News release

Kyowa Kirin Announces Presentations of the Results of Phase 3 Studies of Tenapanor Hydrochloride (KHK7791) for Hemodialysis Patients with Hyperphosphatemia in Japan at the American Society of Nephrology Meeting

TOKYO, October 20, 2022 – Kyowa Kirin Co., Ltd. (TSE:4151, President and CEO: Masashi Miyamoto, "Kyowa Kirin") announces that major results of two phase 3 studies of tenapanor hydrochloride[*1] (KHK7791, "tenapanor") for patients with hyperphosphatemia receiving maintenance dialysis[*2] in Japan will be presented in two poster presentations at the American Society of Nephrology Meeting (ASN Kidney Week 2022, Orlando, Florida), from November 3 to November 6, 2022. The abstracts of these two presentations are available on the ASN website. (https://www.asn-online.org/education/kidneyweek/)

ASN Kidney Week 2022　Poster session
ID:TH-PO160
Session Date, Time: November 3, 2022 from 10:00 AM to 12:00 AM

Title : Efficacy and safety of tenapanor on hyperphosphatemia in Japanese hemodialysis patients: Results of a randomized phase 3 trial

Method

This was a multicenter, randomized, double-blind, placebo-controlled, parallel-group comparative, phase 3 trial for patients with hyperphosphatemia receiving maintenance hemodialysis. The trial comprised three periods which are screening, up to 3-week washout, and 8-week treatment. Patients whose serum phosphorus (sP) level was 3.5−6.0 mg/dL (the target range by Japanese Society for Dialysis Therapy) in screening period were enrolled. After washout of phosphate binders, patients, age ≥ 20 years old, whose serum phosphorus (sP) level were between 6.1−9.9 mg/dL were randomized 1:1 to placebo or tenapanor during the 8-week treatment period. Tenapanor's starting dose was 5 mg administered twice daily and then up-titrated to 10, 20, and 30 mg twice daily based on sP level. The primary endpoint was a mean change in sP level at week 8 from baseline.

Major Results

164 subjects were enrolled (82 subjects per group). The sP level at week 8, a primary endpoint, demonstrated a decrease of -1.89 mg/dL in the tenapanor group and 0.05 mg/dL in the placebo group (difference -1.95 mg/dL [95%CI -2.37 mg/dL, -1.53 mg/dL], p<0.0001). In each group, diarrhea was the most frequent adverse event (tenapanor group: 74.4%, placebo group: 19.5%). In most of the cases, the severity of diarrhea was mild.

Conclusion

Tenapanor demonstrated a statistically significant reduction in sP, as compared to placebo, in patients with hyperphosphatemia receiving maintenance hemodialysis. The safety and tolerability profile for tenapanor in this trial was acceptable, with no new or unexpected findings. These results demonstrate that tenapanor may be a new option for the treatment of patients with hyperphosphatemia receiving maintenance dialysis.

ASN Kidney Week 2022　Poster session
ID:TH-PO161
Session Date, Time: November 3, 2022 from 10:00 AM to 12:00 AM

Title : Efficacy and safety of Tenapanor added to phosphate binders for hemodialysis patients who have poorly controlled hyperphosphatemia on existing phosphate binders: Results of a randomized phase 3 trial

Method

This was a phase 3, multicenter, placebo-controlled, double-blind, randomized, phosphate binder-combination, parallel-group comparative study for patients with hyperphosphatemia receiving maintenance hemodialysis and treated with phosphate binders. Patients, age ≥ 20 years old, whose sP levels were out of target range (6.1–9.9 mg/dL) based upon the Japanese Society for Dialysis Therapy with conventional phosphate binder therapy, were eligible for this study. Enrolled patients were randomized to tenapanor + phosphate binder or placebo + phosphate binder in a 1:1 ratio. Tenapanor 5 mg was administered twice daily as a starting dose with the option to up-titrate to 10, 20, and 30 mg twice daily based on sP levels. The primary endpoint was a mean change in sP level at week 8 from baseline.

Major Results

169 subjects were enrolled (84 subjects to in the tenapanor group and 85 subjects to a placebo group). The mean change in sP level from baseline at week 8 was -2.00 mg/dL in the tenapanor group and -0.24 mg/dL in the placebo group. The difference in the mean change from baseline in sP levels between the tenapanor group vs. the placebo groups was -1.76

mg/dL (95%CI [-2.16 mg/dL, -1.37 mg/dL], p<0.0001). In each group, diarrhea was the most frequent adverse event (tenapanor group:63.1%, placebo group:14.1%). In large part of the cases, the severity of diarrhea was mild.

Conclusion

Tenapanor demonstrated a statistically significant reduction in sP levels when tenapanor was added to conventional phosphate binder therapy compared to phosphate binder therapy alone in patients with poorly controlled hyperphosphatemia with maintenance hemodialysis. The safety and tolerability profile for tenapanor in this trial was acceptable, with no new or unexpected findings. These results suggest that the addition of tenapanor to phosphate binder therapy may provide new treatment option for patients receiving maintenance dialysis who have hyperphosphatemia, refractory to phosphate binders.

Yoshifumi Torii, Ph.D., Executive officer, Vice President, Head of R&D Division at Kyowa Kirin commented, "We believe tenapanor is an important and new, mechanistically unique, approach for the management of hyperphosphatemia for adult patients on dialysis. I'm very excited for patients and the physicians who treat them, as these results demonstrate that tenapanor achieved a statistically significant reduction in serum phosphorus levels both as a monotherapy and in combination with conventional phosphate binders. We will continue to work towards delivering tenapanor to patients with hyperphosphatemia receiving maintenance dialysis."

Kyowa Kirin is also conducting a phase 3 clinical study of tenapanor in hyperphosphatemia patients on peritoneal dialysis and a phase 3 long-term study evaluating serum phosphorus in hyperphosphatemia patients on hemodialysis in Japan who switch from one or more phosphate binders to tenapanor.

Tenapanor, discovered by Ardelyx[*3], is a first-in-class phosphate absorption inhibitor. Kyowa Kirin and Ardelyx initially established a collaborative partnership in November 2017 through a license agreement under which Kyowa Kirin obtained exclusive rights to develop and commercialize tenapanor, for the treatment of cardiorenal diseases, including hyperphosphatemia, in Japan.

The Kyowa Kirin Group companies strive to contribute to the health and well-being of people around the world by creating new value through the pursuit of advances in life sciences and technologies.

***1: About Tenapanor Hydrochloride**

Tenapanor hydrochloride (“tenapanor”), discovered and developed by Ardelyx, is a first-in-class phosphate absorption inhibitor. Tenapanor with a unique blocking mechanism of action, acts locally in the gut to inhibit the sodium hydrogen exchanger 3 (NHE3), reducing phosphate absorption through the paracellular pathway, the primary pathway of phosphate absorption.

***2: About Hyperphosphatemia**

Hyperphosphatemia is a serious condition resulting in an abnormally elevated level of phosphorus in the blood that is estimated to affect more than 745,000 dialysis patients in major developed countries. The kidney is the organ responsible for regulating phosphorus levels, but when kidney function is significantly impaired, phosphorus is not adequately eliminated from the body. As a result, hyperphosphatemia is a nearly universal condition among people with CKD on dialysis with internationally recognized KDIGO treatment guidelines that recommend lowering elevated phosphate levels toward the normal range (2.5-4.5mg/dL).

***3: About Ardelyx Inc.**

Ardelyx was founded with a mission to discover, develop and commercialize innovative first-in-class medicines that meet significant unmet medical needs. Ardelyx’s first approved product, IBSRELA® (tenapanor) is available in the United States and Canada. Ardelyx is developing XPHOZAH® (tenapanor), a novel product candidate to control serum phosphorus in adult patients with CKD on dialysis, which has completed three successful Phase 3 trials. Ardelyx has a Phase 2 potassium lowering compound, RDX013, for the potential treatment of elevated serum potassium, or hyperkalemia, a problem among certain patients with kidney and/or heart disease and an early-stage program in metabolic acidosis, a serious electrolyte disorder in patients with CKD. Ardelyx has established agreements with Kyowa Kirin in Japan, Fosun Pharma in China and Knight Therapeutics in Canada for the development and commercialization of tenapanor in their respective territories.