MALAYSIAN SOCIETY OF OPHTHALMOLOGY

Advertorial by Santen Malaysia

TAFLOTAN®: A NOVEL PROSTAGLANDIN ANALOGS FOR THE TREATMENT OF PRIMARY OPEN ANGLE GLAUCOMA OR OCULAR HYPERTENSION

Tafluprost was developed by Santen Pharmaceutical Co. Ltd. in Osaka, Japan and Asahi Glass Co. Ltd. in Tokyo, Japan. Their original concept having been to develop a novel molecule with an efficacy and safety comparable to or higher than those of latanoprost (a prostanoid FP receptor agonist).

Prost-type PG derivatives (i.e., those other than unoprostone) were discovered as compounds that retained the 15-position hydroxyl group of natural PGF2α, and had high pharmacological activity. The hydroxyl group at the 15-position was considered indispensable for the manifestation of the activity of PGs[1]. However, tafluprost is a novel PGF2α derivative in which the 15-position hydroxyl group is substituted by 2 fluorine atoms (Figure 1). Because of this substitution, ketonization by 15-hydroxy-dehydrogenase (one of the major pathways involved in the metabolization of PGs) does not occur with this compound. As a result, it is metabolized only through beta-oxidation of the alpha-chain of PG skeleton[2]. Because of this lack of one pathway for its metabolization, tafluprost may be expected to have a prolonged action, but it has been shown to lack a tendency to accumulate[2]. In PG derivatives, other than bimatoprost, the alpha-chain ending of the PG skeleton has been isopropyl-esterified, and for this reason these derivatives are converted into an active form (carboxylic acid form) by corneal esterase, and penetrate rapidly into the anterior chamber of the eye. Tafluprost, too, is an isopropylester type of PG derivative.

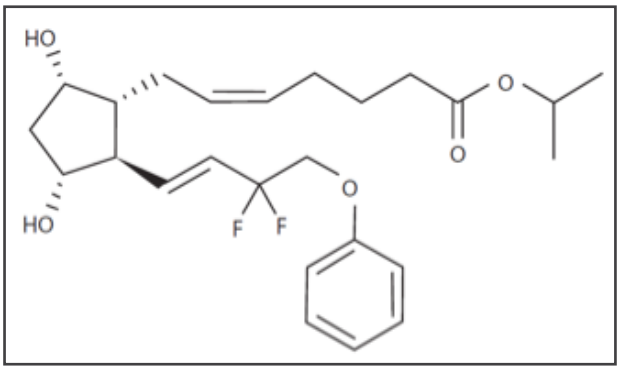

Figure 1 Structure of tafluprost

It has been reported that tafluprost not only has an affinity for the FP receptor that is about 12 times higher than that of latanoprost (Figure 2), but that it has almost no potential to bind to the other receptors[3].

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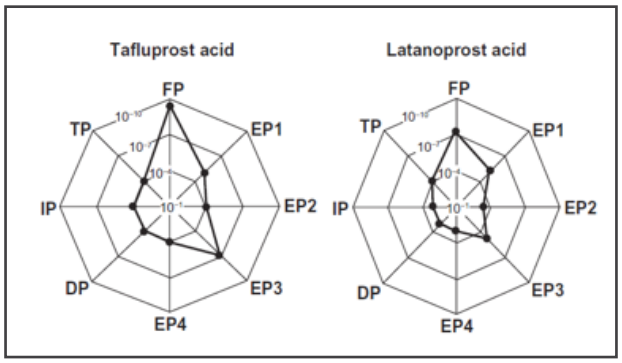

Figure 2 Receptor affinities of prostaglandin derivatives (schematic representation)

In one of the phase III clinical studies conducted in Japan, one was designed as a non-inferiority study aimed at comparing the efficacy of tafluprost with that of latanoprost. A randomized, single-blind comparative study involving 109 patients with primary open angle glaucoma or ocular hypertension (reference drug: latanoprost ophthalmic solution) – the magnitude of the IOP reduction in the tafluprost and latanoprost treatment group after 4-week administration was 6.6 ± 2.5 mmHg (27.6 ± 9.6%) and 6.2 ± 2.5 mmHg (25.9 ± 9.7%), respectively. Thus, endorsing the non-inferiority of this drug versus latanoprost (Figure 3)[4]. Moreover, the percentage of patients showing a reduction of 20% or more in IOP was 80.4% in the tafluprost treatment group against 70.6% in the latanoprost-treatment group.

The second phase III clinical study of tafluprost was designed as a long-term dosing study primarily aimed at evaluating its safety in prolonged use. In that study – involving 351 patients with open angle glaucoma (including normotensive glaucoma) or ocular hypertension – the magnitude of the IOP reduction seen following treatment with tafluprost studied within the range 4.9 to 5.7 mmHg throughout the 52-week study period. Thus, this drug exerted its IOP-lowering effect in a stable manner during prolonged use[5].

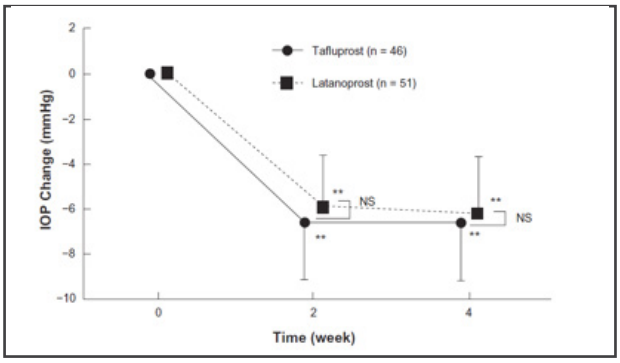

Figure 3 Time course of IOP change in phase III clinical study in patients with primary open angle glaucoma or ocular hypertension (noninferiority study between Tapros® and latanoprost).

Notes: Data represents mean ± SD **P 0.01, vs pre-dosing value (paired-t test).

NS: not significant, comparison between Tapros® and latanoprost (Student t-test).

Abbreviated prescribing information: **Indication:** Reduction of intraocular pressure in patients with primary open-angle glaucoma or ocular hypertension. **Dosage:** Instil 1 drop in the affected eye(s) once daily. **Precautions:** Patient with aphakia or pseudophakia, bronchial asthma or history of bronchial asthma, endophthalmitis, pregnant, parturient and lactating women. **Contraindications:** Patient with history of hypersensitivity to any of the ingredients of this product. **Side effects:** Iris pigmentation, conjunctival injection, corneal epithelium disorder, hypertrichosis of eyelid, abnormality in eyelashes.

***For healthcare professionals only.

References:

1. Resul B, Stjernschantz J. Structure-activity relationships of prostaglandin analogues as ocular hypotensive agents. Curr Opin Ther. 1993;3: 781–795.

2. Fukano Y, Kawazu K. Disposition and metabolism of a novel prostanoid antiglaucoma medication, tafluprost, following ocular administration to rats. Drug Metab Dispos. 2009;37:1622–1634.

3. Takagi Y, Nakajima T, Shimazaki A, et al. Pharmacological characteristics of AFP-168 (tafluprost), a new prostanoid FP receptor agonist, as an ocular hypotensive drug. Exp Eye Res. 2004;78:768–776.

4. Kuwayama Y, Komemusi S. Phase III confirmatory study of 0.0015% DE-085 (Tafluprost) ophthalmic solution as compared to 0.005% Latanoprost ophthalmic solution in patients with open-angle glaucoma or ocular hypertension. Atarashii Ganka. 2008;25:1595–1602.

5. Malaysia Taflotan® package insert updated until April 2016.