Clinical trial results:
An Open-label Extension Study to Evaluate the Long-term Safety of Mavrilimumab in Adult Participants with Rheumatoid Arthritis

Summary

EudraCT number	2011-005648-93
Trial protocol	EE HU CZ DE ES BG GR SK PT GB
Global end of trial date	30 September 2015

Results information

Result version number	v1 (current)
This version publication date	15 March 2017
First version publication date	15 March 2017

Trial information

Trial identification

Sponsor protocol code	CD-IA-CAM-3001-1109

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01712399
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune, LLC.
Sponsor organisation address	Milstein Building, Granta Park, Cambridge, CB21 6GH, United Kingdom,
Public contact	Marius Albulescu, MD, MedImmune, LLC., +44 (0) 301-398-0000, clinicaltrialenquiries@medimmune.com
Scientific contact	Marius Albulescu, MD, MedImmune, LLC., +44 (0) 301-398-0000, clinicaltrialenquiries@medimmune.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	30 September 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 September 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the long-term safety of mavrilimumab in adult participants with moderate-to-severe active Rheumatoid Arthritis (RA) who were previously treated in a qualifying study.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Participating participant signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 February 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 3
Country: Number of subjects enrolled	Argentina: 41
Country: Number of subjects enrolled	Chile: 35
Country: Number of subjects enrolled	Colombia: 25
Country: Number of subjects enrolled	Czech Republic: 69
Country: Number of subjects enrolled	Estonia: 21
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Greece: 3
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Israel: 11
Country: Number of subjects enrolled	Mexico: 10
Country: Number of subjects enrolled	Poland: 34
Country: Number of subjects enrolled	Russian Federation: 53
Country: Number of subjects enrolled	Serbia: 24
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	South Africa: 2
Country: Number of subjects enrolled	Spain: 4

Country: Number of subjects enrolled	Ukraine: 39
Country: Number of subjects enrolled	United Kingdom: 5
Worldwide total number of subjects	397
EEA total number of subjects	157

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)	354
From 65 to 84 years	43
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 409 participants consented and 397 participants received mavrilimumab in this study.

Pre-assignment

Screening details:

A total of 442 participants who received at least one dose of mavrilimumab provided a pooled analysis of safety and efficacy data from this open-label extension study (CD IA CAM 3001 1109) together with the qualifying studies (CD IA CAM 3001 1071 and CD IA CAM 3001 1107).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Mavrilimumab 100 mg

Arm description:

Participants received 100 mg mavrilimumab once in every 2 weeks (Q2W) subcutaneously for up to 3 years.

Arm type	Experimental
Investigational medicinal product name	Mavrilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 100 mg mavrilimumab once in every 2 weeks (Q2W) subcutaneously for up to 3 years.

Number of subjects in period 1	Mavrilimumab 100 mg
Started	397
Completed	0
Not completed	397
Adverse event, serious fatal	1
Consent withdrawn by subject	39
Adverse event, non-fatal	11
Lost to follow-up	1
Study closure	345

Baseline characteristics

Reporting groups	
Reporting group title	Mavrilimumab 100 mg
Reporting group description:	
Participants received 100 mg mavrilimumab once in every 2 weeks (Q2W) subcutaneously for up to 3 years.	

Reporting group values	Mavrilimumab 100 mg	Total	
Number of subjects	397	397	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	354	354	
From 65-84 years	43	43	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	51.1		
standard deviation	± 11.2	-	
Gender, Male/Female Units: Subjects			
Female	339	339	
Male	58	58	
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native	29	29	
Asian	1	1	
Black or African American	1	1	
Native Hawaiian or Other Pacific Islander	0	0	
White	364	364	
Other	2	2	
Region of Enrollment Units: Subjects			
ARGENTINA	41	41	
BULGARIA	3	3	
CHILE	35	35	
COLOMBIA	25	25	
CZECH REPUBLIC	69	69	
ESTONIA	21	21	
GERMANY	8	8	
GREECE	3	3	

HUNGARY	9	9	
ISRAEL	11	11	
MEXICO	10	10	
POLAND	34	34	
RUSSIAN FEDERATION	53	53	
SERBIA	24	24	
SLOVAKIA	1	1	
SOUTH AFRICA	2	2	
SPAIN	4	4	
UKRAINE	39	39	
UNITED KINGDOM	5	5	
Study Specific Characteristic | Weight			
Units: Kilogram			
arithmetic mean	73.25		
standard deviation	± 16.4	-	

End points

End points reporting groups

Reporting group title	Mavrilimumab 100 mg

Reporting group description:

Participants received 100 mg mavrilimumab once in every 2 weeks (Q2W) subcutaneously for up to 3 years.

Primary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)[1]

End point description:

An adverse event (AE) was any untoward medical occurrence attributed to study drug in a participant who received investigational product. A serious adverse event (SAE) was an AE resulting in any of following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. TEAEs were defined as AEs with onset date after the first dose of mavrilimumab 100 mg. The As-treated Population included participants who received at least one dose of mavrilimumab 100 mg Q2W.

End point type	Primary

End point timeframe:

From the start of study drug administration up to 12 weeks after the last dose of study drug (approximately up to 3 years)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Mavrilimumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	397			
Units: Participants				
TEAEs	288			
TESAEs	46			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinical Laboratory Abnormalities Reported as Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Participants With Clinical Laboratory Abnormalities Reported as Treatment-Emergent Adverse Events (TEAEs)[2]

End point description:

Laboratory parameters included hematology, serum chemistry and urinalysis recorded as TEAEs. Clinical laboratory abnormalities recorded as TEAEs were reported. TEAEs were defined as AEs with onset date after the first dose of mavrilimumab 100 mg. The As-treated Population included participants who received at least one dose of mavrilimumab 100 mg Q2W.

End point type	Primary

End point timeframe:

From the start of study drug administration in the study up to 12 weeks after the last dose of study drug (approximately up to 3 years)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Mavrilimumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	397			
Units: Participants				
Anaemia	8			
Eosinophilia	1			
Iron deficiency anaemia	2			
Leukocytosis	1			
Leukopenia	1			
Lymphadenopathy	1			
Neutropenia	2			
Spontaneous haematoma	1			
Alanine aminotransferase increased	8			
Aspartate aminotransferase increased	6			
Blood creatinine increased	1			
Blood glucose increased	1			
Blood pressure increased	3			
C-reactive protein increased	1			
Chest X-ray abnormal	1			
Forced vital capacity abnormal	1			
Gamma-glutamyltransferase increased	2			
Hepatic enzyme increased	2			
Liver function test abnormal	1			
Mycobacterium tuberculosis complex test positive	1			
Neutrophil count decreased	1			
Red blood cell sedimentation rate increased	1			
Transaminases increased	3			
Diabetes mellitus	5			
Dyslipidaemia	4			
Hypercholesterolaemia	9			
Hyperglycaemia	3			
Hyperlipidaemia	2			
Hypertriglyceridaemia	2			
Hypoglycaemia	1			
Type 2 diabetes mellitus	4			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Vital Sign Abnormalities Reported as Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Participants With Vital Sign Abnormalities Reported as Treatment-Emergent Adverse Events (TEAEs)[3]

End point description:

Vital sign assessments included blood pressure, pulse rate, temperature, weight, and respiration rate. Vital sign abnormalities recorded as TEAEs were reported. TEAEs were defined as AEs with onset date after the first dose of mavrilimumab 100 mg. The As-treated Population included participants who received at least one dose of mavrilimumab 100 mg Q2W.

End point type	Primary

End point timeframe:

From the start of study drug administration in the study up to 12 weeks after the last dose of study drug (approximately up to 3 years)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Mavrilimumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	397			
Units: Participants				
Hypertension	26			
Pyrexia	3			
Blood pressure increased	3			
Atrial fibrillation	1			
Palpitations	1			
Sinus tachycardia	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Abnormal Electrocardiogram (ECG) Findings Reported as TEAEs

End point title	Number of Participants With Abnormal Electrocardiogram (ECG) Findings Reported as TEAEs[4]

End point description:

The 12-lead ECG data were summarized and evaluated. TEAEs related to abnormal ECG findings were recorded and reported. TEAEs were defined as AEs with onset date after the first dose of mavrilimumab 100 mg. The As-treated Population included participants who received at least one dose of mavrilimumab 100 mg Q2W.

End point type	Primary

End point timeframe:

From the start of study drug administration in the study up to 12 weeks after the last dose of study drug (approximately up to 3 years)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Mavrilimumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	397			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Forced Expiratory Volume in 1 Second (FEV1) Outside Threshold Values

End point title	Number of Participants With Forced Expiratory Volume in 1 Second (FEV1) Outside Threshold Values[5]

End point description:

Pulmonary function testing was performed by spirometry to assess forced expiratory volume in 1 second (FEV1). FEV1 was the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration.The percentage (%) of predicted values of these pulmonary function tests were calculated based on decrease from baseline and categorized as less than or equal to (=<)15% reduction from baseline, greater than (>)15% to =<20% reduction from baseline, >20% reduction from baseline and >20% reduction to <80%. The threshold values refer to baseline values for each participant. The As-treated Population included participants who received at least one dose of mavrilimumab 100 mg Q2W. Here 'n' represents those participants who were evaluable for this measure at given time points.

End point type	Primary

End point timeframe:

From Week 24 to Week 130 at specified time points

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Mavrilimumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	397			
Units: Participants				
Week 24 (n=236):=<15% reduction	208			
Week 24 (n=236):>15% to =<20%	12			
Week 24 (n=236):>20% reduction	16			
Week 24 (n=236):>20% to <80%	13			
Week 48 (n=231):=<15% reduction	208			
Week 48 (n=231): >15% to =<20%	10			
Week 48 (n=231): >20% reduction	13			
Week 48 (n=231):>20% to <80%	8			
Week 78 (n=178):=<15% reduction	154			
Week 78 (n=178):>15% to =<20%	8			
Week 78 (n=178):>20% reduction	16			
Week 78 (n=178):>20% to <80%	11			
Week 104 (n=29):=<15% reduction	28			
Week 104 (n=29):>15% to =<20%	0			
Week 104 (n=29):>20% reduction	1			
Week 104 (n=29):>20% to <80%	1			

Week 130 (n=3):=<15% reduction	3			
Week 130 (n=3):>15% to =<20%	0			
Week 130 (n=3):>20% reduction	0			
Week 130 (n=3):>20% to <80%	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Forced Expiratory Volume in 6 Seconds (FEV6) Outside Threshold Values

End point title	Number of Participants With Forced Expiratory Volume in 6 Seconds (FEV6) Outside Threshold Values[6]

End point description:

Pulmonary function testing was performed by spirometry to assess forced expiratory volume in 6 seconds (FEV6). FEV6 was the maximal volume of air exhaled in the six second of a forced expiration from a position of full inspiration. The percentage of predicted values of these pulmonary function tests were calculated based on decrease from baseline and categorized as =<15% reduction from baseline, >15% to =<20% reduction from baseline, >20% reduction from baseline and >20% reduction to <80%. The threshold values refer to baseline values for each participant. The As-treated Population included participants who received at least one dose of mavrilimumab 100 mg Q2W. Here 'n' represents those participants who were evaluable for this measure at given time points.

End point type	Primary

End point timeframe:

From Week 24 to Week 130 at specified time points

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Mavrilimumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	397			
Units: Participants				
Week 24 (n=222):=<15% reduction	195			
Week 24 (n=222):>15% to =<20%	14			
Week 24 (n=222):>20% reduction	13			
Week 24 (n=222):>20% to <80%	9			
Week 48 (n=222):=<15% reduction	201			
Week 48 (n=222):>15% to =<20%	13			
Week 48 (n=222):>20% reduction	8			
Week 48 (n=222):>20% to <80%	4			
Week 78 (n=172):=<15% reduction	150			
Week 78 (n=172):>15% to =<20%	8			
Week 78 (n=172):>20% reduction	14			
Week 78 (n=172):>20% to <80%	5			
Week 104 (n=28):=<15% reduction	27			
Week 104 (n=28):>15% to =<20%	0			
Week 104 (n=28):>20% reduction	1			
Week 104 (n=28):>20% to <80%	1			
Week 130 (n=3):=<15% reduction	1			

Week 130 (n=3):>15% to =<20%	0			
Week 130 (n=3):>20% reduction	2			
Week 130 (n=3):>20% to <80%	2			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Forced Vital Capacity (FVC) Outside Threshold Values

End point title	Number of Participants With Forced Vital Capacity (FVC) Outside Threshold Values[7]

End point description:

Pulmonary function testing was performed by spirometry to assess forced vital capacity (FVC). FVC was the volume of air which can be forcibly exhaled from the lungs after taking the deepest breath possible. The percentage of predicted values of these pulmonary function tests were calculated based on decrease from baseline and categorized as =<15% reduction from baseline, >15% to =<20% reduction from baseline, >20% reduction from baseline and >20% reduction to <80%. The threshold values refer to baseline values for each participant. The As-treated Population included participants who received at least one dose of mavrilimumab 100 mg Q2W. Here 'n' represents those participants who were evaluable for this measure at given time points.

End point type	Primary

End point timeframe:

From Week 24 to Week 156 at specified time points

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Mavrilimumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	397			
Units: Participants				
Week 24 (n=233):=<15% reduction	209			
Week 24 (n=233):>15% to =<20%	13			
Week 24 (n=233):>20% reduction	11			
Week 24 (n=233):>20% to <80%	7			
Week 48 (n=239):=<15% reduction	218			
Week 48 (n=239):>15% to =<20%	10			
Week 48 (n=239):>20% reduction	11			
Week 48 (n=239):>20% to <80%	7			
Week 78 (n=177):=<15% reduction	160			
Week 78 (n=177):>15% to =<20%	4			
Week 78 (n=177):>20% reduction	13			
Week 78 (n=177):>20% to <80%	6			
Week 104 (n=32):=<15% reduction	32			
Week 104 (n=32):>15% to =<20%	0			
Week 104 (n=32):>20% reduction	0			
Week 104 (n=32):>20% to <80%	0			
Week 130 (n=5):=<15% reduction	4			
Week 130 (n=5):>15% to =<20%	0			

Week 130 (n=5):>20% reduction	1			
Week 130 (n=5):>20% to <80%	1			
Week 156 (n=2):=<15% reduction	2			
Week 156 (n=2):>15% to =<20%	0			
Week 156 (n=2):>20% reduction	0			
Week 156 (n=2):>20% to <80%	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Meaningful Change in Borg Dyspnea Score Considered as an AE

End point title	Number of Participants With Clinically Meaningful Change in Borg Dyspnea Score Considered as an AE[8]

End point description:

Borg dyspnea score was a validated participant reported outcome assessing participant's perceived difficulty in breathing (dyspnea). The score ranges from 0 (nothing at all) to 10 (maximal difficulty). Higher scores indicated greater difficulty in breathing. The As-treated Population included participants who received at least one dose of mavrilimumab 100 mg Q2W.

End point type	Primary

End point timeframe:

From Week 0 to Week 132 at specified time points

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Mavrilimumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	394			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Oxygen Saturation Levels by Pulse Oximetry

End point title	Oxygen Saturation Levels by Pulse Oximetry[9]

End point description:

Oxygen saturation measured by pulse oximetry which measures the concentration of oxygen in the blood. 99999 indicates non-availability of data as standard error was not calculated due to limited sample size. The As-treated Population included participants who received at least one dose of mavrilimumab 100 mg Q2W. Here 'n' represents those participants who were evaluable for this measure at given time points.

End point type	Primary

End point timeframe:

From Week 0 to Week 132 at specified time points

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Mavrilimumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	397			
Units: Percent saturation				
arithmetic mean (standard error)				
Week 0 (n=397)	97.6 (± 0.1)			
Week 12 (n=384)	97.6 (± 0.1)			
Week 24 (n=1)	98 (± 99999)			
Week 36 (n=357)	97.5 (± 0.1)			
Week 48 (n=327)	97.8 (± 0.1)			
Week 60 (n=281)	97.8 (± 0.1)			
Week 72 (n=233)	97.7 (± 0.1)			
Week 84 (n=222)	97.7 (± 0.1)			
Week 96 (n=188)	97.9 (± 0.1)			
Week 108 (n=58)	97.8 (± 0.2)			
Week 120 (n=18)	97.6 (± 0.3)			
Week 132 (n=7)	97.9 (± 0.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Diffusing Capacity of the Lung for Carbon Monoxide (DLCO)

End point title	Diffusing Capacity of the Lung for Carbon Monoxide (DLCO)[10]

End point description:

DLCO is a pulmonary function testing that measures partial pressure difference between inspired and expired carbon monoxide. The unit mL/min/mmHg refers to milliliter/minute/millimeter of mercury. The As-treated Population included participants who received at least one dose of mavrilimumab 100 mg Q2W. Here 'n' represents those participants who were evaluable for this measure at given time points.

End point type	Primary

End point timeframe:

From Week 12 to Week 156 at specified time points

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Mavrilimumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	397			
Units: mL/min/mmHg				
arithmetic mean (standard deviation)				
Week 12 (n=80)	21.196 (± 5.158)			

Week 24 (n=155)	21.996 (± 5.274)			
Week 48 (n=203)	21.135 (± 4.873)			
Week 78 (n=165)	20.639 (± 4.637)			
Week 104 (n=144)	20.636 (± 5.088)			
Week 130 (n=52)	20.372 (± 4.546)			
Week 156 (n=6)	19.265 (± 4.131)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the start of study drug administration up to 12 weeks after the last dose of study drug (approximately up to 3 years)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Mavrilimumab 100 mg

Reporting group description:

Participants received 100 mg mavrilimumab once in every 2 weeks (Q2W) subcutaneously for up to 3 years.

Serious adverse events	Mavrilimumab 100 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	46 / 397 (11.59%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer female			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fibroadenoma of breast			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyogenic granuloma			

subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
subjects affected / exposed	2 / 397 (0.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ligament rupture			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ligament sprain			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			

Peripheral arterial occlusive disease				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral artery stenosis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral artery thrombosis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Subclavian artery thrombosis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiopulmonary failure				
subjects affected / exposed	2 / 397 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	2 / 397 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Myelitis transverse				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 397 (0.76%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			

subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	2 / 397 (0.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Rheumatoid arthritis			
subjects affected / exposed	4 / 397 (1.01%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendiceal abscess			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis perforated			
subjects affected / exposed	1 / 397 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			

subjects affected / exposed	4 / 397 (1.01%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	2 / 397 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
subjects affected / exposed	2 / 397 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pyomyositis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sialoadenitis				
subjects affected / exposed	1 / 397 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	2 / 397 (0.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Mavrilimumab 100 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	214 / 397 (53.90%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	8 / 397 (2.02%)		
occurrences (all)	8		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	8 / 397 (2.02%)		
occurrences (all)	8		
Vascular disorders			
Hypertension			
subjects affected / exposed	26 / 397 (6.55%)		
occurrences (all)	27		
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 397 (4.28%)		
occurrences (all)	35		
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	8 / 397 (2.02%)		
occurrences (all)	9		
Diarrhoea			
subjects affected / exposed	15 / 397 (3.78%)		
occurrences (all)	15		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 397 (2.02%)		
occurrences (all)	9		

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	12 / 397 (3.02%)		
occurrences (all)	13		
Osteoarthritis			
subjects affected / exposed	12 / 397 (3.02%)		
occurrences (all)	13		
Rheumatoid arthritis			
subjects affected / exposed	38 / 397 (9.57%)		
occurrences (all)	78		
Infections and infestations			
Bronchitis			
subjects affected / exposed	44 / 397 (11.08%)		
occurrences (all)	59		
Gastroenteritis			
subjects affected / exposed	11 / 397 (2.77%)		
occurrences (all)	14		
Influenza			
subjects affected / exposed	23 / 397 (5.79%)		
occurrences (all)	26		
Nasopharyngitis			
subjects affected / exposed	59 / 397 (14.86%)		
occurrences (all)	90		
Oral herpes			
subjects affected / exposed	11 / 397 (2.77%)		
occurrences (all)	13		
Pharyngitis			
subjects affected / exposed	18 / 397 (4.53%)		
occurrences (all)	20		
Respiratory tract infection			
subjects affected / exposed	13 / 397 (3.27%)		
occurrences (all)	21		
Rhinitis			
subjects affected / exposed	9 / 397 (2.27%)		
occurrences (all)	10		
Upper respiratory tract infection			

subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Viral infection subjects affected / exposed occurrences (all)	31 / 397 (7.81%) 43 35 / 397 (8.82%) 53 8 / 397 (2.02%) 10		
Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all)	9 / 397 (2.27%) 9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2012	Reference to the Data safety monitoring board (DSMB) was removed from the Study-stopping Criteria, Definition of the timing of the withdrawal visit was added, Withdrawal criteria item revised to include a definition of inadequate response, A section describing unblinding in the event of a suspected unexpected serious adverse reaction (SUSAR) was added, Responsibilities for the decision to resume administration of investigational product for a participant referred for a specialist pulmonary evaluation were clarified, A DLCO assessment was added, Reference to recording the QT interval during the electrocardiogram (ECG) was removed, Text describing an additional serum sample collection was added, The estimate of volume of blood to be collected was amended and Mention of flow cytometry was deleted from the exploratory endpoints and the protocol abstract

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
30 September 2015	The study was terminated after approximately 3 years due to future clinical development plans, including ethical considerations (the 100 mg Q2W dose was considered suboptimal compared with 150 mg Q2W based on CD-IA-CAM-3001-1071 data).	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated after approximately 3 years due to future clinical development plans, including ethical considerations (the 100 mg Q2W dose was considered suboptimal compared with 150 mg Q2W based on CD-IA-CAM-3001-1071 data).

Notes: