A real-world retrospective study evaluating a Team-based patient Engagement Approach to selexipag initiation and Maintenance in Pulmonary Arterial Hypertension (TEAM PAH)

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Introduction

- Pulmonary arterial hypertension (PAH) is a complex disease that leads to progressive right ventricular failure[1]
- Selexipag is an oral prostacyclin receptor agonist that delays disease progression and reduces the risk of hospitalization for PAH (GRIPHON trial)[2,3]
- Selexipag is typically initiated and titrated in 200 µg twice daily dose increments, usually at weekly intervals, to an individualized maintenance dose (IMD)[3]
  - Side effects associated with the prostacyclin pathway occur more frequently during the dose adjustment phase especially when the incremental dose increase is the highest
- Drug titration and maintenance can be hindered by side effects common to prostacyclin pathway agents, highlighting the need for multidisciplinary collaboration, frequent patient contact, individualized dosing, and symptom management[4]

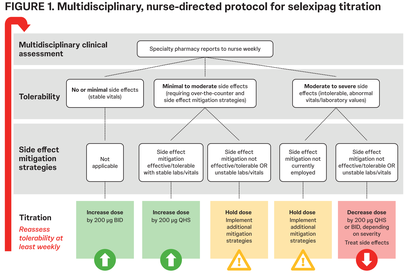
Objective

- To describe real-world oral selexipag dosing patterns and persistence at an expert center in California, USA, that uses a site-specific, multidisciplinary, nurse-directed protocol

Methods

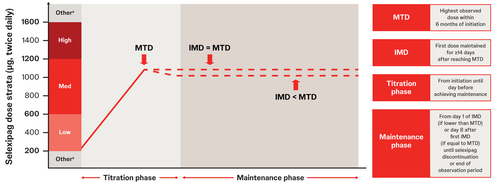
- This was a retrospective chart review of patients with PAH initiated on oral selexipag between January 1, 2016, and March 31, 2023, at a single center using a multidisciplinary, nurse-directed protocol entailing frequent follow-up to individually manage side effects and tailor selexipag titration (**Figure 1**)
- Dosing patterns and persistence were reported during follow-up, which spanned from selexipag initiation (i.e., the index date) to the earliest of 14 months after index, the last assessment, lung transplant, or death
- Study definitions for titration and dosing were adapted from SelexiPag: tHe usErs dRug rEgistry (SPHERE) (**Figure 2**)[5]
- Statistical analysis was conducted as follows:
  - Patient characteristics and dosing patterns were summarized using descriptive statistics
  - Kaplan–Meier analysis was used to describe time to maintenance and persistence
  - Factors associated with selexipag discontinuation were identified via Cox regression analysis

FIGURE 1. Multidisciplinary, nurse-directed protocol for selexipag titration



BID, twice daily; **QHS**, once daily at bedtime.

FIGURE 2. Study definitions adapted from SPHERE[5]



*The 'other' dose category includes doses <200 or >1600 µg twice daily.
IMD, individualized maintenance dose; **Med**, medium; **MTD**, maximum tolerated dose; **SPHERE**, SelixiPag: tHe usErs dRug rEgistry.

Results

Baseline characteristics

- A total of 200 patients initiated oral selexipag and were included in this analysis (**Figure 3**)

FIGURE 3. Baseline demographic and clinical characteristics

Study population	Race/ethnicity[a]	PAH[a]	Comorbidities[a]
200 patients	55% White	Drug/toxin induced[b] 42%	Hypertension 35%
70% female	21% Hispanic/Latino	Idiopathic 16%	Obstructive sleep apnea 29%
	10% Asian	CTD 12%	Coronary artery disease 22%
Median age 52 years	9% Black/African American	60% WHO FC III/IV PAH	Obesity 18%
		Median 1.5 years from diagnosis[c]	41% had a history of methamphetamine use
12% transitioned from other PPA → oral selexipag		71% received PAH-specific triple therapy (selexipag + ERA + PDE5i)	

[a]Categories shown for race/ethnicity, PAH etiology, and comorbidities represent the most common and are not mutually exclusive. [b]Drug- or toxin-induced etiology included drugs such as methamphetamine and fenfluramine/phentermine. [c]Diagnosis date was unknown for 26% of patients.
CTD, connective tissue disease; **ERA**, endothelin receptor antagonist; **PAH**, pulmonary arterial hypertension; **PDE5I**, phosphodiesterase type 5 inhibitor; **PPA**, prostacyclin pathway agent; **WHO FC**, World Health Organization functional class.

Oral selexipag dosing patterns

- Over a median period of 14 months, 178/200 (89%) patients achieved maintenance (median IMD, 900 µg twice daily), with relatively even distribution across low-, medium-, and high-dose strata (**Table 1**)
- During titration, patients had a median of 2.5 dose escalations, with substantial variability among patients in the time between dose escalations (median, 14.0 days [interquartile range 9.5, 21.2]) (**Table 1**)

TABLE 1. Oral selexipag dosing patterns during the titration and maintenance phases

Dosing pattern	Titration phase (n=200)	Maintenance phase (n=178)
Selexipag dose strata, n (%)[a,b]	MTD	IMD
Low (200 to <600 µg twice daily)	43 (22%)	40 (23%)
Medium (600 to <1200 µg twice daily)	76 (38%)	62 (35%)
High (1200 to 1600 µg twice daily)	75 (38%)	71 (40%)
Other (<200 or >1600 µg twice daily)	6 (3%)	5 (3%)
No. of dose escalations		
Mean [median] (IQR)	2.9 [2.5] (1.0, 4.0)	1.7 [1.0] (1.0, 2.0)
Patients with ≥1 dose escalation, n (%)	174 (87%)	160 (90%)
Time between dose escalations, days		
Mean [median] (IQR)	17.7 [14.0] (9.5, 21.2)	57.9 [43.2] (18.5, 83.1)
No. of step-downs		
Mean [median] (IQR)	0.2 [0.0] (0.0, 0.0)	0.9 [1.0] (0.0, 1.0)
Patients with ≥2 step-downs, n (%)	6 (3%)	42 (24%)
Time between step-downs, days		
Mean [median] (IQR)	36.5 [13.0] (6.0, 49.6)	70.2 [43.0] (24.5, 107.4)
Patients who discontinued selexipag, n (%)[c]	20 (10%)	30 (17%)

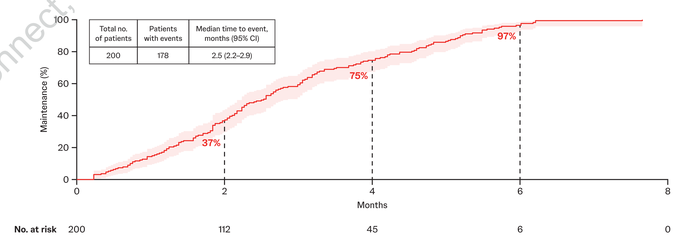
[a]MTD is reported for the titration phase and IMD for the maintenance phase. [b]Percentages do not add to 100% due to rounding. [c]Two patients died during the titration phase and therefore did not reach maintenance.
IMD, individualized maintenance dose; **IQR**, interquartile range; **MTD**, maximum tolerated dose.

- Median time to maintenance based on Kaplan–Meier analysis was 2.5 months (95% confidence interval, 2.2–2.9) (**Figure 4**)

Oral selexipag persistence

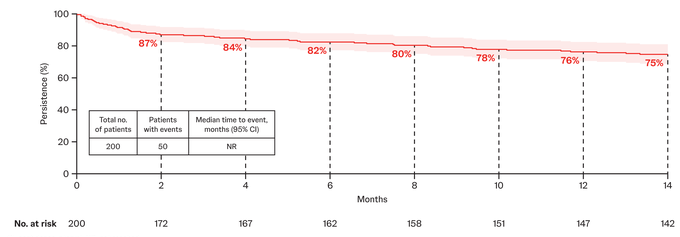
- Persistence was 87% at month 2 and 76% at month 12 in the overall sample (**Figure 5**)
  - Among those achieving maintenance, persistence at month 12 was 85%
- The highest rate of discontinuation occurred within 2 months of treatment initiation, and most discontinuations were due to an inability to tolerate treatment
- Over the study period, 91% of patients experienced adverse events (AEs), with 43% experiencing severe AEs
- The most common AEs were headache (63%), muscle pain (38%), nausea (35%), and diarrhea (35%)
- Compared with patients who continued treatment, a higher proportion of those who discontinued had chronic obstructive pulmonary disease at initiation, as well as AEs that were categorized as severe while using selexipag (**Table 2**)

FIGURE 4. Kaplan–Meier plot for time to maintenance



CI, confidence interval.

FIGURE 5. Kaplan–Meier plot for persistence during the observation period



CI, confidence interval; **NR**, not reached.

TABLE 2. Factors associated with oral selexipag discontinuation

Parameter	Patients who discontinued selexipag (n=50)	Patients who did not discontinue selexipag (n=150)	Hazard ratio (95% CI)[a]	*P*-value[a]
COPD at initiation, n (%)	8 (16%)	10 (7%)	2.2 (1.0–4.7)	<0.05
No. of different AEs				
Mean [median] (IQR)	2.3 [2.0] (1.0, 3.0)	2.8 [3.0] (1.3, 4.0)	0.7 (0.6–0.9)	<0.001
Severe AEs, n (%)	30 (60%)	55 (37%)	3.8 (2.0–7.3)	<0.001

[a]A Cox proportional hazards backward selection model was fit to identify demographic and clinical characteristics associated with oral selexipag discontinuation during the entire observation period. Variables identified as statistically significant (*P*<0.05) are reported here.
AE, adverse event; **CI**, confidence interval; **COPD**, chronic obstructive pulmonary disease; **IQR**, interquartile range.

Limitations

- Due to the retrospective study design, analysis relied on routinely collected clinical data, and a number of patients had missing data of interest (e.g., risk parameters)
- The study findings may not be generalizable to patients with PAH outside of this expert center in California

Conclusions

- Using a multidisciplinary, nurse-directed protocol enabled the majority of patients who initiated oral selexipag to reach their IMD and remain on treatment
- Time between dose titrations was often >2 weeks (longer than protocolized in the GRIPHON trial[2]), suggesting a slower, individualized titration schedule with side effect management may promote persistence
- Consistent with the findings from GRIPHON[2] and SPHERE,[5] median IMD was 900 µg twice daily. These data support titrating to patient tolerability and maximize the potential to treat at an efficacious dose and that titration to higher doses is not necessary to achieve a therapeutic dose
- Most discontinuations occurred within 2 months of treatment initiation, highlighting the importance of greater clinical engagement in the early stages of selexipag treatment

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Disclosures

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Pulmonary Hypertension

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An interim analysis of these results was presented at the ATS 2025 International Conference; San Francisco, CA, USA; May 16–21, 2025

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