Clinical trial results:
Peroperative Tranexamic acid as prophylaxis of bleeding related to benign hysterectomy - a randomized, placebo-controlled trial

Summary

EudraCT number	2012-005407-40
Trial protocol	DK
Global end of trial date	30 December 2014

Results information

Result version number	v1 (current)
This version publication date	18 February 2022
First version publication date	18 February 2022

Trial information

Trial identification

Sponsor protocol code	2011-425

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01940419
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hillerød Hospital
Sponsor organisation address	Dyrehavevej 18, HIllerød, Denmark, 3400
Public contact	Märta Fink Topsøe, Hillerød Hospital, department of gynecology and obstetrics, 0045 28 41 48 17, Maerta.Topsoee-Jensen@regionh.dk
Scientific contact	Märta Fink Topsøe, Hillerød Hospital, department of gynecology and obstetrics, 0045 28 41 48 17, Maerta.Topsoee-Jensen@regionh.dk
Sponsor organisation name	Nordsjællands Hospital
Sponsor organisation address	Dyrehavevej 18, Hillerød, Denmark, 3400
Public contact	Professor Ellen Løkkegaard, Hillerød Hospital, 0045 48294829, Ellen.Christine.Leth.Loekkegaard@regionh.dk
Scientific contact	Professor Ellen Løkkegaard, Hillerød Hospital, 0045 48294829, Ellen.Christine.Leth.Loekkegaard@regionh.dk

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	18 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 December 2014
Global end of trial reached?	Yes
Global end of trial date	30 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the study is primarily to investigate Tranexamic acid's impact on preventing perioperative bleeding in benign hysterectomy. This will be investigated both by individual assessment of the intraoperative bleeding in ml, and by using relevant quantitative and qualitative secondary endpoints. The results are also expected to indicate a possible effect of Tranexamic acid on the number of actual intra- and postoperative bleeding complications, and may in this respect be considered as a pilot study.

Protection of trial subjects:

None as the intervention under study was not considered harmful during trial.

Background therapy:

Standard operative techniques, anaesthesi and pain-treatment in relation to conventional Hysterectomy.

Evidence for comparator: -

Actual start date of recruitment	31 March 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 342
Worldwide total number of subjects	342
EEA total number of subjects	342

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)	298
From 65 to 84 years	43
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Potential participants were identified and screened at the 4 participating Departments if they were scheduled for hysterectomy for any benign indication.

Pre-assignment

Screening details:

All potentially eligible women were informed about the study by a physician or a research nurse. They were excluded if they had thrombophilia, active thrombotic disease, any allergy to Tranexamic Acid, renal impairment, hematuria, malignant disease or received any anti-thrombotic medication.

Pre-assignment period milestones

Number of subjects started	342
Number of subjects completed	332

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 5
Reason: Number of subjects	Physician decision: 1
Reason: Number of subjects	Surgery postponed: 4

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description:

Intervention

Arm type	Placebo
Investigational medicinal product name	Tranexamic Acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Tranexamic Acid 1 gram intravenously

Arm title	Placebo

Arm description:

Placebo

Arm type	Placebo

Investigational medicinal product name	sodium chloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

100 ml intravenously

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: The intervention was blinded to the participants as well as the assessors.

Number of subjects in period 1[2]	Intervention	Placebo
Started	165	167
Completed	165	167

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: We included 342 patients in the trial, 10 were not randomized, and consequently the remaining 332 women concluded the study.

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	332	332	
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			
Age at surgery			
Units: years			
median	48.5		
standard deviation	± 6.8	-	
Gender categorical			
All Women			
Units: Subjects			
Female	332	332	
Male	0	0	
Smoking			
Smoking or not a scheduled operation			
Units: Subjects			
Smoking	332	332	
Planned Abdominal Hysterectomy Units: Subjects			
PAH	332	332	
Planned Vaginal Hysterectomy Units: Subjects			
PVH	332	332	
Planned Laparoscopic Hysterectomy Units: Subjects			
PLH	332	332	
Alcohol			
>8 units per week			
Units: Subjects			
Alcohol	332	332	
Educational Level			

<4			
Units: Subjects			
Education	332	332	
ASA Class			
ASA Class >2			
Units: Subjects			
ASA	332	332	
Comorbidity Units: Subjects			
Comorbidity	332	332	
NSAID Units: Subjects			
NASID	332	332	
Bleeding Indication Units: Subjects			
Bleeding Indication	332	332	
BMI Units: Kg/MeterxMeter			
median	25.5		
inter-quartile range (Q1-Q3)	22.2 to 28.7	-	
Uterine Weight Units: gram(s)			
median	236		
inter-quartile range (Q1-Q3)	104 to 430	-	
Preoperative Hgb Units: g/dl			
arithmetic mean	8.3		
standard deviation	± 0.7	-	

End points

End points reporting groups

Reporting group title	Intervention
Reporting group description: Intervention	
Reporting group title	Placebo
Reporting group description: Placebo	

Primary: Total Blood loss estimates by surgeon

End point title	Total Blood loss estimates by surgeon
End point description: Blood loss estimated by the surgeon	
End point type	Primary
End point timeframe: During surgery	

End point values	Intervention	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	166		
Units: ml				
arithmetic mean (inter-quartile range (Q1-Q3))				
Total Blood loss	98.4 (50 to 200)	134.8 (50 to 300)		

Statistical analyses

Statistical analysis title	T test
Statistical analysis description: T test analysis	
Comparison groups	Intervention v Placebo
Number of subjects included in analysis	330
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

4 weeks

Adverse event reporting additional description:

The participant were assessed at discharge after surgery and again by questionnaire 4 weeks after surgery.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	TA exposed

Reporting group description: -

Reporting group title	Saline Exposed

Reporting group description:

Women having placebo (saline infusion)

Serious adverse events	TA exposed	Saline Exposed	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 164 (0.00%)	0 / 166 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	TA exposed	Saline Exposed	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 164 (0.00%)	0 / 166 (0.00%)	

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: There was indeed no non-serious events in relation to this trial.

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