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A Real-World Multidisciplinary Approach to Successful Patient Adherence and Maintenance on Oral Selexipag Therapy

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Background: Selexipag is an oral selective prostacyclin receptor agonist approved in WHO Group 1 pulmonary arterial hypertension (PAH), with recommended weekly uptitration of 200 mcg BID to a goal of 1600 mcg BID. The side effect profile limits optimization and may result in medication discontinuation. Indeed, 87% of subjects in the GRIPHON trial had ≥ 1 prostacyclin-associated adverse event. Our center developed a nurse directed process to initiate and uptitrate selexipag to recapitulate the success of the GRIPHON trial. Our protocol includes weekly communication with the patient/caregiver and specialty pharmacy to discuss side effects, adherence, and medication administration. To improve retention, we developed a standardized assessment tool by which nurses can modify the titration schedule based on patient needs and severity of side effects. We employed proactive strategies to mitigate side effects and ensure patient tolerance prior to dose escalation, including pharmacologic and non-pharmacologic interventions that target common prostacyclin related issues including diarrhea, GERD, headache, jaw pain, and myalgia. We sought to compare the results of our nurse directed protocol to the adherence observed in the GRIPHON trial.

Methods: We performed retrospective chart review of all patients initiated on oral selexipag at UCSF Medical Center from January 2016 to April 2019. Patients were categorized based on PAH etiology and maximum tolerated selexipag dose. Statistical analyses were performed using Student's T-tests, ANOVA, and Chi2 tests.

Results: Of the 129 patients who initiated selexipag, 69% were female, 53% were Caucasian, mean age was 53 years ± 13.81, and the most common PAH subtypes were methamphetamine-associated PAH (43%); and connective tissue disease PAH (22%) (Table 1). The mean maximum tolerated total daily dose (TDD) of selexipag was 1917 mcg (range 400-4800 mcg), and 39% were on a TDD > 2400 mcg, similar to 43% of patients in the GRIPHON trial (p=0.39). In total, 76% of our cohort remained on selexipag therapy, similar to the GRIPHON retention rate of 77% (p=0.74). Approximately 30% of patients transitioned to selexipag from another form of prostacyclin therapy. Patients who transitioned to selexipag from another prostacyclin tolerated higher doses of selexipag than in prostacyclin naïve patients (p=0.002). We found no differences in rate of discontinuation or dose tolerated when categorized by race, age, gender, or PAH subtype.

Conclusions: Our multidisciplinary team developed an effective, individualized approach to managing oral prostacyclin therapy resulting in high adherence, including in those with a history of methamphetamine use. Our findings from this single center real-world study suggest that a nurse-directed protocol can achieve similar results as in a randomized trial, even in high-risk groups. The difference in dose tolerability between prostacyclin experienced and naïve patients was statistically significant and is clinically important. Patients who have not previously been on prostacyclin therapy may benefit from patient centered titration, intensive side effect management, and close monitoring. Additional studies are needed to better understand the real world factors affecting adherence to and continuation of prostacyclin therapies.

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Figure 1. Table 1: Demographics and clinical characteristics

	All subjects (n= 129)
Age (years)	53 ± 13.81
Female	89 (69%)
Male	40 (31%)
Caucasian	69 (53 %)
African American	17 (13%)
Latino	26 (20%)
Asian	15 (12%)
Other race	2 (2%)
PAH Etiology	
Methamphetamine associated	55 (43%)
CTD	28 (22%)
Idiopathic	18 (14%)
ACHD	14 (11%)
Other	14 (11%)
Clinical Characteristics	
Prostacyclin naïve	47 (36%)
Currently on selexipag	98 (76%)

* Data are presented as mean ± SD or numbers (percent).
† Abbreviations: CTD, connective tissue disease; ACHD, adult congenital heart disease