Clinical trial results:
A Phase 2, Multicenter, Randomized, Double-blind, Placebo-controlled Dose-ranging Study of Vapendavir in Moderate to Severe Asthmatic Adults with Symptomatic Human Rhinovirus Infection.

Summary

EudraCT number	2014-001785-95
Trial protocol	CZ BG PL
Global end of trial date	09 December 2016

Results information

Result version number	v1 (current)
This version publication date	01 January 2019
First version publication date	01 January 2019

Trial information

Trial identification

Sponsor protocol code	BTA798-203

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Biota Pharma Europe Limited
Sponsor organisation address	2500 Northwinds Parkway, Suite 100, Alpharetta, United States, 30009
Public contact	VP, Clinical Development, Biota Pharmaceuticals, Inc., +1 6782213343, a.barry@biotapharma.com
Scientific contact	VP, Clinical Development, Biota Pharmaceuticals, Inc., +1 6782213343, a.barry@biotapharma.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	02 February 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 December 2016
Global end of trial reached?	Yes
Global end of trial date	09 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of vapendavir on asthma control following HRV infection, as measured by the Asthma Control Questionnaire (ACQ-6).

Protection of trial subjects:

The study was performed in accordance with applicable regulatory and ethical guidelines including the Declaration of Helsinki and the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guideline for Good Clinical Practice (GCP), and any applicable national and local laws and regulations.

Background therapy:

At least 264 µg daily of fluticasone

Evidence for comparator:

N/A

Actual start date of recruitment	02 February 2015
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	United States: 265
Country: Number of subjects enrolled	Georgia: 9
Country: Number of subjects enrolled	Czech Republic: 44
Country: Number of subjects enrolled	Bulgaria: 77
Country: Number of subjects enrolled	Poland: 56
Country: Number of subjects enrolled	Romania: 13
Worldwide total number of subjects	464
EEA total number of subjects	190

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	420
From 65 to 84 years	44
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multicenter trial that was conducted at approximately 60 sites among 6 Northern Hemisphere countries in North America and Central Europe.

Pre-assignment

Screening details:

Patients with an established history of moderate to severe asthma and a history of losing asthma control as a result of upper respiratory tract infection (URTI) were screened up to 180 days prior to becoming symptomatic with a common cold infection.

Period 1

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

Blinding implementation details:

Study drug (active and placebo) were identical in physical appearance. Unblinded bioanalytical analysis was only transferred to the blinded study team post database lock. Unblinding via the IWRS could only be performed by personnel with an appropriate level of access.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo dose consists of applicable matching placebo capsules.

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:

Placebo dose consists of applicable matching placebo capsules.

Arm title	264 mg BID vapendavir

Arm description:

264 mg dose consists of 2x 132 mg capsules of vapendavir phosphate

Arm type	Experimental
Investigational medicinal product name	Vapendavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

264 mg BID PO vapendavir achieved with two 132 mg capsules and two matching placebo capsules at each intake for 7 days.

Arm title	528 mg BID vapendavir

Arm description:

264 mg dose consists of 4x 132 mg capsules of vapendavir phosphate

Arm type	Experimental

Investigational medicinal product name	Vapendavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

528 mg BID PO vapendavir achieved with four 132 capsules at each intake for 7 days

Number of subjects in period 1	Placebo	264 mg BID vapendavir	528 mg BID vapendavir
Started	156	153	155
Completed	155	141	150
Not completed	1	12	5
Consent withdrawn by subject	1	6	-
Physician decision	-	-	1
Adverse event, non-fatal	-	3	2
Lost to follow-up	-	1	2
Noncompliance with Study Protocol/Study Visits	-	1	-
Withdrawal of Informed Consent	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo dose consists of applicable matching placebo capsules.	
Reporting group title	264 mg BID vapendavir
Reporting group description:	
264 mg dose consists of 2x 132 mg capsules of vapendavir phosphate	
Reporting group title	528 mg BID vapendavir
Reporting group description:	
264 mg dose consists of 4x 132 mg capsules of vapendavir phosphate	

Reporting group values	Placebo	264 mg BID vapendavir	528 mg BID vapendavir
Number of subjects	156	153	155
Age categorical Units: Subjects			
not recorded	156	153	155
Gender categorical Units: Subjects			
Not Reported	156	153	155

Reporting group values	Total		
Number of subjects	464		
Age categorical Units: Subjects			
not recorded	464		
Gender categorical Units: Subjects			
Not Reported	464		

Subject analysis sets	
Subject analysis set title	Placebo
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
ITT-I: All patients in the ITT population who had laboratory-confirmed HRV infection (by either RVP [Day 1] or RT-PCR for either the NPS or TBM sample on any of Study Days 1, 3, 5, or 7). This was the primary efficacy population.	
Subject analysis set title	264 mg BID
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
ITT-I: All patients in the ITT population who had laboratory-confirmed HRV infection (by either RVP [Day 1] or RT-PCR for either the NPS or TBM sample on any of Study Days 1, 3, 5, or 7). This was the primary efficacy population.	
Subject analysis set title	528 mg BID
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
ITT-I: All patients in the ITT population who had laboratory-confirmed HRV infection (by either RVP [Day	

1] or RT-PCR for either the NPS or TBM sample on any of Study Days 1, 3, 5, or 7). This was the primary efficacy population.

Subject analysis set title	Combined
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

ITT-I: All patients in the ITT population who had laboratory-confirmed HRV infection (by either RVP [Day 1] or RT-PCR for either the NPS or TBM sample on any of Study Days 1, 3, 5, or 7). This was the primary efficacy population.

Reporting group values	Placebo	264 mg BID	528 mg BID
Number of subjects	57	54	57
Age categorical Units: Subjects			
not recorded	57	54	57
Gender categorical Units: Subjects			
Not Reported	57	54	57

Reporting group values	Combined		
Number of subjects	111		
Age categorical Units: Subjects			
not recorded	111		
Gender categorical Units: Subjects			
Not Reported	111		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo dose consists of applicable matching placebo capsules.	
Reporting group title	264 mg BID vapendavir
Reporting group description:	
264 mg dose consists of 2x 132 mg capsules of vapendavir phosphate	
Reporting group title	528 mg BID vapendavir
Reporting group description:	
264 mg dose consists of 4x 132 mg capsules of vapendavir phosphate	
Subject analysis set title	Placebo
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
ITT-I: All patients in the ITT population who had laboratory-confirmed HRV infection (by either RVP [Day 1] or RT-PCR for either the NPS or TBM sample on any of Study Days 1, 3, 5, or 7). This was the primary efficacy population.	
Subject analysis set title	264 mg BID
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
ITT-I: All patients in the ITT population who had laboratory-confirmed HRV infection (by either RVP [Day 1] or RT-PCR for either the NPS or TBM sample on any of Study Days 1, 3, 5, or 7). This was the primary efficacy population.	
Subject analysis set title	528 mg BID
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
ITT-I: All patients in the ITT population who had laboratory-confirmed HRV infection (by either RVP [Day 1] or RT-PCR for either the NPS or TBM sample on any of Study Days 1, 3, 5, or 7). This was the primary efficacy population.	
Subject analysis set title	Combined
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
ITT-I: All patients in the ITT population who had laboratory-confirmed HRV infection (by either RVP [Day 1] or RT-PCR for either the NPS or TBM sample on any of Study Days 1, 3, 5, or 7). This was the primary efficacy population.	

Primary: LS mean change from baseline to Study Day 14 in ACQ-6 total score

End point title	LS mean change from baseline to Study Day 14 in ACQ-6 total score
End point description:	
The Least Square (LS) mean change from baseline (Study Day 1) to Study Day 14 in ACQ-6 total score	
End point type	Primary
End point timeframe:	
From baseline (Study Day 1) to Study Day 14	

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	54	57	111
Units: total score				
least squares mean (standard error)	-0.94 (± 0.181)	-0.75 (± 0.184)	-0.79 (± 0.189)	-0.77 (± 0.174)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.319 [1]
Method	ANCOVA
Confidence interval	

Notes:

[1] - The p-value corresponds to the test of treatment effect from an ANCOVA with fixed effects for treatment, asthma severity, baseline ACQ-6 score, and geographical region.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.319 [2]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	0.8

Notes:

[2] - The p-value corresponds to the test of treatment effect from an ANCOVA with fixed effects for treatment, asthma severity,
baseline ACQ-6 score, and geographical region.

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.319 [3]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	1.5

Notes:

[3] - The p-value corresponds to the test of treatment effect from an ANCOVA with fixed effects for treatment, asthma severity,
baseline ACQ-6 score, and geographical region.

Secondary: Proportion of Patients with a moderate or severe asthma exacerbation

End point title	Proportion of Patients with a moderate or severe asthma exacerbation

End point description:

Proportion of patients with a moderate or severe asthma exacerbation within Study Day 1 to Study Day 14,

End point type	Secondary

End point timeframe:

Within Study Day 1 to Study Day 14

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	54	57	111
Units: Patients	12	14	10	24

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.563 [4]
Method	Cochran-Mantel-Haenszel

Notes:

[4] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.632 [5]
Method	Cochran-Mantel-Haenszel

Notes:

[5] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma
severity.

Statistical analysis title	Statistical Analysis - Combined vs Placbo
Comparison groups	Placebo v Combined

Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.942 [6]
Method	Cochran-Mantel-Haenszel

Notes:

[6] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Secondary: Proportion of patients with a severe asthma exacerbation

End point title	Proportion of patients with a severe asthma exacerbation

End point description:

Proportion of patients with a severe asthma exacerbation within Study Day 1 to Study Day 14, inclusive

End point type	Secondary

End point timeframe:

Within Study Day 1 to Study Day 14

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	54	57	111
Units: Patients	1	2	4	6

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.533 [7]
Method	Cochran-Mantel-Haenszel

Notes:

[7] - The p-value corresponds to the test of no treatment based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placbo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.173 [8]
Method	Cochran-Mantel-Haenszel

Notes:

[8] - The p-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - Combined vs Placbo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.265 [9]
Method	Cochran-Mantel-Haenszel

Notes:

[9] - The p-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Secondary: LS mean change from baseline to Study Day 7 in ACQ-6 total score

End point title	LS mean change from baseline to Study Day 7 in ACQ-6 total score

End point description:

The LS mean change from baseline to Study Day 7 in ACQ-6 total score

End point type	Secondary

End point timeframe:

From baseline to Study Day 7

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	53	56	109
Units: Total Score				
least squares mean (standard deviation)	-0.47 (± 0.177)	-0.34 (± 0.179)	-0.34 (± 0.184)	-0.34 (± 0.169)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.471 [10]
Method	ANCOVA

Notes:

[10] - The p-value corresponds to the test of treatment effect from an ANCOVA with fixed effects for treatment, asthma severity, baseline ACQ-6 score, and geographical region

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID

Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.471 [11]
Method	ANCOVA

Notes:

[11] - The p-value corresponds to the test of treatment effect from an ANCOVA with fixed effects for treatment, asthma severity, baseline ACQ-6 score, and geographical region

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.471 [12]
Method	ANCOVA

Notes:

[12] - The p-value corresponds to the test of treatment effect from an ANCOVA with fixed effects for treatment, asthma severity, baseline ACQ-6 score, and geographical region

Secondary: Proportion of patients with ≥0.5 point reduction in ACQ-6 score

End point title	Proportion of patients with ≥0.5 point reduction in ACQ-6 score

End point description:

Proportion of patients with ≥0.5 point reduction in ACQ-6 score from baseline over the 28 days of the study

End point type	Secondary

End point timeframe:

From baseline over 28 days of study

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	54	57	111
Units: Patients	45	41	46	87

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.673 [13]
Method	Cochran-Mantel-Haenszel

Notes:

[13] - The p-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma
severity.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placbo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.814 [14]
Method	Cochran-Mantel-Haenszel

Notes:

[14] - The p-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma
severity.

Statistical analysis title	Statistical Analysis - Combined vs Placbo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.914 [15]
Method	Cochran-Mantel-Haenszel

Notes:

[15] - The p-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma
severity.

Secondary: Proportion of patients with ≥0.5 point increase in ACQ-6 score

End point title	Proportion of patients with ≥0.5 point increase in ACQ-6 score

End point description:

Proportion of patients with ≥0.5 point increase in ACQ-6 score from baseline over the 28 days of the study

End point type	Secondary

End point timeframe:

From baseline over the 28 days of the study

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	54	57	111
Units: Patients	8	12	11	23

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.267 [16]
Method	Cochran-Mantel-Haenszel

Notes:

[16] - The p-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placbo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.454 [17]
Method	Cochran-Mantel-Haenszel

Notes:

[17] - The p-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - Combined vs Placbo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.292 [18]
Method	Cochran-Mantel-Haenszel

Notes:

[18] - The p-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Secondary: Proportion of patients with a post-Study Day 1 ACQ-6 score of ≤1.5

End point title	Proportion of patients with a post-Study Day 1 ACQ-6 score of ≤1.5

End point description:

Proportion of patients with a post-Study Day 1 ACQ-6 score of ≤1.5

End point type	Secondary

End point timeframe:

post-Study Day 1

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	54	57	111
Units: Patients	41	36	38	74

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	264 mg BID v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.526 [19]
Method	Cochran-Mantel-Haenszel

Notes:

[19] - The p-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placbo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.546 [20]
Method	Cochran-Mantel-Haenszel

Notes:

[20] - The p-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - Combined vs Placbo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.482 [21]
Method	Cochran-Mantel-Haenszel

Notes:

[21] - The p-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Secondary: Daily ß2-agonist use over Study Day 1 to Study Day 14

End point title	Daily ß2-agonist use over Study Day 1 to Study Day 14

End point description:

Daily ß2-agonist use over Study Day 1 to Study Day 14

End point type	Secondary

End point timeframe:

Study Day 1 to Study Day 14

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	54	57	111
Units: ß-agonist uses				
least squares mean (standard error)	1.86 (± 0.451)	1.41 (± 0.455)	1.65 (± 0.470)	1.53 (± 0.432)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.783 [22]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	6.1

Notes:

[22] - The p-value for test of no treatment difference is based on analysis of covariance model with fixed effects for treatment, asthma severity and geographical region. The p-value is from the model with the ranked response variable as dependent variables

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placbo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.783 [23]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	8.6

Notes:

[23] - The p-value for test of no treatment difference is based on analysis of covariance model with fixed effects for treatment, asthma severity and geographical region. The p-value is from the model with the ranked response variable as dependent variables

Statistical analysis title	Statistical Analysis - Combined vs Placbo
Comparison groups	Combined v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.783 [24]
Method	ANCOVA

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	8.6

Notes:

[24] - The p-value for test of no treatment difference is based on analysis of covariance model with fixed effects for treatment, asthma severity and geographical region. The p-value is from the model with the ranked response variable as dependent variables

Secondary: Reliever free days

End point title	Reliever free days

End point description:

Reliever free days over Study Day 1 to Study Day 14

End point type	Secondary

End point timeframe:

Study Day 1 to Study Day 14

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	54	57	111
Units: days				
least squares mean (standard error)	6.8 (± 0.90)	7.2 (± 0.91)	7.5 (± 0.94)	7.4 (± 0.86)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.961 [25]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	10

Notes:

[25] - The p-value for test of no treatment difference is based on analysis of covariance model with fixed effects for treatment, asthama severity and geographical region. The p-value is from the model with ranked response variable as the dependent variable

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placbo
Comparison groups	Placebo v 528 mg BID

Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.525 [26]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	10

Notes:

[26] - The p-value for test of no treatment difference is based on analysis of covariance model with fixed effects for treatment, asthama severity and geographical region. The p-value is from the model with ranked response variable as the dependent variable

Statistical analysis title	Statistical Analysis - Combined vs Placbo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.525 [27]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	10

Notes:

[27] - The p-value for test of no treatment difference is based on analysis of covariance model with fixed effects for treatment, asthama severity and geographical region. The p-value is from the model with ranked response variable as the dependent variable

Secondary: Maximum fall in FEV1

End point title	Maximum fall in FEV1

End point description:

Maximum fall in clinic-based forced expiratory volume in 1 second (FEV1) during Study Day 1 to Study Day 14 as a percent of the Study Day 1 level

End point type	Secondary

End point timeframe:

Study Day 1 to Study Day 14

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	50	57	107
Units: Litres				
least squares mean (standard error)	1.579 (± 5.2133)	-4.780 (± 5.3190)	-1.802 (± 5.4146)	-3.291 (± 4.9958)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.87 [28]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.98
upper limit	34.67

Notes:

[28] - The p-value for test of no treatment difference is based on an analysis of covariance model with fixed effects for treatment, asthma severity, Study Day 1 pre-bronchodilator FEV1, and geographical region.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placbo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.87 [29]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.1
upper limit	47.92

Notes:

[29] - The p-value for test of no treatment difference is based on analysis of covariance model with fixed effects for treatment, asthama severity, Study Day 1 pre-bronchodilator FEV1, and geographical region

Statistical analysis title	Statistical Analysis - Combined vs Placbo
Comparison groups	Combined v Placebo
Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.87 [30]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.1
upper limit	47.92

Notes:

[30] - The p-value for test of no treatment difference is based on an analysis of covariance model with fixed effects for treatment, asthma severity, Study Day 1 pre-bronchodilator FEV1, and geographical region.

Secondary: Maximum increase in clinical-based FEV1

End point title	Maximum increase in clinical-based FEV1

End point description:

Maximum increase in clinic-based FEV1 during Study Days 1 to Study Day 14 as a percent of the Study Day 1 level

End point type	Secondary

End point timeframe:

Study Day 1 to Study Day 14

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	54	57	111
Units: Litres				
least squares mean (standard error)	1.579 (± 5.2133)	-4.780 (± 5.3190)	-1.802 (± 5.4146)	-3.291 (± 4.9958)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	264 mg BID v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.87 [31]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.98
upper limit	34.67

Notes:

[31] - P-value for test of no treatment difference is based on an analysis of covariance model with fixed effects for treatment, asthma severity, Day 1 pre-bronchodilator FEV1, and geographical region.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placbo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.87 [32]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.1
upper limit	47.92

Notes:

[32] - P-value for test of no treatment difference is based on an analysis of covariance model with fixed effects for treatment, asthma severity, Day 1 pre-bronchodilator FEV1, and geographical region.

Statistical analysis title	Statistical Analysis - Combined vs Placbo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.87 [33]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.1
upper limit	47.92

Notes:

[33] - P-value for test of no treatment difference is based on an analysis of covariance model with fixed effects for treatment, asthma severity, Day 1 pre-bronchodilator FEV1, and geographical region.

Secondary: WURSS-21 daily change severity score averaged over the peak infection

End point title	WURSS-21 daily change severity score averaged over the peak infection

End point description:

WURSS-21 daily change severity score averaged over the peak infection Study Day 2 to Study Day 4

End point type	Secondary

End point timeframe:

Study Day 2 to Study Day 4

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	50	57	107
Units: severity score				
least squares mean (standard error)	-24.93 (± 5.169)	-24.61 (± 5.232)	-28.06 (± 5.431)	-26.33 (± 4.976)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.73 [34]
Method	ANCOVA

Notes:

[34] - The p-value for test of no treatment difference was based on an ANCOVA model with fixed effects for treatment, asthma severity, gender and geographical region. It is from the model with the ranked response variable as the dependent variable

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.73 [35]
Method	ANCOVA

Notes:

[35] - The p-value for test of no treatment difference was based on an ANCOVA model with fixed effects for treatment, asthma severity, gender and geographical region. It is from the model with the ranked response variable as the dependent variable

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.73 [36]
Method	ANCOVA

Notes:

[36] - The p-value for test of no treatment difference was based on an ANCOVA model with fixed effects for treatment, asthma severity, gender and geographical region. It is from the model with the ranked response variable as the dependent variable

Secondary: Time to alleviate WURSS-21 cold symptoms

End point title	Time to alleviate WURSS-21 cold symptoms
End point description:	
Time to alleviation (hours) of WURSS-21 cold symptoms	
End point type	Secondary
End point timeframe:	
Length of study	

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	54	57	111
Units: hours				
arithmetic mean (standard deviation)	9.1 (± 0.49)	9.3 (± 0.51)	8.2 (± 0.46)	8.8 (± 0.34)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.212 [37]
Method	Regression, Cox
Confidence interval	
level	95 %
sides	2-sided
lower limit	7
upper limit	13

Notes:

[37] - The p-value for the test of no treatment difference was based on Cox Proportional Hazards model with covariates for asthma
severity, gender, and geographical region.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placbo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.212 [38]
Method	Regression, Cox
Confidence interval	
level	95 %
sides	2-sided
lower limit	7
upper limit	10

Notes:

[38] - The p-value for the test of no treatment difference was based on Cox Proportional Hazards model with covariates for asthma
severity, gender, and geographical region.

Statistical analysis title	Statistical Analysis - Combined vs Placbo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.212 [39]
Method	Regression, Cox
Confidence interval	
level	95 %
sides	2-sided
lower limit	7
upper limit	10

Notes:

[39] - The p-value for the test of no treatment difference was based on Cox Proportional Hazards model with covariates for asthma
severity, gender, and geographical region.

Secondary: Maximum fall in peak expiratory flow (PEF)

End point title	Maximum fall in peak expiratory flow (PEF)

End point description:

Maximum fall in clinic-based peak expiratory flow (PEF) during Study Day 1 to Study Day 14, as a percent of the Study Day 1 level

End point type	Secondary

End point timeframe:

Study Day 1 to Study Day 14

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	50	57	107
Units: L/min				
least squares mean (standard error)	7.6 (± 5.89)	-5.5 (± 5.99)	2.7 (± 6.12)	-1.4 (± 5.64)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.074 [40]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32
upper limit	28

Notes:

[40] - P-value for test of no treatment difference is based on analysis of covariance model with fixed effects for treatment, asthma severity, Day 1 pre-bronchodilator PEF and geographical region.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	528 mg BID v Placebo
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.074 [41]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35
upper limit	71

Notes:

[41] - P-value for test of no treatment difference is based on an analysis of covariance model with fixed effects for treatment, asthma severity,
Day 1 pre-bronchodilator PEF, and geographical region.

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined

Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.074 [42]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35
upper limit	71

Notes:

[42] - P-value for test of no treatment difference is based on an analysis of covariance model with fixed effects for treatment, asthma severity,
Day 1 pre-bronchodilator PEF, and geographical region.

Secondary: Maximum fall in peak expiratoy flow (PEF), post-SABA level

End point title	Maximum fall in peak expiratoy flow (PEF), post-SABA level

End point description:

Maximum absolute fall in clinic-based peak expiratory (PEF) during Study Day 1 to Study Day 14 from Study Day 1, post-SABA level

End point type	Secondary

End point timeframe:

Study Day 1 to Study Day 14

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	50	57	107
Units: L/min				
least squares mean (standard error)	-4.0 (± 14.87)	-4.4 (± 15.19)	6.0 (± 15.52)	0.8 (± 14.30)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.762 [43]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	144
upper limit	658

Notes:

[43] - P-value for test of no treatment difference is based on an analysis of covariance model with fixed effects for treatment, asthma severity,
Day 1 post-bronchodilator PEF, and geographical region.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.762 [44]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-76
upper limit	144

Notes:

[44] - P-value for test of no treatment difference is based on an analysis of covariance model with fixed effects for treatment, asthma severity,
Day 1 post-bronchodilator PEF, and geographical region.

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.762 [45]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-144
upper limit	144

Notes:

[45] - P-value for test of no treatment difference is based on an analysis of covariance model with fixed effects for treatment, asthma severity, Day 1 post-bronchodilator PEF, and geographical region.

Secondary: Maximum fall in FVC

End point title	Maximum fall in FVC

End point description:

Maximum fall in forced vital capacity (FVC) during the Study Day 1 to Study Day 14, as a percent of the Study Day 1 level

End point type	Secondary

End point timeframe:

Study Day 1 to Study Day 14

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	50	57	107
Units: Litres				
least squares mean (standard error)	-0.854 (± 4.3693)	-2.845 (± 4.4395)	-1.931 (± 4.5456)	-2.388 (± 4.1840)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.686 [46]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31
upper limit	40.26

Notes:

[46] - P-value for test of no treatment difference is based on an analysis of covariance model with fixed effects for treatment, asthma severity,
Day 1 pre-bronchodilator FVC, and geographical region.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.686 [47]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.53
upper limit	38.78

Notes:

[47] - P-value for test of no treatment difference is based on an analysis of covariance model with fixed effects for treatment, asthma severity,
Day 1 pre-bronchodilator FVC, and geographical region.

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined

Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.686 [48]
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.53
upper limit	40.26

Notes:

[48] - P-value for test of no treatment difference is based on an analysis of covariance model with fixed effects for treatment, asthma severity,
Day 1 pre-bronchodilator FVC, and geographical region.

Secondary: Proportion of patients with a ≥10% decline in FVC

End point title	Proportion of patients with a ≥10% decline in FVC

End point description:

Proportion of patients with a ≥10% decline from the Study Day 1 level in FVC at any time during Study Day 1 to Study Day 14

End point type	Secondary

End point timeframe:

Study Day 1 to Study Day 14

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	152	151	152	303
Units: Patients	34	35	36	71

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.877 [49]
Method	Cochran-Mantel-Haenszel

Notes:

[49] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID

Number of subjects included in analysis	304
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.786 [50]
Method	Cochran-Mantel-Haenszel

Notes:

[50] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	455
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.798 [51]
Method	Cochran-Mantel-Haenszel

Notes:

[51] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Secondary: Proportion of patients with a ≥10% increase in FVC

End point title	Proportion of patients with a ≥10% increase in FVC

End point description:

Proportion of patients with a ≥10% increase from the Study Day 1 level in FVC at any time during Study Day 1 to Study Day 14

End point type	Secondary

End point timeframe:

Study Day 1 to Study Day 14

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	152	151	152	303
Units: Patients	44	35	49	84

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.249 [52]
Method	Cochran-Mantel-Haenszel

Notes:

[52] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	304
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.534 [53]
Method	Cochran-Mantel-Haenszel

Notes:

[53] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - Combined vs Placbo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	455
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.775 [54]
Method	Cochran-Mantel-Haenszel

Notes:

[54] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Secondary: Proportion of patients with ≥10% decline in FEV1

End point title	Proportion of patients with ≥10% decline in FEV1

End point description:

Proportion of patients with a ≥10% decline from the Study Day 1 level in FEV1 at any time during Study Day 1 to Study Day 14

End point type	Secondary

End point timeframe:

Study Day 1 to Study Day 14

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	55	46	52	98
Units: Patients	18	15	16	31

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.988 [55]
Method	Cochran-Mantel-Haenszel

Notes:

[55] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.825 [56]
Method	Cochran-Mantel-Haenszel

Notes:

[56] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity

Statistical analysis title	Statistical Analysis - Combined vs Placbo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.886 [57]
Method	Cochran-Mantel-Haenszel

Notes:

[57] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity

Secondary: Proportion of patients with a ≥10% increase in FEV1

End point title	Proportion of patients with a ≥10% increase in FEV1

End point description:

Proportion of patients with a ≥10% increase from the Study Day 1 level in FEV1 at any time during Study Day 1 to Study Day 14

End point type	Secondary

End point timeframe:

Study Day 1 to Study Day 14

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	55	46	52	98
Units: Patients	21	15	14	29

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID

Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.568 [58]
Method	Cochran-Mantel-Haenszel

Notes:

[58] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.228 [59]
Method	Cochran-Mantel-Haenszel

Notes:

[59] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity

Statistical analysis title	Statistical Analysis - Combined vs Placbo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.287 [60]
Method	Cochran-Mantel-Haenszel

Notes:

[60] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity

Secondary: LS mean change from baseline to Study Day 21 in ACQ-6 total score

End point title	LS mean change from baseline to Study Day 21 in ACQ-6 total score

End point description:

The LS mean change from baseline to Study Day 21 in ACQ-6 total score

End point type	Secondary

End point timeframe:

Baseline to Study Day 21

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	51	56	107
Units: total score				
least squares mean (standard error)	-1.03 (± 0.177)	-0.66 (± 0.180)	-0.82 (± 0.185)	-0.74 (± 0.170)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02 [61]
Method	ANCOVA

Notes:

[61] - The p-value corresponds to the test of treatment effect from an ANCOVA with fixed effects for treatment, asthma severity, baseline ACQ-6 score, and geographical region

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006 [62]
Method	ANCOVA

Notes:

[62] - p-value corresponds to pairwise comparisons of each active group versus placebo created from linear contrasts of the placebo model. Values are only presented if the test of treatment effect was significant at the 0.05 level

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.105 [63]
Method	ANCOVA

Notes:

[63] - p-value corresponds to pairwise comparisons of each active group versus placebo created from linear contrasts of the placebo model. Values are only presented if the test of treatment effect was significant at the 0.05 level

Secondary: LS mean change from baseline to Study Day 28 in ACQ-6 total score

End point title	LS mean change from baseline to Study Day 28 in ACQ-6 total score

End point description:

The LS mean change from baseline to Study Day 28 in ACQ-6 total score

End point type	Secondary

End point timeframe:

Baseline to Study Day 28

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	48	56	104
Units: total score				
least squares mean (standard error)	-1.13 (± 0.180)	-0.95 (± 0.183)	-0.91 (± 0.187)	-0.93 (± 0.172)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.205 [64]
Method	ANCOVA

Notes:

[64] - The p-value corresponds to the test of treatment effect from an ANCOVA with fixed effects for treatment, asthma severity, baseline ACQ-6 score, and geographical region.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.205 [65]
Method	ANCOVA

Notes:

[65] - The p-value corresponds to the test of treatment effect from an ANCOVA with fixed effects for treatment, asthma severity, baseline ACQ-6 score, and geographical region.

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.205 [66]
Method	ANCOVA

Notes:

[66] - The p-value corresponds to the test of treatment effect from an ANCOVA with fixed effects for treatment, asthma severity, baseline ACQ-6 score, and geographical region.

Secondary: WURSS-21 daily change severity score averaged over the peak infection

End point title	WURSS-21 daily change severity score averaged over the peak infection

End point description:

WURSS-21 daily change severity score averaged over the peak infectionStudy Day 3 to Study Day 5

End point type	Secondary

End point timeframe:

Study Day 3 to Study Day 5

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	50	57	107
Units: severity score				
least squares mean (standard error)	-37.15 (± 5.835)	-35.04 (± 5.913)	-40.43 (± 6.136)	-37.74 (± 5.622)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.531 [67]
Method	ANCOVA

Notes:

[67] - The p-value for test of no treatment difference was based on an ANCOVA model with fixed effects for treatment, asthma severity, gender and geographical region. It is from the model with the ranked response variable as the dependent variable

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.531 [68]
Method	ANCOVA

Notes:

[68] - The p-value for test of no treatment difference was based on an ANCOVA model with fixed effects for treatment, asthma severity, gender and geographical region. It is from the model with the ranked response variable as the dependent variable

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.531 [69]
Method	ANCOVA

Notes:

[69] - The p-value for test of no treatment difference was based on an ANCOVA model with fixed effects for treatment, asthma severity, gender and geographical region. It is from the model with the ranked response variable as the dependent variable

Secondary: WURSS-21 daily change severity score averaged over the peak infection

End point title	WURSS-21 daily change severity score averaged over the peak infection

End point description:
WURSS-21 daily change severity score averaged over the peak infection Study Day 2 to Study Day 7

End point type	Secondary

End point timeframe:
Study Day 2 to Study Day 7

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	57	50	57	107
Units: severity score				
least squares mean (standard error)	-34.49 (± 5.578)	-33.55 (± 5.653)	-38.31 (± 5.866)	-35.93 (± 5.374)

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	264 mg BID v Placebo
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.468 [70]
Method	ANCOVA

Notes:

[70] - The p-value for test of no treatment difference was based on an ANCOVA model with fixed effects for treatment, asthma severity, gender and geographical region.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	528 mg BID v Placebo
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.468 [71]
Method	ANCOVA

Notes:

[71] - The p-value for test of no treatment difference was based on an ANCOVA model with fixed effects for treatment, asthma severity, gender and geographical region.

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.468 [72]
Method	ANCOVA

Notes:

[72] - The p-value for test of no treatment difference was based on an ANCOVA model with fixed effects for treatment, asthma severity, gender and geographical region.

Secondary: Proportion of patients with a ≥10% decline in FVC	
End point title	Proportion of patients with a ≥10% decline in FVC

End point description:

Proportion of patients with a ≥10% decline from the Study Day 1 level in FVC at any time during Study Day 1 to Study Day 28

End point type	Secondary

End point timeframe:

Study Day 1 to Study Day 28

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	152	151	152	303
Units: Patients	41	47	46	93

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.436 [73]
Method	Cochran-Mantel-Haenszel

Notes:

[73] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	304
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.527 [74]
Method	Cochran-Mantel-Haenszel

Notes:

[74] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	455
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.411 [75]
Method	Cochran-Mantel-Haenszel

Notes:

[75] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Secondary: Proportion of patients with a ≥10% increase in FVC

End point title	Proportion of patients with a ≥10% increase in FVC

End point description:

Proportion of patients with a ≥10% increase from the Study Day 1 level in FVC at any time during Study Day 1 to Study Day 28

End point type	Secondary

End point timeframe:

Study Day 1 to Study Day 28

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	152	151	152	303
Units: Patients	44	35	49	84

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	264 mg BID v Placebo
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05 [76]
Method	Cochran-Mantel-Haenszel

Notes:

[76] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	304
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999 [77]
Method	Cochran-Mantel-Haenszel

Notes:

[77] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined

Number of subjects included in analysis	455
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.261 [78]
Method	Cochran-Mantel-Haenszel

Notes:

[78] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity.

Secondary: Proportion of patients with a ≥10% decline in FEV1

End point title	Proportion of patients with a ≥10% decline in FEV1

End point description:

Proportion of patients with a ≥10% decline from the Study Day 1 level in FEV1 at any time during Study Day 1 to Study Day 28

End point type	Secondary

End point timeframe:

Study Day 1 to Study Day 28

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	55	46	52	98
Units: Patients	20	20	17	37

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.474 [79]
Method	Cochran-Mantel-Haenszel

Notes:

[79] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.681 [80]
Method	Cochran-Mantel-Haenszel

Notes:

[80] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.875 [81]
Method	Cochran-Mantel-Haenszel

Notes:

[81] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity

Secondary: Proportion of patients with ≥10 increase in FEV1

End point title	Proportion of patients with ≥10 increase in FEV1

End point description:

Proportion of patients with a ≥10% increase from the Study Day 1 level in FEV1 at any time during Study Day 1 to Study Day 28

End point type	Secondary

End point timeframe:

Study Day 1 to Study 28

End point values	Placebo	264 mg BID	528 mg BID	Combined
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	55	46	52	98
Units: Patients	24	16	16	32

Statistical analyses

Statistical analysis title	Statistical Analysis - 264 mg BID vs Placebo
Comparison groups	Placebo v 264 mg BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.372 [82]
Method	Cochran-Mantel-Haenszel

Notes:

[82] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity

Statistical analysis title	Statistical Analysis - 528 mg BID vs Placebo
Comparison groups	Placebo v 528 mg BID
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.18 [83]
Method	Cochran-Mantel-Haenszel

Notes:

[83] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity

Statistical analysis title	Statistical Analysis - Combined vs Placebo
Comparison groups	Placebo v Combined
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.183 [84]
Method	Cochran-Mantel-Haenszel

Notes:

[84] - P-value corresponds to the test of no treatment difference based on a Cochran-Mantel-Haenszel test stratified by asthma severity

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From initiation of study drug on Study Day 1 up to and including the final follow-up telephone call on Study Day 35

Adverse event reporting additional description:

For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Placebo dose consists of applicable matching placebo capsules.

Reporting group title	264 mg BID vapendavir

Reporting group description:

264 mg dose consists of 2x 132 mg capsules of vapendavir phosphate

Reporting group title	528 mg BID vapendavir

Reporting group description:

528 mg dose consists of 4x 132 mg capsules of vapendavir phosphate

Reporting group title	Combined

Reporting group description: -

Serious adverse events	Placebo	264 mg BID vapendavir	528 mg BID vapendavir
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	1 / 152 (0.66%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Gastroenteritis viral			
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract infection	Additional description: Mild		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
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	Combined		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 303 (0.66%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Gastroenteritis viral			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract infection	Additional description: Mild		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	264 mg BID vapendavir	528 mg BID vapendavir
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 151 (39.74%)	77 / 151 (50.99%)	71 / 152 (46.71%)
Vascular disorders			
Hypertension	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	1 / 151 (0.66%)	2 / 152 (1.32%)
occurrences (all)	1	1	2
Pregnancy, puerperium and perinatal conditions			
Unintended pregnancy	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	1 / 152 (0.66%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Chest discomfort	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	2 / 152 (1.32%)
occurrences (all)	0	0	2
Chest pain	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment		

subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Drug withdrawal syndrome	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Fatigue	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	2 / 152 (1.32%)
occurrences (all)	0	0	2
Pyrexia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	0 / 152 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Menstruation irregular	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Asthma	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	43 / 151 (28.48%)	48 / 151 (31.79%)	36 / 152 (23.68%)
occurrences (all)	43	48	36
Cough	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	3 / 151 (1.99%)	1 / 152 (0.66%)
occurrences (all)	0	3	1
Epistaxis	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	1 / 151 (0.66%)	2 / 152 (1.32%)
occurrences (all)	1	1	2
Nasal dryness	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Rhinitis allergic	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Sleep apnoea syndrome	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		

subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	0 / 152 (0.00%)
occurrences (all)	1	0	0
Wheezing	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	0 / 152 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Abnormal dreams	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Nightmare	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Panic attack	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	1	0	1
Aspartate aminotransferase increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	1	0	1
Blood creatine increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Blood glucose increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	2 / 151 (1.32%)	1 / 151 (0.66%)	1 / 152 (0.66%)
occurrences (all)	2	1	1
Blood pressure increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		

subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Blood thyroid stimulating hormone increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Blood urea increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Electrocardiogram abnormal	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Electrocardiogram T wave inversion	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	0 / 152 (0.00%)
occurrences (all)	1	0	0
Haematocrit increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	0 / 152 (0.00%)
occurrences (all)	1	0	0
Haemoglobin increased			
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	0 / 152 (0.00%)
occurrences (all)	1	0	0
White blood cell count increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Arthropod bite	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		

subjects affected / exposed	0 / 151 (0.00%)	2 / 151 (1.32%)	0 / 152 (0.00%)
occurrences (all)	0	2	0
Contusion	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	0 / 152 (0.00%)
occurrences (all)	1	0	0
Joint dislocation	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Joint injury	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Laceration	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Spinal column injury	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Atrial flutter	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	0 / 152 (0.00%)
occurrences (all)	1	0	0
Bundle branch block right	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Palpitations	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Tachycardia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Nervous system disorders			
Anosmia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		

subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Disturbance in attention	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Dizziness	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	1	0	1
Dysgeusia			
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Headache	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	5 / 151 (3.31%)	7 / 152 (4.61%)
occurrences (all)	1	5	7
Blood and lymphatic system disorders			
Eosinophilia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Leukopenia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Lymphadenopathy	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Neutropenia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear pain	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		

subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	2 / 152 (1.32%)
occurrences (all)	0	0	2
Abdominal pain	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	0 / 152 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	3 / 152 (1.97%)
occurrences (all)	0	0	3
Constipation	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	0 / 152 (0.00%)
occurrences (all)	1	0	0
Dental caries	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	0 / 152 (0.00%)
occurrences (all)	1	0	0
Diarrhoea	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	2 / 151 (1.32%)	1 / 151 (0.66%)	2 / 152 (1.32%)
occurrences (all)	2	1	2
Flatulence	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	0 / 152 (0.00%)
occurrences (all)	1	0	0
Mouth haemorrhage	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Nausea	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	2 / 151 (1.32%)	3 / 152 (1.97%)
occurrences (all)	0	2	3
Umbilical hernia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Vomiting	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	2 / 152 (1.32%)
occurrences (all)	1	0	2
Skin and subcutaneous tissue disorders			

Hyperhidrosis	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Rash papular	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Nephrolithiasis	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Back pain	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	5 / 151 (3.31%)	0 / 152 (0.00%)
occurrences (all)	1	5	0
Muscle spasms	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Tendonitis	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bartholin's abscess	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	0 / 152 (0.00%)
occurrences (all)	1	0	0
Bronchitis	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	3 / 152 (1.97%)
occurrences (all)	0	0	3
Bronchitis bacterial	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		

subjects affected / exposed	1 / 151 (0.66%)	0 / 151 (0.00%)	0 / 152 (0.00%)
occurrences (all)	1	0	0
Candida infection	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Eye infection	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Gastroenteritis viral	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Influenza	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Lower respiratory tract infection viral	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	0 / 152 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	2 / 151 (1.32%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	2	0	1
Sinusitis	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	1 / 152 (0.66%)
occurrences (all)	0	1	1
Sputum purulent	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1
Upper respiratory tract infection	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	3 / 151 (1.99%)	6 / 151 (3.97%)	3 / 152 (1.97%)
occurrences (all)	3	6	3
Urinary tract infection	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	2 / 151 (1.32%)	3 / 151 (1.99%)	2 / 152 (1.32%)
occurrences (all)	2	3	2
Metabolism and nutrition disorders			

Decreased appetite	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	1 / 152 (0.66%)
occurrences (all)	0	1	1
Hyperphosphataemia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 151 (0.00%)	0 / 151 (0.00%)	1 / 152 (0.66%)
occurrences (all)	0	0	1

Non-serious adverse events	Combined		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	148 / 303 (48.84%)		
Vascular disorders			
Hypertension	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	3 / 303 (0.99%)		
occurrences (all)	3		
Pregnancy, puerperium and perinatal conditions			
Unintended pregnancy	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
General disorders and administration site conditions			
Chest discomfort	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Chest pain	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Drug withdrawal syndrome	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Fatigue	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment		
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Pyrexia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment		
subjects affected / exposed	0 / 303 (0.00%)		
occurrences (all)	0		

Reproductive system and breast disorders			
Menstruation irregular	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Asthma	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	84 / 303 (27.72%)		
occurrences (all)	84		
Cough	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	4 / 303 (1.32%)		
occurrences (all)	4		
Epistaxis	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	3 / 303 (0.99%)		
occurrences (all)	3		
Nasal dryness	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Rhinitis allergic	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Sleep apnoea syndrome	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 303 (0.00%)		
occurrences (all)	0		
Wheezing	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 303 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Psychiatric disorders			
Abnormal dreams	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		

Nightmare	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Panic attack	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Aspartate aminotransferase increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Blood creatine increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Blood glucose increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Blood pressure increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Blood thyroid stimulating hormone increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Blood urea increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Electrocardiogram abnormal	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Electrocardiogram QT prolonged	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		

subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Electrocardiogram T wave inversion	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 303 (0.00%)		
occurrences (all)	0		
Haematocrit increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 303 (0.00%)		
occurrences (all)	0		
Haemoglobin increased			
subjects affected / exposed	0 / 303 (0.00%)		
occurrences (all)	0		
White blood cell count increased	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod bite	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Contusion	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Joint dislocation	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Joint injury	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Laceration	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		

subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Spinal column injury	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Cardiac disorders			
Atrial flutter	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 303 (0.00%)		
occurrences (all)	0		
Bundle branch block right	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Palpitations	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Tachycardia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Nervous system disorders			
Anosmia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Disturbance in attention	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Dizziness	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Headache	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		

subjects affected / exposed	12 / 303 (3.96%)		
occurrences (all)	12		
Blood and lymphatic system disorders			
Eosinophilia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Leukopenia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Lymphadenopathy	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Neutropenia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear pain	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal discomfort	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Abdominal pain	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 303 (0.00%)		
occurrences (all)	0		
Abdominal pain upper	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	3 / 303 (0.99%)		
occurrences (all)	3		
Constipation	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 303 (0.00%)		
occurrences (all)	0		
Dental caries	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		

subjects affected / exposed	0 / 303 (0.00%)		
occurrences (all)	0		
Diarrhoea	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	3 / 303 (0.99%)		
occurrences (all)	3		
Flatulence	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 303 (0.00%)		
occurrences (all)	0		
Mouth haemorrhage	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Nausea	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	5 / 303 (1.65%)		
occurrences (all)	5		
Umbilical hernia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Vomiting	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Hyperhidrosis	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Rash papular	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Renal and urinary disorders			
Nephrolithiasis	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			

Arthralgia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Back pain	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	5 / 303 (1.65%)		
occurrences (all)	5		
Muscle spasms	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Tendonitis	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Infections and infestations			
Bartholin's abscess	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 303 (0.00%)		
occurrences (all)	0		
Bronchitis	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	3 / 303 (0.99%)		
occurrences (all)	3		
Bronchitis bacterial	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	0 / 303 (0.00%)		
occurrences (all)	0		
Candida infection	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Eye infection	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Gastroenteritis viral	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Influenza	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		

subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Lower respiratory tract infection viral	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Nasopharyngitis	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Sinusitis	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Sputum purulent	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Upper respiratory tract infection	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	9 / 303 (2.97%)		
occurrences (all)	9		
Urinary tract infection	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	5 / 303 (1.65%)		
occurrences (all)	5		
Metabolism and nutrition disorders			
Decreased appetite	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Hyperphosphataemia	Additional description: For patients who experienced the same coded event more than once, the greatest severity was presented within a treatment.		
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		

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