

Supplementary data

Long-Term Effectiveness of Three Anti-CGRP Monoclonal Antibodies in Drug-Resistant Patients with Chronic Migraine based on the MIDAS score

CNS drugs

Luigi Francesco Iannone^{1,2}, Davide Fattori¹, Silvia Benemei², Alberto Chiarugi^{1,2},
Pierangelo Geppetti^{1,2*} and Francesco De Cesaris²

¹*Headache Center and Clinical Pharmacology Unit, Careggi University Hospital, Florence, Italy.*

²*Section of Clinical Pharmacology and Oncology, Department of Health Sciences, University of Florence, Florence, Italy*

***Author for correspondence:**

Prof. Pierangelo Geppetti

Department of Health Sciences

University of Florence, Florence, Italy

pierangelo.geppetti@unifi.it

Table S1. Outcome variables changes compared to baseline at different follow-up.

	Month 1 (n=184)	Months 3 (n=145)	Months 6 (n=95)	Months 9 (n=62)	Months 12 (n=33)
Migraine days	-8.19 ± 7.6	-10.47 ± 8.3	-12.1 ± 8.7	-12.9 ± 8.2	-10.84 ± 9.1
Days with at least one analgesic used	-8.10 ± 8.0	-10.38 ± 8.0	-12.25 ± 8.5	-12.43 ± 8.8	-10.18 ± 8.8
Number of analgesics used	-16.69 ± 21.9	-20.30 ± 21.3	-25.15 ± 23.3	-26.50 ± 21.1	-27.71 ± 21.0
Medication overuse, n (%)	69 (37.5)	44 (30.3)	29 (30.5)	15 (24.2)	12 (36.3)
HIT-6 total score	-8.28 ± 10.1	-10.50 ± 8.8	-14.53 ± 10.6	-15.74 ± 8.9	-16.09 ± 10.2
MIDAS total score	/	-69.20 ± 52.7	-80.58 ± 62.7	-96.90 ± 63.7	-107.21 ± 62.9

All values are reported as mean ± SD as otherwise specified. HIT-6, Headache Impact Test 6; MIDAS, Migraine Disability Assessment.

Table S2. Bivariate analysis of baseline variables associated to medication overuse and OnabotulinumtoxinA inefficacy.

	Non- medication overuse (n=31)	Medication overuse (n=172)	<i>p</i> value	OnabotulinumtoxinA naive (n=77)	OnabotulinumtoxinA inefficacy (n=126)	<i>p</i> value
Age [years], mean $\pm$ SD	44.5 $\pm$ 14.7	50.3 $\pm$ 11.6	0.02	49.3 $\pm$ 13.1	49.5 $\pm$ 11.7	0.84
Sex female, n (%)	25 (80.6)	134 (77.9)	0.73	56 (72.7)	103 (81.7)	0.13
<i>Migraine features</i>						
Monthly migraine days, mean $\pm$ SD	22.3 $\pm$ 5.8	24.4 $\pm$ 5.8	0.07	22.2 $\pm$ 5.9	25.3 $\pm$ 5.6	<0.0001
Aura, n (%)	3 (9.7)	11 (6.4)	0.38	8 (10.4)	6 (4.8)	0.30
Migraine duration [years], mean $\pm$ SD	29.4 $\pm$ 15.3	33.7 $\pm$ 12.6	0.14	32.4 $\pm$ 13.2	33.4 $\pm$ 13.3	0.77
Chronicization duration [years], mean $\pm$ SD	16.0 $\pm$ 12.4	16.1 $\pm$ 11.4	0.82	14.0 $\pm$ 10.8	17.5 $\pm$ 11.8	0.04
NRS score, mean $\pm$ SD	8.3 $\pm$ 1.4	7.8 $\pm$ 1.2	0.05	7.6 $\pm$ 1.2	8.1 $\pm$ 1.2	<0.0001
<i>Treatments</i>						
Concomitant preventive treatment, mean (SD)	0.3 (0.6)	0.2 (0.4)	0.40	0.3 (0.6)	0.3 (0.6)	0.49
Prior preventive classes failures, mean $\pm$ SD	4.5 $\pm$ 0.8	4.3 $\pm$ 0.8	0.20	3.7 $\pm$ 0.6	4.8 $\pm$ 0.7	<0.0001

Medication overuse headache (MOH), n (%)	/	/	/	65 (84.4)	107 (84.9)	0.92
Monthly analgesic use, median (IQR)	10 (10)	30 (33)	<0.0001	25 (19)	33 (39)	0.01
OnabotulinumtoxinA inefficacy, n (%)	19 (61.3)	107 (62.2)	0.92	/	/	/
<i>Migraine-related clinical burden</i>						
Disability (MIDAS), mean ± SD	84.1 ± 51.5	104.3 ± 65.3	0.14	79.5 ± 52.5	114.6 ± 66.4	<0.0001
Headache-related impact (HIT-6), mean ± SD	67.3 ± 6.1	68.0 ± 5.5	0.70	66.2 ± 5.8	69.0 ± 5.3	<0.0001

Values in bold are statistically significant, percentages are expressed on column total. HIT-6, Headache Impact Test 6; MIDAS, Migraine Disability Assessment.

Table S3. Summary of adverse drug reactions (ADRs) in the safety analysis.

	Patients (n = 203)
Overall ADR rate, n (%)	23 (11.0)
Patients reported at least one ADR, n (%)	16 (7.9)
ADRs leading to drug discontinuation, n (%)	3 (1.5)
<i>ADRs reported, n (%):</i>	
Fatigue	8 (3.9)
Injection site erythema	3 (1.5)
Muscle Pain	3 (1.5)
Constipation	3 (1.5)
Alopecia	2 (0.9)
Flushing	2 (0.9)
Somnolence	1 (0.5)
Vertigo	1 (0.5)

ADR, adverse drug reaction.

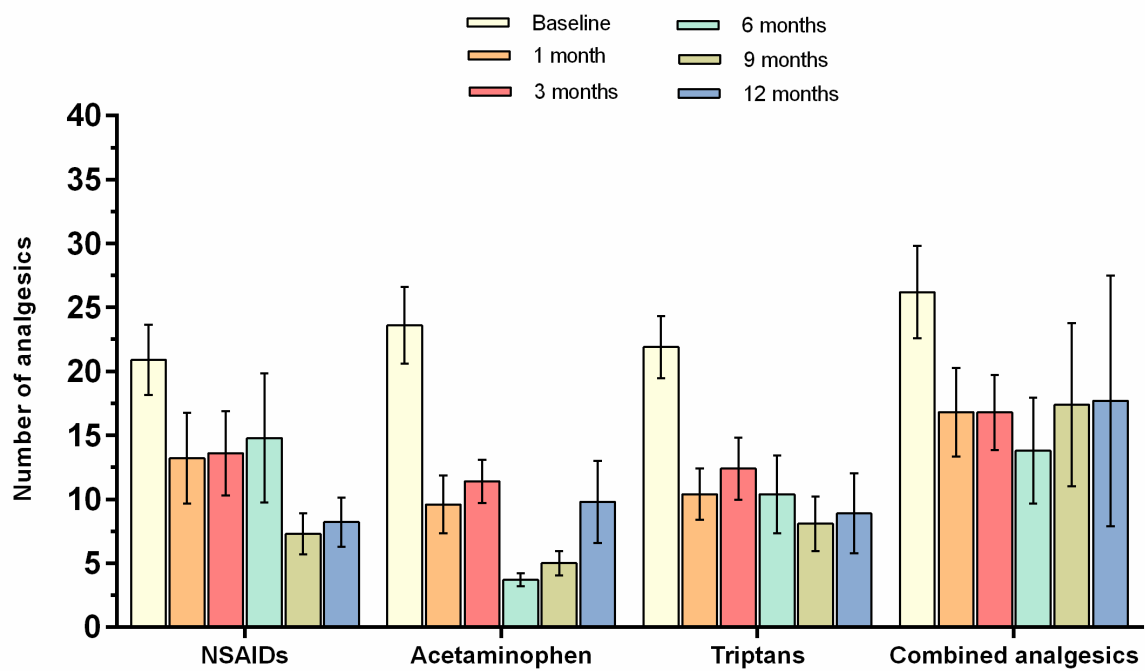


Figure S1. Number of analgesics used subdivided by classes at each follow up.
NSAID, non-steroidal anti-inflammatory drugs.

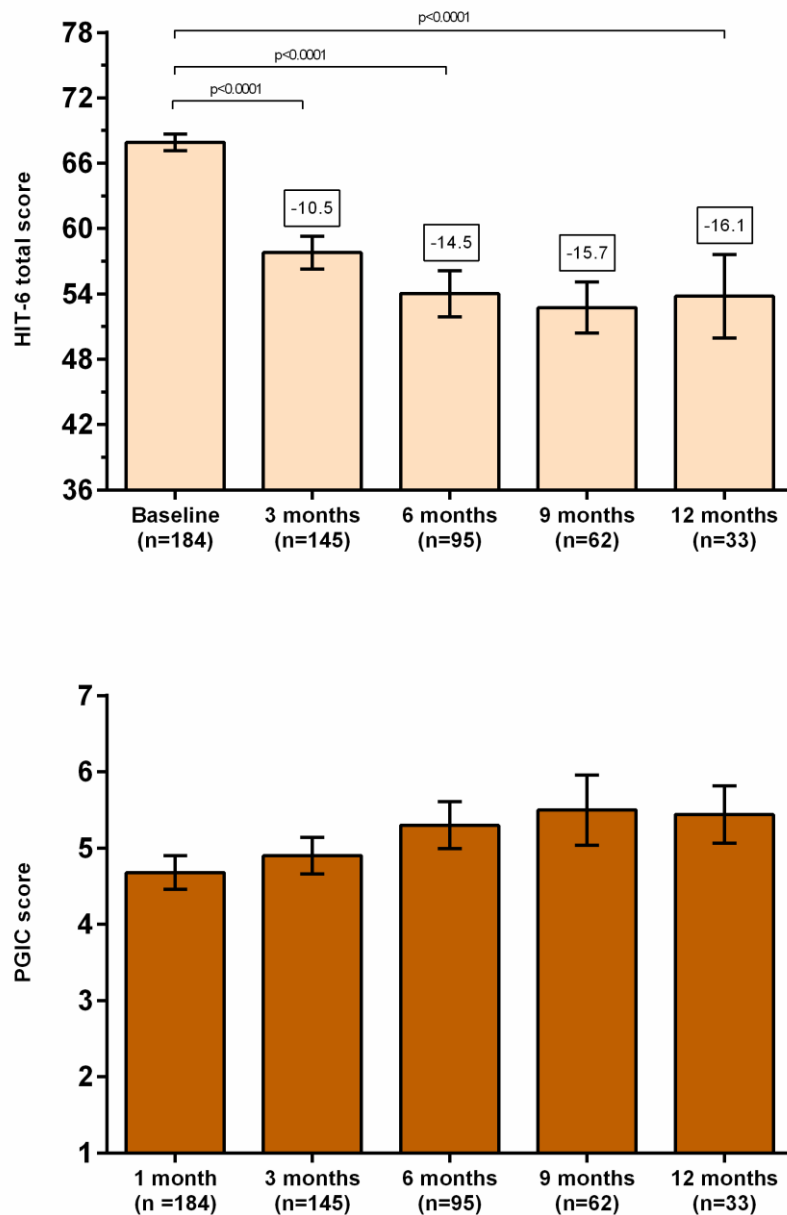


Figure S2. Patient Headache Impact Test 6 (HIT-6) questionnaire total score and Global Impression of Change (PGIC) score during treatment in effectiveness analysis. Error bars represent 95% confidence intervals. Error bars represent 95% confidence intervals.

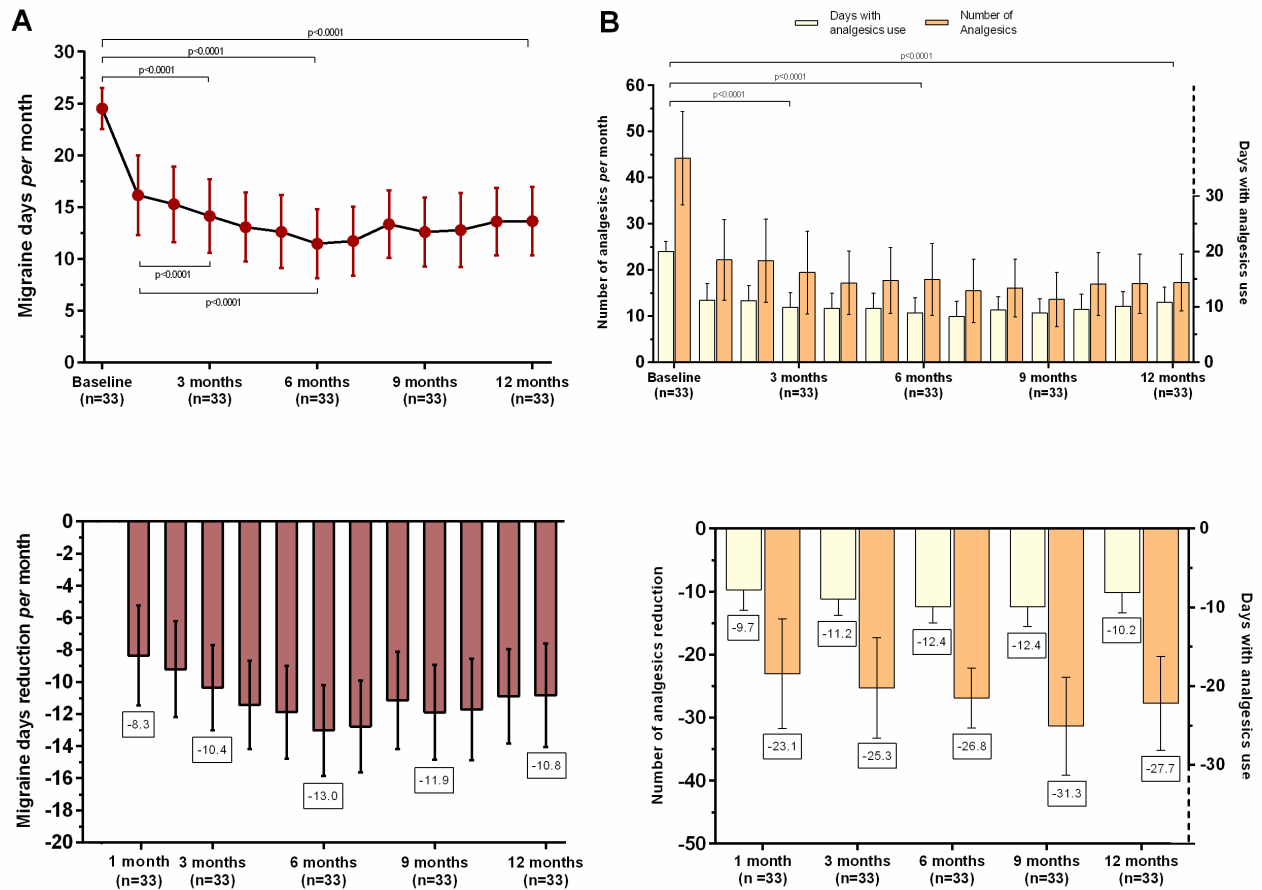


Figure S3. (A) Monthly migraine days (MMD) frequency during anti-CGRP treatment in patients who completed 1-year follow-up and reduction in MMDs compared to baseline at each follow-up. (B) Number of analgesics used and days with at least one analgesic used *per* months and their reduction compared to baseline. Error bars represent 95% confidence intervals. Analgesics include NSAIDs, triptans, analgesic associations (with or without opioids), opioids and ergot derivative.

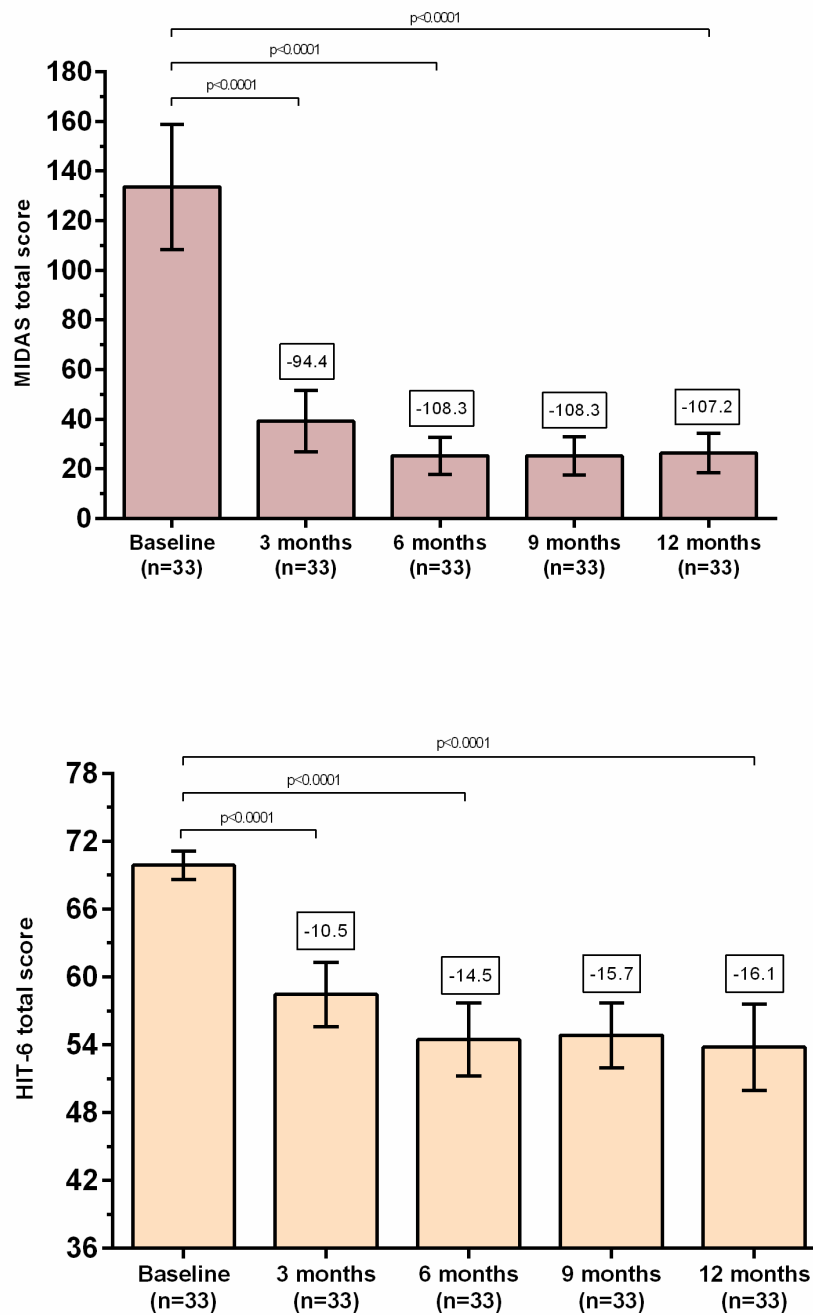


Figure S4. Migraine Disability Assessment (MIDAS) (A) and the Headache Impact Test 6 (HIT-6) (B) questionnaire total scores during treatment follow-up in patients who complete 12 months follow-up. Error bars represent 95% confidence intervals.

Number in square represent mean reduction compared to baseline.

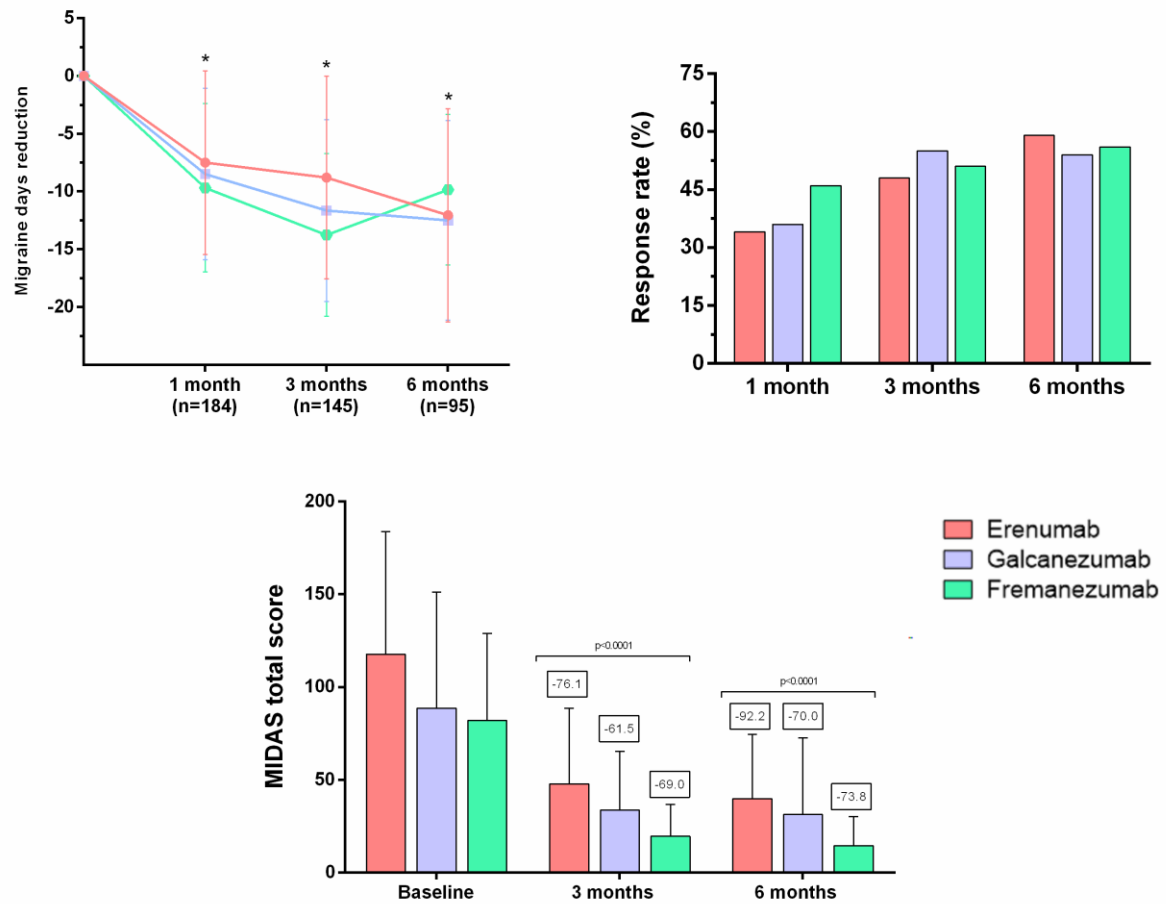


Figure S5. Reduction in monthly migraine days (MMDs) and MIDAS score and responder rate ($\geq 50\%$ reduction in MMDs) with three different anti-CGRP antibodies at different follow-ups. Error bars represent 95% confidence intervals. * $p < 0.0001$ for each anti-CGRP mAbs compared to baseline.