



Clinical trial results:

Evaluation of the subcutaneous administration of 30 mg of S 78989 versus placebo and evaluation of the subcutaneous administration of 60 mg of S78989 versus placebo on the reduction of arterial wall inflammation in patients with marked atherosclerotic plaque inflammation.

A 28-weeks, randomised, double-blind, parallel-group, placebo controlled, international multicentre exploratory pilot study.

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2012-002677-53
Trial protocol	FI NL
Global end of trial date	24 November 2014

Results information

Result version number	v1 (current)
This version publication date	23 July 2016
First version publication date	23 July 2016

Trial information

Trial identification

Sponsor protocol code	CL2-78989-009
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Institut de Recherches Internationales Servier
Sponsor organisation address	50 rue Carnot, Suresnes, France, 92284 Cedex
Public contact	Clinical Studies Department, Institut de Recherches Internationales Servier, 33 155724366, clinicaltrials@servier.com
Scientific contact	Clinical Studies Department, Institut de Recherches Internationales Servier, 33 155724366, clinicaltrials@servier.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No	No

1901/2006 apply to this trial?	
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	24 November 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 November 2014
Global end of trial reached?	Yes
Global end of trial date	24 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to evaluate the effect of 4 successive monthly subcutaneous (SC) administrations of 30 mg of S78989 (gevokizumab) versus placebo as a first step, and 60 mg of S78989 (gevokizumab) versus placebo as a second step, on the reduction of arterial wall inflammation in adult patients with marked arterial wall inflammation following a recent acute coronary syndrome (ACS).

The primary objective was to evaluate the effect of S78989 compared to placebo on arterial wall inflammation assessed by 18-Fluorodeoxyglucose-positron emission tomography/computed tomography (18FDG-PET/CT), in the most diseased region of interest (ROI) of both carotids and thoracic aortic walls.

Part A (gevokizumab 30 mg vs placebo) and Part B (gevokizumab 60 mg vs placebo) are presented in parallel. However, it is to be noted that Part B of the trial was conducted after Part A and involved independent selection, randomisation, treatment and follow-up of patients.

Protection of trial subjects:

This study was conducted in accordance with Good Clinical Practice standards, ethical principles stated in the Declaration of Helsinki and applicable regulatory requirements. After the subject has ended his/her participation in the trial, the investigator provided appropriate medication and/or arranged access to appropriate care for the patient.

Background therapy:

Usual cardiovascular treatment

Evidence for comparator: -

Actual start date of recruitment	19 November 2012
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	Canada: 55
Country: Number of subjects enrolled	Finland: 28
Country: Number of subjects enrolled	Netherlands: 10
Worldwide total number of subjects	93
EEA total number of subjects	38

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)	67
From 65 to 84 years	26
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Selected patients were male or females of non-childbearing potential, 50 years of age or older with a recent ACS defined as association of a chest pain episode or its equivalent and elevated troponin, PCI or significant coronary stenosis and had revascularisation procedures completed and received statins for at least 3 months at a stable dose.

Period 1

Period 1 title	Treatment (W0 to W28) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
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Arm title	Part A: gevokizumab 30 mg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Gevokizumab 30 mg
Investigational medicinal product code	S 78989 Gevokizumab
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Randomised patients received fixed dose 30 mg SC administrations of gevokizumab at baseline and then, every 4 weeks, for 12 weeks.

Arm title	Part A: Placebo
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Randomised patients received SC administrations of matching placebo at baseline and then, every 4 weeks for 12 weeks.

Arm title	Part B: gevokizumab 60 mg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Gevokizumab 60 mg
Investigational medicinal product code	S 78989 Gevokizumab
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Randomised patients received fixed dose 60 mg SC administrations of gevokizumab at baseline and

then, every 4 weeks, for 12 weeks.

Arm title	Part B: Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Randomised patients received SC administrations of matching placebo at baseline and then, every 4 weeks for 12 weeks.

Number of subjects in period 1	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg
Started	32	16	31
Completed	32	16	31

Number of subjects in period 1	Part B: Placebo
Started	14
Completed	14

Baseline characteristics

Reporting groups

Reporting group title	Part A: gevokizumab 30 mg
Reporting group description: -	
Reporting group title	Part A: Placebo
Reporting group description: -	
Reporting group title	Part B: gevokizumab 60 mg
Reporting group description: -	
Reporting group title	Part B: Placebo
Reporting group description: -	

Reporting group values	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg
Number of subjects	32	16	31
Age categorical Units: Subjects			
< 65 years	23	13	20
>= 65 years	9	3	11
Age continuous Units: years			
arithmetic mean	60.3	59.4	60.8
standard deviation	± 6.7	± 6	± 6.1
Gender categorical Units: Subjects			
Female	2	2	4
Male	30	14	27

Reporting group values	Part B: Placebo	Total	
Number of subjects	14	93	
Age categorical Units: Subjects			
< 65 years	11	67	
>= 65 years	3	26	
Age continuous Units: years			
arithmetic mean	59.2		
standard deviation	± 6.5	-	
Gender categorical Units: Subjects			
Female	1	9	
Male	13	84	

End points

End points reporting groups

Reporting group title	Part A: gevokizumab 30 mg
Reporting group description: -	
Reporting group title	Part A: Placebo
Reporting group description: -	
Reporting group title	Part B: gevokizumab 60 mg
Reporting group description: -	
Reporting group title	Part B: Placebo
Reporting group description: -	

Primary: Change from Baseline to W16 in mean max target to background ratio (TBR) assessed by FDG-PET/CT within the most diseased segment (MDS) of the left carotid region of interest (ROI)

End point title	Change from Baseline to W16 in mean max target to background ratio (TBR) assessed by FDG-PET/CT within the most diseased segment (MDS) of the left carotid region of interest (ROI)
End point description:	
End point type	Primary
End point timeframe:	
Baseline to W16	

End point values	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg	Part B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	31	14
Units: standard uptake value				
median (inter-quartile range (Q1-Q3))	0.01 (-0.15 to 0.15)	-0.04 (-0.15 to 0.11)	-0.075 (-0.17 to 0.045)	0.16 (-0.05 to 0.26)

Statistical analyses

Statistical analysis title	Part A: gevokizumab 30 mg versus placebo
Comparison groups	Part A: gevokizumab 30 mg v Part A: Placebo
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	0.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.19

Statistical analysis title	Part B: gevokizumab 60 mg versus placebo
Comparison groups	Part B: gevokizumab 60 mg v Part B: Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.31
upper limit	-0.03

Primary: Change from Baseline to W16 in max mean TBR assessed by FDG-PET/CT within the MDS of the left carotid ROI

End point title	Change from Baseline to W16 in max mean TBR assessed by FDG-PET/CT within the MDS of the left carotid ROI
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End point description:

End point type	Primary
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End point timeframe:

Baseline to W16

End point values	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg	Part B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	31	14
Units: Standard Uptake Value				
median (inter-quartile range (Q1-Q3))	0.05 (-0.14 to 0.17)	0.03 (-0.25 to 0.12)	-0.045 (-0.115 to 0.1)	0.12 (-0.02 to 0.24)

Statistical analyses

Statistical analysis title	Part A: gevokizumab 30 mg versus placebo
Comparison groups	Part A: Placebo v Part A: gevokizumab 30 mg

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.22

Statistical analysis title	Part B: gevokizumab 60 mg versus placebo
Comparison groups	Part B: gevokizumab 60 mg v Part B: Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.02

Primary: Change from Baseline to W16 in average mean TBR assessed by FDG-PET/CT within the MDS of the left carotid ROI

End point title	Change from Baseline to W16 in average mean TBR assessed by FDG-PET/CT within the MDS of the left carotid ROI
End point description:	
End point type	Primary
End point timeframe:	
Baseline to W16	

End point values	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg	Part B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	31	14
Units: Standard Uptake Value				
median (inter-quartile range (Q1-Q3))	0.02 (-0.11 to 0.12)	0.01 (-0.15 to 0.11)	-0.035 (-0.16 to 0.075)	0.16 (-0.04 to 0.22)

Statistical analyses

Statistical analysis title	Part A: gevokizumab 30 mg versus placebo
Comparison groups	Part A: gevokizumab 30 mg v Part A: Placebo
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.15

Statistical analysis title	Part B: gevokizumab 60 mg versus placebo
Comparison groups	Part B: gevokizumab 60 mg v Part B: Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0

Primary: Change from Baseline to W16 in max max TBR assessed by FDG-PET/CT within the MDS of the left carotid ROI

End point title	Change from Baseline to W16 in max max TBR assessed by FDG-PET/CT within the MDS of the left carotid ROI
End point description:	
End point type	Primary
End point timeframe:	
Baseline to W16	

End point values	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg	Part B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	31	14
Units: Standard Uptake Value				
median (inter-quartile range (Q1-Q3))	0.06 (-0.1 to 0.25)	-0.06 (-0.16 to 0.09)	-0.045 (-0.145 to 0.065)	0.13 (-0.06 to 0.29)

Statistical analyses

Statistical analysis title	Part A: gevokizumab 30 mg versus matching placebo
Comparison groups	Part A: gevokizumab 30 mg v Part A: Placebo
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hoges & Lehman estimate
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.3

Statistical analysis title	Part B: gevokizumab 60 mg versus matching placebo
Comparison groups	Part B: gevokizumab 60 mg v Part B: Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	-0.01

Primary: Change from Baseline to W16 in mean max TBR assessed by FDG-PET/CT within the MDS of the right carotid ROI

End point title	Change from Baseline to W16 in mean max TBR assessed by FDG-PET/CT within the MDS of the right carotid ROI
End point description:	
End point type	Primary

End point timeframe:

Baseline to W16

End point values	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg	Part B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	31	14
Units: Standard Uptake Value				
median (inter-quartile range (Q1-Q3))	-0.03 (-0.09 to 0.09)	0.02 (-0.12 to 0.06)	-0.025 (-0.08 to 0.1)	0.04 (-0.14 to 0.12)

Statistical analyses

Statistical analysis title	Part A: gevokizumab 30 mg versus placebo
Comparison groups	Part A: gevokizumab 30 mg v Part A: Placebo
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.12

Statistical analysis title	Part B: gevokizumab 60 mg versus placebo
Comparison groups	Part B: gevokizumab 60 mg v Part B: Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.12

Primary: Change from Baseline to W16 in max mean TBR assessed by FDG-PET/CT within the MDS of the right carotid ROI

End point title	Change from Baseline to W16 in max mean TBR assessed by FDG-PET/CT within the MDS of the right carotid ROI
End point description:	
End point type	Primary
End point timeframe:	
Baseline to W16	

End point values	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg	Part B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	31	14
Units: Standard Uptake Value				
median (inter-quartile range (Q1-Q3))	-0.05 (-0.12 to 0.06)	0 (-0.12 to 0.1)	-0.02 (-0.1 to 0.14)	0.03 (-0.09 to 0.11)

Statistical analyses

Statistical analysis title	Part A: gevokizumab 30 mg versus placebo
Comparison groups	Part A: gevokizumab 30 mg v Part A: Placebo
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.1

Statistical analysis title	Part B: gevokizumab 60 mg versus placebo
Comparison groups	Part B: gevokizumab 60 mg v Part B: Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.13

Primary: Change from Baseline to W16 in average mean TBR assessed by FDG-PET/CT within the MDS of the right carotid ROI

End point title	Change from Baseline to W16 in average mean TBR assessed by FDG-PET/CT within the MDS of the right carotid ROI
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End point description:

End point type	Primary
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End point timeframe:

Baseline to W16

End point values	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg	Part B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	31	14
Units: Standard Uptake Value				
median (inter-quartile range (Q1-Q3))	-0.03 (-0.1 to 0.07)	0 (-0.13 to 0.04)	-0.01 (-0.09 to 0.12)	0.03 (-0.07 to 0.11)

Statistical analyses

Statistical analysis title	Part A: gevokizumab 30 mg versus placebo
Comparison groups	Part A: gevokizumab 30 mg v Part A: Placebo
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.12

Statistical analysis title	Part B: gevokizumab 60 mg versus placebo
Comparison groups	Part B: gevokizumab 60 mg v Part B: Placebo

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.12

Primary: Change from Baseline to W16 in max max TBR assessed by FDG-PET/CT within the MDS of the right carotid ROI

End point title	Change from Baseline to W16 in max max TBR assessed by FDG-PET/CT within the MDS of the right carotid ROI
End point description:	
End point type	Primary
End point timeframe:	
Baseline to W16	

End point values	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg	Part B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	31	14
Units: Standard Uptake Value				
median (inter-quartile range (Q1-Q3))	-0.05 (-0.13 to 0.07)	0.04 (-0.11 to 0.14)	-0.025 (-0.17 to 0.16)	0.05 (-0.1 to 0.1)

Statistical analyses

Statistical analysis title	Part A: gevokizumab 30 mg versus placebo
Comparison groups	Part A: gevokizumab 30 mg v Part A: Placebo
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.1

Statistical analysis title	Part B: gevokizumab 60 mg versus placebo
Comparison groups	Part B: Placebo v Part B: gevokizumab 60 mg
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.15

Primary: Change from Baseline to W16 in mean max TBR assessed by FDG-PET/CT within the MDS of the thoracic aorta ROI

End point title	Change from Baseline to W16 in mean max TBR assessed by FDG-PET/CT within the MDS of the thoracic aorta ROI
End point description:	
End point type	Primary
End point timeframe:	
Baseline to W16	

End point values	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg	Part B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	31	14
Units: Standard Uptake Value				
median (inter-quartile range (Q1-Q3))	0 (-0.12 to 0.17)	-0.12 (-0.28 to 0.06)	0.02 (-0.17 to 0.09)	0.02 (-0.21 to 0.11)

Statistical analyses

Statistical analysis title	Part A; gevokizumab 30 mg versus placebo
Comparison groups	Part A: gevokizumab 30 mg v Part A: Placebo

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.3

Statistical analysis title	Part B: gevokizumab 60 mg versus placebo
Comparison groups	Part B: gevokizumab 60 mg v Part B: Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.25

Primary: Change from Baseline to W16 in max mean TBR assessed by FDG-PET/CT within the MDS of the thoracic aorta ROI

End point title	Change from Baseline to W16 in max mean TBR assessed by FDG-PET/CT within the MDS of the thoracic aorta ROI
End point description:	
End point type	Primary
End point timeframe:	
Baseline to W16	

End point values	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg	Part B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	31	14
Units: Standard Uptake Value				
median (inter-quartile range (Q1-Q3))	0.09 (-0.01 to 0.17)	-0.02 (-0.17 to 0.13)	-0.01 (-0.15 to 0.12)	0.08 (-0.15 to 0.24)

Statistical analyses

Statistical analysis title	Part A: gevokizumab 30 mg versus placebo
Comparison groups	Part A: gevokizumab 30 mg v Part A: Placebo
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.24

Statistical analysis title	Part B: gevokizumab 60 mg versus placebo
Comparison groups	Part B: gevokizumab 60 mg v Part B: Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.11

Primary: Change from Baseline to W16 in average mean TBR assessed by FDG-PET/CT within the MDS of the thoracic aorta ROI

End point title	Change from Baseline to W16 in average mean TBR assessed by FDG-PET/CT within the MDS of the thoracic aorta ROI
End point description:	
End point type	Primary
End point timeframe:	
Baseline to W16	

End point values	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg	Part B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	31	14
Units: Standard Uptake Value				
median (inter-quartile range (Q1-Q3))	0.02 (-0.05 to 0.12)	-0.02 (-0.1 to 0.06)	0.01 (-0.15 to 0.1)	0.05 (-0.12 to 0.24)

Statistical analyses

Statistical analysis title	Part A: gevokizumab 30 mg versus placebo
Comparison groups	Part A: gevokizumab 30 mg v Part A: Placebo
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.16

Statistical analysis title	Part B: gevokizumab 60 mg versus placebo
Comparison groups	Part B: gevokizumab 60 mg v Part B: Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	0.1

Primary: Change from Baseline to W16 in max max TBR assessed by FDG-PET/CT within the MDS of the thoracic aorta ROI

End point title	Change from Baseline to W16 in max max TBR assessed by FDG-PET/CT within the MDS of the thoracic aorta ROI
End point description:	
End point type	Primary

End point timeframe:

Baseline to W16

End point values	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg	Part B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	16	31	14
Units: Standard Uptake Value				
median (inter-quartile range (Q1-Q3))	0.07 (-0.14 to 0.24)	-0.2 (-0.38 to 0.02)	0 (-0.19 to 0.2)	-0.02 (-0.22 to 0.16)

Statistical analyses

Statistical analysis title	Part A: gevokizumab 30 mg versus placebo
Comparison groups	Part A: Placebo v Part A: gevokizumab 30 mg
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.43

Statistical analysis title	Part B: gevokizumab 60 mg versus placebo
Comparison groups	Part B: gevokizumab 60 mg v Part B: Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hodges & Lehman estimate
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.3

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to W28

Adverse event reporting additional description:

The section non-serious adverse events presented emergent adverse events on treatment and included serious adverse events (SAEs). The causality and seriousness of reported SAEs are reported according to the investigator's opinion. The Sponsor took these decisions to be compliant with the existing ICH E3 Clinical Study Report.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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Reporting groups

Reporting group title	Part A: gevokizumab 30 mg
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Reporting group description: -

Reporting group title	Part A: Placebo
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Reporting group description: -

Reporting group title	Part B: gevokizumab 60 mg
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Reporting group description: -

Reporting group title	Part B: Placebo
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Reporting group description: -

Serious adverse events	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 32 (12.50%)	2 / 16 (12.50%)	2 / 31 (6.45%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 32 (0.00%)	1 / 16 (6.25%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 32 (3.13%)	0 / 16 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			

subjects affected / exposed	0 / 32 (0.00%)	0 / 16 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Presyncope			
subjects affected / exposed	1 / 32 (3.13%)	0 / 16 (0.00%)	0 / 31 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 32 (3.13%)	0 / 16 (0.00%)	0 / 31 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 32 (0.00%)	0 / 16 (0.00%)	0 / 31 (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 / 32 (0.00%)	1 / 16 (6.25%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	0 / 32 (0.00%)	0 / 16 (0.00%)	1 / 31 (3.23%)
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	1 / 32 (3.13%)	0 / 16 (0.00%)	0 / 31 (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
Bacterial prostatitis			

subjects affected / exposed	1 / 32 (3.13%)	0 / 16 (0.00%)	0 / 31 (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

Serious adverse events	Part B: Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 14 (14.29%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	0 / 14 (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	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bacterial prostatitis			
subjects affected / exposed	0 / 14 (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	Part A: gevokizumab 30 mg	Part A: Placebo	Part B: gevokizumab 60 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 32 (71.88%)	14 / 16 (87.50%)	14 / 31 (45.16%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 32 (0.00%)	1 / 16 (6.25%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			

Hypertension subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	0 / 16 (0.00%) 0	1 / 31 (3.23%) 1
General disorders and administration site conditions			
Chest pain subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	0 / 16 (0.00%) 0	2 / 31 (6.45%) 2
Fatigue subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 16 (6.25%) 2	2 / 31 (6.45%) 2
Injection site erythema subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1	0 / 31 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	2 / 16 (12.50%) 2	0 / 31 (0.00%) 0
Epistaxis subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	1 / 16 (6.25%) 1	0 / 31 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 16 (0.00%) 0	2 / 31 (6.45%) 2
Psychiatric disorders			
Depressed mood subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 16 (6.25%) 2	0 / 31 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1	0 / 31 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1	0 / 31 (0.00%) 0
Sleep disorder subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 16 (6.25%) 2	0 / 31 (0.00%) 0

Investigations			
Blood glucose increased			
subjects affected / exposed	1 / 32 (3.13%)	1 / 16 (6.25%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 32 (0.00%)	1 / 16 (6.25%)	1 / 31 (3.23%)
occurrences (all)	0	1	1
Blood creatinine phosphokinase increased			
subjects affected / exposed	0 / 32 (0.00%)	1 / 16 (6.25%)	1 / 31 (3.23%)
occurrences (all)	0	1	1
International normalised ratio increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 16 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 32 (3.13%)	1 / 16 (6.25%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Fall			
subjects affected / exposed	0 / 32 (0.00%)	2 / 16 (12.50%)	0 / 31 (0.00%)
occurrences (all)	0	2	0
Ligament sprain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 16 (6.25%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Post-traumatic pain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 16 (6.25%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 32 (0.00%)	1 / 16 (6.25%)	1 / 31 (3.23%)
occurrences (all)	0	1	1
Palpitations			
subjects affected / exposed	0 / 32 (0.00%)	1 / 16 (6.25%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			

Amnesia subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1	0 / 31 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	0 / 16 (0.00%) 0	2 / 31 (6.45%) 2
Blood and lymphatic system disorders			
Neutropenia subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 2	1 / 16 (6.25%) 1	1 / 31 (3.23%) 2
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 16 (0.00%) 0	0 / 31 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1	0 / 31 (0.00%) 0
Eructation subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1	0 / 31 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1	1 / 31 (3.23%) 1
Diarrhoea subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 16 (0.00%) 0	0 / 31 (0.00%) 0
Gastrointestinal inflammation subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 16 (0.00%) 0	2 / 31 (6.45%) 2
Hepatobiliary disorders			
Biliary colic subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1	0 / 31 (0.00%) 0
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 16 (0.00%) 0	0 / 31 (0.00%) 0

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 32 (3.13%)	1 / 16 (6.25%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Bursitis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 16 (0.00%)	2 / 31 (6.45%)
occurrences (all)	2	0	2
Musculoskeletal chest pain			
subjects affected / exposed	1 / 32 (3.13%)	1 / 16 (6.25%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Muscle spasms			
subjects affected / exposed	0 / 32 (0.00%)	1 / 16 (6.25%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 32 (0.00%)	1 / 16 (6.25%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Costochondritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 16 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 32 (15.63%)	4 / 16 (25.00%)	4 / 31 (12.90%)
occurrences (all)	5	4	5
Sinusitis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 16 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Erysipelas			
subjects affected / exposed	0 / 32 (0.00%)	1 / 16 (6.25%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Infected skin ulcer			
subjects affected / exposed	0 / 32 (0.00%)	0 / 16 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 16 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0

Vitamin B12 deficiency subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0	0 / 16 (0.00%) 0	0 / 31 (0.00%) 0
Non-serious adverse events	Part B: Placebo		
Total subjects affected by non-serious adverse events subjects affected / exposed	8 / 14 (57.14%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Colon cancer subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
General disorders and administration site conditions Chest pain subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Injection site erythema subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0 1 / 14 (7.14%) 1 0 / 14 (0.00%) 0		
Psychiatric disorders			

Depressed mood subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Depression subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Insomnia subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Sleep disorder subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Investigations Blood glucose increased subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Blood creatinine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
International normalised ratio increased subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Fall subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Ligament sprain subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		

Post-traumatic pain subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Cardiac disorders			
Angina pectoris subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Palpitations subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Nervous system disorders			
Amnesia subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Dizziness subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Blood and lymphatic system disorders			
Neutropenia subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Eructation subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Diarrhoea subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		

Gastrointestinal inflammation subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Hepatobiliary disorders Biliary colic subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Bursitis subjects affected / exposed occurrences (all) Musculoskeletal chest pain subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) Costochondritis subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 1 / 14 (7.14%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Sinusitis	4 / 14 (28.57%) 4		

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Erysipelas</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Infected skin ulcer</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 14 (0.00%)</p> <p>0</p> <p>0 / 14 (0.00%)</p> <p>0</p> <p>1 / 14 (7.14%)</p> <p>1</p>		
<p>Metabolism and nutrition disorders</p> <p>Hypokalaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vitamin B12 deficiency</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 14 (7.14%)</p> <p>1</p> <p>1 / 14 (7.14%)</p> <p>1</p>		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 January 2013	<ul style="list-style-type: none">- Modification of study duration (28 weeks) at the request of Health Canada- Modification of PET/CT central reading procedure to improve precision and validity of the results- Various minor changes to the protocol
19 February 2013	International harmonisation of the protocol by applying the changes described in the first amendment (31 January 2013) to centres in the Netherlands and Finland.
22 August 2013	<ul style="list-style-type: none">- Addition of a new cohort of 45 patients treated with gevokizumab 60 mg or placebo- Various minor changes to the protocol- Extension of the period of the study from December 2013 to October 2014

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

In this EudraCT report data for Part A and Part B are presented in parallel. However, it is to be noted that Part B of the trial was conducted after Part A and involved independent selection, randomisation, treatment and follow-up of patients.

Notes: