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Survival in Pulmonary Arterial Hypertension for 669 Patients Treated with Selexipag in Clinical Practice: Insights From EXPOSURE

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Relevant Financial Relationship Disclosure Statement

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Stefan Söderberg

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I **will not** discuss off-label use and/or investigational use of any drugs or devices.

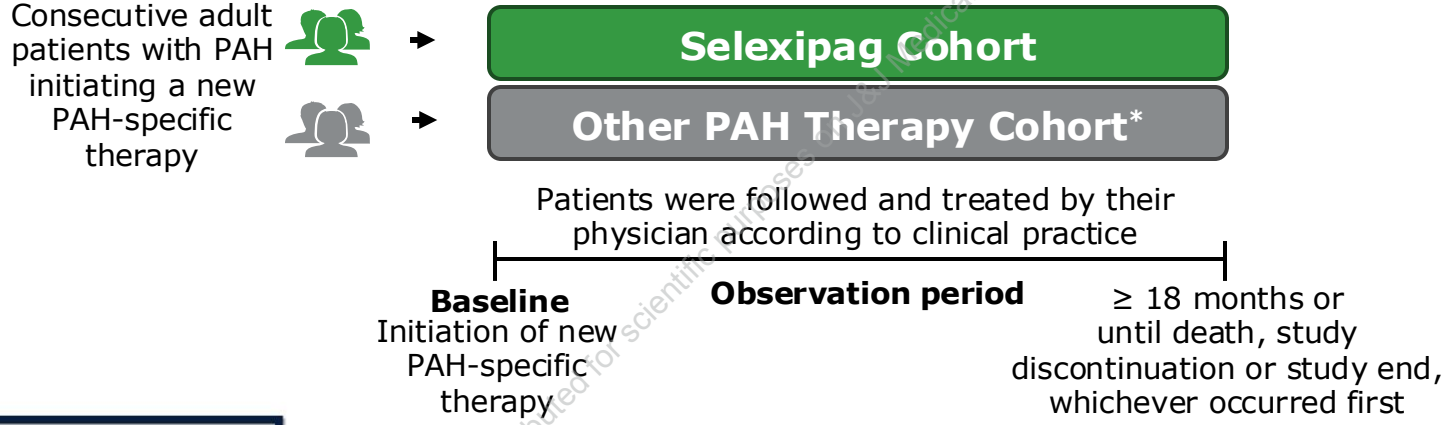
Background

- Evaluating treatment effect on survival in PAH presents challenges in RCTs primarily because the disease is rare and progressive in nature
  - High patient numbers are needed to demonstrate a treatment effect
  - PAH patients typically experience clinical deterioration prior to death, and there is an unequivocal duty of care to provide "rescue therapy" in those who deteriorate
- Real-world studies can be used to understand treatment effect on survival
- EXPOSURE is an observational study specifically designed to further describe the safety profile of selexipag, including patient survival

PAH: pulmonary arterial hypertension; RCT: randomized controlled trial.

EXPOSURE study design

- EXPOSURE (EUPAS19085) is an ongoing, observational, multicenter, prospective study of PAH patients initiating a PAH-specific therapy in Europe and Canada, with recruitment started in 2017



*Allowed therapies were: endothelin receptor antagonists, phosphodiesterase 5 inhibitors, soluble guanylate cyclase stimulators, and prostacyclin and its analogs.

Aim

To perform **comparative survival analyses** between treatment with selexipag versus other PAH therapies, using data from EXPOSURE

Methods

- In real-world studies, treatment choice is not random, which can introduce bias and lead to potential misinterpretation of raw comparisons
- For this reason, propensity score weighting was applied to address differences between cohorts*, with the selexipag cohort as reference
- Treatment effect of selexipag was assessed through comparison of all-cause death between the two cohorts, expressed as a mortality rate ratio (weighted Poisson model)

*Data cut off date: November 2022.

Baseline characteristics (1)

Baseline variable	Unweighted		Propensity Score Weighted*	
	Selexipag N=698	Other PAH therapy N=1411	Selexipag N=658‡	Other PAH therapy N=612‡
Age, mean (SD)	57.6 (15.7)	62.1 (14.8)	57.3 (15.7)	54.0 (9.7)
Female, n (%)	495 (71)	954 (68)	465 (71)	469 (77)
Time since diagnosis, n	650	1367	658	612
Median (Q1, Q3), years	2.0 (0.7, 6.3)	0.0 (0.0, 0.5)	1.9 (0.7, 6.3)	2.0 (0.0, 8.9)
PAH etiology, n (%)				
Idiopathic / heritable / drug- or toxin-induced PAH / HIV-associated	410 (59)	807 (57)	384 (58)	367 (60)
CTD-associated PAH	187 (27)	393 (28)	176 (27)	144 (24)
CHD-associated PAH	82 (12)	129 (9)	80 (12)	76 (13)
Other§	19 (3)	82 (6)	18 (3)	25 (4)
PAH-specific treatment#, n (%)				
Monotherapy	17 (2)	636 (45)	17 (3)	16 (3)
Double combination therapy	90 (13)	671 (48)	90 (14)	90 (15)
Triple combination therapy or more	572 (82)	80 (6)	532 (81)	482 (79)
Missing / Unknown	19 (3)	24 (2)	19 (3)	23 (4)

*Selexipag (reference) cohort: propensity score weighting of 1 applied; Other PAH therapy cohort: propensity score weighting applied based on similarity of baseline characteristics to those of selexipag patients. ‡Data presented are from 1 of 10 multiple imputed datasets; results from other imputed datasets are similar. §Includes patients with portal hypertension, pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis. #For the propensity score weighted other PAH therapy cohort, N=611 due to rounding. CHD: congenital heart disease; CTD: connective tissue disease; HIV: human immunodeficiency virus.

Baseline characteristics (2)

Baseline variable	Unweighted		Propensity Score Weighted*	
	Selexipag N=698	Other PAH therapy N=1411	Selexipag N=658‡	Other PAH therapy N=612‡
WHO FC, n (%)				
I / II	241 (35)	455 (32)	240 (37)	189 (31)
III / IV	358 (51)	868 (62)	356 (54)	372 (61)
Missing / Unknown	99 (14)	88 (6)	62 (9)	51 (8)
6MWD, n	395	846	658	612
Median (Q1, Q3), m	364 (257, 466)	330 (220, 425)	364 (262, 468)	350 (277, 465)
NT-proBNP, n	567	1155	539	495
Abnormal§, n (%)	433 (76)	920 (80)	415 (63)	382 (62)
Hemodynamic parameters				
Mean right atrial pressure, n	430	1126	658	612
Mean (SD), mmHg	9.2 (7.7)	8.6 (6.0)	9.6 (7.6)	9.2 (4.2)
Cardiac index, n	437	1094	658	612
Mean (SD), L/min/m^2	2.7 (0.9)	2.6 (1.3)	2.7 (1.0)	2.7 (0.8)
SvO_2, n	361	938	353	360
>65 %, n (%)	198 (47)	451 (41)	195 (30)	205 (34)

*Selexipag (reference) cohort: propensity score weighting of 1 applied; Other PAH therapy cohort: propensity score weighting applied based on similarity of baseline characteristics to those of selexipag patients. ‡Data presented are from 1 of 10 multiple imputed datasets; results from other imputed datasets are similar. §As per physician judgement. 6MWD: 6-minute walk distance; NT-proBNP: N-terminal pro-brain natriuretic protein; SvO_2: mixed venous oxygen saturation; WHO FC: World Health Organization functional class.

Baseline characteristics (3)

Baseline variable	Unweighted		Propensity Score Weighted*	
	Selexipag N=698	Other PAH therapy N=1411	Selexipag N=658‡	Other PAH therapy N=612‡
Pericardial effusion, n (%)	81 (12)	200 (14)	80 (12)	74 (12)
Renal impairment, n (%)	154 (22)	365 (26)	140 (21)	116 (19)
≥1 Comorbidities§, n (%)	145 (21)**	419 (30)	130 (20)	119 (19)
≥1 Cardiovascular risk factors‡‡, n (%)	423 (61)**	1045 (74)	403 (61)	333 (54)

*Selexipag (reference) cohort: propensity score weighting of 1 applied; Other PAH therapy cohort: propensity score weighting applied based on similarity of baseline characteristics to those of selexipag patients. ‡Data presented are from 1 of 10 multiple imputed datasets; results from other imputed datasets are similar §Comorbidities were recorded in the medical history and included: myocardial ischemia, cardiac arrest, revascularization procedure (coronary and/or carotid), ischemic cerebrovascular disorder, hemorrhagic stroke, cardiac arrhythmia. **n=697. ‡‡Cardiovascular risk factors were recorded in the medical history and included: diabetes mellitus, hyperlipidemia, systemic hypertension, smoking (current or former).

Outcomes

	Propensity Score Weighted*	
	Selexipag	Other PAH therapy
Number of patients, n	669	614
Number of deaths, n (%)	70 (10.5)	108 (17.6)
Treatment exposure (person-years)	827.9	840.5
Mortality rate ratio of selexipag / other PAH therapy (95% CI)	**0.55 (0.31, 0.99)**	

45% reduction in risk of mortality among patients treated with selexipag versus other PAH therapies when baseline patient characteristics were taken into account

Data presented are from the average of 10 imputed datasets. *Selexipag (reference) cohort: propensity score weighting of 1 applied; Other PAH therapy cohort: propensity score weighting applied based on baseline characteristics similarity with selexipag patients. Before weighting was applied, patients from either the selexipag or other PAH therapy cohort with extreme propensity score values were excluded. CI: confidence interval.

Conclusions

- In EXPOSURE, a 45% reduction in risk of mortality among patients treated with selexipag versus other PAH therapies was observed when baseline patient characteristics were accounted for
- These findings:
  - Give an indication of the effectiveness of selexipag in a real-world setting among patients who tolerate the drug
  - Highlight the potential for targeting the prostacyclin pathway with selexipag in contemporary patients with PAH