



## Clinical trial results:

### Double-blind trial investigating the efficacy of different doses of Progesterone compared with Placebo for treatment of vasomotor symptoms

#### Summary

EudraCT number	2016-004386-12
Trial protocol	DE AT
Global end of trial date	06 December 2018

#### Results information

Result version number	v1 (current)
This version publication date	03 June 2021
First version publication date	03 June 2021

#### Trial information

##### Trial identification

Sponsor protocol code	BHR-401-301
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	Besins Healthcare Ltd.
Sponsor organisation address	16 Pembroke Street Upper, Dublin 2, Ireland,
Public contact	Global Clinical Development, Besins Healthcare Ltd., moconnell@besins-healthcare.com
Scientific contact	Global Clinical Development, Besins Healthcare Ltd., moconnell@besins-healthcare.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	05 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 December 2018
Global end of trial reached?	Yes
Global end of trial date	06 December 2018
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the clinical trial is to demonstrate superiority of BHR401 (oral micronized progesterone) versus placebo as a monotherapy for moderate to severe VMS in postmenopausal women.

Protection of trial subjects:

Micronized Progesterone preparations (like BHR-401) are licensed for endometrial protection in the context of menopausal hormone therapy at doses of 200 mg and 300 mg, two of the doses were used in the present study. The safety profile of micronized progesterone at these doses is favorable, with headache, drowsiness and dizziness being the most frequently reported side effects. These are most likely due to the sedating effects of progesterone and its metabolites. Therefore, study medication should be taken in the evening, before bed time, to avoid a burden to the subjects by these otherwise non-serious side effects. The 400 mg dose used in the present study is not licensed in Germany yet; however, oral doses of up to 400 mg/d are licensed for the treatment of secondary amenorrhea in the USA.

Furthermore, based on pharmacokinetic evaluations where even higher doses of progesterone are given (and consequently higher plasma levels of progesterone are achieved), no significant safety concerns, other than those also described for the 200 mg and 300 mg doses, can be currently associated with an oral intake of this dose.

Regardless of the dose, allergic reactions to micronized progesterone have been observed, mainly towards the excipients (e.g. soy lecithin). Therefore, subjects with a soy allergy were excluded from participation in this study.

The risk to subjects was minimized by compliance with eligibility criteria and study procedures as well as close clinical monitoring. Participating subjects benefit from careful monitoring and follow-up during the entire study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 June 2017
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	Switzerland: 4
Country: Number of subjects enrolled	Germany: 70
Worldwide total number of subjects	74
EEA total number of subjects	70

Notes:

<b>Subjects enrolled per age group</b>	
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)	63
From 65 to 84 years	11
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

Number of subjects started	74
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Number of subjects completed	55
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### Pre-assignment subject non-completion reasons

Reason: Number of subjects	Missing: 1
Reason: Number of subjects	Insufficient VMS frequency: 14
Reason: Number of subjects	no aktuell mammographie: 1
Reason: Number of subjects	Smoker: 1
Reason: Number of subjects	Screening period exited: 1
Reason: Number of subjects	mammography suspect: 1

### Period 1

Period 1 title	Treatment Phase (overall period)
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Is this the baseline period?	Yes
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Allocation method	Randomised - controlled
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Blinding used	Double blind
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Roles blinded	Subject, Investigator, Monitor
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### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	BHR-401 200 mg
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Arm description: -

Arm type	Experimental
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Investigational medicinal product name	BHR-401 200mg
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Capsule
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Routes of administration	Oral use
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Dosage and administration details:

3 capsules per day: 1 capsule 200 mg BHR-401, 1 capsule 200mg Placebo, 1 capsule 300 mg Placebo

<b>Arm title</b>	BHR-401 300 mg
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Arm description: -

Arm type	Experimental
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Investigational medicinal product name	BHR-401 300mg
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Capsule
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Routes of administration	Oral use
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Dosage and administration details:

3 capsules per day: 1 capsule 300 mg BHR-401, 2 capsules 200mg Placebo

<b>Arm title</b>	BHR-401 400 mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	BHR-401 400mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
3 capsules per day: 2 capsules 200 mg BHR-401, 1 capsule 300 mg Placebo	
<b>Arm title</b>	Placebo
Arm description: -	
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:	
3 capsules per day: 2 capsules 200 mg Placebo, 1 capsule 300mg Placebo	

<b>Number of subjects in period 1<sup>[1]</sup></b>	BHR-401 200 mg	BHR-401 300 mg	BHR-401 400 mg
Started	13	16	12
Completed	11	13	8
Not completed	2	3	4
holidays	-	-	-
Consent withdrawn by subject	-	2	-
Adverse event, non-fatal	-	-	1
injury of inclusion criteria	1	-	-
SAE	-	-	1
end of study	-	-	-
Lack of efficacy	1	1	2

<b>Number of subjects in period 1<sup>[1]</sup></b>	Placebo
Started	14
Completed	11
Not completed	3
holidays	1
Consent withdrawn by subject	-
Adverse event, non-fatal	1
injury of inclusion criteria	-

SAE	-
end of study	1
Lack of efficacy	-

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Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 19 subject did not finalize the screening period. I.e., 74 subjects were screened and 55 subjects finally were analyzed.

## Baseline characteristics

### Reporting groups

Reporting group title	BHR-401 200 mg
Reporting group description: -	
Reporting group title	BHR-401 300 mg
Reporting group description: -	
Reporting group title	BHR-401 400 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	BHR-401 200 mg	BHR-401 300 mg	BHR-401 400 mg
Number of subjects	13	16	12
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			
arithmetic mean	54.6	57.2	57.4
standard deviation	± 2.57	± 6.79	± 6.74
Gender categorical Units: Subjects			
Female	13	16	12
Male	0	0	0
Age at menarche Units: years			
arithmetic mean	13.3	13.1	13.5
standard deviation	± 1.18	± 1.65	± 1.75
Number of pregnancies Units: number			
arithmetic mean	1.8	1.7	2.3
standard deviation	± 1.14	± 0.79	± 1.19
Number of live births Units: number			
arithmetic mean	1.6	1.6	1.8
standard deviation	± 0.67	± 0.81	± 0.75
Time since beginning of menopause Units: years			

arithmetic mean	5.4	6.7	6.8
standard deviation	± 4.13	± 8.69	± 6.67
Time since first VMS			
Units: years			
arithmetic mean	4.1	4.3	5.6
standard deviation	± 2.82	± 4.54	± 6.24

<b>Reporting group values</b>	Placebo	Total	
Number of subjects	14	55	
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	56.6		
standard deviation	± 5.84	-	
Gender categorical			
Units: Subjects			
Female	14	55	
Male	0	0	
Age at menarche			
Units: years			
arithmetic mean	12.9		
standard deviation	± 0.73	-	
Number of pregnancies			
Units: number			
arithmetic mean	1.9		
standard deviation	± 1.00	-	
Number of live births			
Units: number			
arithmetic mean	1.6		
standard deviation	± 0.51	-	
Time since beginning of menopause			
Units: years			
arithmetic mean	7.4		
standard deviation	± 10.35	-	
Time since first VMS			
Units: years			
arithmetic mean	5.0		
standard deviation	± 6.00	-	



## End points

### End points reporting groups

Reporting group title	BHR-401 200 mg
Reporting group description: -	
Reporting group title	BHR-401 300 mg
Reporting group description: -	
Reporting group title	BHR-401 400 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	SAF
Subject analysis set type	Safety analysis
Subject analysis set description: Safety data set (SAF) comprises all randomized subjects who were administered the study medication at least once.	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description: The Full analysis data set (FAS) includes all subjects of the SAF who provided any post-baseline data related to efficacy.	
Subject analysis set title	PP
Subject analysis set type	Per protocol
Subject analysis set description: The per-protocol (PP) data set includes all subjects from the FAS who did not exhibit a major protocol deviation, e.g. protocol deviations that might have an influence on the outcome of the study.	

### Primary: Absolute change in the frequency of moderate or severe VMS per day between baseline and week 12

End point title	Absolute change in the frequency of moderate or severe VMS per day between baseline and week 12
End point description:	
End point type	Primary
End point timeframe: Change from Baseline to Week 12 (Treatment Phase)	

End point values	BHR-401 200 mg	BHR-401 300 mg	BHR-401 400 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12 <sup>[1]</sup>	16	10 <sup>[2]</sup>	13 <sup>[3]</sup>
Units: number				
arithmetic mean (standard deviation)	-7.70 (± 4.913)	-8.29 (± 7.725)	-9.00 (± 4.046)	-7.40 (± 3.579)

Notes:

[1] - Data from one patient missing

[2] - 11 patients in the FAS, data from 1 patient missing

[3] - Data from 1 patient missing

## Statistical analyses

<b>Statistical analysis title</b>	ANCOVA
Comparison groups	BHR-401 200 mg v Placebo
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8798
Method	ANCOVA

<b>Statistical analysis title</b>	ANCOVA
Comparison groups	BHR-401 300 mg v Placebo
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7457
Method	ANCOVA

<b>Statistical analysis title</b>	ANCOVA
Comparison groups	BHR-401 400 mg v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1397
Method	ANCOVA

## Secondary: Absolute change of VMS severity between baseline and week 12

End point title	Absolute change of VMS severity between baseline and week 12
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End point description:

End point type	Secondary
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End point timeframe:

Change from between baseline to week 12 (Treatment Phase)

<b>End point values</b>	BHR-401 200 mg	BHR-401 300 mg	BHR-401 400 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11 <sup>[4]</sup>	15 <sup>[5]</sup>	9 <sup>[6]</sup>	11 <sup>[7]</sup>
Units: scoring				
arithmetic mean (standard deviation)	-0.58 (± 0.600)	-0.49 (± 0.658)	-0.69 (± 0.809)	-0.44 (± 0.597)

Notes:

[4] - data from 2 patients missing

[5] - data from 1 patient missing

[6] - 11 patients in FAS, data from 2 patients missing

[7] - data from 3 patients missing

### Statistical analyses

<b>Statistical analysis title</b>	ANCOVA
Comparison groups	BHR-401 200 mg v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3744
Method	ANCOVA

<b>Statistical analysis title</b>	ANCOVA
Comparison groups	BHR-401 300 mg v Placebo
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9534
Method	ANCOVA

<b>Statistical analysis title</b>	ANCOVA
Comparison groups	BHR-401 400 mg v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8808
Method	ANCOVA

### Secondary: Absolute change in the frequency of moderate or severe VMS per day between baseline and week 4

End point title	Absolute change in the frequency of moderate or severe VMS per day between baseline and week 4
End point description:	
End point type	Secondary
End point timeframe:	
Change from Baseline to Week 4 (Treatment Phase)	

<b>End point values</b>	BHR-401 200 mg	BHR-401 300 mg	BHR-401 400 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	15	10	11
Units: number				
arithmetic mean (standard deviation)	-6.40 (± 3.441)	-7.04 (± 6.167)	-6.54 (± 2.184)	-6.75 (± 3.880)

### Statistical analyses

<b>Statistical analysis title</b>	ANCOVA
Comparison groups	BHR-401 200 mg v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6978
Method	ANCOVA

<b>Statistical analysis title</b>	ANCOVA
Comparison groups	BHR-401 300 mg v Placebo
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.785
Method	ANCOVA

<b>Statistical analysis title</b>	ANCOVA
Comparison groups	BHR-401 400 mg v Placebo
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4611
Method	ANCOVA

### Secondary: Absolute change of VMS severity between baseline and week 4

End point title	Absolute change of VMS severity between baseline and week 4
End point description:	

End point type	Secondary
End point timeframe:	
Change from baseline to week 4 (Treatment Phase)	

End point values	BHR-401 200 mg	BHR-401 300 mg	BHR-401 400 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	13	10	11
Units: scoring				
arithmetic mean (standard deviation)	-0.36 (± 0.412)	-0.37 (± 0.253)	0.00 (± 0.263)	-0.28 (± 0.499)

### Statistical analyses

<b>Statistical analysis title</b>	ANCOVA
Comparison groups	BHR-401 200 mg v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9122
Method	ANCOVA

<b>Statistical analysis title</b>	ANCOVA
Comparison groups	BHR-401 300 mg v Placebo
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.98
Method	ANCOVA

<b>Statistical analysis title</b>	ANCOVA
Comparison groups	BHR-401 400 mg v Placebo
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4272
Method	ANCOVA

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent AEs (TEAEs) are defined as any event with a start date occurring on or after baseline or, if pre-existing, worsening after baseline, and occurring within the period of treatment with the trial drug, i.e. until visit 5.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

### Reporting groups

Reporting group title	BHR-401 200mg
Reporting group description: -	
Reporting group title	BHR-401 300mg
Reporting group description: -	
Reporting group title	BHR-401 400mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	BHR-401 200mg	BHR-401 300mg	BHR-401 400mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 16 (0.00%)	1 / 12 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 13 (0.00%)	0 / 16 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Syncope			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1.8 %

<b>Non-serious adverse events</b>	BHR-401 200mg	BHR-401 300mg	BHR-401 400mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 13 (30.77%)	6 / 16 (37.50%)	3 / 12 (25.00%)
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 13 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tachycardia paroxysmal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Dental care			
subjects affected / exposed	0 / 13 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 13 (7.69%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Malaise			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			

Vertigo subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 16 (0.00%) 0	0 / 12 (0.00%) 0
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 16 (0.00%) 0	1 / 12 (8.33%) 1
Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all)  Endometrial thickening subjects affected / exposed occurrences (all)  Ovarian cyst subjects affected / exposed occurrences (all)  Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0  0 / 13 (0.00%) 0  0 / 13 (0.00%) 0  0 / 13 (0.00%) 0	0 / 16 (0.00%) 0  0 / 16 (0.00%) 0  0 / 16 (0.00%) 0  1 / 16 (6.25%) 1	1 / 12 (8.33%) 1  1 / 12 (8.33%) 1  1 / 12 (8.33%) 1  2 / 12 (16.67%) 2
Psychiatric disorders Nervousness subjects affected / exposed occurrences (all)  Restlessness subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0  0 / 13 (0.00%) 0	0 / 16 (0.00%) 0  0 / 16 (0.00%) 0	0 / 12 (0.00%) 0  0 / 12 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)  Back pain subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1  0 / 13 (0.00%) 0	0 / 16 (0.00%) 0  0 / 16 (0.00%) 0	0 / 12 (0.00%) 0  0 / 12 (0.00%) 0
Infections and infestations			



Bronchitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	2 / 13 (15.38%)	2 / 16 (12.50%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Nasopharyngitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 16 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

<b>Non-serious adverse events</b>	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 14 (35.71%)		
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Tachycardia paroxysmal			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Surgical and medical procedures			
Dental care			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Malaise			

subjects affected / exposed occurrences (all)  Oedema peripheral subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0  0 / 14 (0.00%) 0		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all)  Endometrial thickening subjects affected / exposed occurrences (all)  Ovarian cyst subjects affected / exposed occurrences (all)  Vaginal haemorrhage subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1  0 / 14 (0.00%) 0  0 / 14 (0.00%) 0  1 / 14 (7.14%) 1		
Psychiatric disorders Nervousness subjects affected / exposed occurrences (all)  Restlessness subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1  1 / 14 (7.14%) 1		
Musculoskeletal and connective tissue disorders Arthralgia			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Cystitis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		

## 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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

No conclusion can be drawn from the study results due to the premature termination of the study. This decision was not based on a safety concern, but due to insufficient subject accrual rate.
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Notes: