Plain Language Summary of Study Results

Astellas is grateful to the people 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 Treatment of Anemia in Chronic Kidney Disease Patients Not on Dialysis.

Why was this Study Needed?

Many people with chronic kidney disease develop anemia, which is a lack of red blood cells. Anemia in these people is thought to be caused by a lack of a hormone (erythropoietin) produced in their kidneys. This hormone helps the body to produce more red blood cells and hemoglobin. Hemoglobin is the part of the red blood cells that carries oxygen from the lungs to the rest of the body. People with chronic kidney disease who develop anemia are given medicines called erythropoiesis-stimulating agents, also called ESAs. ESAs are given by injection (shot) and work by helping the body to make more red blood cells. These people also usually receive iron supplements together with ESAs.

These medicines might not work well for some of these people. There is a need to find a new treatment for anemia in people with chronic kidney disease.

Roxadustat, also called ASP1517, is a new medicine, taken by mouth. In this study, roxadustat is used to treat anemia in people with chronic kidney disease.

In this study, people with chronic kidney disease either took roxadustat tablets or received ESA injections. The ESA used in this study was darbepoetin alfa.

The study started in March 2014 and ended in November 2019. 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 were the main questions the study helped answer?

- How many people had an increase in hemoglobin in their blood after the first 24 weeks of treatment with the study medicines (roxadustat or darbepoetin alfa)?
- Was the number of people with an increase in their hemoglobin lower for those who took roxadustat compared to those who received darbepoetin alfa by a medically important amount?
- Did these people have any medical problems from the study medicines (roxadustat or darbepoetin alfa)?

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 (roxadustat or darbepoetin alfa).

This study included adults at least 18 years of age with moderate to severe chronic kidney disease (stages 3 to 5). These people had anemia and were not on dialysis.

	Number of People
Age Group	
Aged less than 65 years	237
Aged 65 to 74 years	168
Aged 75 years or older	211
Sex	
Men	274
Women	342

What Happened during the Study?

During the study, people visited the clinic several times. At the first visit the study doctor checked if these people could take part in the study. People who could take part were picked for treatment with roxadustat or darbepoetin alfa by chance alone.

- Roxadustat: People in the study took roxadustat tablets 3 times a week. The starting dose was 70 milligrams (mg). If people weighed more than 70 kg, the starting dose was 100 mg.
- Darbepoetin alfa: People in the study received darbepoetin alfa either as an injection (shot) into a vein or under the skin. The starting dose, the way it was given and how often people received darbepoetin alfa was decided by the study doctor. This was based on the specific needs of each person. The 2 choices were:
    - People received 0.45 micrograms (µg) darbepoetin alfa for each kilogram of their body weight. This is also known as 0.45 µg/kg. They received darbepoetin alfa either as an injection (shot) into a vein or under the skin. This happened once a week.
    - Or people received 0.75 µg/kg darbepoetin alfa as an injection under the skin, once every 2 weeks.

After 4 weeks, the study doctor adjusted the dose (roxadustat or darbepoetin alfa) for each person, based on the amount of hemoglobin (in red blood cells) in that person's blood.

Study doctors adjusted the dose in the same way every 4 weeks.

Before treatment and regularly during the course of the study, the study doctors took blood samples from each person. They measured the amount of hemoglobin in the person's blood to see if it had increased by a specific amount after 24 weeks. The specific amount was decided by the researchers before the study had started.

People were treated with roxadustat or darbepoetin alfa for up to 104 weeks (2 years).

Where Did The Study Take Place?

This study took place at 156 clinics in several countries. 616 people were in the study and took at least 1 dose of study medicine (roxadustat or darbepoetin alfa).

	Number of People
Clinic Location	
European Union Countries (*at the time of the study*)	429
Austria	3
Bulgaria	19
Croatia	73
Czech Republic	33
Finland	3
France	18
Germany	37
Hungary	32
Ireland	8
Latvia	4
Netherlands	1
Poland	30
Portugal	17
Romania	16
Slovakia	26
Slovenia	15
Spain	33
United Kingdom	61
Outside European Union	187
Belarus	17
Georgia (Republic)	19
Israel	3
Macedonia	12
Montenegro	4
Russian Federation	48
Serbia	48
Ukraine	36

What Were the Study Results?

A total of 323 people took roxadustat and 293 people received darbepoetin alfa. Of these, 286 people who took roxadustat and 273 people who received darbepoetin alfa had information for the study results in the first 24 weeks of treatment.

How many people had an increase in their hemoglobin in their blood after the first 24 weeks of treatment with the study medicines (roxadustat or darbepoetin alfa)?

- 256 out of 286 people (89.5%) who took roxadustat had a relevant increase in hemoglobin in their blood
- 213 out of 273 people (78.0%) who received darbepoetin alfa had a relevant increase in hemoglobin in their blood.

Was the number of people with a relevant increase in their hemoglobin lower for those who took roxadustat compared to those who received darbepoetin alfa by a medically important amount?

Although these percentages look different, some differences can be due to chance. However, a statistical test showed that the percentage of roxadustat-treated people with a relevant increase in hemoglobin was not lower than those treated with darbepoetin by a medically important amount.

What Adverse Reactions did People Have in this Study?

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 people 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.

78 people (24.1% or 78 out of 323 people) who took roxadustat and 66 people (22.5% or 66 out of 293 people) who received darbepoetin alfa had adverse reactions to the study medicines. This was throughout the long-term treatment of up to 2 years.

The table below shows the most common adverse reactions to the study medicines experienced by people who took at least 1 dose of study medicine in this study.

Adverse Reaction	Roxadustat (out of 323 people)	Darbepoetin alfa (out of 293 people)
High blood pressure	14 (4.3%)	36 (12.3%)
Nausea or the urge to vomit	7 (2.2%)	0
Fatigue or tiredness	5 (1.5%)	4 (1.4%)
Headache or head pain	5 (1.5%)	2 (0.7%)
Belly pain	4 (1.2%)	1 (0.3%)
Itching	4 (1.2%)	0
Blood pressure went up	1 (0.3%)	4 (1.4%)
Not enough iron in the body	1 (0.3%)	6 (2.0%)

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

Did any of the people in this study have serious adverse reactions?

18 people (5.6%, or 18 out of 323 people) who took roxadustat and 9 people (3.1%, or 9 out of 293 people) who received darbopoetin alfa had serious adverse reactions to the study medicines.

The most common serious adverse reactions to the study medicines are shown in the table below.

Serious Adverse Reaction	Roxadustat (out of 323 people)	Darbepoetin alfa (out of 293 people)
Kidney failure which needs kidney dialysis or a kidney transplant for the person to survive	3 (0.9%)	0
Heart Attack	2 (0.6%)	1 (0.3%)
High blood pressure	1 (0.3%)	3 (1.0%)
Blood clot in an abnormal connection between an artery and a vein	0	2 (0.7%)
A severe increase in blood pressure which can lead to a stroke	0	2 (0.7%)

40 people who took roxadustat and 37 people who received darbepoetin alfa passed away during the study. Of these, 2 deaths were judged by the study doctor to be possibly caused by roxadustat. No one passed away during the study because of darbepoetin alfa.

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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