

**Clinical trial results:****A Phase II, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Antiviral Activity, Safety, Pharmacokinetics, and Efficacy of RO7496998 (AT-527) in Non-Hospitalized Adult Patients with Mild or Moderate COVID-19****Summary**

EudraCT number	2020-005366-34
Trial protocol	IE BG ES LV GR LT
Global end of trial date	13 October 2021

Results information

Result version number	v1 (current)
This version publication date	04 October 2022
First version publication date	04 October 2022

Trial information**Trial identification**

Sponsor protocol code	WV43042
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04709835
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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	13 October 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	13 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this Phase II, randomized, double-blind, placebo-controlled study was to evaluate the antiviral activity of selected dose regimens of AT-527 compared with placebo in non-hospitalized adult participants with mild or moderate COVID-19.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 February 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	United Kingdom: 76
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Latvia: 3
Worldwide total number of subjects	100
EEA total number of subjects	23

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)	97
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study enrolled 104 participants at sites in the United Kingdom, Spain, Greece, Latvia, Ireland and Canada.

Pre-assignment

Screening details:

The study enrolled 104 non-hospitalized adult participants with mild or moderate COVID-19. Four enrolled participants were not treated and are not included in the Results.

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	Investigator, Carer, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Pooled Placebo

Arm description:

Participants received placebo matched to 550 mg or 1100 mg AT-527 twice a day (BID) on Days 1-5.

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

Dosage and administration details:

The dose and regimen of the placebo matched that of the respective AT-527 comparator arm.

Arm title	AT-527 550 mg (1x550 mg)
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Arm description:

Participants received 550 mg AT-527 (1x550 mg) twice a day (BID) on Days 1-5.

Arm type	Experimental
Investigational medicinal product name	AT-527
Investigational medicinal product code	
Other name	RO7496998
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 550 mg AT-527 (1x550 mg) twice a day (BID) on Days 1-5.

Arm title	AT-527 1100 mg (4x275 mg)
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Arm description:

Participants received 1100 mg AT-527 (4x275 mg) twice a day (BID) on Days 1-5.

Arm type	Experimental
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Investigational medicinal product name	AT-527
Investigational medicinal product code	
Other name	RO7496998
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 1100 mg AT-527 (4x275 mg) twice a day (BID) on Days 1-5.

Number of subjects in period 1	Pooled Placebo	AT-527 550 mg (1x550 mg)	AT-527 1100 mg (4x275 mg)
Started	40	30	30
Completed	40	29	30
Not completed	0	1	0
Consent withdrawn by subject	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	Pooled Placebo
Reporting group description: Participants received placebo matched to 550 mg or 1100 mg AT-527 twice a day (BID) on Days 1-5.	
Reporting group title	AT-527 550 mg (1x550 mg)
Reporting group description: Participants received 550 mg AT-527 (1x550 mg) twice a day (BID) on Days 1-5.	
Reporting group title	AT-527 1100 mg (4x275 mg)
Reporting group description: Participants received 1100 mg AT-527 (4x275 mg) twice a day (BID) on Days 1-5.	

Reporting group values	Pooled Placebo	AT-527 550 mg (1x550 mg)	AT-527 1100 mg (4x275 mg)
Number of subjects	40	30	30
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	36.8 ± 13.2	32.7 ± 10.9	40.3 ± 15.6
Sex: Female, Male Units:			
Female	22	15	17
Male	18	15	13
Amount of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Virus RNA at Baseline SARS-CoV-2 virus RNA was measured by reverse-transcription polymerase chain reaction (RT-PCR). Units: log10 copies/mL arithmetic mean standard deviation	6.24 ± 1.40	6.98 ± 1.10	5.94 ± 1.46

Reporting group values	Total		
Number of subjects	100		
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	-		
Sex: Female, Male Units:			
Female	54		
Male	46		

Amount of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Virus RNA at Baseline			
SARS-CoV-2 virus RNA was measured by reverse-transcription polymerase chain reaction (RT-PCR).			
Units: log10 copies/mL arithmetic mean standard deviation		-	

End points

End points reporting groups

Reporting group title	Pooled Placebo
Reporting group description: Participants received placebo matched to 550 mg or 1100 mg AT-527 twice a day (BID) on Days 1-5.	
Reporting group title	AT-527 550 mg (1x550 mg)
Reporting group description: Participants received 550 mg AT-527 (1x550 mg) twice a day (BID) on Days 1-5.	
Reporting group title	AT-527 1100 mg (4x275 mg)
Reporting group description: Participants received 1100 mg AT-527 (4x275 mg) twice a day (BID) on Days 1-5.	
Subject analysis set title	Placebo Matched to AT-527 550 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received placebo matched to 550 mg AT-527 twice a day (BID) on Days 1-5.	

Primary: Change from Baseline in the Amount of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Virus RNA for AT-527 550 mg and Matched Placebo

End point title	Change from Baseline in the Amount of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Virus RNA for AT-527 550 mg and Matched Placebo ^[1]
End point description: SARS-CoV-2 virus RNA was measured by reverse-transcription polymerase chain reaction (RT-PCR) from nasopharyngeal (NP) swabs. The change from baseline was estimated from an ANCOVA model with baseline viral load as a covariate. Reported here is the adjusted mean change from baseline. A negative change from baseline indicates an improvement. The modified ITT infected (mITTi) population was defined as all participants randomized in the study who received any amount of study drug and had at least one positive SARS-CoV-2 RT-PCR test result above or equal to the limit of quantification (LOQ) during the study, with participants grouped according to the treatment assignment at randomization. Here, n indicates the number of participants analyzed at each time point.	
End point type	Primary
End point timeframe: Baseline, Day 3, Day 5, Day 7	

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: Results are reported for the arms as indicated in the endpoint title. The other arms are reported in the co-primary endpoint.

End point values	AT-527 550 mg (1x550 mg)	Placebo Matched to AT-527 550 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: log ₁₀ copies/mL				
arithmetic mean (standard error)				
Day 3 (n=29, 30)	-1.26 (± 0.206)	-1.16 (± 0.203)		
Day 5 (n=30, 29)	-2.11 (± 0.226)	-2.42 (± 0.230)		
Day 7 (n=29, 29)	-3.38 (± 0.220)	-3.13 (± 0.220)		

Statistical analyses

Statistical analysis title	Day 3
Comparison groups	AT-527 550 mg (1x550 mg) v Placebo Matched to AT-527 550 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority ^[2]
P-value	= 0.7144
Method	ANCOVA
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.11
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.49
upper limit	0.27
Variability estimate	Standard error of the mean
Dispersion value	0.292

Notes:

[2] - A difference in adjusted means of <0 favors RO7496998 (AT-527).

Statistical analysis title	Day 5
Comparison groups	AT-527 550 mg (1x550 mg) v Placebo Matched to AT-527 550 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	= 0.3373
Method	ANCOVA
Parameter estimate	Difference in Adjusted Means
Point estimate	0.32
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.11
upper limit	0.74
Variability estimate	Standard error of the mean
Dispersion value	0.327

Notes:

[3] - A difference in adjusted means of <0 favors RO7496998 (AT-527).

Statistical analysis title	Day 7
Comparison groups	AT-527 550 mg (1x550 mg) v Placebo Matched to AT-527 550 mg

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority ^[4]
P-value	= 0.426
Method	ANCOVA
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.25
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.66
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.315

Notes:

[4] - A difference in adjusted means of <0 favors RO7496998 (AT-527).

Primary: Change from Baseline in the Amount of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Virus RNA for AT-527 1100 mg and Pooled Placebo

End point title	Change from Baseline in the Amount of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Virus RNA for AT-527 1100 mg and Pooled Placebo ^[5]
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End point description:

SARS-CoV-2 virus RNA was measured by reverse-transcription polymerase chain reaction (RT-PCR) from NP swabs. The change from baseline was estimated from an ANCOVA model with baseline viral load as a covariate. Reported here is the adjusted mean change from baseline. A negative change from baseline indicates an improvement. The modified ITT infected (mITTi) population was defined as all participants randomized in the study who received any amount of study drug and had at least one positive SARS-CoV-2 RT-PCR test result above or equal to the limit of quantification (LOQ) during the study, with participants grouped according to the treatment assignment at randomization. Here, n indicates the number of participants analyzed at each time point.

End point type	Primary
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End point timeframe:

Baseline, Day 3, Day 5, Day 7

Notes:

[5] - 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: Results are reported for the arms as indicated in the endpoint title. The other arms are reported in the co-primary endpoint.

End point values	Pooled Placebo	AT-527 1100 mg (4x275 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	30		
Units: log ₁₀ copies/mL				
arithmetic mean (standard error)				
Day 3 (n=40, 29)	-1.08 (± 0.190)	-1.18 (± 0.223)		
Day 5 (n=38, 30)	-2.21 (± 0.205)	-2.31 (± 0.231)		
Day 7 (n=39, 30)	-2.70 (± 0.207)	-2.78 (± 0.236)		

Statistical analyses

Statistical analysis title	Day 3
Comparison groups	Pooled Placebo v AT-527 1100 mg (4x275 mg)
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority ^[6]
P-value	= 0.7351
Method	ANCOVA
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.1
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.48
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.294

Notes:

[6] - A difference in adjusted means of <0 favors RO7496998 (AT-527).

Statistical analysis title	Day 5
Comparison groups	Pooled Placebo v AT-527 1100 mg (4x275 mg)
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority ^[7]
P-value	= 0.7524
Method	ANCOVA
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.1
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.5
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.31

Notes:

[7] - A difference in adjusted means of <0 favors RO7496998 (AT-527).

