A Phase 3, Randomized, Double-blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Eptinezumab for the Preventive Treatment of Chronic Migraine: Results of the PROMISE-2 (PRevention Of Migraine via Intravenous eptinezumab Safety and Efficacy–2) Trial

Richard B. Lipton,[1] Joel Saper,[2] Messoud Ashina,[3] David Biondi,[4] Suman Bhattacharya,[4] Joe Hirman,[5] Barbara Schaeffler,[4] Roger Cady[4]

[1]Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, NY; [2]Michigan Headache & Neurological Institute, Ann Arbor, MI; [3]Faculty of Health and Medical Sciences, University of Copenhagen, Denmark; [4]Alder BioPharmaceuticals, Inc., Bothell, WA; [5]Pacific Northwest Statistical Consulting, Inc., Woodinville, WA

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Disclosures

R.B. Lipton: Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, Biovision, Boston Scientific, Dr Reddy's Laboratories, electroCore, Eli Lilly, eNeura, GSK, Headache, MSD, National Institute of Neurological Disorders and Stroke, National Institute on Aging, Neurology, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta

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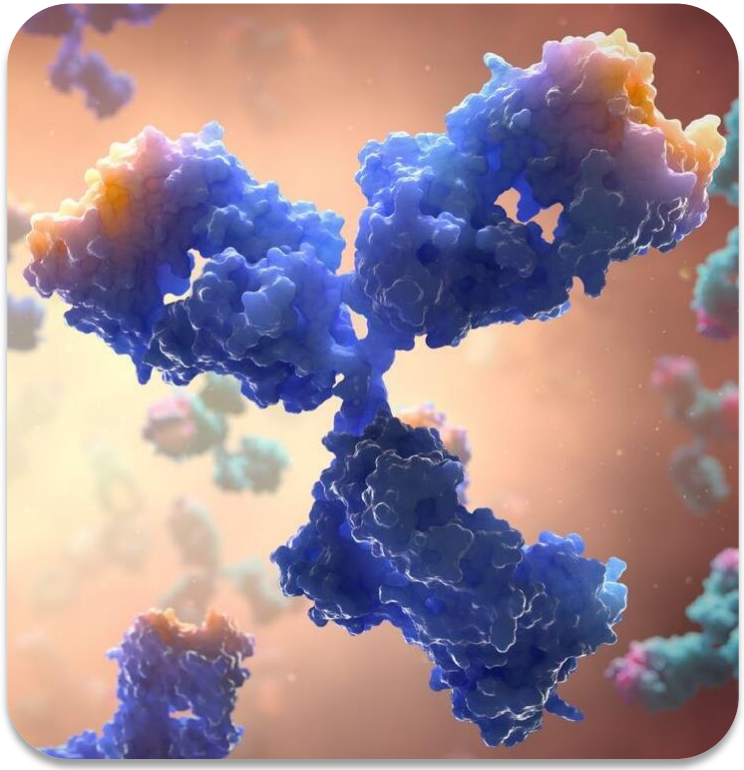
D. Biondi, S. Bhattacharya, J. Hirman, B. Schaeffler, and **R. Cady:** Alder

Eptinezumab (ALD403)
An Anti-CGRP Monoclonal Antibody

- Humanized, IgG1, anti-CGRP monoclonal antibody[1]
  - Selectively and potently inhibits CGRP biological activity
- 5-pM binding affinity for CGRP
- N-glycosylation site mutation to eliminate ADCC/CDC
- Persistent molecular activity ($t_{1/2}$ ~30 days)
- 100% bioavailability when administered by iv infusion
- Quarterly dosing schedule
- Eptinezumab was efficacious and well tolerated in
  - Phase 2 studies in episodic[2] and chronic[3] migraine
  - Phase 3 study in episodic migraine[4]



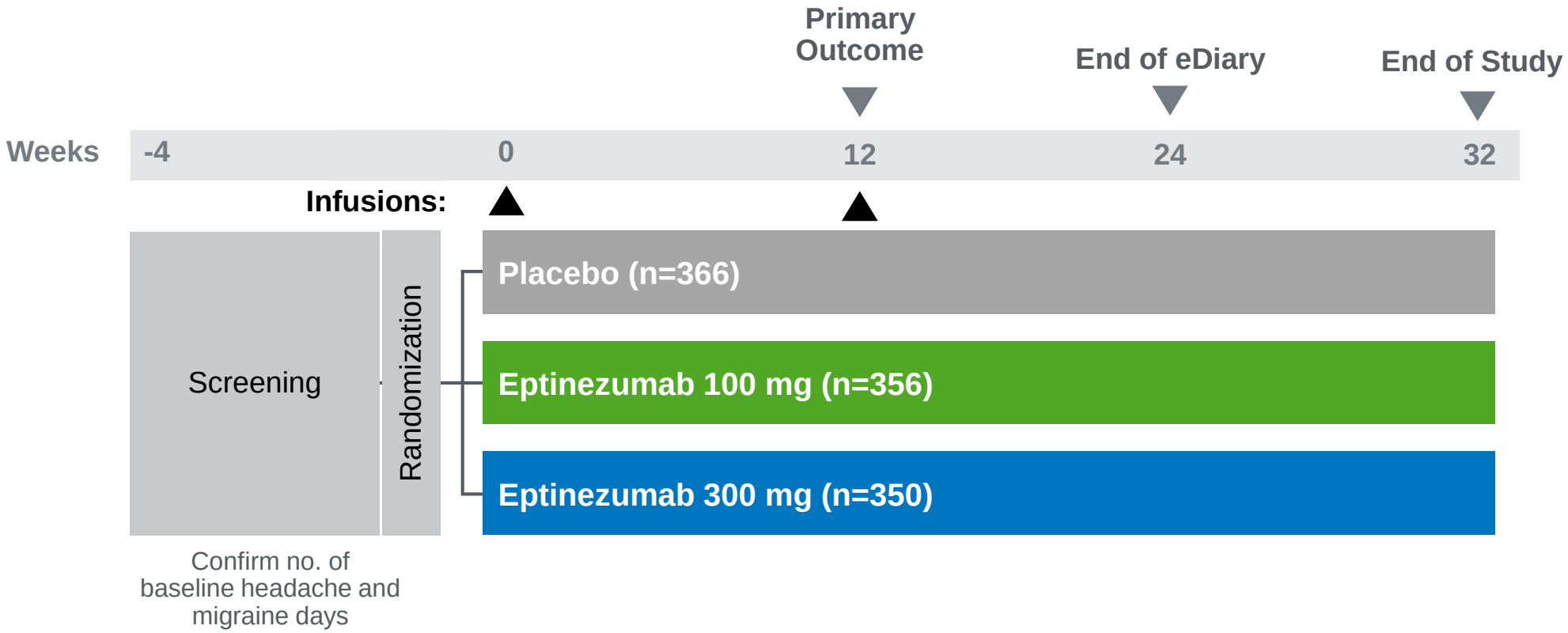
Eptinezumab

ADCC, antibody-dependent cell-mediated cytotoxicity; CDC, cell-dependent cytotoxicity.

1. Baker B, et al. AAN 2017, abstr P2.155; 2. Dodick DW, et al. *Lancet Neurol*. 2016;15:382-90; 3. Smith J, et al. AAN 2017, abstr S52.033. 4. Saper J, et al. AAN 2018, abstr 1356;

Eptinezumab Chronic Migraine Study Design (N=1072) Phase 3 PROMISE-2*

- Patient population: male or female aged 18–65 years, with migraine diagnosis at age ≤50 years (ICHD III beta), migraine history ≥1 year, and ≥15 to ≤26 headache days of which at ≥8 assessed as migraine days during 28-day screening period



*NCT02974153.

Efficacy Endpoints

Primary Endpoint	Mean change from baseline in monthly migraine days	Weeks 1–12
Key Secondary Endpoints	≥75% migraine responder rates*	Weeks 1–4
	≥50% migraine responder rates* ≥75% migraine responder rates*	Weeks 1–12
	% of subjects experiencing migraine	Day 1 postdose

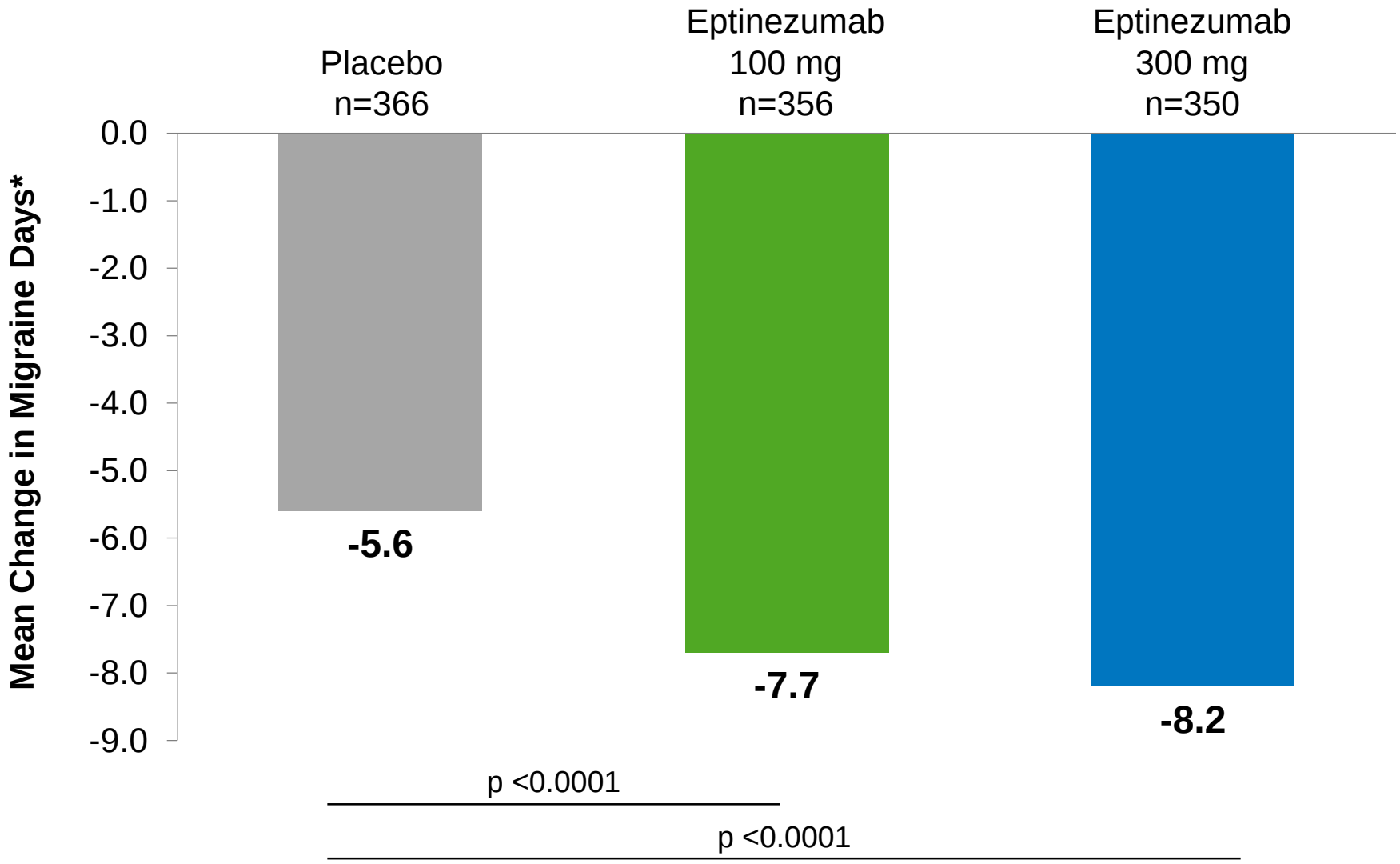
*Responder rate, percent of subjects with migraine response

Baseline Characteristics and Demographics Well Balanced Across Treatment Groups

	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg
Subjects, n	**366**	**356**	**350**
Mean age, year (SD)	39.6 (11.3)	41.0 (11.7)	41.0 (10.4)
Mean BMI, kg/m^2 (SD)	27.0 (5.6)	26.4 (5.0)	26.3 (5.0)
Female, %	89	86	90
Mean years from migraine diagnosis	17.0	18.3	19.0
Mean duration of chronic migraine, year (SD)	11.6 (11.0)	11.6 (12.0)	12.3 (11.2)
Patients with ≥1 prophylactic medication, n (%)	46 (13)	45 (13)	59 (17)
Mean migraine days/month (SD)	16.2 (4.6)	16.1 (4.6)	16.1 (4.8)
Mean headache days/month (SD)	20.4 (3.0)	20.4 (3.1)	20.6 (3.2)
Mean triptan/ergotamine days (SD)*	6.2 (6.7)	6.6 (6.9)	6.7 (6.5)

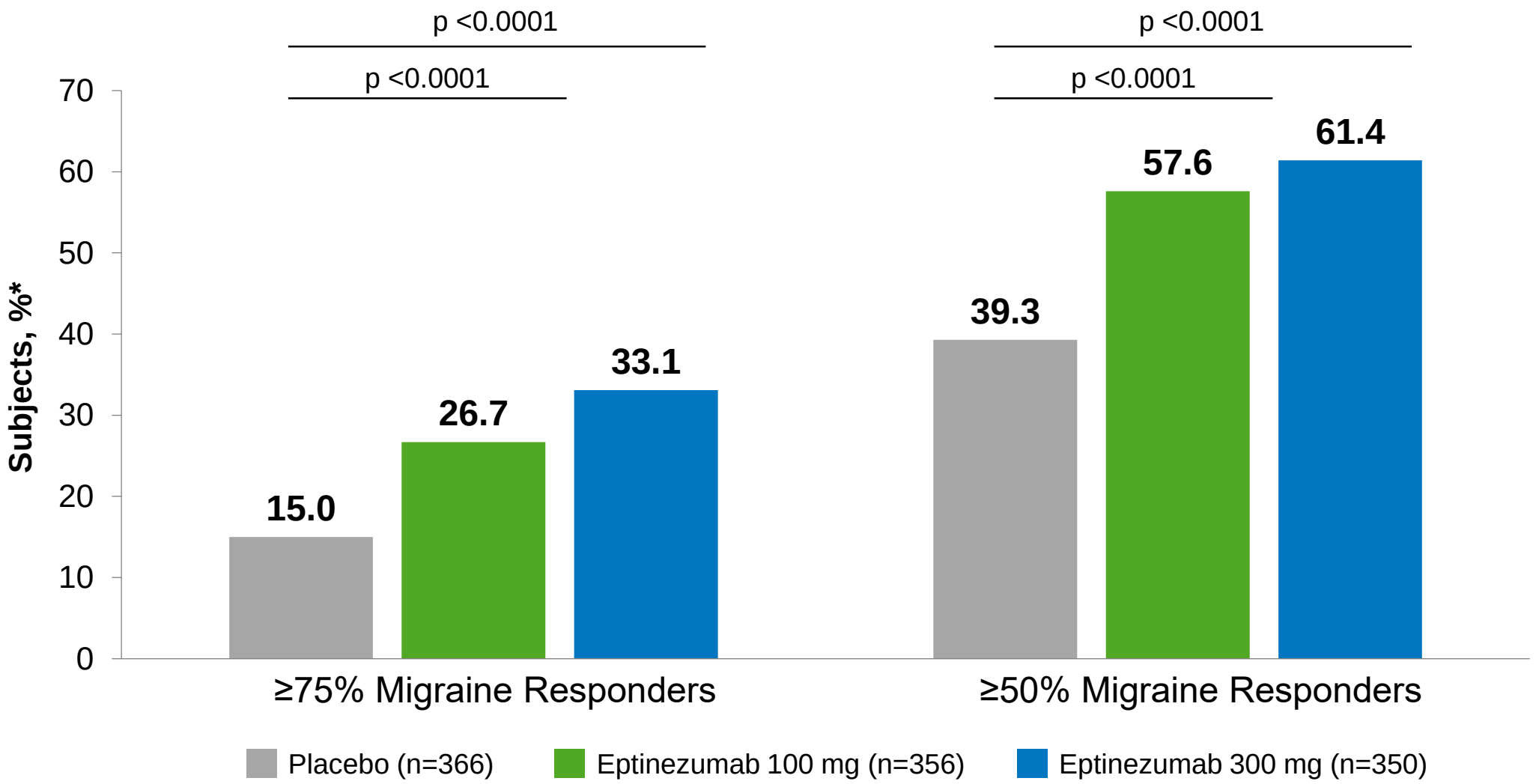
*Days with triptan or ergotamine use as recorded in eDiary averaged over 28-day screening period.

Primary Endpoint
Eptinezumab Significantly Decreased Monthly Migraine Days: Weeks 1–12



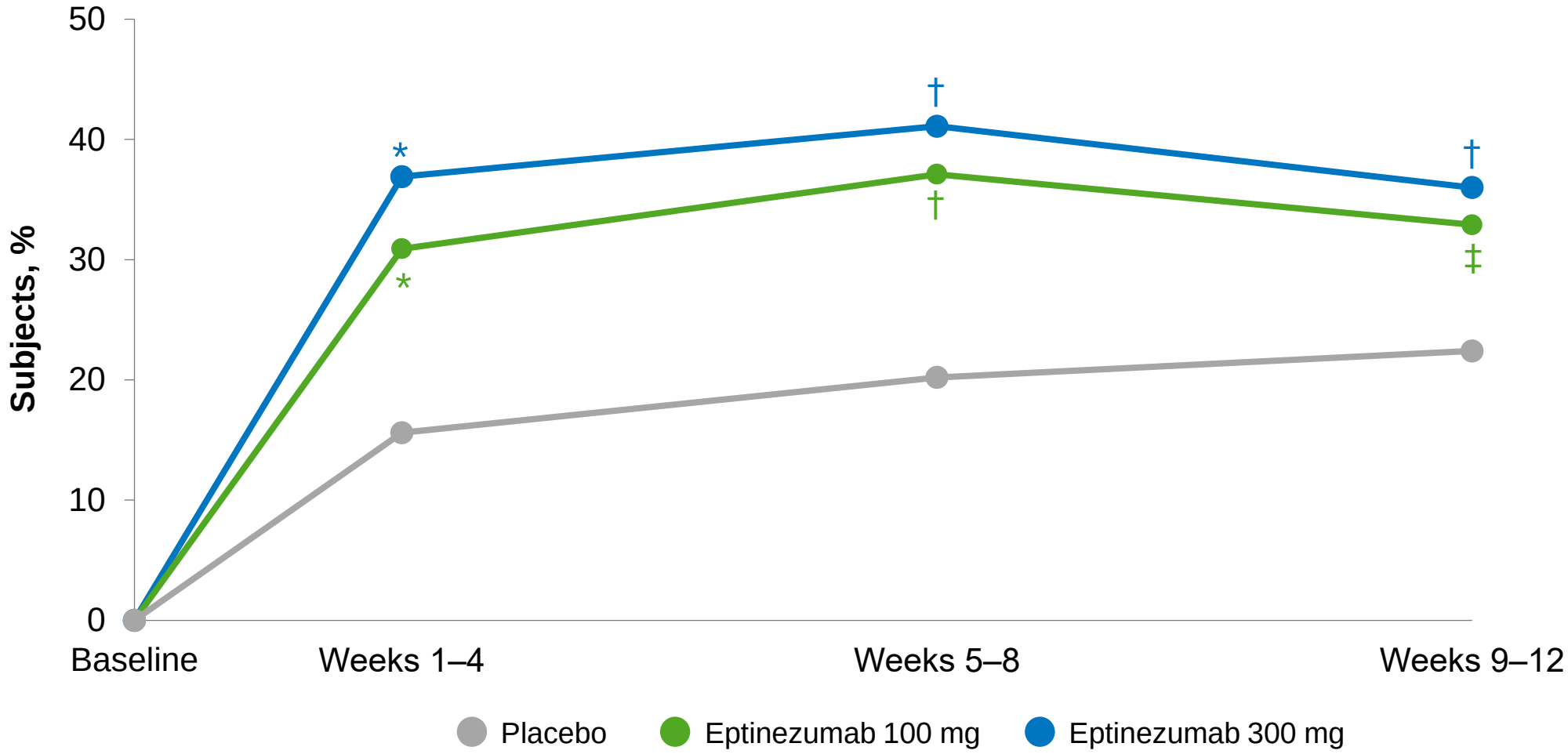
*Analysis of covariance model used to test for differences between treatment groups.

Key Secondary Endpoint
≥75% and ≥50% Migraine Responder Rates: Weeks 1–12



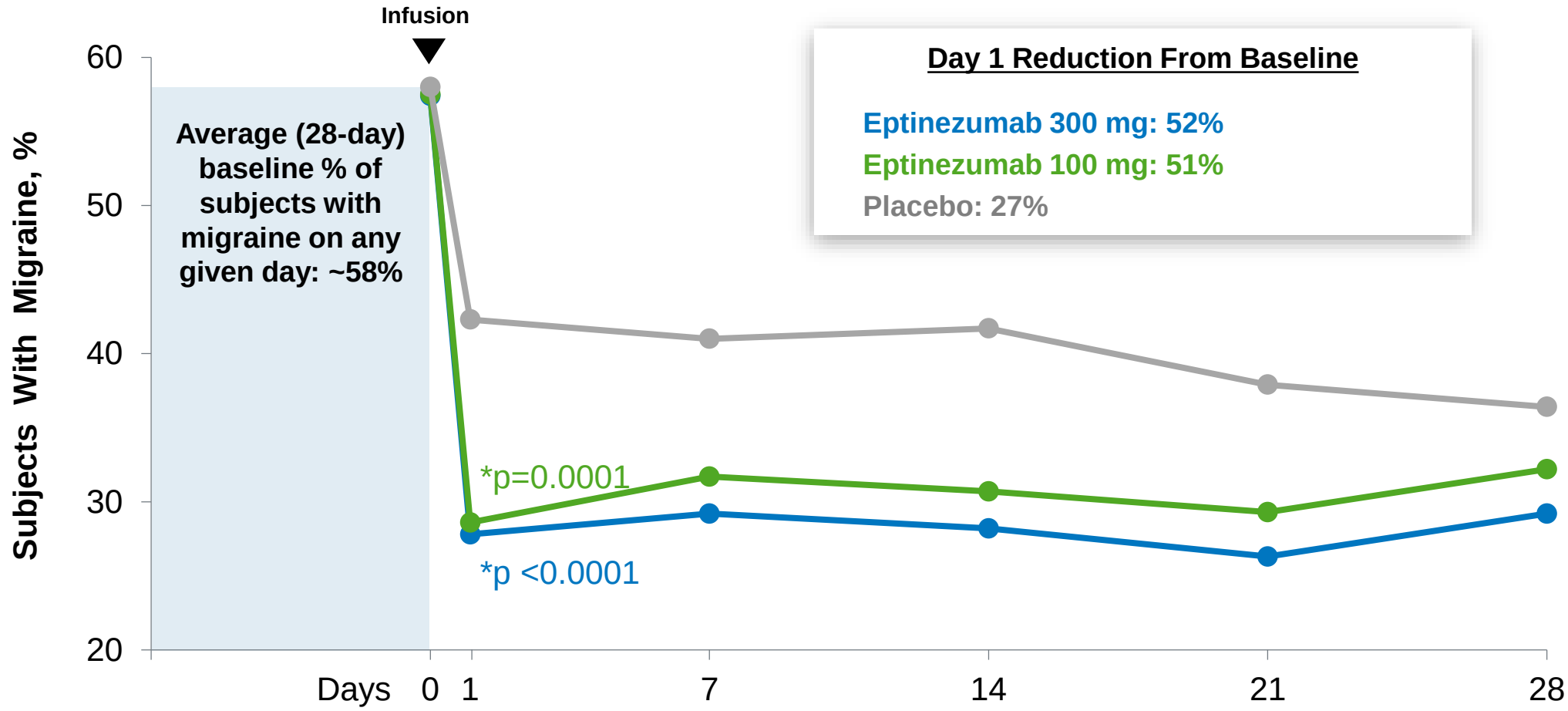
*Cochran–Mantel–Haenszel test used for statistical analysis.

Monthly ≥75% Migraine Responder Rates Following a Single Infusion



*p <0.0001 vs placebo; †p<0.0001, ‡p<0.002 vs placebo (post hoc), a CMH test was used for statistical analysis

Day 1 Reductions From Baseline in % of Subjects With a Migraine



- On Day 1 following eptinezumab infusion, migraine risk was reduced by 52%

*Day 1 % of subjects with migraine between eptinezumab and placebo groups.

Safety Profile: Safety Population

Subjects, n (%)	Placebo n=366	Eptinezumab 100 mg n=356	Eptinezumab 300 mg n=350
Any TEAE	144 (39)	136 (38)	155 (44)
Any serious TEAE*	3 (<1)	3 (<1)	3 (<1)
Any AE leading to drug withdrawal	2 (<1)	2 (<1)	8 (2.3)
Most frequent AEs†			
Nasopharyngitis	15 (4)	13 (4)	22 (6)
Nausea	6 (2)	6 (2)	12 (3)
Upper respiratory tract infection	16 (4)	11 (3)	14 (4)
Urinary tract infection	6 (2)	7 (2)	11 (3)
Arthralgia	3 (<1)	3 (<1)	8 (2)
Dizziness	4 (1)	5 (1)	9 (3)
Anxiety	0	4 (1)	7 (2)
Fatigue	4 (1)	7 (2)	6 (2)

*All serious TEAEs judged unrelated to study drug; †≥2% in any treatment group.

Conclusions

- Eptinezumab-treated subjects showed significant improvements in migraine activity across the primary and all key secondary endpoints
- Eptinezumab 300mg subjects experienced significantly fewer days with migraine
  - Over 33% of subjects achieved a ≥75% reduction in monthly migraine days
  - Over 61% achieved a ≥50% reduction in monthly migraine days
- The % of subjects with a migraine on the first day after eptinezumab infusion dropped by >50% compared with baseline, and the decrease was sustained through Day 28
  - Reductions from baseline were significantly greater than those observed in the placebo group
- TEAE rates were similar to placebo and the safety profile was consistent with previous eptinezumab studies

Acknowledgment

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