Introduction

Prostaglandin analogs (PGAs) and prostamides are commonly prescribed first-line medications for glaucoma or ocular hypertension because of their favorable efficacy and tolerability profiles.1

- Concomitant use of 2 PGAs or prostamides is typically avoided from multidose bottles that contain preservatives to ensure sterility.

- Bimatoprost 0.01% (preserved with 0.02% BAK) (Bimatoprost) has been shown to commonly used preservative in ophthalmic medications.

- While corneal toxicity secondary to BAK has been shown in prior in vitro and rabbit studies, these studies may not accurately replicate ocular surface conditions in patients treated with intracanalicular pressure (IOP-lowering medications preserved with BAK).2

- In a prior clinical study, no statistically significant among-group differences were seen in ocular surface tolerability at 6 months in patients treated with once-daily latanoprost 0.005% (0.02% BAK), latanoprost 0.03% (0.02% BAK), or travoprost 0.004% (0.02% BAK).3

- Recently, a new formulation of bimatoprost 0.01% (0.02% BAK) was approved, which was designed to maintain the IOP-lowering efficacy of bimatoprost 0.01% and provide an improved ocular surface tolerability profile.

Purpose

- To determine the ocular surface tolerability of once-daily latanoprost 0.01% and latanoprost 0.005% (both preserved with 0.02% BAK), and travoprost 0.004% (preserved with sofZia®) in patients previously treated with latanoprost.

Methods

Study design and patient disposition

- Three-month, multicenter (14 sites in US) clinical study to evaluate ocular surface tolerability of latanoprost and Travoprost in patients with ocular hypertension.

- At baseline (day 0), patients discontinued treatment with their current ocular hypotensive medications for 7 days.

- For 4 weeks, patients used 1 drop of latanoprost 0.005% once daily (day 1–28). Patients were then randomized to 1 of 3 treatment groups:

  - Bimatoprost 0.01% preserved with 0.02% BAK (Lumigan, Alcon Laboratories, Inc., Fort Worth, TX, USA)

  - travoprost 0.004% preserved with 0.02% BAK (Zioptin, Allergan, Irvine, CA, USA)

- Following drug administration, patients were instructed to avoid ocular or systemic contact with the preservative (ie, BAK vs sofZia).

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Outcome variables and analyses

- Ocular surface tolerability assessments:

  - Conjunctival hyperemia (primary endpoint)

  - Tear breakup time (TBU)

  - Biomicroscopy

- Safety evaluations

  - AEs

Adverse events

- All AEs were well tolerated and adverse event incidence rates were comparable among groups (Table 4).

Discussion

- This study evaluated 2 PGAs and a prostamide that differed in active ingredients and type of preservative. At 3 months, there were no statistically significant differences among the treatment groups in objective clinical and patients' reports of ocular surface tolerability including hyperemia, corneal staining, or TBUT despite differences in type of preservative.

- Latanoprost, among-group differences were seen in change from baseline to week 1 in conjunctival hyperemia (P = 0.018). While there were no statistically significant changes from the latanoprost-treated baseline in conjunctival hyperemia, corneal staining, or TBUT in latanoprost-treated eyes at any visit, there was a statistically significant increase in hyperemia from latanoprost-treated baseline in conjunctival hyperemia, corneal staining, or TBUT in latanoprost-treated eyes at both weeks 1 (P = 0.001) and 4 (P = 0.04).

- Corneal staining and TBUT were not statistically significantly different among the groups at baseline or at any follow-up visit.

- This study was intended to assess the typical glaucoma patient population and did not exclude patients who may have had dry eye symptoms at baseline. Patients with punctal plugs were excluded to ensure that there were not differences in response times of study medications on the ocular surface.

- While several prick studies, using both in vivo and in vitro models, have suggested that BAK may have deleterious impacts on the ocular surface, the clinical relevance of these findings in humans remains unclear, as the BAK exposure in these reports is typically much greater than that experienced clinically. In rabbits, for example, BAK is absorbed into the conjunctiva where it may remain for 14 days, yet there is no evidence for accumulation of BAK in human conjunctiva.4

- In the present clinical study, there was no effect on the incidence of any ocular surface lesion.

- Long-term studies that evaluate tolerability in patients on multiple topical medications and in patients with severe ocular surface disease are warranted.

Conclusions

- At 12 weeks, patients had comparable ocular tolerability findings between latanoprost and Travoprost, differences in conjunctival hyperemia, corneal staining, and TBUT between latanoprost and Travoprost were not observed in ocular surface tolerability at 3 months. Adverse event incidence rates among groups were comparable.

- No statistically significant differences in conjunctival hyperemia, corneal staining, or TBUT between latanoprost and Travoprost were observed.

Ocular surface tolerability of prostaglandin analogs and prostamides in patients with glaucoma or ocular hypertension

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Table 1. Baseline characteristics of all enrolled patients, n (%)

<table>
<thead>
<tr>
<th>Safety population</th>
<th>Bimatoprost (N=56)</th>
<th>Bimatoprost with sofZia® (N=53)</th>
<th>Latanoprost (N=55)</th>
<th>Latanoprost with sofZia® (N=53)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&lt; 65</td>
<td>39 (69.6)</td>
<td>40 (75.4)</td>
<td>38 (69.1)</td>
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<tr>
<td>≥ 65</td>
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<td>13 (24.6)</td>
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<td>Gender, m</td>
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<td>49 (92.5)</td>
<td>48 (87.3)</td>
<td>48 (89.7)</td>
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<td>10 (18.2)</td>
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<tr>
<td>Black</td>
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<td>9 (17.0)</td>
<td>11 (20.0)</td>
<td>12 (22.9)</td>
</tr>
<tr>
<td>Other</td>
<td>9 (16.1)</td>
<td>8 (15.1)</td>
<td>10 (18.2)</td>
<td>10 (19.2)</td>
</tr>
</tbody>
</table>
| Ocular surface tolerability

- There were no statistically significant differences among groups in ocular surface tolerability at any visit.

- There was no evidence for the occurrence of any ocular surface lesions.

- At baseline, there were no significant differences among treatment groups in patient demographics or ocular diagnosis (Table 1).