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MIRA-4 Phase 3 Trial: The Safety and Efficacy of Phentolamine Ophthalmic Solution for Reversal of Pharmacologically Induced Mydriasis in Subjects Aged 3-11 Years

(Poster ID 90950)

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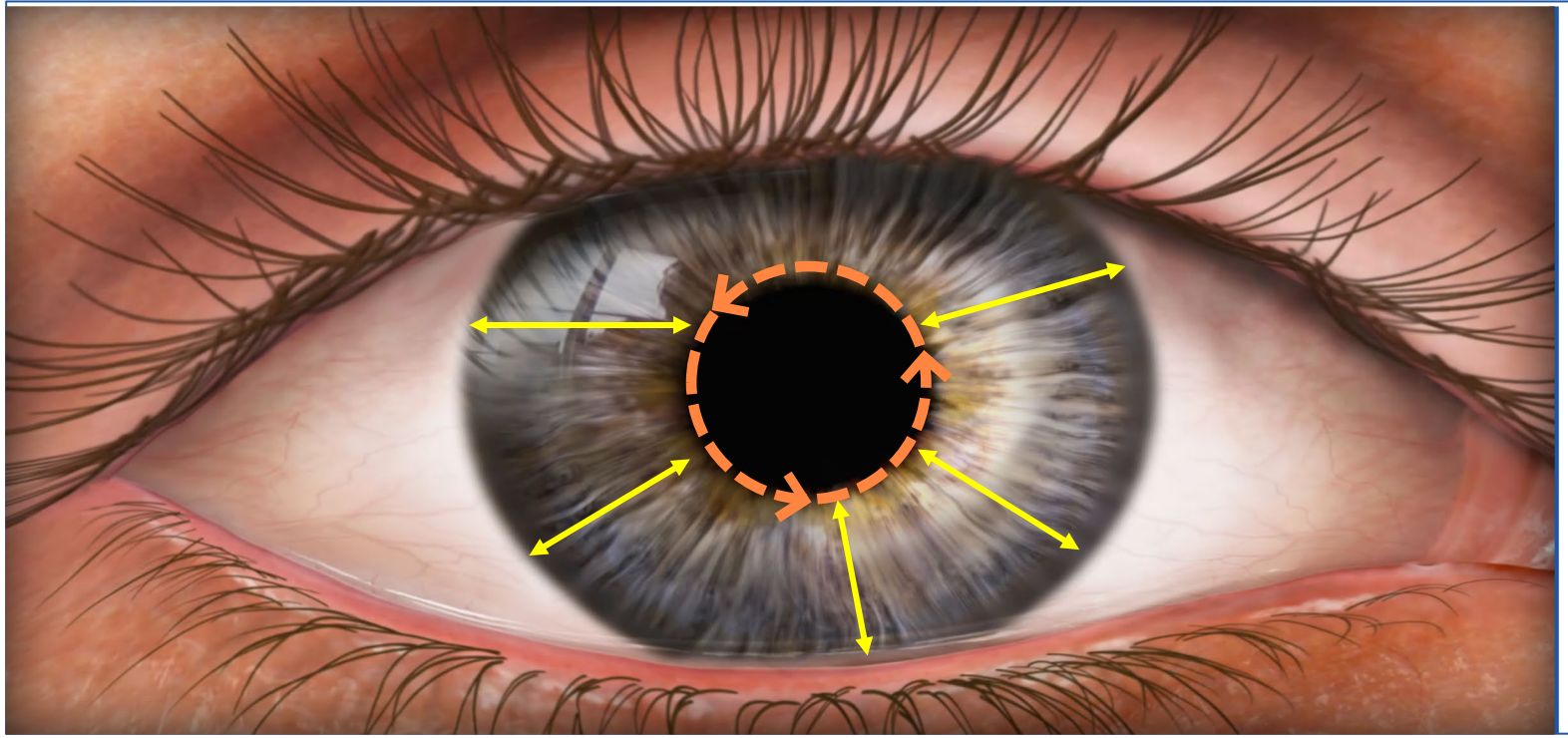
Dr. Chu's financial disclosures:

- Consultant to Ocuphire Phr
- XXX

0.75% Phentolamine Ophthalmic Solution Presbyopia Eye Drops

Differentiated Iris Dilator Inhibition MOA for Moderate Pupil Reduction and Vision Benefits

Phentolamine is the Active Ingredient in Nyxol: a non-selective α1 Antagonist



Phentolamine blocks α1 receptors on the **Iris Dilator Muscle**

↓

Decreases pupil size (moderately) **without affecting the iris sphincter or ciliary muscles**

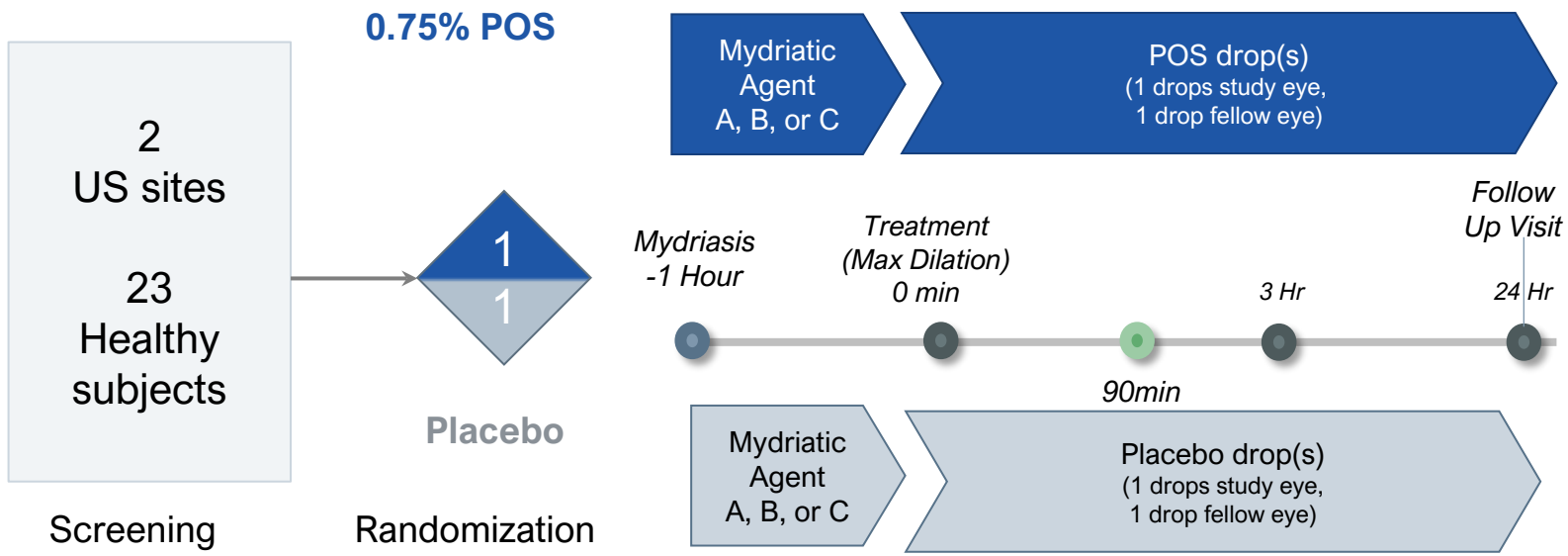
↓

Allows for 3 indications: **RM, Presbyopia and NVD**

Yellow arrows- Iris dilator muscle (alpha antagonists e.g.: Phentolamine)
Orange circle- Iris sphincter muscle (cholinergic agonists e.g.: pilocarpine, carbachol, aceclidine)

MIRA-4 Trial Design

Well-Controlled, Randomized, Double-Masked Placebo-Controlled Trial of Pediatrics Patients



Key Eligibility Criteria

Inclusion: Healthy subjects 3 to 11 years of age, inclusive.

Primary Safety

- Adverse events
- Vitals
- Best-Corrected Distance Visual Acuity (BCDVA)
- Conjunctival hyperemia

Efficacy Endpoints

- % of subjects (study eye) returning to baseline (within 0.2 mm) pupil diameter (PD) at 90 minutes
- Change (in mm) in photopic pupil diameter from baseline at 90 minutes, 3 hours and 24 hours
- Time to return to baseline photopic pupil diameter

Mydriatic Agents 3:1:1 – A: 2.5% phenylephrine (alpha-1 agonist), B: 1% tropicamide (cholinergic blocker), C: Paremyd® (combination)

MIRA-4: Demographics and Baseline Characteristics

Well Balanced Across Treatment and Placebo Arms

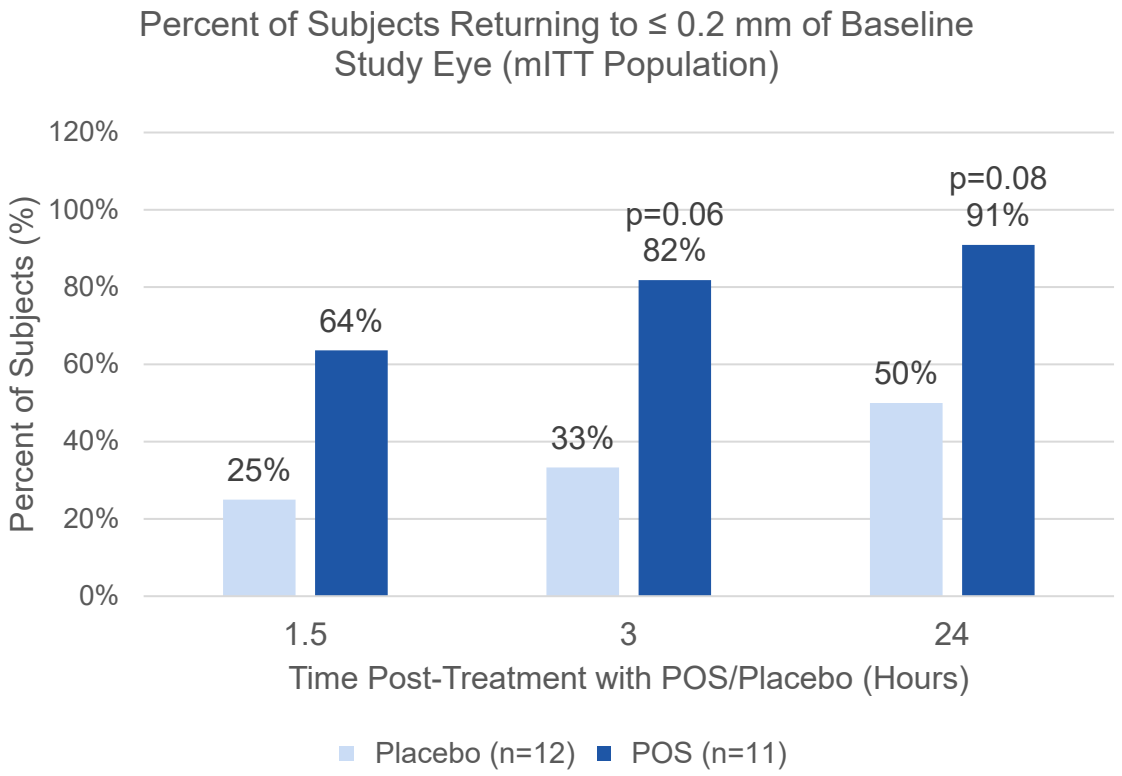
	POS n=11	Placebo n=12	Total n=23
Demographics			
Mean Age (years) (Range)	7 (3-11)	6 (3-10)	6 (3-11)
Age Range Category: 3 to 5 Years n (%) **6 to 11 Years** n (%)	5 (46%) 6 (55%)	6 (50%) 6 (50%)	11 (48%) 12 (52%)
Sex: Male n (%) **Female** n (%)	6 (55%) 5 (46%)	5 (42%) 7 (58%)	11 (48%) 12 (52%)
Race: White n (%) **African American** n (%) **Asian** n (%) **Other^** n (%) *^includes American Indian or Alaska Native; Native Hawaiian or Other Pacific Islander*	11 (100%) 0 (0%) 0 (0%) 0 (0%)	10 (83%) 2 (17%) 0 (0%) 0 (0%)	21 (91%) 2 (9%) 0 (0%) 0 (0%)
Light Iris Color: n (%)	5 (45%)	6 (50%)	11 (48%)
Dark Iris Color: n (%)	6 (55%)	6 (50%)	12 (52%)
Baseline Characteristics			
Baseline Pupil Diameter Mean (mm)	6.1	5.9	6.0
Max Dilated Pupil Diameter Mean (mm)	7.3	7.3	7.3

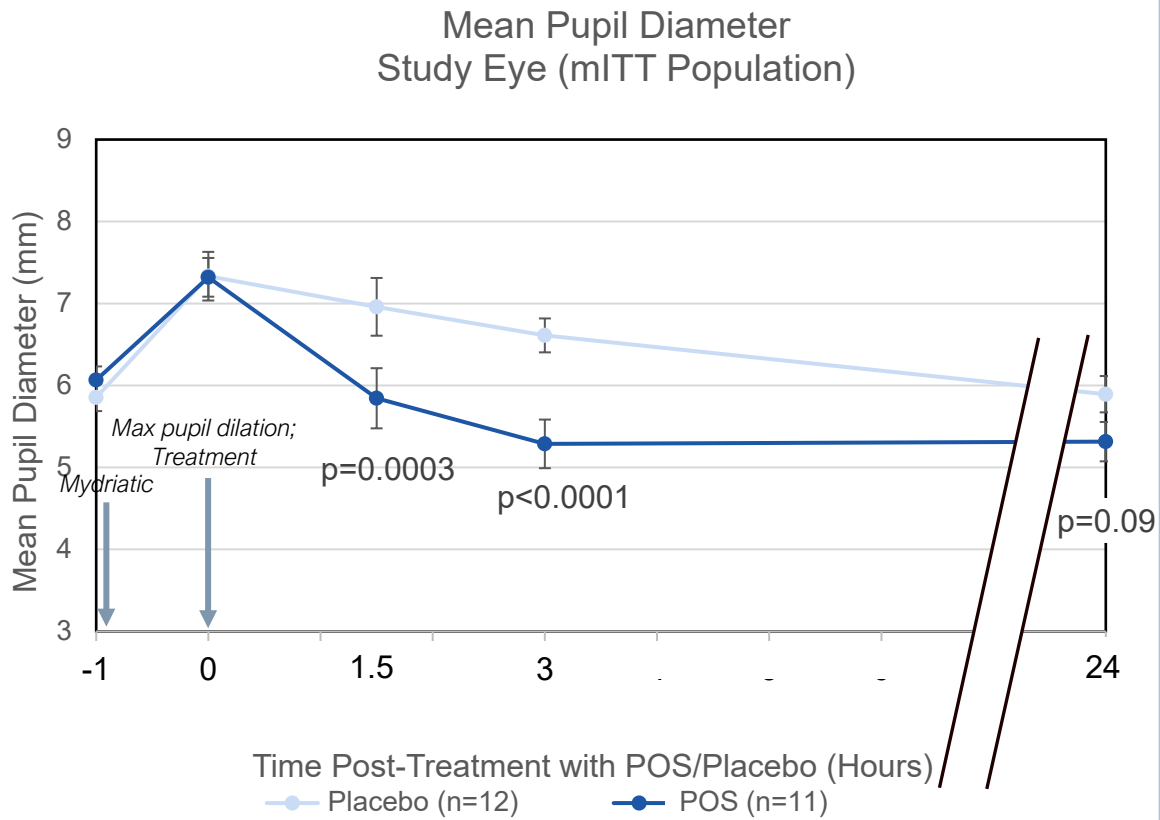
Source: MIRA-4 Results; Data include all three mydriatics (Phenylephrine, Tropicamide, Paremyd)

MIRA-4: Mean and Return to Baseline Pupil Diameter

POS Rapidly Reversed Dilation at 90 Minutes, 3 Hours and 24 Hours and Reduced PD

MIRA-4 Trial





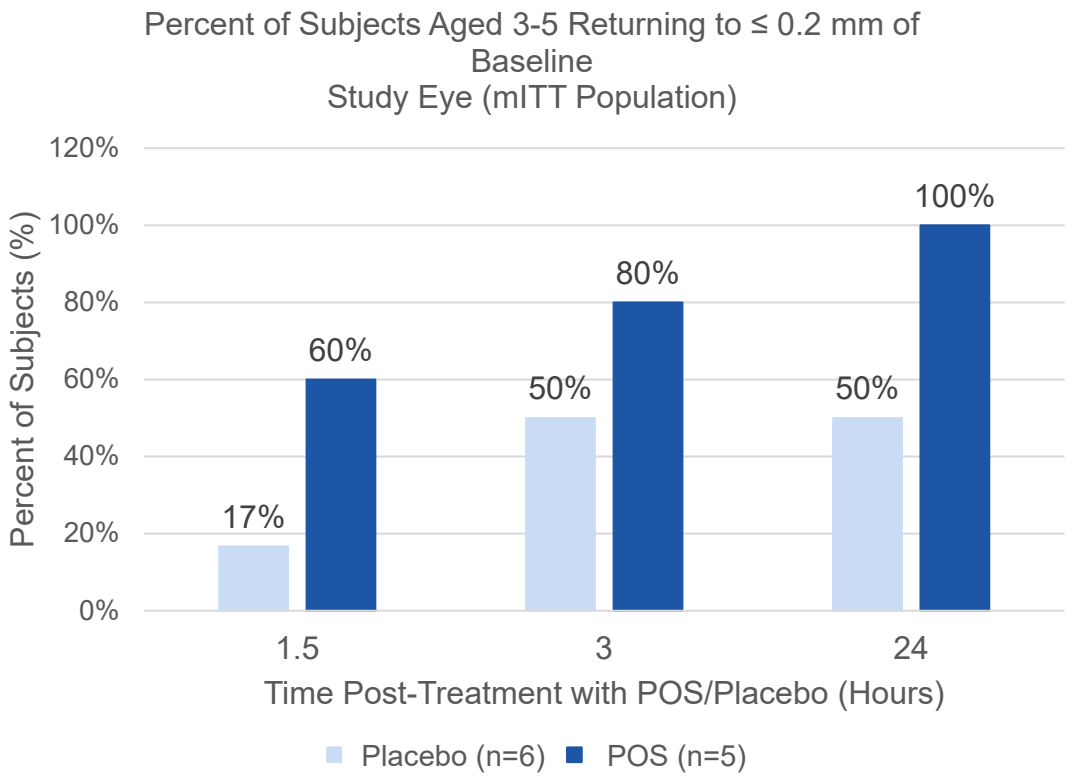
Source: MIRA-4 Results; Data include all three mydriatics (Phenylephrine, Tropicamide, Paremyd)

MIRA-4: Comparison of PD by Pediatric Age Groups

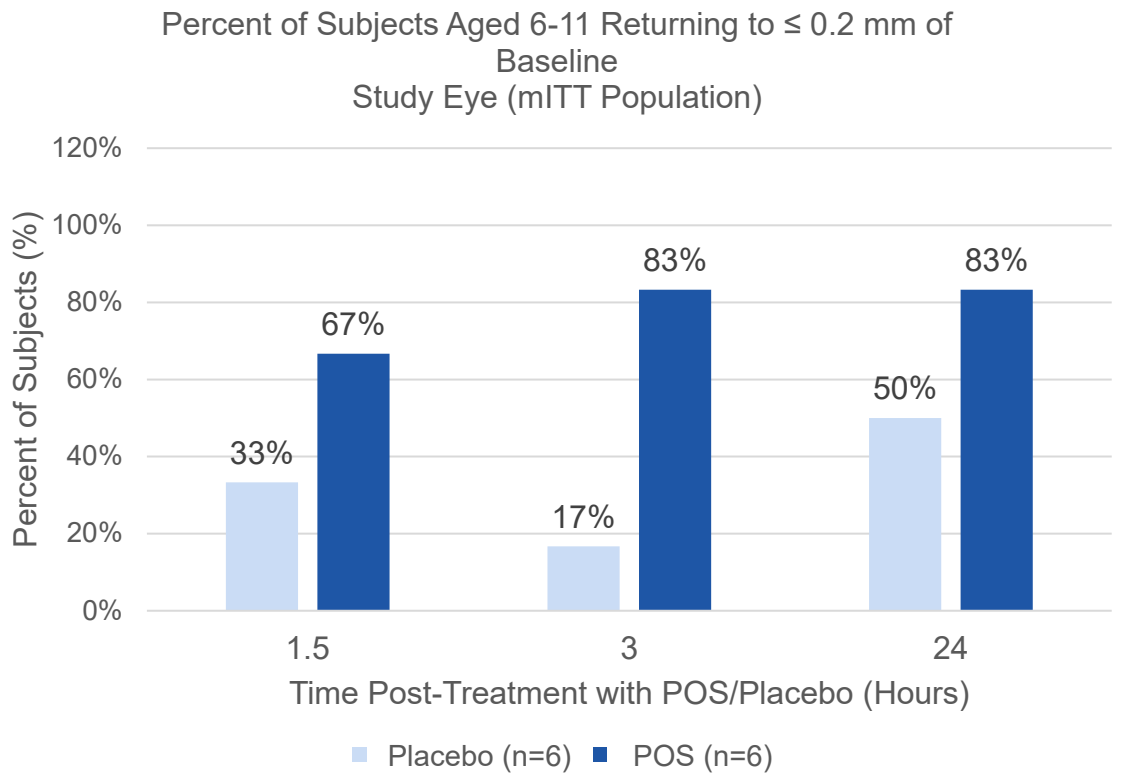
POS Rapidly Reversed Dilation in Young Children 3 to 5 as well as 6 to 11 Years

MIRA-4 Trial

Subjects Aged 3-5



Subjects Aged 6-11



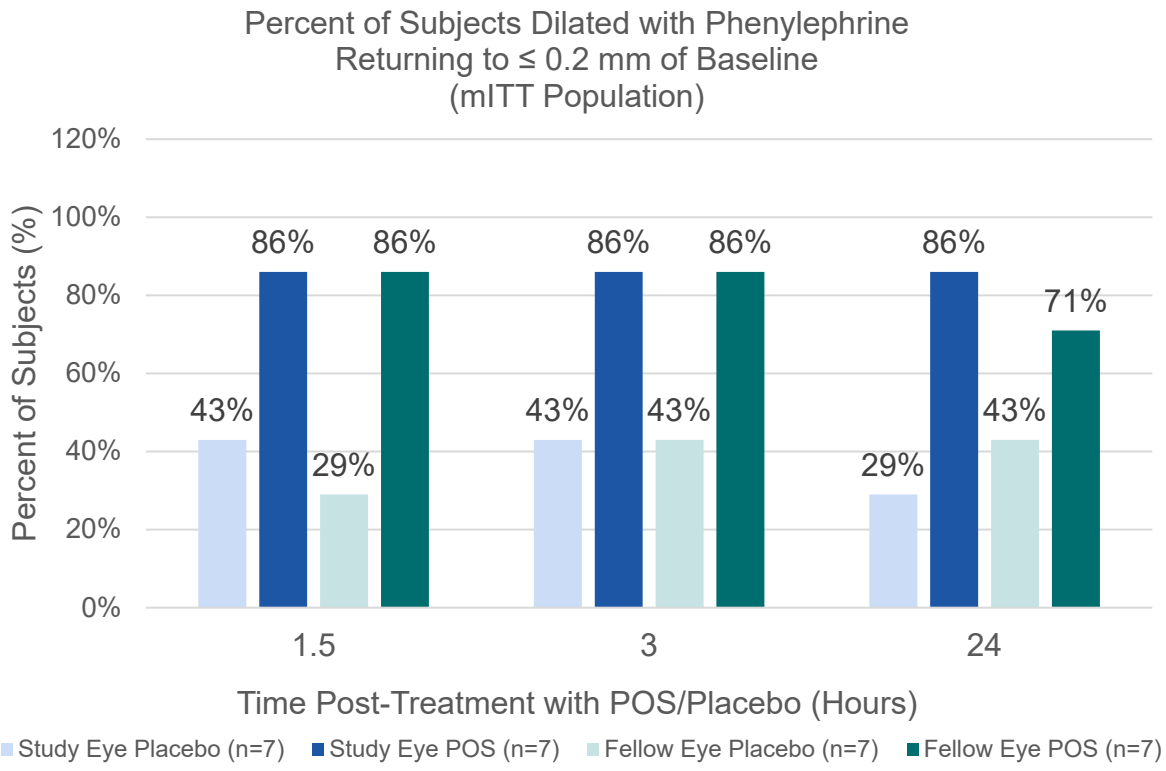
Source: MIRA-4 Results; Data include all three mydriatics (Phenylephrine, Tropicamide, Paremyd)

MIRA-4: Comparison of PD by Mydriatic Agent

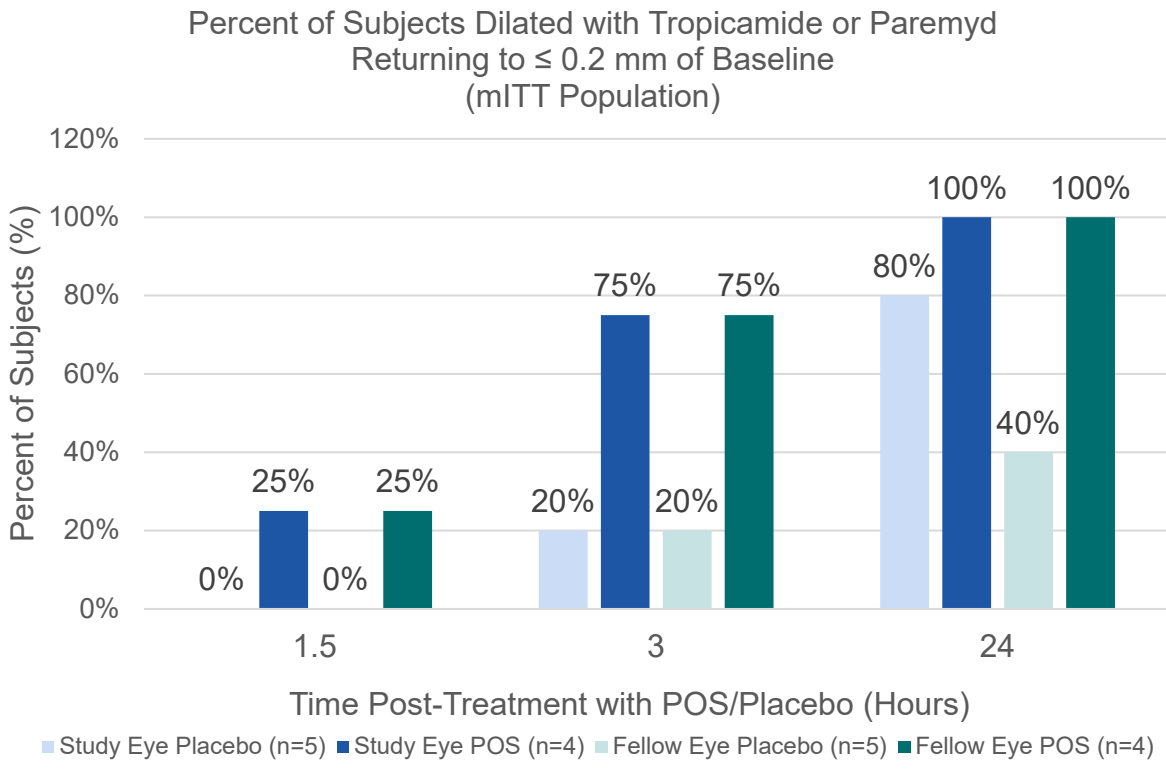
POS Rapidly Reversed Dilation Across All 3 Mydriatic Agents

MIRA-4 Trial

Subjects with Phenylephrine Pretreatment



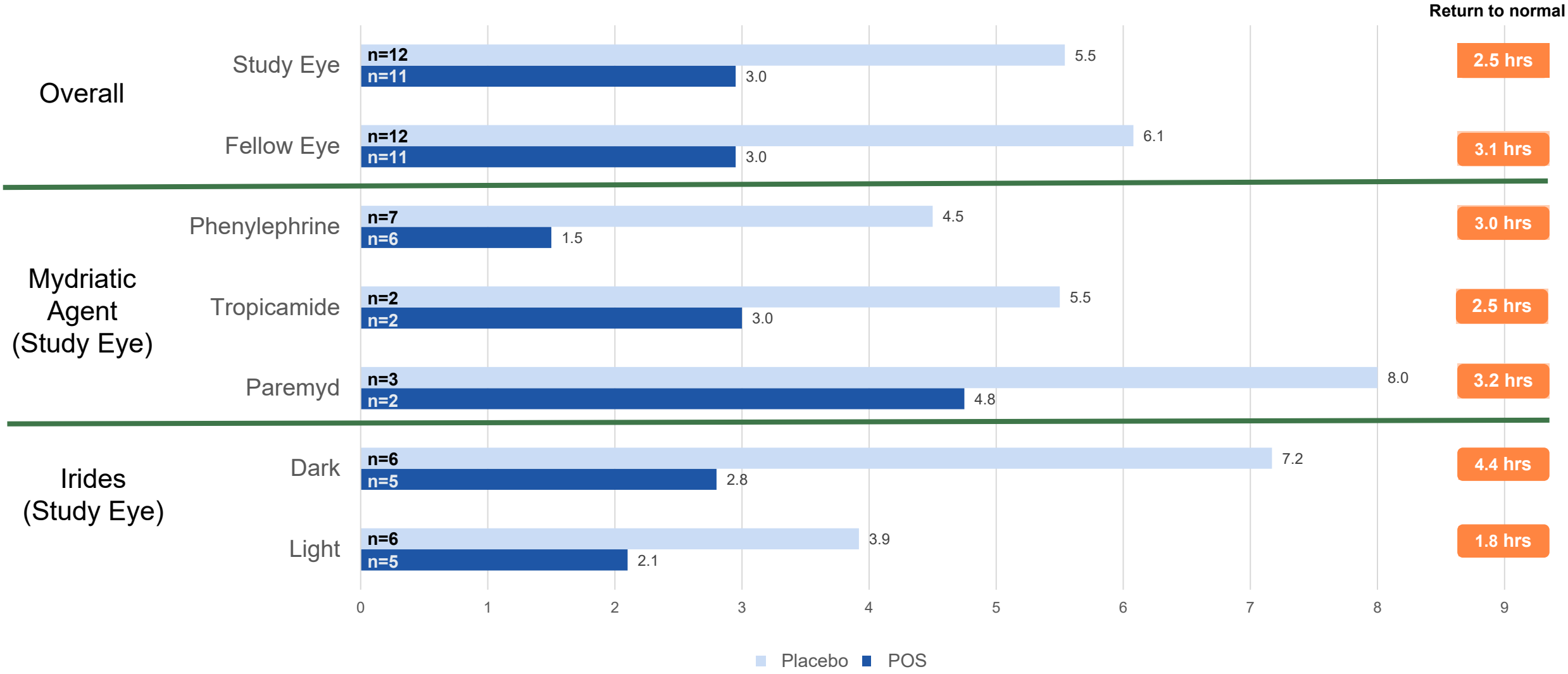
Subjects with Tropicamide or Paremyd Pretreatment



Source: MIRA-4 Results

MIRA-4: Mean Time to Return to Baseline PD

Saving of ~3 Hours in Return to Normal PD Overall and Across Mydriatic Agents



Source: MIRA-4 Results

MIRA-4: Efficacy and Safety Data Summary

Pediatric Results Consistent with Both Phase 3 Trials on Efficacy and Safety Profile

Efficacy

- At 90 minutes post-dose, 64% of POS returned to baseline PD compared to 25% on placebo
- Efficacy seen at 3 timepoints measured from 90 minutes to 24 hours
- Efficacy across all 3 mydriatic agents – phenylephrine, tropicamide, and Paremyd®
- Efficacy in both light and dark iris colors
- Time savings of ~3 hour with one drop of POS

Safety

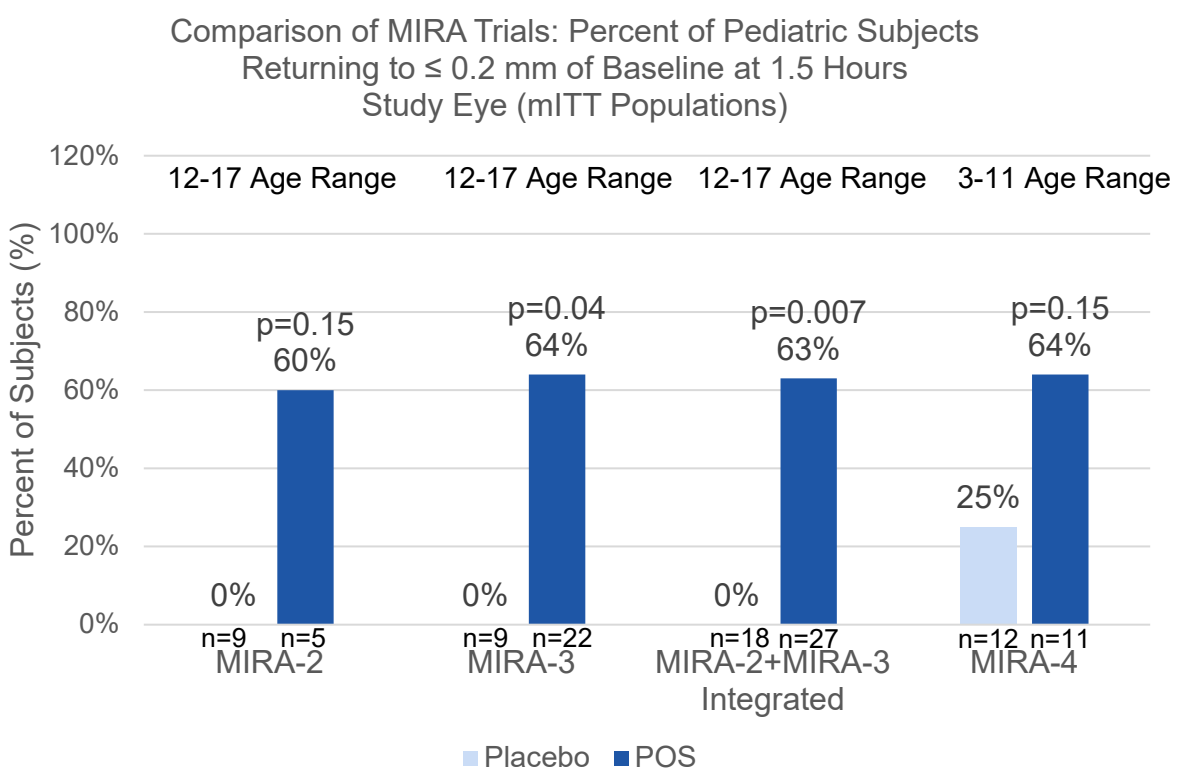
- **No Adverse Events**
- **No** reported instillation site discomfort or pain, burning, stinging, or irritation
- **No** distance visual acuity loss
- **No** change in vital signs (BP, HR, etc.)
- Completion of MIRA-4 study satisfies Pediatric Research Equity Act (PREA) requirement

Source: MIRA-4 Results

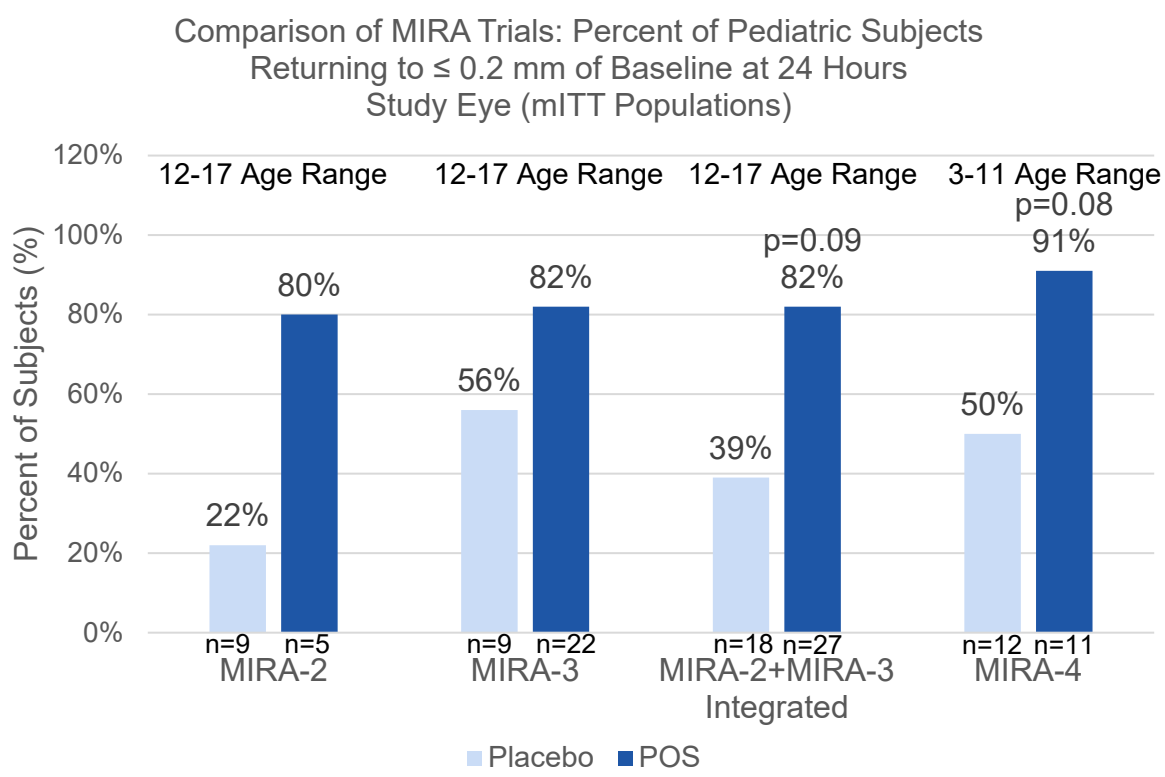
Comparison of Pediatric Subjects in MIRA-4 and MIRA-2/3 Phase 3 Trials

Consistent Pediatric Efficacy Data Across Trials MIRA-2/MIRA-3 and MIRA-4

90 Minute Comparison



24 Hours Comparison



At all timepoints starting at 90 min through 24 hrs, POS rapidly reversed dilation compared to placebo for all pediatric ages across 3 different trials; Additionally, pediatric data was consistent with MIRA-2/3 90 min primary endpoint of % subjects returning to baseline PD (56% POS vs. 6% placebo; p<0.0001)

Source: MIRA-2, MIRA-3, MIRA-2+MIRA-3 Integrated Summary of Efficacy, MIRA-4 Results

Key Takeaways

- Our study suggests that school-aged children experience symptoms resulting from pharmacological dilation for a longer duration than adults, with a higher likelihood of discomfort and slow return to baseline even after 24 hours
- **Today, there are no commercially-available treatments for reversal of mydriasis ➔ POS, if approved, would be a safe and effective option in pediatric patients**
- ***POS New Drug Application PDUFA date is Sept 28, 2023***

Source: MIRA-2, MIRA-3, MIRA-4 Results

We thank all the MIRA-4 study participants, investigators and their staff !!!

Dr. Y. Ralph Chu

MIRA-4 Clinical Trial Sponsor is Ocuphire Pharma
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