



## Clinical trial results:

### Clinical Trials with lozenge as local anaesthesia as treatment of oral pain in burning mouth syndrome and Sjögrens syndrome

#### Summary

EudraCT number	2011-006196-19
Trial protocol	DK
Global end of trial date	15 January 2015

#### Results information

Result version number	v1 (current)
This version publication date	21 September 2019
First version publication date	21 September 2019

#### Trial information

##### Trial identification

Sponsor protocol code	OC003SB
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01584947
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	Clinical Research Centre, Amager and Hvidovre Hospital
Sponsor organisation address	Kettegård allé 30, Hvidovre, Denmark,
Public contact	Charlotte Tredal, Clinical Research Centre, Amager and Hvidovre Hospital, 0045 38626077, sugetablet@gmail.com
Scientific contact	Charlotte Tredal, Clinical Research Centre, Amager and Hvidovre Hospital, 0045 38626077, sugetablet@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	14 January 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 January 2014
Global end of trial reached?	Yes
Global end of trial date	15 January 2015
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The effect of the treatment with respectively bupivacaine- and placebo lozenges on subjective symptoms in burning mouth syndrome, Sjögren's syndrome and lichen planus such as pain in the oral mucosa, oral dryness and taste disturbances

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2012
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: 25
Worldwide total number of subjects	25
EEA total number of subjects	25

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)	21
From 65 to 84 years	4
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The participants were recruited among patients attending or referred to the Oral Medicine clinic, Department of Odontology, Faculty of Health and Medical Sciences, University of Copenhagen, during the period from April 2012 to January 2014

### Pre-assignment

Screening details:

The inclusion criteria were a diagnosis of BMS, age of 18 to 75 years, fertile women had to use effective contraception, ability to speak and understand Danish and ability to give informed consent. The patients were diagnosed with BMS on the basis of symptoms and clinical and paraclinical investigations.

### Period 1

Period 1 title	baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

The randomization allocation list was done by a statistician and was carried out using the statistical program R version 3.0.1. The containers with the lozenges were sequentially numbered and assigned period 1 or period 2 in correlation with the randomization list. The first patient then received container 1, period 1 and container 1, period 2 and so forth.

### Arms

Arm title	baseline
Arm description: -	
Arm type	baseline
Investigational medicinal product name	Bupivacaine lozenge
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Lozenge
Routes of administration	Oral use

Dosage and administration details:

Lozenges containing 5 mg bupivacaine and placebo lozenges both with a size of 12-mm diameter were manufactured by direct compression, at the Pharmacy of the Capital Region, Denmark. Both the placebo and the bupivacaine lozenge were taste masked with liquorice powder as it can disguise the bitter taste of bupivacaine.

Patients were asked to take three lozenges each day in the treatment period, one after breakfast, one after lunch and one after dinner. The lozenges were administrated after meals to sustain the local anesthetic effect as long as possible. Patients were instructed to suck on the lozenge until it was completely dissolved, to avoid the use of other medical lozenges and to avoid intake of food and drinks for a minimum of 30 minutes after the lozenge was dissolved.

Investigational medicinal product name	Placebo lozenge
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Lozenge
Routes of administration	Oromucosal use

Dosage and administration details:

Lozenges containing 5 mg bupivacaine and placebo lozenges both with a size of 12-mm diameter were manufactured by direct compression, at the Pharmacy of the Capital Region, Denmark. Both the placebo and the bupivacaine lozenge were taste masked with liquorice powder as it can disguise the bitter taste of bupivacaine.

Patients were asked to take three lozenges each day in the treatment period, one after breakfast, one after lunch and one after dinner. The lozenges were administrated after meals to sustain the local anesthetic effect as long as possible. Patients were instructed to suck on the lozenge until it was completely dissolved, to avoid the use of other medical lozenges and to avoid intake of food and drinks

for a minimum of 30 minutes after the lozenge was dissolved.

<b>Number of subjects in period 1</b>	baseline
Started	25
Completed	25

## Period 2

Period 2 title	Treatment period 1
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

### Blinding implementation details:

The patients were randomized to receive bupivacaine lozenges in one treatment period and placebo lozenges in another treatment period.

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Lozenge active

### Arm description:

The patients were randomized to receive bupivacaine lozenges

Arm type	Experimental
Investigational medicinal product name	Bupivacaine lozenge
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Lozenge
Routes of administration	Oral use

### Dosage and administration details:

Lozenges containing 5 mg bupivacaine and placebo lozenges both with a size of 12-mm diameter were manufactured by direct compression, at the Pharmacy of the Capital Region, Denmark. Both the placebo and the bupivacaine lozenge were taste masked with liquorice powder as it can disguise the bitter taste of bupivacaine.

Patients were asked to take three lozenges each day in the treatment period, one after breakfast, one after lunch and one after dinner. The lozenges were administered after meals to sustain the local anesthetic effect as long as possible. Patients were instructed to suck on the lozenge until it was completely dissolved, to avoid the use of other medical lozenges and to avoid intake of food and drinks for a minimum of 30 minutes after the lozenge was dissolved.

<b>Arm title</b>	Lozenge placebo
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Arm description:	
The patients were randomized to placebo lozenges	
Arm type	Placebo
Investigational medicinal product name	Placebo lozenge
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Lozenge
Routes of administration	Oral use

**Dosage and administration details:**

Lozenges containing 5 mg bupivacaine and placebo lozenges both with a size of 12-mm diameter were manufactured by direct compression, at the Pharmacy of the Capital Region, Denmark. Both the placebo and the bupivacaine lozenge were taste masked with liquorice powder as it can disguise the bitter taste of bupivacaine.

Patients were asked to take three lozenges each day in the treatment period, one after breakfast, one after lunch and one after dinner. The lozenges were administered after meals to sustain the local anesthetic effect as long as possible. Patients were instructed to suck on the lozenge until it was completely dissolved, to avoid the use of other medical lozenges and to avoid intake of food and drinks for a minimum of 30 minutes after the lozenge was dissolved.

<b>Number of subjects in period 2</b>	Lozenge active	Lozenge placebo
Started	12	13
Completed	10	13
Not completed	2	0
Consent withdrawn by subject	2	-

**Period 3**

Period 3 title	Treatment period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

**Blinding implementation details:**

The randomization allocation list was done by a statistician and was carried out using the statistical program R version 3.0.1. The containers with the lozenges were sequentially numbered and assigned period 1 or period 2 in correlation with the randomization list. The first patient then received container 1, period 1 and container 1, period 2 and so forth.

**Arms**

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Active lozenge

**Arm description:**

The patients were randomized to receive bupivacaine lozenges

Arm type	Experimental
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Investigational medicinal product name	Bupivacaine lozenge
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Lozenge
Routes of administration	Oral use

Dosage and administration details:

Lozenges containing 5 mg bupivacaine and placebo lozenges both with a size of 12-mm diameter were manufactured by direct compression, at the Pharmacy of the Capital Region, Denmark. Both the placebo and the bupivacaine lozenge were taste masked with liquorice powder as it can disguise the bitter taste of bupivacaine.

Patients were asked to take three lozenges each day in the treatment period, one after breakfast, one after lunch and one after dinner. The lozenges were administered after meals to sustain the local anesthetic effect as long as possible. Patients were instructed to suck on the lozenge until it was completely dissolved, to avoid the use of other medical lozenges and to avoid intake of food and drinks for a minimum of 30 minutes after the lozenge was dissolved.

<b>Arm title</b>	Placebo lozenge
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Arm description:

The patients were randomized to receive placebo lozenges

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

Dosage and administration details:

Lozenges containing 5 mg bupivacaine and placebo lozenges both with a size of 12-mm diameter were manufactured by direct compression, at the Pharmacy of the Capital Region, Denmark. Both the placebo and the bupivacaine lozenge were taste masked with liquorice powder as it can disguise the bitter taste of bupivacaine.

Patients were asked to take three lozenges each day in the treatment period, one after breakfast, one after lunch and one after dinner. The lozenges were administered after meals to sustain the local anesthetic effect as long as possible. Patients were instructed to suck on the lozenge until it was completely dissolved, to avoid the use of other medical lozenges and to avoid intake of food and drinks for a minimum of 30 minutes after the lozenge was dissolved.

<b>Number of subjects in period 3</b>	Active lozenge	Placebo lozenge
Started	10	13
Completed	7	8
Not completed	3	5
Consent withdrawn by subject	1	1
Protocol deviation	2	4

## Baseline characteristics

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### Reporting groups

Reporting group title	baseline
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Reporting group description: -

<b>Reporting group values</b>	baseline	Total	
Number of subjects	25	25	
Age categorical Units: Subjects			
Adults (18-64 years)	21	21	
From 65-84 years	4	4	
Age continuous Units: years			
median	60		
full range (min-max)	39 to 71	-	
Gender categorical Units: Subjects			
Female	21	21	
Male	4	4	

## End points

### End points reporting groups

Reporting group title	baseline
Reporting group description: -	
Reporting group title	Lozenge active
Reporting group description: The patients were randomized to receive bupivacaine lozenges	
Reporting group title	Lozenge placebo
Reporting group description: The patients were randomized to placebo lozenges	
Reporting group title	Active lozenge
Reporting group description: The patients were randomized to receive bupivacaine lozenges	
Reporting group title	Placebo lozenge
Reporting group description: The patients were randomized to receive placebo lozenges	

### Primary: Effect

End point title	Effect
End point description:	
End point type	Primary
End point timeframe: Each treatment period lasted for two weeks.	

End point values	Lozenge active	Lozenge placebo	Active lozenge	Placebo lozenge
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	13	10	13
Units: millimeter(s)				
median (full range (min-max))	-5.5 (-7.4 to -3.6)			

### Statistical analyses

Statistical analysis title	Effect
Comparison groups	Lozenge active v Lozenge placebo v Active lozenge v Placebo lozenge

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.4
upper limit	-3.6
Variability estimate	Standard deviation

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

- Bivirkninger eller hændelser relateret til medicinen vil blive registreret fra det øjeblik, patienten modtager medicinen og de efterfølgende 24 timer.
- Opstår der bivirkninger eller hændelser vil de blive fulgt, til de er ophørt.

Assessment type	Systematic
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### Dictionary used

Dictionary name	Lægemiddelstyrelsen
Dictionary version	NA

### Reporting groups

Reporting group title	Burning Mouth Syndrome
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Reporting group description: -

<b>Serious adverse events</b>	Burning Mouth Syndrome		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

<b>Non-serious adverse events</b>	Burning Mouth Syndrome		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 25 (52.00%)		
Skin and subcutaneous tissue disorders			
Burning sensation	Additional description: The side effects regarding the bupivacaine lozenge were mild and included increased but tolerable burning or stinging sensation, swallowing discomfort and ceased or altered taste sensation. Side effects experienced after treatment with the placebo lo		
subjects affected / exposed	13 / 25 (52.00%)		
occurrences (all)	13		

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported