Abstract: P3671

Selexipag dosing and titration in the first 500 patients enrolled in SPHERE (SelexiPag: tHe UsErs dRug rEgistry)

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Pulmonary Hypertension

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Introduction: SPHERE is an ongoing US-based, multicentre, prospective, registry collecting data on use of the oral selective IP prostacyclin receptor agonist selexipag in real-world settings. Here, we report selexipag dosing and titration in the first 500 patients. Methods: SPHERE, initiated in November 2016, will enrol 800 patients newly initiated on or already treated with selexipag at enrollment who have a documented titration regimen. Patients are followed for up to 18 months. Patients were considered "newly initiated" on selexipag if they were enrolled in SPHERE 60 days after starting selexipag and were considered "previously initiated" if they enrolled >60 days after starting selexipag. The highest dose is the maximum dose reached during up-titration within 6 months since initiation. Selexipag "maintenance dose" is defined as the first dose received for 14 days without interruption or change; "titration speed" is defined as the highest dose reached within the first 6 months after initiation divided by the time (in weeks) to reach it.

Results: The data cut-off for this analysis was December 20, 2018. Most patients had Group 1 pulmonary hypertension (PH) (95.4%), which was primarily idiopathic (49.6%) or connective tissue disease associated (26.0%). At selexipag initiation 49.8% of patients had functional class III symptoms. At the time of selexipag initiation, 19.2% of patients were on PH therapy containing a prostacyclin pathway agent (PPA) (8.5% with a parenteral PPA). The median maintenance dose of selexipag was 1200 µg BID (IQR: 800–1600 µg BID) and the median time to reach it was 8.1 wks (IQR: 5.3–11.0 wks). Low (=400 µg BID), medium (600–1000 µg BID), and high (=1200 µg BID) maintenance doses were attained by 15.1%, 30.8%, and 49.5% of patients, respectively (and in 23.2%, 31.2%, and 36.2%, respectively, in GRIPHON). The median titration speed was 175 µg BID/wk (IQR: 110.5–195.3 µg BID/wk), slower than the protocol-outlined 200 µg BID/wk in GRIPHON. In SPHERE, most patients titrated at speeds <200 µg BID/wk, regardless of whether they were newly (175 µg BID/wk; IQR 118.6, 195.3) or previously (175 µg BID/wk; IQR 109.8, 195.3) initiated. As expected, more patients discontinued due to adverse events in the newly (29.0%) versus previously (14.1%) initiated groups. The most common adverse events leading to selexipag discontinuation were worsening pulmonary hypertension (2.2%), headache (2.0%), myalgia (1.4%), and nausea (1.0%).

Conclusion: The median maintenance selexipag dose in SPHERE was 1200 µg BID. While the median titration speed was 175 µg BID/wk, there was marked variation and the vast majority of patients titrated slower than 200 µg BID/wk. No new safety signals were observed.
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