Clinical trial results:
The effects of preoperative high-dose Dexamethasone on inflammatory response and recovery after emergency laparotomy, a randomized, double-blind, placebo-controlled clinical trial - AHA STEROID TRIAL

Summary

EudraCT number	2020-002586-34
Trial protocol	DK
Global end of trial date	02 January 2023

Results information

Result version number	v1 (current)
This version publication date	18 June 2025
First version publication date	18 June 2025

Trial information

Trial identification

Sponsor protocol code	STEROID_MC_1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04791566
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Research Group, Dept. of Anesthesia
Sponsor organisation address	Kettegard alle 30, Hvidovre, Denmark, 2650
Public contact	Research Group, Dept. of Anesthesia, Department of Anesthesiology, Copenhagen University Hospital Hvidovre, Capital Region of Denmark , mirjana.cihoric.03@regionh.dk
Scientific contact	Research Group, Dept. of Anesthesia, Department of Anesthesiology, Copenhagen University Hospital Hvidovre, Capital Region of Denmark , 0045 38620547, mirjana.cihoric.03@regionh.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	02 January 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 January 2023
Global end of trial reached?	Yes
Global end of trial date	02 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

C-reactive protein T24H after surgery.

Protection of trial subjects:

No protection measures put in place-

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 March 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: 120
Worldwide total number of subjects	120
EEA total number of subjects	120

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)	48
From 65 to 84 years	63
85 years and over	9

Subject disposition

Recruitment

Recruitment details:

After a confirmed CT diagnosis of either intestinal obstruction or perforated viscus, the senior surgeon contacted the primary investigator (PI). The PI evaluated and informed the patients, securing written and verbal consent before surgery and before arrival at the operating room. The PI of the trial evaluated and included all patients.

Pre-assignment

Screening details:

Adult patients scheduled for emergency laparotomy for either intestinal obstruction or perforated viscus were eligible. Exclusion criteria were reoperations, traumas, gynaecological, urogenital, and other vascular pathology, dementia, insulin treatment for diabetes, immunolsuppresive treatment, allergy, pregnancy and lack of informed consent.

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:

Sequence generation and preparation of 120 sequentially numbered opaque sealed randomization envelopes were completed by two people independent of the research team and who had no further role in the trial. Personnel, not otherwise involved in the trial opened the randomization envelopes, prepared and blinded the trial medication, and sealed the envelopes again afterwards. Patients, care providers, and data collectors were blinded to allocation.

Arms

Are arms mutually exclusive?	Yes
Arm title	Dexamethasone

Arm description:

A single preoperative dose of 1 mg/kg dexamethasone diluted in 100 ml of physiological saline and administered just after anaesthesia induction as a 15-min infusion.

Arm type	Active comparator
Investigational medicinal product name	dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dexamethasone 10.0 mg/mL (Ratiopharm, Germany) . Patients will receive 1 mg/kg Dexamethasone. Dispensed as Dexamethasone-21-dihydrogenfosfat, diluted in normal saline, with a total volume of 100 mL.

Arm title	Placebo arm

Arm description:

A single preoperative dose of 1 mg/kg of placebo (saline), diluted in 100 ml of physiological saline and administered just after anaesthesia induction as a 15-min infusion.

Arm type	Placebo

Investigational medicinal product name	saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Bolus infusion of normal saline, 100 mL over a 10-15-minute period in addition to standard care (no steroid treatment).

Number of subjects in period 1	Dexamethasone	Placebo arm
Started	60	60
Completed	60	60

Baseline characteristics

Reporting groups	
Reporting group title	Dexamethasone
Reporting group description:	
A single preoperative dose of 1 mg/kg dexamethasone diluted in 100 ml of physiological saline and administered just after anaesthesia induction as a 15-min infusion.	
Reporting group title	Placebo arm
Reporting group description:	
A single preoperative dose of 1 mg/kg of placebo (saline), diluted in 100 ml of physiological saline and administered just after anaesthesia induction as a 15-min infusion.	

Reporting group values	Dexamethasone	Placebo arm	Total
Number of subjects	60	60	120
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	71	68	
inter-quartile range (Q1-Q3)	57 to 78	54 to 76	-
Gender categorical			
Units: Subjects			
Female	30	32	62
Male	30	28	58

End points

End points reporting groups

Reporting group title	Dexamethasone
Reporting group description:	
A single preoperative dose of 1 mg/kg dexamethasone diluted in 100 ml of physiological saline and administered just after anaesthesia induction as a 15-min infusion.	
Reporting group title	Placebo arm
Reporting group description:	
A single preoperative dose of 1 mg/kg of placebo (saline), diluted in 100 ml of physiological saline and administered just after anaesthesia induction as a 15-min infusion.	

Primary: CRP at T24 hours after surgery

End point title	CRP at T24 hours after surgery
End point description:	
End point type	Primary
End point timeframe:	
At 24 hours after surgery, overall cohort	

End point values	Dexamethasone	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	58		
Units: mg/l				
median (inter-quartile range (Q1-Q3))	170 (60 to 260)	220 (150 to 300)		

Statistical analyses

Statistical analysis title	chi sqare
Comparison groups	Dexamethasone v Placebo arm
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Chi-squared
Parameter estimate	Median difference (final values)

Primary: CRP at T24 hours after surgery, intestinal obstruction

End point title	CRP at T24 hours after surgery, intestinal obstruction

End point description:

End point type	Primary

End point timeframe:

At 24 hours after surgery, intestinal obstruction

End point values	Dexamethasone	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	29		
Units: mg/l				
median (inter-quartile range (Q1-Q3))	60 (30 to 160)	160 (100 to 280)		

Statistical analyses

Statistical analysis title	chi square
Comparison groups	Dexamethasone v Placebo arm
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Chi-squared

Secondary: 30 day mortality

End point title	30 day mortality

End point description:

End point type	Secondary

End point timeframe:

30 day postoperatively

End point values	Dexamethasone	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	58		
Units: percentage	7	12		

Statistical analyses

No statistical analyses for this end point

Secondary: 90 day mortality

End point title	90 day mortality

End point description:

End point type	Secondary

End point timeframe:

90 day postoperatively

End point values	Dexamethasone	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	58		
Units: percentage	7	22		

Statistical analyses

No statistical analyses for this end point

Secondary: 30 day postoperative complications

End point title	30 day postoperative complications

End point description:

End point type	Secondary

End point timeframe:

30 days postoperatively

End point values	Dexamethasone	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	58		
Units: percentage	28	45		

Statistical analyses

No statistical analyses for this end point

Secondary: LOS

End point title	LOS

End point description:

End point type	Secondary

End point timeframe:
Length of in-hospital stay

End point values	Dexamethasone	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	58		
Units: days				
median (inter-quartile range (Q1-Q3))	8 (5 to 14)	9 (6 to 21)		

Statistical analyses

No statistical analyses for this end point

Secondary: CRP at T24 hours after surgery, perforated viscus

End point title	CRP at T24 hours after surgery, perforated viscus

End point description:

End point type	Secondary

End point timeframe:
At 24 hours after surgery, perforated viscus

End point values	Dexamethasone	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	29		
Units: mg/l				
median (inter-quartile range (Q1-Q3))	230 (170 to 280)	285 (200 to 330)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Variables registered daily during admission for the first 14 days after randomization

Assessment type	Systematic

Dictionary used

Dictionary name	within protocol
Dictionary version	1

Reporting groups

Reporting group title	Dexamethasone

Reporting group description:

A single preoperative dose of 1 mg/kg dexamethasone diluted in 100 ml of physiological saline and administered just after anaesthesia induction as a 15-min infusion.

Reporting group title	Placebo

Reporting group description:

A single preoperative dose of 1 mg/kg of placebo (saline), diluted in 100 ml of physiological saline and administered just after anaesthesia induction as a 15-min infusion.

Serious adverse events	Dexamethasone	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 60 (16.67%)	13 / 60 (21.67%)	
number of deaths (all causes)	4	13	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
LE	Additional description: Lung embolism		
subjects affected / exposed	1 / 60 (1.67%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
multi-organ failure	Additional description: Postoperative multi organ failure		
subjects affected / exposed	0 / 60 (0.00%)	7 / 60 (11.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Delirium	Additional description: Postoperative incidence of delirium		
subjects affected / exposed	8 / 60 (13.33%)	6 / 60 (10.00%)	
occurrences causally related to treatment / all	0 / 8	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
apoplexia			

subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral derangement	Additional description: Cerebral derangement without apparent cause		
subjects affected / exposed	0 / 60 (0.00%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sepsis	Additional description: Postoperative new onset of sepsis		
subjects affected / exposed	2 / 60 (3.33%)	3 / 60 (5.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection	Additional description: Postoperative surgical infection		
subjects affected / exposed	4 / 60 (6.67%)	4 / 60 (6.67%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Dexamethasone	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 60 (58.33%)	30 / 60 (50.00%)	
Cardiac disorders			
hypertension			
subjects affected / exposed	25 / 60 (41.67%)	25 / 60 (41.67%)	
occurrences (all)	25	25	
palpitations			
subjects affected / exposed	9 / 60 (15.00%)	9 / 60 (15.00%)	
occurrences (all)	9	9	
bradycardia			
subjects affected / exposed	3 / 60 (5.00%)	1 / 60 (1.67%)	
occurrences (all)	3	1	
Nervous system disorders			
headache			

subjects affected / exposed	3 / 60 (5.00%)	4 / 60 (6.67%)	
occurrences (all)	3	4	
sleep disturbance			
subjects affected / exposed	26 / 60 (43.33%)	29 / 60 (48.33%)	
occurrences (all)	26	29	
delirium			
subjects affected / exposed	6 / 60 (10.00%)	4 / 60 (6.67%)	
occurrences (all)	6	4	
Gastrointestinal disorders			
taste disturbance			
subjects affected / exposed	5 / 60 (8.33%)	6 / 60 (10.00%)	
occurrences (all)	5	6	
Endocrine disorders			
flushing			
subjects affected / exposed	3 / 60 (5.00%)	3 / 60 (5.00%)	
occurrences (all)	3	3	
euphoria			
subjects affected / exposed	3 / 60 (5.00%)	2 / 60 (3.33%)	
occurrences (all)	3	2	

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.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/39028763