Long-term tolerability and effectiveness of eptinezumab in Japanese adults with chronic migraine: The 60-week, open-label SUNSET trial

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Data presented here are from an extension of a large-scale phase 3 clinical trial to determine the long-term (60-week) safety, tolerability, and effectiveness of eptinezumab, a monoclonal antibody targeted against calcitonin gene-related peptide, for the preventive treatment of migraine in Japanese adults with chronic migraine.

Background

- In Japan, migraine has a prevalence between 8.6% and 11.0% and is the fourth most common cause of years lived with disability.[1-3]
- There is an unmet need for utilization of preventive migraine treatment options in Japan, not only for the treatment of chronic migraine (CM), but also for the management of the substantial negative impact of migraine on daily functioning and health-related quality of life in Japanese adults.[4-8]
- Eptinezumab, a humanized monoclonal antibody targeted against calcitonin gene-related peptide and approved for migraine prevention,[9] has demonstrated early and sustained reductions in migraine frequency, improvements in patient-reported outcomes, and acceptable tolerability in participants with CM across several clinical trials.[10-13]
- In the large-scale phase 3 SUNRISE trial conducted in a predominantly Asian population with CM, eptinezumab 100 mg and 300 mg met the primary and all key secondary endpoints and was well-tolerated (see presentation **IHC25-PO-318**).

Objective

- To evaluate long-term safety, tolerability, and effectiveness of eptinezumab in Japanese adults with CM.

Methods

- The SUNSET trial (NCT05064371) was an extension of the phase 3, multiregional, randomized, double-blind, placebo-controlled SUNRISE trial (NCT04921384) conducted in adults (18–75 years) diagnosed with CM.
- 159 Japanese participants in SUNRISE were enrolled and treated in SUNSET after completing 12-week, randomized, double-blind treatment with IV eptinezumab 100 mg, 300 mg, or placebo (**Figure 1**).
- SUNSET comprised a 60-week open-label treatment period (during which participants received IV eptinezumab every 12 weeks [5 doses total] and completed a daily electronic diary) and an 8-week safety follow-up period (**Figure 1**).
- All participants received eptinezumab 100 mg at baseline in SUNSET, regardless of the dose received in SUNRISE; participants who did not have a ≥50% reduction from SUNRISE baseline in monthly migraine days (MMDs; SUNSET Weeks 1–12) had their dose increased to 300 mg at SUNSET Week 12 and onward, while all others continued to receive eptinezumab 100 mg.
- The following endpoints were assessed:
  - **Primary endpoints:** Long-term safety and tolerability endpoints, measured as treatment-emergent adverse events (TEAEs), vital signs, weight, laboratory values, electrocardiogram (ECG) data, Columbia–Suicide Severity Rating Scale (C-SSRS) scores, and development of specific anti-drug (anti-eptinezumab) antibodies (ADAs), including neutralizing antibodies (NAbs).
  - **Secondary endpoints:** Change from baseline in the number of MMDs, ≥50% migraine responder rates (MRRs), Patient Global Impression of Change (PGIC) score, patient-identified most bothersome symptom (PI-MBS) score, change from SUNRISE baseline in the 6-item Headache Impact Test (HIT-6) total score, and change from baseline in the EQ-5D-5L visual analog scale (VAS) score.
  - **Exploratory endpoints:** ≥75% MRRs, change from baseline in the Migraine-Specific Quality-of-Life Questionnaire, version 2.1 (MSQ v2.1) domain scores, and change from baseline in the Migraine-specific Work Productivity and Activity Impairment (WPAI:M) questionnaire domain scores.
- Baseline values for efficacy assessments are from the SUNRISE trial.

Results

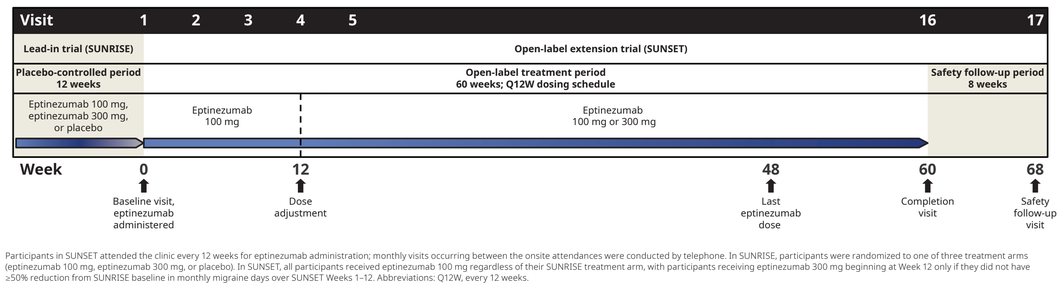
Participants and safety outcomes

- Of 159 participants treated in the SUNSET trial, 141 (89%) completed it (**Figure 2**).
  - All participants had a minimum of 3 months of eptinezumab 100 mg exposure and 123 (77%) had up to 48 weeks of eptinezumab 300 mg exposure (due to having their dose increased at Week 12).
- Evaluable participants were 87% female, with a mean age of 41.9 years, mean of 17.1 MMDs, and 35% with a concurrent diagnosis of medication-overuse headache at baseline of SUNRISE (**Figure 2**).
- Excluding COVID-19 (25%), only nasopharyngitis (11%) occurred as a TEAE in >5% of participants (**Table 1**).
- The proportions of participants with serious adverse events (3%) and TEAEs leading to withdrawal (4%) or infusion interruption (5%) were low (**Table 1**).
- The prevalence of ADAs and NAbs throughout the trial was 21% and 4%, respectively (**Table 1**). None of the participants were ADA-positive at Week 92, and there was no evidence of an impact of ADA or NAb development on the safety or effectiveness of eptinezumab.
- There were no clinically relevant findings related to vital signs, weight, laboratory values, ECGs, and C-SSRS scores.

Effectiveness outcomes

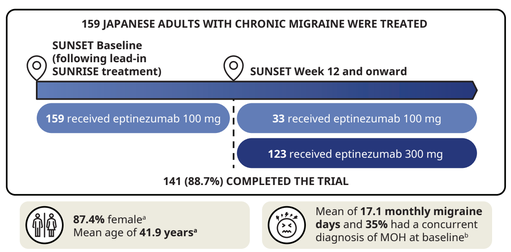
- Eptinezumab resulted in sustained reductions in MMDs from SUNRISE baseline, with least-squares mean changes (± standard error) from baseline in MMDs during SUNSET of -4.4 (0.5) days across Weeks 1–12, -5.0 (0.5) across Weeks 13–24, -5.2 (0.5) across Weeks 25–36, -5.6 (0.5) across Weeks 37–48, and -5.4 (0.6) days across Weeks 49–60.
- Similar effects over time were shown regardless of the lead-in treatment received during the SUNRISE trial (**Figure 3**).
- The proportion of participants with a ≥50% or ≥75% MMD reduction from baseline was maintained or slightly increased throughout the trial (**Figure 4**).
- The proportion of participants indicating their disease status was "much improved" or "very much improved" (PGIC responders) appeared to increase from Week 12 to Week 24, then was maintained through the end of trial to Week 60 (**Figure 4**).
- Improvements from baseline were observed beginning at Week 12 and across 60 weeks of treatment in patient-reported outcomes measuring overall disease status (PGIC), headache-related life impact (HIT-6), and workplace productivity and activity impairment (WPAI:M) (**Figure 5**).
- Sustained improvements in other patient-reported outcome measures, including PI-MBS, MSQ v2.1, and EQ-5D-5L VAS scores, were observed throughout the trial (**Table 2**).

Figure 1. SUNSET clinical trial design



Participants in SUNSET attended the clinic every 12 weeks for eptinezumab administration; monthly visits occurring between the onsite attendances were conducted by telephone. In SUNRISE, participants were randomized to one of three treatment arms (eptinezumab 100 mg, eptinezumab 300 mg, or placebo). In SUNSET, all participants received eptinezumab 100 mg regardless of their SUNRISE treatment arm, with participants receiving eptinezumab 300 mg beginning at Week 12 only if they did not have ≥50% reduction from SUNRISE baseline in monthly migraine days over SUNSET Weeks 1–12. Abbreviations: Q12W, every 12 weeks.

Figure 2. Participants enrolled in the SUNSET clinical trial



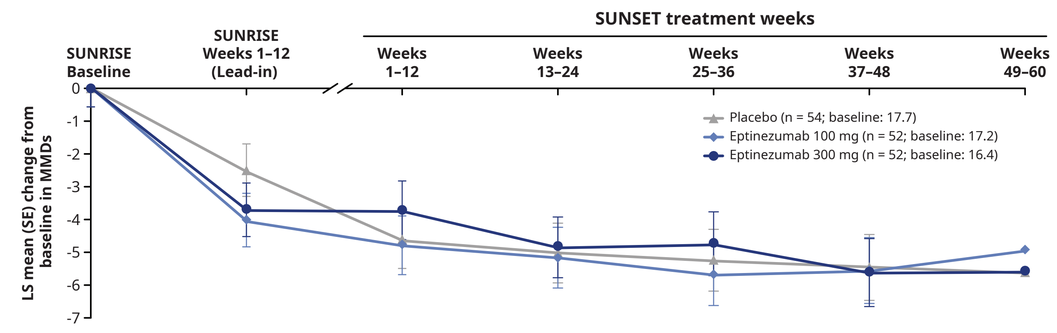
[a]SUNRISE baseline data from all enrolled participants who received an infusion of trial medication in SUNSET. [b]SUNRISE baseline data from all enrolled participants who received an infusion of trial medication, had a valid baseline assessment of monthly migraine days, and had ≥1 valid post-baseline 4-week assessment of monthly migraine days in SUNSET. Abbreviations: MOH, medication-overuse headache.

Table 1. Summary of safety and tolerability

Participants, n (%)	Eptinezumab 100/300 mg (N = 159)
TEAEs	133 (83.6%)
Serious adverse events	5 (3.1%)
TEAEs leading to withdrawal	7 (4.4%)
TEAEs leading to infusion interruption/ termination	8 (5.0%)
Deaths	0
TEAEs occurring in >5% of participants	
COVID-19	40 (25.2%)
Nasopharyngitis	18 (11.3%)
Overall prevalence of ADAs	33 (20.8%)
Overall prevalence of NAbs	7 (4.4%)

Data are from all enrolled participants who received an infusion of trial medication. Abbreviations: ADAs, anti-drug (anti-eptinezumab) antibodies; NAbs, neutralizing antibodies; TEAE, treatment-emergent adverse event.

Figure 3. Change from baseline in MMDs according to lead-in SUNRISE treatment

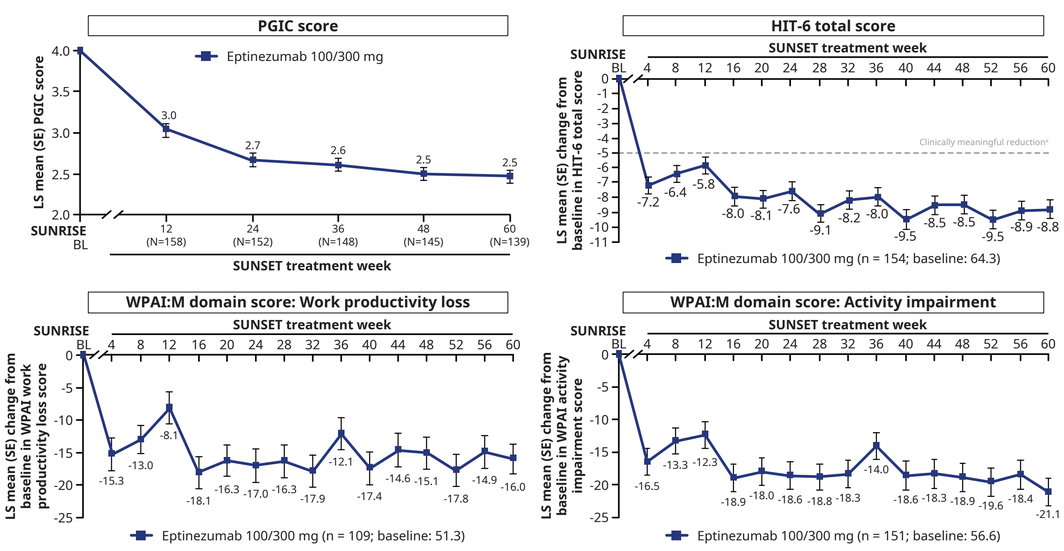


Data are from all enrolled participants who received an infusion of trial medication, had a valid baseline assessment of MMDs, and had ≥1 valid post-baseline 4-week assessment of MMDs in SUNSET. Baseline values are from the SUNRISE trial. The axis break between SUNRISE Weeks 1–12 and SUNSET Weeks 1–12 indicates the transition from SUNRISE trial to SUNSET trial. The estimated LS means were derived from a mixed model for repeated measures with month and prior treatment group as factors, baseline score as a continuous covariate, prior treatment group-by-month interaction, and baseline score-by-month interaction. Abbreviations: LS, least-squares; MMDs, monthly migraine days; SE, standard error.

Figure 4. Proportion of ≥50% and ≥75% responders and PGIC responders

Data are from all enrolled participants who received an infusion of trial medication, had a valid baseline assessment of MMDs, and had ≥1 valid post-baseline 4-week assessment of MMDs in SUNSET. Migraine responder rates across the 4-week intervals were calculated as the mean percent change in MMDs (based on available monthly MMD values). If the MMD value was missing for a given month, responder status was derived based on available values. A ≥50% or ≥75% migraine responder was a participant with ≥50% or ≥75% reduction from SUNRISE baseline, respectively, in MMDs. A PGIC responder was a participant who answered "much improved" or "very much improved" on the 7-point rating scale. Abbreviations: MMDs, monthly migraine days; PGIC, Patient Global Impression of Change.

Figure 5. PGIC score and changes from baseline in HIT-6 total score and selected WPAI:M domain scores



Data are from all enrolled participants who received an infusion of trial medication, had a valid baseline assessment of MMDs, and had ≥1 valid post-baseline 4-week assessment of MMDs in SUNSET. Baseline values are from the SUNRISE trial. For PGIC where the rating scale itself represents a change from baseline, the representative baseline value of 4.0 ("no change") is deterministic and not based on individual data at baseline. For all graphs, axis break between SUNRISE baseline and SUNSET Week 4 represents the 12-week placebo-controlled period in SUNRISE that preceded the SUNSET trial. The estimated LS means for each patient-reported outcome were derived from a mixed model for repeated measures with visit as a factor, baseline score as a continuous covariate, and baseline score-by-month interaction, with the baseline score corresponding to the outcome being analyzed. For PGIC, baseline score was excluded from the model. [a]A ≥5-point decrease from baseline in HIT-6 total score is considered clinically meaningful.[14] Abbreviations: BL, baseline; LS, least-squares; MMDs, monthly migraine days; PGIC, Patient Global Impression of Change; SE, standard error; WPAI:M, Migraine-specific Work Productivity and Activity Impairment questionnaire.

Table 2. Summary of other patient-reported outcomes

	Eptinezumab 100/300 mg			
Participants, n (%)	**SUNRISE Baseline**	**SUNSET Week 12**	**SUNSET Week 24**	**SUNSET Week 60**
PI-MBS, N		157	151	138
LS mean (SE) score at timepoint		3.1 (0.1)	2.7 (0.1)	2.6 (0.1)
Responders[a], n (%)		55 (35.0%)	75 (49.7%)	74 (53.6%)
WPAI:M domain: absenteeism, N	110	99	94	88
Mean baseline score/LS mean (SE) change from baseline at timepoint	3.6	1.6 (1.3)	-1.6 (0.7)	0.6 (1.1)
WPAI:M domain: presenteeism, N	109	98	93	88
Mean baseline score/LS mean (SE) change from baseline at timepoint	50.4	-9.0 (2.4)	-17.2 (2.5)	-17.2 (2.1)
MSQ v2.1 domain: role function-restrictive, N	151	151	145	132
Mean baseline score/LS mean (SE) change from baseline at timepoint	51.9	15.6 (1.4)	18.7 (1.5)	22.2 (1.4)
MSQ v2.1 domain: role function-preventive, N	151	151	145	132
Mean baseline score/LS mean (SE) change from baseline at timepoint	71.1	12.0 (1.2)	12.8 (1.3)	15.6 (1.2)
MSQ v2.1 domain: emotional function, N	151	151	145	132
Mean baseline score/LS mean (SE) change from baseline at timepoint	62.7	10.4 (1.6)	13.9 (1.5)	17.5 (1.6)
EQ-5D-5L visual analogue scale, N	151	151	142	132
Mean baseline score/LS mean (SE) change from baseline at timepoint	71.0	–0.3 (1.7)	1.6 (1.7)	2.9 (2.0)

Data are from all enrolled participants who received an infusion of trial medication, had a valid baseline assessment of MMDs, and had ≥1 valid post-baseline 4-week assessment of MMDs in SUNSET. Baseline values are from the SUNRISE trial. The estimated LS means for each patient-reported outcome were derived from a mixed model for repeated measures with visit as a factor, baseline score as a continuous covariate, and baseline score-by-month interaction, with the baseline score corresponding to the outcome being analyzed. For PI-MBS where the rating scale itself represents a change from baseline, baseline score was excluded from the model. [a]Participants responding "much improved" or "very much improved" on a 7-point rating scale. Abbreviations: LS, least-squares; MMDs, monthly migraine days; MSQ v2.1, Migraine-Specific Quality-of-Life Questionnaire, version 2.1; PI-MBS, patient-identified most bothersome symptom; SE, standard error; WPAI:M, Migraine-specific Work Productivity and Activity Impairment questionnaire.

Key Points

- Long-term (60-week) treatment with eptinezumab 100 mg or 300 mg administered every 12 weeks was well-tolerated, as well as maintained reductions in migraine frequency, patient-reported disease burden, and health-related quality of life in Japanese participants with CM.
- The long-term safety data from the SUNSET trial were similar to previously reported observations in primarily Western trial populations, with no new safety signals identified.

Conclusion

- Symptom reduction within the first 12 weeks of eptinezumab treatment was obtained and/or maintained throughout this 60-week extension trial in Japanese participants with CM, with a long-term safety, tolerability, and effectiveness profile comparable to that observed previously with eptinezumab 100 mg and 300 mg in migraine.

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References

1. Dong L, et al. *Pain Ther.* 2025;14(1):297-315.
2. Statistics Bureau of Japan. Current population estimates as of October 1, 2021. Available online; accessed July 15, 2025.
3. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. *Lancet.* 2017;390(10100):1211-1259.
4. Awaki E, et al. *Neurol Ther.* 2024;13(1):165-182.
5. Danno D, et al. *Neurol Ther.* 2025;14(1):335-356.
6. Matsumori Y, et al. *Neurol Ther.* 2022;11(1):205-222.
7. Kikui S, et al. *J Headache Pain.* 2020;21(1):110.
8. Hirata K, et al. *Curr Med Res Opin.* 2021;37(11):1945-1955.
9. European Medicines Agency. Summary of product characteristics: eptinezumab (Vyepti). Available online; accessed July 15, 2025.
10. Lipton RB, et al. *Neurology.* 2020;94(13):e1365-e1377.
11. Kudrow D, et al. *BMC Neurol.* 2021;21(1):126.
12. Blumenfeld A, et al. *BMC Neurol.* 2022;22(1):251.
13. Tepper SJ, et al. *J Neurol.* 2024;272(1):4.
14. Bayliss MS, Batenhorst AS. The HIT-6™: A User's Guide. 2002.

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