Clinical trial results:
A 12-week double-blind, randomized, multicenter study comparing the efficacy and safety of once monthly subcutaneous 140 mg AMG334 against placebo in adult episodic migraine patients who have failed 2-4 prophylactic treatments (LIBERTY)

Summary

EudraCT number	2016-002211-18
Trial protocol	CZ GB SE DE FI ES AT DK BE GR NL FR IT
Global end of trial date	28 January 2021

Results information

Result version number	v1 (current)
This version publication date	06 February 2022
First version publication date	06 February 2022

Trial information

Trial identification

Sponsor protocol code	CAMG334A2301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03096834
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 January 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of 140 mg AMG334 compared to placebo on the proportion of patients with at least 50% reduction from baseline in monthly migraine days (MMD).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 March 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Austria: 6
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Czechia: 22
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	Finland: 8
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 66
Country: Number of subjects enrolled	Greece: 10
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	Netherlands: 21
Country: Number of subjects enrolled	Norway: 21
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Sweden: 14
Country: Number of subjects enrolled	Switzerland: 8
Country: Number of subjects enrolled	United Kingdom: 9
Worldwide total number of subjects	246
EEA total number of subjects	227

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	246
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

333 participants were screened for the trial

Period 1

Period 1 title	Double-Blind Treatment Epoch
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	AMG334 140 mg DB

Arm description:

AMG334 140 mg subcutaneous injections administered every 4 weeks during Double-Blind Epoch

Arm type	Experimental
Investigational medicinal product name	AMG334
Investigational medicinal product code	AMG334
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Two injections of AMG334 70 mg / 1 mL pre-filled syringe (equaling 140 mg total dose) were administered at Day 1 and Weeks 4 and 8 during DBTP

Arm title	Placebo DB

Arm description:

Matching placebo subcutaneous injections administered every 4 weeks during Double-Blind Epoch

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Two injections of matching placebo were administered at Day 1 and Weeks 4 and 8 during DBTP

Number of subjects in period 1	AMG334 140 mg DB	Placebo DB
Started	121	125
Completed	118	122
Not completed	3	3
Protocol deviation	2	1

Pregnancy	-	1
Subject/guardian decision	1	1

Period 2

Period 2 title	Open-Label Treatment Epoch
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	AMG334 140 mg DB cont on AMG334 140 mg

Arm description:

AMG334 140 mg subcutaneous injections during DB continued on AMG334 140 mg in Open-Label Epoch

Arm type	Experimental
Investigational medicinal product name	AMG334
Investigational medicinal product code	AMG334
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Two injections of AMG334 70 mg / 1 mL pre-filled syringe (equaling 140 mg total dose) were administered at Week 12 and then every 4 weeks during OLTP and PTAP

Arm title	Placebo DB to AMG334 140 mg

Arm description:

Placebo in Double-Blind Epoch (DB) switched to AMG334 140 mg in Open-Label Epoch

Arm type	Experimental
Investigational medicinal product name	AMG334
Investigational medicinal product code	AMG334
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Two injections of AMG334 70 mg / 1 mL pre-filled syringe (equaling 140 mg total dose) were administered at Week 12 and then every 4 weeks during OLTP and PTAP

Number of subjects in period 2	AMG334 140 mg DB cont on AMG334 140 mg	Placebo DB to AMG334 140 mg
Started	118	122
Completed	86	83
Not completed	32	39
Physician decision	1	-
Adverse event, non-fatal	5	6
Pregnancy	1	-
New therapy for study indication	1	1
Subject/guardian decision	9	17
Lack of efficacy	15	15

Period 3

Period 3 title	Safety Follow-Up Epoch
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

No study treatment was administered during this safety follow-up.

Arms

Are arms mutually exclusive?	Yes
Arm title	AMG334 140 mg DB cont on AMG334 140 mg

Arm description:

AMG334 140 mg subcutaneous injections during DB continued on AMG334 140 mg in Open-Label Epoch

Arm type	Experimental
Investigational medicinal product name	AMG334
Investigational medicinal product code	AMG334
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Two injections of AMG334 70 mg / 1 mL pre-filled syringe (equaling 140 mg total dose) were administered at Week 12 and then every 4 weeks during OLTP and PTAP

Arm title	Placebo DB to AMG334 140 mg

Arm description:

Placebo in Double-Blind Epoch (DB) switched to AMG334 140 mg in Open-Label Epoch

Arm type	Experimental
Investigational medicinal product name	AMG334
Investigational medicinal product code	AMG334
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Two injections of AMG334 70 mg / 1 mL pre-filled syringe (equaling 140 mg total dose) were administered at Week 12 and then every 4 weeks during OLTP and PTAP

Number of subjects in period 3[1]	AMG334 140 mg DB cont on AMG334 140 mg	Placebo DB to AMG334 140 mg
Started	66	61
Completed	65	59
Not completed	1	2
Protocol deviation	-	1
Lost to follow-up	1	-
New therapy for study indication	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all participants continued into this Epoch.

Period 4

Period 4 title	Post-Trial Access Epoch
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	AMG334 140 mg DB cont on AMG334 140 mg

Arm description:

AMG334 140 mg subcutaneous injections during DB continued on AMG334 140 mg in Open-Label Epoch

Arm type	Experimental
Investigational medicinal product name	AMG334
Investigational medicinal product code	AMG334
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Two injections of AMG334 70 mg / 1 mL pre-filled syringe (equaling 140 mg total dose) were administered at Week 12 and then every 4 weeks during OLTP and PTAP

Arm title	Placebo DB to AMG334 140 mg

Arm description:

Placebo in Double-Blind Epoch (DB) switched to AMG334 140 mg in Open-Label Epoch

Arm type	Experimental

Investigational medicinal product name	AMG334
Investigational medicinal product code	AMG334
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Two injections of AMG334 70 mg / 1 mL pre-filled syringe (equaling 140 mg total dose) were administered at Week 12 and then every 4 weeks during OLTP and PTAP

Number of subjects in period 4[2]	AMG334 140 mg DB cont on AMG334 140 mg	Placebo DB to AMG334 140 mg
Started	21	15
Completed	21	15

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Post-trial access to treatment was not available if commercially available.

Baseline characteristics

Reporting groups	
Reporting group title	AMG334 140 mg DB
Reporting group description:	
AMG334 140 mg subcutaneous injections administered every 4 weeks during Double-Blind Epoch	
Reporting group title	Placebo DB
Reporting group description:	
Matching placebo subcutaneous injections administered every 4 weeks during Double-Blind Epoch	

Reporting group values	AMG334 140 mg DB	Placebo DB	Total
Number of subjects	121	125	246
Age Categorical			
Participants who continued into Open-Label Epoch were the same participants in Double-Blind Treatment Epoch			
Units: Participants			
Between 18 and 65 years	121	125	246
Sex: Female, Male Units:			
Female	97	103	200
Male	24	22	46
Race/Ethnicity, Customized Units: Subjects			
Caucasian	112	115	227
Asian	0	1	1
Unknown	0	1	1
Other	9	8	17
Monthly Migraine Days at Baseline			
A migraine day was defined as any calendar day in which the subject experienced a qualified migraine headache defined as: with/without aura, lasting ≥ 30 minutes with at least 1 criteria: 1. ≥ 2 of following pain features: unilateral, throbbing, moderate to severe or exacerbated with exercise/physical activity, 2. ≥ 1 of the following symptoms: nausea and/or vomiting, photophobia and phonophobia. If a migraine-specific medication (ie, triptan or ergotamine) was taken during aura, or a headache, it was counted as a migraine day regardless of duration and pain features/associated symptoms.			
Units: Migraine days/month			
arithmetic mean	9.2	9.3	
standard deviation	± 2.56	± 2.72	-

End points

End points reporting groups

Reporting group title	AMG334 140 mg DB

Reporting group description:

AMG334 140 mg subcutaneous injections administered every 4 weeks during Double-Blind Epoch

Reporting group title	Placebo DB

Reporting group description:

Matching placebo subcutaneous injections administered every 4 weeks during Double-Blind Epoch

Reporting group title	AMG334 140 mg DB cont on AMG334 140 mg

Reporting group description:

AMG334 140 mg subcutaneous injections during DB continued on AMG334 140 mg in Open-Label Epoch

Reporting group title	Placebo DB to AMG334 140 mg

Reporting group description:

Placebo in Double-Blind Epoch (DB) switched to AMG334 140 mg in Open-Label Epoch

Reporting group title	AMG334 140 mg DB cont on AMG334 140 mg

Reporting group description:

AMG334 140 mg subcutaneous injections during DB continued on AMG334 140 mg in Open-Label Epoch

Reporting group title	Placebo DB to AMG334 140 mg

Reporting group description:

Placebo in Double-Blind Epoch (DB) switched to AMG334 140 mg in Open-Label Epoch

Reporting group title	AMG334 140 mg DB cont on AMG334 140 mg

Reporting group description:

AMG334 140 mg subcutaneous injections during DB continued on AMG334 140 mg in Open-Label Epoch

Reporting group title	Placebo DB to AMG334 140 mg

Reporting group description:

Placebo in Double-Blind Epoch (DB) switched to AMG334 140 mg in Open-Label Epoch

Subject analysis set title	AMG334 140 mg - All Patients
Subject analysis set type	Safety analysis

Subject analysis set description:

All participants who received AMG334 during trial including participants who switched from placebo

Primary: Percentage of participants with a 50% reduction from baseline of Monthly Migraine Days (MMD) in the last month (last 4 weeks of treatment)

End point title	Percentage of participants with a 50% reduction from baseline of Monthly Migraine Days (MMD) in the last month (last 4 weeks of treatment)

End point description:

A migraine day was defined as any calendar day in which the subject experienced a qualified migraine headache defined as: with/without aura, lasting ≥ 30 minutes with at least 1 criteria: 1. ≥ 2 of following pain features: unilateral, throbbing, moderate to severe or exacerbated with exercise/physical activity, 2. ≥ 1 of the following symptoms: nausea and/or vomiting, photophobia and phonophobia. If a migraine-specific medication (ie, triptan or ergotamine) was taken during aura, or a headache, it was counted as a migraine day regardless of duration and pain features/associated symptoms.

End point type	Primary

End point timeframe:

Baseline, Month 3 (last 4 weeks of treatment)

End point values	AMG334 140 mg DB	Placebo DB		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	124		
Units: Participants				
number (not applicable)	30.3	13.7		

Statistical analyses

Statistical analysis title	Month 3 (last 4 weeks of treatment)
Comparison groups	Placebo DB v AMG334 140 mg DB
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.002
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.43
upper limit	5.19

Secondary: Change from baseline in Monthly Migraine Days (MMD) in the last month (last 4 weeks of treatment)

End point title	Change from baseline in Monthly Migraine Days (MMD) in the last month (last 4 weeks of treatment)

End point description:

A migraine day was defined as any calendar day in which the subject experienced a qualified migraine headache defined as: with/without aura, lasting ≥ 30 minutes with at least 1 criteria: 1. ≥ 2 of following pain features: unilateral, throbbing, moderate to severe or exacerbated with exercise/physical activity, 2. ≥ 1 of the following symptoms: nausea and/or vomiting, photophobia and phonophobia. If a migraine-specific medication (ie, triptan or ergotamine) was taken during aura, or a headache, it was counted as a migraine day regardless of duration and pain features/associated symptoms.

End point type	Secondary

End point timeframe:

Baseline, Month 3 (last 4 weeks of treatment)

End point values	AMG334 140 mg DB	Placebo DB		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	120		
Units: Monthly migraine days				
arithmetic mean (standard error)				
Month 3 n=118,120	-1.75 (± 0.43)	-0.16 (± 0.41)		

Statistical analyses

Statistical analysis title	Month 3
Comparison groups	AMG334 140 mg DB v Placebo DB
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.004
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.67
upper limit	-0.51
Variability estimate	Standard error of the mean
Dispersion value	0.55

Secondary: Change from baseline in physical impairment and everyday activities as measured by the Migraine Physical Function Impact Diary (MPFID) at Month 3

End point title	Change from baseline in physical impairment and everyday activities as measured by the Migraine Physical Function Impact Diary (MPFID) at Month 3

End point description:

MPFID has 2 domains: Everyday Activities, which consisted of 7 items and Physical Impairment with 5 items using a 5-point scale. Scores were summed across each domain and were then transformed and used for analyses. Transforming MPFID domain scores ranged from 0-100, where higher scores were indicative of greater migraine impact (ie, higher burden)

End point type	Secondary

End point timeframe:

Baseline, Month 3 (last 4 weeks of treatment)

End point values	AMG334 140 mg DB	Placebo DB		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	120		
Units: scores on a scale				
arithmetic mean (standard error)				
Physical impairment domain n=118,120	-1.85 (± 0.84)	1.61 (± 0.80)		
Everyday activities domain n=118,120	-3.36 (± 0.83)	0.55 (± 0.81)		

Statistical analyses

Statistical analysis title	Month 3
Statistical analysis description: Physical impairment domain	
Comparison groups	AMG334 140 mg DB v Placebo DB
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.003
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	-1.23
Variability estimate	Standard error of the mean
Dispersion value	1.13

Statistical analysis title	Month 3
Statistical analysis description: Everyday activities domain	
Comparison groups	AMG334 140 mg DB v Placebo DB
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.12
upper limit	-1.7
Variability estimate	Standard error of the mean
Dispersion value	1.12

Secondary: Change in the number of monthly acute migraine-specific medication treatment days at Month 3

End point title	Change in the number of monthly acute migraine-specific medication treatment days at Month 3

End point description:

Number of days on which acute migraine-specific medications were used were recorded in eDiary between each monthly IP dose. Migraine-Specific medications included two categories of medications: triptan-based migraine medications and ergotamine-based migraine medications. Monthly migraine-specific medication use at baseline was the number of migraine-specific medication treatment days in the baseline period.

End point type	Secondary

End point timeframe:

Baseline, Month 3 (last 4 weeks of treatment)

End point values	AMG334 140 mg DB	Placebo DB		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	120		
Units: Migraine treatment specific days/month				
arithmetic mean (standard error)	-1.25 (± 0.24)	0.46 (± 0.28)		

Statistical analyses

Statistical analysis title	Month 3
Comparison groups	AMG334 140 mg DB v Placebo DB
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.43
upper limit	-0.99
Variability estimate	Standard error of the mean
Dispersion value	0.36

Secondary: Percentage of participants with a 75% reduction from baseline of Monthly Migraine Days (MMD) in the last month (last 4 weeks of treatment)

End point title	Percentage of participants with a 75% reduction from baseline of Monthly Migraine Days (MMD) in the last month (last 4 weeks of treatment)

End point description:

A migraine day was defined as any calendar day in which the subject experienced a qualified migraine headache defined as: with/without aura, lasting ≥ 30 minutes with at least 1 criteria: 1. ≥ 2 of following pain features: unilateral, throbbing, moderate to severe or exacerbated with exercise/physical activity, 2. ≥ 1 of the following symptoms: nausea and/or vomiting, photophobia and phonophobia. If a migraine-specific medication (ie, triptan or ergotamine) was taken during aura, or a headache, it was counted as a migraine day regardless of duration and pain features/associated symptoms.

End point type	Secondary

End point timeframe:

Baseline, Month 3 (last 4 weeks of treatment)

End point values	AMG334 140 mg DB	Placebo DB		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	124		
Units: Percentage of participants				
number (not applicable)	11.8	4.0		

Statistical analyses

Statistical analysis title	Month 3
Comparison groups	AMG334 140 mg DB v Placebo DB
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.025
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	9.01

Secondary: Percentage of participants with a 100% reduction from baseline of Monthly Migraine Days (MMD) in the last month (last 4 weeks of treatment)

End point title	Percentage of participants with a 100% reduction from baseline of Monthly Migraine Days (MMD) in the last month (last 4 weeks of treatment)

End point description:

A migraine day was defined as any calendar day in which the subject experienced a qualified migraine headache defined as: with/without aura, lasting ≥ 30 minutes with at least 1 criteria: 1. ≥ 2 of following pain features: unilateral, throbbing, moderate to severe or exacerbated with exercise/physical activity, 2. ≥ 1 of the following symptoms: nausea and/or vomiting, photophobia and phonophobia. If a migraine-specific medication (ie, triptan or ergotamine) was taken during aura, or a headache, it was counted as a migraine day regardless of duration and pain features/associated symptoms.

End point type	Secondary

End point timeframe:

Baseline, Month 3 (last 4 weeks of treatment)

End point values	AMG334 140 mg DB	Placebo DB		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	124		
Units: Percentage of participants				
number (not applicable)	5.9	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who developed anti-AMG334 antibodies

End point title	Number of participants who developed anti-AMG334 antibodies

End point description:

Blood samples for immunogenicity testing were collected for the measurement of anti-AMG334 binding antibodies.

End point type	Secondary

End point timeframe:

Baseline up to 180 weeks

End point values	AMG334 140 mg - All Patients			
Subject group type	Subject analysis set			
Number of subjects analysed	238			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the first dose of study treatment through the completion of the up to 196-week trial for a maximum treatment exposure of 199 weeks (includes 4 week follow-up).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	AMG334 140 mg DB

Reporting group description:

AMG334 140 mg subcutaneous injections administered every 4 weeks during Double-Blind Epoch

Reporting group title	Placebo DB

Reporting group description:

Matching placebo subcutaneous injections administered every 4 weeks during Double-Blind Epoch

Reporting group title	AMG334 140 mg DB cont on AMG334 140 mg

Reporting group description:

AMG334 140 mg subcutaneous injections during DB continued on AMG334 140 mg in Open-Label Epoch

Reporting group title	Placebo DB to MG334 140mg

Reporting group description:

Placebo in Double-Blind Epoch (DB) switched to AMG334 140 mg in Open-Label Epoch

Serious adverse events	AMG334 140 mg DB	Placebo DB	AMG334 140 mg DB cont on AMG334 140 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 119 (1.68%)	1 / 124 (0.81%)	16 / 118 (13.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma stage 0			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelofibrosis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pituitary tumour benign			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postmenopausal haemorrhage			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic fracture			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aura			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medication overuse headache			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	2 / 118 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status migrainosus			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Dacryostenosis acquired			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inflammation of lacrimal passage			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal vein thrombosis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex hepatitis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo DB to MG334 140mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 122 (14.75%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma stage 0			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myelofibrosis			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pituitary tumour benign			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postmenopausal haemorrhage			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	2 / 122 (1.64%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			

Femoral neck fracture				
subjects affected / exposed	0 / 122 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	0 / 122 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Traumatic fracture				
subjects affected / exposed	0 / 122 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Extrasystoles				
subjects affected / exposed	1 / 122 (0.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Aura				
subjects affected / exposed	0 / 122 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	0 / 122 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Medication overuse headache				
subjects affected / exposed	0 / 122 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Migraine				
subjects affected / exposed	2 / 122 (1.64%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Status migrainosus			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Dacryostenosis acquired			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inflammation of lacrimal passage			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Retinal vein thrombosis			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis ischaemic			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Umbilical hernia			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal colic			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic sinusitis			

subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal infection			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Herpes simplex hepatitis			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 122 (0.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 122 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	AMG334 140 mg DB	Placebo DB	AMG334 140 mg DB cont on AMG334 140 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 119 (36.97%)	43 / 124 (34.68%)	94 / 118 (79.66%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 119 (0.84%)	1 / 124 (0.81%)	14 / 118 (11.86%)
occurrences (all)	1	1	14
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 119 (2.52%)	2 / 124 (1.61%)	5 / 118 (4.24%)
occurrences (all)	3	2	8
Headache			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	5 / 118 (4.24%)
occurrences (all)	0	0	5
Migraine			
subjects affected / exposed	0 / 119 (0.00%)	2 / 124 (1.61%)	10 / 118 (8.47%)
occurrences (all)	0	2	12
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 119 (2.52%)	2 / 124 (1.61%)	9 / 118 (7.63%)
occurrences (all)	3	2	11
Influenza like illness			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	11 / 118 (9.32%)
occurrences (all)	0	0	14
Injection site haematoma			
subjects affected / exposed	1 / 119 (0.84%)	2 / 124 (1.61%)	2 / 118 (1.69%)
occurrences (all)	1	3	9
Injection site pain			
subjects affected / exposed	7 / 119 (5.88%)	7 / 124 (5.65%)	8 / 118 (6.78%)
occurrences (all)	21	7	55
Pyrexia			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	8 / 118 (6.78%)
occurrences (all)	1	0	10
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	8 / 118 (6.78%)
occurrences (all)	0	0	12
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 119 (1.68%)	2 / 124 (1.61%)	11 / 118 (9.32%)
occurrences (all)	2	2	11
Diarrhoea			
subjects affected / exposed	2 / 119 (1.68%)	1 / 124 (0.81%)	8 / 118 (6.78%)
occurrences (all)	2	1	11
Nausea			
subjects affected / exposed	3 / 119 (2.52%)	2 / 124 (1.61%)	6 / 118 (5.08%)
occurrences (all)	3	2	6
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	1 / 119 (0.84%)	1 / 124 (0.81%)	10 / 118 (8.47%)
occurrences (all)	1	1	13
Oropharyngeal pain			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	13 / 118 (11.02%)
occurrences (all)	1	0	16
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 119 (1.68%)	1 / 124 (0.81%)	3 / 118 (2.54%)
occurrences (all)	2	2	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 119 (1.68%)	4 / 124 (3.23%)	9 / 118 (7.63%)
occurrences (all)	2	5	15
Back pain			
subjects affected / exposed	5 / 119 (4.20%)	2 / 124 (1.61%)	15 / 118 (12.71%)
occurrences (all)	6	2	23
Neck pain			
subjects affected / exposed	3 / 119 (2.52%)	0 / 124 (0.00%)	9 / 118 (7.63%)
occurrences (all)	3	0	11
Pain in extremity			
subjects affected / exposed	0 / 119 (0.00%)	3 / 124 (2.42%)	5 / 118 (4.24%)
occurrences (all)	0	3	5
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 119 (1.68%)	1 / 124 (0.81%)	8 / 118 (6.78%)
occurrences (all)	2	1	9
Cystitis			
subjects affected / exposed	1 / 119 (0.84%)	2 / 124 (1.61%)	7 / 118 (5.93%)
occurrences (all)	1	3	11
Gastroenteritis			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	13 / 118 (11.02%)
occurrences (all)	1	0	16
Influenza			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	15 / 118 (12.71%)
occurrences (all)	0	0	20

Nasopharyngitis			
subjects affected / exposed	6 / 119 (5.04%)	12 / 124 (9.68%)	45 / 118 (38.14%)
occurrences (all)	6	12	93
Rhinitis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	6 / 118 (5.08%)
occurrences (all)	0	0	6
Sinusitis			
subjects affected / exposed	1 / 119 (0.84%)	1 / 124 (0.81%)	10 / 118 (8.47%)
occurrences (all)	1	1	11
Tonsillitis			
subjects affected / exposed	1 / 119 (0.84%)	1 / 124 (0.81%)	6 / 118 (5.08%)
occurrences (all)	1	1	9
Upper respiratory tract infection			
subjects affected / exposed	4 / 119 (3.36%)	0 / 124 (0.00%)	9 / 118 (7.63%)
occurrences (all)	5	0	23
Urinary tract infection			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	8 / 118 (6.78%)
occurrences (all)	0	1	13

Non-serious adverse events	Placebo DB to MG334 140mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	101 / 122 (82.79%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 122 (7.38%)		
occurrences (all)	13		
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 122 (5.74%)		
occurrences (all)	9		
Headache			
subjects affected / exposed	7 / 122 (5.74%)		
occurrences (all)	7		
Migraine			
subjects affected / exposed	10 / 122 (8.20%)		
occurrences (all)	22		
General disorders and administration			

site conditions Fatigue subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all) Injection site haematoma subjects affected / exposed occurrences (all) Injection site pain subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 8 / 122 (6.56%) 8 6 / 122 (4.92%) 7 7 / 122 (5.74%) 14 8 / 122 (6.56%) 16 7 / 122 (5.74%) 9		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	 6 / 122 (4.92%) 7		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 5 / 122 (4.10%) 5 7 / 122 (5.74%) 11 9 / 122 (7.38%) 12		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain	 10 / 122 (8.20%) 12		

subjects affected / exposed	6 / 122 (4.92%)		
occurrences (all)	7		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	9 / 122 (7.38%)		
occurrences (all)	9		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	12 / 122 (9.84%)		
occurrences (all)	20		
Back pain			
subjects affected / exposed	18 / 122 (14.75%)		
occurrences (all)	24		
Neck pain			
subjects affected / exposed	6 / 122 (4.92%)		
occurrences (all)	11		
Pain in extremity			
subjects affected / exposed	7 / 122 (5.74%)		
occurrences (all)	8		
Infections and infestations			
Bronchitis			
subjects affected / exposed	9 / 122 (7.38%)		
occurrences (all)	11		
Cystitis			
subjects affected / exposed	8 / 122 (6.56%)		
occurrences (all)	12		
Gastroenteritis			
subjects affected / exposed	10 / 122 (8.20%)		
occurrences (all)	12		
Influenza			
subjects affected / exposed	26 / 122 (21.31%)		
occurrences (all)	36		
Nasopharyngitis			
subjects affected / exposed	68 / 122 (55.74%)		
occurrences (all)	164		
Rhinitis			

subjects affected / exposed	5 / 122 (4.10%)		
occurrences (all)	6		
Sinusitis			
subjects affected / exposed	13 / 122 (10.66%)		
occurrences (all)	15		
Tonsillitis			
subjects affected / exposed	2 / 122 (1.64%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	7 / 122 (5.74%)		
occurrences (all)	12		
Urinary tract infection			
subjects affected / exposed	16 / 122 (13.11%)		
occurrences (all)	19		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2016	The purpose of this amendment was to change the AMG 334 dose from 70 mg to 140 mg per administration, and to update the sample size based on new assumptions using 140 mg. The definitions of the formal end of trial (EoT) and final clinical study report (CSR) were expanded upon, in addition to the clarification of various protocol sections based on feedback received from sites and regulatory authorities.
26 October 2017	The purpose of this amendment was to incorporate an additional exploratory analysis based on a consultation with a health technology assessment (HTA) body and due to the fact that amitriptyline was approved in Europe as an additional therapy for migraine prophylaxis.
02 March 2018	The purpose of this amendment was to expand the duration of the Open-Label Treatment Epoch from 52 weeks (1 year) to 156 weeks (3 years), intended to collect further long-term safety and efficacy data on AMG 334 in episodic migraine patients who had previously failed 2 to 4 prophylactic migraine treatments.
27 May 2020	The purpose of this amendment was to provide Post-Trial Access (PTA) for patients who had completed the 3 year Open-Label Treatment Epoch and had demonstrated clinical benefit in the opinion of the Investigator, to ensure continued drug access until erenumab had received country-level launch and subsequent reimbursement decision or until December 2020 whichever came first.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported