Shono and Hyakutake
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RESEARCH

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Efficacy and safety of long-term treatment with elobixibat in hemodialysis patients with chronic constipation: an observational study

Takefumi Shono[1*] and Hiroyuki Hyakutake[1]

Abstract

Background Constipation is a common complication in hemodialysis patients and can impact their quality of life. Elobixibat selectively inhibits ileal bile acid transporter to suppress bile acid reabsorption, increase the amount of bile acid entering the colonic lumen, and promote water secretion and colonic motility in the large intestine. While the efficacy and safety of elobixibat in hemodialysis patients up to 12 weeks after administration have been reported, the long-term efficacy and safety of elobixibat in hemodialysis patients with chronic constipation are yet to be elucidated. This study evaluates the efficacy and safety of long-term treatment with elobixibat in hemodialysis patients with chronic constipation.

Methods This was a single-center observational study. A total of 54 patients who had received elobixibat for at least 24 weeks were enrolled. Data on the frequency of spontaneous bowel movements (SBM), Bristol stool form scale (BSFS), patient satisfaction, constipation scoring system (CSS), interdialytic weight gain, laboratory values including blood electrolyte levels, controlling nutritional status (CONUT) score, and adverse events were collected and retrospectively compared between baseline and the last observation.

Results Long-term elobixibat treatment in the 54 hemodialysis patients with chronic constipation significantly increased ($p < 0.05$) the frequency of SBM and mean stool form score assessed as per the BSFS at the last observation (duration of treatment, 24.4 to 240.0 weeks). Patient satisfaction and CSS also improved ($p < 0.05$). Mean serum phosphorus levels decreased ($p < 0.05$). The treatment was well tolerated.

Conclusions Long-term treatment with elobixibat maintained good bowel movement status and patient satisfaction in hemodialysis patients with chronic constipation. Improved dialysis-related laboratory levels were also demonstrated.

Trial registration: UMIN Clinical Trials Registry, UMIN000049865, 22 December 2022, retrospectively registered.

Keywords Bristol stool form scale, Chronic constipation, Elobixibat, End-stage renal disease, Hemodialysis, Patient satisfaction, Probiotics, Serum phosphorus levels, Spontaneous bowel movement

Background

According to the Report on the Annual Statistical Survey of the Japanese Society for Dialysis Therapy in 2022 [1], 347,474 patients are on hemodialysis in Japan. While the increase in the number of patients has slowed

*Correspondence:
Takefumi Shono
tkfm-shn.3@smile.ocn.ne.jp
[1] Hyakutake Clinic, 2195-26, Ikari, Tagawa-shi, Fukuoka 825-0001, Japan

slightly, their mean age is 69.87 years, and the average age of this patient population continues to increase. The Japanese Guidelines for Clinical Management of Bowel Movement Abnormalities, issued in 2023, reported that constipation is more common in hemodialysis patients than people with normal renal function [2]. In addition, constipation symptoms tend to persist for a prolonged period in hemodialysis patients due to dietary and fluid restriction and the use of phosphate or potassium binders. For the treatment of constipation in hemodialysis patients, the use of magnesium oxide has not been recommended because of the risk of hypermagnesemia. As for stimulant laxatives, resistance develops in long-term continuous use, thus only administration on an as-needed basis or for a short period is recommended. Therefore, long-term use of medications to treat constipation symptoms might be problematic in some cases [3–6]. In recent years, intestinal secretagogues (lubiprostone and linaclotide) and osmotic laxatives (macrogol 4000 + electrolyte preparation and lactulose) have been launched for the treatment of chronic constipation. However, all of them have mechanisms of action that can either increase water secretion or cause water retention.

Elobixibat, a novel drug for the treatment of chronic constipation, was launched in Japan in April 2018. It inhibits the ileal bile acid transporter expressed in the epithelial cells of the terminal ileum and prevents bile acid reabsorption, thereby increasing the amount of bile acids flowing into the colon lumen [7]. Owing to the increased amount of bile acids in the colon, it enhances water and electrolyte secretion into the lumen of the large intestine and induces a high amplitude propagating pressure wave. Elobixibat may therefore be a new treatment option because it improves constipation on the basis of an action mechanism completely different from those of conventional drugs for constipation [8, 9].

A Japanese long-term study has demonstrated that the efficacy and safety of elobixibat was maintained for 52 weeks in patients with chronic constipation [10]. For the efficacy and safety of elobixibat in hemodialysis patients with chronic constipation, an increase in the number of bowel movements, improvement of stool form, and no adverse effect on blood electrolytes have been reported at week 4 [11] and week 12 at the Hyakutake Clinic [12]. However, whether elobixibat adversely affects blood electrolyte levels, which have a significant impact on patients requiring hemodialysis, for an extended period of time is unknown.

This study aimed to evaluate the long-term efficacy and safety of elobixibat in hemodialysis patients who had chronic constipation.

Methods

We conducted a single-center observational study in patients who received elobixibat for at least 24 weeks between 19 April 2018 and 14 December 2022 at the Hyakutake Clinic. In the study, the medical records of subject candidates were reviewed, and those who met all of the following inclusion criteria at the start of elobixibat treatment were determined to be eligible for the study: (1) men and women aged 18 years or older, (2) patients with chronic kidney disease (CKD) who have been on hemodialysis for 3 months or more, (3) patients who meet the Rome IV Diagnostic Criteria for Chronic Constipation, and (4) patients who are confirmed to have received elobixibat in accordance with the dosage and administration for 24 weeks or more (concomitant use of other laxatives permitted).

Patients who met the following exclusion criteria were not enrolled: (1) patients with a history of hypersensitivity to elobixibat; (2) patients with documented or suspected intestinal obstruction due to tumors, hernia, etc.; (3) patients with suspected constipation caused by organic disease; and (4) patients who participated in another clinical trial or interventional study during the period from the baseline observation to the last observation or providing informed consent.

As well as patient background characteristics, the frequency of spontaneous bowel movements (SBM), Bristol stool form scale (BSFS), constipation scoring system (CSS), patient satisfaction [assessed by the patient on a 5-point scale (0, very much satisfied to 4, very much dissatisfied)], interdialytic weight gain (IDWG), laboratory values, concomitant medications, and adverse events were collected from medical records at baseline (before elobixibat treatment), week 12, week 24, week 52, week 78, week 104, week 130, week 156, and the last observation. Since improvement of constipation symptoms may be related to amelioration of the intestinal environment, one blood sample was collected after obtaining written consent from patients who were continuing outpatient treatment as of January 2023.

The primary endpoint of this study was a comparison of the frequency of SBM [bowel movements not induced by laxatives (bisacodyl suppositories)/enema or digital evacuation] between baseline and the last observation, which occurred at week 24 or later. Secondary endpoints were comparisons of the frequency of SBM, BSFS, patient satisfaction, CSS, IDWG, blood electrolyte levels [serum inorganic phosphorus (P), potassium (K), sodium (Na), chlorine (Cl), calcium (Ca), and albumin (Alb) levels], serum low-density lipoproteins (LDL)-cholesterol, serum total cholesterol, total lymphocyte count, and patient satisfaction (the proportions of patients with 0, very

much satisfied and 1, satisfied) over time from baseline. In addition, correlations were compared for the following items:

- Patient satisfaction and each efficacy endpoint
- Nutrition parameters [Alb level, serum total cholesterol, and total lymphocyte count, and controlling nutritional status (CONUT) score [13] calculated from these] in elobixibat responders and nonresponders (patients who required other laxatives at the time of blood collection after informed consent)

For safety endpoints, incidences of adverse events and adverse drug reactions and the rate of elobixibat treatment discontinuation were calculated.

SAS version 9.4 software (SAS Institute Inc., Carey, NC, USA) and R version 4.3.1 software [R Core Team (2021) R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria] were used for preparing analysis datasets and statistical analyses. Reported adverse events were coded using the Medical Dictionary for Regulatory Activities/Japanese version (MedDRA/J Version) 26.0. The efficacy analysis population was defined as patients who met the inclusion criteria, did not meet the exclusion criteria, received elobixibat for at least 24 weeks, and had one or more efficacy assessments at baseline and at week 24 or later. The safety analysis population was defined as patients who met the inclusion criteria and did not meet the exclusion criteria. The comparison of the primary efficacy endpoint was performed by a paired *t*-test. The comparisons of the secondary efficacy endpoints were carried out by a paired *t*-test, Bhapkar test, or Wilcoxon signed-rank test. For the relationships between patient satisfaction and the efficacy endpoints, Spearman's correlation coefficients and maximal information coefficients (MIC) were calculated. The CONUT score was compared between responders and nonresponders by the Wilcoxon signed-rank test. In addition, comparisons of the frequency of SBM and CSS were performed using a paired *t*-test and Wilcoxon signed-rank test in subgroups of patients in the efficacy analysis population that were defined by baseline age ($\geq$ or $<$ 65 years), sex, the status of concomitant use of phosphate binders, potassium binder, or probiotics, baseline CSS ($\geq$ or $<$ 10), the presence or absence of complications, the presence or absence of diabetic nephropathy, the presence or absence of prior treatment for constipation, the status of concomitant use of laxatives, doses (5, 10, or 15 mg), duration of dialysis (mean, $<$ 5.87 years, $\geq$ 5.87 years), and CONUT score (normal, 0–1; mild, 2–4; moderate, 5–8; and severe, $>$ 8) as variables.

The numbers of patients with and incidences of all and each adverse event were calculated in the safety analysis population.

A two-sided significance level of 0.05 was used for the tests.

Results were presented as mean ± standard deviation (SD) or percentage. Statistical analyses for this study were performed by an independent organization (SRD Co., Ltd., Tokyo, Japan).

Results

Patients

All 54 hemodialysis patients who received elobixibat for at least 24 weeks at our clinic between 19 April 2018 and 14 December 2022 were determined to be eligible and thus included in the efficacy and safety analysis populations. Of these, blood and feces samples were collected from 34 patients after obtaining written consent in January 2023 or later. Patient background is summarized in Table 1.

Table 1 Patient background

Number of patients (male/female) (*n*)	**54 (27/27)**
Age (years) (range)	71.4 ± 10.9 (37–91)
Duration of dialysis (years) (range)	5.87 ± 7.64 (0.2–36.3)
Male [*n* (%)]	27 (50.0)
Complications [*n* (%)]	
Yes	53 (98.1)
History of hemodialysis [*n* (%)]	
Diabetic nephropathy	26 (48.1)
Chronic glomerulonephritis	20 (37.0)
Nephrosclerosis	3 (5.6)
Polycystic kidney	2 (3.7)
Chronic pyelonephritis	1 (1.9)
Others	2 (3.7)
Prior medications (during the 2 weeks preceding baseline) [*n* (%)]	
Phosphate binders	38 (70.4)
Laxatives	34 (63.0)
Probiotics	6 (11.1)
Potassium binders	4 (7.4)
Others	52 (96.3)
Concomitant medications [*n* (%)]	
Phosphate binders	47 (87.0)
Laxatives	45 (83.3)
Probiotics	26 (48.1)
Potassium binders	3 (5.6)
Others	54 (100.0)

Data in the table represent mean ± standard deviation (SD) unless otherwise specified

Efficacy

Primary Outcome

Elobixibat treatment significantly increased the frequency of SBM (times/week) from 2.0 ± 1.0 at baseline to 4.5 ± 2.2 at the last observation (Fig. 1a).

Secondary outcomes

Comparisons of the frequency of SBM and BSFS after treatment over time versus baseline The observed frequency of SBM significantly increased at week 12 and later, and the improvement was maintained (Fig. 1a). The stool form score according to the BSFS improved from 1.7 ± 0.7 at baseline to 3.8 ± 1.3 at the last dose; it significantly improved at week 12 and later, and the improvement was maintained (Figs. 1b, 2a).

Comparison of patient satisfaction after treatment over time versus baseline The mean change in patient satisfaction from baseline to each time point (weeks 12, 24, 52, 78, 104, 130, and 156, and the last observation; same applies hereinafter) was −1.8 ± 0.9, −1.9 ± 0.9, −1.9 ± 1.0, −2.0 ± 0.9, −1.9 ± 0.9, −1.7 ± 1.4, −1.9 ± 1.3, and −1.9 ± 1.2, respectively, showing improvement at all timepoints (Fig. 2b).

Comparison of CSS and each component after treatment over time versus baseline The mean changes from

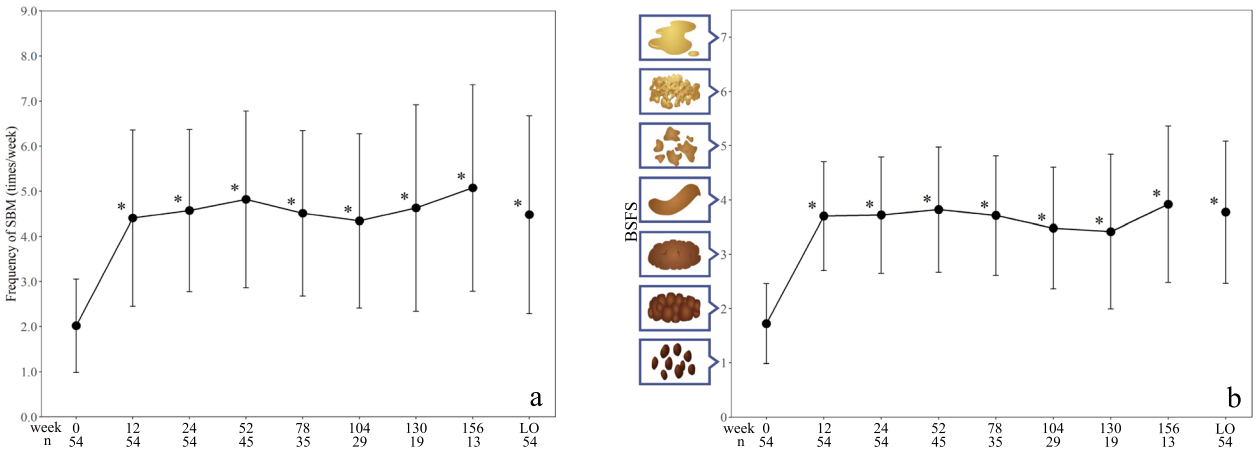

Fig. 1 Changes over time in the mean frequency of SBM and stool form score based on the BSFS. Error bars represent the mean ± standard deviation. *$p < 0.05$. **a** Paired *t* test, frequency of SBM; and **b** Wilcoxon signed-rank test, stool form score based on the BSFS. LO stands for last observation

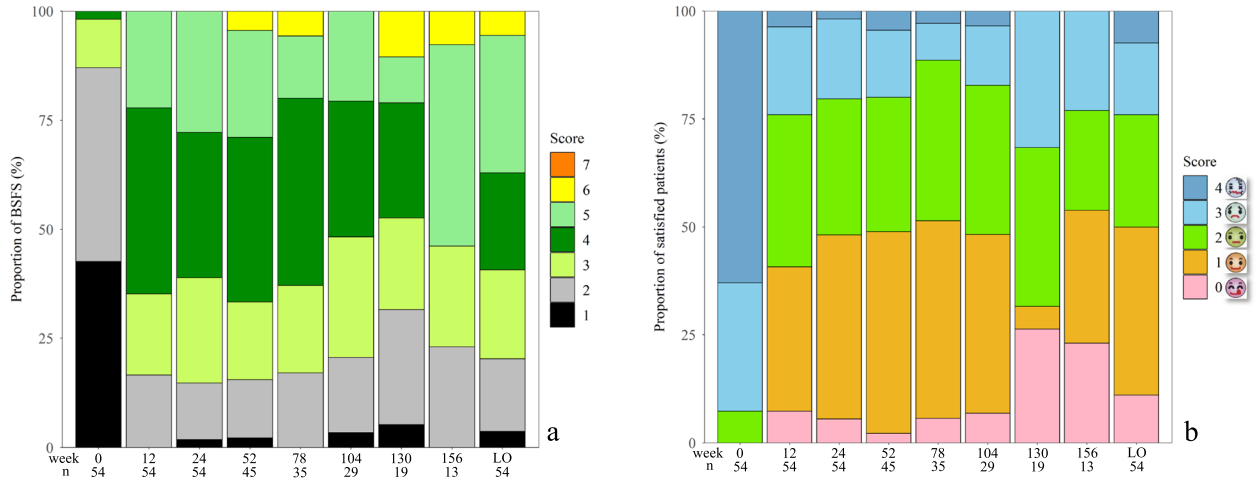

Fig. 2 Proportion of stool form scores based on the BSFS and satisfied patients at each timepoint. The BSFS scores and patient satisfaction scores are color coded. **a** The BSFS scores are as follows: 1–2, hard stools; 3–5, normal stool; and 6–7, soft stool. **b** Patient satisfaction is assessed on a 5-point scale (0, very much satisfied to 4, very much dissatisfied). LO stands for last observation

baseline in the CSS, frequency of bowel movements, painful evacuation, feeling of incomplete evacuation, and unsuccessful attempts for evacuation per 24 h statistically significantly decreased at all timepoints from week 12, and they significantly improved at the last observation as well (Fig. 3). The mean changes from baseline in abdominal pain and minutes in lavatory per attempt significantly improved at the last observation, while no significant difference was found at any timepoints (Fig. 3). For the mean changes from baseline in assistance for evacuation and duration of constipation, no significant difference was found at any of the timepoints (Fig. 3).

Comparison of IDWG, serum LDL-cholesterol, P, K, Na, Cl, Ca, Alb, and BUN levels after treatment over time versus baseline The mean change in IDWG from baseline to each timepoint was −0.19 ± 1.35%, −0.01 ± 1.59%, −0.15 ± 1.54%, −0.42 ± 1.56%, −0.33 ± 1.27%, −0.47 ± 1.23%, −0.68 ± 1.08%, and −0.55 ± 1.74%, respectively; showing a statistically significant decrease at week 156 and at the last observation (Fig. 4a).

The mean change in serum LDL-cholesterol from baseline to each timepoint was −5.7 ± 12.8 mg/dL, −7.4 ± 27.6 mg/dL, −12.1 ± 28.8 mg/dL, −12.8 ± 30.4 mg/dL, −16.9 ± 26.3 mg/dL, −17.1 ± 35.0 mg/dL, −11.2 ± 21.0 mg/dL, and −11.1 ± 29.9 mg/dL, respectively, showing statistically significant decreases at weeks 52, 78, and 104 and at the last observation (Fig. 4b).

The observed serum P level significantly decreased from 5.12 ± 1.19 mg/dL at baseline to 4.40 ± 1.16 mg/dL at the last observation (Fig. 4c). The observed serum K level increased from 4.31 ± 0.84 mEq/L at baseline to 4.43 ± 0.70 mEq/L at the last observation, showing no significant change (Fig. 4d). The observed serum Na level significantly decreased from 138.4 ± 2.9 mEq/L at baseline to 137.3 ± 3.0 mEq/L at the last observation (Fig. 4e). The observed serum Cl level was 103.1 ± 3.1 mEq/L at baseline and 103.1 ± 3.3 mEq/L at the last observation, showing no significant change (Fig. 4f). The observed serum Ca level significantly increased from 8.91 ± 0.46 mg/dL at baseline to 9.24 ± 0.61 mg/dL at the last observation (Fig. 4g). The observed serum Alb level decreased from 3.45 ± 0.31 g/dL at baseline to 3.38 ± 0.41 g/dL at the last observation, showing no significant change (Fig. 4h).

Blood urea nitrogen (BUN) values from baseline to each timepoint did not change. (data not shown).

Spearman's correlation coefficients between patient satisfaction and each efficacy endpoint When assuming

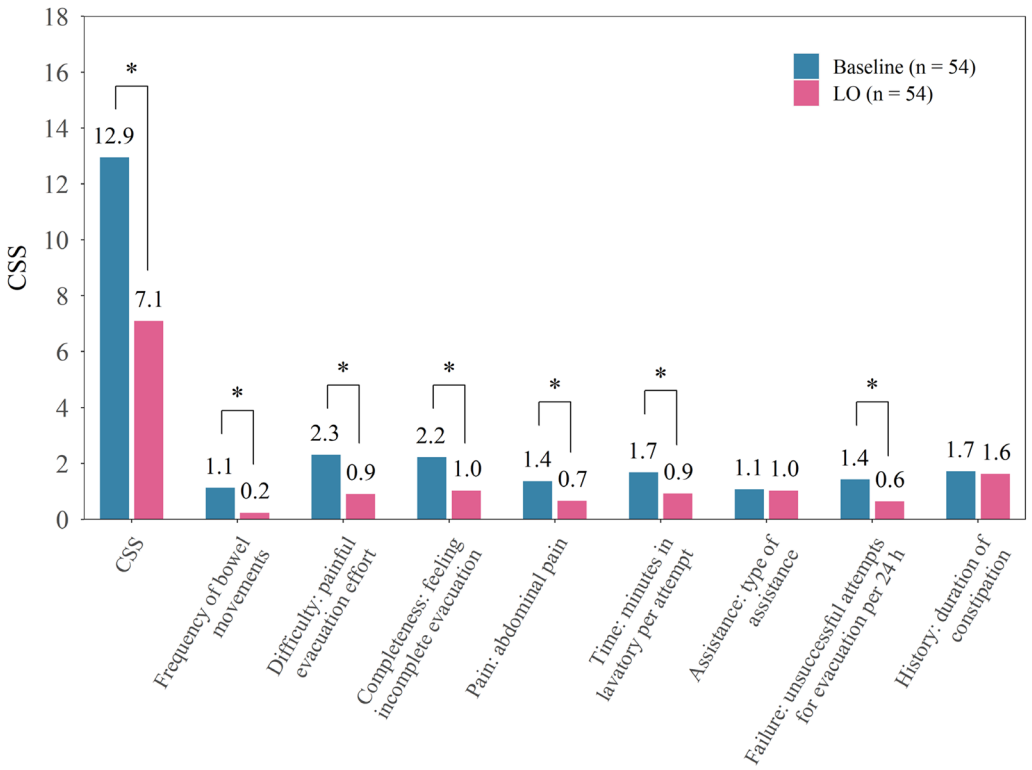

Fig. 3 Bar chart of the mean CSS and each component at each timepoint. CSS is a self-reported measure with a total score of 30 scores. *$p < 0.05$; Wilcoxon signed-rank test. LO stands for last observation

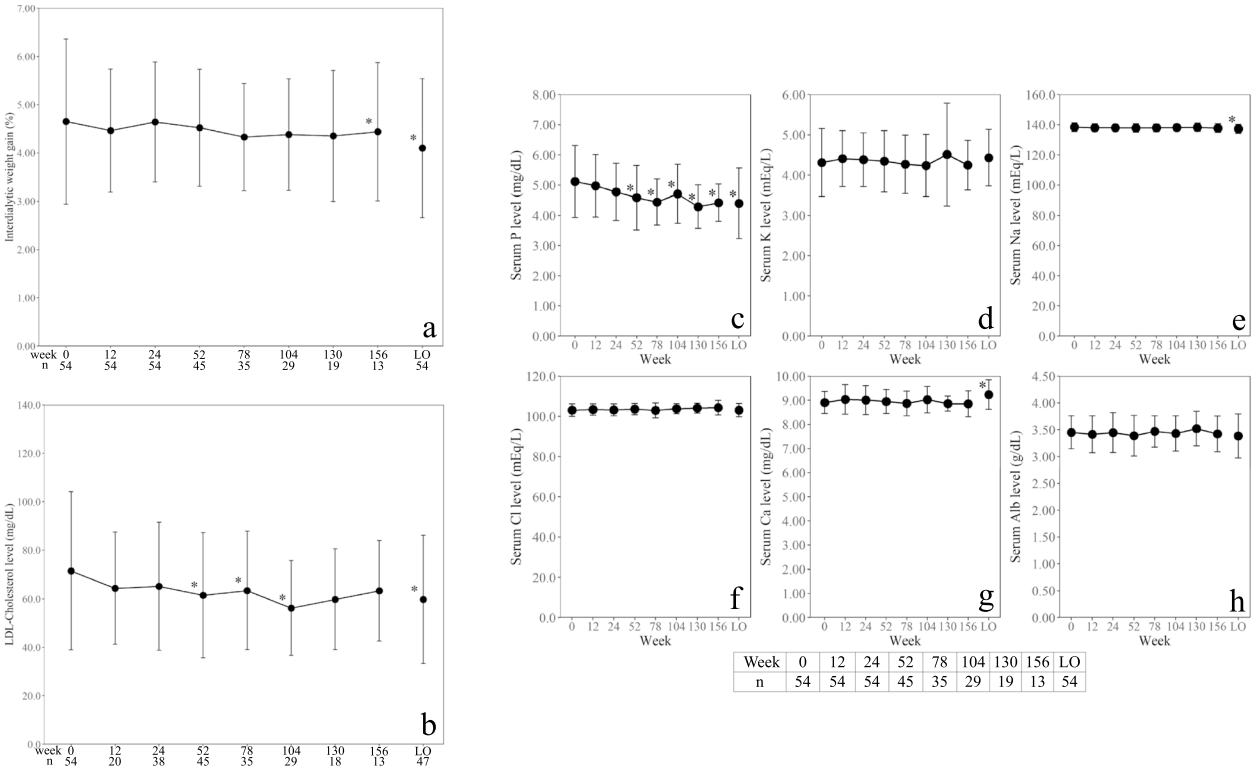

Fig. 4 Changes over time in the mean IDWG, serum LDL-cholesterol, P, K, Na, Cl, Ca, and Alb levels. Error bars represent the mean ± standard deviation. *$p < 0.05$; paired *t*-test. **a** IDWG; **b** serum LDL-cholesterol level; **c** serum P level; **d** serum K level; **e** serum Na level; **f** serum Cl level; **g** serum Ca level; and **h** serum Alb level. LO stands for last observation

that an absolute Spearman's correlation coefficient of 0.6 or greater indicates a strong correlation, the Spearman's correlation coefficient between patient satisfaction and the frequency of SBM was 0.634, 0.643, 0.815, and 0.803 at weeks 24, 78, 104, and 130, respectively, demonstrating a positive correlation. Spearman's correlation coefficient between patient satisfaction and the BSFS score was 0.608, 0.762, 0.647, 0.733, and 0.705 at weeks 52, 78, 104, 130, and 156, respectively, showing a positive correlation. Spearman's correlation coefficient between patient satisfaction and CSS was −0.773, −0.607, −0.776, −0.809, −0.809, and −0.618 at weeks 24, 52, 104, 130, and 156 and at the last observation, respectively, showing a negative correlation (Additional file 1: Table A1).

Furthermore, in case of assuming that an absolute MIC correlation coefficient of 0.6 or greater indicates a strong correlation, the MIC correlation coefficient between patient satisfaction and the frequency of SBM was 0.638 and 0.682 at weeks 104 and 130, respectively, showing a positive correlation. MIC correlation coefficient between patient satisfaction and BSFS was 0.621 and 0.656 at week 78 and at the last observation, respectively, showing a positive correlation. MIC correlation coefficient between patient satisfaction and CSS was 0.626 and 0.661 at weeks 130 and 156, respectively, showing a positive correlation (Additional file 1: Table A2).

Comparison of nutrition index between elobixibat responders and nonresponders The median change in the CONUT score from baseline to each timepoint was 0.0, 0.0, 1.0, 0.0, 1.0, 0.5, 1.0, and 0.0, respectively, showing a significant increase at weeks 12, 52 and 156 (Additional file 1: Table A3).

In the responders, the median change in the CONUT score from baseline to each timepoint was 0.0, −1.0, 0.0, 1.0, 0.0, 0.0, 1.0, and 0.0, respectively, showing no significant change. In the nonresponders, the median change in the CONUT score from baseline to each timepoint was 1.0, 0.5, 1.0, 0.5, 1.0, 1.0, 1.5, and 0.5, respectively, demonstrating a significant increase at weeks 130 and 156. The change was not significant at weeks 12, 24, 52, 78, or 104 or at the last observation. The change between the responders and nonresponders was not significant at any of the timepoints (Additional file 1: Table A4).

Subgroup analyses

For the mean change from baseline in the frequency of SBM, there was no significant change in the subgroup with a baseline CSS of < 10 and baseline CONUT score of 0–1, normal, whereas a significant change was demonstrated in the other subgroups. The median changes from baseline in the CSS and each component were generally similar among all subgroups, and there was no notable change.

Safety

The incidence of adverse events was 18.5% (10/54 patients; 14 cases). That of diarrhea was 18.5% (10/54 patients), abdominal pain was 3.7% (2/54 patients), and nausea was 1.9% (1/54 patients). All reported adverse events were assessed as related to elobixibat. No serious adverse event occurred, and all events were mild in severity (Table 2).

The proportion is the number of patients with an adverse event divided by number of patients in the total analysis population; MedDRA/J (ver.26.0)

Of the reported adverse events, six events resolved without treatment, seven events resolved after a reduction in the elobixibat dose, and one event abated after discontinuation of elobixibat. Elobixibat was discontinued in 3.7% of patients (2/54 patients). The reasons for discontinuation were improvement of symptoms and adverse events in one patient each.

Discussion

Constipation symptoms, which frequently occur in hemodialysis patients, are likely to persist for a prolonged period due to their inherent characteristics, and consequently their treatment may also be prolonged [6]. In recent years, the average age of patients undergoing hemodialysis has been increasing, with a corresponding increase in the incidence of constipation. In this study, data on the long-term efficacy and safety of elobixibat were collected from patients with a range of constipation symptoms [12]. The elderly aged 65 years or older accounted for 80% of the patient population, and the mean duration of dialysis exceeded 5 years. These factors appear to reflect the actual circumstances of elderly hemodialysis patients undergoing prolonged treatment. It was shown that in these patients, elobixibat maintained the improvement in constipation symptoms without reduction in the effect for a maximum of 240.0 weeks (median 104.6 weeks). The symptoms of constipation include not only a decrease in the number of bowel movements, but also hard stools, difficulty in defecation, and abdominal pain [14]. Elobixibat is useful for improving these constipation symptoms (CSS) in hemodialysis patients for an extended period, and patient satisfaction due to improved defecation was maintained.

The cause of constipation unique to hemodialysis patients may be their resistance to the desire to defecate due to anxiety over passing a bowel movement during hemodialysis [15]. Resisting a desire to defecate is known to reduce rectal sensation, which in turn leads to a loss of the desire to defecate. Unpredictable defecation timing can lead to severe anxiety and further limits activities of daily living [15]. Elobixibat has been shown to restore the desire to defecate [16] by decreasing rectal sensory thresholds due to the increase in bile acids [9] and can thus address the cause of constipation specific to hemodialysis patients. In addition, the time until the onset of SBM after administration has been reported to be almost constant [17]; thus, it is expected to eliminate the anxiety of not knowing when the desire to pass a stool might arise. In our study, elobixibat was administered before lunch (68.5%) or dinner (31.5%) after hemodialysis and the findings indicate that treatment can be continued for an extended period by controlling the onset of the desire to defecate during hemodialysis by controlling the administration timing of elobixibat.

It has been reported that hyperphosphatemia elevates the risk of cardiovascular death via vascular calcification [18], and a high IDWG in hemodialysis patients is associated with death [19]. Hence, strict phosphorus management and weight control contribute to improving the life expectancy of hemodialysis patients [20]. This study demonstrated that significant decreases in the serum P level and IDWG by elobixibat shown in the preceding study were maintained for an extended period. For IDWG, while there was a significant difference at the last evaluation point, unlike that in the preceding study [12], it did not improve at week 12. This can be attributed to the fact that there were many patients whose weight was well controlled in this study: baseline IDWG was 5.66% in the preceding study while it was as low as 4.65% in this study. Both improvement of constipation symptoms and long-term reductions in the serum P level and IDWG by elobixibat suggest that the usefulness

Table 2 Summary of adverse events and adverse drug reactions

Number of patients in the analysis population	Any	By severity		
n = 54	*n* (%)	Mild	Moderate	Severe
Adverse events*	10 (18.5)	10 (18.5)	0 (0.0)	0 (0.0)
Gastrointestinal disorders	10 (18.5)	10 (18.5)	0 (0.0)	0 (0.0)
Abdominal pain	2 (3.7)	2 (3.7)	0 (0.0)	0 (0.0)
Diarrhea	10 (18.5)	10 (18.5)	0 (0.0)	0 (0.0)
Nausea	1 (1.9)	1 (1.9)	0 (0.0)	0 (0.0)

*All reported adverse events were assessed as related to elobixibat

of elobixibat in managing phosphorus and controlling weight in hemodialysis patients is maintained for a prolonged period. Therefore, it is reasonable to expect that the life expectancy of hemodialysis patients will be improved.

Laxatives may affect electrolytes: There is a relationship between the abuse of laxatives and a decrease in blood K levels [21] and the risk of hypermagnesemia associated with magnesium oxide. Particularly in hemodialysis patients, renal regulation of the electrolyte balance is inadequate, thus electrolytes must be monitored for any sign of abnormalities. This study showed that long-term elobixibat treatment did not affect serum levels of K or Cl. There were significant changes in serum levels of Na and Ca at the last observation, but the degree of these changes was small, thus elobixibat was not found to have adversely affected them.

In this study, diarrhea, abdominal pain, and nausea were reported to be adverse drug reactions associated with elobixibat. These adverse drug reactions also occurred in a double-blind placebo-controlled study in patients with chronic constipation [10] and a report on the use of elobixibat in hemodialysis patients [12]. All the cases were mild and raised no new safety concerns regarding its long-term use in hemodialysis patients. The incidence of each of these adverse drug reactions is similar to that observed in our preceding study [12], and the incidence did not greatly change even when the study period was extended. Therefore, new adverse drug reactions to elobixibat are unlikely to occur from week 12 onward.

Of note, since this is a single-center study, site bias may have had an effect. This study scale is small, and these findings have little number of cases. In addition, the efficacy evaluation of elobixibat is the result of a retrospective analysis of medical records.

Conclusions

Elobixibat was shown to be an effective treatment for chronic constipation in hemodialysis patients and findings indicate that good bowel movement status and patient satisfaction were maintained even during long-term treatment of 24 weeks or more. Treatment also tended to improve dialysis-related laboratory values such as a decrease in serum P levels.

Abbreviations

Alb	Albumin
BSFS	Bristol stool form scale
BUN	Blood urea nitrogen
Ca	Calcium
CKD	Chronic kidney disease
Cl	Chlorine
CONUT	Controlling nutritional status
CSS	Constipation scoring system
IDWG	Interdialytic weight gain
K	Potassium
LDL	Low-density lipoproteins
MedDRA	Medical dictionary for regulatory activities
MIC	Maximal information coefficient
Na	Sodium
P	Inorganic phosphorus
SBM	Spontaneous bowel movements

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41100-024-00570-y.

Additional file 1.

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Author contributions

T.S. was responsible for planning, conducting, and reporting this work. T.S. and H.H. considered and agreed with manuscript results, discussion, and contributions. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets analyzed in the present study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted after being approved by the institutional review board, Maebashi Hirosegawa Clinic (accreditation no.: 16000033). The study was registered to the University Hospital Medical Information Network Clinical Trials Registry (UMIN-CTR) (registration number: UMIN000049865) on 22 December 2022. This study was carried out in accordance with the principles of the Declaration of Helsinki, Ethical Guidelines for Medical and Biological Research Involving Human Subjects, and the study protocol. Informed consent was obtained in writing or by the opt-out method. Blood and feces samples for the exploratory study were collected after receiving written informed consent.

Consent for publication

Not applicable.

Competing interests

T.S. has received funding from the following companies: Mochida Pharmaceutical Co., Ltd. and EA Pharma Co., Ltd. H.H. has no competing interests.

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References

1. Hanafusa N, Abe M, Joki N, Hoshino J, Taniguchi M, Kikuchi K, et al. Annual dialysis data report. JSDT Renal Data Registry. 2023;56:473–536.
2. Guidelines for Clinical Management of Bowel Movement Abnormalities. edited by The Japanese Gastroenterological Association. Nankodo. 2023: 32–3.
3. Yasuda G, Shibata K, Takizawa T, Ikeda Y, Tokita Y, Umemura S, et al. Prevalence of constipation in continuous ambulatory peritoneal dialysis patients and comparison with hemodialysis patients. Am J Kidney Dis. 2002;39:1292–9.

4. Guerrera MP, Volpe SL, Mao JJ. Therapeutic uses of magnesium. Am Fam Physician. 2009;80:157–62.
5. Locke GR 3rd, Pemberton JH, Phillips SF. AGA technical review on constipation. Am Gastroenterol Assoc Gastroenterol. 2000;119:1766–78.
6. Müller-Lissner SA, Kamm MA, Scarpignato C, Wald A. Myths and misconceptions about chronic constipation. Am J Gastroenterol. 2005;100:232–42.
7. Acosta A, Camilleri M. Elobixibat and its potential role in chronic idiopathic constipation. Ther Adv Gastroenterol. 2014;7:167–75.
8. Wingate DL, Krag E, Mekhjian HS, Phillips SF. Relationships between ion and water movement in the human jejunum, ileum and colon during perfusion with bile acids. Clin Sci Mol Med. 1973;45:593–606.
9. Bampton PA, Dinning PG, Kennedy ML, Lubowski DZ, Cook IJ. The proximal colonic motor response to rectal mechanical and chemical stimulation. Am J Physiol Gastrointest Liver Physiol. 2002;282:G443–9.
10. Nakajima A, Seki M, Taniguchi S, Ohta A, Gillberg PG, Mattsson JP, et al. Safety and efficacy of elobixibat for chronic constipation: results from a randomised, double-blind, placebo-controlled, phase 3 trial and an open-label, single-arm, phase 3 trial. Lancet Gastroenterol Hepatol. 2018;3:537–47.
11. Kamei D, Kamei Y, Nagano M, Mineshima M, Nitta K, Tsuchiya K. Elobixibat alleviates chronic constipation in hemodialysis patients: a questionnaire-based study. BMC Gastroenterol. 2020;20:26.
12. Shono T, Hyakutake H. Efficacy and safety of elobixibat in hemodialysis patients with chronic constipation: a retrospective study. Renal Replacement Therapy. 2020;6:21.
13. Ignacio J, de Ulíbarri A, de González-Madroño NGP, Villar PG, González B, Mancha A, et al. CONUT: A tool for controlling nutritional status. First validation in a hospital population. Nutr Hosp. 2005;20:38–45.
14. Miwa H, Uedo N, Watari J, Mori Y, Sakurai Y, Takanami Y, et al. Randomised clinical trial: efficacy and safety of vonoprazan vs. lansoprazole in patients with gastric or duodenal ulcers—results from two phase 3, non-inferiority randomised controlled trials. Aliment Pharmacol Ther. 2017;45:240–52.
15. Shono T, Hyakutake H. Treatment of chronic constipation in dialysis patients. J Jpn Assoc Dial Physician. 2023;2:212–20.
16. Ishikawa N, Fukuzawa M. Efficacy of elobixibat on defecation desire in patients with chronic constipation: a single-center, retrospective, observational study. Med Consult New Remedies. 2021;58:865–72.
17. Odaka T, Tominaga K. Uncontrolled, open-label pre-dinner administration of elobixibat in Japanese adults with chronic constipation: a retrospective chart review. Curr Ther Res Clin Exp. 2020;93: 100616.
18. Tentori F, Blayney MJ, Albert JM, Gillespie BW, Kerr PG, Bommer J, et al. Mortality risk for dialysis patients with different levels of serum calcium, phosphorus, and PTH: the Dialysis Outcomes and Practice Patterns Study (DOPPS). Am J Kidney Dis. 2008;52:519–30.
19. Foley RN, Herzog CA, Collins AJ; United States Renal Data System. Blood pressure and long-term mortality in United States hemodialysis patients: USRDS Waves 3 and 4 Study. Kidney Int. 2002; 62: 1784–90.
20. Taniguchi M, Fukagawa M, Fujii N, Hamano T, Shoji T, Yokoyama K, et al. Committee of Renal Data Registry of the Japanese Society for Dialysis Therapy. Serum phosphate and calcium should be primarily and consistently controlled in prevalent hemodialysis patients. Ther Apher Dial. 2013; 17: 221–8.
21. Cummings JH. Laxative abuse Gut. 1974;15:758–66.

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