



## Clinical trial results:

**MOVE - A randomized, double-blind, placebo-controlled, multicenter, cross-over study to assess the effects of a 3 week therapy each with QVA149 versus placebo on pulmonary function and average physical activity levels in patients with moderate to severe chronic obstructive pulmonary disease (COPD)**

**Due to EudraCT system limitations, which EMA is aware of, results of crossover studies are not accurately represented in this record. Please go to <https://www.novctrd.com/CtrdWeb/home.nov> for complete trial results.**

## Summary

EudraCT number	2013-001477-25
Trial protocol	DE
Global end of trial date	11 February 2015

## Results information

Result version number	v1 (current)
This version publication date	12 July 2018
First version publication date	12 July 2018

## Trial information

### Trial identification

Sponsor protocol code	CQVA149ADE03
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### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01996319
WHO universal trial number (UTN)	-

Notes:

## Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

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	No

1901/2006 apply to this trial?	
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Notes:

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### Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 February 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 February 2015
Was the trial ended prematurely?	No

Notes:

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### General information about the trial

Main objective of the trial:

To demonstrate superiority of QVA149 (110/50 µg q.d.) over placebo on peak inspiratory capacity (IC) after 21 days of treatment in patients with moderate to severe COPD. Co-primary objective was to evaluate whether QVA149 was superior to placebo with respect to average physical activity level as defined by average daily activity-related energy consumption [kcal/day].

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 April 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

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### Population of trial subjects

#### Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 194
Worldwide total number of subjects	194
EEA total number of subjects	194

Notes:

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#### 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)	109
From 65 to 84 years	85
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

194 were randomized and 194 were exposed to at least one treatment, 96 patients (96/194, 49.5%) were randomized in to the QVA149 - Placebo group and 98 patients (98/194, 50.5%) were randomized into the Placebo - QVA149 group

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind <sup>[1]</sup>
Roles blinded	Subject, Carer

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	QVA149 then Placebo

Arm description:

QVA149 once a day during 22 days cross-over to placebo once a day for up to 22 days

Arm type	Active comparator
Investigational medicinal product name	QVA149 (110/50 µg
Investigational medicinal product code	QVA149
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Inhalation use

Dosage and administration details:

single dose dry powder inhaler

<b>Arm title</b>	Placebo then QVA149
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Arm description:

Placebo once a day during 22 days cross-over to QVA149 once a day for 22 days

Arm type	Placebo
Investigational medicinal product name	Placebo once a day via Breezhaler
Investigational medicinal product code	QVA149
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Inhalation use

Dosage and administration details:

capsules q.d. for inhalation

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: Disposition table verified

<b>Number of subjects in period 1</b>	QVA149 then Placebo	Placebo then QVA149
Started	96	98
Completed	88	95
Not completed	8	3
Adverse event, non-fatal	2	2
Severe or moderate (COPD) Exacerbation	5	1
Protocol deviation	1	-

## Baseline characteristics

### Reporting groups

Reporting group title	QVA149 then Placebo
Reporting group description: QVA149 once a day during 22 days cross-over to placebo once a day for up to 22 days	
Reporting group title	Placebo then QVA149
Reporting group description: Placebo once a day during 22 days cross-over to QVA149 once a day for 22 days	

Reporting group values	QVA149 then Placebo	Placebo then QVA149	Total
Number of subjects	96	98	194
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	42	67	109
From 65-84 years	54	31	85
85 years and over	0	0	0
Age Continuous   Units: Years			
arithmetic mean	64.3	61.2	
standard deviation	± 7.9	± 7.7	-
Gender, Male/Female Units: Participants			
Female	32	35	67
Male	64	63	127

## End points

### End points reporting groups

Reporting group title	QVA149 then Placebo
Reporting group description:	QVA149 once a day during 22 days cross-over to placebo once a day for up to 22 days
Reporting group title	Placebo then QVA149
Reporting group description:	Placebo once a day during 22 days cross-over to QVA149 once a day for 22 days
Subject analysis set title	QVA149
Subject analysis set type	Full analysis
Subject analysis set description:	all randomized patients who applied at least one dose of study medication during at least one study period. all patients were included in these analyses when baseline and day 22 data plus baseline day 36 and day 57 data were available
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	all randomized patients who applied at least one dose of study medication during at least one study period. all patients were included in these analyses when baseline and day 22 data plus baseline day 36 and day 57 data were available
Subject analysis set title	QVA149
Subject analysis set type	Full analysis
Subject analysis set description:	all randomized patients who applied at least one dose of study medication during at least one study period. all patients were included in these analyses when baseline and day 22 data plus baseline day 36 and day 57 data were available
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	all randomized patients who applied at least one dose of study medication during at least one study period. all patients were included in these analyses when baseline and day 22 data plus baseline day 36 and day 57 data were available
Subject analysis set title	QVA149
Subject analysis set type	Full analysis
Subject analysis set description:	all randomized patients who applied at least one dose of study medication during at least one study period. Only patients with baseline and day 22 data, plus baseline on day 36 and day 57 data were included in this analysis
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	all randomized patients who applied at least one dose of study medication during at least one study period. Only patients with baseline and day 22 data, plus baseline on day 36 and day 57 data were included in this analysis
Subject analysis set title	QVA149
Subject analysis set type	Full analysis
Subject analysis set description:	all randomized patients who applied at least one dose of study medication during at least one study period. Only patients with baseline and day 22 data, plus baseline on day 36 and day 57 data were included in this analysis
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	all randomized patients who applied at least one dose of study medication during at least one study

period. Only patients with baseline and day 22 data, plus baseline on day 36 and day 57 data were included in this analysis

Subject analysis set title	QVA149
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Subject analysis set type	Full analysis
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Subject analysis set description:

all randomized patients who applied at least one dose of study medication during at least one study period. Only patients with baseline and day 22 data, plus baseline on day 36 and day 57 data were included in this analysis

Subject analysis set title	Placebo
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Subject analysis set type	Full analysis
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Subject analysis set description:

all randomized patients who applied at least one dose of study medication during at least one study period. Only patients with baseline and day 20 post treatment initiation were included in this analysis.

Subject analysis set title	QVA149
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Subject analysis set type	Full analysis
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Subject analysis set description:

all randomized patients who applied at least one dose of study medication during at least one study period

Subject analysis set title	QVA149
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Subject analysis set type	Full analysis
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Subject analysis set description:

all randomized patients who applied at least one dose of study medication during at least one study period

### **Primary: Change from baseline in peak inspiratory capacity (IC) comparison between QVA149 and Placebo**

End point title	Change from baseline in peak inspiratory capacity (IC) comparison between QVA149 and Placebo
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End point description:

Inspiratory capacity (IC) will be measured with spirometry conducted according to internationally accepted standards. The mean of 3 acceptable measurements will be calculated and reported in liters. In this cross-over trial, we had two baselines collected at day 1 and collected at day 36. From the IC measurements collected on either Day 22 or 57, respectively, the appropriate baseline measurements were subtracted – so either Day 22-Day1 or Day 57-Day36

End point type	Primary
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End point timeframe:

Baseline, day 22, baseline day 36, day 57

<b>End point values</b>	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	189	184		
Units: Liters				
least squares mean (confidence interval 95%)	0.379 (0.3464 to 0.4117)	0.1769 (0.1379 to 0.2159)		

### **Statistical analyses**

<b>Statistical analysis title</b>	Change from baseline in peak inspiratory capacity
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Comparison groups	Placebo v QVA149
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Number of subjects included in analysis	373
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	null hypoth
Point estimate	0.2021
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1583
upper limit	0.246

**Primary: Change from baseline in the comparison of QVA149 versus placebo with respect to average physical activity level**

End point title	Change from baseline in the comparison of QVA149 versus placebo with respect to average physical activity level
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End point description:

Average physical activity level is defined by average daily activity-related energy consumption [Kcal/day], measured via Actinography device. In this cross-over trial, we had two baselines collected at day 1 and collected at day 36. From the activity measurements collected on either Day 22 or 57, respectively, the appropriate baseline measurements were subtracted – so either Day 22-Day1 or Day 57-Day36

End point type	Primary
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End point timeframe:

Baseline, day 22, baseline day 36, day 57

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	175	170		
Units: kcal/day				
least squares mean (confidence interval 95%)	5.1063 (-24.4 to 34.6125)	-31.6063 (-61.5268 to -1.6857)		

**Statistical analyses**

<b>Statistical analysis title</b>	Change from baseline in the comparison of QVA149
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Statistical analysis description:

Change from baseline in the comparison of QVA149 versus placebo with respect to average physical activity level

Comparison groups	QVA149 v Placebo
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Number of subjects included in analysis	345
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0399
Method	ANCOVA
Parameter estimate	Null hypoth
Point estimate	36.7126
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7241
upper limit	71.7011

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**Secondary: Change in the comparison of QVA149 vs. placebo on the average number of steps per day**

End point title	Change in the comparison of QVA149 vs. placebo on the average number of steps per day
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End point description:

The average number of steps per day will be measured via Actinography device. In this cross-over trial, we had two baselines collected at day 1 and collected at day 36. From the activity measurements collected on either Day 22 or 57, respectively, the appropriate baseline measurements were subtracted – so either Day 22-Day 1 or Day 57-Day36

End point type	Secondary
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End point timeframe:

Baseline, day 22, baseline day 36, day 57

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	178	173		
Units: Steps/day				
arithmetic mean (standard deviation)	30.7 (± 1662)	-320.7 (± 1648)		

**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Change in the Duration of at Least Moderate Activity Per Day Comparison of QVA149 Versus Placebo**

End point title	Change in the Duration of at Least Moderate Activity Per Day Comparison of QVA149 Versus Placebo
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End point description:

Least moderate activity (defined as 3,5-7kcal/min) will be measured via Actinography device. In this cross-over trial, we had two baselines collected at day 1 and collected at day 36. From the activity measurements collected on either Day 22 or 57, respectively, the appropriate baseline measurements were subtracted – so either Day 22-Day1 or Day 57-Day36

End point type	Secondary
End point timeframe:	
Baseline, day 22, baseline day 36, day 57	

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	178	173		
Units: Minutes				
arithmetic mean (standard deviation)	-5.5 ( $\pm$ 51.8)	-13 ( $\pm$ 52.3)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in peak IC comparison between QVA149 and Placebo on day 1.

End point title	Change from baseline in peak IC comparison between QVA149 and Placebo on day 1.
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End point description:

Inspiratory capacity (IC) will be measured with spirometry conducted according to internationally accepted standards. The mean of 3 acceptable measurements will be calculated and reported in liters. In this cross-over trial, we had two baselines collected at day 1 and collected at day 36. The IC measurements collected prior to dosing on either Day 1 or 36, respectively, were subtracted from the appropriate peak measures on the same respective days

End point type	Secondary
End point timeframe:	
Day 1 or day 36	

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	193	186		
Units: Liters				
arithmetic mean (standard deviation)	0.486 ( $\pm$ 0.2752)	0.207 ( $\pm$ 0.2114)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in the trough IC comparison between QVA149 and Placebo

End point title	Change from baseline in the trough IC comparison between QVA149 and Placebo
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End point description:

Inspiratory capacity (IC) will be measured with spirometry conducted according to internationally accepted standards. The mean of 3 acceptable measurements will be calculated and reported in liters. In this cross-over trial, we had two baselines collected at day 1 and collected at day 36. From the IC measurements collected on either Day 22 or 57, respectively, the appropriate baseline measurements were subtracted – so either Day 22-Day1 or Day 57-Day36

End point type Secondary

End point timeframe:

Baseline, day 22, baseline day 36, day 57

End point values	QVA149	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	190	183		
Units: Liters				
arithmetic mean (standard deviation)	0.21 ( $\pm$ 0.346)	-0.035 ( $\pm$ 0.279)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Peak forced expiratory volume 1 (FEV1) comparison between QVA149 and Placebo at day 1

End point title Peak forced expiratory volume 1 (FEV1) comparison between QVA149 and Placebo at day 1

End point description:

FEV1 is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation, measured through spirometry testing. The mean of 3 acceptable measurements will be calculated and reported in liters. In this cross-over trial, we had two baselines collected at day 1 and collected at day 36. The FEV1 measurements collected prior to dosing on either Day 1 or 36, respectively, were subtracted from the appropriate peak measures on the same respective days

End point type Secondary

End point timeframe:

Day 1 or day 36

End point values	Placebo	QVA149		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	186	192		
Units: Liters				
arithmetic mean (standard deviation)	0.111 ( $\pm$ 0.179)	0.347 ( $\pm$ 0.176)		

### Statistical analyses

No statistical analyses for this end point

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**Secondary: Trough FEV1 comparison between QVA149 and placebo after 22 days**

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End point title	Trough FEV1 comparison between QVA149 and placebo after 22 days
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End point description:

FEV1 is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation, measured through spirometry testing. The mean of 3 acceptable measurements will be calculated and reported in liters. In this cross-over trial, we had two baselines collected at day 1 and collected at day 36. From the FEV1 measurements collected on either Day 22 or 57, respectively, the appropriate baseline measurements were subtracted – so either Day 22-Day1 or Day 57-Day36

End point type	Secondary
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End point timeframe:

Baseline, day 22, baseline day 36, day 57

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<b>End point values</b>	Placebo	QVA149		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	183	188		
Units: Liters				
arithmetic mean (standard deviation)	-0.058 ( $\pm$ 0.207)	0.245 ( $\pm$ 0.221)		

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**Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Timeframe for AE

Adverse event reporting additional description:

AE additional description

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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### Reporting groups

Reporting group title	QVA149
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Reporting group description:

QVA149

Reporting group title	Placebo
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Reporting group description:

Placebo

<b>Serious adverse events</b>	QVA149	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 193 (2.07%)	2 / 188 (1.06%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bone cancer			
subjects affected / exposed	1 / 193 (0.52%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	0 / 193 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Incisional hernia			
subjects affected / exposed	1 / 193 (0.52%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 193 (0.52%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 193 (0.52%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

<b>Non-serious adverse events</b>	QVA149	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 193 (13.99%)	19 / 188 (10.11%)	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 193 (3.11%)	3 / 188 (1.60%)	
occurrences (all)	7	3	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 193 (1.04%)	0 / 188 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 193 (4.15%)	3 / 188 (1.60%)	
occurrences (all)	8	3	
Dyspnoea			
subjects affected / exposed	2 / 193 (1.04%)	1 / 188 (0.53%)	
occurrences (all)	2	1	
Oropharyngeal pain			
subjects affected / exposed	2 / 193 (1.04%)	0 / 188 (0.00%)	
occurrences (all)	2	0	
Sputum increased			

subjects affected / exposed occurrences (all)	3 / 193 (1.55%) 3	0 / 188 (0.00%) 0	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	3 / 193 (1.55%) 3	3 / 188 (1.60%) 3	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)  Rhinitis subjects affected / exposed occurrences (all)	7 / 193 (3.63%) 7  2 / 193 (1.04%) 2	8 / 188 (4.26%) 8  2 / 188 (1.06%) 2	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 May 2014	The duration of the treatment was corrected to 21 days. The number of randomized patients was corrected to 190. The exclusion criteria were extended adding that patients with a measured GFR <50 ml/min/1,732 (moderate to severe renal impairment) at visit 1 are excluded from the study. Creatinine clearance measured by GFR (MDRD formula) was added to the list of determined laboratory parameters.

Notes:

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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.

Due to EudraCT system limitations, which EMA is aware of, results of crossover studies are not accurately represented in this record. Please go to <https://www.novctrd.com/CtrdWeb/home.nov> for complete trial results.

Notes: