EVALUATION OF 2 MYDRIATIC DOSING REGIMENS DELIVERED BY MICRO-ARRAY PRINT TECHNOLOGY FOR COMPARISON OF PUPIL DILATION SPEED

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Unmet Needs with Topical Ophthalmic Drug Delivery

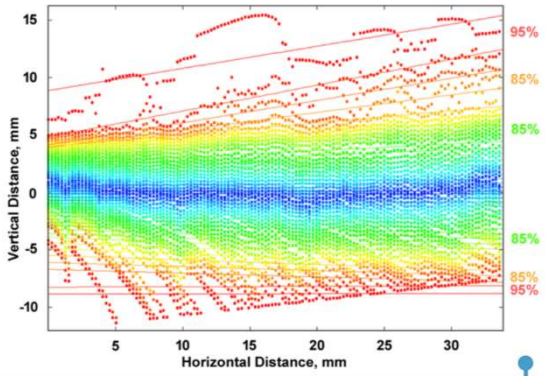
While standard of care, conventional eye drops have several caveats:[1-7]

- Ocular and Systemic side effects[2-4]
- Excess medication volume causing over exposure to medication/preservatives[4]
- Dependent on proper eye drop technique (head angle, squeezing force, etc.)[5]
- Poor compliance[6] and no remote monitoring
- Risk of contamination from protruding tip of multiuse eye drop bottles[7]

1. Grob SR, et al. Management of mydriasis and pain in cataract and intraocular lens surgery: review of current medications and future directions. *Clin Ophthalmol*. 2014;8:1281-1289. 2. Farkouh A, et. al. Systemic side effects of eye drops: a pharmacokinetic perspective. *Clin Ophthalmol*. 10: 2433-2441, 2016. 3. Pasquale LR, et al. Latanoprost with high precision, piezo-print microdose delivery for IOP lowering: clinical results of the PG21 study of 0.4 µg daily microdose. *Clin Ophthalmol*. 2018;12:2451-2457. 4. Ianchulev T, et al. High-precision piezo-ejection ocular microdosing: Phase II study on local and systemic effects of topical phenylephrine. *Ther Deliv*. 2018;9(1):17-27. 5.–Feng A, et al. Success of patient training in improving proficiency of eyedrop administration among various ophthalmic patient populations [published correction appears in *Clin Ophthalmol*. 2017 Feb 14;11:329*]. Clin Ophthalmol*. 2016;10:1505-1511. 6. Tsai JC. A comprehensive perspective on patient adherence to topical glaucoma therapy. *Ophthalmology*. 2009;116(11 Suppl):S30-S36. 7. Daehn T, et al. Contamination of multi dose eyedrops in the intra and perioperative context. *Sci Rep*. 2021;11(1):20364.

Optejet® Microdose Array Print (MAP™) Technology

Administers a microdose volume (6-8 µL) very rapidly (in <100 ms) to deliver topical ophthalmic drug prior to the involuntary human blink[1]



Piezoelectric element delivers a finely controlled microdroplet mist with precisely defined volume, velocity, geometry[1,2]

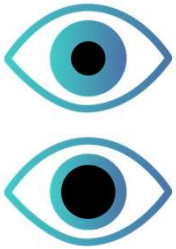
Delivers ophthalmic drug in a horizontal direction as a columnar mist directly to the cornea[1,2]

No protruding nozzle and shutter feature, designed to minimize the risk of touch during administration and therefore to reduce contamination[1]

1.Ianchulev T, et al. Pharmacodynamic profile of mydriatic agents delivered by ocular piezo-ejection microdosing compared with conventional eyedropper. *Ther Deliv*. 2016;7(11):751-760
2.Wirta DL, et al. Mydriasis with micro-array print touch-free tropicamide-phenylephrine fixed combination MIST: pooled randomized Phase III trials. *Ther Deliv*. 2021;12(3):201-214.

The Need for SPEED*

Is one mist as clinically effective as two?



Can dilation be achieved efficiently?

STUDY OBJECTIVE

To determine if 1 single mist (~8µL) of MAP dispenser administered TR-PH FC** solution has similar efficacy to 2 mists (~16 µL) for pupil dilation.

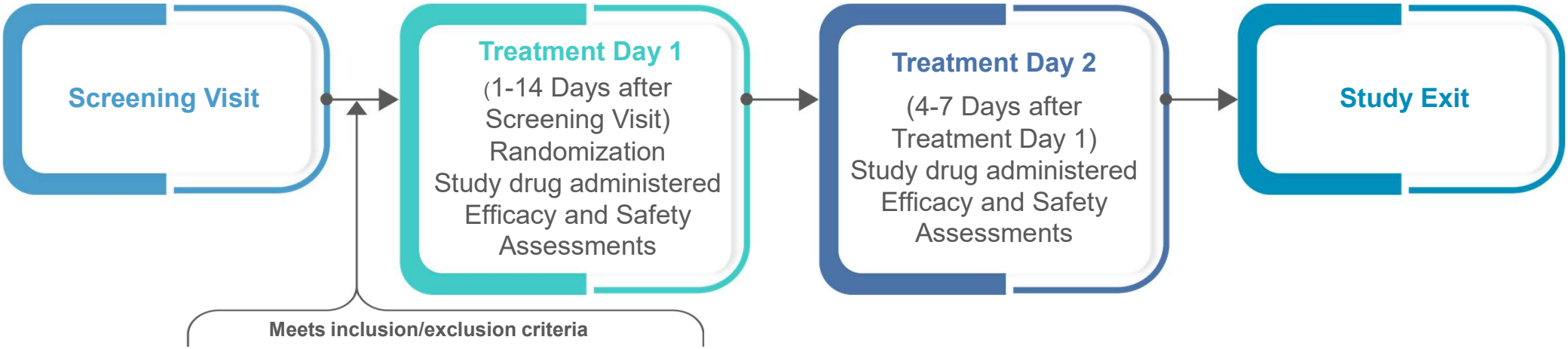
*A SINGLE-CENTER, ASSESSOR-MASKED, ACTIVE-CONTROLLED, PHASE 4 STUDY EVALUATING SPEED OF PUPIL DILATION WITH THE MICRO-ARRAY PRINT (MAP) DISPENSER WHEN COMPARING 2 DOSING REGIMENS OF TROPICAMIDE-PHENYLEPHRINE FIXED COMBINATION OPHTHALMIC SOLUTION (THE SPEED STUDY)

**Tropicamide-Phenylephrine Fixed Combination (TR-PH FC) = T-P OFTENO SOLUCIÓN 50 mg/8 mg/ ml, a commercially available mydriatic product.

SPEED Study Trial Design & Treatment Schedule

- **Single-center**
- Single masked
- Active-controlled
- Cross-over
- Non-inferiority trial

- **Randomized Tx**
  - TR-PH FC solution administered OU via Optejet MAP dispenser over 2 visits:
    - 1 mist OU (either Tx Day 1 or 2)
    - 2 mist OU (either Tx Day 1 or 2)



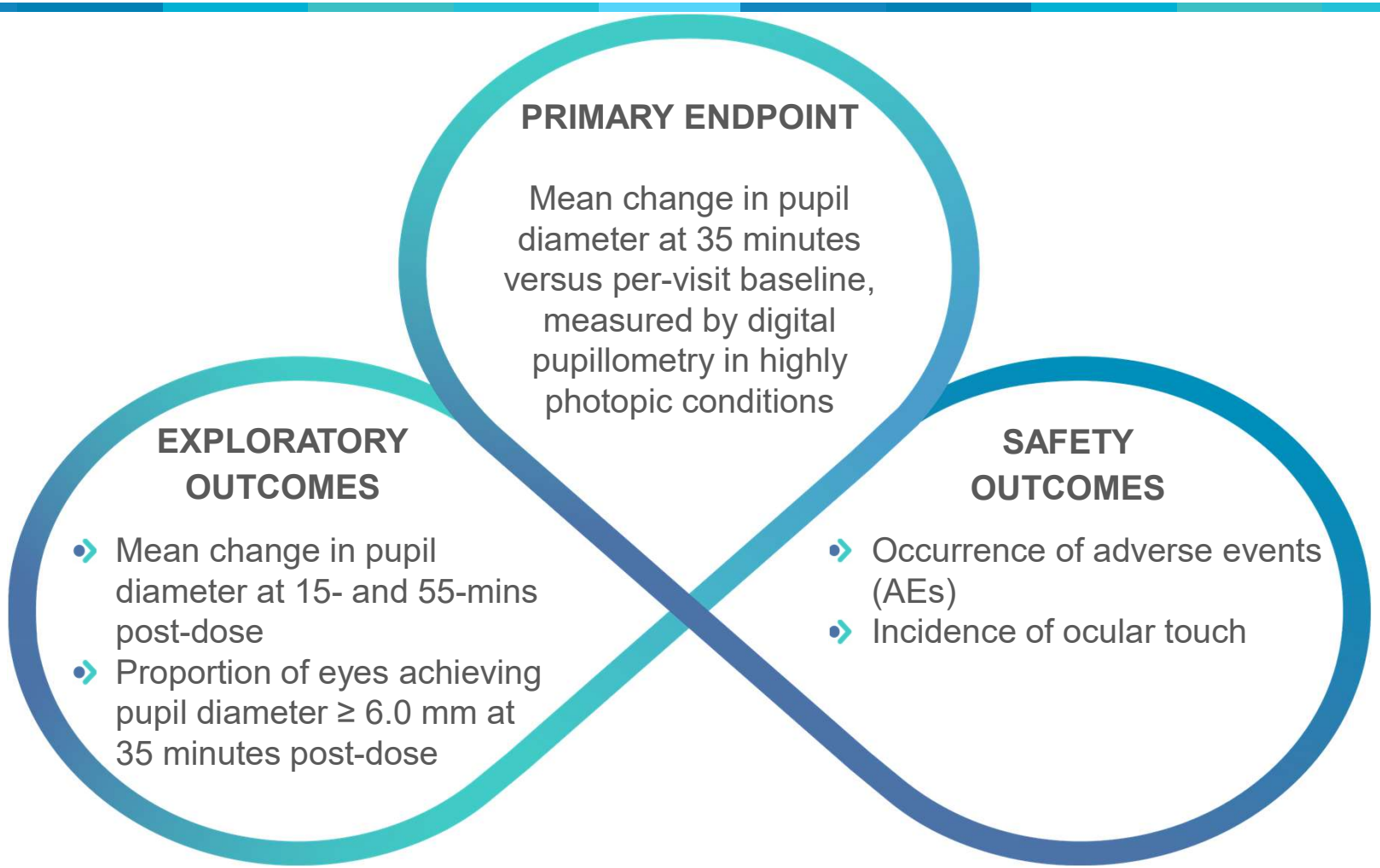
Key inclusion Criteria

- ≥18 years old
- Photopic screening pupil diameter ≤ 3.5 mm in each eye

Key exclusion criteria

- Allergy to active ingredients of pharmaceutical treatment
- Anatomically narrow AC angles or closed-angle glaucoma
- Ocular surgery or laser treatment

SPEED Study Outcome Measures



SPEED Patient Demographics

	n	%
N (subjects)	60 (120 eyes)	
Age (Years)		
Mean (SD)	40.3 (14.2)	
Median	37.0	
Min, Max	[18.0, 69.0]	
Gender		
Male	23	38.3%
Female	37	61.7%
Race		
White	60	100%
Ethnicity		
Hispanic or Latino	59	98.3%
Not Hispanic or Latino	1	1.7%

SPEED Primary Efficacy Endpoints

Primary Endpoint Mean change in pupil diameter (mm) at 35 minutes versus per-visit baseline		
Mean (SD)	**1 mist/eye**	**2 mists/eye**
	4.55 (0.68)	4.88 (0.60)

- In this study, the **primary endpoint** of mean change in pupil diameter at 35 minutes post-dose of 4.55 mm and 4.88 mm for one mist and two mists using commercially available mydriatic T-P OFTENO SOLUCIÓN 50 mg/8 mg/ ml, respectively, was successfully achieved.
- The mean change in pupil diameter from baseline with **a single-mist was non-inferior to two-mists** (estimated difference -0.249 mm).

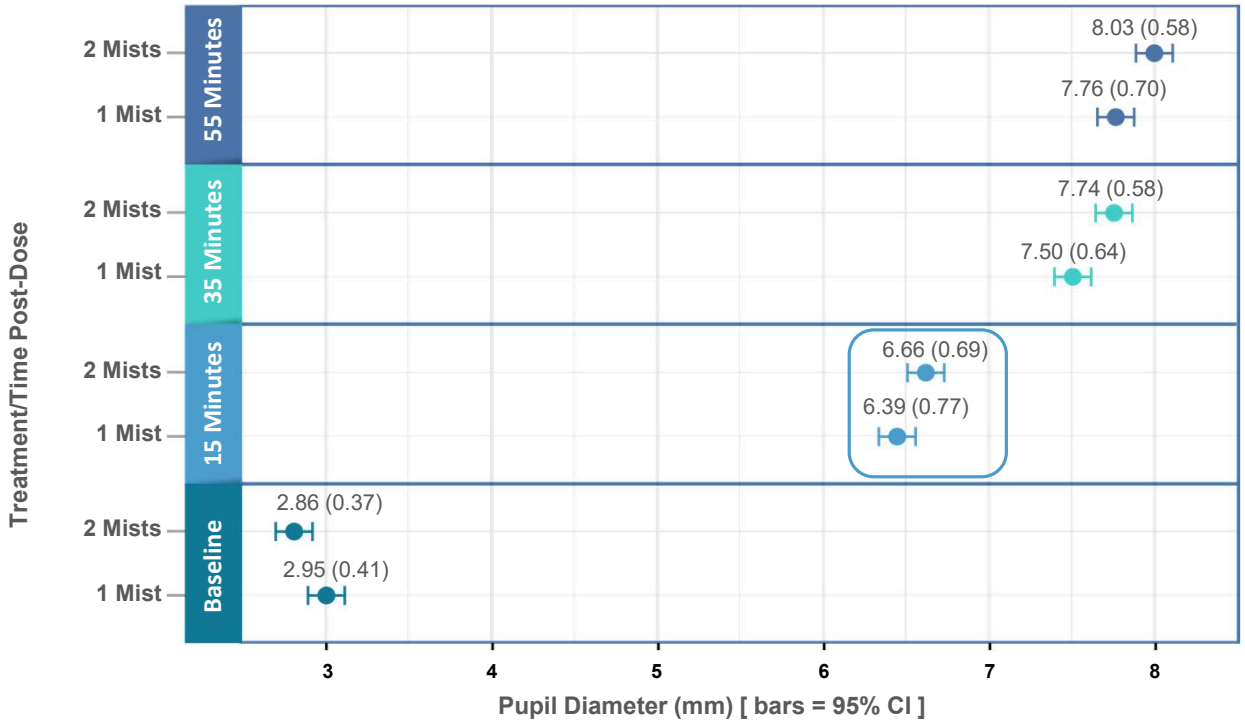
MIST[1]

- A similar mean change in pupil diameter (SE) of 4.72 (0.04) was observed using the same primary endpoint in the MIST clinical trials at 35 min post-administration of 2 mists using a mydriatic investigational agent FC of Tropicamide 1%-Phenylephrine 2.5%.

1.Wirta DL, et al. Mydriasis with micro-array print touch-free tropicamide-phenylephrine fixed combination MIST: pooled randomized Phase III trials. *Ther Deliv*. 2021;12(3):201-214.
FC = fixed combination

SPEED Exploratory Results: Mean Pupil Diameter by Treatment and Time Post Dose

FOREST PLOT OF MEAN PUPIL DIAMETER BY TREATMENT AND TIME POST-DOSE (ITT AND PP POPULATION)



- Clinically relevant dilation was **achieved quickly** at 15 minutes post dose with no significant difference between 1 mist (6.39 mm) and 2 mists (6.66 mm).
- Dilation at 35 minutes was 7.50 mm for 1 mist and 7.74 mm for 2 mists.
- Dilation at 55 minutes dilation was 7.76 for 1 mist and 8.03 for 2 mists.

No significant differences were observed in speed of dilation comparing 1 mist vs. 2 mists at all 3 time points.

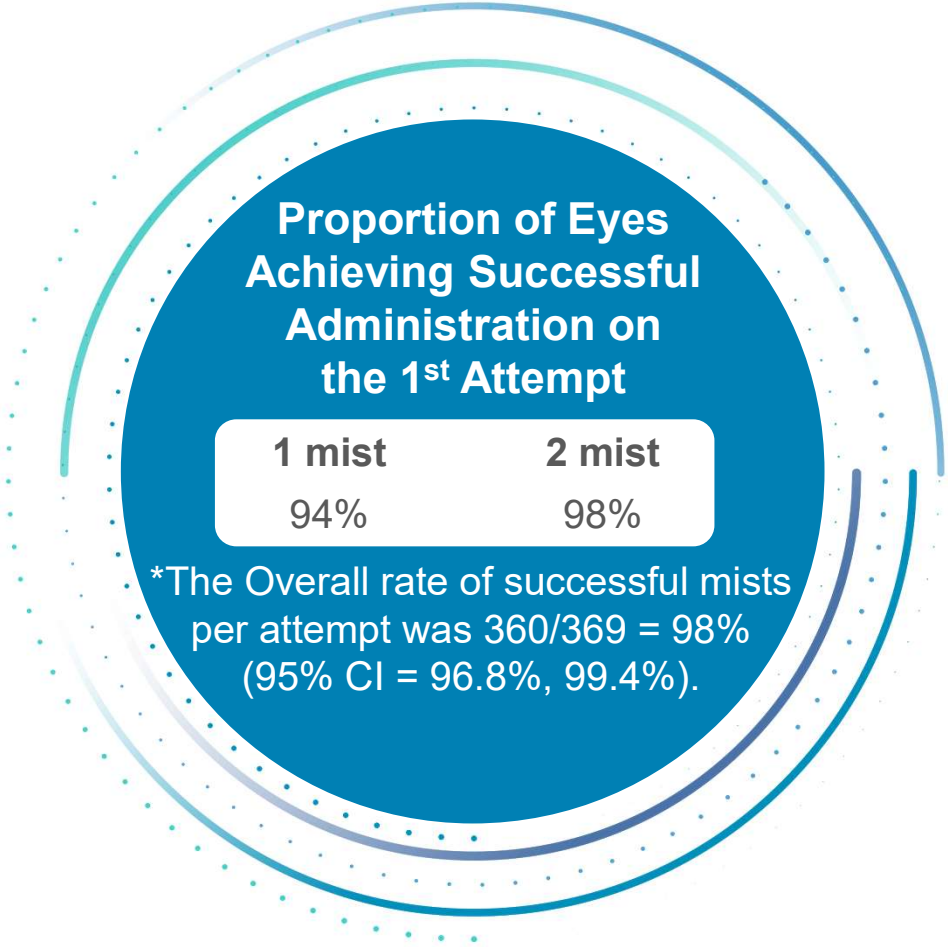
SPEED Safety & Administration

SAFETY

- No Ocular or Systemic Adverse Events were reported during the study.
- Mydriatic delivered by Optejet® was well tolerated with a positive benefit/risk profile.

ADMINISTRATION

- There were no reports of ocular touch.



Clinical Applications for an Eye Exam

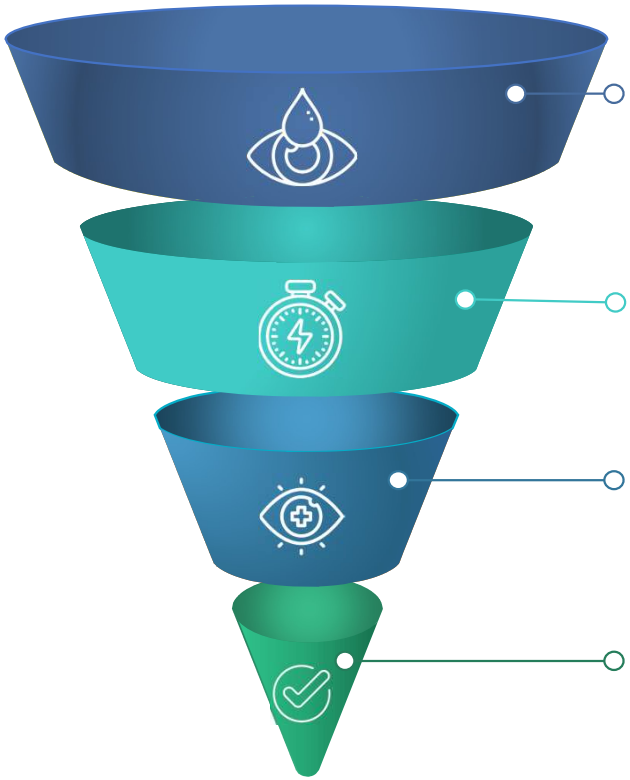
Traditionally, dilation during an eye exam typically takes 20 to 30 min.[1]

Rapid dilation was observed with most eyes in the SPEED study.

Proportion of Patients Achieving Pupil Dilation ≥ 6.0 mm	
	1 mist
15 min	74%
35 min	98%
55 min	99%

1.Boyd D. What are dilating eye drops? American Academy of Ophthalmology. Available at: What Are Dilating Eye Drops? - American Academy of Ophthalmology (aao.org). Accessed February 4, 2022.

SPEED Summary



Optejet® delivered TR-PH FC solution leads to effective pupil dilation with 1 mist.

Clinically effective dilation occurs at 15 minutes post dose.

There is no clinical or statistical benefit with using 2 mists.

Optejet® demonstrates a high rate of successful administration upon first attempt.