Clinical trial results:
Alteplase-Tenecteplase Trial Evaluation for Stroke Thrombolysis – pilot phase

Summary

EudraCT number	2010-024541-67
Trial protocol	GB
Global end of trial date	10 December 2013

Results information

Result version number	v1 (current)
This version publication date	13 March 2020
First version publication date	13 March 2020
Summary attachment (see zip file)	ATTEST Study Publication Summary (2010-024541-67 study publication summary.docx)

Trial information

Trial identification

Sponsor protocol code	1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01472926
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	NHS Greater Glasgow & Clyde
Sponsor organisation address	Grahamston Road, Paisley, UK, United Kingdom, PA2 7DE
Public contact	Prof Keith Muir, University of Glasgow, 44 141 451 5892, k.muir@clinmed.gla.ac.uk
Scientific contact	Dr Maureen Travers, NHS Greater Glasgow & Clyde, 44 141 314 4012 ,

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	01 May 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 December 2013
Global end of trial reached?	Yes
Global end of trial date	10 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The ATTEST pilot phase is a Prospective Randomised Open Blinded End-point (PROBE) study that will compare markers of biological activity to inform the design of a larger definitive trial comparing the efficacy and safety of alteplase and tenecteplase as thrombolytic agents in eligible patients with acute ischaemic stroke.

Protection of trial subjects:

Written informed consent was obtained from each participant, alternatively, if the patient was unable to consent for themselves, then informed assent was provided by the next of kin, or professional. If the participant regains capacity, the participant will be asked to sign a consent form.
Participants underwent baseline measurements followed by routine post-thrombolysis monitoring including adverse event assessment. Participants were followed up at 90 days by the research nurses for evaluation and assessment which included the modified rankin scale (mRS).

Background therapy:

Not applicable

Evidence for comparator:

Intravenous (IV) thrombolysis with the recombinant tissue Plasminogen Activator (rt-PA) alteplase significantly reduces the odds of death or dependence in acute ischaemic stroke when given within 4.5 hours of symptom onset. Alteplase is currently the only treatment licensed for acute stroke. In this study, alteplase will be used in accordance with the current Summary of Product Characteristics with the exception that patients who present within 4.5 hours of stroke symptom onset will be eligible for treatment as per current European Stroke Organisation guidelines. Subjects randomised to treatment this arm will receive the recommended treatment dose of 0.9 mg alteplase/kg body weight (maximum of 90 mg) infused intravenously over 60 minutes with 10 % of the total dose administered as an initial intravenous bolus.

Actual start date of recruitment	01 January 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 104
Worldwide total number of subjects	104
EEA total number of subjects	104

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)	32
From 65 to 84 years	60
85 years and over	12

Subject disposition

Recruitment

Recruitment details:

The pilot study was set in a single site in Glasgow, Scotland

Pre-assignment

Screening details:

355 screened, 157 eligible, 104 enrolled. 8 were excluded final diagnosis of non-stroke 96 full data sets. Inclusion criteria: Males/females>18yr; eligible for treatment with IV alteplase. Exclusion: contraindications to thrombolytic drug treatment for stroke, known impaired renal function precluding contrast CT; allergy to radiological contrast.

Period 1

Period 1 title	Pre-randomisation
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Comparator

Arm description:

Alteplase 0.9mg/kg with 10% of the total dose administered as an initial intravenous bolus and remaining 90% of the total dose administered as an intravenous infusion over 1 hour

Arm type	Active comparator
Investigational medicinal product name	Alteplase
Investigational medicinal product code	
Other name	Actilyse
Pharmaceutical forms	Powder and solvent for solution for injection/infusion
Routes of administration	Intravenous bolus use , Intravenous drip use

Dosage and administration details:

0.9mg/kg with 10% of the total dose administered as a initial intravenous bolus and remaining 90% of the total dose administered as an intravenous infusion over 1 hour

Arm title	Test IMP

Arm description:

Tenecteplase 0.25mg/kg administered as a single rapid intravenous bolus.

Arm type	Experimental
Investigational medicinal product name	Tenecteplase
Investigational medicinal product code	
Other name	Metalyse
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

0.25mg/kg administered as a single rapid IV bolus

Number of subjects in period 1	Comparator	Test IMP
Started	52	52
Completed	52	52

Period 2	
Period 2 title	Randomisation
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Comparator

Arm description:

Alteplase 0.9mg/kg with 10% of the total dose administered as an initial intravenous bolus and remaining 90% of the total dose administered as an intravenous infusion over 1 hour

Arm type	Active comparator
Investigational medicinal product name	Alteplase
Investigational medicinal product code	
Other name	Actilyse
Pharmaceutical forms	Powder and solvent for solution for injection/infusion
Routes of administration	Intravenous bolus use , Intravenous drip use

Dosage and administration details:

0.9mg/kg with 10% of the total dose administered as a initial intravenous bolus and remaining 90% of the total dose administered as an intravenous infusion over 1 hour

Arm title	Test IMP

Arm description:

Tenecteplase 0.25mg/kg administered as a single rapid intravenous bolus.

Arm type	Experimental
Investigational medicinal product name	Tenecteplase
Investigational medicinal product code	
Other name	Metalyse
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

0.25mg/kg administered as a single rapid IV bolus

Number of subjects in period 2	Comparator	Test IMP
Started	52	52
Completed	49	47
Not completed	3	5
Study treatment not received	1	-
excluded final diagnosis of non-stroke	2	5

Period 3

Period 3 title	Post treatment
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Comparator

Arm description:

Alteplase 0.9mg/kg with 10% of the total dose administered as an initial intravenous bolus and remaining 90% of the total dose administered as an intravenous infusion over 1 hour

Arm type	Active comparator
Investigational medicinal product name	Alteplase
Investigational medicinal product code	
Other name	Actilyse
Pharmaceutical forms	Powder and solvent for solution for injection/infusion
Routes of administration	Intravenous drip use , Intravenous bolus use

Dosage and administration details:

0.9mg/kg with 10% of the total dose administered as a initial intravenous bolus and remaining 90% of the total dose administered as an intravenous infusion over 1 hour

Arm title	Test IMP

Arm description:

Tenecteplase 0.25mg/kg administered as a single rapid intravenous bolus.

Arm type	Experimental
Investigational medicinal product name	Tenecteplase
Investigational medicinal product code	
Other name	Metalyse
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

0.25mg/kg administered as a single rapid IV bolus

Number of subjects in period 3	Comparator	Test IMP
Started	49	47
Completed	49	47

Baseline characteristics

Reporting groups	
Reporting group title	Comparator
Reporting group description:	
Alteplase 0.9mg/kg with 10% of the total dose administered as an initial intravenous bolus and remaining 90% of the total dose administered as an intravenous infusion over 1 hour	
Reporting group title	Test IMP
Reporting group description:	
Tenecteplase 0.25mg/kg administered as a single rapid intravenous bolus.	

Reporting group values	Comparator	Test IMP	Total
Number of subjects	52	52	104
Age categorical Units: Subjects			
Adults (18-64 years)	16	16	32
From 65-84 years	30	30	60
85 years and over	6	6	12
Gender categorical Units: Subjects			
Female	26	26	52
Male	26	26	52
smoking history Units: Subjects			
current	26	26	52
former	26	26	52
never	0	0	0
Alcohol Consumption Units: Subjects			
Current	0	0	0
Former	0	0	0
Never	0	0	0
Don't know	52	52	104
Living Status Units: Subjects			
Home alone	26	26	52
Home with family/friends	26	26	52
Sheltered Housing alone	0	0	0
Sheltered housing with family/friends	0	0	0
Residential home (supervised care)	0	0	0
Nursing Home	0	0	0
Long-stay hospitalisation	0	0	0
Systolic Blood Pressure (mmHg) Units: Subjects			
Mean	26	26	52
Median	26	26	52
Min	0	0	0
Max	0	0	0

Diastolic Blood Pressure (mmHg) Units: Subjects			
Mean	26	26	52
Median	26	26	52
Min	0	0	0
Max	0	0	0
Heart rate (bpm) Units: Subjects			
Mean	26	26	52
Median	26	26	52
Min	0	0	0
Max	0	0	0
Temperature (degrees Celsius) Units: Subjects			
Mean	26	26	52
Median	26	26	52
Min	0	0	0
Max	0	0	0
Weight (kg) Units: Subjects			
Mean	26	26	52
Median	26	26	52
Min	0	0	0
Max	0	0	0
Glucose (mmol/L) Units: Subjects			
Mean	26	26	52
Median	26	26	52
Min	0	0	0
Max	0	0	0
ECG Result Units: Subjects			
Normal	26	26	52
Abnormal	26	26	52
Pre-morbid modified Rankin Scale (mRS) Units: Subjects			
No symptoms at all	52	52	104
No significant disability	0	0	0
Slight disability	0	0	0
Moderate disability	0	0	0
Moderately severe disability	0	0	0
Severe disability	0	0	0
Dead	0	0	0
NIH Stroke Scale Units: Subjects			
Mean	52	52	104
Median	0	0	0
Min	0	0	0
Max	0	0	0
ASPECT Score			

Units: Subjects			
Mean	52	52	104
Median	0	0	0
Min	0	0	0
Max	0	0	0
Stroke subtype (side) Units: Subjects			
Right	52	52	104
Left	0	0	0
Both	0	0	0
Stroke subtype (class) Units: Subjects			
TACS	52	52	104
PACS	0	0	0
POCS	0	0	0
LACS	0	0	0
Time from symptom onset and treatment (minutes) Units: Subjects			
Mean	52	52	104
Median	0	0	0
Min	0	0	0
Max	0	0	0
Risk factors: myocardial infarction Units: Subjects			
Yes	52	52	104
Risk factors: Heart disease Units: Subjects			
Yes	52	52	104
Risk factors: stroke Units: Subjects			
Yes	52	52	104
Risk factors: time since previous stroke (days) Units: Subjects			
Mean	52	52	104
Median	0	0	0
Min	0	0	0
Max	0	0	0
Risk factors: type of stroke Units: Subjects			
Ischaemic	0	0	0
Haemoragic	0	0	0
Unknown	52	52	104
Risk factors: Transient Ischaemic Attack (TIA) Units: Subjects			
Yes	0	0	0
Unknown	52	52	104
Risk factors: time since previous TIA (days) Units: Subjects			

Mean	52	52	104
Median	0	0	0
Min	0	0	0
Max	0	0	0
Established peripheral vascular disease Units: Subjects			
Yes	52	52	104
Heart failure Units: Subjects			
Yes	52	52	104
History of diabetes Units: Subjects			
Yes	52	52	104
History of high blood pressure Units: Subjects			
Yes	52	52	104
History of raised cholesterol Units: Subjects			
Yes	52	52	104
Atrial Fibrillation Units: Subjects			
Yes	52	52	104
Type of atrial fibrillation Units: Subjects			
Paroxysmal	26	26	52
Permanent	26	26	52
Carotid endarterectomy Units: Subjects			
Yes	52	52	104
Side of carotid endarterectomy Units: Subjects			
Left	52	52	104
Right	0	0	0
Medical History Units: Subjects			
Blood and lymphatic system disorders	52	52	104
Cardiac Disorders	0	0	0
Congenital, familial and genetic disorders	0	0	0
Ear and labyrinth disorders	0	0	0
Endocrine Disorders	0	0	0
Eye disorders	0	0	0
Gastrointestinal disorders	0	0	0
General disorders & Administration site conditions	0	0	0
Hepatobiliary disorders	0	0	0
Infections and infestations	0	0	0
Injury, poisoning & procedural complications	0	0	0
Investigations	0	0	0
Metabolism and nutrition disorders	0	0	0

Musculoskeletal & connective tissue disorders	0	0	0
Neoplasms benign, malignant & unspecified	0	0	0
Nervous System disorders	0	0	0
Psychiatric disorders	0	0	0
Renal and urinary disorders	0	0	0
Reproductive system and breast disorders	0	0	0
Respiratory, thoracic & mediastinal disorders	0	0	0
Social circumstances	0	0	0
Surgical and medical procedures	0	0	0
Vascular disorders	0	0	0
History of concomitant medication Units: Subjects			
Antidiarrheals, intestinal antiinflammatory,infect	52	52	104
Antiemetics and antinauseants	0	0	0
Digestives, incl. enzymes	0	0	0
Drugs for acid related disorders	0	0	0
Drugs for functional GI disorders	0	0	0
Drugs used in diabetes	0	0	0
Laxatives	0	0	0
Mineral supplements	0	0	0
stomatological preparations	0	0	0
Vitamins	0	0	0
Antimycotics for systemic use	0	0	0
Antibacterials for systemic use	0	0	0
Immunosuppressants	0	0	0
Antiprotozoals	0	0	0
Antianemic preparations	0	0	0
Antithrombotic agents	0	0	0
Agents acting on the renin-angiotensin system	0	0	0
Antihypertensives	0	0	0
Beta blocking agents	0	0	0
Calcium channel blockers	0	0	0
Cardiac Therapy	0	0	0
Diuretics	0	0	0
Lipid modifying agents	0	0	0
Antibiotics & chemotherapeutics for dermatological	0	0	0
Antifungals for dermatological use	0	0	0
Corticosteroids, dermatological preparations	0	0	0
Emollients and protectives	0	0	0
Other dermatological preparations	0	0	0
Urologicals	0	0	0
Antigout preparations	0	0	0
Antiinflammatory and antirheumatic products	0	0	0
Drugs for treatment of bone diseases	0	0	0
Muscle relaxants	0	0	0

Other drugs for disorders of the MSK system	0	0	0
Topical products for joint and muscular pain	0	0	0
Analgesics	0	0	0
Anesthetics	0	0	0
Anti-parkinson drugs	0	0	0
Anti-epileptics	0	0	0
Other nervous system drugs	0	0	0
Psychoanaleptics	0	0	0
Psycholeptics	0	0	0
Antihistamines for systemic use	0	0	0
Cough and cold preparations	0	0	0
Drugs for obstructive airway diseases	0	0	0
Ophthalmological and otological preparations	0	0	0
Ophthamologicals	0	0	0
Corticosteroids for systematic use	0	0	0
Systematichormonalpreps excl. sex hormone&insulin	0	0	0
Pituitary&Hypothalamic hormones & analogues	0	0	0
Thyroid Therapy	0	0	0
All other non-therapeutic products	0	0	0
All other therapeutic products	0	0	0

Subject analysis sets

Subject analysis set title	Comparator (Alteplase)
Subject analysis set type	Per protocol

Subject analysis set description:

49 subjects were included in the protocol analysis as 3 patients were excluded as they had a final diagnosis of non-stroke, also one of those 3 was not treated

Subject analysis set title	Test IMP (Tenecteplase)
Subject analysis set type	Per protocol

Subject analysis set description:

47 subjects were included in the protocol analysis as 5 patients were excluded as they had a final diagnosis of non-stroke

Reporting group values	Comparator (Alteplase)	Test IMP (Tenecteplase)	
Number of subjects	49	47	
Age categorical Units: Subjects			
Adults (18-64 years) From 65-84 years 85 years and over			
Gender categorical Units: Subjects			
Female	18	17	
Male	31	30	

smoking history Units: Subjects			
current	10	13	
former	15	10	
never	24	24	
Alcohol Consumption Units: Subjects			
Current	43	33	
Former	1	2	
Never	5	11	
Don't know	0	1	
Living Status Units: Subjects			
Home alone	10	13	
Home with family/friends	39	33	
Sheltered Housing alone	0	0	
Sheltered housing with family/friends	0	0	
Residential home (supervised care)	0	0	
Nursing Home	0	0	
Long-stay hospitalisation	0	1	
Systolic Blood Pressure (mmHg) Units: Subjects			
Mean	151	146	
Median	153	143	
Min	110	105	
Max	188	192	
Diastolic Blood Pressure (mmHg) Units: Subjects			
Mean	78	75	
Median	78	76	
Min	32	38	
Max	110	112	
Heart rate (bpm) Units: Subjects			
Mean	79	78	
Median	79	72	
Min	52	40	
Max	120	150	
Temperature (degrees Celsius) Units: Subjects			
Mean	36	36	
Median	36	36	
Min	35	35	
Max	37	37	
Weight (kg) Units: Subjects			
Mean	75	76	
Median	74	76	
Min	49	47	
Max	109	102	

Glucose (mmol/L) Units: Subjects			
Mean	7	7	
Median	7	7	
Min	4	4	
Max	15	10	
ECG Result Units: Subjects			
Normal	31	28	
Abnormal	18	19	
Pre-morbid modified Rankin Scale (mRS) Units: Subjects			
No symptoms at all	45	41	
No significant disability	1	3	
Slight disability	3	3	
Moderate disability	0	0	
Moderately severe disability	0	0	
Severe disability	0	0	
Dead	0	0	
NIH Stroke Scale Units: Subjects			
Mean	12	13	
Median	11	12	
Min	3	2	
Max	27	26	
ASPECT Score Units: Subjects			
Mean	7	7	
Median	7	8	
Min	3	2	
Max	10	10	
Stroke subtype (side) Units: Subjects			
Right	23	23	
Left	26	24	
Both	0	0	
Stroke subtype (class) Units: Subjects			
TACS	28	27	
PACS	16	16	
POCS	2	2	
LACS	3	2	
Time from symptom onset and treatment (minutes) Units: Subjects			
Mean	192	184	
Median	200	180	
Min	95	92	
Max	270	265	
Risk factors: myocardial infarction Units: Subjects			

Yes	6	4	
Risk factors: Heart disease Units: Subjects			
Yes	9	12	
Risk factors: stroke Units: Subjects			
Yes	4	6	
Risk factors: time since previous stroke (days) Units: Subjects			
Mean	3484	1016	
Median	2619	973	
Min	0	234	
Max	8697	2043	
Risk factors: type of stroke Units: Subjects			
Ischaemic	4	6	
Haemoragic	0	0	
Unknown	0	0	
Risk factors: Transient Ischaemic Attack (TIA) Units: Subjects			
Yes	8	6	
Unknown	0	1	
Risk factors: time since previous TIA (days) Units: Subjects			
Mean	3562	1736	
Median	3201	1087	
Min	67	0	
Max	8321	7025	
Established peripheral vascular disease Units: Subjects			
Yes	4	0	
Heart failure Units: Subjects			
Yes	1	2	
History of diabetes Units: Subjects			
Yes	7	7	
History of high blood pressure Units: Subjects			
Yes	28	20	
History of raised cholesterol Units: Subjects			
Yes	7	4	
Atrial Fibrillation Units: Subjects			
Yes	15	19	
Type of atrial fibrillation Units: Subjects			
Paroxysmal	7	10	

Permanent	8	9	
Carotid endarterectomy Units: Subjects			
Yes	1	0	
Side of carotid endarterectomy Units: Subjects			
Left	0	0	
Right	1	0	
Medical History Units: Subjects			
Blood and lymphatic system disorders	0	1	
Cardiac Disorders	1	2	
Congenital, familial and genetic disorders	2	0	
Ear and labyrinth disorders	1	0	
Endocrine Disorders	4	0	
Eye disorders	1	0	
Gastrointestinal disorders	8	4	
General disorders & Administration site conditions	0	1	
Hepatobiliary disorders	2	0	
Infections and infestations	0	1	
Injury, poisoning & procedural complications	3	0	
Investigations	0	1	
Metabolism and nutrition disorders	1	2	
Musculoskeletal & connective tissue disorders	2	5	
Neoplasms benign, malignant & unspecified	8	5	
Nervous System disorders	2	0	
Psychiatric disorders	2	4	
Renal and urinary disorders	3	0	
Reproductive system and breast disorders	0	2	
Respiratory, thoracic & mediastinal disorders	8	2	
Social circumstances	0	1	
Surgical and medical procedures	5	6	
Vascular disorders	0	3	
History of concomitant medication Units: Subjects			
Antidiarrheals, intestinal antiinflammatory,infect	35	1	
Antiemetics and antinauseants	6	7	
Digestives, incl. enzymes	1	0	
Drugs for acid related disorders	221	22	
Drugs for functional GI disorders	1	6	
Drugs used in diabetes	4	3	
Laxatives	13	13	
Mineral supplements	4	8	
stomatological preparations	0	3	
Vitamins	5	4	

Antimycotics for systemic use	0	2	
Antibacterials for systemic use	17	21	
Immunosuppressants	1	0	
Antiprotozoals	0	1	
Antianemic preparations	4	2	
Antithrombotic agents	42	45	
Agents acting on the renin-angiotensin system	19	11	
Antihypertensives	2	0	
Beta blocking agents	14	17	
Calcium channel blockers	9	3	
Cardiac Therapy	13	10	
Diuretics	14	7	
Lipid modifying agents	40	39	
Antibiotics & chemotherapeutics for dermatological	0	1	
Antifungals for dermatological use	1	0	
Corticosteroids, dermatological preparations	0	1	
Emollients and protectives	1	0	
Other dermatological preparations	0	1	
Urologicals	6	3	
Antigout preparations	1	4	
Antiinflammatory and antirheumatic products	2	3	
Drugs for treatment of bone diseases	2	2	
Muscle relaxants	0	1	
Other drugs for disorders of the MSK system	0	2	
Topical products for joint and muscular pain	2	0	
Analgesics	32	31	
Anesthetics	1	1	
Anti-parkinson drugs	2	1	
Anti-epileptics	7	3	
Other nervous system drugs	3	3	
Psychoanaleptics	12	6	
Psycholeptics	13	9	
Antihistamines for systemic use	9	9	
Cough and cold preparations	1	0	
Drugs for obstructive airway diseases	13	8	
Ophthalmological and otological preparations	1	0	
Ophthamologicals	5	4	
Corticosteroids for systematic use	1	4	
Systematichormonalpreps excl. sex hormone&insulin	6	5	
Pituitary&Hypothalamic hormones & analogues	0	1	
Thyroid Therapy	5	0	
All other non-therapeutic products	5	1	
All other therapeutic products	1	1	

End points

End points reporting groups

Reporting group title	Comparator
Reporting group description:	
Alteplase 0.9mg/kg with 10% of the total dose administered as an initial intravenous bolus and remaining 90% of the total dose administered as an intravenous infusion over 1 hour	
Reporting group title	Test IMP
Reporting group description:	
Tenecteplase 0.25mg/kg administered as a single rapid intravenous bolus.	
Reporting group title	Comparator
Reporting group description:	
Alteplase 0.9mg/kg with 10% of the total dose administered as an initial intravenous bolus and remaining 90% of the total dose administered as an intravenous infusion over 1 hour	
Reporting group title	Test IMP
Reporting group description:	
Tenecteplase 0.25mg/kg administered as a single rapid intravenous bolus.	
Reporting group title	Comparator
Reporting group description:	
Alteplase 0.9mg/kg with 10% of the total dose administered as an initial intravenous bolus and remaining 90% of the total dose administered as an intravenous infusion over 1 hour	
Reporting group title	Test IMP
Reporting group description:	
Tenecteplase 0.25mg/kg administered as a single rapid intravenous bolus.	
Subject analysis set title	Comparator (Alteplase)
Subject analysis set type	Per protocol
Subject analysis set description:	
49 subjects were included in the protocol analysis as 3 patients were excluded as they had a final diagnosis of non-stroke, also one of those 3 was not treated	
Subject analysis set title	Test IMP (Tenecteplase)
Subject analysis set type	Per protocol
Subject analysis set description:	
47 subjects were included in the protocol analysis as 5 patients were excluded as they had a final diagnosis of non-stroke	

Primary: Percent Penumbral salvage

End point title	Percent Penumbral salvage
End point description:	
End point type	Primary
End point timeframe:	
24-48hrs	

End point values	Comparator (Alteplase)	Test IMP (Tenecteplase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	36[1]	35[2]		
Units: percentage				
Mean	72	68		
Median	79	79		
Min	15	13		
Max	100	100		

Notes:

[1] - 13 missing

[2] - 12 missing

Statistical analyses

Statistical analysis title	Treatment effect (Tenecteplase - Alteplase)
Comparison groups	Test IMP (Tenecteplase) v Comparator (Alteplase)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.8127
Method	Regression, Linear
Parameter estimate	regression coefficient
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.55
upper limit	12.14
Variability estimate	Standard error of the mean
Dispersion value	5.53

Secondary: Total brain infarct volume

End point title	Total brain infarct volume

End point description:

End point type	Secondary

End point timeframe:

24-48 hrs

End point values	Comparator (Alteplase)	Test IMP (Tenecteplase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	47[3]	46[4]		
Units: mL				
Mean	66	75		
Median	31	38		

Min	0	0		
Max	422	474		

Notes:

[3] - 2 missing

[4] - 1 missing

Statistical analyses

Statistical analysis title	Treatment effect (Tenecteplase - Alteplase)
Comparison groups	Comparator (Alteplase) v Test IMP (Tenecteplase)
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.7517
Method	Regression, Linear
Parameter estimate	regression coefficient
Point estimate	4.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.63
upper limit	35.37
Variability estimate	Standard error of the mean
Dispersion value	15.57

Secondary: Co-registered infarct volume

End point title	Co-registered infarct volume

End point description:

End point type	Secondary

End point timeframe:

24 - 48 hours

End point values	Comparator (Alteplase)	Test IMP (Tenecteplase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	45[5]	45[6]		
Units: Percentage				
Mean	47	50		
Median	26	30		
Min	0	0		
Max	243	212		

Notes:

[5] - 4 missing

[6] - 2 missing

Statistical analyses

Statistical analysis title	Treatment effect (Tenecteplase - Alteplase)
Comparison groups	Comparator (Alteplase) v Test IMP (Tenecteplase)
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.9953
Method	Regression, Linear
Parameter estimate	regression coefficient
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.43
upper limit	19.55
Variability estimate	Standard error of the mean
Dispersion value	9.94

Secondary: Recanalisation (TIMI>1 or TICI>2)

End point title	Recanalisation (TIMI>1 or TICI>2)

End point description:

End point type	Secondary

End point timeframe:

24-48 hours

End point values	Comparator (Alteplase)	Test IMP (Tenecteplase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	35[7]	32[8]		
Units: Number				
No	9	11		
Yes	26	21		

Notes:

[7] - 14 missing

[8] - 15 missing

Statistical analyses

Statistical analysis title	Treatment effect (Tenecteplase - Alteplase)
Comparison groups	Comparator (Alteplase) v Test IMP (Tenecteplase)

Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.3789
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	1.8
Variability estimate	Standard error of the mean
Dispersion value	0.55

Secondary: Early clinical improvement in NIHSS scores

End point title	Early clinical improvement in NIHSS scores
End point description:	
End point type	Secondary
End point timeframe:	
at 24 hours	

End point values	Comparator (Alteplase)	Test IMP (Tenecteplase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[9]	47		
Units: Number				
No	36	28		
Yes	12	19		

Notes:
[9] - 1 missing

Statistical analyses

Statistical analysis title	Treatment effect (Tenecteplase - Alteplase)
Comparison groups	Comparator (Alteplase) v Test IMP (Tenecteplase)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.1024
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	5.19
Variability estimate	Standard error of the mean
Dispersion value	0.46

Secondary: Intra-cranial haemorrhage (ICH) and type

End point title	Intra-cranial haemorrhage (ICH) and type
End point description:	
End point type	Secondary
End point timeframe:	
at 24 - 48 hours	

End point values	Comparator (Alteplase)	Test IMP (Tenecteplase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[10]	47		
Units: Number				
No	34	40		
Yes HI1	5	4		
Yes HI2	3	1		
Yes PH1	2	0		
Yes PH2	3	0		
Yes SAH	0	1		
Yes HI1 & SAH	1	0		
Yes PH1 & SAH	0	1		

Notes:
[10] - 1 missing

Statistical analyses

Statistical analysis title	Treatment effect (Tenecteplase - Alteplase)
Comparison groups	Comparator (Alteplase) v Test IMP (Tenecteplase)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.6666
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.37

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	1.07
Variability estimate	Standard error of the mean
Dispersion value	0.56

Secondary: Symptomatic ICH (SITS-MOST definition)

End point title	Symptomatic ICH (SITS-MOST definition)
End point description:	
End point type	Secondary
End point timeframe:	
at 24-48 hours	

End point values	Comparator (Alteplase)	Test IMP (Tenecteplase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[11]	47		
Units: Number				
No	46	46		
Yes	2	1		

Notes:
[11] - 1 missing

Statistical analyses

Statistical analysis title	Treatment effect (Tenecteplase - Alteplase)
Comparison groups	Comparator (Alteplase) v Test IMP (Tenecteplase)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.548
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	5.55
Variability estimate	Standard error of the mean
Dispersion value	1.26

Secondary: mRS favourable clinical outcome (0-1) day 30

End point title	mRS favourable clinical outcome (0-1) day 30

End point description:

End point type	Secondary

End point timeframe:

day 30

End point values	Comparator (Alteplase)	Test IMP (Tenecteplase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[12]	47		
Units: Number				
No	41	40		
Yes	7	7		

Notes:

[12] - 1 missing

Statistical analyses

Statistical analysis title	mRS0-1:Treatment effect Tenecteplase vs. alteplase
Comparison groups	Comparator (Alteplase) v Test IMP (Tenecteplase)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.8925
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	3.52
Variability estimate	Standard error of the mean
Dispersion value	0.6

Secondary: mRS favourable clinical outcome (0-1) day 90

End point title	mRS favourable clinical outcome (0-1) day 90

End point description:

End point type	Secondary

End point timeframe:
day 90

End point values	Comparator (Alteplase)	Test IMP (Tenecteplase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[13]	47		
Units: Number				
No	38	34		
Yes	10	13		

Notes:
[13] - 1 missing

Statistical analyses

Statistical analysis title	mRS0-1:Treatment effect Tenecteplase vs. alteplase
Comparison groups	Comparator (Alteplase) v Test IMP (Tenecteplase)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.2793
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	5.45
Variability estimate	Standard error of the mean
Dispersion value	0.56

Secondary: Number of days at home by day 90

End point title	Number of days at home by day 90

End point description:

End point type	Secondary

End point timeframe:
Day 90

End point values	Comparator (Alteplase)	Test IMP (Tenecteplase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[14]	45[15]		
Units: Number				
Mean	50	45		
Median	65	61		
Min	0	0		
Max	96	104		

Notes:

[14] - 1 missing

[15] - 2 missing

Statistical analyses

Statistical analysis title	Treatment effect (Tenecteplase - Alteplase)
Comparison groups	Comparator (Alteplase) v Test IMP (Tenecteplase)
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.6347
Method	Regression, Linear
Parameter estimate	regression coefficient
Point estimate	-3.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.76
upper limit	9.66
Variability estimate	Standard error of the mean
Dispersion value	6.48

Secondary: Mortality at day 90

End point title	Mortality at day 90

End point description:

End point type	Secondary

End point timeframe:

day 90

End point values	Comparator (Alteplase)	Test IMP (Tenecteplase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	49	47		
Units: Number				
No	43	39		
Yes	6	8		

Statistical analyses

Statistical analysis title	Treatment effect (Tenecteplase - Alteplase)
Comparison groups	Comparator (Alteplase) v Test IMP (Tenecteplase)
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.5135
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	5.23
Variability estimate	Standard error of the mean
Dispersion value	0.63

Statistical analysis title	Treatment effect (Tenecteplase - Alteplase)
Comparison groups	Comparator (Alteplase) v Test IMP (Tenecteplase)
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.6602
Method	Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	3.67
Variability estimate	Standard error of the mean
Dispersion value	0.54

Secondary: mRS favourable clinical outcome (0-2) day 30	
End point title	mRS favourable clinical outcome (0-2) day 30

End point description:

End point type	Secondary

End point timeframe:
day 30

End point values	Comparator (Alteplase)	Test IMP (Tenecteplase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[16]	47		
Units: Number				
No	32	33		
Yes	16	14		

Notes:
[16] - 1 missing

Statistical analyses

Statistical analysis title	mRS0-2:Treatment effect (TenecteplasevsAlteplase)
Comparison groups	Comparator (Alteplase) v Test IMP (Tenecteplase)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.7833
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	2.21
Variability estimate	Standard error of the mean
Dispersion value	0.47

Secondary: mRS favourable clinical outcome (0-2) day 90

End point title	mRS favourable clinical outcome (0-2) day 90

End point description:

End point type	Secondary

End point timeframe:
day 90

End point values	Comparator (Alteplase)	Test IMP (Tenecteplase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[17]	47		
Units: Number				
No	29	30		
Yes	19	17		

Notes:

[17] - 1 missing

Statistical analyses

Statistical analysis title	mRS0-2:Treatment effect (TenecteplasevsAlteplase)
Comparison groups	Comparator (Alteplase) v Test IMP (Tenecteplase)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.8132
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	2.24
Variability estimate	Standard error of the mean
Dispersion value	0.47

Adverse events

Adverse events information	
Timeframe for reporting adverse events: To death or 90 day follow up.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups	
Reporting group title	Comparator
Reporting group description: Alteplase 0.9 mg/kg with 10% of the total dose administered as an initial intravenous bolus and remaining 90% of the total dose administered as an intravenous infusion over 1 hour.	
Reporting group title	Test (Tenecteplase)
Reporting group description: Tenecteplase 0.25 mg/kg administered as a single rapid IV bolus	

Serious adverse events	Comparator	Test (Tenecteplase)	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 51 (31.37%)	22 / 52 (42.31%)	
number of deaths (all causes)	6	8	
number of deaths resulting from adverse events	6	8	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant glioma			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			

Endarterectomy			
subjects affected / exposed	1 / 51 (1.96%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal tube insertion			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hospitalisation			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint resurfacing surgery			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pulmonary sepsis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urosepsis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Postmenopausal haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	2 / 51 (3.92%)	2 / 52 (3.85%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Pulmonary embolism			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional self-injury			

subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Biopsy uterus			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hysteroscopy			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 51 (1.96%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 51 (1.96%)	3 / 52 (5.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	5 / 51 (9.80%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	5 / 5	0 / 0	
deaths causally related to treatment / all	3 / 3	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 51 (1.96%)	2 / 52 (3.85%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 2	
Embolic stroke			

subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 51 (1.96%)	3 / 52 (5.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			

subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Mobility decreased			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchopneumopathy			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Comparator	Test (Tenecteplase)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant glioma			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Deep vein thrombosis			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	2	1	
Haematoma			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Haemorrhage			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Phlebitis			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	2	
Surgical and medical procedures			
Cardiac pacemaker insertion			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Carotid endarterectomy			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	2	1	
Cataract operation			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	

Hospitalisation			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Joint resurfacing surgery			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	3	
Device occlusion			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Drug withdrawal syndrome			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Gait disturbance			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
General physical health deterioration			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Non-cardiac chest pain			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	2	2	
Pneumonia aspiration			

subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	7	9	
Pulmonary embolism			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	2	
Respiratory disorder			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Wheezing			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Psychiatric disorders			
Agitation			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	3	
Depression			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	2	1	
Intentional self-injury			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Investigations			
Blood glucose increased			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Hysteroscopy			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	4	3	
Scratch			

subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Wound haemorrhage			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	1	
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Atrial flutter			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Atrial tachycardia			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Atrial fibrillation			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	2	6	
Bradycardia			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	1	
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	4	1	
Cerebrovascular accident			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	1	
Convulsions local			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	2	
Embolic stroke			

subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Haemorrhage intracranial			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	3	2	
Haemorrhagic transformation stroke			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	8	3	
Headache			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	4	
Intracranial aneurysm			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Partial seizures			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Visual field defect			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Polycythaemia			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Eye disorders			
Blindness			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Constipation			

subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	5	4	
Diarrhoea			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Gingival bleeding			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Haematemesis			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Melaena			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Rectal haemorrhage			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	

Renal and urinary disorders			
Renal failure			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	1	
Renal impairment			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Urinary retention			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	1	
Arthropathy			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	2	0	
Joint swelling			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	1	
Musculoskeletal pain			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchopneumopathy			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Gastroenteritis viral			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	1	

Lower respiratory tract infection			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	2	2	
Pneumonia			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	2	0	
Sepsis			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	1	3	
Urinary tract infection			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	2	7	
Urosepsis			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	2	
Vulvovaginal candidiasis			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Gout			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	
Hyponatraemia			
subjects affected / exposed	36 / 51 (70.59%)	42 / 52 (80.77%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 November 2011	Protocol amendment addressing points raised by the MHRA during its review. Within NHS GG&C the amended protocol (version 2) was approved as part of the Health Board management approval process
09 October 2012	Protocol v2.1 - Addition of definition of acronym (TAT) - Additional tests added (blood test for future coagulation assays) and wording to describe need for additional test - Additional evidence on test drug - Additional wording regarding witnessed verbal consent - Introduction of additional consent form (witnessed verbal consent)

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.

The baseline characteristics 'reporting groups' data is dummy data as we do not have the data for 104 patients. Data only for 96 patients, as 8 patient excluded as final diagnosis as non-stroke.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25726502