When Trials Don't Meet: A Retrospective Statistical Analysis Using Matching-Adjusted Indirect Comparison (MAIC) and Individual Patient Data (IPD) to Compare Catiolanze® with Other Preservative-Free (PF) Latanoprost in Open-Angle Glaucoma (OAG)

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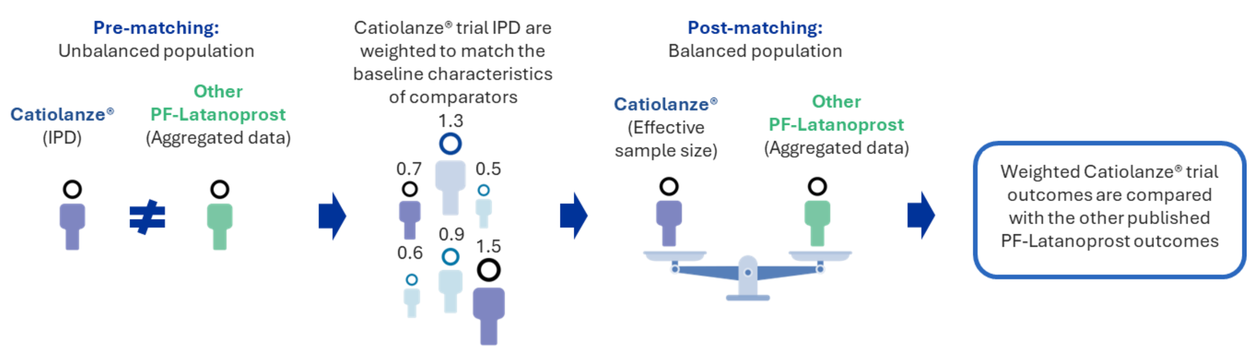
Background & Introduction

- Glaucoma is a progressive and chronic disease and is recognized by the World Health Organization (WHO) as the leading cause of irreversible blindness in the world.[1] OAG is the most prevalent form of glaucoma.[2]
- Topical prostaglandin analogues (PGAs), such as latanoprost, tafluprost, travoprost, and bimatoprost, are recommended as first-line pharmacological treatment options for both OAG and OHT,[3,4] among these options, latanoprost is considered being the preferred PGA based on its favorable risk/benefit profile.[5]
- Catiolanze® (Santen Oy) emulsion, a preservative-free (PF) Latanoprost formulated as a cationic emulsion, demonstrated a treatment options in OAG. PF- products were known to offering improved ocular surface tolerability and potentially enhancing adherence .[6-8]
- Given the absence and inherent difficulty of conducting head-to-head (H2H) trials and the limitations of network meta-analysis (NMA) due to insufficiently comparable data, a matching-adjusted indirect comparison (MAIC) was undertaken to assess the comparative effectiveness of Catiolanze® versus other PF-latanoprost for treating OAG and ocular hypertension (OHT).

Methods

- MAIC, a statistical methodology within indirect treatment comparison (ITC), is designed to minimize bias by applying a weighting approach that adjusts for differences in baseline characteristics between trials (**Figure 1**).
- Screening of PubMed was conducted in May 2025 using all relevant keywords to identify trials engaged PF-latanoprost with no restriction on publication year (24 studies). Those in late or pivotal phases that used preserved latanoprost (Xalatan® (Pfizer)) as the control arm were further reviewed (8 studies). Studies with eye inclusion criteria that differed substantially from the Catiolanze® trial (e.g., selecting the lower IOP eye or a random eye) and studies on switching from preserved to PF-latanoprost without a washout period were excluded (5 studies finally selected, including Catiolanze® trials [8-12]). Given the presence of common control arm in all trials under consideration, an anchored MAIC was carried out. potential trials were identified and analyzed for the applicability of using MAIC methodology, with the Catiolanze® trial serving as the reference study.
- For the eligible trials, baseline characteristics from the Catiolanze® trial IPD were re-weighted to match the mean baseline characteristics of the selected studies with available published aggregate data, and comparable outcomes were weight-adjusted.

Figure 1. Overview of MAIC methodology



Results

Five trials were selected. These trials were conducted across Europe and South Korea to compare PF-latanoprost with Xalatan® in adult patients with OAG or OHT. Among different trials, various baseline intraocular pressure (IOP) criteria were considered, enrollment rate were ranging from 23 to 213 patients per treatment arm. The primary outcomes differed by study designs: three trials evaluated IOP changes from baseline to Days 15, 29, 42, and 84 (Week 12), while one Phase 4 trial assessed corneal/conjunctival staining and ocular surface disease index (OSDI) scores. Other outcomes included safety and tolerability, as well as a range of ocular surface measures.

Baseline Characteristics matching assessment

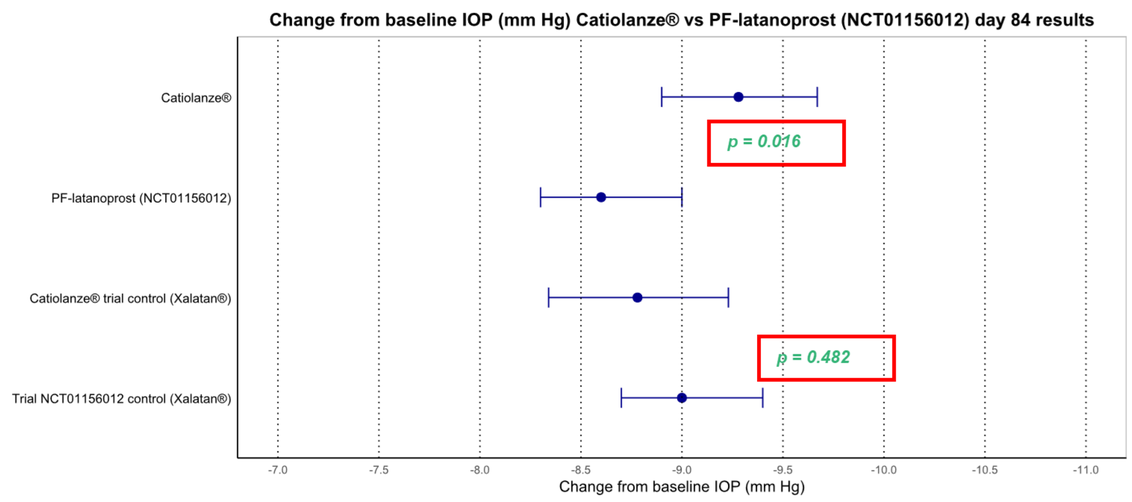
- As shown in the **Table 1**, age, sex, and baseline IOP could be matched across all trials except EudraCT-2018-001727-39, which did not report baseline IOP numerically. Primary diagnosis (percentage of patients with OAG), ethnicity and tear break-up time (TBUT) could only be matched in one trial each (NCT03419975, EudraCT-2018-001727-39 and NCT04743622, respectively).
- Multiple baseline characteristics did not have sufficient data in the publication for matching purposes. For example, prior IOP-lowering therapy was reported in several trials, however the drugs being used were different, whereas no ratio or numerical impact has been reported. Ethnicity could not be selected as a matching characteristic in trials NCT04743622 and NCT03419975 because of differences in study populations (Korean vs. 95.8% White in the Catiolanze® trial) and was not reported in trial NCT01156012. Baseline corneal fluorescein staining (CFS) and conjunctival hyperemia scores were not comparable due to differing assessment methods (Oxford vs. modified Oxford for CFS; Efron 0–4 vs. McMonnies 1–6 for hyperemia assessment scales). Time since diagnosis could not be matched, as only the mean duration of glaucoma diagnosis was reported in the comparator trial, despite both trials including OAG/OHT patients.

Table 1: Demographic and Baseline Characteristics matching assessment

Population characteristics	NCT04133311	NCT01156012	EudraCT-2018-001727-39	NCT04743622	NCT03419975
Age	✓	✓	✓	✓	✓
Sex	✓	✓	✓	✓	✓
Ethnicity	✓		✓		
Primary Diagnosis (%OAG)	✓				✓
Time Since Diagnosis	✓				
Baseline IOP	✓	✓		✓	✓
Corneal thickness				✓	
Baseline CFS Score	✓				
Baseline TBUT	✓			✓	
IOP-lowering drugs prior to study entry	✓				
Baseline Conjunctival hyperemia score	✓				
BMI				✓	✓
Diabetes mellitus (%)					✓
Systolic blood pressure				✓	
diastolic blood pressure				✓	
Pulse rate				✓	
Height				✓	
Weight				✓	
Baseline BCVA				✓	
Baseline OSDI score				✓	

Through MAIC assessment, One trial (NCT01156012) was matched successfully, and the outcomes of IOP change from baseline to Day 84 were compared. Age, sex, and baseline IOP were selected for baseline matching adjustment. The effective sample size (ESS) was 86.31% and 90.09% in the control and treatment arms, respectively. While the control arms between the two trials were comparable (p = 0.482) after matching, the Catiolanze®-treated arm showed a significant reduction in IOP after matching (-0.684 mmHg, p = 0.016) (**Figure 2**).

Figure 2: Catiolanze® vs. Selected PF- latanoprost Matching results and Outcome : Change from baseline IOP at day 84:



Other outcome comparisons across these studies were not feasible due to substantial differences in methodological and patient population:

- Comparisons of safety outcomes of conjunctival hyperemia were limited due to reporting, assessment and scoring methods differences. The inconsistencies on outcome report were also contributed to the matching difficulties, such as IOP reduction reported as percentage changes rather than absolute mmHg values.
- Limited sample sizes presented another challenge: one study included only 25 and 26 patients in PF-latanoprost and preserved latanoprost groups, respectively, from a single-country population. Substantial baseline IOP differences further reduced the effective sample size after matching to 2.50%, making valid statistical comparison impossible.

Discussion

- This analysis demonstrates the methodological applicability of MAIC for comparing Catiolanze® with other PF-latanoprost formulations, showing a statistically significant IOP reduction advantage after matching. During the matching access, substantial limitations were observed across multiple aspects: baseline characteristic matching was less intensive due to incomplete reporting and methodological heterogeneity; safety outcome comparisons were not feasible due to employ different assessment methods; small sample size in some studies resulted in very low effective sample sizes after matching; and outcome reporting inconsistencies made cross-study comparisons challenging. These limitations highlight the inherent difficulties in conducting MAIC studies across PF-latanoprost trials. Although further analysis is needed to confirm the findings, the current study presents a potential approach for assessing ITC when H2H are not feasible.

References
1. GBD 2019 Blindness Vision Impairment Collaborators. Lancet Glob Health 2021;9:e144-e160.
2. Weinreb RN, et al. JAMA 2014;311:1901-11.
3. European Glaucoma Society. Br J Ophthalmology 2021;105:1.
4. Asia-Pacific Glaucoma Society. Asia Pacific Glaucoma Guidelines 2016.
5. Alm A. Clin Ophthalmology 2014:1967-1985.
6. Jaenen N, et al. Eur J Ophthalmology 2007;17:341-9.
7. Pisella PJ, et al. Br J Ophthalmology 2002;86:418-23.
8. Kim DW, et al. Sci Rep 2021;11:14971.
9. Baudouin C, et al. Eye 2025;39:1599-1607.
10. Rouland JF, et al. Br J Ophthalmology 2013;97:196-200.
11. Czumbel N, et al. BMC Ophthalmology 2024;24:313.
12. Kim JM, et al. Int J Ophthalmology 2021;14:1539-1547

Abbreviations:
MAIC: Matching-Adjusted Indirect Comparison; IPD: Individual Patient Data; PF: Preservative-Free; OAG: Open-Angle Glaucoma; H2H: head-to-head ; OHT: ocular hypertension; IOP: intraocular pressure; TBUT: Tear break-up time; CFS: corneal fluorescein staining; ESS: effective sample size; OSD: ocular surface disease; ITC: indirect treatment comparison; OSDI: ocular surface disease index.

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