Clinical trial results:
Safety and efficacy of clopidogrel when added to aspirin and dipyridamole in high risk patients with recent ischaemic stroke or TIA: a randomised controlled trial

Summary

EudraCT number	2007-006749-42
Trial protocol	GB DK
Global end of trial date	30 June 2016

Results information

Result version number	v1 (current)
This version publication date	14 October 2017
First version publication date	14 October 2017

Trial information

Trial identification

Sponsor protocol code	31350

Additional study identifiers

ISRCTN number	ISRCTN47823388
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Nottingham
Sponsor organisation address	Kings Meadow Campus, Lenton Lane, Nottingham, United Kingdom, NG7 2NR
Public contact	TARDIS Trial Office, University of Nottingham, +44 01158230210, tardis@nottingham.ac.uk
Scientific contact	TARDIS Trial Office, University of Nottingham, +44 01158230210, tardis@nottingham.ac.uk

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	Interim
Date of interim/final analysis	15 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2016
Global end of trial reached?	Yes
Global end of trial date	30 June 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the safety of short-term administration (1 month) of intensive antiplatelet therapy (aspirin, dipyridamole and clopidogrel) versus current guideline therapy (dual aspirin and dipyridamole, or clopidogrel monotherapy) in patients with very recent ischaemic stroke or TIA.

Protection of trial subjects:

N/A

Background therapy:

Standard NHS care

Evidence for comparator:

N/A

Actual start date of recruitment	01 April 2009
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: 2955
Country: Number of subjects enrolled	Denmark: 51
Country: Number of subjects enrolled	New Zealand: 7
Country: Number of subjects enrolled	Georgia: 83
Worldwide total number of subjects	3096
EEA total number of subjects	3006

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)	1093
From 65 to 84 years	1798
85 years and over	205

Subject disposition

Recruitment

Recruitment details:

Recruitment commenced in UK on 01/04/09, followed by Denmark on 01/07/13, New Zealand 18/10/13 and Georgia on 19/06/14.

Pre-assignment

Screening details:

Adults at high risk of recurrent ischaemic stroke. Stroke type confirmed by CT/MRI scan.

Period 1

Period 1 title	Randomisation
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Intensive

Arm description:

Clopidogrel, Aspirin and Dipyridamole

Arm type	Experimental
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use, Nasogastric use

Dosage and administration details:

Loading dose of 300mg followed by 30 days of 75mg per day

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use, Nasogastric use

Dosage and administration details:

Loading dose of 300mg at randomisation followed by 75mg for 30 days

Investigational medicinal product name	Dipyridamole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use

Dosage and administration details:

200mg tablet twice per day for 30 days

Arm title	Guideline

Arm description:

Guideline therapy either clopidogrel alone or aspirin and dipyridamole

Arm type	Active comparator

Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use

Dosage and administration details:

Loading dose of 300mg followed by 30 days of 75mg per day

Investigational medicinal product name	aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use

Dosage and administration details:

Loading dose of 300mg followed by daily dose of 75mg for 28 days

Investigational medicinal product name	Dipyridamole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use

Dosage and administration details:

200mg twice daily

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Final assessment completed by blinded assessor

Number of subjects in period 1	Intensive	Guideline
Started	1556	1540
Completed	1556	1540

Period 2

Period 2 title	Baseline
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[2]

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes

Arm title	Intensive
Arm description:	
Clopidogrel, Aspirin and Dipyridamole	
Arm type	Experimental
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use, Nasogastric use
Dosage and administration details:	
Loading dose of 300mg followed by 30 days of 75mg per day	
Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use, Nasogastric use
Dosage and administration details:	
Loading dose of 300mg at randomisation followed by 75mg for 30 days	
Investigational medicinal product name	Dipyridamole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use
Dosage and administration details:	
200mg tablet twice per day for 30 days	
Arm title	Guideline
Arm description:	
Clopidogrel or Aspirin and Dipyridamole	
Arm type	Guideline therapy
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use
Dosage and administration details:	
Loading dose of 300mg followed by 30 days of 75mg per day	
Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use
Dosage and administration details:	
Loading dose of 300mg at randomisation followed by 75mg for 30 days	
Investigational medicinal product name	Dipyridamole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use
Dosage and administration details:	
200mg tablet twice per day for 30 days	

Notes:
[2] - The roles blinded appear inconsistent with a simple blinded trial.
Justification: Final assessment completed by blinded assessor

Number of subjects in period 2	Intensive	Guideline
Started	1556	1540
Completed	1556	1540

Period 3

Period 3 title	Day 7 face to face follow up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Intensive

Arm description:
Clopidogrel, Aspirin and Dipyridamole

Arm type	Experimental
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use, Nasogastric use

Dosage and administration details:
Loading dose of 300mg followed by 30 days of 75mg per day

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use, Nasogastric use

Dosage and administration details:
Loading dose of 300mg at randomisation followed by 75mg for 30 days

Investigational medicinal product name	Dipyridamole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use

Dosage and administration details:
200mg tablet twice per day for 30 days

Arm title	Guideline

Arm description:
Clopidogrel or Aspirin and Dipyridamole

Arm type	Guideline therapy
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use

Dosage and administration details:

Loading dose of 300mg followed by 30 days of 75mg per day

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use

Dosage and administration details:

Loading dose of 300mg at randomisation followed by 75mg for 30 days

Investigational medicinal product name	Dipyridamole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use

Dosage and administration details:

200mg tablet twice per day for 30 days

Number of subjects in period 3	Intensive	Guideline
Started	1556	1540
Recurrent stroke/TIA	41 [3]	57 [4]
Completed	1525	1502
Not completed	31	38
Adverse event, serious fatal	6	6
Consent withdrawn by subject	19	18
Logistical problem	6	14

Notes:

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants were able to withdraw from a particular follow up without having to withdraw fully from the trial. Patients who suffered from a recurrent stroke or TIA were also asked to complete further follow ups. This meant they were still able to complete future follow ups if they wished.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants were able to withdraw from a particular follow up without having to withdraw fully from the trial. Patients who suffered from a recurrent stroke or TIA were also asked to complete further follow ups. This meant they were still able to complete future follow ups if they wished.

Period 4

Period 4 title	Day 35 face to face follow up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[5]

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Intensive

Arm description:

Clopidogrel, Aspirin and Dipyridamole

Arm type	Experimental
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use, Nasogastric use

Dosage and administration details:

Loading dose of 300mg followed by 30 days of 75mg per day

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use, Nasogastric use

Dosage and administration details:

Loading dose of 300mg at randomisation followed by 75mg for 30 days

Investigational medicinal product name	Dipyridamole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use

Dosage and administration details:

200mg tablet twice per day for 30 days

Arm title	Guideline

Arm description:

Clopidogrel or Aspirin and Dipyridamole

Arm type	Guideline therapy
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use

Dosage and administration details:

Loading dose of 300mg followed by 30 days of 75mg per day

Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Nasogastric use , Oral use

Dosage and administration details:

Loading dose of 300mg at randomisation followed by 75mg for 30 days

Investigational medicinal product name	Dipyridamole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use

Dosage and administration details:

200mg tablet twice per day for 30 days

Notes:

[5] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Final assessment completed by blinded assessor

Number of subjects in period 4	Intensive	Guideline
Started	1525	1502
Recurrent stroke/TIA	70 [6]	83 [7]
Completed	1490	1483
Not completed	66	57
Adverse event, serious fatal	14	14
Consent withdrawn by subject	32	27
Logistical problem	20	16
Joined	31	38
Agreed to complete follow up	31	38

Notes:

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants were able to withdraw from a particular follow up without having to withdraw fully from the trial. Patients who suffered from a recurrent stroke or TIA were also asked to complete further follow ups. This meant they were still able to complete future follow ups if they wished.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants were able to withdraw from a particular follow up without having to withdraw fully from the trial. Patients who suffered from a recurrent stroke or TIA were also asked to complete further follow ups. This meant they were still able to complete future follow ups if they wished.

Period 5

Period 5 title	Day 90 telephone follow up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[8]

Blinding implementation details:

Follow up coordinator not involved with participant prior to follow up call and unaware of randomisation

Arms

Are arms mutually exclusive?	Yes

Arm title	Intensive
Arm description:	
Clopidogrel, Aspirin and Dipyridamole	
Arm type	Experimental
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use, Nasogastric use
Dosage and administration details:	
Loading dose of 300mg followed by 30 days of 75mg per day	
Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use, Nasogastric use
Dosage and administration details:	
Loading dose of 300mg at randomisation followed by 75mg for 30 days	
Investigational medicinal product name	Dipyridamole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use
Dosage and administration details:	
200mg tablet twice per day for 30 days	
Arm title	Guideline
Arm description:	
Clopidogrel or Aspirin and Dipyridamole	
Arm type	Guideline therapy
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use
Dosage and administration details:	
Loading dose of 300mg followed by 30 days of 75mg per day	
Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use
Dosage and administration details:	
Loading dose of 300mg at randomisation followed by 75mg for 30 days	
Investigational medicinal product name	Dipyridamole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Nasogastric use , Oral use
Dosage and administration details:	
200mg tablet twice per day for 30 days	

Notes:

[8] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Final assessment completed by blinded assessor

Number of subjects in period 5	Intensive	Guideline
Started	1490	1483
Recurrent stroke/TIA	93 [9]	105 [10]
Completed	1514	1502
Not completed	42	38
Adverse event, serious fatal	26	28
Consent withdrawn by subject	15	5
Reason unknown	1	-
Lost to follow-up	-	5
Joined	66	57
Agreed to complete follow up	66	57

Notes:

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants were able to withdraw from a particular follow up without having to withdraw fully from the trial. Patients who suffered from a recurrent stroke or TIA were also asked to complete further follow ups. This meant they were still able to complete future follow ups if they wished.

[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants were able to withdraw from a particular follow up without having to withdraw fully from the trial. Patients who suffered from a recurrent stroke or TIA were also asked to complete further follow ups. This meant they were still able to complete future follow ups if they wished.

Baseline characteristics

Reporting groups	
Reporting group title	Randomisation
Reporting group description:	
Number of participants recruited in to the trial	

Reporting group values	Randomisation	Total	
Number of subjects	3096	3096	
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)	973	973	
From 65-84 years	1918	1918	
85 years and over	205	205	
Age continuous			
Average age			
Units: years			
arithmetic mean	69		
standard deviation	± 10.1	-	
Gender categorical			
Female			
Units: Subjects			
Female	1151	1151	
Male	1945	1945	

Subject analysis sets	
Subject analysis set title	All participants
Subject analysis set type	Full analysis
Subject analysis set description:	
Analysis of baseline characteristics of all participants	
Subject analysis set title	Stroke
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants randomised with non-cardio embolic ischaemic stroke	
Subject analysis set title	TIA
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants randomised with Transient ischaemic attack	

Reporting group values	All participants	Stroke	TIA
Number of subjects	3096	2143	953
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	973	723	250
From 65-84 years	1918	1281	637
85 years and over	205	139	66
Age continuous			
Average age			
Units: years			
arithmetic mean	69	68.5	70.2
standard deviation	± 10.1	± 10.1	± 9.9
Gender categorical			
Female			
Units: Subjects			
Female	1151	787	364
Male	1945	1356	589

End points

End points reporting groups

Reporting group title	Intensive

Reporting group description:
Clopidogrel, Aspirin and Dipyridamole

Reporting group title	Guideline

Reporting group description:
Guideline therapy either clopidogrel alone or aspirin and dipyridamole

Reporting group title	Intensive

Reporting group description:
Clopidogrel, Aspirin and Dipyridamole

Reporting group title	Guideline

Reporting group description:
Clopidogrel or Aspirin and Dipyridamole

Reporting group title	Intensive

Reporting group description:
Clopidogrel, Aspirin and Dipyridamole

Reporting group title	Guideline

Reporting group description:
Clopidogrel or Aspirin and Dipyridamole

Reporting group title	Intensive

Reporting group description:
Clopidogrel, Aspirin and Dipyridamole

Reporting group title	Guideline

Reporting group description:
Clopidogrel or Aspirin and Dipyridamole

Reporting group title	Intensive

Reporting group description:
Clopidogrel, Aspirin and Dipyridamole

Reporting group title	Guideline

Reporting group description:
Clopidogrel or Aspirin and Dipyridamole

Subject analysis set title	All participants
Subject analysis set type	Full analysis

Subject analysis set description:
Analysis of baseline characteristics of all participants

Subject analysis set title	Stroke
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants randomised with non-cardio embolic ischaemic stroke

Subject analysis set title	TIA
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants randomised with Transient ischaemic attack

Primary: Primary outcome recurrent stroke and TIA by severity	
End point title	Primary outcome recurrent stroke and TIA by severity
End point description: Ordered categorical scale	
End point type	Primary
End point timeframe: By Day 90 follow up	

End point values	Intensive	Guideline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1540	1530		
Units: 3096				
number (not applicable)				
No event	1447	1425		
TIA	32	48		
Stroke MRS 0/1	15	18		
Stroke MRS 2/3	22	23		
Stroke MRS 4/5	11	9		
Fatal stroke MRS 6	13	7		

Statistical analyses

Statistical analysis title	Primary outcome analysis
Statistical analysis description: This analysis has been adjusted for country, index event, guideline comparator choice, age, sex, pre-morbid mRS, time from onset to randomisation, number of antiplatelets on before index event, stroke syndrome, systolic BP, use of gastroprotection medication, use of heparin (low dose), stroke severity (NIHSS), use of rt-PA treatment, ABCD2 score and number of TIAs in the last week.	
Comparison groups	Intensive v Guideline
Number of subjects included in analysis	3070
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.47
Method	Ordinal logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.2

Secondary: Safety outcome, bleeding by severity	
End point title	Safety outcome, bleeding by severity

End point description:

Ordered categorical scale of bleeding events

End point type	Secondary

End point timeframe:

By day 90 follow up

End point values	Intensive	Guideline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1541	1531		
Units: Number				
Fatal bleed	8	3		
Major bleed	31	14		
Moderate bleed	25	13		
Minor bleed	241	109		
No bleeding event	1236	1392		

Statistical analyses

Statistical analysis title	Safety outcome analysis

Statistical analysis description:

This analysis has been adjusted for country, index event, guideline comparator choice, age, sex, pre-morbid mRS, time from onset to randomisation, number of antiplatelets on before index event, stroke syndrome, systolic BP, use of gastroprotection medication, use of heparin (low dose), stroke severity (NIHSS), use of rt-PA treatment, ABCD2 score and number of TIAs in the last week.

Comparison groups	Intensive v Guideline
Number of subjects included in analysis	3072
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Ordinal logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	2.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.05
upper limit	3.16

Secondary: Composite outcome, Stroke or major bleed

End point title	Composite outcome, Stroke or major bleed

End point description:

Composite binary outcome of stroke and major (including fatal) bleeding

End point type	Secondary

End point timeframe:
By day 90 followup

End point values	Intensive	Guideline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1540	1530		
Units: Number				
Stroke or Major bleed	87	69		
No event	1453	1461		

Statistical analyses

Statistical analysis title	Composite outcome analysis

Statistical analysis description:

This analysis has been adjusted for country, index event, guideline comparator choice, age, sex, pre-morbid mRS, time from onset to randomisation, number of antiplatelets on before index event, stroke syndrome, systolic BP, use of gastroprotection medication, use of heparin (low dose), stroke severity (NIHSS), use of rt-PA treatment, ABCD2 score and number of TIAs in the last week.

Comparison groups	Intensive v Guideline
Number of subjects included in analysis	3070
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.19
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.7

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

01/04/09 - 30/06/16

Adverse event reporting additional description:

Clinician assessed during hospitalisation and researcher/patient assessed during follow ups

Assessment type	Non-systematic

Dictionary used

Dictionary name	Excel spreadsheet
Dictionary version	1

Reporting groups

Reporting group title	Intensive

Reporting group description:

Clopidogrel, Aspirin and Dipyridamole

Reporting group title	Guideline

Reporting group description: -

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: All adverse events were adjudicated as serious adverse events

Serious adverse events	Intensive	Guideline	
Total subjects affected by serious adverse events			
subjects affected / exposed	592 / 1556 (38.05%)	496 / 1540 (32.21%)	
number of deaths (all causes)	26	28	
number of deaths resulting from adverse events	7	5	
Cardiac disorders			
Cardiovascular disorder	Additional description: Grouping of all cardiovascular events		
subjects affected / exposed	130 / 1556 (8.35%)	153 / 1540 (9.94%)	
occurrences causally related to treatment / all	7 / 143	4 / 172	
deaths causally related to treatment / all	0 / 2	0 / 3	
Nervous system disorders			
Nervous system disorder			
subjects affected / exposed	191 / 1556 (12.28%)	183 / 1540 (11.88%)	
occurrences causally related to treatment / all	99 / 219	58 / 216	
deaths causally related to treatment / all	5 / 14	5 / 12	
Blood and lymphatic system disorders			
Haematological disorders			
subjects affected / exposed	13 / 1556 (0.84%)	14 / 1540 (0.91%)	
occurrences causally related to treatment / all	10 / 13	12 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Miscellaneous			
subjects affected / exposed	52 / 1556 (3.34%)	51 / 1540 (3.31%)	
occurrences causally related to treatment / all	16 / 52	10 / 55	
deaths causally related to treatment / all	1 / 5	0 / 9	
Immune system disorders			
Immune system disorder			
subjects affected / exposed	4 / 1556 (0.26%)	1 / 1540 (0.06%)	
occurrences causally related to treatment / all	4 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Eye disorder			
subjects affected / exposed	12 / 1556 (0.77%)	6 / 1540 (0.39%)	
occurrences causally related to treatment / all	9 / 12	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal events			
subjects affected / exposed	91 / 1556 (5.85%)	49 / 1540 (3.18%)	
occurrences causally related to treatment / all	67 / 97	31 / 49	
deaths causally related to treatment / all	1 / 3	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Respiratory disorder			
subjects affected / exposed	87 / 1556 (5.59%)	67 / 1540 (4.35%)	
occurrences causally related to treatment / all	62 / 100	32 / 75	
deaths causally related to treatment / all	0 / 2	0 / 3	
Skin and subcutaneous tissue disorders			
Cutaneous			
subjects affected / exposed	159 / 1556 (10.22%)	58 / 1540 (3.77%)	
occurrences causally related to treatment / all	167 / 180	46 / 62	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Genito-urinary			
subjects affected / exposed	46 / 1556 (2.96%)	25 / 1540 (1.62%)	
occurrences causally related to treatment / all	34 / 56	7 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Musculoskeletal disorder			
subjects affected / exposed	9 / 1556 (0.58%)	14 / 1540 (0.91%)	
occurrences causally related to treatment / all	5 / 9	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Metabolic disorder			
subjects affected / exposed	5 / 1556 (0.32%)	8 / 1540 (0.52%)	
occurrences causally related to treatment / all	0 / 5	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Intensive	Guideline	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1556 (0.00%)	0 / 1540 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 February 2012	Guideline group changed from aspirin and dipyridamole to aspirin and dipyridamole or clopidogrel

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.

N/A

Notes: