Clinical trial results:
Biomarkers and antithrombotic treatment in cervical artery dissection (TREAT-CAD)

Summary

EudraCT number	2015-003200-23
Trial protocol	DE DK
Global end of trial date	21 December 2018

Results information

Result version number	v1 (current)
This version publication date	03 December 2021
First version publication date	03 December 2021

Trial information

Trial identification

Sponsor protocol code	2013DR3084

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02046460
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Hospital Basel
Sponsor organisation address	Petersgraben 4, Basel , Switzerland, 4031
Public contact	Stefan Engelter, MD, PI TREA-CAD, University Hospital Basel, stefan.engelter@usb.ch
Scientific contact	Stefan Engelter, MD, PI TREA-CAD, University Hospital Basel, stefan.engelter@usb.ch

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	22 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 December 2018
Global end of trial reached?	Yes
Global end of trial date	21 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of acetylsalicylic acid (ASA) to anti-coagulant treatment (vitamin K antagonists) in patients with cervical artery dissection (CAD) with regard to outcome and complication measures

Protection of trial subjects:

Implementation of data safety monitoring by a data safety monitoring board. Continuous monitoring for adverse and serious adverse events.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 September 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Switzerland: 170
Worldwide total number of subjects	194
EEA total number of subjects	24

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)	188
From 65 to 84 years	6

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between Sept 11, 2013, and Dec 21, 2018, we enrolled 194 patients; 100 (52%) were randomly assigned to the aspirin group and 94 (48%) to the vitamin K antagonist group (78 received phenprocoumon, 12 acenocoumarol, and four warfarin).

Pre-assignment

Screening details:

Patients were screened according to the eligibility criteria for participation in the trial. At screening visit, written informed consent, patient history were obtained and physical examination including the assessment of the NIHSS score was performed.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

We did a randomised, open-label, multicentre, noninferiority trial with blinded assessment of outcome events.

Arms

Are arms mutually exclusive?	Yes
Arm title	Aspirin

Arm description:

Aspirin 300mg/d for 90d

Arm type	Active comparator
Investigational medicinal product name	Aspirin 300mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300mg/d

Arm title	Vitamin K Antagonists

Arm description:

Phenprocoumon, Acenocoumarol or Warfarin with or without bridging with heparin or low-molecular-weight heparin.

Arm type	Experimental
Investigational medicinal product name	Vitamin K Antagonists (Warfarin, Acenocoumarol, Phenprocoumon)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Variable dose with target INR 2-3, oral

Number of subjects in period 1	Aspirin	Vitamin K Antagonists
Started	100	94
Completed	100	94

Baseline characteristics

Reporting groups	
Reporting group title	Aspirin
Reporting group description:	
Aspirin 300mg/d for 90d	
Reporting group title	Vitamin K Antagonists
Reporting group description:	
Phenprocoumon, Acenocoumarol or Warfarin with or without bridging with heparin or low-molecular-weight heparin.	

Reporting group values	Aspirin	Vitamin K Antagonists	Total
Number of subjects	100	94	194
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	46.6	45.5	
standard deviation	± 10.6	± 11.6	-
Gender categorical Units: Subjects			
Female	38	33	71
Male	62	61	123

End points

End points reporting groups

Reporting group title	Aspirin
Reporting group description:	
Aspirin 300mg/d for 90d	
Reporting group title	Vitamin K Antagonists
Reporting group description:	
Phenprocoumon, Acenocoumarol or Warfarin with or without bridging with heparin or low-molecular-weight heparin.	
Subject analysis set title	Per protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
Per protocol population	

Primary: Primary endpoint

End point title	Primary endpoint
End point description:	
Composite of clinical (ischemic stroke, major extracranial hemorrhage, symptomatic intracranial hemorrhage, death) and MRI outcomes (new acute ischemic brain lesion, new hemorrhagic brain lesion)	
End point type	Primary
End point timeframe:	
90 days	

End point values	Aspirin	Vitamin K Antagonists	Per protocol	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	100[1]	94[2]	173	
Units: Number				
Present	22	12	33	
Absent	78	82	140	

Notes:

[1] - Full analysis set

[2] - Full analysis set

Statistical analyses

Statistical analysis title	Full analysis set
Comparison groups	Aspirin v Vitamin K Antagonists
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Regression, Logistic

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 90 days	
Assessment type	Systematic

Dictionary used	
Dictionary name	None
Dictionary version	1

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Overall there were 45 adverse events of which 7 were rated as serious.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 April 2018	Version 3.3

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.

Very rudimentary reporting of results - for full results please refer to the original publication of the trial results.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33765420