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Bimatoprost 0.03% Versus Travoprost 0.004% in Black Americans With Glaucoma or Ocular Hypertension

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ABSTRACT

This randomized, investigator-masked, multicenter, parallel-design trial compared the IOP-lowering efficacy of bimatoprost 0.03% and travoprost 0.004% in African Americans with glaucoma or ocular hypertension. After a washout of all ocular hypotensive agents, patients were assigned to bimatoprost once daily (n=16) or travoprost once daily (n=15) for 3 months. Study visits were at baseline and at months 1, 2, and 3. Primary outcome measures were the percentage of patients who achieved selected target pressures and the mean reduction in IOP from baseline at month 3. Both drugs comparably lowered IOP, but bimatoprost was more likely than travoprost to allow achievement of every target pressure from 12 to 19 mm Hg at month 3. After 3 months, the mean IOP reduction from baseline was 8.4 mm Hg (34%) in the bimatoprost group and 7.9 mm Hg (30%) in the travoprost group. These results are being evaluated further in a larger clinical trial.

Keywords: glaucoma; ocular hypertension; African American; racial differences; bimatoprost; travoprost; IOP

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INTRODUCTION

African-American ancestry has long been recognized as a risk factor for glaucoma.[1,2] Blacks have a much higher prevalence of open-angle glaucoma than do nonblacks,[2-4] as well as onset at an earlier age, more severe disease, and greater damage.[1,3,4] Glaucoma is the leading cause of irreversible blindness in African Americans. Although the incidence of blindness from all causes is approximately three times higher for nonwhites than for whites, blacks are six to eight times more likely than whites to become blind from glaucoma.[1,5]

Some of the differences in the rates of blindness between blacks and nonblacks may be explained by unequal access to health care and undertreatment of glaucoma.[5] Recent studies have suggested, however, that even black patients who are treated tend to respond less well to intraocular pressure (IOP)–lowering therapy than do other ethnic groups.[4,6] The biologic mechanisms underlying these differences are not well understood, but there is an urgent need to identify therapies that are effective in this difficult-to-treat, high-risk population.

Recent clinical studies have evaluated two of the newest ocular hypotensive agents, bimatoprost and travoprost, in black and nonblack patients with glaucoma or ocular hypertension. Bimatoprost, a prostamide, provided equally potent IOP lowering in both populations.[7] Travoprost, a prostaglandin analogue, was less effective in nonblacks than in blacks.[8] Although the respective phase III results suggest comparable IOP-lowering efficacy in black patients, bimatoprost and travoprost have yet to undergo head-to-head comparisons. Hence, the purpose of this study: to compare the efficacy and safety of these drugs in African-American patients with glaucoma or ocular hypertension.

PATIENTS AND METHODS

Study Design

Four centers participated in this prospective, randomized, investigator-masked, parallel-group trial. This pilot study is undergoing expansion.

Patients

Enrolled patients were African Americans of either sex who were at least 18 years of age and had a clinical diagnosis of primary open-angle glaucoma or ocular hypertension. Patients using ocular hypotensive medications completed a washout of appropriate duration prior to study entry (6 weeks for prostamides or prostaglandins; 4 weeks for topical beta blockers; 2 weeks for brimonidine, dipivefrin, and iopidine; and 1 week for systemic or topical carbonic anhydrase inhibitors). The untreated IOP in each eye was at least 22 mm Hg and no more than 34 mm Hg. All participants affirmed their ability to follow instructions and complete all required visits.

Reasons for exclusion were uncontrolled systemic disease; sensitivity/allergy to any component of either study medication; planned or ongoing pregnancy, breast feeding, or nonuse of an adequate birth control method for women of childbearing potential; ocular surgery within the past 6 months; concomitant use of ocular hypotensive medications; and planned alteration of ongoing systemic therapy that might affect IOP.

This study was conducted in accordance with the Declaration of Helsinki and applicable institutional review board regulations (US 21 Code of Federal Regulations [CFR] part 56.103). Participants gave informed consent prior to initiation of any study-related procedures (US 21 CFR part 50).

Intervention and Outcome Measures

Patients were randomly assigned to receive either bimatoprost 0.03% once daily or travoprost 0.004% once daily and instructed to instill study medication at 10 PM. Only the patient identification number was on the overlabeled, masked medication bottles. Investigators and study coordinators were masked to the randomization, and the randomization code was maintained at the central coordination center.

Patients were evaluated at baseline and at months 1, 2, and 3. To control for diurnal variations in IOP, visits were scheduled at 10 AM ± 1 hour. Baseline evaluations consisted of a medical and ophthalmic history and a complete ophthalmic assessment (visual acuity, external examination, slit-lamp biomicroscopy, measurement of IOP, funduscopy, and ophthalmoscopy). Biomicroscopic and ophthalmoscopic findings were rated on a four-point severity scale (0=none, 1=mild, 2=moderate, 3=severe). Adverse events were recorded at each study visit. Use of study medication began following the examination and randomization.

An interim history was taken and complete ocular examination (as at baseline) was performed at follow-up visits. Patients were queried about compliance, and their responses were recorded. IOP was measured at 10 AM ± 1 hour, approximately 12 hours after each dose of medication.

At the final visit, the masked investigators evaluated the clinical success of treatment by considering IOP-lowering efficacy, tolerability, and adverse events in the decision to continue the patients, or not, on the study medication.

The primary outcome measures were the percentage of patients who achieved selected target pressures and the mean change in IOP from baseline at month 3. Secondary outcome measures were mean IOP, incidence of adverse events, and physician evaluation of clinical success.

Statistical Analyses

All analyses concerned the eye with the higher IOP at baseline. If both eyes had the same baseline IOP, the right eye was used for all analyses. Between-group differences in nominal data were analyzed with the χ^2 or Fisher's exact test. Two-sample *t* tests were used for continuous demographic variables and to compare differences in IOP reduction between groups at each evaluation. Paired-sample *t* tests were used to compare within-treatment differences. The *a priori* level of significance for all tests was α=.05.

RESULTS

Demographic and baseline characteristics of the 31 enrolled patients did not differ significantly between the treatment groups (Table).

Two patients in the bimatoprost group discontinued treatment: one patient prior to the month 1 evaluation because of an adverse event unrelated to the study medication

and another, who was lost to follow-up prior to the month 3 evaluation. Twenty-nine patients completed the study as planned.

Patient Demographics at Baseline

	Bimatoprost Group (n=16)	Travoprost Group (n=15)	Between-Group *P* Value
Age, y*	67.2±10.9	62.7±10.3	.244
Sex, no. (%)			
Male	4 (25)	7 (46.7)	.208
Female	12 (75)	8 (53.3)	
Diagnosis, no. (%)			
Open-angle glaucoma	13 (81.3)	15 (100)	.226
Ocular hypertension	3 (18.8)	0	

*Mean ± SD.

Outcome Measures

IOP Lowering

Baseline IOP was comparable in each group (bimatoprost, 25.5 mm Hg; travoprost, 26.5 mm Hg; *P*=.365). Patients were more likely to achieve every target pressure from 12 to 19 mm Hg with bimatoprost than with travoprost (Fig 1) after 3 months, although the between-group differences were not statistically significant.

Both treatments significantly lowered IOP (*P*<.001), and the reductions were comparable in each group (Fig 2). At month 1, the mean IOP reduction was 7.4 mm Hg (29.5%) with bimatoprost and 8.7 mm Hg (33.4%) with travoprost (*P*=.208). After 2 months of treatment, respective mean IOP reductions were 8.5 mm Hg (32.8%) and 7.1 mm Hg (26.2%) (*P*=.321). At the month 3 visit, IOP was lowered by a mean of 8.4 mm Hg (33.7%) with bimatoprost and 7.9 mm Hg (30%) with travoprost (*P*=.671). After the first month of treatment, IOP reductions from baseline were greater with bimatoprost. At each follow-up visit (Fig 3), bimatoprost consistently provided a mean IOP that was as low as or lower than that provided by travoprost.

Adverse Events

The incidence of treatment-related adverse events was low in each group. Ocular redness was most common—in three bimatoprost-treated patients and four travoprost-treated patients. One patient in the travoprost group also had ocular itching. One patient in the bimatoprost group discontinued because of stomach cramps and urticaria not considered treatment related. No significant between-group differences were evident in visual acuity or on biomicroscopy or ophthalmoscopy.

Fig 1. Percentages of patients achieving target IOP levels at month 3.

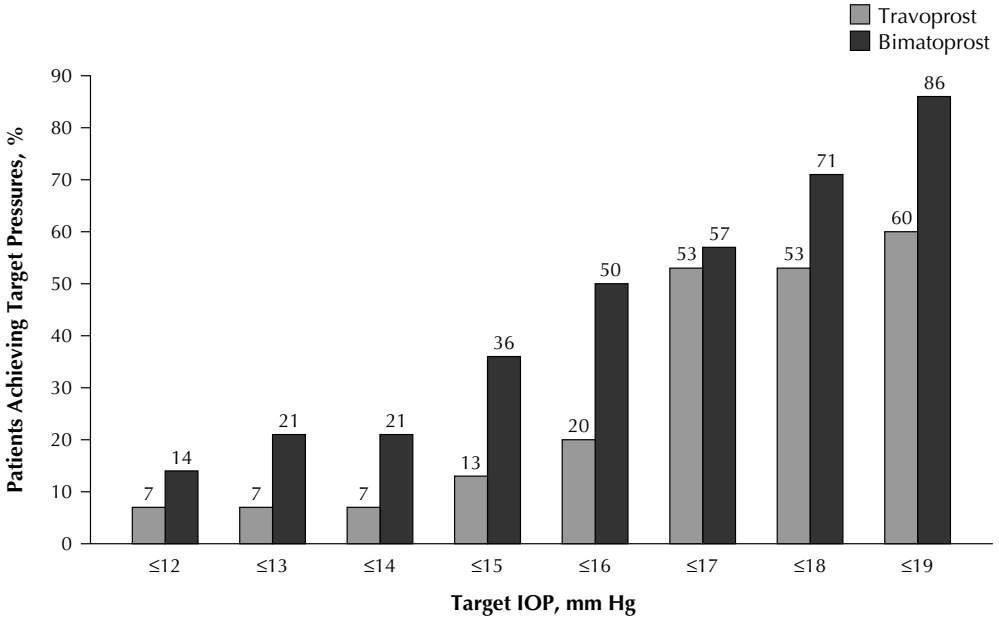


Fig 2. Mean IOP reductions at follow-up visits.

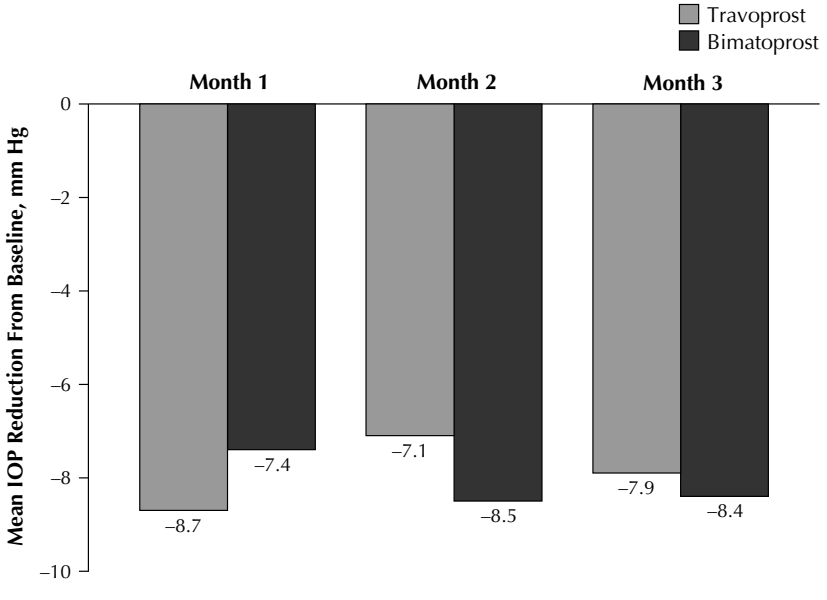
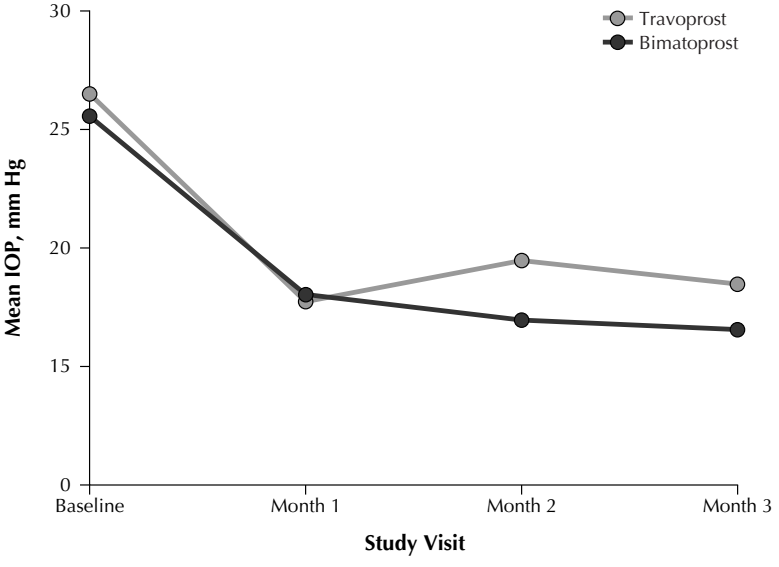


Fig 3. Mean IOP at each study visit.



Clinical Success

The rate of clinical success was similar with each treatment. In the bimatoprost group, 85.7% of patients (12/14) were considered clinically successful, compared with 86.7% (13/15) of the travoprost group ($P>.999$). Data were not available for two bimatoprost patients.

DISCUSSION

While bimatoprost and travoprost lowered IOP in African-American patients with glaucoma or ocular hypertension, bimatoprost allowed more patients to achieve low target IOPs. Mean reductions from baseline in IOP were also greater with bimatoprost at two of the three follow-up visits. None of the between-group differences, however, were statistically significant at any time, probably because of the small sample size. Both medications were well tolerated.

Numerous studies have reported significant differences between blacks and nonblacks in the prevalence of glaucoma[1-4] and the response to treatment.[4,6] Epidemiologic studies have demonstrated that blacks have a greater risk for both glaucoma and the blindness it causes.[4,5] Moreover, recent clinical trials have shown that not all medications are equally effective in both blacks and nonblacks,[8] although the pathophysiologic mechanisms underlying these differences are not yet understood.

The IOP-lowering efficacy of bimatoprost in African Americans demonstrated in our study is consistent with other results. In a large pooled analysis of data from two phase III clinical comparisons of bimatoprost 0.03% with timolol, a subgroup analysis by race showed bimatoprost to be significantly more effective in lowering IOP in both black and nonblack patients.[7] Bimatoprost had equivalent IOP-lowering efficacy in both racial groups, while timolol was notably less effective in blacks than nonblacks (by up to approximately 2 mm Hg).

Conversely, a recent phase III clinical trial comparing travoprost with timolol and latanoprost[8] suggested that travoprost is significantly less effective in nonblack than in black patients. The mean reduction in IOP from baseline in that study ranged from 6.3 to 7.9 mm Hg in nonblacks assigned to travoprost 0.004%, compared with 6.9 to 8.9 mm Hg in black patients randomized to the same treatment. Interestingly, on several evaluations, travoprost provided significantly lower mean IOP in black patients than either latanoprost (also a prostaglandin analogue prodrug) or timolol.

In our study, the mean IOP reduction was larger with travoprost than bimatoprost at month 1 but larger with bimatoprost at months 2 and 3. These findings suggest that the initial reduction with travoprost may not be sustained over the long term. Bimatoprost provided sustained IOP lowering throughout this study, with no evidence of drift.

CONCLUSIONS

Bimatoprost and travoprost both lowered IOP in African-American patients with glaucoma or ocular hypertension, although low target pressures were more likely with bimatoprost, and the mean IOP reductions from baseline were greater with bimatoprost at two of the three follow-up visits. These findings, together with the demonstrated efficacy of bimatoprost in both black and nonblack patients, suggest that bimatoprost may be a more appropriate choice for lowering IOP than travoprost, regardless of race. A large multicenter expansion of this study is ongoing.

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REFERENCES

1. Marshall EC. Racial differences in the presentation of chronic open-angle glaucoma. *J Am Optom Assoc.* 1989;60:760-777.
2. Sommer A, Tielsch JM, Katz J, et al, for the Baltimore Eye Survey Research Group. Relationship between intraocular pressure and primary open angle glaucoma among white and black Americans. *Arch Ophthalmol.* 1991;109:1090-1095.
3. Palmissano P, Hynes M, Mueller L. Glaucoma and race: a case for screening in Connecticut. *Conn Med.* 2000;64:75-78.
4. Sommer A, Tielsch JM, Katz J, et al. Racial differences in the cause-specific prevalence of blindness in east Baltimore. *N Engl J Med.* 1991;325:1412-1417.

5. Javitt JC, McBean AM, Nicholson GA, et al. Undertreatment of glaucoma among black Americans. *N Engl J Med.* 1991;325:1418-1420.
6. AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 9. Comparison of glaucoma outcomes in black and white patients within treatment groups. *Am J Ophthalmol.* 2001;132:311-320.
7. Higgenbotham E, Schuman J, Goldberg I, et al. One-year, randomized study comparing bimatoprost and timolol in glaucoma and ocular hypertension. Bimatoprost Study Groups I and II. *Arch Ophthalmol.* 2002;120:1286-1293.
8. Netland PA, Landry T, Sullivan EK, et al. Travoprost compared with latanoprost and timolol in patients with open-angle glaucoma or ocular hypertension. *Am J Ophthalmol.* 2001;132:472-484.