Increased Migraine-Free Intervals With Eptinezumab Were Associated With Improved Health-Related Quality-of-Life Outcomes Through Week 12: Results From the Phase 3 PROMISE-1 Trial

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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 on Aging, National Institute of Neurological Disorders and Stroke, Neurology, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, Vedanta

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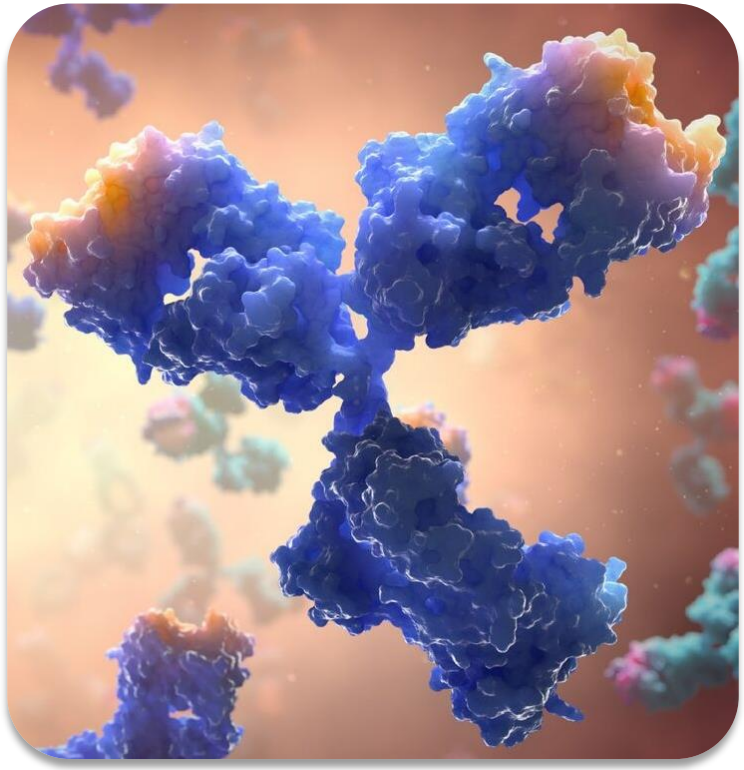
Eptinezumab (ALD403)
An Anti-CGRP Monoclonal Antibody

- 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.

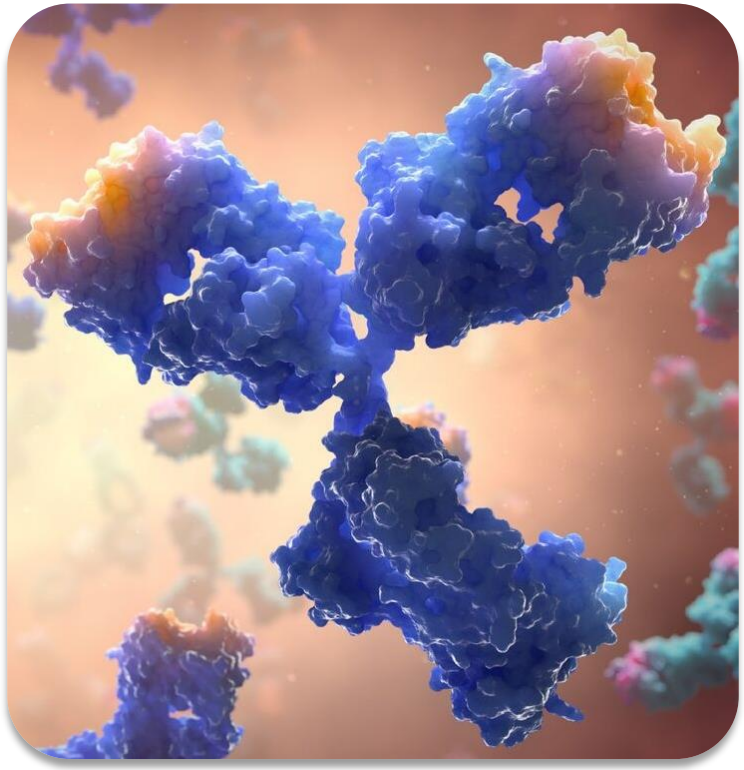
1. Baker B, et al. AAN 2017, abstr P2.155; 2. Dodick DW, et al. *Lancet Neurol*. 2016;15:382-90; 3. Smith J, et al. AAN 2017, abstr S52.033. 4. Saper J, et al. AAN 2018, abstr 1356;

Objectives

- Secondary data analysis of the PROMISE-1 trial, a Phase III study of Eptinezumab in EM prevention[1]
- Regulatory endpoints versus clinically meaningful responders
- Responder Rates better reflect clinical benefit than change in migraine days
- This presentation focuses on the relation of Responder Rates to external validators:

  -Changes in HRQoL

  -Changes in Migraine-Free Intervals

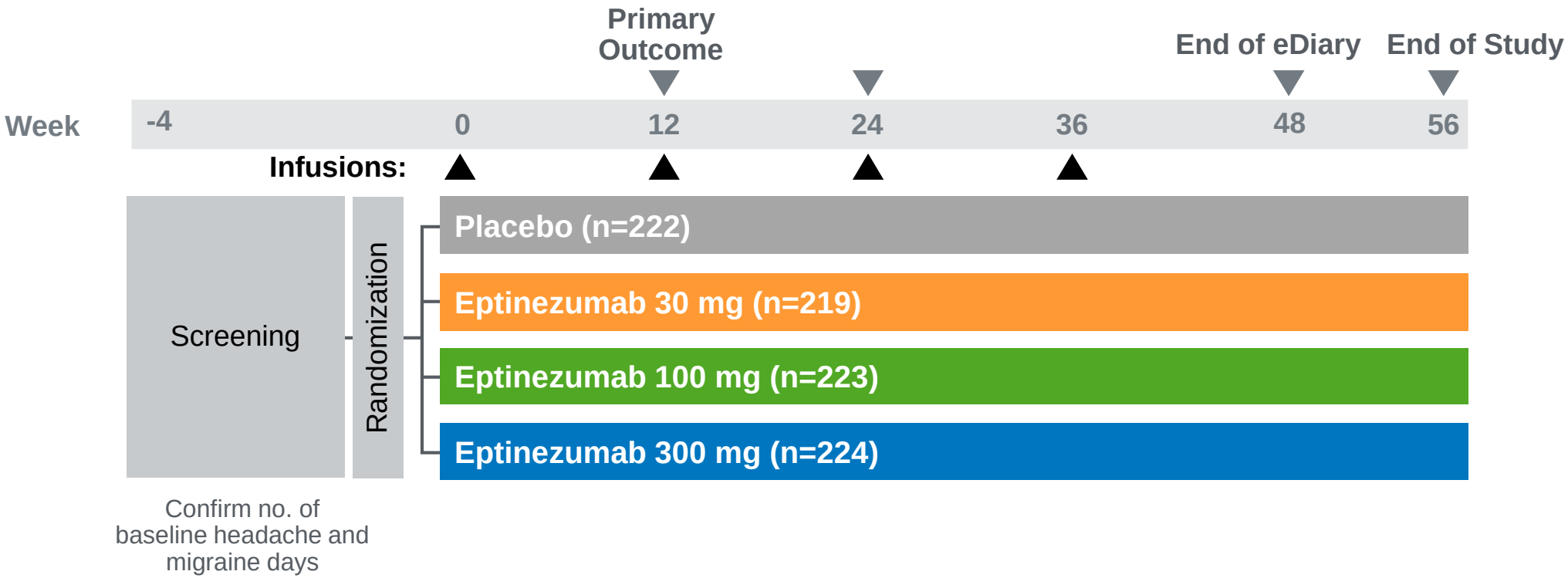


Eptinezumab

1. 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
Other Secondary Endpoint	Short-Form Health Survey (SF-36)	4 week intervals
Exploratory Endpoint	Migraine-Free Intervals	Weeks 1-12

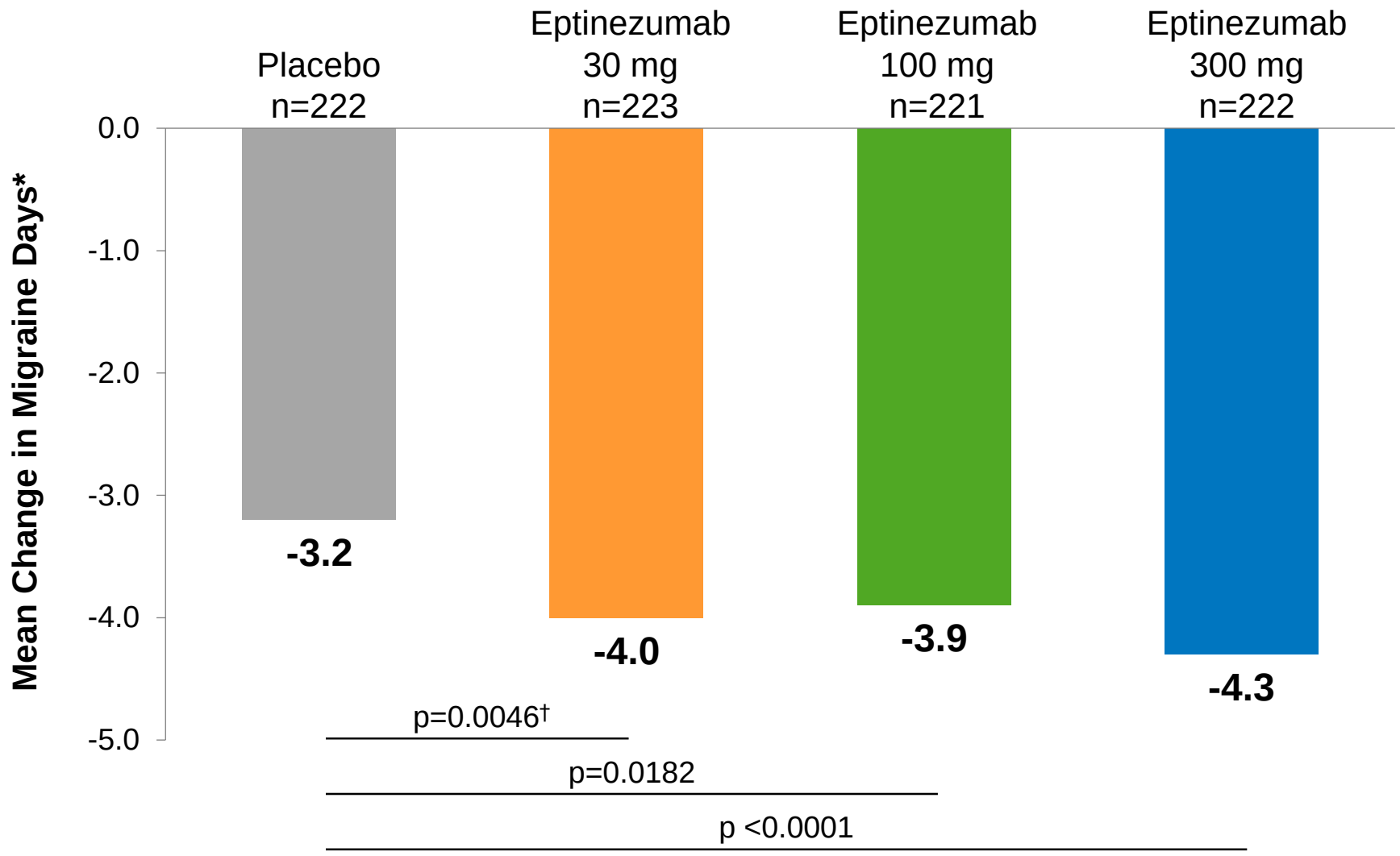
*Responder rate, percent of subjects with migraine response

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 diagnosis	16.9	17.0	17.4	18.2
Subjects with ≥1 prophylactic medication, n (%)	9 (4)	14 (6)	6 (3)	7 (3)
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

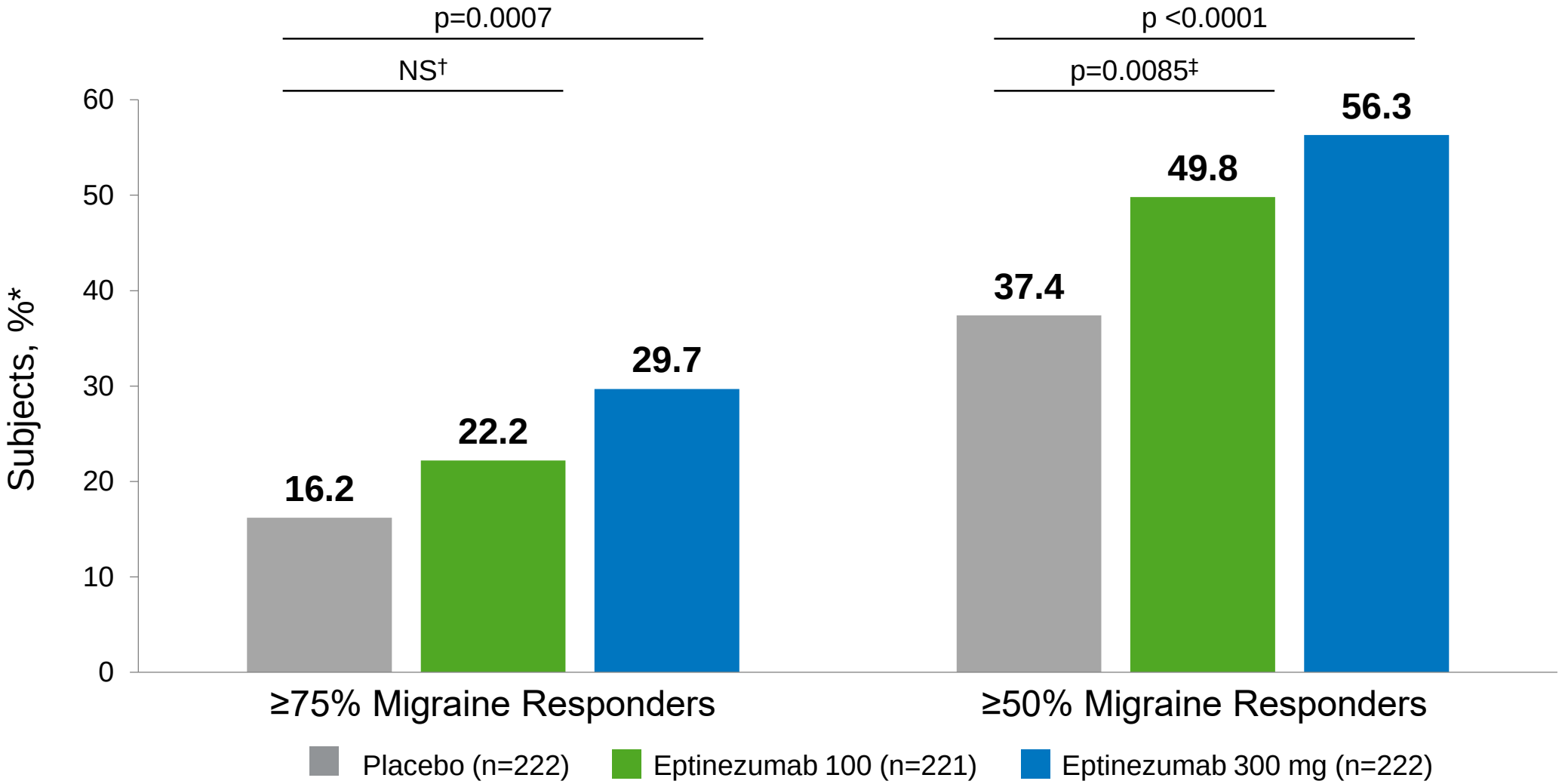
*Days with triptan or ergotamine use as recorded in eDiary averaged over 28-day screening period.

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



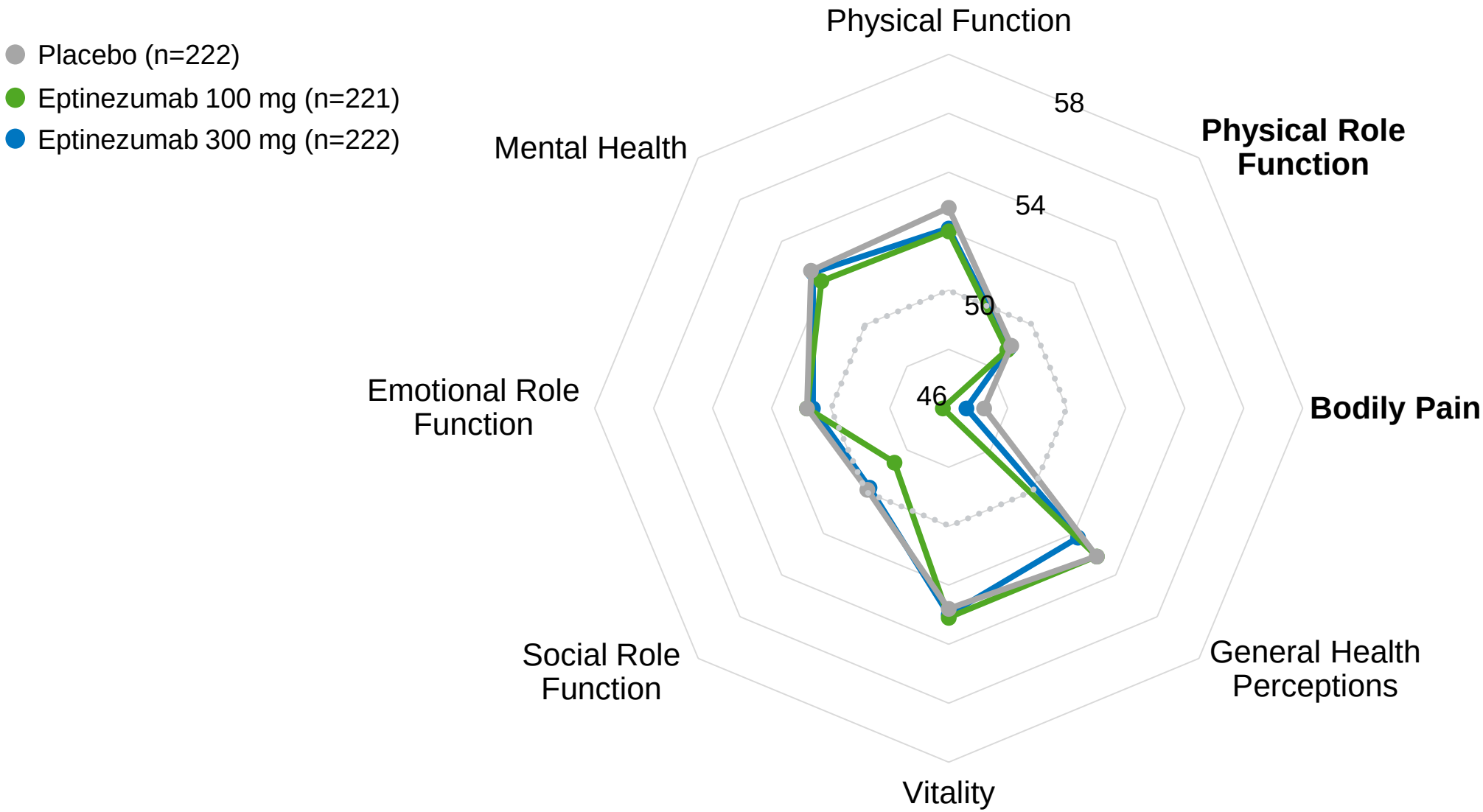
*ANCOVA model used to test for differences between treatment groups., †unadjusted

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



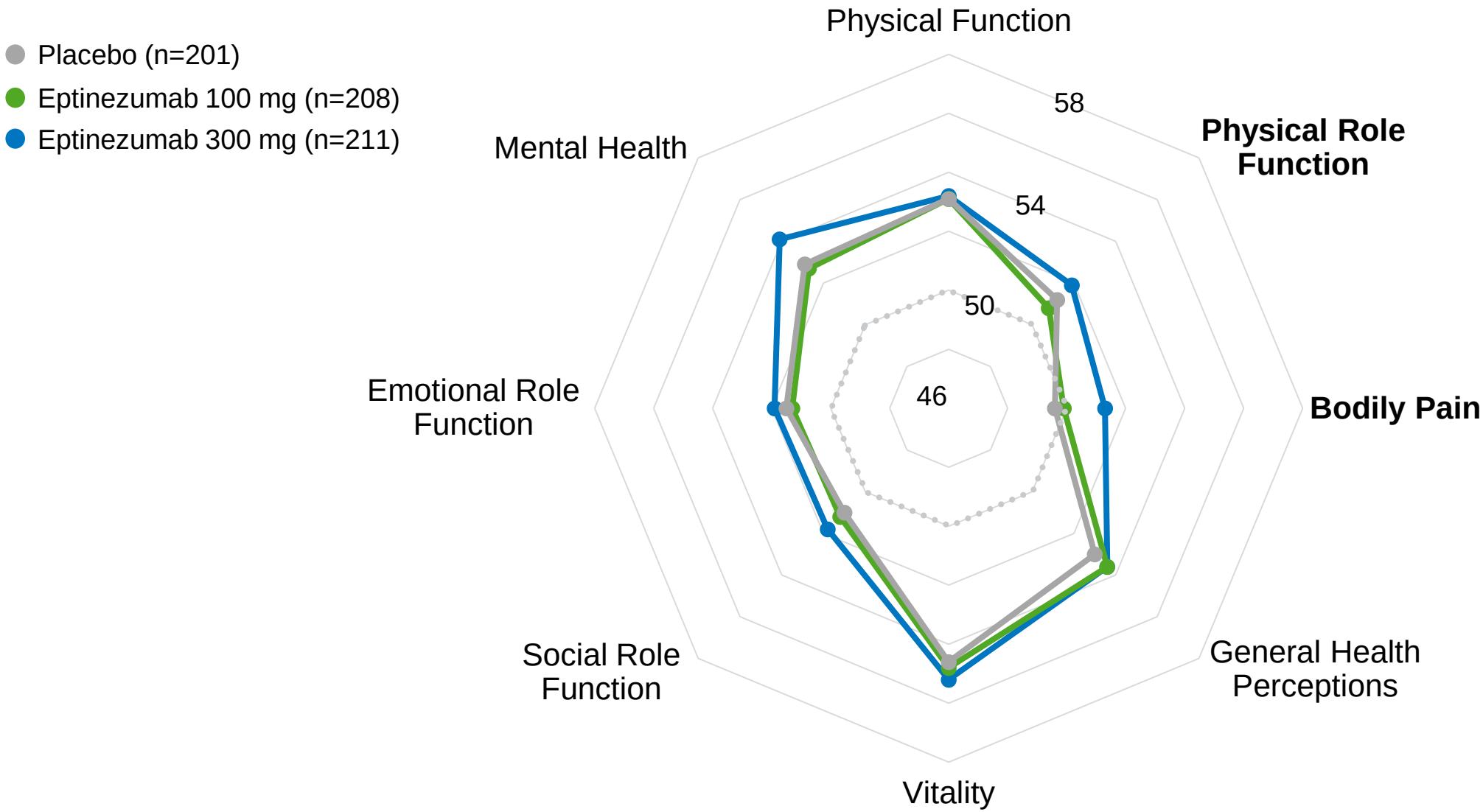
*CMH test used for statistical analysis, †NS= not significant, ‡unadjusted

Mean SF-36 Scores at Baseline in Full Study Population*



*Increasing score = improvement; 50 = normative population score; *bold text* indicates domain most affected at baseline.

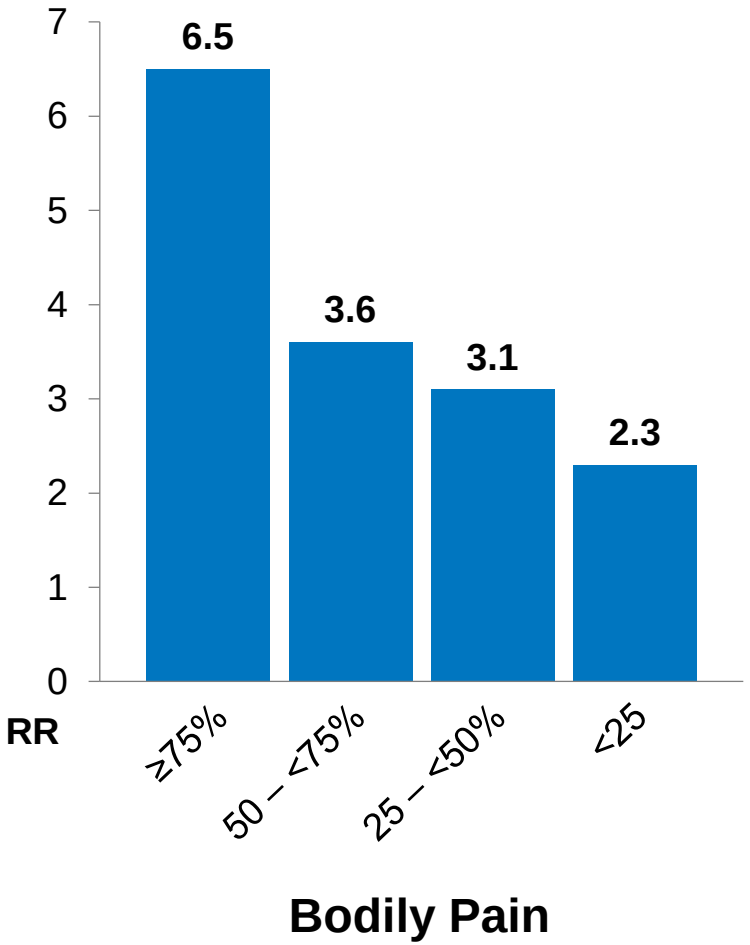
Mean SF-36 Scores at Week 12 in Full Study Population*



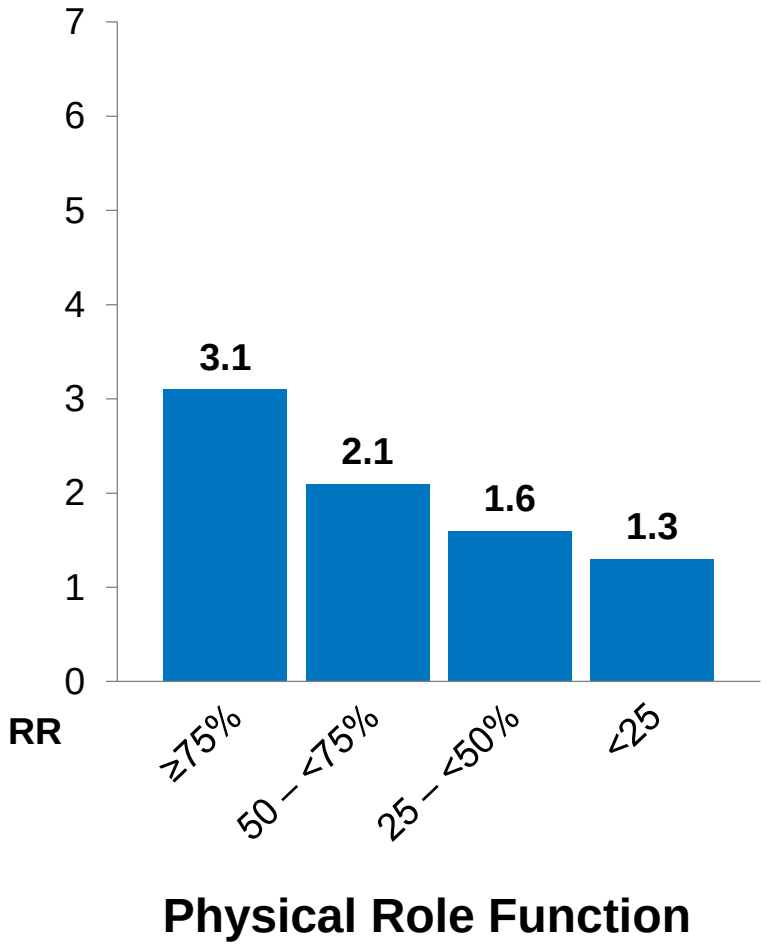
*Increasing score = improvement; 50 = normative population score; *bold text* indicates domain most affected at baseline.

SF-36 Score Improvements in Domains Most Affected By Migraine at Baseline: Week 4

Eptinezumab 300 mg

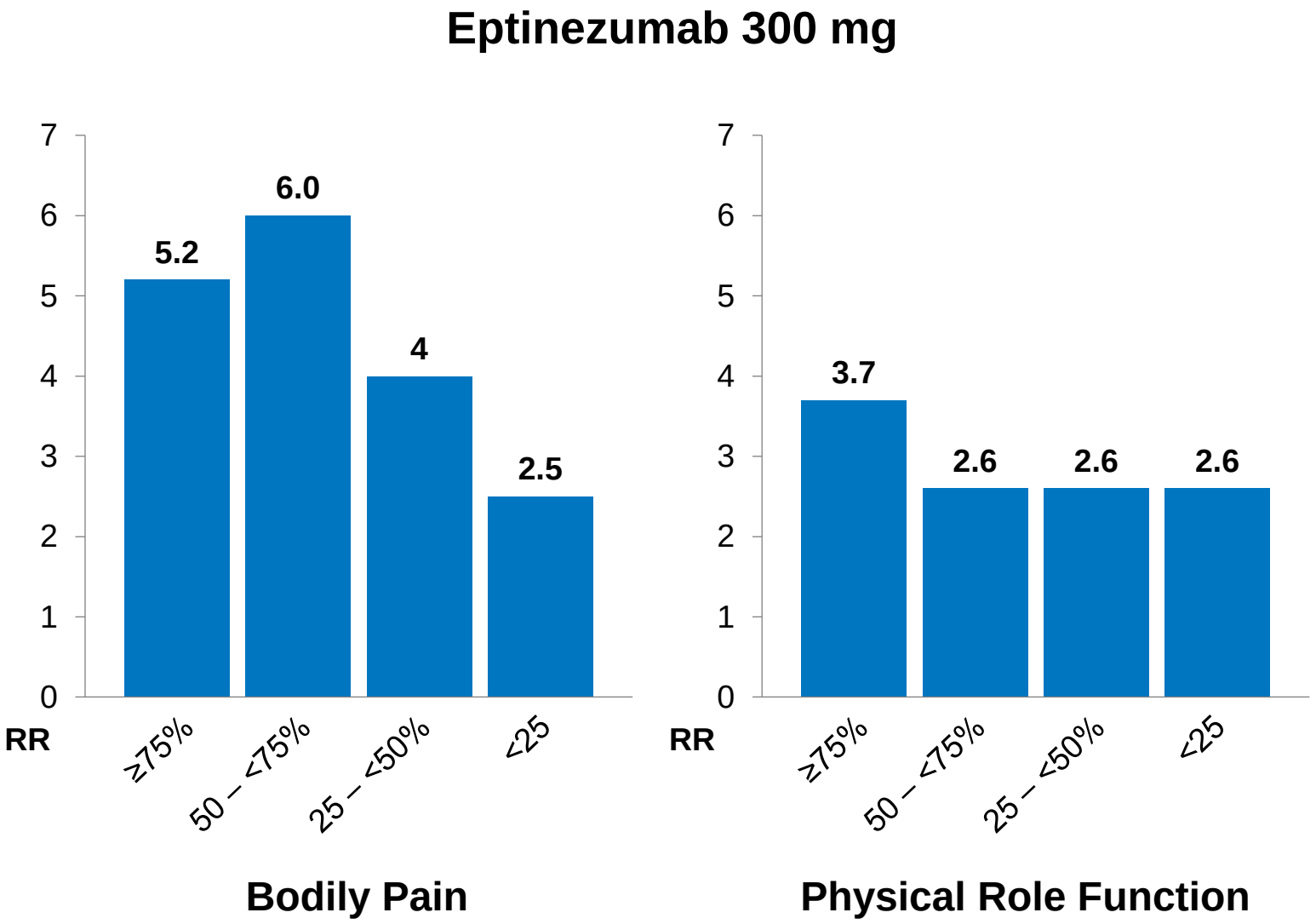


Bodily Pain

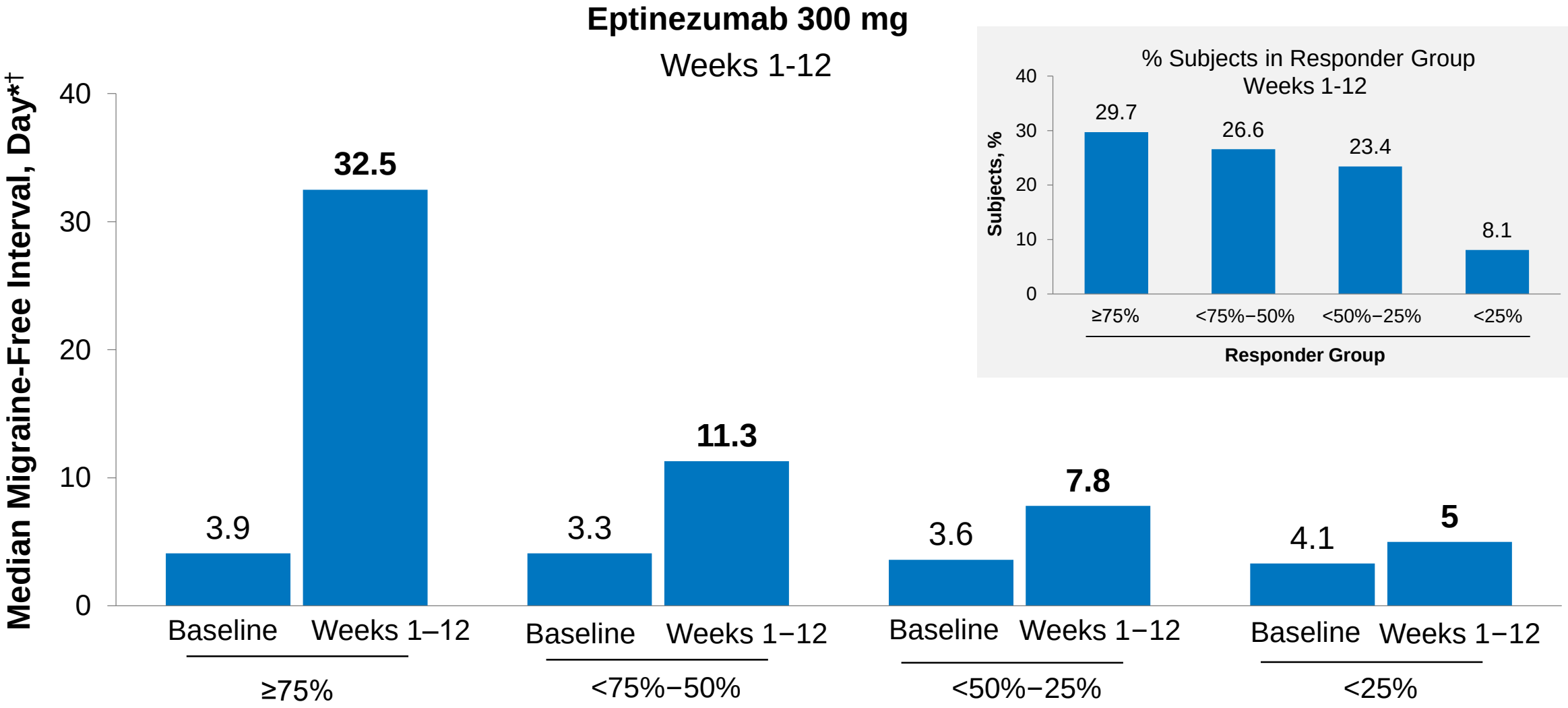


Physical Role Function

SF-36 Score Improvements in Domains Most Affected By Migraine at Baseline: Week 12



Migraine-Free Intervals: ≥75% Migraine Responders Have Over 8-Fold Increase in Days Between Migraine



*Migraine-free interval is days between migraine days., †multiple imputation methodology

Conclusions

- Eptinezumab iv infusion was associated with significant reductions in migraine over Weeks 1-12 in subjects with episodic migraine
  - 29.7% of subjects in the 300 mg dose group achieved a 75% or greater reduction in monthly migraine frequency
- Achieving a ≥75% migraine response rate was associated with more meaningful improvements in physical role function and bodily pain
- Subjects achieving ≥75% response rate experienced an average 8-fold increase in days between migraines
  - Migraine-free interval increased from 3.9 at baseline to 32.5 over Weeks 1-12

Acknowledgment

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