



Clinical trial results:

Does LOW Dose DEXmedetomidine After Cardiopulmonary Bypass Separation

Decrease the Incidence of DELirium: A Double-blind Randomized Placebocontrolled Study (LOWDEXDEL Study)

Summary

EudraCT number	2017-002007-97
Trial protocol	BE
Global end of trial date	30 August 2019

Results information

Result version number	v1 (current)
This version publication date	17 February 2021
First version publication date	17 February 2021

Trial information

Trial identification

Sponsor protocol code	2017/24JUL/374
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03388541
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cliniques universitaires Saint-Luc
Sponsor organisation address	Avenue Hippocrate, 10, Brussels, Belgium, 1200
Public contact	Mona Momeni, Cliniques universitaires Saint-Luc, 0032 27647029, mona.momeni@uclouvain.be
Scientific contact	Mona Momeni, Cliniques universitaires Saint-Luc, 0032 27647029, mona.momeni@uclouvain.be

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	28 October 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 August 2019
Global end of trial reached?	Yes
Global end of trial date	30 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To analyze whether the addition of a low dose DEXMEDETOMIDINE to a sedation regimen based on propofol decreases the incidence of in-hospital delirium compared to propofol sedation with placebo in patients ≥ 60 years undergoing cardiac surgery

Protection of trial subjects:

Any serious adverse events that would have occurred due to the study drug would have been reported to the IDMC. The patients are very closely monitored during the whole period when they receive Dexmedetomidine but also afterwards as they stay during several hours in the ICU. Otherwise, strict rules were followed to protect the subjects. In any case data regarding the patients were kept anonymous.

Background therapy:

DEXMEDETOMIDINE was started at a dose of 0.4 μ g/kg/h (5ml/h) at the moment of the closure of the chest and continued during 10 hours.

Evidence for comparator:

Placebo (NaCl 0.9%) was started at a continuous infusion of 5ml/h at the closure of the chest and was continued during 10 hours

Actual start date of recruitment	07 December 2017
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	Belgium: 420
Worldwide total number of subjects	420
EEA total number of subjects	420

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)	0
From 65 to 84 years	408
85 years and over	12

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from one single center (Cliniques Universitaires Saint Luc)

Pre-assignment

Screening details:

Following written informed consent and before commencing treatment with Dexmedetomidine or Placebo, the patients were screened with Mini Mental State Examination test in order to evaluate the cognitive status of the patient.

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, Monitor, Carer, Assessor

Blinding implementation details:

Randomization and blinding performed by research Pharmacy of Cliniques Universitaires Saint Luc

Arms

Are arms mutually exclusive?	Yes
Arm title	DEXDOR

Arm description:

Patients receiving continuous IV infusion of dexmedetomidine

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

Dosage and administration details:

The drug was prepared at such that 5 ml/h corresponded to 0.4 µg/kg/h

Arm title	PLACEBO
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Arm description:

Patients receiving continuous IV infusion of NaCl0.9%

Arm type	Placebo
Investigational medicinal product name	Sodium Chloride
Investigational medicinal product code	
Other name	Isotonic saline solution, Normal saline solution, Physiological saline solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

The drug was prepared without addition of any other substances and infused at a continuous IV infusion of 5 mL/H.

Number of subjects in period 1	DEXDOR	PLACEBO
Started	210	210
Completed	205	203
Not completed	5	7
Consent withdrawn by subject	2	2
Change in surgical plan	2	2
died before administration of study drug	-	1
Study drug not prepared	1	2

Baseline characteristics

Reporting groups

Reporting group title	DEXDOR
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Reporting group description:

Patients receiving continuous IV infusion of dexmedetomidine

Reporting group title	PLACEBO
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Reporting group description:

Patients receiving continuous IV infusion of NaCl0.9%

Reporting group values	DEXDOR	PLACEBO	Total
Number of subjects	210	210	420
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)	0	0	0
From 65-84 years	205	203	408
85 years and over	5	7	12
Age continuous			
Units: years			
median	71	70	
full range (min-max)	66 to 75	65 to 76	-
Gender categorical			
Units: Subjects			
Female	57	48	105
Male	153	162	315

End points

End points reporting groups

Reporting group title	DEXDOR
Reporting group description:	
Patients receiving continuous IV infusion of dexmedetomidine	
Reporting group title	PLACEBO
Reporting group description:	
Patients receiving continuous IV infusion of NaCl0.9%	

Primary: Postoperative in-hospital delirium

End point title	Postoperative in-hospital delirium
End point description:	
The primary outcome was the incidence of POD at any time during the patient's hospital stay. Delirium assessment in the ICU was performed once the Richmond Agitation-Sedation Scale was ≥ 3 and was based on the Confusion Assessment Method for intubated patients in the ICU (CAM-ICU). The nurses in the ICU evaluated POD every 8 hours with the French version of the CAM-ICU. Delirium assessment at the ward was performed twice a day (08.00 AM and 08.00 PM) with the CAM. Because POD is a fluctuating state, often presenting in the ward and at night, the chart review method was used to detect any episode of POD that was not diagnosed otherwise. The medical chart of the patients was checked for any notifications made by nurses or physicians suggesting for the occurrence of POD (e.g. aggressive, confusion, having been tied, use of haloperidol, hallucinations, inappropriate behaviour,...). Trained study staff then reviewed the medical chart.	
End point type	Primary
End point timeframe:	
After surgical intervention	

End point values	DEXDOR	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	205	203		
Units: percent	18	19		

Statistical analyses

Statistical analysis title	Full study
Statistical analysis description:	
The primary outcome was the incidence of POD at any time during the patient's hospital stay. Delirium assessment in the ICU was performed once the Richmond Agitation Sedation Scale was ≥ 3 and was based on the Confusion Assessment Method for initiated patients in the ICU (CAM-ICU). The nurses in the ICU evaluated OD every 8 hours with French version of the CAM-ICU. Delirium Assessment at the ward was performed twice a day (8/00 AM and 08:00 PM). With the CAM. Because POD is fluctuating state, of	
Comparison groups	DEXDOR v PLACEBO

Number of subjects included in analysis	408
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.687
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.54

Notes:

[1] - This is a superiority trial with an alternative hypothesis being that adding a low dose DEX to propofol sedation would result in a different risk of POD compared to propofol with PL.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

After surgical intervention

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	10.0
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Reporting groups

Reporting group title	DEXDOR
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Reporting group description:

Patients receiving continuous IV infusion of dexmedetomidine

Reporting group title	PLACEBO
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Reporting group description:

Patients receiving continuous IV infusion of NaCl0.9%

Serious adverse events	DEXDOR	PLACEBO	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 205 (0.00%)	0 / 203 (0.00%)	
number of deaths (all causes)	1	10	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	DEXDOR	PLACEBO	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	178 / 205 (86.83%)	153 / 203 (75.37%)	
Vascular disorders			
Surgical revision			
subjects affected / exposed	12 / 205 (5.85%)	8 / 203 (3.94%)	
occurrences (all)	1	1	
Cardiac disorders			
Hypotension requiring norepinephrine			
subjects affected / exposed	178 / 205 (86.83%)	153 / 203 (75.37%)	
occurrences (all)	1	1	
Epicardial pacing			

subjects affected / exposed	116 / 205 (56.59%)	97 / 203 (47.78%)	
occurrences (all)	1	1	
Permanent pace maker			
subjects affected / exposed	6 / 205 (2.93%)	2 / 203 (0.99%)	
occurrences (all)	1	1	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	6 / 205 (2.93%)	10 / 203 (4.93%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2018	An amendment was asked in order to increase the number of patients to include, as the incidence of POD in the Placebo group was lower than expected. We had initially planned to include a total number of 270 patients

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported