# PROSPECTIVE STUDY OF DEXAMETHASONE OPHTHALMIC INSERT FOLLOWING CONCOMITANT MIGS AND CATARACT SURGERY

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# PURPOSE

- Concomitant glaucoma and cataract surgery patients face an outsize postoperative burden. In addition to taking frequent anti-inflammatory eye drops, they often continue at least one glaucoma medication.
- High postoperative eye drop load may worsen the already significant nonadherence reported among glaucoma patients[1], possibly contributing to poorer healing, increased complications, and greater patient dissatisfaction.[2]
- Dexamethasone ophthalmic insert 0.4 mg is a sustained-release corticosteroid placed in the inferior lacrimal punctum that has shown superior control of ocular inflammation and pain versus placebo after cataract surgery.[3]
- The goal of the current study is to compare the safety and efficacy of dexamethasone ophthalmic insert 0.4 mg to standard-of-care prednisolone acetate 1% eye drops after combined minimally-invasive glaucoma surgery and cataract surgery (C-MIGS).

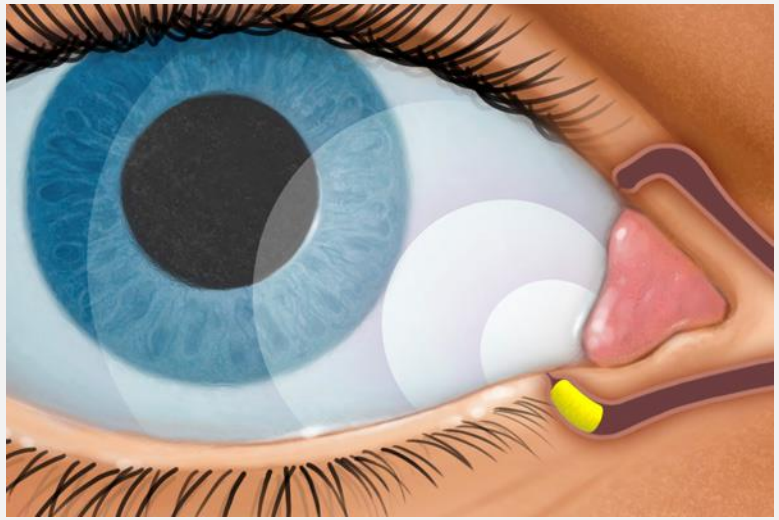


Image credit: https://www.ocutx.com/products/dextenza/

Study approved by Sterling IRB (Atlanta, GA). ClinicalTrials.gov identifier: NCT0420065.


1. Wolfram C, Stahlberg E, Pfeiffer N. Patient-Reported Nonadherence with Glaucoma Therapy. *J Ocul Pharmacol Ther*. 2019;35(4):223-228. doi:10.1089/jop.2018.0134
2. Assil KK, Greenwood MD, Gibson A, Vantipalli S, Metzinger JL, Goldstein MH. Dropless cataract surgery: modernizing perioperative medical therapy to improve outcomes and patient satisfaction. *Curr Opin Ophthalmol*. 2021;32 Suppl 1:S1-S12. doi:10.1097/ICU.0000000000000708
3. Tyson SL, Bafna S, Gira JP, et al. Multicenter randomized phase 3 study of a sustained-release intracanalicular dexamethasone insert for treatment of ocular inflammation and pain after cataract surgery. *J Cataract Refract Surg*. 2019;45(2):204-212. doi:10.1016/j.jcrs.2018.09.023

# METHODS

- Ongoing prospective Phase IV open-label randomized controlled trial with two treatment arms:
  - Dexamethasone ophthalmic insert 0.4 mg placed immediately following C-MIGS.
  - Prednisolone acetate 1% ophthalmic prescribed for 1 month after C-MIGS, tapered from QID dosing to once daily as tolerated.
- All cataract surgeries were performed using phacoemulsification without femtosecond laser. Eligible MIGS types included canaloplasty, the Kahook Dual-Blade, the Hydrus Microstent, and the iStent.
- All eyes received a standard-of-care topical ofloxacin 0.3% regimen QID for one week after surgery.
- All patients were enrolled from a single private practice in the Bronx, NY, and all surgeries were conducted by NMR.
- Block randomization sequence generated on: https://www.sealedenvelope.com. The sequence was unknown to the randomizer and the surgeon, and assignments were concealed in opaque envelopes. Block randomization maximized the odds that an equal number of patients would be randomized to each arm with similar MIGS distributions.
- Patients were followed for 1 day, 1 week, 1 month, and 3 months postop. Main outcomes were measured at 1 and/or 3 months and included Goldmann IOP, logMAR visual acuity, glaucoma meds, adverse events, anti-inflammatory rescue, anterior chamber cell clearance, cystoid macular edema occurrence, and ocular comfort index score.
  - Rescue criteria: Grade 3+ AC cells or flare, moderate to severe photophobia, moderate to severe eye pain, or moderate to severe ciliary or conjunctival injection.
- Intention-to-treat analyses were performed. Statistical software used include Microsoft Excel 2019 and SPSS version 28.0.1.0. Wilcoxon rank-sum test was used for linear outcomes, and Fischer's exact test was used for categorical outcomes. Linear outcomes are reported as means +/- SD. Significance was set at $p<0.05$.

# INCLUSION AND EXCLUSION CRITERIA

**Inclusion Criteria:**

1. Age 21 or older
2. Cataract surgery candidate and glaucoma present in at least one eye
3. MIGS candidate in that same eye as defined by: ocular hypertension requiring a medication, OR mild, moderate, or severe glaucoma that is sufficiently stable and appropriate for operation

**Exclusion Criteria:**

1. Maintains regular use (daily or more) of systemic or ocular steroids at time of enrollment
2. Maintains regular use (daily or more) of systemic or ocular nonsteroidal anti-inflammatory drugs at time of enrollment
3. Anterior chamber cells present at time of enrollment
4. Recent febrile illness that precludes or delays participation for 3 months
5. Pregnancy or lactation
6. Known allergy to dexamethasone or prednisolone
7. Treatment with another investigational drug within the last 20 years
8. Current recreational drug use
9. Preexisting ocular pathology likely to confound the visual acuity or comfort endpoints including but not limited to: severe corneal scarring, ocular surface disease, diabetic retinopathy, or macular edema
10. Corneal or retinal procedures (laser or incisional) during the study period and 6 months prior

# RESULTS

- Enrollment began in January 2020, with a final target of 40 eyes.
- At the time of analysis in January 2022:
  - 25 eyes from 19 patients had been consented.
  - 19 eyes from 15 patients had met inclusion criteria and cleared exclusion criteria, and had been randomized.
  - 17 eyes had received the C-MIGS surgeries. All surgeries performed have been consistent with block assignments.
- Mean age of those randomized was 70.7 ± 9.9, and females comprised 68.4% (N=13). Most enrollees were Hispanic (42.11%, N=8) or black (42.11%, N=8). There were no statistically significant differences in age (p=0.74) or racial distribution (p=0.44) between groups.
- 57.9% (N=11) of those randomized received the dexamethasone ophthalmic insert.
- The most common MIGS type for both groups was canaloplasty, followed by the Hydrus Microstent.

**Figure 1: Racial distribution of randomized eyes**

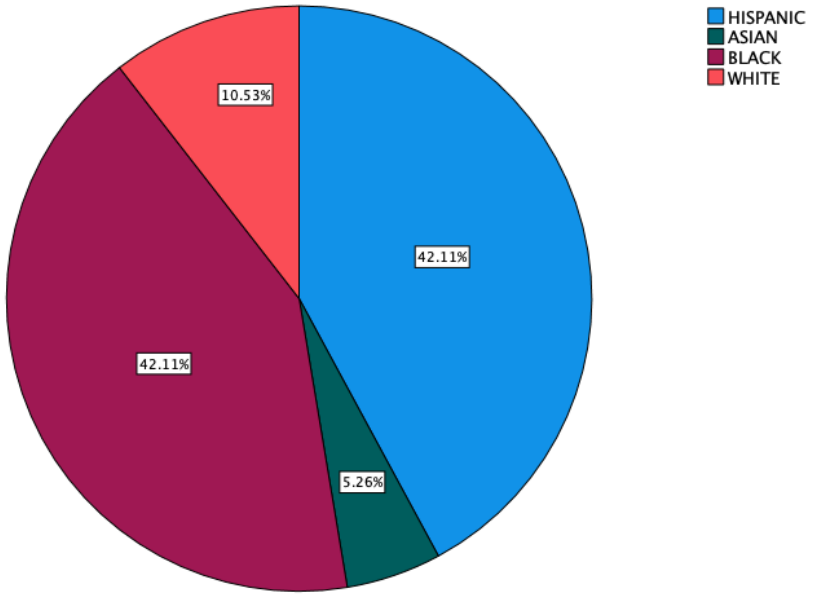
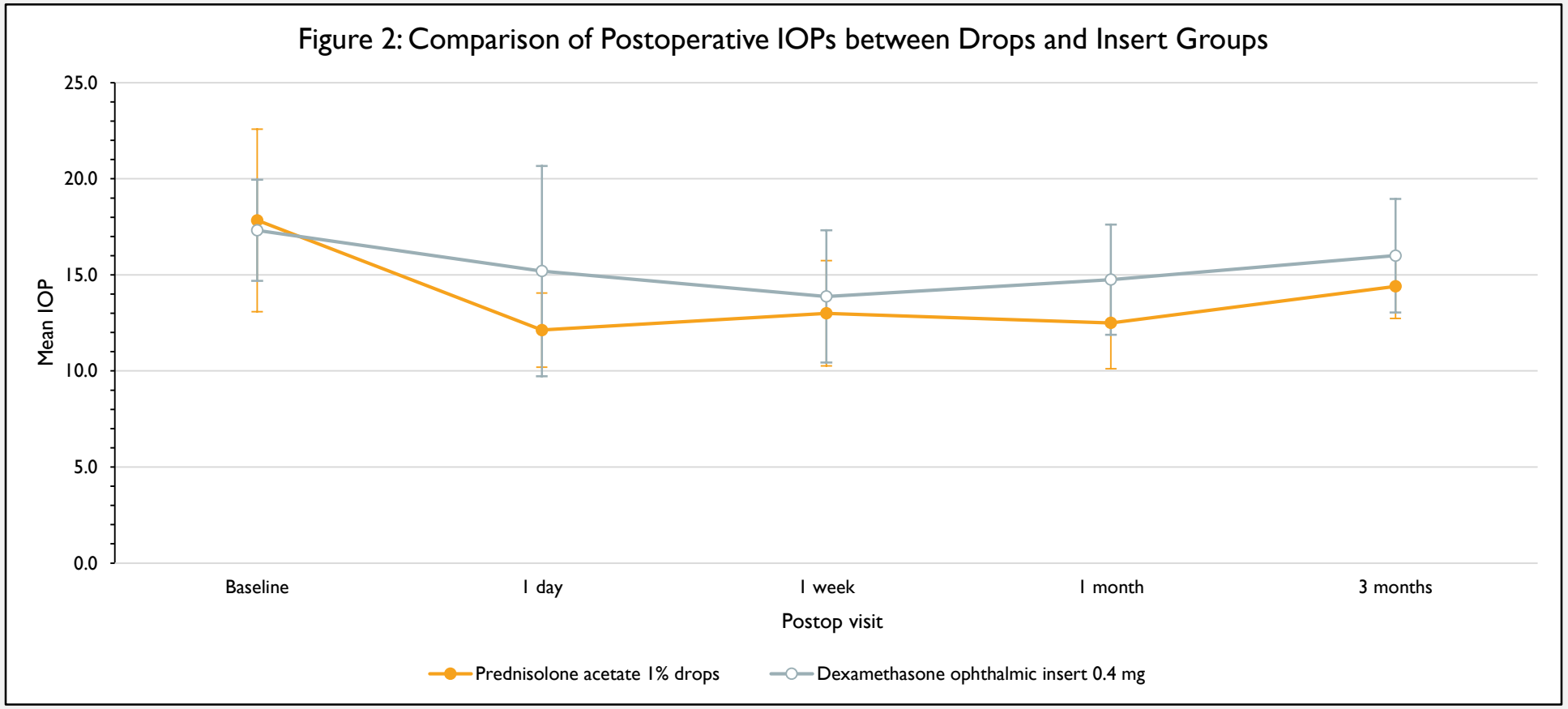



**Table 1: MIGS by Group Randomization**

| | | Treatment | | |
|---|---|---|---|---|
| | | Prednisolone drops | Dexamethasone insert | Total |
| MIGS type | Hydrus | 3 | 3 | 6 |
| | iStent | 0 | 1 | 1 |
| | Canaloplasty | 5 | 7 | 12 |
| Total | | 8 | 11 | 19 |

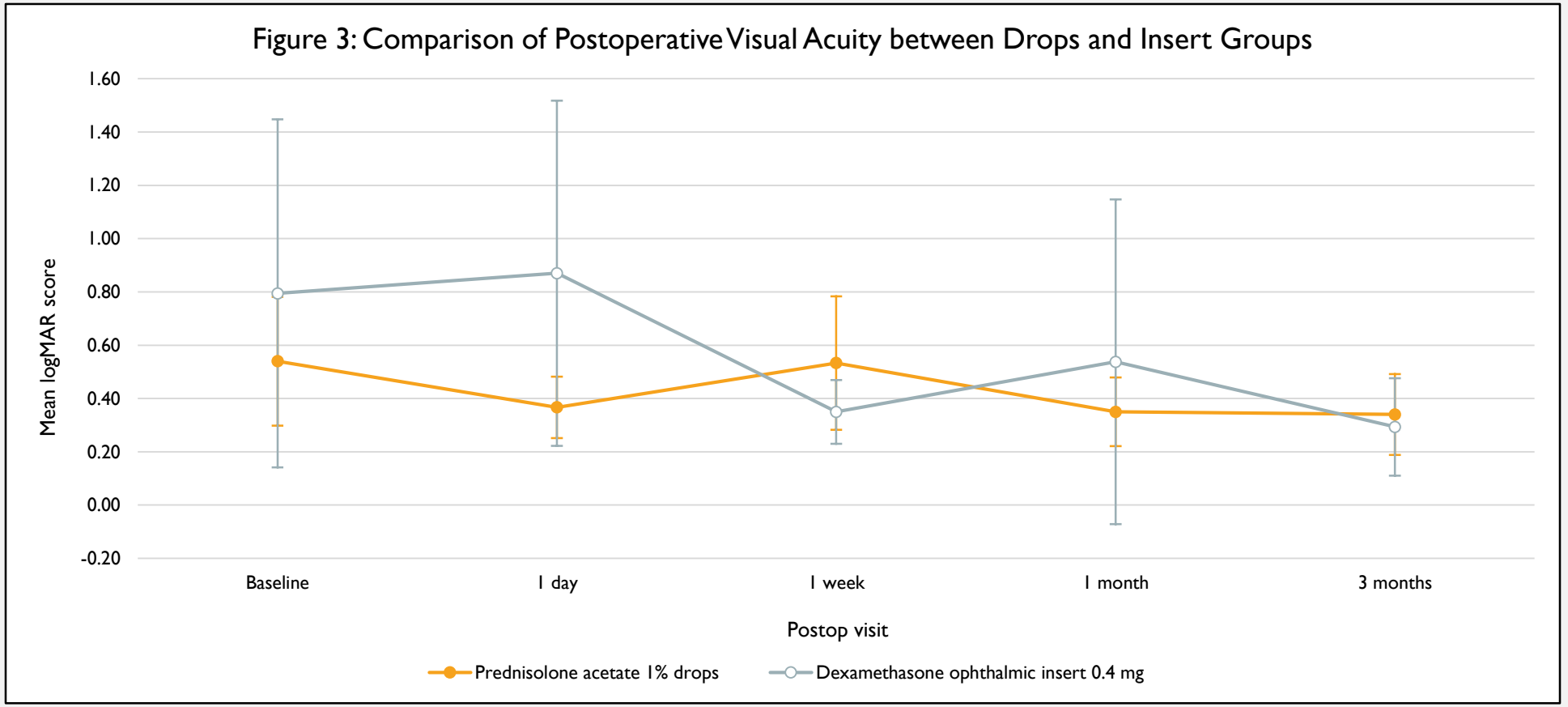
# CHANGES IN INTRAOCULAR PRESSURE




**Baseline to month 1 IOP***: -2.8 ± 2.7 in the insert group (N=8) vs. -6.3 ± 3.7 in the drops group (N=4) (p=0.15)
**Baseline to month 3 IOP***: -1.9 ± 2.5 in the insert group (N=9) vs. -4.6 ± 3.3 in the drops group (N=5) (p=0.18)

*No statistically significant differences were observed. N values indicate # of eyes with IOP data present at month 1 or 3. In the above graph, mean +/- SD IOP for a given time point was calculated using all eyes with IOP data at that time point.

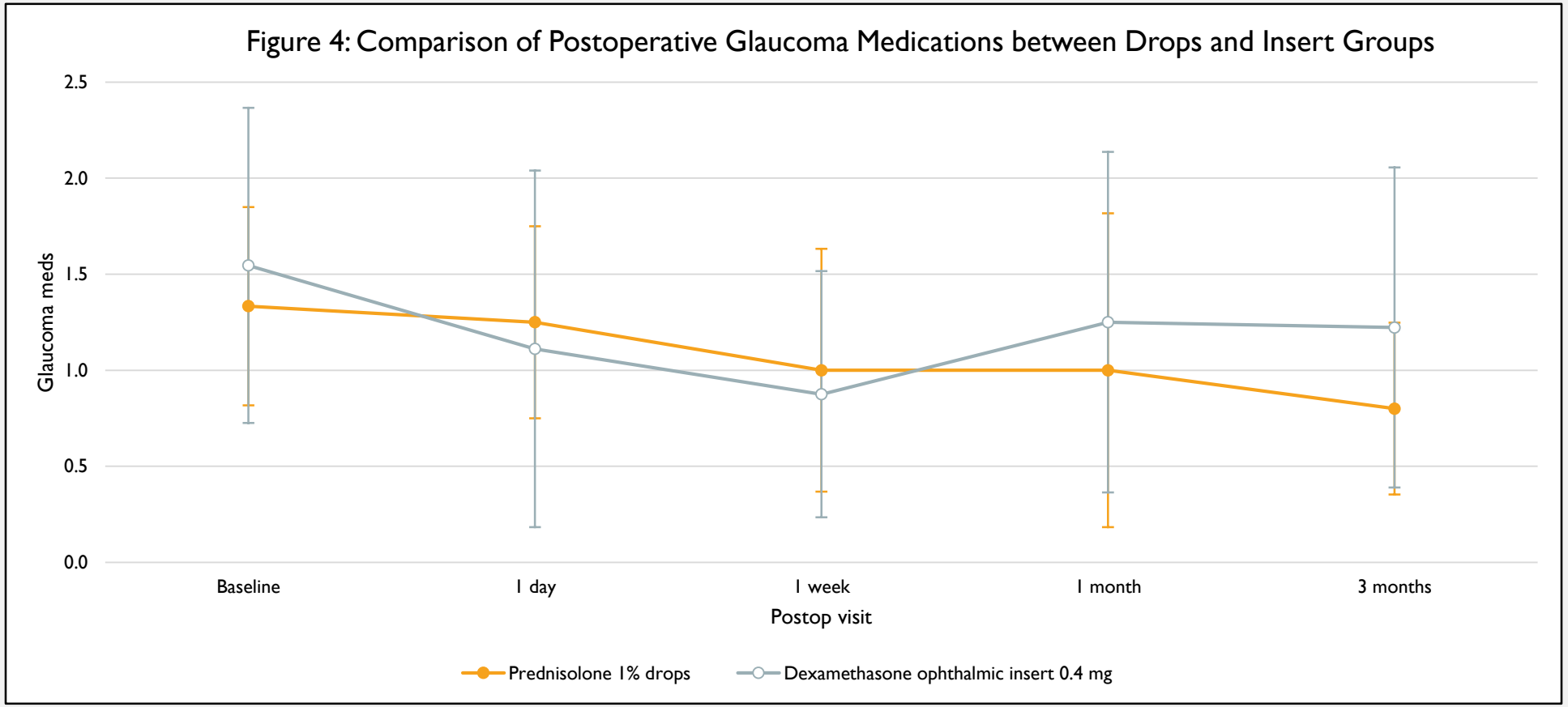
# CHANGES IN VISUAL ACUITY




**Baseline to month 1 logMAR***: -0.6 ± 0.7 in the insert group (N=8) vs. -0.2 ± 0.2 in the drops group (N=4) (p=0.27)
**Baseline to month 3 logMAR***: -0.5 ± 0.7 in the insert group (N=9) vs. -0.2 ± 0.3 in the drops group (N=5) (p=0.35)

* No statistically significant differences were observed. Lower logMAR indicates better visual acuity. N values indicate # of eyes with logMAR data present at month 1 or 3. In the above graph, mean +/- SD logMAR score for a given time point was calculated using all eyes with logMAR data at that time point.

# CHANGES IN MEDICATION BURDEN




**Baseline to month 1 meds***: -0.5 ± 0.9 in the insert group (N=8) vs. -0.5 ± 1.0 in the drops group (N=4) (p=1.0)
**Baseline to month 3 meds***: -0.4 ± 0.7 in the insert group (N=9) vs. -0.6 ± 0.9 in the drops group (N=5) (p=0.75)

* No statistically significant differences were observed. N values indicate # of eyes with medication data present at month 1 or 3. In the above graph, mean +/- SD meds for a given time point was calculated using all eyes with meds data at that time point. Meds were coded by total IOP-lowering chemicals (e.g. dorzolamide-timolol counts as 2).

# INFLAMMATION, COMFORT, AND ADVERSE EVENTS

- Complete resolution of AC cells/flare was noted in all eyes in the drop group, and all but three eyes in the insert group (p=0.26).
- 36.3% (N=4) of the insert group met rescue criteria and required supplemental anti-inflammatory drops.
- Ocular comfort index score at month 1 postop: 29.7 ± 8.0% in the insert group (N=6) vs. 10.7 ± 15.2% in the drops group (N=2) (p=0.13). Lower scores signify less ocular discomfort.
- Ocular comfort index score at month 3 postop: 24.1 ± 14.1% in the insert group (N=9) vs. 16.3 ± 16.5% in the drops group (N=5) (p=0.42).
- There were no serious adverse events or cystoid macular edema cases in either group.
- In the insert group, two patients experienced mild adverse events:
  - One patient reported moderate pain on extraocular movements at the week 1 visit and new-onset upper eyelid twitching at the month 1 visit. The former resolved with supplemental prednisolone drops, and the latter resolved without treatment.
  - One patient had a visually nonsignificant 2 mm hyphema that resolved without intervention.

# CONCLUSIONS

- In the first prospective study comparing the novel dexamethasone ophthalmic insert to standard-of-care prednisolone drops for combined CEIOL-MIGS patients, interim findings revealed that safety and efficacy outcomes were not significantly different.
- Just over a third of the insert group required supplementary anti-inflammatory therapy, which is higher than the pooled measure of 11.7% in previous RCTs comparing the insert to placebo after cataract surgery.[4] This difference may be attributable to increased inflammation from C-MIGS compared to standalone CEIOL.
- Potentially greater inflammatory control in the drops group may reflect the ability to titrate prednisolone dosages based on drop frequency, versus the sustained release of the insert.
- Our findings may apply best to Black and Hispanic patients since they comprised over 80% of our sample.
- The interim analysis is limited by greater dropout in the drops groups compared to the insert group.
- A larger, completed sample will help clarify the early observations in the drops group (possible trend towards greater inflammatory and IOP control) and insert group (possible trend towards more visual improvement).

4. Lee, A., Blair, H.A. Dexamethasone Intracanalicular Insert: A Review in Treating Post-Surgical Ocular Pain and Inflammation. *Drugs* 80, 1101–1108 (2020). https://doi.org/10.1007/s40265-020-01344-6