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ORIGINAL RESEARCH

Safety and efficacy of changing to the travoprost/timolol maleate fixed combination (DuoTrav) from prior mono- or adjunctive therapy

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Purpose: To assess the safety and efficacy of changing to the travoprost/timolol fixed combination (TTFC) from other mono- or adjunctive therapies.

Patients and methods: A prospective, open-label, observational cohort of primary open-angle glaucoma and ocular hypertensive patients whose intraocular pressure (IOP) was uncontrolled on prior therapy or was not on target. Patients were changed from prior mono- or adjunctive treatment at Day 0 to TTFC dosed every evening and underwent active treatment efficacy and safety evaluations at Week 12.

Results: In 474/522 (91%) patients who completed this trial an IOP (mm Hg) of 21.9 ± 2.0 on prior treatment was reduced by TTFC at Month 3: from all prior treatments 5.6 ± 2.6; from monotherapy 5.9 ± 2.3; from adjunctive treatments 4.5 ± 2.9; and from several of the most frequent individual treatments: timolol 5.7 ± 2.2; latanoprost 6.3 ± 2.6; and latanoprost/timolol fixed combination 4.4 ± 1.9. Ocular hyperemia was the most frequent adverse effect (n = 21, 4%). Both patients and physicians preferred TTFC compared to all prior and common individual treatments. The solicited symptom survey showed, following a modified Bonferroni correction ($\alpha/5$), a reduced incidence with TTFC of ocular pain ($P = 0.01$) while the prior medicine had a lower incidence of burning on instillation ($P < 0.001$).

Conclusions: Changing patients from prior mono- or adjunctive therapy to TTFC can provide on average a further reduction in IOP while demonstrating a favorable safety profile and a high patient preference.

Keywords: travoprost/timolol fixed combination, primary open-angle glaucoma, ocular hypertension, safety, efficacy, intraocular pressure

Introduction

Recently the travoprost 0.004%/timolol 0.5% fixed combination (DuoTrav®, Alcon Laboratories, Inc., Fort Worth, TX, USA) gained commercial approval for once daily dosing in the European Union. Barneby and associates showed that patients treated with the travoprost/timolol fixed combination, dosed each morning, had a greater reduction of intraocular pressure from baseline than timolol (1.9 to 3.3 mm Hg) or travoprost (0.9 to 2.4 mm Hg, [dosed each evening]) monotherapy.[1]

An observational study, such as the design of the current trial, may provide additive findings to randomized controlled comparisons by assessing treatment effectiveness in routine clinical practice. Such designs have the potential advantage of analyzing larger, more diverse patient populations than randomized controlled trials. Observational studies might identify differences in effectiveness and safety among more therapeutic options.[2,3]

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The primary objective of this study was to assess the safety and efficacy of changing to travoprost/timolol fixed combination from other mono- or adjunctive (fixed or unfixed combinations) therapies.

Patients and methods

Patients

This study was a prospective, open-label, observational cohort in 19 clinical centers in Germany involving 22 investigators. Patients included were: aged at least 18 years; diagnosed with ocular hypertension, primary open-angle or pigment dispersion glaucoma in at least one eye (study eye); treated with either mono- or adjunctive therapy (in a fixed or unfixed combination) for a minimum of one week at Visit 1 (this time period was chosen because we believed few patients who needed further pressure reduction would gain much greater efficacy following a week or more of treatment that a physician would delay adding a second medicine); demonstrated a need for greater ocular hypotensive efficacy; the last dose of the previous medicine was instilled correctly so the patient was within the dosing cycle of their previous medication(s) at Visit 1; at Visit 1, had a pressure of between 19–35 mm Hg inclusive in at least one eye and ≤35 mm Hg in both eyes on monotherapy or between 19–32 mm Hg inclusive in at least one eye and ≤32 mm Hg in both eyes on adjunctive therapy; and had best-corrected visual acuity of 6/60 (20/200 Snellen, 1.0 logMAR) or better in each eye.

Excluded patients had: a presence of other primary or secondary glaucomas not listed in the inclusion criterion; presence of a narrow angle by gonioscopy not treated successfully by iridectomy; any abnormality preventing reliable applanation tonometry in study eye(s); corneal dystrophies; any opacity or patient uncooperativeness that restricted adequate examination of the ocular fundus or anterior chamber of the study eye(s); concurrent infectious/noninfectious conjunctivitis, keratitis or uveitis in either eye; intraocular conventional surgery or laser surgery in study eye(s) less than 3 months prior to Visit 1; risk of visual field or visual acuity worsening as a consequence of participation in the trial; progressive retinal or optic nerve disease from any cause; women of childbearing potential not using reliable means of birth control; women who were pregnant or lactating; any clinically significant, serious, or severe medical or psychiatric condition; a condition which would present a special risk to the patient; participation in any other investigational study within 30 days prior to Visit 1; known medical history of allergy, hypersensitivity or poor tolerance to any components of the medications to be used in this trial; use of systemic medications known to affect the intraocular pressure which have not been on a stable course for at least 7 days prior to Visit 1 or an anticipated change in the dosage during the course of the study; reactive airway disease; sinus bradycardia (<50 beats per minute); second- or third-degree atrioventricular block; overt cardiac failure; severe allergic rhinitis; unwillingness to risk the possibility of darkened irides or eyelash changes; a history of, or at risk for uveitis, cystoid macular edema or history of ocular herpes simplex.

Procedures

Patients first signed an Ethics Committee-approved Informed Consent before any trial procedures were performed. This trial (NCT00519753) was registered at http://www.clinicaltrials.gov/. At each visit patients underwent Goldmann applanation tonometry and slit lamp biomicroscopy, and had Snellen visual acuity and adverse event assessments performed. Patients completed a symptom survey at Visits 1 and 3 and both patients and physicians provided a global preference response at Visit 3. At the end of Visit 1, qualified patients had their previous glaucoma therapy discontinued and received a commercially available open-label bottle of the travoprost/timolol fixed combination to be used once every evening in the study eye(s).

Patients returned at Week 4 for a safety visit (Visit 2). Visit 2 was scheduled at the same time (±1 hour) as Visit 1. Patients must have been taking travoprost/timolol fixed combination as prescribed or the visit was rescheduled. At this visit, patients received two additional bottles of the study medicine for use until the end of the study. Patients whose intraocular pressure was elevated over baseline (Visit 1), who were considered treatment failures to travoprost/timolol fixed combination, had an intolerable adverse event, or had been noncompliant to therapy, were discontinued from the trial.

Patients returned for the final visit at Week 12 (Visit 3) which was scheduled at the same time (±1 hour) as Visit 1. Patients must have been taking their travoprost/timolol fixed combination as prescribed or the visit was rescheduled. The patient's participation in the trial was considered successful if they completed the study (not discontinued due to noncompliance or an adverse event) and demonstrated a further reduction in intraocular pressure (≥1 mm Hg) from Visit 1. Patients withdrawn from the trial for protocol violations or medication errors were not included in the Per Protocol analysis.

Data analysis

The data were analyzed by PRN Pharmaceutical Research Network, LLC. All data analyses were two-sided and an α-level of 0.05 was used to declare statistical significance. An

average eye, Per Protocol analysis was utilized. Internet- based electronic data capture was used for the trial.

The primary efficacy variable, the change in intraocular pressure between travoprost and the travoprost/timolol fixed combination based on Per Protocol dataset, was analyzed using a paired *t*-test within a one-way analysis of variance (ANOVA) test.[4] A standard deviation of 2.8 mm Hg was assumed to determine the sample size calculation.[5,6] This study provided an 80% power that a difference of 1.5 mm Hg could be excluded between the travoprost/timolol fixed combination and travoprost if at least 27 patients were analyzed for this subgroup.

The secondary efficacy variables: the change of intraocular pressure for the travoprost/timolol fixed combination from other therapeutic regimens (individual or group comparisons) also was analyzed using a paired *t*-test within an ANOVA. Only prior therapies with 27 or more patients who changed to the travoprost/timolol fixed combination were analyzed individually. This helped ensure a normal distribution of patients as well as a similar statistical power as the primary efficacy variable. For the change in pressure for the study cohort as a whole (from any previous therapy) to travoprost/timolol fixed combination, a one-way ANOVA was used.[4] A paired *t*-test within an ANOVA test was also used to evaluate differences in the patient surveys and visual acuity between baseline (Visit 1) and Week 12 (Visit 3). As a result of multiple subgroup assessments (differing prior therapies), a modified Bonferroni correction ($\alpha/5$) was used to adjust the *P*-value.[7]

Adverse events were analyzed with a McNemar's test[6] for intragroup analysis, and global preference by a χ^2 or Fisher's exact test[4] between travoprost/timolol fixed combination and prior therapy, as well as the study cohort as a whole.

Results

Patients

Table 1 describes the disposition of the patients who enrolled in the study and Table 2 details patient characteristics.

Intraocular pressure

Intraocular pressure findings are presented in Table 3. Significant decreases in intraocular pressure were observed from prior treatment (Visit 1, Day 0) with the travoprost/timolol fixed combination on the last exam (Visit 3, Month 3), from all prior mono- and adjunctive treatments, and from prior individual treatments that were analyzable with sufficient statistical power to be clinically meaningful, which included travoprost (primary efficacy variable), timolol, latanoprost, latanoprost/timolol fixed combination, brinzolamide.

Table 1 Relevant population information – Intention-to-Treat population

Population parameter	Patients	Percent
Intention-to-Treat population	522	100
Per Protocol population	474	91
Subjects withdrawn for clinical reasons (more than one reason possible)	28	5
Adverse events	19	4
Withdrew consent	6	1
Noncompliance	2	0.4
Lack of efficacy	1	0.2
Lost to followup	1	0.2
Other reasons	4	1
Subjects withdrawn for protocol deviations	20	14
Date of visit out of time frame	19	4
Comedication not allowed Per Protocol	1	0.2

In addition, there was a significant improvement after changing from bimatoprost, but not bimatoprost/timolol fixed combination ($P < 0.001$ and $P = 0.696$, respectively). Figure 1 shows the intraocular pressure decrease from baseline (Visit 1), irrespective of prior therapy. At each prior intraocular pressure level, there was a further significant decrease in pressure after changing to travoprost/timolol fixed combination ($P < 0.001$).

Safety

The most frequent adverse events are shown in Table 4. In total, there were 93 (18%) patients with at least one ocular or systemic adverse event on travoprost/timolol fixed combination with hyperemia being most frequent (n = 37, 7%). There were 10 (2%) systemic adverse events with headache (n = 5, 1%) being most frequent.

Overall, 20 (4%) patients were discontinued for an adverse event. The most common adverse event resulting in a patient's discontinuation of the study was hyperemia (n = 6, 1%). There were three serious adverse events in patients, while on the travoprost/timolol fixed combination including, kidney stones (n = 1), dizziness (n = 1) and a fractured arm (n = 1). None of these serious events were believed to be related to the study medicine by the investigator.

Product preference and treatment success

Table 5 shows the preference by both the patient and doctor for either the travoprost/timolol fixed combination or the prior prescribed product. Both patients and doctors preferred the travoprost/timolol fixed combination to all prior treatments, both mono- and adjunctive treatments, and from common prior individual treatments.

Table 2 Patient characteristics – Intention-to-Treat population

Characteristic	Variable	Patients	Percent
Gender	Female	318	61
	Male	204	39
Race	Caucasian	516	99
	Black	4	1
	Asian	1	0.2
	Hispanic	1	0.2
Iris color	Blue	248	48
	Brown	155	30
	Green	49	9
	Other	70	13
Age (years)	≤55	70	13
	56–65	123	24
	66–75	196	38
	≥76	133	26
Glaucoma diagnoses	POAG	471	90
	Ocular hypertension	43	8
	Pigmentary glaucoma	8	2
Prior ophthalmic medication (n ≥ 30)	Timolol	149	29
	Latanoprost	64	12
	LTFC	51	10
	Travoprost	51	10
	Brinzolamide	33	6
	Other	174	33
Past medical history (most common)	Arterial hypertension	205	39
	Diabetes	101	19
	Thyroid	49	9
	Lipid disorder	28	5
	Coronary artery disease	22	4
	Hematologic disorder	19	4
	Neurologic seizure disorder	18	3
Concomitant medication (most common)	ACE inhibitor	112	22
	Beta-blocker	74	14
	Hormone therapy	77	15
	Antihyperglycemic	52	10
	Diuretic	44	8

Abbreviations: POAG, primary open-angle glaucoma; LTFC, latanoprost/timolol fixed combination; ACE, angiotensin-converting enzyme.

Table 6 shows the results of the solicited symptom survey. Following the modified Bonferroni correction, there was a reduced incidence of ocular pain with the travoprost/timolol fixed combination ($P = 0.01$) and a reduction in eyelid crusting that was approaching significance ($P = 0.08$). Additionally, the prior medicine had a lower incidence of burning on instillation ($P < 0.001$) although no patients discontinued their participation in the study due to this complaint.

Table 3 Intraocular pressure at each study visit (by prior treatment) – Per Protocol population mean [mm Hg (standard deviation)]

Treatment	Patients	Visit 1	Visit 2	Visit 3	V1–V3	*P*-value
All	474	21.9 (2.1)	16.5 (2.2)	16.3 (2.2)	5.6 (2.6)	<0.001
Monotherapy	352	22.0 (2.2)	16.4 (2.2)	16.1 (1.9)	5.9 (2.4)	<0.001
Combined therapy	122	21.5 (2.0)	16.9 (2.3)	17.0 (2.9)	4.5 (2.8)	<0.001
Travoprost	45	22.1 (2.7)	16.2 (2.6)	15.8 (2.4)	6.3 (2.5)	<0.001
Timolol	130	21.8 (2.0)	16.4 (2.1)	16.1 (1.8)	5.7 (2.3)	<0.001
Latanoprost	60	22.3 (2.4)	16.7 (2.2)	16.0 (2.0)	6.3 (2.8)	<0.001
LTFC	47	21.5 (1.9)	17.6 (2.1)	17.1 (2.1)	4.4 (1.7)	<0.001
Brinzolamide	30	22.7 (2.4)	15.7 (2.5)	16.2 (2.3)	6.5 (2.8)	<0.001
Bimatoprost	16	22.4 (2.1)	16.1 (2.2)	16.3 (1.9)	6.2 (3.1)	<0.001
BTFC	2	20.8 (2.5)	16.0 (7.1)	17.0 (12.73)	3.8 (10.3)	0.70

Notes: The last two analyses were done despite the low number of patients because of the perceived importance of the clinical comparison.
Abbreviations: LTFC, latanoprost/timolol fixed combination; BTFC, bimatoprost/timolol fixed combination.

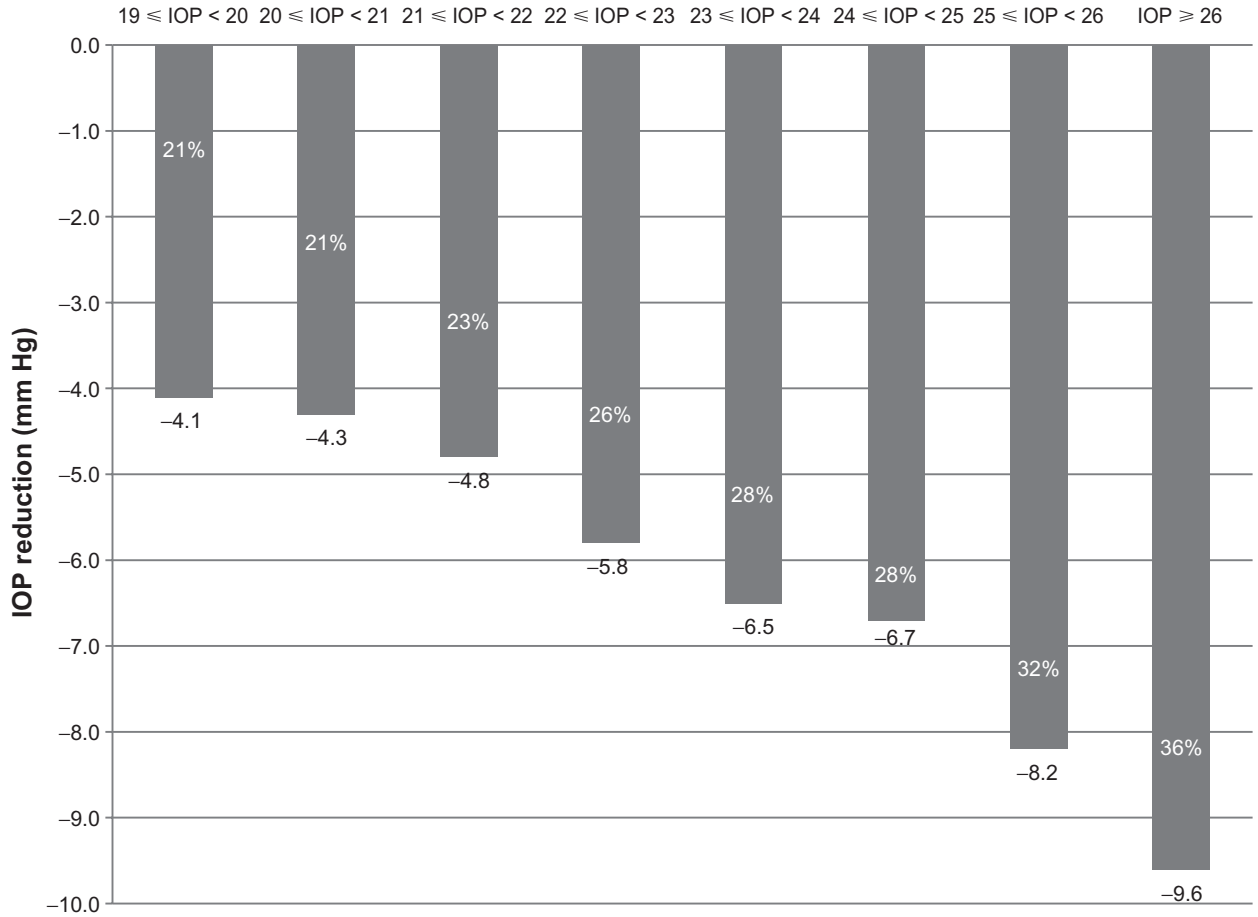

Figure 1 The intraocular pressure (IOP) decrease from baseline (Visit 1), irrespective of prior therapy, for the Per Protocol population.

Of patients initiating treatment, 93% (n = 484) were considered a treatment success by the definition provided in the methods section. Of patients changed from mono- and adjunctive therapy respectively, 94% (n = 364) and 90% (n = 121) were considered a success. From common individual therapies: travoprost, 90% (n = 46); timolol, 93% (n = 138); latanoprost, 92% (n = 59); the latanoprost/timolol fixed combination, 96% (n = 49); and brinzolamide, 97% (n = 32) were considered a success. There was not a statistical difference in success among the above individually considered treatment groups ($P = 0.68$).

Discussion

The primary objective of this study was to assess the safety and efficacy of changing to travoprost/timolol fixed combination from other mono- or adjunctive (fixed or unfixed combinations) therapies.

This study showed significant decreases in intraocular pressure after 3 months of chronic dosing with the travoprost/timolol fixed combination from all common prior treatments analyzed as a group, both mono- and adjunctive treatments analyzed as a group, and from prior individual treatments that were analyzable with sufficient statistical

Table 4 Ocular or systemic adverse events by prior therapy – Intention-to-Treat population patients (%) (>10 occurrences)

Adverse event	All	Monotherapy	Combined therapy	Travoprost	Timolol	Latanoprost	LTFC	Brinzolamide
Patients	522	388	134	51	149	64	51	33
All	93 (18)	65 (17)	28 (21)	9 (18)	33 (22)	5 (8)	3 (6)	4 (12)
Mild	43 (8)	26 (7)	17 (13)	3 (6)	14 (9)	1 (2)	2 (4)	3 (9)
Moderate	35 (7)	27 (7)	8 (6)	4 (8)	15 (10)	3 (5)	1 (2)	0 (0)
Severe	15 (3)	12 (3)	3 (2)	2 (4)	4 (3)	1 (2)	0 (0)	1 (3)
Hyperemia	37 (7)	23 (6)	14 (10)	1 (2)	10 (7)	1 (2)	0 (0)	2 (6)
Ocular itching	13 (3)	10 (3)	3 (2)	1 (2)	6 (4)	0 (0)	1 (2)	0 (0)

Abbreviation: LTFC, latanoprost/timolol fixed combination.

Table 5 Patient and doctor's opinion about TTFC – Per Protocol population

Treatment	Patients	Patient prefers TTFC			Doctor prefers TTFC		
		Percent	Lower 95% CI	Upper 95% CI	Percent	Lower 95% CI	Upper 95% CI
All	474	88	86	91	91	89	94
Monotherapy	352	88	85	92	93	90	95
Combined therapy	122	89	83	94	88	82	94
Travoprost	45	93	86	100	93	86	100
Timolol	130	85	79	92	91	86	96
Latanoprost	60	90	82	98	97	92	100
LTFC	47	85	75	96	83	72	94
Brinzolamide	30	90	77	100	93	84	100
Bimatoprost	16	75	51	99	88	69	100
BTFC	2	100	100	100	50	0	100

Abbreviations: CI, confidence interval; TTFC, travoprost/timolol fixed combination; LTFC, latanoprost/timolol fixed combination; BTFC, bimatoprost/timolol fixed combination.

power to be clinically meaningful, which included travoprost, timolol, latanoprost, latanoprost/timolol fixed combination and brinzolamide. The average decrease in pressure from all prior treatments was 5.6 mm Hg; the average reduction from all prior monotherapy and adjunctive therapy was 5.9 mm Hg and 4.5 mm Hg, respectively. Importantly, this significant decrease in intraocular pressure occurred from prior levels of pressure when the patient was already treated with ocular hypotensive therapy. In addition, there was a significant improvement after changing from bimatoprost, but not the bimatoprost/timolol fixed combination. However, only two patients were available in the latter group. The bimatoprost groups were analyzed because of the importance of this compound in the treatment of glaucoma. Furthermore, there was a significant decrease in pressure after changing to the travoprost/timolol fixed combination regardless of the pressure on common prior therapy (19 to >26 mm Hg). This finding indicates the effectiveness of the travoprost/timolol fixed combination in further reducing intraocular pressure across a wide range of prior therapy.

One of the problems in analyzing data from a trial in which a prior therapy is changed to a switch therapy in an open-label fashion is that the switch therapy has an inherent advantage in intraocular pressure reduction. The reason for this is not known but may result from the 'regression to the mean' phenomenon.[8] This occurs because even a treated intraocular pressure typically fluctuates within a certain range. Accordingly, if the intraocular pressure is measured by chance at the high end of its typical range, it may not have been a true worsening of the disease. Therefore, a physician may adjust a therapeutic regimen to decrease an intraocular pressure that appears too high. By the next clinic visit, if the intraocular pressure appears normalized, any change in therapy from the prior visit may only have appeared to have improved the pressure because it may have regressed towards its mean even on the previous therapeutic regimen.

Nevertheless, in this current trial, the extent of intraocular pressure reduction with the travoprost/timolol fixed combination from prior treatment was higher than expected. Prior studies with similar design (ie, an open-label fashion) have shown an average reduction of 3.6 mm Hg from adjunctive treatment and 3.4 mm Hg from monotherapy treatment, when switched to a fixed combination therapy.[8-14] Nonetheless, because of the unmasked, nonrandomized design of the current study design, further research is required to confirm the results of this study.

Safety results showed that the travoprost/timolol fixed combination was well tolerated in the majority of cases. In the Intention-to-Treat population, 4% of patients discontinued due to an adverse event, most commonly hyperemia (1%). An ocular or systemic adverse event occurred in 18% of patients, with the most common being hyperemia in 7% of patients. Systemic side effects were few, with the most frequent being headache at an incidence rate of 1%.

In total, 93% of patients were considered successfully treated with the travoprost/timolol fixed combination. The preference results showed a clear choice by both doctors and patients for the travoprost/timolol fixed combination. The reason for the strong preference for the fixed combination was not available in the product preference questionnaire. The preference choice may have been influenced by the positive results of the study, which showed that the travoprost based fixed combination appeared to have efficacy advantages, with a favorable safety profile, in comparison to prior therapies. Unfortunately, the results of the solicited patient survey failed to provide further clarity on why patients generally preferred the travoprost/timolol fixed combination. The survey results demonstrated that the travoprost/timolol fixed combination

Table 6 Ocular symptoms summary – Per Protocol population patients (%)

	Level	Visit 1	Visit 3	*P*-value
Have you had dry eyes or dryness around your eyes since your last visit?	None	438 (92)	458 (97)	0.03
	Minimal	8 (2)	5 (1)	
	Mild	16 (3)	8 (2)	
	Moderate	11 (2)	2 (0.4)	
	Severe	1 (0.2)	1 (0.2)	
Have you had pain in or around your eye when in the light since your last visit?	None	465 (98)	471 (99)	0.01
	Minimal	3 (0.6)	0 (0)	
	Mild	1 (0.2)	3 (0.6)	
	Moderate	5 (1)	0 (0)	
Have your eyes teared more than normal since your last visit?	None	455 (96)	464 (98)	0.23
	Minimal	3 (0.6)	3 (0.6)	
	Mild	8 (2)	5 (1)	
	Moderate	6 (1)	2 (0.4)	
	Severe	2 (0.4)	0 (0)	
Did your study eye drops sting or burn when you instilled them?	None	453 (96)	422 (89)	<0.001
	Minimal	12 (3)	29 (6)	
	Mild	7 (2)	4 (0.8)	
	Moderate	2 (0.4)	19 (4)	
Have you had crusting around your eyes since your last visit?	None	458 (97)	467 (99)	0.08
	Minimal	9 (2)	6 (1)	
	Mild	4 (0.8)	1 (0.2)	
	Moderate	3 (0.6)	0 (0)	
Have you had itching of your eyes, eyelids, or the area around your eyes since your last visit?	None	445 (94)	441 (93)	0.93
	Minimal	15 (3)	14 (3)	
	Mild	8 (2)	11 (2)	
	Moderate	5 (1)	7 (2)	
	Severe	1 (0.2)	1 (0.2)	
Since your last visit did you experience a sandy or gritty feeling after you instilled your study drops?	None	454 (96)	453 (96)	0.72
	Minimal	7 (2)	10 (2)	
	Mild	9 (2%)	9 (2)	
	Moderate	3 (0.6)	2 (0.4)	
	Severe	1 (0.2)	0 (0)	
Have you had a feeling or irritation in your eyes since your last visit?	None	460 (97)	454 (96)	0.53
	Minimal	6 (1)	5 (1)	
	Mild	5 (1)	9 (2)	
	Moderate	3 (0.6)	5 (1)	
	Severe	0 (0)	1 (0.2)	
Have you noticed redness in your study eye?	None	458 (97)	439 (93)	0.03
	Minimal	3 (0.6)	11 (2)	
	Mild	9 (2)	11 (2)	
	Moderate	4 (0.8)	12 (3)	
	Severe	0 (0)	1 (0.2)	
Have other people commented about redness in your study eye?	None	461 (97)	444 (94)	0.07
	Minimal	5 (1)	18 (2)	
	Mild	3 (0.6)	10 (2)	
	Moderate	5 (1)	11 (2)	
	Severe	0 (0)	1 (0.2)	
How easy is it for you to get your eye drops in your study eye?	Very difficult	2 (0.4)	4 (0.8)	0.36
	Difficult	16 (3)	13 (3)	
	Easy	335 (71)	355 (75)	
	Very easy	121 (26)	102 (22)	

was associated with less ocular pain but also showed more burning and stinging with the fixed combination. There was a trend towards more patients, and their acquaintances, noticing more ocular redness on the travoprost/timolol fixed combination, but this was not significant after the Bonferroni correction for multiple comparisons.

The data generated from this study are clinically important because they indicate that when an ocular

hypertensive or primary open-angle glaucoma patient, who was previously treated with one or two glaucoma agents, is in need of further intraocular pressure reduction, a physician can generally anticipate greater pressure reduction with a favorable safety profile, high patient preference and a low dropout rate, by changing to the travoprost/timolol fixed combination.

Conclusion

This study suggests that changing patients from prior mono- or adjunctive therapy to the travoprost/timolol fixed combination can provide, on average, a further reduction in intraocular pressure while demonstrating a favorable safety profile and a high patient preference rate.

This study did not evaluate changing patients to the travoprost/timolol fixed combination in a masked, randomized, parallel comparative trial. Consequently our design may have produced potential bias in the results. In addition, this study did not explore the long-term clinical outcomes of using the travoprost/timolol fixed combination. Further research, with a more robust study design, is required to more fully understand the clinical profile of the travoprost/timolol fixed combination in treating primary open-angle glaucoma and ocular hypertension.

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