Clinical trial results:
An Interventional Efficacy and Safety, Phase 2, Randomized, Double-Blind, 3-arm Study to Investigate Nirmatrelvir/Ritonavir in Non-Hospitalized Participants at Least 12 Years of age With Symptomatic COVID-19 who are Immunocompromised

Summary

EudraCT number	2022-001362-35
Trial protocol	ES BG HU SK
Global end of trial date	13 November 2023

Results information

Result version number	v1 (current)
This version publication date	10 May 2024
First version publication date	10 May 2024

Trial information

Trial identification

Sponsor protocol code	C4671034

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05438602
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer Inc., Pfizer ClinicalTrials.gov Call Center, 001 8007181021, ClinicalTrials.gov_Inquires@pfizer.com
Scientific contact	Pfizer Inc., Pfizer ClinicalTrials.gov Call Center, 001 8007181021, ClinicalTrials.gov_Inquires@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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the effect of nirmatrelvir/ritonavir on viral ribonucleic acid (RNA) levels in nasopharyngeal (NP) swabs over time for the treatment of COVID-19 in non-hospitalized symptomatic participants more than or equal to (>=) 12 years of age with COVID-19 who were immunocompromised.

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 participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 August 2022
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	Spain: 51
Country: Number of subjects enrolled	Bulgaria: 1
Country: Number of subjects enrolled	Slovakia: 25
Country: Number of subjects enrolled	Mexico: 24
Country: Number of subjects enrolled	United States: 38
Worldwide total number of subjects	157
EEA total number of subjects	77

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)	1
Adults (18-64 years)	107
From 65 to 84 years	49
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Main study population (MSP): Participants aged >= 12 years weighing >= 40 kilogram(kg) who were immunocompromised and diagnosed with symptomatic COVID-19 were enrolled. Rebound population (RP): Participants with documented, symptomatic COVID-19 rebound within 14 days after 5-day treatment with nirmatrelvir/ritonavir were enrolled.

Pre-assignment

Screening details:

MSP: A total of 156 participants were enrolled and 155 participants were treated. RP: A total of 2 participants were enrolled and treated.

Period 1

Period 1 title	Treatment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Carer, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day

Arm description:

Participants (MSP + RP) received nirmatrelvir 300 milligram (mg) and ritonavir 100 mg orally every 12 hours (q12h) for 5 days. Participants with estimated glomerular filtration rate (eGFR) >=30 to less than (<) 60 milliliters per minute (mL/min)/1.73 square meter (m^2) or estimated creatinine clearance (eCrCl) >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 5 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 10 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Arm type	Experimental
Investigational medicinal product name	Nirmatrelvir
Investigational medicinal product code	PF-07321332
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received nirmatrelvir 300 mg every 12 hours for 5 days.

Investigational medicinal product name	Placebo for Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received placebo for ritonavir every 12 hours for 10 days.

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

Dosage and administration details:

Participants received placebo for nirmatrelvir every 12 hours for 10 days.

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

Dosage and administration details:

Participants received ritonavir 100 mg every 12 hours for 5 days.

Arm title	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day

Arm description:

Participants (MSP + RP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 10 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 10 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 5 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Arm type	Experimental
Investigational medicinal product name	Nirmatrelvir
Investigational medicinal product code	PF-07321332
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received nirmatrelvir 300 mg every 12 hours for 10 days.

Investigational medicinal product name	Placebo for Nirmatrelvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received placebo for nirmatrelvir every 12 hours for 5 days.

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

Dosage and administration details:

Participants received placebo for ritonavir every 12 hours for 5 days.

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

Dosage and administration details:

Participants received ritonavir 100 mg every 12 hours for 10 days.

Arm title	Nirmatrelvir + Ritonavir 15 Day

Arm description:

Participants (MSP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 5 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 15 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

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:

Participants received ritonavir 100 mg every 12 hours for 15 days.

Investigational medicinal product name	Nirmatrelvir
Investigational medicinal product code	PF-07321332
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received nirmatrelvir 300 mg every 12 hours for 15 days.

Number of subjects in period 1	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day
Started	54	52	51
Completed	50	49	43
Not completed	4	3	8
Withdrawal by Participant	2	1	4
No longer met eligibility criteria	-	1	-
Adverse event	2	1	3
Unspecified	-	-	1

Period 2

Period 2 title	Follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Carer, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Nirmatrelvir + Ritonavir 5 day Then Placebo 10 Day

Arm description:

Participants (MSP + RP) received nirmatrelvir 300 milligram (mg) and ritonavir 100 mg orally every 12 hours (q12h) for 5 days. Participants with estimated glomerular filtration rate (eGFR) >=30 to less than (<) 60 milliliters per minute (mL/min)/1.73 square meter (m^2) or estimated creatinine clearance (eCrCl) >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 5 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 10 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Nirmatrelvir + Ritonavir 10-day Then Placebo 5 Day

Arm description:

Participants (MSP + RP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 10 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 10 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 5 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Nirmatrelvir + Ritonavir 15 Day

Arm description:

Participants (MSP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 5 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 15 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Nirmatrelvir + Ritonavir 5 day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10-day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day
Started	50	49	43
Completed	50	50	45
Not completed	4	2	6
Withdrawal by Participant	3	2	6
Adverse event	1	-	-
Joined	4	3	8
Discontinued treatment but followed up	4	3	8

Period 3

Period 3 title	Long-term follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Carer, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Nirmatrelvir + Ritonavir 5 day Then Placebo 10 Day

Arm description:

Participants (MSP + RP) received nirmatrelvir 300 milligram (mg) and ritonavir 100 mg orally every 12 hours (q12h) for 5 days. Participants with estimated glomerular filtration rate (eGFR) >=30 to less than (<) 60 milliliters per minute (mL/min)/1.73 square meter (m^2) or estimated creatinine clearance (eCrCl) >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 5 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 10 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Nirmatrelvir + Ritonavir 10-day Then Placebo 5 Day

Arm description:

Participants (MSP + RP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 10 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 10 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 5 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Nirmatrelvir + Ritonavir 15 Day

Arm description:

Participants (MSP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 5 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 15 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 3	Nirmatrelvir + Ritonavir 5 day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10-day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day
Started	50	50	45
Completed	47	47	44
Not completed	7	5	7
Withdrawal by Participant	4	5	6
Death	1	-	1
Unspecified	1	-	-
Lost to follow-up	1	-	-
Joined	4	2	6
Also eligible for long term follow-up	4	2	6

Baseline characteristics

Reporting groups	
Reporting group title	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day
Reporting group description:	
Participants (MSP + RP) received nirmatrelvir 300 milligram (mg) and ritonavir 100 mg orally every 12 hours (q12h) for 5 days. Participants with estimated glomerular filtration rate (eGFR) >=30 to less than (<) 60 milliliters per minute (mL/min)/1.73 square meter (m^2) or estimated creatinine clearance (eCrCl) >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 5 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 10 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.	
Reporting group title	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day
Reporting group description:	
Participants (MSP + RP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 10 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 10 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 5 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.	
Reporting group title	Nirmatrelvir + Ritonavir 15 Day
Reporting group description:	
Participants (MSP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 5 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 15 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.	

Reporting group values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day
Number of subjects	54	52	51
Age Categorical Units: Participants			
Adolescents (12-17 years)	0	1	0
Adults (18-64 years)	34	35	38
From 65-84 years	20	16	13
Age Continuous Units: years			
arithmetic mean	57.09	54.77	55.63
standard deviation	± 14.77	± 16.20	± 14.44
Gender Categorical Units: Participants			
Female	28	30	26
Male	26	22	25
Race Units: Subjects			
White	50	47	44
Black or African American	1	0	1
American Indian or Alaska Native	1	3	3
Not reported	2	1	3
Asian	0	1	0
Ethnicity Units: Subjects			
Hispanic or Latino	36	33	32

Not Hispanic or Latino	16	19	19
Not Reported	2	0	0

Reporting group values	Total		
Number of subjects	157		
Age Categorical Units: Participants			
Adolescents (12-17 years)	1		
Adults (18-64 years)	107		
From 65-84 years	49		
Age Continuous Units: years arithmetic mean standard deviation	 -		
Gender Categorical Units: Participants			
Female	84		
Male	73		
Race Units: Subjects			
White	141		
Black or African American	2		
American Indian or Alaska Native	7		
Not reported	6		
Asian	1		
Ethnicity Units: Subjects			
Hispanic or Latino	101		
Not Hispanic or Latino	54		
Not Reported	2		

End points reporting groups

Reporting group title	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day

Reporting group description:

Participants (MSP + RP) received nirmatrelvir 300 milligram (mg) and ritonavir 100 mg orally every 12 hours (q12h) for 5 days. Participants with estimated glomerular filtration rate (eGFR) >=30 to less than (<) 60 milliliters per minute (mL/min)/1.73 square meter (m^2) or estimated creatinine clearance (eCrCl) >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 5 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 10 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Reporting group title	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day

Reporting group description:

Participants (MSP + RP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 10 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 10 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 5 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Reporting group title	Nirmatrelvir + Ritonavir 15 Day

Reporting group description:

