



Eren, 2020 (10.1038/s41598-020-68149-1)	n=49	CM	155 UI	3	≥30% fewer MMD	None	N/A	Triptan efficacy
Domínguez Vivero, 2020 (doi.org/10.3390/toxins12080479)	n=62	CM	155 UI	3	≥50% fewer headaches	Age, CGRP levels (> 50 ng/mL), Pentraxin 3 (PTX3) levels (>1000 pg/ml), iron deposition in GP and PAG	mean age difference = 12.2; 95% confidence interval (CI): 5.4–18.9, p = 0.001 CGRP mean difference = 805.0; 95% CI: 37.9–1572.1 μL, p = 0.040 PTX3 mean difference = 69.8; 95% CI: 31.0–108.6 μL, p = 0.008;	Gender, BMI, smoking, headache phenotype, allodynia, presence or location of WML
Moreno-Mayordomo, 2019 (10.1186/s10194-019-0989-9.)	n=156	CM	155 UI	6	≥50% fewer MMD	Polymorphisms : -CALCA rs3781719 - TRPV1 rs222749	p = 0.007, OR = 3.11 (1.33-7.26) and (p = 0.013, OR = 3.29 (1.28-8.43) respectively	23 other SNPs
Schiano di Cola, 2019 (10.3389/fneur.2019.00678. eCollection 2019)	n=84	CM	155-195 UI	12	≥50% fewer headaches	Depressive symptoms, MOH	N/A	N/A
de Tommaso, 2019 (10.1159/000499764.)	n=120	CM	155-195 UI	24	≥50% fewer headaches	Less severe allodynia	relationship between allodynia severity at T0 and reduced headache frequency change at T1 (r = 0.22) and T2 (r = 0.37)	N/A
Young, 2019 (doi.org/10.1186/s10194-018-0952-1)	n=175	CM	155 UI	27	Mean reduction MHD	Absence allodynia	Mean reduction in MMD was significantly greater in patients without allodynia (P=0.044 between-subgroup comparison)	N/A
Domínguez, 2018 (10.1111/head.13211.)	n=62	CM	155 UI	6	≥50% fewer headaches	CGRP levels, PTX3 levels	PTX3 serum levels (1455.4 ± 487.5 pg/mL versus 720.3 ± 334.1 pg/mL, P < .0001) and CGRP serum levels (133.1 ± 86.6 ng/mL versus 58.2 ± 91.7 ng/mL, P = .004) were significantly higher in responders than nonresponders.	TNF-a, IL-10, IL-6, hs-CRP, cFn, S100, NSE,

Domínguez, 2018 (doi.org/10.1111/ene.13523)	n=725	CM	155 UI	12	≥50% fewer headaches	CM duration, Unilateral pain, combined symptomatic treatment, fewer days of disability, milder headache	Correlation analysis of data showed that patients with a shorter duration of disease ( $r=-0.108$ ; $p=0.004$ ), those who had less days of disability per month ( $r=-0.144$ ; $p=0.001$ ), and a milder headache ( $r=-0.098$ ; $p=0.008$ ) had more chances of responding to treatment with OnabotulinumtoxinA. Conversely, we found a positive correlation between unilaterality of pain and effectiveness ( $r=0.093$ ; $p=0.012$ ). The ROC analysis for duration of disease showed an area under the curve of 0.441 (CI 95% 0.388-0.493, $p=0.025$ ), suggesting that a value below 12 months of duration of CM predicts effectiveness with a sensitivity of 72% and a specificity of 78%.	Gender, Migraine with aura, depression, fibromyalgia
Lovati, 2018 (10.1007/s10072-018-3388-0.)	n=44	CM	170-195 UI	12	≥50% fewer MMD	Triptan response	$\chi^2$ test (3 lines $\times$ 3 columns), a significant difference between groups was observed ( $p = 0.016$ ).	N/A
Hubbard, 2016 (doi.org/10.3389/fnhum.2016.00497)	n=23	CM	150 UI	6	≥50% fewer MHD and now EM	Cortical thickness at right SI and aINS, left ParsOp and STG	anti-correlations between the SI seed and lateral occipital (LOC) and dorsomedial prefrontal cortices (DMPFC) in responders, whereas non-responders	N/A

							showed increased connectivity between the ParsOp seed and LOC	
Lee, 2016 (doi.org/10.1016/j.jns.2016.01.054)	n=70	CM	155 UI	1,5	≥50% fewer MMD, ≥50% fewer abortive Rx OR ≥50% fewer mod-severe headache	Disease Duration, MCA/ICA ratio	Longer disease duration was associated with poor treatment outcome (p = 0.019). The ratio of the mean velocity of middle cerebral artery to that of ipsilateral internal carotid artery (MCA/ICA index) was significantly higher in responders than non-responders (p < 0.027).	Age, gender, BMI, concurrent prophylactic medication, MA vs. MoA, psychiatric comorbidity, smoking
Cernuda-Morollón, 2015 (10.1097/j.pain.000000000000119)	n=83	CM	155-195 UI	6	≥50% fewer headaches AND ≥50% reduced VAS	CGRP (76.85 pg/mL vs. 50.45 pg/mL), VIP	Pre-treatment CGRP levels in responders (76.85 pg/mL) were significantly higher than those seen in nonresponders (50.45 pg/mL; P < 0.001).	Clinical features, age, duration of CM, comorbidity, obesity, prophylactic medication

eTable 4. Possible predictive factors for the efficacy of BoNT-A treatment following PREEMPT paradigm, adapted from Ray et al 2021 (<https://doi.org/10.3390/jcm10132898>)

Legend: CM chronic migraine; EM episodic migraine; UI international unit, MMD migraine monthly days, VAS Visual assessment score, MCA middle cerebral artery, ICA internal carotid artery, MOH medication overuse headache