Efficacy and tolerability of a new thermostable formulation of latanoprost in nanoparticles

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BACKGROUND

Benzalkonium chloride (BAK) is known to have toxic effects on the ocular surface on long-term use. A new latanoprost 0.005% BAK-free nanoemulsion (LNe) was engineered as a new alternative to deliver latanoprost to the cornea. The lipophilic properties of the new formulation and the size of the oil nanodroplets prove to be important for absorption and bioavailability, leaving relatively no free molecules to induce ocular surface toxicity. Furthermore, nanoemulsions have been found to restore the tear film and exert protective effects on the ocular surface, resulting in improvements in hyperemia, irritation and dry eye.

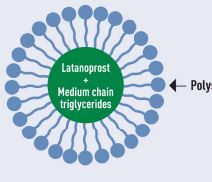


Fig 1: First, latanoprost is dissolved in medium chain triglycerides, forming the oil phase of the emulsion. Then, polysorbate 80 is added to emulsify the oil phase, organizing it into micelles.

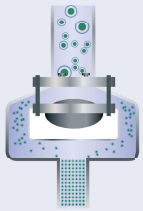
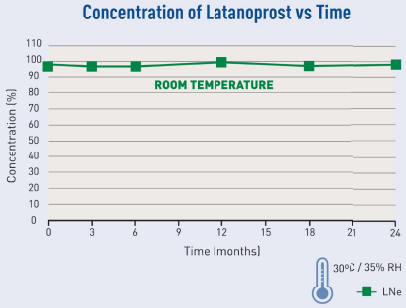


Fig. 2: Finally, a High Technology Microfluidizer reduces the size of the micelles to nanometers (100 - 200 nm), obtaining a homogeneous nanoemulsion.



PURPOSE

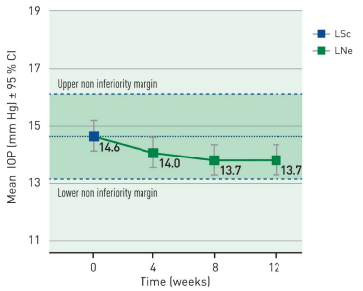
To demonstrate that latanoprost BAK-free nanoemulsion (LNe) has the same intraocular pressure (IOP)-lowering efficacy and is better tolerated than BAK-containing latanoprost solutions (LSc).

METHODS

Adult patients with primary open-angle glaucoma under treatment with LSc for ≥ 6 months (baseline), switched to LNe once daily. As primary outcome, IOP-lowering efficacy was evaluated after 4, 8 and 12 weeks of treatment with LNe. Non inferiority was defined as a mean difference (95% CI) from baseline <1.5 mm Hg at every timepoint after switching. As secondary outcome, ocular surface damage was determined using Ocular Surface Disease Index (OSDI) score, Break-up time (BUT), conjunctival hyperemia and corneal staining at baseline and after 4, 8 and 12 weeks of treatment with LNe.

RESULTS

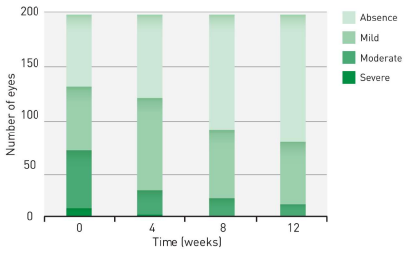
A total of 103 patients (198 eyes) concluded the study. No patient had IOP >20 mm Hg. LNe was non inferior in lowering IOP than LSc, as every 95% CI of mean IOP after switch to LNe was within the 1.5 mm Hg non inferiority margin from baseline IOP (13.1 - 16.1 mm Hg).



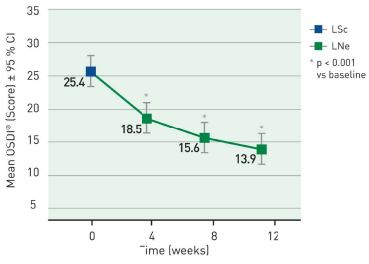
Ocular surface parameters improved from baseline. After 12 weeks of treatment with LNe, OSDI score decreased from 25.4 to 13.9, p<0.05; BUT increased from 7.47 to 9.22 seconds, p<0.05; number of eyes with conjunctival hyperemia decreased by 27.7% (21.7 – 33.7, 95% CI); and number of eyes with corneal staining decreased by 19.2% (14.2 - 24.2, 95% CI).

At baseline out of 103 patients, 67 presented hyperemia. After 3 months of treatment with LNe, 65% of the affected patients benefited from a reduction of at least 1 unit of hyperemia:

- 61% of these patients exhibited a reduction of at least 1 unit of hyperemia after a month of treatment, whereas 89% achieved the same results after 2 months,
- 66% showed no signs of hyperemia after 3 months of treatment,
- 23% achieved a reduction of 2 o 3 units of hyperemia and, in addition, they had no signs of hyperemia at the end of the study.



Mean OSDI score decreased by 11.5 points (7.5 - 15.6, 95% CI) after 12 weeks of treatment with LNe.



SAFETY

Six patients discontinued because of ocular itching, increased tearing, blurred vision, strange body sensation, dry eye or allergic eye reactions. No serious treatment-related adverse effects were reported.

CONCLUSIONS

The new formulation of latanoprost in nanoemulsion showed the same IOP-lowering efficacy as the conventional formulation with significant improvements of ocular surface parameters, adding the advantage of being stored at up to 30°C for 24 months.

REFERENCES:

Wajimbe T, Chelerkar V, Bhagat P, Joshi A, Raut A. Effect of benzalkonium chloride-free latanoprost ophthalmic solution on ocular surface in patients with glaucoma. Clin Ophthalmol. 2016 May 9; 10: 821-7.

Rouland JF, Traverso CE, Stalmans I, Fekih LE, Delval L, Renault D, Baudouin C; T2345 Study Group. Efficacy and safety of preservative-free latanoprost eyedrops, compared with BAK-preserved latanoprost in patients with ocular hypertension or glaucoma. Br J Ophthalmol. 2013 Feb; 97(2):196-200.

Cucherat M, Stalmans I, Rouland JF. Relative efficacy and safety of preservative-free latanoprost (T2345) for the treatment of openangle glaucoma and ocular hypertension: an adjusted indirect comparison meta-analysis of randomized clinical trials. J Glaucoma. 2014 Jan; 23(1): e69-75.

Sarford M. Preservative-Free Latanoprost Eye Drops in Patients with Primary Open-Angle Glaucoma/Ocular Hypertension. Clin Drug Investig. 2014, 34: 521–528.