



Treatment of Open-Angle Glaucoma and Ocular Hypertension with Preservative-Free Tafluprost/Timolol Fixed-Dose Combination Therapy: UK and Ireland Results from the VISIONARY Study

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ABSTRACT

Introduction: Reducing intraocular pressure (IOP), the only modifiable risk factor for open-angle glaucoma (OAG), is important for the preservation of vision and slowing of disease progression. Preservative-free tafluprost (0.0015%)/timolol (0.5%) fixed combination (PF Taf-T FC) is an approved combination

therapy for OAG treatment. The VISIONARY study aimed to evaluate the effectiveness and tolerability of PF Taf-T FC in real-world clinical settings. Here, we present the results from the United Kingdom (UK) and Ireland.

Methods: This observational, multicentre, European, prospective study recorded data during routine clinic appointments on the use of PF Taf-T FC for the treatment of OAG and ocular hypertension (OHT) in patients whose disease was insufficiently controlled on a prostaglandin analogue (PGA) or beta blocker monotherapy or who did not tolerate these medications. Mean change in IOP, symptom severity, changes in clinical signs, and tolerability were investigated over 6 months.

Results: Eighty-two patients were recruited in the UK and Ireland. After 6 months of PF Taf-T FC treatment, mean IOP was significantly reduced from 22.0 to 16.2 mmHg in the UK group and from 18.6 to 14.1 mmHg in the Ireland group. In the UK (65 patients), 49 adverse events (AEs) were reported, of which 3 were serious. No AEs were reported in the Ireland group (17 patients). Overall, 91.9% of UK physicians reported PF Taf-T FC treatment to be the same or better than prior medication for improving clinical signs; 90.0% of UK patients reported PF Taf-T FC treatment to have good or very good tolerability.

Conclusions: Treatment with PF Taf-T FC resulted in significant reductions in mean IOP over 6 months. Patients and physicians reported

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that treatment was well tolerated. These data demonstrate real-world efficacy of PF Taf-T FC for the treatment of OAG and OHT in routine clinical practice in the UK and Ireland.

Trial registration: European Union electronic Register of Post-Authorisation Studies (EU PAS) register number, EUPAS22204.

Keywords: Fixed-dose combination; Ocular hypertension; Open-angle glaucoma; Ophthalmology; Preservative-free topical medication; Tafluprost; Timolol

Key Summary Points

Why carry out this study?

Preservative-free tafluprost (0.0015%)/timolol (0.5%) fixed combination (PF Taf-T FC) is a combination therapy for the treatment of open-angle glaucoma (OAG).

PF Taf-T FC has been shown to reduce intraocular pressure (IOP) in patients with OAG in randomised clinical trials.

This study investigated the effectiveness and tolerability of PF Taf-T FC in real-world clinical settings in Europe. This paper focuses on results from the United Kingdom (UK) and Ireland, where previously prescribed monotherapy is most likely to be prostaglandin analogues.

What was learned from the study?

Country-specific analysis found that, over 6 months, PF Taf-T FC treatment significantly reduced mean IOP in patients with OAG in the UK and Ireland.

This study demonstrates real-world efficacy and tolerability of PF Taf-T FC treatment in routine clinical practice in these countries.

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to <https://doi.org/10.6084/m9.figshare.14261039>.

INTRODUCTION

Increased intraocular pressure (IOP) is an important risk factor for the development of open-angle glaucoma (OAG). Reducing IOP is the only available mechanism for slowing disease progression and is critical for preserving vision and halting visual field loss [1].

Topical IOP-lowering monotherapy medications are first-line treatments for OAG [1–4]. In England, the National Institute for Health and Care Excellence (NICE) recommend prostaglandin analogues (PGA) [3] while other European countries recommend beta blockers [4]. However, if these do not result in a reduction to target IOP, additional therapy is required [4]. Commonly, this is a combination of a PGA and a beta blocker. Fixed-dose combinations of PGAs and beta blockers are often used as they minimise drop requirement and improve adherence [4, 5]. Preservative-free therapies are increasingly being adopted as they are associated with a lower risk of ocular surface disease (OSD) [6, 7] than preserved drops, which further promotes adherence. Preservative-free tafluprost (0.0015%)/timolol (0.5%) fixed combination (PF Taf-T FC) is a preservative-free PGA/beta blocker fixed combination treatment approved for the treatment of OAG [8]. Previous clinical trials have shown a low rate of hyperaemia with PF Taf-T FC treatment [8, 9].

Randomised controlled trials (RCTs) are the gold standard for the collection of robust safety and efficacy data. However, they are unable to represent the full spectrum of real-world scenarios [10]. Real-world evidence from observational studies recording data from standard clinical practice can complement the rigorous safety and efficacy data produced by RCTs by comparing the results of RCTs with those

pragmatically collected through standard clinical practice [11].

The VISIONARY study evaluated the effectiveness and tolerability of PF Taf-T FC treatment in patients with OAG or ocular hypertension (OHT) over 6 months who previously had an insufficient response to either PGA or beta blocker monotherapy, or who did not tolerate these medications, and were judged by their physician to benefit from preservative-free eye drops. Results from the full data set have previously been published [12]. This paper presents the data and further country-specific analysis for patients in the UK and Ireland, and discusses the potential differences between these countries and the full data set. The UK cohort was chosen to be included in this country-specific analysis as, unlike most European countries, UK guidelines recommend PGAs rather than beta blockers as first-line treatments for OAG. Differences in the methodology to measure mean IOP in Ireland (Goldmann vs iCARE tonometry methods), according to standard clinical practice in the country, mean that detailed analysis may allow exploration of the differences in IOP change that may be experienced by patients in real-world practice.

METHODS

Patients

The inclusion and exclusion criteria are summarised in Supplementary Table S1. Details of the trial design are published elsewhere [12]. In brief, male or female patients aged at least 18 years with a diagnosis of OAG or OHT were recruited. Patients with insufficient IOP control on, or intolerance to, monotherapy with topical beta blockers or PGAs, and who were judged by their physician to benefit from preservative-free eye drops, were recruited to the study. All eligible patients attending participating clinics were invited to participate in the study. Patients were required to provide informed consent before enrolling.

Study Design

In line with European Medicines Agency (EMA) requirements, the study was registered under the European Network of Centres for Pharmacoeconomics and Pharmacovigilance (ENCePP[®]) European Union electronic Register of Post-Authorisation Studies (EU PAS Register) (EU PAS register number EUPAS22204). The study complied with the principles of the Declaration of Helsinki. The study protocol was approved by the institutional review board (IRB) or independent ethics committee (IEC) at each centre/institution. The study centres/institutions are listed in the Acknowledgments alongside the relevant principal investigator.

A 6-month, observational, multicentre, prospective study was undertaken (Fig. 1). Eleven countries were included in the study; however, this paper presents results from the UK and Ireland only [12]. Data were recorded during routine clinical visits and were entered into electronic case report forms. Patients were prescribed PF Taf-T FC treatment as one drop daily [12]. Baseline data were recorded within 7 days of PF Taf-T FC treatment initiation. Follow-up clinical visits were completed after 4 weeks (± 7 days), 12 weeks (± 7 days) and 6 months (± 45 days) of PF Taf-T FC treatment. However, data collection at 4 and 12 weeks was optional.

Study Procedures and Evaluations

The primary endpoint of the study was mean absolute IOP change (mmHg) from baseline to 6 months after PF Taf-T FC treatment initiation. Secondary endpoints were mean absolute IOP change from baseline at interim visits (weeks 4 and 12) and patient responder rate, defined as the percentage of patients with an IOP change from baseline of at least 20% at week 12. Changes in ocular signs and severity of symptoms, including conjunctival hyperaemia and visual acuity, at week 4, week 12 and month 6 were investigated. Additionally, change in subjective symptoms with PF Taf-T FC treatment were explored, including differences in severity. Effectiveness and patient compliance as

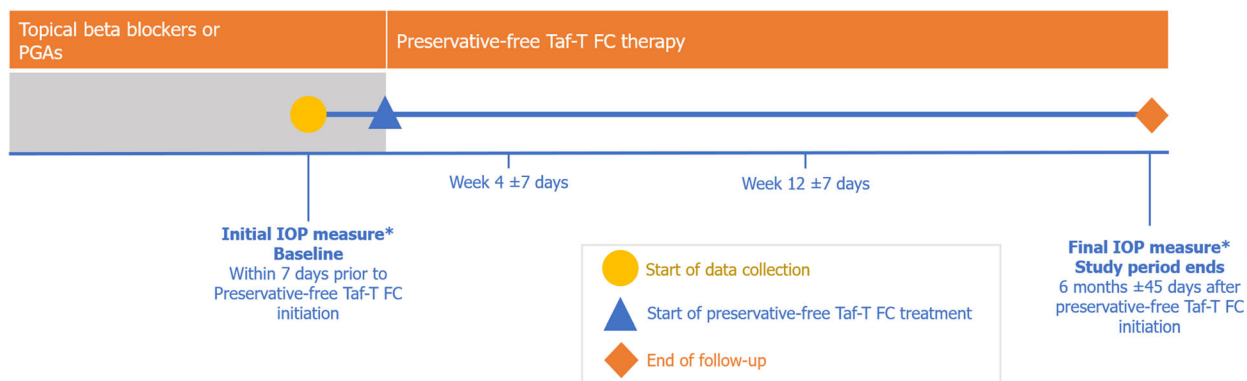


Fig. 1 VISIONARY study design. *Mandatory visit. *IOP* intraocular pressure, *PGA* prostaglandin analogue, *Taf-T FC* tafluprost/timolol fixed combination

assessed by the physician, and tolerability as assessed by the patient, of PF Taf-T FC were also investigated.

Demographic, diagnosis and previous treatment data were recorded at baseline (Table 1). In addition, a baseline IOP measurement was recorded, including the time of day at which the measurement took place. IOP was measured by Goldmann applanation tonometry in the UK, as per routine clinical practice recommended by NICE guidance [3]. At the study enrolment visit in Ireland, IOP was measured using iCARE applanation tonometry for most patients; however, for some patients Goldmann tonometry was used. As outlined in local clinical standard guidelines, at the study clinic in Ireland, standard practice was to use iCARE tonometry for follow-up tests, with results being confirmed with Goldmann tonometry if IOP readings were less than 10 mmHg or over 20 mmHg. In the overall study analysis, assessments using the iCARE method were excluded [12]; however, in these country-specific analyses they were included as a separate group to ensure patients were as reflective of the Irish patient population as possible. For all patients, the same method of IOP measurement was used at baseline and month 6. The clinical signs and subjective symptoms of glaucoma were also recorded at baseline (Table 1).

During the follow-up visits, the duration of PF Taf-T FC treatment was recorded. Conjunctival hyperaemia and corneal fluorescein staining (CFS) assessments were mandatory at

month 6, and optional at weeks 4 and 12. Additional data were reported by physicians and patients. Physician evaluations included the effectiveness and clinical outcomes of PF Taf-T FC treatment, as well as patient compliance (judged as better, the same, or worse than prior medication). Patients assessed the tolerability of PF Taf-T FC treatment (very good, good, satisfactory or poor), reasons for discontinuation of treatment if applicable, and any adverse events (AEs) occurring throughout the study.

Statistical Analysis

For patients who had both eyes treated, the eye with the higher IOP reading at baseline was designated the index eye and included in the analysis. If both eyes had an equal IOP reading, the right eye was included. Analysis was completed on the full UK and Ireland data set, which included any patients who provided informed consent, were prescribed PF Taf-T FC at least once and had at least one IOP measurement at 6 months (± 45 days) after treatment initiation. Analysis of any specific endpoint included patients with complete data on the variables required. Patients were included in the follow-up period regardless of whether they had discontinued PF Taf-T FC, with the aim of reflecting the real-life treatment environment. The primary endpoint was assessed for both countries, regardless of the number of patients included; however, secondary endpoints were only investigated if the study

Table 1 Data collected at baseline

Category	Data collected
Patient demographics	Age
	Gender
Diagnosis (specifying the affected eye)	OHT
	POAG
	Normal tension glaucoma
	Pseudoexfoliative glaucoma
	Pigmentary glaucoma
Previous treatment	Other glaucoma
	Type
	Duration
Reason(s) for change of treatment	Insufficient IOP control
	Progression of glaucoma
	Conversion of OHT first glaucomatous damage
	Poor local tolerance
	Poor compliance
Any concomitant therapy	Other reasons
IOP	Value (mmHg) ^a
	Time of measurement
Clinical signs under prior treatment	Conjunctival hyperaemia
	BCVA ^b
	CFS (0–V) ^{c,d}
	Schirmer's test ^d
Evaluation of subjective symptoms under prior treatment (severity: none–severe)	TBUT ^d
	Dry eye
	Irritation
	Itching eyes
	Foreign body sensation
	Eye pain
	Other

BCVA best corrected visual acuity, CFS corneal fluorescein staining, IOP intraocular pressure, OHT ocular hypertension, POAG primary open-angle glaucoma, TBUT tear break-up time

^a IOP was measured by Goldmann applanation tonometry in the UK, as per routine clinical practice recommended by National Institute for Health and Care Excellence (NICE) guidance [3]. At the study enrolment visit in Ireland, IOP was measured using iCARE applanation tonometry for most patients; however, for some patients Goldmann tonometry was used

^b Data were collected either in decimal, logMAR or fraction (foot or metres) scales. All values were then converted into decimal scale for calculation purposes using appropriate conversion charts for analysis. Based on site's usual practice of measuring visual acuity with or without correction. BCVA was reported by the sites and used in the analysis

^c Oxford scale grade

^d Data collection was optional at baseline

population for the country was at least 20 patients. Normality tests were carried out and, if the results were normally distributed, a paired *t* test was conducted to assess statistical significance. If the results were not normally distributed, a Wilcoxon signed rank test was conducted.

AEs were summarised using system organ class (SOC) terms and preferred terms (PTs) [13]. Severity, causality, relatedness to PF Taf-T FC and outcomes were also recorded.

RESULTS

Patient Disposition and Baseline Characteristics

The proportion of patients included and excluded from the full analysis set overall, across all countries included in the VISIONARY study, has been previously reported [12]. In total, 65 patients were enrolled from the UK and 17 patients were enrolled from Ireland (Table 2). As the Ireland group included fewer than 20 patients, primary endpoints were analysed for both the UK and Ireland, but secondary endpoints were only analysed for the UK, in accordance with the statistical analysis plan (SAP). The baseline characteristics are summarised in Table 2. At baseline, the mean (standard deviation [SD]) IOP was 22.0 (4.5) mmHg for the UK patient group. In Ireland, patients who had their IOP measured using the Goldmann method had a mean (SD) measurement of 17.0 (2.7) mmHg; for patients in the iCARE method group, the mean (SD) IOP was 18.6 (5.1) mmHg.

Mean IOP Reduced with PF Taf-T FC Treatment

PF Taf-T FC treatment significantly reduced mean (SD) IOP at month 6 in patients from the UK, from 22.0 (4.5) mmHg at baseline to 16.2 (2.9) mmHg at month 6 ($p < 0.0001$; Fig. 2a). In patients in the Ireland group, mean (SD) IOP was significantly reduced at month 6 compared to baseline for the iCARE subgroup ($n = 14$;

baseline, 18.6 [5.1] mmHg; month 6, 14.1 [3.0] mmHg; $p = 0.003$; Fig. 2b). For patients in the Goldmann subgroup ($n = 3$) mean IOP reduced from 17.0 (2.7) mmHg at baseline to 13.3 (1.2) mmHg after 6 months of PF Taf-T FC treatment; however, the number of patients in this category was too small to meaningfully assess statistical significance (Fig. 2b). In the UK group, significant reductions ($p < 0.0001$) were also seen at weeks 4 and 12 compared to baseline (baseline [$n = 65$], 22.0 [4.5] mmHg; week 4 [$n = 52$], 17.2 [3.6] mmHg; week 12 [$n = 52$], 16.6 [3.3] mmHg; Fig. 2a). For the UK patient group, the percentage of responders was 61.5% at 6 months (Fig. 2a).

Change in CFS Score in UK Patients Over Time

For patients in the UK group, CFS score change over time was analysed. Most UK patients had a CFS score of 0 throughout the study (Fig. 3). The percentage of patients with a CFS score of 0 ranged from 52.5% to 60.9% across time points. Throughout the study, all patients had a score of III or less, except for one patient who had a score of IV at month 6. Improvements in CFS scores at week 4, week 12 or month 6 compared with baseline were not statistically significant using a Bhapkar test (week 4, $p = 0.51$; week 12, $p = 0.18$; month 6, $p = 0.28$).

Change in Conjunctival Hyperaemia Severity in UK Patients Over Time

Most UK patients had mild conjunctival hyperaemia at baseline (Fig. 4). The percentage of patients with mild conjunctival hyperaemia decreased from 61.3% at baseline to 49.2% at month 6; this was reflected in an increase in patients with no conjunctival hyperaemia (19.4% of patients at baseline, compared to 35.4% of patients at month 6). However, improvements in conjunctival hyperaemia grade at week 4, week 12 or month 6 compared to baseline were not statistically significant using a Bhapkar test (week 4, $p = 0.32$; week 12, $p = 0.10$; month 6, $p = 0.06$).

Table 2 Patient baseline characteristics

<i>n</i> (%), unless otherwise stated	UK (<i>N</i> = 65)	Ireland (<i>N</i> = 17)	
Sex, female	37 (56.9)	9 (52.9)	
Age, years, mean (SD)	68.9 (11.0)	72.4 (10.6)	
Diagnosis			
POAG	43 (66.2)	7 (41.2)	
OHT	16 (24.6)	3 (17.6)	
Pseudoexfoliative glaucoma	2 (3.1)	0	
Normal tension glaucoma	4 (6.2)	7 (41.2)	
Study eye, right	41 (63.1)	8 (47.1)	
Previous treatment			
Beta blocker therapy	6 (9.2)	1 (5.9)	
PGA therapy	59 (90.8)	16 (94.1)	
IOP at baseline, mmHg, mean (SD)	22.0 (4.5)	Goldmann (<i>n</i> = 3)	iCARE (<i>n</i> = 14)
		17.0 (2.7)	18.6 (5.1)
CFS score, Oxford grade scale, mean (SD)	0.6 (0.9)	N/A	
BCVA decimal score, median (IQR)	0.7 (0.3)	0.8 (0.5)	
TBUT, s, median (IQR)	5.0 (7.0)	N/A	

BCVA best corrected visual acuity, *CFS* corneal fluorescein staining, *IQR* interquartile range, *IOP* intraocular pressure, *OHT* ocular hypertension, *PGA* prostaglandin analogue, *POAG* primary open-angle glaucoma, *SD* standard deviation, *s* seconds, *TBUT* tear break-up time

Other Clinical Signs in UK Patients Over Time

In the UK, best corrected visual acuity (BCVA) data were available for 62 patients at baseline with a median decimal score of 0.7 (interquartile range [IQR] 0.3). BCVA data were available for 49 patients at week 4 (median 1.0; IQR 0.3), 52 patients at week 12 (median 0.9; IQR 0.3) and 62 patients at month 6 (median 0.8; IQR 0.3). The change in BCVA decimal score from baseline to any time point was not statistically significant ($p \geq 0.35$ for all time points). For Schirmer's test, no data were recorded at baseline in the UK; therefore, no change from baseline data could be calculated. Tear break-up time (TBUT [seconds]) was recorded for 41 patients at baseline (median 5.0; IQR 7.0), 38 patients at week 4 (median 9.0; IQR 5.0), 41 patients at week 12 (median 6.0; IQR 5.0) and 47 patients at month 6 (median 6.0; IQR 5.0). For the 33 patients for whom TBUT data were available at baseline and week 4, a change of 4.0 s from baseline was statistically significant ($p = 0.001$); changes at week 12 and month 6 were not statistically significant compared to baseline ($p \geq 0.14$).

Subjective Symptoms in UK Patients at Month 6

Analysis of the subjective symptoms recorded in the UK found that, of those who answered, 100% of physicians reported PF Taf-T FC treatment to be the same or better than prior medication for IOP control after 6 months of treatment (Table 3). Similarly, 91.9% of physicians rated PF Taf-T FC treatment as the same or better than prior medication for improving clinical signs, and 100% of physicians rated the treatment as the same or better than prior medication for patient compliance after 6 months of treatment (Table 3). At month 6, of the 60 patients who answered, 90.0% reported PF Taf-T FC treatment to have good or very good tolerability (Table 3).

Safety Outcomes

In the UK group, 49 AEs were recorded (Table 4; Supplementary Table S2). Of these, 31 (63.3%) were mild, 13 (26.5%) were moderate, and 5 (10.2%) were severe. There were three (6.1%) serious AEs reported; one case of retinal vein occlusion, one case of renal impairment and one case of cerebrovascular accident. There were no fatal AEs. As assessed by the investigator, 26 (53.1%) were related to PF Taf-T FC treatment.

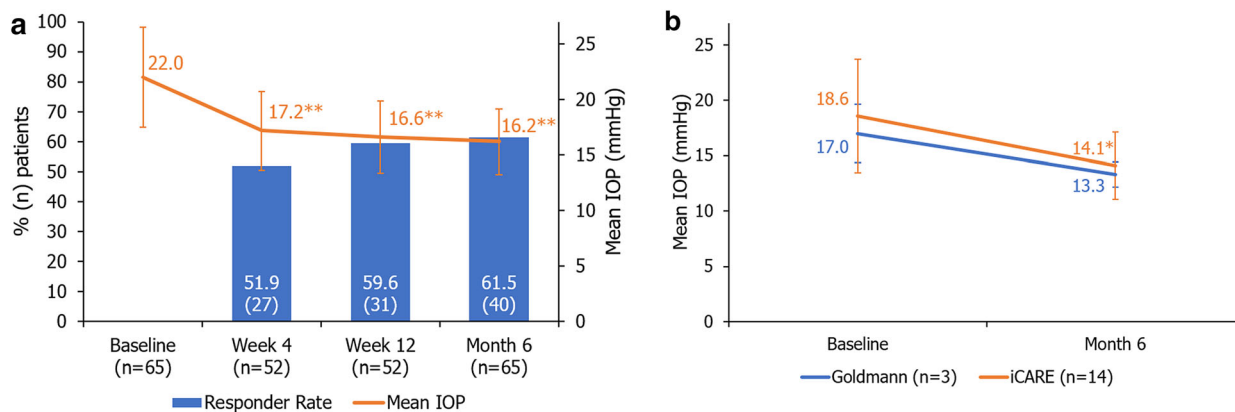


Fig. 2 Mean IOP change in the UK and Ireland patient groups over time. **a** Mean IOP change and responder rates over time in the UK patient group; **b** mean IOP change, split by method of IOP measurement, in the Ireland patient group. * $p < 0.01$; ** $p < 0.0001$ using two-sided

paired t test. Responders are patients with change in IOP of $\geq 20\%$ from baseline. Error bars indicate SD . IOP intraocular pressure, SD standard deviation

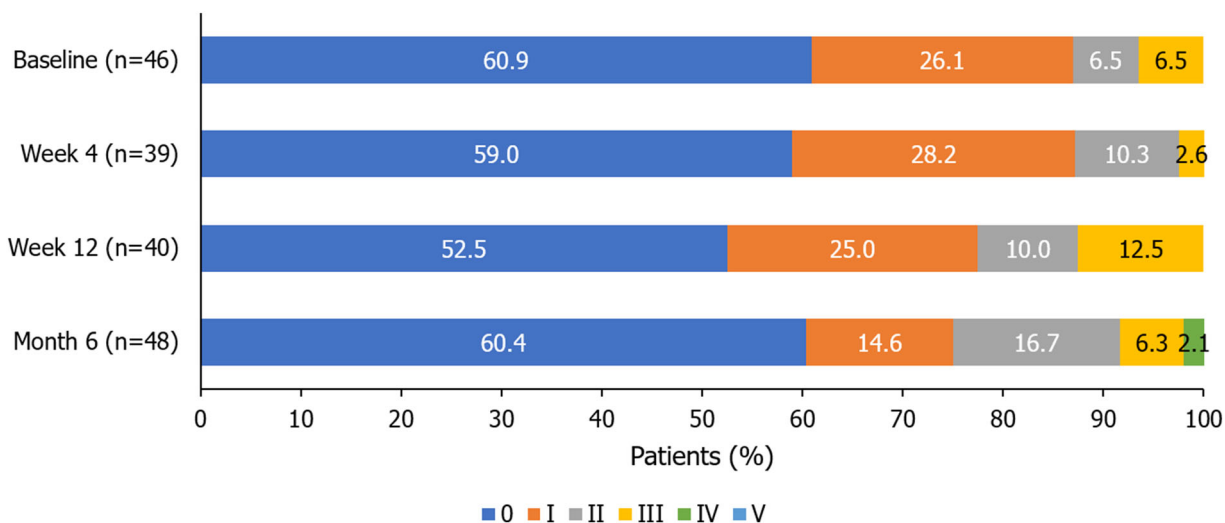


Fig. 3 CFS score* change in UK patients over time. *Oxford grade scale. CFS corneal fluorescein staining

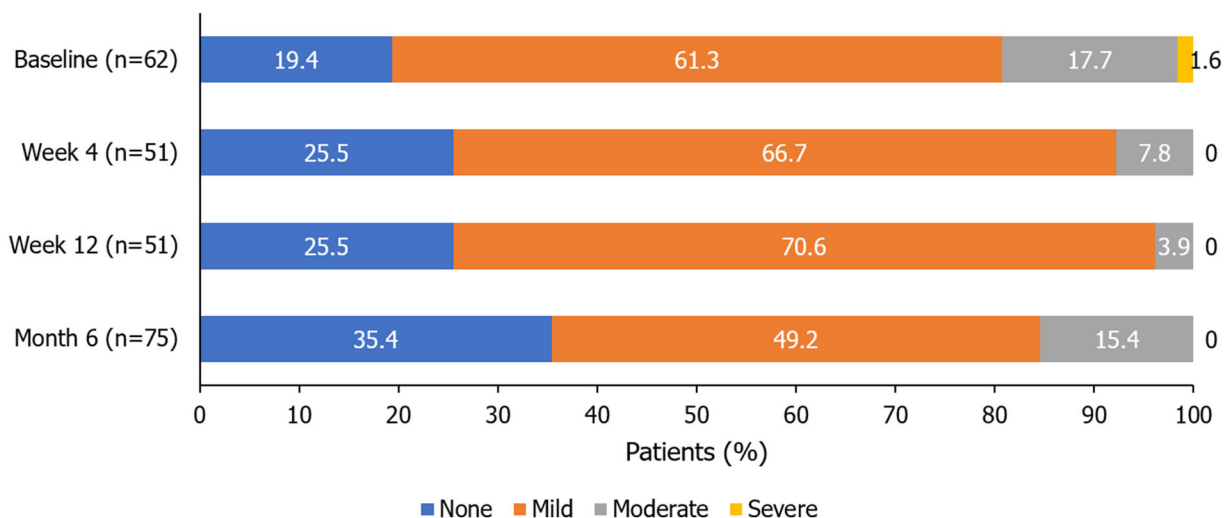


Fig. 4 Conjunctival hyperaemia severity change in UK patients over time

The most common AEs were classified as eye disorders (34 events; 69.4% of AEs), including eye pain (14; 28.6%) and dry eye (3; 6.1%). There were no AEs reported in the Ireland group.

DISCUSSION

PF Taf-T FC treatment resulted in a significant reduction in mean IOP at month 6 in both the UK and Ireland (iCARE) patient populations, supporting its effectiveness as a treatment for

OAG and OHT. This reduction was seen from week 4 in the UK patient population ($p < 0.0001$; 51.9% patients showed more than 20% reduction in mean IOP). There was no statistical difference in the other clinical symptoms measured. Physicians reported that PF Taf-T FC treatment was effective, and patients reported that it showed good tolerability. Safety data indicate that PF Taf-T FC treatment was well tolerated, with few serious AEs.

In the Ireland patient group, IOP was measured by two different methods, which have

Table 3 Subjective symptoms in UK patients at month 6 ($n = 65$)

Physician assessment			
Clinician response; n (% of those who answered)^a	Effectiveness (IOP development) ($n = 61$)	Clinical signs ($n = 62$)	Physician assessment of patient compliance ($n = 63$)
Better than prior medication	53 (86.9)	28 (45.2)	14 (22.2)
Same as prior medication	8 (13.1)	29 (46.8)	49 (77.8)
Worse than prior medication	0	5 (8.1)	0
Missing	4 (6.2)	3 (4.6)	2 (3.1)
Patient response; n (% of those who answered)*			Patient reported tolerability ($n = 60$)
Very good			30 (50.0)
Good			24 (40.0)
Satisfactory			4 (6.7)
Poor			2 (3.3)
Missing			5 (7.7)

IOP intraocular pressure

^a With the exception of the % of missing patients, which were calculated out of the total of 65 patients in the UK group

been found to produce comparable results for patients with low to moderate IOP [14, 15]. Reductions in IOP measured using the iCARE method were statistically significant ($p < 0.01$). In Ireland both the iCARE and Goldmann methods are used and by including both methods in these analyses, this study better reflects real-world practice in Ireland.

Compared with the overall results from this study [12], patients in the UK and Ireland were more likely to be switching from PGA therapy, in line with NICE treatment guidelines [3]. In the full study population, the percentage of patients switching from PGA range from 39.2% in Latvia, to 90.8% in the UK and 94.1% in Ireland [12]. PF Taf-T FC treatment has been found to result in a smaller reduction in mean IOP in patients switching from PGA therapy, compared with those switching from beta blockers [12]. However, in this country-specific analysis, reductions in mean IOP are clinically and statistically significant despite the smaller sample size and more than 90% of patients switching from PGA therapy, demonstrating

that reductions with PF Taf-T FC treatment are likely to be found regardless of previous treatment.

The analysis of the overall results also demonstrated a statistically significant reduction in CFS score and conjunctival hyperaemia with PF Taf-T FC treatment [12]. This statistical significance was not seen in these country-specific treatment groups; however, there was a trend towards a reduction in both likely reflecting the smaller numbers in these patient groups. This may also be due to the difference in previous monotherapies between the UK and Ireland and the other countries in this study. Patient numbers in the CFS and conjunctival hyperaemia analyses were lower at weeks 4 and 12 than month 6. This is likely to be due to the recording of these data being optional at these interim follow-up visits. Although these data do not demonstrate significant improvements in CFS and conjunctival hyperaemia, they also do not suggest that these clinical symptoms worsen with combination therapy. An improvement in CFS would be expected when patients

switch to a preservative-free therapy; however, data assessing the number of patients previously taking preservative-free treatment were not recorded, so it was not possible to investigate this change.

This study demonstrates PF Taf-T FC effectiveness in routine clinical practice, supporting safety and efficacy data from RCTs [9, 16, 17]. Patients included in RCTs often do not represent the full spectrum of patients diagnosed with a disease, as patients with comorbidities are often excluded because they do not meet the strict inclusion criteria of such trials [18]. Additionally, non-pragmatic RCTs do not accurately reflect variations in routine clinical practice where it may be necessary to balance perceived ideal treatments with practical considerations and ensure the best quality of life for patients is achieved. In the present study, however, no washout period between previous treatment and PF Taf-T FC treatment initiation and a wider range of patients included than in clinical trials (e.g. patients with ocular surface abnormalities) are examples of how these data are more reflective of routine clinical practice than previous clinical trials investigating PR Taf-T FC efficacy. This study provides ophthalmologists with data that may be more reflective of real-world treatment with PF Taf-T FC, particularly in UK and Ireland. Real-world data on time to response, the percentage of responders and the range of glaucoma diagnoses for which PF Taf-T FC treatment is effective may help guide treatment decisions in the clinic.

Limitations

The sample size, particularly in the Ireland group, is small; therefore these results may not be generalisable to wider patient populations in the UK and Ireland. Additionally, since this study investigated adult patients with OAG and OHT, the results are not applicable to angle-closure glaucoma and childhood glaucomas. In the Ireland group, the inclusion of both Goldmann and iCARE subgroups adds some noise to the study analysis. However, the presence of both patient groups is reflective of real-world clinical practice in Ireland, where there are no

Table 4 Summary of adverse events in UK patients

	UK n (%)
AEs	49
Serious AEs ^a	3 (6.1)
Treatment-related AEs ^b	26 (53.1)
Intensity of AEs	
Mild	31 (63.3)
Moderate	13 (26.5)
Severe	5 (10.2)
Outcome of AEs	
Fatal	0
Not recovered/resolved	13 (26.5)
Recovered/resolved	25 (51.0)
Recovering/resolving	6 (12.2)
Unknown	5 (10.2)
AEs by SOC and PT	
Eye disorders	34 (69.4)
Infections and infestations	3 (6.1)
Nervous system disorders	7 (14.3)

AE adverse event, *PT* preferred term, *SOC* system organ class

^a The three serious AEs reported were one case of retinal vein occlusion, one case of renal impairment and one case of cerebrovascular accident

^b Assessed by the investigator

guidelines that recommend the use of Goldmann IOP measurement methods in all patients with glaucoma. The study did not take into account the reported disparities between the two instruments that were used for measuring IOP among patients in the study, iCARE applanation tonometry and Goldmann tonometry [14, 15], though the same method of IOP measurement was used at baseline and month 6 for all patients. In-depth details relating to the methods of IOP measurement were lacking. For example, no information was recorded to understand whether the same physician

measured and recorded IOP and if these measurements were taken at the same time of day. It was also unclear if only one reading was taken and reported, or if several IOP readings were taken and the average value reported. Patients in this study had only previously been treated with monotherapies; improvements may not be the same if switching from a different combination therapy to PF Taf-T FC treatment. Further, data regarding whether patients were previously on preservative-free treatment, how long patients had been on monotherapy prior to baseline or which medications were used by patients after discontinuation of PF Taf-T FC were not recorded, which limited the exploration of these variables.

CONCLUSION

In patients, in the UK and Ireland, with OAG and OHT that was insufficiently controlled by monotherapies, PF Taf-T FC treatment demonstrated real-life efficacy in routine clinical practice. A statistically significant reduction in mean IOP was shown from 4 weeks of treatment. This reduction was maintained up to 6 months. In addition, safety data and physician- and patient-reported data demonstrate PF Taf-T FC treatment is well tolerated.

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Compliance with Ethics Guidelines. The study complied with the principles of the Declaration of Helsinki. The study protocol was approved by the institutional review board (IRB) or independent ethics committee (IEC) at each centre/institution listed above. All patients were required to provide informed consent before enrolling.

Data Availability. The datasets used during and/or analysed during the current study are available from the corresponding author on reasonable request.

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