



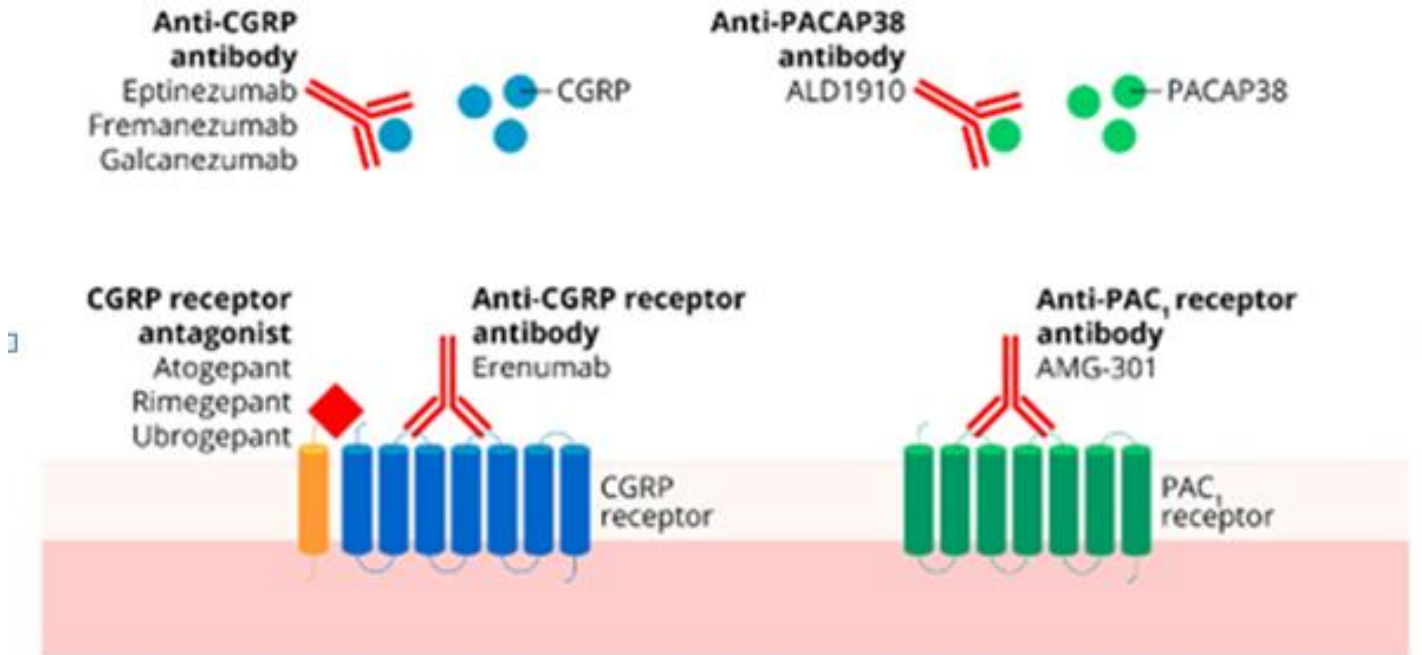
ReFORMÚLaTE

CONTROVERSIA: TRATAMIENTO DE LA MIGRAÑA

“Switch con anti-CGRP y medicina de precisión”

Pablo Selvi Sabater

*Servicio Murciano de Salud / Especialista en
Farmacia Hospitalaria/ Servicio de Gestión
Farmacéutica*





INFORME DE POSICIONAMIENTO TERAPÉUTICO

Informe de Posicionamiento Terapéutico de fremanezumab (Ajovy®) en la profilaxis de migraña

IPT, 11/2020. V1

Fecha de publicación: 28 de julio de 2020¹

Corrección de 3 de noviembre de 2020 (ver al final)

Se carece de datos comparativos directos con otras alternativas en profilaxis, como topiramato, toxina botulínica, betabloqueantes, flunarizina o amitriptilina, o incluso otros fármacos con el mismo mecanismo de acción (erenumab, galcanezumab). La limitada evidencia disponible muestra un beneficio clínico modesto y no permite considerar la superioridad frente a otras opciones disponibles en profilaxis de la migraña.

Ante la ausencia de comparaciones directas y de beneficio añadido respecto a las alternativas de tratamiento, el uso de fremanezumab podría considerarse en pacientes en los que no exista mejoría o que presenten intolerancia a las otras opciones de profilaxis antimigrañosa, siendo en este escenario una alternativa a erenumab y galcanezumab.

Por el momento, no hay evidencia para recomendar la secuenciación tras fracaso terapéutico entre estos fármacos (erenumab, galcanezumab o fremanezumab).

NOTA: este IPT, que es el último adoptado, recoge las conclusiones más actualizadas para el posicionamiento de los distintos medicamentos en profilaxis de migraña.

Sacco et al. *The Journal of Headache and Pain* (2022) 23:67
<https://doi.org/10.1186/s10194-022-01431-x>

The Journal of Headache
and Pain

CONSENSUS ARTICLE

Open Access

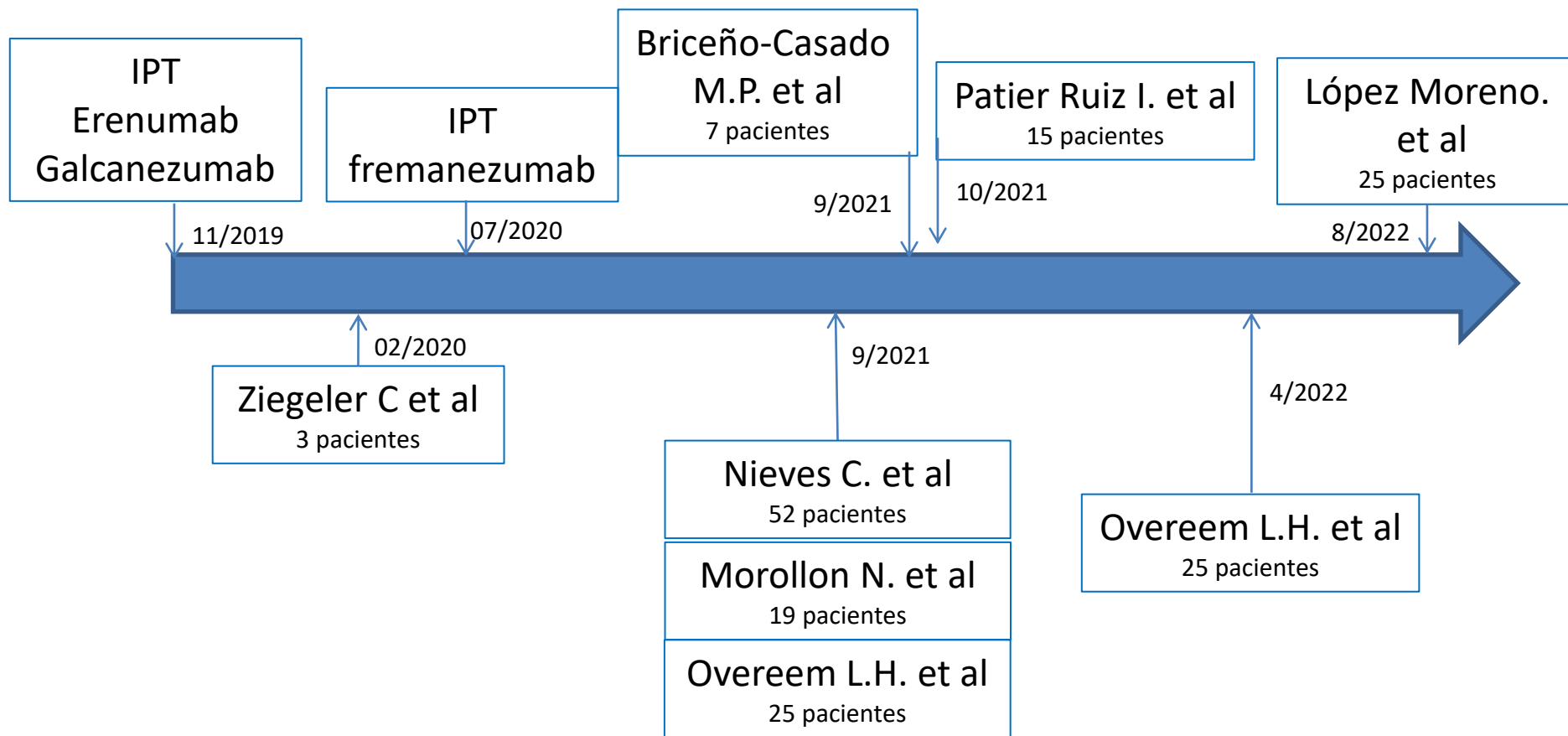


European Headache Federation guideline on the use of monoclonal antibodies targeting the calcitonin gene related peptide pathway for migraine prevention – 2022 update

Simona Sacco^{1*}, Faisal Mohammad Amin^{2,3}, Messoud Ashina², Lars Bendtsen², Christina I. Deligianni², Raquel Gil-Gouveia^{4,5}, Zaza Katsarava^{6,7}, Antoinette MaassenVanDenBrink⁸, Paolo Martelletti⁹, Dimos-Dimitrios Mitsikostas¹⁰, Raffaele Ornello¹, Uwe Reuter^{11,12}, Margarita Sanchez-del-Rio¹³, Alexandra J. Sinclair^{14,15}, Gisela Terwindt¹⁶, Derya Uluduz¹⁷, Jan Versijpt¹⁸ and Christian Lampl¹⁹

6. In individuals with migraine who are non-responders to one monoclonal antibody targeting the CGRP pathway, is switching to a different antibody an option?

In individuals with migraine with inadequate response to one monoclonal antibody targeting the CGRP pathway, there is insufficient evidence on the potential benefits of antibody switch but switching may be an option.



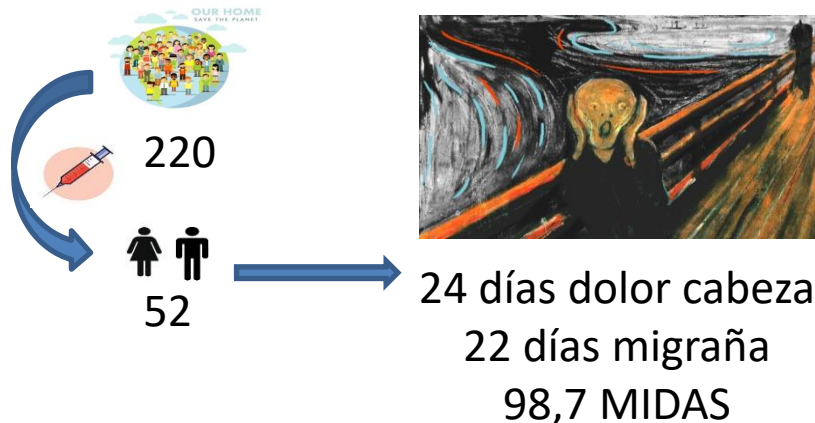
MEETING ABSTRACTS

Open Access

The International Headache Congress – IHS
and EHF joint congress 2021

Virtual. 8-12 September 2021

Published: 7 September 2021



P0105

Treatment failure with anti-CGRP therapy: should we discontinue the treatment or switch it?

C. Nieves Castellanos, M. Losada López, M. I. Fabrich Marín, J. Pérez García, S. Díaz Insa

Hospital Universitari i Politècnic la Fe de Valencia, Valencia, Spain

Correspondence: C. Nieves Castellanos

The Journal of Headache and Pain 2021, 22(Suppl 1):P0105

3 months after the switch with a second a-CGRP
mAb, 46,15% wanted to continue with the
treatment

n=24



36% reducen un 25% DM
2 pacientes reducen un 75% DM

Un 36% de 24 pacientes (9 pacientes). **Un total de 9 respondedores de 52 pacientes = 17%**

The Journal of Headache and Pain 2021, 22(Suppl 1):103
<https://doi.org/10.1186/s10194-021-01293-9>

The Journal of Headache
and Pain

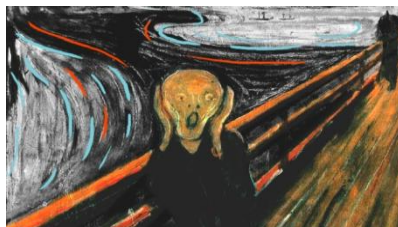
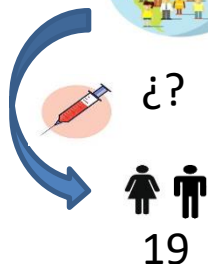
MEETING ABSTRACTS

Open Access

The International Headache Congress – IHS and EHF joint congress 2021

Virtual. 8-12 September 2021

Published: 7 September 2021



¿? días dolor cabeza
¿? días migraña
¿? MIDAS



Cambio de MA
(salvo dos casos)

P0291

What if a monoclonal antibody doesn't work as a migraine preventive treatment? Description of the experience in switching between monoclonals antibodies in a Headache Unit

N. Morollón¹, R. Belvis¹, A. De Dios², N. Pagès², M. Massip²

¹Hospital de la Santa Creu i Sant Pau, Neurology, Barcelona, Spain;

²Hospital de la Santa Creu i Sant Pau, Pharmacy, Barcelona, Spain

Correspondence: N. Morollón

The Journal of Headache and Pain 2021, 22(Suppl 1):P0291



33,3% reducen un 50% DM

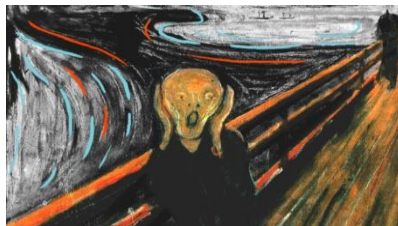
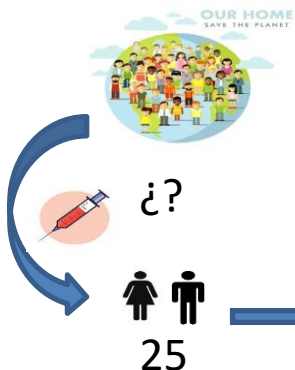
MEETING ABSTRACTS

Open Access

The International Headache Congress – IHS and EHF joint congress 2021

Virtual. 8-12 September 2021

Published: 7 September 2021



20,8 días dolor cabeza

17,8 días dolor cabeza



Cambio de MA



32% reducen un 30% DH
12% reducen un 50% DH

P0328

Effect of antibody switch in non-responders to a CGRP receptor antibody treatment in migraine: A multi-center retrospective cohort study

L. H. Overeem¹, A. Peikert², M. D. Hofacker¹, K. Kamm³, R. Ruscheweyh³, A. Gendolla⁴, B. Raffaelli¹, U. Reuter¹, L. Neeb¹

¹Charité University Hospital Berlin, Neurology, Berlin, Germany;

²Neurologicum Bremen, Bremen, Germany; ³Ludwig Maximilians

University, Neurology, Munich, Germany; ⁴Praxis Gendolla, Essen,

Germany

Correspondence: L. H. Overeem

The Journal of Headache and Pain 2021, 22(Suppl 1):P0328

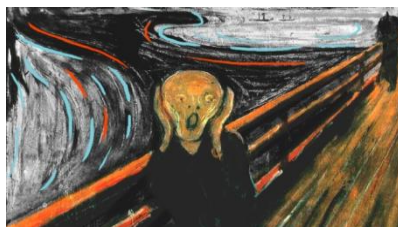
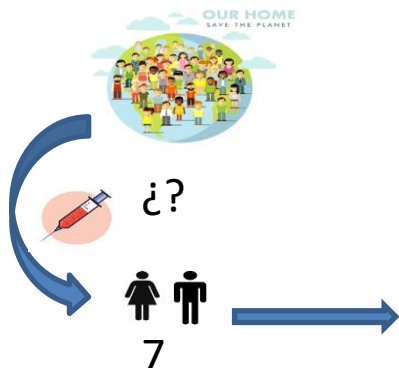
> Eur J Hosp Pharm. 2021 Sep 14;ejhpharm-2021-002946. doi: 10.1136/ejhpharm-2021-002946.
Online ahead of print.

Switching of monoclonal antibodies against calcitonin gene-related peptide in chronic migraine in clinical practice: a case series

María Del Pilar Briceño-Casado¹, Manuel David Gil-Sierra^{2,3}, Beatriz De-La-Calle-Riaguas⁴

Affiliations + expand

PMID: 34521726 DOI: 10.1136/ejhpharm-2021-002946



¿? días migraña
¿? MIDAS



Cambio de MA
2 casos sin cambio de MA

Case report

Table 1 Individual results from patients with chronic migraine treated with CGRP mAb switching

Patient	1	2	3	4	5	6	7
Gender	Female	Male	Male	Female	Female	Female	Female
Approximate age (years)	50–55	25–30	45–50	45–50	40–45	65–70	25–30
Baseline migraine days	≥8	≥8	≥8	≥10	≥10	≥8	≥15
Previous treatments	Botulinum toxin A, flunarizine, mirtazapine, propranolol, topiramate (n=5)	Botulinum toxin A, flunarizine, propranolol, topiramate, zonisamide (n=5)	Botulinum toxin A, amitrityptiline, atenolol, escitalopram, flunarizine, gabapentin, pregabalin, venlafaxine, zonisamide (n=10)	Botulinum toxin A, candesartan, gabapentin, propranolol, venlafaxine, zonisamide (n=6)	Botulinum toxin A, amitrityptiline, flunarizine, nadolol, propranolol, topiramate (n=6)	Botulinum toxin A, amitrityptiline, duloxetine, pregabalin (n=4)	Botulinum toxin A, amitrityptiline, flunarizine, nadolol, topiramate (n=5)
First CGRP mAb	Galcanezumab	Galcanezumab	Galcanezumab	Galcanezumab	Galcanezumab	Galcanezumab	Erenumab
Duration of first CGRP mAb therapy (months)	10	9	9	4	4	6	6
Reduction ≥50% of monthly migraine days with respect to baseline with first CGRP mAb	At 3 months: Yes At 6 months: No	Yes No	Yes No	No Not reached	No Not reached	No No	No No
Reduction in pain intensity with first CGRP mAb	At 3 months: Yes At 6 months: No	No No	Yes No	No Not reached	No Not reached	No No	No No
Reason for switching	No response	No response	No response	No response	No response	No response	No response
Second CGRP mAb	Erenumab	Erenumab	Fremanezumab	Erenumab	Erenumab	Fremanezumab	Galcanezumab
Duration of second CGRP mAb therapy (months)	6	7	3	14	7	3	5
Reduction ≥50% of monthly migraine days with respect to baseline with second CGRP mAb	At 3 months: Yes At 6 months: No	No No	Yes Not reached	Yes Yes	No No	No Not reached	No Not reached
Reduction in pain intensity with second CGRP mAb	At 3 months: No At 6 months: No	No No	Yes Not reached	Yes Yes	No No	No Not reached	No Not reached

CGRP mAb, monoclonal antibodies directed against the calcitonin gene-related peptide pathway.



42%* reducen un 50% DM 3 meses
14% reducen un 50% DM 6 meses

*dos de los tres pacientes ya habían reducido también a los 3 meses con el 1º mAb

Early Experiences in Switching between Monoclonal Antibodies in Patients with Nonresponsive Migraine in Spain: A Case Series

Ignacio Patier Ruiz^a Javier Sánchez-Rubio Ferrández^a Alba Cárcamo Fonfría^b
Teresa Molina García^a

^aPharmacy Service, Getafe University Hospital, Getafe, Spain; ^bNeurology Service, Getafe University Hospital, Getafe, Spain



8/15 (53%) reducen un 30% DM
Y de estos, 4 (27%) consiguen 50% DM

Table 1. Baseline characteristics and main outcomes

	Switch group (n = 15)	Nonswitch group (n = 15)	Total (n = 30)
Age (mean $\pm$ SD), years	51.07 ($\pm$ 10.82)	45.45 ($\pm$ 11.62)	50.26 ($\pm$ 11.06)
Sex, n (%)	Female: 11/15 (73.33) Male: 4/15 (26.66)	Female: 13/15 (86.66) Male: 2/15 (13.33)	Female: 24/30 (80) Male: 6/30 (20)
Diagnostic, n (%)	EM: 4/15 (26.66) CM: 11/15 (73.33)	EM: 11/15 (73.33) CM: 4/15 (26.66)	EM: 15/30 (50) CM: 15/30 (50)
Prior preventive treatment failures, mean $\pm$ SD	5.4 ($\pm$ 1.24)	4.53 ($\pm$ 1.46)	4.96 ($\pm$ 1.4)
Duration of treatment with ERE (median IQR), days	112 (112–168)	364 (280–462)	224 (112–385)
ERE doses (mean $\pm$ SD), n	6 ($\pm$ 3.4)	13.13 ($\pm$ 3.98)	9 ($\pm$ 5.28)
Titration to 140 mg of ERE	15/15 (100%)	80% (12/15)	27/30 (90%)
Duration of treatment with GAL (median IQR), days	182.93 (84–224)	–	–
GAL doses (mean $\pm$ SD), n	7 ($\pm$ 5)	–	–
MDM basal, mean $\pm$ SD	23.93 ($\pm$ 7.13)	16.67 ($\pm$ 5.6)	20.3 ($\pm$ 7.3)
Acute medication use basal (mean $\pm$ SD), days/month	19.87 ($\pm$ 9.27)	11.53 ($\pm$ 7.58)	15.7 ($\pm$ 9.34)

Effect of antibody switch in non-responders to a CGRP receptor antibody treatment in migraine: A multi-center retrospective cohort study

Lucas Hendrik Overeem^{1,*}, Andreas Peikert^{2,*},
Maxi Dana Hofacker¹, Katharina Kamm³,
Ruth Ruscheweyh³, Astrid Gendolla⁴, Bianca Raffaelli¹,
Uwe Reuter^{1,5} and Lars Neeb¹

Cephalalgia

2022, Vol. 42(4-5) 291-301

© International Headache Society 2021



Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/03331024211048765

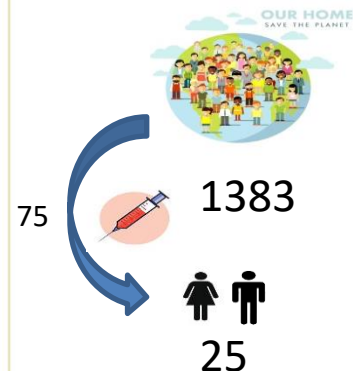
journals.sagepub.com/home/cep



8/28 (32%) reducen un 30% DM
Y de estos, 3 (12%) consiguen 50% DM

Table 4. Monthly headache days and acute medication days after switch during observation period 2.

		(Change from baseline)				p-value for repeated measures ^a
Observation Period 2		Baseline Mean (SD)	Month 1 Mean difference (95% CI)	Month 2 Mean difference (95% CI)	Month 3 Mean difference (95% CI)	
Total cohort	n					
30% responder rate, n (%) ^b	25		4 (16)	7 (28)	8 (32)	
50% responder rate, n (%) ^b	25		2 (8)	3 (12)	3 (12)	
Monthly Headache Days	25	20.8 (7.1)	-1.5 (-3.1 to 0.2)	-2.9 (-4.8 to -0.9)	-3.1 (-5.0 to -1.2)	0.001
p vs baseline ^c			0.208	0.005	0.003	
Corrected p vs baseline ^d			0.623	0.016	0.009	
Acute Medication Days	17	9.1 (4.7)	-1.6 (-4.1 to 0.8)	-1.7 (-4.1 to 0.6)	-1.9 (-4.3 to 0.4)	0.367
Non-daily headache						
30% responder rate, n (%) ^b	16		4 (25)	7 (44)	8 (50)	
50% responder rate, n (%) ^b	16		2 (13)	3 (19)	3 (19)	
Monthly Headache Days	16	17.1 (6.1)	-1.9 (-4.4 to 0.6)	-4.2 (-6.9 to -1.4)	-4.6 (-7.2 to -1.9)	0.002
p vs baseline ^c			0.171	0.003	0.001	
Corrected p vs baseline ^d			0.513	0.010	0.002	
Acute Medication Days	10	9.2 (4.6)	-1.1 (-4.7 to 2.5)	-1.8 (-4.3 to 0.7)	-2.0 (-5.4 to 1.4)	0.324
Daily headache						
30% responder rate, n (%) ^b	9		0 (0)	0 (0)	0 (0)	
50% responder rate, n (%) ^b	9		0 (0)	0 (0)	0 (0)	
Monthly Headache Days	9	27.6 (1.3)	-0.7 (-2.5 to 1.2)	-0.6 (-2.6 to 1.4)	-0.4 (-1.9 to 1.0)	0.719
Acute Medication Days	7	3.2 (5.3)	-2.4 (-6.6 to 1.8)	-1.6 (-7.3 to 4.2)	-1.9 (-6.3 to 2.6)	0.882

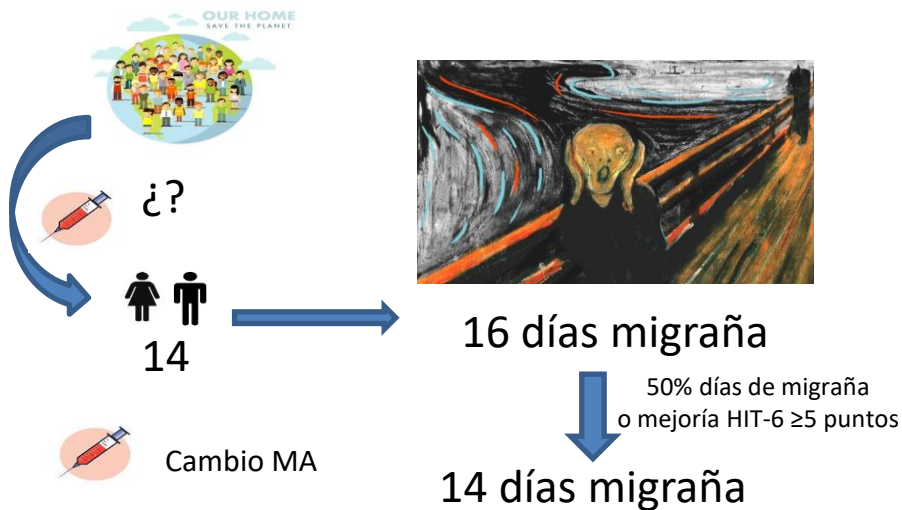


[Failure of an anti-CGRP monoclonal antibody in the treatment of migraine. Is it worthwhile trying another one?]

[Article in Spanish]

Y López-Moreno ¹, M V Castro-Sánchez ¹, L García-Trujillo ¹, P Serrano-Castro ¹

ACTIONS



Solo se dispone datos de pre/post HIT-6 de 6 pacientes

Tabla II. Resultados del tratamiento.

	Paciente													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
DCM basal	20	30	17	15	30	30	15	30	30	15	30	20	30	30
DMM basal	12	20	17	15	10	8	15	15	30	9	16	12	30	13
EVA basal	7	7	9	9							10		10	7.5
MIDAS basal	20	36	29	43	18			75	30	153	97	21	260	115
HIT-6 basal	65	67	74	70	57			65	66	78	68	78	78	68
Primer monoclonal	Ere	Ere	Ere	Galca	Ere	Galca	Galca	Ere	Ere	Ere	Ere	Ere	Galca	Ere
DCM tras el primer monoclonal	13	16	16	8	12	30	30	30	28	13	30	14	30	15
DMM tras el primer monoclonal	13	16	16	8	12	12	7	10	28	8	13	11	30	6
EVA tras el primer monoclonal	8		9	9	8		10	7		9	8	10		8
MIDAS tras el primer monoclonal	28		23	43		42	150	115		47				44
HIT-6 tras el primer monoclonal	66		74	70	52	71	74	74		76		78		65
Respuesta inicial	Si	Si	Si	Si	Si	No	Si	No	Si	No	No	No	No	Si
Tiempo hasta el cambio (meses)	7	8	19	13	13	11	13	7	7	5	7	9	7	16
Segundo monoclonal	Galca	Galca	Galca	Ere	Galca	Ere	Ere	Galca	Galca	Galca	Galca	Frema	Ere	Galca
DCM tras el cambio	8	6	12	9	9	15	12	30	23	9	30	15	30	6
DMM tras el cambio	8	4	12	9	9	15	12	30	23	5	13	15	30	6
EVA tras el cambio		5	7	8	10	8	10		7	8				
MIDAS tras el cambio		14		101	54	32	135		65	65				
HIT-6 tras el cambio		59		66	76	66	70		61	61	74			
EA	Est	Est	No	Est	No	No	No	Est	No	Est	Alopecia	No	No	No

DCM: días de cefalea al mes; DMM: días de migraña al mes; EVA: escala visual analógica de dolor; EA: efectos adversos; Ere: erenumab; Est: estreñimiento; Frema: fremanezumab; Galca: galcanezumab; HIT-6: Headache Impact Test-6; MIDAS: Migraine Disability Assessment Scale.

4/14 (29%) alcanzan variable combinada (RDM o HIT-6)

6/14 (43%) 30% DM y de estos, 2/14 (14%) reducen un 50% DM



Autor	n	RDM >25%	RDM>50%	
Nieves C. et al	52	17%		
Morollon N. et al	19		33%	
Overeem L.H. et al	25	32%	12%	
Briceño-Casado M.P. et al	7		42% -> 14%	
Patier Ruiz I. et al	15	53%	27%	
Overeem L.H. et al	25	32%	12%	
Lopez Moreno et al	14	43%	14%	

29%

20%

Observational Study > J Neurol. 2021 Oct;268(10):3789-3798. doi: 10.1007/s00415-021-10523-8.

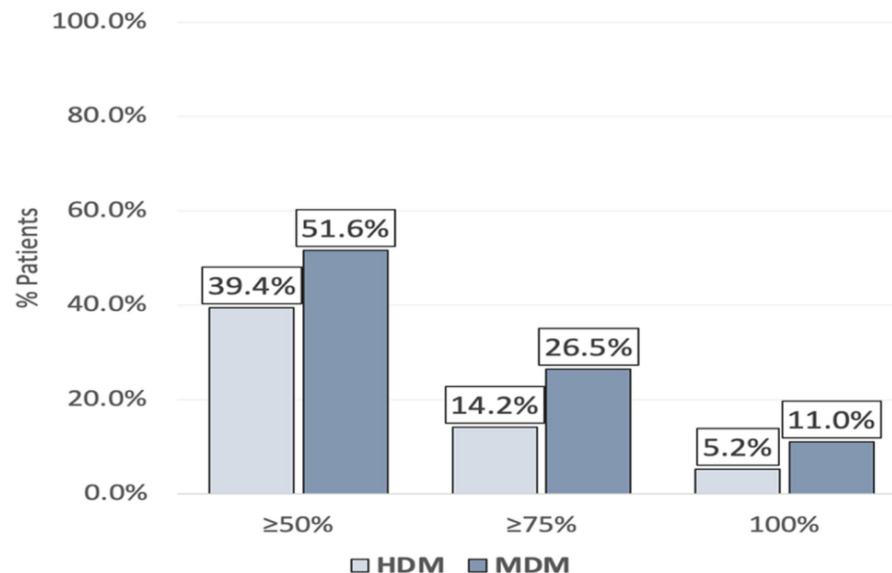
Epub 2021 Mar 27.

The impact of anti-CGRP monoclonal antibodies in resistant migraine patients: a real-world evidence observational study

Marta Torres-Ferrús^{1 2}, Víctor J Gallardo², Alicia Alpuente^{1 2}, Edoardo Caronna²,
Eulalia Gine-Cipres^{1 2}, Patricia Pozo-Rosich^{3 4}

Affiliations ☐ collapse

Response Rate at 3 months





Neurol Ther (2021) 10:293–306
<https://doi.org/10.1007/s40120-021-00245-4>

ORIGINAL RESEARCH

Real-World Treatment Profiles, Clinical Outcomes, and Healthcare Resource Utilization of Patients with Migraine Prescribed Erenumab: A Multicenter Chart-Review Study of US Headache Centers

Elizabeth Faust · Irina Pivneva · Karen Yang · Keith A. Betts · Zubair Ahmed · Shivang Joshi · Rebecca Hogan · Andrew Blumenfeld · Jack Schim · Alexander Feoktistov · Kenneth Carnes · Mark Bensink · Eric Q. Wu · Denise E. Chou · David Chandler

Neurological Sciences (2020) 41 (Suppl 2):S487–S488
<https://doi.org/10.1007/s10072-020-04669-y>

BRIEF COMMUNICATION

Effectiveness, safety, and tolerability of galcanezumab in a real-life setting in patients with migraine in Italy (the GARLIT study)

Fabrizio Vernieri¹ · Claudia Altamura¹ · Cinzia Aurilia² · Nicoletta Brunelli¹ · Gabriella Egeo² · Luisa Fofi² · Carmelina Maria Costa¹ · Adriana Fallacara¹ · Valentina Favoni³ · Giulia Pierangeli³ · Marco Aguggia⁴ · Davide Bertuzzo⁴ · Maria Albanese⁵ · Paola Di Fiore⁶ · Fabio Frediani⁶ · Sabina Cevoli³ · Piero Barbanti²

Headache
© 2020 American Headache Society

ISSN 0017-8748
doi: 10.1111/head.13951
Published by Wiley Periodicals, LLC.

Research Submission

Real-World Patient Experience With Erenumab for the Preventive Treatment of Migraine

Jennifer Robblee, MD, MSc ; Katrina L. Devick, PhD; Natasha Mendez, APRN; Jamie Potter, APRN; Jennifer Slonaker, APRN; Amaal J. Starling, MD

35% RDM50%

75% RDM50%

54% RDM50%

79% RDM50%

Salivary CGRP can monitor the different migraine phases: CGRP (in)dependent attacks

Alicia Alpuente^{1,2} , Victor J Gallardo² , Laila Asskour²,
Edoardo Caronna^{1,2} , Marta Torres-Ferrus^{1,2} and
Patricia Pozo-Rosich^{1,2}

Cephalalgia

2022, Vol. 42(3) 186–196

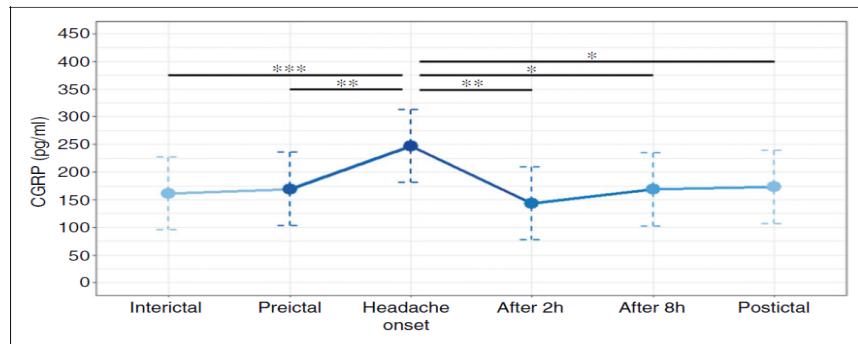
© International Headache Society 2021

Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/03331024211040467

journals.sagepub.com/home/cep



cantly associated with nCGRP group (Table 3). When we analyzed migraine patients, 13 out of 22 patients only showed dCGRP migraine attacks; 3 out of 22 patients only showed nCGRP migraine attacks and 6 patients showed both types of migraine attacks.

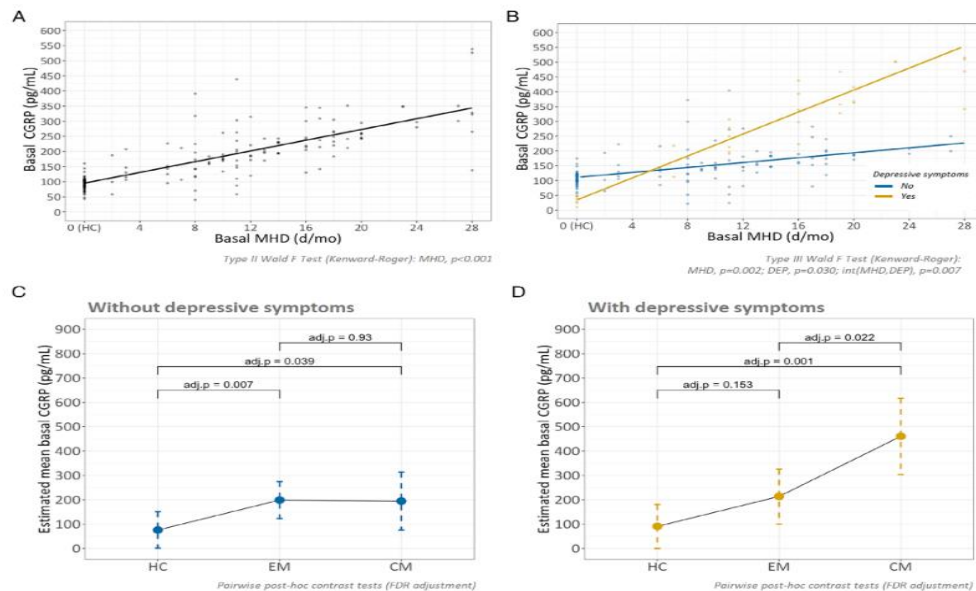
173.0 [107.8–238.0]). Patients were classified as having CGRP-dependent (79.6% and non-CGRP dependent migraine attacks (20.4%) according to the magnitude of change between preictal and ictal phase. Accompanying symptoms such as photophobia and phonophobia were significantly associated to the first group.

Research Article | [Full Access](#)

Salivary CGRP and Erenumab Treatment Response: Towards Precision Medicine in Migraine

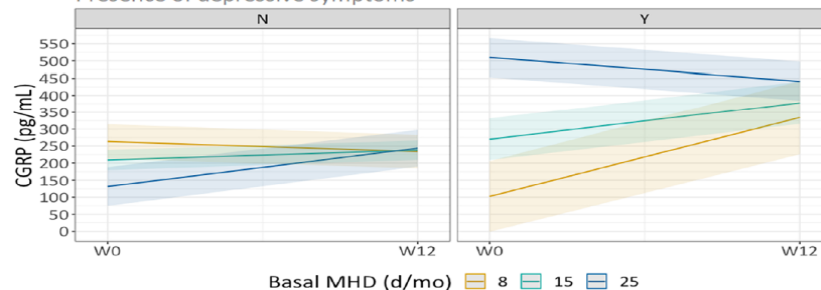
Alicia Alpuente MD, Victor J Gallardo MSc, Laila Asskour MLT, Edoardo Caronna MD, Marta Torres-Ferrus MD, PhD, Patricia Pozo-Rosich MD, PhD

First published: 07 August 2022 | <https://doi.org/10.1002/ana.26472>



Basal salivary CGRP line plots according to basal MHD

Salivary CGRP levels pre-post CGRP-mAb treatment Presence of depressive symptoms



Interpretation: Patients with migraine not only have higher CGRP levels compared with HCs, but also the presence of depressive symptoms seems to increase salivary CGRP levels and we have evidence, for the first time, that baseline salivary CGRP concentration is associated with treatment response to erenumab.

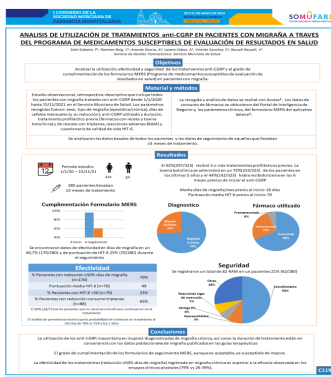


Reducción 50%
días de migraña

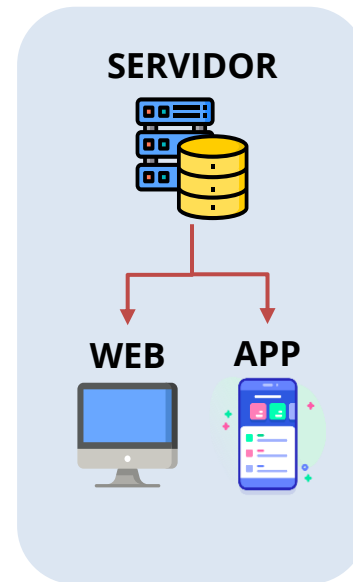


Reducción 30%
días de migraña
+
Reducción 30%
dosis de triptanes/mes
+
Mejora HIT-6
>5 puntos

Reducción 30%
días de migraña
+
Reducción 50%
dosis de triptanes/mes



500 pacientes



LISTADO DE PACIENTES CON RIESGO DE ABUSO DE

Centro de Salud	CIAS	CIPA	DDD mensual	Prioridad	CGRP
C.S. ALCANTARILLA-SANGONERA LA			27	2	SI
C.S. ALCANTARILLA-SANGONERA LA			33	1	SI
C.S. ALCANTARILLA-SANGONERA LA			27	2	NO
C.S. ALHAMA			16	3	NO
C.S. ALHAMA			19	3	NO

Received: 30 November 2021 | Revised: 12 December 2021 | Accepted: 14 December 2021

DOI: 10.1111/jcpt.13595

CASE REPORT

Two possible cases of erenumab-induced xerostomia

Pablo Selvi-Sabater PhD¹ | Miguel Angel Carvajal-Sanchez PharmD² | Francisco Javier Carrera-Hueso PhD³

CONCLUSIONS

- ① Evidencia incipiente (discutible) del Switch
Respuesta entorno al 20-30%
- ② Protocolos de seguimiento <-> Feedback Real World Data
- ③ Factores predictivos de respuesta.
Buscar al paciente que se puede beneficiar del Switch



@paselsab



Gracias por su atención

Gràcies per la seva atenció

Eskerrik asko zure arretagatik

Grazas pola súa atención