



Clinical trial results:

Ciclosporin to Protect Renal function In Cardiac Surgery. CiPRICS. A Phase II Double Blind Randomized Placebo Controlled Study.

Summary

EudraCT number	2014-004610-29
Trial protocol	SE
Global end of trial date	06 October 2016

Results information

Result version number	v1 (current)
This version publication date	22 December 2018
First version publication date	22 December 2018
Summary attachment (see zip file)	Clinical_study_report (170512_CiPRICS_Final_CSR_redacted_Sign.pdf)

Trial information

Trial identification

Sponsor protocol code	2014.001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02397213
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Skanes University Hospital
Sponsor organisation address	Getingevägen 4, Lund, Sweden, 22185
Public contact	Dept of Cardiothoracic Surgery, Skanes University Hospital, 46 461753495349, henrik.bjursten@skane.se
Scientific contact	Dept of Cardiothoracic Surgery, Skanes University Hospital, 46 461753495349, henrik.bjursten@skane.se

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	12 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2016
Global end of trial reached?	Yes
Global end of trial date	06 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To study the efficacy of ciclosporin, with brand name CicloMulsion®, given preoperatively in CABG study patients to reduce the degree of AKI after CABG surgery. A number of biological markers for kidney function will be evaluated as mentioned in 4.4.

Protection of trial subjects:

Treated in routine care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 April 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 154
Worldwide total number of subjects	154
EEA total number of subjects	154

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)	37
From 65 to 84 years	115

85 years and over	2
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

446 patients planned for non-emergent CABG with high risk of developing acute kidney injury where assessed for eligibility. 292 patients were excluded, 154 included:

- 30 did not meet inclusion criteria.
- 140 met exclusion criteria
- 44 declined to participate
- 77 were excluded for other reasons
- 1 included in safety analysis only.

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Ciclosporin

Arm description: -

Arm type	Experimental
Investigational medicinal product name	CicloMulsion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intravenous use

Dosage and administration details:

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Arm title	Placebo
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intravenous use

Dosage and administration details:

III

Number of subjects in period 1	Ciclosporin	Placebo
Started	75	79
Completed	75	79

Baseline characteristics

Reporting groups

Reporting group title	Ciclosporin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Ciclosporin	Placebo	Total
Number of subjects	75	79	154
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			
arithmetic mean	69.7	69.1	
standard deviation	± 8.1	± 8.3	-
Gender categorical Units: Subjects			
Female	13	11	24
Male	62	68	130

End points

End points reporting groups

Reporting group title	Ciclosporin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Relative change in P-Cystatin C from Baseline to postoperative Day 3

End point title	Relative change in P-Cystatin C from Baseline to postoperative Day 3
End point description:	
End point type	Primary
End point timeframe:	
From Day -1 to Day 3.	

End point values	Ciclosporin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	78		
Units: mmol/L				
arithmetic mean (standard deviation)	136.38 (\pm 35.64)	115.87 (\pm 30.82)		

Statistical analyses

Statistical analysis title	Mixed linear model
Comparison groups	Placebo v Ciclosporin
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The reporting of AE began after administration of study medication and lasted until the follow-up phone call was made 1 month after the operation day.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Ciclosporin
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Ciclosporin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 76 (13.16%)	11 / 79 (13.92%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Investigations			
Liver function test abnormal			
subjects affected / exposed	1 / 76 (1.32%)	0 / 79 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Postpericardiotomy syndrome			
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion	Additional description: Vascular Graft Occlusion and Myocardial infarction.		
subjects affected / exposed	1 / 76 (1.32%)	0 / 79 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 76 (1.32%)	1 / 79 (1.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 76 (1.32%)	0 / 79 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorder			
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 76 (1.32%)	0 / 79 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest	Additional description: Cardiac arrest, Myocardial Infarction and Pulmonary Oedema.		
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 76 (0.00%)	2 / 79 (2.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
General disorders and administration site conditions			
Non-cardiac chest pain			

subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain	Additional description: Chest pain, Nausea and Vomiting.		
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal haemorrhage	Additional description: Gastrointestinal haemorrhage was reported for one patient in the Placebo group. Gastrointestinal Haemorrhage and Cardiac Arrest was reported for one patient in the Ciclosporin Group.		
subjects affected / exposed	1 / 76 (1.32%)	1 / 79 (1.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	3 / 76 (3.95%)	0 / 79 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis	Additional description: Hydronephrosis and Ureteral Stenosis		
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 76 (1.32%)	1 / 79 (1.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon gangrene			
subjects affected / exposed	1 / 76 (1.32%)	0 / 79 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			

subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mediastinitis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 76 (1.32%)	0 / 79 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Ciclosporin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 76 (27.63%)	20 / 79 (25.32%)	
Investigations			
Liver function test abnormal			
subjects affected / exposed	1 / 76 (1.32%)	1 / 79 (1.27%)	
occurrences (all)	1	1	
Hepatic enzyme increased			
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Postpericardiotomy syndrome			
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences (all)	0	1	
Vascular graft occlusion	Additional description: Vascular graft occlusion, myocardial infarction		
subjects affected / exposed	1 / 76 (1.32%)	0 / 79 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences (all)	0	1	

Hypertension subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1	0 / 79 (0.00%) 0	
Cardiac disorders			
Pericardial effusion subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1	1 / 79 (1.27%) 1	
Angina pectoris subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	1 / 79 (1.27%) 1	
Atrial fibrillation subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1	0 / 79 (0.00%) 0	
Cardiac disorder subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	1 / 79 (1.27%) 1	
Cardiac failure subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1	0 / 79 (0.00%) 0	
Ventricular arrhythmia subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	1 / 79 (1.27%) 1	
Cardiac arrest subjects affected / exposed occurrences (all)	Additional description: Cardiac arrest, myocardial infarction, pulmonary oedema		
	0 / 76 (0.00%) 0	1 / 79 (1.27%) 1	
Nervous system disorders			
Cerebrovascular accident subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	2 / 79 (2.53%) 2	
Syncope subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1	0 / 79 (0.00%) 0	
General disorders and administration site conditions			
Non-cardiac chest pain subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	1 / 79 (1.27%) 1	

Chest pain	Additional description: Chest pain was reported for one patient in the Ciclosporin group. Chest pain, nausea, and vomiting was reported for one patient in the Placebo group.		
subjects affected / exposed	1 / 76 (1.32%)	1 / 79 (1.27%)	
occurrences (all)	1	1	
Pyrexia	Additional description: Pyrexia, C-reactive protein increased		
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences (all)	0	1	
Gastrointestinal haemorrhage	Additional description: Gastrointestinal haemorrhage was reported for one patient in the Placebo group. Gastrointestinal haemorrhage and cardiac arrest was reported for one patient in the Ciclosporin group.		
subjects affected / exposed	1 / 76 (1.32%)	1 / 79 (1.27%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	6 / 76 (7.89%)	2 / 79 (2.53%)	
occurrences (all)	6	2	
Pneumothorax			
subjects affected / exposed	2 / 76 (2.63%)	0 / 79 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	1 / 76 (1.32%)	0 / 79 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 76 (0.00%)	2 / 79 (2.53%)	
occurrences (all)	0	2	
Sleep disorder			
subjects affected / exposed	1 / 76 (1.32%)	0 / 79 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			

Renal failure			
subjects affected / exposed	1 / 76 (1.32%)	0 / 79 (0.00%)	
occurrences (all)	1	0	
Urinary retention			
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences (all)	0	1	
Hydronephrosis	Additional description: Hydronephrosis, ureteral stenosis		
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences (all)	0	1	
Infections and infestations			
Pneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 76 (5.26%)	1 / 79 (1.27%)	
occurrences (all)	4	1	
Postoperative wound infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 76 (1.32%)	2 / 79 (2.53%)	
occurrences (all)	1	2	
Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 76 (1.32%)	1 / 79 (1.27%)	
occurrences (all)	1	1	
Colon gangrene			
subjects affected / exposed	1 / 76 (1.32%)	0 / 79 (0.00%)	
occurrences (all)	1	0	
Infection			
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences (all)	0	1	
Mediastinitis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 79 (1.27%)	
occurrences (all)	0	1	
Respiratory infection			
subjects affected / exposed	1 / 76 (1.32%)	0 / 79 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 May 2016	- Based on the patient population available at the site, the size of the stratum was changed from "at least 60" to "approximately 50" patients from the group with an ...

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported