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 Phase 3, Randomized, Double-Blind, Placebo Controlled Study of the Efficacy and Safety of Roxadustat for the Treatment of Anemia in Chronic Kidney Disease Patients not on Dialysis. This is also known as the ALPS study.

Why was this Study Needed?

Kidneys filter the blood and make a hormone that tells the soft tissue within the bone (bone marrow) to make red blood cells. Patients with chronic kidney disease often have a lack of enough red blood cells as the kidney hormone function is decreased. This results in their hemoglobin being too low (kidney anemia). Hemoglobin is the part of red blood cells that carries oxygen from the lungs to the rest of the body. Erythropoiesis-stimulating agents (ESAs) are medicines that replace the function of the kidney hormone. ESA medicines together with iron supplements are used to treat kidney anemia. But these medicines may not work well for some patients. And they are given via injection (as a shot). Therefore, there was a need to study new treatments for kidney anemia. Roxadustat (also known as FG-4592 and ASP1517) is a new oral medicine (taken by mouth) for the treatment of kidney anemia.

This study looked at how well roxadustat worked to treat kidney anemia. This was done by measuring the change in hemoglobin level after patients took study medicine for up to 52 weeks. The patients took roxadustat or placebo. (The section below describes what placebo tablets are). It was also important to find out what unwanted effects these patients had from the study medicines.

The study started in September 2013 and ended in November 2017. 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 a "double-blinded" study. That means that the patients and the study doctors did not know who took which of the study medicines (roxadustat or placebo). This helps make study results fair and unbiased. A "placebo" is a dummy treatment that looks like a medicine, but does not have any medicine in it.

This study included adults with chronic kidney disease aged at least 18 years, who had kidney anemia. Their hemoglobin was low. They did not need a treatment called "dialysis" to filter out wastes and extra salt and fluid from the blood.

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 were treated with roxadustat or placebo by chance alone. It was planned that twice as many patients were to be treated with roxadustat than with placebo.

- Roxadustat: Patients took roxadustat tablets 3 times a week. The starting dose was 70 mg. If patients weighed more than 70 kg, the starting dose was 100 mg. The study doctor adjusted the roxadustat dose based on the specific needs of the patient.
- Placebo: Patients took placebo tablets 3 times a week.

Patients took study medicine for at least 52 weeks and up to 104 weeks.

At times, the study medicine may not have increased the patient's hemoglobin level well enough. The patient could then receive a "rescue medicine." The "rescue medicine" could be an ESA medicine. Or it could be iron given through a needle or tube inserted into a vein. That is called an intravenous infusion or IV for short. Or it could be a red blood cell transfusion. This means that red blood cells donated by someone else were put into the patient's bloodstream through an IV.

This study took place at 153 clinics in several countries. 594 patients were in the study and took at least 1 dose of study medicine.

	Number of Patients
Age Group	
Aged less than 65 years	335
Aged 65 to 74 years	163
Aged 75 years or older	96
Sex	
Men	268
Women	326
Clinic Location	
European Union Countries (*at the time of the study*)	192
Belgium	9
Bulgaria	35
Estonia	1
Greece	6
Hungary	12
Italy	6
Poland	48
Romania	46
Spain	17
The UK	12
Outside European Union	402
Belarus	12
Colombia	3
Dominican Republic	12
Georgia (Republic)	17
Guatemala	27
Panama	12
Peru	3
Russian Federation	98
Serbia	85
South Africa	16
Turkey	19
Ukraine	98

What Were the Study Results?

This study in patients with chronic kidney disease with anemia looked at the change in hemoglobin level in the blood after patients took study medicine for up to 52 weeks. The study looked at this change in patients who took no "rescue medicine". And it looked at the change in all patients.

Study doctors made a decision before the study began. They decided what a meaningful increase in hemoglobin was for patients who took no rescue medicine. This increase was seen in 308 out of 389 (79.2%) patients who took roxadustat and no "rescue medicine" for the first 24 weeks. And it was seen in 20 out of 203 (9.9%) patients who took placebo and no "rescue medicine" for the first 24 weeks. A statistical test showed that the difference was not likely to be due to chance.

All patients included patients who took "rescue medicine" and those who did not. For all patients, the study looked at the average hemoglobin level during weeks 28 to 52 of treatment. This level was compared to the hemoglobin level at the start of the study. For all patients who took roxadustat, the average increase in hemoglobin level was 1.992 g/dL (1.992 g of hemoglobin in 1 dL of blood). For all patients who took placebo, the average increase in hemoglobin level was 0.300 g/dL. A statistical test showed that the difference was not likely to be due to chance.

Roxadustat increased the hemoglobin level in the blood more than placebo. Therefore, it was effective in treating kidney anemia in these 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	**Roxadustat (out of 391 patients)**	**Placebo (out of 203 patients)**
Any adverse reaction	81 (20.7%)	27 (13.3%)
High blood pressure	15 (3.8%)	3 (1.5%)
Nausea or the urge to vomit	11 (2.8%)	2 (1.0%)
Not enough iron in the body	10 (2.6%)	1 (0.5%)

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

Serious adverse reactions were experienced by 25 patients (6.4%, or 25 out of 391 patients) who took roxadustat; and by 4 patients (2.0%, or 4 out of 203 patients) who took placebo.

65 patients died during the study: 45 patients who took roxadustat (11.5%, 45 out of 391) and 20 patients (9.9%, 20 out of 203) who took placebo. The deaths of 5 of the patients who took roxadustat could have been related to roxadustat.

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.astellasclinicalstudy results.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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