



Clinical trial results:

Effect of preoperative intravenous highdose methylprednisolone on orthostatic intolerance, sleeping pattern, glucose homeostasis and immune signaling in patients scheduled for total hip-arthroplasty

Summary

EudraCT number	2015-000102-19
Trial protocol	DK
Global end of trial date	02 January 2017

Results information

Result version number	v1 (current)
This version publication date	22 May 2022
First version publication date	22 May 2022
Summary attachment (see zip file)	Orthostatic hypotension and intolerance (Lindberg-Larsen et al. 2018 OH ad OI.pdf)

Trial information

Trial identification

Sponsor protocol code	HL_VL_01_2015
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02445898
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Copenhagen university Hospital Rigshospitalet
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark, 2100
Public contact	Viktoria Oline Lindberg-Larsen, Section for Surgical Pathophysiology, Rigshospitalet, 0045 28791991, viktorina_oline@hotmail.com
Scientific contact	Viktoria Oline Lindberg-Larsen, Section for Surgical Pathophysiology, Rigshospitalet, 0045 28791991, viktorina_oline@hotmail.com

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	01 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 December 2016
Global end of trial reached?	Yes
Global end of trial date	02 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect of intravenous highdose injection of methylprednisolone on orthostatic hypotension and intolerance in patients undergoing total hip-arthroplasty

Protection of trial subjects:

All trial patients followed standard treatment regarding surgery and postoperative regime. Information regarding physical testing and extra blood sampling was given prior til inclusion.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2015
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	Denmark: 59
Worldwide total number of subjects	59
EEA total number of subjects	59

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)	20
From 65 to 84 years	39
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patient were recruited at the ambulatory at Bispebjerg University Hospital visit when planned for total hip arthroplasty surgery.

190 patients were screened for inclusion, 64 patients were included, and 59 patients completed the study. The 5 patients excluded the trial due to protocol violations, primarily conversion to general anesthesia.

Pre-assignment

Screening details:

- Age 55-80 years
- Hip osteoarthritis
- Planned for primary total hip arthroplasty (THA)
- Able to speak and understand Danish
- Have given informed consent

Pre-assignment period milestones

Number of subjects started	59
Number of subjects completed	59

Period 1

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

Blinding implementation details:

A research assistant not otherwise involved in the trial performed a computer-generated random allocation sequence (1:1 allocation rate) concealed in 64 consecutively numbered, opaque, sealed envelopes determining active treatment or placebo. On the morning of surgery the envelopes were opened consecutively, and the trial drug was prepared by 2 anesthetist nurses not otherwise involved in the collection of trial data.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Isotonic saline (2 mL)

Arm type	Placebo
Investigational medicinal product name	Isotonic saline
Investigational medicinal product code	PL1
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

2 mL isotonic saline administered IV after induction of anaesthesia

Arm title	Steroid
Arm description: -	
Arm type	Active comparator

Investigational medicinal product name	Solu-Medrol
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

125 mg Solu-Medrol administered IV after induction of anaesthesia

Number of subjects in period 1	Placebo	Steroid
Started	30	29
Completed	30	29

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Isotonic saline (2 mL)	
Reporting group title	Steroid
Reporting group description: -	

Reporting group values	Placebo	Steroid	Total
Number of subjects	30	29	59
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	67.2 ± 6.7	67.4 ± 5.4	-
Gender categorical Units: Subjects			
Female	12	17	29
Male	18	12	30
ASA Units: Subjects			
ASA1	6	6	12
ASA2	24	22	46
ASA3	0	1	1
BMI Units: BMI arithmetic mean standard deviation	27.5 ± 4.3	26.9 ± 4.1	-
Hemoglobin Units: g/dL arithmetic mean standard deviation	8.7 ± 0.6	8.7 ± 0.7	-
C-reactive protein Units: mg/l median inter-quartile range (Q1-Q3)	2.5 1.0 to 4.0	1.0 1.0 to 3.0	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Isotonic saline (2 mL)	
Reporting group title	Steroid
Reporting group description: -	

Primary: Orthostatic hypotension 6 hrs

End point title	Orthostatic hypotension 6 hrs
End point description:	
End point type	Primary
End point timeframe: Orthostatic challenge 6 hrs postoperatively	

End point values	Placebo	Steroid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: project patients				
OH	11	11		

Statistical analyses

Statistical analysis title	RR
Comparison groups	Placebo v Steroid
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Fisher exact

Secondary: Orthostatic intolerance 6 hrs

End point title	Orthostatic intolerance 6 hrs
End point description:	
End point type	Secondary
End point timeframe: Orthostatic challenge 6 hrs postoperatively	

End point values	Placebo	Steroid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: project patients				
OI	13	9		

Statistical analyses

Statistical analysis title	RR
Comparison groups	Placebo v Steroid
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Fisher exact

Secondary: Orthostatic hypotension 24 hrs

End point title	Orthostatic hypotension 24 hrs
End point description:	
End point type	Secondary
End point timeframe:	
Orthostatic challenge 24 hrs postoperatively	

End point values	Placebo	Steroid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: project patients				
OH	5	2		

Statistical analyses

Statistical analysis title	RR
Comparison groups	Placebo v Steroid

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Fisher exact

Secondary: Orthostatic intolerance 24 hrs

End point title	Orthostatic intolerance 24 hrs
End point description:	
End point type	Secondary
End point timeframe:	
Orthostatic challenge 24 hrs postoperatively	

End point values	Placebo	Steroid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: project patients				
OI	5	1		

Statistical analyses

Statistical analysis title	RR
Comparison groups	Placebo v Steroid
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Fisher exact

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

From time of trial medication administration until 20 hrs after administration (5 x T½)

Adverse event reporting additional description:

Following postoperative conditions will not be registered as AEs, as they are common following anaesthesia and surgery:

Moderate hypotension (MAP <60 mmHg)

Shivering

Pain from the surgical field

Urine retention

Intraoperative bleeding

nausea and vomiting

Dizziness

Fatigue

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	10
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Frequency threshold for reporting non-serious adverse events: 2 %

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: There were no adverse events in the small clinical trial

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/29573263>

<http://www.ncbi.nlm.nih.gov/pubmed/32719355>