Clinical trial results:
A randomised, two-period cross-over, multicentre, double-blind, single-dose, placebo-controlled trial to assess the local analgesic effect of CAM2028 in head-and-neck cancer patients suffering from radiation-induced oral mucositis

Summary

EudraCT number	2007-000163-26
Trial protocol	BG
Global end of trial date	16 November 2007

Results information

Result version number	v1 (current)
This version publication date	19 April 2019
First version publication date	19 April 2019

Trial information

Trial identification

Sponsor protocol code	HS-05-161

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Camurus AB
Sponsor organisation address	Ideon Science Park, Sölvegatan 41, Lund, Sweden, SE-223 70
Public contact	Clinical and Regulatory Development, Camurus AB, +46 462865730, info@camurus.com
Scientific contact	Clinical and Regulatory Development, Camurus AB, +46 462865730, info@camurus.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	17 December 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 November 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To prove the local analgesic effect of a new formulation of Benzydamine Hydrochloride (BZD) (CAM2028) over at least six hours after single dosing in subjects with oral mucositis.

Protection of trial subjects:

The protocol and the statement of informed consent were approved in Bulgaria by an Independent Ethics Committee (IEC) prior to each centre's initiation. The trial was conducted in accordance with the Declaration of Helsinki and its revisions as well as with the valid local and national law(s) of Bulgaria, with the International Conference on Harmonisation (ICH) Harmonised Tripartite Guideline for Good Clinical Practice (GCP) (E6) issued in July 1996, and with the Commission Directives 2001/20/EC, 2005/28/EC and 2001/83/EC. Written Informed Consent was received from all subjects prior to enrolment into the trial, as dictated by the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 June 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 38
Worldwide total number of subjects	38
EEA total number of subjects	38

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)	35
From 65 to 84 years	3

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at five centres in Bulgaria.

Pre-assignment

Screening details:

The screening period was up to seven days. Assessments were done as per the schedule of assessment.

Period 1

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

Blinding implementation details:

The investigators, staff at the trial sites, trial monitors, and data analysis/management personnel were blinded to the subject assignment in order to ensure that information that could potentially bias handling of data was not disclosed.

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence: CAM2028- Placebo

Arm description:

Randomized subjects received CAM2028 on Day 1, and placebo on Day 3. Subjects were treated with trial medication after radiotherapy on Days 1 and 3, respectively. There was a >24 hour wash-out period between treatments.

Arm type	Experimental
Investigational medicinal product name	CAM2028
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal solution
Routes of administration	Oromucosal use

Dosage and administration details:

Dose was 1 mL + 1 mL with 5 min interval between the 2 doses; 30 mg/g BZD (28.2 mg/mL).

One mL of the liquid trial medication was administered into the subject's mouth with a syringe. The subject was to swirl the trial medication around in his or her mouth for approximately 15 seconds to achieve spreading throughout the mouth and then was to spit out any residual formulation. This procedure was repeated after 5 minutes.

Investigational medicinal product name	CAM2028 placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal solution
Routes of administration	Oromucosal use

Dosage and administration details:

Dose was 1 mL + 1 mL with 5 min interval between the 2 doses.

One mL of the liquid trial medication was administered into the subject's mouth with a syringe. The subject was to swirl the trial medication around in his or her mouth for approximately 15 seconds to achieve spreading throughout the mouth and then was to spit out any residual formulation. This procedure was repeated after 5 minutes.

Arm title	Sequence: Placebo - CAM2028

Arm description:

Randomized subjects received placebo on Day 1, and CAM2028 on Day 3. Subjects were treated with trial medication after radiotherapy on Days 1 and 3, respectively. There was a >24 hour wash-out period between treatments.

Arm type	Experimental
Investigational medicinal product name	CAM2028 placebo
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Number of subjects in period 1	Sequence: CAM2028- Placebo	Sequence: Placebo - CAM2028
Started	20	18
Completed	20	18

Baseline characteristics

Reporting groups	
Reporting group title	Sequence: CAM2028- Placebo
Reporting group description:	
Randomized subjects received CAM2028 on Day 1, and placebo on Day 3. Subjects were treated with trial medication after radiotherapy on Days 1 and 3, respectively. There was a >24 hour wash-out period between treatments.	
Reporting group title	Sequence: Placebo - CAM2028
Reporting group description:	
Randomized subjects received placebo on Day 1, and CAM2028 on Day 3. Subjects were treated with trial medication after radiotherapy on Days 1 and 3, respectively. There was a >24 hour wash-out period between treatments.	

Reporting group values	Sequence: CAM2028- Placebo	Sequence: Placebo - CAM2028	Total
Number of subjects	20	18	38
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	50.9	53.3	
standard deviation	± 9.93	± 7.72	-
Gender categorical Units: Subjects			
Female	1	5	6
Male	19	13	32

End points

End points reporting groups

Reporting group title	Sequence: CAM2028- Placebo

Reporting group description:

Randomized subjects received CAM2028 on Day 1, and placebo on Day 3. Subjects were treated with trial medication after radiotherapy on Days 1 and 3, respectively. There was a >24 hour wash-out period between treatments.

Reporting group title	Sequence: Placebo - CAM2028

Reporting group description:

Randomized subjects received placebo on Day 1, and CAM2028 on Day 3. Subjects were treated with trial medication after radiotherapy on Days 1 and 3, respectively. There was a >24 hour wash-out period between treatments.

Subject analysis set title	CAM2028 (Full analysis set)
Subject analysis set type	Full analysis

Subject analysis set description:

Full analysis set included all subjects in the safety set who provided data regarding the primary efficacy variable in both treatment periods.

Subject analysis set title	Placebo (Full analysis set)
Subject analysis set type	Full analysis

Subject analysis set description:

Full analysis set included all subjects in the safety set who provided data regarding the primary efficacy variable in both treatment periods.

Subject analysis set title	CAM2028 (Per Protocol Set)
Subject analysis set type	Per protocol

Subject analysis set description:

Per-protocol set included all subjects in the full analysis set who completed the trial with no major protocol violations.

Subject analysis set title	Placebo (Per Protocol Set)
Subject analysis set type	Per protocol

Subject analysis set description:

Per-protocol set included all subjects in the full analysis set who completed the trial with no major protocol violations.

Primary: Pain intensity difference (PID) at 6 h after dosing assessed using the 0- 10 Likert pain score

End point title	Pain intensity difference (PID) at 6 h after dosing assessed using the 0- 10 Likert pain score[1]

End point description:

The primary variable for this trial was the change in oromucosal pain during six hours after dosing. Data on pain scores were collected using an 11 point Likert pain scale (0=No pain, 10 = Worst possible pain). The subject received a subject diary in which he/she noted the pain score.

End point type	Primary

End point timeframe:

At 6 hours on Days 1 and 3

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: All tests were two-sided with a significance level of 5%. The efficacy parameters were summarised for per protocol set, full analysis set, and each centre for the full analysis set if the centre x treatment interaction was significant. The primary efficacy hypothesis was a confirmatory analysis. Adjustment of alpha-value was not applied.

End point values	CAM2028 (Full analysis set)	Placebo (Full analysis set)	CAM2028 (Per Protocol Set)	Placebo (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	38	38	32	32
Units: Unit on a scale				
arithmetic mean (standard deviation)	2.2 (± 1.82)	2.1 (± 1.82)	2.5 (± 1.76)	2.2 (± 1.86)

Statistical analyses

No statistical analyses for this end point

Secondary: PID at 8 hours after dosing

End point title	PID at 8 hours after dosing

End point description:

PID was measured at 8 hours after dosing using the 0-10 Likert pain score. Data on pain scores were collected using an 11 point Likert pain scale (0=No pain, 10 = Worst possible pain). The subject received a subject diary in which he/she noted the pain score.

End point type	Secondary

End point timeframe:

At 8 hours on Days 1 and 3

End point values	CAM2028 (Full analysis set)	Placebo (Full analysis set)	CAM2028 (Per Protocol Set)	Placebo (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	38	38	32	32
Units: Unit on a scale				
arithmetic mean (standard deviation)	2.1 (± 1.79)	1.9 (± 1.65)	2.4 (± 1.68)	2.0 (± 1.67)

Statistical analyses

No statistical analyses for this end point

Secondary: The area under the curve (AUC) of the pain intensity difference (SPID) during 8 h after dosing

End point title	The area under the curve (AUC) of the pain intensity difference (SPID) during 8 h after dosing

End point description:

AUC of pain intensity difference during 8 h after dosing was assessed. Data on pain scores were collected using an 11 point Likert pain scale (0=No pain, 10 = Worst possible pain). The subject received a subject diary in which he/she noted the pain score.

End point type	Secondary

End point timeframe:

At 8 hours on Days 1 and 3

End point values	CAM2028 (Full analysis set)	Placebo (Full analysis set)	CAM2028 (Per Protocol Set)	Placebo (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	38	38	32	32
Units: Unit on a scale				
arithmetic mean (standard deviation)	1033.82 (± 803.222)	1011.05 (± 788.447)	1181.09 (± 783.686)	1064.77 (± 828.706)

Statistical analyses

No statistical analyses for this end point

Secondary: Peak pain intensity difference (PPID) during 8 h after dosing, the maximal pain intensity

End point title	Peak pain intensity difference (PPID) during 8 h after dosing, the maximal pain intensity

End point description:

PPID during 8 h after dosing was assessed. Data on pain scores were collected using an 11 point Likert pain scale (0=No pain, 10 = Worst possible pain). The subject received a subject diary in which he/she noted the pain score.

End point type	Secondary

End point timeframe:

At 8 hours on Days 1 and 3

End point values	CAM2028 (Full analysis set)	Placebo (Full analysis set)	CAM2028 (Per Protocol Set)	Placebo (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	38	38	32	32
Units: Unit on a scale				
arithmetic mean (standard deviation)	2.5 (± 1.62)	2.6 (± 1.57)	2.8 (± 1.61)	2.7 (± 1.65)

Statistical analyses

No statistical analyses for this end point

Secondary: Difficulty in swallowing intensity before and after lunch and dinner on the day of dosing

End point title	Difficulty in swallowing intensity before and after lunch and dinner on the day of dosing

End point description:

To assess the functional response to a single dose of trial medication in terms of difficulty in swallowing. Data on difficulty in swallowing was collected 30 minutes before and 30 minutes after each meal using a

11 point Likert scale (0=No difficulty, 10 = Worst possible difficulty). The score was noted in the subject diary.

End point type	Secondary

End point timeframe:

At 30 min before and after meals on Day 1 and Day 3

End point values	CAM2028 (Full analysis set)	Placebo (Full analysis set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	38	38		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Before Lunch on Day of Dosing (n = 38, 37)	5.2 (± 2.13)	5.2 (± 2.12)		
After Lunch on Day of Dosing (n = 37, 37)	5.4 (± 2.16)	5.1 (± 2.18)		
Before Dinner on Day of Dosing (n = 38, 38)	5.1 (± 2.01)	5.1 (± 2.08)		
After Dinner on Day of Dosing (n = 37, 38)	5.2 (± 2.12)	5.2 (± 2.30)		

Statistical analyses

No statistical analyses for this end point

Secondary: Difficulty in swallowing intensity before and after lunch and dinner on the day of dosing

End point title	Difficulty in swallowing intensity before and after lunch and dinner on the day of dosing

End point description:

To assess the functional response to a single dose of trial medication in terms of difficulty in swallowing. Data on difficulty in swallowing was collected 30 minutes before and 30 minutes after each meal using a 11 point Likert scale (O=No difficulty, 10 = Worst possible difficulty). The score was noted in the subject diary.

End point type	Secondary

End point timeframe:

At 30 min before and after meals on Day 1 and Day 3

End point values	CAM2028 (Per Protocol Set)	Placebo (Per Protocol Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	32		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Before Lunch on Day of Dosing (n = 32, n =32)	4.9 (± 1.98)	5.1 (± 2.05)		
After Lunch on Day of Dosing (n = 31, n =32)	5.2 (± 2.16)	5.0 (± 2.08)		

Before Dinner on Day of Dosing (n = 32, n = 32)	5.1 (± 2.05)	4.9 (± 2.02)		
After Dinner on Day of Dosing (n = 31, 32)	5.3 (± 2.18)	5.0 (± 2.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum difficulty in swallowing during 24 h after dosing

End point title	Minimum difficulty in swallowing during 24 h after dosing

End point description:

To assess the functional response to a single dose of trial medication in terms of difficulty in swallowing. Data on difficulty in swallowing was collected 30 minutes before and 30 minutes after each meal using a 11 point Likert scale (0=No difficulty, 10 = Worst possible difficulty). The score was noted in the subject diary.

End point type	Secondary

End point timeframe:

At 24 hours on Days 1 to 5

End point values	CAM2028 (Full analysis set)	Placebo (Full analysis set)	CAM2028 (Per Protocol Set)	Placebo (Per Protocol Set)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	38	38	32	32
Units: Unit on a scale				
arithmetic mean (standard deviation)	4.6 (± 2.04)	4.6 (± 1.95)	4.6 (± 2.05)	4.4 (± 1.93)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Days 1, 3, and 5

Adverse event reporting additional description:

An adverse event (AE) was any untoward medical occurrence in a subject administered a pharmaceutical product which did not necessarily have a causal relationship with the treatment.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	CAM2028

Reporting group description:

For the Sequence: CAM2028- Placebo, randomized subjects received CAM2028 on Day 1, and placebo on Day 3. Subjects were treated with trial medication after radiotherapy on Days 1 and 3, respectively. There was a >24 hour wash-out period between treatments. For the Sequence: Placebo - CAM2028, randomized subjects received placebo on Day 1, and CAM2028 on Day 3. Subjects were treated with trial medication after radiotherapy on Days 1 and 3, respectively. There was a >24 hour wash-out period between treatments.

Reporting group title	Placebo

Reporting group description:

For the Sequence: CAM2028- Placebo, randomized subjects received CAM2028 on Day 1, and placebo on Day 3. Subjects were treated with trial medication after radiotherapy on Days 1 and 3, respectively. There was a >24 hour wash-out period between treatments. For the Sequence: Placebo - CAM2028, randomized subjects received placebo on Day 1, and CAM2028 on Day 3. Subjects were treated with trial medication after radiotherapy on Days 1 and 3, respectively. There was a >24 hour wash-out period between treatments.

Serious adverse events	CAM2028	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	CAM2028	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 38 (7.89%)	2 / 38 (5.26%)	
Gastrointestinal disorders			
Nausea			

subjects affected / exposed	2 / 38 (5.26%)	2 / 38 (5.26%)	
occurrences (all)	2	2	
Vomiting			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	

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