Clinical trial results:
Randomized, placebo-controlled, double-blind trial to evaluate the efficacy and safety of topical application of tranexamic acid for saving blood losses in patients subjected to prosthetic knee surgery.

Summary

EudraCT number	2017-002480-17
Trial protocol	ES
Global end of trial date	18 February 2020

Results information

Result version number	v1 (current)
This version publication date	21 March 2021
First version publication date	21 March 2021
Summary attachment (see zip file)	results report (Resumen resultados final_FPS-TRA-2017-02.pdf)

Trial information

Trial identification

Sponsor protocol code	FPS-TRA-2017-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03386656
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fundación Pública Andaluza Progreso y Salud
Sponsor organisation address	Parque Científico y Tecnológico Cartuja Avda. Américo Vespucio, 15. Edificio S-2. 41092 Sevilla, Seville, Spain, 41092
Public contact	Marta Reboredo Ares, Fundación Pública Andaluza Progreso y Salud, 0034 955040450, gestionensayosclinicos.fps@juntadeandalucia.es
Scientific contact	Marta Reboredo Ares, Fundación Pública Andaluza Progreso y Salud, 0034 955040450, gestionensayosclinicos.fps@juntadeandalucia.es

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 February 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 February 2020
Global end of trial reached?	Yes
Global end of trial date	18 February 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim objective is to compare the efficacy and safety of topical tranexamic acid versus placebo in patients diagnosed of severe knee osteoarthritis in total primary knee prosthesis, in blood loss decrease (estimated blood loss, low hemoglobin, low hematocrit), and to assess the safety profile of topical tranexamic acid in patients subjected to prosthetic knee surgery.

Protection of trial subjects:

The trial will be conducted in accordance with the recommendations for Clinical Trials and Investigational Product Evaluation in humans, as contained in the Declaration of Helsinki, as revised at successive World Assemblies (WMA, 2013) (see Annex IV), and the current Spanish Clinical Trial Legislation (RD 1090/2015). The ICH-GCP standards (CPMP/ICH/135/95) will be followed.

The sponsor will obtain authorisation from the Health Authorities (AEMPS), in accordance with all applicable country-specific legal requirements. The study will not commence until AEMPS authorisation and Ethics Committee approval has been obtained.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 September 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 150
Worldwide total number of subjects	150
EEA total number of subjects	150

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)	31
From 65 to 84 years	119
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The sample of this study is made up of patients of both sexes aged between 18 and 80 diagnosed with severe osteoarthritis of the knee who have an indication for Primary Prosthetic Knee Surgery, under follow-up by the Lower Limb Unit of the Puerta del Mar Hospital at the date of the start of the study.

Pre-assignment

Screening details:

Selection criteria, written, signed and dated informed consent, socio-demographic data, anthropometric data, concomitant pharmacological treatment, record of comorbidities and pregnancy test shall be performed.

Period 1

Period 1 title	recruitment and patient follow-up
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The medication in both treatment groups will have the same packaging and labelling, as well as the same volume, weight and organoleptic characteristics. Each package will be identified with an individual randomisation code corresponding to a patient. The clinical management of the patient should be identical, regardless of the assigned treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description: -

Arm type	Experimental
Investigational medicinal product name	tranexamic acid (Amchafibrin)
Investigational medicinal product code	B02AA02
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Topical use

Dosage and administration details:

3 g topical solution

Arm title	Control

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Physiological Saline Solution 0.9%
Investigational medicinal product code	B05BB
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Topical use

Dosage and administration details:

3 g in a 30 cc aqueous solution

Number of subjects in period 1	Intervention	Control
Started	75	75
Completed	75	75

Period 2	
Period 2 title	Data analysis
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description: -

Arm type	Experimental
Investigational medicinal product name	tranexamic acid (Amchafibrin)
Investigational medicinal product code	B02AA02
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Topical use

Dosage and administration details:

3 g topical solution

Arm title	Control

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Physiological Saline Solution 0.9%
Investigational medicinal product code	B05BB
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Topical use

Dosage and administration details:

3 g in a 30 cc aqueous solution

Number of subjects in period 2	Intervention	Control
Started	75	75
Completed	75	75

Baseline characteristics

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

Reporting group values	Intervention	Control	Total
Number of subjects	75	75	150
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	16	15	31
From 65-84 years	59	60	119
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	69.17	69.17	
full range (min-max)	48 to 85	48 to 85	-
Gender categorical Units: Subjects			
Female	53	53	106
Male	22	22	44
Weight Units: Kg			
arithmetic mean	83	83	
full range (min-max)	56 to 122	56 to 122	-
Height Units: metres			
arithmetic mean	1.59	1.59	
full range (min-max)	1.40 to 1.84	1.40 to 1.84	-
IMC Units: Kg/m2			
arithmetic mean	32.73	32.73	
full range (min-max)	21.6 to 44.28	21.6 to 44.28	-

End points

End points reporting groups

Reporting group title	Intervention
Reporting group description: -	
Reporting group title	Control
Reporting group description: -	
Reporting group title	Intervention
Reporting group description: -	
Reporting group title	Control
Reporting group description: -	

Primary: Previous Haemoglobin

End point title	Previous Haemoglobin[1]
End point description:	

End point type	Primary
End point timeframe:	
During the study	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As we do not have information on all the sections required in this point, we have decided not to complete it, however, we will upload a pdf with the results report that includes reference to this point.

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	73		
Units: Haemoglobin				
arithmetic mean (standard deviation)	13.7 (± 4.4)	13.7 (± 4.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Posterior haemoglobin

End point title	Posterior haemoglobin[2]
End point description:	

End point type	Primary
End point timeframe:	
During the study	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As we do not have information on all the sections required in this point, we have decided

not to complete it, however, we will upload a pdf with the results report that includes reference to this point.

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	73		
Units: Haemoglobin				
arithmetic mean (standard deviation)	11.6 (± 1.4)	11.6 (± 1.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Total blood loss (TBL)

End point title	Total blood loss (TBL)[3]

End point description:

It can be stated that there are significant differences in total blood loss (TBL) comparing the group treated with tranexamic acid versus placebo. The patients who did not receive tranexamic acid had a greater blood loss than those who did not.

End point type	Primary

End point timeframe:

During the study

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As we do not have information on all the sections required in this point, we have decided not to complete it, however, we will upload a pdf with the results report that includes reference to this point.

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	73		
Units: Blood				
arithmetic mean (full range (min-max))	662.3 (600.8 to 723.7)	831.5 (752.8 to 910.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Evolution

End point title	Evolution

End point description:

End point type	Secondary

End point timeframe:

During the follow-up

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	73		
Units: Participants				
2 days	1	5		
3 days	48	38		
4 days	14	23		
5 days	7	5		
6 days	1	1		
11 days	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Beginning of Bipedestation

End point title	Beginning of Bipedestation

End point description:

The distribution of the time of onset of standing according to treatment is homogeneous in percentage terms. The fisher's exact test was performed to compare all categories due to the low number of observations in the latter categories. No statistically significant differences were found (p-value=0.55).

End point type	Secondary

End point timeframe:

During the follow-up

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	73		
Units: Participants				
1 day	41	39		
2 days	25	24		
3 days	5	8		
4 days	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: EVA scale one month after the intervention

End point title	EVA scale one month after the intervention

End point description:

The distribution of scores on the EVA scale according to treatment is homogeneous in percentage terms. The x2 test was performed to compare all defined ranges of the scale. No statistically significant differences were found (p-value=0.82).

End point type	Secondary

End point timeframe:

One month after the intervention

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	73		
Units: Participants				
EVA 0	20	20		
EVA 1-3	13	16		
EVA 4-6	25	21		
EVA 7-9	13	16		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first visit of first patient to last visit of last patient.

Adverse event reporting additional description:

Most of the adverse events (AEs) recorded were not related to the trial medication, but to knee oedema (in 1 subject, in addition to oedema, mild haematoma was detected) (no treatment required); or pain treated by home treatment in hospital. In addition, diarrhoea was detected in 1 subject who did not require treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	4.0

Reporting groups

Reporting group title	Intervention
Reporting group description: -	
Reporting group title	Control

Reporting group description: -

Serious adverse events	Intervention	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 75 (0.00%)	2 / 75 (2.67%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Cardiac disorders			
Death due to cardiorespiratory arrest			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 75 (0.00%)	1 / 75 (1.33%)	
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: 4 %

Non-serious adverse events	Intervention	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 75 (9.33%)	7 / 75 (9.33%)	
Vascular disorders			
Oedema			
subjects affected / exposed	2 / 75 (2.67%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Slight bruising			
subjects affected / exposed	2 / 75 (2.67%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	3 / 75 (4.00%)	3 / 75 (4.00%)	
occurrences (all)	3	3	

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.

- Subjects are not necessarily representative of the entire population in Cadiz.
- Refusal to participate.
- Losses in the follow-up.

Notes: