Received: 8 November 2022 | Accepted: 12 June 2023

DOI: 10.1111/aos.15725

Acta Ophthalmologica

REVIEW ARTICLE

How latanoprost changed glaucoma management

Maria Francesca Cordeiro[1,2,3] | **Stefano Gandolfi**[4] | **Konstantin Gugleta**[5] | **Eduardo M. Normando**[3] | **Francesco Oddone**[6]

[1]Imperial College Healthcare NHS Trust, Western Eye Hospital, London, UK

[2]UCL Institute of Ophthalmology, London, UK

[3]Department of Surgery & Cancer, Irish Clinical Oncology Research Group, Imperial College London, London, UK

[4]Ophthalmology Unit, University Hospital of Parma, Parma, Italy

[5]University Hospital and University of Basel, Basel, Switzerland

[6]Glaucoma Unit, IRCSS-Fondazione Bietti, Rome, Italy

Correspondence
Maria Francesca Cordeiro, Western Eye Hospital, Imperial College Healthcare NHS Trust, London, UK.
Email: m.cordeiro@ucl.ac.uk

Funding information
Viatris Inc

Abstract

Glaucoma is currently considered one of the leading causes of severe visual impairment and blindness worldwide. Topical medical therapy represents the treatment of choice for many glaucoma patients. Introduction of latanoprost, 25 years ago, with an entirely new mechanism of action from that of the antiglaucoma drugs used up to that time was a very important milestone. Since then, due mainly to their efficacy, limited systemic side effects and once daily dosing, prostaglandin analogues (PGAs) have become as the first-choice treatment for primary open-angle glaucoma. PGAs are in general terms well tolerated, although they are associated with several mild to moderate ocular and periocular adverse events. Among them, conjunctival hyperemia, eyelash changes, eyelid pigmentation, iris pigmentation and hypertrichosis around the eyes are the most prevalent. The objective of this paper is to review the role of PGAs in the treatment of glaucoma over the 25 years since the launch of Latanoprost and their impact on clinical practice outcomes.

KEYWORDS

glaucoma, Latanoprost, medical treatment, open-angle glaucoma, progression, prostaglandin analogues

1 | INTRODUCTION

Life expectancy has been increasing in recent decades and all countries. Western countries are experiencing growth in both the size and the proportion of older persons in the population (World Health Organization, 2021). According to a report by the World Health Organization, between 2015 and 2050, the proportion of the world's population over 60 years will nearly double from 12% to 22% (World Health Organization, 2021). The aging population is paralleled by an increase in the prevalence of sight-threatening diseases, including glaucoma, age-related macular degeneration, diabetes and diabetic retinopathy, and cataract (Tham et al., 2014; GBD 2019 Blindness and Vision Impairment Collaborators & Vision Loss Expert Group of the Global Burden of Disease Study, 2021).

Under the umbrella of the term glaucoma coexist a series of chronic and progressive optic neuropathies characterized by retinal ganglion cell death and subsequent visual field defects (Weinreb et al., 2014). Glaucoma is currently considered one of the leading causes of severe visual impairment and blindness worldwide, affecting more than 70 million people (Prum et al., 2016; Quigley & Broman, 2006). Among the different types of glaucoma, primary open-angle glaucoma (POAG) is the most common form of glaucoma and accounts for approximately 70% of the total glaucoma cases worldwide (Tham et al., 2014).

Pathogenesis of POAG is multifactorial and largely unknown. Several risk factors have been identified, including elevated intraocular pressure (IOP), family history, age and race (Jonas et al., 2017; McMonnies, 2017; Tham et al., 2014; Weinreb et al., 2014). Among them, elevated IOP has been identified as a primary and independent risk factor, not only for the onset but also for the progression of glaucomatous damage (Leske et al., 2003, 2007; Nouri-Mahdavi et al., 2004; The Advanced Glaucoma Intervention Study (AGIS): 7, 2000). Therefore, lowering elevated IOP (enough to achieve a therapeutic goal in the 'target IOP range') is still the main approach for preserving visual function in patients with glaucoma (Boland et al., 2013; Damji et al., 2003). In most patients, medical treatment represents the first therapeutic step

for glaucoma (American Academy of Ophthalmology Preferred Practice Pattern Glaucoma Committee, 2020).

IOP levels are determined by the balance between the production of aqueous humour by the ciliary body and its drainage by two independent pathways (namely, the trabecular meshwork and uveoscleral outflow pathway) (Weinreb et al., 2014).

Currently, we have different classes of drugs to lower IOP through different mechanisms. For example, beta-blockers and carbonic anhydrase inhibitors (CAIs) suppress aqueous formation; while prostaglandin analogues (PGAs) lower IOP by increasing aqueous humour flow through the uveoscleral pathway (Cvenkel & Kolko, 2020; Gaton et al., 2001).

PGAs are currently considered as first choice treatment for POAG, because of their efficacy, limited systemic side effects and once daily dosing (EGS Guidelines 2020; Li et al., 2016; Li et al., 2018; Weinreb et al., 2014).

Latanoprost 0.005% (Xalatan®) was the first topical PGA for treating glaucoma available on the market. Its launch, 25 years ago, meant a profound change in the paradigm of medical treatment of glaucoma (Alm et al., 1997; Alm & Stjernschantz, 1995; Camras, 1996; Camras et al., 1996).

2 | THE BURDEN OF GLAUCOMA

Glaucoma is a leading cause of irreversible blindness worldwide. It has been estimated in 2020 that glaucoma represents the cause of moderate or severe visual impairment in 4.1 million people and blindness in 3.6 million (Flaxman et al., 2017; GBD 2019 Blindness and Vision Impairment Collaborators & Vision Loss Expert Group of the Global Burden of Disease Study, 2021; Prum et al., 2016; Quigley & Broman, 2006; Sun et al., 2022; Tham et al., 2014).

POAG accounts for approximately two-thirds of cases, with primary angle-closure glaucoma (PACG) the next most common form of the condition (Tham et al., 2014).

The prevalence of glaucoma varies among different nations and regions. It has been reported to be greater among persons of African descent (ranging from 6.5% to 7.3%) (Ashaye et al., 2013; Budenz et al., 2013), followed by East Asian populations (ranging from 2.59% to 3.54%) (Song et al., 2017; Sun et al., 2022; Tham et al., 2014). The prevalence in European-derived populations seems to be slightly lower, with figures around 2% (Höhn et al., 2018; Keel et al., 2019).

Glaucoma is also largely a disease of an aging population, therefore, an increase in its prevalence is expected as the population ages (Ashaye et al., 2013; GBD 2019 Blindness and Vision Impairment Collaborators & Vision Loss Expert Group of the Global Burden of Disease Study, 2021; Jonas et al., 2017; Slettedal et al., 2020; Song et al., 2017).

The burden of visual impairment from glaucoma may generally be expected to follow the rising prevalence. The global prevalence of blindness and vision loss due to glaucoma was 75.6 (95% confidence interval [CI]: 65.0–88.1) per 100 000 in 2017. However, the prevalence of blindness due to glaucoma varies greatly between regions with figures ranging from the 171.5 (95% CI: 146.9–200.2) subjects/100 000 in African region to the 61.1 (95% CI: 52.6–70.7) subjects/100 000 in North American region (Sun et al., 2022).

The aim of glaucoma treatment is to slow the rate of progression, so that it has no significant impact on patients' quality of life (Terminology and Guidelines for Glaucoma, 2020). Treatment options include medical, laser or surgical therapies. In many cases, medical treatment represents the first therapeutic step for glaucoma (American Academy of Ophthalmology Preferred Practice Pattern Glaucoma Committee, 2020).

In glaucoma, the introduction of latanoprost ophthalmic solution (Xalatan®), 25 years ago, has resulted in a paradigm shift in medical treatment and in significant therapeutic benefits for patients.

3 | OBJECTIVES OF THIS REVIEW

It has been 25 years since the launch of Latanoprost, the first topical prostaglandin analogue marketed for the treatment of glaucoma (Alm, 2014; Alm et al., 1997; Alm & Stjernschantz, 1995; Camras, 1996; Camras et al., 1996). Its introduction represented an important change in the therapeutic management of glaucoma. In these 25 years, PGAs have become mainly the first-line medical treatment for POAG, due to their good efficacy/safety profile and their convenient dosage (once daily dosing) (Terminology and Guidelines for Glaucoma, 2020; Li et al., 2016, 2018; Weinreb et al., 2014).

The objective of this paper is to review the role of PGAs in the treatment of glaucoma during these 25 years and their impact on clinical practice outcomes.

4 | CURRENT MEDICAL TREATMENT OPTIONS IN GLAUCOMA

IOP is recognized as the main known and modifiable risk factor, both for the development and progression of glaucoma (AGIS 2000; Leske et al., 2003, 2007; Nouri-Mahdavi et al., 2004). Hence, lowering IOP has been a cornerstone of glaucoma treatment and achieving an IOP lowering by 20%–40% has been shown to be effective for significantly reducing disease progression (Boland et al., 2013; Damji et al., 2003; EGS Guidelines 2020).

Different types of ocular hypotensive medications are currently available in Europe. They include PGAs; β-Blockers; CAIs (systemic and topical); α-2 adrenergic agonists; and parasympathomimetic drugs. They have different mechanisms of action and different IOP-lowering profiles. Table 1 summarizes their main efficacy and safety outcomes, as well as their mechanism of action.

Several landmark studies have shown the efficacy of lowering IOP using ocular hypotensive medications in preventing the development of glaucoma and slowing

TABLE 1 Overview of the ocular hypotensive medications: efficacy, safety and mechanism of action.

Medication class	Active principle	IOP reduction (%)	Mechanism of action				Local adverse effects	Systemic adverse effects
			Increases uveoscleral outflow	Increases trabecular outflow	Decreases aqueous production	Decreases episcleral venous pressure		
Prostaglandin analogues	Bimatoprost, latanoprost, tafluprost, travoprost	25–35	Yes	No	No	No	Conjunctival hyperemia, lengthening and darkening of eyelashes, brown discoloration of the iris, uveitis, macular oedema	Minimal systemic adverse effects; may be related to headaches
β-Blockers								
(i) Nonselective	Timolol, levobonolol, carteolol, metipranolol	20–25	No	No	Yes	No	Ocular irritation and dry eyes	Contraindicated in patients with asthma, chronic pulmonary obstructive disease, and bradycardia
(ii) β1-Selective	Betaxolol	20	No	No	Yes	No		
Carbonic anhydrase inhibitors								
(i) Topical	Dorzolamide, brinzolamide	20	No	No	Yes	No	Ocular irritation, dry eyes, burning sensation with topical agents	Topical form has minimal systemic adverse effects
(ii) Systemic	Acetazolamide, methazolamide, dichlorphenamide	30–40	No	No	Yes	No	None	Paresthesias, nauseas, diarrhoea, loss of appetite and taste, lassitude, or renal stones
Adrenergic agonists								
(i) α-2 Selective	Brimonidine, apraclonidine	20–25	Yes	No	Yes	No	Ocular irritation, dry eyes, allergic reaction is relatively common	Central nervous system effects and respiratory arrest in young children; caution in patients with cerebral or coronary insufficiency, postural hypotension, and renal or hepatic failure
(ii) Nonselective	Dipivefrin, epinephrine	15–20	Yes	No	Yes	No		
Parasympathomimetics	Pilocarpine, echothiophate	20–25	No	Yes	No	No	Ocular irritation, induced myopia and decreased vision due to ciliary spasm	Ciliary spasm leading to headaches in young patients

Note: Adapted from Cvenkel & Kolko, 2020; and Weinreb et al., 2014.

disease progression (Heijl et al., 2002; Kass et al., 2002; Lichter et al., 2001).

- The Ocular Hypertension Treatment Study assessed the efficacy of medical treatment in delaying or preventing the onset of POAG in patients with ocular hypertension. After 5 years of follow-up, the probability of developing glaucoma was significantly lower in the treated group than in the control group (hazard ratio (HR): 0.40; 95% CI: 0.27–0.59; $p<0.0001$) (Kass et al., 2002).
- The Early Manifest Glaucoma Trial compared the effect of early treatment (argon laser trabeculoplasty and topical betaxolol twice daily) versus no treatment/late treatment on the progression of newly diagnosed open-angle glaucoma patients. After a median follow-up of 6 years, progression rate was significantly lower in the treatment group (45%) than in the control group (62%) ($p=0.007$) (Heijl et al., 2002).
- Additionally, the Collaborative Initial Glaucoma Treatment Study compared the effect of medical treatment versus trabeculectomy on the disease-progression of newly diagnosed open-angle glaucoma patients. After 5-years of follow-up, visual field loss did not differ significantly by initial treatment (Lichter et al., 2001).
- The United Kingdom Glaucoma Treatment Study assessed the effect of intraocular-lowering treatment with latanoprost on vision preservation in patients with newly diagnosed open-angle glaucoma. This was the first specific study of the effect of PGAs. At Month 24, mean IOP lowering was 3.8 ± 4.0 mmHg and 0.9 ± 3.8 mmHg in the latanoprost and placebo groups, respectively. Moreover, with respect to visual function, the time to first deterioration was significantly longer in the latanoprost group than in the placebo group (adjusted HR 0.44; 95% CI: 0.28–0.69; $p=0.0003$) (Garway-Heath et al., 2015), showing a strong effect of PGA treatment on visual field preservation.

5 | THE ROLE OF PROSTAGLANDIN ANALOGUES

5.1 | Historical aspects of prostaglandin analogues

Prostaglandins were initially isolated from prostate tissue in 1935 (Von Euler, 1935). They are a family of lipids derived from essential fatty acids and have a wide range of effects throughout the body, including constriction and relaxation of smooth muscles and regulation of the immune response (Hata & Breyer, 2004; The LipidWebb, 2022; Winkler & Fautsch, 2014). $PGF_{2\alpha}$, a prostaglandin released following trauma to the eye, produces a powerful IOP lowering (Perkins, 1975). Camras et al. (1977) reported that the administration of prostaglandin F2α (PGF2α) and E2 (PGE2) to uncannulated rabbit eyes lowered IOP in a dose-dependent manner following an early ocular hypertensive effect. In an experimental study conducted in cynomolgus monkey, the IOP lowering effect of $PGF_{2\alpha}$ was demonstrated to be due largely if not exclusively to an increase in uveoscleral outflow pathway (Gabelt & Kaufman, 1989).

In healthy human eyes, the prostaglandin analogue PhXA34 lowered IOP 12 h post dose. This IOP lowering effect might be explained by increased aqueous humour outflow facility (Alm & Villumsen, 1991).

Latanoprost 0.005%, the first commercially available topical PGA, latanoprost ophthalmic solution (Xalatan®) prostaglandin analogue for treating glaucoma, was launched in 1996 (Alm et al., 1997; Alm & Stjernschantz, 1995; Camras, 1996; Camras et al., 1996). These papers showed that latanoprost 0.005% effectively and safely reduced IOP in patients with glaucoma and provided evidence for its usefulness in chronic glaucoma therapy (Alm et al., 1997; Alm & Stjernschantz, 1995; Camras, 1996; Camras et al., 1996).

5.2 | Mechanism of action

Studies of aqueous humour dynamics in humans and nonhuman primates have demonstrated that the IOP lowering is mainly due to an enhanced uveoscleral outflow, with minor effects on trabecular outflow and aqueous flow (Toris et al., 1997, 2008; Weinreb et al., 2002).

In order to achieve their effect, PGAs must bind to specific receptors, located in the cell membrane and nuclear envelope (Schlötzer-Schrehardt et al., 2002). So far 9 prostaglandin receptors have been identified and their designation is primarily based on the prostaglandin for which binding is most specific (Hata & Breyer, 2004; Sharif et al., 2003; Swymer & Neville, 2012). $PGF_{2\alpha}$ binds the FP, EP1 and EP3 receptors with significant affinity, while travoprost binds the FP receptor (Abramovitz et al., 2000; Sharif et al., 2003).

As aforementioned, IOP is regulated by the balance between the production of aqueous humour by the ciliary body and its removal through the trabecular and the uveoscleral pathways (Weinreb et al., 2014).

PGAs and $PGF_{2\alpha}$ bind to EP and FP receptors in the ciliary muscle, which cause its relaxation and increased aqueous humour outflow (Alm & Nilsson, 2009; Winkler & Fautsch, 2014). Binding of prostaglandins and PGAs to ciliary muscle FP receptors also disrupts extracellular matrix turnover (Lindsey et al., 1997; Weinreb et al., 2020). Matrix metalloproteinases degrade and remodel the extracellular matrix in the ciliary muscle, iris root, and sclera, reducing outflow resistance to fluid flow (Lindsey et al., 1997; Weinreb & Lindsey, 2002). In general terms, it seems that $PGF_{2\alpha}$ and PGAs increases the amount of matrix metalloproteinases, while maintaining tissue inhibitor of metalloproteinase expression. This causes further degradation and remodelling of the extracellular matrix, which enhances outflow facility (Lindsey et al., 1997; Weinreb

et al., 2020; Weinreb & Lindsey, 2002; Winkler & Fautsch, 2014).

5.3 | IOP lowering effect of prostaglandin analogues

5.3.1 | Prostaglandin analogues in monotherapy

IOP lowering effect

Topical ocular hypotensive therapy remains the most common initial method of lowering IOP (American Academy of Ophthalmology Preferred Practice Pattern Glaucoma Committee, 2020). PGAs represent, due to their good efficacy and safety profile and their convenient posology (once daily), the first-choice therapy for treating glaucoma in many patients (EGS Guidelines 2020; Li et al., 2016; Li et al., 2018; Weinreb et al., 2014).

Latanoprost has been very well studied, with numerous publications of clinical trials, meta-analyses, and reviews (Alm, 2014; Digiuni et al., 2012). A review of three masked multicenter Phase III studies in 829 patients with elevated IOP in Scandinavia, the USA, and the UK showed that 6 months treatment with latanoprost reduced IOP by 35%, if given in the evening, and by 31%, if given in the morning (Alm et al., 1997). Additionally, in a randomized, double-masked, placebo-controlled crossover study, once daily latanoprost 0.005% lowered significantly the IOP (21.3%; $p < 0.001$) in normal tension glaucoma patients (Rulo et al., 1996).

Currently available PGAs include latanoprost 0.005%, travoprost 0.004%, bimatoprost (available in two doses, 0.03% and 0.01%) and tafluprost 0.0015%.

PGAs have demonstrated better IOP-lowering effect than β-blockers with fewer systemic adverse events (Eyawo et al., 2009; Garway-Heath et al., 2015; Quaranta et al., 2015). The IOP lowering starts 2–4 h after first administration, with the therapeutic effect reaching a peak at 8–12 h. These agents also minimize IOP fluctuations during a 24-h period, with a maximum effect achieved 3–5 weeks after initiation of therapy (Cvenkel & Kolko, 2020; Eyawo et al., 2009). Topical administration of PGAs leads to a mean IOP reduction from 25% to 32%, which is sustained throughout the 24-h cycle (Alm, 2014; Eyawo et al., 2009; Garway-Heath et al., 2015; Huang et al., 2011; Quaranta et al., 2015; Riva et al., 2014).

In a meta-analysis of randomized clinical trials, van der Valk et al. (2005) reported that the PGAs bimatoprost, travoprost and latanoprost were all effective in lowering IOP. These agents achieved a mean IOP reduction that ranged between 6.5–8.4 mmHg of reduction at trough and peak time points, respectively, corresponding to a mean IOP percentage reduction ranging from 28% to 31% from trough to peak time points, respectively (van der Valk et al., 2005).

Current evidence strongly suggests that the clinical profile of the PGAs is similar (Islam & Spry, 2020). Parrish et al. (2003), in a 12-week randomized clinical trial, reported that the overall mean IOP-lowering achieved by the respective agents was similar throughout the diurnal period (8.6 ± 0.3 mmHg, 8.7 ± 0.3 mmHg, 8.0 ± 0.3 mmHg lowering for patients treated with latanoprost, bimatoprost and travoprost, respectively; $p = 0.128$).

Conversely, some studies have reported greater IOP-lowering efficacy with bimatoprost compared with latanoprost (Cheng & Wei, 2008; DuBiner et al., 2001; Gandolfi et al., 2001; Noecker et al., 2003). However, there are some methodological issues that may limit their findings, including the post hoc nature of analysis and differences in baseline IOPs among treatment groups (DuBiner et al., 2001; Gandolfi et al., 2001).

Regarding tafluprost 0.0015%, it has shown comparable IOP lowering profile to latanoprost for open-angle glaucoma and ocular hypertension (Uusitalo et al., 2010; Yang et al., 2020).

Although glaucoma treatment has to follow a patient-tailored approach, PGAs can be considered the first-choice in many different situations, such as ocular hypertension; POAG; and pseudoexfoliative glaucoma among others (American Academy of Ophthalmology Preferred Practice Pattern Glaucoma Committee, 2020; EGS Guidelines 2020). Additionally, due to their mechanism of action, PGAs may be indicated in cases of angle recession glaucoma (If possible, not during active phase) (Clement & Goldberg, 2011). On the negative side, PGAs would be considered the last choice in patients with elevated IOP secondary to trauma, inflammatory glaucoma, active macularoedema and so forth. (American Academy of Ophthalmology Preferred Practice Pattern Glaucoma Committee, 2020; EGS Guidelines 2020) (Table 2).

Safety

Although PGAs are in general terms well tolerated, they are associated with several mild to moderate ocular and periocular adverse events (AEs). Ocular and periocular AEs associated with the use of PGAs include conjunctival hyperemia, eyelash changes, eyelid pigmentation, iris pigmentation, hypertrichosis around the eyes, corneal epithelium disorder, appearance of iritis, cystoid

TABLE 2 Overview of the main indications and contraindications of prostaglandin analogues.

First choice	Last choice

• Ocular hypertension
• Primary open-angle glaucoma
• Pseudoexfoliative glaucoma
• Pigmentary glaucoma
• Angle recession glaucoma[a]
	• Elevated IOP secondary to trauma
	• Inflammatory glaucoma
	  • Glaucomatocyclitic iritis (aka Possner-Schlossman)
	  • Fuch's Heterochromic iridocyclitis
	  • IOP increases due to herpetic disease
	• Active macular oedema
	• Diabetic with macular oedema, epiretinal membrane
	• Steroid induced glaucoma
	• Post-surgical IOP spike
	• Neovascular glaucoma
	• Unilateral treatment[b]

Note: Adapted from American Academy of Ophthalmology Preferred Practice Pattern Glaucoma Committee (2020) and European Glaucoma Society (EGS) Guidelines (2020).

Abbreviation: IOP, Intraocular pressure.

[a]If possible, not during active phase (Clement & Goldberg, 2011).

[b]For aesthetic reasons.

maculaoedema and deepening of the upper eyelid sulcus (Alm, 2014; Alm et al., 1997; Honrubia et al., 2009; Inoue et al., 2012; Li et al., 2018; Wang et al., 2021; Weinreb et al., 2014).

Tafluprost has been found to have higher rates of hyperemia than latanoprost and most other commonly used PGAs, which is likely related to its higher pro-inflammatory effects (Inoue et al. 2012; Inoue et al. 2020). Additionally, the results of a meta-analysis found that latanoprost 0.005% caused a lower incidence of conjunctival hyperemia than travoprost 0.004% (OR = 0.51; 95% CI 0.39–0.67, $p < 0.00001$) and bimatoprost 0.003% (OR = 0.32; 95% CI 0.24–0.42, $p < 0.00001$) (Honrubia et al., 2009).

Regarding eyelid pigmentation, its incidence with the use of PGAs ranged from 0% (Elgin et al., 2006) to 5.9% (Inoue et al. 2006) with latanoprost 0.005%; from 2.9% (Parrish et al., 2003) to 15.4% (Birt et al., 2010) with travoprost; and from 1.6% (Kampik et al., 2002) to 25.9% (Birt et al., 2010) with bimatoprost.

The incidence of eyelash changes in patients treated with PGAs ranged from 0% (Parrish et al., 2003) to 77% (Demitsu et al., 2001) with latanoprost; from 0.7% (Parrish et al., 2003) to 57.1% (Netland et al., 2001) with travoprost; from 2.9% (Parrish et al., 2003) to 53.8% (Inoue et al., 2012) with bimatoprost and from 4% (Oddone et al., 2022) to 34% (Inoue et al., 2012) with tafluprost.

Both eyelid pigmentation and eyelash changes were associated with duration of treatment. The incidence of eyelid pigmentation ranged between 1.5%–2.9% in subjects with <3 months of medication use and from 0%–25.9% in patients with >3 months of medication use (Inoue et al., 2012). Similarly, the incidence of eyelash growth ranged from 0% to 33.8% in patients with <3 months of use and from 0.7% to 77% in patients with >3 months of use (Inoue et al., 2012).

There is evidence suggesting that PGA therapy might decrease central corneal thickness (Hatanaka et al., 2009; Park et al., 2021; Schlote et al., 2009). Corneal and scleral thickness reduction after using PGAS might be related with the increased uveoscleral outflow (Park et al., 2021).

Iris pigmentation associated with the use of PGAs often occurs in Europeans and Americans, in whom iris pigments are green-brown, yellow-brown, blue-brown and/or of mixed colour (Camras et al., 1996). After 2 years of latanoprost use, Watson (1998) reported that increased in iris pigmentation occurred in 18.8% of the patients. In Japanese people, iris pigment changes occurred in 31.7% of latanoprost patients, 37.9% of travoprost patients, 34.5% off tafluprost patients and 50.0% of bimatoprost patients (Inoue et al., 2006).

Another adverse effect to consider, mainly due to its potential impact on surgery outcomes, is deepening of the upper eyelid sulcus. The first report associating the occurrence of deepening of the upper eyelid sulcus in patients treated with a PGAs (bimatoprost) was published in 2004 (Peplinski & Albiani Smith, 2004). The incidence of deepening of the upper eyelid sulcus differs among PGAs and seems to be related to the ability of $PGF_{2\alpha}$ to inhibit fat production (Park et al., 2011). The condition occurred in 60%, 50%, 24%, and 18% of patients using bimatoprost, travoprost, latanoprost and tafluprost, respectively (Inoue et al., 2013).

Further ocular adnexal changes associated with the use of PGAs have been described, including upper lid ptosis, loss of the inferior orbital fat pads, and enophthalmos (Filippopoulos et al., 2008; Peplinski & Albiani Smith, 2004). Prostaglandin-associated periorbitopathy was more frequent in patients receiving bimatoprost or travoprost than in those treated with latanoprost or tafluprost (Shah et al., 2013).

One of the most controversial points related to the use of PGAs has been its relationship with the appearance of macular oedema or the reactivation of uveitis. A retrospective analysis of 94 patients found that 6.4% and 2.1% of patients developed anterior uveitis and cystoid macular oedema, respectively, while being treated with latanoprost (Warwar et al., 1998). It has been proposed to avoid the use of PGAs in patients at risk of developing cystoid macular oedema (such as those with diabetic retinopathy, retinal vein occlusion, history of epiretinal membrane, surgery complicated with posterior capsule rupture and vitreous humour loss, etc.) (Holló et al., 2020). Nevertheless, a systematic review of uveitis and cystoid macular oedema associated with topical PGAs use refutes the commonly believed association between prostaglandin analogue treatment and these conditions (Hu et al., 2020).

5.3.2 | Prostaglandin analogues in combination with other agents

According to the Terminology and Guidelines for Glaucoma (2020), if monotherapy treatment is well tolerated, but does not achieve target IOP, adding a second drug may be considered (Figure 1).

More than 50% of patients who fill prescriptions for glaucoma medications take more than one drug (Kass et al., 2002; Lichter et al., 2001). The different side effects associated with the use of different medical therapies are shown in Table 3.

When selecting a combination therapy, it is essential to take into account its mechanisms of action. The best option is to combine drugs with different mechanisms of action (EGS Guidelines 2020). As previously mentioned, the IOP reduction mechanism of PGAs is through an increase in aqueous humour outflow (uveoscleral/trabecular). Therefore, the best combination option would be to associate PGAs with drugs that inhibit aqueous production, such as β-Blockers, CAIs (systemic and topics) and α-2 adrenergic agonists.

Prostaglandin analogues in combination with β-Blocker

PGAs/timolol fixed combination is currently one of the most widely used topical anti- glaucoma fixed-combination eye drops (Wang et al., 2021). Latanoprost/timolol fixed combination (LTFC) provided better IOP lowering than either latanoprost or timolol monotherapy (Higginbotham et al., 2010). Additionally, Zhao et al. (2011) found no differences in IOP lowering between LTFC and non-fixed combination of latanoprost and timolol.

Different papers have evaluated the IOP lowering effect of travoprost/timolol (TTFC) and bimatoprost/

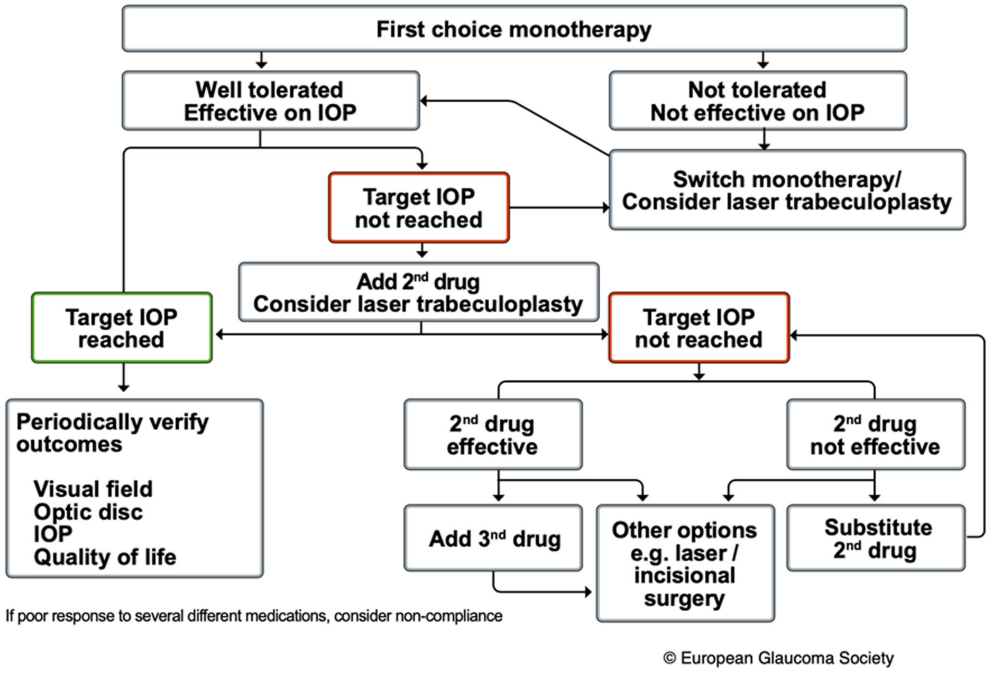

FIGURE 1 Therapeutic algorithm in glaucoma medical therapy. Reproduced from EGS Guidelines (2020).

timolol (BTFC) fixed combinations. The results of these studies point in the same general direction, indicating that both provided a good IOP lowering effect (Konstas et al., 2012, 2013; Lewis et al., 2010; Martínez & Sánchez, 2007, 2008, 2009; Nakano et al., 2015).

Tafluprost/timolol fixed combination has a superior IOP lowering effect compared with agents used as monotherapy (Kaarniranta et al., 2016; Konstas et al., 2018; Pfeiffer et al., 2014).

Fixed combination and non-fixed combination of PGAs and β-blockers result in a similar IOP lowering effect, and both are superior to monotherapy. Overall, PGAs/β-Blocker fixed or unfixed combinations provided a percentage IOP lowering ranging between 32% and 38% (Wang et al., 2021).

In addition to the adverse effects of PGAs, the adverse effects of β-Blockers must be taken into account.

Ocular adverse reactions to β-blockers include conjunctival hyperemia, ocular surface discomfort, reduction in tear flow and worsening of the dryness in the eye, while the systemic AEs include bradycardia, heart block and arrhythmia, bronchospasm and worsening of underlying asthma or chronic obstructive pulmonary disease (Dikopf et al., 2017). Although topical β-blockers were not associated with greater cardiovascular mortality (Pinnock et al., 2016), their use is not recommended in patients with asthma, chronic obstructive pulmonary disease, bradycardia, heart block or uncontrolled heart failure (Marshall et al., 2018).

An association between the use of topical β-blockers and the development of impotence has been suggested (Stewart & Castelli, 1996). However, there seems to be an association between erectile dysfunction and glaucoma that cannot be only attributed to topical β-blockers use (Nathoo et al., 2015). Hence, young patients should be warned about the possibility of erectile dysfunction since they may not associate the use of eye drops with this problem.

Prostaglandin analogues in combination with α-2 agonists

Combination of brimonidine tartrate (0.1%, 0.15%, 0.2%) twice daily and latanoprost (0.005%) once daily can be considered an effective therapy for lowering IOP (Stewart et al., 2004). When added to latanoprost, adjunctive therapy with brimonidine purite 0.15% lead to an additional IOP lowering of 5.8 and 3.3 mmHg at peak and trough drug effect, respectively (Mundorf et al., 2007). Additionally, in patients with pigmentary and pseudoexfoliative glaucoma, the combined therapy with latanoprost 0.005% / brimonidine 0.20% was significantly more effective than dorzolamide/timolol fixed combination in lowering IOP (9 vs. 6.5 mmHg, respectively, $p=0.044$) (Zabriskie et al., 2003).

However, when added to travoprost, timolol seemed to be more effective than brimonidine for lowering IOP (3.9 vs. 2.3 mmHg, respectively; $p=0.01$) (Reis et al., 2006).

Regarding safety, ocular AEs associated with long-term α2-agonist use included conjunctival hyperemia, pupil dilation, and allergic conjunctivitis (Butler et al., 1995). Systemic adverse reactions associated with long-term α2-agonists use include decreases in blood pressure and pulse, drowsiness, dizziness and dry mouth (Abrams et al., 1987).

Prostaglandin analogues in combination with carbonic anhydrase inhibitors

Several randomized clinical trials reported that the non-fixed combination of latanoprost 0.005% and brinzolamide 1% exerts a better IOP reducing effect than latanoprost monotherapy (Nakamoto & Yasuda, 2007; Nakano et al., 2016; Shoji et al., 2005).

TABLE 3 Main ocular and systemic adverse reactions of glaucoma medical therapy.

Class	Ocular AEs	Systemic AEs
PGAs	• Eyelash growth • Iris/eyelid pigment • Deepening of upper eyelid sulcus • Recurrence of herpes • Macular oedema post cataract surgery	• Rarely, upper respiratory infection • Rarely, myalgia
β-blockers	• Conjunctival allergy • Hyperemia • Corneal epithelial disorders • Reduced corneal sensitivity • Blurry vision	• Decrease blood pressure/pulse • Bradycardia • Worsen asthma/COPD • Depression • Impotence • Lethargy
CAIs	• Ocular irritation • Foreign body sensation • Itching • Stinging • Blurred vision • Corneal epithelial disorders	Topical use: • Bitter taste • Fatigue • Diuresis • Gastrointestinal upset Oral use: • Nausea • Unpleasant taste • Dysesthesia of fingers/lips • Anorexia • Metabolic acidosis
α2-adrenergic agonists	• Allergic conjunctivitis • Hyperemia • Mydriasis • Dry eye	• Affects blood pressure/pulse • Drowsiness • Dizziness • Dry mouth • Dysarthria
Parasympathomimetic/ Cholinergic- agonist	• Miosis • Visual field constriction • Night vision loss • Myopia • Red eye • Brow ache • Retinal detachment • Cataract	Direct-acting: • Rare systemic reactions Indirect-acting: • Sweating • Tearing • Nausea/vomiting • Diarrhoea • Bradycardia • Stomach ache

Note: Adapted from Bucolo et al., 2015 and Inoue, 2014.

Abbreviations: AEs, adverse events; CAIs, carbonic anhydrase inhibitors; COPD, chronic obstructive pulmonary disease; PGAs, prostaglandin analogues.

Additionally, latanoprost/brinzolamide non-fixed combination reduces both daytime and night-time IOP, whereas latanoprost/timolol non-fixed combination only reduced IOP during daytime, with little effect on the night-time value (Liu et al., 2009).

Non-fixed combination of 0.03% bimatoprost once in the morning and 2% dorzolamide twice daily in patients with POAG exerts an additional hypotensive effect and reduces vascular resistance in the ophthalmic artery compared to bimatoprost monotherapy (Stankiewicz et al., 2010, 2011).

Ocular adverse reactions associated with carbonic anhydrase inhibitors include conjunctival allergy, conjunctival hyperemia, corneal epithelial disorders, blepharitis, Stevens–Johnson syndrome and toxic epidermal necrosis (Silver, 2000; Strahlman et al., 1995). Because carbonic anhydrase naturally exists in the corneal endothelium, caution is needed in patients with corneal endothelial disorders (Konowal et al., 1999).

Different systemic adverse reactions have been associated with topical carbonic anhydrase inhibitor use, including headache, urticaria, angioedema, pruritus, asthenia, dizziness, paresthesia and transient myopia (EGS Guidelines 2020).

5.3.3 | Benzalkonium chloride (BAK)-free prostaglandin analogues formulations

Because many PGAs ophthalmic solutions were marketed as multi-dose, there were a need for using antimicrobial agents. In the vast majority of preserved products, Benzalkonium chloride (BAK) is used as the antimicrobial agent. Reports suggest that about 70% of eye drops are preserved with this substance (Freeman & Kahook, 2009; Steven et al., 2018). Additionally, there is evidence suggesting that preservative intolerance impacts significantly on treatment adherence, particularly in chronic disease like glaucoma (Holló et al., 2018; Tang et al., 2019).

In terms of IOP lowering, BAK-free PGAs formulations are not inferior to those containing BAK but better tolerated (Holló et al., 2018). Regarding latanoprost, according to the results of a post-hoc pooled analysis, BAK-free formulation of latanoprost significantly reduced IOP, with no significant difference versus BAK-containing formulations (Harasymowycz et al., 2021). Moreover, the results of the RELIEF study found that preservative-free latanoprost provided similar IOP lowering effect that benzalkonium chloride-latanoprost

but with a better tolerability profile (Misiuk-Hojlo et al., 2019).

With regards BAK-free Travoprost, it has shown a comparable safety, efficacy and duration of IOP-lowering effect to travoprost preserved with BAK (Gandolfi et al., 2012).

Preservative free 0.03% bimatoprost was non-inferior and equivalent to bimatoprost 0.03% ophthalmic solution in terms of lowering IOP with a safety profile similar to bimatoprost (Day et al., 2013). Finally, Bimatoprost 0.1 mg/mL preservative-free eye drops provided a similar IOP lowering profile compared to preservative-free bimatoprost 0.03% and preserved bimatoprost 0.03%, although showed a better tolerability profile (Filippelli et al., 2022).

6 | THE IMPACT OF PROSTAGLANDIN ANALOGUES ON GLAUCOMA SURGERY

The arrival to the market of new therapeutic agents has expanded the treatment options, as well as the possible combinations of medical therapies. Clinicians mainly prescribe from one of five classes of IOP-lowering medications: PGAs, β-blockers, CAIs, α2-adrenergic agonists and parasympathomimetic-/cholinergic-agonist (Bucolo et al., 2015; Inoue, 2014).

Each class may cause local and systemic adverse events, and clinicians must take all of them into consideration when choosing the right therapy for each patient (Table 3).

Before the introduction of latanoprost in 1996, the glaucoma treatment algorithm was quite simple and the concept of maximal medical therapy encompassed two topical ocular hypotensive drugs (usually β-blockers + Parasympathomimetic/Cholinergic-agonist) and systemic carbonic anhydrase inhibitors. This algorithm became more complex as medical treatment options expanded (Figure 1).

Although topical hypotensive medication is usually the first treatment approach, many patients do not achieve adequate glaucoma control attributed to different reasons, including poor adherence, side effects or lack of maintained efficacy (Lichter et al., 2001; Newman-Casey et al., 2015).

When topical antiglaucoma treatment does not adequately control the disease, laser therapy and/or surgery is considered next (Burr et al., 2012; Musch et al., 2009; Ting et al., 2014). Trabeculectomy is regarded as the gold standard in glaucoma surgery, due mainly to its well-established efficacy at lowering IOP (Landers et al., 2012). Additionally, in difficult and/or refractory cases, where trabeculectomy is expected to provide worse clinical outcomes, drainage devices (Molteno and Baerveldt implants, and Ahmed valve) may represent a viable option (Bar-David & Blumenthal, 2018; Freedman & Rubin, 1991; Huang et al., 1999).

The introduction of PGAs had a significant impact on the number of trabeculectomies. According to a population-based analysis based on Medicare beneficiaries between 1995 and 2004, the number of trabeculectomies decreased from 59 645 in 1996 to 24 178 in 2004 (Ramulu et al., 2007).

Moreover, from 1996 to 2001 the number of argon (photocoagulative) laser-trabeculoplasty procedures decreased from 148 816 to 75 647, respectively (Ramulu et al., 2007). This reduction may have been as a consequence of an increased utilization of newly available medical therapy, obviating the need for glaucoma procedures.

Similar results have been reported by Walland (2004), who found rates of argon (photocoagulative) laser trabeculoplasty and trabeculectomy surgery fell by 60% and 58%, respectively, between 1993 and 2003 in Australia. Moreover, the results of a retrospective analysis of the Scottish Morbidity Record revealed that, between 1994 and 1999, the number of trabeculectomies decreased from 1714 to 951, respectively (Bateman et al., 2001).

The number of US Medicare patients with a diagnosis of glaucoma remained constant from 1994 through 1999, while the total number of glaucoma procedures markedly decreased by 42.7% from 1994 (147 740 procedures) to 1999 (84 680 procedures) (Strutton & Walt, 2004). These findings seem to indicate that the introduction of PGAs reduced, or at least delayed, the need for surgical treatment in patients with glaucoma.

Interestingly, in Australia, there was a very significant increase in PGAs prescriptions between 1997 and 2003, while the number of prescriptions for other ocular hypotensive medications did not decrease to the same extent (Walland, 2004), suggesting that PGAs were rapidly and widely accepted by ophthalmologists, mainly due to their good efficacy/safety profile and convenient dosage.

Similar to what happened with the advent of PGAs, the approval of selective laser trabeculoplasty (SLT) by the United States Food and Drug Administration (FDA) represented a paradigm shift in the treatment of glaucoma (National Institute for Health and Care Excellence (NICE), 2022). Current evidence suggests that SLT is an effective and safe treatment for patients with open-angle glaucoma, providing good long-term IOP control and reduced need for incisional glaucoma and cataract. The increasingly frequent fact that SLT is being proposed as first-line therapy has led to a reduction in the number of prescriptions for ocular hypotensive drugs (Gazzard et al., 2019a; Gazzard et al., 2019b; Gazzard et al., 2023; National Institute for Health and Care Excellence (NICE), 2022).

However, a very important point to take into consideration is whether the increase in the complexity of glaucoma medical therapeutic regimen would not negatively influence surgery outcomes. In a paper published by Lavin et al. (1990), the success rate of trabeculectomy was found to be significantly higher in eyes that underwent primary trabeculectomy as compared with those who had received at least 1 year of topical glaucoma therapy before undergoing trabeculectomy ($p = 0.001$).

Nevertheless, it has been reported that, in patients who have undergone trabeculectomy, 6 months of additive preoperative treatment with latanoprost did not have any significant effect on either success rate or postoperative IOP (Berthold & Pfeiffer, 2006).

In a retrospective study conducted on POAG patients with medically uncontrolled IOP who underwent primary trabeculectomy, the use of bimatoprost was identified as an independent factor for surgery failure (Miki et al., 2017). In fact, the proportion of patients with no recurrence of IOP elevation was significantly lower in the eyes without deepening of the upper eyelid sulcus (34.7%) than in those with (74.3%), $p < 0.0001$ (Miki et al., 2017).

7 | WHAT DO WE NOT KNOW AND WANT TO KNOW ABOUT PROSTAGLANDIN ANALOGUES?

As previously mentioned, the pathogenesis of glaucoma is multifactorial. Although several risk factors have been associated with the onset of glaucoma and its progression (Jonas et al., 2017; McMonnies, 2017; Tham et al., 2014; Weinreb et al., 2014), the exact mechanism by which ganglion-cell death occurs remains unknown.

The translaminar pressure (TLP) may be defined as the difference between the IOP and the cerebral spinal fluid pressure (CSFP) [TLP = IOP − CSFP] (Jonas et al., 2003). Several studies have shown a reduced CSFP in open-angle glaucoma patients (Berdahl et al., 2008; Jonas et al., 2013; Ren et al., 2010; Siaudvytyte et al., 2014). However, direct determinization of CSFP is complex and not free of complications (Siaudvytyte et al., 2015).

Retinal vessel pulsation may be used as a surrogate of CSFP (Georgevsky et al., 2019). Current evidence suggests that the assessment of spontaneous retinal venous pulsations (SVP) may be a proxy approach to TLP difference evaluation (Golzan et al., 2011, 2012a, 2012b; Levine & Bebie, 2016; Morgan et al., 2022). Additionally, it has been reported that elevated IOP did not induce retinal vein collapse. Moreover, IOP and retinal vein diameters seem to be in phase, which may suggest the IOP is not the major driving force of retinal vein pulsations (Bollinger et al., 2020).

A literature search in PubMed performed in July 14, 2022, using the search terms "prostaglandin analogues, "ophthalmic" and "cerebral spinal fluid pressure" has shown no publications (PubMed, 2022a). Similar results were obtained with the search terms "Prostaglandin analogues (ophthalmic)" AND "Retinal vein/Venous pressure" (PubMed, 2022b).

Vascular factors are involved in the pathogenesis of POAG (Flammer et al., 2002; Grzybowski et al., 2020; Leske et al., 2003; Marjanovic et al., 2012; Martínez & Sánchez, 2005; Martínez & Sánchez-Salorio, 2010).

Different studies have evaluated the impact of PGAs on ocular hemodynamic parameters. According to published evidence, PGAs appear to have some effect on blood vessels. Experimental studies have suggested that PGAs may have, in vitro, some vasoactive properties in porcine ciliary arteries (Allemann et al., 2003a; Brogiolo et al., 2001; Vysniauskiene et al., 2006), although not all the studies have confirmed these findings (Allemann et al., 2003b).

In healthy subjects, latanoprost had a small effect on corneal temperature, which suggested that latanoprost did not have any impact on the blood flow to the anterior segment of the patient's eye (Konieczka et al., 2019).

Assessment of ocular perfusion pressure (OPP) showed latanoprost was associated with a significant increase of OPP in glaucoma patients. In patients with normal-tension glaucoma, latanoprost significantly increased mean 24-h OPP (Costagliola et al., 2008; Drance et al., 1998; Greve et al., 1997; Liu et al., 2002). Similarly, Quaranta et al. (2008) found that in POAG patients, latanoprost, and dorzolamide/timolol fixed combination equally enhanced 24-h diastolic OPP. However, Ishibashi et al. (2006) did not find any significant effect of latanoprost on OPP, despite significantly lowering IOP.

Investigations of ocular blood flow revealed that latanoprost had mostly neutral effects on ocular circulation in healthy subjects and glaucoma patients (Arkasu et al. 2004; Harris et al., 2009; Inan et al., 2003; Nicolela et al., 1996; Zeitz et al., 2005). Koz et al. (2007) reported that PGAs significantly lowered IOP and increased OPP in patients with POAG or ocular hypertension. In addition, latanoprost and travoprost were able to significantly reduce the resistivity index in the ophthalmic and central retinal arteries, respectively (Koz et al., 2007). Similarly, travoprost and bimatoprost increased significantly end-diastolic velocity of central retinal artery in newly diagnosed open-angle glaucoma patients (Alagoz et al., 2008). In previously untreated POAG patients, Gherghel et al. (2008) observed an increase in mean OPP and improvement in ocular perfusion at the optic nerve head and retina levels when treated with Latanoprost 0.005%.

Analysis of the new PGAs in healthy subjects showed that latanoprostene bunod 0.024% was associated with a significant increase in optic nerve head blood volume and oxygen saturation (Samaha et al., 2022). Additionally, latanoprostene bunod caused relaxation in previously contracted human trabecular meshwork cells by endothelin-1 (Cavet et al., 2015).

8 | CONCLUSIONS

PGAs, particularly latanoprost, have formed part of the glaucoma armamentarium for 25 years. During that time, a large number of scientific publications have been generated. They have highlighted its good efficacy and safety profile. PGAs are currently considered as the first-choice in many cases.

Regarding their safety, PGAs have been associated with different ocular AEs, most of them of an aesthetic nature, such as hyperemia, change in eyelid and iris pigmentation, hypertrichosis around the eyes, or eyelash growth. Their relationship with the appearance of postoperative macular oedema has not been fully elucidated and seems to depend on other risk factors. However, it has been suggested to avoid the use of PGAs in patients at risk of developing cystoid macular oedema.

Another adverse event that deserves special attention, mainly due to its potential impact on surgery outcomes, are the ocular adnexal changes associated with the use of PGAs. In fact, deepening of the upper eyelid sulcus was an independent factor for surgery failure.

Because of their efficacy, limited systemic side effects and once daily dosing, PGAs have changed the paradigm of glaucoma treatment, as evidenced by the large reduction in the number of laser procedures and trabeculectomies since their launch.

Beyond the deepening of the upper eyelid sulcus, the use of PGAs has not been associated with worsening surgical outcomes.

The pathogenesis of glaucoma is known to be multifactorial. Beyond their IOP-lowering effect, the role of PGAs on other factors related to the onset of glaucoma and its progression has been evaluated. Despite promising evidence, more ocular hemodynamic data and on the prevention of glaucomatous damage progression are needed.

Overall, PGAs are an effective and well-tolerated treatment for lowering IOP.

ACKNOWLEDGEMENTS

Medical writing and Editorial assistant services have been provided by Antonio Martinez (MD) of Ciencia y Deporte S.L.

This review was supported by an educational grant from Viatris Inc.

ORCID

Maria Francesca Cordeiro https://orcid.org/0000-0001-8663-6525

REFERENCES

Abramovitz, M., Adam, M., Boie, Y., Carrière, M., Denis, D., Godbout, C. et al. (2000) The utilization of recombinant prostanoid receptors to determine the affinities and selectivities of prostaglandins and related analogs. *Biochimica et Biophysica Acta*, 1483(2), 285–293.

Abrams, D.A., Robin, A.L., Pollack, I.P., DeFaller, J.M. & DeSantis, L. (1987) The safety and efficacy of topical 1% ALO 2145 (p-aminoclonidine hydrochloride) in normal volunteers. *Archives of Ophthalmology*, 105(9), 1205–1207.

Akarsu, C., Bilgili, Y.K., Taner, P., Unal, B. & Ergin, A. (2004) Short-term effect of latanoprost on ocular circulation in ocular hypertension. *Clinical & Experimental Ophthalmology*, 32(4), 373–377.

Alagoz, G., Gürel, K., Bayer, A., Serin, D., Celebi, S. & Kukner, S. (2008) A comparative study of bimatoprost and travoprost: effect on intraocular pressure and ocular circulation in newly diagnosed glaucoma patients. *Ophthalmologica*, 222(2), 88–95.

Allemann, R., Flammer, J. & Haefliger, I.O. (2003a) Vasoactive properties of bimatoprost in isolated porcine ciliary arteries. *Klinische Monatsblätter für Augenheilkunde*, 220(3), 161–164.

Allemann, R., Flammer, J. & Haefliger, I.O. (2003b) Absence of vasoactive properties of travoprost in isolated porcine ciliary arteries. *Klinische Monatsblätter für Augenheilkunde*, 220(3), 152–155.

Alm, A. (2014) Latanoprost in the treatment of glaucoma. *Clinical Ophthalmology*, 8, 1967–1985.

Alm, A., Camras, C.B. & Watson, P.G. (1997) Phase III latanoprost studies in Scandinavia, the United Kingdom and the United States. *Survey of Ophthalmology*, 41(Suppl 2), S105–S110.

Alm, A. & Nilsson, S.F. (2009) Uveoscleral outflow–a review. *Experimental Eye Research*, 88(4), 760–768.

Alm, A. & Stjernschantz, J. (1995) Effects on intraocular pressure and side effects of 0.005% latanoprost applied once daily, evening or morning. A comparison with timolol. Scandinavian Latanoprost study group. *Ophthalmology*, 102(12), 1743–1752.

Alm, A. & Villumsen, J. (1991) PhXA34, a new potent ocular hypotensive drug. A study on dose-response relationship and on aqueous humor dynamics in healthy volunteers. *Archives of Ophthalmology*, 109(11), 1564–1568.

American Academy of Ophthalmology Preferred Practice Pattern Glaucoma Committee. (2020) Primary Open-Angle Glaucoma PPP 2020. Available from: https://www.aao.org/preferred-practice-pattern/primary-open-angle-glaucoma-ppp [Accessed July 5, 2022].

Ashaye, A., Ashaolu, O., Komolafe, O., Ajayi, B.G., Olawoye, O., Olusanya, B. et al. (2013) Prevalence and types of glaucoma among an indigenous African population in southwestern Nigeria. *Investigative Ophthalmology & Visual Science*, 54(12), 7410–7416.

Bar-David, L. & Blumenthal, E.Z. (2018) Evolution of glaucoma surgery in the last 25 years. *Rambam Maimonides Med J*, 9(3), e0024.

Bateman, D.N., Clark, R., Azuara-Blanco, A., Bain, M. & Forrest, J. (2001) The impact of new drugs on management of glaucoma in Scotland: observational study. *BMJ*, 323(7326), 1401–1402.

Berdahl, J.P., Allingham, R.R. & Johnson, D.H. (2008) Cerebrospinal fluid pressure is decreased in primary open-angle glaucoma. *Ophthalmology*, 115, 763–768.

Berthold, S. & Pfeiffer, N. (2006) Effect of additive preoperative latanoprost treatment on the outcome of filtration surgery. *Graefe's Archive for Clinical and Experimental Ophthalmology*, 244(8), 1029–1034.

Birt, C.M., Buys, Y.M., Ahmed, I.I., Trope, G.E. & Toronto Area Glaucoma Society. (2010) Prostaglandin efficacy and safety study undertaken by race (the PRESSURE study). *Journal of Glaucoma*, 19(7), 460–467.

Boland, M.V., Ervin, A.M., Friedman, D.S., Jampel, H.D., Hawkins, B.S., Vollenweider, D. et al. (2013) Comparative effectiveness of treatments for open-angle glaucoma: a systematic review for the U.S. preventive services task force. *Annals of Internal Medicine*, 158(4), 271–279.

Bollinger, O., Saruhan, Y. & Gugleta, K. (2020) Analysis of retinal vessel pulsations with electrocardiographic gating. *Klinische Monatsblätter für Augenheilkunde*, 237(4), 464–468.

Brogiolo, G., Flammer, J. & Haefliger, I.O. (2001) Latanoprost is a vasoconstrictor in isolated porcine ciliary arteries. *Klinische Monatsblätter für Augenheilkunde*, 218(5), 373–375.

Bucolo, C., Platania, C.B., Reibaldi, M., Bonfiglio, V., Longo, A., Salomone, S. et al. (2015) Controversies in glaucoma: current medical treatment and drug development. *Current Pharmaceutical Design*, 21(32), 4673–4681.

Budenz, D.L., Barton, K., Whiteside-de Vos, J., Schiffman, J., Bandi, J., Nolan, W. et al. (2013) Prevalence of glaucoma in an urban west African population: the Tema eye survey. *JAMA Ophthalmol*, 131(5), 651–658.

Burr, J., Azuara-Blanco, A., Avenell, A. & Tuulonen, A. (2012) Medical versus surgical interventions for open angle glaucoma. *Cochrane Database of Systematic Reviews*, (9), CD004399.

Butler, P., Mannschreck, M., Lin, S., Hwang, I. & Alvarado, J. (1995) Clinical experience with the long-term use of 1% apraclonidine. *Incidence of Allergic Reactions. Arch Ophthalmol*, 113(3), 293–296.

Camras, C.B. (1996) Comparison of latanoprost and timolol in patients with ocular hypertension and glaucoma: a six-month masked, multicenter trial in the United States. The United States Latanoprost study group. *Ophthalmology*, 103(1), 138–147.

Camras, C.B., Alm, A., Watson, P. & Stjernschantz, J. (1996) Latanoprost, a prostaglandin analog, for glaucoma therapy. Efficacy and safety after 1 year of treatment in 198 patients. Latanoprost study groups. *Ophthalmology*, 103(11), 1916–1924.

Camras, C.B., Bito, L.Z. & Eakins, K.E. (1977) Reduction of intraocular pressure by prostaglandins applied topically to the eyes of conscious rabbits. *Investigative Ophthalmology & Visual Science*, 16(12), 1125–1134.

Cavet, M.E., Vollmer, T.R., Harrington, K.L., VanDerMeid, K. & Richardson, M.E. (2015) Regulation of Endothelin-1-induced trabecular meshwork cell contractility by Latanoprostene Bunod. *Investigative Ophthalmology & Visual Science*, 56(6), 4108–4116.

Cheng, J.W. & Wei, R.L. (2008) Meta-analysis of 13 randomized controlled trials comparing bimatoprost with latanoprost in patients with elevated intraocular pressure. *Clinical Therapeutics*, 30(4), 622–632.

Clement, C.I. & Goldberg, I. (2011) The management of complicated glaucoma. *Indian Journal of Ophthalmology*, 59(Suppl 1), S141–S147.

Costagliola, C., Parmeggiani, F., Virgili, G., Lamberti, G., Incorvaia, C., Perri, P. et al. (2008) Circadian changes of intraocular pressure and ocular perfusion pressure after timolol or latanoprost in Caucasians with normal-tension glaucoma. *Graefe's Archive for Clinical and Experimental Ophthalmology*, 246(3), 389–396.

Cvenkel, B. & Kolko, M. (2020) Current medical therapy and future trends in the Management of Glaucoma Treatment. *Journal of Ophthalmology*, 2020, 6138132.

Damji, K.F., Behki, R., Wang, L. & Target IOP Workshop participants. (2003) Canadian perspectives in glaucoma management: setting target intraocular pressure range. *Canadian Journal of Ophthalmology*, 38(3), 189–197.

Day, D.G., Walters, T.R., Schwartz, G.F., Mundorf, T.K., Liu, C., Schiffman, R.M. et al. (2013) Bimatoprost 0.03% preservative-free ophthalmic solution versus bimatoprost 0.03% ophthalmic solution (Lumigan) for glaucoma or ocular hypertension: a 12-week, randomised, double-masked trial. *The British Journal of Ophthalmology*, 97(8), 989–993.

Demitsu, T., Manabe, M., Harima, N., Sugiyama, T., Yoneda, K. & Yamada, N. (2001) Hypertrichosis induced by latanoprost. *Journal of the American Academy of Dermatology*, 44(4), 721–723.

Digiuni, M., Fogagnolo, P. & Rossetti, L. (2012) A review of the use of latanoprost for glaucoma since its launch. *Expert Opinion on Pharmacotherapy*, 13(5), 723–745.

Dikopf, M.S., Vajaranant, T.S. & Edward, D.P. (2017) Topical treatment of glaucoma: established and emerging pharmacology. *Expert Opinion on Pharmacotherapy*, 18(9), 885–898.

Drance, S.M., Crichton, A. & Mills, R.P. (1998) Comparison of the effect of latanoprost 0.005% and timolol 0.5% on the calculated ocular perfusion pressure in patients with normal-tension glaucoma. *American Journal of Ophthalmology*, 125(5), 585–592.

DuBiner, H., Cooke, D., Dirks, M., Stewart, W.C., VanDenburgh, A.M. & Felix, C. (2001) Efficacy and safety of bimatoprost in patients with elevated intraocular pressure: a 30-day comparison with latanoprost. *Survey of Ophthalmology*, 45(Suppl 4), S353–S360.

Elgin, U., Batman, A., Berker, N. & Ilhan, B. (2006) The comparison of eyelash lengthening effect of latanoprost therapy in adults and children. *European Journal of Ophthalmology*, 2, 247–250.

Eyawo, O., Nachega, J., Lefebvre, P., Meyer, D., Rachlis, B., Lee, C.W. et al. (2009) Efficacy and safety of prostaglandin analogues in patients with predominantly primary open-angle glaucoma or ocular hypertension: a meta-analysis. *Clinical Ophthalmology*, 3, 447–456.

Filippelli, M., Campagna, G., Ciampa, N., Fioretto, G., Giannini, R., Marino, P.F. et al. (2022) Ocular tolerability of Bimatoprost 0.1 mg/mL preservative-free versus Bimatoprost 0.1 mg/mL with Benzalkonium chloride or Bimatoprost 0.3 mg/mL preservative-free in patients with primary open-angle glaucoma. *Journal of Clinical Medicine*, 11(12), 3518.

Filippopoulos, T., Paula, J.S., Torun, N., Hatton, M.P., Pasquale, L.R. & Grosskreutz, C.L. (2008) Periorbital changes associated with topical bimatoprost. *Ophthalmic Plastic & Reconstructive Surgery*, 24(4), 302–307.

Flammer, J., Orgül, S., Costa, V.P., Orzalesi, N., Krieglstein, G.K., Serra, L.M. et al. (2002) The impact of ocular blood flow in glaucoma. *Progress in Retinal and Eye Research*, 21(4), 359–393.

Flaxman, S.R., Bourne, R.R.A., Resnikoff, S., Ackland, P., Braithwaite, T., Cicinelli, M.V. et al. (2017) Global causes of blindness and distance vision impairment 1990-2020: a systematic review and meta-analysis. *The Lancet Global Health*, 5(12), e1221–e1234.

Freedman, J. & Rubin, B. (1991) Molteno implants as a treatment for refractory glaucoma in black patients. *Archives of Ophthalmology*, 109(10), 1417–1420.

Freeman, P.D. & Kahook, M.Y. (2009) Preservatives in topical ophthalmic medications: historical and clinical perspectives expert. *Review of Ophthalmology*, 4, 59–64. Available from: https://doi.org/10.1586/17469899.4.1.59

Gabelt, B.T. & Kaufman, P.L. (1989) Prostaglandin F2 alpha increases uveoscleral outflow in the cynomolgus monkey. *Experimental Eye Research*, 49(3), 389–402.

Gandolfi, S., Paredes, T., Goldberg, I., Coote, M., Wells, A., Volksone, L. et al. (2012) Travoprost Bak-free clinical study group. Comparison of a travoprost BAK-free formulation preserved with polyquaternium-1 with BAK- preserved travoprost in ocular hypertension or open-angle glaucoma. *European Journal of Ophthalmology*, 22(1), 34–44.

Gandolfi, S., Simmons, S.T., Sturm, R., Chen, K., VanDenburgh, A.M. & Bimatoprost Study Group 3. (2001) Three-month comparison of bimatoprost and latanoprost in patients with glaucoma and ocular hypertension. *Advances in Therapy*, 18(3), 110–121.

Garway-Heath, D.F., Crabb, D.P., Bunce, C., Lascaratos, G., Amalfitano, F., Anand, N. et al. (2015) Latanoprost for open-angle glaucoma (UKGTS): a randomised, multicentre, placebo-controlled trial. *Lancet*, 385(9975), 1295–1304.

Gaton, D.D., Sagara, T., Lindsey, J.D., Gabelt, B.T., Kaufman, P.L. & Weinreb, R.N. (2001) Increased matrix metalloproteinases 1, 2, and 3 in the monkey uveoscleral outflow pathway after topical prostaglandin F(2 alpha)-isopropyl ester treatment. *Archives of Ophthalmology*, 119(8), 1165–1170.

Gazzard, G., Konstantakopoulou, E., Garway-Heath, D., Adeleke, M., Vickerstaff, V., Ambler, G. et al. (2023) Laser in glaucoma and ocular hypertension (LiGHT) trial: six-year results of primary selective laser Trabeculoplasty versus eye drops for the treatment of glaucoma and ocular hypertension. *Ophthalmology*, 130(2), 139–151.

Gazzard, G., Konstantakopoulou, E., Garway-Heath, D., Garg, A., Vickerstaff, V., Hunter, R. et al. (2019a) Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre 33andomized controlled trial. *Lancet*, 393(10180), 1505–1516.

Gazzard, G., Konstantakopoulou, E., Garway-Heath, D., Garg, A., Vickerstaff, V., Hunter, R. et al. (2019b) Selective laser trabeculoplasty versus drops for newly diagnosed ocular hypertension and glaucoma: the LiGHT RCT. *Health Technology Assessment*, 31, 1–102.

GBD 2019 Blindness and Vision Impairment Collaborators & Vision Loss Expert Group of the Global Burden of Disease Study. (2021) Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the right to sight: an analysis for the global burden of disease study. *The Lancet Global Health*, 9(2), e144–e160.

Georgevsky, D., Gangoda, S.V.S. & Golzan, S.M. (2019) Postural effects on spontaneous retinal venous pulsations in healthy individuals. *Acta Ophthalmologica*, 97(6), e839–e843.

Gherghel, D., Hosking, S.L., Cunliffe, I.A. & Armstrong, R.A. (2008) First-line therapy with latanoprost 0.005% results in improved ocular circulation in newly diagnosed primary open-angle glaucoma patients: a prospective, 6-month, open-label study. *Eye (London, England)*, 22(3), 363–369.

Golzan, S.M., Avolio, A. & Graham, S.L. (2012) Hemodynamic interactions in the eye: a review. *Ophthalmologica*, 228, 214–221.

Golzan, S.M., Graham, S.L., Leaney, J. & Avolio, A. (2011) Dynamic association between intraocular pressure and spontaneous pulsations of retinal veins. *Current Eye Research*, 36, 53–59.

Golzan, S.M., Kim, M.O., Seddighi, A.S., Avolio, A. & Graham, S.L. (2012) Non-invasive estimation of cerebrospinal fluid pressure waveforms by means of retinal venous pulsatility and central aortic blood pressure. *Annals of Biomedical Engineering*, 40, 1940–1948.

Greve, E.L., Rulo, A.H., Drance, S.M., Crichton, A.C., Mills, R.P. & Hoyng, P.F. (1997) Reduced intraocular pressure and increased ocular perfusion pressure in normal tension glaucoma: a review of short-term studies with three dose regimens of latanoprost treatment. *Survey of Ophthalmology*, 41(Suppl 2), S89–S92.

Grzybowski, A., Och, M., Kanclerz, P., Leffler, C. & Moraes, C.G. (2020) Primary open angle glaucoma and vascular risk factors: a review of population based studies from 1990 to 2019. *Journal of Clinical Medicine*, 9(3), 761.

Harasymowycz, P., Hutnik, C., Rouland, J.F., Negrete, F.J.M., Economou, M.A., Denis, P. et al. (2021) Preserved versus preservative-free Latanoprost for the treatment of glaucoma

and ocular hypertension: a post hoc pooled analysis. *Advances in Therapy*, 38(6), 3019–3031.
Harris, A., Garzozi, H.J., McCranor, L., Rechtman, E., Yung, C.W. & Siesky, B. (2009) The effect of latanoprost on ocular blood flow. *International Ophthalmology*, 29(1), 19–26.
Hata, A.N. & Breyer, R.M. (2004) Pharmacology and signaling of prostaglandin receptors: multiple roles in inflammation and immune modulation. *Pharmacology & Therapeutics*, 103(2), 147–166.
Hatanaka, M., Vessani, R.M., Elias, I.R., Morita, C. & Susanna, R., Jr. (2009) The effect of prostaglandin analogs and prostamide on central corneal thickness. *Journal of Ocular Pharmacology and Therapeutics*, 25(1), 51–53.
Heijl, A., Leske, M.C., Bengtsson, B., Hyman, L., Bengtsson, B., Hussein, M. et al. (2002) Reduction of intraocular pressure and glaucoma progression: results from the early manifest glaucoma trial. *Archives of Ophthalmology*, 120(10), 1268–1279.
Higginbotham, E.J., Olander, K.W., Kim, E.E., Grunden, J.W., Kwok, K.K., Tressler, C.S. et al. (2010) Fixed combination of latanoprost and timolol vs individual components for primary open-angle glaucoma or ocular hypertension: a randomized, double-masked study. *Archives of Ophthalmology*, 128(2), 165–172.
Höhn, R., Nickels, S., Schuster, A.K., Wild, P.S., Münzel, T., Lackner, K.J. et al. (2018) Prevalence of glaucoma in Germany: results from the Gutenberg health study. *Graefe's Archive for Clinical and Experimental Ophthalmology*, 256(9), 1695–1702.
Holló, G., Aung, T., Cantor, L.B. & Aihara, M. (2020) Cystoid macular edema related to cataract surgery and topical prostaglandin analogs: mechanism, diagnosis, and management. *Survey of Ophthalmology*, 65(5), 496–512.
Holló, G., Katsanos, A., Boboridis, K.G., Irkec, M. & Konstas, A.G.P. (2018) Preservative-free prostaglandin analogs and prostaglandin/Timolol fixed combinations in the treatment of glaucoma: efficacy. *Safety and Potential Advantages. Drugs*, 78(1), 39–64.
Honrubia, F., García-Sánchez, J., Polo, V., de la Casa, J.M. & Soto, J. (2009) Conjunctival hyperaemia with the use of latanoprost versus other prostaglandin analogues in patients with ocular hypertension or glaucoma: a meta-analysis of randomised clinical trials. *The British Journal of Ophthalmology*, 93(3), 316–321.
Hu, J., Vu, J.T., Hong, B. & Gottlieb, C. (2020) Uveitis and cystoid macular oedema secondary to topical prostaglandin analogue use in ocular hypertension and open angle glaucoma. *The British Journal of Ophthalmology*, 104(8), 1040–1044.
Huang, H.L., Sun, X.H. & Xiao, M. (2011) Comparison of intraocular pressure reducing effects of three prostaglandin eyedrops in open-angle glaucoma. *Zhonghua Yan Ke Za Zhi*, 47(2), 109–113.
Huang, M.C., Netland, P.A., Coleman, A.L., Siegner, S.W., Moster, M.R. & Hill, R.A. (1999) Intermediate-term clinical experience with the Ahmed glaucoma valve implant. *American Journal of Ophthalmology*, 127(1), 27–33.
Inan, U.U., Ermis, S.S., Yücel, A. & Oztürk, F. (2003) The effects of latanoprost and brimonidine on blood flow velocity of the retrobulbar vessels: a 3-month clinical trial. *Acta Ophthalmologica Scandinavica*, 81(2), 155–160.
Inoue, K. (2014) Managing adverse effects of glaucoma medications. *Clinical Ophthalmology*, 8, 903–913.
Inoue, K., Ishida, K., Tomita, G. & Noma, H. (2020) A scoping review and network meta-analysis for efficacy and safety of glaucoma medication in Japanese patients. *Japanese Journal of Ophthalmology*, 64(2), 103–113.
Inoue, K., Shiokawa, M., Higa, R., Sugahara, M., Soga, T., Wakakura, M. et al. (2012) Adverse periocular reactions to five types of prostaglandin analogs. *Eye (London, England)*, 26(11), 1465–1472.
Inoue, K., Shiokawa, M., Wakakura, M. & Tomita, G. (2013) Deepening of the upper eyelid sulcus caused by 5 types of prostaglandin analogs. *Journal of Glaucoma*, 22(8), 626–631.
Inoue, K., Wakakura, M., Inoue, J., Matsuo, H., Hara, T. & Tomita, G. (2006) Adverse reaction after use of latanoprost in Japanese glaucoma patients. *Nippon Ganka Gakkai Zasshi*, 110(8), 581–587.
Ishibashi, S., Hirose, N., Tawara, A. & Kubota, T. (2006) Effect of latanoprost on the diurnal variations in the intraocular and ocular perfusion pressure in normal tension glaucoma. *Journal of Glaucoma*, 15(5), 354–357.
Islam, S. & Spry, C. (2020) *Prostaglandin Analogues for Ophthalmic Use: A Review of Comparative Clinical Effectiveness, Cost-Effectiveness, and Guidelines [Internet]*. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health. Available from: https://www.ncbi.nlm.nih.gov/books/NBK562924/ [Accessed July 12, 2022].
Jonas, J.B., Aung, T., Bourne, R.R., Bron, A.M., Ritch, R. & Panda-Jonas, S. (2017) Glaucoma. *Lancet*, 390(10108), 2183–2193.
Jonas, J.B., Berenshtein, E. & Holbach, L. (2003) Anatomic relationship between lamina cribrosa, intraocular space, and cerebrospinal fluid space. *Investigative Ophthalmology & Visual Science*, 44, 5189–5195.
Jonas, J.B., Nangia, V., Wang, N., Bhate, K., Nangia, P., Nangia, P. et al. (2013) Trans-lamina cribrosa pressure difference and open-angle glaucoma. The Central India eye and medical study. *PLoS One*, 8, e82284.
Kaarniranta, K., Ikäheimo, K., Mannermaa, E. & Ropo, A. (2016) Pharmacokinetics, efficacy, and safety of the preservative-free fixed combination of Tafluprost 0.0015% and Timolol 0.5% in healthy volunteers: a phase I comparison vs. the corresponding preservative-free monotherapies. *Clinical Pharmacokinetics*, 55(4), 485–494.
Kampik, A., Arias-Puente, A., O'Brart, D.P., Vuori, M.L. & European Latanoprost Study Group. (2002) Intraocular pressure-lowering effects of latanoprost and brimonidine therapy in patients with open-angle glaucoma or ocular hypertension: a randomized observer-masked multicenter study. *Journal of Glaucoma*, 11(2), 90–96.
Kass, M.A., Heuer, D.K., Higginbotham, E.J., Johnson, C.A., Keltner, J.L., Miller, J.P. et al. (2002) The ocular hypertension treatment study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. *Archives of Ophthalmology*, 120(6), 701–713 discussion 829-830.
Keel, S., Xie, J., Foreman, J., Lee, P.Y., Alwan, M., Fahy, E.T. et al. (2019) Prevalence of glaucoma in the Australian National eye Health Survey. *The British Journal of Ophthalmology*, 103(2), 191–195.
Konieczka, K., Koch, S., Hauenstein, D., Chackathayil, T.N., Binggeli, T., Schoetzau, A. et al. (2019) Effects of the glaucoma drugs Latanoprost and Brimonidine on corneal temperature. *Translational Vision Science & Technology*, 8(3), 47.
Konowal, A., Morrison, J.C., Brown, S.V., Cooke, D.L., Maguire, L.J., Verdier, D.V. et al. (1999) Irreversible corneal decompensation in patients treated with topical dorzolamide. *American Journal of Ophthalmology*, 127(4), 403–406.
Konstas, A.G., Holló, G., Mikropoulos, D.G., Haidich, A.B., Dimopoulos, A.T., Empeslidis, T. et al. (2013) 24-hour efficacy of the bimatoprost-timolol fixed combination versus latanoprost as first choice therapy in subjects with high-pressure exfoliation syndrome and glaucoma. *The British Journal of Ophthalmology*, 97(7), 857–861.
Konstas, A.G., Katsanos, A., Athanasopoulos, G.P., Voudouragkaki, I.C., Panagiotou, E.S., Pagkalidou, E. et al. (2018) Preservative-free tafluprost/timolol fixed combination: comparative 24-h efficacy administered morning or evening in open-angle glaucoma patients. *Expert Opinion on Pharmacotherapy*, 19(18), 1981–1988.
Konstas, A.G., Quaranta, L. & Realini, T. (2012) Overview of the [corrected] travoprost/timolol BAK-free fixed combination. *Expert Opinion on Pharmacotherapy*, 13(5), 757–766.
Koz, O.G., Ozsoy, A., Yarangumeli, A., Kose, S.K. & Kural, G. (2007) Comparison of the effects of travoprost, latanoprost and bimatoprost on ocular circulation: a 6-month clinical trial. *Acta Ophthalmologica Scandinavica*, 85(8), 838–843.
Landers, J., Martin, K., Sarkies, N., Bourne, R. & Watson, P. (2012) A twenty-year follow-up study of trabeculectomy: risk factors and outcomes. *Ophthalmology*, 119(4), 694–702.
Lavin, M.J., Wormald, R.P., Migdal, C.S. & Hitchings, R.A. (1990) The influence of prior therapy on thesuccess of trabeculectomy. *Arch Ophthalmol*, 108(11):1543–1548.
Leske, M.C., Heijl, A., Hussein, M., Bengtsson, B., Hyman, L., Komaroff, E. et al. (2003) Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. *Archives of Ophthalmology*, 121(1), 48–56.

Leske, M.C., Heijl, A., Hyman, L., Bengtsson, B., Dong, L., Yang, Z. et al. (2007) Predictors of long-term progression in the early manifest glaucoma trial. *Ophthalmology*, 114(11), 1965–1972.

Levine, D.N. & Bebie, H. (2016) Phase and amplitude of spontaneous retinal vein pulsations: an extended constant inflow and variable outflow model. *Microvascular Research*, 106, 67–79.

Lewis, R.A., Gross, R.L., Sall, K.N., Schiffman, R.M., Liu, C.C., Batoosingh, A.L. et al. (2010) The safety and efficacy of bimatoprost/timolol fixed combination: a 1-year double-masked, randomized parallel comparison to its individual components in patients with glaucoma or ocular hypertension. *Journal of Glaucoma*, 19(6), 424–426.

Li, F., Huang, W. & Zhang, X. (2018) Efficacy and safety of different regimens for primary open-angle glaucoma or ocular hypertension: a systematic review and network meta-analysis. *Acta Ophthalmologica*, 96(3), e277–e284.

Li, T., Lindsley, K., Rouse, B., Hong, H., Shi, Q., Friedman, D.S. et al. (2016) Comparative effectiveness of first-line medications for primary open-angle glaucoma: a systematic review and network meta-analysis. *Ophthalmology*, 123(1), 129–140.

Lichter, P.R., Musch, D.C., Gillespie, B.W., Guire, K.E., Janz, N.K., Wren, P.A. et al. (2001) Interim clinical outcomes in the collaborative initial glaucoma treatment study comparing initial treatment randomized to medications or surgery. *Ophthalmology*, 108(11), 1943–1953.

Lindsey, J.D., Kashiwagi, K., Kashiwagi, F. & Weinreb, R.N. (1997) Prostaglandin action on ciliary smooth muscle extracellular matrix metabolism: implications for uveoscleral outflow. *Survey of Ophthalmology*, 41(Suppl 2), S53–S59.

Liu, C.J., Ko, Y.C., Cheng, C.Y., Chiu, A.W., Chou, J.C., Hsu, W.M. et al. (2002) Changes in intraocular pressure and ocular perfusion pressure after latanoprost 0.005% or brimonidine tartrate 0.2% in normal-tension glaucoma patients. *Ophthalmology*, 109(12), 2241–2247.

Liu, J.H., Medeiros, F.A., Slight, J.R. & Weinreb, R.N. (2009) Comparing diurnal and nocturnal effects of brinzolamide and timolol on intraocular pressure in patients receiving latanoprost monotherapy. *Ophthalmology*, 116(3), 449–454.

Marjanovic, I., Milic, N., Martínez, A. & Benitez-del-Castillo, J. (2012) Retrobulbar hemodynamic parameters in open-angle and angle-closure glaucoma patients. *Eye (London, England)*, 26(4), 523–528.

Marshall, L.L., Hayslett, R.L. & Stevens, G.A. (2018) Therapy for open-angle glaucoma. *The Consultant Pharmacist*, 33(8), 432–445.

Martínez, A. & Sánchez, M. (2005) Predictive value of colour Doppler imaging in a prospective study of visual field progression in primary open-angle glaucoma. *Acta Ophthalmologica Scandinavica*, 83(6), 716–722.

Martínez, A. & Sánchez, M. (2007) A comparison of the safety and intraocular pressure lowering of bimatoprost/timolol fixed combination versus latanoprost/timolol fixed combination in patients with open-angle glaucoma. *Current Medical Research and Opinion*, 23(5), 1025–1032.

Martínez, A. & Sánchez, M. (2008) Efficacy and safety of bimatoprost/timolol fixed combination in the treatment of glaucoma or ocular hypertension. *Expert Opinion on Pharmacotherapy*, 9(1), 137–143.

Martínez, A. & Sánchez, M. (2009) Bimatoprost/timolol fixed combination vs latanoprost/timolol fixed combination in open-angle glaucoma patients. *Eye (London, England)*, 23(4), 810–818.

Martínez, A. & Sánchez-Salorio, M. (2010) Predictors for visual field progression and the effects of treatment with dorzolamide 2% or brinzolamide 1% each added to timolol 0.5% in primary open-angle glaucoma. *Acta Ophthalmologica*, 88(5), 541–552.

McMonnies, C.W. (2017) Glaucoma history and risk factors. *Journal of Optometry*, 10(2), 71–78.

Miki, T., Naito, T., Fujiwara, M., Araki, R., Kiyoi, R., Shiode, Y. et al. (2017) Effects of pre-surgical administration of prostaglandin analogs on the outcome of trabeculectomy. *PLoS One*, 12(7), e0181550.

Misiuk-Hojlo, M., Pomorska, M., Mulak, M., Rekas, M., Wierzbowska, J., Prost, M. et al. (2019 Mar) The RELIEF study: tolerability and efficacy of preservative-free latanoprost in the treatment of glaucoma or ocular hypertension. *European Journal of Ophthalmology*, 29(2), 210–215.

Morgan, W.H., Vukmirovic, A., Abdul-Rahman, A., Khoo, Y.J., Kermode, A.G., Lind, C.R. et al. (2022) Zero retinal vein pulsation amplitude extrapolated model in non-invasive intracranial pressure estimation. *Scientific Reports*, 12(1), 5190.

Mundorf, T., Noecker, R.J. & Earl, M. (2007) (2007): ocular hypotensive efficacy of brimonidine 0.15% as adjunctive therapy with latanoprost 0.005% in patients with open-angle glaucoma or ocular hypertension. *Advances in Therapy*, 24(2), 302–309.

Musch, D.C., Gillespie, B.W., Lichter, P.R., Niziol, L.M., Janz, N.K. & CIGTS Study Investigators. (2009) Visual field progression in the collaborative initial glaucoma treatment study the impact of treatment and other baseline factors. *Ophthalmology*, 116(2), 200–207.

Nakamoto, K. & Yasuda, N. (2007) Effect of concomitant use of latanoprost and brinzolamide on 24-hour variation of IOP in normal-tension glaucoma. *Journal of Glaucoma*, 4, 352–357.

Nakano, T., Inoue, R., Kimura, T., Suzumura, H., Tanino, T., Yamazaki, Y. et al. (2016) Effects of Brinzolamide, a topical carbonic anhydrase inhibitor, on corneal endothelial cells. *Advances in Therapy*, 33(8), 1452–1459.

Nakano, T., Mizoue, S., Fuse, N., Iwase, A., Matsumoto, S. & Yoshikawa, K. (2015) Fixed combination of Travoprost and Timolol maleate reduces intraocular pressure in Japanese patients with primary open-angle glaucoma or ocular hypertension: a prospective multicenter open-label study. *Advances in Therapy*, 32(9), 823–837.

Nathoo, N.A., Etminan, M. & Mikelberg, F.S. (2015) Association between glaucoma, glaucoma therapies, and erectile dysfunction. *Journal of Glaucoma*, 24(2), 135–137.

National Institute for Health and Care Excellence (NICE). (2022) *Evidence Reviews for Selective Laser Trabeculoplasty in Ocular Hypertension or Chronic Open-angle Glaucoma Adult Patients: Glaucoma: Diagnosis and Management*. London: National Institute for Health and Care Excellence. Available from: https://www.ncbi.nlm.nih.gov/books/NBK579557/ [Accessed May 25, 2023]

Netland, P.A., Landry, T., Sullivan, E.K., Andrew, R., Silver, L., Weiner, A. et al. (2001) Travoprost compared with latanoprost and timolol in patients with open-angle glaucoma or ocular hypertension. *American Journal of Ophthalmology*, 132(4), 472–484.

Newman-Casey, P.A., Robin, A.L., Blachley, T., Farris, K., Heisler, M., Resnicow, K. et al. (2015) The Most common barriers to glaucoma medication adherence: a cross-sectional survey. *Ophthalmology*, 122(7), 1308–1316.

Nicolela, M.T., Buckley, A.R., Walman, B.E. & Drance, S.M. (1996) A comparative study of the effects of timolol and latanoprost on blood flow velocity of the retrobulbar vessels. *American Journal of Ophthalmology*, 122(6), 784–789.

Noecker, R.S., Dirks, M.S., Choplin, N.T., Bernstein, P., Batoosingh, A.L., Whitcup, S.M. et al. (2003) A six-month randomized clinical trial comparing the intraocular pressure-lowering efficacy of bimatoprost and latanoprost in patients with ocular hypertension or glaucoma. *American Journal of Ophthalmology*, 135(1), 55–63.

Nouri-Mahdavi, K., Hoffman, D., Coleman, A.L., Liu, G., Li, G., Gaasterland, D. et al. (2004) Predictive factors for glaucomatous visual field progression in the advanced glaucoma intervention study. *Ophthalmology*, 111(9), 1627–1635.

Oddone, F., Scorcia, V., Iester, M., Sisto, D., De Cilla, S., Bettin, P. et al. (2022) Treatment of open-angle glaucoma and ocular hypertension with the fixed-dose combination of preservative-free Tafluprost/Timolol: clinical outcomes from ophthalmology clinics in Italy. *Clinical Ophthalmology*, 16, 1707–1719.

Park, J., Cho, H.K. & Moon, J.I. (2011) Changes to upper eyelid orbital fat from use of topical bimatoprost, travoprost, and latanoprost. *Japanese Journal of Ophthalmology*, 55(1), 22–27.

Park, J.H., Yoo, C., Chung, H.W. & Kim, Y.Y. (2021) Effect of prostaglandin analogues on anterior scleral thickness and corneal thickness in patients with primary open-angle glaucoma. *Scientific Reports*, 11(1), 11098.

Parrish, R.K., Palmberg, P., Sheu, W.P. & XLT Study Group. (2003) A comparison of latanoprost, bimatoprost, and travoprost in

patients with elevated intraocular pressure: a 12-week, randomized, masked-evaluator multicenter study. *American Journal of Ophthalmology*, 135(5), 688–703.

Peplinski, L.S. & Albiani Smith, K. (2004) Deepening of lid sulcus from topical bimatoprost therapy. *Optometry and Vision Science*, 81(8), 574–547.

Perkins, E.S. (1975) Prostaglandins and the eye. *Advances in Ophthalmology*, 29, 2–21.

Pfeiffer, N., Traverso, C.E., Lorenz, K., Saarela, V., Liinamaa, J., Uusitalo, H. et al. (2014) A 6-month study comparing efficacy, safety, and tolerability of the preservative-free fixed combination of tafluprost 0.0015% and timolol 0.5% versus each of its individual preservative-free components. *Advances in Therapy*, 31(12), 1228–1246.

Pinnock, C., Yip, J.L., Khawaja, A.P., Luben, R., Hayat, S., Broadway, D.C. et al. (2016) Topical Beta-blockers and cardiovascular mortality: systematic review and meta-analysis with data from the EPIC-Norfolk cohort study. *Ophthalmic Epidemiology*, 23(5), 277–284.

Prum, B.E., Jr., Rosenberg, L.F., Gedde, S.J., Mansberger, S.L., Stein, J.D., Moroi, S.E. et al. (2016) Primary open-angle glaucoma preferred practice pattern(®) guidelines. *Ophthalmology*, 123(1), P41–P111.

PubMed (2022a). Available from: https://pubmed.ncbi.nlm.nih.gov/?term=Prostaglandin+analogues+%28ophthalmic%29+and+cerebral+spinal+fluid+pressure&schema=all&sort=pubdate&size=200 [Accessed July 14, 2022].

PubMed (2022b). Available from: https://pubmed.ncbi.nlm.nih.gov/?term=Prostaglandin+analogues+%28ophthalmic%29+and+Retinal+vein%2FVenous+pressure&sort=pubdate&size=200 [Accessed July 14, 2022].

Quaranta, L., Miglior, S., Floriani, I., Pizzolante, T. & Konstas, A.G. (2008) Effects of the timolol-dorzolamide fixed combination and latanoprost on circadian diastolic ocular perfusion pressure in glaucoma. *Investigative Ophthalmology & Visual Science*, 49(10), 4226–4231.

Quaranta, L., Riva, I., Katsanos, A., Floriani, I., Centofanti, M. & Konstas, A.G. (2015) Safety and efficacy of travoprost solution for the treatment of elevated intraocular pressure. *Clinical Ophthalmology*, 9, 633–643.

Quigley, H.A. & Broman, A.T. (2006) The number of people with glaucoma worldwide in 2010 and 2020. *The British Journal of Ophthalmology*, 90(3), 262–267. Available from: https://doi.org/10.1136/bjo.2005.081224

Ramulu, P.Y., Corcoran, K.J., Corcoran, S.L. & Robin, A.L. (2007) Utilization of various glaucoma surgeries and procedures in Medicare beneficiaries from 1995 to 2004. *Ophthalmology*, 114(12), 2265–2270.

Reis, R., Queiroz, C.F., Santos, L.C., Avila, M.P. & Magacho, L. (2006) A randomized, investigator-masked, 4-week study comparing timolol maleate 0.5%, brinzolamide 1%, and brimonidine tartrate 0.2% as adjunctive therapies to travoprost 0.004% in adults with primary open-angle glaucoma or ocular hypertension. *Clinical Therapeutics*, 28(4), 552–559.

Ren, R., Jonas, J.B., Tian, G., Zhen, Y., Ma, K., Li, S. et al. (2010) Cerebrospinal fluid pressure in glaucoma: a prospective study. *Ophthalmology*, 117, 259–266.

Riva, I., Katsanos, A., Floriani, I., Biagioli, E., Konstas, A.G., Centofanti, M. et al. (2014) Long-term 24-hour intraocular pressure control with travoprost monotherapy in patients with primary open-angle glaucoma. *Journal of Glaucoma*, 23(8), 535–540.

Rulo, A.H., Greve, E.L., Geijssen, H.C. & Hoyng, P.F. (1996) Reduction of intraocular pressure with treatment of latanoprost once daily in patients with normal-pressure glaucoma. *Ophthalmology*, 103(8), 1276–1282.

Samaha, D., Diaconu, V., Bouchard, J.F., Desalliers, C. & Dupont, A. (2022) Effect of Latanoprostene Bunod on optic nerve head blood flow. *Optometry and Vision Science*, 99(2), 172–176.

Schlote, T., Tzamalis, A. & Kynigopoulos, M. (2009) Central corneal thickness during treatment with travoprost 0.004% in glaucoma patients. *Journal of Ocular Pharmacology and Therapeutics*, 25(5), 459–462.

Schlötzer-Schrehardt, U., Zenkel, M. & Nüsing, R.M. (2002) Expression and localization of FP and EP prostanoid receptor subtypes in human ocular tissues. *Investigative Ophthalmology & Visual Science*, 43(5), 1475–1487.

Shah, M., Lee, G., Lefebvre, D.R., Kronberg, B., Loomis, S., Brauner, S.C. et al. (2013) A cross-sectional survey of the association between bilateral topical prostaglandin analogue use and ocular adnexal features. *PLoS One*, 8(5), e61638.

Sharif, N.A., Kelly, C.R., Crider, J.Y., Williams, G.W. & Xu, S.X. (2003) Ocular hypotensive FP prostaglandin (PG) analogs: PG receptor subtype binding affinities and selectivities, and agonist potencies at FP and other PG receptors in cultured cells. *Journal of Ocular Pharmacology and Therapeutics*, 19(6), 501–515.

Shoji, N., Ogata, H., Suyama, H., Ishikawa, H., Suzuki, H., Morita, T. et al. (2005) Intraocular pressure lowering effect of brinzolamide 1.0% as adjunctive therapy to latanoprost 0.005% in patients with open angle glaucoma or ocular hypertension: an uncontrolled, open-label study. *Current Medical Research and Opinion*, 21(4), 503–508.

Siaudvytyte, L., Januleviciene, I., Ragauskas, A., Bartusis, L., Meiliuniene, I., Siesky, B. et al. (2014) The difference in translaminar pressure gradient and neuroretinal rim area in glaucoma and healthy subjects. *Journal of Ophthalmology*, 2014, 937360.

Siaudvytyte, L., Januleviciene, I., Ragauskas, A., Bartusis, L., Siesky, B. & Harris, A. (2015) Update in intracranial pressure evaluation methods and translaminar pressure gradient role in glaucoma. *Acta Ophthalmologica*, 93(1), 9–15.

Silver, L.H. (2000) Ocular comfort of brinzolamide 1.0% ophthalmic suspension compared with dorzolamide 2.0% ophthalmic solution: results from two multicenter comfort studies. Brinzolamide comfort study group. *Survey of Ophthalmology*, 44 Suppl 2, S141–S145.

Slettedal, J.K., Traustadóttir, V.D., Sandvik, L. & Ringvold, A. (2020) The prevalence and incidence of glaucoma in Norway 2004-2018: a nationwide population-based study. *PLoS One*, 15(12), e0242786.

Song, P., Wang, J., Bucan, K., Theodoratou, E., Rudan, I. & Chan, K.Y. (2017) National and subnational prevalence and burden of glaucoma in China: a systematic analysis. *Journal of Global Health*, 7(2), 020705.

Stankiewicz, A., Misiuk-Hojło, M., Grabska-Liberek, I., Romanowska-Dixon, B., Wierzbowska, J., Wasyluk, J. et al. (2011) Intraocular pressure and ocular hemodynamics in patients with primary open-angle glaucoma treated with the combination of morning dosing of bimatoprost and dorzolamide hydrochloride. *Acta Ophthalmologica*, 89(1), e57–e63.

Stankiewicz, A., Wierzbowska, J., Siemiatkowska, A., Fuksinska, B., Robaszkiewicz, J., Zegadlo, A. et al. (2010) The additive effect of dorzolamide hydrochloride (Trusopt) and a morning dose of bimatoprost (Lumigan) on intraocular pressure and retrobulbar blood flow in patients with primary open-angle glaucoma. *The British Journal of Ophthalmology*, 94(10), 1307–1311.

Steven, D.W., Alaghband, P. & Lim, K.S. (2018) Preservatives in glaucoma medication. *The British Journal of Ophthalmology*, 102(11), 1497–1503.

Stewart, W.C. & Castelli, W.P. (1996) Systemic side effects of topical beta-adrenergic blockers. *Clinical Cardiology*, 19(9), 691–697.

Stewart, W.C., Stewart, J.A., Day, D.G., Sharpe, E.D. & Jenkins, J.N. (2004), Efficacy and safety of the latanoprost/timolol maleate fixed combination vs concomitant brimonidine and latanoprost therapy. *Eye (London, England)*, 18(10), 990–905.

Strahlman, E., Tipping, R. & Vogel, R. (1995) A double-masked, randomized 1-year study comparing dorzolamide (Trusopt), timolol, and betaxolol. International Dorzolamide Study Group. *Archives of Ophthalmology*, 113(8), 1009–1016.

Strutton, D.R. & Walt, J.G. (2004) Trends in glaucoma surgery before and after the introduction of new topical glaucoma pharmacotherapies. *Journal of Glaucoma*, 13(3), 221–226.

Sun, Y., Chen, A., Zou, M., Zhang, Y., Jin, L., Li, Y. et al. (2022) Time trends, associations and prevalence of blindness and vision loss due to glaucoma: an analysis of observational data from the global burden of disease study 2017. *BMJ Open*, 12(1), e053805.

Swymer, C. & Neville, M.W. (2012) Tafluprost: the first preservative-free prostaglandin to treat open-angle glaucoma and ocular hypertension. *The Annals of Pharmacotherapy*, 46(11), 1506–1510.

Tang, W., Zhang, F., Liu, K. & Duan, X. (2019) Efficacy and safety of prostaglandin analogues in primary open-angle glaucoma or ocular hypertension patients: a meta-analysis. *Medicine (Baltimore)*, 98(30), e16597.

Terminology and Guidelines for Glaucoma. (2020) In: Azuara-Blanco, A. & Traverso, C.E. (Eds.) *Savona*. Italy: European Glaucoma Society.

Tham, Y.C., Li, X., Wong, T.Y., Quigley, H.A., Aung, T. & Cheng, C.Y. (2014) Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology*, 121(11), 2081–2090.

The Advanced Glaucoma Intervention Study (AGIS): 7. (2000) The relationship between control of intraocular pressure and visual field deterioration. The AGIS investigators. *American Journal of Ophthalmology*, 130(4), 429–440.

The LipidWebb. (2022) Prostanoids: Prostaglandins, Prostacyclins and Thromboxanes. Available from: https://www.lipidmaps.org/resources/lipidweb/lipidweb_html/lipids/fa-eic/eicprost/index.htm [Accessed July 6, 2022].

Ting, N.S., Li Yim, J.F. & Ng, J.Y. (2014) Different strategies and cost-effectiveness in the treatment of primary open angle glaucoma. *Clinicoecon Outcomes Res*, 6, 523–530.

Toris, C.B., Camras, C.B., Yablonski, M.E. & Brubaker, R.F. (1997) Effects of exogenous prostaglandins on aqueous humor dynamics and blood-aqueous barrier function. *Survey of Ophthalmology*, 41(Suppl 2), S69–S75.

Toris, C.B., Gabelt, B.T. & Kaufman, P.L. (2008) Update on the mechanism of action of topical prostaglandins for intraocular pressure reduction. *Survey of Ophthalmology*, 53(Suppl 1), S107–S120.

Uusitalo, H., Pillunat, L.E., Ropo, A. & Phase III Study Investigators. (2010) Efficacy and safety of tafluprost 0.0015% versus latanoprost 0.005% eye drops in open-angle glaucoma and ocular hypertension: 24-month results of a randomized, double-masked phase III study. *Acta Ophthalmologica*, 88(1), 12–19.

van der Valk, R., Webers, C.A., Schouten, J.S., Zeegers, M.P., Hendrikse, F. & Prins, M.H. (2005) Intraocular pressure-lowering effects of all commonly used glaucoma drugs: a meta-analysis of randomized clinical trials. *Ophthalmology*, 112(7), 1177–1185.

Von Euler, U.S. (1935) Über die spezifische blutdrucksenkende Substanz des menschlichen Prostata- und Samenblasensekrets. *Wiener Klinische Wochenschrift*, 14, 1182–1183. Available from: http://link.springer.com/article/ 10.1007%2FBF01778029

Vysniauskiene, I., Allemann, R., Flammer, J. & Haefliger, I.O. (2006) Vasoactive responses ofvU46619, PGF2alpha, latanoprost, and travoprost in isolated porcine ciliary arteries. *Investigative Ophthalmology & Visual Science*, 47(1), 295–298.

Walland, M.J. (2004) Glaucoma treatment in Australia: changing patterns of therapy 1994-2003. *Clinical & Experimental Ophthalmology*, 32(6), 590–596.

Wang, T., Cao, L., Jiang, Q. & Zhang, T. (2021) Topical medication therapy for glaucoma and ocular hypertension. *Frontiers in Pharmacology*, 12, 749858.

Warwar, R.E., Bullock, J.D. & Ballal, D. (1998) Cystoid macular edema and anterior uveitis associated with latanoprost use. Experience and incidence in a retrospective review of 94 patients. *Ophthalmology*, 105(2), 263–268.

Watson, P.G. (1998) Latanoprost. Two years' experience of its use in the United Kingdom. Latanoprost study group. *Ophthalmology*, 105(1), 82–87.

Weinreb, R.N., Aung, T. & Medeiros, F.A. (2014) The pathophysiology and treatment of glaucoma: a review. *JAMA*, 311(18), 1901–1911.

Weinreb, R.N. & Lindsey, J.D. (2002) Metalloproteinase gene transcription in human ciliary muscle cells with latanoprost. *Investigative Ophthalmology & Visual Science*, 43(3), 716–722.

Weinreb, R.N., Robinson, M.R., Dibas, M. & Stamer, W.D. (2020) Matrix metalloproteinases and glaucoma treatment. *Journal of Ocular Pharmacology and Therapeutics*, 36(4), 208–228.

Weinreb, R.N., Toris, C.B., Gabelt, B.T., Lindsey, J.D. & Kaufman, P.L. (2002) Effects of prostaglandins on the aqueous humor outflow pathways. *Survey of Ophthalmology*, 47(Suppl 1), S53–S64.

Winkler, N.S. & Fautsch, M.P. (2014) Effects of prostaglandin analogues on aqueous humor outflow pathways. *Journal of Ocular Pharmacology and Therapeutics*, 30(2–3), 102–109.

World Health Organization. (2021) Aging and Health. Available from: https://www.who.int/news-room/fact-sheets/detail/ageing-and-health [Accessed July 5, 2022].

Yang, X.T., Zhao, L., Wang, L.J., Zhang, Y., Liao, D.Y. & Wang, J.M. (2020) Efficacy and safety of 0.0015% tafluprost versus 0.005% latanoprost in primary open angle glaucoma, ocular hypertension: a meta-analysis. *International Journal of Ophthalmology*, 13(3), 474–480.

Zabriskie, N., Netland, P.A. & Brimonidine with Latanoprost Study Groups 1 and 2. (2003) Comparison of brimonidine/latanoprost and timolol/dorzolamide: two randomized, double-masked, parallel clinical trials. *Advances in Therapy*, 20(2), 92–100.

Zeitz, O., Matthiessen, E.T., Reuss, J., Wiermann, A., Wagenfeld, L., Galambos, P. et al. (2005) Effects of glaucoma drugs on ocular hemodynamics in normal tension glaucoma: a randomized trial comparing bimatoprost and latanoprost with dorzolamide [ISRCTN18873428]. *BMC Ophthalmology*, 5, 6.

Zhao, J.L., Ge, J., Li, X.X., Li, Y.M., Sheng, Y.H., Sun, N.X. et al. (2011) Comparative efficacy and safety of the fixed versus unfixed combination of latanoprost and timolol in Chinese patients with open-angle glaucoma or ocular hypertension. *BMC Ophthalmology*, 11, 23.

How to cite this article: Cordeiro, M.F., Gandolfi, S., Gugleta, K., Normando, E.M. & Oddone, F. (2023) How latanoprost changed glaucoma management. *Acta Ophthalmologica*, 00, 1–16. Available from: https://doi.org/10.1111/aos.15725