Supplementary table 1. Achievement of ≥50% reduction in MMD during the OLEP: shift table by treatment arm and responder status during the DBTP (open-label analysis set)

Criteria for DBTP	Percentage of OLEP visits reaching 50% responder criteria among visits with non-missing MMD values											
	Patients on erenumab 140 mg in DBTP who continued erenumab in OLEP						Patients on placebo in DBTP who switched to erenumab in OLEP					
	Total	**0**	**≥30%**	**≥50%**	**≥80%**	**100%**	**Total**	**0**	**≥30%**	**≥50%**	**≥80%**	**100%**
0 visit with 50% response	62	24 (38.7)	19 (30.6)	10 (16.1)	3 (4.8)	0	97	30 (30.9)	47 (48.5)	39 (40.2)	15 (15.5)	6 (6.2)
1 visit with 50% response	27	6 (22.2)	13 (48.1)	10 (37.0)	3 (11.1)	0	12	3 (25.0)	9 (75.0)	8 (66.7)	3 (25.0)	0
2 visits with 50% response	17	1 (5.9)	14 (82.4)	11 (64.7)	7 (41.2)	4 (23.5)	10	0	10 (100)	8 (80.0)	6 (60.0)	4 (40.0)
3 visits with 50% response	12	0	11 (91.7)	9 (75.0)	8 (66.7)	7 (58.3)	2	0	2 (100)	2 (100)	1 (50.0)	1 (50.0)
≥1 visit with 50% response	56	7 (12.5)	38 (67.9)	30 (53.6)	18 (32.1)	11 (19.6)	24	3 (12.5)	21 (87.5)	18 (75.0)	10 (41.7)	5 (20.8)
≥2 visits with 50% response	29	1 (3.4)	25 (86.2)	20 (69.0)	15 (51.7)	11 (37.9)	12	0	12 (100)	10 (83.3)	7 (58.3)	5 (41.7)
50% responder at Week 12 only	10	1 (10.0)	8 (80.0)	7 (70.0)	2 (20.0)	0	6	2 (33.3)	4 (66.7)	3 (50.0)	1 (16.7)	0

50% responder at week 12 and ≥1 other visit	25	1 (4.0)	21 (84.0)	17 (68.0)	13 (52.0)	10 (40.0)	11	0	11 (100)	9 (81.8)	6 (54.5)	5 (45.5)

50% responder is defined as achievement of ≥50% reduction in MMD.

DBTP, double-blind treatment phase; MMD, monthly migraine days; OLEP, open-label extension phase

Supplementary appendix 1

List of Independent Ethics Committees (IEC) or Institutional Review Boards (IRB) by study centre

Centre No.	Ethics Committee or Institutional Review Board	Department / Organization	City, State/Province, Postal Code Country	IRB/IEC Approval number
1003	Austin Health Human Research Ethics Committee	Office for Research	Heidelberg Victoria 3084 Australia	HREC/16/AUSTIN/398
1011	Ethikkommission der Med. Universität Wien	Ethikkommission	Vienna A-1090 Austria	1946/2016
1013	Ethikkommission der Med. Universität Wien	Ethikkommission	Vienna A-1090 Austria	1946/2016
1021	Commissie voor Medische Ethiek UZ Gent	Commissie Medische Ethiek	Gent 9000 Belgium	2016/290
1022	Commissie voor Medische Ethiek UZ Gent	Commissie Medische Ethiek	Gent 9000 Belgium	2016/290
1023	Commissie voor Medische Ethiek UZ Gent	Commissie Medische Ethiek	Gent 9000 Belgium	2016/290
1024	Commissie voor Medische Ethiek UZ Gent	Commissie Medische Ethiek	Gent 9000 Belgium	2016/290
1031	Etická komise IKEM a TN, Thomayerova nemocnice	Vídeňská 800	Praha 4 140 59 Czech Republic	M-16-50
1033	Etická komise IKEM a TN, Thomayerova nemocnice	Vídeňská 800	Praha 4 140 59 Czech Republic	M-16-50
1034	Etická komise IKEM a TN, Thomayerova nemocnice	Vídeňská 800	Praha 4 140 59 Czech Republic	M-16-50

Centre No.	Ethics Committee or Institutional Review Board	Department / Organization	City, State/Province, Postal Code Country	IRB/IEC Approval number
1041	De Videnskabsetiske Komiteer for Region Hovedstaden	Regionsgården, Center for sundhed, Kongens Vænge 2	Hillerød 3400 Denmark	H-16038336
1051	Varsinais-Suomen eettinen toimikunta		Turku 20521 Finland	EC dnro 101/1800/2016
1053	Varsinais-Suomen eettinen toimikunta		Turku 20521 Finland	EC dnro 101/1800/2016
1054	Varsinais-Suomen eettinen toimikunta		Turku 20521 Finland	EC dnro 101/1800/2016
1061	Comite de protection des personnes Sud Mediterranee I		Marseille 13274 France	16 89 MS 3
1063	Comite de protection des personnes Sud Mediterranee I		Marseille 13274 France	16 89 MS 3
1065	Comite de protection des personnes Sud Mediterranee I		Marseille 13274 France	16 89 MS 3
1071	Landesamt für Gesundheit und Soziales, Ethik-Kommission des Landes Berlin		Berlin 10707 Germany	16/0297 – EK 15

Centre No.	Ethics Committee or Institutional Review Board	Department / Organization	City, State/Province, Postal Code Country	IRB/IEC Approval number
1072	Ludwig-Maximilians-Universität München, Medizinische Fakultät Ethikkommission		München 80336 Germany	16/0297 – EK 15
1073	Christian-Albrechts-Universität zu Kiel, Ethik-Kommission der Medizinischen Fakultät		Kiel 24105 Germany	16/0297 – EK 15
1074	Ärztekammer Hamburg, Geschäftsstelle der Ethik-Kommission		Hamburg 22083 Germany	16/0297 – EK 15
1075	Landesärztekammer Hessen, Ethik-Kommission		Frankfurt am Main 60488 Germany	16/0297 – EK 15
1076	Landesamt für Gesundheit und Soziales, Ethik-Kommission des Landes Berlin		Berlin 10707 Germany	16/0297 – EK 15
1077	Sächsische Landesärztekammer, Ethik-Kommission		Dresden 01099 Germany	16/0297 – EK 15
1078	Universitätsklinikum Essen, Medizinische Fakultät der Universität Duisburg-Essen Ethik-Kommission		Essen 45147 Germany	16/0297 – EK 15

Centre No.	Ethics Committee or Institutional Review Board	Department / Organization	City, State/Province, Postal Code Country	IRB/IEC Approval number
1079	Ethik-Kommission an der Medizinischen Fakultät der Eberhard-Karls-Universität und am Universitätsklinikum Tübingen		Tübingen 72074 Germany	16/0297 – EK 15
1081	Ethik-Kommission der Ärztekammer Westfalen-Lippe und der Westfälischen Wilhelms-Universität Münster		Münster 48147 Germany	16/0297 – EK 15
1082	Ethik-Kommission der Ärztekammer Westfalen-Lippe und der Westfälischen Wilhelms-Universität Münster		Münster 48147 Germany	16/0297 – EK 15
1084	Friedrich-Alexander-Universität Erlangen-Nürnberg, Medizinische Fakultät Ethik-Kommission		Erlangen 91054 Germany	16/0297 – EK 15
2001	National Ethics Committee		Cholargos Attica 15562 Greece	62648/2018, dated 18-Jun-2018
2003	National Ethics Committee		Cholargos Attica 15562 Greece	62648/2018, dated 18-Jun-2018

Centre No.	Ethics Committee or Institutional Review Board	Department / Organization	City, State/Province, Postal Code Country	IRB/IEC Approval number
2004	National Ethics Committee		Cholargos Attica 15562 Greece	62648/2018, dated 18-Jun-2018
2011	Comitato Etico dell'Università Sapienza	Policlinico Universitario Umberto I	Roma 00161 Italy	2011: 114 SA/2018 2012: 2018-147 CINECA 10151 2013: NA 2014: 06/2018 2015: 131/2018 2016: 64/2016 2017: 158-16131/2018/Em003/AUSLBO
2012	Comitato Etico Regione Toscana Area Vasta Centro	Azienda Ospedaliero Universitaria Careggi di Firenze	Firenze 50134 Italy	2011: 114 SA/2018 2012: 2018-147 CINECA 10151 2013: NA 2014: 06/2018 2015: 131/2018 2016: 64/2016 2017: 158-16131/2018/Em003/AUSLBO
2014	Comitato Etico Palermo	AOU Policlinico P. Giaccone di Palermo	Palermo 90127 Italy	2011: 114 SA/2018 2012: 2018-147 CINECA 10151 2013: NA 2014: 06/2018 2015: 131/2018

Centre No.	Ethics Committee or Institutional Review Board	Department / Organization	City, State/Province, Postal Code Country	IRB/IEC Approval number
				2016: 64/2016 2017: 158-16131/2018/Em003/AUSLBO
2015	Comitato Etico Seconda Università degli Studi di Napoli - Università degli Studi della Campania L. Vanvitelli	AOU SUN-AORN Ospedale dei Colli	Napoli 80138 Italy	2011: 114 SA/2018 2012: 2018-147 CINECA 10151 2013: NA 2014: 06/2018 2015: 131/2018 2016: 64/2016 2017: 158-16131/2018/Em003/AUSLBO
2016	Comitato Etico Regione Lombardia - Sezione della Fondazione IRCCS	Istituto Neurologico Carlo Besta	Milano 20133 Italy	2011: 114 SA/2018 2012: 2018-147 CINECA 10151 2013: NA 2014: 06/2018 2015: 131/2018 2016: 64/2016 2017: 158-16131/2018/Em003/AUSLBO
2017	Comitato Etico di Area Vasta Emilia Centro della Regione Emilia-Romagna CE AVEC	AOU di Bologna, Policlinico S.Orsola-Malpighi	Bologna 40138 Italy	2011: 114 SA/2018 2012: 2018-147 CINECA 10151 2013: NA 2014: 06/2018 2015: 131/2018

Centre No.	Ethics Committee or Institutional Review Board	Department / Organization	City, State/Province, Postal Code Country	IRB/IEC Approval number
				2016: 64/2016 2017: 158-16131/2018/Em003/AUSLBO
2028	METC LUCM	Commissie Medische Ethiek	Leiden N/A 2300 PC the Netherlands	NL58509.058.16 CME number: P16.250
2029	METC LUCM	Commissie Medische Ethiek	Leiden N/A 2300 PC the Netherlands	NL58509.058.16 CME number: P16.250
2030	METC LUCM	Commissie Medische Ethiek	Leiden N/A 2300 PC the Netherlands	NL58509.058.16 CME number: P16.250
2041	Regionale komiteer for medisinsk og helsefaglig forskningsetikk	REK sor-ost B	Oslo 0484 Norway	2016/1429/REK sør-øst B, dated: 18-Jun-2018
2043	Regionale komiteer for medisinsk og helsefaglig forskningsetikk	REK sor-ost B	Oslo 0484 Norway	2016/1429/REK sør-øst B, dated: 18-Jun-2018
2051	CEIC Grupo Hospitalario Quirón en Barcelona	Centro Médico Teknon	Barcelona Barcelona 08022 Spain	G.3/PROT.HIP
2052	CEIC Grupo Hospitalario Quirón en Barcelona	Centro Médico Teknon	Barcelona Barcelona 08022 Spain	G.3/PROT.HIP
2053	CEIC Grupo Hospitalario Quirón en Barcelona	Centro Médico Teknon	Barcelona Barcelona 08022 Spain	G.3/PROT.HIP

Centre No.	Ethics Committee or Institutional Review Board	Department / Organization	City, State/Province, Postal Code Country	IRB/IEC Approval number
2055	CEIC Grupo Hospitalario Quirón en Barcelona	Centro Médico Teknon	Barcelona Barcelona 08022 Spain	G.3/PROT.HIP
2056	CEIC Grupo Hospitalario Quirón en Barcelona	Centro Médico Teknon	Barcelona Barcelona 08022 Spain	G.3/PROT.HIP
2057	CEIC Grupo Hospitalario Quirón en Barcelona	Centro Médico Teknon	Barcelona Barcelona 08022 Spain	G.3/PROT.HIP
2067	Etikprövningsmyngdigheten		Uppsala 750 02 Sweden	2018-122, dated: 27-Jul-2018
2069	Etikprövningsmyngdigheten		Uppsala 750 02 Sweden	2018-122, dated: 27-Jul-2018
2070	Etikprövningsmyngdigheten		Uppsala 750 02 Sweden	2018-122, dated: 27-Jul-2018
2072	Etikprövningsmyngdigheten		Uppsala 750 02 Sweden	2018-122, dated: 27-Jul-2018
2073	Etikprövningsmyngdigheten		Uppsala 750 02 Sweden	2018-122, dated: 27-Jul-2018
2081	Kantonale Ethikkommission Zürich		Zürich 8090 Switzerland	EC Ref no 2016-01326
2082	Kantonale Ethikkommission Zürich		Zürich 8090 Switzerland	EC Ref no 2016-01326
2083	Kantonale Ethikkommission Zürich		Zürich 8090 Switzerland	EC Ref no 2016-01326

Centre No.	Ethics Committee or Institutional Review Board	Department / Organization	City, State/Province, Postal Code Country	IRB/IEC Approval number
2091	East Midlands - Leicester Central Research Ethics Committee	The Old Chapel, Royal Standard Place	Nottingham NG1 6FS United Kingdom	IRAS: 211113 REC reference: 16/EM/0386
2092	East Midlands - Leicester Central Research Ethics Committee	The Old Chapel, Royal Standard Place	Nottingham NG1 6FS United Kingdom	IRAS: 211113 REC reference: 16/EM/0386
2094	East Midlands - Leicester Central Research Ethics Committee	The Old Chapel, Royal Standard Place	Nottingham NG1 6FS United Kingdom	IRAS: 211113 REC reference: 16/EM/0386

Supplementary appendix 2

Inclusion criteria

Patients eligible for inclusion in this study must have fulfilled all of the following criteria. For inclusion purposes, one month equals one calendar month.

During the Screening Epoch:

- Written informed consent was obtained before any assessment was performed
- Adults ≥18 to ≤65 years of age upon entry into screening
- Documented history of migraine (with or without aura) for ≥12 months prior to screening according to the International Classification of Headache Disorders-(ICHD-3 beta)
- 4 to 14 days per month (in at least two separate attacks) of migraine symptoms (based on ICHD-3 criteria) on average across the 3 months prior to screening based on retrospective reporting
- <15 days per month of headache symptoms (i.e., migraine and non-migraine)

Patients must have*:

- Failed 2 to 4 prior migraine prophylaxis treatments out of the following: propranolol/metoprolol, topiramate, flunarizine, valproate/divalproex, amitriptyline, venlafaxine, lisinopril, candesartan, locally approved products (e.g. oxetorone or pizotifen)
- Failed one AND failed or not be suitable for a second of the following:
  - Propranolol OR metoprolol
  - Topiramate
  - Flunarizine
- Failed or not be suitable for valproate or divalproex

* The following definitions were applicable for inclusion criteria 6-8:

- Efficacy failure was defined as “no meaningful reduction in headache frequency after administration of the respective medication for an adequate period of time (at least 2-3 months are recommended by the European Headache Federation treatment guidelines) at generally accepted therapeutic dose(s) based on the investigator’s assessment within the last 5 years prior to screening.”
- Tolerability failure was defined as “documented discontinuation due to adverse events of the respective medication at any previous time.”
- “Not suitable” for the purpose of this study was defined as “patient was not considered to be suitable for the treatment for medical reasons such as contraindications or precautions included in local labels, national guidelines or other locally binding documents, or other medically relevant reasons” as confirmed by the treating physician.

During the Baseline Epoch:

- Migraine frequency of 4 to 14 migraine days during the Baseline Epoch, confirmed by the eDiary
- ≥80% eDiary compliance during the Baseline Epoch

Exclusion criteria

Patients fulfilling any of the following criteria were not eligible for inclusion in this study. No additional exclusions were applied by the investigator, in order to ensure that the study population was representative of all eligible patients. Calendar months were used for exclusion purposes.

- Older than 50 years of age at migraine onset
- Unable to differentiate migraine from other headaches
- History of cluster headache or hemiplegic migraine headache
- Failed more than 4 prior migraine prophylaxis treatments out of the following:

  - Propranolol/metoprolol, topiramate, flunarizine, valproate/divalproex, amitriptyline, venlafaxine, lisinopril, candesartan, locally approved products (e.g. oxetorone or pizotifen)
- Use of a prophylactic migraine medication within 5 half-lives, or a device or procedure within one month prior to the start of the baseline phase or during the baseline phase
- Prior Botulinum toxin A treatment in the head/neck region (including cosmetic use or other licensed indications for Botox®) within 4 months prior to the start of the baseline epoch or during the baseline epoch
- Use of the following for any indication in the 1 month prior to the start of the baseline phase or during the baseline phase:
  - Ergotamines or triptans ≥10 days/month, or
  - Simple analgesics (nonsteroidal anti-inflammatory drugs [NSAIDs], acetaminophen, paracetamol) ≥15 days/month, or
  - Opioid- or butalbital-containing analgesics ≥4 days/month
- Anticipated to require any excluded medication or device (such as occipital nerve stimulators, transcranial magnetic stimulation) during the study
- Active chronic pain syndromes (such as fibromyalgia or chronic pelvic pain)
- History or current evidence of major psychiatric disorder (such as schizophrenia, bipolar disorder or type B personality disorder that might interfere with the ability to properly report clinical outcomes)
- Evidence of drug or alcohol abuse or dependence within 12 months prior to screening, based on medical records or patient self-report
- Current evidence of depression based on a Beck Depression Inventory (BDI)-II total score of >19 at screening. Patients with anxiety disorder and/or major depressive disorder were permitted in the study if they were considered by the investigator to be

stable and were taking no more than one medication per disorder. Patients must have been on a stable dose within the 3 months prior to the start of the baseline phase

- History of seizure disorder or other significant neurological conditions other than migraine 14. Score “yes” on item 4 or item 5 of the Suicidal Ideation section of the Columbia Suicide Severity Rating Scale (C-SSRS), if this ideation occurred in the past 6 months, or “yes” on any item of the Suicidal Behaviour section, except for the “Non-Suicidal Self-Injurious Behaviour” (item also included in the Suicidal Behaviour section), if this behaviour occurred in the past 2 years
- Myocardial infarction, stroke, transient ischemic attack, unstable angina, or coronary artery bypass surgery or other revascularization procedures within 12 months prior to screening
- History or current diagnosis of electrocardiogram abnormalities indicating significant risk of safety for patients participating in the study
- History of malignancy of any organ system (other than localized basal cell carcinoma of the skin or in situ cervical cancer), treated or untreated, within the past 5 years, regardless of whether there is evidence of local recurrence or metastases
- Hepatic disease by history or total bilirubin ≥2 x upper limit of normal (ULN) or alanine transaminase (ALT) or aspartate aminotransferase (AST) ≥3.0 x ULN as assessed by central laboratory at initial screening
- Pregnant or nursing (lactating) women
- Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using highly effective methods of contraception during dosing and for 110 days after stopping of study medication. Highly effective contraception methods include:
    - Total abstinence (when this is in line with the preferred and usual lifestyle of the patient). Periodic abstinence (e.g. calendar, ovulation, symptothermal,

post-ovulation methods) and withdrawal were not acceptable methods of contraception

- Female sterilization (have had surgical bilateral oophorectomy with or without hysterectomy) total hysterectomy or tubal ligation at least six weeks before taking investigational drug. In case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment
- Male sterilization (at least 6 months prior to screening). For female patients on the study, the vasectomized male partner should be the sole partner for that patient
- Use of oral (oestrogen and progesterone), injected or implanted hormonal methods of contraception or placement of an intrauterine device (IUD) or intrauterine system (IUS) or other forms of hormonal contraception that have comparable efficacy (failure rate <1%), e.g. hormone vaginal ring or transdermal hormone contraception
- In case of use of oral contraception women should have been stable on the same pill for a minimum of 3 months before taking investigational drug
- Women are considered post-menopausal and not of child bearing potential if they have had 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (e.g. age appropriate, history of vasomotor symptoms) or have had surgical bilateral oophorectomy (with or without hysterectomy), total hysterectomy or tubal ligation at least six weeks ago. In the case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment is she considered not of child bearing potential.

- Use of other investigational drugs within 5 half-lives of enrolment, or until the expected pharmacodynamic effect has returned to baseline, whichever is longer
- History of hypersensitivity to the study drug or its excipients
- Any prior exposure to investigational products targeting the calcitonin gene-related peptide pathway, including previous erenumab studies
- Unlikely to be able to complete all protocol required study visits or procedures, and/or to comply with all required study procedures (e.g. independent completion of electronic diary items) to the best of the patient's and investigator's knowledge.