Poster: TH-PO143

Optimal Initiation of Tenapanor Treatment Analyzed by Baseline Phosphate Binder Dose: A Sub-Analysis of the OPTIMIZE Study

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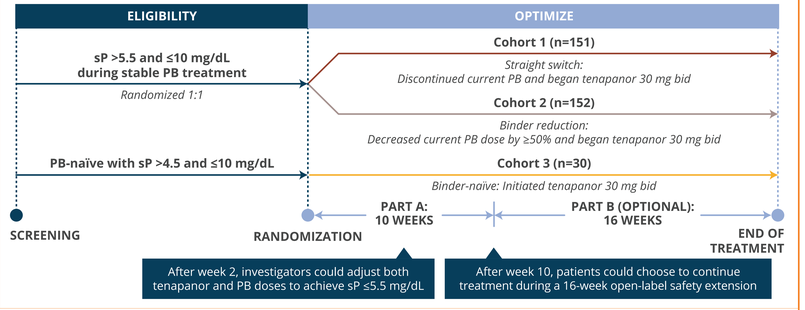
Background

- Tenapanor is a first-in-class, minimally absorbed phosphate absorption inhibitor that decreases paracellular phosphate absorption by selectively inhibiting intestinal sodium/hydrogen exchanger isoform 3.[1–3]
- Real-world data show that nearly 80% of patients on dialysis are unable to consistently maintain adequate control of serum phosphate (sP) for a 6-month period with the use of phosphate binders (PB) alone.[4]
- Tenapanor offers an alternative mechanism of action to PBs for control of sP in adult patients with chronic kidney disease on maintenance dialysis.[5,6]
- OPTIMIZE (NCT04549597) evaluated how to best manage hyperphosphatemia treatment in patients on dialysis using tenapanor.[6]
  - In this sub-analysis of OPTIMIZE, we evaluated sP control, pill burden, and quality of life with different strategies of tenapanor initiation among patients with high and low baseline PB dose.

Methods

- In the OPTIMIZE study, patients with sP >5.5 and ≤10 mg/dL while taking PBs were randomized to two cohorts 1:1 (**Figure 1**).[6]
  - In Cohort 1 (*Straight Switch*; n=151) patients stopped PBs and initiated tenapanor 30 mg twice a day.
  - In Cohort 2 (*Binder Reduction*; n=152) patients reduced PB dose by ≥50% and added tenapanor 30 mg twice a day.
- Patients with sP >4.5 and ≤10 mg/dL who had never taken PB therapy were enrolled in Cohort 3 (*Binder-Naïve*; n=30).
- The PB/tenapanor dose could be adjusted to achieve sP ≤5.5 mg/dL; dose up-titration for PBs was not allowed until week 2.
- A patient experience questionnaire was administered at the end of the 10-week treatment period.
- For the current analysis, patients in Cohort 1 and Cohort 2 were categorized into two groups based on phosphate-binder dose at baseline: Low phosphate binder (LPB; ≤6 pills/day) and high phosphate binder (HPB; >6 pills/day).
  - sP response during Part A (defined as sP reduction ≥1.2 mg/dL at ≥2 of 3 measurements) was evaluated at weeks 1–4 (early sP response) and at weeks 6–10 (late sP response) of treatment.

Figure 1. OPTIMIZE Study Design[a]



[a]If patients were taking an odd number of PB pills, they decreased by more than 50%. For example: 3 pills were decreased to 1; 5 pills were decreased to 2.
bid, twice a day; PB, phosphate binder; sP, serum phosphorus.

Results

Patients

- Overall, 87 HPB patients and 60 LPB patients were randomized to Cohort 1 (Straight Switch) while 93 HPD and 55 LPB were randomized to Cohort 2 (Binder Reduction). The 8 randomized patients (4 per cohort) whose daily PB pill number at baseline was not available were excluded from this analysis.
- Baseline demographics and characteristics were generally well balanced between baseline PB dose groups within each tenapanor initiation strategy cohort (**Table 1**).

Table 1. Baseline Demographics and Disease Characteristics (Full Analysis Set)[a]

	Cohort 1 (*Straight Switch*)		Cohort 2 (*Binder Reduction*)	
	HPB (N=87)	LPB (N=60)	HPB (N=93)	LPB (N=55)
Mean age, years (SD)	51.2 (11.2)	54.2 (11.0)	53.7 (11.4)	52.6 (13.0)
Female, n (%)	28 (32.2)	15 (25)	27 (29)	23 (41.8)
Race, n (%)				
Black or African American	33 (37.9)	33 (55.0)	44 (47.3)	24 (43.6)
White	38 (43.7)	24 (40)	35 (37.6)	26 (47.3)
Asian	10 (11.5)	2 (3.3)	2 (2.2)	1 (1.8)
Native American or Alaskan	2 (2.3)	1 (1.7)	4 (4.3)	2 (3.6)
Native Hawaiian or Pacific Islander	2 (2.3)	0 (0)	2 (2.2)	2 (3.6)
Other/Unknown	2 (2.3)	0 (0)	6 (6.5)	0 (0)
Mean BMI, kg/m² (SD)	33.2 (9.0)	32.0 (7.9)	32.2 (7.6)	32.0 (9.4)
Duration since first dialysis at baseline, months (SD)	61.2 (52.0)	52.9 (54.2)	62.8 (50.5)	48.2 (47.6)
Type of PB taken at screening, n (%)				
Sevelamer binder	35 (40.2)	20 (33.3)	35 (37.6)	22 (40)
Calcium-based binder	16 (18.4)	7 (11.7)	15 (16.1)	5 (9.1)
Iron-based binder	12 (13.8)	27 (45)	18 (19.4)	23 (41.8)
Other non-sevelamer binder	2 (2.3)	4 (6.7)	1 (1.1)	3 (5.5)
Combination	22 (25.3)	2 (3.3)	24 (25.8)	2 (3.6)
Median PB dose per day, pills (range)	9 (7–22)	6 (3–6)	9 (7–23)	6 (3–6)
Mean sP, mg/dL (SD)	7.10 (1.02)	7.14 (1.09)	6.95 (1.09)	7.52 (1.13)

Data are mean (SD) unless otherwise noted. Baseline is the last observed measurement collected before the first dose of tenapanor.
[a]The full analysis set includes the planned treatment group.
HPB, high phosphate binder; LPB, low phosphate binder; PB, phosphate binder; SD, standard deviation; BMI, body mass index; sP, serum phosphate.

Serum Phosphate Response

- Early sP response was achieved by 24.1% and 47.3% of HPB patients in Cohort 1 (*Straight Switch*) and Cohort 2 (*Binder Reduction*), respectively; and by 38.3% and 47.3% of LPB patients in Cohort 1 and Cohort 2, respectively (**Figure 2A**).
- Overall, based on observed data, 57%–80% of early sP responders continued to achieve the late sP response (**Figure 2B**).

Mean Serum Phosphate by Week

- Both cohorts achieved consistent sP control (sP ≤5.5 mg/dL) throughout the 10-week treatment period by adding tenapanor, independent of how tenapanor was initiated (**Figure 3**).
- A reduction in sP from baseline of ~1 mg/dL was observed throughout the 10-week treatment period in both cohorts following the addition of tenapanor (**Figure 3**).

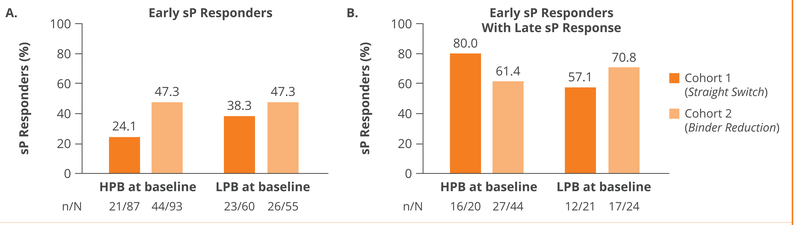
Pill Burden

- At week 4, the median sP-lowering pill number reduction (including tenapanor) was 7 and 4 pills/day for HPB patients in Cohort 1 (*Straight Switch*) and Cohort 2 (*Binder Reduction*), respectively; it was 2.5 and 1 pill/day for LPB patients in Cohort 1 (*Straight Switch*) and Cohort 2 (*Binder Reduction*), respectively. Pill burden increased slightly through week 10.

Quality of Life

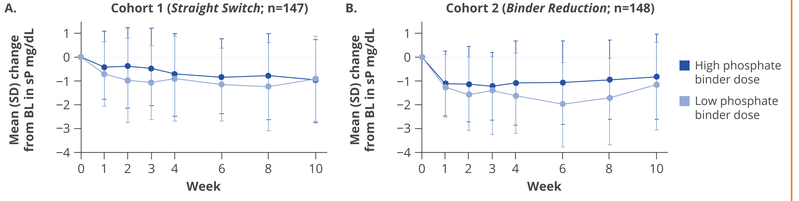
- Of the 243 patients in Cohort 1 (*Straight Switch*; n=121) and Cohort 2 (*Binder Reduction*; n=122) who completed the patient experience questionnaire, 205 patients (84.4%) indicated that their phosphate management routine had improved (minimally, much, or very much), while 8 (3.3%) felt that it had worsened (minimally or very much).
  - A similar proportion of patients in each cohort indicated an improvement in their routine (Cohort 1 [*Straight Switch*], 83.5%; Cohort 2 [*Binder Reduction*], 85.2%) or a worsening in their routine (3.3% for both).
- Of the 213 patients in Cohort 1 (*Straight Switch*) and Cohort 2 (*Binder Reduction*) who changed their perspective of the phosphate management routine during the treatment period, most selected the change in medication burden (either daily dose frequency, pill size, or number of pills) or the change in the frequency of bowel movements as the primary reason for their changed perspective (**Figure 4**).
- Most patients in both cohorts (Cohort 1 [*Straight Switch*], 67.8%; Cohort 2 [*Binder Reduction*], 70.5%) indicated that it was much less or somewhat less difficult to control their phosphate during the study than before the study.

Figure 2. sP Response by Cohort and Baseline PB Pill Number



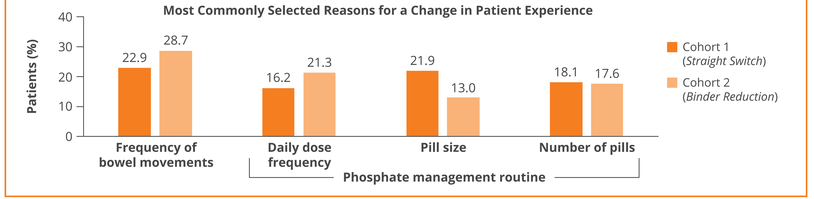
HPB, high phosphate binder; LPB, low phosphate binder; PB, phosphate binder; sP, serum phosphate.

Figure 3. Change in sP From Baseline Up to Week 10



BL, baseline; SD, standard deviation; sP, serum phosphate.

Figure 4. Top 4 Reasons for Change in Perception of Phosphate Management Routine



Conclusions

Both cohorts experienced improved sP control and quality of life, and a reduction in pill burden.

HPB patients may have better early sP control by initiating tenapanor with a 50% reduction in PB dose than completely switching to tenapanor, while LPB patients appeared to have similar early sP control regardless of tenapanor initiation strategy.

Disclosures

Stuart M. Sprague receives research grants from and is a consultant for Ardelyx, Inc. Jill M. Meyer have no commercial interests or conflicts of interest to declare. David P. Rosenbaum, Susan Edelstein, Yang Yang, Suling Zhao, and David M. Spiegel are employees of Ardelyx, Inc.

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