AR-13324-CS208 Japan Phase 2 Study Topline Results

November 6, 2019

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Japan Phase 2 Executive Summary

- 28-day prospective, double-masked, placebo-controlled, dose-ranging study of netarsudil efficacy and safety in Japanese subjects with open-angle glaucoma (OAG) or ocular hypertension (OHT)
- Netarsudil 0.01%, 0.02% and 0.04% were efficacious and met primary endpoint of superiority to placebo in mean diurnal IOP at Week 4[1]
  - Baseline mean diurnal IOPs 20-21 mmHg across study arms[2] (Japanese IOPs ~3 – 4 mmHg lower than in Caucasians)
  - Week 4 mean diurnal IOP was 16.3 (-4.1), 15.4 (-4.8), 16.2 (-4.8) and 19.3 (-1.7) mmHg in the netarsudil 0.01%, 0.02%, 0.04%, and placebo groups, respectively[2]
- Netarsudil 0.01%, 0.02% and 0.04% were safe and generally well tolerated in Japanese subjects
  - No serious adverse events
- Netarsudil 0.02% provided optimal efficacy and safety profile
  - Most common AEs were Conjunctival Hyperemia (37.0%) and Eye Irritation (9.3%)
  - Discontinuations rate was 1.9% (1/54 subjects)
  - Hyperemia and discontinuation rates lower than in US trials[3-5]

1. ANCOVA with MCMC imputation. 2. Observed data. 3. Bacharach J, et al. Ophthalmology. 2015 Feb;122(2):302-7. 4. Serle JB, et al. Am J Ophthalmol. 2018 Feb;186:116-127. 5. Khouri AS, et al. Am J Ophthalmol. 2019 Aug;204:97-104.

Study Design

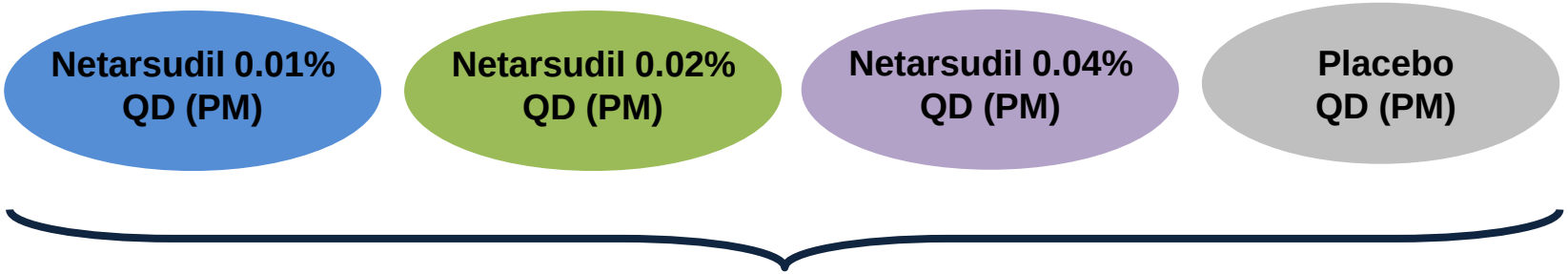
Japanese patients with

Open Angle Glaucoma (OAG) with IOP (unmedicated) ≥ 15 mmHg and < 35 mmHg

or

Ocular Hypertension (OHT) with IOP (unmedicated) ≥ 22 mmHg and < 35 mmHg

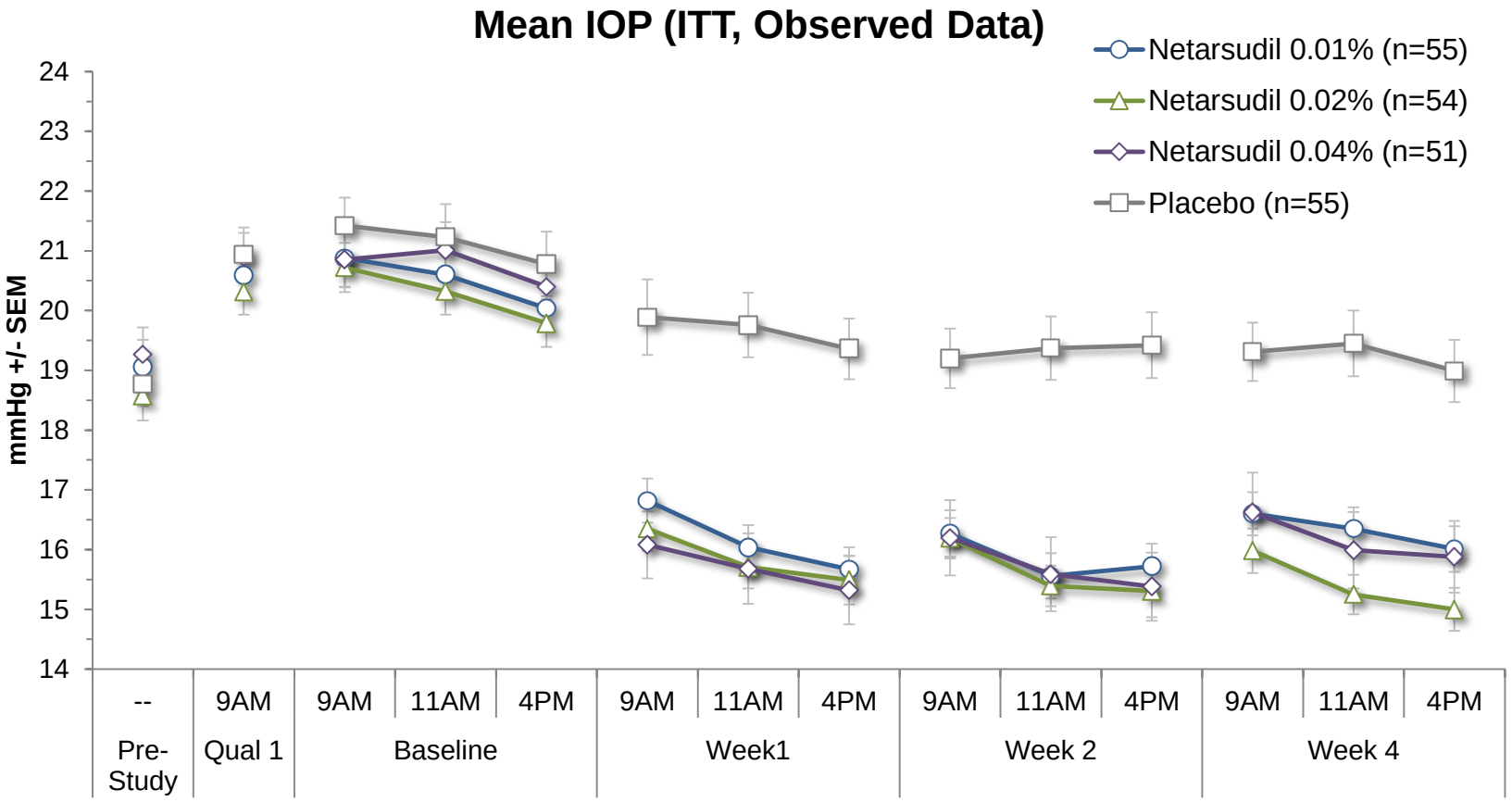
N = 215 subjects randomized (1:1:1:1)



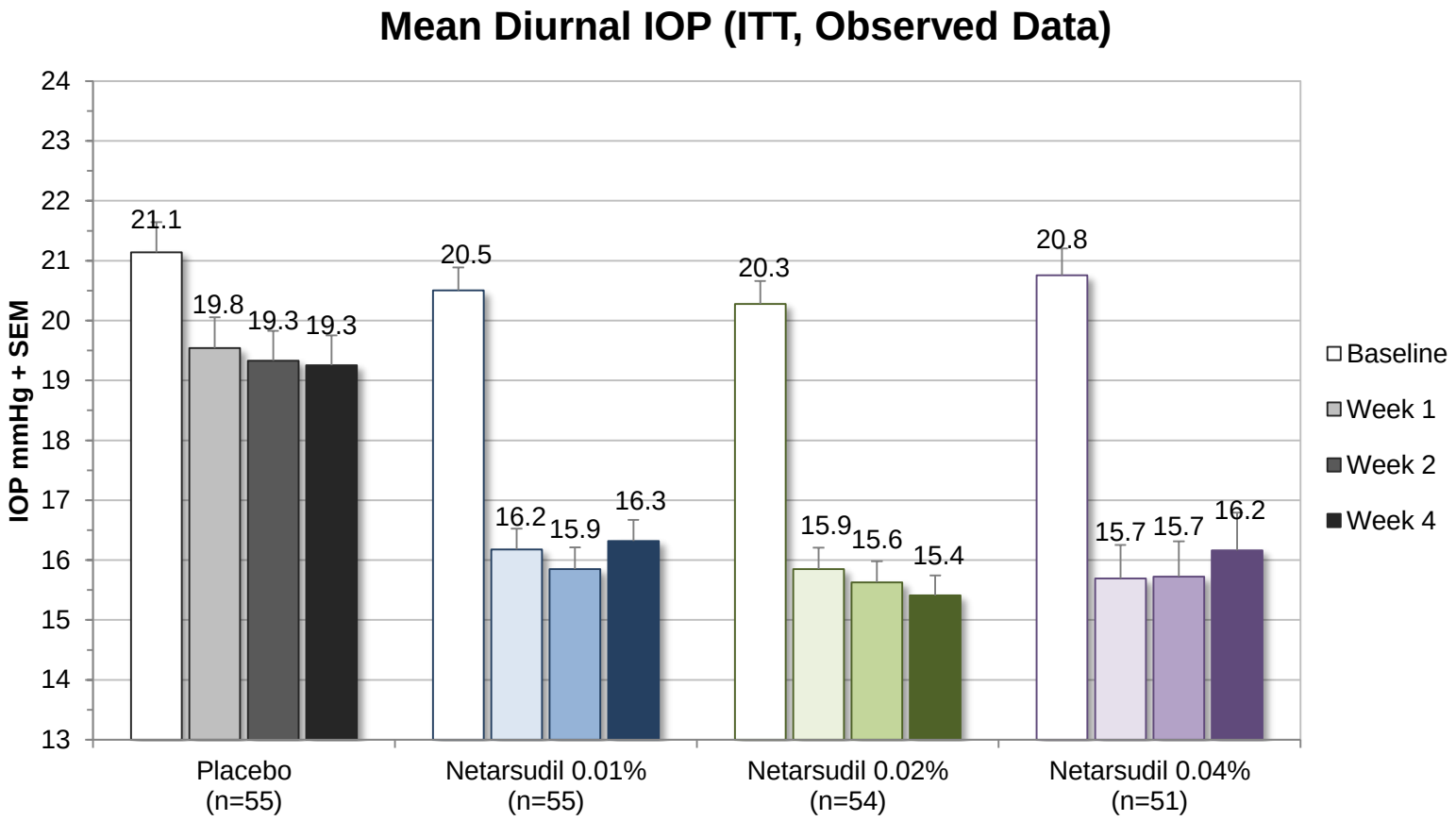
Primary Endpoints

- Efficacy: Mean diurnal IOP at Week 4
- Safety: Ocular/Systemic safety during a 4-week treatment period

Efficacy – Mean IOP at Each Time Point



Primary Endpoint – Mean Diurnal IOP



- P<0.0001 vs. placebo at Week 4 for all dose levels[1]
- 0.02% achieved lowest mean diurnal IOP at Week 4

1. ANCOVA with MCMC imputation

Safety Summary

- There were no serious adverse events
- 6 of 215 subjects (1 each in netarsudil 0.01% and 0.02%, and 4 in netarsudil 0.04%) had early discontinuation due to an AE

Any TEAEs ≥ 2% System Organ Class Preferred Term	Netarsudil 0.01% QD (N=55) n (%)	Netarsudil 0.02% QD (N=54) n (%)	Netarsudil 0.04% QD (N=51) n (%)	Placebo (N=55) n (%)
Eye Disorders	16 (29.1)	22 (40.7)	32 (62.7)	3 (5.5)
Conjunctival hyperemia	13 (23.6)	20 (37.0)	29 (56.9)	1 (1.8)
Eye irritation	3 (5.5)	5 (9.3)	2 (3.9)	0
Conjunctival hemorrhage	0	3 (5.6)	3 (5.9)	0
Eye discharge	1 (1.8)	1 (1.9)	1 (2.0)	0
Vision blurred	1 (1.8)	1 (1.9)	1 (2.0)	0
Visual acuity reduced	0	1 (1.9)	1 (2.0)	0
Conjunctival follicles	0	0	1 (2.0)	0
Dry eye	0	0	1 (2.0)	0
Eye pain	0	0	1 (2.0)	0
Keratitis	0	0	1 (2.0)	0
Vernal keratoconjunctivitis	0	0	1 (2.0)	0
General disorders/admin site conditions	0	2 (3.7)	1 (2.0)	0
Instillation site irritation	0	1 (1.9)	1 (2.0)	0
Infections and Infestations	1 (1.8)	0	2 (3.9)	0
Conjunctivitis	1 (1.8)	0	2 (3.9)	0

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- Efficacy at low baseline IOPs predicts efficacy in Normal Tension Glaucoma
- Meeting with PMDA in 1H'20 and expect start of P3 trials in 2H '20

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