Characteristics and clinical course of the first 500 patients (pts) from SPHERE (SelexiPag: the users Drug Registry) receiving selexipag in real-world clinical practice

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Background: SPHERE is a US, multicentre, prospective registry collecting real-world data from pts with pulmonary arterial hypertension (PAH) treated with selexipag, a selective oral IP prostacyclin receptor agonist.

Methods: SPHERE (planned N=800) included newly initiated (NI, receiving selexipag ≤60 days) and previously initiated (PI) pts. We describe disease characteristics, selexipag dose and clinical course of the first 500 pts and risk assessment based on REVEAL 2.0 risk calculator and COMPERA risk assessment strategy.

Results: Disease characteristics at initiation were: 75.0% female, median age 61.0 years, idiopathic etiology (49.2%) or associated with connective tissue disease (26.4%). Pts were mostly WHO functional class (FC) II (31.0%) or III (49.6%) (unknown for 9.2%). Median time from PAH diagnosis to selexipag initiation was 3.4 years. Of the first 500 pts enrolled, 138 (28%) were NI and 362 (72%) were PI; characteristics were consistent between NI and PI.

Risk classification at initiation differed depending on method used: with REVEAL 2.0, low/intermediate/high risk were 41.8%/29.6%/28.6% (38.4%/26.1%/35.5% for NI and 43.1%/30.9%/26.0% for PI, respectively) and with COMPERA were 22.0%/67.2%/9.6% (13.8%/73.2%/10.9% for NI and 25.1%/64.9%/9.1% for PI), respectively. Note, missing variables in real-world registry data may affect risk assessment.

In both cohorts, median individualised maintenance dose was 1200 µg twice daily (NI 1000 µg, PI 1200 µg); median time to individualised maintenance dose was 8.1 weeks. Median treatment duration was 21.7 months (17.7 months NI, 25.8 months PI). Overall, 32.4% of pts discontinued selexipag (46.4% NI, 27.1% PI), most commonly (22.8%) for adverse events (AEs) (34.8% NI, 18.2% PI). Of note, disease progression is classified as an AE. No selexipag-related deaths were reported.

At 18 months, WHO FC improved/remained stable in the majority of pts (205/235, 87%; improved, 24%; stable, 63%), but worsened in 12.8% of pts. At 18 months, the majority of pts had improved/stable risk by REVEAL 2.0 (265/334, 79% [improved, 22%; stable, 57%]) and by COMPERA (255/316, 81% [improved, 23%; stable, 58%]). This was consistent for NI and PI.

For both risk assessment tools higher risk was associated with increased risk of death. With REVEAL 2.0, risk of death was 2.9 and 9.3 times higher for intermediate and high risk, respectively vs low risk. Similarly with COMPERA, risk of death was 3.2 and 11.4 times higher in intermediate and high risk, respectively vs low risk.

Conclusions: Of the first 500 pts in SPHERE, the vast majority were prevalent PAH cases in FC II or III. Around one-quarter of pts had improved FC and/or risk; the majority of pts remained stable risk. Higher risk was associated with increased mortality risk. Over 50% of pts completed 18 months of selexipag. Discontinuations
were most commonly for AEs and/or PAH progression.