EU Clinical Trials Register

Clinical trial results:
A Phase 2/3, Randomized, Double-Blind, Double-Dummy, Placebo-Controlled Study to Evaluate the Safety and Efficacy of 2 Regimens of Orally Administered PF-07321332/Ritonavir in Preventing Symptomatic SARS-CoV-2 Infection in Adult Household Contacts of an Individual With Symptomatic COVID-19

Summary

EudraCT number	2021-002894-24
Trial protocol	ES BG HU
Global end of trial date	12 April 2022

Results information

Result version number	v1 (current)
This version publication date	27 April 2023
First version publication date	27 April 2023

Trial information

Trial identification

Sponsor protocol code	C4671006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05047601
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.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	27 May 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of 5-day and 10-day regimens of PF-07321332/ritonavir versus placebo in preventing symptomatic Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) or Rapid Antigen Test (RAT)-confirmed SARS-CoV-2 infection in adult subjects who have a negative RT-PCR result at baseline and who are household contacts of an individual with symptomatic COVID-19.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 September 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Brazil: 3
Country: Number of subjects enrolled	Bulgaria: 229
Country: Number of subjects enrolled	Colombia: 3
Country: Number of subjects enrolled	Czechia: 3
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Japan: 10
Country: Number of subjects enrolled	Malaysia: 2
Country: Number of subjects enrolled	Mexico: 195
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Russian Federation: 127
Country: Number of subjects enrolled	South Africa: 140
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Thailand: 4
Country: Number of subjects enrolled	Turkey: 8
Country: Number of subjects enrolled	Ukraine: 99
Country: Number of subjects enrolled	United States: 1902
Worldwide total number of subjects	2736
EEA total number of subjects	237

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	2508
From 65 to 84 years	221
85 years and over	7

Subject disposition

Recruitment

Recruitment details:

Subjects who had a negative screening severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) rapid antigen test result and were asymptomatic household contacts of individuals who were symptomatic and recently tested positive for SARS-CoV-2, were included in the study.

Pre-assignment

Screening details:

A total of 2880 subjects were screened. Out of which, 122 subjects were screen failures. 22 subjects were not screen failures and were not randomised. 2736 subjects were randomised and 2721 subjects received study drug.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days

Arm description:

Subjects were randomised to receive nirmatrelvir 300 milligrams (mg) and ritonavir 100 mg orally every 12 hours from Day 1 to 5, followed by matching placebo every 12 hours from Day 6 through Day 10.

Arm type	Experimental
Investigational medicinal product name	Nirmatrelvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Nirmatrelvir 300 mg every 12 hours

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo every 12 hours

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ritonavir 100 mg every 12 hours

Arm title	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days

Arm description:

Subjects were randomised to receive nirmatrelvir 300 mg and ritonavir 100 mg orally every 12 hours from Day 1 to 10.

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

Dosage and administration details:

Ritonavir 100 mg every 12 hours

Investigational medicinal product name	Nirmatrelvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Nirmatrelvir 300 mg every 12 hours

Arm title	Placebo

Arm description:

Subjects were randomised to receive placebo matched to nirmatrelvir/ritonavir every 12 hours for 10 days from Day 1 through Day 10.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo every 12 hours

Number of subjects in period 1	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo
Started	921	917	898
Treated	913	911	897
Completed	877	864	863
Not completed	44	53	35
Consent withdrawn by subject	25	36	23
Unspecified	10	6	5
Lost to follow-up	9	11	7

Baseline characteristics

Reporting groups

Reporting group title	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days
Reporting group description:	

Subjects were randomised to receive nirmatrelvir 300 milligrams (mg) and ritonavir 100 mg orally every 12 hours from Day 1 to 5, followed by matching placebo every 12 hours from Day 6 through Day 10.

Reporting group title	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days
Reporting group description:	

Subjects were randomised to receive nirmatrelvir 300 mg and ritonavir 100 mg orally every 12 hours from Day 1 to 10.

Reporting group title	Placebo
Reporting group description:	

Subjects were randomised to receive placebo matched to nirmatrelvir/ritonavir every 12 hours for 10 days from Day 1 through Day 10.

Reporting group values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo
Number of subjects	921	917	898
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	842	834	832
From 65-84 years	76	81	64
85 years and over	3	2	2
Age Continuous			
Units: Years			
arithmetic mean	43.92	42.85	42.39
standard deviation	± 14.88	± 15.02	± 14.36
Sex: Female, Male			
Units: Subjects			
Female	502	479	474
Male	419	438	424
Race			
Units: Subjects			
American Indian or Alaska Native	58	52	49
Asian	8	15	11
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	139	136	132
White	714	711	704
More than one race	1	1	1

Unknown or Not Reported	1	2	1
Ethnicity			
Units: Subjects			
Hispanic or Latino	664	642	643
Not Hispanic or Latino	257	275	255
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	2736		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	2508		
From 65-84 years	221		
85 years and over	7		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Subjects			
Female	1455		
Male	1281		
Race			
Units: Subjects			
American Indian or Alaska Native	159		
Asian	34		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	407		
White	2129		
More than one race	3		
Unknown or Not Reported	4		
Ethnicity			
Units: Subjects			
Hispanic or Latino	1949		
Not Hispanic or Latino	787		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days

Reporting group description:

Subjects were randomised to receive nirmatrelvir 300 milligrams (mg) and ritonavir 100 mg orally every 12 hours from Day 1 to 5, followed by matching placebo every 12 hours from Day 6 through Day 10.

Reporting group title	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days

Reporting group description:

Subjects were randomised to receive nirmatrelvir 300 mg and ritonavir 100 mg orally every 12 hours from Day 1 to 10.

Reporting group title	Placebo

Reporting group description:

Subjects were randomised to receive placebo matched to nirmatrelvir/ritonavir every 12 hours for 10 days from Day 1 through Day 10.

Primary: Percentage of Subjects who Developed Symptomatic RT-PCR or RAT Confirmed SARS-CoV-2 Infection Through Day 14: Among Participants With Negative RT-PCR at Baseline

End point title	Percentage of Subjects who Developed Symptomatic RT-PCR or RAT Confirmed SARS-CoV-2 Infection Through Day 14: Among Participants With Negative RT-PCR at Baseline

End point description:

Percentage of subjects who developed symptomatic RT-PCR or RAT confirmed SARS-Cov-2 infection were reported in this end point. Modified Intent-To-Treat (mITT) population included all subjects randomly assigned to study intervention who received at least 1 dose of study intervention and had a negative RT-PCR result at baseline.

End point type	Primary

End point timeframe:

From Day 1 to Day 14

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	844	830	840	
Units: Percentage of subjects				
number (not applicable)	2.607	2.410	3.929	

Statistical analyses

Statistical analysis title	Nirmatrelvir300 mg+Ritonavir100 mg10 Days,Placebo

Statistical analysis description:

Model included the fixed effects of treatment, geographic regions and presence of risk factors.

Compound symmetry variance-covariance structure.

Comparison groups	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days v Placebo
Number of subjects included in analysis	1670
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1163
Method	GEE
Parameter estimate	Risk ratio (RR)
Point estimate	0.645
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.373
upper limit	1.115

Statistical analysis title	Nirmatrelvir300 mg +Ritonavir100mg 5 Days,Placebo

Statistical analysis description:

Model included the fixed effects of treatment, geographic regions and presence of risk factors. Compound symmetry variance-covariance structure.

Comparison groups	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days v Placebo
Number of subjects included in analysis	1684
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1722
Method	Generalized estimating equation (GEE)
Parameter estimate	Risk ratio (RR)
Point estimate	0.702
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.422
upper limit	1.167

Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious AEs and AEs Leading to Study and Study Drug Discontinuation

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious AEs and AEs Leading to Study and Study Drug Discontinuation

End point description:

An AE was defined as any untoward medical occurrence in a subject temporally associated with the use of study intervention, whether or not considered related to the study intervention. An SAE was defined as any untoward medical occurrence at any dose that resulted in any of the following outcomes: death; life-threatening ; required inpatient hospitalisation or prolongation of existing hospitalisation; persistent or significant disability/incapacity ; congenital anomaly/birth defect; or that was considered as an important medical event. TEAEs were defined as events that started on or after the study medication start date and time. AEs included both serious and all non-serious adverse events. AEs that led to study discontinuation and AEs that led to discontinuation of study intervention and then continued study were also reported in this end point. Safety analysis set included all subjects randomly assigned to study intervention and who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

From start of study intervention (Day 1) up to end of safety follow-up (Day 38)

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	912	911	898	
Units: Subjects				
TEAEs	218	212	195	
SAEs	3	1	2	
AEs led to discontinuation of study	0	0	0	
AEs:discontinue study intervention,continued study	10	11	14	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Developed Symptomatic RT-PCR or RAT Confirmed SARS-CoV-2 Infection Through Day 14: Among Subjects With Negative RT-PCR at Baseline With Increased Risk of Severe COVID-19 Illness

End point title	Percentage of Subjects who Developed Symptomatic RT-PCR or RAT Confirmed SARS-CoV-2 Infection Through Day 14: Among Subjects With Negative RT-PCR at Baseline With Increased Risk of Severe COVID-19 Illness

End point description:

Percentage of subjects who had a symptomatic RT-PCR or RAT confirmed SARS-Cov-2 infection were reported in this end point. The risk factors associated with severe covid-19 illness included age greater than or equal to 60 years, body mass index greater than 25, social history of smoking and presence of comorbidities. Modified Intent-To-Treat (mITT2) population included all subjects randomly assigned to study intervention who received at least 1 dose of study intervention and had a negative RT-PCR result at baseline and were at increased risk of severe COVID-19 illness.

End point type	Secondary

End point timeframe:

From Day 1 to Day 14

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	627	605	606	
Units: Percentage of subjects				
number (not applicable)	2.871	2.645	3.465	

Statistical analyses

Statistical analysis title	Nirmatrelvir300 mg+Ritonavir100 mg 10 Days,Placebo
Statistical analysis description:	
Model included the fixed effects of treatment, geographic regions. Compound symmetry variance-covariance structure.	
Comparison groups	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days v Placebo
Number of subjects included in analysis	1211
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.507
Method	GEE
Parameter estimate	Risk ratio (RR)
Point estimate	0.809
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.433
upper limit	1.512

Statistical analysis title	Nirmatrelvir300 mg+Ritonavir100 mg 5 Days,Placebo
Statistical analysis description:	
Model included the fixed effects of treatment, geographic regions. Compound symmetry variance-covariance structure.	
Comparison groups	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days v Placebo
Number of subjects included in analysis	1233
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6766
Method	GEE
Parameter estimate	Risk ratio (RR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.484
upper limit	1.602

Secondary: Percentage of Subjects With COVID-19 Related Hospitalization or Death

From any Cause Through Day 28: Among Subjects With Negative RT-PCR at Baseline With Increased Risk of Severe COVID-19 Illness

End point title	Percentage of Subjects With COVID-19 Related Hospitalization or Death From any Cause Through Day 28: Among Subjects With Negative RT-PCR at Baseline With Increased Risk of Severe COVID-19 Illness

End point description:

The risk factors associated with severe covid-19 illness included age greater than or equal to 60 years, body mass index greater than 25, social history of smoking and presence of comorbidities. mITT2 population included all subjects randomly assigned to study intervention who received at least 1 dose of study intervention and had a negative RT-PCR result at baseline and were at increased risk of severe COVID-19 illness.

End point type	Secondary

End point timeframe:

From Day 1 to Day 28

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	627	605	606	
Units: Percentage of subjects				
number (not applicable)	0	0	0.165	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Asymptomatic RT-PCR or RAT Confirmed SARS-CoV-2 Infection Through Day 14: Among Subjects With Negative RT-PCR at Baseline

End point title	Percentage of Subjects With Asymptomatic RT-PCR or RAT Confirmed SARS-CoV-2 Infection Through Day 14: Among Subjects With Negative RT-PCR at Baseline

End point description:

Percentage of subjects who had asymptomatic RT-PCR or RAT confirmed SARS-CoV-2 infection through day 14 among subjects with negative RT-PCR at baseline were reported in this end point. Index case was defined as subjects with symptomatic COVID-19. mITT population included all subjects randomly assigned to study intervention who received at least 1 dose of study intervention and had a negative RT-PCR result at baseline.

End point type	Secondary

End point timeframe:

From Day 1 to Day 14

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	844	830	840	
Units: Percentage of subjects				
number (not applicable)	2.014	1.928	3.095	

Statistical analyses

Statistical analysis title	Nirmatrelvir 300 mg+Ritonavir100mg 10 Days,Placebo
Statistical analysis description:	
Model included the fixed effects of treatment, geographic regions and presence of risk factors. Compound symmetry variance-covariance structure.	
Comparison groups	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days v Placebo
Number of subjects included in analysis	1670
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1221
Method	GEE
Parameter estimate	Risk ratio (RR)
Point estimate	0.633
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.355
upper limit	1.13

Statistical analysis title	Nirmatrelvir300 mg+Ritonavir100 mg 5 Days,Placebo
Statistical analysis description:	
Model included the fixed effects of treatment, geographic regions and presence of risk factors. Compound symmetry variance-covariance structure.	
Comparison groups	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days v Placebo
Number of subjects included in analysis	1684
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1869
Method	GEE
Parameter estimate	Risk ratio (RR)
Point estimate	0.672
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.373
upper limit	1.213

Secondary: Time to RT-PCR or RAT Confirmed SARS-CoV-2 Infection Through Day 14: Among Subjects With Negative RT-PCR at Baseline

End point title	Time to RT-PCR or RAT Confirmed SARS-CoV-2 Infection Through Day 14: Among Subjects With Negative RT-PCR at Baseline

End point description:

Number of days between first dose and confirmation of the SARS-CoV-2 infection by RT-PCR or RAT was reported in this end point. mITT population included all subjects randomly assigned to study intervention who received at least 1 dose of study intervention and had a negative RT-PCR result at baseline. 99999 indicates median and the corresponding 95% confidence interval could not be calculated as there were less number of subjects with event.

End point type	Secondary

End point timeframe:

From Day 1 to Day 14

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	844	830	840	
Units: Days				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

Statistical analysis title	Nirmatrelvir300 mg+Ritonavir100 mg 10 Days,Placebo
Comparison groups	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days v Placebo
Number of subjects included in analysis	1670
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0186
Method	Logrank

Statistical analysis title	Nirmatrelvir300 mg+Ritonavir100mg 5 Days,Placebo
Comparison groups	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days v Placebo

Number of subjects included in analysis	1684
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0368
Method	Logrank

Secondary: Percentage of Subjects With Symptomatic RT-PCR or RAT Confirmed SARS-CoV-2 Infection Through Day 14: Among Subjects With Positive RT-PCR at Baseline

End point title	Percentage of Subjects With Symptomatic RT-PCR or RAT Confirmed SARS-CoV-2 Infection Through Day 14: Among Subjects With Positive RT-PCR at Baseline

End point description:

Percentage of subjects with a positive RT-PCR result at baseline who had a symptomatic SARS-CoV-2 infection confirmed by RAT or RT-PCR through Day 14 were reported in this end point. mITT1 population included all subjects randomly assigned to study intervention who received at least 1 dose of study intervention and had a positive RT-PCR result at baseline.

End point type	Secondary

End point timeframe:

From Day 1 to Day 14

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	48	29	
Units: Percentage of subjects				
number (not applicable)	28.947	45.833	37.931	

Statistical analyses

Statistical analysis title	Nirmatrelvir300 mg+Ritonavir100 mg 10 Days,Placebo

Statistical analysis description:

Model included the fixed effects of treatment, geographic regions and presence of risk factors. Compound symmetry variance-covariance structure.

Comparison groups	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days v Placebo
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4273
Method	GEE
Parameter estimate	Risk ratio (RR)
Point estimate	1.244

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.725
upper limit	2.135

Statistical analysis title	Nirmatrelvir300 mg+Ritonavir100 mg 5 Days,Placebo

Statistical analysis description:

Model included the fixed effects of treatment, geographic regions and presence of risk factors. Compound symmetry variance-covariance structure.

Comparison groups	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4126
Method	GEE
Parameter estimate	Risk ratio (RR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.378
upper limit	1.491

Secondary: Percentage of Subjects With Symptomatic RT-PCR or RAT Confirmed SARS-CoV-2 Infection Through Day 14: Among Subjects With Negative, Positive or Missing RT-PCR at Baseline

End point title	Percentage of Subjects With Symptomatic RT-PCR or RAT Confirmed SARS-CoV-2 Infection Through Day 14: Among Subjects With Negative, Positive or Missing RT-PCR at Baseline

End point description:

Percentage of subjects with a negative, positive, or missing RT-PCR result at baseline, who had a symptomatic SARS-CoV-2 infection confirmed by RAT or RT-PCR through Day 14 were reported in this end point. Index case was defined as subjects with symptomatic COVID-19. Modified Intent-To-Treat (mITT3) population included all subjects randomly assigned to study intervention who received at least 1 dose of study intervention and had a negative, positive or missing RT-PCR result at baseline.

End point type	Secondary

End point timeframe:

From Day 1 to Day 14

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	889	887	873	
Units: Percentage of subjects				
number (not applicable)	3.712	4.848	5.269	

Statistical analyses

Statistical analysis title	Nirmatrelvir300 mg+Ritonavir100 mg 5 Days,Placebo
Statistical analysis description:	
Model included the fixed effects of treatment, geographic regions and presence of risk factors. Compound symmetry variance-covariance structure.	
Comparison groups	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days v Placebo
Number of subjects included in analysis	1762
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1333
Method	GEE
Parameter estimate	Risk ratio (RR)
Point estimate	0.726
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.478
upper limit	1.103

Statistical analysis title	Nirmatrelvir 300 mg + Ritonavir 100 mg 10 Days
Statistical analysis description:	
Model included the fixed effects of treatment, geographic regions and presence of risk factors. Compound symmetry variance-covariance structure.	
Comparison groups	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days v Placebo
Number of subjects included in analysis	1760
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8088
Method	GEE
Parameter estimate	Risk ratio (RR)
Point estimate	0.953
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.645
upper limit	1.408

Secondary: Percentage of Subjects With no, Mild, Moderate, or Severe Signs and Symptoms Attributed to COVID-19 Through Day 28: Among Subjects With Negative RT-PCR at Baseline

End point title	Percentage of Subjects With no, Mild, Moderate, or Severe Signs and Symptoms Attributed to COVID-19 Through Day 28: Among Subjects With Negative RT-PCR at Baseline

End point description:

Subjects were categorised according to severity of signs and symptoms as no, mild, moderate, severe in this end point. The 12 signs and symptoms included stuffy or runny nose, sore throat, shortness of breath or difficulty breathing, cough, low energy or tiredness, muscle or body aches, headache, chills or shivering, feeling hot or feverish, nausea, vomiting, diarrhea. Subjects recorded their daily severity rating of their symptoms over the past 24 hours based on a 4-point scale in which 0 was reported if no symptoms were present; 1 if mild; 2 if moderate; and 3 if severe. mITT population included all subjects randomly assigned to study intervention who received at least 1 dose of study intervention and had a negative RT-PCR result at baseline.

End point type	Secondary

End point timeframe:

From Day 1 to Day 28

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	844	830	840	
Units: Percentage of subjects				
number (not applicable)				
No	81.517	83.373	81.667	
Mild	7.820	8.193	7.619	
Moderate	6.872	5.060	7.143	
Severe	2.133	2.048	2.738	
Missing	1.659	1.325	0.833	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Days of Symptomatic RT-PCR or RAT Confirmed SARS-CoV- 2 Infection Through Day 28: Among Subjects With Negative RT-PCR at Baseline

End point title	Number of Days of Symptomatic RT-PCR or RAT Confirmed SARS-CoV- 2 Infection Through Day 28: Among Subjects With Negative RT-PCR at Baseline

End point description:

This end point has been reported in terms of number of subjects according to days of symptomatic SARS-CoV-2 infection through Day 28. mITT population included all subjects randomly assigned to study intervention who received at least 1 dose of study intervention and had a negative RT-PCR result at baseline. Here, "Number of Subjects Analysed" signifies subjects evaluable for this end point.

End point type	Secondary

End point timeframe:
From Day 1 to Day 28

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	20	33	
Units: Subjects				
1 Day of Symptoms	1	7	2	
2 Days of Symptoms	2	0	1	
3 Days of Symptoms	0	1	4	
4 Days of Symptoms	5	0	2	
5 Days of Symptoms	1	3	3	
6 Days of Symptoms	0	1	3	
7 Days of Symptoms	3	4	4	
8 Days of Symptoms	2	0	5	
9 Days of Symptoms	0	1	1	
10 Days of Symptoms	0	0	1	
11 Days of Symptoms	0	1	1	
12 Days of Symptoms	2	0	4	
13 Days of Symptoms	1	1	2	
14 Days of Symptoms	1	1	0	
18 Days of Symptoms	2	0	0	
20 Days of Symptoms	1	0	0	
26 Days of Symptoms	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration Versus Time Summary of Nirmatrelvir (PF-07321332)

End point title	Plasma Concentration Versus Time Summary of Nirmatrelvir (PF-07321332)[1]

End point description:

Safety analysis set included all subjects randomly assigned to study intervention and who received at least 1 dose of study intervention. This end point was not planned to be analyzed for placebo arm. Here, ''Overall Number of Subjects Analysed signifies subjects evaluable for this end point and ''Number Analyzed'' signifies subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:
Day 1: 1 hour post dose; Day 5: 2 hours pre-dose

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only descriptive analysis was planned for this endpoint.

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	476	476		
Units: Nanograms per milliliter				
arithmetic mean (standard deviation)				
Day 1: 1 hour post-dose (n=159, 156)	1489 (± 1481.4)	1472 (± 1488.2)		
Day 5: 2 hours pre-dose (n=476, 476)	1688 (± 2093.3)	1657 (± 2068.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Viral Load in Nasal Samples Over Time: Among Subjects With Negative RT-PCR at Baseline

End point title	Viral Load in Nasal Samples Over Time: Among Subjects With Negative RT-PCR at Baseline

End point description:

Nasal samples were collected to estimate the viral load in terms of logarithm to base 10 (log10) copies per millilitre in subjects with negative RT-PCR at baseline and were reported in this end point. mITT population included all subjects randomly assigned to study intervention who received at least 1 dose of study intervention and had a negative RT-PCR result at baseline. Here 'Number Analyzed' signifies subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

From Day 1 to Day 14

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	844	830	840	
Units: Log 10 copies per millilitre				
arithmetic mean (standard deviation)				
Day 1(n=844, 830,840)	0.042 (± 0.265)	0.035 (± 0.241)	0.038 (± 0.253)	
Day 2(n=810,802,809)	0.078 (± 0.523)	0.053 (± 0.409)	0.108 (± 0.611)	
Day 3(n=823, 812,812)	0.090 (± 0.586)	0.048 (± 0.374)	0.147 (± 0.760)	

Day 4(n=820,808,813)	0.081 (± 0.537)	0.057 (± 0.409)	0.165 (± 0.859)
Day 5(n=736,737,742)	0.079 (± 0.528)	0.074 (± 0.573)	0.217 (± 1.063)
Day 6(n=817,799,812)	0.074 (± 0.575)	0.090 (± 0.670)	0.189 (± 0.978)
Day 7(n=815,798,806)	0.088 (± 0.586)	0.053 (± 0.536)	0.186 (± 0.883)
Day 8(n=814,796,805)	0.096 (± 0.627)	0.081 (± 0.669)	0.159 (± 0.860)
Day 9(n=810,795,807)	0.094 (± 0.672)	0.062 (± 0.596)	0.135 (± 0.784)
Day 10(n=733,715,714)	0.080 (± 0.616)	0.064 (± 0.590)	0.133 (± 0.725)
Day 11(n=797,789,793)	0.103 (± 0.673)	0.053 (± 0.511)	0.115 (± 0.707)
Day 12(n=803,783,798)	0.106 (± 0.748)	0.051 (± 0.447)	0.103 (± 0.662)
Day 13(n=797,791,794)	0.085 (± 0.642)	0.052 (± 0.425)	0.117 (± 0.714)
Day 14(n=696,670,686)	0.108 (± 0.717)	0.035 (± 0.386)	0.146 (± 0.798)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Death Event Through Day 38: Among Participants With Negative RT-PCR at Baseline

End point title	Percentage of Subjects With Death Event Through Day 38: Among Participants With Negative RT-PCR at Baseline

End point description:

Percentage of subjects with death (all-cause) event were reported in this end point. mITT population included all participants randomly assigned to study intervention who received at least 1 dose of study intervention and had a negative RT-PCR result at baseline.

End point type	Secondary

End point timeframe:

From Day 1 to Day 38

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	844	830	840	
Units: Percentage of subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Viral Load in Nasal Samples Over Time: Among Subjects With Positive RT-PCR at Baseline

End point title	Viral Load in Nasal Samples Over Time: Among Subjects With Positive RT-PCR at Baseline

End point description:

Nasal samples were collected to estimate the viral load in terms of logarithm to base 10 (log10) copies per millilitre in subjects with negative RT-PCR at baseline and were reported in this end point. mITT1 population included all subjects randomly assigned to study intervention who received at least 1 dose of study intervention and had a positive RT-PCR result at baseline. Here 'Number Analyzed' signifies subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

From Day 1 to Day 14

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	48	29	
Units: Log 10 copies per millilitre				
arithmetic mean (standard deviation)				
Day 1(n=38,48,29)	4.870 (± 2.041)	4.470 (± 1.542)	4.837 (± 1.577)	
Day 2(n=38,45,28)	3.286 (± 2.534)	2.724 (± 2.208)	3.104 (± 2.909)	
Day 3(n=38,46,28)	2.880 (± 2.641)	2.051 (± 2.212)	3.255 (± 2.702)	
Day 4(n=36,47,28)	2.600 (± 2.427)	1.514 (± 2.064)	2.721 (± 2.640)	
Day 5(n=35,43,27)	1.470 (± 2.057)	1.413 (± 1.745)	2.994 (± 2.677)	
Day 6(n=38,44,28)	1.065 (± 1.656)	0.997 (± 1.696)	2.466 (± 2.561)	
Day 7(n=37,45,28)	1.199 (± 1.747)	0.913 (± 1.762)	1.478 (± 2.212)	
Day 8(n=37,45,28)	1.212 (± 1.829)	0.942 (± 1.908)	1.072 (± 1.663)	
Day 9(n=38,44,28)	1.169 (± 1.852)	0.766 (± 1.858)	1.103 (± 1.545)	
Day 10(n=35,45,28)	0.819 (± 1.656)	0.541 (± 1.605)	0.965 (± 1.514)	
Day 11(n=36,44,28)	0.623 (± 1.170)	0.603 (± 1.044)	0.707 (± 1.116)	
Day 12(n=37,44,28)	0.532 (± 1.136)	0.670 (± 1.204)	0.436 (± 0.919)	
Day 13(n=36,45,26)	0.413 (± 1.098)	0.313 (± 1.018)	0.361 (± 0.770)	
Day 14(n=31,40,25)	0.284 (± 1.040)	0.345 (± 0.808)	0.358 (± 0.735)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Days of Hospitalisation and Intensive Care Unit (ICU) Stay: Among Subjects With Negative RT-PCR at Baseline

End point title	Number of Days of Hospitalisation and Intensive Care Unit (ICU) Stay: Among Subjects With Negative RT-PCR at Baseline
End point description:	

This end point has been presented in terms of subjects according to number of days of hospitalisation and in ICU as 0 days and more than or equal to 1 day. mITT population included all subjects randomly assigned to study intervention who received at least 1 dose of study intervention and had a negative RT-PCR result at baseline.

End point type	Secondary
End point timeframe:	

From Day 1 to Day 28

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	844	830	840	
Units: Subjects				
ICU Visits: 0 Day	844	830	840	
ICU Visits: More than or equal to 1 day	0	0	0	
Hospitalization Visits: 0 Day	844	830	839	
Hospitalization Visit: More than or equal to 1 day	0	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of COVID-19 Related Medical Visits Through Day 28: Among Subjects With Negative RT-PCR at Baseline

End point title	Number of COVID-19 Related Medical Visits Through Day 28: Among Subjects With Negative RT-PCR at Baseline
End point description:	

In this end point, number of COVID-19 related medical visits per day were reported. Number of medical visits per day = number of medical visits/number of days follow up through day 28 visit or the last collection date on or before day 28, if day 28 visit was missing. mITT population included all subjects randomly assigned to study intervention who received at least 1 dose of study intervention and had a

negative RT-PCR result at baseline.

End point type	Secondary
End point timeframe: From Day 1 to Day 28	

End point values	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	844	830	840	
Units: Medical visits per day				
arithmetic mean (standard deviation)	0.0067 (± 0.0200)	0.0057 (± 0.0201)	0.0066 (± 0.0182)	

Statistical analyses

Statistical analysis title	Nirmatrelvir300 mg+Ritonavir100 mg 5 Days,Placebo
Comparison groups	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days v Placebo
Number of subjects included in analysis	1684
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7991
Method	Negative binomial regression model
Parameter estimate	LS Mean Ratio
Point estimate	0.969
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.758
upper limit	1.238

Statistical analysis title	Nirmatrelvir 300 mg + Ritonavir 100 mg 10 Days
Comparison groups	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days v Placebo
Number of subjects included in analysis	1670
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1985
Method	Negative binomial regression model
Parameter estimate	LS Mean Ratio
Point estimate	0.847

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.657
upper limit	1.091

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
From Day 1 to Day 38	
Adverse event reporting additional description:	
Same event may appear as both SAE and non-SAE but are distinct events. An event may be categorised as serious in 1 subject and non-serious in another, or a subject may have experienced both SAE and non-SAE. Safety population comprised of all subjects who received at least 1 dose of study intervention during the study.	
Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days
Reporting group description:	
Subjects were randomised to receive nirmatrelvir 300 mg and ritonavir 100 mg orally every 12 hours from Day 1 to 5, followed by matching placebo every 12 hours from Day 6 through Day 10.	
Reporting group title	Placebo
Reporting group description:	
Subjects were randomised to receive placebo matched to nirmatrelvir/ritonavir every 12 hours for 10 days from Day 1 through Day 10.	
Reporting group title	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days
Reporting group description:	
Subjects were randomised to receive nirmatrelvir 300 mg and ritonavir 100 mg orally every 12 hours from Day 1 to 10.	

Serious adverse events	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Placebo	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 912 (0.33%)	2 / 898 (0.22%)	1 / 911 (0.11%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 912 (0.00%)	1 / 898 (0.11%)	0 / 911 (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
Road traffic accident			

subjects affected / exposed	1 / 912 (0.11%)	0 / 898 (0.00%)	0 / 911 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	1 / 912 (0.11%)	0 / 898 (0.00%)	0 / 911 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 912 (0.11%)	0 / 898 (0.00%)	0 / 911 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 912 (0.11%)	1 / 898 (0.11%)	1 / 911 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 5 Days	Placebo	Nirmatrelvir (PF-07321332) 300 mg + Ritonavir 100 mg 10 Days
Total subjects affected by non-serious adverse events			
subjects affected / exposed	176 / 912 (19.30%)	152 / 898 (16.93%)	173 / 911 (18.99%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 912 (0.22%)	11 / 898 (1.22%)	6 / 911 (0.66%)
occurrences (all)	2	12	8
Activated partial thromboplastin time prolonged			
subjects affected / exposed	11 / 912 (1.21%)	22 / 898 (2.45%)	14 / 911 (1.54%)
occurrences (all)	11	23	15
Fibrin D dimer increased			
subjects affected / exposed	18 / 912 (1.97%)	4 / 898 (0.45%)	13 / 911 (1.43%)
occurrences (all)	18	5	13
Blood thyroid stimulating hormone			

increased			
subjects affected / exposed	11 / 912 (1.21%)	10 / 898 (1.11%)	8 / 911 (0.88%)
occurrences (all)	11	11	8
Blood creatine phosphokinase increased			
subjects affected / exposed	12 / 912 (1.32%)	13 / 898 (1.45%)	15 / 911 (1.65%)
occurrences (all)	12	14	15
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 912 (1.64%)	29 / 898 (3.23%)	17 / 911 (1.87%)
occurrences (all)	16	31	19
Dysgeusia			
subjects affected / exposed	54 / 912 (5.92%)	6 / 898 (0.67%)	62 / 911 (6.81%)
occurrences (all)	54	6	62
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 912 (1.10%)	17 / 898 (1.89%)	7 / 911 (0.77%)
occurrences (all)	11	18	7
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	23 / 912 (2.52%)	15 / 898 (1.67%)	22 / 911 (2.41%)
occurrences (all)	24	15	26
Nausea			
subjects affected / exposed	16 / 912 (1.75%)	14 / 898 (1.56%)	12 / 911 (1.32%)
occurrences (all)	16	16	13
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 912 (1.10%)	12 / 898 (1.34%)	2 / 911 (0.22%)
occurrences (all)	11	15	2
Nasal congestion			
subjects affected / exposed	4 / 912 (0.44%)	10 / 898 (1.11%)	3 / 911 (0.33%)
occurrences (all)	5	10	3
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	20 / 912 (2.19%)	18 / 898 (2.00%)	17 / 911 (1.87%)
occurrences (all)	21	19	17
Nasopharyngitis			

subjects affected / exposed	13 / 912 (1.43%)	6 / 898 (0.67%)	9 / 911 (0.99%)
occurrences (all)	13	6	9
COVID-19			
subjects affected / exposed	27 / 912 (2.96%)	36 / 898 (4.01%)	26 / 911 (2.85%)
occurrences (all)	27	36	26

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 January 2022	Updated the secondary objective and secondary endpoint to assess viral titers in subjects with a positive RT-PCR result at baseline.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported