A COMPARATIVE STUDY OF DIFLUPREDNATE 0.05% NANOEMULSION VS PREDNISOLONE ACETATE 1% + PHENYLEPHRINE HYDROCHLORIDE 0.12% SUSPENSION FOR POSTOPERATIVE INFLAMMATION TREATMENT FOLLOWING CATARACT SURGERY

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BACKGROUND:

Cataracts, defined as partial or total opacification of the lens, are estimated to affect 95 million people worldwide and are considered the leading cause of blindness in middle-income and low-income countries. Up to now cataract surgery remains the unique treatment option. Surgical procedures have upgraded, developing methods that allow faster recovery improving visual outcomes, such as microincision cataract surgery using phacoemulsification, which has largely replaced extracapsular cataract extraction. However, postsurgical visual rehabilitation is sometimes delayed by inflammatory processes induced by mechanical transmission of energy into the eye. Controlling and preventing ocular inflammation is one of the most important concerns for surgeons in order to recover visual acuity during the first days after surgery and to prevent development of post-operative complications.

Difluprednate 0.05% was approved by US Food and Drug Administration in 2008 for postsurgical cataract inflammation and pain treatment. This new synthetic steroid, formulated as a nanoemulsion, presents structural modifications with respect to its predecessor, Prednisolone acetate. Changes in molecule structure and novel formulation in nanoemulsion allow achieving **greater potency, penetration, and bioavailability** which may enable a reduced posology.

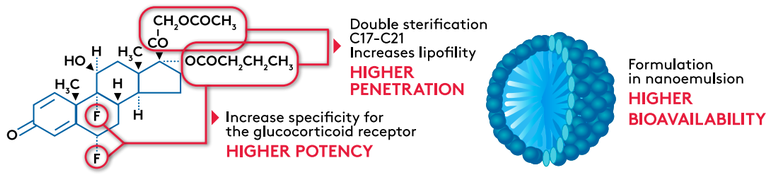

Figure 1. Molecular and formulation factors that improve the characteristics of Difluprednate.

PURPOSE:

To investigate if Difluprednate 0.05% nanoemulsion (DIFL) administered twice a day (BID) is non-inferior than Prednisolone acetate 1% + Phenylephrine hydrochloride 0.12% (PRED) administered four times a day (QID), for postsurgical inflammation treatment following cataract surgery.

METHODS:

A non-inferiority, prospective, multicenter, double-blind, randomized, controlled, parallel-group study was performed.
A total of 259 patients who underwent phacoemulsification randomly received DIFL or PRED starting the day before surgery and continuing for 28 days. All patients received two bottles (A & B) of anti-inflammatory medication. For DIFL group bottle A had Difluprednate 0.05% while bottle B had vehicle. For PRED group both bottles had Prednisolone acetate 1% + Phenylephrine 0.12%. All patients were told to alternate one drop of bottle A and B every 6 hours starting the day before the surgery and continuing for the next 14 days postoperatively. For the remaining 14 days of treatment patients were told to alternate one drop from each bottle every 12 hours.
The primary endpoint was corneal thickness. Non-inferior anti-inflammatory efficacy was considered if the difference of corneal thickness between baseline and Day 4 did not differ beyond 17 µm between treatments. Secondary endpoints were cells & flare, corrected distance visual acuity (CDVA), endothelial cell count, OCT-central macular thickness, and intraocular pressure (IOP). All outcomes were evaluated at baseline (Day -1), Day 1, 4, and 28 after surgery.

RESULTS:

Of 259 patients that met eligibility criteria, 225 finished the follow-up assessments.

CORNEAL THICKNESS

The difference in corneal thickness at baseline and Day 4 did not differ beyond 17 µm between treatments (IC95% -2.78 µm – 14.84 µm), with no statistically significant differences between treatments (p = 0.523).

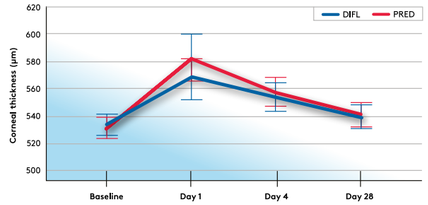

Figure 2. Mean ± CI 95% Corneal Thickness (µm) over time.

CELLS & FLARE

There were no statistically significant differences between groups in cells & flare at all study times (p > 0.05).

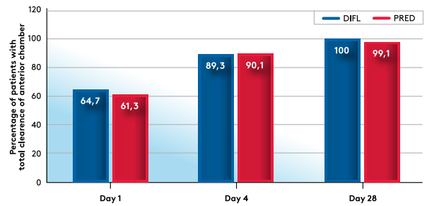

Figure 3. Percentage of patients with anterior chamber total clearance (cells & flare grade 0) by time.

BEST CORRECTED VISUAL ACUITY

No statistically significant differences between treatments in BCVA were reported (p = 0.455), although BCVA LogMAR improved in DIFL group at Day 1 (from 0.198 to 0.177), while PRED group did not improve (from 0.219 to 0.234).

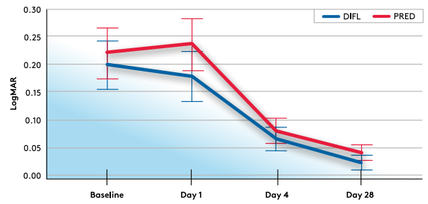

Figure 4. Mean ± CI95% Logarithm of the minimum angle of resolution over time.

ENDOTHELIAL CELL COUNT

No statistically significant differences between groups in endothelial cell count were reported (p = 0.811).

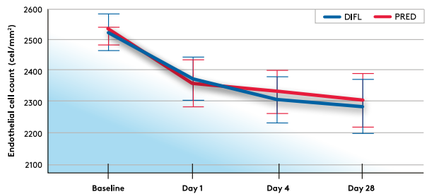

Figure 5. Mean ± CI 95% endothelial cell count (cells/mm²) over time.

MACULAR THICKNESS

No statistically significant differences between treatments in OCT-central macular thickness were reported (p = 0.869).

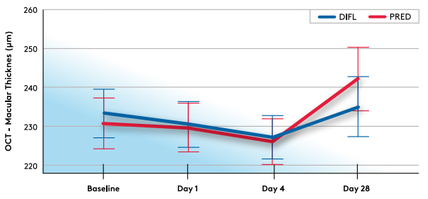

Figure 6. Mean ± CI 95% OCT- central macular thickness (µm) over time.

INTRAOCULAR PRESSURE

No statistically significant differences between group in intraocular pressure outcome were reported (p = 0.316). At Day 28, four patients reported elevated IOP (> 21 mmHg), three of which belonged to PRED group.

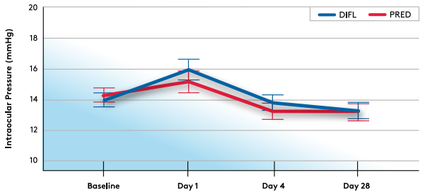

Figure 7. Mean ± CI 95% Intraocular pressure (mmHg) over time.

CONCLUSION:

- **Difluprednate 0.05% ophthalmic nanoemulsion administered BID is at least as effective as Prednisolone acetate 1% + Phenylephrine hydrochloride 0.12% suspension administered QID for managing cataract postsurgical inflammation.**
- **This suggests that Difluprednate permits a reduced posology, achieving equivalent clinical outcomes and improving treatment compliance with additional pharmacotechnical advantages that avoid unnecessary exposure to BAK and allow a stable formulation that ensures therapeutical levels in each drop of ophthalmic nanoemulsion.**

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