



Clinical trial results:

REVACEPT, AN INHIBITOR OF PLATELET ADHESION IN SYMPTOMATIC CAROTID STENOSIS: A PHASE II, MULTICENTRE; RANDOMISED, DOSE-FINDING, DOUBLE-BLIND AND PLACEBO-CONTROLLED SUPERIORITY STUDY WITH PARALLEL GROUPS

Summary

EudraCT number	2011-001006-10
Trial protocol	DE GB
Global end of trial date	23 September 2019

Results information

Result version number	v1 (current)
This version publication date	15 November 2020
First version publication date	15 November 2020
Summary attachment (see zip file)	CSR Summary 2020-09-10 (Revacept-CS-02 Clinical Study Synopsis.100920.pdf)

Trial information

Trial identification

Sponsor protocol code	Revacept/CS/02
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01645306
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	advanceCOR GmbH
Sponsor organisation address	Fraunhoferstraße 9A, Martinsried, Germany, 82152
Public contact	Prof. Dr. med. Götz Münch, advanceCOR GmbH, 0049 892000 20410, muench@advancecor.com
Scientific contact	Prof. Dr. med. Götz Münch, advanceCOR GmbH, 0049 892000 20410, muench@advancecor.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	23 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 September 2019
Global end of trial reached?	Yes
Global end of trial date	23 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Efficacy objectives are:

- Assessment of incidence of microembolic signals (MES) by transcranial Doppler (TCD) examination (before and after treatment)
- Rate of MES per hour (before and after treatment)
- Cerebral lesion analysis by DWI-NMR
- Assessment of neurological status (NIH Stroke Scale)
- Clinical endpoints will be summarised cumulatively i.e. before treatment, after treatment, at 3 months and at 12 months. The following endpoints will be recorded:
 - o Rate of all cause death
 - o Rate of stroke-related death
 - o Any TIA, amaurosis fugax or stroke including haemorrhagic stroke
- Assessment of cardiovascular outcome including myocardial infarction and re-intervention up to 3 and 12 months

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

The study and all substantial amendments were reviewed by an Independent Ethics Committee in the United Kingdom: NRES Committee East of England – Cambridge South, The Old Chapel, Royal Standard Court, Nottingham, NG16FS and the lead Ethics Committee Germany: Ethikkommission der Fakultät für Medizin der Technischen Universität München, Ismaninger Straße 22, 81675 München.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2012
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	United Kingdom: 57
Country: Number of subjects enrolled	Germany: 101
Worldwide total number of subjects	158
EEA total number of subjects	158

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)	59
From 65 to 84 years	94
85 years and over	5

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total 160 subjects were enrolled in the study. Of those randomised, 53 subjects received 120 mg Revacept, 54 patients 40 mg Revacept and 51 patients placebo by a single IV infusion. Two subjects received no study medication because they no longer met the eligibility criteria.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

single dose

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Phosphate buffered saline (PBS), 1% sucrose, 4% mannitol
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

single dose

Arm title	40 mg Revacept
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Arm description:

single dose

Arm type	Experimental
Investigational medicinal product name	40 mg Revacept
Investigational medicinal product code	
Other name	GPVI-Fc
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 mg Revacept, single dose

Arm title	120 mg Revacept
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Arm description:

single dose

Arm type	Experimental
Investigational medicinal product name	120 mg Revacept
Investigational medicinal product code	
Other name	GPVI-Fc
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

120 mg Revacept, single dose

Number of subjects in period 1	Placebo	40 mg Revacept	120 mg Revacept
Started	51	54	53
Completed	51	54	53

Baseline characteristics

Reporting groups

Reporting group title	Randomisation
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Reporting group description: -

Reporting group values	Randomisation	Total	
Number of subjects	158	158	
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)	59	59	
From 65-84 years	94	94	
85 years and over	5	5	
Age continuous			
Units: years			
arithmetic mean	68.1		
standard deviation	± 10.13	-	
Gender categorical			
Units: Subjects			
Female	38	38	
Male	120	120	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: single dose	
Reporting group title	40 mg Revacept
Reporting group description: single dose	
Reporting group title	120 mg Revacept
Reporting group description: single dose	

Primary: Exploratory

End point title	Exploratory ^[1]
End point description: see Synopsis of Clinical Study Report attached	
End point type	Primary
End point timeframe: exploratory	

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: Exploratory trial design - see summary of clinical study report attached for details.

End point values	Placebo	40 mg Revacept	120 mg Revacept	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	54	53	
Units: exploratory				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

IMP administration to 365 days thereafter.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

single dose

Reporting group title	40 mg Revacept
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Reporting group description:

single dose

Reporting group title	120 mg Revacept
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Reporting group description:

single dose

Serious adverse events	Placebo	40 mg Revacept	120 mg Revacept
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 51 (33.33%)	17 / 54 (31.48%)	15 / 53 (28.30%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glottis carcinoma			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Laryngeal cancer			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Lung neoplasm malignant			

subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Malignant melanoma			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Sarcoma of skin			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Hypertensive crisis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Carotid endarterectomy			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chemotherapy			

subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Coronary angioplasty			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary arterial stent insertion			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Skin lesion removal			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Vocal cordectomy			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Chest discomfort			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Chest pain			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Pneumonia aspiration			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Pulmonary embolism			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Psychiatric disorders			
Panic attack			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Investigations			
Angiogram			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Biopsy larynx			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Cardiac clearance			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Diffusion-weighted brain MRI abnormal			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Weight decreased subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Injury, poisoning and procedural complications			
Cerebral hyperperfusion syndrome subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Fall subjects affected / exposed	2 / 51 (3.92%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Rib fracture subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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			
Acute myocardial infarction subjects affected / exposed	2 / 51 (3.92%)	2 / 54 (3.70%)	2 / 53 (3.77%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Bradycardia subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac arrest			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Myocardial infarction			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ataxia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery stenosis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Cerebellar infarction			

subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Cerebral haemorrhage			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	1 / 51 (1.96%)	2 / 54 (3.70%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cerebral ischaemia			
subjects affected / exposed	2 / 51 (3.92%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clumsiness			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Dizziness			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Epilepsy			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Headache			

subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Hypoaesthesia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Intracranial aneurysm			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Loss of consciousness			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinsonism			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Postictal paralysis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Seizure			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			

subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Stroke in evolution			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Syncope			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Transient ischaemic attack			
subjects affected / exposed	2 / 51 (3.92%)	1 / 54 (1.85%)	4 / 53 (7.55%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Gastrointestinal disorders			
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Muscular weakness			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Osteonecrosis of jaw			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (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
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Pneumonia			
subjects affected / exposed	2 / 51 (3.92%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Urinary tract infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (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
Ketoacidosis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	40 mg Revacept	120 mg Revacept
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 51 (68.63%)	41 / 54 (75.93%)	32 / 53 (60.38%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Glottis carcinoma			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Laryngeal cancer			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Lung neoplasm malignant			

subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Malignant melanoma			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Sarcoma of skin			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Arteriosclerosis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Circulatory collapse			
subjects affected / exposed	2 / 51 (3.92%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	2	0	0
Haematoma			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	2 / 53 (3.77%)
occurrences (all)	1	0	2
Hypertension			
subjects affected / exposed	4 / 51 (7.84%)	2 / 54 (3.70%)	2 / 53 (3.77%)
occurrences (all)	4	2	2
Hypertensive crisis			
subjects affected / exposed	0 / 51 (0.00%)	2 / 54 (3.70%)	1 / 53 (1.89%)
occurrences (all)	0	2	1
Hypotension			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	2 / 53 (3.77%)
occurrences (all)	1	1	2
Ischaemia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Lymphoedema			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0

Phlebitis subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 54 (0.00%) 0	1 / 53 (1.89%) 1
Surgical and medical procedures			
Carotid endarterectomy subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	1 / 54 (1.85%) 1	1 / 53 (1.89%) 1
Chemotherapy subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Coronary angioplasty subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 54 (0.00%) 0	1 / 53 (1.89%) 1
Coronary arterial stent insertion subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Gastrointestinal tube insertion subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Skin lesion removal subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Ureteral catheterisation subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Vocal cordectomy subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Catheter site pain subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Chest discomfort			

subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Condition aggravated			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Facial pain			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Feeling hot			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Impaired healing			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	1 / 53 (1.89%)
occurrences (all)	0	1	1
Oedema peripheral			
subjects affected / exposed	2 / 51 (3.92%)	5 / 54 (9.26%)	2 / 53 (3.77%)
occurrences (all)	2	5	2
Pain			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Peripheral swelling			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Sensation of foreign body			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Vascular stent stenosis			

subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	0 / 51 (0.00%)	2 / 54 (3.70%)	1 / 53 (1.89%)
occurrences (all)	0	2	1
Dysphonia			
subjects affected / exposed	2 / 51 (3.92%)	1 / 54 (1.85%)	1 / 53 (1.89%)
occurrences (all)	2	1	1
Dyspnoea			
subjects affected / exposed	3 / 51 (5.88%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	3	1	0
Emphysema			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Laryngeal oedema			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Pneumonia aspiration			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Pulmonary embolism			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			

Abnormal dreams			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Alcohol abuse			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Depressed mood			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	2 / 53 (3.77%)
occurrences (all)	0	1	2
Hallucination, visual			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Panic attack			
subjects affected / exposed	2 / 51 (3.92%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	2	0	0
Panic disorder			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Post stroke depression			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Angiocardiogram			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Biopsy larynx			

subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Blood creatine increased			
subjects affected / exposed	1 / 51 (1.96%)	2 / 54 (3.70%)	0 / 53 (0.00%)
occurrences (all)	1	2	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Blood glucose increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Blood potassium decreased			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Blood urea increased			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Blood urine present			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Breath sounds abnormal			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
C-reactive protein increased			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Cardiac clearance			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Cardiac murmur			
subjects affected / exposed	3 / 51 (5.88%)	1 / 54 (1.85%)	1 / 53 (1.89%)
occurrences (all)	3	1	1

Diffusion-weighted brain MRI abnormal			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	1 / 51 (1.96%)	3 / 54 (5.56%)	0 / 53 (0.00%)
occurrences (all)	1	3	0
Heart rate decreased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Inflammatory marker increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Myocardial necrosis marker increased			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Oxygen saturation decreased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Troponin increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	1 / 53 (1.89%)
occurrences (all)	0	1	1
Weight decreased			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
White blood cell count increased			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			

Burns second degree			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Carotid artery restenosis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Cerebral hyperperfusion syndrome			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	1	0	1
Fall			
subjects affected / exposed	3 / 51 (5.88%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	3	0	1
Foot fracture			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Head injury			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Post procedural contusion			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Post procedural haematoma			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Post procedural haemorrhage			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Post procedural oedema			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Post procedural swelling			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0

Postoperative hypertension subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Postoperative hypotension subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 54 (0.00%) 0	2 / 53 (3.77%) 2
Postoperative wound complication subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Procedural haemorrhage subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Procedural headache subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Procedural hypotension subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Procedural nausea subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Procedural pain subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 3	1 / 54 (1.85%) 1	2 / 53 (3.77%) 2
Rib fracture subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Skin procedural complication subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Synovial rupture subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Wound complication subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	2 / 54 (3.70%) 2	0 / 53 (0.00%) 0

Wound haematoma subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Wound secretion subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Cardiac disorders			
Acute myocardial infarction subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2	2 / 54 (3.70%) 2	2 / 53 (3.77%) 2
Angina pectoris subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Atrioventricular block complete subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Atrioventricular block first degree subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Bradycardia subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 54 (0.00%) 0	2 / 53 (3.77%) 2
Bundle branch block left subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Cardiac arrest subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 54 (0.00%) 0	1 / 53 (1.89%) 1
Cardiac disorder subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Cardiac failure subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	1 / 53 (1.89%) 1
Cardiogenic shock			

subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Coronary artery disease			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Myocardial infarction			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Aphasia			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Ataxia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Carotid artery disease			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Carotid artery occlusion			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Carotid artery stenosis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Cerebellar infarction			
subjects affected / exposed	2 / 51 (3.92%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	2	0	0
Cerebral haemorrhage			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Cerebral infarction			
subjects affected / exposed	2 / 51 (3.92%)	2 / 54 (3.70%)	2 / 53 (3.77%)
occurrences (all)	2	2	2

Cerebral ischaemia			
subjects affected / exposed	2 / 51 (3.92%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	2	1	0
Cerebrovascular accident			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	1 / 53 (1.89%)
occurrences (all)	0	1	1
Cerebrovascular insufficiency			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Clonus			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Clumsiness			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	2 / 51 (3.92%)	0 / 54 (0.00%)	2 / 53 (3.77%)
occurrences (all)	2	0	2
Dysaesthesia			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Dysarthria			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Epilepsy			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Facial paralysis			
subjects affected / exposed	1 / 51 (1.96%)	2 / 54 (3.70%)	1 / 53 (1.89%)
occurrences (all)	1	2	1
Facial paresis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	2 / 51 (3.92%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	2	1	0

Hemiplegia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	2 / 51 (3.92%)	2 / 54 (3.70%)	1 / 53 (1.89%)
occurrences (all)	2	2	1
Hypoglossal nerve paresis			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Intracranial aneurysm			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Ischaemic stroke			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Loss of consciousness			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	1 / 53 (1.89%)
occurrences (all)	0	1	1
Monoparesis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	1 / 53 (1.89%)
occurrences (all)	0	1	1
Muscle spasticity			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	3 / 53 (5.66%)
occurrences (all)	0	1	3
Paralysis recurrent laryngeal nerve			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Parkinsonism			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Peroneal nerve palsy			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0

Postictal paralysis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Seizure			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	1 / 53 (1.89%)
occurrences (all)	1	1	1
Status epilepticus			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Stroke in evolution			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	1 / 51 (1.96%)	2 / 54 (3.70%)	1 / 53 (1.89%)
occurrences (all)	1	2	1
Transient ischaemic attack			
subjects affected / exposed	2 / 51 (3.92%)	1 / 54 (1.85%)	4 / 53 (7.55%)
occurrences (all)	2	1	4
Visual field defect			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Leukopenia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Eye disorders			

Blepharospasm			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
blindness			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Retinal artery occlusion			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Visual impairment			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	2 / 51 (3.92%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	2	1	0
Diarrhoea			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Nausea			

subjects affected / exposed	1 / 51 (1.96%)	3 / 54 (5.56%)	1 / 53 (1.89%)
occurrences (all)	1	3	1
Oesophageal discomfort			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Paraesthesia oral			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 51 (0.00%)	3 / 54 (5.56%)	0 / 53 (0.00%)
occurrences (all)	0	3	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Cold sweat			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Drug eruption			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Generalised erythema			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Lividity			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Pemphigoid			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0

Pigmentation disorder			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Pruritus generalised			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	1 / 51 (1.96%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Rash macular			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Rash pruritic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Scab			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Bladder irritation			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Micturition urgency			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Renal failure			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	2 / 51 (3.92%)	1 / 54 (1.85%)	1 / 53 (1.89%)
occurrences (all)	2	1	1
Musculoskeletal and connective tissue disorders			

Ankylosing spondylitis subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 54 (0.00%) 0	1 / 53 (1.89%) 1
Back pain subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2	2 / 54 (3.70%) 2	1 / 53 (1.89%) 1
Intervertebral disc protrusion subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Joint swelling subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Muscle spasms subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	1 / 53 (1.89%) 1
Muscular weakness subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2	1 / 54 (1.85%) 1	1 / 53 (1.89%) 1
Musculoskeletal pain subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Osteonecrosis of jaw subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2	3 / 54 (5.56%) 3	2 / 53 (3.77%) 2
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 54 (0.00%) 0	0 / 53 (0.00%) 0
Cellulitis subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 54 (1.85%) 1	0 / 53 (0.00%) 0
Gastroenteritis viral			

subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Infection			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	2 / 51 (3.92%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	2	0	0
Oral candidiasis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Pathogen resistance			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	4 / 51 (7.84%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	4	0	0
Postoperative wound infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Pyelonephritis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Sepsis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Staphylococcal sepsis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	3 / 51 (5.88%)	1 / 54 (1.85%)	2 / 53 (3.77%)
occurrences (all)	3	1	2
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Gout			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	1	0	1
Hyponatraemia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Ketoacidosis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 51 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 April 2013	Protocol Version 7.1 (15.04.2013): Amendment of eligibility criteria to improve recruitment rates.
12 September 2013	Protocol Version 7.3 (12.09.2013): Safety Reporting timeframes updated upon request of MHRA.
22 July 2014	Protocol Version 7.4 (22.07.2014): Amendment of eligibility criteria to improve recruitment rates
27 May 2015	Prolongation of study due to slower than anticipated recruitment rates. Original proposed study end date: 2015. Revised proposed study end date: 2017.
22 June 2015	Protocol Version 8 (22.06.2015): Change to exploratory study design upon recommendation of the DSMB due to restrictive eligibility criterion required for primary endpoint.
14 September 2017	Prolongation of study due to slower than anticipated recruitment rates. Original proposed study end date: 2017. Revised proposed study end date: 2018.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported