Treatment of open angle glaucoma or ocular hypertension with preservative-free tafluprost/timolol fixed dose combination in a real-world setting: analysis by diagnostic subgroup and prior treatment at study entry

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Introduction

Topical prostaglandin analogue (PGA) and β-blocker monotherapies are among the first-line treatments recommended for the lowering of intraocular pressure (IOP) in people with open-angle glaucoma (OAG) and/or ocular hypertension (OHT).[1,2] Fixed-dose combination therapies are designed to provide the benefits of both treatment types.

The preservative-free tafluprost (0.0015%) and timolol (0.5%) fixed-dose combination (PF tafluprost/timolol FC) has demonstrated IOP-lowering efficacy alongside a good tolerability profile in randomized trials and observational studies.[3-9]

The VISIONARY study was a large multicenter observational trial, which demonstrated statistically and clinically significant IOP reductions with PF tafluprost/timolol FC treatment in patients with OAG and OHT who were insufficiently controlled on PGA or β-blocker monotherapy.[9]

The current analysis examined data from the VISIONARY study to investigate the IOP reduction achieved with PF tafluprost/timolol FC therapy according to glaucoma diagnosis and prior treatment type.

Methods

Data were collected during routine consultations at 66 ophthalmology clinics in Austria, Denmark, Hungary, Ireland, Italy, Latvia, Netherlands, Norway, Russia, Spain, Sweden and the United Kingdom. Treatment outcomes were assessed at Week 4, Week 12 and Month 6 following initiation of PF tafluprost/timolol FC treatment. Baseline and Month 6 study visits were mandatory, while attendance at Week 4 and Week 12 visits was optional.

Inclusion criteria

- Male/female adults (aged ≥18 years)
- OAG or OHT diagnosis
- Insufficient response to previous PGA or β-blocker monotherapy
- Likely to benefit from PF eye drops (judged by physician)

Exclusion criteria

- Treated with PF tafluprost/timolol FC (previously or currently)
- Ophthalmic surgery (within 6 months)
- Pregnancy or breastfeeding

Primary study endpoint

- Mean absolute change in IOP from baseline at Month 6 after a switch to PF tafluprost/timolol FC

Exploratory endpoints

- Mean (standard deviation [SD]) change in IOP from baseline at Month 6 and interim study visits according to:
  - Baseline glaucoma diagnosis
  - Prior monotherapy type (PGA or β-blocker)
- Discontinuations from study drug due to poor local tolerance or insufficient IOP control

Statistical analysis

- Change from baseline concerning IOP was assessed using a two-sided t-test
- The two-sided Wilcoxon signed rank test was used for subgroup analysis according to diagnostic group and prior monotherapy

Results

Patient demographics

In total, 577 patients were included in the analysis.

At baseline, 425 participants were diagnosed with primary open-angle glaucoma (POAG), 110 had OHT, 19 were diagnosed with pseudoexfoliative glaucoma (PEX), 13 had normal tension glaucoma (NTG) and 10 were categorised as having another type of glaucoma, outside of these main categories.

IOP change according to glaucoma diagnosis

Table 1 shows the mean (SD) IOP change at each study visit according to glaucoma diagnosis.

At Month 6, mean (SD) IOP was significantly reduced in each of the diagnostic subgroups assessed:

- POAG: 5.8 (4.02) mmHg (25.4%; p <0.0001)
- OHT: 6.2 (4.18) mmHg (26.1%; p <0.0001)
- PEX: 3.9 (4.65) mmHg (17.6%: p = 0.002)
- NTG: 2.9 (3.17) mmHg (15.8%; p = 0.006)

The study was not powered to assess statistical differences between unplanned subgroups.

