Twenty-four–Hour Control With Latanoprost-Timolol–Fixed Combination Therapy vs Latanoprost Therapy

Anastasios G. P. Konstas, MD, PhD; Kostantinos Boboridis, MD; Despina Tzetzi, MD; Kostantinos Kallinderis, MD; Jessica N. Jenkins, BS; William C. Stewart, MD

Objective: To evaluate the 24-hour efficacy and safety of the latanoprost-timolol maleate–fixed combination vs latanoprost therapy in patients with primary open-angle glaucoma.

Methods: A prospective, observer-masked, crossover, active-controlled, randomized comparison in which after a 6-week medicine-free period, patients were randomized to either latanoprost-timolol–fixed combination therapy or latanoprost therapy, both dosed once each evening, alone for 8 weeks. Patients were then switched to the opposite treatment for 8 weeks. At the end of the washout and treatment periods, a 24-hour diurnal curve was performed.

Results: The baseline untreated mean±SD diurnal curve in 37 patients who completed the study was 24.2±2.0 mm Hg. The mean diurnal curve was 19.2±2.6 mm Hg for those who received latanoprost therapy alone and 16.7±2.1 mm Hg for those who received the fixed combination therapy (P<.001). The fixed combination therapy also provided a lower absolute intraocular pressure level (1.5-2.9 mm Hg, P<.001) and a greater intraocular pressure reduction from the untreated baseline (P<.001). Stinging was statistically lower with latanoprost therapy alone (P=.04), but itching was statistically increased compared with the fixed combination therapy (P=.04).

Conclusion: The result of this study suggests that the latanoprost-timolol–fixed combination compared with latanoprost therapy alone provides improved intraocular pressure reduction over the 24-hour diurnal curve and for each individual time point in patients with primary open-angle glaucoma.


The 0.005% LATANOPROST-0.5% timolol maleate–fixed combination therapy (Xalacom, Pfizer Inc, New York, NY) was recently commercially released. In regulatory trials Pfeiffer and associates¹ and Higginbotham et al² showed that morning dosing of the fixed combination therapy reduced the intraocular pressure (IOP) further compared with latanoprost therapy alone by 1.1 to 1.2 mm Hg following a run-in period of timolol dosed twice daily. In the study by Pfeiffer and associates¹ latanoprost was dosed in the morning and in the study by Higginbotham et al² it was dosed in the evening.

The reduction provided by the fixed combination in the regulatory trials was less than might be anticipated based on the known efficacy of once-daily timolol therapy.¹,² The reason for the relative lack of efficacy has not been completely explained. However, it may be in part because the fixed combination therapy was instilled in the morning in the regulatory studies, whereas latanoprost therapy alone was dosed in the evening in the study by Higginbotham et al.² Previous data, by Alm et al³ and Konstas and associates,⁴,⁵ have demonstrated that nighttime dosing of latanoprost provides lower daytime IOPs. In addition, the diurnal data in the regulatory studies were limited to 3 daytime time points. Unfortunately, little data exist that more completely evaluate 24-hour diurnal IOPs or describe the IOP with the latanoprost-timolol–fixed combination therapy compared with latanoprost therapy alone, both dosed in the evening.

In this trial we evaluated the 24-hour efficacy and safety of the 0.005% latanoprost-0.5% timolol maleate–fixed combination therapy vs 0.005% latanoprost therapy, both dosed each evening, in patients with primary open-angle glaucoma. We wished to determine if a more complete evaluation of the diurnal ocu-
lar hypotensive effect, and time of instillation, could influence differences in efficacy between these products.

**METHODS**

**PATIENTS**

Patients were recruited for this prospective study from the Glaucoma Unit of the University Department of Ophthalmology, Australasian Hellenic Educational Progressive Association Hospital, Thessaloniki, Greece. All patients who agreed to participate in the study and met the inclusion and exclusion criteria were enrolled. We enrolled patients of either sex, older than 39 years, who demonstrated a willingness to comply with the investigators’ and protocol’s instructions and to sign the institutional review board–approved informed consent document; had a clinical diagnosis of primary open-angle glaucoma in at least 1 eye (study eye); at screening had an IOP at a level in both eyes to ensure clinical stability of vision and the optic nerve throughout the trial; and at baseline had an untreated IOP of 24 to 36 mm Hg inclusive at the 10-o’clock position measurement (visit 2). Patients with glaucoma were defined as those having typical glaucomatous optic atrophy (neural rim thinning, notching, saucerization, or nerve fiber layer disc hemorrhage) with or without typical glaucomatous visual field damage (arcuate, Seidel or paracentral scotoma, or nasal step).

We excluded patients who received therapy if they had either a history of unresponsiveness (deemed to be an IOP reduction of <10%) to any antiglaucoma medication, including latanoprost or timolol, or a history of noncompliance. Patients were also excluded from this study if they demonstrated unreliable applanation tonometry, inadequate visualization of the ocular fundus or anterior chamber, a concurrent infectious-noninfectious conjunctivitis, keratitis or uveitis, or a history of hypersensitivity to any components of the preparations used in this trial; were a woman of childbearing potential or not using reliable birth control; were pregnant or lactating; had a risk of visual field or visual acuity worsening as a consequence of participation in the trial, a cup-disc ratio of 0.8 or worse, or a mean deviation of worse than 14 dB on visual field testing (not attributable to cataract); were unable to give informed consent; anticipated change in systemic hypotensive therapy during the active treatment portion of the trial (visits 2-6); had undergone intraocular conventional surgery or laser surgery; had a risk of visual field or visual acuity worsening as a consequence of participation in the trial, a cup-disc ratio of 0.8 or worse, or a mean deviation of worse than 14 dB on visual field testing; were participating (or current participation) in any investigational drug or device trial within the previous 30 days prior to the screening visit; had undergone intraocular conventional surgery or laser surgery; had a history of unresponsiveness to any components of the preparations used in the trial; were a woman of childbearing potential or not using reliable birth control; were pregnant or lactating; had a risk of visual field or visual acuity worsening as a consequence of participation in the trial, a cup-disc ratio of 0.8 or worse, or a mean deviation of worse than 14 dB on visual field testing (not attributable to cataract); were unable to give informed consent; anticipated change in systemic hypotensive therapy during the active treatment portion of the trial (visits 2-6); had progressive retinal or optic nerve disease apart from glaucoma; were unwilling to accept the risk of iris color change, saucerization, or nerve fiber layer disc hemorrhage; were at risk for uveitis or cystoid macular edema; were at risk for uveitis or cystoid macular edema in this trial; or had a history of ocular herpes simplex, reactive airway disease, second- or third-degree heart block, poorly compensated congestive heart failure, or concomitant use of systemic beta-blockers.

All patients signed an informed consent agreement approved by an institutional review board before any procedures were performed. The Treaty of Helsinki was followed for this study. At visit 1 subjects had an ophthalmic and systemic history taken and had dilated funduscopy and automated full-threshold perimetry performed (Humphrey 24-2 test, Swedish Interactive Thresholding Algorithm [SITA] standard). At this visit, as well as at all other visits, the IOP (2 measurements at each time point were averaged) was measured and Snellen visual acuity and slit-lamp biomicroscopy were performed. Qualified patients were then washed out of their glaucoma medications and asked to return in 6 weeks for the baseline visit (visit 2).

At visit 2, and at all other diurnal curve visits (visits 4 and 6), patients had IOP measurements at 6 and 10 AM, 2, 6, and 11 PM, and 2 AM. Patients who met the IOP inclusion requirements were randomly assigned to receive either the 0.005% latanoprost-0.3% timolol–fixed combination or 0.005% latanoprost once every evening at 8 PM for the first 8-week treatment period.

A safety evaluation was performed after 2 weeks of treatment (visit 3). At the end of period 1 a diurnal curve was again performed (visit 4). Patients were then switched to the second study medicine for period 2. A safety visit was again performed after 2 weeks of treatment (visit 5) and a diurnal curve was performed at the end of the second 8-week treatment period (visit 6).

The same investigators at each site measured the IOP and used the same calibrated instruments (Goldmann applanation tonometer) to perform diurnal curves of the IOP. During the study the investigators and staff were masked to the treatment regimen. Medicine labels were concealed with a study-specific cover and kept in an opaque medicine vial. Patients were only aware of the color top of the study treatment.

Patients were instructed regarding correct medication instillation and compliance. In this study all patients were instructed to perform nasolacrimal occlusion for 1 minute after instillation of each study eyedrop. At each visit local and systemic adverse effects that occurred during the treatment period were recorded. Adverse effects were evaluated by asking patients a general query about their state of health. Patients also were queried as to their compliance to the study medicine.

**STATISTICS**

Statistical analyses comparing the IOP responses to the drug regimens were performed using a paired t test for both individual time points and the entire diurnal curve (average mean IOPs measured throughout the day).6-12 These data were also evaluated by a repeated-measures of analysis. The significance level was set at 5% and a 2-way analysis was used for all tests. The primary efficacy variable was the level of the diurnal IOP between study treatments. This study had an 80% power to identify a 1.5-mm Hg difference between individual time points and between mean diurnal IOPs assuming an SD of 2.8 mm Hg between treatments.13-16 The secondary efficacy variables, the level of IOP at each time point, the reduction of IOP from untreated baseline for each time point as well as the diurnal curve, and the mean range if the diurnal curve (the average of each patient’s difference between the highest and the lowest IOP throughout the 24-hour period) were also analyzed by a repeated-measures of analysis. If both eyes qualified, 1 eye was randomly chosen to be analyzed by a computerized randomization number list. Adverse events were evaluated by McNemar test.17

**RESULTS**

**PATIENTS**

Thirty-seven patients with primary open-angle glaucoma, with a mean age ± SD of 65.8 ± 7.9 years, were enrolled in this trial. All patients were ethnic Greek in origin. Fourteen were men and 23 were women. Five patients were newly diagnosed, whereas 32 were receiving previous therapy. Of these, all patients were receiving combination therapies except for 3 patients who were receiv-
ing latanoprost alone and 1 patient who was receiving timolol alone. One additional patient each was excluded because of previous unresponsiveness to latanoprost therapy alone and timolol therapy alone. The mean±SD visual acuity was 0.9±0.2 (mean of the denominator of the Snellen chart divided into the numerator). The mean±SD cup-disc ratio was 0.6±0.1 and the mean±SD visual field defect was −7.5±4.3 dB.

**INTRAOCULAR PRESSURE**

The absolute IOP levels are listed in Table 1 as well as shown in Figure 1 and Figure 2. The reductions in IOP from baseline are given in Table 2. Both 0.005% latanoprost and the 0.005% latanoprost-0.5% timolol maleate–fixed combination therapy dosed at 8 PM reduced the IOP from baseline at each time point and for the 24-hour diurnal curve (P<.001). Also, the fixed combination therapy provided an additional IOP reduction compared with latanoprost therapy alone at each time point and for the diurnal curve (P<.001). The range of the diurnal IOP showed a trend to be decreased more with the fixed combination therapy compared with latanoprost therapy alone (P= .08). Further, the IOP reduction from baseline with the fixed combination therapy was significantly greater compared with latanoprost therapy alone for each time point and for the diurnal curve (P≤ .002).

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Baseline</th>
<th>0.005% Latanoprost Therapy Alone</th>
<th>0.005% Latanoprost-0.5% Timolol Maleate–Fixed Combination Therapy</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 AM</td>
<td>25.0 ± 3.2</td>
<td>19.1 ± 3.6</td>
<td>16.2 ± 2.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>10 AM</td>
<td>26.5 ± 2.8</td>
<td>19.2 ± 3.4</td>
<td>16.4 ± 2.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2 PM</td>
<td>24.5 ± 1.9</td>
<td>19.0 ± 2.5</td>
<td>17.1 ± 2.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6 PM</td>
<td>23.8 ± 2.3</td>
<td>18.9 ± 2.9</td>
<td>17.4 ± 2.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>11 PM</td>
<td>22.7 ± 2.4</td>
<td>19.5 ± 2.1</td>
<td>16.5 ± 2.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2 AM</td>
<td>22.9 ± 3.1</td>
<td>19.1 ± 2.8</td>
<td>16.5 ± 2.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diurnal</td>
<td>24.2 ± 2.0</td>
<td>19.2 ± 2.6</td>
<td>16.7 ± 2.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mean range</td>
<td>5.9 ± 2.1</td>
<td>4.4 ± 1.8</td>
<td>3.9 ± 1.3</td>
<td>.08</td>
</tr>
</tbody>
</table>

†P values are between treatments only.

