Clinical trial results:
STOP-AUST: The Spot sign and Tranexamic acid On Preventing ICH growth – AUStralasia Trial

Summary

EudraCT number	2013-001262-42
Trial protocol	FI
Global end of trial date	13 November 2019

Results information

Result version number	v1 (current)
This version publication date	06 December 2020
First version publication date	06 December 2020

Trial information

Trial identification

Sponsor protocol code	NTA1201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01702636
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	The Florey Institute of Neuroscience and Mental Health
Sponsor organisation address	245 Burgundy Street, Heidelberg, Australia, VIC 3084
Public contact	Neuroscience Trials Australia, The Florey Institute of Neuroscience and Mental Health, 61 3-9035-7232,
Scientific contact	Neuroscience Trials Australia, The Florey Institute of Neuroscience and Mental Health, 61 3-9035-7232,

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	28 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 November 2019
Global end of trial reached?	Yes
Global end of trial date	13 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To test the hypothesis that ICH patients selected with CTA "spot sign" will have lower rates of haematoma growth when treated with intravenous tranexamic acid within 4.5 hours of stroke onset, compared to placebo.

Protection of trial subjects:

Independent data monitoring committee, according to charter.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 December 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 23
Country: Number of subjects enrolled	Australia: 65
Country: Number of subjects enrolled	Taiwan: 12
Worldwide total number of subjects	100
EEA total number of subjects	23

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)	100
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

We recruited 100 participants between March 1, 2013, and Aug 13, 2019.

Pre-assignment

Screening details:

3325 patients with intracerebral patients seen at 7 hospitals during trial recruitment period (2.6 % of patients recruited into the trial).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Tranexamic acid

Arm description: -

Arm type	Experimental
Investigational medicinal product name	tranexamic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1 gram tranexamic acid in 100 mL NaCl 0.9% infusion over 10 minutes followed by 1 gram tranexamic acid in 500 mL NaCl 0.9% infusion over 8 hours.

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	NaCl 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

10 mL NaCl 0.9% in 100 mL NaCl 0.9% infusion over 10 minutes followed by 10 mL NaCl 0.9% in 500 mL NaCl 0.9% infusion over 8 hours.

Number of subjects in period 1	Tranexamic acid	Placebo
Started	50	50
Completed	50	50

Baseline characteristics

Reporting groups	
Reporting group title	Tranexamic acid
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Tranexamic acid	Placebo	Total
Number of subjects	50	50	100
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			
median	73	71	
inter-quartile range (Q1-Q3)	55 to 78	58 to 79	-
Gender categorical			
Units: Subjects			
Female	15	23	38
Male	35	27	62

Subject analysis sets	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Intention to treat full analysis set	

Reporting group values	ITT		
Number of subjects	100		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			

Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years median inter-quartile range (Q1-Q3)	 71 57 to 79		
Gender categorical Units: Subjects			
Female Male	38 62		

End points

End points reporting groups	
Reporting group title	Tranexamic acid
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: Intention to treat full analysis set	

Primary: intracerebral haemorrhage growth of at least 33% or 6 mL from baseline	
End point title	intracerebral haemorrhage growth of at least 33% or 6 mL from baseline
End point description:	
End point type	Primary
End point timeframe: 24 h (±3) after start of study drug	

End point values	Tranexamic acid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: 2	22	26		

Statistical analyses

Statistical analysis title	Primary outcome
Comparison groups	Tranexamic acid v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.41
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	1.59

Secondary: absolute intracerebral haemorrhage growth volume

End point title	absolute intracerebral haemorrhage growth volume
End point description:	
End point type	Secondary
End point timeframe:	
24 h +/- 3h	

End point values	Tranexamic acid	Placebo	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	49	50	99	
Units: mL				
median (inter-quartile range (Q1-Q3))	1.9 (0.2 to 9.5)	3.4 (0.0 to 16.0)	2.7 (0.1 to 13.7)	

Statistical analyses

Statistical analysis title	absolute ICH growth
Comparison groups	Tranexamic acid v Placebo
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.28
Method	median regression
Parameter estimate	Median difference (final values)
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.2
upper limit	1.5

Secondary: absolute intraventricular haemorrhage growth

End point title	absolute intraventricular haemorrhage growth
End point description:	
End point type	Secondary
End point timeframe:	
24 +/- 3 h	

End point values	Tranexamic acid	Placebo	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	49	50	99[1]	
Units: mL				
median (inter-quartile range (Q1-Q3))	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.6)	0.0 (0.0 to 0.0)	

Notes:

[1] - Missing data for one tranexamic acid patient.

Statistical analyses

Statistical analysis title	absolute intraventricula haemorrhage growth
Comparison groups	Tranexamic acid v Placebo
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.99
Method	median regression
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Secondary: mRS 0–4 or return to prestroke score at 90 days	
End point title	mRS 0–4 or return to prestroke score at 90 days

End point description:

End point type	Secondary

End point timeframe:

90 days

End point values	Tranexamic acid	Placebo	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	50	50	100	
Units: mRS 0-4 or back to prestroke	34	40	74	

Statistical analyses

Statistical analysis title	mRS 0-4 or back to baseline
Comparison groups	Tranexamic acid v Placebo v ITT
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	1.23

Secondary: mRS 0–3 or return to prestroke score at 90 days	
End point title	mRS 0–3 or return to prestroke score at 90 days
End point description:	
End point type	Secondary
End point timeframe:	
90 days	

End point values	Tranexamic acid	Placebo	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	50	50	100	
Units: mRS 0-3 or back to prestroke	28	23	51	

Statistical analyses

Statistical analysis title	mRS 0-3 or back to baseline
Comparison groups	Placebo v Tranexamic acid v ITT
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.31
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.64

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	4.24

Secondary: categorical shift in mRS at 90 days

End point title	categorical shift in mRS at 90 days

End point description:

End point type	Secondary

End point timeframe:

90 days

End point values	Tranexamic acid	Placebo	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	50	50	100	
Units: OR				
number (confidence interval 95%)	1.01 (0.63 to 1.61)	1.01 (0.63 to 1.61)	1.01 (0.63 to 1.61)	

Statistical analyses

Statistical analysis title	mRS categorical shift
Comparison groups	Tranexamic acid v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.97
Method	assumption-free Wilcoxon-Mann-Whitney ge
Parameter estimate	Odds ratio (OR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.61

Notes:

[2] - assumption-free Wilcoxon-Mann-Whitney generalised OR

Secondary: major thromboembolic events

End point title	major thromboembolic events

End point description:

End point type	Secondary

End point timeframe:
90 days

End point values	Tranexamic acid	Placebo	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	50	50	100	
Units: Number of events	1	2	3	

Statistical analyses

Statistical analysis title	major thromboembolic events
Comparison groups	Tranexamic acid v Placebo v ITT
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.57
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	5.58

Secondary: Death

End point title	Death

End point description:

End point type	Secondary

End point timeframe:
90 days

End point values	Tranexamic acid	Placebo	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	50	50	100	
Units: Deaths				
number (confidence interval 95%)	13 (13 to 13)	8 (8 to 8)	2.38 (0.66 to 8.67)	

Statistical analyses

Statistical analysis title	death within 90 days
Comparison groups	Tranexamic acid v Placebo v ITT
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.19
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	8.67

Adverse events

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

Dictionary used	
Dictionary name	NA
Dictionary version	NA

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: Not reported.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33128912