Clinical trial results:
Oral dexamethasone as an adjunct to a brachial plexus block in patients undergoing orthopaedic surgery of the forearm and hand. A randomised, blinded, placebo-controlled, parallel, triple-arm clinical trial.

Summary

EudraCT number	2021-000428-36
Trial protocol	DK
Global end of trial date	03 May 2023

Results information

Result version number	v1 (current)
This version publication date	29 March 2024
First version publication date	29 March 2024

Trial information

Trial identification

Sponsor protocol code	ADJUNCT-1-2021

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04853446
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Zealand University Hospital
Sponsor organisation address	Lykkebækvej 1, Køge, Denmark, 4600
Public contact	Department of Anaesthesiology, Centre for Anaesthesiological Research, Department of Anaesthesiology, Zealand University Hospital, mmaag@regionsjaelland.dk
Scientific contact	Department of Anaesthesiology, Centre for Anaesthesiological Research, Department of Anaesthesiology, Zealand University Hospital, mmaag@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	21 October 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 May 2023
Global end of trial reached?	Yes
Global end of trial date	03 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the beneficial and harmful effects of oral dexamethasone as an adjunct to a lateral infraclavicular block in patients undergoing surgery of the bones of the forearm or hand.

Protection of trial subjects:

Standard care other than the experimental intervention.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 May 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 180
Worldwide total number of subjects	180
EEA total number of subjects	180

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)	104
From 65 to 84 years	76
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adults >=18 years, unilateral surgery of forearm/hand, ASA 1-3, BMI 18-40, min. weight 50kg. Exclusion: pregnancy, inability to provide informed consent, allergy, daily morphine >30mg, daily prednisolone >5mg, alcohol/drug abuse, glaucoma, other surgery needed, other trauma needing opioids.

Period 1

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

Blinding implementation details:

Trial medication was prepared by the pharmacy in identically appearing opaque capsules containing either placebo or 12mg dexamethasone. The trial medication was packaged in identical containers with two capsules in each container, resulting in the possibility of being allocated to placebo, 12mg dexamethasone, or 24mg dexamethasone.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Capsules containing placebo.

Arm type	Placebo
Investigational medicinal product name	Glucosemonohydrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo capsule, administered 30-60min before block performance.

Arm title	Dexamethasone 12mg

Arm description:

Capsules containing 12mg dexamethasone.

Arm type	Active comparator
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

12mg dexamethasone administered 30-60min before block performance.

Arm title	Dexamethasone 24mg

Arm description:

Capsules containing 24mg of dexamethasone.

Arm type	Experimental

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

24mg dexamethasone administered 30-60min before block performance.

Number of subjects in period 1	Placebo	Dexamethasone 12mg	Dexamethasone 24mg
Started	61	61	58
Completed	61	59	55
Not completed	0	2	3
Consent withdrawn by subject	-	-	1
Did not receive nerve block.	-	2	-
did not receive nerve block	-	-	1
Dementia	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Capsules containing placebo.	
Reporting group title	Dexamethasone 12mg
Reporting group description:	
Capsules containing 12mg dexamethasone.	
Reporting group title	Dexamethasone 24mg
Reporting group description:	
Capsules containing 24mg of dexamethasone.	

Reporting group values	Placebo	Dexamethasone 12mg	Dexamethasone 24mg
Number of subjects	61	61	58
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			
arithmetic mean	61.3	59.4	62.7
standard deviation	± 14.1	± 17.2	± 14.6
Gender categorical Units: Subjects			
Female	47	42	47
Male	14	19	11
Diabetes Units: Subjects			
Diabetes	3	3	0
No diabetes	58	58	58
Type of surgery Units: Subjects			
Fracture	57	50	51
Non-fracture	4	11	7
Use of analgesics Units: Subjects			
Paracetamol	19	23	28
NSAIDs	7	12	14
Anti-depressants	7	8	5

Opioids	4	3	6
No use	24	15	5

Weight			
Units: kilogram(s)			
arithmetic mean	78.6	78.8	74.3
standard deviation	± 15.6	± 16.5	± 14.8
Height			
Units: centimetre			
arithmetic mean	171	172	170
standard deviation	± 9.3	± 9.8	± 8.8
Body Mass Index			
Units: kilogram(s)/cubic metre			
arithmetic mean	26.9	26.7	25.8
standard deviation	± 4.7	± 4.6	± 4.5
Pre-operative pain			
Measured on the Numerical Rating Scale 0-10 points (0 no pain, 10 worst pain)			
Units: points			
median	3	3	2
inter-quartile range (Q1-Q3)	0 to 4	1 to 4	0 to 5

Reporting group values	Total		
Number of subjects	180		
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			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	136		
Male	44		
Diabetes			
Units: Subjects			
Diabetes	6		
No diabetes	174		
Type of surgery			
Units: Subjects			
Fracture	158		
Non-fracture	22		

Use of analgesics Units: Subjects			
Paracetamol	70		
NSAIDs	33		
Anti-depressants	20		
Opioids	13		
No use	44		
Weight Units: kilogram(s) arithmetic mean standard deviation	- -		
Height Units: centimetre arithmetic mean standard deviation	- -		
Body Mass Index Units: kilogram(s)/cubic metre arithmetic mean standard deviation	- -		
Pre-operative pain			
Measured on the Numerical Rating Scale 0-10 points (0 no pain, 10 worst pain)			
Units: points median inter-quartile range (Q1-Q3)	- -		

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description: Capsules containing placebo.	
Reporting group title	Dexamethasone 12mg
Reporting group description: Capsules containing 12mg dexamethasone.	
Reporting group title	Dexamethasone 24mg
Reporting group description: Capsules containing 24mg of dexamethasone.	

Primary: Duration of analgesia	
End point title	Duration of analgesia
End point description: Participants noted their date and time of their first perception of pain in the surgical area.	
End point type	Primary
End point timeframe: 0-48 hours postoperatively	

End point values	Placebo	Dexamethasone 12mg	Dexamethasone 24mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	59	55	
Units: minute				
arithmetic mean (standard deviation)	818 (± 292)	1171 (± 318)	1256 (± 395)	

Statistical analyses

Statistical analysis title	Placebo vs 12mg dexamethasone
Comparison groups	Placebo v Dexamethasone 12mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	354

Confidence interval	
level	Other: 98.33 %
sides	2-sided
lower limit	218
upper limit	490

Statistical analysis title	Placebo vs 24mg dexamethasone
Comparison groups	Placebo v Dexamethasone 24mg
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	437
Confidence interval	
level	Other: 98.33 %
sides	2-sided
lower limit	280
upper limit	594

Statistical analysis title	12 vs 24mg dexamethasone
Comparison groups	Dexamethasone 24mg v Dexamethasone 12mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.21
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	85
Confidence interval	
level	Other: 98.33 %
sides	2-sided
lower limit	-78
upper limit	249

Secondary: Duration of motor block	
End point title	Duration of motor block
End point description:	
Participants noted their date and time of their first ability to activate their biceps muscle.	
End point type	Secondary
End point timeframe:	
0-48 hours postoperatively	

End point values	Placebo	Dexamethasone 12mg	Dexamethasone 24mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	59	55	
Units: minute				
median (inter-quartile range (Q1-Q3))	813 (660 to 1087)	1144 (973 to 1335)	1144 (915 to 1325)	

Statistical analyses

Statistical analysis title	Placebo vs 12mg dexamethasone
Comparison groups	Placebo v Dexamethasone 12mg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	VanElteren
Parameter estimate	Hodges-Lehmann pseudomedian difference
Point estimate	283
Confidence interval	
level	95 %
sides	2-sided
lower limit	148
upper limit	394

Statistical analysis title	Placebo vs 24mg dexamethasone
Comparison groups	Dexamethasone 24mg v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	VanElteren
Parameter estimate	Hodges-Lehmann pseudomedian difference
Point estimate	232
Confidence interval	
level	95 %
sides	2-sided
lower limit	121
upper limit	356

Statistical analysis title	12mg vs 24mg dexamethasone

Comparison groups	Dexamethasone 24mg v Dexamethasone 12mg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.63
Method	VanElteren
Parameter estimate	Hodges-Lehmann pseudomedian difference
Point estimate	-30
Confidence interval	
level	95 %
sides	2-sided
lower limit	-149
upper limit	81

Secondary: Quality of sleep night 1

End point title	Quality of sleep night 1
End point description:	
Measured on the Numerical Rating Scale 0-10 points (0 worst sleep, 10 best sleep)	
End point type	Secondary
End point timeframe:	
First postoperative night	

End point values	Placebo	Dexamethasone 12mg	Dexamethasone 24mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	59	55	
Units: points				
median (inter-quartile range (Q1-Q3))	5 (4 to 7)	6 (3.5 to 8)	6 (3 to 8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of sleep night 2

End point title	Quality of sleep night 2
End point description:	
Measured on the Numerical Rating Scale 0-10 points (0 worst sleep, 10 best sleep)	
End point type	Secondary
End point timeframe:	
Second postoperative night	

End point values	Placebo	Dexamethasone 12mg	Dexamethasone 24mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	59	55	
Units: points				
median (inter-quartile range (Q1-Q3))	8 (7 to 9)	8 (7 to 9)	8 (7 to 10)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Pain at rest 24 hours postoperatively

End point title	Pain at rest 24 hours postoperatively
End point description: Measured on the Numerical Rating Scale 0-10 points (0 no pain, 10 worst pain)	
End point type	Other pre-specified
End point timeframe: 24 hours postoperatively	

End point values	Placebo	Dexamethasone 12mg	Dexamethasone 24mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	59	55	
Units: points				
median (inter-quartile range (Q1-Q3))	4 (2 to 6)	3 (1 to 4)	2 (0.5 to 5)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Pain at rest 48 hours postoperatively

End point title	Pain at rest 48 hours postoperatively
End point description: Measured on the Numerical Rating Scale 0-10 points (0 no pain, 10 worst pain)	
End point type	Other pre-specified
End point timeframe: 48 hours postoperatively	

End point values	Placebo	Dexamethasone 12mg	Dexamethasone 24mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	59	55	
Units: Points				
median (inter-quartile range (Q1-Q3))	2 (1 to 3)	2 (1 to 3)	2.5 (1 to 4)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Average pain 0-24 hours

End point title	Average pain 0-24 hours

End point description:

Measured on the Numerical Rating Scale 0-10 points (0 no pain, 10 worst pain)

End point type	Other pre-specified

End point timeframe:

0-24 hours postoperatively

End point values	Placebo	Dexamethasone 12mg	Dexamethasone 24mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	59	55	
Units: points				
median (inter-quartile range (Q1-Q3))	4 (2 to 5)	2 (0.5 to 4)	2 (1 to 3)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Average pain 24-48 hours

End point title	Average pain 24-48 hours

End point description:

Measured on the Numerical Rating Scale 0-10 points (0 no pain, 10 worst pain)

End point type	Other pre-specified

End point timeframe:

24-48 hours postoperatively

End point values	Placebo	Dexamethasone 12mg	Dexamethasone 24mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	59	55	
Units: points				
median (inter-quartile range (Q1-Q3))	2.5 (1.8 to 4)	3 (1 to 4)	3 (2 to 4)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Worst pain 0-24 hours

End point title	Worst pain 0-24 hours

End point description:

Measured on the Numerical Rating Scale 0-10 points (0 no pain, 10 worst pain)

End point type	Other pre-specified

End point timeframe:

0-24 hours postoperatively

End point values	Placebo	Dexamethasone 12mg	Dexamethasone 24mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	59	55	
Units: points				
median (inter-quartile range (Q1-Q3))	7 (5.8 to 8)	5 (2 to 6.5)	4 (1.5 to 7)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Worst pain 24-48 hours

End point title	Worst pain 24-48 hours

End point description:

Measured on the Numerical Rating Scale 0-10 points (0 no pain, 10 worst pain)

End point type	Other pre-specified

End point timeframe:

24-48 hours postoperatively

End point values	Placebo	Dexamethasone 12mg	Dexamethasone 24mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	59	55	
Units: points				
median (inter-quartile range (Q1-Q3))	4 (2 to 5.3)	4 (2 to 7)	5 (2 to 7)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Cumulative opioid consumption 0-24 hours

End point title	Cumulative opioid consumption 0-24 hours
End point description: Measured in oral oxycodone equivalents	
End point type	Other pre-specified
End point timeframe: 0-24 hours postoperatively	

End point values	Placebo	Dexamethasone 12mg	Dexamethasone 24mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	59	55	
Units: milligram(s)r				
median (inter-quartile range (Q1-Q3))	10 (0 to 15)	0 (0 to 10)	0 (0 to 10)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Cumulative opioid consumption 0-48 hours

End point title	Cumulative opioid consumption 0-48 hours
End point description:	
End point type	Other pre-specified
End point timeframe: 0-48 hours postoperatively	

End point values	Placebo	Dexamethasone 12mg	Dexamethasone 24mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	59	55	
Units: milligram(s)				
median (inter-quartile range (Q1-Q3))	20 (10 to 30)	10 (0 to 22.5)	5 (0 to 22.5)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 0-48 hours for adverse events and up until 30 days for serious adverse events.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27

Reporting groups	
Reporting group title	Placebo
Reporting group description: Capsules containing placebo.	
Reporting group title	Dexamethasone 12mg
Reporting group description: Capsules containing 12mg dexamethasone.	
Reporting group title	Dexamethasone 24mg
Reporting group description: Capsules containing 24mg of dexamethasone.	

Serious adverse events	Placebo	Dexamethasone 12mg	Dexamethasone 24mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 61 (1.64%)	1 / 61 (1.64%)	2 / 58 (3.45%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Surgery	Additional description: Internal fixation failure and re-operation		
subjects affected / exposed	1 / 61 (1.64%)	0 / 61 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome	Additional description: Acute coronary syndrome suspected and ruled out		
subjects affected / exposed	0 / 61 (0.00%)	1 / 61 (1.64%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fracture	Additional description: Fall and fracture of the femoral head.		

subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	Dexamethasone 12mg	Dexamethasone 24mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 61 (13.11%)	5 / 61 (8.20%)	9 / 58 (15.52%)
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 61 (0.00%)	1 / 61 (1.64%)	2 / 58 (3.45%)
occurrences (all)	0	1	2
Confusional state			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	1 / 61 (1.64%)	0 / 61 (0.00%)	1 / 58 (1.72%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Nauseaea			
subjects affected / exposed	3 / 61 (4.92%)	2 / 61 (3.28%)	1 / 58 (1.72%)
occurrences (all)	3	2	1
Pyrexia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	1
Flushing			

subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Haemorrhage	Additional description: Bandage seep through		
subjects affected / exposed	2 / 61 (3.28%)	1 / 61 (1.64%)	1 / 58 (1.72%)
occurrences (all)	2	1	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	3 / 61 (4.92%)	1 / 61 (1.64%)	0 / 58 (0.00%)
occurrences (all)	3	1	0
Reflux gastritis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 61 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 61 (0.00%)	0 / 61 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	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

None reported