Statistical analysis title	Day 7
Comparison groups	Pooled Placebo v AT-527 1100 mg (4x275 mg)

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority ^[8]
P-value	= 0.8083
Method	ANCOVA
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.08
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.48
upper limit	0.33
Variability estimate	Standard error of the mean
Dispersion value	0.314

Notes:

[8] - A difference in adjusted means of <0 favors RO7496998 (AT-527).

Secondary: Time to Cessation of SARS-CoV-2 Viral Shedding

End point title	Time to Cessation of SARS-CoV-2 Viral Shedding
End point description:	
Time to cessation of viral shedding was defined as the time between the initiation of any study treatment and the first time when a negative or below the limit of detection RT-PCR test result was obtained. RT-PCR was measured from NP swabs. Median, 25th and 75th percentiles were estimated from the Kaplan-Meier curve. The mITTi population was defined as all participants randomized in the study who received any amount of study drug and had at least one positive SARS-CoV-2 RT-PCR test result above or equal to the limit of quantification (LOQ) during the study, with participants grouped according to the treatment assignment at randomization. "99999" indicates that the value was not estimable due to low number of participants with events.	
End point type	Secondary
End point timeframe:	
Up to Day 7	

End point values	Pooled Placebo	AT-527 550 mg (1x550 mg)	AT-527 1100 mg (4x275 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	30	30	
Units: hours				
median (inter-quartile range (Q1-Q3))	99999 (144.2 to 99999)	99999 (143.8 to 99999)	99999 (141.1 to 99999)	

Statistical analyses

Statistical analysis title	Placebo versus AT-527 550 mg
Statistical analysis description:	
Hazard ratio (80% CI) was estimated with a Cox proportional hazards model (unadjusted).	
Comparison groups	Pooled Placebo v AT-527 550 mg (1x550 mg)

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.96
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.53
upper limit	1.74

Statistical analysis title	Placebo versus AT-527 1100 mg
Statistical analysis description:	
Hazard ratio (80% CI) was estimated with a Cox proportional hazards model (unadjusted).	
Comparison groups	Pooled Placebo v AT-527 1100 mg (4x275 mg)
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	1.33
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.76
upper limit	2.32

Secondary: Time to Sustained Non-Detectable SARS-CoV-2 Virus RNA

End point title	Time to Sustained Non-Detectable SARS-CoV-2 Virus RNA
End point description:	
Time to sustained non-detectable SARS-CoV-2 virus RNA was defined as the time between the initiation of any study treatment and first time when a negative or below the limit of detection test result by RT-PCR is obtained after which no positive test above or equal to the limit of detection was reported. RT-PCR was measured from NP swabs. Median, 25th and 75th percentiles were estimated from the Kaplan-Meier curve. The mITTi population was defined as all participants randomized in the study who received any amount of study drug and had at least one positive SARS-CoV-2 RT-PCR test result above or equal to the limit of quantification (LOQ) during the study, with participants grouped according to the treatment assignment at randomization. "99999" indicates that the value was not estimable due to low number of participants with events.	
End point type	Secondary
End point timeframe:	
Up to Day 7	

End point values	Pooled Placebo	AT-527 550 mg (1x550 mg)	AT-527 1100 mg (4x275 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	30	30	
Units: hours				
median (inter-quartile range (Q1-Q3))	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

Statistical analysis title	Placebo versus AT-527 550 mg
Statistical analysis description: Hazard ratio (80% CI) was estimated with a Cox proportional hazards model (unadjusted).	
Comparison groups	Pooled Placebo v AT-527 550 mg (1x550 mg)
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.44
upper limit	1.7

Statistical analysis title	Placebo versus AT-527 1100 mg
Statistical analysis description: Hazard ratio (80% CI) was estimated with a Cox proportional hazards model (unadjusted).	
Comparison groups	Pooled Placebo v AT-527 1100 mg (4x275 mg)
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	1.06
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.56
upper limit	2.03

Secondary: Percentage of Participants Positive for SARS-CoV-2 Virus RNA at Specified Timepoints

End point title	Percentage of Participants Positive for SARS-CoV-2 Virus RNA at Specified Timepoints
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End point description:

Reported here is the percentage of participants with a positive virus RNA by RT-PCR test result above or equal to the limit of quantification (LOQ). RT-PCR was measured from NP swabs. The mITTi population was defined as all participants randomized in the study who received any amount of study drug and had at least one positive SARS-CoV-2 RT-PCR test result above or equal to the limit of quantification (LOQ) during the study, with participants grouped according to the treatment assignment at randomization. Here, n indicates the number of participants analyzed at each time point.

End point type Secondary

End point timeframe:

Baseline, Day 3, Day 5, Day 7

End point values	Pooled Placebo	AT-527 550 mg (1x550 mg)	AT-527 1100 mg (4x275 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	30	30	
Units: percentage of participants number (not applicable)				
Baseline (n=40, 30, 30)	100	100	96.7	
Day 3 (n=40, 30, 29)	95.0	100	93.1	
Day 5 (n=38, 30, 30)	84.2	90.0	83.3	
Day 7 (n=39, 29, 30)	76.9	79.3	76.7	

Statistical analyses

Statistical analysis title Day 3 Placebo versus AT-527 550 mg

Statistical analysis description:

Confidence interval estimated with the Farrington-Manning method.

