Clinical trial results:
Repeat dose steroid to prevent pain relapse after Total Knee Arthroplasty in patients with high pain response - A randomized blinded placebo-controlled trial

Summary

EudraCT number	2020-006110-20
Trial protocol	DK
Global end of trial date	19 April 2024

Results information

Result version number	v1 (current)
This version publication date	09 July 2025
First version publication date	09 July 2025

Trial information

Trial identification

Sponsor protocol code	RepeatDoseTKAHPR2020

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05563155
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vejle sygehus
Sponsor organisation address	Beriderbakken 4, Vejle, Denmark, 7100
Public contact	Forskningsenheden Ortopædkirurgisk, Ortopædkirurgisk Department. Vejle Sygehus. Denmark, + 4579405779, clausvarnum@gmail.com
Scientific contact	Forskningsenheden Ortopædkirurgisk, Ortopædkirurgisk Department. Vejle Sygehus. Denmark, + 4579405779, clausvarnum@gmail.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 July 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 April 2024
Global end of trial reached?	Yes
Global end of trial date	19 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the study is to compare the effect of a repeat moderate dose of glucocorticoids postoperatively after preoperative high dose upon postoperative pain after TKA in an HPR population to a standard single high dose systemic preoperative administration in an HPR population.

Protection of trial subjects:

The study will not bring other changes to the patient’s course of treatment in relation to the preoperative preparation, level of information, type of anesthesia, surgical procedure, postoperative care, physiotherapy and discharge, the exceptions being the repeat-dosing program, Dexamethasone vs. Placebo. All these other steps will be following our Fast-Track program.

Background therapy:

Standardised fast-track regime according to local guidelines.

Evidence for comparator: -

Actual start date of recruitment	02 May 2022
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: 110
Worldwide total number of subjects	110
EEA total number of subjects	110

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)	44
From 65 to 84 years	64

85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Between 25 November 2021 and 20 March 2024, 110 patients were included and randomised. The inclusion took place at Hvidovre and Vejle Hospitals in Denmark.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	287[1]
Number of subjects completed	110

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 30
Reason: Number of subjects	Not meeting criteria: 118
Reason: Number of subjects	Protocol deviation: 21
Reason: Number of subjects	Discharged on day 0: 5
Reason: Number of subjects	Could not complete primary outcome: 3

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 10 subjects were added as an amendment.

Period 1

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

Blinding implementation details:

The randomization-sequence will be stored in a sealed envelope at the Pharmacy at Lillebaelt Hospital who carried out the packaging-process. The randomization personnel have no contact to the patient. Sealed coding-envelopes containing data on randomization are stored in a locked cabinet at Dept. of Orthopaedic Surgery, Lillebaelt Hospital – Vejle and Dept. of Anesthesiology, Hvidovre Hospital.

Arms

Are arms mutually exclusive?	Yes
Arm title	Dexamethasone

Arm description:

Patients receiving the active regime of repeat dose oral dexamethasone 24 mg.

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:

24 mg oral dexamethasone administered on the evening of day 1 after surgery.

Arm title	Placebo

Arm description:

Subjects receiving inactive placebo.

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

Dosage and administration details:

Placebo capsule administered on the evening on day 1 after surgery.

Number of subjects in period 1	Dexamethasone	Placebo
Started	55	55
Completed	48	53
Not completed	7	2
Consent withdrawn by subject	4	2
Lost to follow-up	1	-
Protocol deviation	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Dexamethasone
Reporting group description:	
Patients receiving the active regime of repeat dose oral dexamethasone 24 mg.	
Reporting group title	Placebo
Reporting group description:	
Subjects receiving inactive placebo.	

Reporting group values	Dexamethasone	Placebo	Total
Number of subjects	55	55	110
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	67	68	
full range (min-max)	50 to 81	50 to 87	-
Gender categorical Units: Subjects			
Female	28	31	59
Male	27	24	51

End points

End points reporting groups	
Reporting group title	Dexamethasone
Reporting group description:	
Patients receiving the active regime of repeat dose oral dexamethasone 24 mg.	
Reporting group title	Placebo
Reporting group description:	
Subjects receiving inactive placebo.	

Primary: Moderate to severe pain (VAS > 30) upon ambulation in a 5-meter walk test, on the morning of day 2 after TKA surgery.	
End point title	Moderate to severe pain (VAS > 30) upon ambulation in a 5-meter walk test, on the morning of day 2 after TKA surgery.
End point description:	
End point type	Primary
End point timeframe:	
Assessed 48 hours after surgery.	

End point values	Dexamethasone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	53		
Units: Number of patients	31	42		

Statistical analyses

Statistical analysis title	Primary outcome
Comparison groups	Dexamethasone v Placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	1.16

Secondary: Cumulated pain upon ambulation in a 5-meter walk test day 2-3

End point title	Cumulated pain upon ambulation in a 5-meter walk test day 2-3

End point description:

End point type	Secondary

End point timeframe:

Days 2 to 3 after surgery

End point values	Dexamethasone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	52		
Units: VAS				
arithmetic mean (standard deviation)	168 (± 75)	186 (± 68)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulated pain score at rest from day 2-7

End point title	Cumulated pain score at rest from day 2-7

End point description:

End point type	Secondary

End point timeframe:

Days 2 to 7 after surgery.

End point values	Dexamethasone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	52		
Units: VAS				
arithmetic mean (standard deviation)	425 (± 219)	405 (± 206)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulated pain score upon ambulation in a 5-meter walk test from day 2-7

End point title	Cumulated pain score upon ambulation in a 5-meter walk test from day 2-7

End point description:

End point type	Secondary

End point timeframe:

Days 2 to 7 after surgery

End point values	Dexamethasone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	52		
Units: VAS				
arithmetic mean (standard deviation)	477 (± 218)	486 (± 213)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulated pain score at night from day 2-7

End point title	Cumulated pain score at night from day 2-7

End point description:

End point type	Secondary

End point timeframe:

Days 2 to 7 after surgery

End point values	Dexamethasone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	52		
Units: VAS				
arithmetic mean (standard deviation)	228 (± 111)	219 (± 109)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulated pain at rest on days 2-3

End point title	Cumulated pain at rest on days 2-3

End point description:

End point type	Secondary

End point timeframe:

Days 2 to 3 postoperatively

End point values	Dexamethasone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	52		
Units: VAS				
arithmetic mean (standard deviation)	137 (± 75)	152 (± 64)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulated pain at night days 2-3

End point title	Cumulated pain at night days 2-3

End point description:

End point type	Secondary

End point timeframe:

Days 2 to 3 after surgery

End point values	Dexamethasone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	52		
Units: VAS				
arithmetic mean (standard deviation)	76 (± 40)	79 (± 42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative use of rescue analgesics per day from day 2-7

End point title	Cumulative use of rescue analgesics per day from day 2-7

End point description:

End point type	Secondary

End point timeframe:
Days 2 to 7 after surgery

End point values	Dexamethasone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	52		
Units: MME				
median (inter-quartile range (Q1-Q3))	15 (5 to 30)	19 (7 to 35)		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of sleep from days 2-7

End point title	Quality of sleep from days 2-7

End point description:
Assessed on scale of 0-10, 0 being best and 10 being worst

End point type	Secondary

End point timeframe:
Days 2 to 7 after surgery

End point values	Dexamethasone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	52		
Units: Numeric				
median (inter-quartile range (Q1-Q3))	3 (2.3 to 4.2)	3 (2.4 to 4.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Lethargy on days 2-7

End point title	Lethargy on days 2-7

End point description:
Assessed on scale of 0-10, 0 being best and 10 being worst

End point type	Secondary

End point timeframe:
Days 2 to 7 after surgery

End point values	Dexamethasone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	52		
Units: Numeric				
median (inter-quartile range (Q1-Q3))	3.4 (1.7 to 4.8)	3.1 (2.0 to 4.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Dizziness from days 2-7

End point title	Dizziness from days 2-7
End point description: Assessed on scale of 0-10, 0 being best and 10 being worst	
End point type	Secondary
End point timeframe: Days 2 to 7 after surgery	

End point values	Dexamethasone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	52		
Units: Numeric				
median (inter-quartile range (Q1-Q3))	0.4 (0 to 1.6)	0.3 (0 to 1.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Nausea on days 2-7

End point title	Nausea on days 2-7
End point description: Assessed on scale of 0-10, 0 being best and 10 being worst	
End point type	Secondary
End point timeframe: Days 2 to 7 postoperatively	

End point values	Dexamethasone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	52		
Units: Numeric				
median (inter-quartile range (Q1-Q3))	0 (0 to 1.7)	0.3 (0 to 1.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient satisfaction with analgesic regimen

End point title	Patient satisfaction with analgesic regimen
End point description:	
Assessed on scale of 0-10, 0 being most and 10 being least	
End point type	Secondary
End point timeframe:	
Assessed on day 7 postoperatively	

End point values	Dexamethasone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	52		
Units: Numeric				
median (inter-quartile range (Q1-Q3))	1.5 (0 to 5)	2 (0 to 5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Length of hospital stay

End point title	Length of hospital stay
End point description:	
Number of days in hospital after surgery	
End point type	Secondary
End point timeframe:	
Within 30 days after surgery	

End point values	Dexamethasone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	52		
Units: Days				
median (inter-quartile range (Q1-Q3))	1 (1 to 1)	1 (1 to 1)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
30 days after surgery	
Adverse event reporting additional description:	
Only serious adverse events were reported	
Assessment type	Systematic

Dictionary used	
Dictionary name	None used
Dictionary version	0

Reporting groups	
Reporting group title	Dexamethasone
Reporting group description:	
Patients receiving the active regime of repeat dose oral dexamethasone 24 mg.	
Reporting group title	Placebo
Reporting group description:	
Subjects receiving inactive placebo.	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: We did not report non-serious adverse events as per protocol, since the active drug dexamethasone is a well-known drug with well-described adverse events.

Serious adverse events	Dexamethasone	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 49 (6.12%)	0 / 54 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Vasovagal syncope	Additional description: Patient was dehydrated		
subjects affected / exposed	1 / 49 (2.04%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Prosthetic joint infection	Additional description: Infection around the prostesis treated with antibiotics and sof-tissue revision.		
subjects affected / exposed	2 / 49 (4.08%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Dexamethasone	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 49 (0.00%)	0 / 54 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 November 2022	10 subjects were added to the study group (5 in each arm) due to drop-outs.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/40364780