

Selexipag As A Treatment of Pulmonary Arterial Hypertension

Niswah Hamidah Al Udzmaa¹, Amik Yuliati¹

¹Faculty of Medicine Universitas Pembangunan Nasional Veteran Jawa Timur

Corresponding Author

Niswah Hamidah Al Udzmaa

Faculty of Medicine Universitas Pembangunan Nasional Veteran Jawa Timur

Rungkut Madya Street Number 191, Rungkut Kidul, Rungkut District, Surabaya, Jawa Timur 60293

Tel/Fax: +6282141837745

E-mail: 24091010021@student.upnjatim.ac.id

Abstract

Background. To review the current evidence regarding the use of selexipag in the treatment of PAH, evaluating its effectiveness and safety.

Methods. Literature searching was conducted by collecting data through databases such as PubMed, Google Scholar, and ScienceDirect using search terms included "pulmonary arterial hypertension," and "selexipag."

Discussion. It is necessary to look at the relationship between abnormalities in PAH patients and how Selexipag itself works and to look at the side effects that occur in the research that has been carried out.

Conclusion. Giving selexipag is a good method because it is effective in treating PAH patients even with comorbid diseases or connective tissue diseases. However, not much is known about the use of selexipag and the results of research on selxipag can be said to be still limited. This review highlights the ability of selexipag to improve comfort and effectiveness in the treatment of PAH patients.

Keywords. Pulmonary Arterial Hypertension, Selexipag

Introduction

Pulmonary arterial hypertension is a devastating progressive disease mediated by different pathophysiologic pathways that result in progressive increase in pulmonary vascular resistance along with right ventricular failure and eventually premature death.¹ There are roughly 10.6 cases of PAH for a million adults in the United States.²

On December 22, 2015, US FDA authorized Selexipag for the treatment of pulmonary arterial hypertension (PAH) for the treatment of pulmonary arterial hypertension (PAH) to delay disease progression and decrease the risk of hospitalization.³

This literature review examines the effectiveness of selexipag treatment in PAH patients by looking at the impact and side effects based on research that has been written in various sources listed.

Methods

A systematic review of articles, reports, and journals by collecting data through a database source such as PubMed, Google Scholar, and ScienceDirect using search terms included "pulmonary arterial hypertension," and "selexipag" that was limited to publications in the last 5 years (2019 to 2024).

Discussion

Pulmonary arterial hypertension (PAH) is a life-threatening disease that is characterized by pulmonary arterial endothelial dysfunction that leads to arterial tree's adverse remodeling with cell proliferation, loss of vascular compliance, vasoconstriction, and chronic inflammation, which raises vascular resistance with subsequent increase in right ventricular afterload and eventual development of right ventricular dysfunction and heart failure, which is the main cause of mortality among patients with PAH if left untreated.^{4,5} Prostacyclin (PGI₂) is released by vascular endothelial cells, serving as a potent vasodilator and prevents platelet aggregation.⁶

Selexipag is a first-in-class, oral, long-acting, selective, non-prostanoid agonist of the prostacyclin receptor (IP receptor) which promotes vasodilation in pulmonary vasculature and is used to treat pulmonary arterial hypertension (PAH).^{3,7} This comparative effectiveness study, designed to simulate a theoretical trial with 2,966 commercially insured PAH patients, found a decrease in the risks of overall hospitalization, PAH-related hospitalizations, and the progression of PAH-related disease.⁸ The most frequently reported side effects are related to known effects of prostacyclin and/or the underlying disease. At 1,

3, 5, and 7 years, the corresponding Kaplan-Meier survival estimates (95%CI) were 92.0% (89.4, 94.0), 79.3% (75.4, 82.6), 71.2% (66.5, 75.3), and 63.0% (57.4, 68.1).⁹ In individuals with repaired CHD- PAH, selexipag is well tolerated and may slow the course of the condition. These results contribute to the growing evidence that patients with repaired CHD-PAH can benefit from PAH treatments.¹⁰ Regardless of the patient's comorbidity level, selexipag lowers the risk of a morbidity or mortality event when compared to a placebo, indicating that comorbidity status has no bearing on the medication's effectiveness.¹¹ Selexipag has been shown to be effective in improving a composite outcome of morbidity and mortality in adult patients with pulmonary arterial hypertension (PAH), primarily those with idiopathic PAH, PAH associated with connective tissue disease, or PAH secondary to corrected congenital heart defects. It was effective in patients with WHO Functional Class II and III, either as a monotherapy or as part of a sequential treatment regimen alongside an endothelin receptor antagonist or a phosphodiesterase type 5 inhibitor.¹² Although it is indicated as a treatment of symptomatic adult pulmonary arterial hypertension (PAH), oral selexipag use in children with PAH is well endured and secure when closely monitored.¹³

Conclusions

Giving selexipag is a good method because it is effective in treating PAH patients even with comorbid diseases or connective tissue diseases. However, not much is known about the use of selexipag and the results of research on selxipag can be said to be still limited. This review highlights the ability of selexipag to improve comfort and effectiveness in the treatment of PAHpatients.

References

1. Beshay S, Sahay S, Humbert M. Evaluation and management of pulmonary arterial hypertension. *Respir Med.* 2020;171:106099.
2. Ruopp NF, Cockrill BA. Diagnosis and treatment of pulmonary arterial hypertension: A review. *JAMA.* 2022;327(14):1379–1391.
3. National Center for Biotechnology Information. PubChem Compound Summary for CID 9913767, Selexipag. PubChem. 2024 Dec 14 [cited 2024 Dec 14]. Available from:<https://pubchem.ncbi.nlm.nih.gov/compound/Selexipag>.
4. Hardin EA, Chin KM. Selexipag in the treatment of pulmonary arterial hypertension: design, development, and therapy. *Drug Des Devel Ther.*

2016;10:3747–3754.

5. Luna-López R, Ruiz Martín A, Escribano Subías P. Pulmonary arterial hypertension. *Medicina Clínica(Engl Ed)*. 2022;158(12):622–629.
6. Stitham J, Midgett C, Martin KA, Hwa J. Prostacyclin: an inflammatory paradox. *FrontPharmacol*. 2011;2:24.
7. Panagiotidou E, Boutou A, Pitsiou G. An evaluation of selexipag for the treatment of pulmonary hypertension. *Expert Opin Pharmacother*. 2020;22(1):29–36.
8. Burger CD, Tang W, Tsang Y, Panjabi S. Early addition of selexipag to double therapy for pulmonary arterial hypertension. *JAMA Netw Open*. 2024;7(9):e2434691.
9. Galiè N, Gaine S, Channick R, et al. Long-term survival, safety and tolerability with selexipag in patients with pulmonary arterial hypertension: Results from GRIPHON and its open-label extension. *Adv Ther*. 2022;39:796–810.
10. Beghetti M, Channick RN, et al. Selexipag treatment for pulmonary arterial hypertension associated with congenital heart disease after defect correction: insights from the randomised controlled GRIPHON study. *Eur J Heart Fail*. 2019;21(3):352–359.
11. Rosenkranz S, Channick R, Chin KM, et al. The impact of comorbidities on selexipag treatment effect in patients with pulmonary arterial hypertension: insights from the GRIPHON study. *Eur J Heart Fail*. 2022;24(1):205–214.
12. Genecand L, Wacker J, Beghetti M, Lador F. Selexipag for the treatment of pulmonaryarterial hypertension. *Expert Rev Respir Med*. 2020;15(5):583–595.
13. Hansmann G, Meinel K, Bukova M, Chouvarine P, Wählander H, Koestenberger M. Selexipag for the treatment of children with pulmonary arterial hypertension: First multicenter experience in drug safety and efficacy. *J Heart Lung Transplant*.2020;39(7):695-706.