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Bimatoprost 0.01% or 0.03% After Latanoprost 0.005% Treatment in Glaucoma or Ocular Hypertension: Two Randomized 12-Week Trials

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Background

- The prostaglandin/prostamide (PG/PM) topical ophthalmic medications reduce intraocular pressure (IOP) effectively[1] and have become first-line therapy for many patients with open-angle glaucoma (OAG) or ocular hypertension (OHT)
- When patients treated with a PG/PM need additional IOP lowering, switching within class to a different PG/PM may provide further IOP reduction[2] and is recommended before adding a second medication[3]
- Among the PG/PM medications, the PM bimatoprost has excellent IOP-lowering efficacy; bimatoprost 0.03% has been seen in meta-analyses to achieve greater IOP lowering compared with travoprost and latanoprost[4]
- The most frequent side effect of bimatoprost 0.03% treatment has been conjunctival hyperemia[5]
- To improve its tolerability profile while maintaining its efficacy in reducing IOP, the bimatoprost 0.03% ophthalmic solution was reformulated, and bimatoprost 0.01% was approved by the United States Food and Drug Administration in August 2010
- In a phase 3 clinical study, bimatoprost 0.01% demonstrated equivalent IOP lowering to bimatoprost 0.03% and was associated with less frequent and less severe conjunctival hyperemia[6]
- Two randomized clinical trials with similar design were conducted to evaluate monotherapy and combination therapy regimens for OAG and OHT patients using latanoprost monotherapy who need additional IOP lowering
- This presentation focuses on the study arms that evaluated bimatoprost 0.01% or 0.03% monotherapy in these patients

Objective

- To evaluate the intraocular pressure (IOP)–lowering efficacy and safety of monotherapy with bimatoprost 0.01% or 0.03% in patients treated with latanoprost 0.005% monotherapy who require additional IOP lowering for their OHT or OAG

Methods

- Two prospective, investigator-masked, randomized, parallel-group, multicenter studies enrolled patients with OHT or OAG who had baseline IOP of ≥20 mm Hg after at least 30 days of latanoprost 0.005% monotherapy
- Entry criteria for both studies included best-corrected visual acuity of 20/100 or better in both eyes, use of ≤2 (Study 1) or ≤ 3 (Study 2) IOP-lowering medications at screening, and IOP in the study eye ≥20 mm Hg and <34 mm Hg at 8 AM and 10 AM (Study 1) or at 8 AM (Study 2) at baseline after at least a 30-day run-in on monotherapy with latanoprost 0.005% (Falcon Pharmaceuticals, Ltd, Fort Worth, TX, USA [Study 1] or Pfizer Inc., New York, NY, USA [Study 2])
- Following baseline measurements after a 1-month run-in on latanoprost, patients discontinued latanoprost and were randomized to 12 weeks of study treatment with a bimatoprost 0.01% (Study 1) or bimatoprost 0.03% (Study 2) monotherapy or combination therapy regimen **(Figure 1)**
- Patient evaluations at weeks 4 and 12 included IOP at 8 AM, 10 AM, and 4 PM and safety assessments (adverse events and slit-lamp biomicroscopy)
- The primary efficacy endpoint was mean change from baseline in diurnal IOP (average of the 8 AM, 10 AM, and 4 PM measurements) at week 12 in Study 1 and mean diurnal IOP at week 12 in Study 2

Figure 1. Study design

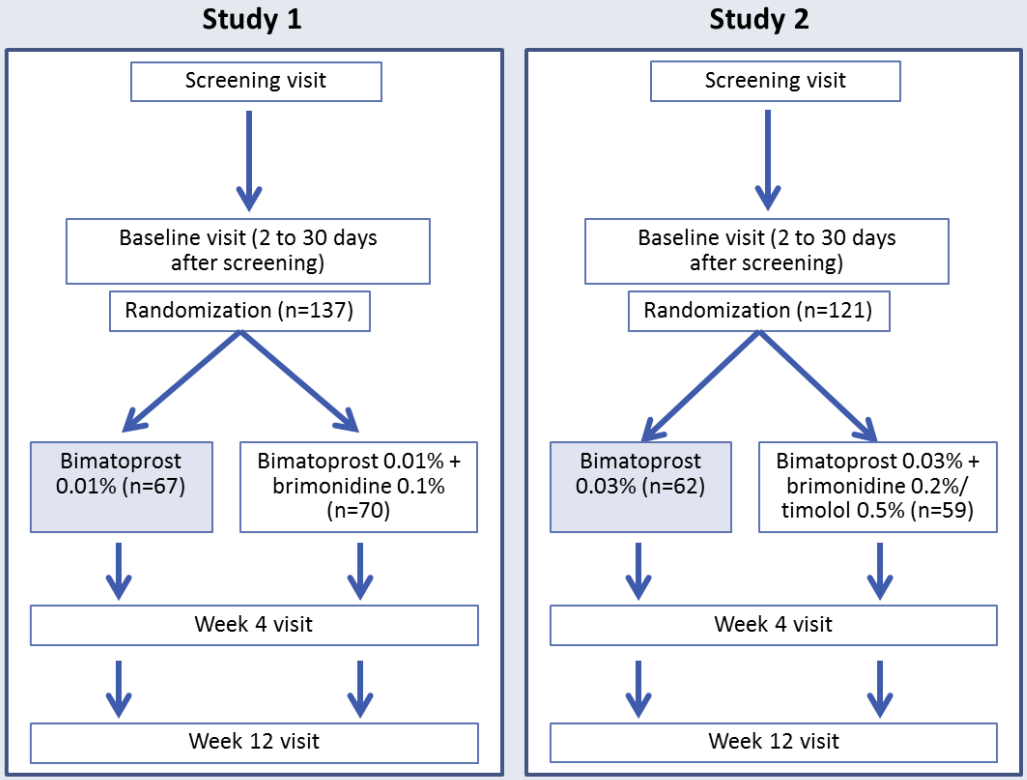
Patients with glaucoma or ocular hypertension begin washout of any IOP-lowering medication other than latanoprost and start run-in on open-label latanoprost 0.005% monotherapy

Eligible patients with latanoprost-treated baseline IOP ≥20 mm Hg and <34 mm Hg in study eye discontinue latanoprost and are randomized to monotherapy or combination therapy

Bimatoprost 0.01% or 0.03% was dosed once daily in the evening at 8 PM

Outcome assessments at 4 and 12 weeks include IOP, biomicroscopy, and adverse events

IOP, intraocular pressure.



Analysis

- This presentation reports outcomes in the study arms evaluating monotherapy (bimatoprost 0.01% or 0.03%)
- Efficacy was evaluated in the study eye (eye with higher IOP at baseline) using observed values in the per-protocol population of all patients who completed the study without significant protocol violations
- Safety was evaluated in all patients who received study treatment

Results

Table 1. Baseline patient characteristics (safety population)

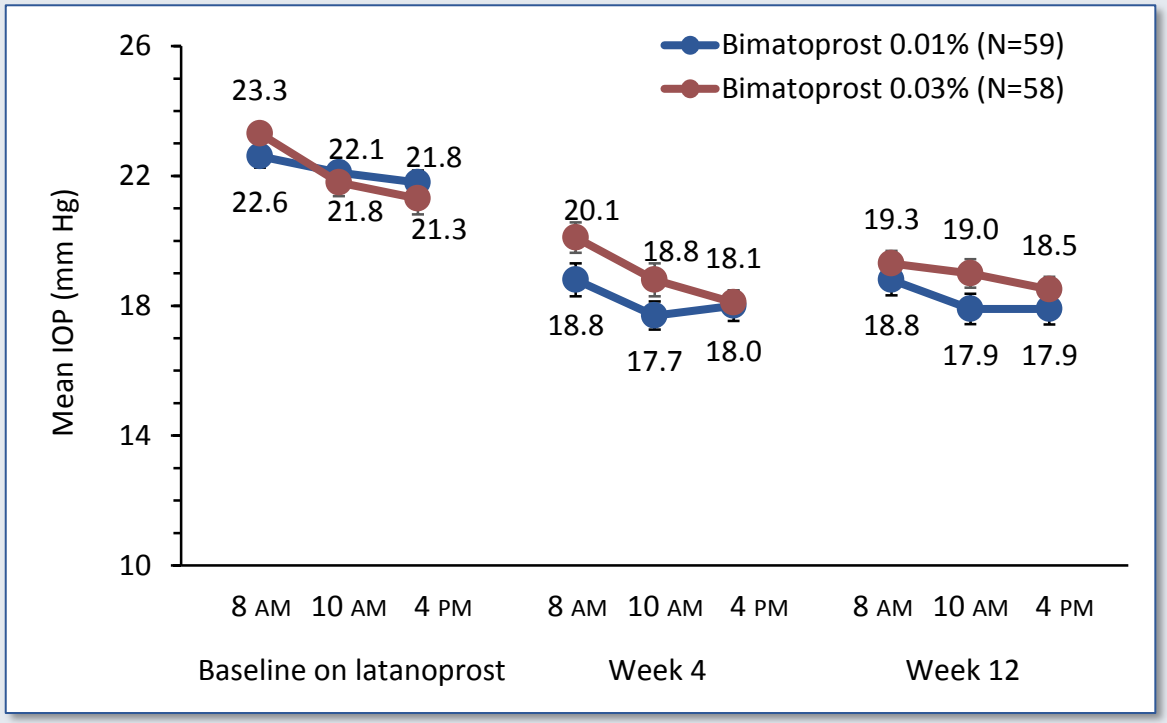
Characteristic	Bimatoprost 0.01% N=67	Bimatoprost 0.03% N=62
Mean age (SD), years	61.1 (13.9)	62.6 (13.2)
Range	21–86	21–83
Male, n (%)	34 (50.7)	26 (41.9)
Race/ethnicity, n (%)		
Caucasian	32 (47.8)	32 (51.6)
Hispanic	12 (17.9)	19 (30.6)
Black/African-American	21 (31.3)	11 (17.7)
Asian	2 (3.0)	0 (0.0)
Diagnosis in study eye, n (%)		
Glaucoma	53 (79.1)	51 (82.3)
Ocular hypertension	14 (20.9)	11 (17.7)
Using IOP-lowering medication at screening, n (%)	62 (92.5)	58 (93.5)
Prostaglandin or prostamide	44 (65.7%)	56 (90.3)
Mean central corneal thickness (SD), µm	555 (34)	550 (36)

- Most patients in each treatment arm were diagnosed with glaucoma and were using IOP-lowering medication at screening **(Table 1)**

Patient disposition

- Study completion rates were 92.5% with bimatoprost 0.01% and 96.8% with bimatoprost 0.03%
- Fifty-nine (88.1%) patients treated with bimatoprost 0.01% and 58 (93.5%) treated with bimatoprost 0.03% completed the study without significant protocol violations and were included in the efficacy analyses

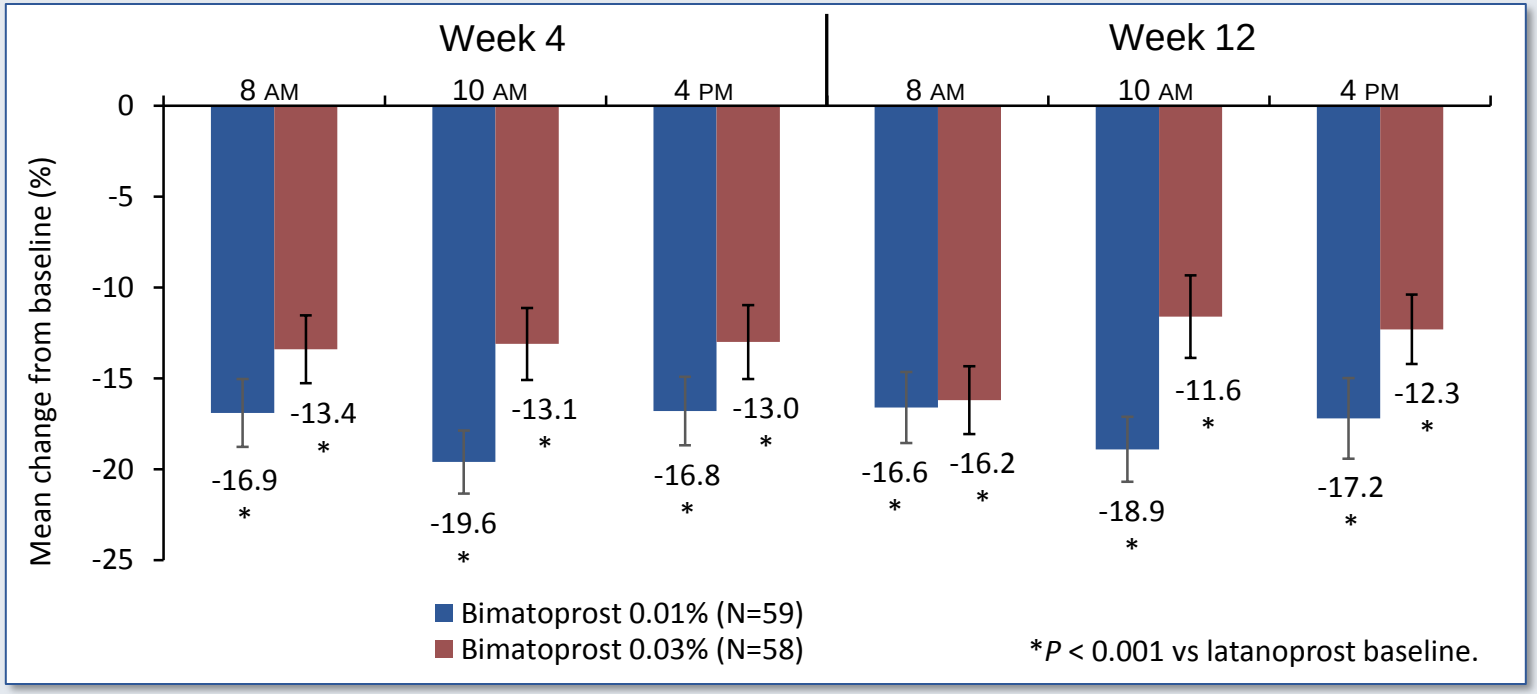
Figure 2. Mean IOP at each time point



Error bars, standard error of the mean.

- Latanoprost-treated baseline mean diurnal IOP was 22.2 mm Hg and 22.1 mm Hg in the bimatoprost 0.01% and bimatoprost 0.03% treatment arms, respectively
- After replacement of latanoprost, mean IOP at follow-up (8 AM, 10 AM, and 4 PM at weeks 4 and 12) ranged from 17.7 to 18.8 mm Hg with bimatoprost 0.01% and 18.1 to 20.1 mm Hg with bimatoprost 0.03%
- Mean IOP was numerically lower in the bimatoprost 0.01% treatment arm at each follow-up time point **(Figure 2)**

Figure 3. Mean percentage change in IOP from latanoprost baseline at each time point during follow-up



Error bars, standard error of the mean.

- In both treatment arms, mean reduction in IOP from latanoprost-treated baseline was statistically significant at each time point at both follow-up visits (*P*<.001) ranging from 3.7 mm Hg (17.0%) to 4.4 mm Hg (19.9%) with bimatoprost 0.01% and 2.8 mm Hg (12.8%) to 3.9 mm Hg (16.7%) with bimatoprost 0.03%
- The mean percentage IOP reduction from latanoprost-treated baseline was numerically greater with bimatoprost 0.01% than bimatoprost 0.03% throughout follow-up **(Figure 3)**

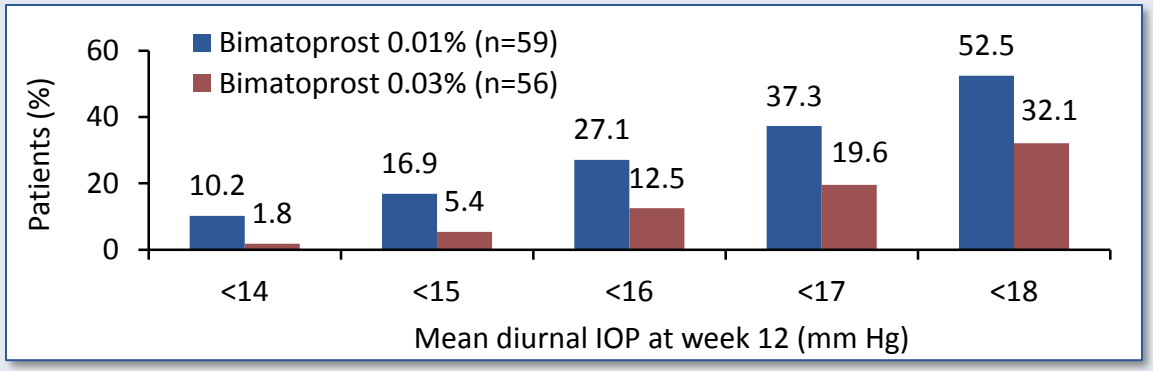
Table 2. Diurnal IOP (primary endpoint)

Parameter	Bimatoprost 0.01% N=59	Bimatoprost 0.03% N=58
Baseline		
Mean diurnal IOP on latanoprost (SEM), mm Hg	22.2 (0.32)	22.1 (0.36)
Week 4		
Mean diurnal IOP (SEM), mm Hg	18.2 (0.41)	19.1 (0.46)
Mean change from baseline diurnal IOP (SEM), mm Hg	–4.0 (0.37)	–3.0 (0.41)
Mean percentage change from baseline diurnal IOP (SEM), %	–17.9 (1.6)	–13.2 (1.7)
Week 12		
Mean diurnal IOP (SEM), mm Hg	18.2 (0.46)	18.9 (0.35)
Mean change from baseline diurnal IOP (SEM), mm Hg	–4.0 (0.42)	–3.2 (0.38)
Mean percentage change from baseline diurnal IOP (SEM), %	–17.7 (1.8)	–13.8 (1.7)

IOP, intraocular pressure; SEM, standard error of the mean.

- Latanoprost-treated baseline mean diurnal IOP was within 0.1 mm Hg in the two studies
- At 4 and 12 weeks after replacement of latanoprost with bimatoprost, mean change from baseline diurnal IOP was –4.0 mm Hg in the bimatoprost 0.01% arm and ranged from –3.0 to –3.2 mm Hg in the bimatoprost 0.03% arm **(Table 2)**
- The mean reduction in diurnal IOP from latanoprost-treated baseline was 0.8 to 1.0 mm Hg larger in the bimatoprost 0.01% arm compared with the bimatoprost 0.03% arm **(Table 2)**

Figure 4. Achievement of specific diurnal IOPs at week 12

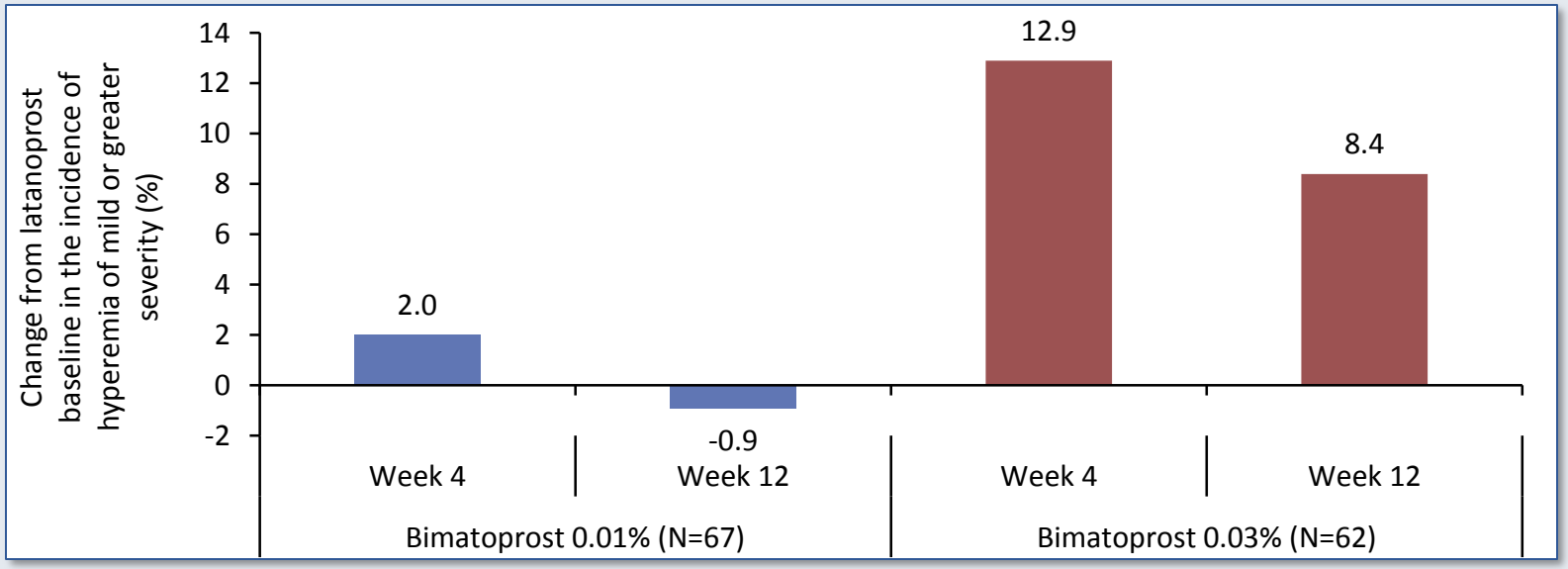


- Patients in the bimatoprost 0.01% arm were more likely to achieve low diurnal IOPs at week 12 **(Figure 4)**

Safety assessments

- The incidence of adverse events was similar in the two treatment arms
- Ocular adverse events were reported in 6 (9.0%) patients treated with bimatoprost 0.01% and 7 patients (11.3%) treated with bimatoprost 0.03%
- On biomicroscopy, mean scores of conjunctival hyperemia remained in the none-to-trace range with both bimatoprost 0.01% and bimatoprost 0.03%
- The incidence of conjunctival hyperemia of mild or greater severity increased from latanoprost baseline after 12 weeks of treatment only in the bimatoprost 0.03% treatment arm **(Figure 5)**

Figure 5. Change from latanoprost-treated baseline in the percentage of patients with mild or greater severity of conjunctival hyperemia



Discussion

- These studies showed significant additional mean IOP lowering after replacement of latanoprost with either bimatoprost 0.01% or 0.03%, but both the efficacy and the safety results favored the bimatoprost 0.01% formulation
- Bimatoprost 0.01% provided a greater percentage reduction in IOP from latanoprost-treated baseline at all 6 follow-up time points and was associated with less conjunctival hyperemia compared with bimatoprost 0.03%
- The results are consistent with the phase 3 clinical trial showing a lower incidence and less severe hyperemia with bimatoprost 0.01% compared with bimatoprost 0.03% in patients washed out of previous treatment[6] and demonstrate a discernible difference in the hyperemia profiles of bimatoprost 0.01% and bimatoprost 0.03%
- The results are also consistent with a recent observational study (the CLEAR study) showing a significant decrease in conjunctival hyperemia in patients switched from bimatoprost 0.03% to bimatoprost 0.01%[7]
- Limitations of this analysis are that the two bimatoprost formulations were tested in separate studies, and the latanoprost used for run-in was from two different manufacturers, but the studies were otherwise almost identical in study design and the study populations were similar in demographic characteristics and in latanoprost-treated baseline diurnal IOP

Conclusions

- These studies were designed to evaluate alternative monotherapies for patients who do not meet target IOP with latanoprost 0.005% alone
- The studies demonstrated that many patients who do not reach their target IOP on latanoprost can achieve additional IOP lowering and maintain monotherapy by replacing latanoprost with bimatoprost
- Of the available bimatoprost formulations, bimatoprost 0.01% has the more favorable efficacy and safety profile
  - Reductions in IOP from latanoprost baseline in these studies were larger with bimatoprost 0.01% than with bimatoprost 0.03%
  - Changes in conjunctival hyperemia from the latanoprost baseline were minimized with the switch to bimatoprost 0.01%

References

1. van der Valk R, et al. *J Clin Epidemiol.* 2009;62(12):1279–1283. **2.** Law SK, et al. *Ophthalmology.* 2005;112(12):2123–2130. **3.** European Glaucoma Society. *Terminology and Guidelines for Glaucoma.* 2008. **4.** Kymes SM, et al. *Ther Clin Risk Manag.* 2011;7:283–290. **5.** Aptel F, et al. *J Glaucoma.* 2008;17(8):667–673. **6.** Katz LJ, et al. *Am J Ophthalmol.* 2010;149(4):661–671. **7.** Crichton AC, et al. *Clin Ophthalmol*. 2013;7:1–8.

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