patients who could remain in the study took tacrolimus for 6 months. For the first 3 months, patients took 2 mg tacrolimus per day (or 1.5 mg if they were older than 65 years). The study doctor then adjusted the dose based on the specific needs of the patient. Patients took between 1 and 3 mg tacrolimus per day for the last 3 months.

A total of 121 patients were in this study and received at least 1 dose of study medicine.

	Number of Patients (out of 121 patients)
Age Group	
Aged 20 to 65 years	106
Aged older than 65 years	15
Sex	
Men	14
Women	107
Clinic Location	
European Union Countries	0
Outside European Union	121
South Korea	121

What Were the Study Results?

This study was conducted in patients with rheumatoid arthritis who did not get relief from their usual antirheumatic medicines. They took tacrolimus for 6 months. The study looked at how many of these patients improved at least 20% in their rheumatoid arthritis symptoms.

After patients took tacrolimus for 6 months, 78 of the 121 patients (64.5%) improved at least 20% in their rheumatoid arthritis symptoms.

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 received at least 1 dose of study medicine.

Adverse Reaction	**Tacrolimus (out of 121 patients)**
Heartburn	4 (3.3%)
Nausea or the urge to vomit	3 (2.5%)
Common cold	3 (2.5%)

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care. One patient experienced a serious adverse reaction. The patient had a broken foot.

Where Can I Learn More About This Study?

Astellas may perform additional studies to better understand tacrolimus.

This summary of the clinical study results is available 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. If you have questions about tacrolimus, please discuss these with your doctor.

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