8 November 2019 07:00 GMT

Roxadustat significantly increased haemoglobin levels for chronic kidney disease patients with anaemia in Phase III OLYMPUS and ROCKIES trials

OLYMPUS demonstrated a mean increase of 1.75g/dL averaged over weeks 28 to 52, compared to 0.40g/dL with placebo

ROCKIES demonstrated a mean increase of 0.77g/dL averaged over weeks 28 to 52, compared to 0.68g/dL with epoetin alfa

AstraZeneca today presented detailed results from the Phase III OLYMPUS and ROCKIES trials showing that roxadustat significantly increased haemoglobin (Hb) levels in non-dialysis-dependent (NDD) and dialysis-dependent (DD) patients with anaemia from chronic kidney disease (CKD), respectively.

The OLYMPUS trial compared roxadustat to placebo while the ROCKIES trial compared roxadustat to epoetin alfa. The results were presented today during two oral sessions at the American Society of Nephrology (ASN) Kidney Week 2019 in Washington, D.C., US.

Mene Pangalos, Executive Vice President, BioPharmaceuticals R&D, said: "Anaemia is a common, serious condition among patients with chronic kidney disease. It occurs when the body has fewer healthy red blood cells than normal and low levels of haemoglobin, which may leave patients fatigued and short of breath. Results from OLYMPUS and ROCKIES reinforce the potential role that roxadustat could play in increasing haemoglobin levels and managing anaemia, which is often underdiagnosed and undertreated."

Steven Fishbane, MD, Zucker School of Medicine at Hofstra/Northwell, Great Neck, New York, US and primary investigator on the OLYMPUS and ROCKIES trials, said: "These data demonstrated that roxadustat effectively increased haemoglobin levels for patients with anaemia from chronic kidney disease, including those who show signs of inflammation. Patients who experience chronic inflammation are often more difficult to treat than the overall chronic kidney disease patient population, emphasising the need for new treatment options."

In the OLYMPUS trial, roxadustat demonstrated a statistically significant improvement in Hb levels from baseline, with a mean increase of 1.75g/dL averaged over weeks 28 to 52, compared to 0.40g/dL with placebo, the primary efficacy endpoint.

Roxadustat also improved Hb levels from baseline in a subgroup of patients with elevated high-sensitivity C-reactive protein (hsCRP) levels of greater than 5mg/L, with a statistically significant mean increase of 1.73 g/dL, compared to 0.62g/dL with placebo, a secondary endpoint. hsCRP is a protein in the blood that increases when inflammation is present.

Overall safety findings are generally consistent with the NDD-CKD patient population. For all patients, the most frequently reported adverse events in the intent to treat analysis set were end-stage renal disease, pneumonia, urinary tract infection and hypertension. Additional serious adverse events reported were azotaemia, sepsis, acute kidney injury and hyperkalaemia.

In the ROCKIES trial, roxadustat demonstrated a statistically significant improvement in Hb levels from baseline with a mean increase of 0.77g/dL averaged over weeks 28 to 52, compared to 0.68g/dL with epoetin alfa, the primary efficacy endpoint.

Roxadustat also improved Hb levels from baseline in a subgroup of patients with elevated hsCRP levels of greater than 5 mg/L, demonstrating a statistically significant improvement with a mean

increase of 0.80g/dL compared to 0.59g/dL with epoetin alfa, a secondary endpoint. Patients treated with roxadustat used less monthly intravenous (IV) iron (mean = 59mg) compared to those treated with epoetin alfa (mean = 91mg) from week 36 to the end of the study.

Adverse events with roxadustat were generally similar to those seen in patients treated with epoetin alfa and commonly found in DD-CKD patients. In roxadustat treated patients, the most frequently reported adverse events were diarrhoea, hypertension, pneumonia, headache and arteriovenous fistula thrombosis. Additional serious adverse events reported were sepsis and acute myocardial infarction.

Cardiovascular (CV) safety data from these trials will be reported as part of the pooled efficacy and CV safety analyses of DD-CKD and NDD-CKD patients from the global Phase III programme, which is being presented in the oral late-breaking abstract session "High-Impact Clinical Trials" at ASN Kidney Week on 8 November 2019.

Roxadustat is currently approved in China for the treatment of anaemia in patients with CKD, regardless of whether they require dialysis. Data from the Phase III OLYMPUS and ROCKIES trials, together with the efficacy and pooled CV safety data from the global Phase III programme, will form part of the regulatory submission in the US, anticipated in Q4 2019.

About roxadustat
Roxadustat is a hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI) that promotes erythropoiesis by increasing endogenous production of erythropoietin and improving iron regulation and overcoming the negative impact of inflammation on haemoglobin synthesis and red blood cell production by downregulating hepcidin. Use of roxadustat has been shown to induce coordinated erythropoiesis, increasing red blood cell count while maintaining plasma erythropoietin levels within or near normal physiologic range, in multiple subpopulations of CKD patients, including in the presence of inflammation and without a need for supplemental IV iron.

About the Phase III programme
FibroGen, Inc., (FibroGen) and AstraZeneca are collaborating on the development and commercialisation of roxadustat for the treatment of anaemia in patients with CKD in the US, China, and other global markets. FibroGen and Astellas Pharma Inc. (Astellas) are collaborating on the development and commercialisation of roxadustat for the treatment of anaemia in patients with CKD in territories including Japan, Europe, the Commonwealth of Independent States, the Middle East, and South Africa.

The global Phase III programme consisted of seven trials in more than 9,000 patients and was conducted by AstraZeneca, FibroGen and Astellas.

About OLYMPUS
OLYMPUS is a Phase III, randomised, double blind, placebo-controlled trial designed to evaluate the efficacy and safety of roxadustat vs. placebo for the treatment of NDD patients with anaemia from CKD stages 3, 4 and 5 . OLYMPUS evaluated 2,781 patients with anaemia (Hb<10.0g/dL) in NDD-CKD stages 3-5 who were randomised 1:1 to roxadustat or placebo across 26 countries. Top-line results announced in December 2018 showed OLYMPUS met its primary efficacy endpoint. OLYMPUS is one of two AstraZeneca-sponsored trials that are part of the global Phase III clinical trials programme.

About ROCKIES
ROCKIES is a Phase III, randomised, open-label, active-controlled trial designed to assess the efficacy and safety of roxadustat vs. epoetin alfa, for the treatment of patients with anaemia in DD-CKD. ROCKIES evaluated 2,133 DD-CKD patients with anaemia either currently treated with an erythropoietin analogue (Hb<12g/dL) or not currently treated with an erythropoietin analogue (Hb<10g/dL) randomised 1:1 to roxadustat or epoetin alfa across 18 countries. Oral iron was

allowed; IV iron was used as standard of care (SoC) in the epoetin alfa arm and with evidence of iron deficiency in the roxadustat arm. Top-line results announced in December 2018 showed ROCKIES met its primary efficacy endpoint. ROCKIES is one of two AstraZeneca-sponsored trials that are part of the global Phase III clinical trials programme.

About anaemia from CKD

Anaemia can be a serious medical condition in which patients have insufficient red blood cells and low levels of haemoglobin, a protein in red blood cells that carries oxygen to cells throughout the body.[1,2] Anaemia from CKD is associated with increased risk of hospitalisation, CV complications and death,[3] also frequently causing significant fatigue, cognitive dysfunction and decreased quality of life.[4] Severe anaemia is common in patients with CKD, cancer, myelodysplastic syndrome, inflammatory diseases and other serious illnesses.

Anaemia is particularly prevalent in patients with CKD. CKD affects more than 200 million patients worldwide and is generally a progressive disease characterised by gradual loss of kidney function that may eventually lead to kidney failure.

According to the United States Renal Data System, about 80% of the approximately 507,000 patients receiving dialysis in the US in 2016 were being treated with erythropoiesis-stimulating agents (ESA).[5] Patients seldom receive ESA treatment until they initiate dialysis therapy.

About AstraZeneca in CVRM

Cardiovascular, Renal & Metabolism (CVRM) together forms one of AstraZeneca's three therapy areas and is a key growth driver for the Company. By following the science to understand more clearly the underlying links between the heart, kidneys and pancreas, AstraZeneca is investing in a portfolio of medicines to protect organs and improve outcomes by slowing disease progression, reducing risks and tackling co-morbidities. The Company's ambition is to modify or halt the natural course of CVRM diseases and potentially regenerate organs and restore function, by continuing to deliver transformative science that improves treatment practices and cardiovascular health for millions of patients worldwide.

About AstraZeneca

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three therapy areas - Oncology, CVRM, and Respiratory. AstraZeneca operates in over 100 countries, and its innovative medicines are used by millions of patients worldwide. For more information, please visit astrazeneca.com and follow the Company on Twitter @AstraZeneca.

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