Primary Results of PROMISE-1 (PRevention Of Migraine via Intravenous eptinezumab Safety and Efficacy–1) Trial: a Phase 3, Randomized, Double-blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Eptinezumab for Prevention of Frequent Episodic Migraine

Joel R. Saper,[1] Richard B. Lipton,[2] David B. Kudrow,[3] Joe Hirman,[4] David W. Dodick,[5] Stephen Silberstein,[6] George Chakhava,[7] Jeff Smith[8]

[1]Michigan Headache & Neurological Institute, Ann Arbor, MI; [2]Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, NY; [3]California Medical Clinic for Headache, Harbor-UCLA Medical Center, David Geffen School of Medicine at UCLA, Los Angeles, CA; [4]Pacific Northwest Statistical Consulting, Inc., Woodinville, WA; [5]Mayo Clinic, Phoenix, AZ; [6]Jefferson Headache Center, Philadelphia, PA; [7]Multiprofile Clinic Consilium Medulla, Georgian Association of Medical Specialties, Tbilisi, Georgia; [8]Alder BioPharmaceuticals Limited, Dublin, Ireland

2018 AAN Annual Meeting

Disclosures

J.R. Saper: Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, CoLucid, Dr. Reddy's Laboratories, Eli Lilly, Impax, Migraine Research Foundation, Scion Neuro Stim, Supernus, Teva, Zosano.

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

D.B. Kudrow: Alder, Allergan, Amgen, Biohaven, CoLucid, Ely Lilly, Genentech-Roche, Teva

J. Hirman: Alder (contracted service provider)

D.W. Dodick: Alder, Academy for Continued Healthcare Learning, Acorda, Alcobra, Albert Einstein University, Allergan, American Academy of Neurology, American Headache Society, Amgen, Arteaus, Autonomic Technologies, Biohaven, Bioventric, BMS, Boston Scientific, Canadian Headache Society, Chameleon Communications, Charleston Laboratories, CoLucid, Decision Resources, Dr. Reddy's Laboratories, electroCore, Eli Lilly, eNeura, Epien, Ethicon, GBS/Nocira, Global Scientific Communications, Gore, Haymarket Medical Education, Healint, HealthLogix, Impax, Insys, IntraMed, King-Devick Technologies, Labrys, Lundbeck, Magellan, MAP, Medicom, MedNet, Medscape, Medtronic, MeetingLogiX, Miller Medical, MSD, Myndshft, NeuroAssessment Systems, Novartis, NuPathe, Oregon Health Science Center, Oxford University Press, Patent 17189376.1-1466:vTitle: Botulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis (no compensation), Peer View Institute for Medical Education, Pfizer, Sage Publishing, Second Opinion, St Jude, Starr Clinical, Sun Pharma, Supernus, Synergy, Teva, Theranica, Tonix, Universal Meeting Management, University of Toronto, UptoDate, WebMD, West Virginia University Foundation, Wiley Blackwell, Xenon, Zogenix, Zosano

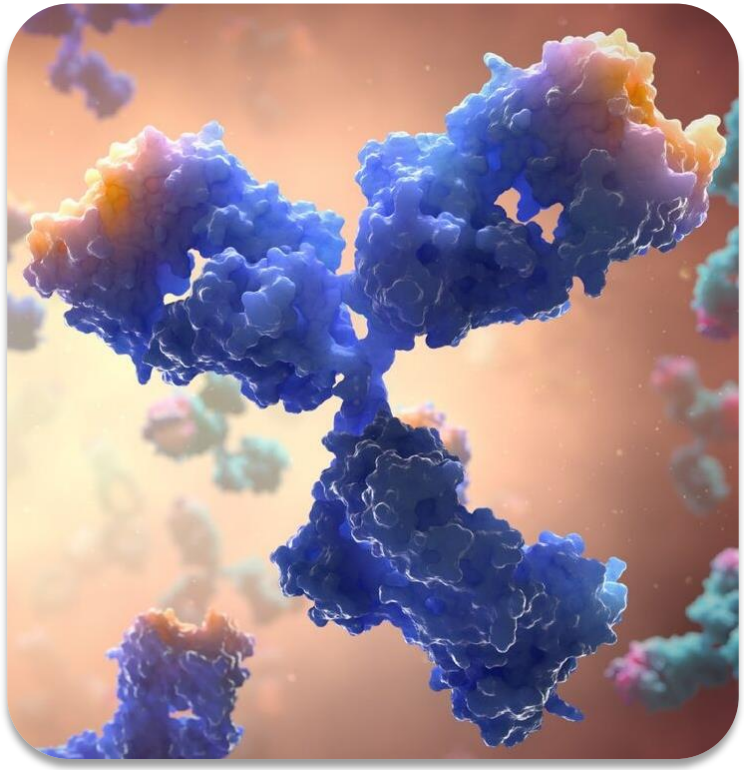
S. Silberstein: Alder, Allergan, Amgen, Avanir, Curelator, Dr. Reddy's Laboratories, eNeura, electroCore, Eli Lilly, Medscape, National Institute of Neurological Disorders and Stroke, Supernus, Teva, Theranica, Trigemina

G. Chakhava: Alder

J. Smith: Alder (full-time employee, founder, and share holder)

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]



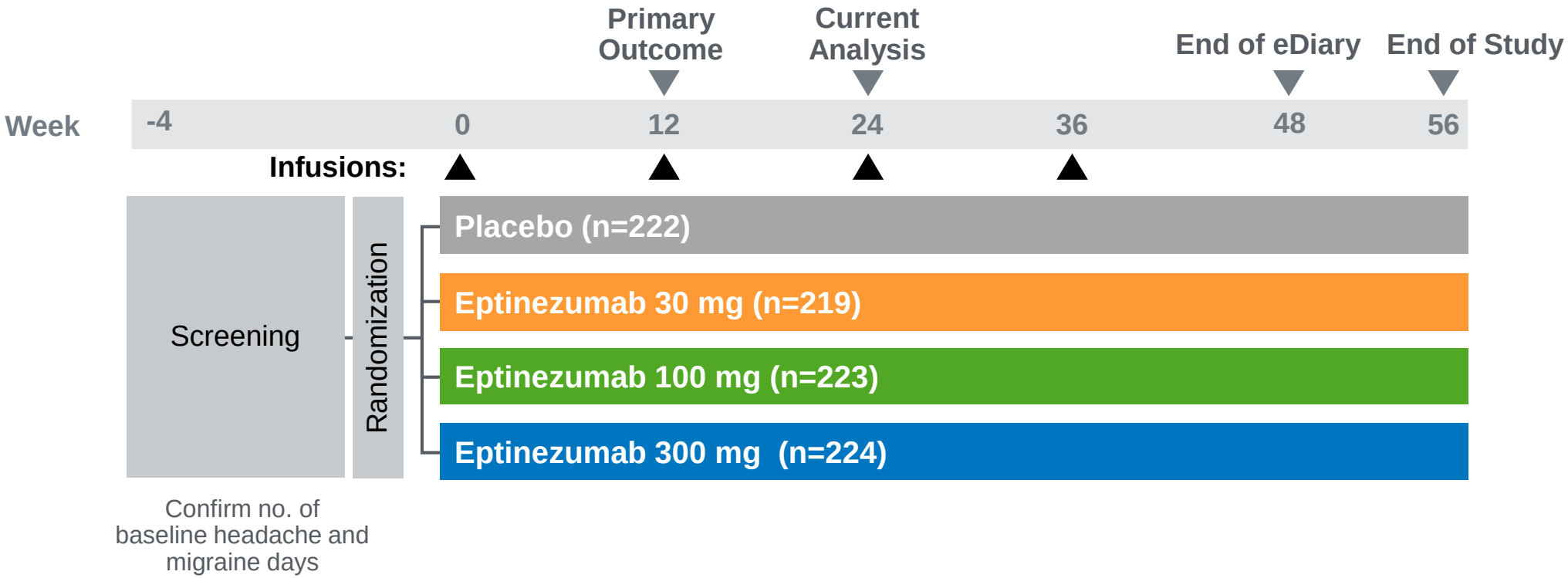
Eptinezumab

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 Episodic Migraine Study Design (N=888) Phase 3 PROMISE-1*

- Subject population: male or female aged 18–75 years, with migraine diagnosis at age ≤50 years (ICHD-II), migraine history ≥12 month at a frequency of ≤14 headache days/month of which 4 must be migraine days



*NCT02559895.

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 a migraine	Day 1 postdose

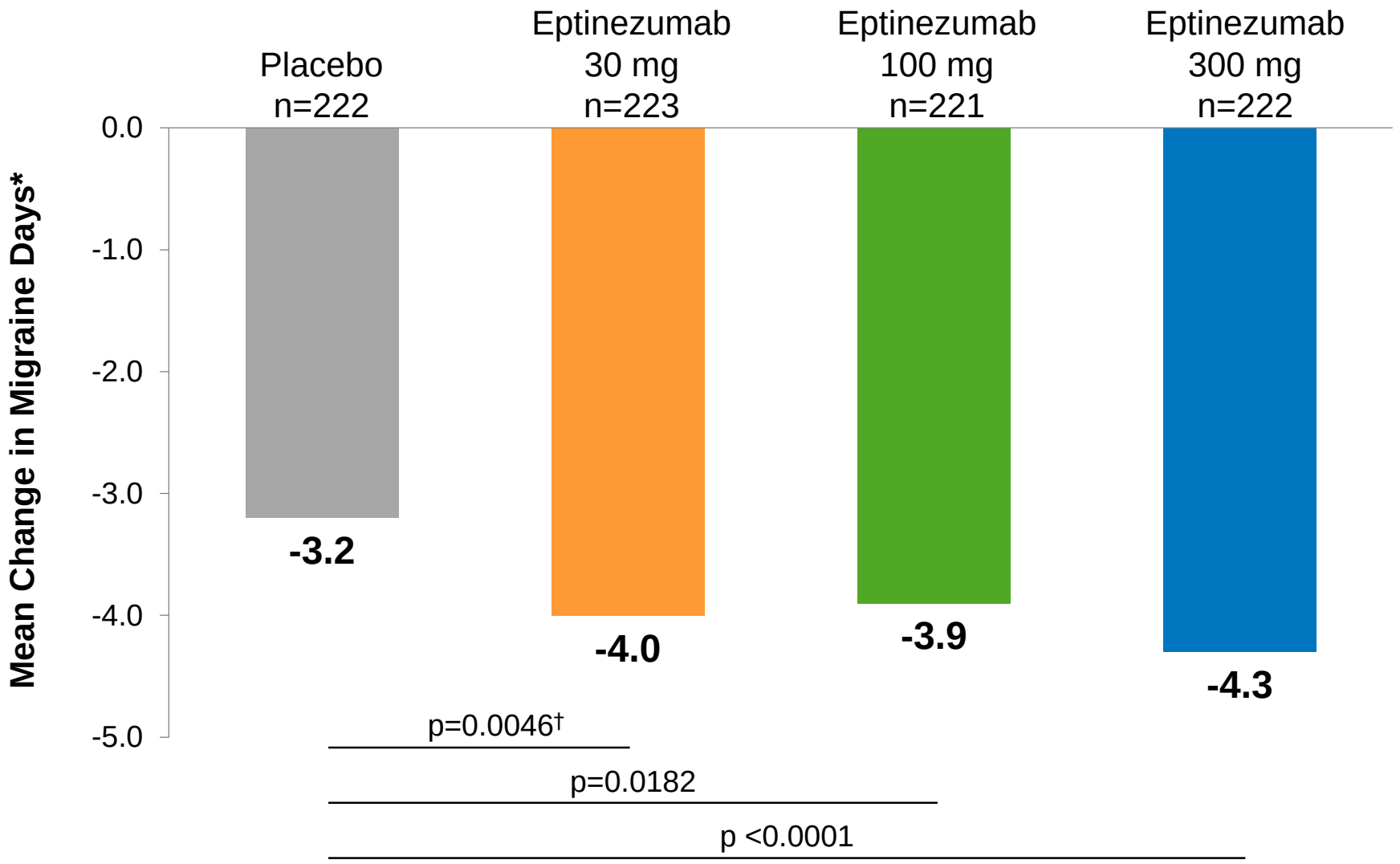
*Responder rate, percent of subjects with migraine response

Baseline Characteristics and Demographics Well Balanced Across Treatment Groups

	Placebo	Eptinezumab		
		30 mg	100 mg	300 mg
Safety population, n	**222**	**219**	**223**	**224**
Mean age, year	39.9	39.1	40.0	40.2
Mean weight, kg	82.4	82.0	82.4	80.2
Female, %	84	85	80	89
Mean years from migraine diagnosis	16.9	17.0	17.4	18.2
Subjects with ≥1 prophylactic medication, n (%)	10 (5)	14 (6)	9 (4)	8 (4)
Efficacy population, n	**222**	**223**	**221**	**222**
Mean migraine days/month	8.4	8.7	8.7	8.6
Mean headache days/month	9.9	10.2	10.0	10.1
Mean triptan/ergotamine days*	1.5	1.4	1.5	1.6

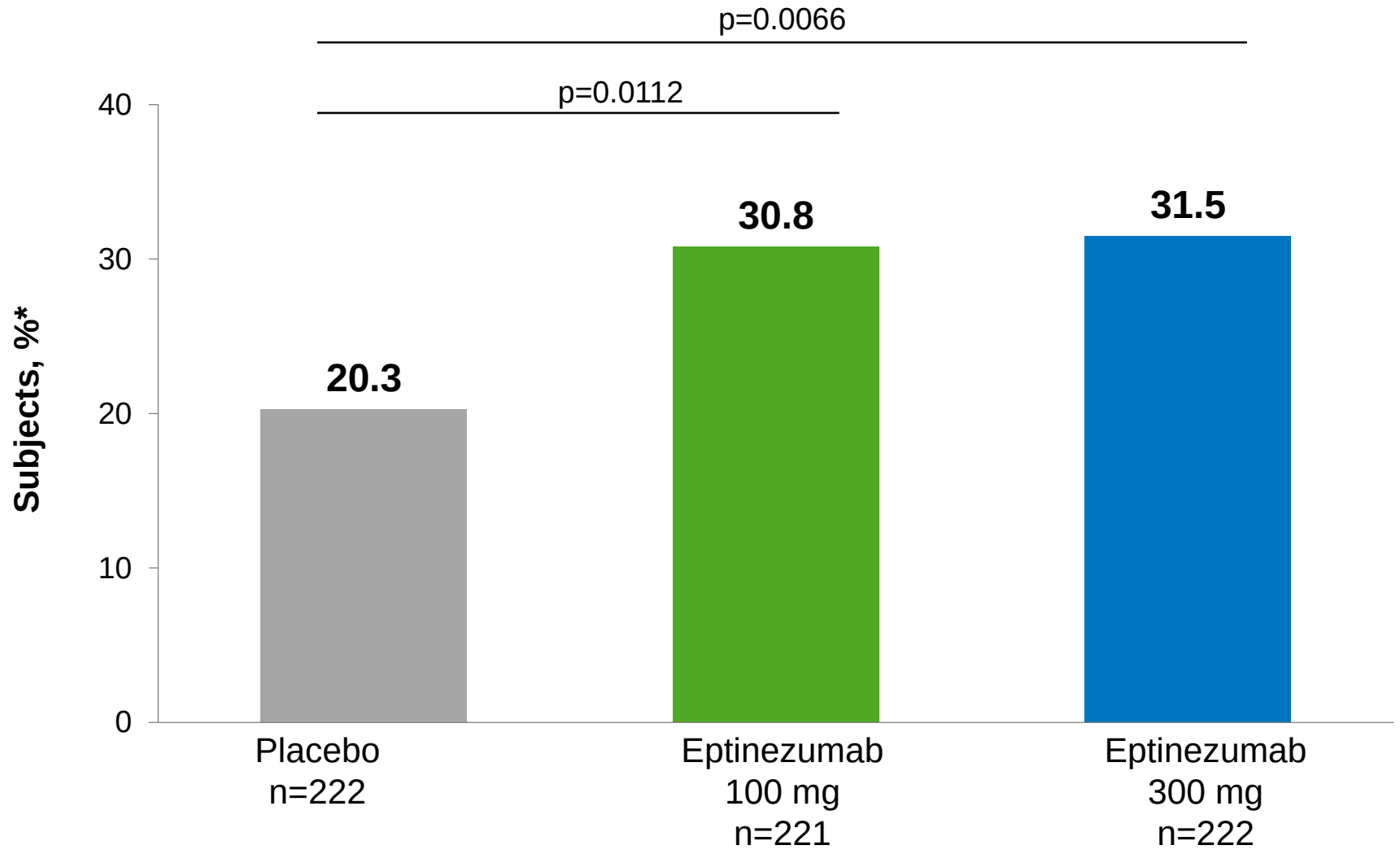
*Days with triptan or ergotamine use as recorded in eDiary averaged over 28-day screening period.

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



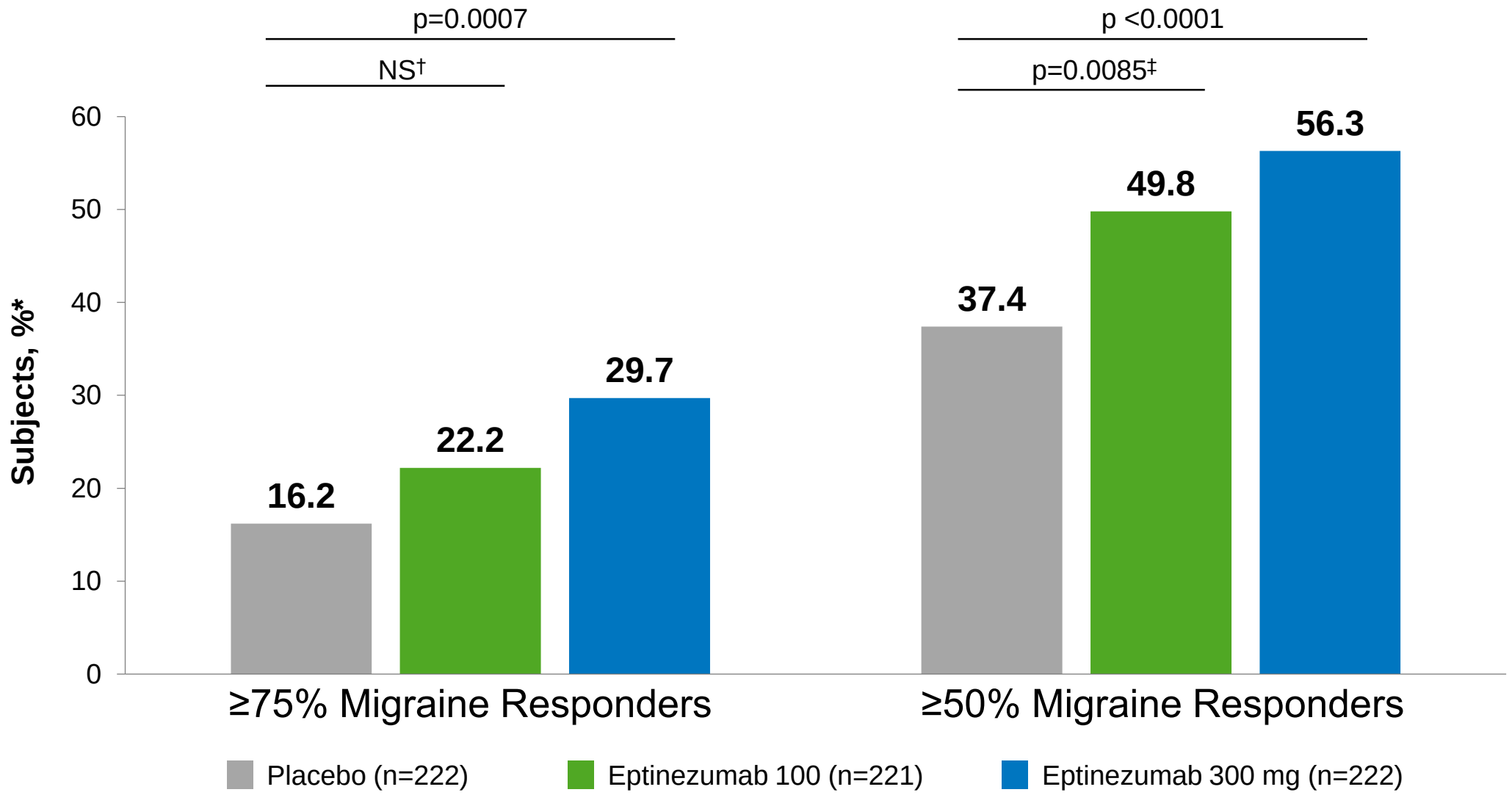
*ANCOVA model used to test for differences between treatment groups., †unadjusted

Key Secondary Endpoint
≥75% Migraine Responder Rate: Weeks 1–4



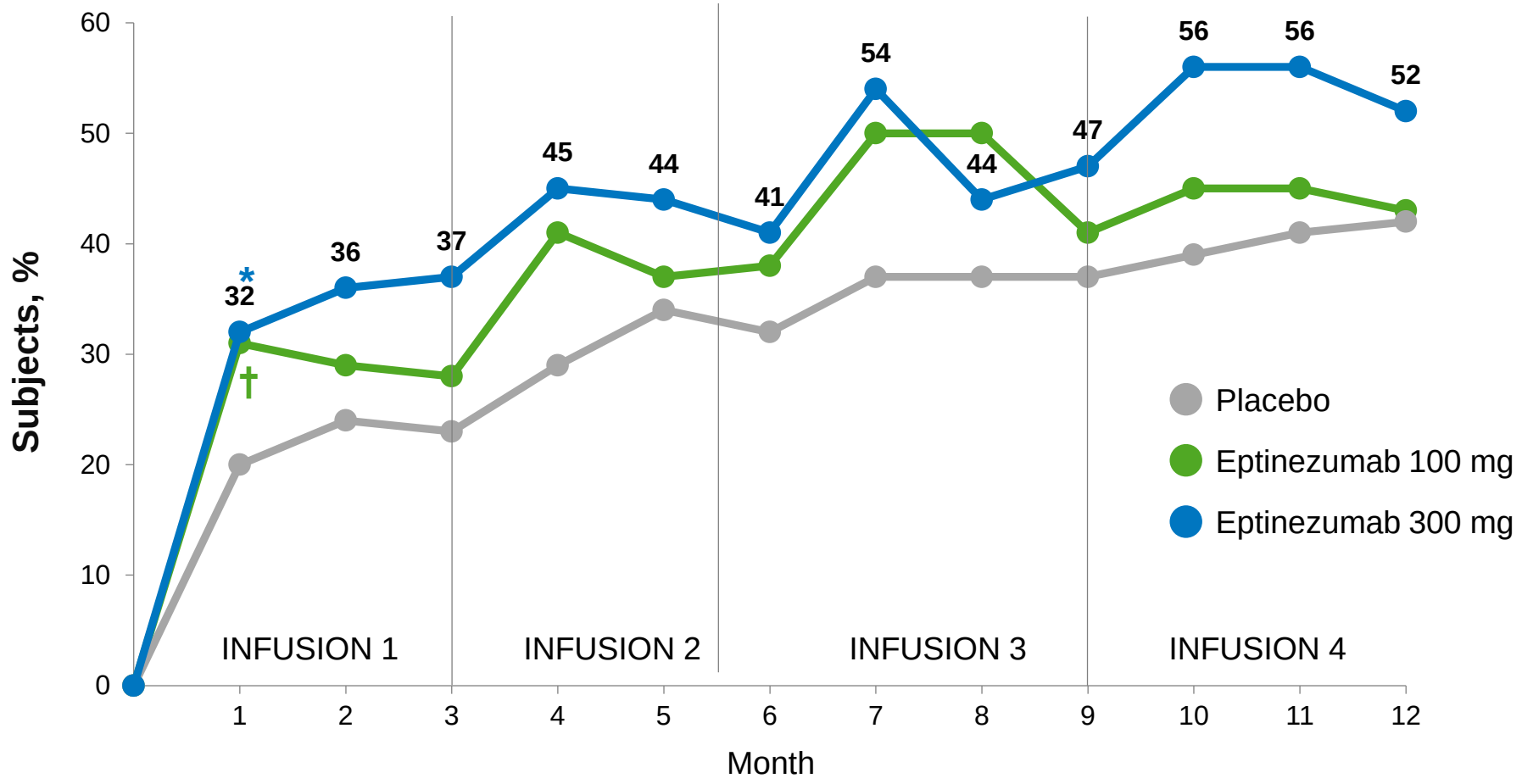
*CMH test used for statistical analysis.

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



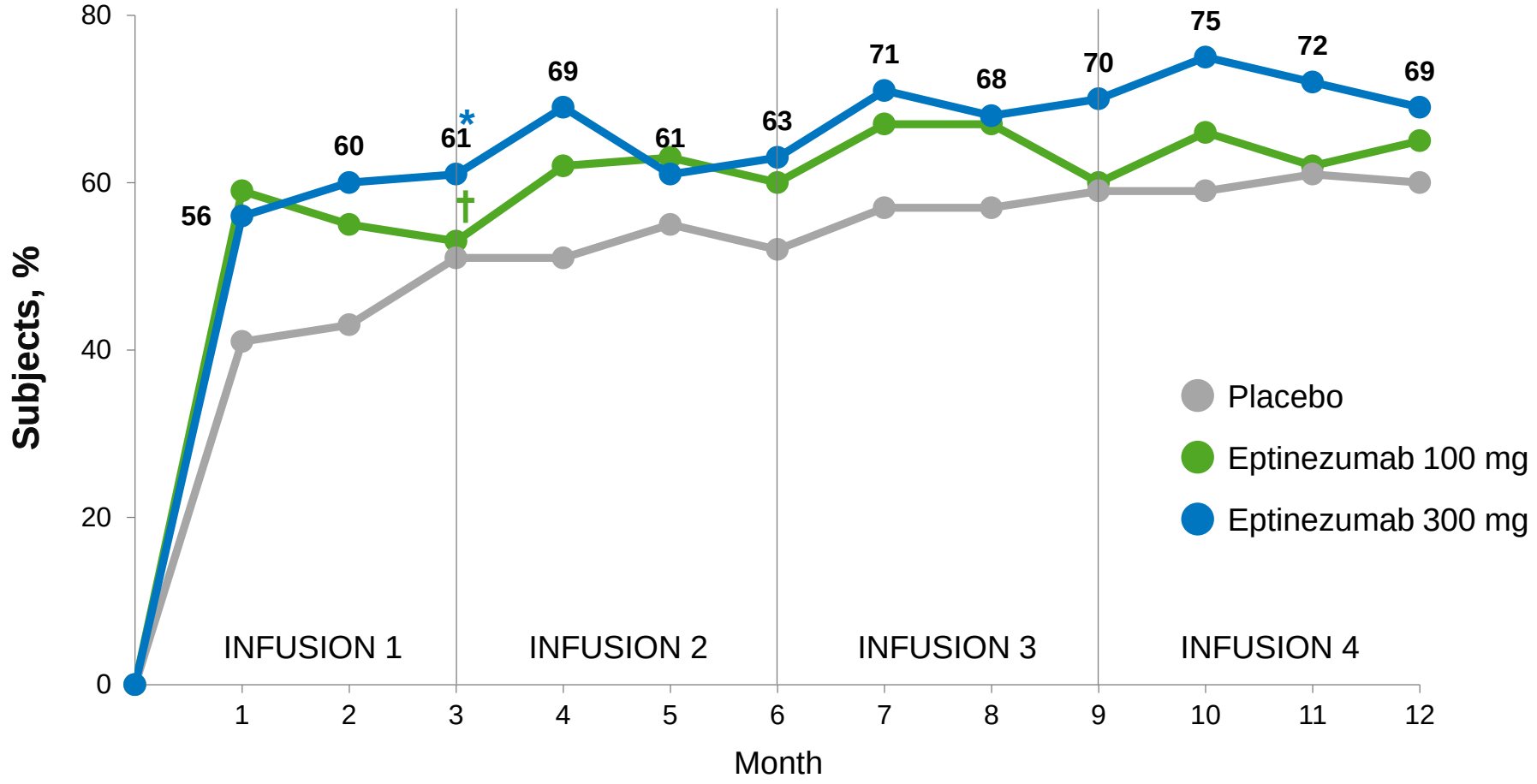
*CMH test used for statistical analysis; †NS= not tested; ‡unadjusted p value

Over 51% of Eptinezumab 300 mg Subjects Achieved ≥75% Reduction in Migraine Days After 3rd and 4th Infusion



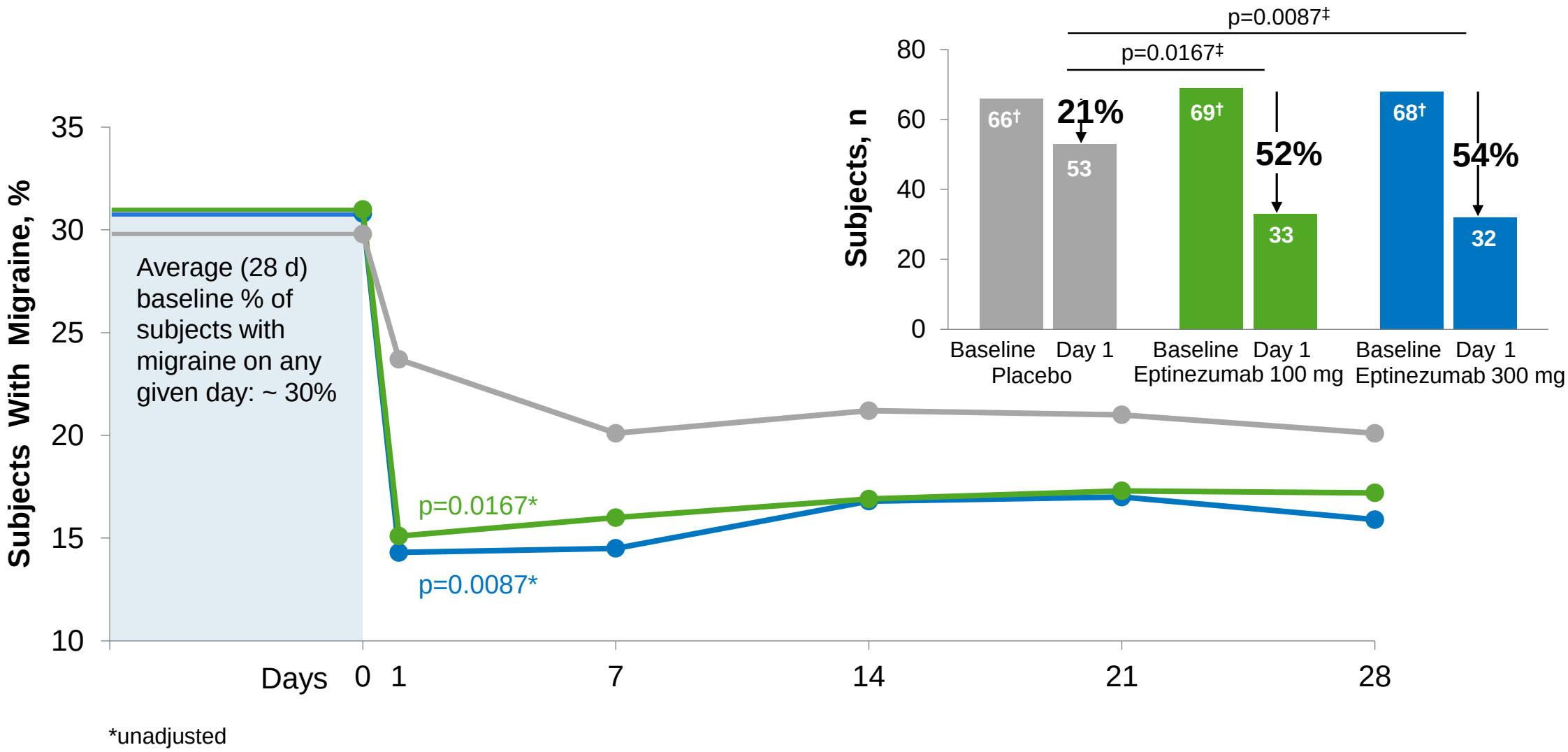
*p=0.0066; †p=0.0112

Over 70% of Eptinezumab 300 mg Subjects Achieved ≥50% Reduction in Migraine Days After 3rd and 4th Infusion



*p=0.0001, †p=0.0085 vs placebo.

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



*unadjusted

Safety Profile: Safety Population

Subjects, n (%)	Placebo n=222	Eptinezumab 30 mg n=219	Eptinezumab 100 mg n=223	Eptinezumab 300 mg n=224
Any TEAE	132 (60)	128 (58)	141 (63)	129 (58)
Any serious TEAE*	6 (3)	4 (2)	4 (2)	3 (1)
Any serious TEAE leading to drug withdrawal	6 (3)	12 (6)	6 (3)	5 (2)
Most-frequent TEAEs†				
Upper respiratory tract infection	16 (7)	25 (11)	22 (10)	23 (10)
Nasopharyngitis	12 (5)	14 (6)	17 (8)	14 (6)
Sinusitis	14 (6)	7 (3)	6 (3)	11 (5)

*All serious TEAEs judged unrelated to study drug; †≥5% in any treatment group.

- Occurrences of TEAEs were similar among treatment and placebo groups

Conclusions

- Subjects with episodic migraine who received eptinezumab 300 mg experienced a significant reduction in mean monthly migraine days over Weeks 1-12, reaching statistical significance for the primary and all key secondary endpoints
- Migraine day prevalence dropped over 50% on Day 1 and reduction was sustained through Day 28 in subjects receiving eptinezumab
- Subjects experienced significantly fewer days with migraine
  - 32% achieved a ≥75% reduction in monthly migraine days over Weeks 1– 4 and 37% over Weeks 1-12 for the 300 mg dose group
  - 61% achieved a ≥50% reduction in monthly migraine days over Weeks 1-12 for the 300 mg dose group
- Responder rates further improved with subsequent infusions for the 300 mg dose group
  - Over 51% achieved a ≥75% reduction in monthly migraine days
  - Over 70% achieved a ≥50% reduction in monthly migraine days
- Overall TEAE rates were similar to placebo and the safety profile was consistent with previous eptinezumab studies

Acknowledgment

This study was funded by Alder BioPharmaceuticals, Inc.

Back-up

Serious Adverse Events

Serious AE, n (%)*	Placebo n=222	Eptinezumab 30 mg n=219	Eptinezumab 100 mg n=223	Eptinezumab 300 mg n=224
Abdominal wound dehiscence	0	0	0	1 (<1)
Benign breast neoplasm	0	0	0	1 (<1)
Postprocedural complication	0	0	0	1 (<1)
Vertigo	0	0	0	1 (<1)
Cholecystitis	0	0	1 (<1)	0
Panic attack	0	0	1 (<1)	0
Postprocedural constipation	0	0	1 (<1)	0
Procedural pain	0	0	1 (<1)	0
Suicide attempt	0	0	1 (<1)	0
Suicidal ideation	0	0	1 (<1)	0
Cholestatic hepatitis	0	1 (<1)	0	0
Incisional hernia	0	1 (<1)	0	0
Nephrolithiasis	0	1 (<1)	0	0
Acute renal failure	0	1 (<1)	0	0
Rhabdomyolysis	0	1 (<1)	0	0
Apnea	1 (<1)	0	0	0
Breast cancer stage II	1 (<1)	0	0	0
Cellulitis	1 (<1)	0	0	0
Chronic obstructive pulmonary disease	1 (<1)	0	0	0
Intervertebral disc protrusion	1 (<1)	0	0	0
Migraine	1 (<1)	0	0	0
Syncope	1 (<1)	0	0	0
Uterine prolapse	1 (<1)	0	0	0

*Some patients experienced >1 serious AE.