



## Clinical trial results:

### Effect of high versus low dose intravenous dexamethason on complications in the immediate postoperative setting after mastectomy - a randomized, double-blind, controlled trial

#### Summary

EudraCT number	2017-000227-27
Trial protocol	DK
Global end of trial date	29 April 2018

#### Results information

Result version number	v1 (current)
This version publication date	06 November 2019
First version publication date	06 November 2019

#### Trial information

##### Trial identification

Sponsor protocol code	DEXMAS01
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03125941
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Rigshospitalet
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark, 2100
Public contact	Kristin Julia Steinhorsdottir, Rigshospitalet, 0045 31666112, kste0050@regionh.dk
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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	21 October 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 April 2018
Global end of trial reached?	Yes
Global end of trial date	29 April 2018
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To investigate the effect of high versus low dose intravenous dexamethasone on complications in the immediate postoperative setting after mastectomy. Main objective is proportion of patientes needing admission to postanaesthesia care unit after operation.

Protection of trial subjects:

Study medication was medication already being used, just in two different doses

Background therapy:

All other therapy followed local standard protocol

Evidence for comparator:

4-8 mg of dexamethasone is a standard prophylactic treatment for post-operative nausea and vomiting. 125 mg methylprednisolone (equivalent to 24 mg of dexamethasone) has been shown to reduce pain in the first days after hip and knee replacements (Lunn TH, 2011, 2013).

Actual start date of recruitment	03 April 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	Denmark: 130
Worldwide total number of subjects	130
EEA total number of subjects	130

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)	51
From 65 to 84 years	74

85 years and over	5
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## Subject disposition

### Recruitment

Recruitment details:

recruitment by investigator or study personell at the pre-operative consultation, at the department of breast surgery

### Pre-assignment

Screening details:

Screening by doctors from the department of breast surgery and investigator: all adult patients undergoing mastectomy were screened for inclusion

### 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, Data analyst, Carer, Assessor

Blinding implementation details:

Personnel not otherwise involved in trial prepared study drug: either 6 ml dexamethasone (24 mg) or 2 ml dexamethasone (8 mg) and 4 ml nacl. Syringes containing both solutions were clear and identical in appearance.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Dexamethasone 8 mg

Arm description:

Single-shot preoperative injection

Arm type	Active comparator
Investigational medicinal product name	dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

8 mg (2 ml) with 4 ml nacl, injected single-shot

<b>Arm title</b>	Dexamethasone 24 mg
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Arm description:

Single shot pre-operative injection, 24 mg

Arm type	Experimental
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

24 mg (6 ml) injected as a pre-operative single-shot

<b>Number of subjects in period 1</b>	Dexamethasone 8 mg	Dexamethasone 24 mg
Started	65	65
Completed	63	64
Not completed	2	1
Protocol deviation	2	1

## Baseline characteristics

### Reporting groups

Reporting group title	overall trial
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Reporting group description:

130 patients were randomized, 3 pre-intervention exclusions, so 127 received the intervention. Baseline characteristics reported for all patients, endpoints only for patients receiving intervention

Reporting group values	overall trial	Total	
Number of subjects	130	130	
Age categorical			
Units: Subjects			
Adults (18-64 years)	81	81	
From 65-84 years	44	44	
85 years and over	5	5	
Age continuous			
Units: years			
arithmetic mean	65		
full range (min-max)	24 to 87	-	
Gender categorical			
Units: Subjects			
Female	128	128	
Male	2	2	
BMI			
Units: kg/m2			
arithmetic mean	25		
standard deviation	± 5	-	

## End points

### End points reporting groups

Reporting group title	Dexamethasone 8 mg
Reporting group description:	
Single-shot preoperative injection	
Reporting group title	Dexamethasone 24 mg
Reporting group description:	
Single shot pre-operative injection, 24 mg	

### Primary: proportion of patients transferred to PACU

End point title	proportion of patients transferred to PACU
End point description:	
Proportion of patients transferred to the post-anesthesia care unit after operation (vs. patients transferred directly to the ward)	
End point type	Primary
End point timeframe:	
1 hour	

End point values	Dexamethasone 8 mg	Dexamethasone 24 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63 <sup>[1]</sup>	64 <sup>[2]</sup>		
Units: patients	23	23		

Notes:

[1] - 1 pre-intervention exclusion

[2] - 2 pre-intervention exclusion

### Statistical analyses

Statistical analysis title	Primary endpoint
Statistical analysis description:	
patients meeting criteria for transfer to PACU according to standardized discharge score	
Comparison groups	Dexamethasone 8 mg v Dexamethasone 24 mg
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	2.05

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**Secondary: Discharge scores**

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End point title	Discharge scores
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End point description:

Standardized discharge score (modified Aldrete criteria), at extubation and transfer from operating room and upon arrival at the ward

End point type	Secondary
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End point timeframe:

12 h

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End point values	Dexamethasone 8 mg	Dexamethasone 24 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63 <sup>[3]</sup>	64 <sup>[4]</sup>		
Units: score				
median (inter-quartile range (Q1-Q3))				
extubation	0 (0 to 2)	1 (0 to 2)		
transfer from OR	1 (0 to 2)	1 (0 to 2)		
arrival at ward	1 (1 to 2)	1 (1 to 2)		

Notes:

[3] - 2 pre-intervention exclusion

[4] - 1 pre-intervention exclusion

**Statistical analyses**

<b>Statistical analysis title</b>	discharge scores
Comparison groups	Dexamethasone 8 mg v Dexamethasone 24 mg
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.114 <sup>[5]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[5] - at transfer 0.294, ward 0.076

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**Secondary: Pain scores**

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End point title	Pain scores
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End point description:

Pain scores at extubation, transfer from the operating room and arrival at ward

End point type	Secondary
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End point timeframe:

12 h

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End point values	Dexamethason e 8 mg	Dexamethason e 24 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63 <sup>[6]</sup>	64 <sup>[7]</sup>		
Units: numeric rating scale				
median (inter-quartile range (Q1-Q3))				
extubation	0 (0 to 0)	0 (0 to 0)		
transfer from OR	0 (0 to 0)	0 (0 to 0)		
arrival at ward	2 (1 to 3)	1 (0 to 3)		

Notes:

[6] - 2 pre-intervention exclusion

[7] - 1 pre-intervention exclusion

## Statistical analyses

Statistical analysis title	pain scores
Comparison groups	Dexamethasone 8 mg v Dexamethasone 24 mg
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009 <sup>[8]</sup>
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)

Notes:

[8] - at transfer 0.416, arrival at ward 0.097

## Secondary: Lenght of stay

End point title	Lenght of stay
End point description:	
lenght of stay, measured from start of operation to discharge from hospital (hospital), or end of operation to discharge from PACU (PACU)	
End point type	Secondary
End point timeframe:	
30 days	

End point values	Dexamethason e 8 mg	Dexamethason e 24 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63 <sup>[9]</sup>	64 <sup>[10]</sup>		
Units: hours				
median (inter-quartile range (Q1-Q3))				
LOS, Hospital	9.2 (7.4 to 24.4)	11 (8.1 to 23.5)		
LOS, PACU	2 (1.4 to 2.4)	1.5 (1.4 to 2.1)		

Notes:

[9] - 2 pre-intervention exclusion

[10] - 1 pre-intervention exclusion

## Statistical analyses

<b>Statistical analysis title</b>	LOS
Comparison groups	Dexamethasone 8 mg v Dexamethasone 24 mg
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.217 <sup>[11]</sup>
Method	Wilcoxon (Mann-Whitney)

Notes:

[11] - PACU 0.350

## Secondary: Readmission

End point title	Readmission
End point description:	any readmission (other than scheduled oncological)
End point type	Secondary
End point timeframe:	30 days

End point values	Dexamethason e 8 mg	Dexamethason e 24 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63 <sup>[12]</sup>	64 <sup>[13]</sup>		
Units: number of patients	4	4		

Notes:

[12] - 2 pre-intervention exclusion

[13] - 2 pre-intervention exclusion

## Statistical analyses

<b>Statistical analysis title</b>	readmissions
Comparison groups	Dexamethasone 8 mg v Dexamethasone 24 mg
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.97
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.243
upper limit	4.3

## Secondary: Seroma

End point title	Seroma
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End point description: no of patients with seroma requiring drainage	
End point type	Secondary
End point timeframe: 14 days	

End point values	Dexamethason e 8 mg	Dexamethason e 24 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63 <sup>[14]</sup>	64 <sup>[15]</sup>		
Units: number of patients	51	60		

Notes:

[14] - 2 pre-intervention exclusion

[15] - 1 pre-intervention exclusion

### Statistical analyses

Statistical analysis title	seroma
Comparison groups	Dexamethasone 8 mg v Dexamethasone 24 mg
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	3.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	11.6

### Secondary: wound infection

End point title	wound infection
End point description: no of patients with wound infection req treatment	
End point type	Secondary
End point timeframe: 30 days	

End point values	Dexamethason e 8 mg	Dexamethason e 24 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63 <sup>[16]</sup>	64 <sup>[17]</sup>		
Units: no of patients	1	3		

Notes:

[16] - 2 pre-intervention exclusion

[17] - 1 pre-intervention exclusion

### Statistical analyses

Statistical analysis title	wound infection
Comparison groups	Dexamethasone 8 mg v Dexamethasone 24 mg
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.315
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	3.24

### Post-hoc: Proportion of patients actually transferred

End point title	Proportion of patients actually transferred
End point description:	
Post-hoc analysis of patients actually transferred to PACU, since not all patients who met the criteria for transfer were actually transferred	
End point type	Post-hoc
End point timeframe:	
1 h	

End point values	Dexamethason e 8 mg	Dexamethason e 24 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63 <sup>[18]</sup>	64 <sup>[19]</sup>		
Units: patients	12	12		

Notes:

[18] - 2 pre-intervention exclusion

[19] - 1 pre-intervention exclusion

### Statistical analyses

Statistical analysis title	post hoc primary endpoint
Comparison groups	Dexamethasone 8 mg v Dexamethasone 24 mg

Number of subjects included in analysis	127
Analysis specification	Post-hoc
Analysis type	superiority
P-value	> 0.999
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	2.43

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

60 hours from intervention administration

Adverse event reporting additional description:

Patient charts, patient questionnaire

Assessment type	Systematic
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### Dictionary used

Dictionary name	SNOMED CT
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Dictionary version	2019-09-30
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### Reporting groups

Reporting group title	Dexamethasone 8 mg
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Reporting group description:

Single-shot preoperative injection

Reporting group title	Dexamethasone 24 mg
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Reporting group description:

Single shot pre-operative injection, 24 mg

Serious adverse events	Dexamethasone 8 mg	Dexamethasone 24 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 63 (7.94%)	3 / 64 (4.69%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			
Haemorrhage	Additional description: postoperative wound hemorrhage/hematoma		
subjects affected / exposed	5 / 63 (7.94%)	3 / 64 (4.69%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Dexamethasone 8 mg	Dexamethasone 24 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 63 (9.52%)	8 / 64 (12.50%)	
Surgical and medical procedures			
Haemorrhage			
subjects affected / exposed	6 / 63 (9.52%)	3 / 64 (4.69%)	
occurrences (all)	6	3	



## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported