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Title: Calcitonin Gene-Related Peptide Monoclonal Antibody Utilization and Treatment Gaps in People with Migraine in Japan: Results from the OVERCOME (Japan) 2nd Study

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Supplementary files

Table S1: Patient-reported outcomes

PRO	Evaluation	Scoring	Grading
MIDAS	Quantifies headache-related disability over a 3-month period. It measures the number of days missed or with reduced productivity at work, home, or social events.	The total score is a summation of five items (scored 0–90); higher values indicate greater disability.	Grade I (0–5) – little or no disability, Grade II (6–10) – mild disability, Grade III (11–20) – moderate disability, and Grade IV (21+) – severe disability.
MIDAS additional question on pain severity	Patients self-report average headache pain severity on an 11-point numerical rating scale.	0 (no pain at all) to 10 (pain as bad as it could be).	-
MIBS-4	A 4-item instrument that measures headache-related burden in the time between attacks. The items address disruption at work and school, diminished family and social life, difficulty planning, and emotional difficulty.	The total score range is 0–12.	Level of interictal burden is categorized as None (0), Mild (1–2), Moderate (3–4), and Severe (5+).

Abbreviations: MIBS – Migraine Interictal Burden Scale-4, MIDAS – Migraine Disability Assessment Scale, PRO – Patient-Reported Outcome.

Table S2. Variables used in the univariate analysis (CGRP mAb never use vs. ever use [CGRP mAb current and discontinued groups])

Variable	Odds ratio (95% CI)	p-value
Age	0.98 (0.97, 1.00)	0.017
Gender	0.49 (0.34, 0.70)	<0.001
Region		
Kanto	reference	-
Hokkaido	0.57 (0.17, 1.90)	0.360
Tohoku	0.64 (0.28, 1.44)	0.282
Chubu	1.14 (0.69, 1.88)	0.606
Kinki/Kansai	0.94 (0.57, 1.58)	0.825
Chugoku	1.04 (0.51, 2.12)	0.914
Shikoku	0.71 (0.21, 2.36)	0.573
Kyushu	0.45 (0.21, 0.97)	0.042
Okinawa	1.19 (0.27, 5.35)	0.818
Marital status	1.61 (1.12, 2.31)	0.010
Medical history		
Hypertension	2.71 (1.87, 3.93)	<0.001
Diabetes	3.20 (2.02, 5.08)	<0.001
Hypercholesterolemia/Hyperlipidemia/Dyslipidemia	1.32 (0.86, 2.04)	0.205
Tension-type headache	1.37 (0.94, 1.99)	0.103
Cluster headache	2.49 (1.51, 4.11)	<0.001
Medication-overuse headache	2.97 (1.77, 4.99)	<0.001
insomnia	1.99 (1.37, 2.89)	<0.001
Depression	1.51 (1.04, 2.18)	0.030

Anxiety/ panic disorder	1.18 (0.76, 1.82)	0.456
Employment status	2.41 (1.46, 3.96)	<0.001
Household income	2.29 (1.51, 3.49)	<0.001
Age at onset of headache	0.99 (0.97, 1.01)	0.301
MHD	1.00 (0.98, 1.03)	0.824
EM/CM	1.19 (0.79, 1.78)	0.411
Degree of disability in past 3 months	0.62 (0.29, 1.33)	0.217
MIDAS score	1.01 (1.00, 1.01)	0.001
MIBS-4	1.09 (1.04, 1.14)	<0.001
Healthcare status		
Currently not consulted	reference	-
CGRP mAb prescribable department	6.98 (3.51, 13.90)	<0.001
CGRP mAb non-prescribable department	2.71 (1.08, 6.78)	0.033
Currently consulted department	2.58 (1.32, 5.02)	0.005
OTC medication use experience	1.23 (0.69, 2.19)	0.478
NSAIDs use experience	2.42 (1.56, 3.74)	<0.001
Triptan use experience	8.27 (5.28, 12.94)	<0.001
Experience discussing treatment goals with physicians	3.22 (1.90, 5.46)	<0.001
Attitude towards headache	1.27 (0.50, 3.22)	0.615
Perception: Improvable by Preventive Medication	2.14 (1.50, 3.06)	<0.001

Variables with a p-value <0.05 in the univariate analysis were included in the multivariate model. The number of respondents included in the analysis was 1484, except for employment status (n = 1453), household income (n = 1166), currently consulted department (n = 1063), and experience discussing treatment goals with physicians (n = 1063). Abbreviations: CGRP mAb - Calcitonin gene-related peptide monoclonal antibody, CI – Confidence interval, CM – chronic migraine, EM – Episodic migraine, MHD – Monthly headache days, MIBS-4 - Migraine interictal burden scale-4, MIDAS - Migraine disability assessment scale, NSAIDs- Nonsteroidal anti-inflammatory drugs, OR – Odds ratio, OTC – Over-the-counter

Table S3. Reasons for not initiating CGRP mAbs by the respondents

	Eligible	Ineligible
	No CGRP mAb n = 56	No CGRP mAb n = 186
Worried about the cost	21 (37.5)	33 (17.7)
I wasn't sure if it would be worth the cost	17 (30.4)	34 (18.3)
There is no facility nearby that can prescribe it (the facility that can prescribe is far away)	11 (19.6)	36 (19.4)
I don't know the difference from the current treatment	10 (17.9)	21 (11.3)
I'm worried about new drugs	10 (17.9)	21 (11.3)
I don't like the administration method (injection)	9 (16.1)	23 (12.4)
I'm satisfied with my current treatment	8 (14.3)	34 (18.3)
I didn't know if the treatment was right for my migraine	8 (14.3)	42 (22.6)
I don't want to increase the number of drugs I use	8 (14.3)	29 (15.6)
I was worried about side effects	12 (21.4)	31 (16.7)
The doctor told me that I didn't know if it would work	7 (12.5)	32 (17.2)
The doctor recommended another treatment, saying it was still too early	7 (12.5)	22 (11.8)
I don't like the administration method (number of times)	7 (12.5)	19 (10.2)
I don't think the effect will be the same as the current treatment	11 (19.6)	27 (14.5)
Other reasons	8 (14.3)	25 (13.4)

Abbreviations: CGRP – Calcitonin gene-related peptide monoclonal antibody, n – Number of respondents

Table S4. Reasons for CGRP mAb discontinuation, suspension, resumption, and switching

Variable	Eligible		Ineligible	
	Current CGRP mAb	Discontinued CGRP mAb	Current CGRP mAb	Discontinued CGRP mAb
Reason for CGRP mAb discontinuation, n (%)	-	n = 58	-	n = 176
The doctor advised me to stop	-	12 (20.7)	-	22 (12.5)
I was concerned about the side effects of injections	-	11 (19.0)	-	16 (9.1)
The injection does not work or no longer works	-	9 (15.5)	-	22 (12.5)
Regular hospital visits became impossible or wanted to stop	-	5 (8.6)	-	13 (7.4)
With information on the Internet	-	3 (5.2)	-	25 (14.2)
Due to the high cost	-	4 (6.9)	-	15 (8.5)
The injection was effective enough, and I thought I would stop once	-	4 (6.9)	-	13 (7.4)
I wanted to stop the injection itself, because the injection was painful	-	3 (5.2)	-	12 (6.8)
I thought other prevention methods might work better	-	2 (3.4)	-	14 (8.0)

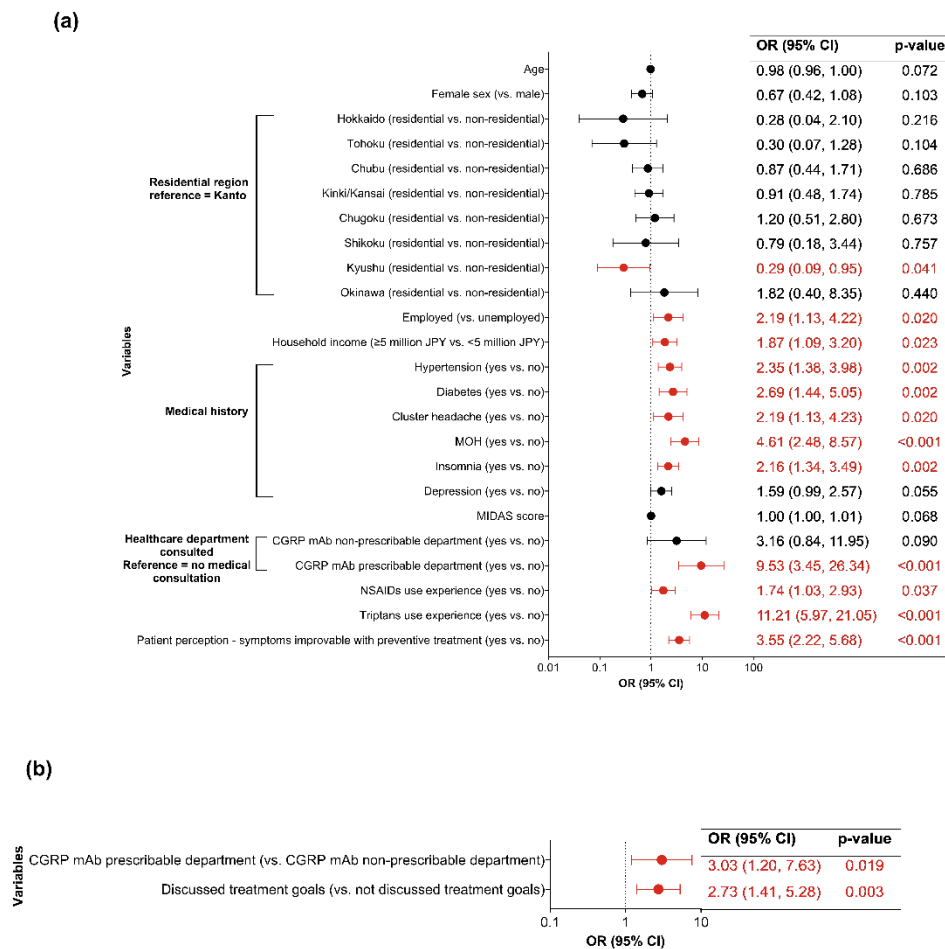
Thinking about pregnancy	-	2 (3.4)	-	6 (3.4)
At the recommendation of friends and family	-	1 (1.7)	-	7 (4.0)
Other reasons	-	2 (3.4)	-	11 (6.3)
Reason for CGRP mAb suspension, n (%)	n = 37	n = 38	n = 68	n = 113
With information on the Internet	6 (16.2)	1 (2.6)	6 (8.8)	12 (10.6)
Due to high cost	5 (13.5)	6 (15.8)	9 (13.2)	8 (7.1)
I thought other prevention methods might work better	5 (13.5)	2 (5.3)	3 (4.4)	11 (9.7)
The doctor advised me to stop	3 (8.1)	6 (15.8)	8 (11.8)	16 (14.2)
The injection does not work or no longer works	4 (10.8)	5 (13.2)	12 (17.6)	11 (9.7)
I was concerned about the side effects of injections	3 (8.1)	5 (13.2)	5 (7.4)	13 (11.5)
I wanted to stop the injection itself, because the injection was painful	3 (8.1)	4 (10.5)	7 (10.3)	7 (6.2)
Regular hospital visits became impossible or wanted to stop	3 (8.1)	2 (5.3)	6 (8.8)	8 (7.1)
The injection was effective enough and I thought I would stop once	2 (5.4)	4 (10.5)	9 (13.2)	17 (15.0)
Thinking about pregnancy	2 (5.4)	3 (7.9)	-	4 (3.5)

At the recommendation of friends and family	-	-	3 (4.4)	1 (0.9)
Other reasons	1 (2.7)	-	-	5 (4.4)
Reason for resuming CGRP mAb, n (%)	n = 37	n = 38	n = 68	n = 113
The headache started to come back	7 (18.9)	6 (15.8)	11 (16.2)	19 (16.8)
My headache got worse	7 (18.9)	6 (15.8)	5 (7.4)	10 (8.8)
It got worse when I stopped	7 (18.9)	-	8 (11.8)	11 (9.7)
The frequency of headache attacks has increased	5 (13.5)	5 (13.2)	13 (19.1)	17 (15.0)
I expected the headache to get worse	3 (8.1)	2 (5.3)	5 (7.4)	5 (4.4)
The doctor suggested that I resume	2 (5.4)	5 (13.2)	7 (10.3)	18 (15.9)
I was able to pay for it	2 (5.4)	3 (7.9)	5 (7.4)	10 (8.8)
I can go to the hospital	1 (2.7)	5 (13.2)	9 (13.2)	12 (10.6)
It was recommended by family and friends	1 (2.7)	4 (10.5)	5 (7.4)	6 (5.3)
Other reasons	2 (5.4)	2 (5.3)	-	5 (4.4)
Reason for switching CGRP mAb formulation, n (%)	n = 28	-	n = 40	-
The number of days I have headaches with the previous injection has increased	6 (21.4)	-	4 (10.0)	-

I thought the current injection might work better	4 (14.3)	-	4 (10.0)	-
The doctor recommended that I change to my current injection	3 (10.7)	-	6 (15.0)	-
With information on the Internet	3 (10.7)	-	3 (7.5)	-
I want to try something different	3 (10.7)	-	3 (7.5)	-
I was worried about the side effects of the previous injection	2 (7.1)	-	6 (15.0)	-
The number and method of injections are right for me	2 (7.1)	-	4 (10.0)	-
The severity of the headache has worsened with the previous injection	1 (3.6)	-	5 (12.5)	-
The syringe of the current injection is more suitable for me	1 (3.6)	-	2 (5.0)	-
The current injection is cheaper than the previous injection	1 (3.6)	-	2 (5.0)	-
On the recommendation of friends and family	1 (3.6)	-	-	-
Other reasons	1 (3.6)	-	1 (2.5)	-

Abbreviations: CGRP – Calcitonin gene-related peptide monoclonal antibody, n – Number of respondents

Figure S1. Factors associated with the CGRP mAb treatment experience (ever used [current CGRP mAb group] vs. never used)



(a) Includes respondents eligible for CGRP mAbs but had no CGRP mAb experience (n = 1,348) and respondents eligible for CGRP mAbs and current users (n=78) and (b) Includes respondents who visited a medical institution in the past year: eligible for CGRP mAbs but had no CGRP mAb experience (n = 936) and respondents eligible for CGRP mAbs and current users (n = 74). Age was adjusted for sex, and vice versa; MIDAS total score was adjusted for age and sex; and all other variables were adjusted for age, sex, and MHD in the regression model. Red color indicates the variables that significantly (p<0.05) affect CGRP mAb treatment experience (current CGRP mAb vs. No CGRP mAb group).

Abbreviations: CGRP mAb - Calcitonin gene-related peptide monoclonal antibody, CI – Confidence interval, JPY – Japanese Yen, MHD – Monthly headache days, MIDAS - Migraine disability assessment scale, MOH – Medication-overuse headache, NSAID - Nonsteroidal anti-inflammatory drugs, OR – Odds ratio