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, Open-Label, Active-Controlled Study to Evaluate the Efficacy and Safety of Roxadustat in the Maintenance Treatment of Anemia in End Stage Renal Disease Patients on Stable Dialysis. This was also known as the PYRENEES 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.

End stage renal disease means kidneys are working at a very low level. They can no longer filter blood well enough. Patients with this disease need kidney dialysis or a kidney transplant to survive. Dialysis is a treatment to filter out wastes and extra salt and fluid from the blood. Patients with end stage renal disease usually have kidney anemia. This study looked at how well roxadustat worked to treat kidney anemia in patients with end stage renal disease who were on dialysis. 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 ESA medicine. This study looked at how well roxadustat worked to treat kidney anemia in patients with end stage renal disease who were on dialysis. And it was compared to ESA medicines. It was also important to find out what unwanted effects these patients had from the study medicines.

The study started in November 2014 and ended in July 2018. 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 an “open-label” study. This means that each patient and the study doctors knew which study medicine that patient took (roxadustat or ESA).

This study included adult patients at least 18 years of age with end stage renal disease. They had been on dialysis for at least 4 months before their first dose of study medicine. The patients had kidney anemia. Patients had received an ESA medicine (epoetin or darbepoetin

alfa) for at least 8 weeks before their first dose of study medicine. Their weekly dose of epoetin or darbepoetin alfa was the same for at least the past 4 weeks.

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 ESA medicine by chance alone. The study doctor adjusted the dose of study medicines based on the specific needs of the patient.

- Roxadustat: Patients took roxadustat tablets 3 times a week. The starting dose was 100, 150 or 200 mg depending on what their weekly ESA dose used to be.
- ESA: Patients received epoetin alfa or darbepoetin alfa as a shot. Their average weekly dose was about the same as before the study started.

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 a red blood cell transfusion. This means that donated red blood cells were given through a tube inserted into a vein of the patient. For patients who took roxadustat, the "rescue medicine" could also be an ESA medicine.

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

This study took place at 150 clinics in several countries. 834 patients were in the study and took at least 1 dose of study medicine.

	Number of Patients
Age Group	
Aged less than 65 years	451
Aged from 65 to 74 years	229
Aged 75 years or older	154
Sex	
Men	480
Women	354
Clinic Location	
European Union Countries (*at the time of the study*)	644
Belgium	31
Bulgaria	156
Croatia	59
Czech Republic	16
France	12
Germany	34
Hungary	136
Italy	39
Poland	29
Portugal	17
Romania	40
Slovakia	32
Spain	29

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The United Kingdom	14
Outside European Union	190
Georgia (Republic)	6
Russia	98
Serbia	86

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.

In patients who took no "rescue medicine", the average hemoglobin level in the blood during weeks 28 to 36 of treatment was compared to the level at the start of the study. For patients who took roxadustat, the average change in hemoglobin level was 0.428 g/dL (0.428 g of hemoglobin in 1 dL of blood). For patients who took ESA medicine, the average change in hemoglobin level was 0.193 g/dL. A statistical test showed that the change was similar between patients who took roxadustat and patients who took ESA medicine.

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 patients who took roxadustat, the average change in hemoglobin level was 0.363 g/dL (0.363 g of hemoglobin in 1 dL of blood). For patients who took ESA, the average change in hemoglobin level was 0.192 g/dL. A statistical test showed that the change was similar between patients who took roxadustat and patients who took ESA medicine.

Roxadustat was not worse than ESA medicines in keeping up the level of hemoglobin. Therefore, roxadustat was not worse than ESA medicines in treatment of anemia in patients with end stage renal disease who were on dialysis.

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 414 patients)	ESA (out of 420 patients)
Any adverse reaction	77 (18.6%)	35 (8.3%)
High blood pressure	14 (3.4%)	4 (1.0%)
Blood clot in a connection between an artery and a vein. Connection is needed for dialysis procedure.	12 (2.9%)	4 (1.0%)
Nausea or the urge to vomit	8 (1.9%)	0
Diarrhea	4 (1.0%)	0
Not enough iron in the body	4 (1.0%)	10 (2.4%)
Lack of enough red blood cells (anemia)	4 (1.0%)	0

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

Serious adverse reactions in this study were experienced by 33 patients (8.0%, or 33 out of 414 patients) who took roxadustat. And by 10 patients (2.4%, or 10 out of 420 patients) who took ESA medicines.

137 patients died during the study: 78 patients (18.8%, 78 out of 414) who took roxadustat and 59 patients (14.0%, 59 out of 420) who took ESA medicine. The deaths of 5 patients who took roxadustat could have been related to roxadustat. The deaths of 2 patients who took ESA medicines could have been related to the ESA medicine.

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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