Table 1. Change in mean (SD) IOP from baseline according to diagnosis

Visit	N	Mean (SD) IOP, mmHg	Mean (SD) IOP reduction from baseline, mmHg	Mean % IOP reduction from baseline	p value*
POAG					
Baseline	425	21.5 (5.00)			
Week 4	399	16.2 (3.32)	5.4 (3.76)	23.5	<0.0001
Week 12	378	15.6 (2.91)	5.9 (3.98)	25.7	<0.0001
Month 6	425	15.6 (3.01)	5.8 (4.02)	25.4	<0.0001
OHT					
Baseline	110	22.3 (4.30)			
Week 4	104	16.2 (3.09)	6.1 (3.80)	25.9	<0.0001
Week 12	91	16.1 (3.23)	6.4 (3.68)	27.0	<0.0001
Month 6	110	16.1 (3.33)	6.2 (4.18)	26.1	<0.0001
PEX					
Baseline	19	21.7 (4.13)			
Week 4	17	17.2 (3.65)	4.6 (3.74)	20.1	0.0001
Week 12	15	16.9 (2.90)	5.3 (3.46)	22.9	<0.0001
Month 6	19	17.8 (5.11)	3.9 (4.65)	17.6	0.002
NTG					
Baseline	13	17.2 (2.68)			
Week 4	11	14.5 (2.02)	2.7 (2.76)	14.5	0.008
Week 12	10	14.3 (1.70)	2.7 (2.36)	14.7	0.006
Month 6	13	14.3 (2.56)	2.9 (3.17)	15.8	0.006

*Significance testing using two-sided Wilcoxon sign rank test

IOP change according to prior monotherapy

Table 2 shows the mean (SD) IOP change at each study visit according to the monotherapy used prior to initiating PF tafluprost/timolol FC treatment.

- Prior PGA monotherapies comprised latanoprost, tafluprost, bimatoprost and travoprost
- At Month 6, those previously treated with PGA monotherapy demonstrated mean (SD) IOP reductions from baseline of 5.4 (4.04) mmHg (23.6%; p<0.0001)
- Prior β-blocker users showed mean (SD) Month 6 IOP reductions of 6.6 (4.16) mmHg (28.5%; p<0.0001)

Table 2. Change in mean (SD) IOP from baseline at each study visit according to previous therapy

Visit	N	Mean (SD) IOP, mmHg	Mean (SD) IOP reduction from baseline, mmHg	Mean % IOP reduction from baseline	p value*
Previous PGA users					
Baseline	416	21.4 (4.48)			
Week 4	384	16.2 (3.21)	5.3 (3.83)	23.1	<0.0001
Week 12	362	15.8 (2.97)	5.6 (3.97)	24.6	<0.0001
Month 6	416	16.0 (3.23)	5.4 (4.04)	23.6	<0.0001
Previous β-blocker users					
Baseline	161	21.9 (4.36)			
Week 4	157	16.2 (3.44)	5.8 (3.56)	25.2	<0.0001
Week 12	141	15.5 (3.00)	6.5 (3.63)	28.1	<0.0001
Month 6	161	15.3 (3.10)	6.6 (4.16)	28.5	<0.0001

*Significance testing using two-sided Wilcoxon sign rank test

Discontinuations from PF tafluprost/timolol FC

Overall, 14 patients discontinued use of PF tafluprost/timolol FC therapy due to poor local tolerance or insufficient IOP control (Table 3).

Table 3. Discontinuations from study drug due to poor local tolerance or insufficient IOP control

Diagnosis	Number of discontinuations	
	Insufficient IOP control	Poor local tolerance
POAG	2	7
OHT	0	3
PEX	0	1
NTG	0	1

Discussion

- In routine clinical practice, a switch to PF tafluprost/timolol FC therapy from PGA or β-blocker monotherapy was associated with significant mean IOP reductions among those diagnosed with POAG, OHT, PEX and NTG
- Statistically significant IOP reductions were observed with PF tafluprost/timolol FC therapy, regardless of whether a PGA or β-blocker was used prior to the treatment switch
- Statistically and clinically significant IOP reductions were demonstrated from Week 4 and sustained through Month 6 in each of the diagnostic and prior treatment subgroups examined
- Relatively few patients discontinued from PF tafluprost/timolol FC therapy as a consequence of insufficient IOP control or poor local tolerance

Conclusions

In this real-world study, PF tafluprost/timolol FC provided IOP-lowering efficacy in patients previously insufficiently controlled on β-blocker or PGA monotherapy, irrespective of initial diagnosis or the type of prior medication used. In each of the subgroups examined, significant IOP reductions were observed at Week 4 and maintained throughout the study period.

Disclosures
Francesco Oddone has received consultancy fees from Santen, Allergan, Sooft, Omikron Italia, Centervue and Novartis
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