Clinical trial results:
Impact of eradication of asymptomatic bacteriuria on reducing the incidence of early infection in patients with periprosthetic femoral fractures requiring hip hemiarthroplasty

Summary

EudraCT number	2016-001108-47
Trial protocol	ES
Global end of trial date	01 January 2019

Results information

Result version number	v1 (current)
This version publication date	21 October 2021
First version publication date	21 October 2021

Trial information

Trial identification

Sponsor protocol code	BARIFER

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	VHIR
Sponsor organisation address	Passeig Vall Hebron 119-129, Barcelona, Spain, 08035
Public contact	Joaquin Lopez-Soriano, VHIR, joaquin.lopez.soriano@vhir.org
Scientific contact	Inmaculada Fuentes, VHIR - Unitat de Suport a la Investigació Clinica (USIC), usic@vhir.org

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	30 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2018
Global end of trial reached?	Yes
Global end of trial date	01 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the clinical impact of eradication of asymptomatic bacteriuria on reducing the incidence of early periprosthetic infection in patients with femur fracture requiring hip hemiarthroplasty.

Protection of trial subjects:

Urine analysis was performed before HHA surgery. Preoperative antibiotic prophylaxis was decided according to each center protocol. All patients were followed for three months after HHA or until early-PJIs or death was diagnosed, whichever occurred first.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 May 2016
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: 594
Worldwide total number of subjects	594
EEA total number of subjects	594

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)	94
From 65 to 84 years	450
85 years and over	50

Subject disposition

Recruitment	
Recruitment details: -	
Pre-assignment	
Screening details: -	
Pre-assignment period milestones	
Number of subjects started	594
Number of subjects completed	594

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
Arms	
Are arms mutually exclusive?	Yes
Arm title	Fosfomycin
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Fosfomycin
Investigational medicinal product code	
Other name	Monuril, Monurol, Monural
Pharmaceutical forms	Oral powder in single-dose container
Routes of administration	Oral use
Dosage and administration details: 3 g of fosfomycin-trometamol (oral route) vs. no treatment, between 24 and 6h before surgery.	
Arm title	No treatment
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Non ASB
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Fosfomycin	No treatment	Non ASB
Started	77	75	442
Completed	77	75	442

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	594	594	
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	84.3		
standard deviation	± 8.34	-	
Gender categorical Units: Subjects			
Female	420	420	
Male	174	174	

End points

End points reporting groups

Reporting group title	Fosfomycin
Reporting group description: -	
Reporting group title	No treatment
Reporting group description: -	
Reporting group title	Non ASB
Reporting group description: -	

Primary: Cumulative incidence PJI

End point title	Cumulative incidence PJI
End point description:	
Cumulative incidence of early PJI (periprosthetic joint infection) after preoperative ASB (asymptomatic bacteriuria) treatment in patients with hip hemiarthroplasty (HHA) for fracture.	
End point type	Primary
End point timeframe:	
12 weeks	

End point values	Fosfomycin	No treatment	Non ASB	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	77	75	442	
Units: percent				
number (not applicable)	2	2	11	

Statistical analyses

Statistical analysis title	Early PJI
Comparison groups	No treatment v Fosfomycin
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

12 weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Total cohort

Reporting group description: -

Serious adverse events	Total cohort		
Total subjects affected by serious adverse events			
subjects affected / exposed	100 / 594 (16.84%)		
number of deaths (all causes)	54		
number of deaths resulting from adverse events	54		
Cardiac disorders			
Heart failure			
subjects affected / exposed	9 / 594 (1.52%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Ischaemic heart disease			
subjects affected / exposed	7 / 594 (1.18%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Arrhythmia			
subjects affected / exposed	4 / 594 (0.67%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 594 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Stroke			

subjects affected / exposed	1 / 594 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Haemorrhage			
subjects affected / exposed	9 / 594 (1.52%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	4 / 594 (0.67%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute renal failure			
subjects affected / exposed	2 / 594 (0.34%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			
subjects affected / exposed	63 / 594 (10.61%)		
occurrences causally related to treatment / all	0 / 63		
deaths causally related to treatment / all	0 / 54		

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

Non-serious adverse events	Total cohort		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	109 / 594 (18.35%)		
Surgical and medical procedures			
Other Medical adverse events	Additional description: Adverse events related to surgery		
subjects affected / exposed	109 / 594 (18.35%)		
occurrences (all)	109		
Nervous system disorders			

Disorientation subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	25 / 594 (4.21%) 25 1 / 594 (0.17%) 1 3 / 594 (0.51%) 3		
Metabolism and nutrition disorders Electrolyte imbalance subjects affected / exposed occurrences (all)	9 / 594 (1.52%) 9		

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.

The main limitation was the small sample size. The difficulty of obtaining the informed consent signed and all study requirements at least 6h before surgery made our inclusion rate slow

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33864153