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Review Article

Rocklatan Could Raise Hopes for Glaucoma Patients

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Abstract

Purpose: To assess the effectiveness of ROCKLATAN, a topical therapy comprising netarsudil and latanoprost ophthalmic solution 0.02%/0.005%, in patients with open-angle glaucoma and ocular hypertension.

Method: Two randomized and controlled clinical trials were conducted to evaluate the effectiveness of ROCKLATAN (a solution containing netarsudil and latanoprost for ophthalmic use) with a concentration of 0.02%/0.005%.

Results: The results showed that ROCKLATAN was superior to either netarsudil or latanoprost alone in reducing intraocular pressure (IOP). After three months of treatment, 58.4% of patients on ROCKLATAN achieved an IOP of 16 mmHg or lower compared to 37.3% of patients on latanoprost alone. Additionally, 30.9% of patients on ROCKLATAN achieved at least a 40% reduction in mean diurnal IOP compared to 5.9% on netarsudil alone and 8.5% on latanoprost alone. These results were maintained over the 12-month study period.

Conclusion: ROCKLATAN with once-daily dosing, has shown to be more effective than using either netarsudil or latanoprost alone. This combination has the potential to decrease the treatment burden and improve adherence and clinical outcomes for patients with open-angle glaucoma or ocular hypertension.

Keywords: Glaucoma; Open-angle glaucoma; Ocular Hypertension; Rocklatan; Netarsudil atanprost

Introduction

Glaucoma is a group of conditions that cause progressive damage to the optic nerve, resulting in the loss of retinal ganglion cells, thinning of the retinal nerve fiber layer, and excavation of the optic disc [1]. This leads to visual impairment, including loss of peripheral vision, impaired contrast, and color perception. The causes of retinal ganglion cell loss are not fully understood [2], but intraocular pressure is a modifiable risk factor. Other risk factors include older age, non-white race, and family history. Glaucoma can be categorized into open-angle and angle-closure, and diagnosis and monitoring involve tests such as intraocular pressure measurement, perimetry, and optical coherence tomography. Treatment involves reducing intraocular pressure through medications, laser, or surgical procedures [3].

Netarsudil ophthalmic solution 0.02% inhibits a Rhoassociated protein kinase (ROCK) and norepinephrine transporters found in the trabecular pathway that primarily reduces intraocular pressure (IOP) by increasing the outflow of aqueous humor through the trabecular meshwork pathway, decreasing episcleral venous pressure, and reducing aqueous humor production. Latanoprost decreases IOP by increasing uveoscleral out flow. The combination

of netarsudil/latanoprost was developed as a once-daily, effective, and safe treatment for open-angle glaucoma and ocular hypertension [4-7].

Method

ROCKLATAN, a solution containing netarsudil and latanoprost, was studied in two controlled clinical trials (PG324-CS301 and PG324-CS302) involving patients with open-angle glaucoma and ocular hypertension. These trials compared the once-daily ROCKLATAN to once-daily netarsudil 0.02% and latanoprost 0.005% administered separately, with a treatment duration of 12 months for Study 301(MERCURY-1) and 3 months for Study 302 (MERCURY-2). Results showed that ROCKLATAN was able to lower IOP by 1 to 3 mmHg more than either monotherapy during the 3-month period and maintained the IOP reductions throughout 12 months in Study 301. In addition, the MERCURY-1 study, conducted in the USA for 12 months, and the MERCURY-2 study, conducted in the USA and Canada for 3 months, evaluated the safety and efficacy of treatment to reduce elevated IOP in patients with open-angle glaucoma or ocular hypertension. Both studies were phase 3, randomized, double-masked, multicenter, active controlled, parallel-group studies.

Results

Studies 301 and 302 involved participants whose IOP levels were lower than 36 mmHg. These studies aimed to compare the efficacy of ROCKLATAN when administered once daily to the individual administration of netarsudil 0.02% once daily and latanoprost 0.005% once daily in lowering IOP. The duration of treatment was 12 months for Study 301 and 3 months for Study 302. During the three-month period, ROCKLATAN demonstrated an IOP lowering effect that was 1 to 3 mmHg greater than the effect of either netarsudil 0.02% or latanoprost 0.005% when administered alone. In Study 301, the reduction in IOP levels was maintained throughout the 12-month period.

The phase 3 trials for FCNL were MERCURY-1 and MERCURY-2, which were conducted in the USA. In MERCURY-1, patients were split into three groups: FCNL, netarsudil 0.02%, and latanoprost 0.005%. The average baseline IOP across three time points was 22.4-24.8 mm Hg for all groups. Between week 2 and month 3 of treatment, the mean IOP for FCNL ranged from 14.8 to 16.2 mm Hg, compared to 17.2-19 mm Hg for netarsudil and 16.7-17.8 mm Hg for latanoprost. FCNL was able to lower IOP by an additional 1.8-3.0 mm Hg compared to netarsudil and 1.3-2.5 mm Hg compared to latanoprost, which met the criteria for superiority to each individual component. The percentage reduction in mean IOP from baseline was 30.9-36.7%, 21.8-24.9%, and 23.3-28.8% for FCNL, netarsudil, and latanoprost respectively. A high percentage of patients (64.5%) treated with FCNL achieved a ≥30% reduction in mean diurnal IOP compared to netarsudil (28.8%) or latanoprost (37.2%).

In MERCURY-2, patients were also split into three groups: FCNL, netarsudil 0.02%, and latanoprost 0.005%. The average baseline IOP across three time points was 22.4-24.8 mm Hg for all groups. Between week 2 and month 3 of treatment, the mean IOP for FCNL ranged from 15.3 to 16.5 mm Hg, compared to 17.4-19.8 mm Hg for netarsudil and 17.1-18.1 mm Hg for latanoprost. FCNL was able to lower IOP by an additional 2.2-3.3 mm Hg compared to netarsudil and 1.5-2.4 mm Hg compared to latanoprost, which met the criteria for superiority to each individual component. The percentage reduction in mean IOP from baseline was 30.3-34.8%, 19.5-23.0%, and 23.6-27.3% for FCNL, netarsudil, and latanoprost respectively. A high percentage of patients (58.8%) treated with FCNL achieved a ≥30% reduction in mean diurnal IOP compared to netarsudil (20.6%) or latanoprost (29.4%). These results demonstrate that once daily FCNL is clinically superior to monotherapy with either netarsudil or latanoprost in reducing IOP.

The initial average IOP during the day was similar for all three groups (netarsudil/latanoprost FDC, netarsudil, and latanoprost), with values ranging from 23.5 to 23.6 mmHg. At week 2, 6, and 12, the mean diurnal IOP for each group decreased, with the netarsudil/latanoprost FDC consistently achieving a greater reduction compared to the individual components ($p < 0.0001$ for all nine time points). At the three-month mark, a higher percentage of patients in the netarsudil/latanoprost FDC and latanoprost groups achieved an IOP of ≤ 16 mmHg compared to the netarsudil group (58.4% vs 37.3%, $p < 0.0001$). Moreover, a greater percentage of patients in the netarsudil/latanoprost FDC group achieved at least a 40% reduction from baseline in mean diurnal IOP compared to the netarsudil and latanoprost groups (30.9% vs 5.9%, $p < 0.0001$, and 8.5%, $p < 0.0001$, respectively). The combined safety results were consistent with the individual MERCURY studies [8-11].

Conclusion

The combination of netarsudil and latanoprost, administered once daily, has shown to be more effective in reducing intraocular pressure (IOP) than using either netarsudil or latanoprost alone offering potential benefits for glaucoma patients, including improved adherence and clinical outcomes. Although netarsudil/latanoprost FDC therapy is associated with a slightly higher risk of corneal hyperemia, this is usually mild and does not result in discontinuation of medication. Therefore, the use of netarsudil/latanoprost FDC therapy should be considered in glaucoma patients. Further research is necessary to determine the efficacy and safety of this treatment for patients who have not responded to other medications or are resistant to latanoprost.

Glaucoma patients face challenges with drug compliance and require long-acting, potent medications to control IOP and prevent vision-threatening complications. With the introduction of new drugs such as latanoprostene bunod, netarsudil, and fixed combination netarsudil-latanoprost, the need for surgery may be delayed if the IOPs are well controlled on medications. This combination may be used in patients who require additional IOP-lowering effects. The simplicity of once-daily dosing also improves patient compliance. While prostaglandin analogues are typically

used as first-line glaucoma medications, patients with active inflammation, cystoid macular edema, or allergies to its constituents may benefit from netarsudil as an alternative treatment option. As further research is conducted on the safety and efficacy of new medications, the choice of glaucoma treatments may evolve.

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