Clinical trial results:
Dexamethasone twice for pain treatment of total knee arthroplasty (DEX-2-TKA)
A randomized blinded placebo-controlled clinical trial

Summary

EudraCT number	2018-001099-39
Trial protocol	DK
Global end of trial date	07 June 2020

Results information

Result version number	v1 (current)
This version publication date	01 March 2022
First version publication date	01 March 2022

Trial information

Trial identification

Sponsor protocol code	SM1-KAKG-2018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03506789
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Department of Anaesthesiology
Sponsor organisation address	Ringstedgade 61, Næstved, Denmark, 4700
Public contact	Daniel Hägi-Pedersen, Department of Anaesthesiology, Naestved Hospital, 0045 56514002, anaestesisekretariat@regionsjaelland.dk
Scientific contact	Daniel Hägi-Pedersen, Department of Anaesthesiology, Naestved Hospital, 0045 56514002, anaestesisekretariat@regionsjaelland.dk

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	27 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 March 2020
Global end of trial reached?	Yes
Global end of trial date	07 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this trial is to investigate the analgesic efficacy and safety of one or two doses of dexamethasone after total knee arthroplasty

Protection of trial subjects:

Subjects received a Patient Controlled Analgesia Pump with morphine, where they could steer their own pain treatment. Thus reducing patients discomfort in trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 October 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 485
Worldwide total number of subjects	485
EEA total number of subjects	485

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)	179
From 65 to 84 years	296

85 years and over	10

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All participants scheduled for primary, unilateral total knee arthroplasty were screened for enrolment. 1599 patients were assessed for eleigibility.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	DEX1

Arm description:

24 mg dexamethasone i.v. perioperatively and placebo (isotonic saline) i.v. on the first postoperative day

Arm type	Active comparator
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

24 milligramme intravenous after start of anaesthesia.

Investigational medicinal product name	NaCl (Sodium Chloride)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Placebo (isotonic saline) i.v. on the first postoperative day 6 ml. 24 hours after last suture.

Arm title	DEX2

Arm description:

24 mg dexamethasone i.v. perioperatively and 24 mg dexamethasone i.v. on the first postoperative day

Arm type	Active comparator
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

24 mg dexamethasone i.v. perioperatively and 24 mg dexamethasone i.v. on the first postoperative day, 24 hours after last suture.

Arm title	Placebo

Arm description:

Placebo (isotonic saline) i.v. perioperatively and placebo (isotonic saline) i.v. on the first postoperative day

Arm type	Placebo
Investigational medicinal product name	NaCl (Sodium Chloride)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Placebo (isotonic saline) i.v. perioperatively 6 ml and placebo (isotonic saline) i.v. on the first postoperative day 6 ml, 24 hours after last suture.

Number of subjects in period 1	DEX1	DEX2	Placebo
Started	161	162	162
Completed	161	162	162

Baseline characteristics

Reporting groups	
Reporting group title	DEX1
Reporting group description:	
24 mg dexamethasone i.v. perioperatively and placebo (isotonic saline) i.v. on the first postoperative day	
Reporting group title	DEX2
Reporting group description:	
24 mg dexamethasone i.v. perioperatively and 24 mg dexamethasone i.v. on the first postoperative day	
Reporting group title	Placebo
Reporting group description:	
Placebo (isotonic saline) i.v. perioperatively and placebo (isotonic saline) i.v. on the first postoperative day	

Reporting group values	DEX1	DEX2	Placebo
Number of subjects	161	162	162
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Age in years			
Units: years			
arithmetic mean	69	67	68
standard deviation	± 9	± 9	± 9
Gender categorical			
Sex			
Units: Subjects			
Female	81	87	88
Male	80	75	74
American Society of Anesthesiologists physical status			
American Society of Anesthesiologists physical status			
Units: Subjects			
Healthy	28	28	19
Mild systemic disease	102	114	120
Severe systemic disease	31	20	23
Type 2 diabetes			
Type 2 diabetes			
Units: Subjects			

No	145	146	145
Yes	16	16	17
Type of Anaesthesia			
Units: Subjects			
Spinal	128	131	132
General	30	28	26
Conversion of spinal to general	3	3	4
Use of PONV prophylaxis			
Administration of 4 mg ondansetron PONV prophylaxis			
Units: Subjects			
Yes	140	146	151
No	21	16	11
Local infiltration analgesia			
Administration of local infiltration analgesia			
Units: Subjects			
Yes	157	162	161
No	4	0	1
Type of knee arthroplasty			
Type of knee arthroplasty			
Units: Subjects			
Cemented	97	96	94
Cement less	5	2	4
Hybrid	59	64	64
Height			
Height in cm			
Units: centimetre			
arithmetic mean	173	172	172
standard deviation	± 10	± 9	± 10
Weight			
Weight in kg			
Units: kilogram(s)			
arithmetic mean	86	88	89
standard deviation	± 17	± 15	± 16
BMI			
Body mass index			
Units: kilogram(s)/square metre			
arithmetic mean	29	30	30
standard deviation	± 5	± 4	± 4
Median use of sufentanil under GA			
Mean (SD) amount of sufentanil used if general anaesthesia (µg)			
Units: microgram(s)			
arithmetic mean	26.6	26.2	27.8
standard deviation	± 6.1	± 4.7	± 8.7
Median amonut bupivacaine in spinal			
Median (IQR) amount of bupivacaine in spinal anaesthesia (mg)			
Units: milligram(s)			
median	11	11	11
inter-quartile range (Q1-Q3)	10 to 11.5	10 to 12	10 to 12
Intraoperative bloodloss			
Median (IQR) intraoperative blood loss (mL). Intraoperative blood loss was registered at the end of surgery, comprising blood in the suction bottle and gauze			

Units: millilitre(s)			
median	150	150	150
inter-quartile range (Q1-Q3)	50 to 250	100 to 200	56 to 250
Duration of surgery			
Median (IQR) duration of surgery (min)			
Units: minute'			
median	61	62	63
inter-quartile range (Q1-Q3)	55 to 71	53 to 73	54 to 71
Median use of morphine			
Previous median (IQR) amount of opioid used (mg).			
Units: milligram(s)			
median	12.5	15	20
inter-quartile range (Q1-Q3)	11.3 to 13.8	10 to 20	20 to 20

Reporting group values	Total		
Number of subjects	485		
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			
Age in years			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Sex			
Units: Subjects			
Female	256		
Male	229		
American Society of Anesthesiologists physical status			
American Society of Anesthesiologists physical status			
Units: Subjects			
Healthy	75		
Mild systemic disease	336		
Severe systemic disease	74		
Type 2 diabetes			
Type 2 diabetes			
Units: Subjects			
No	436		
Yes	49		
Type of Anaesthesia			

Units: Subjects			
Spinal	391		
General	84		
Conversion of spinal to general	10		
Use of PONV prophylaxis			
Administration of 4 mg ondansetron PONV prophylaxis			
Units: Subjects			
Yes	437		
No	48		
Local infiltration analgesia			
Administration of local infiltration analgesia			
Units: Subjects			
Yes	480		
No	5		
Type of knee arthroplasty			
Type of knee arthroplasty			
Units: Subjects			
Cemented	287		
Cement less	11		
Hybrid	187		
Height			
Height in cm			
Units: centimetre			
arithmetic mean			
standard deviation	-		
Weight			
Weight in kg			
Units: kilogram(s)			
arithmetic mean			
standard deviation	-		
BMI			
Body mass index			
Units: kilogram(s)/square metre			
arithmetic mean			
standard deviation	-		
Median use of sufentanil under GA			
Mean (SD) amount of sufentanil used if general anaesthesia (µg)			
Units: microgram(s)			
arithmetic mean			
standard deviation	-		
Median amonut bupivacaine in spinal			
Median (IQR) amount of bupivacaine in spinal anaesthesia (mg)			
Units: milligram(s)			
median			
inter-quartile range (Q1-Q3)	-		
Intraoperative bloodloss			
Median (IQR) intraoperative blood loss (mL). Intraoperative blood loss was registered at the end of surgery, comprising blood in the suction bottle and gauze			
Units: millilitre(s)			
median			
inter-quartile range (Q1-Q3)	-		

Duration of surgery			
Median (IQR) duration of surgery (min)			
Units: minute' median inter-quartile range (Q1-Q3)	- - -		
Median use of morphine			
Previous median (IQR) amount of opioid used (mg).			
Units: milligram(s) median inter-quartile range (Q1-Q3)	- - -		

End points

End points reporting groups

Reporting group title	DEX1
Reporting group description:	
24 mg dexamethasone i.v. perioperatively and placebo (isotonic saline) i.v. on the first postoperative day	
Reporting group title	DEX2
Reporting group description:	
24 mg dexamethasone i.v. perioperatively and 24 mg dexamethasone i.v. on the first postoperative day	
Reporting group title	Placebo
Reporting group description:	
Placebo (isotonic saline) i.v. perioperatively and placebo (isotonic saline) i.v. on the first postoperative day	

Primary: Median morphine consumption at 0-48 h

End point title	Median morphine consumption at 0-48 h
End point description:	
End point type	Primary
End point timeframe:	
Morphine consumption from last suture of operation to 48 hours after last suture.	

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: milligram(s)				
median (confidence interval 98.3%)	37.9 (20.7 to 56.7)	35.0 (20.6 to 52.0)	43 (28.7 to 64.0)	

Statistical analyses

Statistical analysis title	Median diffrence between DEX2 and DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.3 [2]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	-2.7

Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	-9.3
upper limit	3.7

Notes:

[1] - Hodges-Lehman median diffrence

[2] - Because three intervention groups were included, we used an α of 0.0167 (Bonferroni correction; two sided)

Statistical analysis title	Median diffrence between DEX2 and DEX1
Comparison groups	Placebo v DEX1
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.008 [4]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	7.8
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	0.7
upper limit	14.7

Notes:

[3] - Hodges-Lehman median diffrence

[4] - Because three intervention groups were included, we used an α of 0.0167 (Bonferroni correction; two sided)

Statistical analysis title	Median diffrence between DEX2 and placebo group
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.001 [6]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	10.7
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	4
upper limit	17.3

Notes:

[5] - Hodges-Lehman median diffrence

[6] - Because three intervention groups were included, we used an α of 0.0167 (Bonferroni correction; two sided)

Secondary: Pain intensity level; knee flexion

End point title	Pain intensity level; knee flexion

End point description:

End point type	Secondary

End point timeframe:
24 hours postoperatively

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	50 (32 to 69.5)	50 (35 to 68)	60 (44 to 80)	

Statistical analyses

Statistical analysis title	Pain int level; knee flex at 24 h, DEX2 vs DEX1
Statistical analysis description:	
Pain intensity level; knee flexion at 24 h (mm)	
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.91 [7]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	5

Notes:
[7] - Significance level 0.05.

Statistical analysis title	Pain int level; knee flex at 24 h, Plac and DEX1
Statistical analysis description:	
Pain intensity level; knee flexion at 24 h (mm)	
Comparison groups	Placebo v DEX1
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [8]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	4
upper limit	15

Notes:
[8] - Significance level 0.05.

Statistical analysis title	Pain int level; knee flex at 24 h, Plac and DEX2
Statistical analysis description: Pain intensity level; knee flexion at 24 h (mm)	
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [9]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	15

Notes:
[9] - Significance level 0.05.

Secondary: Pain intensity level at rest 24 h

End point title	Pain intensity level at rest 24 h
End point description:	
End point type	Secondary
End point timeframe: 24 hours postoperatively	

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	20 (8 to 31)	20 (10 to 35)	24.5 (14 to 45)	

Statistical analyses

Statistical analysis title	Median diff pain rest, DEX2 vs DEX1
Statistical analysis description: Pain intensity level at rest	
Comparison groups	DEX1 v DEX2

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.25 [10]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	6

Notes:

[10] - Significance level 0.05

Statistical analysis title	Median diff pain rest, Plac vs DEX1
Statistical analysis description:	
Pain intensity level at rest	
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [11]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	7
Confidence interval	
level	95 %
sides	2-sided
lower limit	3
upper limit	11

Notes:

[11] - Significance level 0.05

Statistical analysis title	Median diff pain rest, Plac vs DEX2
Statistical analysis description:	
Pain intensity level at rest	
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.031 [12]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	10

Notes:
[12] - Significance level 0.05

Secondary: Level of highest pain 0-24h

End point title	Level of highest pain 0-24h

End point description:

End point type	Secondary

End point timeframe:
From last suture to 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	70 (50 to 85)	69 (50 to 82)	80 (66 to 90)	

Statistical analyses

Statistical analysis title	Median diff highest pain, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.81 [13]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	5

Notes:
[13] - Significance level 0.05.

Statistical analysis title	Median diff highest pain, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [14]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	10

Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	15

Notes:
[14] - Significance level 0.05.

Statistical analysis title	Median diff highest pain, Plac vs DEX2
Comparison groups	DEX2 v Placebo
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [15]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	15

Notes:
[15] - Significance level 0.05.

Secondary: Pain Intensity level, knee flexion 48 h	
End point title	Pain Intensity level, knee flexion 48 h
End point description:	
End point type	Secondary
End point timeframe:	
48 hours postoperatively	

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	55 (40 to 70)	40 (30 to 50)	50 (35 to 63.5)	

Statistical analyses

Statistical analysis title	Medeian difference pain, knee flex, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [16]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	-15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20
upper limit	-10

Notes:

[16] - Significance level 0.05

Statistical analysis title	Medeian difference pain, knee flex, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011 [17]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	-6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	0

Notes:

[17] - Significance level 0.05

Statistical analysis title	Medeian difference pain, knee flex, Plac vs DEX2
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [18]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	3
upper limit	11

Notes:

[18] - Significance level 0.05

Secondary: Pain Intensity level at rest at 48h

End point title	Pain Intensity level at rest at 48h

End point description:

End point type	Secondary

End point timeframe:

48 hours postoperatively

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	30 (10 to 40)	15 (9 to 30)	20 (10 to 35)	

Statistical analyses

Statistical analysis title	Median diff pain, rest DEX2 vs DEX1

Statistical analysis description:

Median diffrence of pain intensity level at rest 48 hours postoperatively

Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [19]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	-10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	-5

Notes:

[19] - Significance level 0.05

Statistical analysis title	Median diff pain, rest Plac vs DEX1

Statistical analysis description:

Median diffrence of pain intensity level at rest 48 hours postoperatively

Comparison groups	Placebo v DEX1
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01 [20]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	-3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	0

Notes:
[20] - Significance level 0.05

Statistical analysis title	Median diff pain, rest Plac vs DEX2

Statistical analysis description:
Median diffrence of pain intensity level at rest 48 hours postoperatively

Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [21]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	10

Notes:
[21] - Significance level 0.05

Secondary: Level for highest pain intensity 24–48 h

End point title	Level for highest pain intensity 24–48 h

End point description:

End point type	Secondary

End point timeframe:
24 hours to 48 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	70 (50 to 84)	60 (40 to 71)	70 (52 to 80)	

Statistical analyses

Statistical analysis title	Median diff highest pain, DEX2 vs DEX1

Statistical analysis description:	
Median diffrence of the level for highest pain intensity between 24–48 hours postoperatively	
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [22]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	-10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20
upper limit	-10

Notes:

[22] - Significance level 0.05

Statistical analysis title	Median diff highest pain, Plac vs DEX1
Statistical analysis description:	
Median diffrence of the level for highest pain intensity between 24–48 hours postoperatively	
Comparison groups	Placebo v DEX1
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.89 [23]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	5

Notes:

[23] - Significance level 0.05

Statistical analysis title	Median diff highest pain, Plac vs DEX2
Statistical analysis description:	
Median diffrence of the level for highest pain intensity between 24–48 hours postoperatively	
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [24]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	11

Confidence interval	
level	95 %
sides	2-sided
lower limit	10
upper limit	20

Notes:
[24] - Significance level 0.05

Secondary: Adverse Events 0- 48 hours postoperatively

End point title	Adverse Events 0- 48 hours postoperatively

End point description:

End point type	Secondary

End point timeframe:
Adverse events from last suture of operation to 48 hours after last suture.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: Events	7	4	10	

Statistical analyses

Statistical analysis title	Odds ratio, AE, DEX2 vs DEX1

Statistical analysis description:
Adverse events 0- 48 hours postoperatively, odds ratio.

Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.35 [25]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	1.92

Notes:
[25] - Significance level 0.05.

Statistical analysis title	Odds ratio, AE, Plac vs DEX1

Statistical analysis description:
Adverse events 0- 48 hours postoperatively, odds ratio.

Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.45 [26]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	4.09

Notes:

[26] - Significance level 0.05.

Statistical analysis title	Odds ratio, AE, Plac vs DEX2

Statistical analysis description:

Adverse events 0- 48 hours postoperatively, odds ratio.

Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1 [27]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	9.25

Notes:

[27] - Significance level 0.05.

Other pre-specified: Serious adverse events within 90 days

End point title	Serious adverse events within 90 days

End point description:

End point type	Other pre-specified

End point timeframe:

From the day of surgery until 90 days postoperatively

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: Events	21	9	18	

Statistical analyses

Statistical analysis title	Odds ratio, SAE 90 days, DEX2 vs DEX1
Comparison groups	DEX2 v DEX1
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023 [28]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	0.88

Notes:

[28] - Significance level 0.05

Statistical analysis title	Odds ratio, SAE 90 days, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.06 [29]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	1.64

Notes:

[29] - Significance level 0.05

Statistical analysis title	Odds ratio, SAE 90 days, Plac vs DEX2
Comparison groups	Placebo v DEX2

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.075 [30]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	4.9

Notes:

[30] - Significance level 0.05

Other pre-specified: Nausea 24 hours	
End point title	Nausea 24 hours

End point description:

End point type	Other pre-specified

End point timeframe:

Nausea at 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: patients	57	76	108	

Statistical analyses

Statistical analysis title	Odds ratio nausea 24h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.035
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	2.56

Statistical analysis title	Odds ratio nausea 24h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.57
upper limit	6.7

Statistical analysis title	Odds ratio nausea 24h, Plac vs DEX2
Comparison groups	DEX2 v Placebo
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.54
upper limit	3.85

Other pre-specified: Nausea 48 hours	
End point title	Nausea 48 hours
End point description:	

End point type	Other pre-specified
End point timeframe:	
Nausea at 48 hours postoperatively.	

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: patients	63	46	72	

Statistical analyses

Statistical analysis title	Odds ratio nausea 48 h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05 [31]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	1

Notes:

[31] - Significance level 0.05

Statistical analysis title	Odds ratio nausea 48 h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.24 [32]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	2.06

Notes:

[32] - Significance level 0.05

Statistical analysis title	Odds ratio nausea 48 h, Plac vs DEX2
Comparison groups	DEX2 v Placebo

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [33]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.31
upper limit	3.38

Notes:

[33] - Significance level 0.05

Other pre-specified: Sedation 24 hours	
End point title	Sedation 24 hours

End point description:

End point type	Other pre-specified

End point timeframe:

Sedation at 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: patients	49	74	93	

Statistical analyses

Statistical analysis title	Odds ratio sedation 24 h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [34]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.25
upper limit	3.13

Notes:
[34] - Significane level 0.05.

Statistical analysis title	Odds ratio sedation 24 h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [35]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.08
upper limit	5.28

Notes:
[35] - Significane level 0.05.

Statistical analysis title	Odds ratio sedation 24 h, Plac vs DEX2
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.027 [36]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	2.59

Notes:
[36] - Significane level 0.05.

Other pre-specified: Sedation 48 hours	
End point title	Sedation 48 hours

End point description:

End point type	Other pre-specified

End point timeframe:
Sedation at 48 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: patients	59	53	75	

Statistical analyses

Statistical analysis title	Odds ratio sedation 48h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.43 [37]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.33

Notes:

[37] - Significance level 0.05.

Statistical analysis title	Odds ratio sedation 48h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047 [38]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	2.5

Notes:

[38] - Significance level 0.05.

Statistical analysis title	Odds ratio sedation 48h, Plac vs DEX2
Comparison groups	Placebo v DEX2

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007 [39]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.19
upper limit	3

Notes:

[39] - Significance level 0.05.

Other pre-specified: Dizziness 24 hours

End point title	Dizziness 24 hours

End point description:

End point type	Other pre-specified

End point timeframe:

Dizziness at 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: patients	60	71	104	

Statistical analyses

Statistical analysis title	Odds ratio dizziness 24h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.21 [40]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	2.08

Notes:
[40] - Significance level 0.05

Statistical analysis title	Odds ratio dizziness 24h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [41]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.06
upper limit	5.21

Notes:
[41] - Significance level 0.05

Statistical analysis title	Copy of Odds ratio dizziness 24h, Plac vs DEX2
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [42]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.54
upper limit	3.8

Notes:
[42] - Significance level 0.05

Other pre-specified: Dizziness 48 hours	
End point title	Dizziness 48 hours

End point description:

End point type	Other pre-specified

End point timeframe:
Dizziness at 48 hours postoperatively

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: patients	47	40	54	

Statistical analyses

Statistical analysis title	Odds ratio dizziness 48 h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.38 [43]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.32

Notes:

[43] - Significance level 0.05.

Statistical analysis title	Odds ratio dizziness 48 h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.34 [44]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	2.04

Notes:

[44] - Significance level 0.05.

Statistical analysis title	Odds ratio dizziness 48 h, Plac vs DEX2
Comparison groups	Placebo v DEX2

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.068 [45]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	2.58

Notes:

[45] - Significance level 0.05.

Other pre-specified: Vomiting episodes 0-24 h

End point title	Vomiting episodes 0-24 h

End point description:

End point type	Other pre-specified

End point timeframe:

Vomiting episodes between 0 hours and 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: episodes	31	35	66	

Statistical analyses

Statistical analysis title	Odds ratio vomiting 0-24h, DEX2 vs DEX1
Comparison groups	DEX2 v DEX1
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.65 [46]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.96

Notes:
[46] - Significance level 0.05.

Statistical analysis title	Odds ratio vomiting 0-24h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [47]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.89
upper limit	5.34

Notes:
[47] - Significance level 0.05.

Statistical analysis title	Odds ratio vomiting 0-24h, Plac vs DEX2
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [48]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	4.29

Notes:
[48] - Significance level 0.05.

Other pre-specified: Vomiting episodes 24-48 hours

End point title	Vomiting episodes 24-48 hours

End point description:

End point type	Other pre-specified

End point timeframe:
Vomiting episodes between 24 hours and 48 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: episodes	17	11	28	

Statistical analyses

Statistical analysis title	Odds ratio vomiting 24-48h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.24 [49]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	1.37

Notes:

[49] - Significance level 0.05.

Statistical analysis title	Odds ratio vomiting 24-48h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.065 [50]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	3.54

Notes:

[50] - Significance level 0.05.

Statistical analysis title	Odds ratio vomiting 24-48h, Plac vs DEX2
Comparison groups	Placebo v DEX2

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [51]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.41
upper limit	6.17

Notes:

[51] - Significance level 0.05.

Other pre-specified: Ondansetron used 0-24 h

End point title	Ondansetron used 0-24 h

End point description:

End point type	Other pre-specified

End point timeframe:

Ondansetron used i milligrams between 0 hours until 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: milligram(s)				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 1)	0 (0 to 2)	

Statistical analyses

Statistical analysis title	Median diff ondansetron 0-24h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.066
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Statistical analysis title	Median diff ondansetron 0-24h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Statistical analysis title	Median diff ondansetron 0-24h, Plac vs DEX2
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Other pre-specified: Ondansetron used 24-48 hours	
End point title	Ondansetron used 24-48 hours
End point description:	

End point type	Other pre-specified
End point timeframe:	
Ondansetron used between 24 hours until 48 hours postoperatively.	

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: milligram(s)				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	

Statistical analyses

Statistical analysis title	Odds ratio ondansetron 24-48h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.86 [52]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Notes:

[52] - Significance level 0.05

Statistical analysis title	Odds ratio ondansetron 24-48h, Plac vs DEX1
Comparison groups	Placebo v DEX1
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005 [53]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Notes:

[53] - Significance level 0.05

Statistical analysis title	Odds ratio ondansetron 24-48h, Plac vs DEX2
Comparison groups	Placebo v DEX2

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007 [54]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Notes:
[54] - Significance level 0.05

Other pre-specified: Droperidol used 0-24 hours

End point title	Droperidol used 0-24 hours

End point description:

End point type	Other pre-specified

End point timeframe:
Droperidol used between 0 hours and 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: milligram(s)				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	

Statistical analyses

Statistical analysis title	Odds ratio droperidol 0-24 h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.36 [55]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Notes:
[55] - Significance level 0.05.

Statistical analysis title	Odds ratio droperidol 0-24 h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [56]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Notes:
[56] - Significance level 0.05.

Statistical analysis title	Odds ratio droperidol 0-24 h, Plac vs DEX2
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.031 [57]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Notes:
[57] - Significance level 0.05.

Other pre-specified: Droperidol used 24-48 h

End point title	Droperidol used 24-48 h

End point description:

End point type	Other pre-specified

End point timeframe:
Droperidol used between 0 hours and 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: milligram(s)				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	

Statistical analyses

Statistical analysis title	Odds ratio droperidol 24-48 h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.66 [58]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Notes:

[58] - Significance level 0.05.

Statistical analysis title	Odds ratio droperidol 24-48 h,Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12 [59]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Notes:

[59] - Significance level 0.05.

Statistical analysis title	Odds ratio droperidol 24-48 h,Plac vs DEX2
Comparison groups	Placebo v DEX2

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.054 [60]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Notes:

[60] - Significance level 0.05.

Other pre-specified: Morphine consumption 0-24 hours

End point title	Morphine consumption 0-24 hours

End point description:

End point type	Other pre-specified

End point timeframe:

Morphine consumption between 0 hours and 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: milligram(s)				
median (inter-quartile range (Q1-Q3))	28 (17.0 to 42.0)	28 (16.0 to 42.0)	36.3 (22.0 to 52.0)	

Statistical analyses

Statistical analysis title	Median diff morphine 0-24 h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.646
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	4

Statistical analysis title	Median diff morphine 0-24 h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	6
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	12

Statistical analysis title	Median diff morphine 0-24 h, Plac vs DEX2
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.7
upper limit	12

Other pre-specified: Morphine consumption 24-48 hours	
End point title	Morphine consumption 24-48 hours
End point description:	

End point type	Other pre-specified
End point timeframe:	
Morphine consumption between 24 hours and 48 hours postoperatively.	

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: milligram(s)				
median (inter-quartile range (Q1-Q3))	6.7 (3.3 to 13.3)	6.7 (0.0 to 10.0)	6.7 (3.3 to 13.3)	

Statistical analyses

Statistical analysis title	Median diff morphine 24-48h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012 [61]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	0

Notes:

[61] - Significance level 0.05.

Statistical analysis title	Median diff morphine 24-48h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.258 [62]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	3.3

Notes:

[62] - Significance level 0.05.

Statistical analysis title	Median diff morphine 24-48h, Plac vs DEX2
Comparison groups	Placebo v DEX2

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [63]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	3.3

Notes:

[63] - Significance level 0.05.

Other pre-specified: Pain intensity llevel, knee flexion at 6 h

End point title	Pain intensity llevel, knee flexion at 6 h

End point description:

End point type	Other pre-specified

End point timeframe:

Pain intensitiy level with knee flexion at 6 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	50 (30 to 66)	45 (25 to 64.5)	59 (39 to 75)	

Statistical analyses

Statistical analysis title	Median diff pain int flex 6h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.538 [64]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8
upper limit	5

Notes:
[64] - Significance level 0.05.

Statistical analysis title	Median diff pain int flex 6h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [65]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	16

Notes:
[65] - Significance level 0.05.

Statistical analysis title	Median diff pain int flex 6h, Plac vs DEX2
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [66]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	11
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	19

Notes:
[66] - Significance level 0.05.

Other pre-specified: Pain intensitiy level at rest at 6 h	
End point title	Pain intensitiy level at rest at 6 h

End point description:

End point type	Other pre-specified

End point timeframe:
Pain intensitiy level at rest at 6 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	23 (10 to 42)	24 (11 to 39)	34 (20 to 50)	

Statistical analyses

Statistical analysis title	Median diff pain intens rest 6h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.658 [67]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	4

Notes:

[67] - Significance level 0.05.

Statistical analysis title	Median diff pain intens rest 6h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [68]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	4
upper limit	15

Notes:

[68] - Significance level 0.05.

Statistical analysis title	Median diff pain intens rest 6h, Plac vs DEX2
Comparison groups	Placebo v DEX2

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [69]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	15

Notes:

[69] - Significance level 0.05.

Other pre-specified: Nausea 6 h

End point title	Nausea 6 h

End point description:

End point type	Other pre-specified

End point timeframe:

Nausea at 6 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: patients	11	22	45	

Statistical analyses

Statistical analysis title	Odds ratio nausea 6h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.054 [70]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	4.56

Notes:
[70] - Significance level 0.05.

Statistical analysis title	Odds ratio nausea 6h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [71]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.73
upper limit	11.32

Notes:
[71] - Significance level 0.05.

Statistical analysis title	Odds ratio nausea 6h, Plac vs DEX2
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [72]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.44
upper limit	4.51

Notes:
[72] - Significance level 0.05.

Other pre-specified: Sedation 6 h

End point title	Sedation 6 h

End point description:

End point type	Other pre-specified

End point timeframe:
Sedation at 6 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: Patients	43	49	61	

Statistical analyses

Statistical analysis title	Median diff sedation 6h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.538
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.91

Statistical analysis title	Median diff sedation 6h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.024
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	2.82

Statistical analysis title	Median diff sedation 6h, Plac vs DEX2
Comparison groups	Placebo v DEX2

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.098
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	2.39

Other pre-specified: Dizziness at 6 h	
End point title	Dizziness at 6 h
End point description:	

End point type	Other pre-specified
End point timeframe:	
Dizziness at 6 hours postoperatively.	

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: patients	22	28	44	

Statistical analyses

Statistical analysis title	Median diff dizziness 6h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.41 [73]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	2.41

Notes:
[73] - Significance level 0.05.

Statistical analysis title	Median diff dizziness 6h, Plac vs DEX1
Comparison groups	Placebo v DEX1
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [74]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.36
upper limit	4.28

Notes:
[74] - Significance level 0.05.

Statistical analysis title	Median diff dizziness 6h, Plac vs DEX2
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025 [75]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	3.2

Notes:
[75] - Significance level 0.05.

Other pre-specified: Level for average pain intensity 0-24 h

End point title	Level for average pain intensity 0-24 h

End point description:

End point type	Other pre-specified

End point timeframe:
Level for average pain intensity between 0 hours until 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	37 (25 to 48)	39 (30 to 50)	48 (39 to 57)	

Statistical analyses

Statistical analysis title	Med diff pain average 0-24h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.268
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	6

Statistical analysis title	Med diff pain average 0-24h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	7
upper limit	15

Statistical analysis title	Med diff pain average 0-24h, Plac vs DEX2
Comparison groups	Placebo v DEX2

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	12

Other pre-specified: Level for average pain intensity between 24-48 h

End point title	Level for average pain intensity between 24-48 h

End point description:

End point type	Other pre-specified

End point timeframe:

Level for average pain intensity between 24 hours until 48 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	45 (30 to 52)	30 (20 to 50)	40 (30 to 50)	

Statistical analyses

Statistical analysis title	Median diff pain average 24-48h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [76]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	-10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15
upper limit	-5

Notes:
[76] - Significance level 0.05

Statistical analysis title	Median diff pain average 24-48h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.431 [77]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	0

Notes:
[77] - Significance level 0.05

Statistical analysis title	Median diff pain average 24-48h, Plac vs DEX2
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [78]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	12

Notes:
[78] - Significance level 0.05

Other pre-specified: Quality of sleep 24 h	
End point title	Quality of sleep 24 h

End point description:

End point type	Other pre-specified

End point timeframe:
Quality of sleep at 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: patients	70	73	87	

Statistical analyses

Statistical analysis title	Odds ratio sleep 24h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.819
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.64

Statistical analysis title	Odds ratio sleep 24h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	2.46

Statistical analysis title	Odds ratio sleep 24h, Plac vs DEX2
Comparison groups	DEX2 v Placebo

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.073
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	2.33

Other pre-specified: Quality of sleep at 24 h

End point title	Quality of sleep at 24 h

End point description:

End point type	Other pre-specified

End point timeframe:

Quality of sleep at 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: Patients	44	26	35	

Statistical analyses

Statistical analysis title	Odds ratio sleep 48 h, DEX2 vs DEX1
Comparison groups	DEX2 v DEX1
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015 [79]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	0.88

Notes:
[79] - Significance level 0.05.

Statistical analysis title	Odds ratio sleep 48 h,Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.283 [80]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	1.26

Notes:
[80] - Significance level 0.05.

Statistical analysis title	Copy of Odds ratio sleep 48 h,Plac vs DEX2
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.187 [81]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	2.59

Notes:
[81] - Significance level 0.05.

Other pre-specified: Fatigue at 24 h	
End point title	Fatigue at 24 h

End point description:

End point type	Other pre-specified

End point timeframe:
Fatigue at 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: patients	70	81	120	

Statistical analyses

Statistical analysis title	Odds ratio fatigue 24 h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.222
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	2.05

Statistical analysis title	Odds ratio fatigue 24 h, Plac vs DEX1
Comparison groups	Placebo v DEX1
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.54
upper limit	6.66

Statistical analysis title	Odds ratio fatigue 24 h, Plac vs DEX2
Comparison groups	Placebo v DEX2

Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.92
upper limit	5.02

Other pre-specified: Fatigue at 48 h

End point title	Fatigue at 48 h

End point description:

End point type	Other pre-specified

End point timeframe:

Fatigue at 48 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: patients	133	116	135	

Statistical analyses

Statistical analysis title	Odds ratio fatigue 48 h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.024
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.92

Statistical analysis title	Odds ratio fatigue 48 h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.289
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	2.79

Statistical analysis title	Odds ratio fatigue 48 h, Plac vs DEX2
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.47
upper limit	5.08

Other pre-specified: Failure to fulfill timed up and go test 24 h	
End point title	Failure to fulfill timed up and go test 24 h
End point description:	

End point type	Other pre-specified
End point timeframe:	
Timed up and go test at 24 hours postoperatively.	

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	156	158	
Units: patients	46	48	62	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time for completion of timed up and go test 24 h

End point title	Time for completion of timed up and go test 24 h

End point description:

End point type	Other pre-specified

End point timeframe:

Time for completion of timed up and go test 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	112	108	96	
Units: second				
median (inter-quartile range (Q1-Q3))	30.5 (22 to 44)	31 (20 to 41)	40 (26.5 to 54.5)	

Statistical analyses

Statistical analysis title	Median diff TUG time 24h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.413 [82]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	2

Notes:

[82] - Significance level 0.05.

Statistical analysis title	Median diff TUG time 24h, Plac vs DEX1
Comparison groups	DEX1 v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.058 [83]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	12

Notes:

[83] - Significance level 0.05.

Statistical analysis title	Median diff TUG time 24h, Plac vs DEX2
Comparison groups	Placebo v DEX2
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [84]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	4
upper limit	14

Notes:

[84] - Significance level 0.05.

Other pre-specified: Level for highest pain intensitiy during TUG 24 h

End point title	Level for highest pain intensitiy during TUG 24 h

End point description:

End point type	Other pre-specified

End point timeframe:

Level for highest pain intensitiy during timed up and go test at 24 hours postoperatively.

End point values	DEX1	DEX2	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	112	108	96	
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	49 (30 to 60)	42 (25 to 58)	48 (34.5 to 61.5)	

Statistical analyses

Statistical analysis title	Med diff highest pain TUG 24 h, DEX2 vs DEX1
Comparison groups	DEX1 v DEX2
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.164 [85]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	1

Notes:

[85] - Significance level 0.05.

Statistical analysis title	Med diff highest pain TUG 24 h, Plac vs DEX1
Comparison groups	Placebo v DEX1
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.466 [86]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	9

Notes:

[86] - Significance level 0.05.

Statistical analysis title	Med diff highest pain TUG 24 h, Plac vs DEX2
Comparison groups	Placebo v DEX2

Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026 [87]
Method	Van Elteren test
Parameter estimate	Hodges-Lehmann
Point estimate	7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	13

Notes:

[87] - Significance level 0.05.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were reported from the intervention is given to 48 hours postoperatively. SAE were followed up to 90 days.	
Adverse event reporting additional description:	
SAE were followed by patient charts until 90 days postoperatively.	
Assessment type	Systematic

Dictionary used	
Dictionary name	ICH-GCP
Dictionary version	Revision 2

Reporting groups	
Reporting group title	DEX1
Reporting group description:	
24 mg dexamethasone i.v. perioperatively and placebo (isotonic saline) i.v. on the first postoperative day	
Reporting group title	DEX2
Reporting group description:	
24 mg dexamethasone i.v. perioperatively and 24 mg dexamethasone i.v. on the first postoperative day	
Reporting group title	Placebo
Reporting group description:	
Placebo (isotonic saline) i.v. perioperatively and placebo (isotonic saline) i.v. on the first postoperative day	

Serious adverse events	DEX1	DEX2	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 161 (13.04%)	9 / 162 (5.56%)	18 / 162 (11.11%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer			
subjects affected / exposed	1 / 161 (0.62%)	0 / 162 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis/lung embolism			
subjects affected / exposed	1 / 161 (0.62%)	3 / 162 (1.85%)	1 / 162 (0.62%)
occurrences causally related to treatment / all	1 / 1	1 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			

Infection	Additional description: Surgical site infection		
subjects affected / exposed	2 / 161 (1.24%)	1 / 162 (0.62%)	5 / 162 (3.09%)
occurrences causally related to treatment / all	1 / 2	1 / 1	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound related problems			
subjects affected / exposed	2 / 161 (1.24%)	0 / 162 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mechanical problems with prosthesis			
subjects affected / exposed	6 / 161 (3.73%)	1 / 162 (0.62%)	7 / 162 (4.32%)
occurrences causally related to treatment / all	1 / 6	1 / 1	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Morphine side effects			
subjects affected / exposed	1 / 161 (0.62%)	0 / 162 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hospital admittance longer than 4 days			
subjects affected / exposed	1 / 161 (0.62%)	0 / 162 (0.00%)	2 / 162 (1.23%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Unknown			
subjects affected / exposed	1 / 161 (0.62%)	0 / 162 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiovascular disorder			
subjects affected / exposed	1 / 161 (0.62%)	2 / 162 (1.23%)	1 / 162 (0.62%)
occurrences causally related to treatment / all	1 / 1	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral disorder			
subjects affected / exposed	2 / 161 (1.24%)	0 / 162 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pain			
subjects affected / exposed	1 / 161 (0.62%)	0 / 162 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Low haemoglobin			
subjects affected / exposed	1 / 161 (0.62%)	0 / 162 (0.00%)	1 / 162 (0.62%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 161 (0.62%)	0 / 162 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 161 (0.00%)	1 / 162 (0.62%)	1 / 162 (0.62%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fracture, not anatomically related			
subjects affected / exposed	1 / 161 (0.62%)	0 / 162 (0.00%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 162 (0.62%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection not anatomically related			
subjects affected / exposed	3 / 161 (1.86%)	1 / 162 (0.62%)	0 / 162 (0.00%)
occurrences causally related to treatment / all	1 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	DEX1	DEX2	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 161 (4.35%)	4 / 162 (2.47%)	10 / 162 (6.17%)
Cardiac disorders			
Hypotension			
subjects affected / exposed	1 / 161 (0.62%)	1 / 162 (0.62%)	0 / 162 (0.00%)
occurrences (all)	1	1	0
Syncope during mobilisation			
subjects affected / exposed	0 / 161 (0.00%)	0 / 162 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	0 / 161 (0.00%)	0 / 162 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Nervous system disorders			
Confusion			
subjects affected / exposed	2 / 161 (1.24%)	0 / 162 (0.00%)	2 / 162 (1.23%)
occurrences (all)	2	0	2
Headache			
subjects affected / exposed	1 / 161 (0.62%)	0 / 162 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 161 (0.00%)	0 / 162 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 162 (0.00%)	0 / 162 (0.00%)
occurrences (all)	1	0	0
Stomach ache			
subjects affected / exposed	0 / 161 (0.00%)	0 / 162 (0.00%)	1 / 162 (0.62%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Itching			
subjects affected / exposed	1 / 161 (0.62%)	1 / 162 (0.62%)	1 / 162 (0.62%)
occurrences (all)	1	1	1

Renal and urinary disorders Elevated creatinine subjects affected / exposed occurrences (all)	1 / 161 (0.62%) 1	2 / 162 (1.23%) 2	3 / 162 (1.85%) 3

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/34983775