Participants (MSP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 5 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 15 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Reporting group title	Nirmatrelvir + Ritonavir 5 day Then Placebo 10 Day

Reporting group description:

Participants (MSP + RP) received nirmatrelvir 300 milligram (mg) and ritonavir 100 mg orally every 12 hours (q12h) for 5 days. Participants with estimated glomerular filtration rate (eGFR) >=30 to less than (<) 60 milliliters per minute (mL/min)/1.73 square meter (m^2) or estimated creatinine clearance (eCrCl) >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 5 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 10 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Reporting group title	Nirmatrelvir + Ritonavir 10-day Then Placebo 5 Day

Reporting group description:

Participants (MSP + RP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 10 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 10 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 5 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Reporting group title	Nirmatrelvir + Ritonavir 15 Day

Reporting group description:

Participants (MSP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 5 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 15 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Reporting group title	Nirmatrelvir + Ritonavir 5 day Then Placebo 10 Day

Reporting group description:

Participants (MSP + RP) received nirmatrelvir 300 milligram (mg) and ritonavir 100 mg orally every 12 hours (q12h) for 5 days. Participants with estimated glomerular filtration rate (eGFR) >=30 to less than (<) 60 milliliters per minute (mL/min)/1.73 square meter (m^2) or estimated creatinine clearance (eCrCl) >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 5 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 10 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Reporting group title	Nirmatrelvir + Ritonavir 10-day Then Placebo 5 Day

Reporting group description:

Participants (MSP + RP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 10 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 10 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 5 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Reporting group title	Nirmatrelvir + Ritonavir 15 Day

Reporting group description:

Participants (MSP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 5 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 15 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Primary: Percentage of Participants With Sustained Nasopharyngeal (NP) Swab Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Ribonucleic Acid (RNA) < Lower Limit of Quantitation (LLOQ) From Day 15 to Day 44: MSP

End point title	Percentage of Participants With Sustained Nasopharyngeal (NP) Swab Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Ribonucleic Acid (RNA) < Lower Limit of Quantitation (LLOQ) From Day 15 to Day 44: MSP[1]

End point description:

An NP swab was collected by healthcare professional (HCP) from participants and were sent to the central laboratory for viral RNA level testing real-time reverse transcriptase-polymerase chain reaction(RT-PCR). Sustained was defined as NP swab SARS-CoV-2 RNA level not >=2.0 log10 copies/mL at any study visit (through Day 44) following the first study visit where the participant's NP swab SARS-CoV-2 RNA <LLOQ (<2.0 log10 copies/mL). Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention.

End point type	Primary

End point timeframe:

From Day 15 to Day 44

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned for this endpoint.

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Percentage of participants				
number (not applicable)	61.54	70.83	66.00	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With SARS-CoV-2 RNA < LLOQ in Plasma Over Time at Each Visit Through Week 24: MSP

End point title	Percentage of Participants With SARS-CoV-2 RNA < LLOQ in Plasma Over Time at Each Visit Through Week 24: MSP

End point description:

A 6-mL blood sample was collected for adult and paediatric participants and was analysed to measure SARS-CoV-2 RNA by RT-PCR. The LLOQ is <2.0 log10 copies/mL. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Baseline; Days 5, 10, 15, 21, 28, 35, and 44; Weeks 12 and 24

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Percentage of participants				
number (not applicable)				
Baseline	98.08	97.92	92.00	
Day 5	90.38	93.75	92.00	
Day 10	92.31	95.83	92.00	
Day 15	88.46	91.67	88.00	
Day 21	86.54	93.75	88.00	
Day 28	84.62	95.83	78.00	
Day 35	82.69	93.75	84.00	
Day 44	86.54	91.67	88.00	
Week 12	73.08	87.50	78.00	
Week 24	69.23	85.42	84.00	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Sustained NP Swab SARS-CoV-2 RNA < LLOQ for Participants Through Day 44 With NP Swab SARS-CoV-2 RNA >= LLOQ at Baseline: MSP

End point title	Time to First Sustained NP Swab SARS-CoV-2 RNA < LLOQ for Participants Through Day 44 With NP Swab SARS-CoV-2 RNA >= LLOQ at Baseline: MSP

End point description:

An NP swab was collected by HCP from participants and were sent to the central laboratory for viral RNA level testing RT-PCR. Sustained was defined as NP swab SARS-CoV-2 RNA level not >=2.0 log10 copies/mL at any study visit (through Day 44) following the first study visit where the participant's NP swab SARS-CoV-2 RNA <LLOQ (<2.0 log10 copies/mL). The LLOQ is <2.0 log10 copies/mL. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention. Here, 'Number of Participants Analysed' signifies with non-missing data in the analysis set.

End point type	Secondary

End point timeframe:

Day 1 through Day 44

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	44	45	
Units: Days				
median (confidence interval 95%)	15.000 (9.000 to 16.000)	11.000 (10.000 to 15.000)	10.000 (9.000 to 16.000)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First NP Swab SARS-Cov-2 RNA <LLOQ for Participants with NP Swab SARS-CoV-2 RNA >= LLOQ at Baseline: MSP

End point title	Time to First NP Swab SARS-Cov-2 RNA <LLOQ for Participants with NP Swab SARS-CoV-2 RNA >= LLOQ at Baseline: MSP

End point description:

An NP swab was collected by HCP from participants and were sent to the central laboratory for viral RNA level testing RT-PCR. The LLOQ is <2.0 log10 copies/mL. Kaplan-Meier method was used for analysis. Time (days) to first NP swab SARS-CoV-2 RNA<LLOQ was calculated as (First Event Date) - (First Dose Date) +1. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention. Here, 'Number of Participants Analysed' signifies with non-missing data in the analysis set.

End point type	Secondary

End point timeframe:

Day 1 through Day 44

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	44	45	
Units: Days				
median (confidence interval 95%)	9.500 (6.000 to 15.000)	11.000 (10.000 to 15.000)	9.000 (6.000 to 11.000)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With SARS-CoV-2 RNA <LLOQ in NP Swabs at Each Study Visit Through Day 44: MSP

End point title	Percentage of Participants With SARS-CoV-2 RNA <LLOQ in NP Swabs at Each Study Visit Through Day 44: MSP

End point description:

An NP swab was collected by HCP from adult and paediatric participants and were sent to the central laboratory for viral RNA level testing RT-PCR. The LLOQ is <2.0 log10 copies/mL. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Baseline; Days 5, 10, 15, 21, 28, 35 and 44

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Percentage of participants				
number (not applicable)				
Baseline	5.77	8.33	4.00	
Day 5	38.46	29.17	38.00	
Day 10	51.92	64.58	58.00	
Day 15	69.23	77.08	72.00	
Day 21	71.15	91.67	78.00	
Day 28	80.77	93.75	76.00	
Day 35	80.77	91.67	84.00	
Day 44	78.85	91.67	88.00	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in SARS-CoV-2 RNA Level in NP Swabs at Days 5, 10, 15, 21, 28, 35 and 44: MSP

End point title	Change From Baseline in SARS-CoV-2 RNA Level in NP Swabs at Days 5, 10, 15, 21, 28, 35 and 44: MSP

End point description:

An NP swab was collected by HCP from adult and paediatric participants and were sent to the central laboratory for viral RNA level testing RT-PCR. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention. Here, "n" signifies participants with non-missing data in the analysis set and evaluable at specified time points. Here "Number of Participants Analysed" were participants evaluable for this outcome measure. All participants reported under 'Number of Participants Analysed' contributed data to table but may not have evaluable data for every row.

End point type	Secondary

End point timeframe:

Baseline; Day 5, 10, 15, 21, 28, 35 and 44

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: log10 copies/mL				
arithmetic mean (standard deviation)				
Change at Day 5 (n=45, 43, 45)	-3.449 (± 1.730)	-3.621 (± 1.521)	-3.746 (± 1.687)	
Change at Day 10 (n=45, 43, 45)	-4.167 (± 2.292)	-4.931 (± 1.899)	-5.002 (± 1.942)	
Change at Day 15 (n=44, 42, 42)	-4.827 (± 2.476)	-5.773 (± 1.473)	-6.009 (± 2.093)	
Change at Day 21 (n=42, 42, 40)	-5.472 (± 2.028)	-6.328 (± 1.472)	-6.319 (± 1.967)	
Change at Day 28 (n=43, 42, 38)	-5.938 (± 2.138)	-6.509 (± 1.571)	-6.530 (± 1.770)	
Change at Day 35 (n=40, 41, 42)	-6.237 (± 1.746)	-6.596 (± 1.453)	-6.633 (± 1.816)	
Change at Day 44 (n=42, 42, 42)	-5.916 (± 1.865)	-6.597 (± 1.445)	-6.707 (± 1.922)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in SARS-CoV-2 RNA Level in Plasma at Days 5, 10, 15, 21, 28, 35 and 44

End point title	Change From Baseline in SARS-CoV-2 RNA Level in Plasma at Days 5, 10, 15, 21, 28, 35 and 44

End point description:

A 6-mL blood sample was collected for adult and paediatric participants and was analysed to measure SARS-CoV-2 RNA by RT-PCR. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention. Here, "n" signifies participants with non-missing data in the analysis set and evaluable at specified time points. Here, ‘Number of Participants Analyzed’ signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline; Days 5, 10, 15, 21, 28, 35 and 44

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	10	15	
Units: log10 copies/mL				
arithmetic mean (standard deviation)				
Change at Day 5 (n=7, 10, 15)	-1.457 (± 0.643)	-1.360 (± 0.717)	-1.528 (± 0.626)	
Change at Day 10 (n=8, 9, 14)	-1.487 (± 0.601)	-1.700 (± 0.000)	-1.880 (± 0.380)	

Change at Day 15 (n=8, 9, 14)	-1.700 (± 0.000)	-1.700 (± 0.000)	-1.880 (± 0.380)	
Change at Day 21 (n=7, 10, 14)	-1.700 (± 0.000)	-1.700 (± 0.000)	-1.880 (± 0.380)	
Change at Day 28 (n=7, 10, 12)	-1.700 (± 0.000)	-1.700 (± 0.000)	-1.910 (± 0.405)	
Change at Day 35 (n= 7, 10, 13)	-1.700 (± 0.000)	-1.700 (± 0.000)	-1.894 (± 0.392)	
Change at Day 44 (n= 7, 10, 14)	-1.700 (± 0.000)	-1.700 (± 0.000)	-1.880 (± 0.380)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Rebound in SARS-CoV-2 RNA Level in NP Swabs at Follow up: MSP

End point title	Number of Participants With Rebound in SARS-CoV-2 RNA Level in NP Swabs at Follow up: MSP

End point description:

Rebound in SARS-CoV-2 RNA level in NP swabs at follow up (ie, any study visit after end of treatment through Day 44) was defined as a half (0.5) log10 copies/mL increase or greater in SARS-CoV-2 RNA level relative to end of treatment SARS-CoV-2 RNA level based on treatment regimen, with a follow-up viral RNA level >= 2.5 log10 copies/mL. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Day 16 through Day 44

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Participants	9	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs) and Adverse Events (AEs) Leading to Treatment Discontinuation: MSP

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs) and Adverse Events (AEs) Leading to Treatment Discontinuation: MSP

End point description:

An adverse event (AE) was any untoward medical occurrence that did not necessarily have a causal

relationship with study treatment. TEAE was an AE that occurred after initiation of study treatment that was not present at the time of treatment start or an AE that increased in severity after the initiation of medication, if the event was present at the time of treatment start emerges. SAE was an AE resulting in any of the following outcomes or considered medically significant: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly or birth defect. Safety population included all randomised participants who received at least 1 dose of the study intervention.

End point type	Secondary

End point timeframe:

Day 1 of dosing up to Week 24

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	51	51	
Units: Participants				
TEAEs	28	34	31	
SAEs	5	1	4	
AEs Leading to Study Treatment Discontinuation	1	1	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With COVID-19-Related Hospitalisation >24 Hours (h) or Death Through Day 28: MSP

End point title	Percentage of Participants With COVID-19-Related Hospitalisation >24 Hours (h) or Death Through Day 28: MSP

End point description:

Hospitalisation >24 h is defined as >24h of acute care in a hospital or similar acute care facility, including emergency rooms or temporary facilities instituted to address medical needs of those with severe COVID-19. This included specialised acute medical care unit within an assisted living facility or nursing home. This did not include hospitalisation for the purposes of public health and/or clinical trial execution. Kaplan-Meier method was used for evaluation. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Day 1 through Day 28

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Percentage of participants				
number (not applicable)				
Hospitalisation	3.846	0	0	
Death	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With COVID-19-Related Hospitalisation Through Day 44 and Week 24: MSP

End point title	Percentage of Participants With COVID-19-Related Hospitalisation Through Day 44 and Week 24: MSP

End point description:

COVID-19 related hospitalisation is defined as >24h of acute care in a hospital or similar acute care facility, including emergency rooms or temporary facilities instituted to address medical needs of those with severe COVID-19. This included specialised acute medical care unit within an assisted living facility or nursing home. This did not include hospitalisation for the purposes of public health and/or clinical trial execution. Kaplan-Meier method was used for evaluation. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Day 1 through Day 44 and Day 1 through Week 24

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Percentage of participants				
number (not applicable)				
Through Day 44	3.846	0	0	
Through Week 24	3.846	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Death Through Week 24: MSP

End point title	Percentage of Participants With Death Through Week 24: MSP

End point description:

Death due to any cause through week 24 was considered. Kaplan-Meier method was used for evaluation. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Day 1 through Week 24

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Percentage of participants				
number (not applicable)	1.923	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With COVID-19-Related Intensive Care Unit (ICU) Admission Through Day 44 and Week 24: MSP

End point title	Percentage of Participants With COVID-19-Related Intensive Care Unit (ICU) Admission Through Day 44 and Week 24: MSP

End point description:

Kaplan-Meier method was used for evaluation. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Day 1 through Day 44 and Day 1 through Week 24

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Percentage of participants				
number (not applicable)				
Through Day 44	1.923	0	0	
Through Week 24	1.923	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Invasive Mechanical Ventilation or Extracorporeal Membrane Oxygenation (ECMO) Through Day 44 and Week 24: MSP

End point title	Percentage of Participants With Invasive Mechanical Ventilation or Extracorporeal Membrane Oxygenation (ECMO) Through Day 44 and Week 24: MSP

End point description:

Invasive mechanical ventilation or ECMO were types of oxygen support received in hospital. Kaplan-Meier method was used for evaluation. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Day 1 through Day 44 and Day 1 through Week 24

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Percentage of participants				
number (not applicable)				
Through Day 44	0	0	0	
Through Week 24	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Days in Hospital and ICU Stay Through Day 44 and Through Week 24: MSP

End point title	Number of Days in Hospital and ICU Stay Through Day 44 and Through Week 24: MSP

End point description:

Hospitalization >24 hours is defined as >24h of acute care in a hospital or similar acute care facility, including Emergency Rooms or temporary facilities instituted to address medical needs of those with severe COVID-19. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Day 1 through Day 44 and Day 1 through Week 24

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Days				
arithmetic mean (standard deviation)				
Hospital Stay: Up to Day 44	0.635 (± 3.453)	0.000 (± 0.000)	0.000 (± 0.000)	
Hospital Stay: Up to Week 24	0.635 (± 3.453)	0.000 (± 0.000)	0.000 (± 0.000)	
ICU Stay: Up to Day 44	0.442 (± 3.190)	0.000 (± 0.000)	0.000 (± 0.000)	
ICU Stay: Up to Week 24	0.442 (± 3.190)	0.000 (± 0.000)	0.000 (± 0.000)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of COVID-19-Related Medical Visits Through Day 44 and Through Week 24: MSP

End point title	Number of COVID-19-Related Medical Visits Through Day 44 and Through Week 24: MSP

End point description:

Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Day 1 through Day 44 and Day 1 through Week 24

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Medical visits				
arithmetic mean (standard deviation)				
Through Day 44	0.115 (± 0.615)	0.000 (± 0.000)	0.000 (± 0.000)	
Through Week 24	0.115 (± 0.615)	0.000 (± 0.000)	0.020 (± 0.141)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Alleviation of Each Targeted Signs and Symptoms Through Day 44: MSP

End point title	Time to First Alleviation of Each Targeted Signs and Symptoms Through Day 44: MSP

End point description:

Symptoms alleviation through day44 of each targeted COVID-19 sign/symptom was defined as first time when each targeted symptom scored as moderate/severe at study entry are scored as mild or absent and a targeted symptom scored mild or absent at study entry are scored as absent.COVID-19 targeted signs/symptoms were muscle or body aches,shortness of breath(SOB)or difficulty breathing,chills or shivering, cough,diarrhoea,feeling hot or feverish,headache,nausea,stuffy or runny nose,sense of smell,sense of taste,sore throat,low energy or tiredness, vomit. KM method was used for analysis.Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention.Here,"n"signifies number of participants with non-missing data and with baseline severity of mild,moderate and severe of targeted signs/symptoms.Here'99999'suggests that upper limit/lower limit of CI could not be estimated due to insufficient number of participants with

End point type	Secondary

End point timeframe:

