Early experience with selexipag for the treatment of adults with pulmonary arterial hypertension associated with congenital heart disease

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Funding Acknowledgement: Type of funding source: Other. Main funding source(s): Actelion Pharmaceuticals

Background: Recently, selexipag, a new orally available and selective prostacyclin receptor agonist, has become available for treatment of pulmonary arterial hypertension (PAH), but experience in patients with PAH associated with congenital heart disease (CHD) is limited to patients with closed defects.

Purpose: We present our early multi-centre experience using selexipag in the heterogeneous PAH-CHD population.

Methods: We prospectively evaluated adults with PAH-CHD from five PAH-CHD expert centres who were treated with selexipag. Patients were titrated to highest tolerable individualized dose (200 to 1,600 μg twice daily), after which patients entered the maintenance phase. Data on functional class (FC), 6-minute walk distance (6MWD), imaging and biochemical (N terminal pro-brain natriuretic peptide [NT-proBNP]) parameters were collected.

Results: Thirty-four patients (age 43±14 years, 56% female, 60% Eisenmenger syndrome, 22% Down syndrome, 60% dual PAH therapy) were started on selexipag. All patients experienced at least 2 side effects during the initial uptitration phase. Most side effects were manageable and diminished after reaching the maintenance dose, but eight patients discontinued treatment due to side effects during the titration phase. The most frequent side effects were consistent with the known side effects of prostacyclins, including headache, nausea, diarrhoea and jaw pain. Majority (68%) of patients reached lower maintenance doses of 200–600 μg. At 12 months, FC improved in three patients and remained unchanged in the others. 6-minute walk distance remained stable throughout follow-up (475 to 470 m; p=n.s.) in patients who remained on-treatment compared to patients who stopped selexipag (485 to 370 m). NT-proBNP levels remained stable in patients on-treatment (520 to 600 ng/L) but worsened in patients who stopped (700 to 1000 ng/L). One patient died during follow-up from end-stage heart failure.

Conclusion: There is a promising role for selexipag in the treatment of adults with PAH-CHD. However, based on our experience, the use is challenging due to complexity in dosing and side effect profiles, which limit patients' tolerability and acceptance during the titration phase.