Comparison groups	Pooled Placebo v AT-527 550 mg (1x550 mg)
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in Percentage of Positivity
Point estimate	5
Confidence interval level	Other: 80 %
sides	2-sided
lower limit	-0.16
upper limit	10.16

Statistical analysis title Day 3 Placebo versus AT-527 1100 mg

Statistical analysis description:

Confidence interval estimated with the Farrington-Manning method.

Comparison groups	Pooled Placebo v AT-527 1100 mg (4x275 mg)
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Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in Percentage of Positivity
Point estimate	-1.9
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-9.2
upper limit	5.41

Statistical analysis title	Day 5 Placebo versus AT-527 550 mg
Statistical analysis description:	
Confidence interval estimated with the Farrington-Manning method.	
Comparison groups	Pooled Placebo v AT-527 550 mg (1x550 mg)
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in Percentage of Positivity
Point estimate	5.79
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-4.82
upper limit	16.4

Statistical analysis title	Day 5 Placebo versus AT-527 1100 mg
Statistical analysis description:	
Confidence interval estimated with the Farrington-Manning method.	
Comparison groups	Pooled Placebo v AT-527 1100 mg (4x275 mg)
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in Percentage of Positivity
Point estimate	-0.88
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-12.4
upper limit	10.65

Statistical analysis title	Day 7 Placebo versus AT-527 550 mg
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Statistical analysis description:

Confidence interval estimated with the Farrington-Manning method.

Comparison groups	Pooled Placebo v AT-527 550 mg (1x550 mg)
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in Percentage of Positivity
Point estimate	2.39
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-10.64
upper limit	15.42

Statistical analysis title	Day 7 Placebo versus AT-527 1100 mg
Statistical analysis description:	
Confidence interval estimated with the Farrington-Manning method.	
Comparison groups	Pooled Placebo v AT-527 1100 mg (4x275 mg)
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in Percentage of Positivity
Point estimate	-0.26
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-13.39
upper limit	12.88

Secondary: Area Under the Curve (AUC) in the Amount of SARS-CoV-2 Virus RNA

End point title	Area Under the Curve (AUC) in the Amount of SARS-CoV-2 Virus RNA
End point description:	
AUC is the amount of SARS-CoV-2 virus RNA from baseline to the last sample timepoint and was calculated using the trapezoidal method. RT-PCR was measured from NP swabs. The mITTi population was defined as all participants randomized in the study who received any amount of study drug and had at least one positive SARS-CoV-2 RT-PCR test result above or equal to the limit of quantification (LOQ) during the study, with participants grouped according to the treatment assignment at randomization.	
End point type	Secondary
End point timeframe:	
Baseline, Day 3, Day 5, Day 7	

End point values	Pooled Placebo	AT-527 550 mg (1x550 mg)	AT-527 1100 mg (4x275 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	30	30	
Units: log10 copies/mL*hour				
arithmetic mean (standard deviation)	651.56 (± 189.10)	733.70 (± 146.63)	618.62 (± 194.88)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Alleviation or Improvement of COVID-19 Symptoms (21.5 hours)

End point title	Time to Alleviation or Improvement of COVID-19 Symptoms (21.5 hours)
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End point description:

COVID-19 symptoms were evaluated using the first 12 items in the COVID-19 Symptom Diary, which included the following 12 items: nasal congestion or runny nose, sore throat, cough, shortness of breath, muscle or body aches, fatigue, headache, chills/sweats, feeling hot or feverish, nausea, vomiting, and diarrhea. The symptoms were scored on the 4-point Likert scale (0=none, 1=mild, 2=moderate, 3=severe). Time to alleviation or improvement is defined as the length of time taken from start of treatment to the point at which all of the following three criteria are met and maintained for a concurrent duration of at least 21.5 hours: "new" symptoms with a score of 0 or 1; "pre-existing and worsened due to COVID-19" symptoms with at least a single category improvement from baseline; "pre-existing and not worsened due to COVID-19" symptoms remaining the same or at least a single category improvement from baseline. mITTI population was analyzed for this endpoint.

End point type	Secondary
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End point timeframe:

Up to 28 Days

End point values	Pooled Placebo	AT-527 550 mg (1x550 mg)	AT-527 1100 mg (4x275 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	30	30	
Units: hours				
median (inter-quartile range (Q1-Q3))	43.4 (9.3 to 104.7)	57.2 (9.0 to 115.8)	56.4 (2.5 to 96.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Alleviation or Improvement of COVID-19 Symptoms (43 hours)

End point title	Time to Alleviation or Improvement of COVID-19 Symptoms (43 hours)
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End point description:

COVID-19 symptoms were evaluated using the first 12 items in the COVID-19 Symptom Diary, which included the following 12 items: nasal congestion or runny nose, sore throat, cough, shortness of breath, muscle or body aches, fatigue, headache, chills/sweats, feeling hot or feverish, nausea, vomiting, and diarrhea. The symptoms were scored on the 4-point Likert scale (0=none, 1=mild, 2=moderate, 3=severe). Time to alleviation or improvement is defined as the length of time taken from start of treatment to the point at which all of the following three criteria are met and maintained for a concurrent duration of at least 43 hours: "new" symptoms with a score of 0 or 1; "pre-existing and worsened due to COVID-19" symptoms with at least a single category improvement from baseline; "pre-existing and not worsened due to COVID-19" symptoms remaining the same or at least a single category improvement from baseline. mITTI population was analyzed for this endpoint.

End point type Secondary

End point timeframe:

Up to 28 Days

End point values	Pooled Placebo	AT-527 550 mg (1x550 mg)	AT-527 1100 mg (4x275 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	30	30	
Units: hours				
median (inter-quartile range (Q1-Q3))	43.4 (9.3 to 104.7)	57.2 (9.0 to 141.2)	58.1 (2.5 to 118.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Alleviation of COVID-19 Symptoms (21.5 hours)

End point title Time to Alleviation of COVID-19 Symptoms (21.5 hours)

End point description:

COVID-19 symptoms were evaluated using the first 12 items in the COVID-19 Symptom Diary, which included the following 12 items: nasal congestion or runny nose, sore throat, cough, shortness of breath, muscle or body aches, fatigue, headache, chills/sweats, feeling hot or feverish, nausea, vomiting, and diarrhea. The symptoms were scored on the 4-point Likert scale (0=none, 1=mild, 2=moderate, 3=severe). Time to alleviation of COVID-19 symptoms is defined as the length of time taken from start of treatment to the point at which the following criterion is met and maintained for at least 21.5 hours: Score of 0 or 1 on Items 1-12 of the COVID-19 Symptom Diary, regardless of if the symptom is pre-existing or new. mITTI population was analyzed for this endpoint.

End point type Secondary

End point timeframe:

Up to 28 Days

End point values	Pooled Placebo	AT-527 550 mg (1x550 mg)	AT-527 1100 mg (4x275 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	30	30	
Units: hours				
median (inter-quartile range (Q1-Q3))	43.4 (9.3 to 104.7)	57.2 (9.0 to 115.8)	56.4 (8.2 to 96.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Alleviation of COVID-19 Symptoms (43 hours)

End point title	Time to Alleviation of COVID-19 Symptoms (43 hours)
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End point description:

COVID-19 symptoms were evaluated using the first 12 items in the COVID-19 Symptom Diary, which included the following 12 items: nasal congestion or runny nose, sore throat, cough, shortness of breath, muscle or body aches, fatigue, headache, chills/sweats, feeling hot or feverish, nausea, vomiting, and diarrhea. The symptoms were scored on the 4-point Likert scale (0=none, 1=mild, 2=moderate, 3=severe). Time to alleviation of COVID-19 symptoms is defined as the length of time taken from start of treatment to the point at which the following criterion is met and maintained for at least 43 hours: Score of 0 or 1 on Items 1-12 of the COVID-19 Symptom Diary, regardless of if the symptom is pre-existing or new. mITTi population was analyzed for this endpoint.

End point type	Secondary
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End point timeframe:

Up to 28 Days

End point values	Pooled Placebo	AT-527 550 mg (1x550 mg)	AT-527 1100 mg (4x275 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	30	30	
Units: hours				
median (inter-quartile range (Q1-Q3))	43.4 (9.3 to 104.7)	57.2 (9.0 to 141.2)	58.1 (8.2 to 118.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Fever

End point title	Duration of Fever
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End point description:

Duration of fever was defined as the time from start of treatment to return to an afebrile state (temperature $\leq 37.5^{\circ}\text{C}$) maintained for at least 21.5 hours. The mITTi population was defined as all participants randomized in the study who received any amount of study drug and had at least one positive SARS-CoV-2 RT-PCR test result above or equal to the limit of quantification (LOQ) during the study, with participants grouped according to the treatment assignment at randomization.

End point type	Secondary
End point timeframe:	
Up to 28 Days	

End point values	Pooled Placebo	AT-527 550 mg (1x550 mg)	AT-527 1100 mg (4x275 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2 ^[9]	0 ^[10]	0 ^[11]	
Units: hours				
median (inter-quartile range (Q1-Q3))	10.6 (9.6 to 11.7)	(to)	(to)	

Notes:

[9] - Only participants who had a fever (temperature > 37.5 degrees Celsius) at baseline are included.

[10] - Only participants who had a fever (temperature > 37.5 degrees Celsius) at baseline are included.

[11] - Only participants who had a fever (temperature > 37.5 degrees Celsius) at baseline are included.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with COVID-19 Related Complications

End point title	Percentage of Participants with COVID-19 Related Complications
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End point description:

COVID-19 related complications include death, hospitalization, radiologically confirmed pneumonia, acute respiratory failure, sepsis, coagulopathy, pericarditis, myocarditis, and cardiac failure. The mITTi population was defined as all participants randomized in the study who received any amount of study drug and had at least one positive SARS-CoV-2 RT-PCR test result above or equal to the limit of quantification (LOQ) during the study, with participants grouped according to the treatment assignment at randomization.

End point type	Secondary
End point timeframe:	
Up to 33 Days	

End point values	Pooled Placebo	AT-527 550 mg (1x550 mg)	AT-527 1100 mg (4x275 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	30	30	
Units: percentage of participants				
number (not applicable)	0	3.3	3.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Alleviation of an Individual Symptom

End point title	Time to Alleviation of an Individual Symptom
End point description:	
<p>The COVID-19 Symptom Diary included 14 items: nasal congestion or runny nose, sore throat, cough, shortness of breath, muscle or body aches, fatigue, headache, chills/sweats, feeling hot or feverish, nausea, vomiting, diarrhea, sense of smell over the past 7 days, sense of taste over the past 7 days. The severity of items 1-12 was recorded on a 4-point Likert scale (none=0, mild=1, moderate=2, severe=3). Items 13-14 were recorded on a 3-point Likert scale (same as usual=0, less than usual=1, no sense=2). Time to alleviation: the time from the start of treatment to the point at which the following criterion was met and maintained for at least 21.5 hours: score of 0 or 1 for Items 1-12; score of 0 for Items 13-14. mITTi population: only participants with a baseline score of > 1 for Items 1 - 12 or > 0 for Items 13 - 14 were included in the analysis. Here, "n" is the number of participants analyzed for the individual symptom. "99999": not estimable due to low number of events.</p>	
End point type	Secondary
End point timeframe:	
Up to 28 Days	

End point values	Pooled Placebo	AT-527 550 mg (1x550 mg)	AT-527 1100 mg (4x275 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	30	30	
Units: hours				
median (inter-quartile range (Q1-Q3))				
Nasal Congestion/Runny Nose (n=12, 8, 10)	27.6 (11.3 to 59.9)	34.2 (15.8 to 82.4)	32.7 (10.0 to 57.7)	
Sore Throat (n=5, 5, 2)	20.5 (14.1 to 22.7)	24.1 (9.8 to 45.0)	111.7 (22.1 to 201.4)	
Cough (n=11, 6, 7)	22.6 (11.8 to 129.3)	90.7 (23.7 to 140.4)	33.9 (20.5 to 119.2)	
Shortness of Breath (n=3, 2, 1)	23.9 (11.5 to 99999)	68.9 (68.5 to 69.2)	11.6 (11.6 to 11.6)	
Aches and Pains (n=8, 8, 4)	33.1 (11.8 to 60.4)	22.3 (16.3 to 62.2)	94.4 (48.1 to 177.7)	
Fatigue (n=15, 10, 11)	47.8 (22.6 to 178.1)	44.4 (10.5 to 94.5)	70.6 (22.6 to 106.0)	
Headache (n=13, 7, 11)	32.0 (10.1 to 95.8)	11.7 (9.8 to 93.6)	34.4 (21.8 to 105.4)	
Chills/Sweats (n=8, 3, 4)	11.8 (9.8 to 24.1)	12.0 (9.0 to 35.8)	25.0 (17.1 to 41.4)	
Feeling Hot or Feverish (n=6, 2, 4)	26.5 (11.8 to 35.7)	48.0 (24.0 to 72.0)	40.3 (15.9 to 63.4)	
Nausea (n=2, 0, 0)	99999 (21.1 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Vomiting (n=2, 0, 0)	99999 (11.0 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Diarrhea (n=1, 0, 1)	99999 (99999 to 99999)	99999 (99999 to 99999)	9.8 (9.8 to 9.8)	
Sense of Smell (n=19, 14, 18)	261.5 (164.9 to 99999)	290.2 (130.7 to 99999)	213.1 (129.7 to 513.7)	
Sense of Taste (n=16, 12, 17)	221.1 (165.3 to 297.6)	214.1 (94.1 to 99999)	178.5 (105.5 to 391.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Adverse Events (AEs)

End point title | Percentage of Participants with Adverse Events (AEs)

End point description:

An AE is any untoward medical occurrence in a clinical investigation subject administered a pharmaceutical product, regardless of causal attribution. An AE can therefore be any of the following: any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the medicinal product, any new disease or exacerbation of an existing disease, recurrence of an intermittent medical condition not present at baseline or related to a protocol-mandated intervention. Safety population consisted of all participants who received any amount of study drug and were grouped according to the treatment that the participants actually received rather than the treatment assigned at randomization.

End point type | Secondary

End point timeframe:

Up to 33 Days

End point values	Pooled Placebo	AT-527 550 mg (1x550 mg)	AT-527 1100 mg (4x275 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	30	30	
Units: percentage of participants				
number (not applicable)	27.5	20.0	33.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of AT-511, AT-551, AT-229 and AT-273 for Participants Treated with 550 mg AT-527

End point title | Plasma Concentrations of AT-511, AT-551, AT-229 and AT-273 for Participants Treated with 550 mg AT-527^[12]

End point description:

AT-511 is the free base form of AT-527. Its major metabolites are AT-551, AT-229, and AT-273. The pharmacokinetic-evaluable population consisted of all participants randomized into the study who had at least one post-dose drug concentration measurement at a scheduled visit timepoint. Here, n indicates the number of participants analyzed at each time point.

End point type | Secondary

End point timeframe:

Day 1: pre-dose, 1 hour, 3 hours; Day 3: pre-dose; Day 5: pre-dose, 3 hours, 48 hours

Notes:

[12] - 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: Results are presented for the arm as indicated in the endpoint title. Plasma concentrations were only evaluated in the arms treated with AT-527.

End point values	AT-527 550 mg (1x550 mg)			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
AT-511: Day 1, pre-dose (n=30)	1.3 (± 4.5)			
AT-511: Day 1, 1 hour (n=30)	1950.5 (± 2365.0)			
AT-511: Day 1, 3 hours (n=29)	441.4 (± 645.8)			
AT-511: Day 3, pre-dose (n=28)	254.2 (± 943.1)			
AT-511: Day 5, pre-dose (n=30)	5.6 (± 21.9)			
AT-511: Day 5, 3 hours (n=30)	415.7 (± 445.5)			
AT-511: Day 5, 48 hours (n=29)	0.5 (± 0.0)			
AT-551: Day 1, pre-dose (n=30)	0.5 (± 0.0)			
AT-551: Day 1, 1 hour (n=30)	347.5 (± 334.1)			
AT-551: Day 1, 3 hours (n=29)	375.8 (± 303.9)			
AT-551: Day 3, pre-dose (n=28)	56.9 (± 100.1)			
AT-551: Day 5, pre-dose (n=30)	26.6 (± 22.7)			
AT-551: Day 5, 3 hours (n=30)	323.8 (± 168.3)			
AT-551: Day 5, 48 hours (n=29)	1.7 (± 1.4)			
AT-229: Day 1, pre-dose (n=30)	0.5 (± 0.0)			
AT-229: Day 1, 1 hour (n=30)	268.5 (± 318.5)			
AT-229: Day 1, 3 hours (n=29)	427.4 (± 275.8)			
AT-229: Day 3, pre-dose (n=28)	290.3 (± 152.3)			
AT-229: Day 5, pre-dose (n=30)	295.4 (± 145.0)			
AT-229: Day 5, 3 hours (n=30)	773.9 (± 340.8)			
AT-229: Day 5, 48 hours (n=29)	89.2 (± 87.8)			
AT-273: Day 1, pre-dose (n=30)	0.5 (± 0.0)			
AT-273: Day 1, 1 hour (n=30)	26.5 (± 29.0)			
AT-273: Day 1, 3 hours (n=29)	132.2 (± 66.7)			
AT-273: Day 3, pre-dose (n=28)	135.9 (± 47.6)			
AT-273: Day 5, pre-dose (n=30)	138.1 (± 53.0)			
AT-273: Day 5, 3 hours (n=30)	236.9 (± 79.9)			
AT-273: Day 5, 48 hours (n=29)	40.9 (± 22.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of AT-511, AT-551, AT-229 and AT-273 for Participants Treated with 1100 mg AT-527

End point title	Plasma Concentrations of AT-511, AT-551, AT-229 and AT-273
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End point description:

AT-511 is the free base form of AT-527. Its major metabolites are AT-551, AT-229, and AT-273. The pharmacokinetic-evaluable population consisted of all participants randomized into the study who had at least one post-dose drug concentration measurement at a scheduled visit timepoint. Here, n indicates the number of participants analyzed at each time point.

End point type

Secondary

End point timeframe:

Day 1: pre-dose, 1 hour, 4 hours; Day 3: pre-dose; Day 5: pre-dose, 1 hour, 4 hours, 48 hours

Notes:

[13] - 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: Results are presented for the arm as indicated in the endpoint title. Plasma concentrations were only evaluated in the arms treated with AT-527.

End point values	AT-527 1100 mg (4x275 mg)			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
AT-511: Day 1, pre-dose (n=29)	0.5 (± 0.0)			
AT-511: Day 1, 1 hour (n=29)	3575.0 (± 2883.6)			
AT-511: Day 1, 4 hours (n=30)	852.4 (± 1513.2)			
AT-511: Day 3, pre-dose (n=24)	9.6 (± 15.9)			
AT-511: Day 5, pre-dose (n=26)	316.7 (± 1544.7)			
AT-511: Day 5, 1 hour (n=25)	3568.9 (± 3352.1)			
AT-511: Day 5, 4 hours (n=23)	1323.3 (± 2883.5)			
AT-511: Day 5, 48 hours (n=24)	0.6 (± 0.6)			
AT-551: Day 1, pre-dose (n=29)	0.5 (± 0.0)			
AT-551: Day 1, 1 hour (n=29)	592.2 (± 576.9)			
AT-551: Day 1, 4 hours (n=30)	640.4 (± 446.3)			
AT-551: Day 3, pre-dose (n=25)	84.0 (± 72.1)			
AT-551: Day 5, pre-dose (n=26)	71.3 (± 61.6)			
AT-551: Day 5, 1 hour (n=25)	302.8 (± 222.1)			
AT-551: Day 5, 4 hours (n=23)	342.1 (± 254.9)			
AT-551: Day 5, 48 hours (n=24)	4.4 (± 4.8)			
AT-229: Day 1, pre-dose (n=29)	0.5 (± 0.0)			
AT-229: Day 1, 1 hour (n=29)	371.9 (± 460.3)			
AT-229: Day 1, 4 hours (n=30)	865.4 (± 494.2)			
AT-229: Day 3, pre-dose (n=25)	682.8 (± 351.7)			
AT-229: Day 5, pre-dose (n=26)	797.8 (± 459.9)			
AT-229: Day 5, 1 hour (n=25)	990.9 (± 505.3)			

AT-229: Day 5, 4 hours (n=23)	1357.2 (± 825.3)			
AT-229: Day 5, 48 hours (n=24)	279.4 (± 285.3)			
AT-273: Day 1, pre-dose (n=29)	0.5 (± 0.0)			
AT-273: Day 1, 1 hour (n=29)	35.7 (± 47.4)			
AT-273: Day 1, 4 hours (n=30)	231.8 (± 111.4)			
AT-273: Day 3, pre-dose (n=25)	245.6 (± 122.8)			
AT-273: Day 5, pre-dose (n=26)	263.6 (± 107.3)			
AT-273: Day 5, 1 hour (n=25)	252.1 (± 97.4)			
AT-273: Day 5, 4 hours (n=23)	310.6 (± 107.5)			
AT-273: Day 5, 48 hours (n=24)	84.4 (± 45.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 33 days

Adverse event reporting additional description:

Safety Population consisted of all participants who received any amount of study drug and were grouped according to the treatment that the participants actually received rather than the treatment assigned at randomization.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	Pooled Placebo
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Reporting group description:

Participants received placebo matched to 550 mg or 1100 mg AT-527 twice a day (BID) on Days 1-5.

Reporting group title	AT-527 1100 mg (4x275 mg)
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Reporting group description:

Participants received 1100 mg AT-527 (4x275 mg) twice a day (BID) on Days 1-5.

Reporting group title	AT-527 550 mg (1x550 mg)
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Reporting group description:

Participants received 550 mg AT-527 (1x550 mg) twice a day (BID) on Days 1-5.

Serious adverse events	Pooled Placebo	AT-527 1100 mg (4x275 mg)	AT-527 550 mg (1x550 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 40 (2.50%)	1 / 30 (3.33%)	1 / 30 (3.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	1 / 40 (2.50%)	0 / 30 (0.00%)	0 / 30 (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	0 / 40 (0.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	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	Pooled Placebo	AT-527 1100 mg (4x275 mg)	AT-527 550 mg (1x550 mg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 40 (2.50%)	5 / 30 (16.67%)	1 / 30 (3.33%)
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 40 (2.50%)	3 / 30 (10.00%)	1 / 30 (3.33%)
occurrences (all)	1	3	1
Vomiting			
subjects affected / exposed	1 / 40 (2.50%)	5 / 30 (16.67%)	0 / 30 (0.00%)
occurrences (all)	1	5	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 December 2020	The purpose of amendment version 2 was primarily to remove the use of historical severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) test results for eligibility assessment and to clarify the timing of safety data required for dose-selection decision making.
05 February 2021	The purpose of country-specific amendment version 3 was to incorporate changes requested by the Irish Health Products Regulatory Authority.
24 February 2021	The purpose of amendment version 4 was primarily to broaden the patient population by allowing all subjects with mild or moderate COVID-19 to be enrolled, not only those considered otherwise healthy, and to enable Cohorts B-E to be conducted in an outpatient setting. The parameters for the dose selection decision were also modified.
13 May 2021	The purpose of amendment version 5 was primarily to incorporate additional secondary efficacy endpoints and updated information related to cautionary therapies.
17 September 2021	The purpose of amendment version 6 was primarily to enable further evaluation of the antiviral efficacy and safety of RO7496998 (AT-527) using the dose regimen selected from previous cohorts. No patients were enrolled under this protocol version as the study closed after recruitment of Cohort A and Cohort B.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported