Clinical trial results:
Tranexamic acid in major vascular surgery (Tranex-AAA)

Summary

EudraCT number	2014-001456-39
Trial protocol	IT
Global end of trial date	01 February 2019

Results information

Result version number	v1 (current)
This version publication date	17 February 2022
First version publication date	17 February 2022

Trial information

Trial identification

Sponsor protocol code	Tranex-AAA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02335359
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IRCCS Ospedale San Raffaele
Sponsor organisation address	Via Olgettina, 60, Milano, Italy, 20132
Public contact	Dip di Anestesia e Rianimazione, IRCCS Ospedale San Raffaele , 0039 0226436151, landoni.giovanni@hsr.it
Scientific contact	Dip di Anestesia e Rianimazione, IRCCS Ospedale San Raffaele , 0039 0226436151, landoni.giovanni@hsr.it

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 February 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study was to determine if tranexamic acid reduces blood loss in open abdominal aortic aneurysm (AAA) surgery.

Protection of trial subjects:

Approval by the local Ethics Committee was obtained before the beginning of the study and written informed consent was obtained from all patients at time of enrolment. Patients care was carried out by a multidisciplinary team, including 14 vascular surgeons (five first operators) and 10 anaesthesiologists. All patients underwent a full preoperative work-up. Non-aspirin antiplatelet agents were discontinued before surgery whereas aspirin was continued throughout the perioperative period. Warfarin was stopped 5 days before surgery, whereas novel oral anticoagulants were suspended 48 h before surgery. To prevent deep venous thrombosis and pulmonary thromboembolism, all patients received 4000 units of low molecular weight heparin once a day, from the evening before surgery until 4 weeks after surgery. Patient undergoing open AAA repair at our institution receive an enhanced recovery after surgery (ERAS) approach, which has been adopted since 2012.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 March 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 100
Worldwide total number of subjects	100
EEA total number of subjects	100

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)	27
From 65 to 84 years	73
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This single-centre, double-blinded, parallel-group, randomised clinical trial involved 100 patients older than 50yr undergoing open AAA surgical repair. Patients were asked to signed informed consent form on the day before surgery. Patients were enrolled between March 2015 and October 2017. One year of follow up was completed in November 2018

Pre-assignment

Screening details:

Patients undergoing urgent surgery, noncollaborating or psychiatric, with known history of allergy to tranexamic acid, seizures, acute venous or arterial thrombosis, fibrinolytic conditions, severe renal insufficiency , haematuria, and with ocular disturbances, including blurred vision, poor sight or altered colour perception were excluded.

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

Blinding implementation details:

Trial participants, care providers, and data collectors were blinded to group assignment. The treatment was prepared by a nurse who was not involved in the study or in the care of the patient.The bottle with the loading dose and the syringe for continuous i.v. infusion were labelled only with the acronym of the trial and the number of randomisation of the patient; bottles containing tranexamic acid and those containing placebo were indistinguishable

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	Ugurol
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

A loading dose of 500 mg of tranexamic acid diluted in 100 ml saline was intravenously infused slowly 20 min before surgery, and a continuous intravenous infusion of tranexamic acid was then administered at a rate of 250 mg h-1 (2.5 ml h-1, using nondiluted tranexamic acid contained in the vials) from surgical incision until skin closure

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Sodium Chloride 0.9%
Investigational medicinal product code	
Other name	Saline solution
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients randomised to the control group received placebo with identical volumes and rates of infusion of patients randomised to the experimental group.

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			
Adults (18-64 years)	18	9	27
From 65-84 years	32	41	73
Gender categorical Units: Subjects			
Female	7	0	7
Male	43	50	93

End points

End points reporting groups	
Reporting group title	Tranexamic Acid
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Intraoperative blood loss	
End point title	Intraoperative blood loss
End point description:	
End point type	Primary
End point timeframe:	
At the end of the surgery	

End point values	Tranexamic Acid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: millilitre(s)				
median (inter-quartile range (Q1-Q3))	400 (300 to 1050)	500 (360 to 1000)		

Statistical analyses

Statistical analysis title	Groups comparation
Comparison groups	Tranexamic Acid v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Patients receiving RBC	
End point title	Patients receiving RBC
End point description:	
End point type	Secondary
End point timeframe:	
During surgery and until hospital discharge	

End point values	Tranexamic Acid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: number	6	10		

Statistical analyses

Statistical analysis title	Groups comparation
Comparison groups	Tranexamic Acid v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared corrected

Secondary: 28-day mortality

End point title	28-day mortality

End point description:

End point type	Secondary

End point timeframe:

28 days after surgery

End point values	Tranexamic Acid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: number	0	0		

Statistical analyses

Statistical analysis title	Groups comparation
Comparison groups	Tranexamic Acid v Placebo

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared corrected

Secondary: 1-yr mortality

End point title	1-yr mortality

End point description:

End point type	Secondary

End point timeframe:

1 year after surgery

End point values	Tranexamic Acid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: number	0	3		

Statistical analyses

Statistical analysis title	Groups comparation
Comparison groups	Tranexamic Acid v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared corrected

Secondary: Occurrence of thromboembolic events

End point title	Occurrence of thromboembolic events

End point description:

End point type	Secondary

End point timeframe:

28-days and one year after surgery

End point values	Tranexamic Acid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: number	0	0		

Statistical analyses

Statistical analysis title	Groups comparation
Comparison groups	Tranexamic Acid v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared corrected

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: During hospitalization and during follow-up phone calls	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20

Frequency threshold for reporting non-serious adverse events: 5 %

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: No non-serious adverse event associated to the IMPs were recorded.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 December 2014	Changes to protocol (inclusion criteria - concomitant medication) and informed consent form relating to safety and integrity of subjects

Notes:

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/31607387