Clinical trial results:
Different dosis of corticosteroids in mandibular third molar surgery. A randomized, blinded clinical trial assessing pain, trismus, edema and quality of life outcome measurements.

Summary

EudraCT number	2017-000622-35
Trial protocol	DK
Global end of trial date	01 July 2019

Results information

Result version number	v1 (current)
This version publication date	30 July 2019
First version publication date	30 July 2019

Trial information

Trial identification

Sponsor protocol code	56872

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aalborg University Hospital
Sponsor organisation address	Hobrovej 18-22, Aalborg, Denmark, 9000
Public contact	Department of Oral and Maxillofacial Surgery, Aalborg University Hospital, 0045 97 66 00 00, marie.kjaergaard@rn.d
Scientific contact	Department of Oral and Maxillofacial Surgery, Aalborg University Hospital, 0045 97 66 00 00, marie.kjaergaard@rn.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	01 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 June 2019
Global end of trial reached?	Yes
Global end of trial date	01 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effects of treatment with intramuscular methylprednisolone on the postoperative morbidity after removal of mandibular third molar.

Protection of trial subjects:

Clinical examination

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 January 2018
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: 52
Worldwide total number of subjects	52
EEA total number of subjects	52

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)	52
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited to the study from January to May 2018.

Pre-assignment

Screening details:

Medical assessment

Pre-assignment period milestones

Number of subjects started	52
Number of subjects completed	52[1]

Notes:

[1] - The number of subjects reported to be in the pre-assignment period is not consistent with the number starting period 1. It is expected that the number completing the pre-assignment period are also present in the arms in period 1.
Justification: The study is a split-mouth trial. Every patient gets two arms.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Natriumklorid isotonisk SAD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

2mL isotonic NaCl solution

Arm title	20 mg methylprednisolone

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Solu-Medrol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

20 mg methylprednisolone

Arm title	30 mg methylprednisolone

Arm description: -

Arm type	Experimental

Investigational medicinal product name	Solu-Medrol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:
30 mg methylprednisolone

Arm title	40 mg methylprednisolone

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Solu-Medrol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:
40 mg methylprednisolone

Number of subjects in period 1	Placebo	20 mg methylprednisolone	30 mg methylprednisolone
Started	26	26	26
Completed	26	26	26

Number of subjects in period 1	40 mg methylprednisolone
Started	26
Completed	26

Baseline characteristics

Reporting groups	
Reporting group title	Intervention

Reporting group description: -

Reporting group values	Intervention	Total	
Number of subjects	52	52	
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	25.9		
standard deviation	± 6	-	
Gender categorical Units: Subjects			
Female	36	36	
Male	16	16	
Eosinophils Units: Amount			
median	0.1		
standard deviation	± 0.1	-	
Leucocytes Units: Amount			
median	6.3		
standard deviation	± 1.4	-	
Neutrophils Units: Amount			
median	3.2		
standard deviation	± 1.1	-	
C-reactive protein Units: Amount			
median	1.3		
standard deviation	± 0.1	-	
Trismus Units: mm			
median	51		
standard deviation	± 5.9	-	

Pain			
Units: mm			
median	0		
standard deviation	± 14	-	

Subject analysis sets

Subject analysis set title	Corticosteroids
Subject analysis set type	Full analysis

Subject analysis set description:

The data contain data from 53 people, however one person is excluded due to missing values on a number of variables (including the treatment group). Thus all analyses are based on 52 people.

Reporting group values	Corticosteroids		
Number of subjects	52		
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	25.9		
standard deviation	± 6		
Gender categorical			
Units: Subjects			
Female	36		
Male	16		
Eosinophils			
Units: Amount			
median	0.1		
standard deviation	± 0.1		
Leucocytes			
Units: Amount			
median	6.3		
standard deviation	± 1.4		
Neutrophils			
Units: Amount			
median	3.2		
standard deviation	± 1.1		
C-reactive protein			
Units: Amount			
median	1.3		
standard deviation	± 0.1		

Trismus Units: mm median standard deviation	 51 ± 5.9		
Pain Units: mm median standard deviation	 0 ± 14		

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	20 mg methylprednisolone
Reporting group description: -	
Reporting group title	30 mg methylprednisolone
Reporting group description: -	
Reporting group title	40 mg methylprednisolone
Reporting group description: -	
Subject analysis set title	Corticosteroids
Subject analysis set type	Full analysis
Subject analysis set description:	
The data contain data from 53 people, however one person is excluded due to missing values on a number of variables (including the treatment group). Thus all analyses are based on 52 people.	

Primary: VAS	
End point title	VAS
End point description:	
End point type	Primary
End point timeframe:	
One days postoperatively	

End point values	Placebo	20 mg methylprednisolone	30 mg methylprednisolone	40 mg methylprednisolone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	26	26	26
Units: mm				
median (standard deviation)	52 (± 28.4)	43.8 (± 25.5)	41 (± 20.5)	45.5 (± 22.5)

Statistical analyses

Statistical analysis title	VAS Placebo-20mg
Comparison groups	Placebo v 20 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.53

Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.15
upper limit	15.1
Variability estimate	Standard error of the mean
Dispersion value	8

Statistical analysis title	VAS Placebo-30mg
Comparison groups	Placebo v 30 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	-11.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.88
upper limit	4.34
Variability estimate	Standard error of the mean
Dispersion value	8.2

Statistical analysis title	VAS Placebo-40mg
Comparison groups	Placebo v 40 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.94
upper limit	14.18
Variability estimate	Standard error of the mean
Dispersion value	7.7

Secondary: Trismus	
End point title	Trismus

End point description:

End point type	Secondary
End point timeframe:	
Three days postoperatively	

End point values	Placebo	20 mg methylprednisolone	30 mg methylprednisolone	40 mg methylprednisolone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	26	26	26
Units: mm				
median (standard deviation)	31.6 (± 9.5)	31 (± 11.2)	34.4 (± 8)	32.9 (± 9.5)

Statistical analyses

Statistical analysis title	Trismus Placebo-20mg
Comparison groups	Placebo v 20 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.71
upper limit	6.16
Variability estimate	Standard error of the mean
Dispersion value	2.5

Statistical analysis title	Trismus Placebo-30mg
Comparison groups	Placebo v 30 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.44

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.99
upper limit	6.87
Variability estimate	Standard error of the mean
Dispersion value	2.8

Statistical analysis title	Trismus Placebo-40mg
Comparison groups	Placebo v 40 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.53
upper limit	8.01
Variability estimate	Standard error of the mean
Dispersion value	2.7

Secondary: Leucocytes

End point title	Leucocytes
End point description:	
End point type	Secondary
End point timeframe:	
Three days postoperatively	

End point values	Placebo	20 mg methylprednisolone	30 mg methylprednisolone	40 mg methylprednisolone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	26	26	26
Units: Number				
median (standard deviation)	7.2 (± 1.6)	8.2 (± 2.2)	8.3 (± 2.7)	7.8 (± 2)

Statistical analyses

Statistical analysis title	Leucocytes Placebo-20mg
Comparison groups	Placebo v 20 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	0.5

Statistical analysis title	Leucocytes Placebo-30mg
Comparison groups	Placebo v 30 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.42
upper limit	1.04
Variability estimate	Standard error of the mean
Dispersion value	0.63

Statistical analysis title	Leucocytes Placebo-40mg
Comparison groups	Placebo v 40 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	1.16
Variability estimate	Standard error of the mean
Dispersion value	0.55

Secondary: Eosinophils

End point title	Eosinophils
End point description:	
End point type	Secondary
End point timeframe:	
Three days postoperatively	

End point values	Placebo	20 mg methylprednisolone	30 mg methylprednisolone	40 mg methylprednisolone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	26	26	26
Units: Amount				
median (standard deviation)	0.1 (± 0.1)	0.2 (± 0.1)	0.1 (± 0.1)	0.1 (± 0.1)

Statistical analyses

Statistical analysis title	Eosinophils Placebo-20mg
Comparison groups	Placebo v 20 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Eosinophils Placebo-30mg
Comparison groups	Placebo v 30 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.001
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Eosinophils Placebo-40mg
Comparison groups	Placebo v 40 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.005
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.02

Secondary: Neutrophils	
End point title	Neutrophils
End point description:	

End point type	Secondary
End point timeframe:	
Three days postoperatively	

End point values	Placebo	20 mg methylprednisolone	30 mg methylprednisolone	40 mg methylprednisolone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	26	26	26
Units: Amount				
median (standard deviation)	4.5 (± 1.7)	5.2 (± 2)	5.1 (± 2.3)	4.7 (± 1.9)

Statistical analyses

Statistical analysis title	Neutrophils Placebo-20mg
Comparison groups	Placebo v 20 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.5

Statistical analysis title	Neutrophils Placebo-30mg
Comparison groups	Placebo v 30 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.61
upper limit	0.72
Variability estimate	Standard error of the mean
Dispersion value	0.59

Statistical analysis title	Neutrophils Placebo-40mg
Comparison groups	Placebo v 40 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.28
upper limit	0.68
Variability estimate	Standard error of the mean
Dispersion value	0.5

Secondary: C-reactive protein	
End point title	C-reactive protein
End point description:	
End point type	Secondary
End point timeframe:	
Three days postoperatively	

End point values	Placebo	20 mg methylprednisolone	30 mg methylprednisolone	40 mg methylprednisolone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	26	26	26
Units: Amount				
median (standard deviation)	20.6 (± 24.3)	16.1 (± 25.5)	11.4 (± 13.4)	11.5 (± 22.8)

Statistical analyses

Statistical analysis title	C-reactive protein Placebo-20mg
Comparison groups	Placebo v 20 mg methylprednisolone

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	-4.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.65
upper limit	8.08
Variability estimate	Standard error of the mean
Dispersion value	6.6

Statistical analysis title	C-reactive protein Placebo-30mg
Comparison groups	Placebo v 30 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	-10.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.31
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	5.1

Statistical analysis title	C-reactive protein Placebo-40mg
Comparison groups	Placebo v 40 mg methylprednisolone
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	GEE analysis
Parameter estimate	Mean difference (final values)
Point estimate	-9.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.17
upper limit	2.32

Variability estimate	Standard error of the mean
Dispersion value	6.2

Adverse events

Adverse events information	
Timeframe for reporting adverse events: The time point is January 2019.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20

Reporting groups	
Reporting group title	Adverse events

Reporting group description: -

Serious adverse events	Adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 52 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 52 (42.31%)		
Infections and infestations			
Infections			
subjects affected / exposed	22 / 52 (42.31%)		
occurrences (all)	22		

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