Clinical trial results:
Effect of Combinations of Paracetamol, Ibuprofen, and Dexamethasone on Patient-Controlled Morphine Consumption in the First 24 Hours After Total Hip Arthroplasty. The RECIPE Randomized Clinical Trial

Summary

EudraCT number	2019-002844-25
Trial protocol	DK
Global end of trial date	15 February 2023

Results information

Result version number	v1 (current)
This version publication date	16 October 2024
First version publication date	16 October 2024

Trial information

Trial identification

Sponsor protocol code	SM1-JOAST-2019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04123873
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	RCAI, Department of Anaethesiology, Næstved-Slagelse-Ringsted Hospitals
Sponsor organisation address	Ringstedgade 61, Næstved, Denmark, 4700
Public contact	Dept of Anaesthesiology, Næstved Hospital, 0045 56514002, anaestesisekretariat@regionsjaelland.dk
Scientific contact	Dept of Anaesthesiology, Næstved 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	15 February 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 February 2023
Global end of trial reached?	Yes
Global end of trial date	15 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the analgesic effects, by differences in 24-hour morphine consumption, of different combinations of paracetamol, ibuprofen, and dexamethasone after total hip 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	01 January 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 1060
Worldwide total number of subjects	1060
EEA total number of subjects	1060

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)	348
From 65 to 84 years	680
85 years and over	32

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All participants scheduled for primary, unilateral total hip arthroplasty were screened for enrolment. 4468 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	Paracetamol plus ibuprofen plus dexamthesone

Arm description:

Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg. The first dose of oral medication was given as premedication 1 h before surgery. The three remaining doses were continued postoperatively with 6 h intervals until 24 h postoperatively. The intravenous medication was given immediately after the onset of spinal anaesthesia or after the induction of general anaesthesia.

Arm type	Experimental
Investigational medicinal product name	Paracetamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The first dose of oral medication 1000 mg was given as premedication 1 h before surgery. The three remaining doses (1000 mg each) were continued postoperatively with 6 h intervals until 24 h postoperatively.

Investigational medicinal product name	Ibuprofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The first dose of oral medication 400 mg was given as premedication 1 h before surgery. The three remaining doses (each 400 mg) were continued postoperatively with 6 h intervals until 24 h postoperatively.

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:

Dexamthasone 24 mg was given immediately after the onset of spinal anaesthesia or afterthe induction of general anaesthesia.

Arm title	Ibuprofen plus dexamthasone

Arm description:

Oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching paracetamol.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Oral placebo 1000 mg. The first dose of oral medication was given as premedication 1 h before surgery. The three remaining doses were continued postoperatively with 6 h intervals until 24 h postoperatively.

Investigational medicinal product name	Ibuprofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The first dose of oral medication 400 mg was given as premedication 1 h before surgery. The three remaining doses (each 400 mg) were continued postoperatively with 6 h intervals until 24 h postoperatively.

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:

Dexamthasone 24 mg was given immediately after the onset of spinal anaesthesia or afterthe induction of general anaesthesia.

Arm title	Paracetamol plus dexatmethasone

Arm description:

Oral paracetamol 1000 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching ibuprofen.

Arm type	Experimental
Investigational medicinal product name	Paracetamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The first dose of oral medication 1000 mg was given as premedication 1 h before surgery. The three remaining doses (1000 mg each) were continued postoperatively with 6 h intervals until 24 h postoperatively.

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:

Dexamthasone 24 mg was given immediately after the onset of spinal anaesthesia or afterthe induction of general anaesthesia.

Investigational medicinal product name	Placebo to Ibuprofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Oral placebo 400 mg. The first dose of oral medication was given as premedication 1 h before surgery. The three remaining doses were continued postoperatively with 6 h intervals until 24 h postoperatively.

Arm title	Paracetamol plus Ibuprofen

Arm description:

Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus placebo matching dexamethasone.

Arm type	Experimental
Investigational medicinal product name	Paracetamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The first dose of oral medication 1000 mg was given as premedication 1 h before surgery. The three remaining doses (1000 mg each) were continued postoperatively with 6 h intervals until 24 h postoperatively.

Investigational medicinal product name	Ibuprofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The first dose of oral medication 400 mg was given as premedication 1 h before surgery. The three remaining doses (each 400 mg) were continued postoperatively with 6 h intervals until 24 h postoperatively.

Investigational medicinal product name	Placebo to Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

The intravenous placebo (sodium chloride 6 ml) was given immediately after the onset of spinal anaesthesia or after the induction of general anaesthesia.

Number of subjects in period 1	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone
Started	265	265	265
Completed	258	262	262
Not completed	7	3	3
Consent withdrawn by subject	-	-	1
Physician decision	-	-	2
Expiration of interventional drugs	1	1	-
Surgery cancelled	5	2	-
Trial personnel overlooked surgery	1	-	-

Number of subjects in period 1	Paracetamol plus Ibuprofen
Started	265
Completed	261
Not completed	4
Consent withdrawn by subject	2
Physician decision	1
Expiration of interventional drugs	-
Surgery cancelled	1
Trial personnel overlooked surgery	-

Baseline characteristics

Reporting groups	
Reporting group title	Paracetamol plus ibuprofen plus dexamthesone
Reporting group description:	
Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg. The first dose of oral medication was given as premedication 1 h before surgery. The three remaining doses were continued postoperatively with 6 h intervals until 24 h postoperatively. The intravenous medication was given immediately after the onset of spinal anaesthesia or after the induction of general anaesthesia.	
Reporting group title	Ibuprofen plus dexamthasone
Reporting group description:	
Oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching paracetamol.	
Reporting group title	Paracetamol plus dexatmethasone
Reporting group description:	
Oral paracetamol 1000 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching ibuprofen.	
Reporting group title	Paracetamol plus Ibuprofen
Reporting group description:	
Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus placebo matching dexamethasone.	

Reporting group values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone
Number of subjects	265	265	265
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 Units: years			
median	69	69	69
inter-quartile range (Q1-Q3)	62 to 74	60 to 75	61 to 76
Gender categorical Units: Subjects			
Female	148	141	153
Male	117	124	112
American Society of Anesthesiologists score Units: Subjects			
Healthy	64	67	58
Mild systemic disease	171	168	179

Severe systemic disease	30	30	28
Diabetes Units: Subjects			
Type 2 diabetes	16	8	18
No diabetes	249	257	247
Use of paracetamol before surgery Units: Subjects			
None	40	39	36
As needed	111	101	105
Daily use	114	125	124
Use of NSAID before surgery Units: Subjects			
None	117	131	128
As needed	96	79	79
Daily use	52	55	58
Daily opioid users: type of opioid Units: Subjects			
Morphine	6	8	4
Oxycodone	4	4	6
Tramadol	6	5	7
None	249	248	248
Use of gabapentinoids before surgery Units: Subjects			
None	255	252	255
As needed	0	4	3
Daily use	10	9	7
Use of antidepressants before surgery Units: Subjects			
None	245	251	253
As needed	0	0	0
Daily use	13	11	9
Unknown	7	3	3
Surgery type Units: Subjects			
Uncemented	206	204	204
Hybrid	35	36	33
Cemented	21	21	23
Not registred	3	4	5
Anaesthesia method Units: Subjects			
Spinal	194	202	203
General anaesthesia	58	48	49
Conversion from spinal to general anaesthesia	13	15	13
Spinal type plain Units: Subjects			
Spinal type plain	202	214	213
No spinal	63	51	52
Sufentanil administrated			
Sufentanil administrated for participants in general			

anaesthesia (planned or converted from spinal)			
Units: Subjects			
Sufentanil administrated	54	48	53
No sufentanil administrated	211	217	212
Ondansetron administrated			
Ondansetron 4 mg administrated			
Units: Subjects			
Ondansetron administrated	252	254	251
No ondansetron adminstrated	13	11	14
Perioperative local infiltration analgesia			
Units: Subjects			
Perioperative local infiltration analgesia	0	0	0
None	265	265	265
Height			
Units: centimetre			
arithmetic mean	172.1	172.2	171.6
standard deviation	± 8.9	± 8.1	± 9.2
Weigth			
Units: kilogram(s)			
arithmetic mean	82	79.8	80.9
standard deviation	± 17.4	± 15.5	± 15.5
BMI			
Units: kilogram(s)/square metre			
arithmetic mean	27.4	26.8	27.4
standard deviation	± 4.6	± 4.2	± 4.2
Morphine users: daily dose, mg			
Units: milligram(s)			
median	10.0	10.0	20.0
inter-quartile range (Q1-Q3)	10.0 to 11.5	10.0 to 16.3	20.0 to 22.5
Oxycodone users: daily dose, mg			
Units: milligram(s)			
median	20.0	10.0	20.0
inter-quartile range (Q1-Q3)	16.3 to 22.5	8.8 to 15.0	12.5 to 20.0
Tramadol users: daily dose, mg			
Units: milligram(s)			
median	75.0	100.0	100.0
inter-quartile range (Q1-Q3)	50.0 to 100.0	100.00 to 100.00	50.0 to 125.0
Pain at rest VAS			
Units: millimetre(s)			
median	20.0	20.0	17.0
inter-quartile range (Q1-Q3)	1.5 to 40.0	4.8 to 35.0	2.5 to 35.0
Pain during mobilisation VAS			
Units: millimetre			
median	45.5	44.0	41.0
inter-quartile range (Q1-Q3)	21.0 to 70.0	20.0 to 65.5	20.0 to 64.0
Surgery duration			
Units: minute			
median	55	55	55
inter-quartile range (Q1-Q3)	45 to 68	45 to 69	45 to 69
Bupivacaine dose			

Units: milligram(s)			
median	12.0	12.5	12.5
inter-quartile range (Q1-Q3)	11.0 to 12.5	11.0 to 12.5	11.0 to 12.5
Sufentanil dose			
Sufentanil administrated for participants in general anaesthesia (planned or converted from spinal) Sufentanil dose			
Units: microgram(s)			
median	22.5	22.8	22.5
inter-quartile range (Q1-Q3)	19.0 to 27.3	20.0 to 26.4	20.0 to 26.9
Blood loss			
Units: millilitre(s)			
median	300	300	250
inter-quartile range (Q1-Q3)	200 to 443	200 to 440	175 to 400

Reporting group values	Paracetamol plus Ibuprofen	Total	
Number of subjects	265	1060	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
median	70		
inter-quartile range (Q1-Q3)	62 to 76	-	
Gender categorical			
Units: Subjects			
Female	156	598	
Male	109	462	
American Society of Anesthesiologists score			
Units: Subjects			
Healthy	56	245	
Mild systemic disease	182	700	
Severe systemic disease	27	115	
Diabetes			
Units: Subjects			
Type 2 diabetes	12	54	
No diabetes	253	1006	
Use of paracetamol before surgery			
Units: Subjects			
None	45	160	
As needed	94	411	
Daily use	126	489	

Use of NSAID before surgery Units: Subjects			
None	123	499	
As needed	76	330	
Daily use	66	231	
Daily opioid users: type of opioid Units: Subjects			
Morphine	7	25	
Oxycodone	6	20	
Tramadol	7	25	
None	245	990	
Use of gabapentinoids before surgery Units: Subjects			
None	255	1017	
As needed	2	9	
Daily use	8	34	
Use of antidepressants before surgery Units: Subjects			
None	252	1001	
As needed	1	1	
Daily use	8	41	
Unknown	4	17	
Surgery type Units: Subjects			
Uncemented	209	823	
Hybrid	32	136	
Cemented	18	83	
Not registred	6	18	
Anaesthesia method Units: Subjects			
Spinal	187	786	
General anaesthesia	59	214	
Conversion from spinal to general anaesthesia	19	60	
Spinal type plain Units: Subjects			
Spinal type plain	203	832	
No spinal	62	228	
Sufentanil administrated			
Sufentanil administrated for participants in general anaesthesia (planned or converted from spinal)			
Units: Subjects			
Sufentanil administrated	61	216	
No sufentanil administrated	204	844	
Ondansetron administrated			
Ondansetron 4 mg administrated			
Units: Subjects			
Ondansetron administrated	250	1007	
No ondansetron adminstrated	15	53	
Perioperative local infiltration analgesia			

Units: Subjects			
Perioperative local infiltration analgesia	1	1	
None	264	1059	
Height			
Units: centimetre			
arithmetic mean	171.7		
standard deviation	± 9.4	-	
Weigth			
Units: kilogram(s)			
arithmetic mean	81.6		
standard deviation	± 17.0	-	
BMI			
Units: kilogram(s)/square metre			
arithmetic mean	27.6		
standard deviation	± 4.5	-	
Morphine users: daily dose, mg			
Units: milligram(s)			
median	10.0		
inter-quartile range (Q1-Q3)	10.0 to 15.0	-	
Oxycodone users: daily dose, mg			
Units: milligram(s)			
median	10.0		
inter-quartile range (Q1-Q3)	6.3 to 13.8	-	
Tramadol users: daily dose, mg			
Units: milligram(s)			
median	100.0		
inter-quartile range (Q1-Q3)	100.0 to 100.0	-	
Pain at rest VAS			
Units: millimetre(s)			
median	19.0		
inter-quartile range (Q1-Q3)	0.0 to 40.0	-	
Pain during mobilisation VAS			
Units: millimetre			
median	46.0		
inter-quartile range (Q1-Q3)	20.0 to 69.0	-	
Surgery duration			
Units: minute			
median	55		
inter-quartile range (Q1-Q3)	45 to 70	-	
Bupivacaine dose			
Units: milligram(s)			
median	12.5		
inter-quartile range (Q1-Q3)	11.0 to 12.5	-	
Sufentanil dose			
Sufentanil administrated for participants in general anaesthesia (planned or converted from spinal) Sufentanil dose			
Units: microgram(s)			
median	25.0		
inter-quartile range (Q1-Q3)	20.0 to 27.0	-	
Blood loss			
Units: millilitre(s)			

median	300		
inter-quartile range (Q1-Q3)	200 to 494	-	

End points

End points reporting groups

Reporting group title	Paracetamol plus ibuprofen plus dexamthesone
Reporting group description:	
Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg. The first dose of oral medication was given as premedication 1 h before surgery. The three remaining doses were continued postoperatively with 6 h intervals until 24 h postoperatively. The intravenous medication was given immediately after the onset of spinal anaesthesia or after the induction of general anaesthesia.	

Reporting group title	Ibuprofen plus dexamthasone
Reporting group description:	
Oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching paracetamol.	

Reporting group title	Paracetamol plus dexatmethasone
Reporting group description:	
Oral paracetamol 1000 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching ibuprofen.	

Reporting group title	Paracetamol plus Ibuprofen
Reporting group description:	
Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus placebo matching dexamethasone.	

Primary: 24-h morphine consumption

End point title	24-h morphine consumption
End point description:	

End point type	Primary
End point timeframe:	
Morphine consumption from last suture to 24 hours after last suture	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	262	262	261
Units: milligram(s)				
median (inter-quartile range (Q1-Q3))	15 (8 to 26)	16 (10 to 30)	20 (12 to 32)	24 (12 to 38)

Statistical analyses

Statistical analysis title	Median difference
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus ibuprofen plus dexamthesone

Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.14
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-2
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-4
upper limit	2

Statistical analysis title	Median difference
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0013
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-4
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-8
upper limit	-1

Statistical analysis title	Median difference
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	519
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-6
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-10
upper limit	-3

Statistical analysis title	Median difference
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.033
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-2
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-6
upper limit	0

Statistical analysis title	Median difference
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-4.5
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-8
upper limit	-2

Statistical analysis title	Median difference
Comparison groups	Paracetamol plus dexatmethasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-2
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-6
upper limit	2

Secondary: Adverse events, 0 to 24 h postoperatively

End point title	Adverse events, 0 to 24 h postoperatively
End point description:	

End point type	Secondary
End point timeframe:	
0 to 24 hours postoperatively	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	262	262	261
Units: events	91	99	103	165

Statistical analyses

Statistical analysis title	Relative Risk
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.55
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.14

Statistical analysis title	Relative Risk
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone

Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.34
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.15

Statistical analysis title	Relative Risk
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	519
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	0.66

Statistical analysis title	Relative Risk
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.73
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.22

Statistical analysis title	Relative Risk
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	0.7

Statistical analysis title	Relative Risk
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	0.73

Secondary: Pain at rest 24 hours postoperatively	
End point title	Pain at rest 24 hours postoperatively
End point description:	

End point type	Secondary
End point timeframe:	
24 hours postoperatively	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	262	262	261
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	10 (1 to 20)	12 (0 to 28)	13 (1 to 25)	12 (1 to 25)

Statistical analyses

Statistical analysis title	Pairwise comparisons between the median pain score
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-5
upper limit	0

Statistical analysis title	Pairwise comparisons between the median pain score
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-5
upper limit	0

Statistical analysis title	Pairwise comparisons between the median pain score
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen

Number of subjects included in analysis	519
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.14
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-5
upper limit	0

Statistical analysis title	Pairwise comparisons between the median pain score
Comparison groups	Paracetamol plus dexatmethasone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.72
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-2
upper limit	1

Statistical analysis title	Pairwise comparisons between the median pain score
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.72
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-2
upper limit	1

Statistical analysis title	Pairwise comparisons between the median
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.92
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-2
upper limit	2

Secondary: Pain during mobilisation at 24 h postoperatively	
End point title	Pain during mobilisation at 24 h postoperatively
End point description:	
End point type	Secondary
End point timeframe:	
24 hours postoperatively	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	262	262	261
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	31 (18 to 50)	32 (18 to 50)	40 (20 to 60)	43 (27 to 65)

Statistical analyses

Statistical analysis title	Pairwise comparisons pain score mobilisation
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0

Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-6
upper limit	5

Statistical analysis title	Pairwise comparisons pain score mobilisation
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0031
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-6
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-12
upper limit	0

Statistical analysis title	Pairwise comparisons pain score mobilisation
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	519
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-10
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-16
upper limit	-5

Statistical analysis title	Pairwise comparisons pain score mobilisation
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone

Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.016
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-5
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-10
upper limit	0

Statistical analysis title	Pairwise comparisons pain score mobilisation
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-10
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-15
upper limit	-4

Statistical analysis title	Pairwise comparisons pain score mobilisation
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.058
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-5
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-10
upper limit	2

Secondary: Maximum pain during 5 m walk	
End point title	Maximum pain during 5 m walk
End point description:	

End point type	Secondary
End point timeframe:	
24 h postoperatively	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	262	262	261
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	27 (15 to 41)	30 (16 to 46)	35 (20 to 50)	35 (20 to 51)

Statistical analyses

Statistical analysis title	Pairwise comparisons max pain score walk
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-3
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-8
upper limit	2

Statistical analysis title	Pairwise comparisons max pain score walk
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-6

Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-12
upper limit	-1

Statistical analysis title	Pairwise comparisons max pain score walk
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	519
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-9
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-14
upper limit	3

Statistical analysis title	Pairwise comparisons max pain score walk
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.078
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-3
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-9
upper limit	2

Statistical analysis title	Pairwise comparisons max pain score walk
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen

Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.016
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-5
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-10
upper limit	0

Statistical analysis title	Copy of Pairwise comparisons max pain score walk
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.37
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-2
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-8
upper limit	4

Other pre-specified: Pain at rest 6h

End point title	Pain at rest 6h
End point description:	

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

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	262	262	261
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	16 (10 to 31)	20 (8 to 30)	25 (10 to 40)	29 (11 to 48)

Statistical analyses

Statistical analysis title	Pairwise comparisons pain rest 6h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.73
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-4
upper limit	3

Statistical analysis title	Pairwise comparisons pain rest 6h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0076
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-5
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-10
upper limit	0

Statistical analysis title	Pairwise comparisons pain rest 6h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen

Number of subjects included in analysis	519
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-10
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-14
upper limit	-4

Statistical analysis title	Pairwise comparisons pain rest 6h
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0048
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-5
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-10
upper limit	0

Statistical analysis title	Pairwise comparisons pain rest 6h
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-10
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-14
upper limit	-4

Statistical analysis title	Pairwise comparisons pain rest 6h
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.032
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-4
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-10
upper limit	0

Other pre-specified: Pain during mobilisation, 6 h	
End point title	Pain during mobilisation, 6 h
End point description:	
End point type	Other pre-specified
End point timeframe:	
6 hours postoperatively	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	262	262	261
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	30 (15 to 51)	30 (15 to 50)	37 (20 to 55)	48 (25 to 69)

Statistical analyses

Statistical analysis title	Pairwise comparisons pain mobilisation 6h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.32
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0

Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-5
upper limit	7

Statistical analysis title	Pairwise comparisons pain mobilisation 6h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-5
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-10
upper limit	1

Statistical analysis title	Pairwise comparisons pain mobilisation 6h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	519
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-13
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-20
upper limit	-6

Statistical analysis title	Pairwise comparisons pain mobilisation 6h
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone

Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-5
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-11
upper limit	0

Statistical analysis title	Pairwise comparisons pain mobilisation 6h
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-15
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-20
upper limit	-8

Statistical analysis title	Pairwise comparisons pain mobilisation 6h
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-9
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-15
upper limit	-2

Other pre-specified: Nausea, 6 h	
End point title	Nausea, 6 h
End point description:	
End point type	Other pre-specified
End point timeframe:	
6 hours postoperatively	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	248	251	244	243
Units: patients	21	19	23	49

Statistical analyses

Statistical analysis title	Relative Risk Nausea 6h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.71
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	1.78

Statistical analysis title	Relative Risk Nausea 6h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.68
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.89

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	2.02

Statistical analysis title	Relative Risk Nausea 6h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	0.63

Statistical analysis title	Relative Risk Nausea 6h
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.041
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.83

Statistical analysis title	Relative Risk Nausea 6h
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen

Number of subjects included in analysis	494
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	0.57

Statistical analysis title	Relative Risk Nausea 6h
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	487
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0012
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	0.69

Other pre-specified: Nausea 24 h

End point title	Nausea 24 h
End point description:	

End point type	Other pre-specified
End point timeframe:	
24 hours postoperatively	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	256	261	257	257
Units: patients	49	68	70	125

Statistical analyses

Statistical analysis title	Relative Risk Nausea 24h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.058
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	0.97

Statistical analysis title	Relative Risk Nausea 24h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	513
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.02

Statistical analysis title	Relative Risk Nausea 24h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen

Number of subjects included in analysis	513
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	0.5

Statistical analysis title	Relative Risk Nausea 24h
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	518
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.76
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.33

Statistical analysis title	Relative Risk Nausea 24h
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	518
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	0.67

Statistical analysis title	Relative Risk Nausea 24h
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	514
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	0.69

Other pre-specified: Vomiting 0-24 h	
End point title	Vomiting 0-24 h
End point description:	
End point type	Other pre-specified
End point timeframe:	
0 to 24 hours postoperatively	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	256	261	255	257
Units: patients	23	29	33	81

Statistical analyses

Statistical analysis title	Relative Risk Vomiting 0-24h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.42
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.81

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	1.22

Statistical analysis title	Relative Risk Vomiting 0-24h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.16
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.39

Statistical analysis title	Relative Risk Vomiting 0-24h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	513
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	0.41

Statistical analysis title	Relative Risk Vomiting 0-24h
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone

Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.52
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.6

Statistical analysis title	Relative Risk Vomiting 0-24h
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	518
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	0.49

Statistical analysis title	Relative Risk Vomiting 0-24h
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	512
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	0.56

Other pre-specified: Dizziness walk test, 24 h	
End point title	Dizziness walk test, 24 h
End point description:	

End point type	Other pre-specified
End point timeframe:	
24 hours postoperatively	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	233	237	230	221
Units: Patients	27	33	25	48

Statistical analyses

Statistical analysis title	Relative Risk Dizziness walk test 24h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	470
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.47
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	1.23

Statistical analysis title	Relative Risk Dizziness walk test 24h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	463
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.78
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	1.07

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	2.18

Statistical analysis title	Relative Risk Dizziness walk test 24h
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0042
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	0.77

Statistical analysis title	Relative Risk Dizziness walk test 24h
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	467
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.34
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	2.46

Statistical analysis title	Relative Risk Dizziness walk test 24h
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen

Number of subjects included in analysis	458
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	0.9

Statistical analysis title	Relative Risk Dizziness walk test 24h
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	451
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0023
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	0.73

Other pre-specified: Anti–emetic use, 0–24 h

End point title	Anti–emetic use, 0–24 h
End point description:	

End point type	Other pre-specified
End point timeframe:	
0 to 24 hours postoperatively	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	257	261	261	263
Units: patients	36	49	65	95

Statistical analyses

Statistical analysis title	Relative Risk Anti-emetic use
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	518
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	1.03

Statistical analysis title	Relative Risk Anti-emetic use
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	518
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0017
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	0.89

Statistical analysis title	Relative Risk Anti-emetic use
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen

Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	0.51

Statistical analysis title	Relative Risk Anti-emetic use
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.089
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.12

Statistical analysis title	Relative Risk Anti-emetic use
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	0.67

Statistical analysis title	Relative Risk Anti-emetic use
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0037
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	0.86

Other pre-specified: Sleep quality	
End point title	Sleep quality
End point description: VAS 0-100, 0 worst to 100 best.	
End point type	Other pre-specified
End point timeframe: 24 hours postoperatively	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	262	262	261
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	50 (30 to 79)	50 (30 to 80)	50 (30 to 75)	58 (40 to 80)

Statistical analyses

Statistical analysis title	Median difference sleep quality
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.65
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	4

Statistical analysis title	Median difference sleep quality
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	6

Statistical analysis title	Median difference sleep quality
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	519
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.51
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	0

Statistical analysis title	Median difference sleep quality
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone

Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.27
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	8

Statistical analysis title	Median difference sleep quality
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	0

Statistical analysis title	Median difference sleep quality
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0073
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	-1

Other pre-specified: Intra–operative blood loss	
End point title	Intra–operative blood loss
End point description:	

End point type	Other pre-specified
End point timeframe:	
Intra-operative blood loss	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	262	262	261
Units: millilitre(s)				
median (inter-quartile range (Q1-Q3))	300 (200 to 450)	300 (200 to 440)	250 (175 to 400)	300 (200 to 500)

Statistical analyses

Statistical analysis title	Median difference blood loss
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.77
Method	Hodges-Lehmann
Parameter estimate	Median difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	50

Statistical analysis title	Median difference blood loss
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone

Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13
Method	Hodges-Lehmann
Parameter estimate	Median difference (net)
Point estimate	20
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	50

Statistical analysis title	Median difference blood loss
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	519
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.26
Method	Hodges-Lehmann
Parameter estimate	Median difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50
upper limit	0

Statistical analysis title	Median difference blood loss
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044
Method	Hodges-Lehmann
Parameter estimate	Median difference (net)
Point estimate	40
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	60

Statistical analysis title	Median difference blood loss
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.46
Method	Hodges-Lehmann
Parameter estimate	Median difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50
upper limit	25

Statistical analysis title	Median difference blood loss
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	Hodges-Lehmann
Parameter estimate	Median difference (net)
Point estimate	-50
Confidence interval	
level	95 %
sides	2-sided
lower limit	-75
upper limit	0

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:	
Within 90 days postoperatively.	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	262	262	261
Units: patients	20	24	31	35

Statistical analyses

Statistical analysis title	Relative Risk Adverse events 90 days
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.58
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	1.33

Statistical analysis title	Relative Risk Adverse events 90 days
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.38

Statistical analysis title	Relative Risk Adverse events 90 days
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen

Number of subjects included in analysis	519
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	0.88

Statistical analysis title	Relative Risk Adverse events 90 days
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.32
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.54

Statistical analysis title	Relative Risk Adverse events 90 days
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	1.01

Statistical analysis title	Relative Risk Adverse events 90 days
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.55
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.26

Other pre-specified: Oxford Hip Score at 90 days

End point title	Oxford Hip Score at 90 days
End point description:	
End point type	Other pre-specified
End point timeframe:	
90 days postoperatively	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	262	262	261
Units: points				
median (inter-quartile range (Q1-Q3))	41 (36 to 450)	41 (36 to 45)	41 (34 to 45)	42 (36 to 45)

Statistical analyses

Statistical analysis title	Median difference Oxford Hip Score
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.52
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1

Statistical analysis title	Median difference Oxford Hip Score
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.14
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	2

Statistical analysis title	Median difference Oxford Hip Score
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	519
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.99
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1

Statistical analysis title	Median difference Oxford Hip Score
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone

Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.49
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2

Statistical analysis title	Median difference Oxford Hip Score
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.74
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1

Statistical analysis title	Median difference Oxford Hip Score
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.34
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0

Other pre-specified: EQ5D5L index score	
End point title	EQ5D5L index score
End point description:	
End point type	Other pre-specified
End point timeframe:	
90 days postoperatively	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	262	262	261
Units: score				
median (inter-quartile range (Q1-Q3))	0.93 (0.87 to 1)	0.93 (0.88 to 1)	0.93 (0.87 to 1)	0.93 (0.87 to 1)

Statistical analyses

Statistical analysis title	Median difference EQ5D5L index score
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.78
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.004
upper limit	0

Statistical analysis title	Median difference EQ5D5L index score
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone

Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.68
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.005

Statistical analysis title	Median difference EQ5D5L index score
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	519
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.77
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Statistical analysis title	Median difference EQ5D5L index score
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.56
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.008

Statistical analysis title	Median difference EQ5D5L index score
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.58
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.004

Statistical analysis title	Median difference EQ5D5L index score
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.91
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.002

Other pre-specified: EQ5D5L VAS score 90 days	
End point title	EQ5D5L VAS score 90 days
End point description:	

End point type	Other pre-specified
End point timeframe:	
90 days postoperatively	

End point values	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone	Paracetamol plus Ibuprofen
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	262	262	261
Units: millimetre(s)				
median (inter-quartile range (Q1-Q3))	85 (75 to 90)	85 (75 to 90)	85 (75 to 90)	85 (75 to 90)

Statistical analyses

Statistical analysis title	Median difference EQ5D5L VAS score
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.71
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	3

Statistical analysis title	Median difference EQ5D5L VAS score
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	520
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.75
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	2

Statistical analysis title	Median difference EQ5D5L VAS score
Comparison groups	Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen

Number of subjects included in analysis	519
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.59
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	3

Statistical analysis title	Median difference EQ5D5L VAS score
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone
Number of subjects included in analysis	524
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.48
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	5

Statistical analysis title	Median difference EQ5D5L VAS score
Comparison groups	Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.86
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Statistical analysis title	Median difference EQ5D5L VAS score
Comparison groups	Paracetamol plus Ibuprofen v Paracetamol plus dexatmethasone
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.46
Method	Hodges-Lehmann
Parameter estimate	Median difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	0

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
0 to 24 hours postoperatively	
Assessment type	Systematic

Dictionary used	
Dictionary name	ICH-GCP
Dictionary version	Revision 2

Reporting groups	
Reporting group title	Paracetamol plus ibuprofen plus dexamthesone
Reporting group description:	
Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg. The first dose of oral medication was given as premedication 1 h before surgery. The three remaining doses were continued postoperatively with 6 h intervals until 24 h postoperatively. The intravenous medication was given immediately after the onset of spinal anaesthesia or after the induction of general anaesthesia.	
Reporting group title	Ibuprofen plus dexamthasone
Reporting group description:	
Oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching paracetamol.	
Reporting group title	Paracetamol plus dexatmethasone
Reporting group description:	
Oral paracetamol 1000 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching ibuprofen.	
Reporting group title	Paracetamol plus Ibuprofen
Reporting group description:	
Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus placebo matching dexamethasone.	

Serious adverse events	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 258 (2.33%)	5 / 262 (1.91%)	3 / 262 (1.15%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Cardiac arrhythmia			
subjects affected / exposed	0 / 258 (0.00%)	0 / 262 (0.00%)	1 / 262 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemodynamic instability			
subjects affected / exposed	1 / 258 (0.39%)	0 / 262 (0.00%)	0 / 262 (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

Surgical and medical procedures			
Complete and incomplete prosthetic dislocation			
subjects affected / exposed	1 / 258 (0.39%)	1 / 262 (0.38%)	1 / 262 (0.38%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Neuropathic pain			
subjects affected / exposed	0 / 258 (0.00%)	0 / 262 (0.00%)	0 / 262 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drop foot			
subjects affected / exposed	0 / 258 (0.00%)	1 / 262 (0.38%)	0 / 262 (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
General disorders and administration site conditions			
Worsening of known symptoms from previous critical illness			
subjects affected / exposed	0 / 258 (0.00%)	0 / 262 (0.00%)	0 / 262 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hospitalisation 4 or more days			
subjects affected / exposed	3 / 258 (1.16%)	3 / 262 (1.15%)	1 / 262 (0.38%)
occurrences causally related to treatment / all	3 / 3	3 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 258 (0.39%)	0 / 262 (0.00%)	0 / 262 (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
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 258 (0.00%)	0 / 262 (0.00%)	0 / 262 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Paracetamol plus Ibuprofen		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 261 (4.98%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Cardiac arrhythmia			
subjects affected / exposed	0 / 261 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemodynamic instability			
subjects affected / exposed	1 / 261 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Complete and incomplete prosthetic dislocation			
subjects affected / exposed	1 / 261 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Neuropathic pain			
subjects affected / exposed	1 / 261 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Drop foot			
subjects affected / exposed	1 / 261 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Worsening of known symptoms from previous critical illness			
subjects affected / exposed	1 / 261 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hospitalisation 4 or more days			

subjects affected / exposed	7 / 261 (2.68%)		
occurrences causally related to treatment / all	7 / 7		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 261 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 261 (0.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Paracetamol plus ibuprofen plus dexamthesone	Ibuprofen plus dexamthasone	Paracetamol plus dexatmethasone
Total subjects affected by non-serious adverse events			
subjects affected / exposed	122 / 258 (47.29%)	150 / 262 (57.25%)	167 / 262 (63.74%)
Cardiac disorders			
Vasovagal episode or syncope			
subjects affected / exposed	8 / 258 (3.10%)	1 / 262 (0.38%)	5 / 262 (1.91%)
occurrences (all)	8	1	5
Cardiac arrhythmia			
subjects affected / exposed	1 / 258 (0.39%)	0 / 262 (0.00%)	1 / 262 (0.38%)
occurrences (all)	1	0	1
Hypotensive episode			
subjects affected / exposed	0 / 258 (0.00%)	1 / 262 (0.38%)	1 / 262 (0.38%)
occurrences (all)	0	1	1
Surgical and medical procedures			
Blood transfusion			
subjects affected / exposed	0 / 258 (0.00%)	2 / 262 (0.76%)	4 / 262 (1.53%)
occurrences (all)	0	2	4
Blood oozing from surgical wound			

subjects affected / exposed	0 / 258 (0.00%)	1 / 262 (0.38%)	2 / 262 (0.76%)
occurrences (all)	0	1	2
Perioperative fracture			
subjects affected / exposed	1 / 258 (0.39%)	0 / 262 (0.00%)	2 / 262 (0.76%)
occurrences (all)	1	0	2
Haematoma			
subjects affected / exposed	1 / 258 (0.39%)	0 / 262 (0.00%)	0 / 262 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness during 5 m walk			
subjects affected / exposed	27 / 258 (10.47%)	33 / 262 (12.60%)	25 / 262 (9.54%)
occurrences (all)	27	33	25
Confusion			
subjects affected / exposed	1 / 258 (0.39%)	1 / 262 (0.38%)	1 / 262 (0.38%)
occurrences (all)	1	1	1
Delirium			
subjects affected / exposed	0 / 258 (0.00%)	0 / 262 (0.00%)	0 / 262 (0.00%)
occurrences (all)	0	0	0
Worsening of known neurologic symptoms			
subjects affected / exposed	0 / 258 (0.00%)	1 / 262 (0.38%)	0 / 262 (0.00%)
occurrences (all)	0	1	0
Pain and logistics			
subjects affected / exposed	0 / 258 (0.00%)	0 / 262 (0.00%)	0 / 262 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 258 (0.00%)	0 / 262 (0.00%)	1 / 262 (0.38%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Non-surgical drop in hemoglobin level			
subjects affected / exposed	0 / 258 (0.00%)	0 / 262 (0.00%)	1 / 262 (0.38%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Delayed mobilisation or discharge			
subjects affected / exposed	2 / 258 (0.78%)	7 / 262 (2.67%)	8 / 262 (3.05%)
occurrences (all)	2	7	8

Immune system disorders			
Urticaria			
subjects affected / exposed	0 / 258 (0.00%)	0 / 262 (0.00%)	4 / 262 (1.53%)
occurrences (all)	0	0	4
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	57 / 258 (22.09%)	70 / 262 (26.72%)	75 / 262 (28.63%)
occurrences (all)	57	70	75
Vomiting			
subjects affected / exposed	23 / 258 (8.91%)	29 / 262 (11.07%)	34 / 262 (12.98%)
occurrences (all)	23	29	34
Stomach discomfort or pain			
subjects affected / exposed	0 / 258 (0.00%)	1 / 262 (0.38%)	0 / 262 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Pneumonia			
subjects affected / exposed	0 / 258 (0.00%)	1 / 262 (0.38%)	0 / 262 (0.00%)
occurrences (all)	0	1	0
Desaturation			
subjects affected / exposed	0 / 258 (0.00%)	1 / 262 (0.38%)	0 / 262 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Impaired kidney function			
subjects affected / exposed	1 / 258 (0.39%)	0 / 262 (0.00%)	2 / 262 (0.76%)
occurrences (all)	1	0	2
Urinary infection			
subjects affected / exposed	0 / 258 (0.00%)	1 / 262 (0.38%)	1 / 262 (0.38%)
occurrences (all)	0	1	1
Urinary retention			
subjects affected / exposed	0 / 258 (0.00%)	0 / 262 (0.00%)	0 / 262 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Paracetamol plus Ibuprofen		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	248 / 261 (95.02%)		
Cardiac disorders			

Vasovagal episode or syncope			
subjects affected / exposed	5 / 261 (1.92%)		
occurrences (all)	5		
Cardiac arrhythmia			
subjects affected / exposed	1 / 261 (0.38%)		
occurrences (all)	1		
Hypotensive episode			
subjects affected / exposed	3 / 261 (1.15%)		
occurrences (all)	3		
Surgical and medical procedures			
Blood transfusion			
subjects affected / exposed	1 / 261 (0.38%)		
occurrences (all)	1		
Blood oozing from surgical wound			
subjects affected / exposed	0 / 261 (0.00%)		
occurrences (all)	0		
Perioperative fracture			
subjects affected / exposed	3 / 261 (1.15%)		
occurrences (all)	3		
Haematoma			
subjects affected / exposed	0 / 261 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness during 5 m walk			
subjects affected / exposed	48 / 261 (18.39%)		
occurrences (all)	48		
Confusion			
subjects affected / exposed	1 / 261 (0.38%)		
occurrences (all)	1		
Delirium			
subjects affected / exposed	1 / 261 (0.38%)		
occurrences (all)	1		
Worsening of known neurologic symptoms			
subjects affected / exposed	0 / 261 (0.00%)		
occurrences (all)	0		
Pain and logistics			

subjects affected / exposed	1 / 261 (0.38%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	0 / 261 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Non-surgical drop in hemoglobin level			
subjects affected / exposed	0 / 261 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Delayed mobilisation or discharge			
subjects affected / exposed	9 / 261 (3.45%)		
occurrences (all)	9		
Immune system disorders			
Urticaria			
subjects affected / exposed	1 / 261 (0.38%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	133 / 261 (50.96%)		
occurrences (all)	133		
Vomiting			
subjects affected / exposed	81 / 261 (31.03%)		
occurrences (all)	81		
Stomach discomfort or pain			
subjects affected / exposed	2 / 261 (0.77%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Pneumonia			
subjects affected / exposed	0 / 261 (0.00%)		
occurrences (all)	0		
Desaturation			
subjects affected / exposed	0 / 261 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			

Impaired kidney function subjects affected / exposed occurrences (all)	2 / 261 (0.77%) 2		
Urinary infection subjects affected / exposed occurrences (all)	0 / 261 (0.00%) 0		
Urinary retention subjects affected / exposed occurrences (all)	1 / 261 (0.38%) 1		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None reported

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/38458208