Ocular Hypotensive Efficacy of Netarsudil Ophthalmic Solution 0.02% Over a 24-Hour Period: A Pilot Study

James H. Peace, M.D.[1],
Casey K. Kopczynski, Ph.D.[2], and Theresa Heah, M.D.[2]

[1] Inglewood, CA
[2] Aerie Pharmaceuticals, Inc., Durham NC and Bedminster, NJ

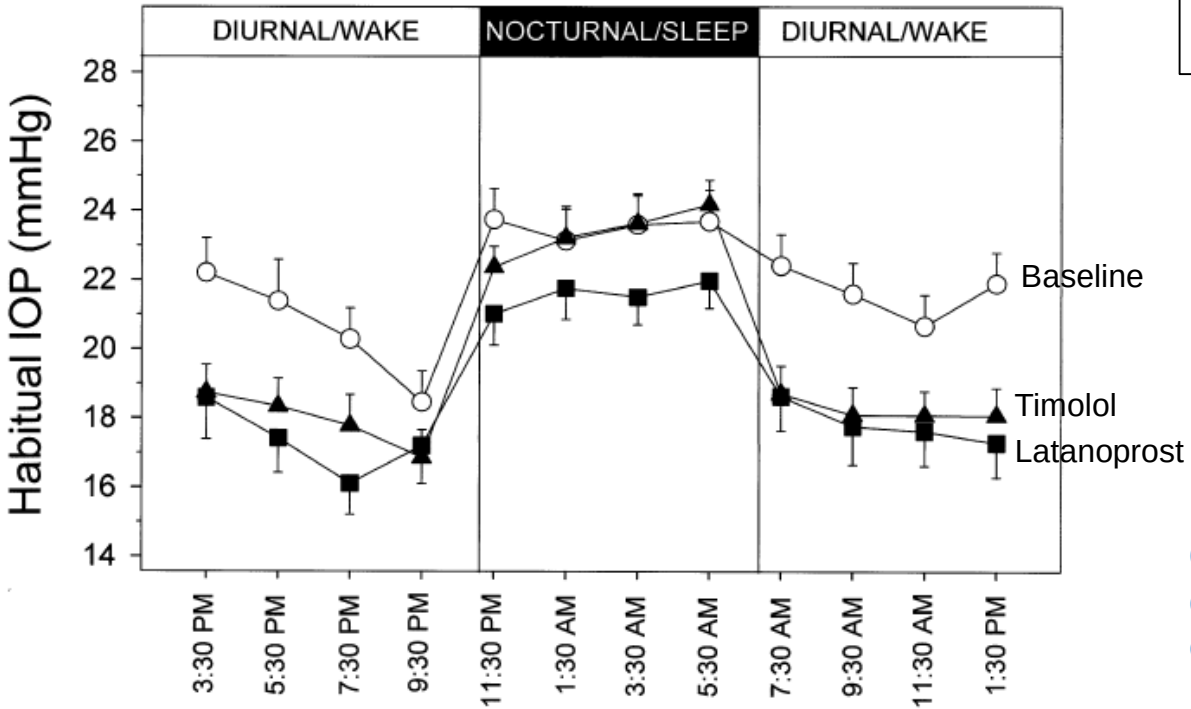
Nocturnal IOP Elevation Presents an ***Unmet Need:***

- **Large diurnal fluctuations in IOP** are an independent risk factor in patients with glaucoma (Asrani 2000).

- Peak IOP is related to glaucoma progression (Bagga 2009), and previous studies have shown that **IOP peaks** in glaucoma patients frequently **occur during nocturnal hours** (2004 Liu).

- A main objective in treating glaucoma should be to lower the patients' IOP to the point that further damage to the optic nerve is prevented, and to achieve this without sacrificing safety or convenience

Timolol, Latanoprost: 24 HOUR DATA



Liu JH, et al.
Am J Ophthalmol. 2004; 138:389

- Timolol did not reduce IOP during the nocturnal period
- Latanoprost reduced IOP less effectively during the nocturnal period than during the day (approx. -2.0 vs. -3.5 mmHg, resp.)

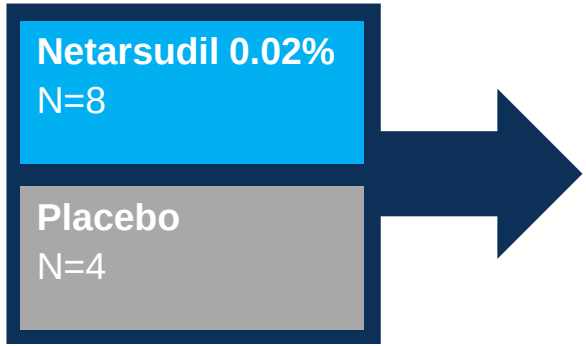
Current glaucoma medications either have no efficacy at night or reduced efficacy at night[1 - 6]

1. Liu JH, et al. Am J Ophthalmol. 2004; 138:389-395. 2. Gulati V, et al. Arch Ophthalmol. 2012; 130:677-684. 3. Liu JH, et al. Ophthalmology. 2009; 116:449-454. 4. Liu JH, et al. Ophthalmology. 2010; 117:2075-9. 5. Fan S et al. J Glaucoma. 2014; 23:276-81. 6. Liu JH, et al. Am J Ophthalmol. 2016;169:249-257.

Netarsudil 24 Hour IOP: PILOT STUDY DESIGN

A double-masked, randomized, single-center, placebo-controlled study comparing the **nocturnal and diurnal IOP-lowering effect of netarsudil** ophthalmic solution 0.02% **in habitual positions over a 24-hour period.**

Patients randomized 2:1



PRIMARY Objective:

To evaluate the **ocular hypotensive efficacy of netarsudil** ophthalmic solution 0.02% (Netarsudil) **over a 24-hour period**

Primary Endpoint:
Mean **change** from baseline in **mean nocturnal IOP** *(mean of the 4 nocturnal time points: **9:00 pm, 12:00 am, 3:00am, and 6:00am) at Day 8/Day 9**.*

Netarsudil 24 Hour IOP: STUDY VISITS

Day 1/Day 2

At Center
IOP measured over 24 hours

Randomization
Dose q.d. PM Day 2

Days 3–7

At home

Dose q.d. PM

Day 8/Day 9

At Center
IOP measured over 24 hours

Dose q.d. PM Day 8
Exit study

Day 2–Day 7: Study drugs self-administered as 1 drop in each eye, once daily between 8:00 PM and 10:00 PM.

Day 8: Study center personnel administered final evening dose.

Netarsudil 24 Hour IOP: STUDY ENVIRONMENT

Habitual Position

- **Nocturnal hours measured supine**
- **Diurnal hours measured seated**

IOP measurements taken by Perkins Tonometer

Netarsudil 24 Hour IOP: PATIENT ELIGIBILITY

Main Inclusion Criteria

- 18 years of age or greater
- Diagnosis of OAG or OHT in both eyes (OAG in one eye and OHT in the fellow eye acceptable).
- Unmedicated (post-washout) IOP > 17 mmHg in one or both eyes and < 30 mmHg in both eyes at Qualification Visit.

Netarsudil 24 Hour IOP: PATIENT ELIGIBILITY

Main Exclusion Criteria

- Glaucoma: pseudoexfoliation or pigment dispersion component, history of angle closure, or narrow angles.
- IOP ≥ 30 mmHg at the Qualification Visit.
- Use of more than 2 ocular hypotensive medications within 30 days of screening. Note: fixed dose combinations count as 2 medications.
- Known hyper-sensitivity to any component of the test formulations or to medications used routinely during a clinical eye examination, such as topical anesthetics.
- Previous glaucoma intraocular surgery or glaucoma laser procedures in the study eye(s).

Netarsudil 24 Hour IOP: DEMOGRAPHICS

8 patients in Netarsudil group; 4 patients in Placebo group	
Age (yrs)	**Number (Proportion)**
64.4 ± 8.58, 47 – 75	
> 65	4 (33.3%)
≥ 65 years old	8 (66.7%)
Gender	
Male	6 (50.0%)
Female	6 (50.0%)
Ethnicity, n (%)	
Hispanic or Latino	2 (16.7%)
Not Hispanic or Latino	10 (83.3%)
Race, n (%)	
White	3 (25.0%)
Black/African American	9 (75.0%)
Asian	0 (0.0%)
Multiple	0 (0.0%)
Iris Color (study eye), n (%)	
Brown/Black	12 (100.0%)
Blue/Grey/Green, Hazel, Other	0 (0.0%)

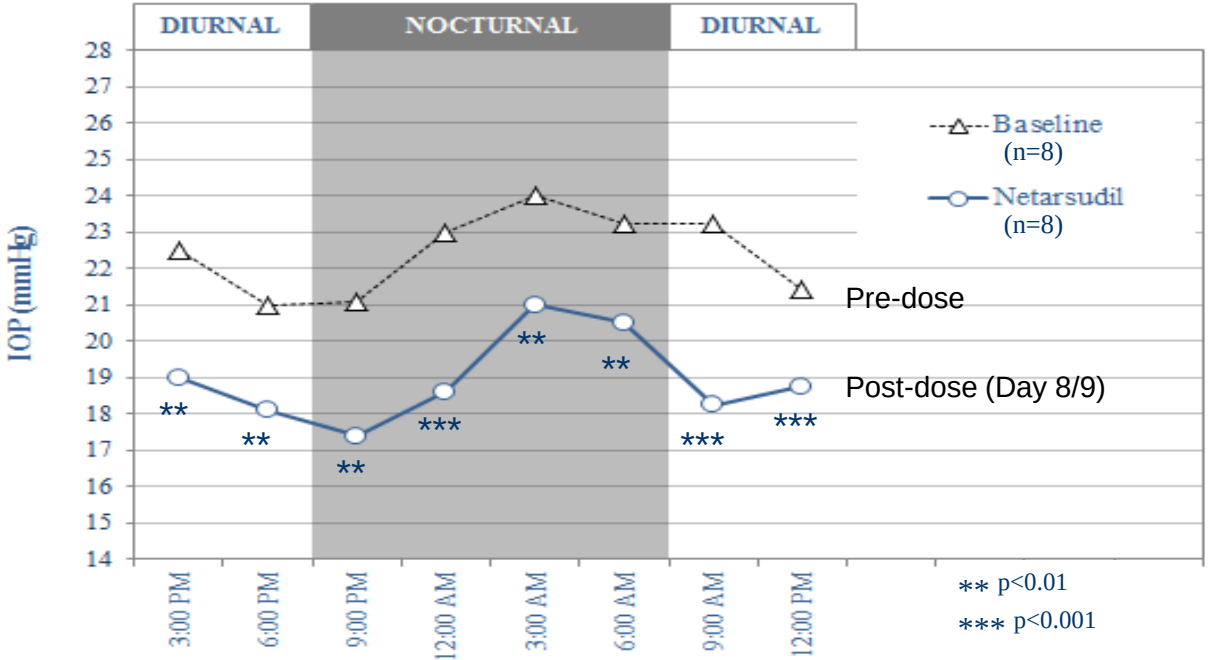
Netarsudil 24 Hour IOP: BASELINE CHARACTERISTICS

Study Eye Diagnosis n (%)	
Ocular Hypertension	1 (8.3%)
Open Angle Glaucoma	11 (91.7%)
Time Since Current Diagnosis (weeks)	
Mean ± SD	387 ± 310
Time on Current Hypotensive Therapy (weeks)	
Mean ± SD	62 ± 110

Netarsudil 24 Hour IOP: BASELINE CHARACTERISTICS

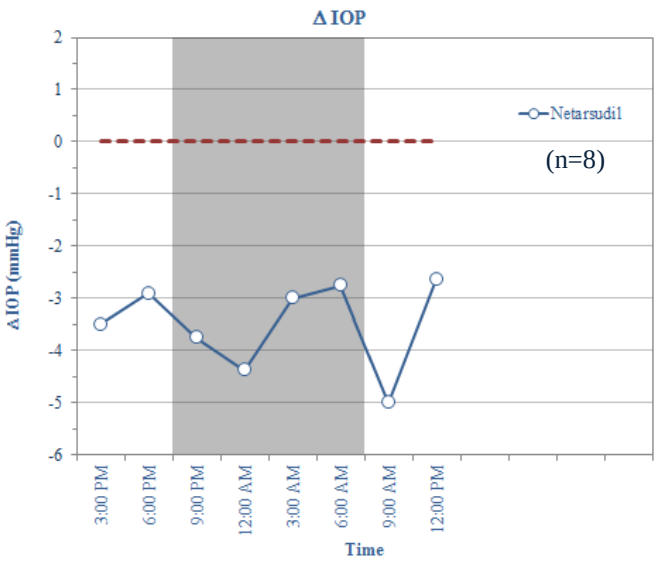
IOP Study Eye (mmHg)	Mean ± SD
Screening	18.0 ± 2.8
Mean Nocturnal	23.1 ± 2.1
Mean Diurnal	22.1 ± 1.7
Mean 24-hour	22.6 ± 1.8
Central Corneal Thickness (µm)	
Study Eye	540.3 ± 29.4
Fellow Eye	541.1 ± 28.0
Cup to Disc Ratio	
Study Eye	0.55 ± 0.07
Fellow Eye	0.55 ± 0.07
Visual Field Mean Deviation (dB)	
Study Eye	-0.64 ± 3.04
Fellow Eye	-1.12 ± 3.78

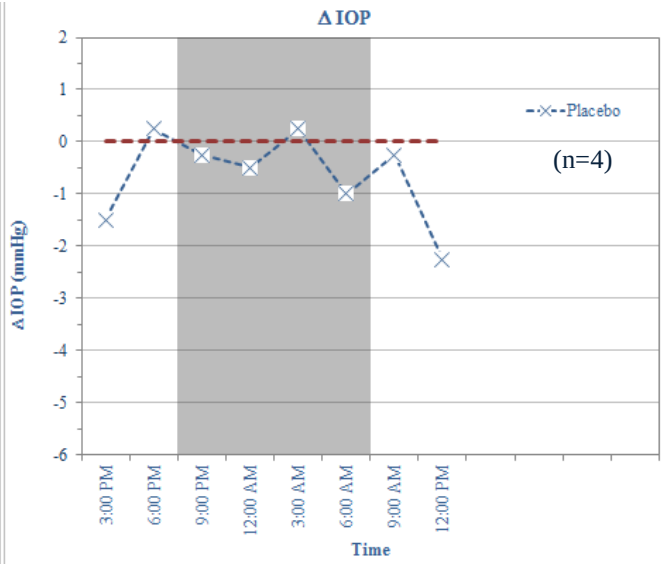
Netarsudil 24 Hour IOP: ITT POPULATION



- Netarsudil equally effective during diurnal and nocturnal periods
- No reported AEs

Netarsudil 24 Hour IOP: ITT POPULATION





Netarsudil change from baseline IOP similar during diurnal and nocturnal periods

Statistically significant vs. baseline at all time points

Netarsudil 24 Hour IOP: RESULTS SUMMARY

(Netarsudil Ophthalmic Solution) 0.02% dosed QD in the evening **met the primary efficacy endpoint** demonstrating a statistical significant **mean change from baseline of 3.5 mmHg** in mean nocturnal IOP ($p<0.05$)

Netarsudil mean change from baseline IOP was **consistent during diurnal and nocturnal periods (-3.5 mmHg vs -3.5 mmHg respectively)**

Netarsudil 24 Hour IOP: CONCLUSION

- IOP goes up at night when pressure is not routinely monitored
- One goal for new ocular hypotensive medications should be to provide sustained IOP reduction during nocturnal + diurnal periods
- Netarsudil maintained consistent IOP reduction throughout the 24-hour period
- Recommend a larger confirmatory study