IOR04

Eptinezumab Achieved Meaningful Reductions in Migraine Activity as Early as Day 1:PROMISE-2 (PRevention Of Migraine via Intravenous eptinezumab Safety and Efficacy-2) Phase 3 Trial in Chronic Migraine

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Disclosures

David Kudrow: Alder, Allergan, Amgen, Biohaven, CoLucid, Eli Lilly, Genentech-Roche, Teva

Merle Diamond: No conflicts reported

Lora McGill: No conflicts reported

Roger Cady: Alder full-time employee

Suman Bhattacharya: Alder full-time employee

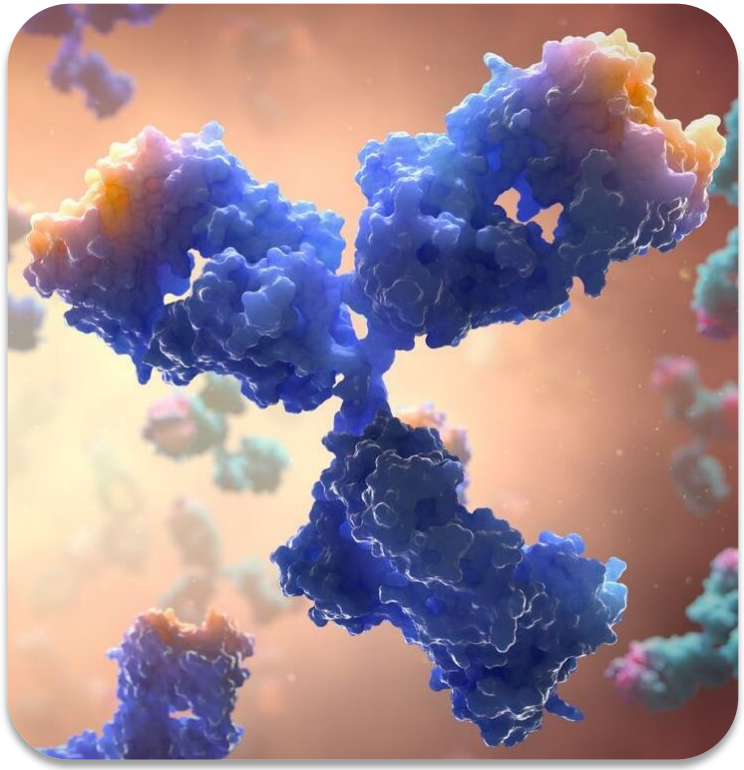
David Biondi: Alder full-time employee

Joe Hirman: Alder (contract service provider)

Jeff Smith: Alder full-time employee

Eptinezumab (ALD403)
An Anti-CGRP Monoclonal Antibody

- IgG1, anti-CGRP monoclonal antibody[1]
  - Selectively and potently inhibits both CGRP ligands*
- 5-pM binding affinity for CGRP
- Glycoengineered for reduced immune activation
- Reliable ~30 days $t_{1/2}$
- 100% bioavailability within hours after iv administration
- Quarterly dosing schedule
- Eptinezumab was efficacious and well tolerated in
  - Phase 2 and Phase 3 studies in episodic[2,3] and chronic[4,5] migraine



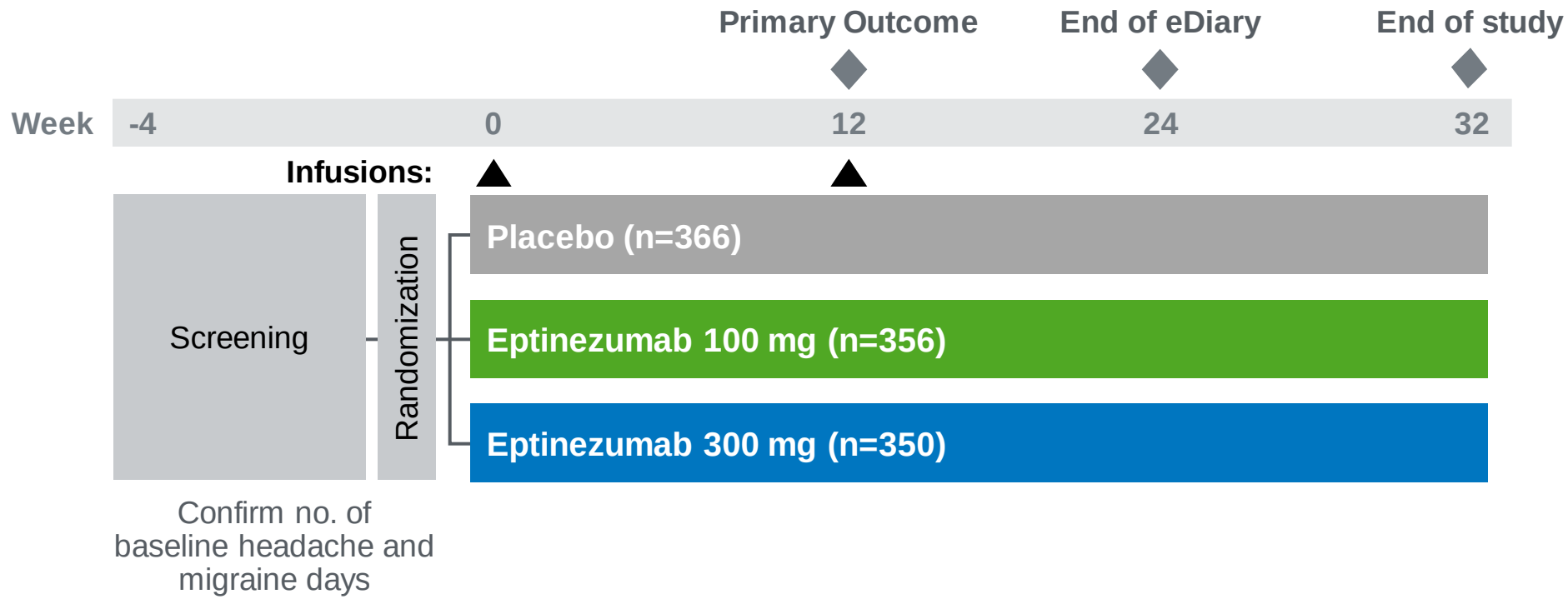
Eptinezumab

*α-CGRP and β-CGRP. CGRP, calcitonin gene-related protein.

1. Baker B, et al. AAN 2017, abstr P2.155; 2. Dodick DW, et al. *Lancet Neurol*. 2014;13:1100-07; 3. Saper J, et al. *Cephalalgia*. 2017;37(suppl):319-74; 4. Dodick D, et al. *Neurology*. 2017;88(suppl 16):S52.033; 5. Lipton RB, et al. *Neurology*. 2018;90(suppl 15):S32.

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-3 beta), migraine history ≥1 year, and ≥15 to ≤26 headache days, of which ≥8 assessed as migraine days during 28-day screening period



*NCT02974153. ICHD-3, International Classification of Headache Disorders, 3rd Edition (beta).

Efficacy Endpoints

Primary Endpoint	Mean change from baseline in monthly migraine days (MMD)	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 with a migraine	Day 1 postdose
	Daily % of subjects with a migraine	Week 1, 2, 3, and 4

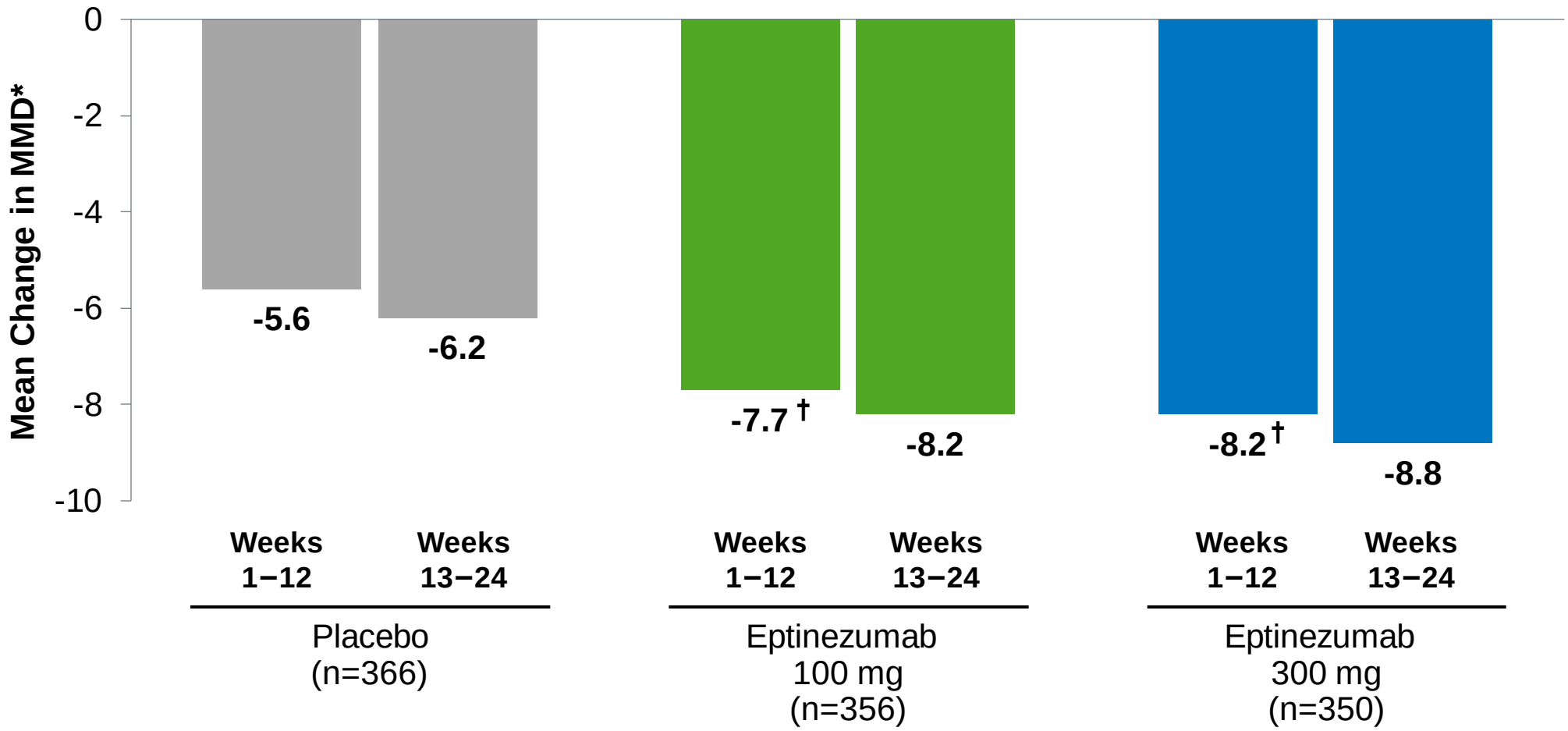
*Responder rate, percent of subjects with prespecified migraine response (reduction in MMD from baseline).

Baseline Characteristics and Demographics

	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg
Subjects, n	**366**	**356**	**350**
Mean age, years (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, years (SD)	11.6 (10.9)	11.6 (11.7)	12.4 (11.2)
≥1 prophylactic medication, n (%)*	163 (44.5)	161 (45.2)	155 (44.3)
Mean migraine days/month (SD)	16.2 (4.6)	16.1 (4.6)	16.1 (4.8)
Mean headache days/month (SD)	20.6 (3.0)	20.4 (3.1)	20.4 (3.2)

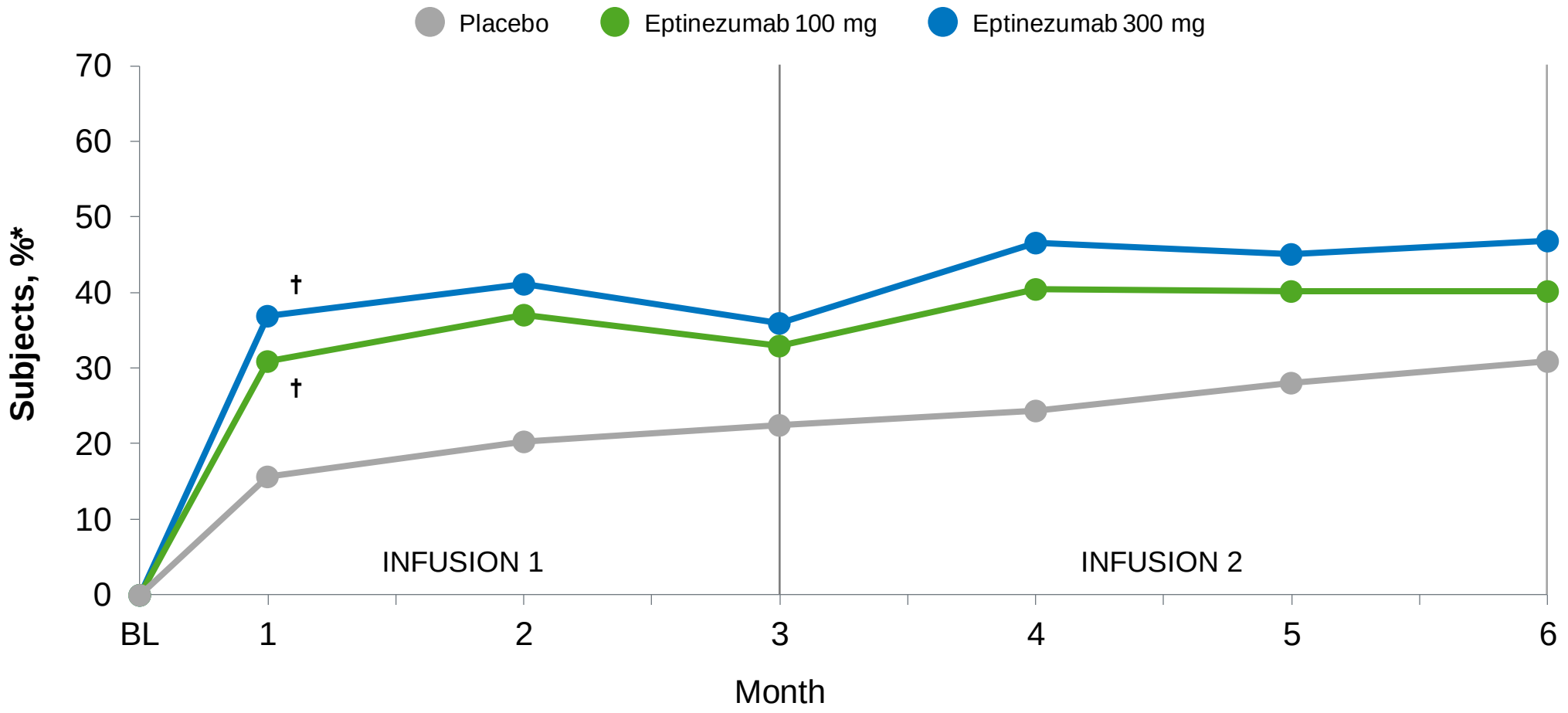
*According to American Academy of Neurology/American Headache Society guidelines for migraine preventive treatment (medications identified by clinical review of coded medical data); BMI, body mass index; SD, standard deviation.

Mean Change in Monthly Migraine Days Through 2 Dose Intervals



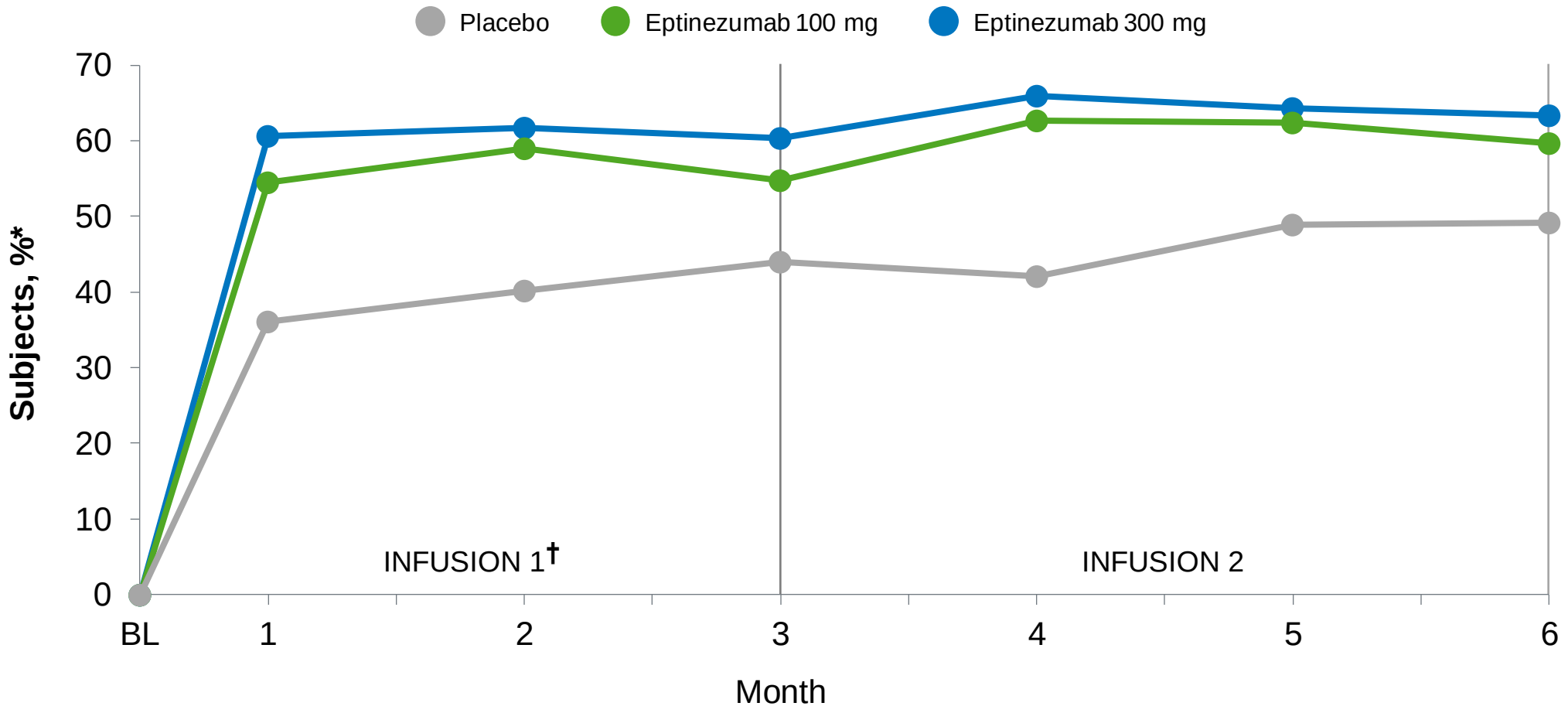
*Analysis of covariance model used to test for difference between treatment arms; †p <0.0001 vs placebo.

≥75% Migraine Responder Rate Through 2 Dose Intervals



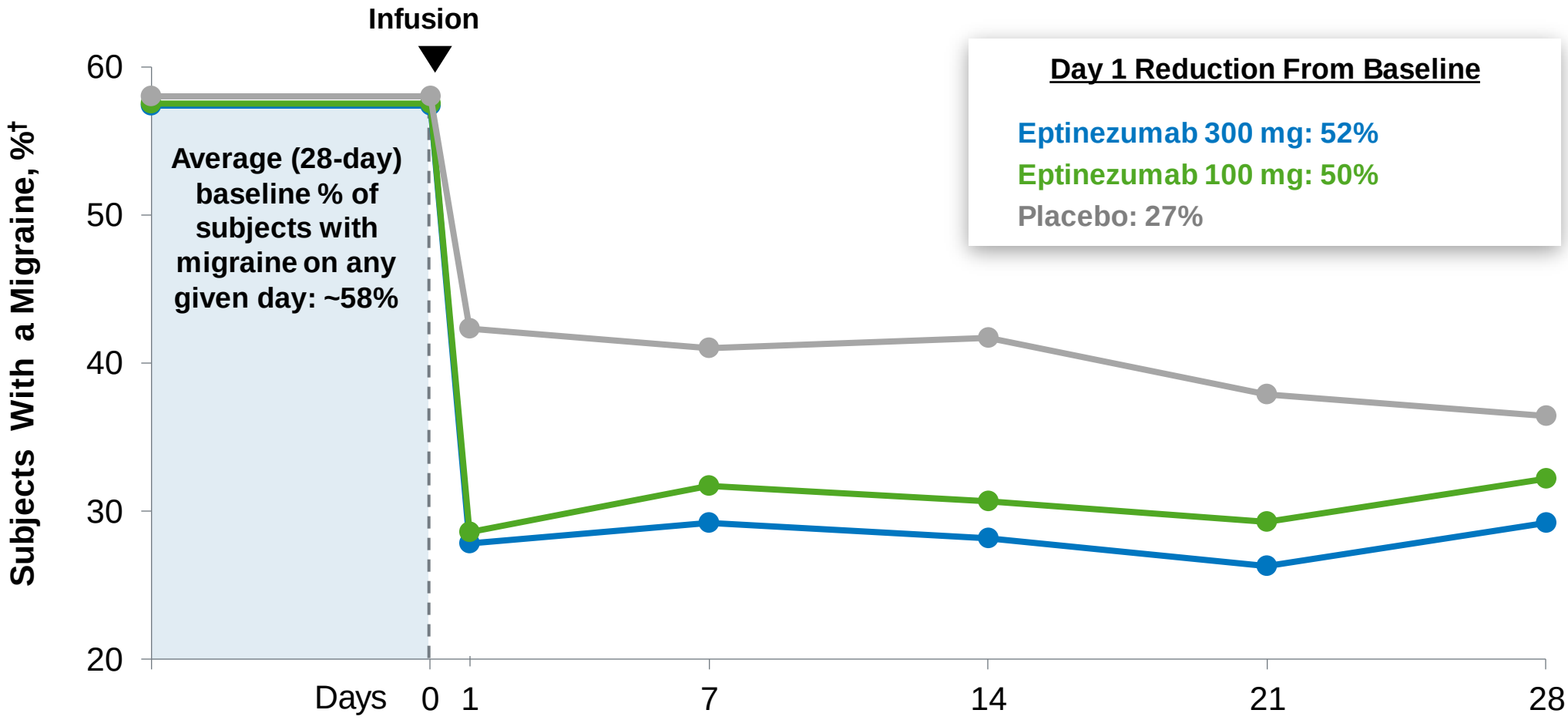
*Stratified Cochran–Mantel–Haenszel test used for statistical analysis; †p <0.0001 vs placebo (Weeks 1-4). BL, baseline.

≥50% Migraine Responder Rate Through 2 Dose Intervals



*Stratified Cochran–Mantel–Haenszel test used for statistical analysis; †p <0.0001 vs placebo for 300- and 100-mg doses (Weeks 1–12). BL, baseline.

Key Secondary Endpoint:
Day 1 Reductions From Baseline in Percentages of Subjects With a Migraine Maintained, on Average, Through 28 Days*



*Day 1 % of subjects with a migraine in eptinezumab vs placebo groups ($p<0.0001$ for both doses; Stratified Cochran–Mantel–Haenszel test used for statistical analysis) and daily % of subjects with a migraine averaged weekly for Days 1–28 in eptinezumab vs placebo groups ($p<0.0001$ for both doses; endpoint repeated measure used for statistical analysis).

Safety Profile Through Week 32*

Subjects, n (%)	Placebo n=366	Eptinezumab 100 mg n=356	Eptinezumab 300 mg n=350
Any TEAE	171 (47)	155 (44)	182 (52)
Any serious TEAE†	3 (<1)	3 (<1)	4 (1)
Any TEAE leading to drug withdrawal	2 (<1)	3 (<1)	8 (2)
Most frequent TEAEs‡			
Nasopharyngitis	22 (6)	19 (5)	33 (9)
Upper respiratory tract infection	20 (6)	15 (4)	19 (5)
Nausea	7 (2)	6 (2)	12 (3)
Urinary tract infection	6 (2)	8 (2)	12 (3)
Arthralgia	3 (<1)	5 (1)	11 (3)
Influenza	9 (3)	1 (<1)	10 (3)
Dizziness	4 (1)	5 (1)	9 (3)
Sinusitis	15 (4)	7 (2)	9 (3)
Migraine	16 (4)	6 (2)	8 (2)
Anxiety	1 (<1)	4 (1)	7 (2)
Fatigue	7 (2)	8 (2)	6 (2)
Back pain	6 (2)	7 (2)	6 (2)
Bronchitis	8 (2)	7 (2)	4 (1)

*Safety profile represents safety population; †All serious TEAEs reported unrelated to study drug; ‡≥2% in any active treatment group. TEAE, treatment-emergent adverse event.

Conclusions

- In subjects with CM, beginning on Day 1 post a single infusion, eptinezumab substantially reduced monthly migraine days (MMD) through a 2nd infusion
- The average daily percentage of subjects with a migraine on Day 1 was reduced by ≥50% following eptinezumab infusion and the reduction was sustained, on average, through Day 28
- 33% of subjects treated with eptinezumab 300 mg experienced a ≥75% reduction in MMD over Weeks 1–12, which increased to 43% of subjects after the 2nd infusion
- 61% of subjects treated with eptinezumab 300 mg experienced a ≥50% reduction in MMD over Weeks 1–12, which increased to 64% of subjects after the 2nd infusion
- Overall TEAE rates for eptinezumab were similar to placebo and the safety profile was consistent with previous eptinezumab studies

Acknowledgment

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Back-up

Subject Disposition

Randomized subjects, n (%)	Placebo 375	Eptinezumab 100 mg 372	Eptinezumab 300 mg 374	Overall 1121*
Full analysis population†	366 (98)	356 (96)	350 (94)	1072 (96)
Week 12‡	356 (95)	349 (94)	344 (92)	1049 (94)
Week 24**	396 (90)	333 (90)	331 (89)	1000 (89)
Discontinued treatment early‡	24 (7)	16 (5)	15 (4)	55 (5)
Adverse event	3 (<1)	3 (<1)	8 (2)	14 (1)
Subject consent withdrawal/ lost to follow-up	19 (2)	10 (1)	7 (1)	36 (3)
Other	2 (<1)	3 (<1)	0	5 (<1)

*All randomized: N=1121; all randomized and dosed: n=1072, all randomized, dosed, and captured at Week 12: n=1049; †Includes all randomized subjects who received eptinezumab or placebo; ‡Subjects by visit, percentages based on all randomized subjects; **Percentages based on full analysis population.