**ADVERSE EVENTS AND DISCONTINUED PATIENTS**

Stinging was statistically lower with latanoprost therapy alone (P=.04), but itching was statistically increased compared with the fixed combination therapy (P=.04). Five patients (14%) receiving latanoprost alone and 3 patients (8%) receiving fixed combination therapy reported conjunctival hyperemia (P=.50). Of these, none of the patients receiving latanoprost therapy alone and 1 of the patients receiving the fixed combination therapy also reported anterior segment adverse effects (ie, itching, burning) (P=.99). No other statistical differences were observed between study medicines (P>.05).

Two patients discontinued the trial early prior to the diurnal assessment and were excluded from the analysis. The reasons for discontinuation were as follows: one patient was lost to follow-up and the other demonstrated poor compliance. There were no reported serious adverse events.

**COMMENT**

Most patients with primary open-angle glaucoma are treated with a prostaglandin or a beta-blocker as first-line therapy. When more efficacy is required, the choice...
of a second product, and how the product is delivered, becomes of primary importance. One avenue of delivering a second medication is through a fixed combination product that has the advantage of providing 2 medicines within 1 drop. Such a product potentially reduces confusion from multiple bottles, aids compliance, and eliminates the need to separate drops given from separate bottles.18 In addition, theoretically safety might be increased by using a fixed combination product because of limiting the exposure to benzalkonium chloride, the preservative in most eyedrops. This compound has been shown to be irritating to the corneal epithelium in in vitro studies.29 However, for a fixed combination product to be truly clinically advantageous, it must increase efficacy beyond each of its individual components given as monotherapy while not worsening safety.

Regulatory trials for the latanoprost-timolol–fixed combination therapy, although showing a statistically significant increase in efficacy over latanoprost and timolol each given alone, were limited to 3 time points.1,2 Few comparative studies exist in patients with glaucoma that examine the fixed combination product compared with the individual components over multiple time points throughout the 24-hour or daytime diurnal curve.

Stewart et al30 and Konstas et al31 previously evaluated the 12-hour diurnal curve, measured every 2 hours, of the latanoprost-timolol–fixed combination therapy. They found a further 2.8– to 3.0-mm Hg decrease in IOP with the fixed combination therapy when dosed in the morning or evening, respectively, vs twice-daily timolol. Larsson22 has evaluated the fixed combination therapy over a 24-hour diurnal curve and found a 4.7–mm Hg mean reduction vs placebo with no efficacy in the early morning hours (3-6 AM).

The purpose of this trial was to evaluate the 24-hour efficacy and safety of 0.005% latanoprost-0.5% timolol–fixed combination therapy vs 0.005% latanoprost therapy alone, both dosed once each evening, in patients with primary open-angle glaucoma using a crossover design. The crossover design had the advantage of increasing the statistical power of the study because each patient acted as his or her own control. However, the fewer numbers could potentially limit the types of adverse effects described. In addition, despite the 2-month treatment period the period 1 treatment theoretically could influence the results of period 2.

This study showed that both treatments provided a statistically significant IOP reduction from untreated baseline over a 24-hour diurnal curve and for each individual time point. However, when both treatment groups were compared directly, the fixed combination provided an additional IOP reduction compared with latanoprost alone over the 24-hour diurnal curve and for each individual time point, ranging from 1.5 mm Hg at 6 PM to 2.9 mm Hg at 6 AM. In addition, the IOP decrease from untreated baseline was greater with the latanoprost-timolol–fixed combination therapy compared with latanoprost therapy alone for the 24-hour diurnal curve and for each individual time point.

Apart from a statistical difference in IOP, regulatory agencies typically define a clinically important separation between glaucoma medicines as 1.5 mm Hg. Therefore, it also may be clinically important that the latanoprost-timolol–fixed combination therapy provided at least a greater than 1.5–mm Hg reduction than latanoprost therapy alone at each time point and a mean 24-hour reduction of approximately 2.5 mm Hg in this trial. However, the definition of a “clinically important reduction” is not clearly constituted by the ophthalmic community. Consequently, individual physicians must determine for themselves what constitutes a clinically important hypotensive effect in their practice. Nevertheless, both the results of the Ocular Hypertension Treatment Study and Early Manifest Glaucoma Trial have indicated the importance of a 1.0–mm Hg further reduction in IOP in both ocular hypertension and primary open-angle glaucoma.23,24

The results of this study appear to show better efficacy for the latanoprost-timolol–fixed combination therapy than the 1.1– to 1.2–mm Hg further reduction compared with latanoprost therapy alone in the regulatory trials.1,2 The reason for the difference in results between these studies and our trial is not completely clear but may have resulted in part from 2 potential reasons. First, in this trial the 24-hour comparison of the latanoprost-timolol–fixed combination therapy to latanoprost therapy alone may have provided a more complete picture of the efficacy between these products than previously available. Second, since latanoprost demonstrates more daytime ocular hypotensive efficacy when dosed at night, it may have provided a greater effect than in the study by Higginbotham et al2 in which the latanoprost-timolol–fixed combination therapy was dosed in the

### Table 2: Intraocular Pressure Reduction From Baseline for 37 Patients With Primary Open-angle Glaucoma

<table>
<thead>
<tr>
<th>Time Point, h</th>
<th>0.005% Latanoprost Therapy Alone</th>
<th>0.005% Latanoprost-0.5% Timolol Maleate–Fix Combination Therapy</th>
<th>Difference</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 AM</td>
<td>5.8 ± 2.4</td>
<td>8.7 ± 2.2</td>
<td>2.9 ± 2.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>10 AM</td>
<td>7.2 ± 2.5</td>
<td>10.1 ± 2.4</td>
<td>2.9 ± 2.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2 PM</td>
<td>5.5 ± 2.3</td>
<td>7.3 ± 2.8</td>
<td>1.8 ± 2.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6 PM</td>
<td>4.9 ± 2.5</td>
<td>6.4 ± 2.4</td>
<td>1.5 ± 2.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>11 PM</td>
<td>3.1 ± 2.5</td>
<td>6.1 ± 2.5</td>
<td>3.0 ± 2.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2 AM</td>
<td>3.8 ± 1.9</td>
<td>6.4 ± 2.5</td>
<td>2.6 ± 2.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diurnal</td>
<td>5.1 ± 1.5</td>
<td>7.5 ± 1.7</td>
<td>2.5 ± 1.6</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

†P values are between treatments only.

*Data are given as mean ± SD in millimeters of mercury.
morning and latanoprost therapy alone was dosed in the evening.

The current results also differ from the study by Larsson,22 which showed a limited mean ocular hypotensive effect of the latanoprost-timolol–fixed combination from untreated baseline and no statistical effect in the early morning. Our study demonstrated a mean reduction of 7.5 ± 1.7 mm Hg with the latanoprost-timolol–fixed combination therapy compared with baseline at each time point over the 24-hour diurnal curve, including the early morning hours.22 The reason for this difference in efficacy between studies is not completely clear. In the study by Larsson22 the patients were diagnosed as having ocular hypertension. However, the highest mean untreated IOP at any time point was 21.8 mm Hg and the mean diurnal untreated IOP was 19.4 mm Hg.22 Consequently, possibly some of these patients may not have actually had ocular hypertension. In addition, the number of patients evaluated was small (n = 19).22 In the current study, we entered a larger sample size (n = 37) of patients with morning IOPs of 24 mm Hg or higher. These differences might have allowed a better characterization of the diurnal curve response for the latanoprost-timolol–fixed combination therapy.

In contrast the mean range of the IOP between the latanoprost-timolol–fixed combination and latanoprost therapies was not significantly different although a trend was observed to a narrower range with the adjunctive therapy. The mean range noted in this study for both preparations was similar to previous studies, however.6,7,16 The lack of significance of the study may have been due, in part, to the number of patients included in this study. A larger sample size may have provided a statistical difference.

This study suggests that the latanoprost-timolol–fixed combination therapy compared with latanoprost therapy alone provides a further statistical IOP reduction over the 24-hour diurnal curve, and for each individual time point, in patients with primary open-angle glaucoma.

This study did not evaluate the long-term additional efficacy of the latanoprost-timolol–fixed combination therapy compared with latanoprost therapy alone. Further, a direct 24-hour comparison between morning and evening dosing of the latanoprost-timolol–fixed combination therapy would be helpful in addressing the issue of its preferred dosing in the future. In addition, the effect of corneal thickness was not evaluated in this study. Previous work has noted corneal thickness can influence the beta-blocker ocular hypotensive response.23 Also, this study included only Greek ethnic patients who typically have darker irides. How the ethnic makeup could have influenced the results of this study remains unknown. Further research might help to better define the efficacy of the latanoprost-timolol–fixed combination therapy compared with latanoprost therapy alone.

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Phakic Status Affects Vitreous Penetration of Topical Moxifloxacin

We commend Hariprasad et al1 on their study regarding the aqueous and vitreous penetration of topically administered 0.5% moxifloxacin. We have no critiques of their study design, methods, or conclusions, but further review of their data reveals an additional interesting finding. Although their statistical analysis comparing aqueous and vitreous concentration values in phakic and pseudophakic eyes was not significant, we decided to further evaluate the potential effect of lens status on vitreous penetration by asking the questions, “Does phakic status effect the distribution of topically administered moxifloxacin from the aqueous into the vitreous?” and “What percentage of moxifloxacin entering the aqueous cavity diffuses posteriorly into the vitreous cavity, and does phakic status alter this percentage?” We feel convinced that penetration across the conjunctival, scleral, and retinochoroidal barriers into the vitreous is negligible; therefore, any topical moxifloxacin entering the vitreous cavity would do so via corneal penetration into the aqueous and from there must diffuse posteriorly around the lens.

Grouping their data for all of the 18 patients who had both aqueous and vitreous samples, a mean of only 4.2% of moxifloxacin that had accumulated in the aqueous diffused posteriorly into the vitreous. However, subgroup analysis reveals that these mean percentages were 2.2% (range, 1.4%-3.7%; median, 2.6%) in phakic eyes and 9.6% (range, 3.7%-16.7%; median, 10.0%) in pseudophakic eyes. This represents a more than 4-fold higher rate of posterior diffusion based on phakic status, and this difference was statistically significant (P<.001). We suggest that the absence of a native lens provides less of a barrier for the diffusion of moxifloxacin from the aqueous to the vitreous cavities than the presence of a native lens. This finding may have implications for the treatment and prophylaxis of intraocular infections with topical 0.5% moxifloxacin in phakic vs pseudophakic eyes.

Jeffrey J. Fuller, MD
Gerald McGwin, Jr, MS, PhD

In reply

We thank Drs Fuller and McGwin for their kind comments and interest in our research. It makes intuitive sense that phakic status would alter the penetration pharmacokinetics of topically administered moxifloxacin into the posterior segment. We had not performed the subgroup analysis described by Drs Fuller and McGwin, and we commend them for their detailed analysis of our data.

Their analysis implies that penetration of 0.5% moxifloxacin into the posterior segment is greater in pseudophakic eyes compared with phakic eyes. Therefore, this lends further support for the use of the fourth-generation fluoroquinolones after cataract surgery for prophylaxis against endophthalmitis. Further research is warranted to truly delineate the role of the fourth-generation fluoroquinolones through various routes of administration for the treatment of or prophylaxis against intraocular infections.

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Financial Disclosure: None.

Correction

Incorrect Dosage of Combination Therapy in Tables 1 and 2. In the Clinical Sciences article titled “Twenty-four–Hour Control With Latanoprost–Timolol–Fixed Combination Therapy vs Lantanoprost Therapy” by Anastasios G. P. Konstas et al, published in the July 2005 issue of the ARCHIVES (2005;123:898-902), the combination therapy should have been 0.005% Latanoprost-0.3% Timolol Maleate–Fixed Combination Therapy as column headings in Tables 1 and 2 on pages 900 and 901, respectively.