Migraine prevention in the real world: Exploring the role of anti-CGRP antibodies

Disclaimer

- *Unapproved products or unapproved uses of approved products may be discussed by the faculty; these situations may reflect the approval status in one or more jurisdictions*
- *The presenting faculty have been advised by touchIME to ensure that they disclose any such references made to unlabelled or unapproved use*
- *No endorsement by touchIME of any unapproved products or unapproved uses is either made or implied by mention of these products or uses in touchIME activities*
- *touchIME accepts no responsibility for errors or omissions*

Anti-CGRP antibodies for migraine prevention: Insights from real-world evidence

Prof. Mamoru Shibata
Department of Neurology
Tokyo Dental College
Ichikawa General Hospital
Chiba, Japan

touch™ NEUROLOGY

- **What is the value of real-world evidence in supporting clinical decision making for preventive migraine treatment with anti-CGRP antibodies?**

Japanese Headache Society guidance on anti-CGRP antibodies

Preventive therapy indication:[1]
When acute therapy for migraine cannot adequately treat the disability experienced in daily life

Preventive drug selection based on:[1]

- Headache characteristics
- Comorbidities
- Contraindications
- Efficacy
- Side effects

Use of anti-CGRP antibodies:[1]
In cases when existing prophylactic drugs provide insufficient efficacy or if side effects occur

Galcanezumab, fremanezumab and erenumab:[2–4]
Preventive treatment of migraine in adult patients with ≥4 MMDs for ≥3 months

CGRP, calcitonin gene-related peptide; MMD, monthly migraine day.

1. The Japanese Society of Neurology/The Japanese Headache Society/The Japanese Society of Neurotherapy. 2021. Available at: www.jhsnet.net/pdf/guideline_2021.pdf (accessed 14 June 2023); 2. The Japanese Headache Society. CQ- 3: Galcanezumab. Available at: www.jhsnet.net/GUIDELINE/CGRP/4.pdf (accessed 27 June 2023); 3. The Japanese Headache Society. CQ- 4: Fremanezumab. Available at: www.jhsnet.net/GUIDELINE/CGRP/5.pdf (accessed 27 June 2023); 4. The Japanese Headache Society. CQ-5: Erenumab. Available at: www.jhsnet.net/GUIDELINE/CGRP/7.pdf (accessed 27 June 2023).

touch™ NEUROLOGY

RWD on anti-CGRP antibodies: Insights for clinical decision making

Effects of **discontinuation** and optimal **treatment strategies**[1]

Safety and efficacy in **large, heterogeneous populations or subgroups,** e.g. aged ≥65 years, difficult to treat, country specific[3–5]

Potential **predictors of response** or **non-response** to treatment[2]

Long-term safety and efficacy data[6,7]

CGRP, calcitonin gene-related peptide; RWD, real-world data.

1. Gantenbein AR, et al. *Cephalalgia*. 2021;41:1181–6; 2. Raffaelli B, et al. *J Headache Pain*. 2023;24:16; 3. Muñoz-Vendrell A, et al. *J Headache Pain*. 2023;24:63; 4. Schiano di Cola F, et al. *Neurol Sci.* 2022;43:5763–4; 5. Kim B, et al. Presented at: 65th AHS Annual Scientific Meeting, Austin, TX, USA. 15–18 June 2023. P-65; 6. Iannone LF, et al. *CNS Drugs.* 2022;36:191–202; 7. Troy E, et al. *J Headache Pain*. 2023;24:5.

touch™ NEUROLOGY

Does real-world evidence support the clinical trial data for anti-CGRP antibodies?

RWD and RCT data for anti-CGRP antibodies

In patients with prior unsuccessful preventive treatment

	Erenumab		Eptinezumab		Fremanezumab		Galcanezumab	
Study type	**RCTs*[1]**	**RWD[1]**	**RCTs*[1]**	**RWD[2]**	**RCTs*[1]**	**RWD[1]**	**RCTs*[1]**	**RWD[1]**
MMDs or MHDs change	-1.8	0 to -15	100 mg: -4.8 300 mg: -5.3	Approx. 100 mg: -6.9 300 mg: -6.9	Monthly: -4.1 Quarterly: -3.7	EM: -5.0 CM: -10.0	-4.0	EM: -8.0 CM: -14.0
MMDs ≥50% response rate	30%	27–88%	100 mg: 42% 300 mg: 49%	>60%	Monthly: 34% Quarterly: 34%	64%	38%	EM: 77% CM: 64%
Frequent AEs	Injection site erythema: 6%	Constipation: 10–65%	COVID-19: 100 mg: 6% 300 mg: 7%	No new safety signals identified	Injection site erythema: 7%	Injection site erythema: 8%	Injection site erythema: 7%	Constipation: 20%; injection site erythema: 8%

Real-world data generally support the efficacy and safety of anti-CGRP antibodies observed in RCTs

*12-week trial results. Data cannot be directly compared due to major differences in study designs and patient characteristics.

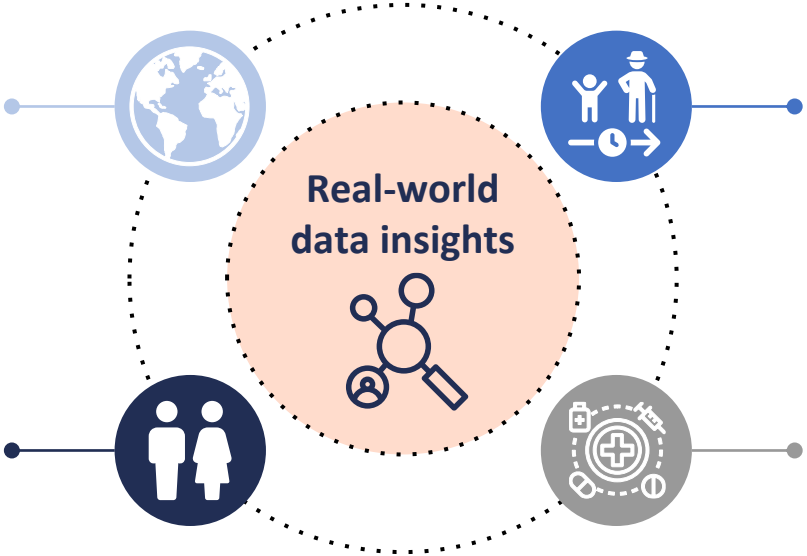
AE, adverse event; CGRP, calcitonin gene-related peptide; CM, chronic migraine; EM, episodic migraine; MHD, monthly headache day; MMD, monthly migraine day; RCT, randomized controlled trial; RWD, real-world data.

1. Lee MJ, et al. *Cephalalgia*. 2023;43:1–15; 2. Starling A, et al. Presented at: 65th AHS Annual Scientific Meeting, Austin, TX, USA. 15–18 June 2023. P-114.

Have there been any interesting real-world evidence outcomes in specific populations of patients using anti-CGRP antibodies?

touch™ NEUROLOGY

Anti-CGRP antibodies in specific patient populations



Different countries

e.g. South Korea,[1] Brazil[2] and Australia[3]

Different ages

e.g. patients aged ≥65 years[4] and adolescents[5]

Different genders

e.g. men and women[6,7]

Difficult to treat

e.g. highly treatment refractory patients[8–10]

Real-world data studies support the efficacy and safety of anti-CGRP antibodies in specific subgroups of patients

CGRP, calcitonin gene-related peptide.

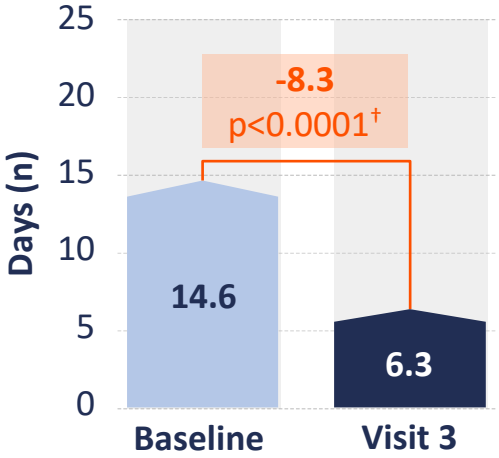
1. Kim B, et al. Presented at: 65th AHS Annual Scientific Meeting, Austin, TX, USA. 15–18 June 2023. P-65; 2. Krymchantowski AV, et al. *Avanços em Medicina.* 2021;1:24–9; 3. Ray J, et al. *J Headache Pain.* 2022;23(Suppl. 1):P52; 4. Biswas S, et al. Presented at: 65th AHS Annual Scientific Meeting, Austin, TX, USA. 15–18 June 2023. P-233; 5. Katsuki M, et al. *Cureus.* 15:e33689; 6. Ornello R, et al. *Front Neurol*. 12:774341; 7. Ornello R, et al. *J Headache Pain*. 2022;23:38; 8. Argyriou AA, et al. *Eur J Neurol*. 2023;30:1435–42; 9. Scheffler A, et al. *J Headache Pain*. 2020;21:84; 10. Schiano di Cola F. *Neurol Sci.* 2022;43:5763–4.

touch™ NEUROLOGY

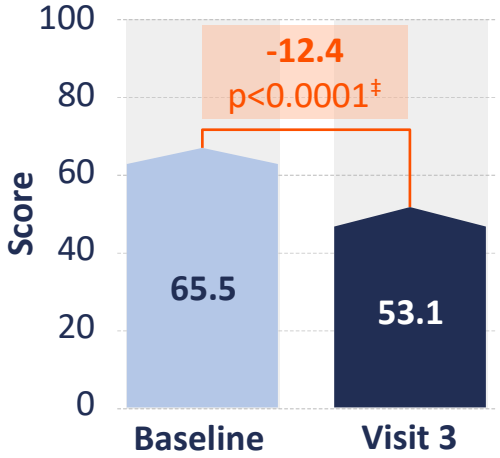
Anti-CGRP antibodies for migraine prevention in Japanese patients

Single-centre prospective cohort study of patients who had treatment failure with ≥1 preventive drug (N=30)*

Change in MMDs



Change in HIT-6 score



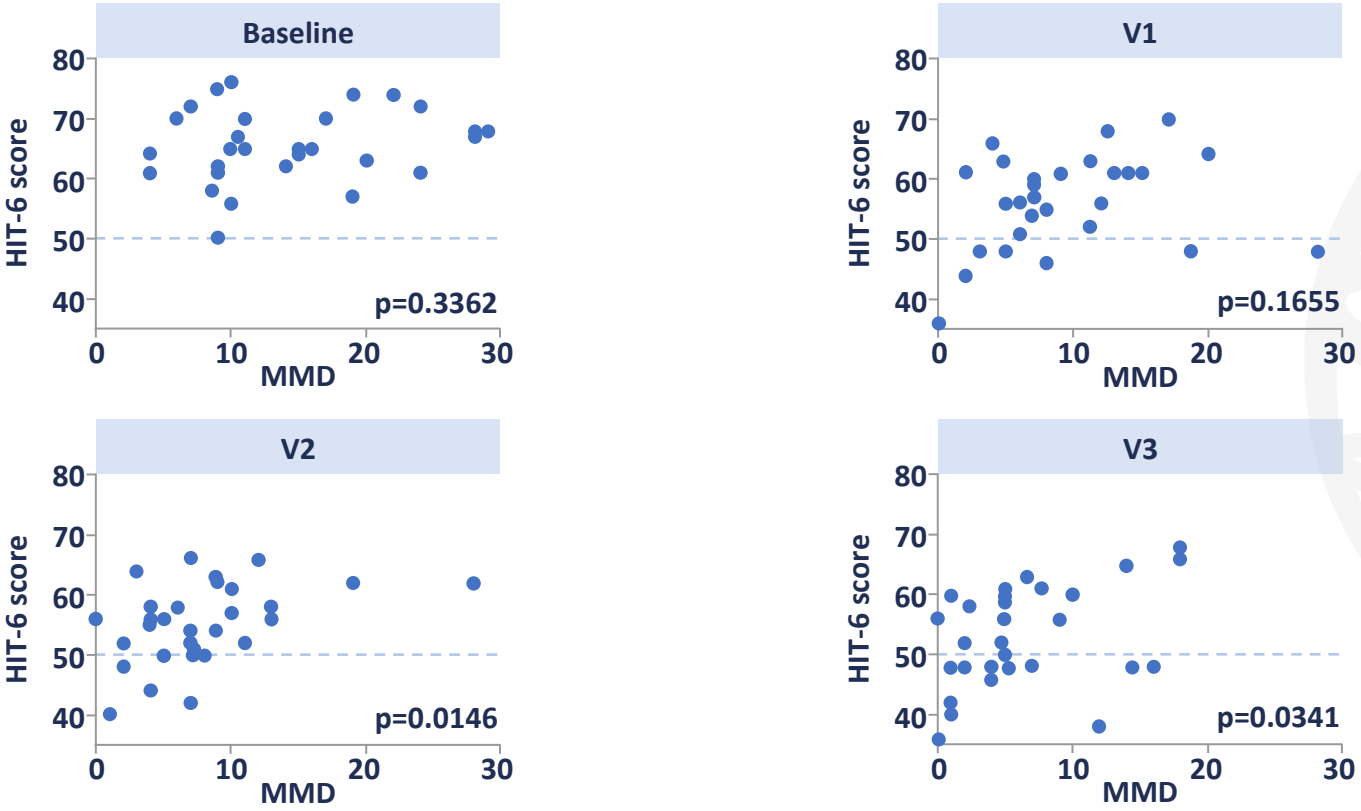
TEAEs

Total	30%
Constipation	16.7%
Injection site reactions	6.7%
Blood pressure elevation	3.3%
Alopecia	3.3%
Diarrhoea	3.3%

*Data shown are for the whole CGRP-treated cohort: galcanezumab, n=15; fremanezumab, n=8; erenumab, n=7. After the baseline period of ≥4 weeks, patients received three doses of CGRP antibody treatment in total; †Friedman's test with Dunn's post hoc test; ‡One-way ANOVA with Dunnett's post hoc test.
CGRP, calcitonin gene-related peptide; HIT-6, Headache Impact Test-6; MMD, monthly migraine day; TEAE, treatment-emergent adverse event.
Shibata M, et al. Presented at: 65th AHS Annual Scientific Meeting, Austin, TX, USA. 15–18 June 2023. P-164.

touch™ NEUROLOGY

Correlation between MMD and HIT-6 score



HIT-6, Headache Impact Test-6; MMD, monthly migraine day; V, visit.

Shibata M, et al. Presented at: 65th AHS Annual Scientific Meeting, Austin, TX, USA. 15–18 June 2023. P-164.

What do available real-world data indicate with regards to treatment optimization with anti-CGRP antibodies?

touch™ NEUROLOGY

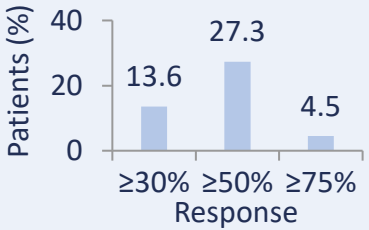
Switching to and from anti-CGRP antibodies

Iannone LF, et al. 2023[1]
Retrospective, single-centre study (N=22)

Chronic (n=19) or episodic migraine (n=3)

- Erenumab (n=11) to galcanezumab (n=11)
- Galcanezumab (n=8) or fremanezumab (n=3) to erenumab (n=11)

Outcomes at month 3 vs switch baseline:



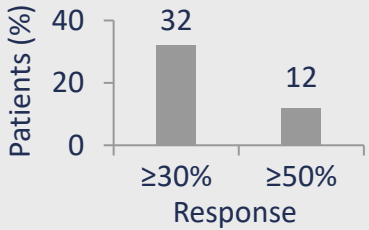
Significant reductions in MHDs and AMDs (both p<0.003)

Overeem LH, et al. 2022[2]
Retrospective, multicentre study (N=25)

Chronic (n=22) or episodic migraine (n=3)

Erenumab (n=25) to galcanezumab (n=12) or fremanezumab (n=13)

Outcomes at month 3 vs switch baseline:



Significant reduction in MHDs (p<0.009)

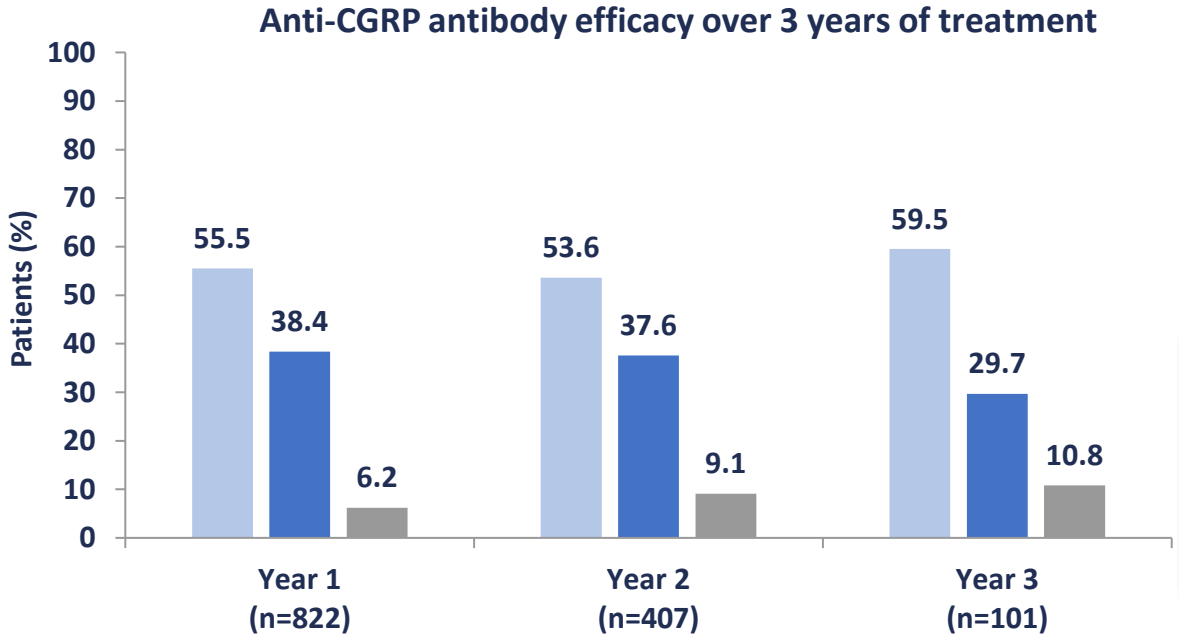
For patients who did not respond to an anti-CGRP antibody treatment, switching to another anti-CGRP antibody agent provided clinical benefit

Data cannot be directly compared due to major differences in study designs and patient characteristics.
AMD, analgesic medication day; CGRP, calcitonin gene-related peptide; MHD, monthly headache day; MMD, monthly migraine day.
1. Iannone LF, et al. *Cephalalgia*. 2023;43:1–11; 2. Overeem LH, et al. *Cephalalgia*. 2022;42:291–301.

touch™ NEUROLOGY

Long-term treatment with anti-CGRP antibodies

Longitudinal US-based EMR analysis (n=2,025)



Anti-CGRP antibodies were associated with sustained efficacy over extended periods of treatment, with only a minority losing benefit over time

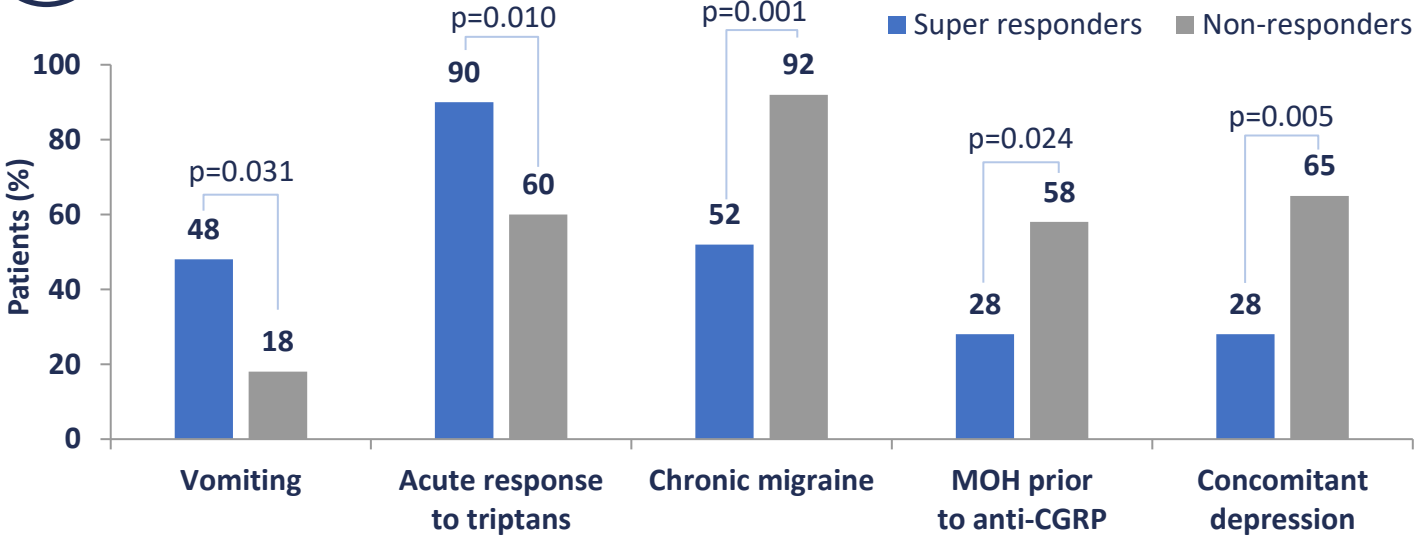
CGRP, calcitonin gene-related peptide; EMR, electronic medical record; MMD, monthly migraine day.

Salim A, et al. *J Headache Pain*. 2022;23(Suppl. 1):P59.

touch™ NEUROLOGY

Identifying super responders and non-responders to anti-CGRP antibodies

Single-centre retrospective cohort study of super responders (n=29) and non-responders (n=26)*



Non-responders also had higher MHDs ($p<0.001$) and MMDs ($p<0.035$) vs super responders

*Super responders: ≥75% reduction of MHD in third month after anti-CGRP initiation vs baseline (erenumab, 41%; fremanezumab, 35%; galcanezumab, 24%). Non-responders: ≤25% reduction in MHD in third month after anti-CGRP initiation vs baseline with both anti-CGRPs (first anti-CGRP: erenumab, 54%; fremanezumab, 15%; galcanezumab, 31%; Second anti-CGRP: erenumab, 46%; fremanezumab, 8%; galcanezumab, 46%).

CGRP, calcitonin gene-related peptide; MHD, monthly headache day; MMD, monthly migraine day; MOH, medication overuse headache.

Raffaelli B, et al. *J Headache Pain*. 2023;24:16.