Day 1 through Day 44

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Days				
median (confidence interval 95%)				
Muscle or body aches (n= 36, 39, 41)	6.000 (4.000 to 9.000)	9.000 (4.000 to 9.000)	9.000 (5.000 to 13.000)	
SOB or difficulty breathing(n=26,32,26)	6.000 (4.000 to 9.000)	9.000 (4.000 to 9.000)	6.000 (4.000 to 13.000)	
Chills or shivering (n= 27, 34, 33)	5.000 (4.000 to 6.000)	4.000 (4.000 to 5.000)	5.000 (4.000 to 5.000)	
Cough (n= 50, 44, 44)	6.000 (5.000 to 9.000)	9.000 (6.000 to 9.000)	10.000 (5.000 to 13.000)	
Diarrhea (n= 22, 12, 14)	9.000 (5.000 to 10.000)	5.000 (4.000 to 9.000)	9.000 (4.000 to 22.000)	
Feeling hot or feverish (n= 39, 32, 34)	5.000 (4.000 to 6.000)	4.000 (4.000 to 5.000)	5.000 (4.000 to 5.000)	
Headache (n= 33, 37, 38)	9.000 (4.000 to 15.000)	5.000 (4.000 to 9.000)	5.000 (4.000 to 9.000)	
Nausea (n= 11, 18, 13)	9.000 (4.000 to 13.000)	4.000 (4.000 to 5.000)	6.000 (4.000 to 13.000)	
Stuffy or runny nose (n= 46, 46, 47)	9.000 (6.000 to 11.000)	9.000 (5.000 to 9.000)	9.000 (5.000 to 10.000)	
Sense of smell (n= 15, 21, 20)	9.000 (6.000 to 10.000)	9.000 (4.000 to 10.000)	9.000 (5.000 to 10.000)	
Sense of taste (n= 15, 18, 24)	10.000 (5.000 to 10.000)	9.000 (4.000 to 10.000)	9.000 (6.000 to 13.000)	
Sore throat (n= 33, 38, 37)	6.000 (4.000 to 6.000)	5.000 (4.000 to 9.000)	5.000 (4.000 to 9.000)	
Low energy or tiredness (n= 45, 46, 46)	9.000 (6.000 to 13.000)	9.000 (5.000 to 10.000)	9.000 (5.000 to 14.000)	
Vomit (n= 5, 4, 6)	6.000 (4.000 to 99999)	4.000 (-99999 to 99999)	4.500 (4.000 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Resolution of Each Targeted Signs and Symptoms Through Day 44: MSP

End point title	Time to First Resolution of Each Targeted Signs and Symptoms Through Day 44: MSP

End point description:

Symptoms resolution through day 44 of each targeted COVID-19 sign/symptom was defined as the first time when each targeted symptom scored as mild, moderate or severe at study entry are scored as absent. COVID -19 targeted signs/symptoms were muscle or body aches, SOB or difficulty breathing, chills or shivering, cough, diarrhoea, feeling hot or feverish, headache, nausea, stuffy or runny nose, sense of smell, sense of taste, sore throat, low energy or tiredness, vomit. KM method was used for analysis. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention. Here, "n" signifies number of participants with non-missing data and with baseline severity of mild, moderate and severe of targeted signs and symptoms.
Here'99999'suggests that upper limit of CI could not be estimated due to insufficient number of participants with event.

End point type	Secondary

End point timeframe:

Day 1 through Day 44

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Days				
median (confidence interval 95%)				
Muscle or body aches (n=36, 39, 41)	14.500 (10.000 to 19.000)	11.000 (9.000 to 21.000)	10.000 (6.000 to 20.000)	
SOB or difficulty breathing (n=26, 32, 26)	9.000 (5.000 to 13.000)	9.500 (9.000 to 19.000)	12.000 (6.000 to 19.000)	
Chills or shivering (n=27, 34, 33)	6.000 (4.000 to 9.000)	4.000 (4.000 to 9.000)	5.000 (4.000 to 6.000)	
Cough (n=50, 44, 44)	13.000 (10.000 to 20.000)	12.000 (9.000 to 21.000)	19.500 (11.000 to 22.000)	
Diarrhea (n= 22, 12, 14)	9.000 (6.000 to 10.000)	9.000 (4.000 to 13.000)	16.500 (4.000 to 26.000)	
Feeling hot or feverish (n= 39, 32, 34)	9.000 (5.000 to 9.000)	7.000 (4.000 to 9.000)	5.000 (4.000 to 6.000)	
Headache (n=33, 37, 38)	13.000 (9.000 to 15.000)	10.000 (9.000 to 15.000)	9.000 (5.000 to 11.000)	
Nausea (n=11, 18, 13)	9.000 (4.000 to 14.000)	4.000 (4.000 to 9.000)	9.000 (4.000 to 13.000)	

Stuffy or runny nose (n= 46, 46, 47)	14.000 (10.000 to 22.000)	13.000 (9.000 to 15.000)	13.000 (9.000 to 16.000)	
Sense of smell (n= 15, 21, 20)	10.000 (9.000 to 15.000)	9.000 (5.000 to 11.000)	9.000 (5.000 to 10.000)	
Sense of taste (n= 15, 18, 24)	10.000 (9.000 to 14.000)	10.500 (9.000 to 21.000)	10.000 (6.000 to 13.000)	
Sore throat (n=33, 38, 37)	9.000 (5.000 to 11.000)	9.500 (9.000 to 13.000)	9.000 (9.000 to 10.000)	
Low energy or tiredness (n= 45, 46, 46)	27.000 (13.000 to 33.000)	20.000 (13.000 to 35.000)	22.000 (15.000 to 99999)	
Vomit (n=5, 4, 6)	6.000 (4.000 to 99999)	4.000 (4.000 to 99999)	4.500 (4.000 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Any Severe Targeted Signs and Symptoms Attributed to COVID-19 Through Day 44: MSP

End point title	Percentage of Participants With Any Severe Targeted Signs and Symptoms Attributed to COVID-19 Through Day 44: MSP

End point description:

COVID -19 targeted signs/symptoms were muscle or body aches, SOB or difficulty breathing, chills or shivering, cough, diarrhoea, feeling hot or feverish, headache, nausea, stuffy or runny nose, sense of smell, sense of taste, sore throat, low energy or tiredness, vomit. Evaluable analysis set included all participants assigned to study intervention and who took at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Day 1 through Day 44

End point values	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day	Nirmatrelvir + Ritonavir 15 Day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Percentage of participants				
number (not applicable)	28.85	31.25	38.00	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 of dosing up to Week 24

Adverse event reporting additional description:

Safety analysis set included all participants randomly assigned to study intervention.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day

Reporting group description:

Participants (MSP + RP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 5 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl>=30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 5 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 10 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Reporting group title	Nirmatrelvir + Ritonavir 15 Day

Reporting group description:

Participants (MSP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 5 days. Participants with eGFR >=30 to <60 mL/min/1.73 m^2 or eCrCl >=30 to <60 mL/min received nirmatrelvir 150mg and ritonavir 100mg orally q12h for 15 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Reporting group title	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day

Reporting group description:

Participants (MSP + RP) received nirmatrelvir 300 mg and ritonavir 100 mg orally q12h for 10 days. Participants with eGFR >= 30 to <60 mL/min/1.73 m^2 or eCrCl >= 30 to <60 mL/min received nirmatrelvir 150 mg and ritonavir 100 mg orally q12h for 10 days. Participants then received placebo for nirmatrelvir and placebo for ritonavir q12h for next 5 days. Participants had follow-up through Day 44. Participants had long term follow-up through Week 24.

Serious adverse events	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 15 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 54 (9.26%)	4 / 51 (7.84%)	1 / 52 (1.92%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Follicular lymphoma			
subjects affected / exposed	1 / 54 (1.85%)	0 / 51 (0.00%)	0 / 52 (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
Nervous system disorders			

Haemorrhage intracranial			
subjects affected / exposed	0 / 54 (0.00%)	1 / 51 (1.96%)	0 / 52 (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
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 51 (1.96%)	0 / 52 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 51 (0.00%)	0 / 52 (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
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	1 / 54 (1.85%)	0 / 51 (0.00%)	0 / 52 (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			
Pseudomonas infection			
subjects affected / exposed	0 / 54 (0.00%)	1 / 51 (1.96%)	0 / 52 (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
Urinary tract infection			
subjects affected / exposed	1 / 54 (1.85%)	0 / 51 (0.00%)	0 / 52 (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
Pneumonia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 51 (1.96%)	0 / 52 (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
COVID-19			

subjects affected / exposed	1 / 54 (1.85%)	0 / 51 (0.00%)	0 / 52 (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
Fungal infection			
subjects affected / exposed	0 / 54 (0.00%)	0 / 51 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Nirmatrelvir + Ritonavir 5 Day Then Placebo 10 Day	Nirmatrelvir + Ritonavir 15 Day	Nirmatrelvir + Ritonavir 10 Day Then Placebo 5 Day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 54 (22.22%)	19 / 51 (37.25%)	19 / 52 (36.54%)
Investigations			
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 54 (0.00%)	3 / 51 (5.88%)	0 / 52 (0.00%)
occurrences (all)	0	3	0
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	6 / 54 (11.11%)	14 / 51 (27.45%)	12 / 52 (23.08%)
occurrences (all)	6	14	12
Headache			
subjects affected / exposed	1 / 54 (1.85%)	1 / 51 (1.96%)	3 / 52 (5.77%)
occurrences (all)	1	1	4
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 54 (1.85%)	5 / 51 (9.80%)	2 / 52 (3.85%)
occurrences (all)	1	5	2
Diarrhoea			
subjects affected / exposed	5 / 54 (9.26%)	4 / 51 (7.84%)	4 / 52 (7.69%)
occurrences (all)	5	5	4

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 September 2022	This protocol was amended based on regulatory feedback to update the primary analysis and include an additional population of nonhospitalized symptomatic participants who are immunocompromised with a rebound in COVID-19.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Primary endpoint data not reported for RP, since there was 1 participant each in 2 arms, it could have led to re-identification of participants. In other sections of results data for RP and MSP have been combined.

Notes: