Clinical trial results:
A Cluster Crossover Trial Comparing Conventionl vs Incremental Antibiotic Therapy for the Prevention or Arrhytmia Device Infection

Summary

EudraCT number	2014-000459-10
Trial protocol	NL
Global end of trial date	08 September 2017

Results information

Result version number	v1 (current)
This version publication date	30 July 2021
First version publication date	30 July 2021

Trial information

Trial identification

Sponsor protocol code	PADIT

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01628666
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Canadian Institutes of Health Research
Sponsor organisation address	160 Elgin Street, 10th Floor , Ottawa, Canada, 4809A
Public contact	Marco Alings, Werkgroep Cardiologische Centra Nederland, +31 76595 4166, marco@alings.org
Scientific contact	Marco Alings, Werkgroep Cardiologische Centra Nederland, +31 76595 4166, marco@alings.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	18 October 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The goal of the study is to compare whether a centre-wide policy of incremental antibiotic therapy will reduce device infection compared to a policy of conventional antibiotic prophylaxis in high-risk patients undergoing arrhythmia device procedures.

Protection of trial subjects:

Standard non-antibiotic operating procedures to reduce infection will be continued in each centre.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 December 2012
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	Canada: 18893
Country: Number of subjects enrolled	Netherlands: 710
Worldwide total number of subjects	19603
EEA total number of subjects	710

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)	19603
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited in 28 centers. 24 centers in Canada and 4 centers in the Netherlands.

Pre-assignment

Screening details:

Because there is a risk of infection with every device procedure, it would be reasonable to include data from all patients receiving a device in the analysis. However we will only include data from patients at higher risk of infection for reasons of study efficiency.

Period 1

Period 1 title	Randomisation (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Both patient and operator were aware of the open-label treatment. Design was cluster randomisation.

Arms

Are arms mutually exclusive?	Yes
Arm title	Conventional arm

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Cefazolin/Vancomycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

CONVENTIONAL THERAPY
Conventional antibiotic therapy will be a single preoperative dose of intravenous Cefazolin 1-2g iv 60 minutes prior to skin incision. In penicillin-allergic patients, Vancomycin will be used instead at a dose of 1-1.5g iv given over 60-90 minutes, 60-90 minutes prior to skin incision.

Arm title	Incremental therapy

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Bacitracin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Topical use

Dosage and administration details:

INCREMENTAL THERAPY
Pre-procedure antibiotics will consist of a single dose of both Cefazolin 1-2g iv 60 minutes prior to skin incision plus a single dose of Vancomycin 1-1.5g iv given over 60-90 minutes, 60-90 minutes prior to incision. Because only a single dose of Vancomycin is administered, there is no need to adjust dosing in patients with renal failure. Penicillin-allergic patients will only receive Vancomycin.
Patients will also receive intracavitary antibacterial wash with 50,000 units Bacitracin powder diluted in 10 ml sterile saline in the vial, shaken to dissolve the Bacitracin powder, and then placed in 50 ml sterile saline in a bowl on the sterile field, and injected into the pocket.
Patients will also receive postoperative antibiotic prescription to last for 2 days after the procedure. This can be either Cefalexin 500 mg PO TID OR Cephadroxil 1000 mg BID.

Penicillin-allergic patients will receive Clindamycin 150-300 mg TID

Number of subjects in period 1	Conventional arm	Incremental therapy
Started	9627	9976
Device implantation	9627	9976
Completed	9605	9954
Not completed	22	22
Lost to follow-up	22	22

Baseline characteristics

Reporting groups

Reporting group title	Randomisation

Reporting group description: -

Reporting group values	Randomisation	Total	
Number of subjects	19603	19603	
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			
72.0 +/- 13.1			
Units: years			
arithmetic mean	72.0		
standard deviation	± 13.1	-	
Gender categorical Units: Subjects			
Female	6652	6652	
Male	12951	12951	

End points

End points reporting groups

Reporting group title	Conventional arm
Reporting group description: -	
Reporting group title	Incremental therapy
Reporting group description: -	

Primary: hospitalisation attributed to device infection

End point title	hospitalisation attributed to device infection[1]
End point description:	
End point type	Primary
End point timeframe:	
12 months post procedure	

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: See publication for more statistical details. Link is added in more information tab

End point values	Conventional arm	Incremental therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	66		
Units: patients	77	66		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 12 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	N/A
Dictionary version	N/A

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

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: See publication for more Adverse event details. Link is added in more information tab

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30545448