Clinical trial results:
A randomised controlled trial of topical intranasal tranexamic acid versus placebo to reduce the need for nasal packing in patients presenting to the Emergency Department with spontaneous epistaxis.

Summary

EudraCT number	2016-001530-10
Trial protocol	GB
Global end of trial date	22 July 2019

Results information

Result version number	v1 (current)
This version publication date	02 August 2020
First version publication date	02 August 2020

Trial information

Trial identification

Sponsor protocol code	NoPac01

Additional study identifiers

ISRCTN number	ISRCTN34153772
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	IRAS: 197027, EudraCT: 2016-001530-10

Notes:

Sponsors

Sponsor organisation name	Royal Devon & Exeter NHS Foundation Trust
Sponsor organisation address	Bowmoor House, Wonford Road, Exeter, United Kingdom, EX2 5DW
Public contact	Clinical Trial Manager, Peninsula Clinical Trials Unit, 44 (0)1752 315252, nopac@plymouth.ac.uk
Scientific contact	Clinical Trial Manager, Peninsula Clinical Trials Unit, 44 (0)1752 315252, nopac@plymouth.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	Final
Date of interim/final analysis	24 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 July 2019
Global end of trial reached?	Yes
Global end of trial date	22 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the study is to test the effectiveness of topical intranasal tranexamic acid (TXA) in reducing the need for anterior nasal packing in adult patients presenting to the Emergency Department (ED) with spontaneous. The objectives are to compare the effect of topical TXA versus placebo on the need for nasal packing; need for hospital admission; subsequent length of hospital stay; requirement for blood products; re-bleeding rate for patients subsequently discharged from the ED; adverse events, including thrombotic complications.

In lay language, the research question is: For patients attending the Emergency Department (Accident and Emergency) with a serious nosebleed, can tranexamic acid applied inside the bleeding nostril reduce the need for nasal packing (a large dressing filling the nostril)?

Protection of trial subjects:

Specific measures that were put in place to protect trial subjects, for example measures to minimise pain and distress, were:
1) An epistaxis nasal clip was provided for each participant. The use of the nasal clip allowed patients to read the study information and take part in the consent process unimpeded by having to hold their nose during this time.
2) In the event that the patient was willing to participate in the study but was unable to sign and/or date the consent form because of practical difficulties (e.g. unable easily to hold a pen due to contamination of hands with blood), a witness may sign and/or date the consent form on the patient's behalf.

Background therapy:

Treatments that were not test or comparator products that were used across all arms/groups in this trial were:

During the index ED attendance:
Standardised vasoconstrictor therapy (not formally part of the study i.e. not part of the research process requiring participant consent):Phenylephedrine and lignocaine; adrenaline and lignocaine; adrenaline; cocaine HCL/Spray; lignocaine.

During the index ED attendance and/or during the follow-up period:
Nasal cautery; intranasal vasoconstrictor; TXA; resorbable nasal pack; Vitamin K; nasal ligation; blood transfusion (the majority of participants who required a blood transfusion were given packed red cells).

Evidence for comparator:

The rationale for the comparator used in this trial, i.e. water for injection (for topical use), is that the excipient for the active IMP is water for injection. On inspection, the comparator is indistinguishable to the active IMP by sight, taste or smell.

Actual start date of recruitment	05 May 2017
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: 496
Worldwide total number of subjects	496
EEA total number of subjects	496

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)	136
From 65 to 84 years	274
85 years and over	86

Subject disposition

Recruitment

Recruitment details:

A total of 496 participants were recruited to this trial, from 5 May 2017 to 31 March 2019, from 25 NHS hospitals in the UK (24 hospitals in England; 1 in Scotland).

Pre-assignment

Screening details:

Inclusion criteria: aged 18 or over; present to the ED with spontaneous, atraumatic epistaxis, unresolved with simple first aid and standard initial therapy. Exclusion criteria apply.

Pre-assignment period milestones

Number of subjects started	496
Number of subjects completed	496

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Control

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Water for injections
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Impregnated plug
Routes of administration	Intranasal use

Dosage and administration details:

Up to two doses of placebo may be given, each dose being approximately 2mL of water for injections. One dental roll (supplied) will be inserted into the vial of trial solution and soaked in the allocated trial solution until saturated. This will leave approximately half of the 4mL trial solution in the vial. The soaked dental roll will be inserted into the bleeding nostril and gentle pressure applied with an epistaxis nasal clip for at least ten minutes. If the epistaxis persists (as defined by the presence of fresh blood on the upper lip or philtrum after wiping), a second dental roll should be soaked in the remaining trial solution until saturated or no solution remains. The saturated roll will be inserted into the affected nostril, with gentle pressure applied for at least a further ten minutes.

Arm title	Active

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Tranexamic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Impregnated plug
Routes of administration	Intranasal use

Dosage and administration details:

Up to two doses of active IMP may be given, each dose being approximately 2mL of 100mg/mL TXA in

water for injection. One dental roll (supplied) will be inserted into the vial of trial solution and soaked in the allocated trial solution until saturated. This will leave approximately half of the 4mL trial solution in the vial. The soaked dental roll will be inserted into the bleeding nostril and gentle pressure applied with an epistaxis nasal clip for at least ten minutes. If the epistaxis persists (as defined by the presence of fresh blood on the upper lip or philtrum after wiping), a second dental roll should be soaked in the remaining trial solution until saturated or no solution remains. The saturated roll will be inserted into the affected nostril, with gentle pressure applied for at least a further ten minutes.

Number of subjects in period 1	Control	Active
Started	242	254
Completed	242	254

Period 2	
Period 2 title	Overall Trial
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Assessor

Arms	
Are arms mutually exclusive?	Yes
Arm title	Control

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Water for injections
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Impregnated plug
Routes of administration	Intranasal use

Dosage and administration details:

Up to two doses of placebo may be given, each dose being approximately 2mL of water for injections. One dental roll (supplied) will be inserted into the vial of trial solution and soaked in the allocated trial solution until saturated. This will leave approximately half of the 4mL trial solution in the vial. The soaked dental roll will be inserted into the bleeding nostril and gentle pressure applied with an epistaxis nasal clip for at least ten minutes. If the epistaxis persists (as defined by the presence of fresh blood on the upper lip or philtrum after wiping), a second dental roll should be soaked in the remaining trial solution until saturated or no solution remains. The saturated roll will be inserted into the affected nostril, with gentle pressure applied for at least a further ten minutes.

Arm title	Active

Arm description: -

Arm type	Experimental

Investigational medicinal product name	Tranexamic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Impregnated plug
Routes of administration	Intranasal use

Dosage and administration details:

Up to two doses of active IMP may be given, each dose being approximately 2mL of 100mg/mL TXA in water for injections. One dental roll (supplied) will be inserted into the vial of trial solution and soaked in the allocated trial solution until saturated. This will leave approximately half of the 4mL trial solution in the vial. The soaked dental roll will be inserted into the bleeding nostril and gentle pressure applied with an epistaxis nasal clip for at least ten minutes. If the epistaxis persists (as defined by the presence of fresh blood on the upper lip or philtrum after wiping), a second dental roll should be soaked in the remaining trial solution until saturated or no solution remains. The saturated roll will be inserted into the affected nostril, with gentle pressure applied for at least a further ten minutes.

Number of subjects in period 2	Control	Active
Started	242	254
Completed	242	254

Baseline characteristics

Reporting groups	
Reporting group title	Control
Reporting group description: -	
Reporting group title	Active
Reporting group description: -	

Reporting group values	Control	Active	Total
Number of subjects	242	254	496
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	72.3	70.1	
standard deviation	± 13.9	± 15.6	-
Gender categorical Units: Subjects			
Female	100	126	226
Male	142	128	270
Anticoagulant medication Units: Subjects			
No	76	99	175
Yes	166	155	321
Hypertension Units: Subjects			
No	93	101	194
Yes	149	153	302
Ischemic heart disease Units: Subjects			
No	183	205	388
Yes	59	49	108
Diabetes Units: Subjects			
No	204	221	425
Yes	38	33	71
Thromboembolic disease Units: Subjects			

No	226	228	454
Yes	16	26	42
Alcoholic liver disease Units: Subjects			
No	241	252	493
Yes	1	2	3
Any bleeding disorder Units: Subjects			
No	234	249	483
Yes	8	5	13
Systolic blood pressure Units: mm/Hg			
arithmetic mean	150.7	150.2	
standard deviation	± 25.8	± 27.9	-
Diastolic blood pressure Units: mm/Hg			
arithmetic mean	87.0	85.8	
standard deviation	± 15.3	± 18.4	-
Pulse Units: bpm			
arithmetic mean	82.2	82.6	
standard deviation	± 16.6	± 17.2	-

End points

End points reporting groups

Reporting group title	Control
Reporting group description: -	
Reporting group title	Active
Reporting group description: -	
Reporting group title	Control
Reporting group description: -	
Reporting group title	Active
Reporting group description: -	
Subject analysis set title	Placebo Treatment Compliant
Subject analysis set type	Per protocol
Subject analysis set description:	
Placebo treatment group excluding any participant who did not complete the first dose or second dose (if indicated).	
Subject analysis set title	TXA Treatment Compliant
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants allocated to TXA excluding any participant who did not complete the first dose or second dose (if indicated).	
Subject analysis set title	Placebo Protocol Compliant
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants allocated to placebo excluding any participant who did receive vasoconstrictor therapy prior to the trial intervention and/or did not complete the first dose or second dose (if indicated).	
Subject analysis set title	TXA Protocol Compliant
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants allocated to TXA excluding any participant who did receive vasoconstrictor therapy prior to the trial intervention and/or did not complete the first dose or second dose (if indicated).	
Subject analysis set title	Placebo Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants allocated to placebo in the safety population. The safety population is those in the ITT population who have at least one (of the possible two) dental rolls soaked in the allocated solution, fully inserted into their nose (even if removed before the intended 10 minutes).	
Subject analysis set title	TXA Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants allocated to TXA in the safety population. The safety population is those in the ITT population who have at least one (of the possible two) dental rolls soaked in the allocated solution, fully inserted into their nose (even if removed before the intended 10 minutes).	
Subject analysis set title	Placebo - anticoagulant
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
subjects in the placebo group on anticoagulant medication	
Subject analysis set title	TXA - anticoagulant
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants allocated to TXA on anticoagulant medication	
Subject analysis set title	Placebo - no anticoagulant
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants allocated to placebo not on anticoagulant medication

Subject analysis set title	TXA - no anticoagulant
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants allocated to TXA not taking anticoagulant medication

Primary: Proportion of subjects with anterior nasal packing in index ED visit

End point title	Proportion of subjects with anterior nasal packing in index ED visit

End point description:

End point type	Primary

End point timeframe:

Index ED

End point values	Control	Active	Placebo Treatment Compliant	TXA Treatment Compliant
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	242	254	227	246
Units: 496				
No	142	143	137	141
Yes	100	111	90	106

End point values	Placebo Protocol Compliant	TXA Protocol Compliant	Placebo - anticoagulant	TXA - anticoagulant
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	224	242	166	155
Units: 496				
No	135	136	96	83
Yes	89	106	70	72

End point values	Placebo - no anticoagulant	TXA - no anticoagulant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	76	99		
Units: 496				
No	46	60		
Yes	30	39		

Statistical analyses

Statistical analysis title	Primary analysis
Statistical analysis description:	
Binomial logistic regression to compare allocated groups	
Comparison groups	Active v Control
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.585
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.107
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.769
upper limit	1.594

Notes:

[1] - Mixed effects logistic regression, adjusting for study center as a random effect and allocated group as a fixed effect.

Statistical analysis title	Sensitivity Analysis Treatment PP
Statistical analysis description:	
Logistic regression	
Comparison groups	Placebo Treatment Compliant v TXA Treatment Compliant
Number of subjects included in analysis	473
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.346
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.822
upper limit	1.752

Notes:

[2] - Mixed effects logistic regression, adjusting for study center as a random effect and allocated group as a fixed effect.

Statistical analysis title	Sensitivity Analysis Compliance PP
Comparison groups	Placebo Protocol Compliant v TXA Protocol Compliant
Number of subjects included in analysis	466
Analysis specification	Post-hoc
Analysis type	superiority[3]
P-value	= 0.374
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.182

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.818
upper limit	1.71

Notes:

[3] - Mixed effects logistic regression, adjusting for study center as a random effect and allocated group as a fixed effect.

Statistical analysis title	Sub-group analysis

Statistical analysis description:

Sub-group analysis to see if there might be an interaction between allocated groups and anticoagulant medication.

Comparison groups	Placebo - no anticoagulant v TXA - no anticoagulant v TXA - anticoagulant v Placebo - anticoagulant
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	other[4]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.288
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.591
upper limit	2.809

Notes:

[4] - mixed effects logistic regression model, adjusting for study center as a random effect. Interpretation focused on the interaction between anticoagulant medication and allocated group as a fixed effect. Interpretations were exploratory.

Primary: Any Packing during index ED or after

End point title	Any Packing during index ED or after

End point description:

A slight modification to the definition of the primary outcome, need for packing during the indexed ED admission or after.

End point type	Primary

End point timeframe:

Overall trial

End point values	Control	Active		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	254		
Units: 496				
No	125	120		
Yes	117	134		

Statistical analyses

Statistical analysis title	Sensitivity Analysis
Statistical analysis description:	
Sensitivity analysis on a modification of the primary outcome	
Comparison groups	Control v Active
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.312
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.204
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.752

Notes:

[5] - Mixed effects logistic regression adjusting for study center as a random effect and allocated group as a fixed effect.

Secondary: Any ED treatment

End point title	Any ED treatment
End point description:	
any treatment for epistaxis during the indexed ED visit	
End point type	Secondary
End point timeframe:	
Indexed ED	

End point values	Control	Active		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	254		
Units: 496				
No	95	97		
Yes	147	157		

Statistical analyses

Statistical analysis title	Primary analysis
Comparison groups	Active v Control
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.807
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.046

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.729
upper limit	1.501

Notes:

[6] - Mixed effects binomial logistic regression comparing allocated groups adjusting for study center as a random effect

Secondary: Hospital admission

End point title	Hospital admission

End point description:

Hospital admission following ED visit

End point type	Secondary

End point timeframe:

Overall

End point values	Control	Active		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	254		
Units: 496				
No	132	144		
Yes	110	110		

Statistical analyses

Statistical analysis title	Primary analysis
Comparison groups	Control v Active
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.63
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.917
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.643
upper limit	1.307

Notes:

[7] - Mixed effects logistic regression, adjusting for study center as a random effect and allocated group as a fixed effect.

Secondary: Length of hospital stay

End point title	Length of hospital stay

End point description:

End point type	Secondary

End point timeframe:
overall trial

End point values	Control	Active		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	254		
Units: 496				
median (inter-quartile range (Q1-Q3))	2 (1 to 3)	1.5 (1 to 2)		

Statistical analyses

Statistical analysis title	Primary analysis
Comparison groups	Control v Active
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.651
Method	Regression, negative binomial
Parameter estimate	between group difference
Point estimate	0.049
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.185
upper limit	0.282

Notes:
[8] - Mixed effects, negative binomial, regression model

Secondary: Blood transfusion

End point title	Blood transfusion

End point description:

End point type	Secondary

End point timeframe:
overall trial

End point values	Control	Active		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	254		
Units: 496				
No	236	247		
Yes	6	7		

Statistical analyses

Statistical analysis title	Primary analysis
Comparison groups	Control v Active
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.847
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.115
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.369
upper limit	3.365

Notes:

[9] - Mixed effects logistic regression, adjusting for study center as a random effect and allocated group as a fixed effect.

Secondary: Recurrent epistaxis

End point title	Recurrent epistaxis

End point description:

End point type	Secondary

End point timeframe:

overall trial

End point values	Control	Active		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	252[10]		
Units: 494				
No	203	203		
Yes	39	49		

Notes:

[10] - Two participants were missing outcome data

Statistical analyses

Statistical analysis title	Primary analysis
Comparison groups	Control v Active
Number of subjects included in analysis	494
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.335
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.257
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	2.002

Notes:

[11] - Mixed effects logistic regression, adjusting for study center as a random effect and allocated group as a fixed effect.

Secondary: Thrombotic evens

End point title	Thrombotic evens

End point description:

End point type	Secondary

End point timeframe:

overall trial

End point values	Control	Active		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	251[12]		
Units: 493				
No	241	251		
Yes	1	0		

Notes:

[12] - Missing outcome data on three participants

Statistical analyses

No statistical analyses for this end point

Secondary: Any treatment for epistaxis

End point title	Any treatment for epistaxis

End point description:

Any treatment of epistaxis during index ED visit or 7 days post discharge

End point type	Secondary

End point timeframe:

overall trial

End point values	Control	Active		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	254		
Units: 496				
No	68	70		
yes	174	184		

Statistical analyses

Statistical analysis title	Primary analysis
Comparison groups	Control v Active
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.836
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.043
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.697
upper limit	1.561

Notes:

[13] - Mixed effects logistic regression, adjusting for study center as a random effect and allocated group as a fixed effect.

Secondary: Adverse reactions

End point title	Adverse reactions

End point description:

End point type	Secondary

End point timeframe:

Overall trial

End point values	Placebo Safety	TXA Safety		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	241[14]	254		
Units: 495				
No	238	245		
Yes	3	9		

Notes:
[14] - 1 participant did not have any trial treatment

Statistical analyses

Statistical analysis title	Safety Analysis
Comparison groups	Placebo Safety v TXA Safety
Number of subjects included in analysis	495
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.111
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.975
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.779
upper limit	11.353

Notes:
[15] - Mixed effects logistic regression, adjusting for study center as a random effect and allocated group as a fixed effect.

Secondary: Serious adverse events

End point title	Serious adverse events

End point description:

End point type	Secondary

End point timeframe:
Overall trial

End point values	Placebo Safety	TXA Safety		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	241[16]	254		
Units: 495				
No	236	244		
Yes	5	10		

Notes:
[16] - 1 participant did not begin trial treatment

Statistical analyses

Statistical analysis title	Safety Analysis
Comparison groups	Placebo Safety v TXA Safety

Number of subjects included in analysis	495
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.235
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.935
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.651
upper limit	5.745

Notes:

[17] - mixed effects logistic regression model, adjusting for study center as a random effect and allocated group as a fixed effect.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall trial

Adverse event reporting additional description:

AE additional description

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Experimental

Reporting group description: -

Reporting group title	Control

Reporting group description: -

Serious adverse events	Experimental	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 254 (4.33%)	5 / 242 (2.07%)	
number of deaths (all causes)	3	2	
number of deaths resulting from adverse events	3	2	
Investigations			
Investigations	Additional description: Investigations		
subjects affected / exposed	1 / 254 (0.39%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Additional description: Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
subjects affected / exposed	1 / 254 (0.39%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Vascular disorders	Additional description: Vascular disorders		
subjects affected / exposed	1 / 254 (0.39%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Cardiac disorders	Additional description: Cardiac disorders		
subjects affected / exposed	2 / 254 (0.79%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Nervous system disorders			
Nervous system disorders	Additional description: Nervous system disorders		
subjects affected / exposed	2 / 254 (0.79%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	3 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Blood and lymphatic system disorders	Additional description: Blood and lymphatic system disorders		
subjects affected / exposed	1 / 254 (0.39%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: Gastrointestinal disorders		
subjects affected / exposed	1 / 254 (0.39%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: Respiratory, thoracic and mediastinal disorders		
subjects affected / exposed	2 / 254 (0.79%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infections and infestations			
Infections and infestations	Additional description: Infections and infestations		
subjects affected / exposed	2 / 254 (0.79%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

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

Non-serious adverse events	Experimental	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 254 (2.76%)	3 / 242 (1.24%)	
Nervous system disorders			
Nervous system disorders	Additional description: Nervous system disorders		
subjects affected / exposed	5 / 254 (1.97%)	2 / 242 (0.83%)	
occurrences (all)	5	2	
General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: General disorders and administration site conditions		
subjects affected / exposed	2 / 254 (0.79%)	1 / 242 (0.41%)	
occurrences (all)	2	1	

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None.

Notes: