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Anhang 4-G 1: RKI-mITT2-Population

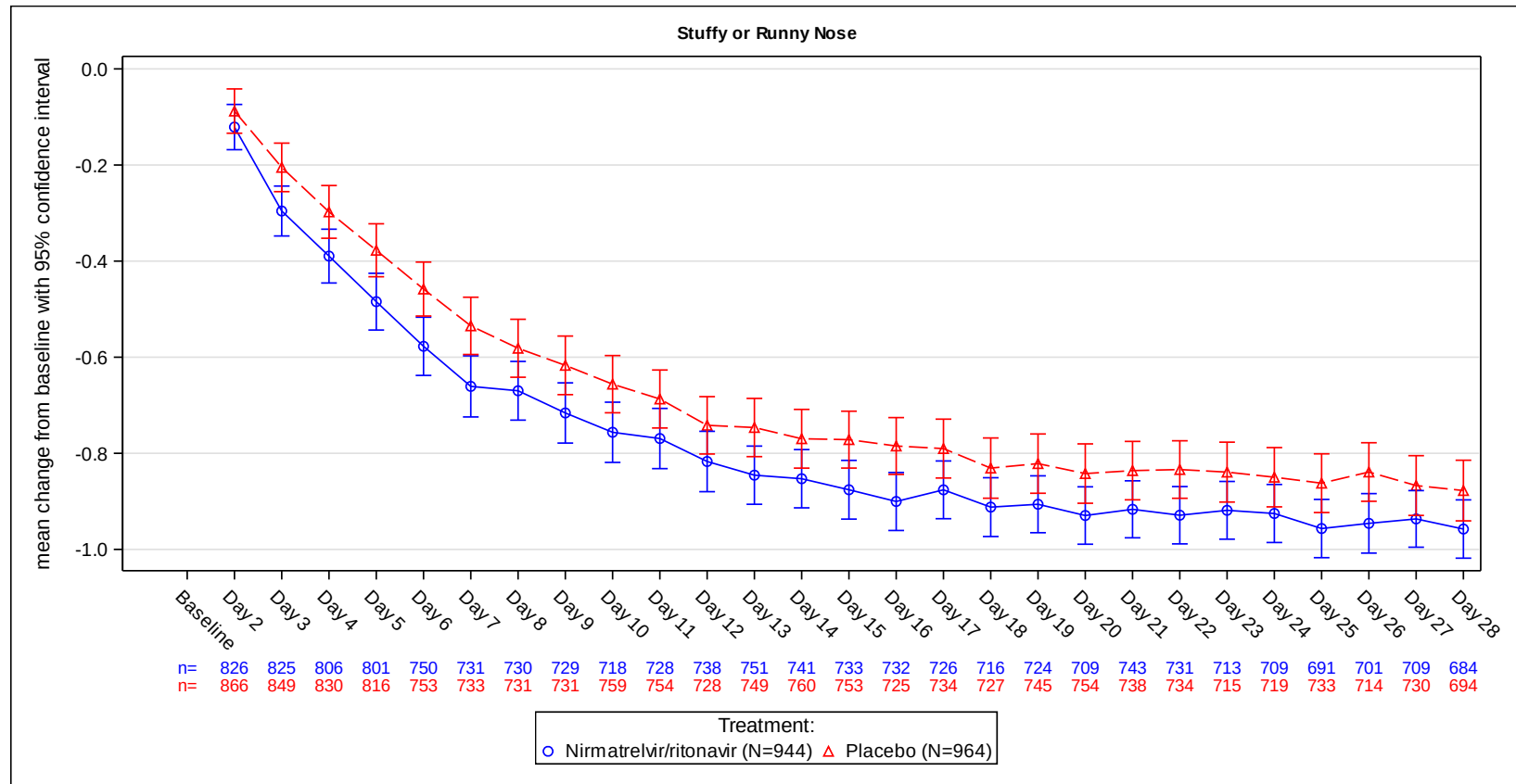
Anhang 4-G 1.1: Krankheitsbedingte Symptome

**Anhang 4-G 1.1.1: Mittlere Veränderung der krankheitsbedingten Symptome -
Verlaufskurven (insgesamt und für Patienten mit schweren
Symptomen zu Studienbeginn)**

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms - Stuffy or Runny Nose

Final

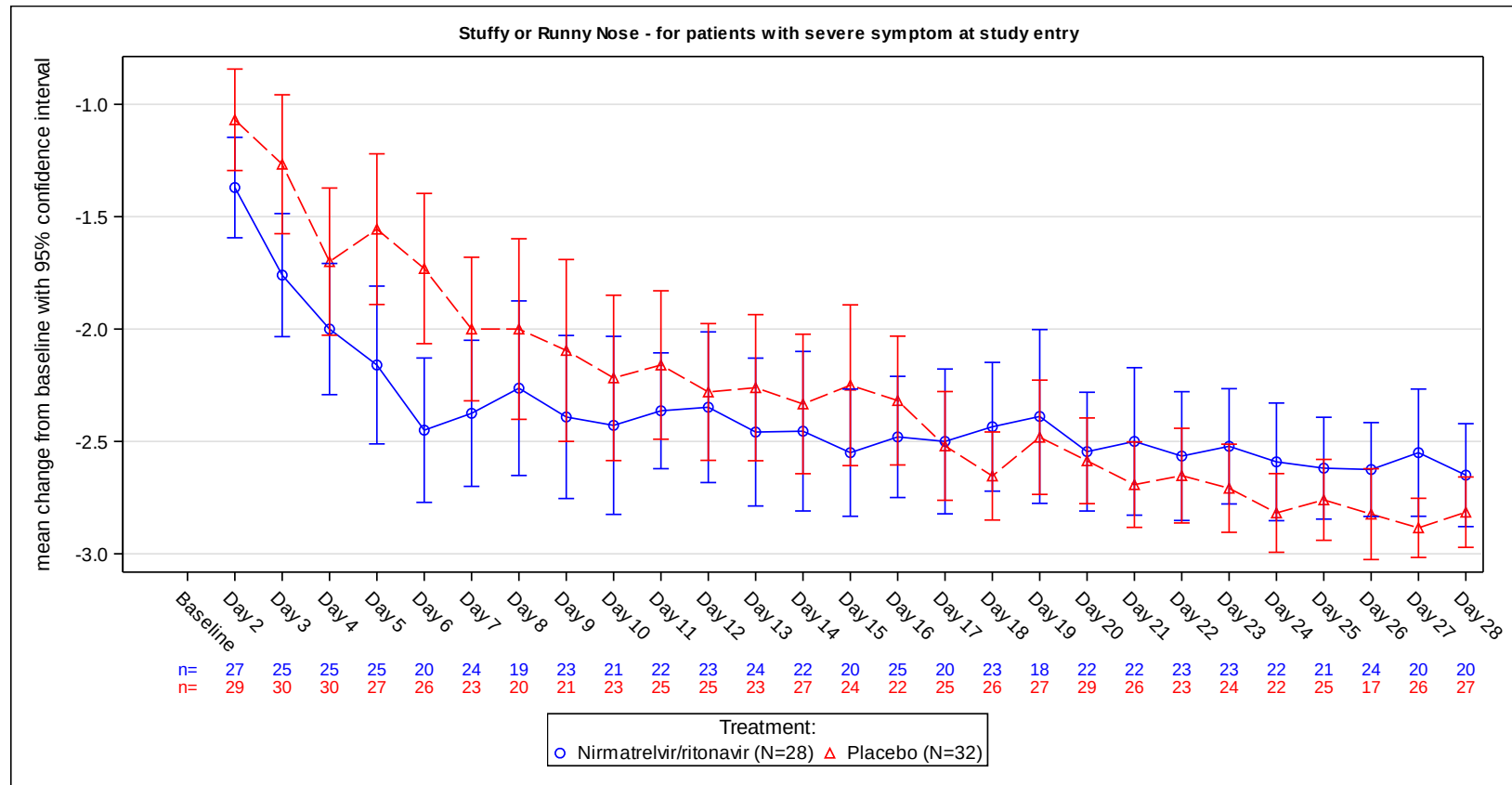


N = Number of participants, n = Number of participants with non missing values

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms for patients with severe symptom at study entry - Stuffy or Runny Nose

Final

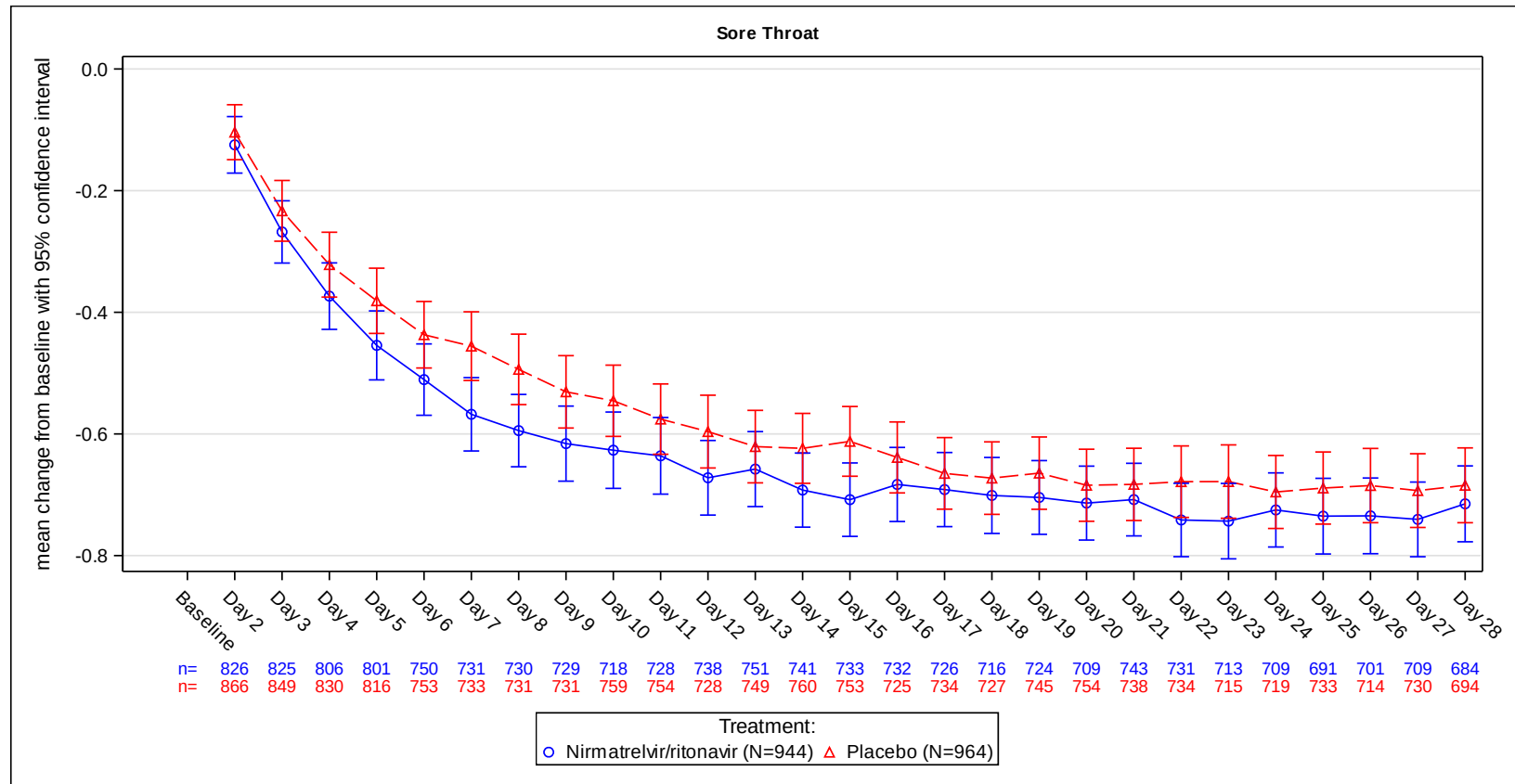


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms - Sore Throat

Final

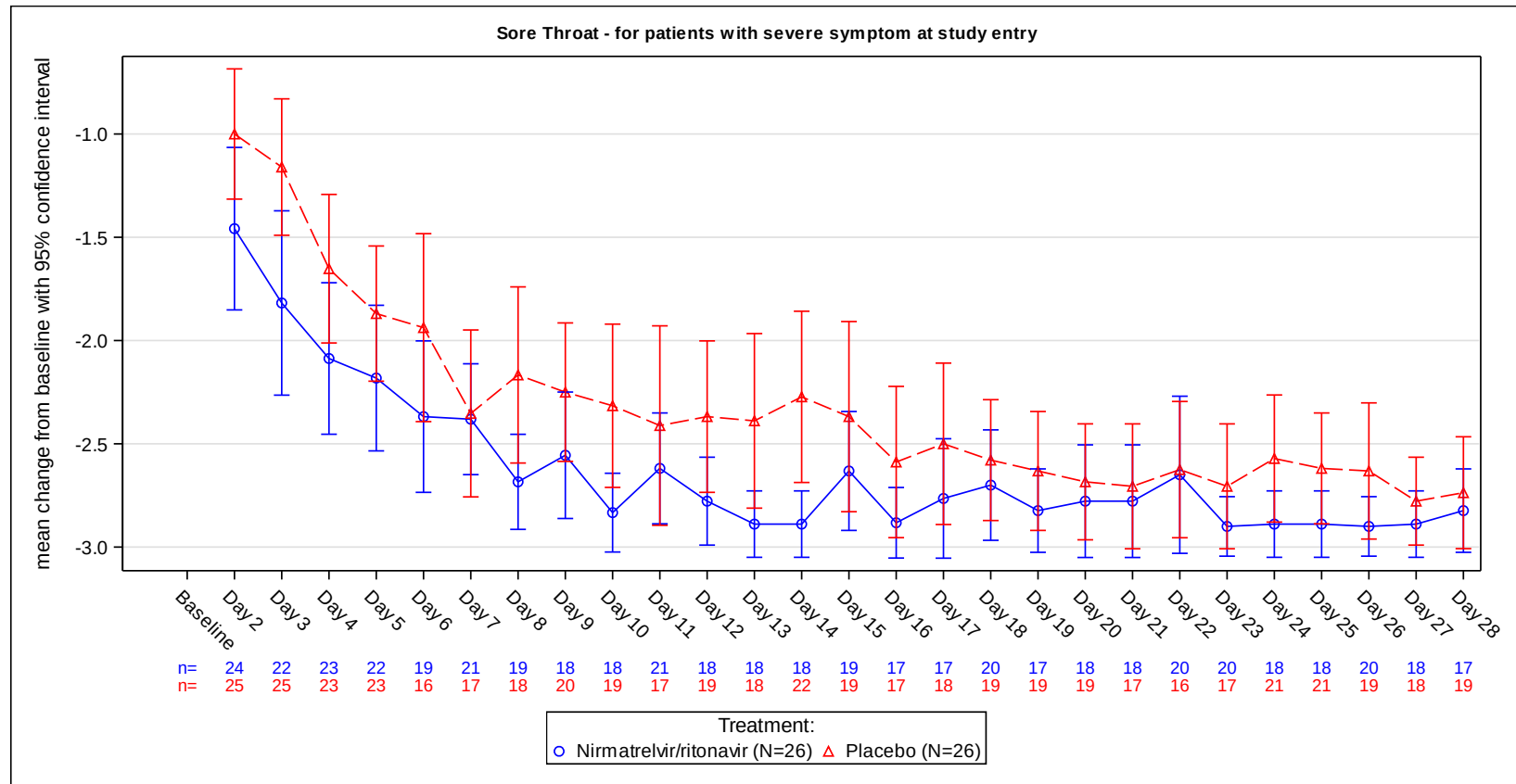


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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 Overall Study population
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Final

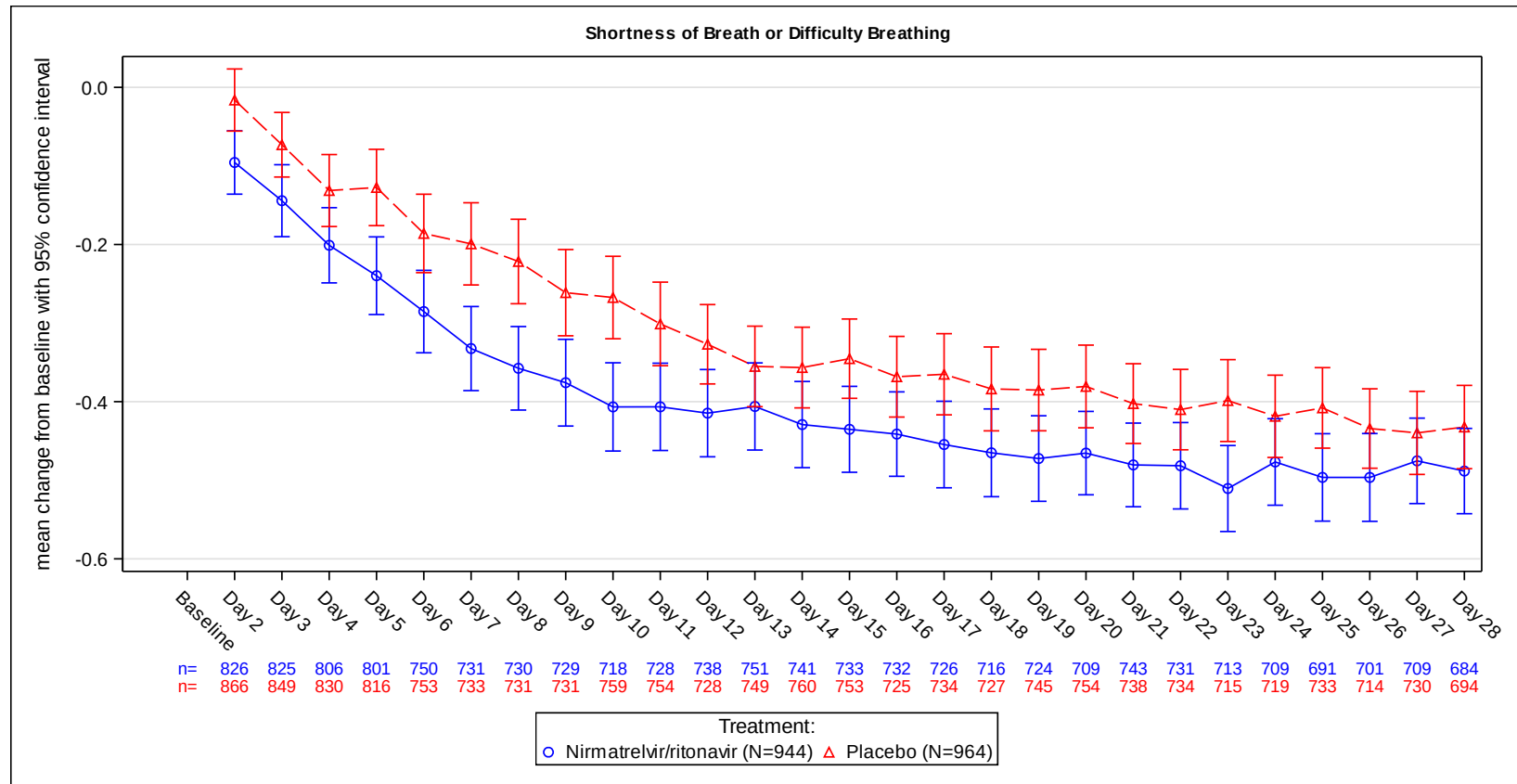


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms - Shortness of Breath or Difficulty Breathing

Final

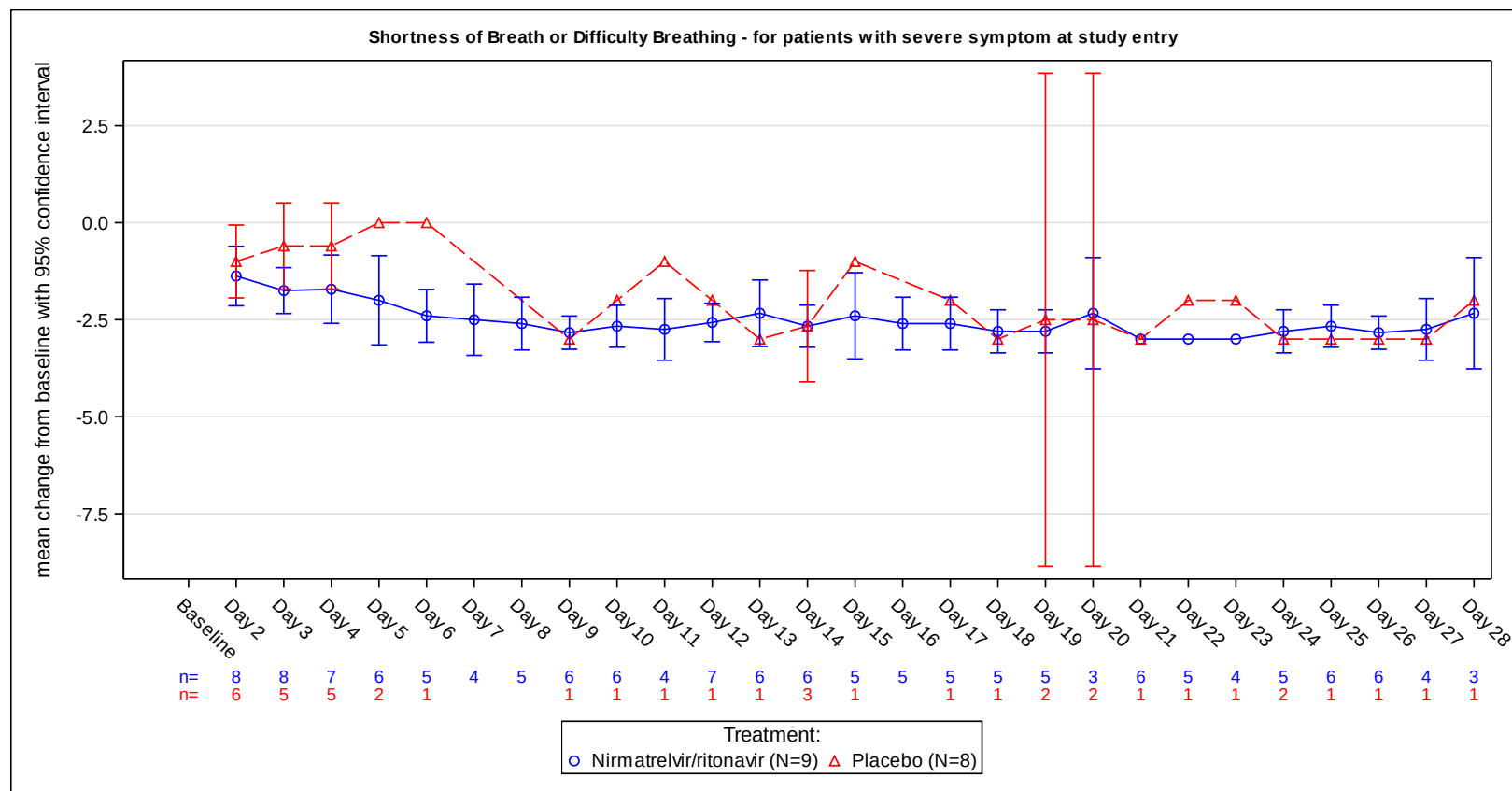


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms for patients with severe symptom at study entry - Shortness of Breath or Difficulty Breathing

Final

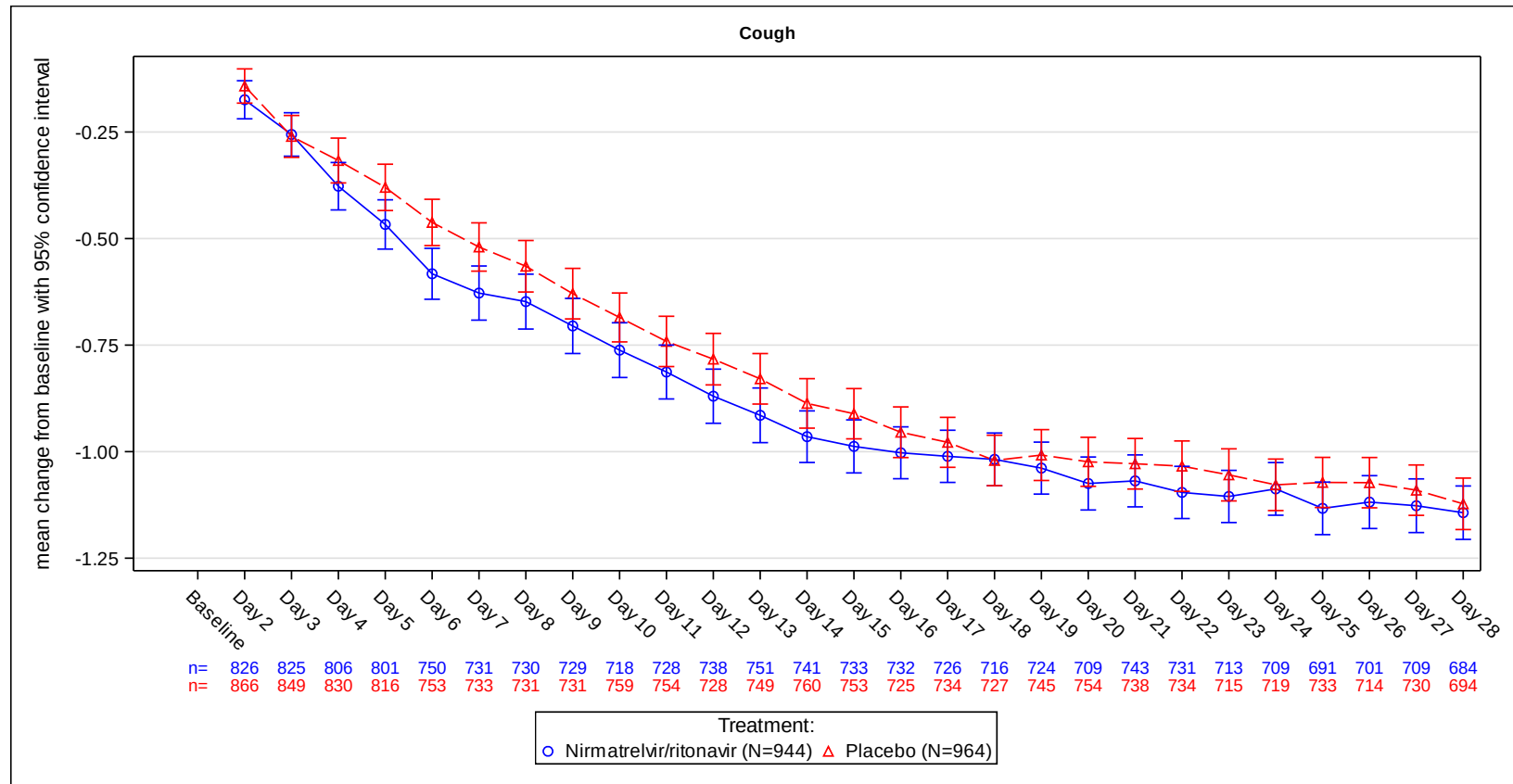


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms - Cough

Final

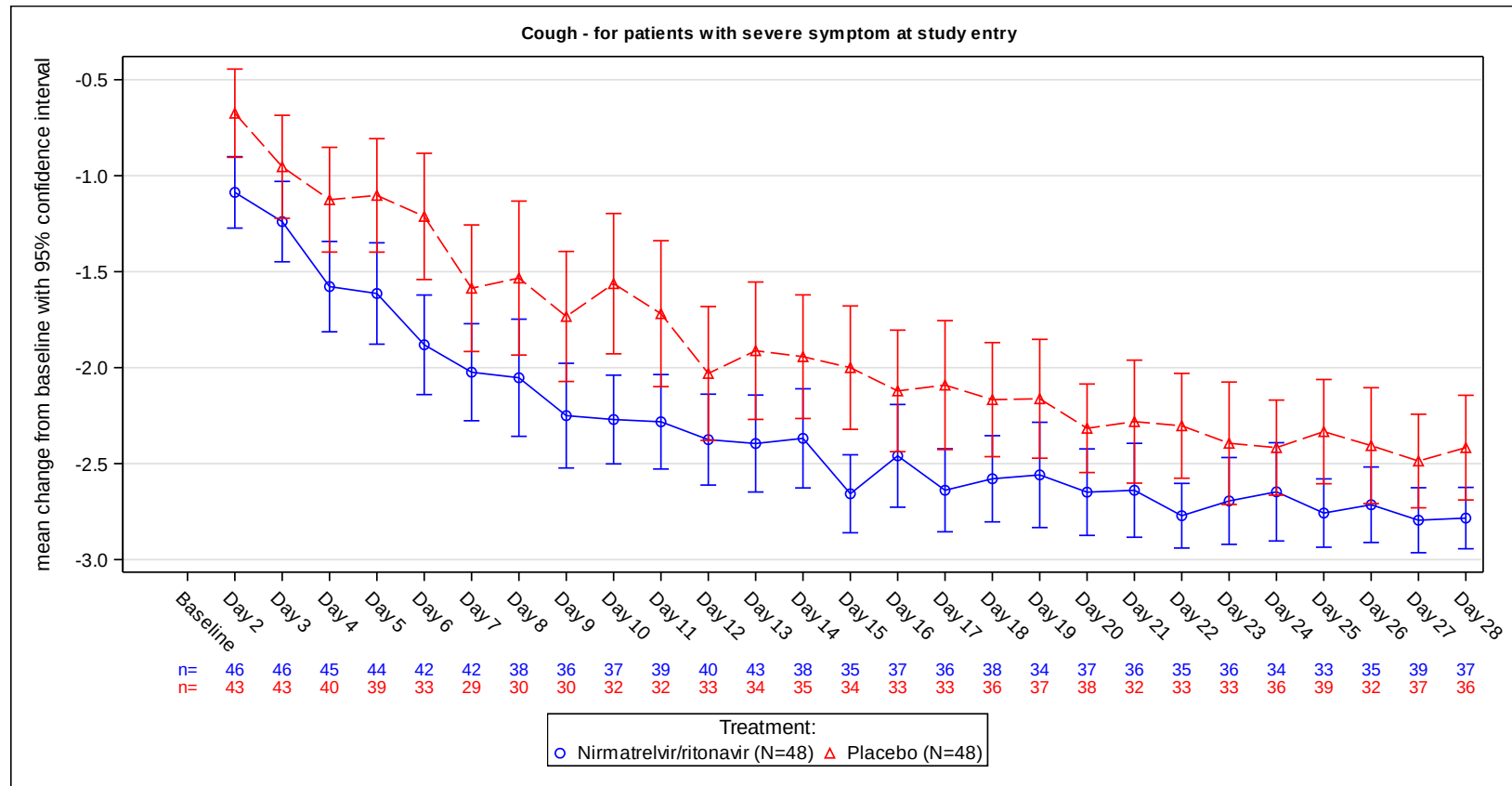


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms for patients with severe symptom at study entry - Cough

Final

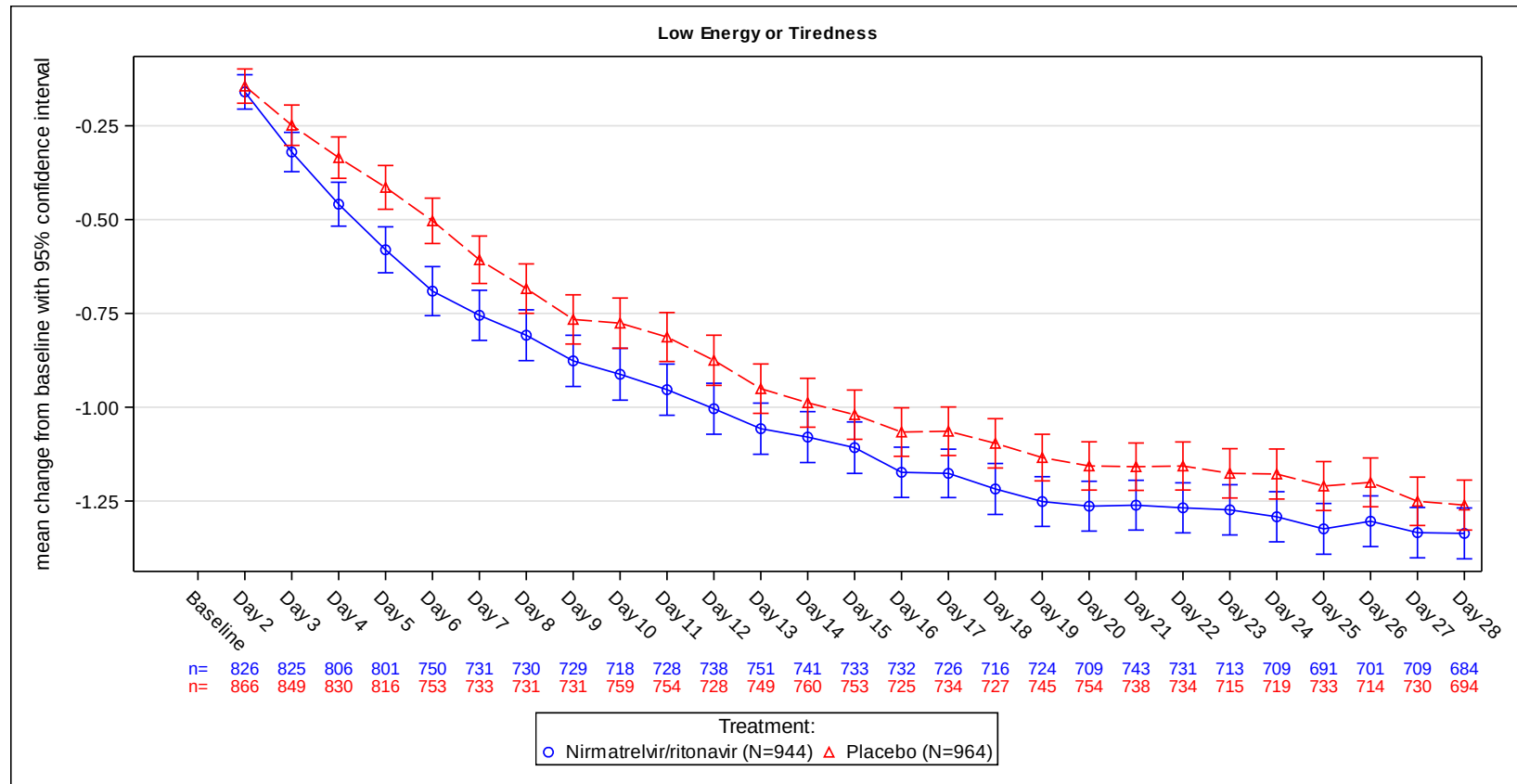


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Signs and Symptoms - Fatigue (low energy or tiredness)

Final

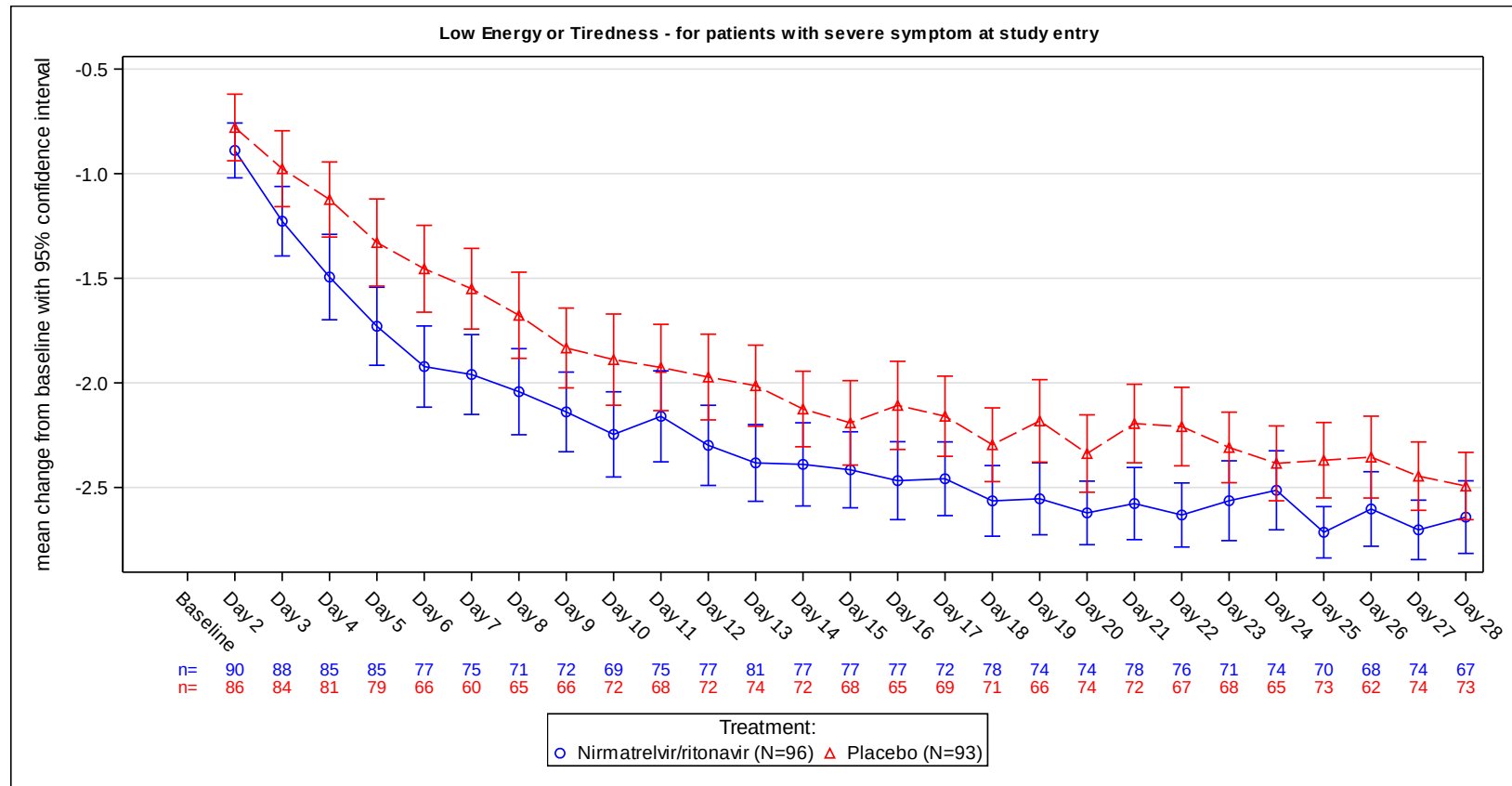


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Signs and Symptoms for patients with severe symptom at study entry - Fatigue (low energy or tiredness)

Final

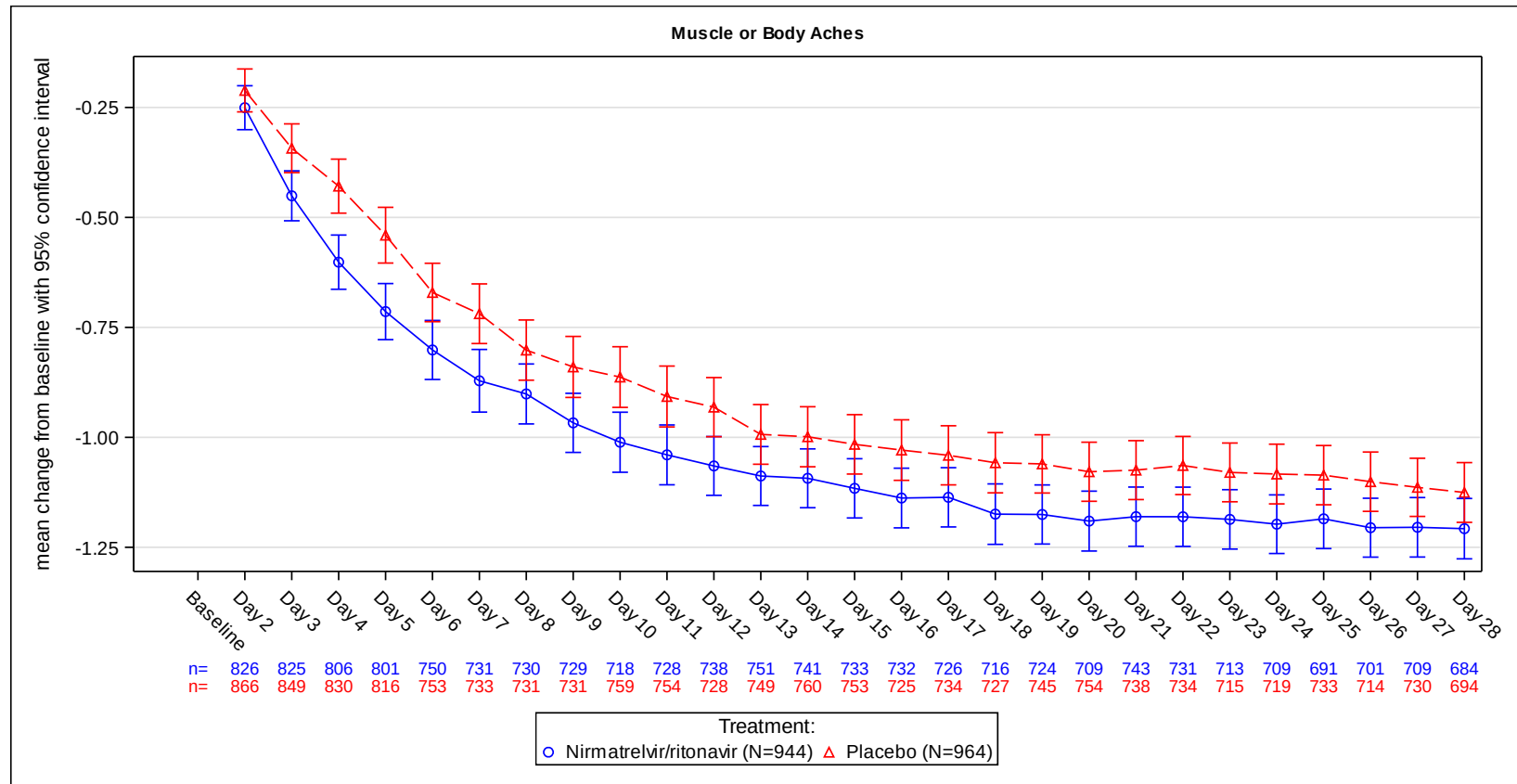


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms - Muscle or Body Aches

Final

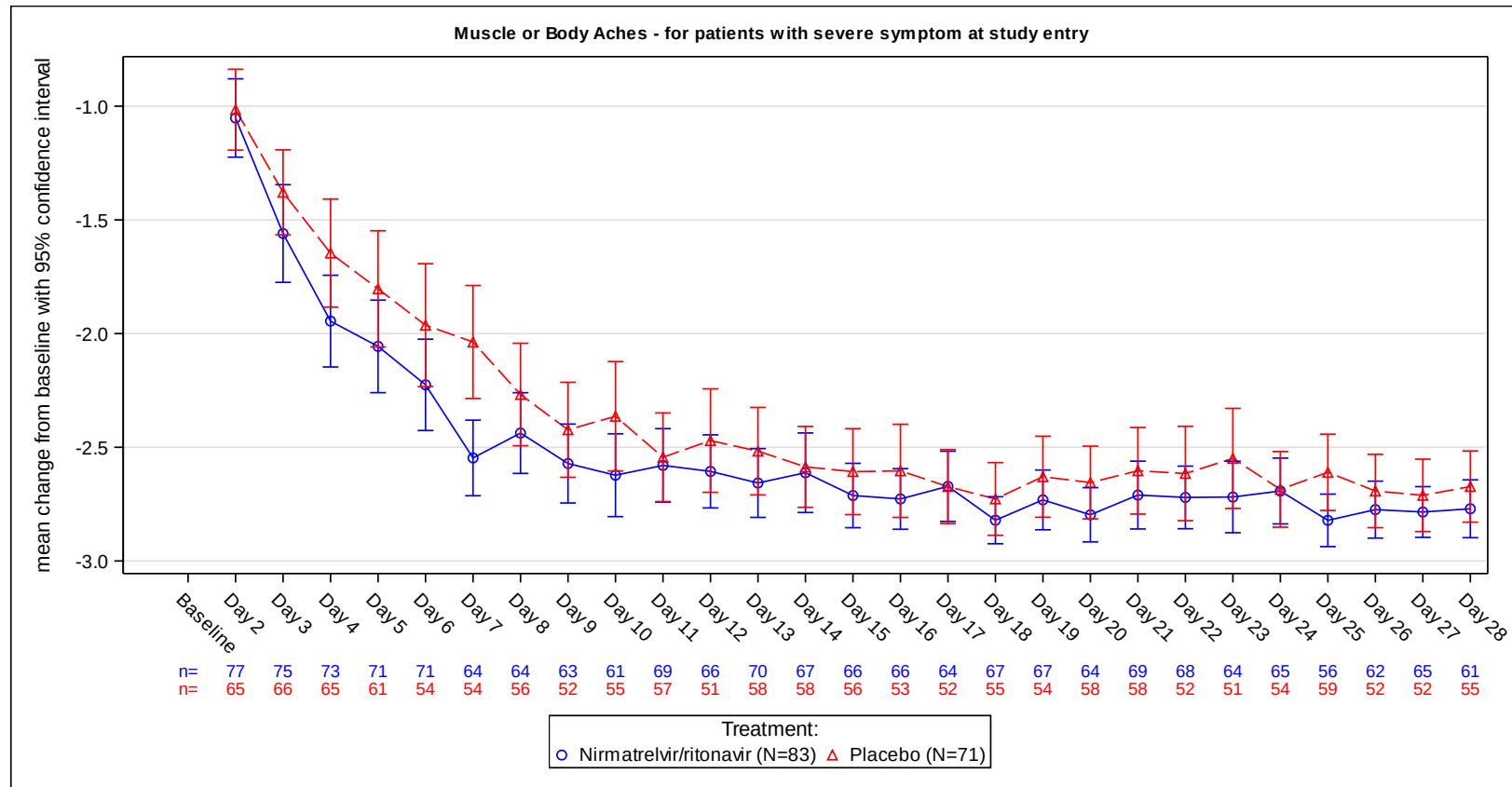


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms for patients with severe symptom at study entry - Muscle or Body Aches

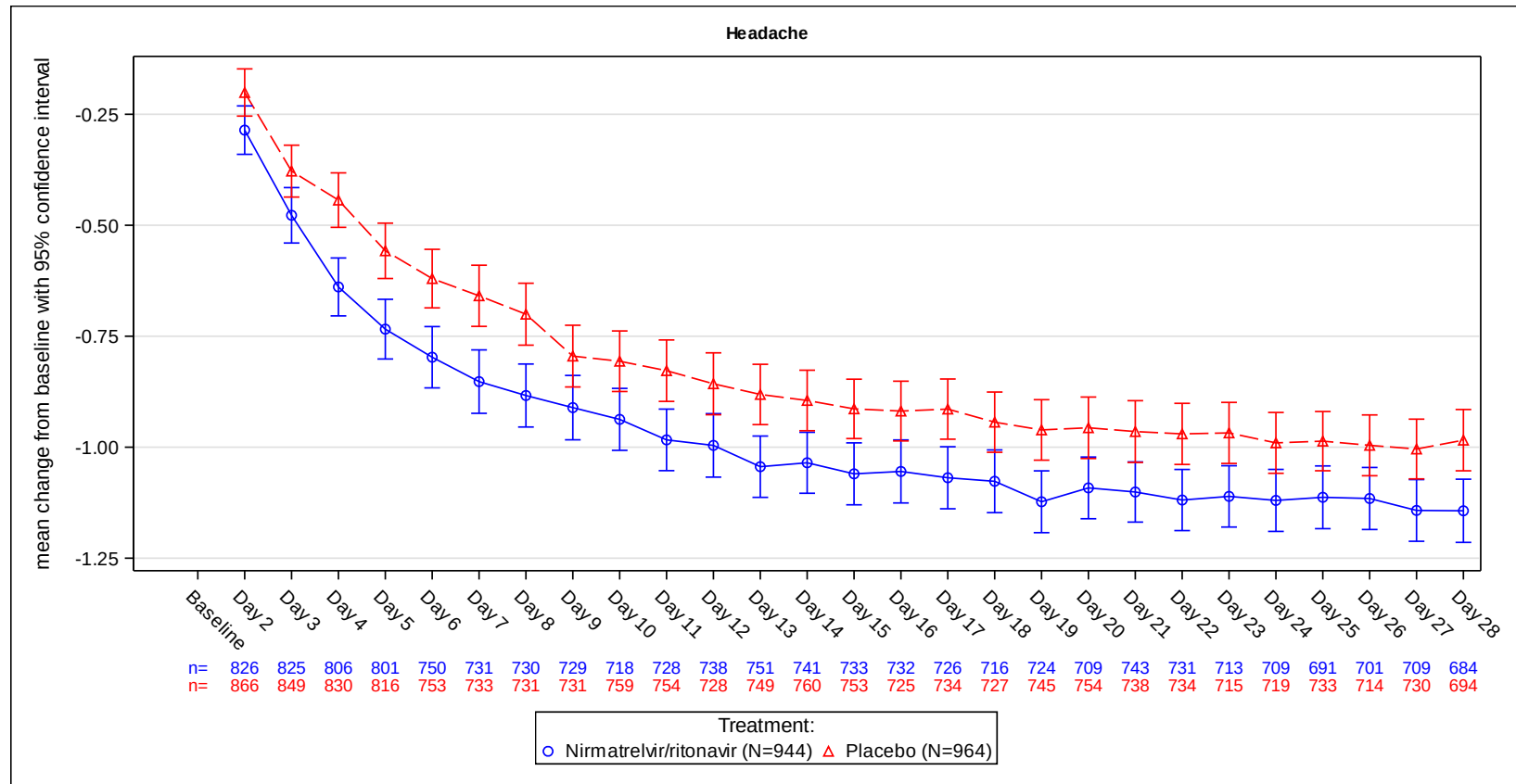
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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms - Headache

Final

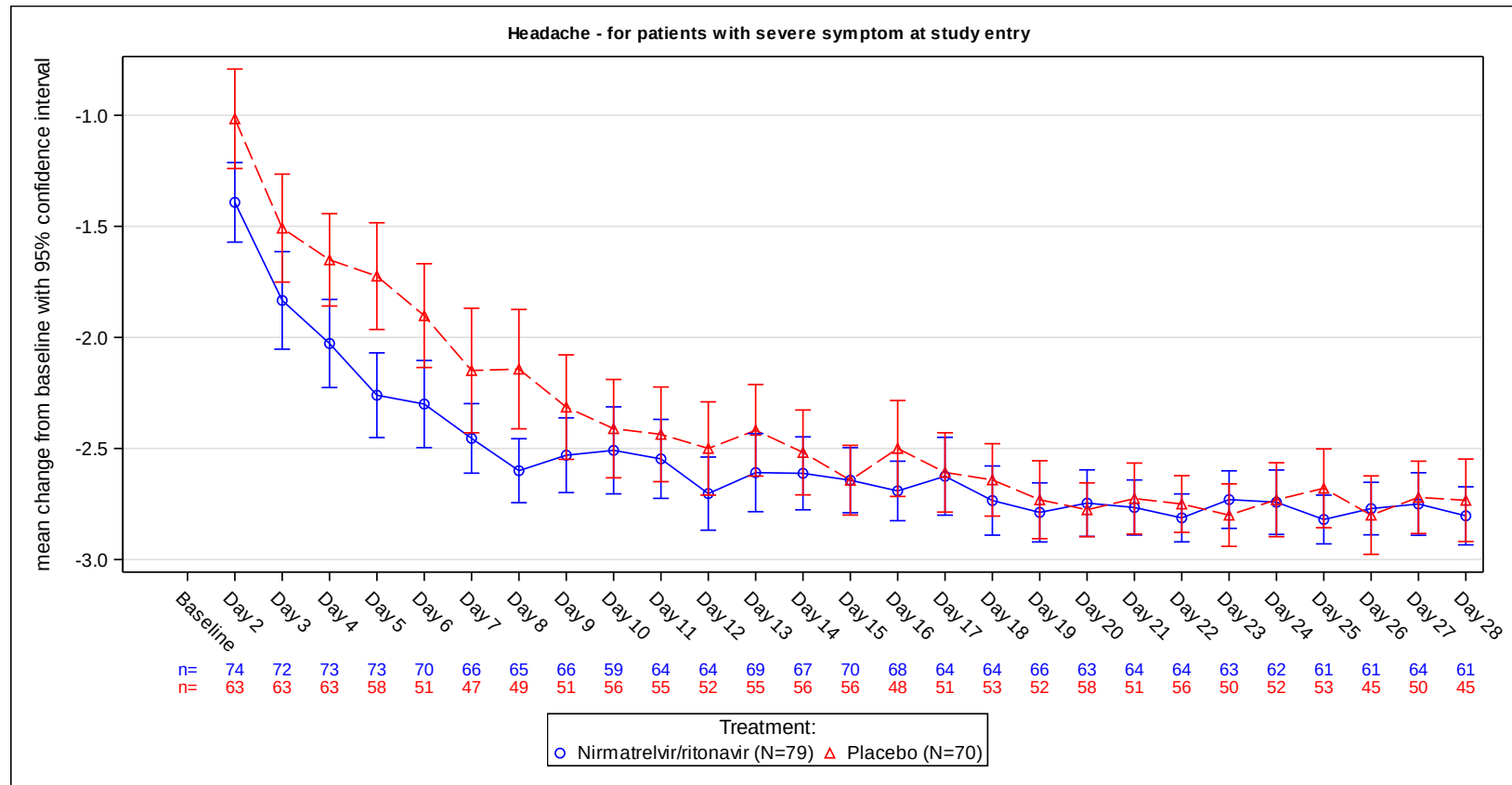


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms for patients with severe symptom at study entry - Headache

Final

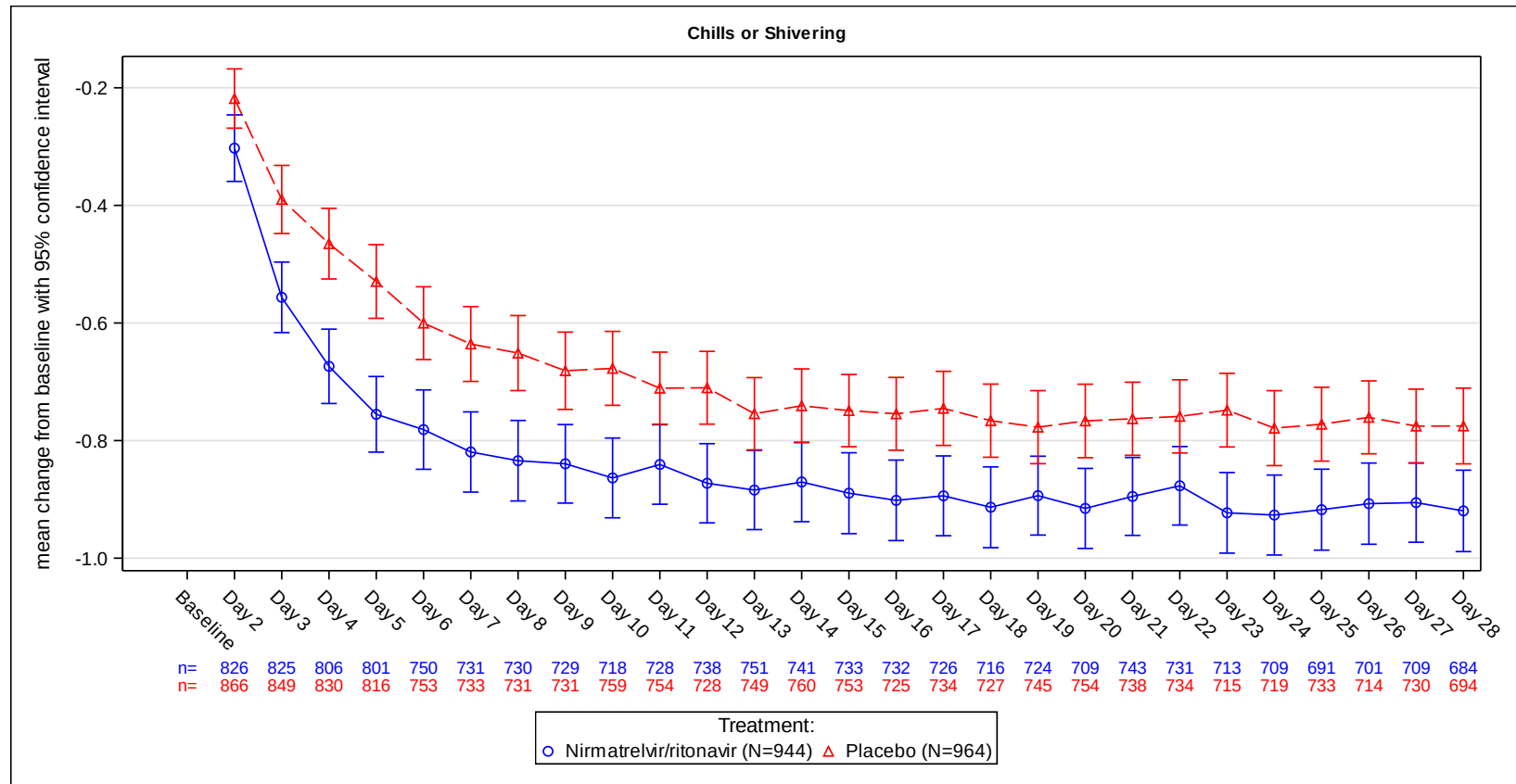


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms - Chills or Shivering

Final

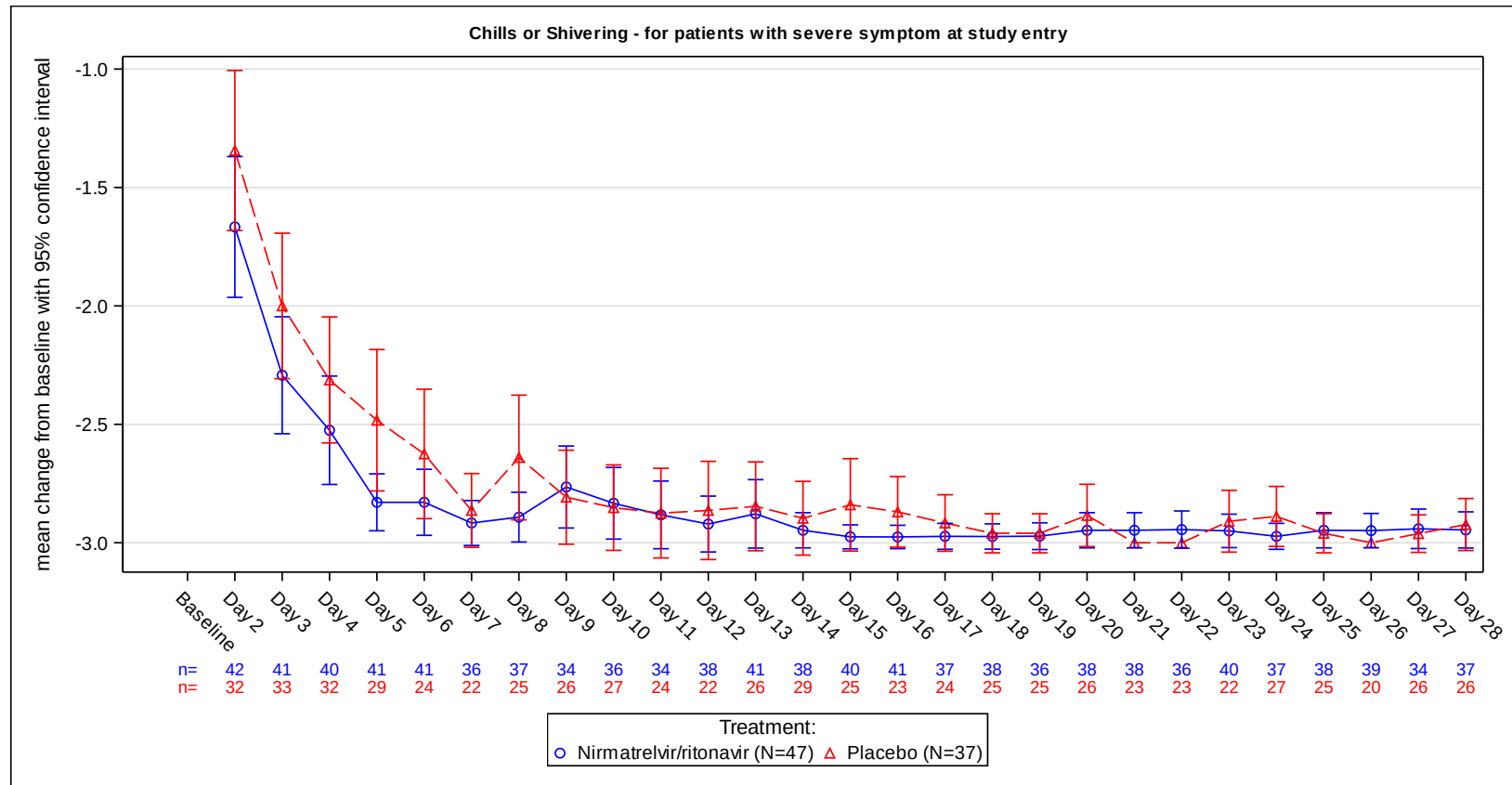


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms for patients with severe symptom at study entry - Chills or Shivering

Final

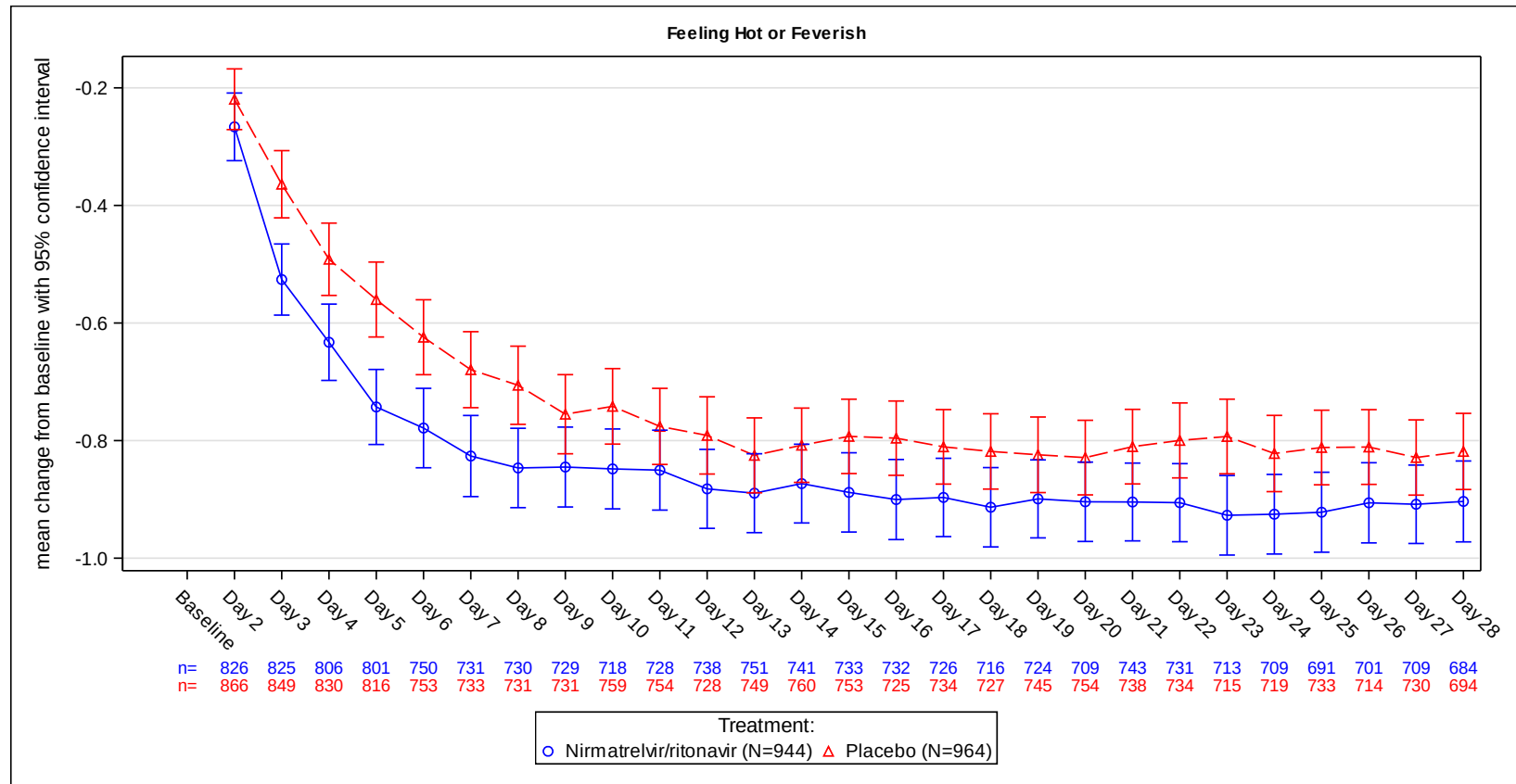


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms - Feeling Hot or Feverish

Final

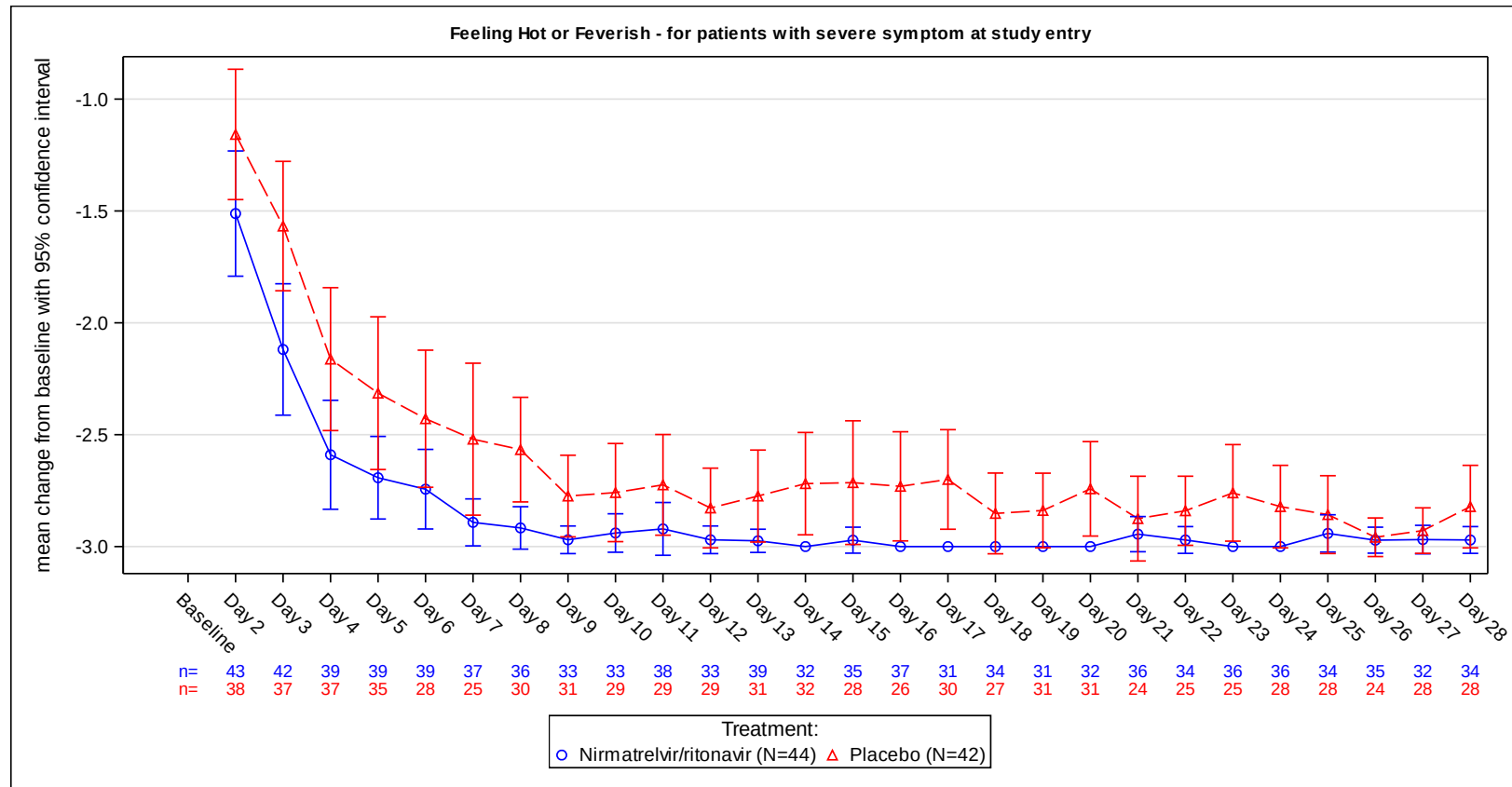


N = Number of participants, n = Number of participants with non missing values

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms for patients with severe symptom at study entry - Feeling Hot or Feverish

Final

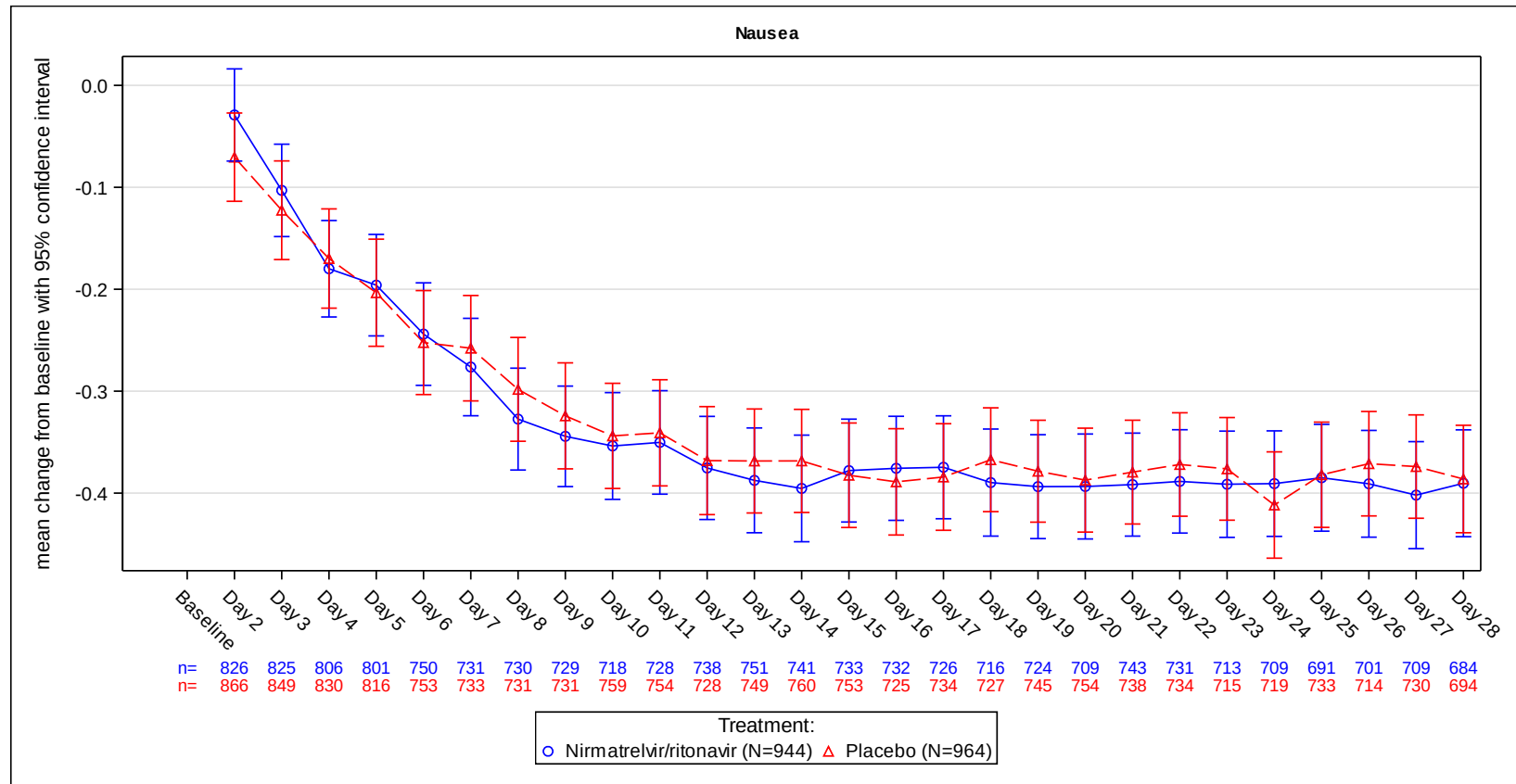


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms - Nausea

Final

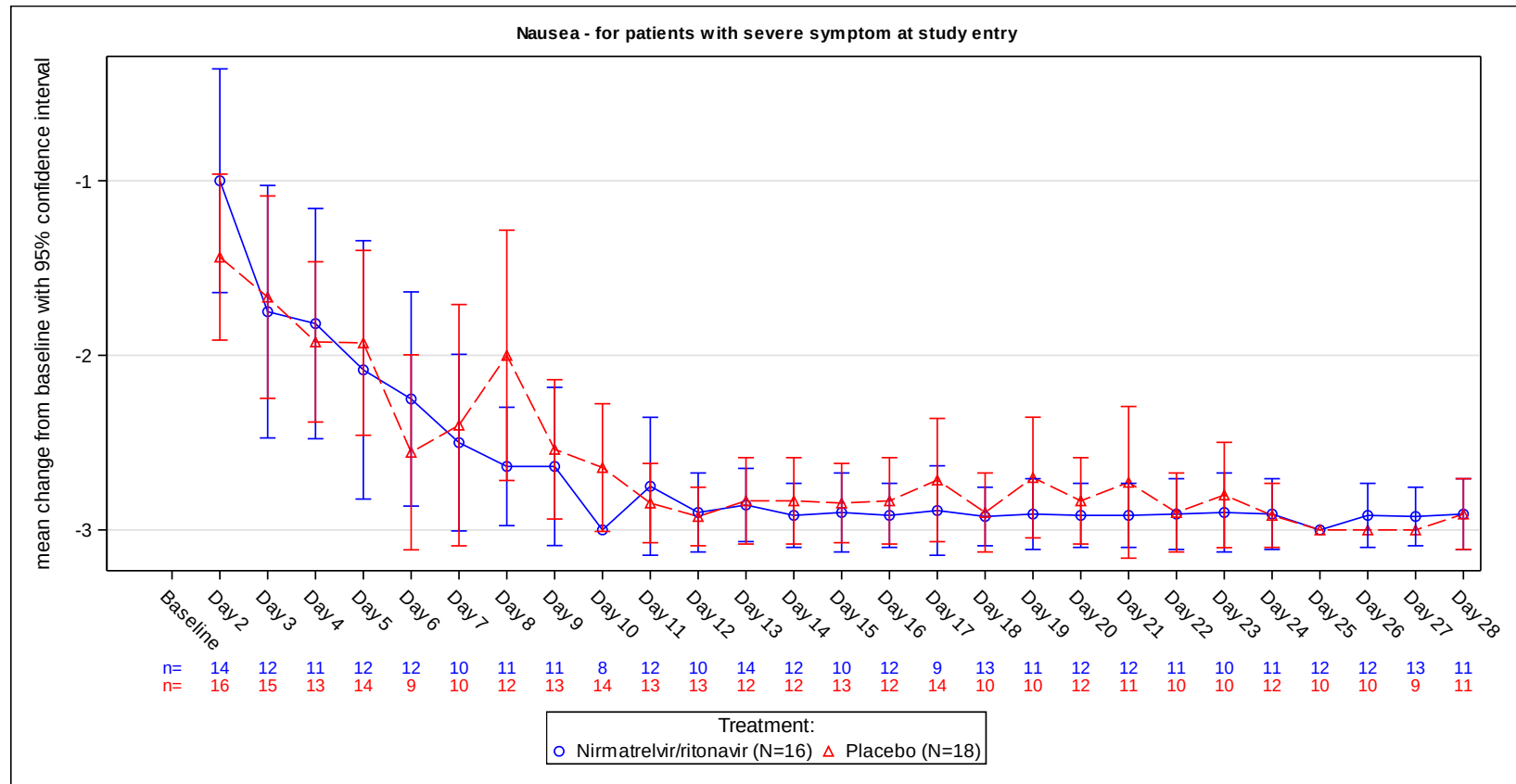


N = Number of participants, n = Number of participants with non missing values

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms for patients with severe symptom at study entry - Nausea

Final

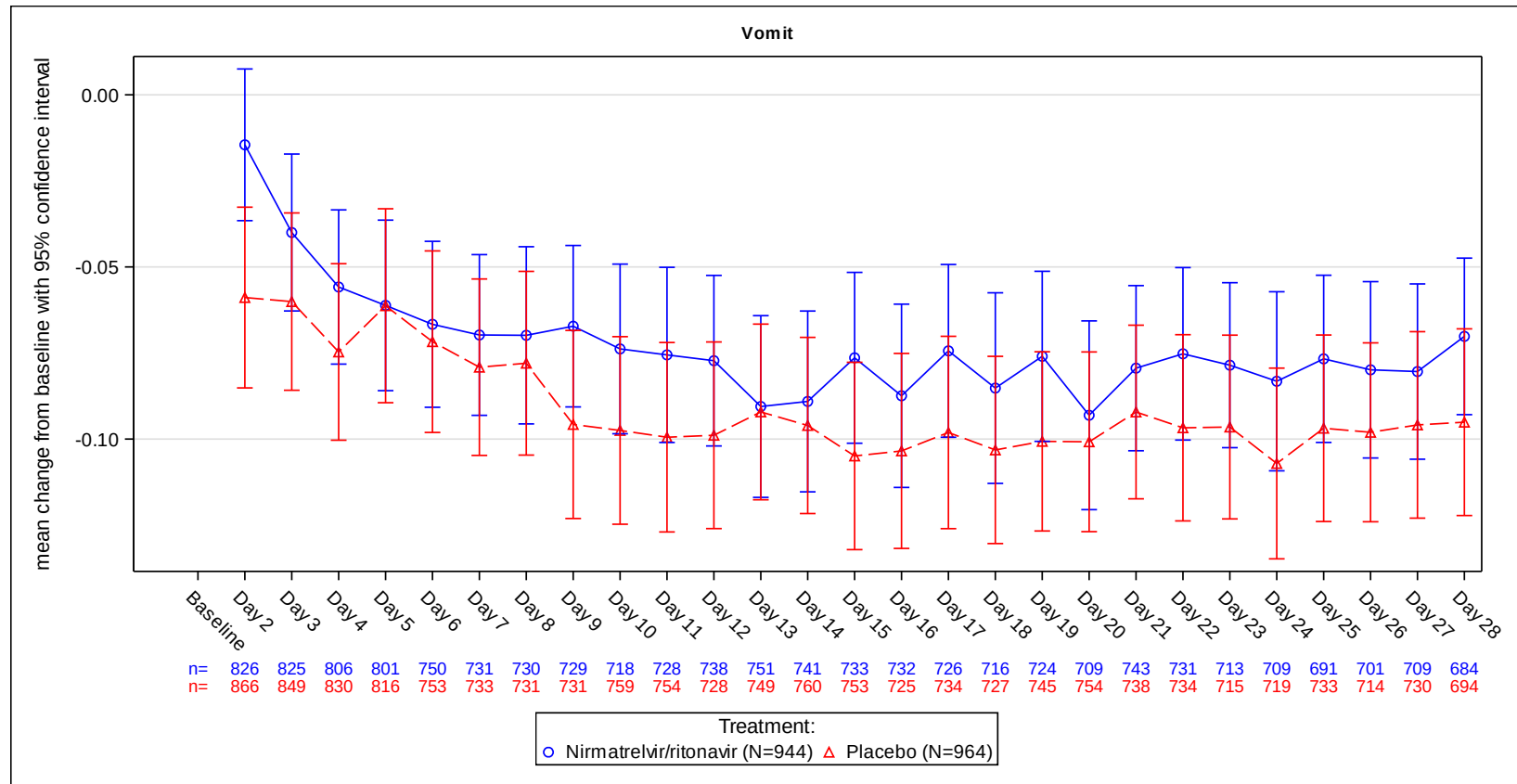


N = Number of participants, n = Number of participants with non missing values

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms - Vomit

Final

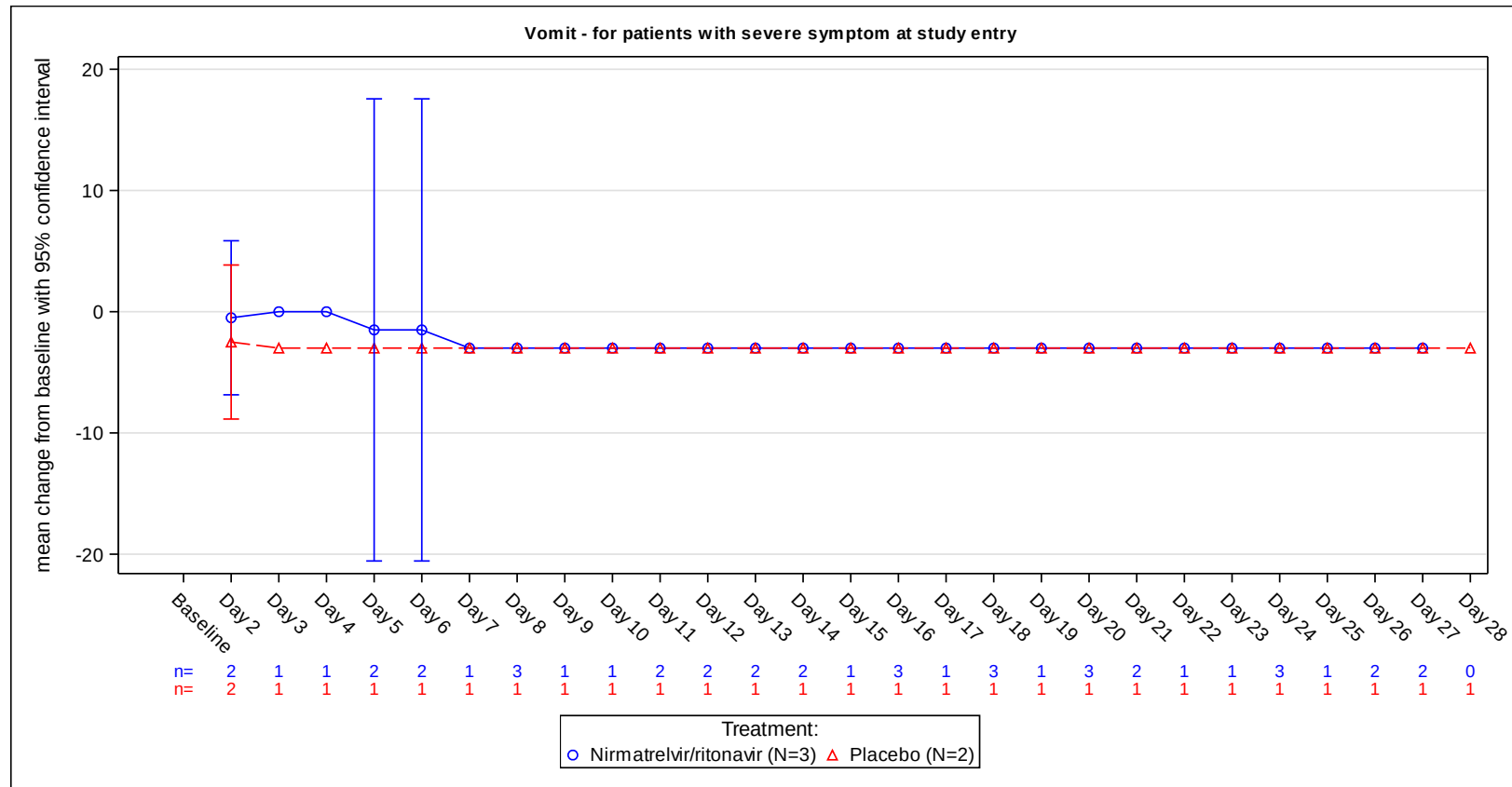


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms for patients with severe symptom at study entry - Vomit

Final

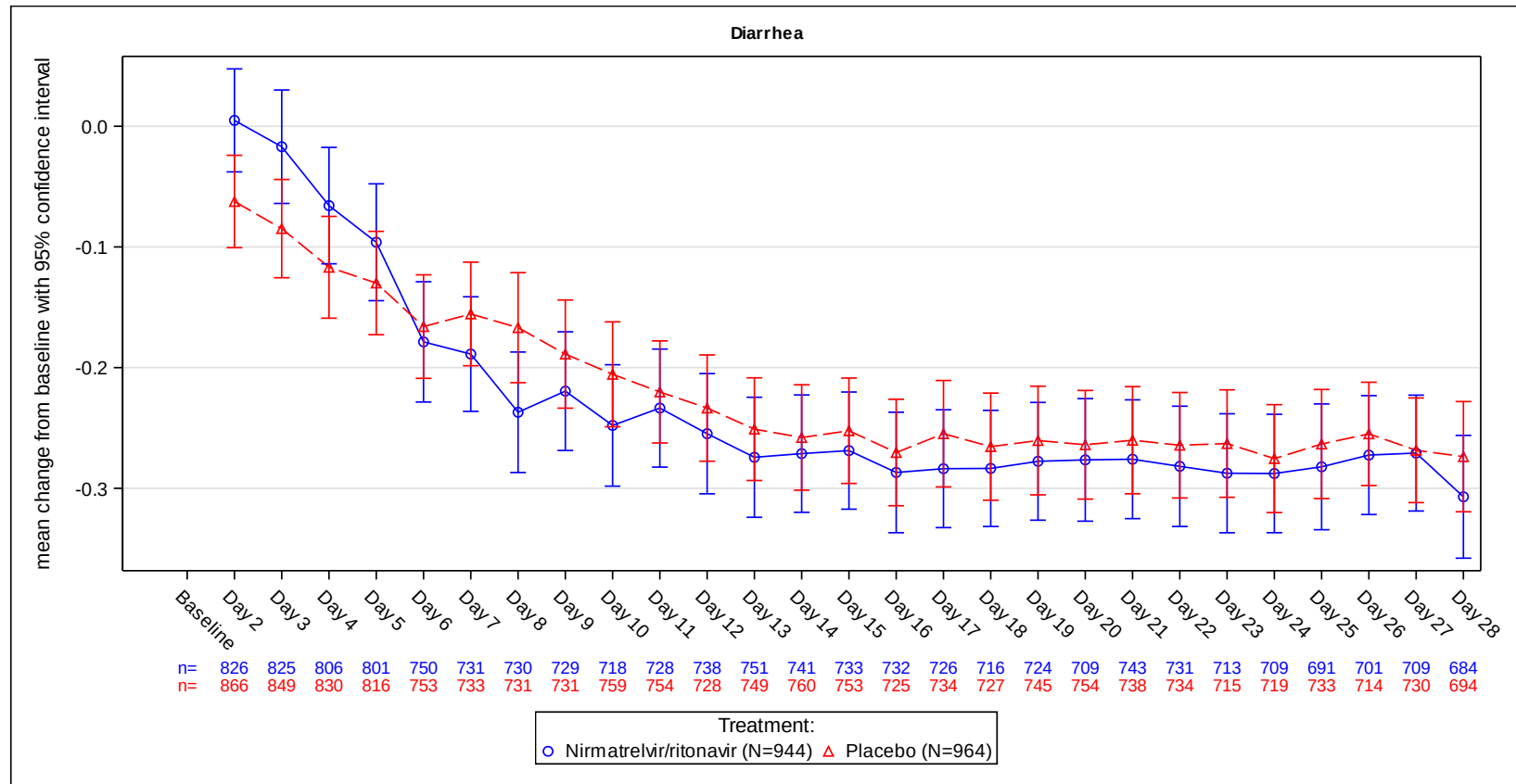


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms - Diarrhea

Final

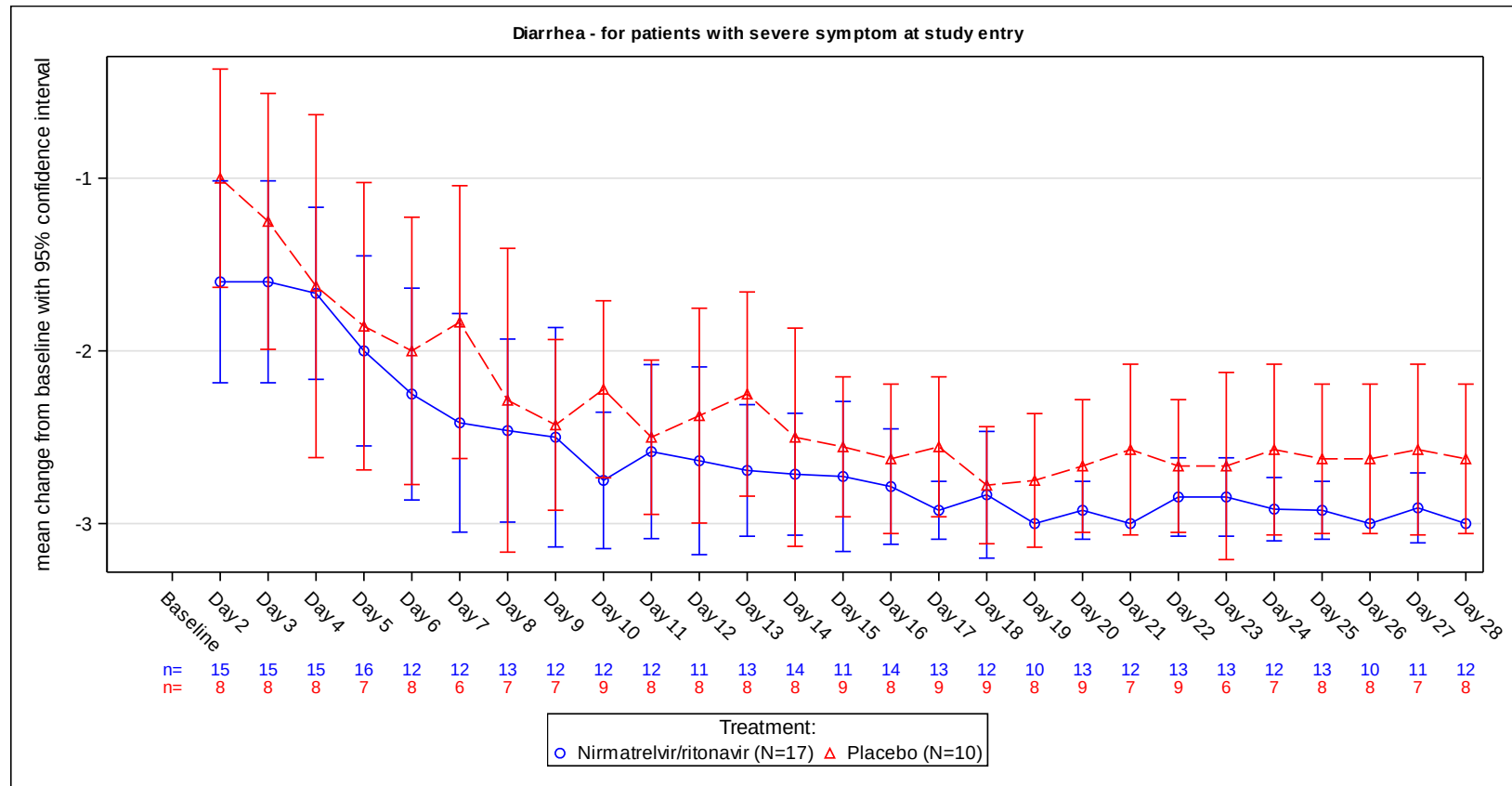


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Each Targeted Signs and Symptoms for patients with severe symptom at study entry - Diarrhea

Final

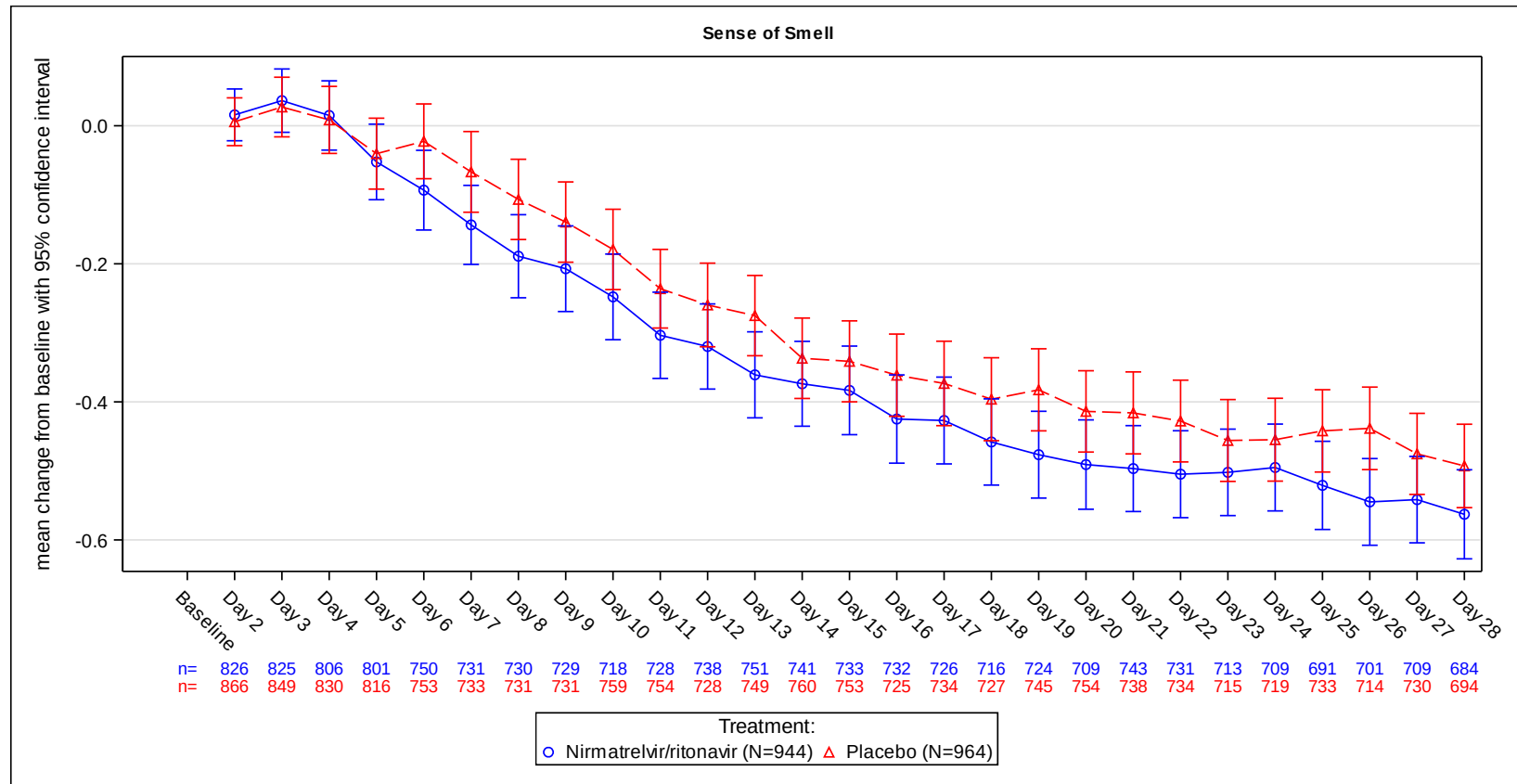


N = Number of participants, n = Number of participants with non missing values

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Signs and Symptoms - Loss of smell

Final

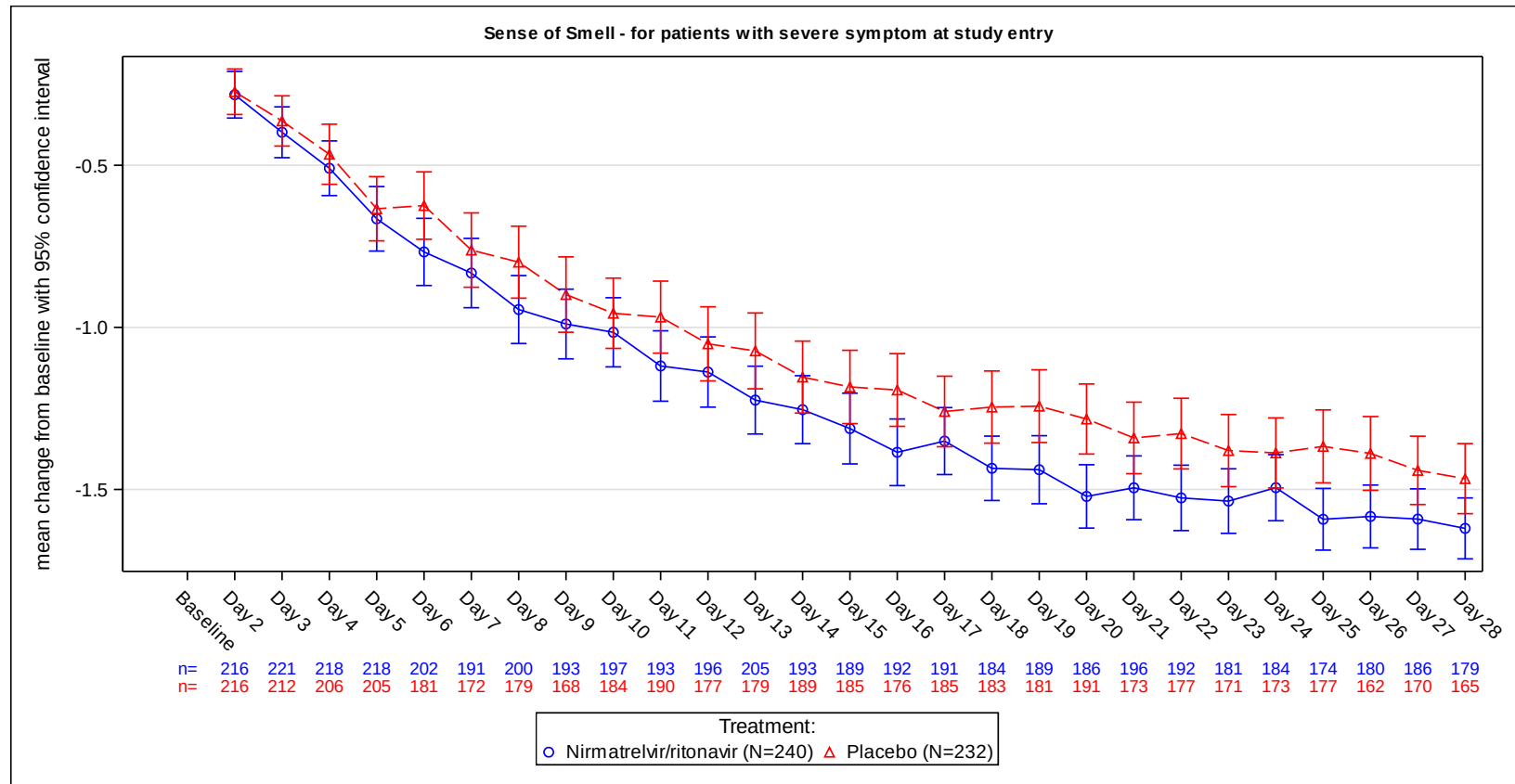


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Signs and Symptoms for patients with severe symptom at study entry - Loss of smell

Final

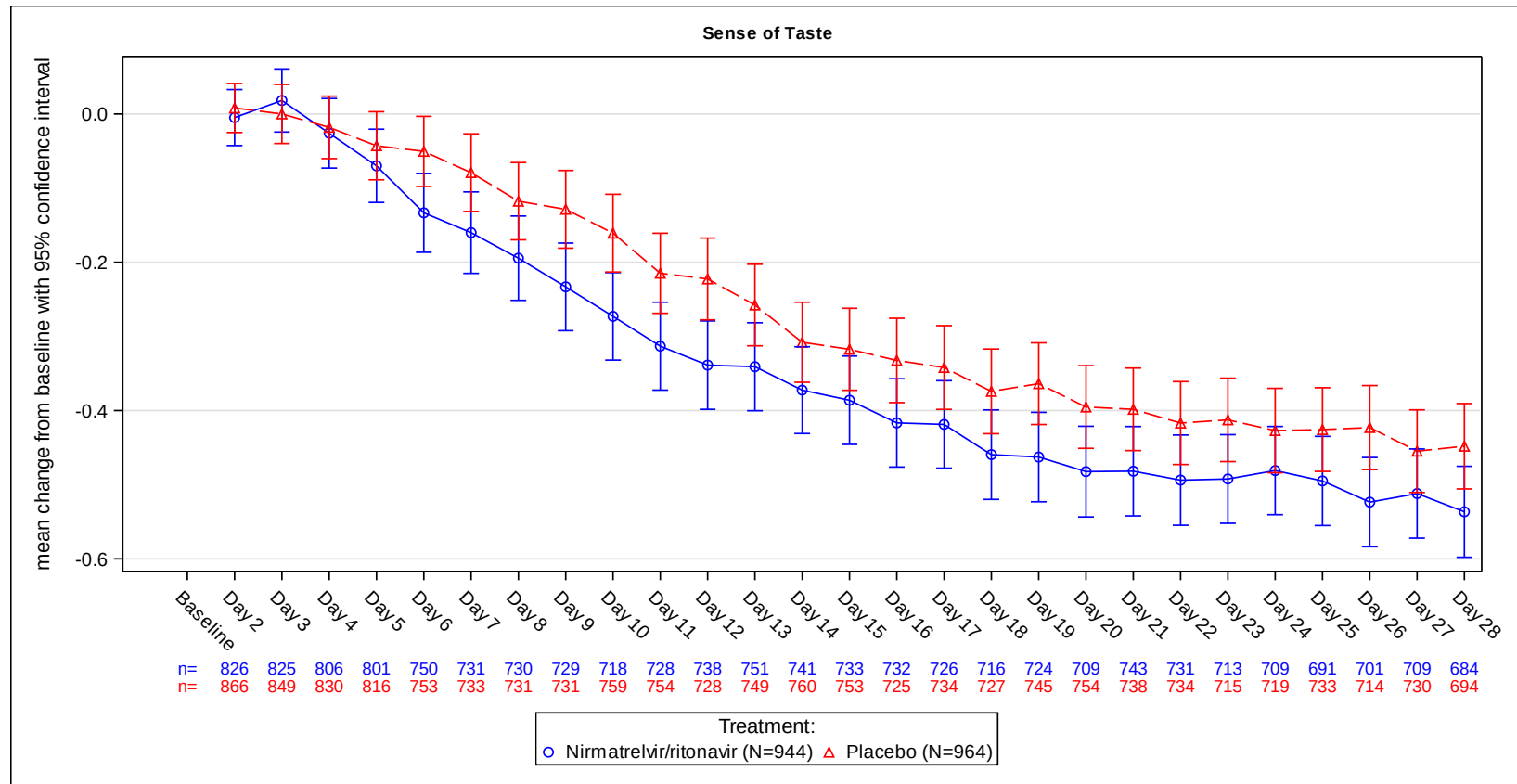


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Signs and Symptoms - Loss of taste

Final

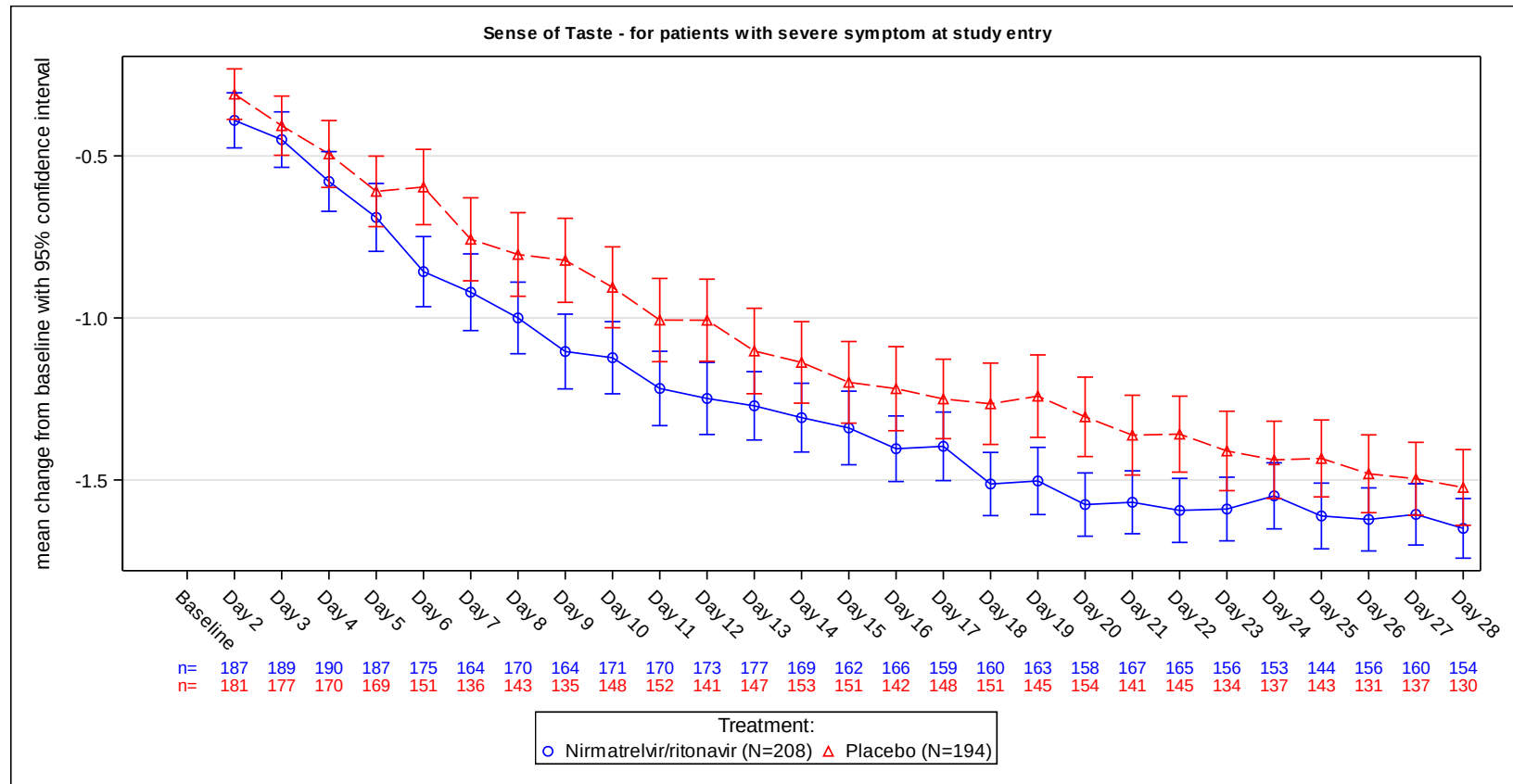


N = Number of participants, n = Number of participants with non missing values

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Signs and Symptoms for patients with severe symptom at study entry - Loss of taste

Final



N = Number of participants, n = Number of participants with non missing values

Anhang 4-G 1.1.2: Krankheitsbedingte Symptome (Verslechterung des Status in einem oder mehreren Symptom(en) (Gesamtrate) (OC) - Sensitivitätsanalyse)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with Progression of Worsening Status in 1 or More Signs and Symptoms (OC)

Final

	Nirmatrelvir/ritonavir (N=865)	Placebo (N=903)
Number of subjects with Response, n (%)	718 (83.0)	728 (80.6)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.170 (0.914, 1.499) 0.213	
Relative Risk (95% CI)	1.018 (0.974, 1.063) 0.427	
Risk Difference (95% CI)	0.017 (-0.019, 0.053) 0.362	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.174 (0.921, 1.496) 0.194	
Relative Risk (95% CI)	1.030 (0.985, 1.076) 0.193	
Risk Difference (95% CI)	0.024 (-0.012, 0.060) 0.193	

N: Number of participants with observed data, CI: Confidence Interval, NE: Not estimable

Only observed cases (OC), no Imputation approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Anhang 4-G 1.1.3: Krankheitsbedingte Symptome (Präspezifizierte Analysen gemäß SAP (11 Symptome) - maßgebliche Analyse)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with Any Severe Targeted Signs and Symptoms

Final

	Nirmatrelvir/ritonavir (N=928)	Placebo (N=955)
Number of subjects with Response, n (%)	185 (19.9)	200 (20.9)
Adjusted analysis [1] Odds Ratio (95% CI)	0.966 (0.761, 1.226) 0.774	
Relative Risk (95% CI)	0.977 (0.821, 1.164) 0.797	
Risk Difference (95% CI)	NE (NE, NE) NE	
Unadjusted analysis [2] Odds Ratio (95% CI)	0.940 (0.751, 1.176) 0.588	
Relative Risk (95% CI)	0.952 (0.796, 1.138) 0.588	
Risk Difference (95% CI)	-0.010 (-0.046, 0.026) 0.588	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Overall Study population
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 Analysis of Participants with Any Severe Targeted Signs and Symptoms (NRI)

Final

	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)
Number of subjects with Response, n (%)	175 (18.5)	192 (19.9)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.925 (0.727, 1.177) 0.526	
Relative Risk (95% CI)	0.949 (0.792, 1.137) 0.569	
Risk Difference (95% CI)	NE (NE, NE) NE	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.915 (0.729, 1.149) 0.445	
Relative Risk (95% CI)	0.931 (0.774, 1.119) 0.445	
Risk Difference (95% CI)	-0.014 (-0.049, 0.022) 0.445	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Analysis of Participants with Progression of Worsening Status in 1 or More Targeted Signs and Symptoms

Final

	Nirmatrelvir/ritonavir (N=928)	Placebo (N=955)
Number of subjects with Response, n (%)	702 (75.6)	706 (73.9)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.094 (0.881, 1.359) 0.416	
Relative Risk (95% CI)	1.013 (0.963, 1.065) 0.629	
Risk Difference (95% CI)	0.012 (-0.026, 0.051) 0.528	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.096 (0.890, 1.349) 0.390	
Relative Risk (95% CI)	1.023 (0.971, 1.078) 0.390	
Risk Difference (95% CI)	0.017 (-0.022, 0.056) 0.390	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Final

	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)
Number of subjects with Response, n (%)	702 (74.4)	706 (73.2)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.061 (0.858, 1.312) 0.587	
Relative Risk (95% CI)	1.005 (0.954, 1.059) 0.844	
Risk Difference (95% CI)	0.007 (-0.032, 0.046) 0.720	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.060 (0.864, 1.300) 0.575	
Relative Risk (95% CI)	1.015 (0.963, 1.071) 0.575	
Risk Difference (95% CI)	0.011 (-0.028, 0.051) 0.575	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Analysis of Participants with Progression of Worsening Status in 1 or More Targeted Signs and Symptoms (OC)

Final

	Nirmatrelvir/ritonavir (N=865)	Placebo (N=903)
Number of subjects with Response, n (%)	669 (77.3)	682 (75.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.121 (0.892, 1.408) 0.327	
Relative Risk (95% CI)	1.012 (0.963, 1.065) 0.629	
Risk Difference (95% CI)	0.013 (-0.026, 0.052) 0.507	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.106 (0.888, 1.378) 0.369	
Relative Risk (95% CI)	1.024 (0.972, 1.078) 0.369	
Risk Difference (95% CI)	0.018 (-0.021, 0.058) 0.368	

N: Number of participants with observed data, CI: Confidence Interval, NE: Not estimable

Only observed cases (OC), no Imputation approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 RKI-conform mITT2 Analysis set
 Analysis of Time to Sustained Alleviation of All Targeted Signs and Symptoms Through Day 28

Final

	Nirmatrelvir/ritonavir (N=928)	Placebo (N=955)
Number of subjects with events, n (%)	684 (73.7)	621 (65.0)
Number of censored subjects, n (%)	244 (26.3)	334 (35.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	13.0 (12.0, 13.0)	15.0 (14.0, 17.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.291 (1.155, 1.442)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.308 (1.173, 1.458)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

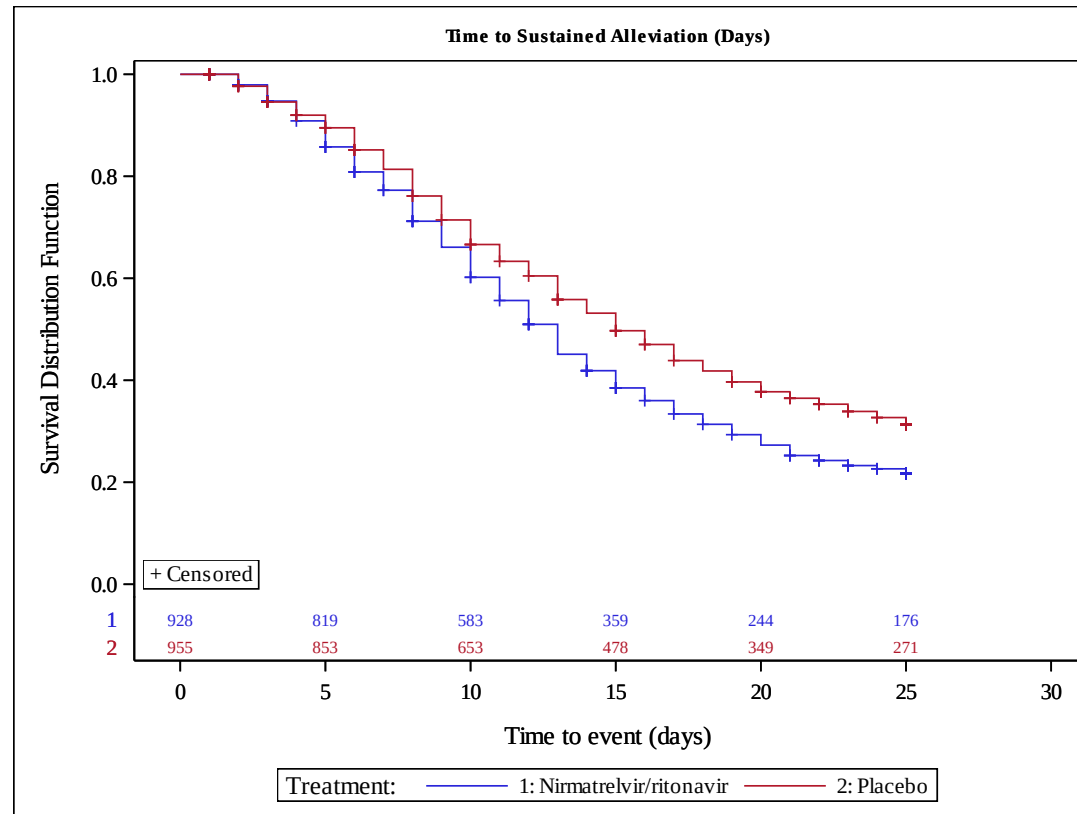
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Kaplan-Meier Plot of Time to Sustained Alleviation of All Targeted Signs and Symptoms Through Day 28

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Analysis of Time to Sustained Alleviation of All Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry

Final

	Nirmatrelvir/ritonavir (N=188)	Placebo (N=178)
Number of subjects with events, n (%)	161 (85.6)	136 (76.4)
Number of censored subjects, n (%)	27 (14.4)	42 (23.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (4.0, 5.0)	8.0 (7.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.417 (1.118, 1.796)	
p-value [3]	0.004	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.501 (1.194, 1.889)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

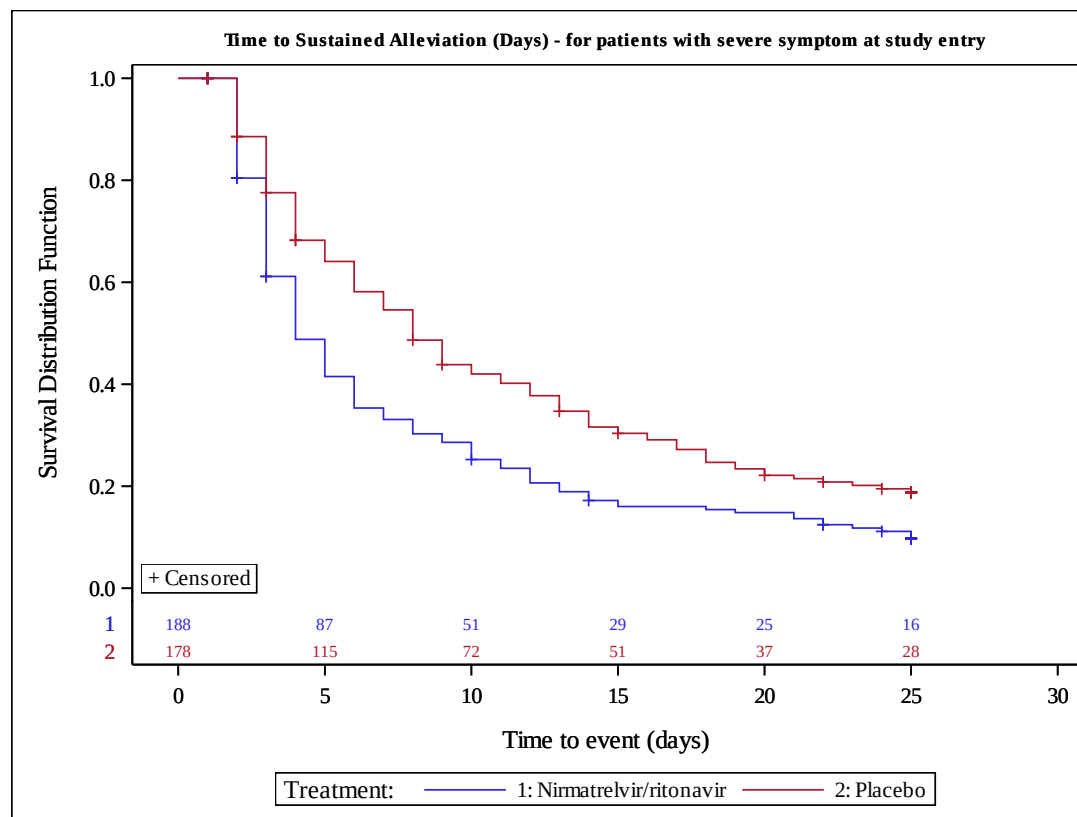
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 RRI-conform mITT2 Analysis set
 Analysis of Time to Sustained Resolution of All Targeted Signs and Symptoms Through Day 28

Final

	Nirmatrelvir/ritonavir (N=928)	Placebo (N=955)
Number of subjects with events, n (%)	602 (64.9)	556 (58.2)
Number of censored subjects, n (%)	326 (35.1)	399 (41.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	17.0 (15.0, 18.0)	19.0 (17.0, 20.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.205 (1.071, 1.355)	
p-value [3]	0.002	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.220 (1.087, 1.369)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

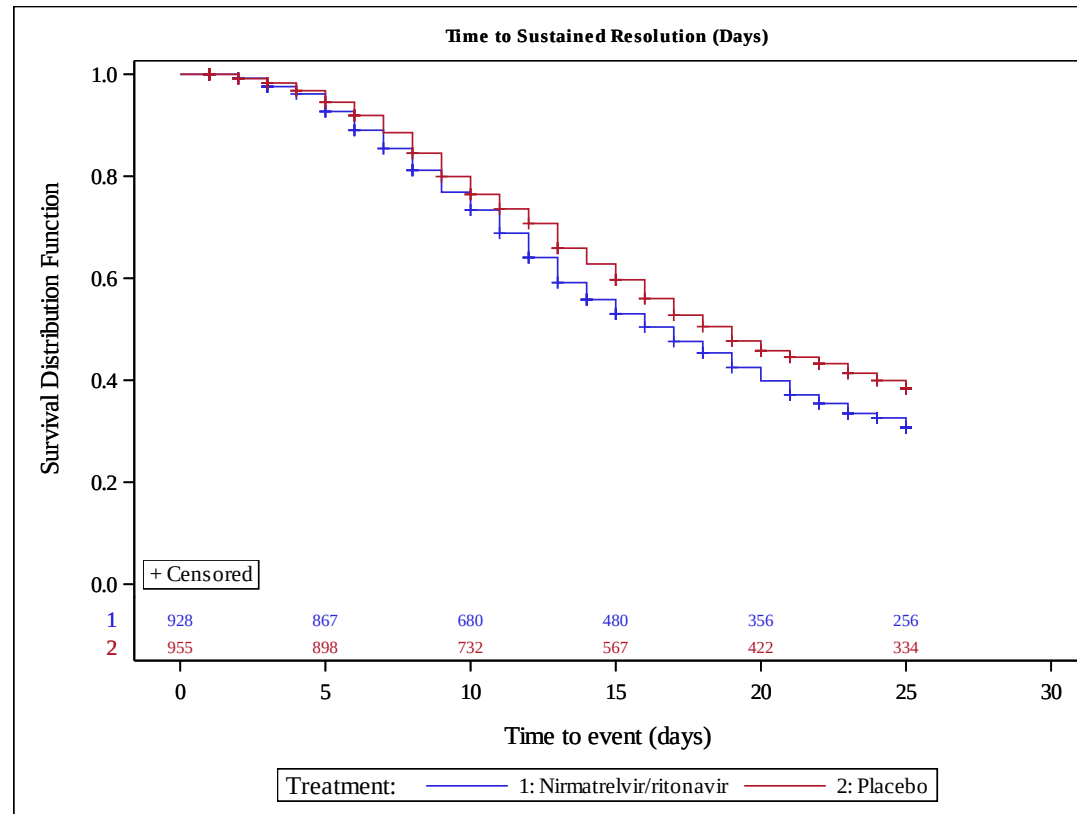
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

	Nirmatrelvir/ritonavir (N=188)	Placebo (N=178)
Number of subjects with events, n (%)	128 (68.1)	101 (56.7)
Number of censored subjects, n (%)	60 (31.9)	77 (43.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	12.0 (11.0, 15.0)	18.0 (16.0, 23.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.420 (1.084, 1.860)	
p-value [3]	0.011	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.496 (1.152, 1.943)	
p-value [3]	0.003	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

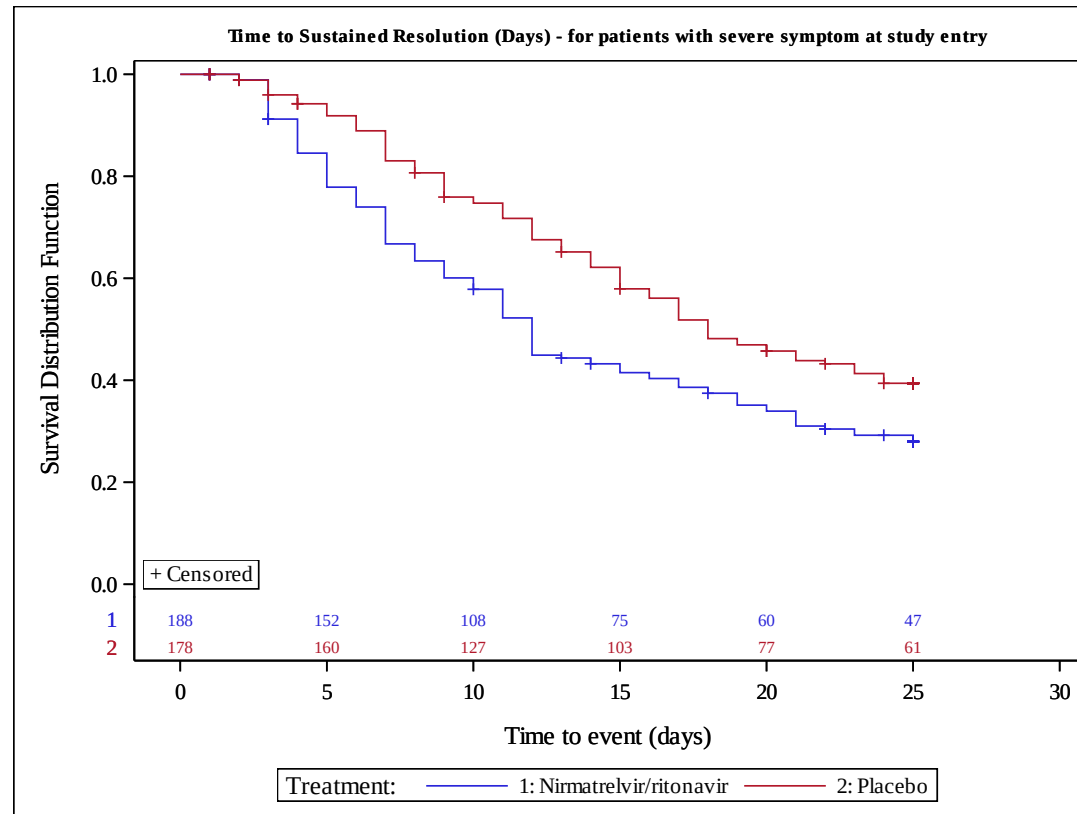
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Anhang 4-G 1.1.4: Langzeit-COVID-19 bezogene Symptome (Deskriptive Darstellung sowie Responderanalysen [insgesamt und nach Schweregrad] - supportive Analyse)

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 Descriptive Statistics on Proportion of Participants With Signs and Symptoms Severity Levels at Week 24

Final

Endpoint	Severity	Nirmatrelvir/ritonavir (N=944) n (%)	Placebo (N=964) n (%)	Total (N=1908) n (%)
Any pre-specified symptom, n (%)	None	852 (95.8%)	858 (96.2%)	1710 (96.0%)
	Mild	31 (3.5%)	27 (3.0%)	58 (3.3%)
	Moderate	5 (0.6%)	7 (0.8%)	12 (0.7%)
	Severe	1 (0.1%)	0 (0.0%)	1 (0.1%)
Cough, n (%)	None	882 (99.2%)	890 (99.8%)	1772 (99.5%)
	Mild	7 (0.8%)	2 (0.2%)	9 (0.5%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Shortness of breath, n (%)	None	887 (99.8%)	890 (99.8%)	1777 (99.8%)
	Mild	2 (0.2%)	1 (0.1%)	3 (0.2%)
	Moderate	0 (0.0%)	1 (0.1%)	1 (0.1%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Difficulty breathing, n (%)	None	886 (99.7%)	891 (99.9%)	1777 (99.8%)
	Mild	3 (0.3%)	1 (0.1%)	4 (0.2%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fever, n (%)	None	888 (99.9%)	892 (100.0%)	1780 (99.9%)
	Mild	1 (0.1%)	0 (0.0%)	1 (0.1%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chills, n (%)	None	889 (100.0%)	892 (100.0%)	1781 (100.0%)
	Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fatigue, n (%)	None	875 (98.4%)	882 (98.9%)	1757 (98.7%)
	Mild	10 (1.1%)	7 (0.8%)	17 (1.0%)
	Moderate	4 (0.4%)	3 (0.3%)	7 (0.4%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Malaise, n (%)	None	883 (99.3%)	881 (98.8%)	1764 (99.0%)
	Mild	5 (0.6%)	10 (1.1%)	15 (0.8%)
	Moderate	1 (0.1%)	1 (0.1%)	2 (0.1%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Muscle pain, n (%)	None	888 (99.9%)	890 (99.8%)	1778 (99.8%)
	Mild	1 (0.1%)	1 (0.1%)	2 (0.1%)
	Moderate	0 (0.0%)	1 (0.1%)	1 (0.1%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diarrhea, n (%)	None	888 (99.9%)	892 (100.0%)	1780 (99.9%)
	Mild	1 (0.1%)	0 (0.0%)	1 (0.1%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nausea, n (%)	None	889 (100.0%)	892 (100.0%)	1781 (100.0%)
	Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)

N: Number of participants

Percentages are based on Number of participants with non-missing data.

The severity of Any pre-specified symptom was derived based on the maximum severity of the 18 pre-specified symptoms.

A participant can report severity on more than one Other symptoms. The severity of Other symptoms was derived based on the maximum severity of the reported symptoms (Alopecia, Arthralgia, Snoring and Parosmia).

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 RRI-conform mITT2 Analysis set
 Descriptive Statistics on Proportion of Participants With Signs and Symptoms Severity Levels at Week 24

Final

Endpoint	Severity	Nirmatrelvir/ritonavir (N=944) n (%)	Placebo (N=964) n (%)	Total (N=1908) n (%)
Vomiting, n (%)	None	888 (99.9%)	892 (100.0%)	1780 (99.9%)
	Mild	1 (0.1%)	0 (0.0%)	1 (0.1%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Headache, n (%)	None	882 (99.2%)	882 (98.9%)	1764 (99.0%)
	Mild	6 (0.7%)	8 (0.9%)	14 (0.8%)
	Moderate	1 (0.1%)	2 (0.2%)	3 (0.2%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sore throat, n (%)	None	887 (99.8%)	892 (100.0%)	1779 (99.9%)
	Mild	2 (0.2%)	0 (0.0%)	2 (0.1%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rhinorrhea, n (%)	None	887 (99.8%)	890 (99.8%)	1777 (99.8%)
	Mild	2 (0.2%)	1 (0.1%)	3 (0.2%)
	Moderate	0 (0.0%)	1 (0.1%)	1 (0.1%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Loss of taste/smell, n (%)	None	883 (99.3%)	889 (99.7%)	1772 (99.5%)
	Mild	3 (0.3%)	3 (0.3%)	6 (0.3%)
	Moderate	2 (0.2%)	0 (0.0%)	2 (0.1%)
	Severe	1 (0.1%)	0 (0.0%)	1 (0.1%)
Difficulty with concentration, n (%)	None	885 (99.6%)	888 (99.6%)	1773 (99.6%)
	Mild	3 (0.3%)	4 (0.4%)	7 (0.4%)
	Moderate	1 (0.1%)	0 (0.0%)	1 (0.1%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sleep disturbances, n (%)	None	883 (99.3%)	880 (98.7%)	1763 (99.0%)
	Mild	5 (0.6%)	12 (1.3%)	17 (1.0%)
	Moderate	1 (0.1%)	0 (0.0%)	1 (0.1%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Heart palpitations, n (%)	None	888 (99.9%)	886 (99.3%)	1774 (99.6%)
	Mild	1 (0.1%)	6 (0.7%)	7 (0.4%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other symptoms, n (%)	None	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Mild	0 (0.0%)	1 (100.0%)	1 (100.0%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)

N: Number of participants

Percentages are based on Number of participants with non-missing data.

The severity of Any pre-specified symptom was derived based on the maximum severity of the 18 pre-specified symptoms.

A participant can report severity on more than one Other symptoms. The severity of Other symptoms was derived based on the maximum severity of the reported symptoms (Alopecia, Arthralgia, Snoring and Parosmia).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with any prespecified symptom of long term COVID-19 Symptoms regardless of severity at Week 24

Final

	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)
Number of subjects with Response, n (%)	37 (3.9)	34 (3.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.154 (0.709, 1.877) 0.565	
Relative Risk (95% CI)	NE (NE, NE) NE	
Risk Difference (95% CI)	NE (NE, NE) NE	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.116 (0.694, 1.793) 0.651	
Relative Risk (95% CI)	1.111 (0.704, 1.755) 0.651	
Risk Difference (95% CI)	0.004 (-0.013, 0.021) 0.651	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with any prespecified symptom of long term COVID-19 Symptoms with severity mild at Week 24

Final

	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)
Number of subjects with Response, n (%)	33 (3.5)	29 (3.0)
Adjusted analysis [1] Odds Ratio (95% CI)	1.213 (0.721, 2.041) 0.466	
Relative Risk (95% CI)	NE (NE, NE) NE	
Risk Difference (95% CI)	NE (NE, NE) NE	
Unadjusted analysis [2] Odds Ratio (95% CI)	1.168 (0.703, 1.939) 0.549	
Relative Risk (95% CI)	1.162 (0.711, 1.898) 0.549	
Risk Difference (95% CI)	0.005 (-0.011, 0.021) 0.549	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with any prespecified symptom of long term COVID-19 Symptoms with severity moderate at Week 24

Final

	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)
Number of subjects with Response, n (%)	6 (0.6)	7 (0.7)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.884 (0.295, 2.654) 0.827	
Relative Risk (95% CI)	NE (NE, NE) NE	
Risk Difference (95% CI)	NE (NE, NE) NE	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.875 (0.293, 2.612) 0.810	
Relative Risk (95% CI)	0.875 (0.295, 2.595) 0.810	
Risk Difference (95% CI)	-0.001 (-0.008, 0.006) 0.810	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with any prespecified symptom of long term COVID-19 Symptoms with severity severe at Week 24

Final

	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)
Number of subjects with Response, n (%)	1 (0.1)	0 (0.0)
Adjusted analysis [1]		
Odds Ratio (95% CI)	NE (NE, NE)	
Relative Risk (95% CI)	NE (NE, NE)	
Risk Difference (95% CI)	NE (NE, NE)	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	3.067 (0.125, 75.376) 0.493	
Relative Risk (95% CI)	3.063 (0.125, 75.106) 0.493	
Risk Difference (95% CI)	0.001 (-0.001, 0.003) 0.317	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

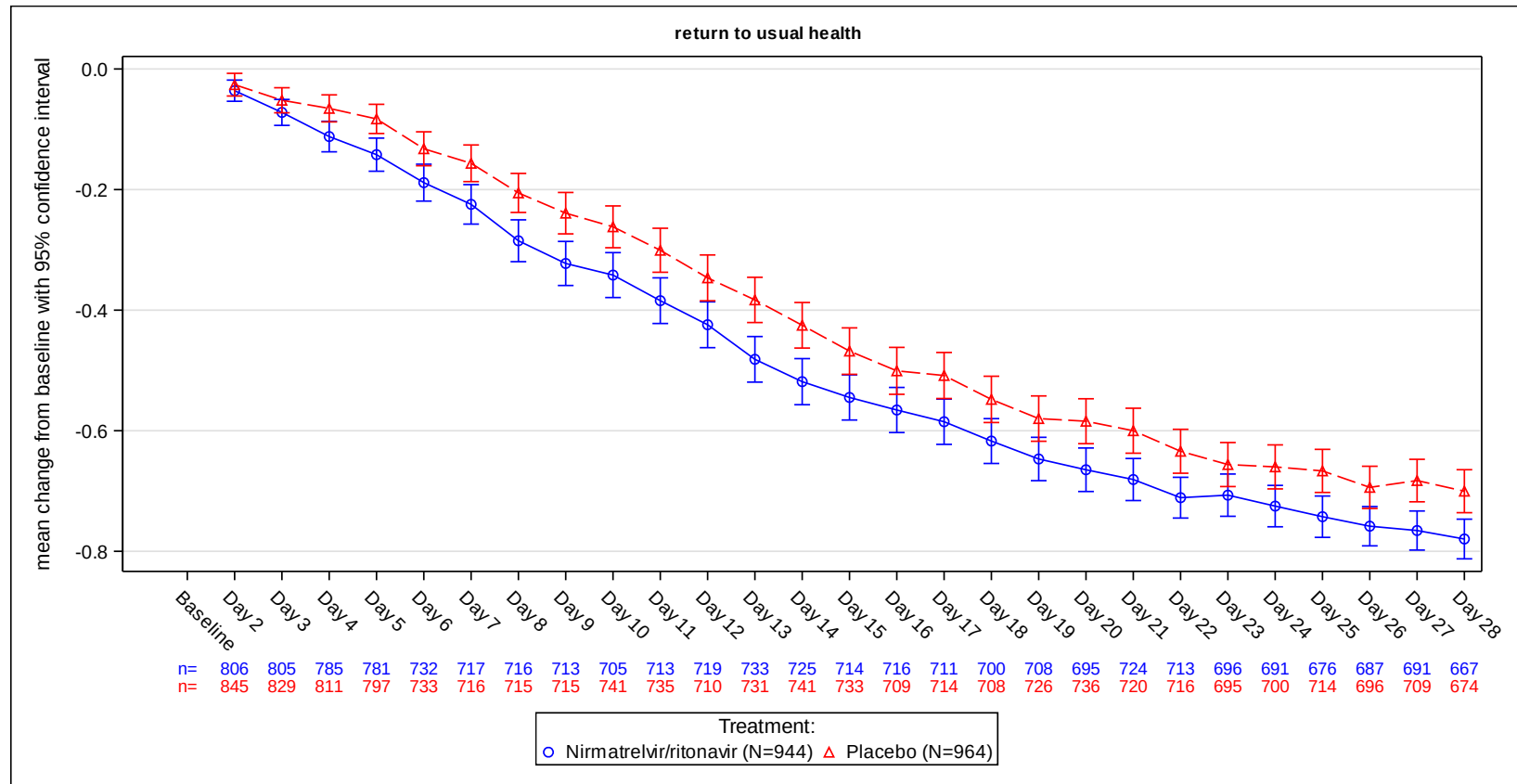
Anhang 4-G 1.2: Global Impression Questions (Symptomatik)

**Anhang 4-G 1.2.1: Mittlere Veränderung der Global Impression Questions
(Symptomatik) - Verlaufskurven**

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Global Impression Questionnaire: return to usual health

Final

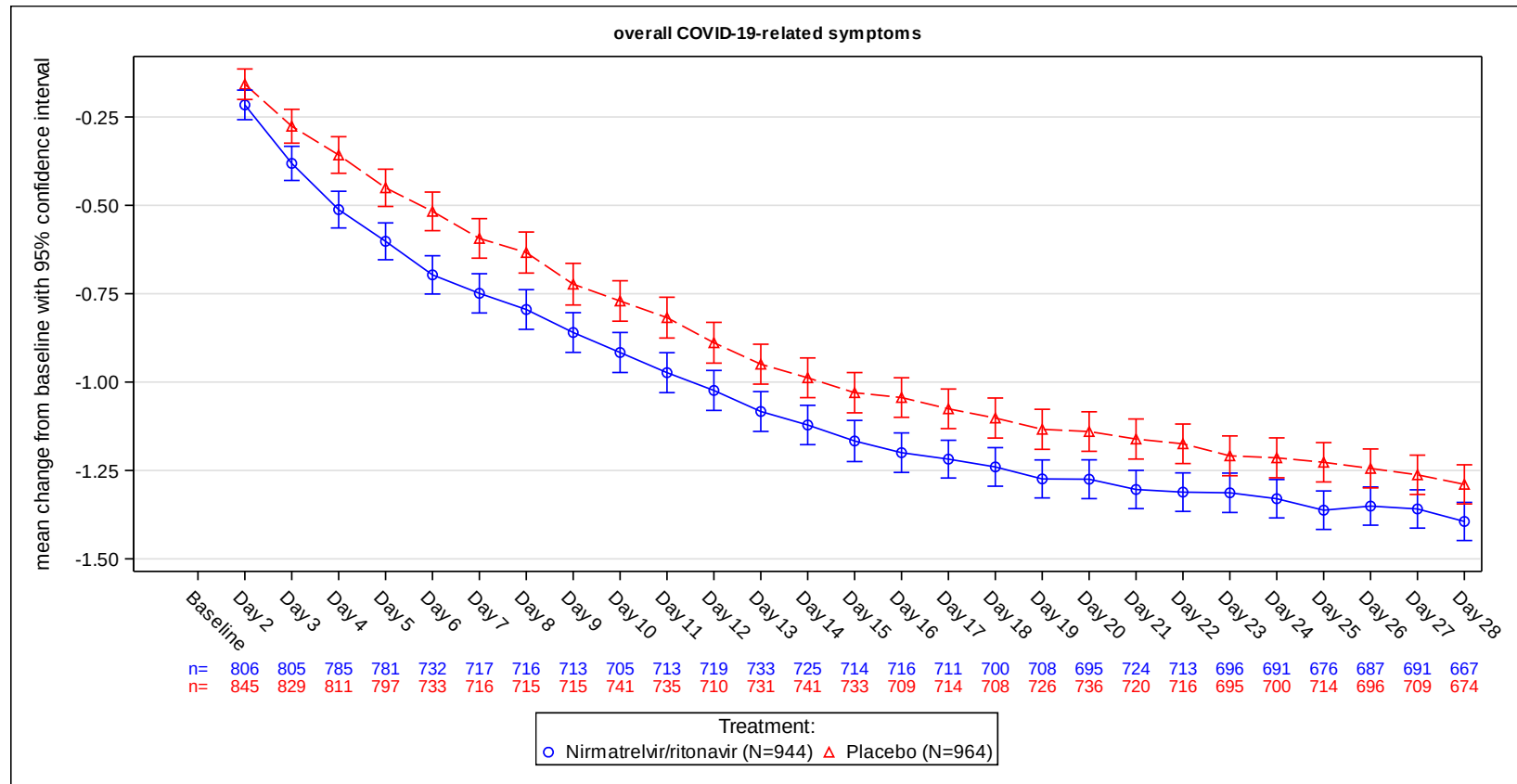


N = Number of participants, n = Number of participants with non missing values

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for Global Impression Questionnaire: overall COVID-19-related symptoms

Final



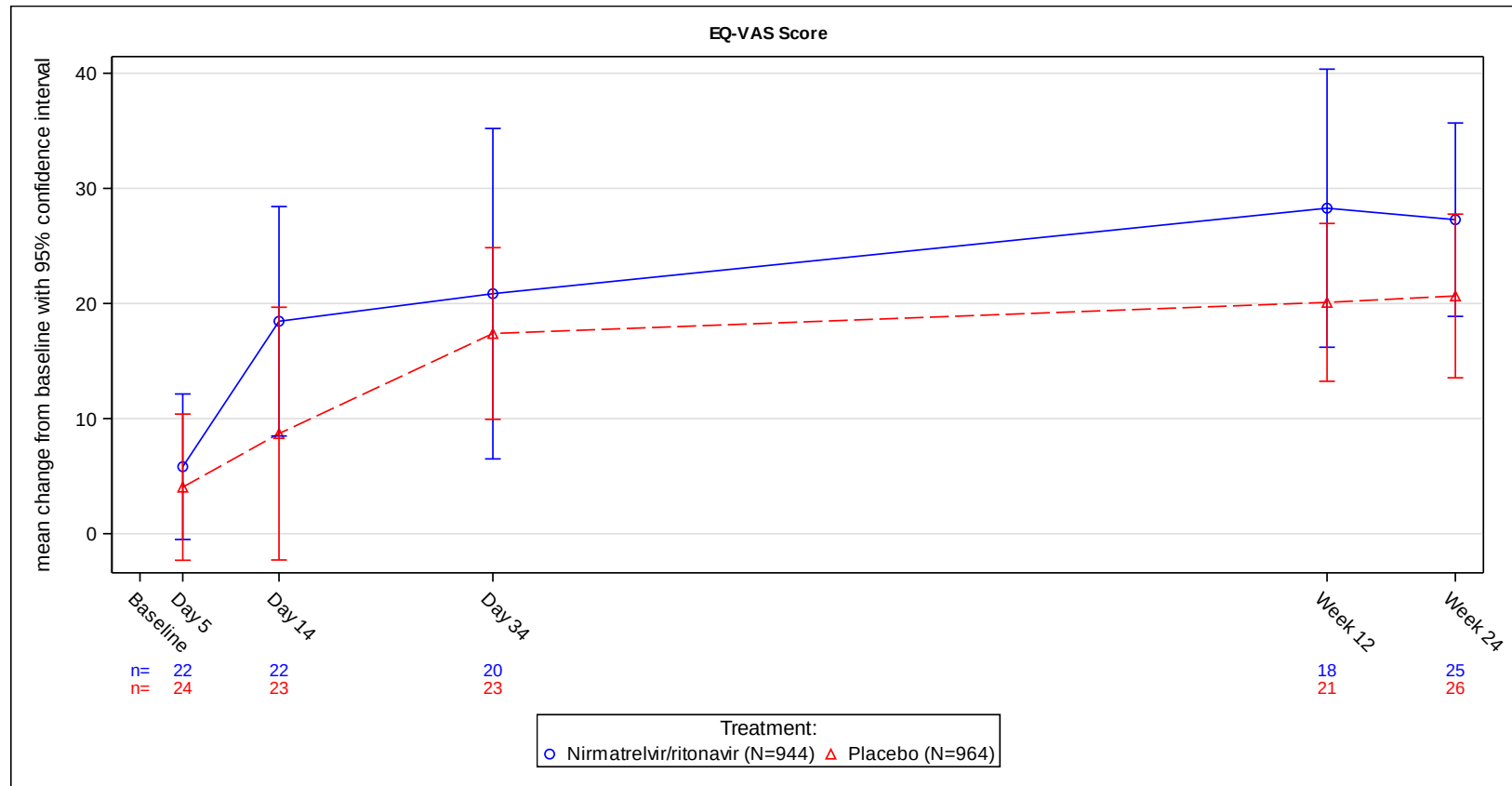
N = Number of participants, n = Number of participants with non missing values

Anhang 4-G 1.3: Gesundheitszustand (EQ-5D VAS)

**Anhang 4-G 1.3.1: Mittlere Veränderung des Gesundheitszustandes (EQ-5D VAS) -
Verlaufskurven**

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for EQ-5D VAS

Final



N = Number of participants, n = Number of participants with non missing values

**Anhang 4-G 1.4: Periphere Sauerstoffsättigung im Ruhezustand
(Verlaufsbeobachtungen - supportive Analyse)**

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Observed Means and Change from Baseline for Resting peripheral oxygen saturation (%)

Final

Visit	Nirmatrelvir/ritonavir (N=944)				Placebo (N=964)			
	Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
Baseline	944	97.01 (1.53)			964	96.93 (1.56)		
Day 3	890	97.19 (1.54)	890	0.17 (1.28)	908	97.02 (1.94)	908	0.06 (1.65)
Day 5	881	97.44 (1.49)	881	0.42 (1.41)	883	97.13 (1.76)	883	0.17 (1.62)
Day 14	841	97.74 (1.26)	841	0.74 (1.50)	823	97.59 (1.38)	823	0.64 (1.53)
Day 34	763	97.99 (1.41)	763	0.97 (1.78)	775	97.97 (1.19)	775	0.98 (1.55)

N = Number of participants, n = Number of participants with non missing values, SD = Standard Deviation, NE = Not estimable

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Between Treatment Comparison (Mixed Effects Model) of Change from Baseline for Resting peripheral oxygen saturation (%)

Final

Visit	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Difference of		p-Value	Hedges' g (95% CI) [2]		p-Value
	N [1]	LS Mean (SE)	N [1]	LS Mean (SE)	LS Means (95% CI)					
Day 3		0.01 (0.07)		-0.14 (0.07)						
Day 5		0.26 (0.07)		-0.04 (0.07)						
Day 14		0.58 (0.06)		0.44 (0.06)						
Day 34		0.82 (0.07)		0.81 (0.07)						
OVERALL	924	0.42 (0.06)	937	0.27 (0.06)	0.15 (0.07, 0.24)	<.001	0.09 (-0.00, 0.18)		0.054	

N = Number of participants, n = Number of participants with non missing values, SD = Standard Deviation, NE = Not estimable, LS: Least Squares, MMRM: mixed-effects model with repeated measures

Stratification factors: geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

MMRM analysis: treatment, visit, visit by treatment interaction as fixed effects and stratification variables along with participant as a random effect.

[1] N displays number of participants included in the mixed effects model.

[2] An approximate standard deviation was calculated for each arm based on the standard error of the LS mean to obtain the pooled standard deviation for Hedges'g.

Anhang 4-G 1.5: Viruslast (Verlaufsbeobachtungen - supportive Analyse)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Observed Means and Change from Baseline for Log10 Transformed Viral Load (copies/mL)

Final

Visit	Nirmatrelvir/ritonavir (N=944)				Placebo (N=964)			
	Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
Baseline	746	5.73 (2.08)			779	5.50 (2.17)		
Day 3	702	3.95 (2.13)	702	-1.76 (1.76)	728	4.33 (2.38)	728	-1.14 (1.70)
Day 5	678	2.73 (1.84)	678	-3.02 (1.80)	698	3.32 (2.26)	698	-2.15 (1.75)
Day 10	670	1.43 (1.62)	670	-4.32 (2.11)	666	1.72 (1.77)	666	-3.72 (2.04)
Day 14	679	0.89 (1.28)	679	-4.83 (2.14)	704	0.99 (1.32)	704	-4.46 (2.12)

N = Number of participants, n = Number of participants with non missing values, SD = Standard Deviation, NE = Not estimable

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Between Treatment Comparison (Mixed Effects Model) of Change from Baseline for Log10 Transformed Viral Load (copies/mL)

Final

Visit	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Difference of		p-Value	Hedges' g (95% CI) [2]		p-Value
	N [1]	LS Mean (SE)	N [1]	LS Mean (SE)	LS Means (95% CI)					
Day 3		-1.62 (0.09)		-1.15 (0.09)						
Day 5		-2.88 (0.09)		-2.19 (0.09)						
Day 10		-4.17 (0.09)		-3.78 (0.09)						
Day 14		-4.68 (0.08)		-4.49 (0.08)						
OVERALL	725	-3.34 (0.08)	757	-2.90 (0.08)	-0.44 (-0.55, -0.33)	<.001	-0.21 (-0.31, -0.11)	<.001		

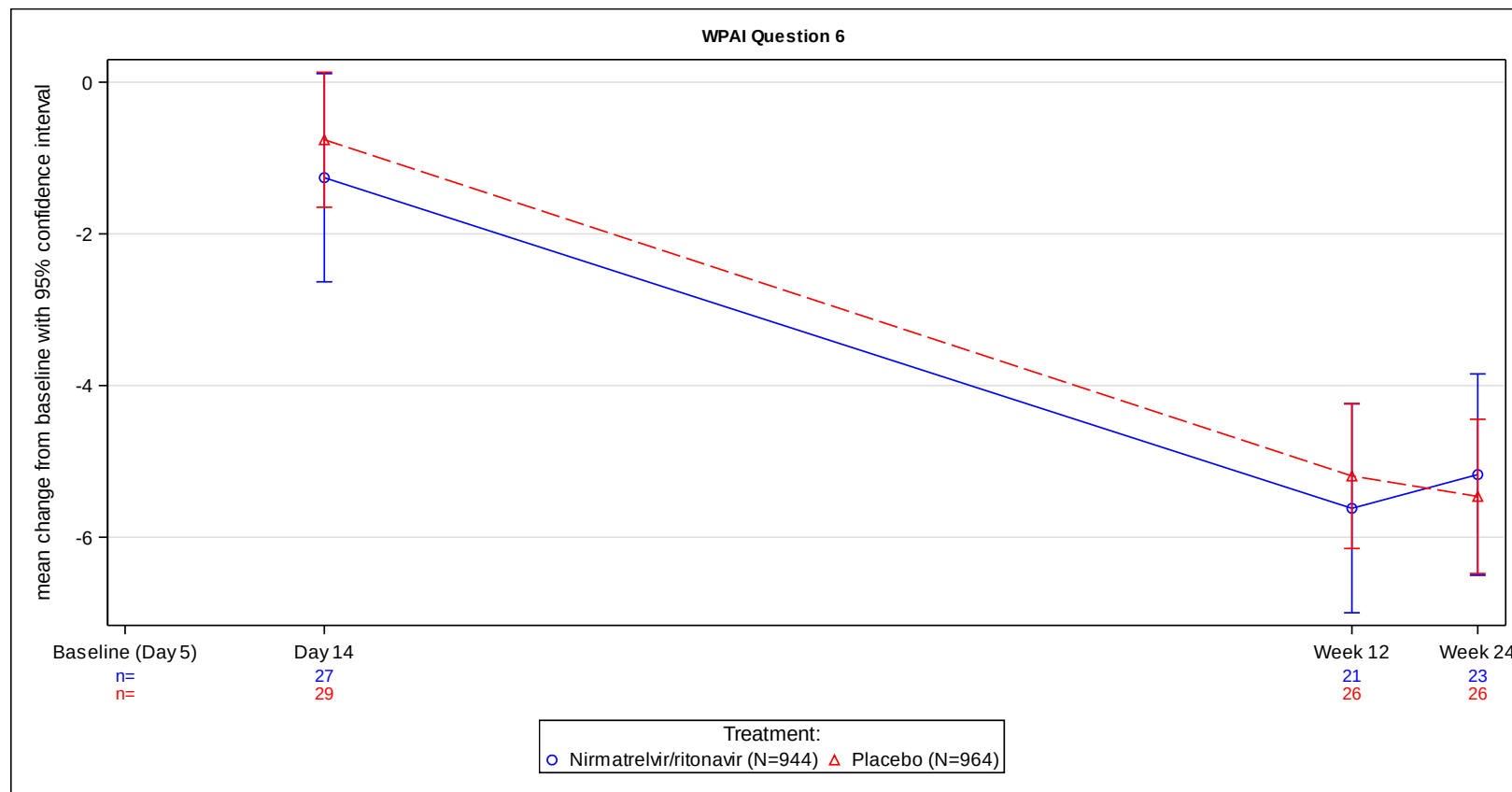
N = Number of participants, n = Number of participants with non missing values, SD = Standard Deviation, NE = Not estimable, LS: Least Squares, MMRM: mixed-effects model with repeated measures
 Stratification factors: geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status, baseline viral load and nasopharyngeal sample site.
 MMRM analysis: treatment, visit, visit by treatment interaction as fixed effects and stratification variables along with participant as a random effect.
 [1] N displays number of participants included in the mixed effects model.
 [2] An approximate standard deviation was calculated for each arm based on the standard error of the LS mean to obtain the pooled standard deviation for Hedges'g.

Anhang 4-G 1.6: WPAI (Beeinträchtigung täglicher Aktivitäten)

Anhang 4-G 1.6.1: Mittlere Veränderung des WPAI (Beeinträchtigung täglicher Aktivitäten) - Verlaufskurven

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Progression Curve over Time for mean Change from Baseline for WPAI Question 6

Final



N = Number of participants, n = Number of participants with non missing values

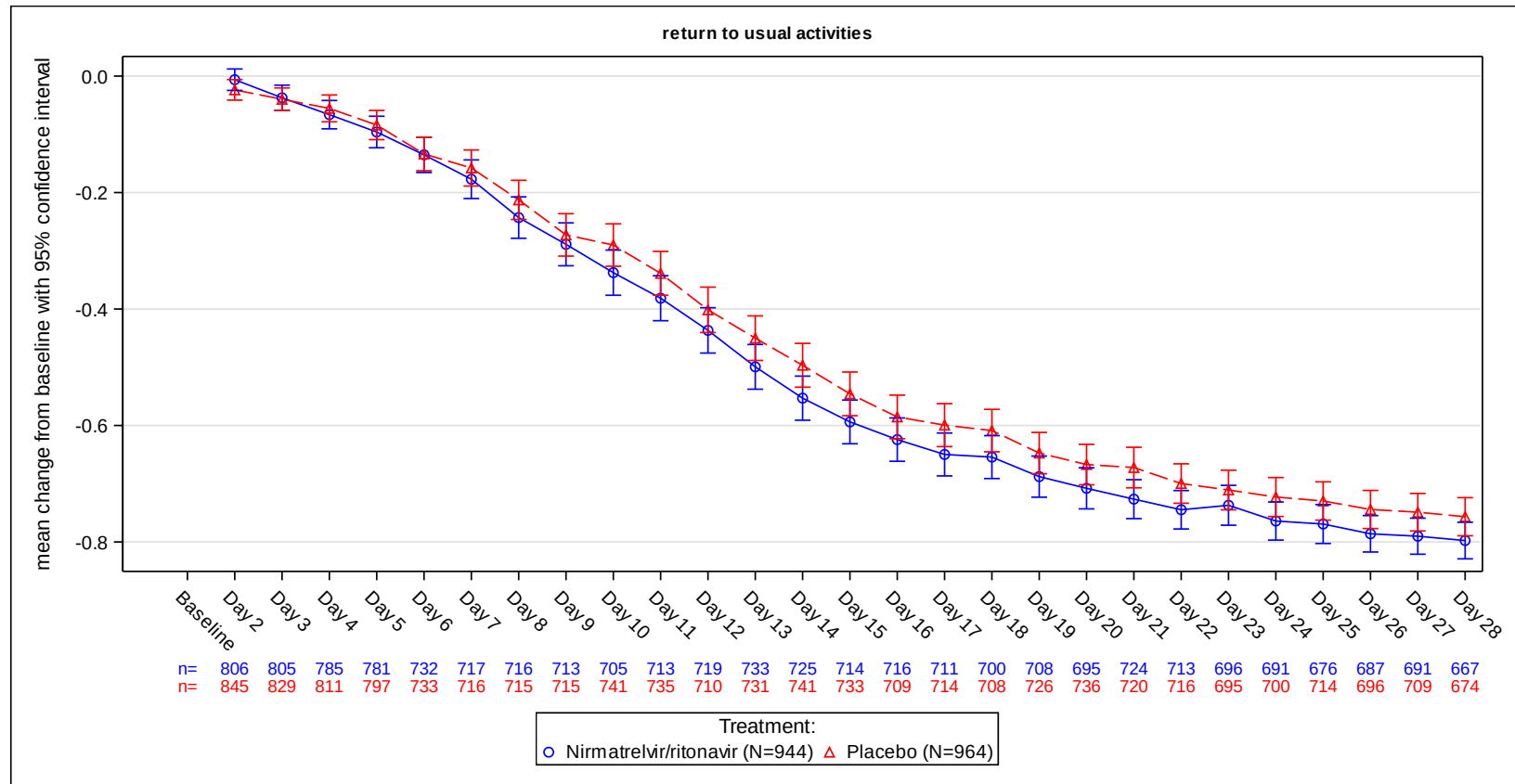
Anhang 4-G 1.7: Global Impression Questions (Lebensqualität)

**Anhang 4-G 1.7.1: Mittlere Veränderung der Global Impression Questions
(Lebensqualität) - Verlaufskurven**

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Progression Curve over Time for mean Change from Baseline for Global Impression Questionnaire: return to usual activities

Final



N = Number of participants, n = Number of participants with non missing values

Anhang 4-G 1.8: Verträglichkeit

Anhang 4-G 1.8.1: Liste der prädefinierten, spezifischen UE

Protocol C4671005 (PF-07321332) Statistical Analysis Plan

Appendix 4. List of pre-specified AESIs

Table Adverse Events of Special Interest

Category of Interest	Medra version 24 Criteria/Programming Details
Hemodynamic events	Arrhythmia related investigations, signs and symptoms (SMQ); Cardiac arrhythmia terms (incl bradyarrhythmias and tachyarrhythmias) (SMQ); Bradycardia; Heart rate decreased; Heart rate abnormal; Maximum heart rate decreased;Tachycardia;Heart rate increased; Maximum heart rate increased;Hypertension;Hypotension Hyperfibrinogenaemia; Prothrombin level abnormal; Prothrombin level increased; Prothrombin time prolonged; Prothrombin time abnormal; Thrombocytosis; Leukocytosis; White blood cell count increased; White blood cell count abnormal;Blood fibrinogen increased; Blood fibrinogen abnormal; Activated partial thromboplastin time prolonged; Activated partial thromboplastin time abnormal; Platelet count abnormal; Platelet count increased; Fibrin D dimer increased; Haptoglobin abnormal; Haptoglobin increased; Blood albumin abnormal; Protein total abnormal; Albumin globulin ratio abnormal; C-reactive protein abnormal; C-reactive protein increased; Neutrophilia; Neutrophil count abnormal; Lymphocytosis; Lymphocyte count abnormal; Eosinophilia; Eosinophil count abnormal;
Inflammatory events	Monocytosis; Monocyte count abnormal
thyroid-related events	Blood thyroid stimulating hormone abnormal;Blood thyroid stimulating hormone increased;Thyroxine free abnormal; Thyroxine free increased; Thyroxine abnormal; Thyroxine increased

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DMB02-GSOP-RF02 5.0 Statistical Analysis Plan Template 05-Dec-2019

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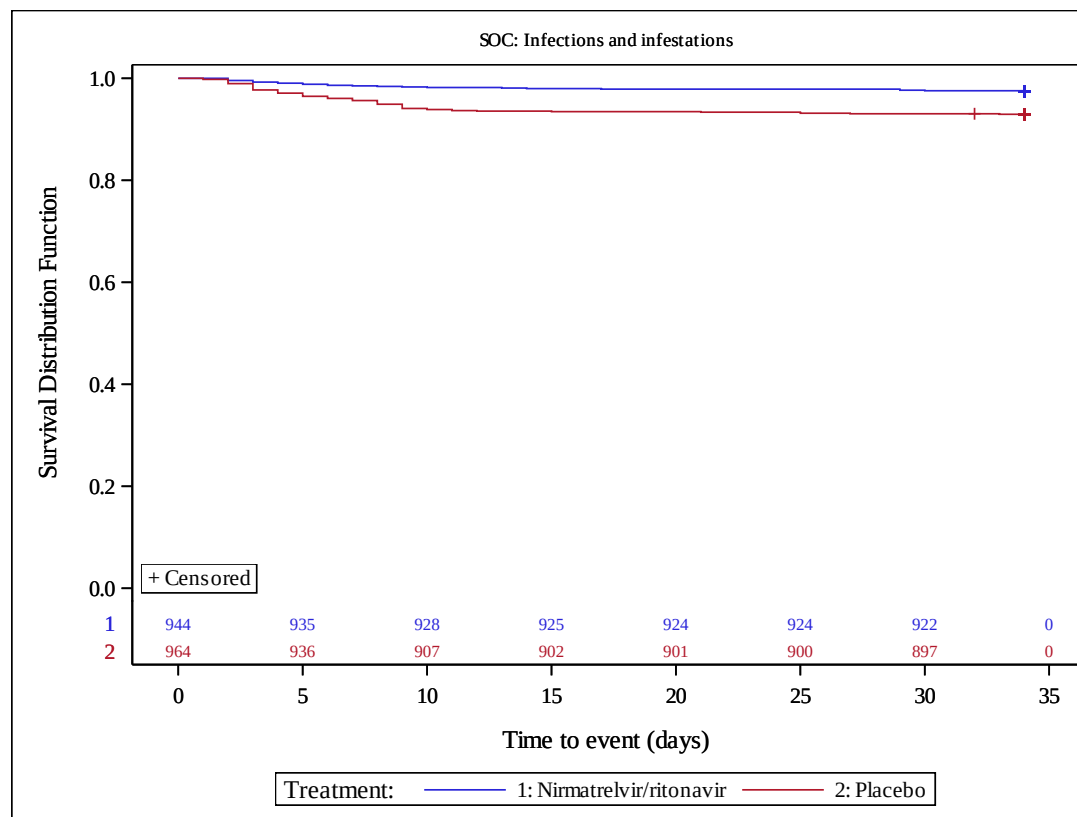
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**Anhang 4-G 1.8.2: UE nach SOC und PT (jeglicher DAIDS-Grad) - Kaplan-Meier
Kurven**

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or >=10 patients)

Final

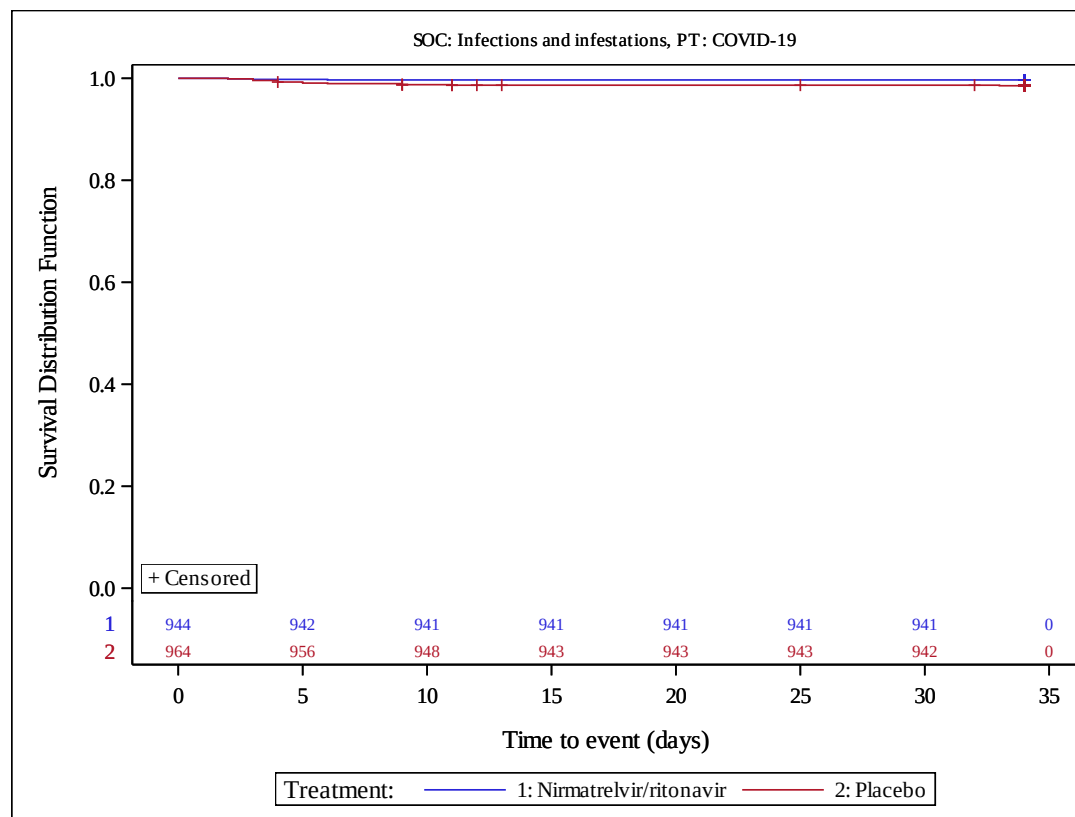


Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or >=10 patients)

Final

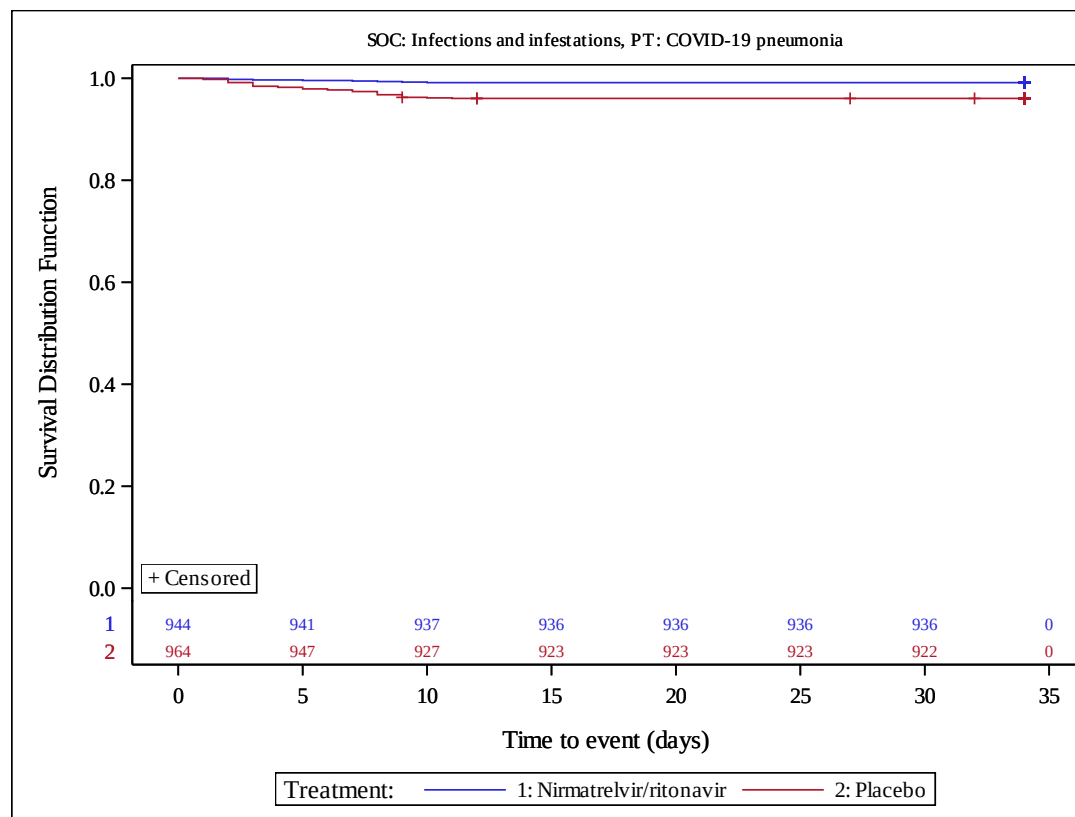


Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or >=10 patients)

Final

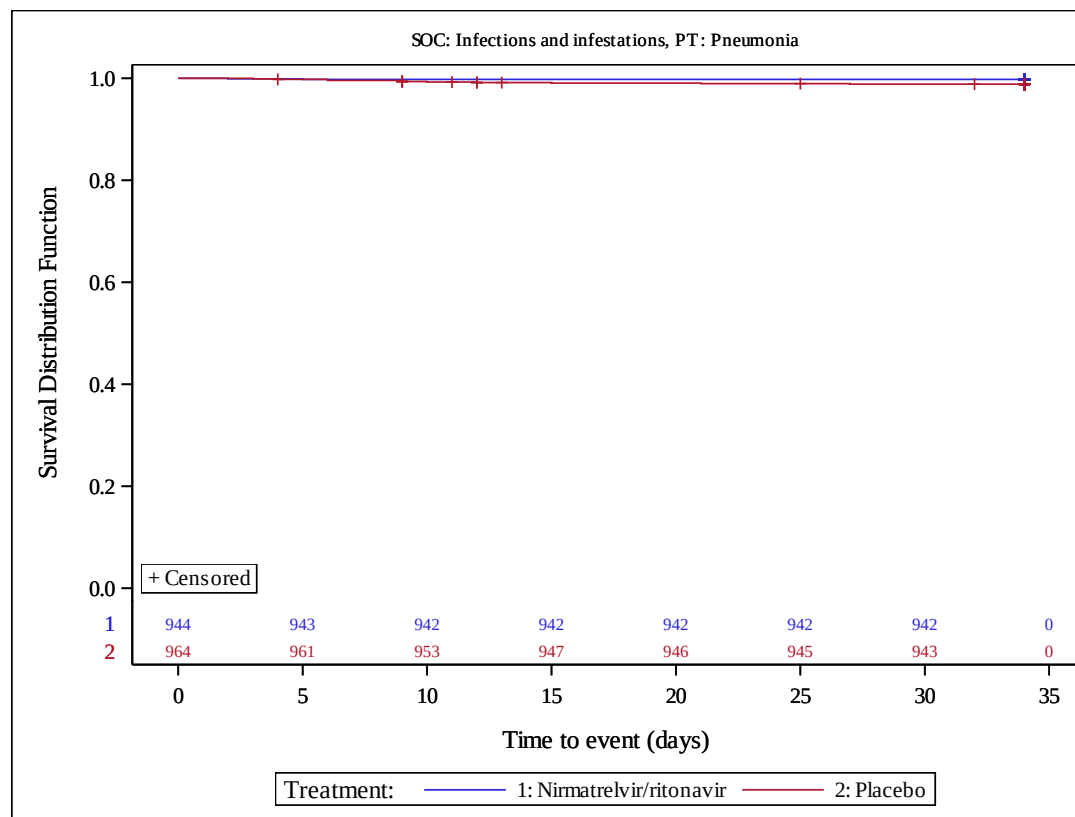


Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Kaplan-Meier Plot of Time to First Frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or >=10 patients)

Final

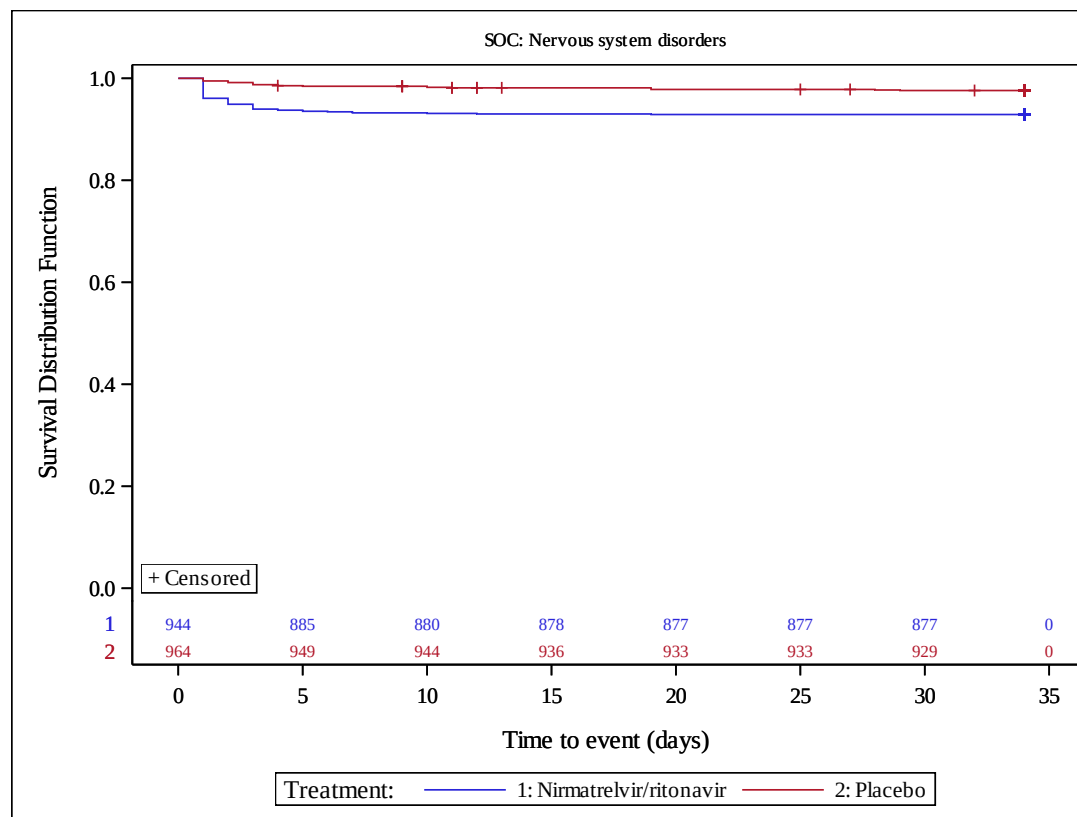


Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)
Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or >=10 patients)

Final

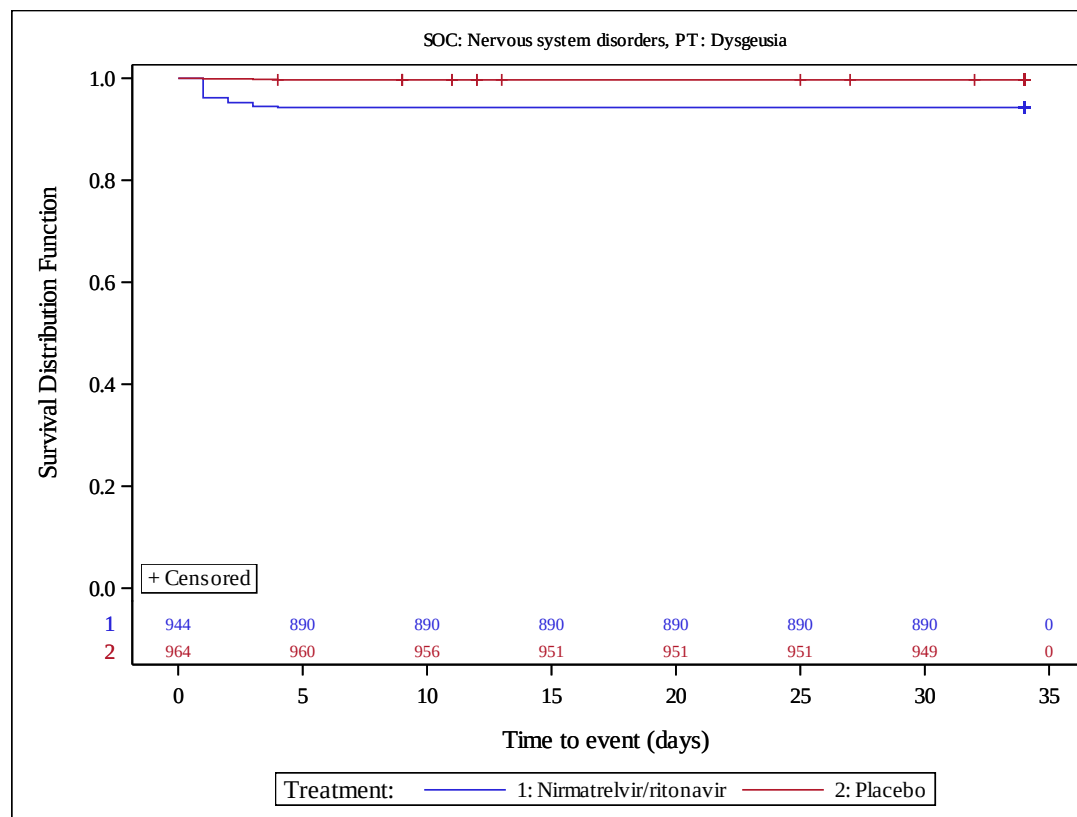


Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or >=10 patients)

Final



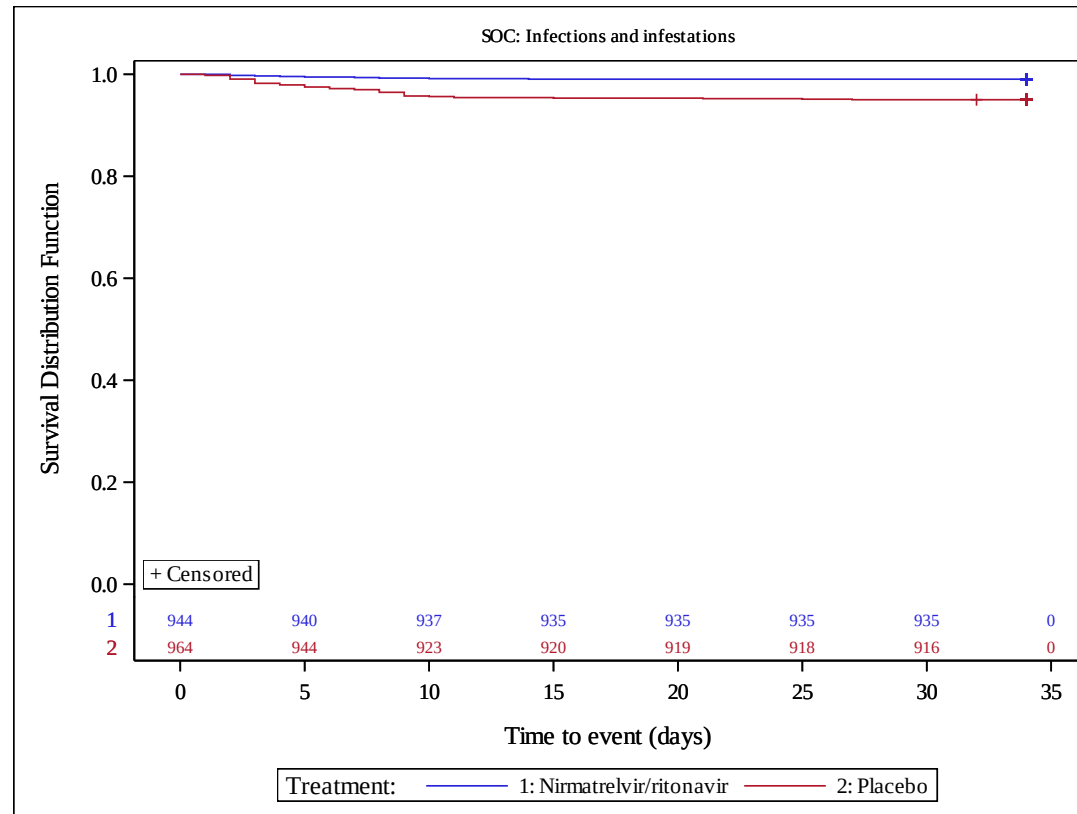
Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

Anhang 4-G 1.8.3: Schwere UE nach SOC und PT (DAIDS-Grad ≥ 3) - Kaplan-Meier Kurven

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Frequent Severe Adverse Events (DAIDS >=3) by SOC and PT (incidence in either arm >= 5% or >=10 patients)

Final

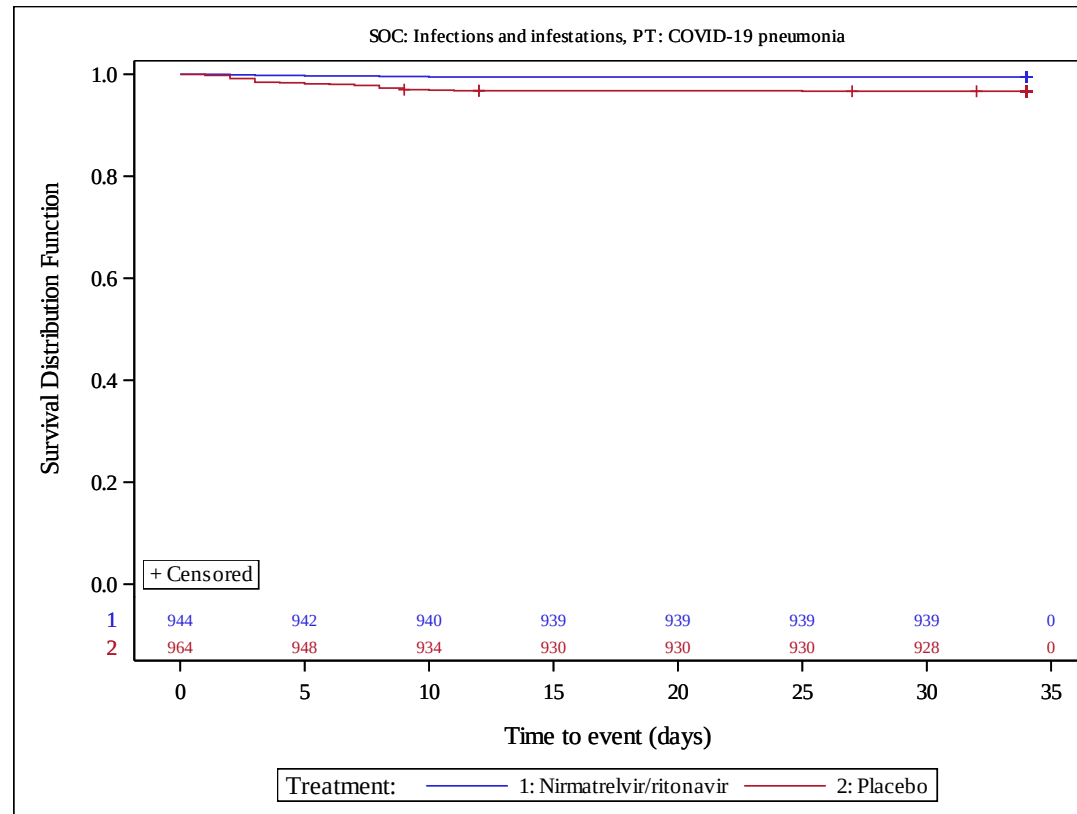


Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Frequent Severe Adverse Events (DAIDS >=3) by SOC and PT (incidence in either arm >= 5% or >=10 patients)

Final

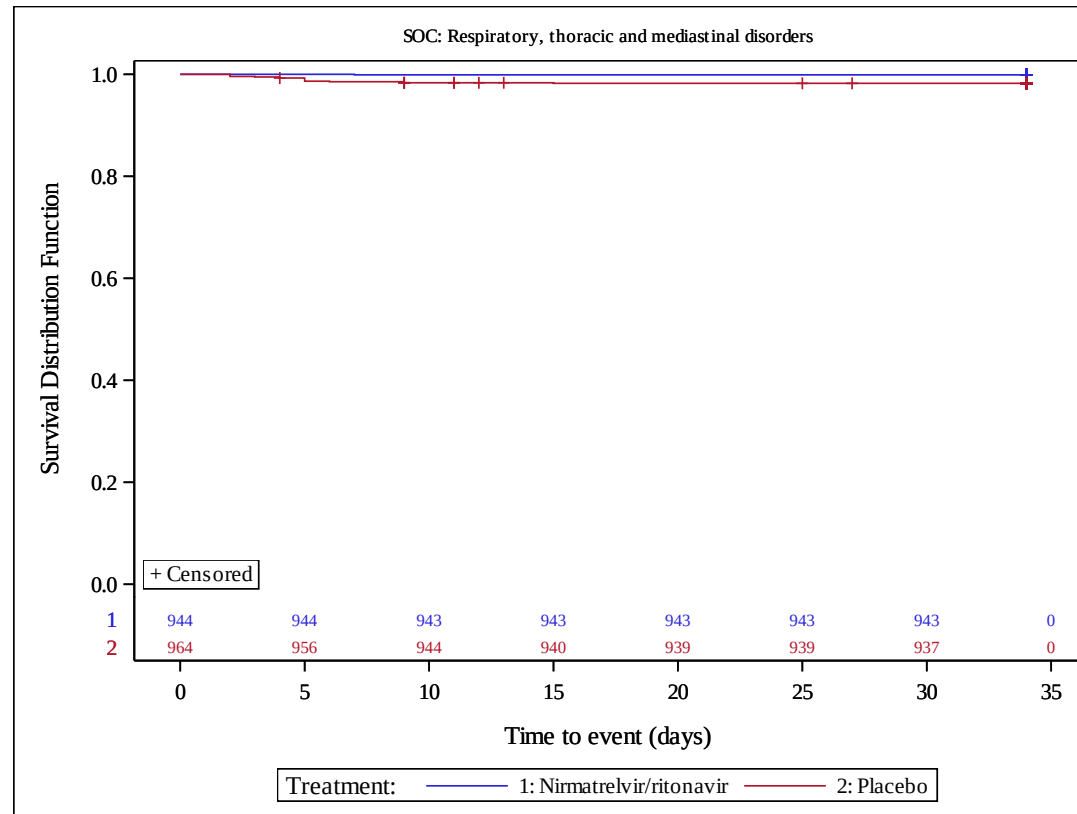


Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Frequent Severe Adverse Events (DAIDS >=3) by SOC and PT (incidence in either arm >= 5% or >=10 patients)

Final



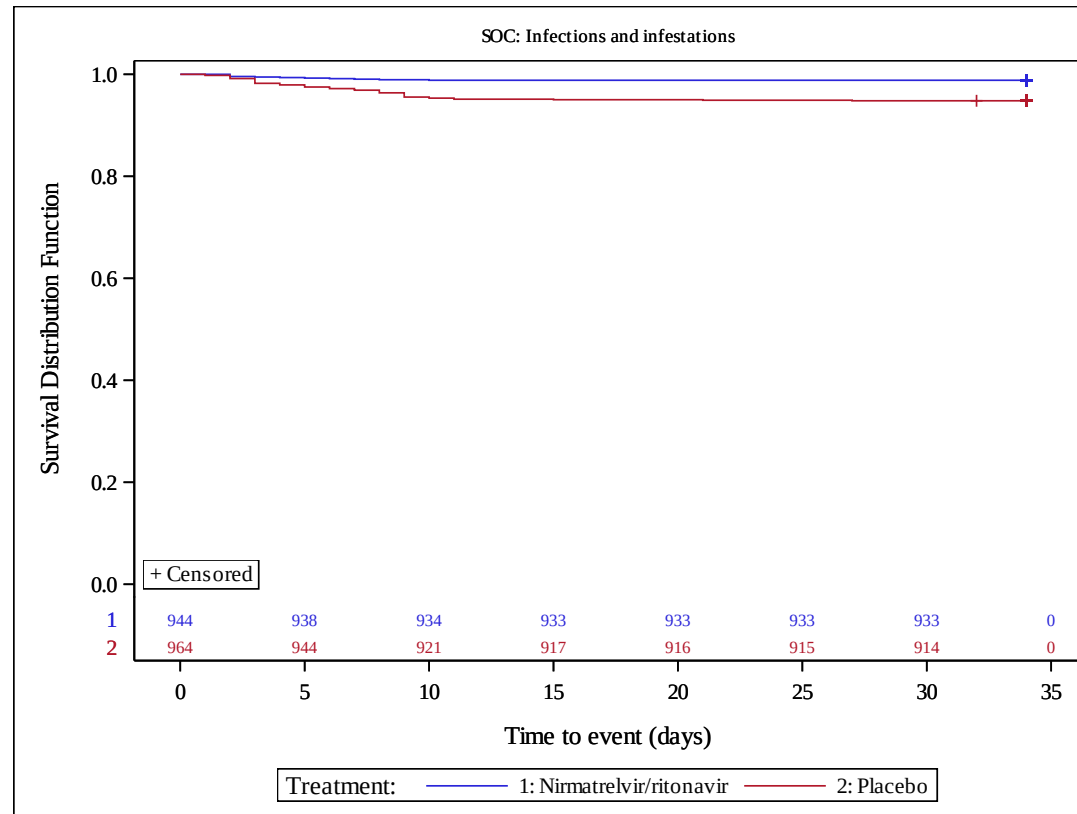
Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

Anhang 4-G 1.8.4: SUE nach SOC und PT - Kaplan-Meier Kurven

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Frequent Serious Adverse Event by SOC and PT (incidence in either arm >= 5% or >=10 patients)

Final

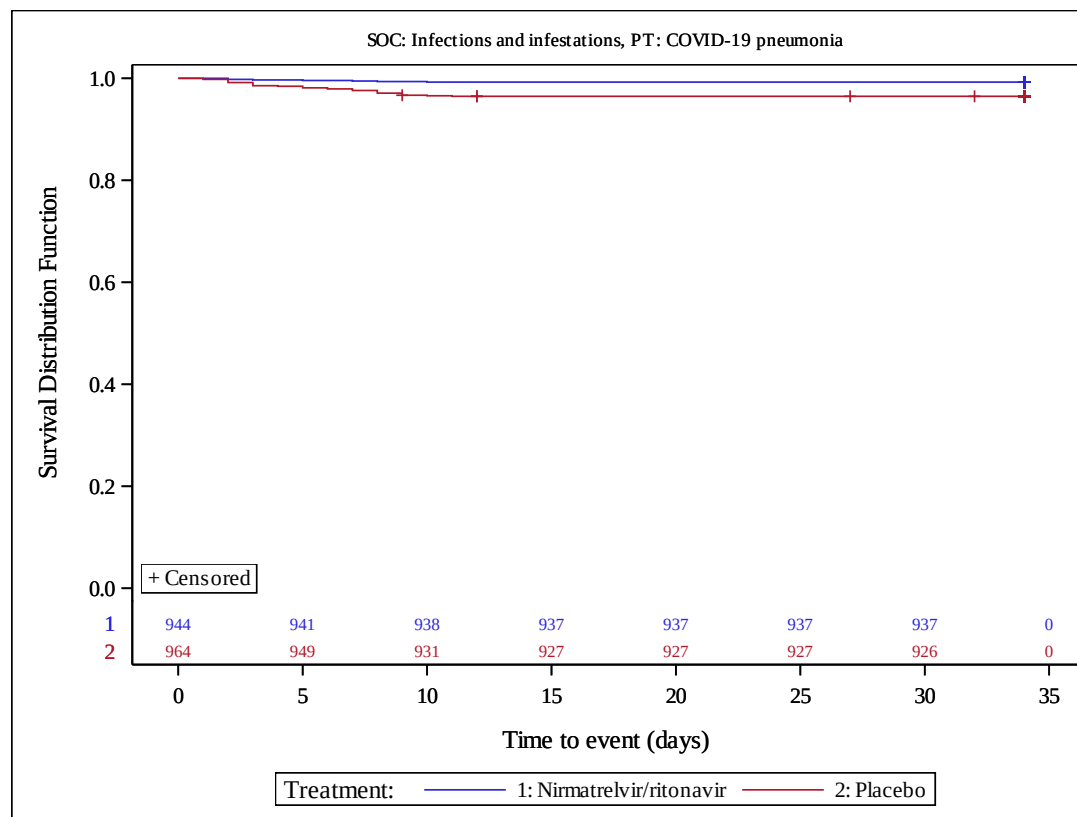


Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Frequent Serious Adverse Event by SOC and PT (incidence in either arm >= 5% or >=10 patients)

Final



Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

Anhang 4-G 1.8.5: UE, die an Tag 35 oder später auftraten (Deskriptive Darstellung - maßgebliche Analyse)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Incidence of Adverse Events that started after Day 34 by SOC, PT and Maximum DAIDS Grade

Final

System Organ Class (SOC) Preferred Term (PT)	Nirmatrelvir/ritonavir (N=944)						Placebo (N=964)					
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Participants with events	13 (1.4)	8 (0.8)	2 (0.2)	0	0	23 (2.4)	10 (1.0)	5 (0.5)	2 (0.2)	0	1 (0.1)	18 (1.9)
Investigations	4 (0.4)	1 (0.1)	2 (0.2)	0	0	7 (0.7)	2 (0.2)	1 (0.1)	0	0	0	3 (0.3)
Fibrin D dimer increased	3 (0.3)	0	0	0	0	3 (0.3)	1 (0.1)	0	0	0	0	1 (0.1)
Alanine aminotransferase increased	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
Aspartate aminotransferase increased	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
Blood calcium increased	0	0	0	0	0	0	1 (0.1)	0	0	0	0	1 (0.1)
Blood glucose increased	0	0	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0
Coagulation time prolonged	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
Creatinine renal clearance decreased	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
Haemoglobin decreased	0	0	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0
Hepatitis C virus test positive	0	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0
Oxygen saturation decreased	0	0	0	0	0	0	0	1 (0.1)	0	0	0	1 (0.1)
Infections and infestations	4 (0.4)	2 (0.2)	0	0	0	6 (0.6)	2 (0.2)	0	0	0	0	2 (0.2)
COVID-19	4 (0.4)	2 (0.2)	0	0	0	6 (0.6)	1 (0.1)	0	0	0	0	1 (0.1)
Respiratory tract infection viral	0	0	0	0	0	0	1 (0.1)	0	0	0	0	1 (0.1)
Respiratory, thoracic and mediastinal disorders	1 (0.1)	2 (0.2)	0	0	0	3 (0.3)	2 (0.2)	0	0	0	1 (0.1)	3 (0.3)
Dyspnoea	0	2 (0.2)	0	0	0	2 (0.2)	0	0	0	0	0	0
Epistaxis	0	0	0	0	0	0	1 (0.1)	0	0	0	0	1 (0.1)
Nasal obstruction	0	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0
Oropharyngeal pain	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
Pneumonitis	0	0	0	0	0	0	0	0	0	0	1 (0.1)	1 (0.1)
Pulmonary mass	0	0	0	0	0	0	1 (0.1)	0	0	0	0	1 (0.1)
Gastrointestinal disorders	2 (0.2)	1 (0.1)	0	0	0	3 (0.3)	1 (0.1)	0	0	0	0	1 (0.1)
Abdominal pain upper	2 (0.2)	0	0	0	0	2 (0.2)	0	0	0	0	0	0
Diarrhoea	0	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0
Toothache	0	0	0	0	0	0	1 (0.1)	0	0	0	0	1 (0.1)
General disorders and administration site conditions	0	1 (0.1)	0	0	0	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.1)
Asthenia	0	0	0	0	0	0	1 (0.1)	0	0	0	0	1 (0.1)
Chills	0	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0
Fatigue	0	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0
Hepatobiliary disorders	0	2 (0.2)	0	0	0	2 (0.2)	1 (0.1)	0	0	0	0	1 (0.1)
Hepatic function abnormal	0	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0
Hepatic steatosis	0	0	0	0	0	0	1 (0.1)	0	0	0	0	1 (0.1)
Steatohepatitis	0	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0
Nervous system disorders	1 (0.1)	1 (0.1)	0	0	0	2 (0.2)	0	1 (0.1)	0	0	0	1 (0.1)
Facial paralysis	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
Paraesthesia	0	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0
Tension headache	0	0	0	0	0	0	0	1 (0.1)	0	0	0	1 (0.1)
Vascular disorders	1 (0.1)	0	0	0	0	1 (0.1)	1 (0.1)	1 (0.1)	0	0	0	2 (0.2)
Hypertension	1 (0.1)	0	0	0	0	1 (0.1)	1 (0.1)	1 (0.1)	0	0	0	2 (0.2)
Musculoskeletal and connective tissue disorders	1 (0.1)	0	0	0	0	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.1)
Back pain	1 (0.1)	0	0	0	0	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.1)
Blood and lymphatic system disorders	0	0	0	0	0	0	1 (0.1)	0	0	0	0	1 (0.1)
Anaemia	0	0	0	0	0	0	1 (0.1)	0	0	0	0	1 (0.1)
Endocrine disorders	0	0	0	0	0	0	0	1 (0.1)	0	0	0	1 (0.1)

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started after Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 N: Number of participants, n: Number of participants with event

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Incidence of Adverse Events that started after Day 34 by SOC, PT and Maximum DAIDS Grade

Final

System Organ Class (SOC) Preferred Term (PT)	Nirmatrelvir/ritonavir (N=944)						Placebo (N=964)					
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Thyroiditis chronic	0	0	0	0	0	0	0	1 (0.1)	0	0	0	1 (0.1)
Injury, poisoning and procedural complications	0	0	0	0	0	0	0	0	1 (0.1)	0	0	1 (0.1)
Ligament rupture	0	0	0	0	0	0	0	0	1 (0.1)	0	0	1 (0.1)
Renal and urinary disorders	0	0	0	0	0	0	0	0	1 (0.1)	0	0	1 (0.1)
Nephrosclerosis	0	0	0	0	0	0	0	0	1 (0.1)	0	0	1 (0.1)
Skin and subcutaneous tissue disorders	0	0	0	0	0	0	0	1 (0.1)	0	0	0	1 (0.1)
Alopecia	0	0	0	0	0	0	0	1 (0.1)	0	0	0	1 (0.1)

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started after Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 N: Number of participants, n: Number of participants with event

Anhang 4-G 1.9: Subgruppenanalysen - Gesamtmortalität

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with Death from any Cause through Day 28 - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944) n/N (%)	Placebo (N=964) n/N (%)	Adjusted Analysis [1]		Interaction p-Value	Unadjusted Analysis [2]		Interaction p-Value
			Relative Risk (95% CI)	p-Value		Relative Risk (95% CI)	p-Value	
Age								
< 65	0/ 804 (0.0)	4/ 816 (0.5)						
>= 65	0/ 140 (0.0)	8/ 148 (5.4)						
Gender								
Male	0/ 474 (0.0)	8/ 510 (1.6)						
Female	0/ 470 (0.0)	4/ 454 (0.9)						
Geographic region								
United States	0/ 387 (0.0)	3/ 395 (0.8)						
Europe	0/ 322 (0.0)	8/ 321 (2.5)						
India	0/ 74 (0.0)	0/ 78 (0.0)						
Rest of World	0/ 161 (0.0)	1/ 170 (0.6)						
COVID-19 therapeutic mAb treatment at randomisation								
Yes	0/ 60 (0.0)	0/ 60 (0.0)	NE (NE, NE)	NE	NE	NE (NE, NE)	NE	NE
No	0/ 884 (0.0)	12/ 904 (1.3)	NE (NE, NE)	NE		0.041 (0.002, 0.690)	0.027	
Baseline viral load 1								
< 10 ⁴ copies/mL	0/ 340 (0.0)	0/ 356 (0.0)	NE (NE, NE)	NE	NE	NE (NE, NE)	NE	NE
>= 10 ⁴ copies/mL	0/ 579 (0.0)	10/ 582 (1.7)	NE (NE, NE)	NE		0.048 (0.003, 0.815)	0.036	
Baseline viral load 2								
< 10 ⁷ copies/mL	0/ 663 (0.0)	4/ 707 (0.6)						
>= 10 ⁷ copies/mL	0/ 256 (0.0)	6/ 231 (2.6)						
Baseline serology status								
Negative	0/ 439 (0.0)	11/ 457 (2.4)	NE (NE, NE)	NE	NE	0.045 (0.003, 0.766)	0.032	0.359
Positive	0/ 494 (0.0)	1/ 495 (0.2)	NE (NE, NE)	NE		0.334 (0.014, 8.179)	0.502	
Symptom onset days to first dose date								
<= 3	0/ 637 (0.0)	9/ 632 (1.4)						
> 3	0/ 307 (0.0)	3/ 332 (0.9)						
BMI group								
< 25	0/ 216 (0.0)	1/ 213 (0.5)						
25 - < 30	0/ 324 (0.0)	4/ 336 (1.2)						
>= 30	0/ 403 (0.0)	7/ 415 (1.7)						
Ethnicity								
White	0/ 712 (0.0)	10/ 725 (1.4)	NE (NE, NE)	NE	NE	0.048 (0.003, 0.826)	0.036	0.588
Black or African American	0/ 45 (0.0)	1/ 42 (2.4)	NE (NE, NE)	NE	NE	0.312 (0.013, 7.444)	0.471	
Asian	0/ 118 (0.0)	0/ 127 (0.0)	NE (NE, NE)	NE	NE	NE (NE, NE)	NE	
Others	0/ 69 (0.0)	1/ 70 (1.4)	NE (NE, NE)	NE	NE	0.338 (0.014, 8.159)	0.504	
Number of baseline comorbidities present								
0-1	0/ 720 (0.0)	5/ 734 (0.7)						
2-3	0/ 220 (0.0)	7/ 224 (3.1)						
>= 4	0/ 4 (0.0)	0/ 6 (0.0)						
Presence of risk factor: Smoking								
Yes	0/ 423 (0.0)	2/ 442 (0.5)	NE (NE, NE)	NE	NE	0.209 (0.010, 4.340)	0.312	0.487
No	0/ 519 (0.0)	10/ 522 (1.9)	NE (NE, NE)	NE		0.048 (0.003, 0.815)	0.036	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with Death from any Cause through Day 28 - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)	Adjusted Analysis [1]				Interaction	Unadjusted Analysis [2]			Interaction	
	n/N (%)	n/N (%)	Relative Risk (95% CI)			p-Value	p-Value	Relative Risk (95% CI)			p-Value	p-Value
Presence of risk factor: Diabetes mellitus												
Yes	0/ 135 (0.0)	4/ 137 (2.9)										
No	0/ 808 (0.0)	8/ 827 (1.0)										
Presence of risk factor: Immunosuppression												
Yes	0/ 6 (0.0)	0/ 7 (0.0)	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
No	0/ 937 (0.0)	12/ 957 (1.3)	NE (	NE,	NE)	NE		0.041 (	0.002,	0.689)	0.027	
Presence of risk factor: Chronic lung disease												
Yes	0/ 62 (0.0)	0/ 39 (0.0)	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
No	0/ 881 (0.0)	12/ 925 (1.3)	NE (	NE,	NE)	NE		0.042 (	0.002,	0.708)	0.028	
Presence of risk factor: Hypertension												
Yes	0/ 358 (0.0)	11/ 375 (2.9)	NE (	NE,	NE)	NE	NE	0.046 (	0.003,	0.770)	0.032	0.359
No	0/ 585 (0.0)	1/ 589 (0.2)	NE (	NE,	NE)	NE		0.336 (	0.014,	8.222)	0.503	
Presence of risk factor: Cardiovascular disorder												
Yes	0/ 42 (0.0)	3/ 49 (6.1)										
No	0/ 901 (0.0)	9/ 915 (1.0)										
Presence of risk factor: Chronic kidney disease												
Yes	0/ 6 (0.0)	0/ 8 (0.0)	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
No	0/ 937 (0.0)	12/ 956 (1.3)	NE (	NE,	NE)	NE		0.041 (	0.002,	0.688)	0.026	
Presence of risk factor: HIV Infection												
Yes	0	0/ 1 (0.0)										
No	0/ 943 (0.0)	12/ 962 (1.2)										
Presence of risk factor: Sickle Cell Disease												
No	0/ 943 (0.0)	12/ 964 (1.2)										
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0/ 2 (0.0)	0/ 1 (0.0)										
No	0/ 941 (0.0)	12/ 963 (1.2)										
Presence of risk factor: Cancer												
Yes	0/ 5 (0.0)	0/ 6 (0.0)	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
No	0/ 938 (0.0)	12/ 958 (1.3)	NE (	NE,	NE)	NE		0.041 (	0.002,	0.689)	0.027	
Presence of risk factor: Device Dependence												
Yes	0/ 4 (0.0)	0/ 3 (0.0)										
No	0/ 930 (0.0)	11/ 953 (1.2)										

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochran's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Analysis of Participants with Death from any Cause through Week 24 - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)	Adjusted Analysis [1]				Interaction	Unadjusted Analysis [2]			Interaction
	n/N (%)	n/N (%)	Relative Risk (95% CI)		p-Value	p-Value	Relative Risk (95% CI)	p-Value	p-Value		
Age											
< 65	0/ 804 (0.0)	6/ 816 (0.7)									
>= 65	0/ 140 (0.0)	9/ 148 (6.1)									
Gender							NE			0.689	
Male	0/ 474 (0.0)	11/ 510 (2.2)	NE (	NE,	NE)	NE		0.047 (0.003, 0.792)	0.034		
Female	0/ 470 (0.0)	4/ 454 (0.9)	NE (	NE,	NE)	NE		0.107 (0.006, 1.988)	0.134		
Geographic region							NE			0.759	
United States	0/ 387 (0.0)	3/ 395 (0.8)	NE (	NE,	NE)	NE		0.146 (0.008, 2.813)	0.202		
Europe	0/ 322 (0.0)	10/ 321 (3.1)	NE (	NE,	NE)	NE		0.047 (0.003, 0.807)	0.035		
India	0/ 74 (0.0)	0/ 78 (0.0)	NE (	NE,	NE)	NE		NE (	NE,	NE)	
Rest of World	0/ 161 (0.0)	2/ 170 (1.2)	NE (	NE,	NE)	NE		0.211 (0.010, 4.364)	0.314		
COVID-19 therapeutic mAb treatment at randomisation							NE			NE	
Yes	0/ 60 (0.0)	0/ 60 (0.0)	NE (	NE,	NE)	NE		NE (	NE,	NE)	
No	0/ 884 (0.0)	15/ 904 (1.7)	NE (	NE,	NE)	NE		0.033 (0.002, 0.550)	0.018		
Baseline viral load 1							NE			NE	
< 10^4 copies/mL	0/ 340 (0.0)	0/ 356 (0.0)	NE (	NE,	NE)	NE		NE (	NE,	NE)	
>= 10^4 copies/mL	0/ 579 (0.0)	13/ 582 (2.2)	NE (	NE,	NE)	NE		0.037 (0.002, 0.625)	0.022		
Baseline viral load 2											
< 10^7 copies/mL	0/ 663 (0.0)	5/ 707 (0.7)									
>= 10^7 copies/mL	0/ 256 (0.0)	8/ 231 (3.5)									
Baseline serology status							NE			0.554	
Negative	0/ 439 (0.0)	12/ 457 (2.6)	NE (	NE,	NE)	NE		0.042 (0.002, 0.701)	0.027		
Positive	0/ 494 (0.0)	3/ 495 (0.6)	NE (	NE,	NE)	NE		0.143 (0.007, 2.764)	0.198		
Symptom onset days to first dose date							NE			0.621	
<= 3	0/ 637 (0.0)	11/ 632 (1.7)	NE (	NE,	NE)	NE		0.043 (0.003, 0.730)	0.029		
> 3	0/ 307 (0.0)	4/ 332 (1.2)	NE (	NE,	NE)	NE		0.120 (0.006, 2.222)	0.155		
BMI group											
< 25	0/ 216 (0.0)	3/ 213 (1.4)									
25 - < 30	0/ 324 (0.0)	5/ 336 (1.5)									
>= 30	0/ 403 (0.0)	7/ 415 (1.7)									
Ethnicity							NE			0.681	
White	0/ 712 (0.0)	12/ 725 (1.7)	NE (	NE,	NE)	NE		0.041 (0.002, 0.687)	0.026		
Black or African American	0/ 45 (0.0)	1/ 42 (2.4)	NE (	NE,	NE)	NE		0.312 (0.013, 7.444)	0.471		
Asian	0/ 118 (0.0)	1/ 127 (0.8)	NE (	NE,	NE)	NE		0.359 (0.015, 8.716)	0.529		
Others	0/ 69 (0.0)	1/ 70 (1.4)	NE (	NE,	NE)	NE		0.338 (0.014, 8.159)	0.504		
Number of baseline comorbidities present											
0-1	0/ 720 (0.0)	6/ 734 (0.8)									
2-3	0/ 220 (0.0)	9/ 224 (4.0)									
>= 4	0/ 4 (0.0)	0/ 6 (0.0)									
Presence of risk factor: Smoking							NE			0.530	
Yes	0/ 423 (0.0)	3/ 442 (0.7)	NE (	NE,	NE)	NE		0.149 (0.008, 2.881)	0.208		
No	0/ 519 (0.0)	12/ 522 (2.3)	NE (	NE,	NE)	NE		0.040 (0.002, 0.678)	0.026		

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochran's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with Death from any Cause through Week 24 - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)	Adjusted Analysis [1]				Interaction	Unadjusted Analysis [2]			Interaction	
	n/N (%)	n/N (%)	Relative Risk (95% CI)			p-Value	p-Value	Relative Risk (95% CI)			p-Value	p-Value
Presence of risk factor: Diabetes mellitus												
Yes	0/ 135 (0.0)	4/ 137 (2.9)	NE (	NE,	NE)	NE	NE	0.113 (0.006,	2.074)	0.142	0.654	
No	0/ 808 (0.0)	11/ 827 (1.3)	NE (	NE,	NE)	NE		0.044 (0.003,	0.754)	0.031		
Presence of risk factor: Immunosuppression												
Yes	0/ 6 (0.0)	1/ 7 (14.3)	NE (	NE,	NE)	NE	NE	0.381 (0.018,	7.929)	0.533	0.260	
No	0/ 937 (0.0)	14/ 957 (1.5)	NE (	NE,	NE)	NE		0.035 (0.002,	0.590)	0.020		
Presence of risk factor: Chronic lung disease												
Yes	0/ 62 (0.0)	0/ 39 (0.0)	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
No	0/ 881 (0.0)	15/ 925 (1.6)	NE (	NE,	NE)	NE		0.034 (0.002,	0.565)	0.018		
Presence of risk factor: Hypertension												
Yes	0/ 358 (0.0)	13/ 375 (3.5)	NE (	NE,	NE)	NE	NE	0.039 (0.002,	0.650)	0.024	0.436	
No	0/ 585 (0.0)	2/ 589 (0.3)	NE (	NE,	NE)	NE		0.201 (0.010,	4.185)	0.301		
Presence of risk factor: Cardiovascular disorder												
Yes	0/ 42 (0.0)	3/ 49 (6.1)	NE (	NE,	NE)	NE	NE	0.166 (0.009,	3.127)	0.231	0.498	
No	0/ 901 (0.0)	12/ 915 (1.3)	NE (	NE,	NE)	NE		0.041 (0.002,	0.685)	0.026		
Presence of risk factor: Chronic kidney disease												
Yes	0/ 6 (0.0)	0/ 8 (0.0)	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
No	0/ 937 (0.0)	15/ 956 (1.6)	NE (	NE,	NE)	NE		0.033 (0.002,	0.549)	0.017		
Presence of risk factor: HIV Infection												
Yes	0	0/ 1 (0.0)										
No	0/ 943 (0.0)	15/ 962 (1.6)										
Presence of risk factor: Sickle Cell Disease												
No	0/ 943 (0.0)	15/ 964 (1.6)										
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0/ 2 (0.0)	0/ 1 (0.0)										
No	0/ 941 (0.0)	15/ 963 (1.6)										
Presence of risk factor: Cancer												
Yes	0/ 5 (0.0)	1/ 6 (16.7)	NE (	NE,	NE)	NE	NE	0.389 (0.019,	7.883)	0.538	0.254	
No	0/ 938 (0.0)	14/ 958 (1.5)	NE (	NE,	NE)	NE		0.035 (0.002,	0.590)	0.020		
Presence of risk factor: Device Dependence												
Yes	0/ 4 (0.0)	0/ 3 (0.0)										
No	0/ 930 (0.0)	14/ 953 (1.5)										

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Anhang 4-G 1.10: Subgruppenanalysen - COVID-19 bedingte Aufenthalte in medizinischen Einrichtungen

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Analysis of Number of COVID-19 related hospitalizations - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavi (N=944)		Placebo (N=964)		Adjusted Analysis [1]				Interaction p-Value	Unadjusted Analysis [2]				Interaction p-Value
	n	Events	n	Events	LS mean	Ratio	(95% CI)	p-Value		LS mean	Ratio	(95% CI)	p-Value	
Age														
< 65	9	9	41	42	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
>= 65	1	1	19	19	0.054 (	0.007,	0.405)	0.005		NE (	NE,	NE)	NE	
Gender														
Male	6	6	39	40	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
Female	4	4	21	21	0.207 (	0.071,	0.604)	0.004		0.185 (	0.063,	0.539)	0.002	
Geographic region														
United States	3	3	12	12	0.264 (	0.074,	0.950)	0.042	NE	NE (	NE,	NE)	NE	NE
Europe	4	4	36	37	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE	
India	0	0	0	0	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE	
Rest of World	3	3	12	12	NE (	NE,	NE)	NE		0.265 (	0.075,	0.939)	0.040	
COVID-19 therapeutic mAb treatment at randomisation														
Yes	1	1	2	2	0.480 (	0.043,	5.377)	0.552	NE	NE (	NE,	NE)	NE	NE
No	9	9	58	59	0.163 (	0.080,	0.329)	<.001		0.155 (	0.077,	0.313)	<.001	
Baseline viral load 1														
< 10^4 copies/mL	2	2	3	3	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
>= 10^4 copies/mL	8	8	54	55	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE	
Baseline viral load 2														
< 10^7 copies/mL	8	8	33	34	0.256 (	0.118,	0.553)	<.001	NE	NE (	NE,	NE)	NE	0.116
>= 10^7 copies/mL	2	2	24	24	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE	
Baseline serology status														
Negative	8	8	52	53	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
Positive	2	2	8	8	0.250 (	0.053,	1.186)	0.081		NE (	NE,	NE)	NE	
Symptom onset days to first dose date														
<= 3	5	5	40	41	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	0.244
> 3	5	5	20	20	NE (	NE,	NE)	NE		0.270 (	0.101,	0.719)	0.009	
BMI group														
< 25	1	1	9	9	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
25 - < 30	3	3	22	23	NE (	NE,	NE)	NE		0.130 (	0.039,	0.438)	0.001	
>= 30	6	6	29	29	NE (	NE,	NE)	NE		0.210 (	0.087,	0.506)	<.001	
Ethnicity														
White	9	9	50	51	0.194 (	0.095,	0.395)	<.001	NE	0.179 (	0.088,	0.364)	<.001	NE
Black or African American	0	0	1	1	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE	
Asian	1	1	3	3	NE (	NE,	NE)	NE		0.367 (	0.038,	3.528)	0.385	
Others	0	0	6	6	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE	
Number of baseline comorbidities present														
0-1	5	5	37	37	NE (	NE,	NE)	NE	NE	0.136 (	0.054,	0.347)	<.001	NE
2-3	5	5	23	24	NE (	NE,	NE)	NE		0.213 (	0.081,	0.562)	0.002	
>= 4	0	0	0	0	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE	
Presence of risk factor: Smoking														
Yes	5	5	17	18	0.323 (	0.117,	0.893)	0.029	NE	NE (	NE,	NE)	NE	0.185
No	5	5	43	43	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE	

N: Number of participants, n: Number of participants with event, CI: Confidence Interval, NE: Not estimable, I: Infinity, LS: Least Squares
Medical Visits and Hospitalization events are limited through Day 34 visit. Number of events per day = Number of events/Number of days follow up limited to Day 37.
Stratification factors: geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.
[1] Negative binomial regression model includes main effects of treatment, stratification factors and the log number of days follow up as the participant offset variable.
[2] Negative binomial regression model includes main effects of treatment and the log number of days follow up as the participant offset variable.
p-Value for interaction from same negative binomial regression model with additional factors for subgroup and subgroup*treatment interaction.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Analysis of Number of COVID-19 related hospitalizations - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Adjusted Analysis [1]				Interaction	Unadjusted Analysis [2]				Interaction
	n	Events	n	Events	LS mean Ratio (95% CI)		p-Value		p-Value	LS mean Ratio (95% CI)		p-Value		p-Value
Presence of risk factor: Diabetes mellitus														
Yes	3	3	9	9	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	0.262
No	7	7	51	52	NE (	NE,	NE)	NE		0.137 (	0.062,	0.301)	<.001	
Presence of risk factor: Immunosuppression														
Yes	0	0	0	0	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
No	10	10	60	61	0.174 (	0.089,	0.341)	<.001		NE (	NE,	NE)	NE	
Presence of risk factor: Chronic lung disease														
Yes	0	0	2	2	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
No	10	10	58	59	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE	
Presence of risk factor: Hypertension														
Yes	5	5	42	43	NE (	NE,	NE)	NE	NE	0.121 (	0.048,	0.306)	<.001	0.234
No	5	5	18	18	0.306 (	0.112,	0.836)	0.021		0.278 (	0.103,	0.749)	0.011	
Presence of risk factor: Cardiovascular disorder														
Yes	0	0	11	11	NE (	NE,	NE)	NE	NE	0.000 (	0.000,	378E134)	0.940	NE
No	10	10	49	50	0.215 (	0.109,	0.426)	<.001		NE (	NE,	NE)	NE	
Presence of risk factor: Chronic kidney disease														
Yes	0	0	0	0	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
No	10	10	60	61	NE (	NE,	NE)	NE		0.166 (	0.085,	0.324)	<.001	
Presence of risk factor: HIV Infection														
Yes	0	0	0	0										
No	10	10	60	61										
Presence of risk factor: Sickie Cell Disease														
No	10	10	60	61										
Presence of risk factor: Neurodevelopmental Disorder														
Yes	0	0	0	0										
No	10	10	60	61										
Presence of risk factor: Cancer														
Yes	0	0	0	0	NE (	NE,	NE)	NE	NE	NE (	NE,	NE)	NE	NE
No	10	10	60	61	NE (	NE,	NE)	NE		0.166 (	0.085,	0.325)	<.001	
Presence of risk factor: Device Dependence														
Yes	0	0	0	0										
No	10	10	59	60										

N: Number of participants, n: Number of participants with event, CI: Confidence Interval, NE: Not estimable, I: Infinity, LS: Least Squares
 Medical Visits and Hospitalization events are limited through Day 34 visit. Number of events per day = Number of events/Number of days follow up limited to Day 37.
 Stratification factors: geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.
 [1] Negative binomial regression model includes main effects of treatment, stratification factors and the log number of days follow up as the participant offset variable.
 [2] Negative binomial regression model includes main effects of treatment and the log number of days follow up as the participant offset variable.
 p-Value for interaction from same negative binomial regression model with additional factors for subgroup and subgroup*treatment interaction.
 Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Anhang 4-G 1.11: Subgruppenanalysen - Krankheitsbedingte Symptome

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Stuffy or Runny Nose - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]		Interaction p-Value	Unadjusted analysis [2]		Interaction p-Value
			Relative Risk (95% CI)	p-Value		Relative Risk (95% CI)	p-Value	
Age								
< 65	194/ 790 (24.6)	201/ 810 (24.8)	0.981 (0.825, 1.167)	0.830	0.081	0.990 (0.834, 1.174)	0.905	0.083
>= 65	17/ 138 (12.3)	30/ 145 (20.7)	0.555 (0.316, 0.974)	0.040		0.595 (0.344, 1.029)	0.063	
Gender								
Male	104/ 463 (22.5)	111/ 507 (21.9)	1.018 (0.803, 1.292)	0.882	0.378	1.026 (0.810, 1.299)	0.831	0.287
Female	107/ 465 (23.0)	120/ 448 (26.8)	0.864 (0.685, 1.088)	0.214		0.859 (0.685, 1.077)	0.188	
Geographic region								
United States	91/ 375 (24.3)	84/ 387 (21.7)	1.126 (0.861, 1.473)	0.387	0.139	1.118 (0.862, 1.450)	0.401	0.120
Europe	83/ 322 (25.8)	90/ 321 (28.0)	0.911 (0.701, 1.182)	0.482		0.919 (0.712, 1.186)	0.518	
India	7/ 74 (9.5)	6/ 78 (7.7)	1.214 (0.430, 3.429)	0.715		1.230 (0.433, 3.490)	0.698	
Rest of World	30/ 157 (19.1)	51/ 169 (30.2)	0.638 (0.429, 0.949)	0.026		0.633 (0.426, 0.940)	0.023	
COVID-19 therapeutic mAb treatment at randomisation								
Yes	11/ 57 (19.3)	14/ 60 (23.3)	0.758 (0.377, 1.524)	0.437	0.623	0.827 (0.410, 1.668)	0.596	0.713
No	200/ 871 (23.0)	217/ 895 (24.2)	0.943 (0.795, 1.119)	0.503		0.947 (0.801, 1.120)	0.526	
Baseline viral load 1								
< 10^4 copies/mL	64/ 335 (19.1)	74/ 354 (20.9)	0.906 (0.670, 1.225)	0.521	0.850	0.914 (0.677, 1.233)	0.556	0.866
>= 10^4 copies/mL	139/ 569 (24.4)	149/ 575 (25.9)	0.943 (0.773, 1.151)	0.565		0.943 (0.772, 1.151)	0.563	
Baseline viral load 2								
< 10^7 copies/mL	127/ 652 (19.5)	149/ 699 (21.3)	0.910 (0.736, 1.126)	0.387	0.868	0.914 (0.740, 1.129)	0.403	0.883
>= 10^7 copies/mL	76/ 252 (30.2)	74/ 230 (32.2)	0.935 (0.720, 1.215)	0.615		0.937 (0.719, 1.222)	0.633	
Baseline serology status								
Negative	122/ 435 (28.0)	134/ 456 (29.4)	0.945 (0.764, 1.168)	0.598	0.865	0.954 (0.776, 1.174)	0.659	0.848
Positive	85/ 482 (17.6)	93/ 487 (19.1)	0.911 (0.698, 1.189)	0.492		0.923 (0.708, 1.205)	0.557	
Symptom onset days to first dose date								
<= 3	153/ 624 (24.5)	159/ 624 (25.5)	0.940 (0.773, 1.142)	0.532	0.854	0.962 (0.794, 1.166)	0.695	0.618
> 3	58/ 304 (19.1)	72/ 331 (21.8)	0.915 (0.667, 1.254)	0.579		0.877 (0.644, 1.194)	0.405	
BMI group								
< 25	46/ 215 (21.4)	59/ 213 (27.7)	0.789 (0.559, 1.112)	0.175	0.247	0.772 (0.552, 1.081)	0.132	0.264
25 - < 30	72/ 319 (22.6)	67/ 332 (20.2)	1.125 (0.835, 1.517)	0.438		1.118 (0.833, 1.502)	0.457	
>= 30	93/ 393 (23.7)	105/ 410 (25.6)	0.890 (0.693, 1.144)	0.364		0.924 (0.725, 1.177)	0.523	
Ethnicity								
White	165/ 699 (23.6)	176/ 718 (24.5)	0.965 (0.799, 1.166)	0.715	0.191	0.963 (0.800, 1.159)	0.690	0.394
Black or African American	15/ 43 (34.9)	11/ 40 (27.5)	1.485 (0.739, 2.987)	0.267		1.268 (0.664, 2.425)	0.472	
Asian	17/ 117 (14.5)	21/ 127 (16.5)	NE (NE, NE)	NE		0.879 (0.488, 1.582)	0.667	
Others	14/ 69 (20.3)	23/ 70 (32.9)	NE (NE, NE)	NE		0.618 (0.347, 1.098)	0.100	
Number of baseline comorbidities present								
0-1	167/ 710 (23.5)	175/ 728 (24.0)	0.953 (0.789, 1.152)	0.620	0.900	0.978 (0.813, 1.177)	0.818	0.596
2-3	43/ 214 (20.1)	55/ 221 (24.9)	0.885 (0.626, 1.252)	0.490		0.807 (0.568, 1.148)	0.233	
>= 4	1/ 4 (25.0)	1/ 6 (16.7)	NE (NE, NE)	NE		1.500 (0.127, 17.667)	0.747	
Presence of risk factor: Smoking								
Yes	96/ 417 (23.0)	96/ 438 (21.9)	1.034 (0.804, 1.330)	0.793	0.242	1.050 (0.819, 1.347)	0.699	0.250
No	115/ 509 (22.6)	135/ 517 (26.1)	0.856 (0.686, 1.067)	0.166		0.865 (0.697, 1.074)	0.190	
Presence of risk factor: Diabetes mellitus					0.702			0.609

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Stuffy or Runny Nose - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value	
Yes	24/ 130 (18.5)	30/ 136 (22.1)	NE (	NE,	NE)	NE		0.837 (	0.518,	1.352)	0.467	
No	187/ 797 (23.5)	201/ 819 (24.5)	0.946 (	0.792,	1.130)	0.542		0.956 (	0.804,	1.137)	0.612	
Presence of risk factor: Immunosuppression							NE					0.558
Yes	0/ 6 (0.0)	1/ 7 (14.3)	NE (	NE,	NE)	NE		0.381 (	0.018,	7.929)	0.533	
No	211/ 921 (22.9)	230/ 948 (24.3)	0.933 (	0.790,	1.101)	0.413		0.944 (	0.802,	1.112)	0.492	
Presence of risk factor: Chronic lung disease							0.997					0.826
Yes	11/ 62 (17.7)	8/ 39 (20.5)	0.891 (	0.377,	2.104)	0.792		0.865 (	0.382,	1.960)	0.728	
No	200/ 865 (23.1)	223/ 916 (24.3)	0.941 (	0.795,	1.115)	0.484		0.950 (	0.804,	1.122)	0.544	
Presence of risk factor: Hypertension							0.251					0.322
Yes	87/ 348 (25.0)	89/ 371 (24.0)	1.033 (	0.797,	1.338)	0.807		1.042 (	0.806,	1.347)	0.753	
No	124/ 579 (21.4)	142/ 584 (24.3)	0.856 (	0.691,	1.062)	0.158		0.881 (	0.713,	1.088)	0.240	
Presence of risk factor: Cardiovascular disorder							0.195					0.193
Yes	8/ 42 (19.0)	16/ 49 (32.7)	NE (	NE,	NE)	NE		0.583 (	0.278,	1.225)	0.154	
No	203/ 885 (22.9)	215/ 906 (23.7)	0.960 (	0.809,	1.140)	0.644		0.967 (	0.817,	1.143)	0.692	
Presence of risk factor: Chronic kidney disease							0.341					0.460
Yes	1/ 6 (16.7)	3/ 8 (37.5)	NE (	NE,	NE)	NE		0.444 (	0.060,	3.285)	0.427	
No	210/ 921 (22.8)	228/ 947 (24.1)	0.940 (	0.796,	1.111)	0.469		0.947 (	0.804,	1.116)	0.516	
Presence of risk factor: HIV Infection												
Yes	0	0/ 1 (0.0)										
No	211/ 927 (22.8)	231/ 953 (24.2)										
Presence of risk factor: Sickle Cell Disease												
No	211/ 927 (22.8)	231/ 955 (24.2)										
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0/ 2 (0.0)	0/ 1 (0.0)										
No	211/ 925 (22.8)	231/ 954 (24.2)										
Presence of risk factor: Cancer							0.174					0.170
Yes	3/ 5 (60.0)	1/ 6 (16.7)	NE (	NE,	NE)	NE		3.600 (	0.524,	24.728)	0.193	
No	208/ 922 (22.6)	230/ 949 (24.2)	0.927 (	0.785,	1.095)	0.373		0.931 (	0.790,	1.097)	0.392	
Presence of risk factor: Device Dependence												
Yes	0/ 4 (0.0)	2/ 3 (66.7)										
No	210/ 914 (23.0)	228/ 944 (24.2)										

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=659)			Placebo (N=653)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	490/ 568	(86.3)	6.0 (6.0, 7.0)	443/ 562	(78.8)	7.0 (7.0, 8.0)	1.277 (1.119, 1.458)	<.001		0.083	1.271 (1.117, 1.446)	<.001		0.078
>= 65	87/ 91	(95.6)	5.0 (4.0, 6.0)	70/ 91	(76.9)	6.0 (4.0, 8.0)	1.664 (1.195, 2.316)	0.003			1.655 (1.201, 2.280)	0.002		
Gender														
Male	275/ 312	(88.1)	6.0 (5.0, 6.0)	263/ 340	(77.4)	7.0 (7.0, 8.0)	1.447 (1.214, 1.725)	<.001		0.176	1.424 (1.200, 1.688)	<.001		0.181
Female	302/ 347	(87.0)	6.0 (5.0, 7.0)	250/ 313	(79.9)	7.0 (6.0, 9.0)	1.218 (1.025, 1.448)	0.025			1.233 (1.042, 1.458)	0.015		
Geographic region														
United States	220/ 268	(82.1)	6.0 (5.0, 8.0)	202/ 266	(75.9)	6.0 (5.0, 8.0)	1.141 (0.939, 1.387)	0.185		0.221	1.130 (0.933, 1.368)	0.212		0.111
Europe	197/ 215	(91.6)	6.0 (5.0, 7.0)	167/ 211	(79.1)	7.0 (6.0, 8.0)	1.457 (1.174, 1.807)	<.001			1.445 (1.174, 1.780)	<.001		
India	53/ 55	(96.4)	7.0 (5.0, 8.0)	51/ 54	(94.4)	7.0 (6.0, 9.0)	1.387 (0.931, 2.067)	0.108			1.306 (0.884, 1.928)	0.180		
Rest of World	107/ 121	(88.4)	5.0 (3.0, 6.0)	93/ 122	(76.2)	10.0 (7.0, 11.0)	1.598 (1.198, 2.132)	0.001			1.646 (1.242, 2.182)	<.001		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	37/ 46	(80.4)	7.0 (3.0, 9.0)	44/ 53	(83.0)	8.0 (4.0, 10.0)	1.036 (0.663, 1.620)	0.876		0.300	1.074 (0.693, 1.664)	0.749		0.336
No	540/ 613	(88.1)	6.0 (5.0, 6.0)	469/ 600	(78.2)	7.0 (7.0, 8.0)	1.351 (1.189, 1.535)	<.001			1.343 (1.186, 1.521)	<.001		
Baseline viral load 1														
< 10^4 copies/mL	204/ 233	(87.6)	6.0 (5.0, 7.0)	185/ 226	(81.9)	6.0 (5.0, 7.0)	1.161 (0.949, 1.420)	0.147		0.099	1.125 (0.922, 1.374)	0.245		0.071
>= 10^4 copies/mL	354/ 407	(87.0)	6.0 (5.0, 6.0)	315/ 409	(77.0)	8.0 (7.0, 10.0)	1.431 (1.226, 1.670)	<.001			1.429 (1.226, 1.665)	<.001		
Baseline viral load 2														
< 10^7 copies/mL	390/ 457	(85.3)	6.0 (5.0, 7.0)	371/ 464	(80.0)	7.0 (6.0, 8.0)	1.211 (1.049, 1.398)	0.009		0.027	1.198 (1.039, 1.382)	0.013		0.024
>= 10^7 copies/mL	168/ 183	(91.8)	6.0 (5.0, 7.0)	129/ 171	(75.4)	8.0 (7.0, 11.0)	1.746 (1.374, 2.219)	<.001			1.682 (1.334, 2.121)	<.001		
Baseline serology status														
Negative	272/ 309	(88.0)	6.0 (5.0, 7.0)	227/ 307	(73.9)	9.0 (7.0, 11.0)	1.531 (1.277, 1.837)	<.001		0.074	1.526 (1.277, 1.822)	<.001		0.050
Positive	299/ 343	(87.2)	6.0 (5.0, 6.0)	277/ 336	(82.4)	6.0 (5.0, 7.0)	1.197 (1.013, 1.413)	0.035			1.171 (0.994, 1.380)	0.059		
Symptom onset days to first dose date														
<= 3	393/ 437	(89.9)	6.0 (5.0, 7.0)	344/ 424	(81.1)	7.0 (6.0, 8.0)	1.315 (1.133, 1.526)	<.001		0.713	1.312 (1.134, 1.517)	<.001		0.732
> 3	184/ 222	(82.9)	5.0 (5.0, 7.0)	169/ 229	(73.8)	8.0 (7.0, 9.0)	1.342 (1.080, 1.667)	0.008			1.332 (1.080, 1.642)	0.007		
BMI group														
< 25	138/ 151	(91.4)	6.0 (5.0, 7.0)	117/ 141	(83.0)	7.0 (6.0, 8.0)	1.321 (1.013, 1.723)	0.040		0.853	1.308 (1.021, 1.677)	0.034		0.719
25 - < 30	186/ 216	(86.1)	6.0 (5.0, 7.0)	173/ 227	(76.2)	7.0 (6.0, 8.0)	1.401 (1.132, 1.734)	0.002			1.386 (1.125, 1.707)	0.002		
>= 30	253/ 292	(86.6)	6.0 (5.0, 7.0)	223/ 285	(78.2)	8.0 (6.0, 9.0)	1.299 (1.077, 1.566)	0.006			1.273 (1.062, 1.525)	0.009		
Ethnicity														
White	432/ 494	(87.4)	6.0 (5.0, 7.0)	379/ 493	(76.9)	7.0 (6.0, 8.0)	1.309 (1.135, 1.510)	<.001		0.653	1.315 (1.145, 1.510)	<.001		0.653
Black or African American	16/ 24	(66.7)	5.0 (4.0, 21.0)	15/ 23	(65.2)	5.0 (2.0, 19.0)	1.106 (0.527, 2.317)	0.790			1.034 (0.509, 2.103)	0.926		
Asian	79/ 85	(92.9)	6.0 (5.0, 7.0)	76/ 82	(92.7)	7.0 (6.0, 9.0)	1.350 (0.971, 1.875)	0.074			1.282 (0.934, 1.760)	0.124		
Others	50/ 56	(89.3)	4.0 (3.0, 7.0)	43/ 55	(78.2)	10.0 (5.0, 12.0)	1.701 (1.108, 2.610)	0.015			1.679 (1.105, 2.553)	0.015		
Number of baseline comorbidities present														
0-1	443/ 507	(87.4)		383/ 491	(78.0)									
2-3	132/ 150	(88.0)		127/ 159	(79.9)									
>= 4	2/ 2	(100.0)		3/ 3	(100.0)									
Presence of risk factor: Smoking														
Yes	262/ 298	(87.9)	6.0 (5.0, 7.0)	248/ 313	(79.2)	7.0 (7.0, 8.0)	1.370 (1.145, 1.640)	<.001		0.896	1.324 (1.112, 1.577)	0.002		0.871
No	314/ 359	(87.5)	6.0 (5.0, 6.0)	265/ 340	(77.9)	8.0 (6.0, 8.0)	1.312 (1.109, 1.552)	0.002			1.328 (1.126, 1.565)	<.001		

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=659)			Placebo (N=653)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus										0.239				0.186
Yes	84/	95 (88.4)	4.0 (3.0, 6.0)	73/	89 (82.0)	7.0 (5.0, 10.0)	1.512 (1.084, 2.109)	0.015			1.556 (1.132, 2.138)	0.007		
No	492/	563 (87.4)	6.0 (6.0, 7.0)	440/	564 (78.0)	7.0 (7.0, 8.0)	1.298 (1.137, 1.481)	<.001			1.286 (1.131, 1.464)	<.001		
Presence of risk factor: Immunosuppression										0.913				0.918
Yes	5/	5 (100.0)	3.0 (2.0, 21.0)	6/	6 (100.0)	8.5 (2.0, 13.0)	1.833 (0.263, 12.777)	0.541			1.333 (0.363, 4.893)	0.665		
No	571/	653 (87.4)	6.0 (5.0, 7.0)	507/	647 (78.4)	7.0 (7.0, 8.0)	1.324 (1.171, 1.497)	<.001			1.321 (1.171, 1.489)	<.001		
Presence of risk factor: Chronic lung disease										0.665				0.684
Yes	43/	47 (91.5)	5.0 (4.0, 7.0)	22/	27 (81.5)	9.0 (5.0, 10.0)	1.645 (0.942, 2.872)	0.080			1.525 (0.910, 2.557)	0.109		
No	533/	611 (87.2)	6.0 (5.0, 7.0)	491/	626 (78.4)	7.0 (7.0, 8.0)	1.312 (1.156, 1.489)	<.001			1.308 (1.156, 1.479)	<.001		
Presence of risk factor: Hypertension										0.997				0.856
Yes	200/	234 (85.5)	6.0 (5.0, 7.0)	194/	252 (77.0)	7.0 (6.0, 8.0)	1.289 (1.050, 1.583)	0.015			1.273 (1.044, 1.552)	0.017		
No	376/	424 (88.7)	6.0 (5.0, 7.0)	319/	401 (79.6)	7.0 (7.0, 9.0)	1.355 (1.163, 1.580)	<.001			1.348 (1.160, 1.566)	<.001		
Presence of risk factor: Cardiovascular disorder										0.227				0.544
Yes	24/	25 (96.0)	5.0 (4.0, 9.0)	20/	26 (76.9)	8.0 (4.0, 11.0)	1.936 (0.982, 3.815)	0.056			1.565 (0.860, 2.846)	0.142		
No	552/	633 (87.2)	6.0 (5.0, 7.0)	493/	627 (78.6)	7.0 (7.0, 8.0)	1.306 (1.153, 1.479)	<.001			1.311 (1.160, 1.481)	<.001		
Presence of risk factor: Chronic kidney disease										0.761				0.685
Yes	5/	6 (83.3)	5.0 (2.0, 7.0)	5/	6 (83.3)	4.5 (2.0, NE)	1.390 (0.254, 7.613)	0.704			1.683 (0.437, 6.480)	0.449		
No	571/	652 (87.6)	6.0 (5.0, 7.0)	508/	647 (78.5)	7.0 (7.0, 8.0)	1.324 (1.171, 1.498)	<.001			1.320 (1.171, 1.489)	<.001		
Presence of risk factor: HIV Infection														
Yes	0			1/	1 (100.0)									
No	576/	658 (87.5)		511/	651 (78.5)									
Presence of risk factor: Sickel Cell Disease														
No	576/	658 (87.5)		513/	653 (78.6)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/	2 (100.0)		1/	1 (100.0)									
No	574/	656 (87.5)		512/	652 (78.5)									
Presence of risk factor: Cancer														
Yes	1/	1 (100.0)		6/	6 (100.0)									
No	575/	657 (87.5)		507/	647 (78.4)									
Presence of risk factor: Device Dependence														
Yes	2/	3 (66.7)		1/	2 (50.0)									
No	569/	648 (87.8)		509/	645 (78.9)									

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

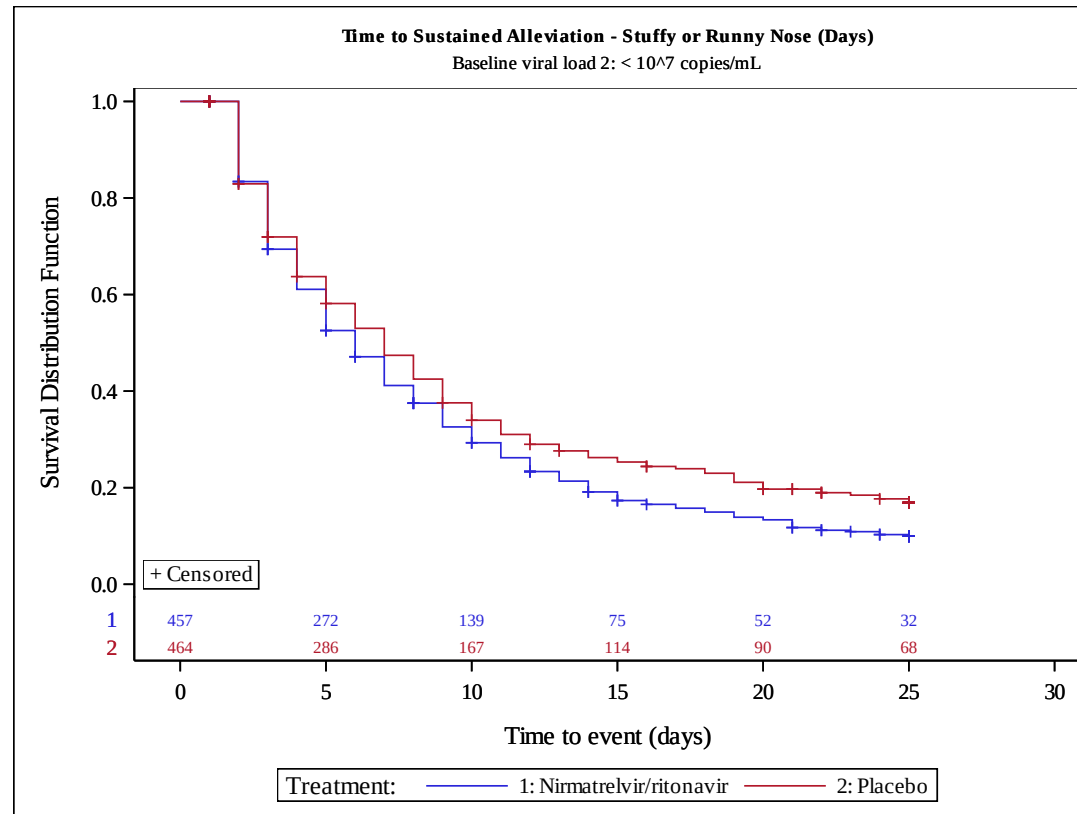
[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Final

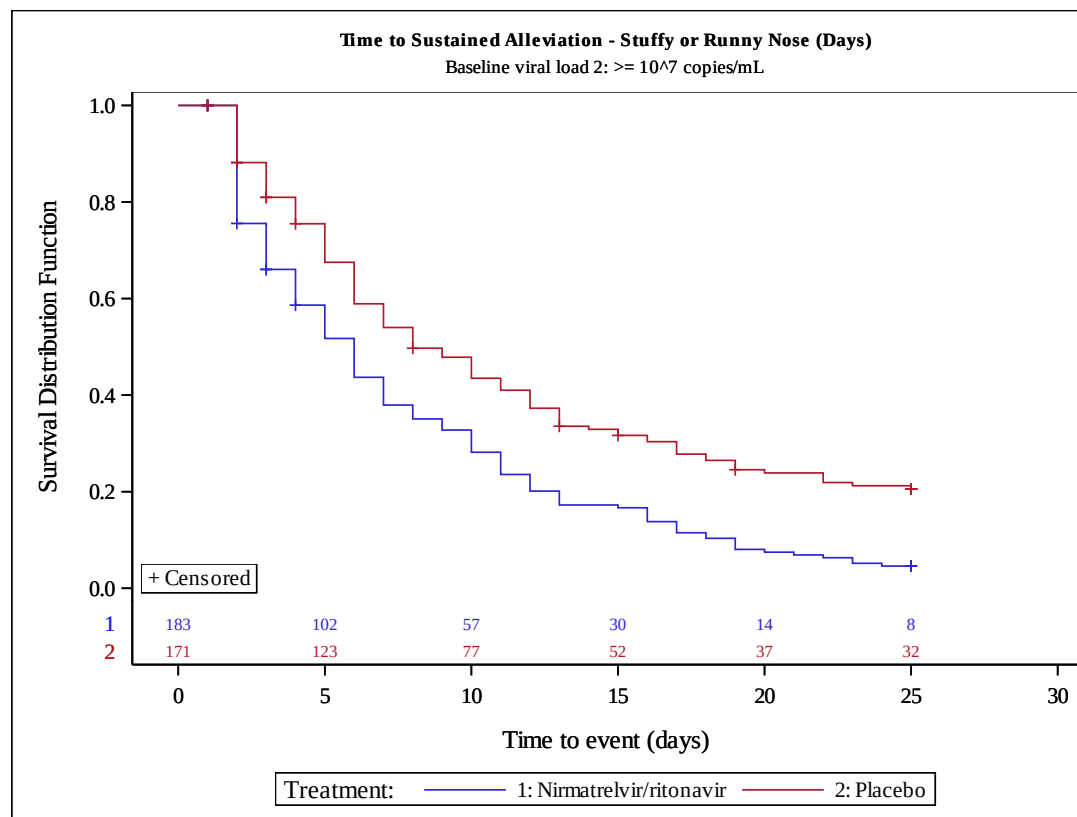


Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=28)			Placebo (N=32)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Age												
< 65	22/	27 (81.5)		26/	30 (86.7)							
>= 65	1/	1 (100.0)		2/	2 (100.0)							
Gender									0.249			0.176
Male	11/	15 (73.3)	3.0 (2.0, 23.0)	8/	10 (80.0)	7.0 (2.0, 12.0)	1.085 (0.258, 4.562)	0.911		0.695 (0.269, 1.796)	0.453	
Female	12/	13 (92.3)	7.5 (2.0, 20.0)	20/	22 (90.9)	9.5 (5.0, 16.0)	1.064 (0.440, 2.572)	0.891		1.100 (0.531, 2.279)	0.798	
Geographic region												
United States	12/	17 (70.6)		11/	15 (73.3)							
Europe	6/	6 (100.0)		9/	9 (100.0)							
India	0/	0		0/	0							
Rest of World	5/	5 (100.0)		8/	8 (100.0)							
COVID-19 therapeutic mAb treatment at randomisation												
Yes	0/	2 (0.0)		2/	2 (100.0)							
No	23/	26 (88.5)		26/	30 (86.7)							
Baseline viral load 1									0.031			0.029
< 10^4 copies/mL	3/	5 (60.0)	16.0 (3.0, NE)	5/	5 (100.0)	3.0 (2.0, 6.0)	0.169 (0.015, 1.944)	0.154		0.151 (0.017, 1.346)	0.090	
>= 10^4 copies/mL	19/	22 (86.4)	4.5 (2.0, 11.0)	23/	26 (88.5)	10.0 (7.0, 16.0)	1.116 (0.560, 2.223)	0.755		1.038 (0.557, 1.936)	0.906	
Baseline viral load 2									0.472			0.876
< 10^7 copies/mL	11/	15 (73.3)	6.5 (3.0, 22.0)	20/	22 (90.9)	8.0 (4.0, 16.0)	1.013 (0.432, 2.374)	0.976		0.780 (0.367, 1.658)	0.518	
>= 10^7 copies/mL	11/	12 (91.7)	7.5 (2.0, 21.0)	8/	9 (88.9)	9.0 (2.0, 12.0)	0.919 (0.232, 3.635)	0.904		0.818 (0.313, 2.135)	0.681	
Baseline serology status									0.962			0.862
Negative	14/	18 (77.8)	9.0 (3.0, 21.0)	17/	19 (89.5)	9.5 (6.0, 14.0)	1.013 (0.439, 2.341)	0.975		0.821 (0.393, 1.716)	0.601	
Positive	9/	10 (90.0)	4.5 (2.0, 11.0)	11/	13 (84.6)	7.0 (2.0, 16.0)	1.250 (0.405, 3.864)	0.698		0.903 (0.363, 2.249)	0.826	
Symptom onset days to first dose date									0.988			0.601
<= 3	18/	20 (90.0)	3.0 (2.0, 11.0)	18/	18 (100.0)	8.5 (4.0, 14.0)	0.845 (0.400, 1.783)	0.658		0.854 (0.425, 1.717)	0.658	
> 3	5/	8 (62.5)	10.0 (2.0, NE)	10/	14 (71.4)	10.0 (3.0, 17.0)	0.623 (0.142, 2.727)	0.530		0.725 (0.245, 2.140)	0.560	
BMI group									0.878			0.852
< 25	4/	5 (80.0)	6.5 (3.0, 10.0)	6/	6 (100.0)	8.5 (2.0, 19.0)	2.633 (0.117, 59.004)	0.542		1.312 (0.325, 5.286)	0.703	
25 - < 30	6/	7 (85.7)	6.0 (2.0, 23.0)	8/	10 (80.0)	7.0 (2.0, 20.0)	1.239 (0.326, 4.716)	0.753		0.912 (0.297, 2.798)	0.872	
>= 30	13/	16 (81.3)	6.5 (3.0, 21.0)	14/	16 (87.5)	10.0 (4.0, 14.0)	0.832 (0.349, 1.984)	0.678		0.787 (0.359, 1.722)	0.548	
Ethnicity												
White	17/	22 (77.3)		23/	26 (88.5)							
Black or African American	2/	2 (100.0)		1/	1 (100.0)							
Asian	2/	2 (100.0)		2/	2 (100.0)							
Others	2/	2 (100.0)		2/	3 (66.7)							
Number of baseline comorbidities present												
0-1	20/	24 (83.3)		22/	26 (84.6)							
2-3	3/	4 (75.0)		6/	6 (100.0)							
>= 4	0/	0		0/	0							
Presence of risk factor: Smoking									0.459			0.913
Yes	8/	9 (88.9)	9.0 (2.0, 22.0)	14/	15 (93.3)	9.0 (4.0, 16.0)	0.514 (0.121, 2.174)	0.366		0.798 (0.318, 2.003)	0.631	
No	15/	19 (78.9)	4.5 (3.0, 20.0)	14/	17 (82.4)	9.0 (4.0, 14.0)	1.358 (0.552, 3.339)	0.505		0.927 (0.442, 1.946)	0.842	

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Stuffy or Runny Nose - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=28)			Placebo (N=32)			Adjusted Analysis [2]			Unadjusted Analysis [3]			
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	
Presence of risk factor: Diabetes mellitus													
Yes	1/	1 (100.0)		3/	3 (100.0)								
No	22/	27 (81.5)		25/	29 (86.2)								
Presence of risk factor: Immunosuppression													
Yes	0			0									
No	23/	28 (82.1)		28/	32 (87.5)								
Presence of risk factor: Chronic lung disease													
Yes	6/	6 (100.0)		2/	2 (100.0)								
No	17/	22 (77.3)		26/	30 (86.7)								
Presence of risk factor: Hypertension													
Yes	4/	7 (57.1)	13.0 (2.0, NE)	8/	9 (88.9)	7.0 (2.0, 16.0)	0.868 (0.112, 6.749)	0.892	0.310	0.532 (0.139, 2.034)	0.357	0.161	
No	19/	21 (90.5)	6.0 (3.0, 10.0)	20/	23 (87.0)	10.0 (5.0, 14.0)	0.993 (0.486, 2.028)	0.985		1.024 (0.540, 1.944)	0.942		
Presence of risk factor: Cardiovascular disorder													
Yes	0			2/	2 (100.0)								
No	23/	28 (82.1)		26/	30 (86.7)								
Presence of risk factor: Chronic kidney disease													
Yes	0			0									
No	23/	28 (82.1)		28/	32 (87.5)								
Presence of risk factor: HIV Infection													
Yes	0			0									
No	23/	28 (82.1)		28/	32 (87.5)								
Presence of risk factor: Sickle Cell Disease													
No	23/	28 (82.1)		28/	32 (87.5)								
Presence of risk factor: Neurodevelopmental Disorder													
Yes	0			0									
No	23/	28 (82.1)		28/	32 (87.5)								
Presence of risk factor: Cancer													
Yes	0			0									
No	23/	28 (82.1)		28/	32 (87.5)								
Presence of risk factor: Device Dependence													
Yes	0/	1 (0.0)		0									
No	22/	26 (84.6)		28/	32 (87.5)								

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[3] Estimated by cox regression model assuming proportional hazards.

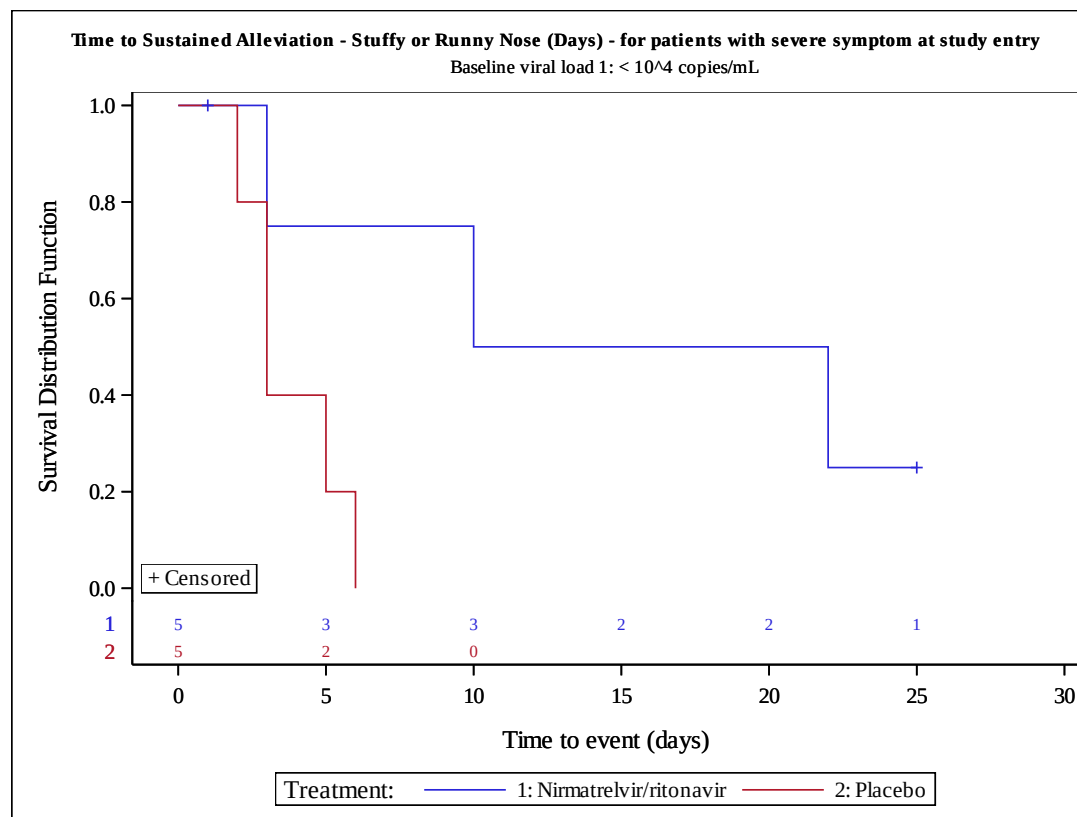
p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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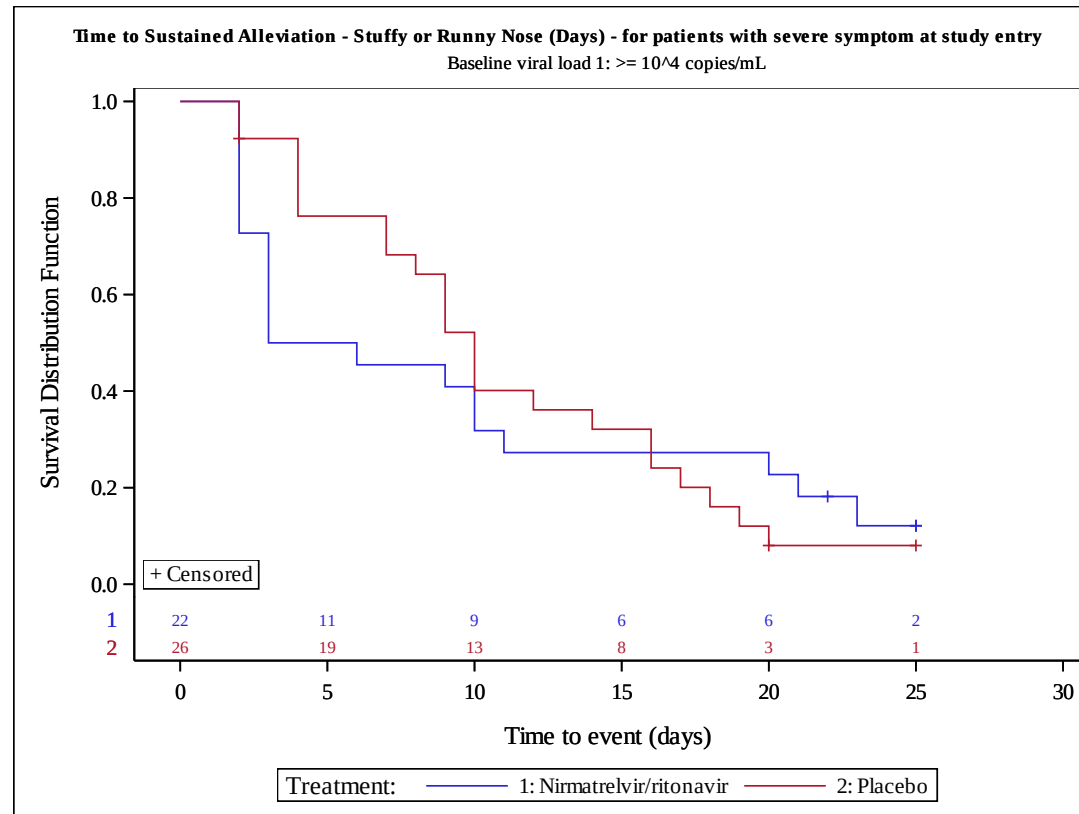


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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=659)			Placebo (N=653)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	444/ 568	(78.2)	10.0 (9.0, 11.0)	396/ 562	(70.5)	11.0 (10.0, 12.0)	1.281 (1.115, 1.473)	<.001		0.114	1.261 (1.101, 1.445)	<.001		0.062
>= 65	81/ 91	(89.0)	7.5 (6.0, 9.0)	62/ 91	(68.1)	10.0 (8.0, 15.0)	1.676 (1.186, 2.368)	0.003			1.724 (1.234, 2.408)	0.001		
Gender														
Male	254/ 312	(81.4)	8.0 (7.0, 9.0)	242/ 340	(71.2)	10.0 (9.0, 11.0)	1.418 (1.182, 1.702)	<.001		0.332	1.392 (1.166, 1.662)	<.001		0.357
Female	271/ 347	(78.1)	11.0 (10.0, 12.0)	216/ 313	(69.0)	12.0 (11.0, 15.0)	1.258 (1.047, 1.512)	0.014			1.276 (1.066, 1.526)	0.008		
Geographic region														
United States	200/ 268	(74.6)	11.0 (9.0, 12.0)	171/ 266	(64.3)	12.0 (9.0, 15.0)	1.300 (1.055, 1.602)	0.014		0.877	1.284 (1.046, 1.576)	0.017		0.654
Europe	173/ 215	(80.5)	11.0 (9.0, 12.0)	149/ 211	(70.6)	12.0 (10.0, 15.0)	1.301 (1.037, 1.633)	0.023			1.298 (1.042, 1.617)	0.020		
India	53/ 55	(96.4)	7.0 (5.0, 8.0)	51/ 54	(94.4)	8.0 (6.0, 9.0)	1.391 (0.933, 2.073)	0.105			1.306 (0.885, 1.929)	0.179		
Rest of World	99/ 121	(81.8)	7.0 (6.0, 10.0)	87/ 122	(71.3)	12.0 (10.0, 15.0)	1.523 (1.132, 2.050)	0.006			1.545 (1.157, 2.064)	0.003		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	36/ 46	(78.3)	11.0 (8.0, 13.0)	40/ 53	(75.5)	12.0 (9.0, 17.0)	1.058 (0.666, 1.680)	0.812		0.376	1.179 (0.750, 1.851)	0.476		0.565
No	489/ 613	(79.8)	9.0 (9.0, 10.0)	418/ 600	(69.7)	11.0 (10.0, 12.0)	1.349 (1.180, 1.543)	<.001			1.330 (1.167, 1.516)	<.001		
Baseline viral load 1														
< 10^4 copies/mL	192/ 233	(82.4)	8.0 (7.0, 10.0)	166/ 226	(73.5)	9.0 (8.0, 10.0)	1.302 (1.055, 1.606)	0.014		0.921	1.249 (1.014, 1.538)	0.036		0.712
>= 10^4 copies/mL	317/ 407	(77.9)	10.0 (9.0, 11.0)	281/ 409	(68.7)	12.0 (11.0, 14.0)	1.336 (1.135, 1.572)	<.001			1.339 (1.140, 1.573)	<.001		
Baseline viral load 2														
< 10^7 copies/mL	363/ 457	(79.4)	9.0 (8.0, 10.0)	330/ 464	(71.1)	10.0 (9.0, 11.0)	1.332 (1.146, 1.550)	<.001		0.802	1.309 (1.127, 1.521)	<.001		0.914
>= 10^7 copies/mL	146/ 183	(79.8)	11.0 (9.0, 12.0)	117/ 171	(68.4)	12.0 (10.0, 15.0)	1.306 (1.019, 1.674)	0.035			1.313 (1.029, 1.675)	0.028		
Baseline serology status														
Negative	243/ 309	(78.6)	11.0 (10.0, 12.0)	195/ 307	(63.5)	14.0 (12.0, 18.0)	1.508 (1.242, 1.830)	<.001		0.158	1.520 (1.257, 1.837)	<.001		0.110
Positive	277/ 343	(80.8)	8.0 (7.0, 9.0)	254/ 336	(75.6)	9.0 (8.0, 10.0)	1.211 (1.018, 1.439)	0.030			1.197 (1.009, 1.419)	0.039		
Symptom onset days to first dose date														
<= 3	359/ 437	(82.2)	9.0 (9.0, 10.0)	310/ 424	(73.1)	11.0 (10.0, 12.0)	1.300 (1.113, 1.519)	<.001		0.591	1.298 (1.115, 1.512)	<.001		0.641
> 3	166/ 222	(74.8)	10.0 (8.0, 12.0)	148/ 229	(64.6)	12.0 (9.0, 15.0)	1.368 (1.088, 1.720)	0.007			1.353 (1.083, 1.689)	0.008		
BMI group														
< 25	127/ 151	(84.1)	7.0 (7.0, 8.0)	110/ 141	(78.0)	10.0 (8.0, 12.0)	1.426 (1.082, 1.878)	0.012		0.973	1.341 (1.038, 1.732)	0.025		0.968
25 - < 30	169/ 216	(78.2)	9.0 (8.0, 10.0)	159/ 227	(70.0)	11.0 (9.0, 13.0)	1.317 (1.056, 1.643)	0.015			1.334 (1.073, 1.657)	0.009		
>= 30	229/ 292	(78.4)	11.0 (10.0, 12.0)	189/ 285	(66.3)	12.0 (10.0, 14.0)	1.359 (1.113, 1.661)	0.003			1.306 (1.077, 1.585)	0.007		
Ethnicity														
White	383/ 494	(77.5)	11.0 (9.0, 11.0)	330/ 493	(66.9)	12.0 (11.0, 14.0)	1.314 (1.130, 1.529)	<.001		0.652	1.322 (1.140, 1.532)	<.001		0.741
Black or African American	16/ 24	(66.7)	9.0 (5.0, 17.0)	11/ 23	(47.8)	19.0 (5.0, NE)	1.402 (0.590, 3.333)	0.444			1.566 (0.722, 3.396)	0.257		
Asian	78/ 85	(91.8)	7.0 (5.0, 8.0)	76/ 82	(92.7)	7.0 (7.0, 9.0)	1.265 (0.910, 1.757)	0.161			1.213 (0.883, 1.666)	0.233		
Others	48/ 56	(85.7)	9.5 (5.0, 12.0)	41/ 55	(74.5)	12.0 (9.0, 17.0)	1.544 (1.007, 2.368)	0.046			1.564 (1.026, 2.383)	0.038		
Number of baseline comorbidities present														
0-1	402/ 507	(79.3)		352/ 491	(71.7)									
2-3	121/ 150	(80.7)		103/ 159	(64.8)									
>= 4	2/ 2	(100.0)		3/ 3	(100.0)									
Presence of risk factor: Smoking														
Yes	243/ 298	(81.5)	9.0 (8.0, 10.0)	215/ 313	(68.7)	11.0 (10.0, 13.0)	1.528 (1.265, 1.847)	<.001		0.101	1.490 (1.239, 1.792)	<.001		0.098
No	281/ 359	(78.3)	10.0 (9.0, 11.0)	243/ 340	(71.5)	10.0 (9.0, 12.0)	1.178 (0.988, 1.405)	0.068			1.192 (1.004, 1.416)	0.045		

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Subgroup Level	Nirmatrelvir/ritonavir (N=659)			Placebo (N=653)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Presence of risk factor: Diabetes mellitus									0.444			0.227
Yes	79/	95 (83.2)	6.0 (5.0, 7.0)	67/	89 (75.3)	10.0 (8.0, 12.0)	1.485 (1.055, 2.089)	0.023		1.499 (1.080, 2.081)	0.016	
No	445/	563 (79.0)	10.0 (9.0, 11.0)	391/	564 (69.3)	11.0 (10.0, 13.0)	1.315 (1.144, 1.512)	<.001		1.289 (1.125, 1.477)	<.001	
Presence of risk factor: Immunosuppression									0.806			0.723
Yes	4/	5 (80.0)	5.0 (2.0, NE)	5/	6 (83.3)	10.5 (2.0, NE)	13.316 (0.617, 287.52)	0.099		1.092 (0.285, 4.181)	0.898	
No	520/	653 (79.6)	9.0 (9.0, 10.0)	453/	647 (70.0)	11.0 (10.0, 12.0)	1.329 (1.168, 1.513)	<.001		1.322 (1.165, 1.500)	<.001	
Presence of risk factor: Chronic lung disease									0.918			0.943
Yes	34/	47 (72.3)	10.0 (5.0, 13.0)	18/	27 (66.7)	13.0 (8.0, 24.0)	1.363 (0.746, 2.490)	0.315		1.324 (0.747, 2.346)	0.336	
No	490/	611 (80.2)	9.0 (9.0, 10.0)	440/	626 (70.3)	11.0 (10.0, 12.0)	1.330 (1.165, 1.518)	<.001		1.323 (1.163, 1.506)	<.001	
Presence of risk factor: Hypertension									0.952			0.844
Yes	178/	234 (76.1)	10.0 (9.0, 11.0)	171/	252 (67.9)	11.0 (10.0, 13.0)	1.296 (1.045, 1.608)	0.018		1.275 (1.033, 1.574)	0.024	
No	346/	424 (81.6)	9.0 (8.0, 10.0)	287/	401 (71.6)	11.0 (9.0, 12.0)	1.344 (1.144, 1.579)	<.001		1.336 (1.142, 1.564)	<.001	
Presence of risk factor: Cardiovascular disorder									0.253			0.631
Yes	24/	25 (96.0)	11.0 (5.0, 14.0)	19/	26 (73.1)	10.5 (8.0, 14.0)	1.932 (0.965, 3.867)	0.063		1.465 (0.800, 2.684)	0.217	
No	500/	633 (79.0)	9.0 (9.0, 10.0)	439/	627 (70.0)	11.0 (10.0, 12.0)	1.306 (1.145, 1.489)	<.001		1.309 (1.151, 1.488)	<.001	
Presence of risk factor: Chronic kidney disease									0.797			0.866
Yes	4/	6 (66.7)	8.0 (4.0, NE)	4/	6 (66.7)	11.0 (2.0, NE)	1.541 (0.056, 42.042)	0.798		1.358 (0.334, 5.527)	0.669	
No	520/	652 (79.8)	9.0 (9.0, 10.0)	454/	647 (70.2)	11.0 (10.0, 12.0)	1.326 (1.166, 1.509)	<.001		1.318 (1.161, 1.495)	<.001	
Presence of risk factor: HIV Infection												
Yes	0			1/	1 (100.0)							
No	524/	658 (79.6)		456/	651 (70.0)							
Presence of risk factor: Sickle Cell Disease												
No	524/	658 (79.6)		458/	653 (70.1)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	2/	2 (100.0)		0/	1 (0.0)							
No	522/	656 (79.6)		458/	652 (70.2)							
Presence of risk factor: Cancer												
Yes	1/	1 (100.0)		5/	6 (83.3)							
No	523/	657 (79.6)		453/	647 (70.0)							
Presence of risk factor: Device Dependence												
Yes	2/	3 (66.7)		1/	2 (50.0)							
No	517/	648 (79.8)		454/	645 (70.4)							

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=28)				Placebo (N=32)				Adjusted Analysis [2]				Unadjusted Analysis [3]			
	n/N	(%)	Median	(95% CI)[1]	n/N	(%)	Median	(95% CI)[1]	Hazard Ratio (95% CI)	p-Value	p-Value	Hazard Ratio (95% CI)	p-Value	p-Value		
Age																
< 65	16/	27 (59.3)			16/	30 (53.3)										
>= 65	0/	1 (0.0)			2/	2 (100.0)										
Gender											0.688			0.432		
Male	9/	15 (60.0)	13.0 (6.0, NE)		6/	10 (60.0)	13.5 (3.0, NE)		0.379 (0.096, 1.498)	0.167		0.747 (0.266, 2.101)	0.581			
Female	7/	13 (53.8)	16.5 (4.0, NE)		12/	22 (54.5)	24.0 (14.0, NE)		0.766 (0.261, 2.245)	0.627		1.275 (0.501, 3.247)	0.610			
Geographic region																
United States	8/	17 (47.1)			5/	15 (33.3)										
Europe	3/	6 (50.0)			8/	9 (88.9)										
India	0/				0/											
Rest of World	5/	5 (100.0)			5/	8 (62.5)										
COVID-19 therapeutic mAb treatment at randomisation																
Yes	0/	2 (0.0)			0/	2 (0.0)										
No	16/	26 (61.5)			18/	30 (60.0)										
Baseline viral load 1											0.163			0.175		
< 10^4 copies/mL	2/	5 (40.0)	NE (10.0, NE)		4/	5 (80.0)	7.0 (3.0, NE)		0.461 (0.058, 3.681)	0.465		0.406 (0.073, 2.255)	0.303			
>= 10^4 copies/mL	13/	22 (59.1)	16.5 (7.0, NE)		14/	26 (53.8)	24.0 (17.0, NE)		1.268 (0.546, 2.944)	0.581		1.281 (0.601, 2.731)	0.521			
Baseline viral load 2											0.326			0.862		
< 10^7 copies/mL	7/	15 (46.7)	NE (6.0, NE)		13/	22 (59.1)	21.0 (14.0, NE)		0.902 (0.321, 2.538)	0.846		0.955 (0.380, 2.398)	0.922			
>= 10^7 copies/mL	8/	12 (66.7)	15.5 (5.0, NE)		5/	9 (55.6)	14.5 (3.0, NE)		0.450 (0.106, 1.910)	0.279		1.053 (0.344, 3.224)	0.928			
Baseline serology status											0.593			0.550		
Negative	8/	18 (44.4)	NE (9.0, NE)		10/	19 (52.6)	24.0 (17.0, NE)		1.241 (0.405, 3.801)	0.705		0.972 (0.383, 2.466)	0.953			
Positive	8/	10 (80.0)	9.5 (4.0, 20.0)		8/	13 (61.5)	15.5 (3.0, NE)		1.778 (0.507, 6.240)	0.369		1.357 (0.506, 3.643)	0.544			
Symptom onset days to first dose date											0.323			0.651		
<= 3	13/	20 (65.0)	12.5 (6.0, NE)		14/	18 (77.8)	17.0 (9.0, 24.0)		0.926 (0.399, 2.151)	0.859		0.936 (0.439, 1.993)	0.864			
> 3	3/	8 (37.5)	NE (4.0, NE)		4/	14 (28.6)	NE (4.0, NE)		1.553 (0.207, 11.650)	0.669		1.398 (0.311, 6.278)	0.662			
BMI group											0.128			0.138		
< 25	2/	5 (40.0)	NE (6.0, NE)		5/	6 (83.3)	14.5 (3.0, NE)		1.229 (0.062, 24.313)	0.892		0.518 (0.100, 2.677)	0.432			
25 - < 30	3/	7 (42.9)	NE (5.0, NE)		7/	10 (70.0)	17.0 (4.0, 24.0)		0.288 (0.038, 2.185)	0.228		0.513 (0.130, 2.020)	0.340			
>= 30	11/	16 (68.8)	12.5 (5.0, NE)		6/	16 (37.5)	NE (9.0, NE)		2.072 (0.657, 6.542)	0.214		2.142 (0.788, 5.821)	0.135			
Ethnicity																
White	10/	22 (45.5)			15/	26 (57.7)										
Black or African American	2/	2 (100.0)			0/	1 (0.0)										
Asian	2/	2 (100.0)			2/	2 (100.0)										
Others	2/	2 (100.0)			1/	3 (33.3)										
Number of baseline comorbidities present																
0-1	14/	24 (58.3)			14/	26 (53.8)										
2-3	2/	4 (50.0)			4/	6 (66.7)										
>= 4	0/				0/											
Presence of risk factor: Smoking											0.981			0.377		
Yes	6/	9 (66.7)	10.0 (4.0, NE)		8/	15 (53.3)	24.0 (7.0, NE)		1.707 (0.282, 10.342)	0.561		1.639 (0.563, 4.766)	0.365			
No	10/	19 (52.6)	20.5 (9.0, NE)		10/	17 (58.8)	18.5 (9.0, NE)		1.200 (0.420, 3.427)	0.733		0.879 (0.365, 2.115)	0.773			

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum (last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Stuffy or Runny Nose - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=28)			Placebo (N=32)			Adjusted Analysis [2]			Unadjusted Analysis [3]		
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus												
Yes	1/	1 (100.0)		2/	3 (66.7)							
No	15/	27 (55.6)		16/	29 (55.2)							
Presence of risk factor: Immunosuppression												
Yes	0			0								
No	16/	28 (57.1)		18/	32 (56.3)							
Presence of risk factor: Chronic lung disease												
Yes	3/	6 (50.0)		1/	2 (50.0)							
No	13/	22 (59.1)		17/	30 (56.7)							
Presence of risk factor: Hypertension									0.364			0.062
Yes	2/	7 (28.6)	NE (4.0, NE)	7/	9 (77.8)	17.0 (3.0, NE)	0.842 (0.077, 9.170)	0.888		0.380 (0.079, 1.829)	0.227	
No	14/	21 (66.7)	12.0 (7.0, NE)	11/	23 (47.8)	24.0 (12.0, NE)	1.215 (0.483, 3.059)	0.679		1.661 (0.751, 3.673)	0.211	
Presence of risk factor: Cardiovascular disorder												
Yes	0			2/	2 (100.0)							
No	16/	28 (57.1)		16/	30 (53.3)							
Presence of risk factor: Chronic kidney disease												
Yes	0			0								
No	16/	28 (57.1)		18/	32 (56.3)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	16/	28 (57.1)		18/	32 (56.3)							
Presence of risk factor: Sickle Cell Disease												
No	16/	28 (57.1)		18/	32 (56.3)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0			0								
No	16/	28 (57.1)		18/	32 (56.3)							
Presence of risk factor: Cancer												
Yes	0			0								
No	16/	28 (57.1)		18/	32 (56.3)							
Presence of risk factor: Device Dependence												
Yes	0/	1 (0.0)		0								
No	15/	26 (57.7)		18/	32 (56.3)							

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final

Overall Study population
RKI-conform mITT2 Analysis set

Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Sore Throat - Subgroup analysis

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]		Interaction p-Value	Unadjusted analysis [2]		Interaction p-Value
			Relative Risk (95% CI)	p-Value		Relative Risk (95% CI)	p-Value	
Age								
< 65	175/ 790 (22.2)	193/ 810 (23.8)	0.921 (0.768, 1.104)	0.372	0.650	0.930 (0.777, 1.113)	0.426	0.719
>= 65	25/ 138 (18.1)	31/ 145 (21.4)	0.825 (0.515, 1.324)	0.425		0.847 (0.528, 1.359)	0.492	
Gender								
Male	84/ 463 (18.1)	109/ 507 (21.5)	0.832 (0.643, 1.077)	0.163	0.379	0.844 (0.654, 1.089)	0.192	0.414
Female	116/ 465 (24.9)	115/ 448 (25.7)	0.965 (0.769, 1.210)	0.756		0.972 (0.778, 1.214)	0.802	
Geographic region								
United States	96/ 375 (25.6)	98/ 387 (25.3)	1.034 (0.807, 1.323)	0.793	0.167	1.011 (0.793, 1.289)	0.930	0.222
Europe	67/ 322 (20.8)	78/ 321 (24.3)	0.822 (0.612, 1.104)	0.193		0.856 (0.642, 1.142)	0.290	
India	7/ 74 (9.5)	3/ 78 (3.8)	NE (NE, NE)	NE		2.459 (0.661, 9.157)	0.180	
Rest of World	30/ 157 (19.1)	45/ 169 (26.6)	0.729 (0.486, 1.095)	0.128		0.718 (0.477, 1.079)	0.111	
COVID-19 therapeutic mAb treatment at randomisation								
Yes	15/ 57 (26.3)	16/ 60 (26.7)	0.957 (0.527, 1.739)	0.886	0.856	0.987 (0.539, 1.805)	0.966	0.811
No	185/ 871 (21.2)	208/ 895 (23.2)	0.903 (0.757, 1.077)	0.256		0.914 (0.767, 1.088)	0.313	
Baseline viral load 1								
< 10^4 copies/mL	78/ 335 (23.3)	83/ 354 (23.4)	1.000 (0.765, 1.307)	0.998	0.386	0.993 (0.758, 1.302)	0.960	0.401
>= 10^4 copies/mL	116/ 569 (20.4)	137/ 575 (23.8)	0.854 (0.686, 1.062)	0.156		0.856 (0.688, 1.065)	0.162	
Baseline viral load 2								
< 10^7 copies/mL	132/ 652 (20.2)	152/ 699 (21.7)	0.938 (0.763, 1.152)	0.542	0.543	0.931 (0.757, 1.146)	0.499	0.541
>= 10^7 copies/mL	62/ 252 (24.6)	68/ 230 (29.6)	0.847 (0.631, 1.138)	0.272		0.832 (0.620, 1.117)	0.221	
Baseline serology status								
Negative	97/ 435 (22.3)	113/ 456 (24.8)	0.882 (0.695, 1.120)	0.303	0.799	0.900 (0.710, 1.141)	0.384	0.822
Positive	100/ 482 (20.7)	108/ 487 (22.2)	0.937 (0.736, 1.191)	0.593		0.936 (0.735, 1.191)	0.588	
Symptom onset days to first dose date								
<= 3	140/ 624 (22.4)	150/ 624 (24.0)	0.909 (0.741, 1.115)	0.358	0.917	0.933 (0.763, 1.142)	0.503	0.764
> 3	60/ 304 (19.7)	74/ 331 (22.4)	0.897 (0.663, 1.214)	0.482		0.883 (0.652, 1.195)	0.420	
BMI group								
< 25	42/ 215 (19.5)	40/ 213 (18.8)	1.033 (0.696, 1.534)	0.871	0.711	1.040 (0.705, 1.535)	0.843	0.774
25 - < 30	73/ 319 (22.9)	86/ 332 (25.9)	0.878 (0.668, 1.153)	0.349		0.883 (0.673, 1.159)	0.371	
>= 30	84/ 393 (21.4)	98/ 410 (23.9)	0.861 (0.661, 1.120)	0.264		0.894 (0.692, 1.156)	0.393	
Ethnicity								
White	161/ 699 (23.0)	185/ 718 (25.8)	0.890 (0.739, 1.072)	0.221	0.387	0.894 (0.744, 1.074)	0.232	0.668
Black or African American	12/ 43 (27.9)	8/ 40 (20.0)	NE (NE, NE)	NE		1.395 (0.637, 3.057)	0.405	
Asian	12/ 117 (10.3)	12/ 127 (9.4)	NE (NE, NE)	NE		1.085 (0.508, 2.320)	0.832	
Others	15/ 69 (21.7)	19/ 70 (27.1)	NE (NE, NE)	NE		0.801 (0.444, 1.444)	0.461	
Number of baseline comorbidities present								
0-1	158/ 710 (22.3)	170/ 728 (23.4)	0.930 (0.768, 1.127)	0.461	0.310	0.953 (0.788, 1.153)	0.620	0.576
2-3	42/ 214 (19.6)	52/ 221 (23.5)	0.862 (0.598, 1.244)	0.428		0.834 (0.582, 1.196)	0.324	
>= 4	0/ 4 (0.0)	2/ 6 (33.3)	NE (NE, NE)	NE		0.280 (0.017, 4.656)	0.375	
Presence of risk factor: Smoking								
Yes	87/ 417 (20.9)	101/ 438 (23.1)	0.913 (0.709, 1.175)	0.479	0.905	0.905 (0.702, 1.166)	0.439	0.858
No	113/ 509 (22.2)	123/ 517 (23.8)	0.894 (0.713, 1.121)	0.332		0.933 (0.746, 1.168)	0.545	
Presence of risk factor: Diabetes mellitus					0.380			0.347

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value	
Yes	26/ 130 (20.0)	36/ 136 (26.5)	0.713 (0.458, 1.110)			0.134		0.756 (0.485, 1.177)			0.215	
No	174/ 797 (21.8)	188/ 819 (23.0)	0.937 (0.780, 1.125)			0.485		0.951 (0.793, 1.141)			0.588	
Presence of risk factor: Immunosuppression							0.253					0.372
Yes	3/ 6 (50.0)	2/ 7 (28.6)	NE (NE, NE)			NE		1.750 (0.424, 7.229)			0.439	
No	197/ 921 (21.4)	222/ 948 (23.4)	0.901 (0.760, 1.069)			0.232		0.913 (0.771, 1.082)			0.294	
Presence of risk factor: Chronic lung disease							0.352					0.269
Yes	19/ 62 (30.6)	9/ 39 (23.1)	1.366 (0.689, 2.710)			0.372		1.328 (0.670, 2.633)			0.417	
No	181/ 865 (20.9)	215/ 916 (23.5)	0.880 (0.738, 1.050)			0.157		0.891 (0.749, 1.061)			0.197	
Presence of risk factor: Hypertension							0.203					0.343
Yes	69/ 348 (19.8)	89/ 371 (24.0)	0.793 (0.598, 1.053)			0.109		0.827 (0.626, 1.092)			0.180	
No	131/ 579 (22.6)	135/ 584 (23.1)	0.986 (0.797, 1.218)			0.894		0.979 (0.792, 1.209)			0.842	
Presence of risk factor: Cardiovascular disorder							0.215					0.360
Yes	5/ 42 (11.9)	10/ 49 (20.4)	NE (NE, NE)			NE		0.583 (0.216, 1.572)			0.287	
No	195/ 885 (22.0)	214/ 906 (23.6)	0.925 (0.779, 1.099)			0.375		0.933 (0.787, 1.106)			0.424	
Presence of risk factor: Chronic kidney disease							0.267					0.296
Yes	1/ 6 (16.7)	4/ 8 (50.0)	NE (NE, NE)			NE		0.333 (0.049, 2.271)			0.262	
No	199/ 921 (21.6)	220/ 947 (23.2)	0.915 (0.772, 1.085)			0.309		0.930 (0.786, 1.101)			0.400	
Presence of risk factor: HIV Infection												
Yes	0	0/ 1 (0.0)										
No	200/ 927 (21.6)	224/ 953 (23.5)										
Presence of risk factor: Sickie Cell Disease												
No	200/ 927 (21.6)	224/ 955 (23.5)										
Presence of risk factor: Neurodevelopmental Disorder												
Yes	1/ 2 (50.0)	0/ 1 (0.0)										
No	199/ 925 (21.5)	224/ 954 (23.5)										
Presence of risk factor: Cancer							0.152					0.383
Yes	1/ 5 (20.0)	0/ 6 (0.0)	NE (NE, NE)			NE		3.500 (0.173, 70.944)			0.415	
No	199/ 922 (21.6)	224/ 949 (23.6)	0.902 (0.761, 1.068)			0.232		0.914 (0.773, 1.082)			0.297	
Presence of risk factor: Device Dependence												
Yes	1/ 4 (25.0)	3/ 3 (100.0)										
No	198/ 914 (21.7)	218/ 944 (23.1)										

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

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[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

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Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Sore Throat - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=514)			Placebo (N=538)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	389/ 449	(86.6)	5.0 (4.0, 6.0)	363/ 461	(78.7)	6.0 (5.0, 7.0)	1.329 (1.147, 1.540)	<.001		0.248	1.310 (1.134, 1.513)	<.001		0.152
>= 65	63/ 65	(96.9)	3.0 (2.0, 4.0)	64/ 77	(83.1)	4.0 (3.0, 7.0)	1.660 (1.150, 2.398)	0.007			1.651 (1.156, 2.357)	0.006		
Gender														
Male	220/ 252	(87.3)	4.0 (4.0, 5.0)	205/ 261	(78.5)	6.0 (5.0, 8.0)	1.426 (1.171, 1.737)	<.001		0.462	1.401 (1.156, 1.698)	<.001		0.459
Female	232/ 262	(88.5)	5.0 (4.0, 6.0)	222/ 277	(80.1)	6.0 (5.0, 7.0)	1.307 (1.082, 1.580)	0.006			1.288 (1.070, 1.549)	0.007		
Geographic region														
United States	168/ 210	(80.0)	5.0 (4.0, 6.0)	177/ 229	(77.3)	6.0 (5.0, 8.0)	1.147 (0.924, 1.424)	0.214		0.229	1.153 (0.933, 1.425)	0.186		0.223
Europe	150/ 157	(95.5)	4.0 (4.0, 5.0)	135/ 166	(81.3)	5.0 (4.0, 7.0)	1.530 (1.198, 1.953)	<.001			1.488 (1.174, 1.884)	<.001		
India	43/ 46	(93.5)	6.0 (5.0, 7.0)	35/ 38	(92.1)	8.0 (6.0, 10.0)	1.380 (0.861, 2.213)	0.181			1.305 (0.831, 2.049)	0.247		
Rest of World	91/ 101	(90.1)	4.0 (3.0, 5.0)	80/ 105	(76.2)	6.0 (4.0, 9.0)	1.551 (1.135, 2.119)	0.006			1.578 (1.163, 2.141)	0.003		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	27/ 32	(84.4)	3.0 (2.0, 7.0)	36/ 42	(85.7)	6.0 (5.0, 9.0)	1.343 (0.790, 2.284)	0.276		0.852	1.254 (0.760, 2.071)	0.376		0.811
No	425/ 482	(88.2)	5.0 (4.0, 5.0)	391/ 496	(78.8)	6.0 (5.0, 7.0)	1.364 (1.184, 1.572)	<.001			1.350 (1.176, 1.551)	<.001		
Baseline viral load 1														
< 10^4 copies/mL	154/ 177	(87.0)	5.0 (4.0, 6.0)	154/ 192	(80.2)	6.0 (4.0, 7.0)	1.257 (1.001, 1.580)	0.049		0.404	1.253 (1.001, 1.570)	0.049		0.423
>= 10^4 copies/mL	281/ 319	(88.1)	4.0 (4.0, 5.0)	264/ 334	(79.0)	6.0 (5.0, 7.0)	1.393 (1.174, 1.653)	<.001			1.392 (1.175, 1.648)	<.001		
Baseline viral load 2														
< 10^7 copies/mL	292/ 344	(84.9)	5.0 (4.0, 6.0)	307/ 389	(78.9)	6.0 (5.0, 7.0)	1.239 (1.054, 1.457)	0.009		0.078	1.233 (1.050, 1.448)	0.011		0.084
>= 10^7 copies/mL	143/ 152	(94.1)	4.0 (3.0, 5.0)	111/ 137	(81.0)	6.0 (5.0, 8.0)	1.675 (1.288, 2.177)	<.001			1.652 (1.283, 2.127)	<.001		
Baseline serology status														
Negative	209/ 235	(88.9)	4.0 (4.0, 5.0)	200/ 257	(77.8)	6.0 (5.0, 7.0)	1.400 (1.147, 1.709)	<.001		0.671	1.391 (1.144, 1.692)	<.001		0.622
Positive	238/ 274	(86.9)	5.0 (4.0, 6.0)	224/ 277	(80.9)	6.0 (5.0, 7.0)	1.345 (1.115, 1.622)	0.002			1.317 (1.096, 1.582)	0.003		
Symptom onset days to first dose date														
<= 3	312/ 342	(91.2)	5.0 (4.0, 5.0)	281/ 338	(83.1)	6.0 (5.0, 7.0)	1.405 (1.189, 1.660)	<.001		0.546	1.378 (1.170, 1.621)	<.001		0.639
> 3	140/ 172	(81.4)	5.0 (4.0, 6.0)	146/ 200	(73.0)	7.0 (6.0, 9.0)	1.251 (0.984, 1.589)	0.067			1.269 (1.005, 1.601)	0.045		
BMI group														
< 25	106/ 121	(87.6)	4.0 (3.0, 6.0)	93/ 107	(86.9)	5.0 (4.0, 7.0)	1.187 (0.886, 1.590)	0.252		0.679	1.238 (0.935, 1.638)	0.136		0.809
25 - < 30	149/ 171	(87.1)	5.0 (4.0, 6.0)	150/ 189	(79.4)	7.0 (5.0, 8.0)	1.411 (1.116, 1.784)	0.004			1.377 (1.095, 1.731)	0.006		
>= 30	197/ 222	(88.7)	5.0 (4.0, 6.0)	184/ 242	(76.0)	6.0 (5.0, 8.0)	1.400 (1.136, 1.726)	0.002			1.362 (1.112, 1.668)	0.003		
Ethnicity														
White	332/ 378	(87.8)	4.0 (4.0, 5.0)	321/ 405	(79.3)	6.0 (5.0, 7.0)	1.347 (1.150, 1.577)	<.001		0.330	1.331 (1.141, 1.554)	<.001		0.366
Black or African American	12/ 17	(70.6)	7.0 (3.0, 11.0)	15/ 21	(71.4)	7.0 (3.0, 23.0)	0.851 (0.351, 2.063)	0.720			1.112 (0.519, 2.381)	0.785		
Asian	68/ 75	(90.7)	6.0 (4.0, 7.0)	63/ 69	(91.3)	6.0 (5.0, 8.0)	1.157 (0.805, 1.663)	0.432			1.167 (0.827, 1.647)	0.380		
Others	40/ 44	(90.9)	4.0 (3.0, 5.0)	28/ 43	(65.1)	8.0 (5.0, 16.0)	1.963 (1.178, 3.272)	0.010			1.908 (1.167, 3.120)	0.010		
Number of baseline comorbidities present														
0-1	349/ 397	(87.9)		317/ 399	(79.4)									
2-3	101/ 115	(87.8)		108/ 137	(78.8)									
>= 4	2/ 2	(100.0)		2/ 2	(100.0)									
Presence of risk factor: Smoking														
Yes	190/ 218	(87.2)	5.0 (4.0, 6.0)	177/ 230	(77.0)	6.0 (5.0, 8.0)	1.423 (1.149, 1.762)	0.001		0.511	1.391 (1.131, 1.712)	0.002		0.500
No	260/ 294	(88.4)	5.0 (4.0, 6.0)	250/ 308	(81.2)	6.0 (5.0, 7.0)	1.292 (1.082, 1.543)	0.005			1.293 (1.087, 1.540)	0.004		

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=514)			Placebo (N=538)			Adjusted Analysis [2]			Interaction		Unadjusted Analysis [3]			Interaction	
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	p-Value			Hazard Ratio (95% CI)	p-Value	p-Value		
Presence of risk factor: Diabetes mellitus										0.910					0.997	
Yes	65/	76 (85.5)	4.0 (3.0, 6.0)	67/	81 (82.7)	7.0 (5.0, 9.0)	1.403 (0.986, 1.998)	0.060				1.330 (0.943, 1.877)	0.104			
No	386/	437 (88.3)	5.0 (4.0, 5.0)	360/	457 (78.8)	6.0 (5.0, 7.0)	1.359 (1.172, 1.576)	<.001				1.341 (1.160, 1.550)	<.001			
Presence of risk factor: Immunosuppression																
Yes	4/	4 (100.0)		3/	3 (100.0)											
No	447/	509 (87.8)		424/	535 (79.3)											
Presence of risk factor: Chronic lung disease										0.311					0.216	
Yes	29/	34 (85.3)	6.0 (3.0, 7.0)	20/	22 (90.9)	6.0 (4.0, 9.0)	0.886 (0.479, 1.639)	0.700				0.936 (0.528, 1.660)	0.822			
No	422/	479 (88.1)	5.0 (4.0, 5.0)	407/	516 (78.9)	6.0 (5.0, 7.0)	1.381 (1.200, 1.589)	<.001				1.368 (1.193, 1.570)	<.001			
Presence of risk factor: Hypertension										0.366					0.538	
Yes	168/	192 (87.5)	4.0 (4.0, 5.0)	168/	217 (77.4)	6.0 (4.0, 8.0)	1.426 (1.143, 1.780)	0.002				1.380 (1.112, 1.712)	0.003			
No	283/	321 (88.2)	5.0 (4.0, 6.0)	259/	321 (80.7)	6.0 (5.0, 7.0)	1.303 (1.095, 1.551)	0.003				1.313 (1.108, 1.555)	0.002			
Presence of risk factor: Cardiovascular disorder										0.488					0.459	
Yes	20/	20 (100.0)	3.0 (2.0, 7.0)	21/	25 (84.0)	6.0 (3.0, 8.0)	1.539 (0.756, 3.133)	0.235				1.678 (0.897, 3.139)	0.105			
No	431/	493 (87.4)	5.0 (4.0, 5.0)	406/	513 (79.1)	6.0 (5.0, 7.0)	1.342 (1.167, 1.543)	<.001				1.329 (1.160, 1.524)	<.001			
Presence of risk factor: Chronic kidney disease										0.229					0.201	
Yes	5/	5 (100.0)	4.0 (2.0, 12.0)	4/	6 (66.7)	16.0 (2.0, NE)	6.398 (0.844, 48.470)	0.072				3.504 (0.797, 15.416)	0.097			
No	446/	508 (87.8)	5.0 (4.0, 5.0)	423/	532 (79.5)	6.0 (5.0, 7.0)	1.345 (1.173, 1.542)	<.001				1.327 (1.161, 1.518)	<.001			
Presence of risk factor: HIV Infection																
Yes	0			1/	1 (100.0)											
No	451/	513 (87.9)		425/	536 (79.3)											
Presence of risk factor: Sickel Cell Disease																
No	451/	513 (87.9)		427/	538 (79.4)											
Presence of risk factor: Neurodevelopmental Disorder																
Yes	1/	1 (100.0)		1/	1 (100.0)											
No	450/	512 (87.9)		426/	537 (79.3)											
Presence of risk factor: Cancer																
Yes	1/	1 (100.0)		3/	3 (100.0)											
No	450/	512 (87.9)		424/	535 (79.3)											
Presence of risk factor: Device Dependence																
Yes	0/	1 (0.0)		1/	1 (100.0)											
No	446/	506 (88.1)		424/	533 (79.5)											

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=26)			Placebo (N=26)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Age												
< 65	20/	24 (83.3)		18/	25 (72.0)							
>= 65	1/	2 (50.0)		1/	1 (100.0)							
Gender									0.235			0.905
Male	9/	12 (75.0)	4.0 (2.0, NE)	7/	12 (58.3)	9.0 (6.0, NE)	0.648 (0.102, 4.111)	0.646		1.759 (0.649, 4.768)	0.267	
Female	12/	14 (85.7)	3.0 (2.0, 14.0)	12/	14 (85.7)	6.0 (3.0, 17.0)	1.966 (0.605, 6.382)	0.261		1.750 (0.766, 3.994)	0.184	
Geographic region												
United States	9/	13 (69.2)		8/	12 (66.7)							
Europe	3/	3 (100.0)		6/	8 (75.0)							
India	0			0								
Rest of World	9/	10 (90.0)		5/	6 (83.3)							
COVID-19 therapeutic mAb treatment at randomisation												
Yes	2/	3 (66.7)		0/	1 (0.0)							
No	19/	23 (82.6)		19/	25 (76.0)							
Baseline viral load 1									0.548			0.655
< 10^4 copies/mL	5/	7 (71.4)	11.0 (2.0, NE)	4/	5 (80.0)	23.0 (3.0, 23.0)	0.540 (0.100, 2.920)	0.474		1.349 (0.354, 5.143)	0.661	
>= 10^4 copies/mL	16/	19 (84.2)	3.5 (2.0, 6.0)	15/	21 (71.4)	7.0 (5.0, 16.0)	2.125 (0.903, 4.999)	0.084		1.806 (0.886, 3.680)	0.104	
Baseline viral load 2									0.474			0.990
< 10^7 copies/mL	11/	15 (73.3)	4.5 (2.0, 22.0)	12/	18 (66.7)	16.0 (6.0, 23.0)	1.855 (0.682, 5.042)	0.226		1.456 (0.640, 3.312)	0.371	
>= 10^7 copies/mL	10/	11 (90.9)	2.5 (2.0, 6.0)	7/	8 (87.5)	5.0 (2.0, 9.0)	0.828 (0.156, 4.404)	0.825		1.407 (0.518, 3.820)	0.503	
Baseline serology status									0.873			0.899
Negative	9/	13 (69.2)	4.0 (2.0, 14.0)	13/	18 (72.2)	7.0 (4.0, 23.0)	1.741 (0.611, 4.962)	0.299		1.533 (0.652, 3.604)	0.327	
Positive	12/	13 (92.3)	4.0 (2.0, 8.0)	6/	8 (75.0)	9.0 (2.0, 23.0)	1.300 (0.405, 4.174)	0.659		1.563 (0.577, 4.237)	0.380	
Symptom onset days to first dose date									0.197			0.152
<= 3	20/	21 (95.2)	4.0 (2.0, 5.0)	14/	16 (87.5)	8.5 (3.0, 16.0)	2.346 (1.035, 5.322)	0.041		1.895 (0.942, 3.814)	0.073	
> 3	1/	5 (20.0)	NE (18.0, NE)	5/	10 (50.0)	23.0 (2.0, NE)	0.829 (0.051, 13.490)	0.895		0.358 (0.041, 3.135)	0.353	
BMI group												
< 25	3/	5 (60.0)		2/	3 (66.7)							
25 - < 30	6/	7 (85.7)		8/	11 (72.7)							
>= 30	12/	14 (85.7)		9/	12 (75.0)							
Ethnicity												
White	13/	17 (76.5)		14/	20 (70.0)							
Black or African American	2/	2 (100.0)		3/	3 (100.0)							
Asian	3/	3 (100.0)		1/	1 (100.0)							
Others	3/	4 (75.0)		1/	2 (50.0)							
Number of baseline comorbidities present												
0-1	19/	23 (82.6)		13/	20 (65.0)							
2-3	2/	3 (66.7)		6/	6 (100.0)							
>= 4	0			0								
Presence of risk factor: Smoking									0.475			0.431
Yes	9/	10 (90.0)	4.0 (2.0, 4.0)	6/	10 (60.0)	9.0 (2.0, NE)	0.895 (0.220, 3.634)	0.877		1.821 (0.638, 5.194)	0.262	
No	11/	15 (73.3)	6.0 (2.0, 14.0)	13/	16 (81.3)	8.0 (5.0, 23.0)	1.512 (0.580, 3.941)	0.397		1.245 (0.557, 2.786)	0.593	

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Subgroup Level	Nirmatrelvir/ritonavir (N=26)			Placebo (N=26)			Adjusted Analysis [2]			Unadjusted Analysis [3]				
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)		p-Value	Interaction p-Value	Hazard Ratio (95% CI)		p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus														
Yes	1/	2 (50.0)		3/	3 (100.0)									
No	19/	23 (82.6)		16/	23 (69.6)									
Presence of risk factor: Immunosuppression														
Yes	0			0										
No	20/	25 (80.0)		19/	26 (73.1)									
Presence of risk factor: Chronic lung disease														
Yes	0			1/	1 (100.0)									
No	20/	25 (80.0)		18/	25 (72.0)									
Presence of risk factor: Hypertension										0.923				0.337
Yes	6/	9 (66.7)	4.5 (2.0, NE)	8/	9 (88.9)	8.0 (2.0, 23.0)	1.960 (0.420, 9.146)	0.392			0.928 (0.319, 2.700)	0.891		
No	14/	16 (87.5)	4.0 (2.0, 6.0)	11/	17 (64.7)	9.0 (3.0, 23.0)	1.484 (0.562, 3.916)	0.425			1.949 (0.875, 4.343)	0.103		
Presence of risk factor: Cardiovascular disorder														
Yes	1/	1 (100.0)		3/	3 (100.0)									
No	19/	24 (79.2)		16/	23 (69.6)									
Presence of risk factor: Chronic kidney disease														
Yes	0			0										
No	20/	25 (80.0)		19/	26 (73.1)									
Presence of risk factor: HIV Infection														
Yes	0			0										
No	20/	25 (80.0)		19/	26 (73.1)									
Presence of risk factor: Sickle Cell Disease														
No	20/	25 (80.0)		19/	26 (73.1)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	0			0										
No	20/	25 (80.0)		19/	26 (73.1)									
Presence of risk factor: Cancer														
Yes	0			0										
No	20/	25 (80.0)		19/	26 (73.1)									
Presence of risk factor: Device Dependence														
Yes	0/	1 (0.0)		0										
No	20/	23 (87.0)		19/	26 (73.1)									

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	n/N	(%)	Median	(95% CI)	[1]		n/N	(%)	Median	(95% CI)	[1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value					
Age																						
< 65	365/ 58	449/ 65	(81.3)	(89.2)	7.0	(7.0, 8.0)	(4.0, 7.0)	5.0	(4.0, 7.0)	336/ 60	461/ 77	(72.9)	(77.9)	9.0	(8.0, 11.0)	(7.0, 12.0)	1.304 (1.120, 1.518)	<.001	0.337	1.307 (1.126, 1.517)	<.001	0.281
>= 65																	1.631 (1.121, 2.374)	0.011		1.561 (1.085, 2.245)	0.016	
Gender																						
Male	211/ 212	252/ 262	(83.7)	(80.9)	7.0	(6.0, 7.0)	(6.0, 9.0)	8.0	(6.0, 9.0)	195/ 201	261/ 277	(74.7)	(72.6)	9.0	(7.0, 10.0)	(8.0, 12.0)	1.352 (1.106, 1.652)	0.003	0.768	1.377 (1.132, 1.676)	0.001	0.594
Female																	1.308 (1.074, 1.593)	0.008		1.294 (1.066, 1.570)	0.009	
Geographic region																						
United States	163/ 135	210/ 157	(77.6)	(86.0)	8.0	(6.0, 11.0)	(7.0, 8.0)	8.0	(6.0, 8.0)	164/ 122	229/ 166	(71.6)	(73.5)	9.0	(8.0, 11.0)	(7.0, 12.0)	1.186 (0.949, 1.481)	0.133	0.701	1.221 (0.983, 1.518)	0.072	0.754
Europe																	1.429 (1.111, 1.839)	0.006		1.407 (1.099, 1.799)	0.007	
India	43/ 82	46/ 101	(93.5)	(81.2)	7.0	(5.0, 8.0)	(5.0, 8.0)	7.0	(5.0, 8.0)	35/ 75	38/ 105	(92.1)	(71.4)	9.0	(7.0, 11.0)	(6.0, 15.0)	1.381 (0.857, 2.225)	0.184		1.364 (0.868, 2.144)	0.178	
Rest of World																	1.398 (1.010, 1.935)	0.043		1.427 (1.041, 1.955)	0.027	
COVID-19 therapeutic mAb treatment at randomisation																						
Yes	27/ 396	32/ 482	(84.4)	(82.2)	8.5	(4.0, 11.0)	(6.0, 8.0)	7.0	(6.0, 8.0)	36/ 360	42/ 496	(85.7)	(72.6)	7.0	(6.0, 9.0)	(8.0, 11.0)	0.930 (0.551, 1.569)	0.786	0.213	0.968 (0.587, 1.596)	0.898	0.219
No																	1.363 (1.178, 1.578)	<.001		1.369 (1.186, 1.580)	<.001	
Baseline viral load 1																						
< 10^4 copies/mL	146/ 262	177/ 319	(82.5)	(82.1)	7.0	(6.0, 9.0)	(6.0, 8.0)	7.0	(6.0, 8.0)	141/ 248	192/ 334	(73.4)	(74.3)	8.0	(7.0, 10.0)	(8.0, 12.0)	1.244 (0.982, 1.575)	0.070	0.656	1.282 (1.017, 1.618)	0.036	0.766
>= 10^4 copies/mL																	1.343 (1.126, 1.601)	0.001		1.345 (1.130, 1.602)	<.001	
Baseline viral load 2																						
< 10^7 copies/mL	275/ 133	344/ 152	(79.9)	(87.5)	7.0	(6.0, 8.0)	(6.0, 8.0)	7.0	(6.0, 8.0)	284/ 105	389/ 137	(73.0)	(76.6)	9.0	(8.0, 11.0)	(7.0, 12.0)	1.275 (1.078, 1.507)	0.004	0.512	1.268 (1.074, 1.498)	0.005	0.467
>= 10^7 copies/mL																	1.408 (1.079, 1.837)	0.012		1.447 (1.119, 1.872)	0.005	
Baseline serology status																						
Negative	198/ 222	235/ 274	(84.3)	(81.0)	7.0	(6.0, 8.0)	(6.0, 8.0)	7.0	(6.0, 8.0)	184/ 209	257/ 277	(71.6)	(75.5)	10.0	(8.0, 13.0)	(8.0, 10.0)	1.474 (1.200, 1.810)	<.001	0.219	1.494 (1.220, 1.829)	<.001	0.187
Positive																	1.229 (1.013, 1.490)	0.036		1.241 (1.027, 1.500)	0.025	
Symptom onset days to first dose date																						
<= 3	291/ 132	342/ 172	(85.1)	(76.7)	7.0	(6.0, 8.0)	(6.0, 11.0)	7.0	(6.0, 11.0)	260/ 136	338/ 200	(76.9)	(68.0)	9.0	(8.0, 10.0)	(8.0, 14.0)	1.349 (1.137, 1.601)	<.001	0.697	1.353 (1.144, 1.601)	<.001	0.747
> 3																	1.257 (0.981, 1.611)	0.071		1.289 (1.014, 1.639)	0.038	
BMI group																						
< 25	97/ 139	121/ 171	(80.2)	(81.3)	6.0	(5.0, 8.0)	(5.0, 9.0)	6.0	(5.0, 9.0)	88/ 140	107/ 189	(82.2)	(74.1)	9.5	(7.0, 12.0)	(8.0, 11.0)	1.198 (0.879, 1.631)	0.253	0.605	1.259 (0.942, 1.684)	0.119	0.772
25 - < 30																	1.346 (1.058, 1.712)	0.016		1.307 (1.033, 1.654)	0.026	
>= 30	187/ 187	222/ 222	(84.2)		7.0	(6.0, 9.0)		7.0		168/ 168	242/ 242	(69.4)		9.0	(8.0, 12.0)		1.416 (1.141, 1.756)	0.002		1.402 (1.137, 1.728)	0.002	
Ethnicity																						
White	307/ 12	378/ 17	(81.2)	(70.6)	7.0	(6.0, 8.0)	(6.0, 15.0)	11.0	(6.0, 15.0)	294/ 13	405/ 21	(72.6)	(61.9)	9.0	(8.0, 11.0)	(11.0, 6.0)	1.318 (1.119, 1.552)	<.001	0.743	1.323 (1.126, 1.553)	<.001	0.817
Black or African American																	0.764 (0.283, 2.065)	0.596		1.278 (0.578, 2.824)	0.544	
Asian	67/ 37	75/ 75	(89.3)		7.0	(5.0, 8.0)		7.0		62/ 62	69/ 69	(89.9)		7.0	(6.0, 9.0)		1.159 (0.803, 1.674)	0.430		1.235 (0.872, 1.749)	0.234	
Others	37/ 37	44/ 44	(84.1)		8.0	(5.0, 12.0)		8.0		27/ 27	43/ 43	(62.8)		12.0	(6.0, 24.0)		1.620 (0.966, 2.716)	0.068		1.643 (0.996, 2.710)	0.052	
Number of baseline comorbidities present																						
0-1	327/ 94	397/ 115	(82.4)	(81.7)						303/ 91	399/ 137	(75.9)	(66.4)									
2-3																						
>= 4	2/ 2									2/ 2												
Presence of risk factor: Smoking																						
Yes	179/ 243	218/ 294	(82.1)	(82.7)	7.0	(6.0, 8.0)	(6.0, 9.0)	7.0	(6.0, 9.0)	160/ 236	230/ 308	(69.6)	(76.6)	10.0	(8.0, 13.0)	(8.0, 10.0)	1.535 (1.227, 1.922)	<.001	0.129	1.534 (1.236, 1.903)	<.001	0.084
No																	1.211 (1.009, 1.452)	0.040		1.208 (1.010, 1.445)	0.039	

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=514)			Placebo (N=538)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus										0.247				0.372
Yes	59/	76 (77.6)	7.0 (5.0, 11.0)	62/	81 (76.5)	9.0 (7.0, 11.0)	1.182 (0.818, 1.708)	0.375			1.142 (0.799, 1.632)	0.468		
No	363/ 437	(83.1)	7.0 (6.0, 8.0)	334/ 457	(73.1)	9.0 (8.0, 11.0)	1.380 (1.184, 1.608)	<.001			1.371 (1.180, 1.591)	<.001		
Presence of risk factor: Immunosuppression														
Yes	4/	4 (100.0)		3/	3 (100.0)									
No	418/ 509	(82.1)		393/ 535	(73.5)									
Presence of risk factor: Chronic lung disease										0.365				0.283
Yes	27/	34 (79.4)	9.5 (6.0, 13.0)	18/	22 (81.8)	9.0 (5.0, 15.0)	0.955 (0.507, 1.800)	0.887			0.963 (0.530, 1.750)	0.902		
No	395/ 479	(82.5)	7.0 (6.0, 8.0)	378/ 516	(73.3)	9.0 (8.0, 11.0)	1.348 (1.167, 1.558)	<.001			1.359 (1.179, 1.566)	<.001		
Presence of risk factor: Hypertension										0.321				0.485
Yes	152/	192 (79.2)	8.0 (6.0, 10.0)	149/	217 (68.7)	10.0 (8.0, 14.0)	1.399 (1.113, 1.760)	0.004			1.388 (1.106, 1.741)	0.005		
No	270/ 321	(84.1)	7.0 (6.0, 8.0)	247/ 321	(76.9)	9.0 (7.0, 10.0)	1.253 (1.048, 1.498)	0.013			1.291 (1.086, 1.536)	0.004		
Presence of risk factor: Cardiovascular disorder										0.720				0.699
Yes	20/	20 (100.0)	4.5 (2.0, 13.0)	20/	25 (80.0)	6.0 (5.0, 10.0)	1.281 (0.638, 2.573)	0.487			1.502 (0.800, 2.822)	0.206		
No	402/ 493	(81.5)	7.0 (6.0, 8.0)	376/ 513	(73.3)	9.0 (8.0, 11.0)	1.321 (1.144, 1.525)	<.001			1.328 (1.153, 1.530)	<.001		
Presence of risk factor: Chronic kidney disease										0.206				0.208
Yes	5/	5 (100.0)	4.0 (2.0, 12.0)	4/	6 (66.7)	16.0 (5.0, NE)	16.031 (1.222, 210.38)	0.035			3.354 (0.788, 14.269)	0.101		
No	417/ 508	(82.1)	7.0 (6.0, 8.0)	392/ 532	(73.7)	9.0 (8.0, 11.0)	1.313 (1.140, 1.511)	<.001			1.320 (1.149, 1.516)	<.001		
Presence of risk factor: HIV Infection														
Yes	0			1/	1 (100.0)									
No	422/ 513	(82.3)		394/ 536	(73.5)									
Presence of risk factor: Sickel Cell Disease														
No	422/ 513	(82.3)		396/ 538	(73.6)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	1/	1 (100.0)		0/	1 (0.0)									
No	421/ 512	(82.2)		396/ 537	(73.7)									
Presence of risk factor: Cancer														
Yes	1/	1 (100.0)		3/	3 (100.0)									
No	421/ 512	(82.2)		393/ 535	(73.5)									
Presence of risk factor: Device Dependence														
Yes	0/	1 (0.0)		1/	1 (100.0)									
No	417/ 506	(82.4)		393/ 533	(73.7)									

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Final

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Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Sore Throat - Subgroup analysis

Subgroup Level	Nirmatrelvir/ritonavir (N=26)			Placebo (N=26)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Age												
< 65	16/	24 (66.7)		14/	25 (56.0)							
>= 65	1/	2 (50.0)		1/	1 (100.0)							
Gender									0.094			0.165
Male	7/	12 (58.3)	18.0 (6.0, NE)	7/	12 (58.3)	15.0 (6.0, NE)	0.165 (0.022, 1.256)	0.082		0.828 (0.289, 2.368)	0.725	
Female	10/	14 (71.4)	11.0 (2.0, 18.0)	8/	14 (57.1)	21.5 (7.0, NE)	2.859 (0.765, 10.681)	0.118		2.205 (0.863, 5.634)	0.099	
Geographic region												
United States	8/	13 (61.5)		7/	12 (58.3)							
Europe	3/	3 (100.0)		5/	8 (62.5)							
India	0			0								
Rest of World	6/	10 (60.0)		3/	6 (50.0)							
COVID-19 therapeutic mAb treatment at randomisation												
Yes	2/	3 (66.7)		0/	1 (0.0)							
No	15/	23 (65.2)		15/	25 (60.0)							
Baseline viral load 1									0.522			0.730
< 10^4 copies/mL	4/	7 (57.1)	20.5 (2.0, NE)	3/	5 (60.0)	23.0 (7.0, NE)	0.310 (0.043, 2.228)	0.244		1.089 (0.240, 4.938)	0.912	
>= 10^4 copies/mL	13/	19 (68.4)	12.5 (7.0, 16.0)	12/	21 (57.1)	15.0 (10.0, NE)	1.876 (0.733, 4.801)	0.189		1.452 (0.661, 3.189)	0.353	
Baseline viral load 2									0.122			0.474
< 10^7 copies/mL	9/	15 (60.0)	17.0 (7.0, NE)	10/	18 (55.6)	23.0 (7.0, NE)	1.327 (0.452, 3.893)	0.606		1.109 (0.450, 2.731)	0.822	
>= 10^7 copies/mL	8/	11 (72.7)	10.0 (2.0, 14.0)	5/	8 (62.5)	15.0 (6.0, NE)	9.952 (1.429, 69.312)	0.020		1.820 (0.590, 5.609)	0.297	
Baseline serology status									0.716			0.598
Negative	7/	13 (53.8)	14.0 (4.0, NE)	11/	18 (61.1)	15.0 (6.0, NE)	1.170 (0.388, 3.527)	0.780		1.150 (0.445, 2.972)	0.773	
Positive	10/	13 (76.9)	13.0 (2.0, 23.0)	4/	8 (50.0)	23.0 (7.0, NE)	1.456 (0.363, 5.835)	0.596		1.671 (0.523, 5.336)	0.386	
Symptom onset days to first dose date									0.229			0.220
<= 3	16/	21 (76.2)	12.0 (6.0, 16.0)	10/	16 (62.5)	16.5 (7.0, NE)	1.910 (0.790, 4.619)	0.151		1.563 (0.707, 3.458)	0.270	
> 3	1/	5 (20.0)	NE (18.0, NE)	5/	10 (50.0)	19.0 (6.0, NE)	0.835 (0.051, 13.573)	0.899		0.350 (0.040, 3.057)	0.343	
BMI group												
< 25	3/	5 (60.0)		2/	3 (66.7)							
25 - < 30	5/	7 (71.4)		7/	11 (63.6)							
>= 30	9/	14 (64.3)		6/	12 (50.0)							
Ethnicity												
White	12/	17 (70.6)		11/	20 (55.0)							
Black or African American	2/	2 (100.0)		2/	3 (66.7)							
Asian	2/	3 (66.7)		1/	1 (100.0)							
Others	1/	4 (25.0)		1/	2 (50.0)							
Number of baseline comorbidities present												
0-1	15/	23 (65.2)		10/	20 (50.0)							
2-3	2/	3 (66.7)		5/	6 (83.3)							
>= 4	0			0								
Presence of risk factor: Smoking									0.947			0.949
Yes	6/	10 (60.0)	17.5 (2.0, NE)	5/	10 (50.0)	25.0 (7.0, NE)	0.424 (0.087, 2.062)	0.288		1.318 (0.402, 4.328)	0.649	
No	10/	15 (66.7)	14.0 (4.0, 18.0)	10/	16 (62.5)	15.0 (6.0, NE)	1.810 (0.673, 4.874)	0.240		1.342 (0.557, 3.232)	0.512	

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=26)						Placebo (N=26)						Adjusted Analysis [2]		Unadjusted Analysis [3]													
	n/N	(%)	Median (95% CI) [1]				n/N	(%)	Median (95% CI) [1]				Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value										
Presence of risk factor: Diabetes mellitus																												
Yes	0/	2	(	0.0)			2/	3	(	66.7)																		
No	16/	23	(	69.6)			13/	23	(	56.5)																		
Presence of risk factor: Immunosuppression																												
Yes	0						0																					
No	16/	25	(	64.0)			15/	26	(	57.7)																		
Presence of risk factor: Chronic lung disease																												
Yes	0						1/	1	(	100.0)																		
No	16/	25	(	64.0)			14/	25	(	56.0)																		
Presence of risk factor: Hypertension																												
Yes	6/	9	(	66.7)	12.0	(	2.0,	NE)	7/	9	(	77.8)	11.0	(	2.0,	NE)	2.168	(	0.435,	10.807)	0.345	0.701	1.038	(	0.347,	3.108)	0.946	0.544
No	10/	16	(	62.5)	14.0	(	7.0,	NE)	8/	17	(	47.1)	25.0	(	10.0,	NE)	1.651	(	0.552,	4.932)	0.370							
Presence of risk factor: Cardiovascular disorder																												
Yes	1/	1	(	100.0)			3/	3	(	100.0)																		
No	15/	24	(	62.5)			12/	23	(	52.2)																		
Presence of risk factor: Chronic kidney disease																												
Yes	0						0																					
No	16/	25	(	64.0)			15/	26	(	57.7)																		
Presence of risk factor: HIV Infection																												
Yes	0						0																					
No	16/	25	(	64.0)			15/	26	(	57.7)																		
Presence of risk factor: Sickle Cell Disease																												
No	16/	25	(	64.0)			15/	26	(	57.7)																		
Presence of risk factor: Neurodevelopmental Disorder																												
Yes	0						0																					
No	16/	25	(	64.0)			15/	26	(	57.7)																		
Presence of risk factor: Cancer																												
Yes	0						0																					
No	16/	25	(	64.0)			15/	26	(	57.7)																		
Presence of risk factor: Device Dependence																												
Yes	0/	1	(	0.0)			0																					
No	16/	23	(	69.6)			15/	26	(	57.7)																		

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Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Shortness of Breath or Difficulty Breathing - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)		p-Value			Relative Risk (95% CI)		p-Value		
Age							0.057					0.045
< 65	189/ 790 (23.9)	230/ 810 (28.4)	0.819 (0.693, 0.967)		0.018			0.843 (0.714, 0.994)		0.043		
>= 65	22/ 138 (15.9)	45/ 145 (31.0)	0.500 (0.316, 0.793)		0.003			0.514 (0.326, 0.808)		0.004		
Gender							0.479					0.402
Male	100/ 463 (21.6)	130/ 507 (25.6)	0.809 (0.643, 1.016)		0.069			0.842 (0.670, 1.058)		0.141		
Female	111/ 465 (23.9)	145/ 448 (32.4)	0.731 (0.591, 0.903)		0.004			0.738 (0.598, 0.910)		0.005		
Geographic region							0.057					0.053
United States	99/ 375 (26.4)	102/ 387 (26.4)	0.983 (0.771, 1.253)		0.888			1.002 (0.790, 1.270)		0.989		
Europe	72/ 322 (22.4)	112/ 321 (34.9)	0.627 (0.484, 0.811)		<.001			0.641 (0.498, 0.825)		<.001		
India	3/ 74 (4.1)	8/ 78 (10.3)	NE (NE, NE)		NE			0.395 (0.109, 1.433)		0.158		
Rest of World	37/ 157 (23.6)	53/ 169 (31.4)	0.756 (0.534, 1.071)		0.115			0.751 (0.525, 1.076)		0.119		
COVID-19 therapeutic mAb treatment at randomisation							0.216					0.179
Yes	15/ 57 (26.3)	13/ 60 (21.7)	NE (NE, NE)		NE			1.215 (0.635, 2.322)		0.557		
No	196/ 871 (22.5)	262/ 895 (29.3)	0.754 (0.642, 0.886)		<.001			0.769 (0.655, 0.902)		0.001		
Baseline viral load 1							0.036					0.029
< 10^4 copies/mL	68/ 335 (20.3)	69/ 354 (19.5)	1.010 (0.750, 1.361)		0.947			1.041 (0.772, 1.405)		0.791		
>= 10^4 copies/mL	138/ 569 (24.3)	198/ 575 (34.4)	0.702 (0.585, 0.843)		<.001			0.704 (0.586, 0.846)		<.001		
Baseline viral load 2							0.434					0.473
< 10^7 copies/mL	141/ 652 (21.6)	185/ 699 (26.5)	0.807 (0.667, 0.976)		0.027			0.817 (0.675, 0.989)		0.039		
>= 10^7 copies/mL	65/ 252 (25.8)	82/ 230 (35.7)	0.716 (0.545, 0.940)		0.016			0.723 (0.551, 0.950)		0.020		
Baseline serology status							0.048					0.069
Negative	113/ 435 (26.0)	171/ 456 (37.5)	0.683 (0.560, 0.835)		<.001			0.693 (0.568, 0.844)		<.001		
Positive	94/ 482 (19.5)	102/ 487 (20.9)	0.948 (0.737, 1.219)		0.676			0.931 (0.725, 1.196)		0.576		
Symptom onset days to first dose date							0.510					0.574
<= 3	143/ 624 (22.9)	187/ 624 (30.0)	0.747 (0.619, 0.902)		0.002			0.765 (0.634, 0.922)		0.005		
> 3	68/ 304 (22.4)	88/ 331 (26.6)	0.832 (0.633, 1.094)		0.188			0.841 (0.639, 1.108)		0.219		
BMI group							0.033					0.014
< 25	31/ 215 (14.4)	64/ 213 (30.0)	0.522 (0.355, 0.767)		<.001			0.480 (0.327, 0.705)		<.001		
25 - < 30	82/ 319 (25.7)	91/ 332 (27.4)	0.948 (0.733, 1.227)		0.685			0.938 (0.726, 1.211)		0.623		
>= 30	98/ 393 (24.9)	120/ 410 (29.3)	0.769 (0.609, 0.970)		0.026			0.852 (0.678, 1.070)		0.169		
Ethnicity							0.292					0.262
White	174/ 699 (24.9)	221/ 718 (30.8)	0.802 (0.676, 0.952)		0.012			0.809 (0.683, 0.958)		0.014		
Black or African American	11/ 43 (25.6)	13/ 40 (32.5)	0.859 (0.403, 1.831)		0.694			0.787 (0.400, 1.550)		0.489		
Asian	9/ 117 (7.7)	24/ 127 (18.9)	NE (NE, NE)		NE			0.407 (0.197, 0.839)		0.015		
Others	17/ 69 (24.6)	17/ 70 (24.3)	NE (NE, NE)		NE			1.014 (0.566, 1.820)		0.962		
Number of baseline comorbidities present							0.841					0.604
0-1	165/ 710 (23.2)	207/ 728 (28.4)	0.783 (0.655, 0.935)		0.007			0.817 (0.685, 0.975)		0.025		
2-3	45/ 214 (21.0)	67/ 221 (30.3)	0.718 (0.520, 0.991)		0.044			0.694 (0.500, 0.963)		0.029		
>= 4	1/ 4 (25.0)	1/ 6 (16.7)	NE (NE, NE)		NE			1.500 (0.127, 17.667)		0.747		
Presence of risk factor: Smoking							0.630					0.736
Yes	87/ 417 (20.9)	112/ 438 (25.6)	0.811 (0.635, 1.036)		0.094			0.816 (0.638, 1.043)		0.105		
No	124/ 509 (24.4)	163/ 517 (31.5)	0.746 (0.611, 0.911)		0.004			0.773 (0.633, 0.943)		0.011		
Presence of risk factor: Diabetes mellitus							0.874					0.703

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

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[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928)		Placebo (N=955)		Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
	n/N (%)		n/N (%)		Relative Risk (95% CI)		p-Value	Relative Risk (95% CI)		p-Value				
Yes	31/ 130	(23.8)	44/ 136	(32.4)	0.705 (0.489, 1.016)		0.061		0.737 (0.498, 1.090)		0.127			
No	180/ 797	(22.6)	231/ 819	(28.2)	0.780 (0.658, 0.925)		0.004		0.801 (0.676, 0.948)		0.010			
Presence of risk factor: Immunosuppression								0.652				0.638		
Yes	2/ 6	(33.3)	2/ 7	(28.6)	NE (NE, NE)		NE		1.167 (0.229, 5.946)		0.853			
No	209/ 921	(22.7)	273/ 948	(28.8)	0.771 (0.659, 0.901)		0.001		0.788 (0.674, 0.921)		0.003			
Presence of risk factor: Chronic lung disease								0.575				0.511		
Yes	17/ 62	(27.4)	11/ 39	(28.2)	0.890 (0.472, 1.679)		0.720		0.972 (0.511, 1.851)		0.931			
No	194/ 865	(22.4)	264/ 916	(28.8)	0.762 (0.648, 0.895)		<.001		0.778 (0.663, 0.914)		0.002			
Presence of risk factor: Hypertension								0.918				0.568		
Yes	77/ 348	(22.1)	110/ 371	(29.6)	0.745 (0.579, 0.959)		0.022		0.746 (0.580, 0.960)		0.023			
No	134/ 579	(23.1)	165/ 584	(28.3)	0.778 (0.638, 0.947)		0.013		0.819 (0.673, 0.997)		0.047			
Presence of risk factor: Cardiovacular disorder								0.639				0.595		
Yes	9/ 42	(21.4)	16/ 49	(32.7)	NE (NE, NE)		NE		0.656 (0.324, 1.328)		0.242			
No	202/ 885	(22.8)	259/ 906	(28.6)	0.780 (0.665, 0.916)		0.002		0.798 (0.681, 0.936)		0.006			
Presence of risk factor: Chronic kidney disease								0.592				0.571		
Yes	1/ 6	(16.7)	3/ 8	(37.5)	NE (NE, NE)		NE		0.444 (0.060, 3.285)		0.427			
No	210/ 921	(22.8)	272/ 947	(28.7)	0.777 (0.664, 0.908)		0.001		0.794 (0.680, 0.927)		0.004			
Presence of risk factor: HIV Infection														
Yes	0		0/ 1	(0.0)										
No	211/ 927	(22.8)	275/ 953	(28.9)										
Presence of risk factor: Sickie Cell Disease														
No	211/ 927	(22.8)	275/ 955	(28.8)										
Presence of risk factor: Neurodevelopmental Disorder														
Yes	0/ 2	(0.0)	0/ 1	(0.0)										
No	211/ 925	(22.8)	275/ 954	(28.8)										
Presence of risk factor: Cancer								0.360				0.743		
Yes	1/ 5	(20.0)	1/ 6	(16.7)	NE (NE, NE)		NE		1.200 (0.098, 14.690)		0.887			
No	210/ 922	(22.8)	274/ 949	(28.9)	0.774 (0.663, 0.905)		0.001		0.789 (0.675, 0.921)		0.003			
Presence of risk factor: Device Dependence														
Yes	0/ 4	(0.0)	2/ 3	(66.7)										
No	209/ 914	(22.9)	272/ 944	(28.8)										

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

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[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=425)			Placebo (N=435)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	302/	365 (82.7)	6.0 (5.0, 7.0)	267/	366 (73.0)	9.0 (7.0, 10.0)	1.368 (1.154, 1.622)	<.001		0.112	1.357 (1.150, 1.601)	<.001		0.093
>= 65	55/	60 (91.7)	6.0 (3.0, 7.0)	50/	69 (72.5)	10.0 (7.0, 15.0)	2.310 (1.512, 3.530)	<.001			2.004 (1.353, 2.966)	<.001		
Gender														
Male	163/	193 (84.5)	6.0 (4.0, 7.0)	156/	218 (71.6)	9.0 (7.0, 11.0)	1.546 (1.229, 1.944)	<.001		0.373	1.519 (1.217, 1.896)	<.001		0.395
Female	194/	232 (83.6)	7.0 (5.0, 8.0)	161/	217 (74.2)	8.0 (7.0, 11.0)	1.339 (1.079, 1.663)	0.008			1.363 (1.105, 1.680)	0.004		
Geographic region														
United States	159/	201 (79.1)	7.0 (5.0, 9.0)	138/	199 (69.3)	9.0 (7.0, 12.0)	1.309 (1.037, 1.653)	0.024		0.464	1.331 (1.059, 1.673)	0.014		0.427
Europe	119/	132 (90.2)	7.0 (6.0, 8.0)	115/	146 (78.8)	9.0 (6.0, 10.0)	1.425 (1.089, 1.864)	0.010			1.412 (1.091, 1.828)	0.009		
India	16/	16 (100.0)	4.5 (3.0, 8.0)	10/	11 (90.9)	7.0 (3.0, 9.0)	1.728 (0.683, 4.367)	0.248			1.182 (0.526, 2.655)	0.685		
Rest of World	63/	76 (82.9)	4.5 (3.0, 6.0)	54/	79 (68.4)	9.0 (7.0, 15.0)	1.860 (1.273, 2.718)	0.001			1.803 (1.247, 2.607)	0.002		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	27/	33 (81.8)	10.0 (5.0, 16.0)	23/	33 (69.7)	11.5 (4.0, 18.0)	1.171 (0.649, 2.111)	0.600		0.475	1.294 (0.741, 2.260)	0.365		0.664
No	330/	392 (84.2)	6.0 (5.0, 7.0)	294/	402 (73.1)	8.0 (7.0, 10.0)	1.460 (1.241, 1.718)	<.001			1.450 (1.238, 1.698)	<.001		
Baseline viral load 1														
< 10^4 copies/mL	130/	154 (84.4)	6.0 (5.0, 7.0)	120/	158 (75.9)	7.0 (5.0, 9.0)	1.290 (0.999, 1.666)	0.051		0.178	1.279 (0.997, 1.641)	0.053		0.263
>= 10^4 copies/mL	212/	255 (83.1)	6.0 (5.0, 7.0)	189/	263 (71.9)	11.0 (9.0, 12.0)	1.566 (1.282, 1.912)	<.001			1.526 (1.252, 1.858)	<.001		
Baseline viral load 2														
< 10^7 copies/mL	255/	310 (82.3)	7.0 (5.0, 7.0)	239/	319 (74.9)	8.0 (7.0, 9.0)	1.295 (1.082, 1.549)	0.005		0.011	1.289 (1.080, 1.538)	0.005		0.015
>= 10^7 copies/mL	87/	99 (87.9)	4.0 (3.0, 6.0)	70/	102 (68.6)	12.0 (9.0, 16.0)	2.077 (1.482, 2.911)	<.001			1.968 (1.430, 2.710)	<.001		
Baseline serology status														
Negative	154/	186 (82.8)	7.0 (5.0, 9.0)	148/	211 (70.1)	10.0 (8.0, 12.0)	1.585 (1.255, 2.002)	<.001		0.657	1.491 (1.188, 1.870)	<.001		0.649
Positive	199/	234 (85.0)	6.0 (4.0, 7.0)	163/	217 (75.1)	8.0 (6.0, 9.0)	1.398 (1.130, 1.730)	0.002			1.386 (1.125, 1.707)	0.002		
Symptom onset days to first dose date														
<= 3	227/	270 (84.1)	6.0 (5.0, 7.0)	216/	278 (77.7)	8.0 (6.0, 9.0)	1.323 (1.092, 1.603)	0.004		0.147	1.320 (1.094, 1.592)	0.004		0.163
> 3	130/	155 (83.9)	6.0 (4.0, 8.0)	101/	157 (64.3)	11.0 (8.0, 15.0)	1.707 (1.301, 2.239)	<.001			1.689 (1.300, 2.195)	<.001		
BMI group														
< 25	80/	92 (87.0)	3.0 (3.0, 5.0)	58/	78 (74.4)	8.5 (6.0, 12.0)	1.927 (1.320, 2.813)	<.001		0.166	1.916 (1.359, 2.700)	<.001		0.174
25 - < 30	117/	137 (85.4)	7.0 (6.0, 8.0)	114/	157 (72.6)	8.0 (6.0, 10.0)	1.349 (1.030, 1.766)	0.030			1.354 (1.044, 1.756)	0.022		
>= 30	160/	196 (81.6)	7.0 (5.0, 9.0)	145/	200 (72.5)	10.0 (7.0, 12.0)	1.368 (1.085, 1.726)	0.008			1.333 (1.064, 1.670)	0.013		
Ethnicity														
White	278/	334 (83.2)	7.0 (5.0, 7.0)	258/	352 (73.3)	9.0 (7.0, 11.0)	1.361 (1.143, 1.622)	<.001		0.680	1.381 (1.165, 1.637)	<.001		0.677
Black or African American	14/	19 (73.7)	7.0 (4.0, 14.0)	12/	18 (66.7)	7.0 (3.0, NE)	1.325 (0.519, 3.384)	0.556			1.321 (0.604, 2.887)	0.485		
Asian	34/	36 (94.4)	3.0 (2.0, 6.0)	27/	33 (81.8)	7.0 (6.0, 9.0)	1.760 (1.006, 3.080)	0.048			1.678 (1.004, 2.806)	0.048		
Others	31/	36 (86.1)	5.0 (2.0, 11.0)	20/	32 (62.5)	11.0 (7.0, 18.0)	1.751 (0.973, 3.154)	0.062			1.871 (1.056, 3.316)	0.032		
Number of baseline comorbidities present														
0-1	269/	318 (84.6)		214/	295 (72.5)									
2-3	87/	106 (82.1)		100/	137 (73.0)									
>= 4	1/	1 (100.0)		3/	3 (100.0)									
Presence of risk factor: Smoking														
Yes	154/	180 (85.6)	6.0 (5.0, 7.0)	146/	199 (73.4)	8.0 (6.0, 10.0)	1.437 (1.131, 1.825)	0.003		0.670	1.408 (1.121, 1.768)	0.003		0.883
No	202/	244 (82.8)	6.0 (5.0, 8.0)	171/	236 (72.5)	9.0 (8.0, 11.0)	1.479 (1.200, 1.824)	<.001			1.452 (1.183, 1.781)	<.001		

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=425)			Placebo (N=435)			Adjusted Analysis [2]			Interaction		Unadjusted Analysis [3]			Interaction	
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	p-Value			Hazard Ratio (95% CI)	p-Value	p-Value		
Presence of risk factor: Diabetes mellitus										0.676					0.674	
Yes	48/ 60	(80.0)	5.0 (3.0, 7.0)	57/ 74	(77.0)	8.0 (6.0, 11.0)	1.601 (1.057, 2.425)	0.026				1.297 (0.882, 1.907)	0.187			
No	309/ 365	(84.7)	6.0 (5.0, 7.0)	260/ 361	(72.0)	9.0 (7.0, 10.0)	1.490 (1.255, 1.769)	<.001				1.463 (1.239, 1.727)	<.001			
Presence of risk factor: Immunosuppression																
Yes	3/ 3	(100.0)		2/ 3	(66.7)											
No	354/ 422	(83.9)		315/ 432	(72.9)											
Presence of risk factor: Chronic lung disease										0.361					0.311	
Yes	26/ 33	(78.8)	7.0 (4.0, 13.0)	19/ 24	(79.2)	9.0 (5.0, 15.0)	1.099 (0.576, 2.099)	0.775				1.074 (0.594, 1.944)	0.813			
No	331/ 392	(84.4)	6.0 (5.0, 7.0)	298/ 411	(72.5)	9.0 (7.0, 10.0)	1.467 (1.247, 1.726)	<.001				1.465 (1.251, 1.715)	<.001			
Presence of risk factor: Hypertension										0.384					0.572	
Yes	142/ 168	(84.5)	6.0 (5.0, 7.0)	147/ 202	(72.8)	9.0 (7.0, 11.0)	1.506 (1.186, 1.914)	<.001				1.488 (1.179, 1.877)	<.001			
No	215/ 257	(83.7)	6.0 (5.0, 7.0)	170/ 233	(73.0)	9.0 (7.0, 11.0)	1.373 (1.115, 1.691)	0.003				1.388 (1.134, 1.699)	0.001			
Presence of risk factor: Cardiovascular disorder										0.457					0.945	
Yes	15/ 19	(78.9)	7.5 (2.0, 14.0)	17/ 24	(70.8)	10.0 (4.0, 19.0)	1.631 (0.748, 3.555)	0.218				1.347 (0.672, 2.701)	0.401			
No	342/ 406	(84.2)	6.0 (5.0, 7.0)	300/ 411	(73.0)	9.0 (7.0, 10.0)	1.425 (1.215, 1.672)	<.001				1.436 (1.229, 1.679)	<.001			
Presence of risk factor: Chronic kidney disease																
Yes	2/ 2	(100.0)		4/ 5	(80.0)											
No	355/ 423	(83.9)		313/ 430	(72.8)											
Presence of risk factor: HIV Infection																
Yes	0			1/ 1	(100.0)											
No	357/ 425	(84.0)		315/ 433	(72.7)											
Presence of risk factor: Sickel Cell Disease																
No	357/ 425	(84.0)		317/ 435	(72.9)											
Presence of risk factor: Neurodevelopmental Disorder																
Yes	2/ 2	(100.0)		1/ 1	(100.0)											
No	355/ 423	(83.9)		316/ 434	(72.8)											
Presence of risk factor: Cancer																
Yes	0			2/ 2	(100.0)											
No	357/ 425	(84.0)		315/ 433	(72.7)											
Presence of risk factor: Device Dependence																
Yes	0/ 1	(0.0)		0/ 1	(0.0)											
No	354/ 420	(84.3)		316/ 431	(73.3)											

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

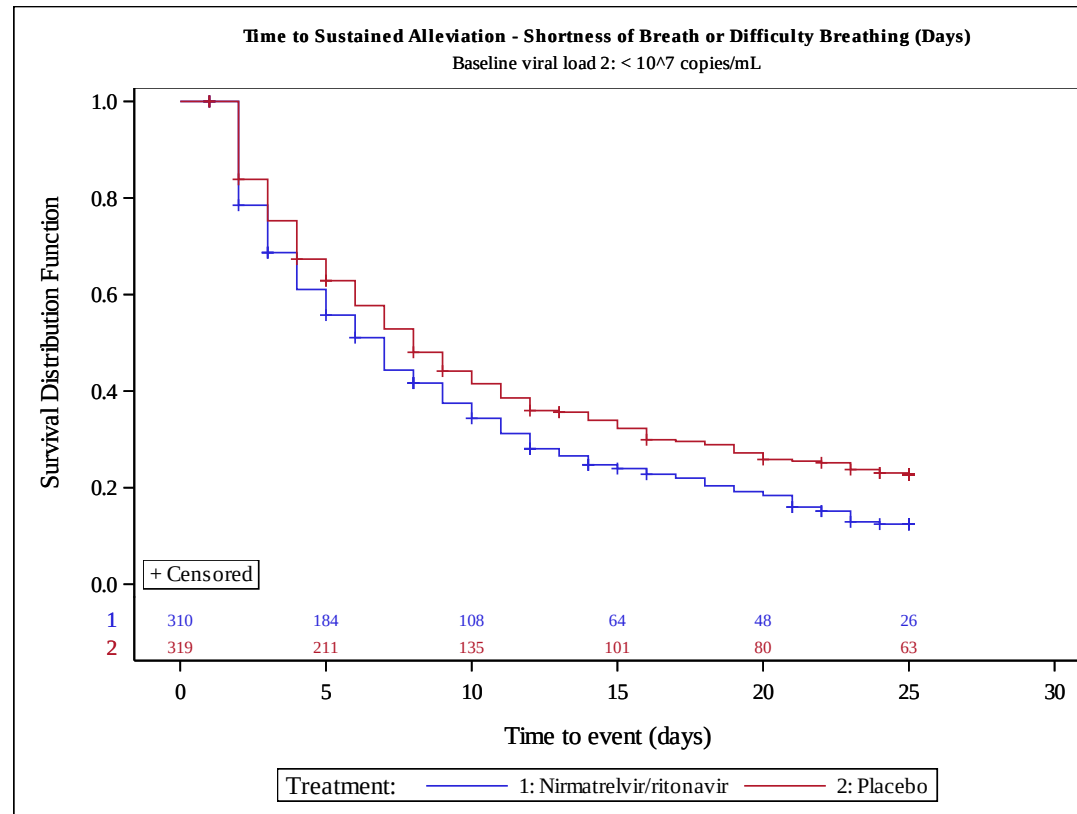
[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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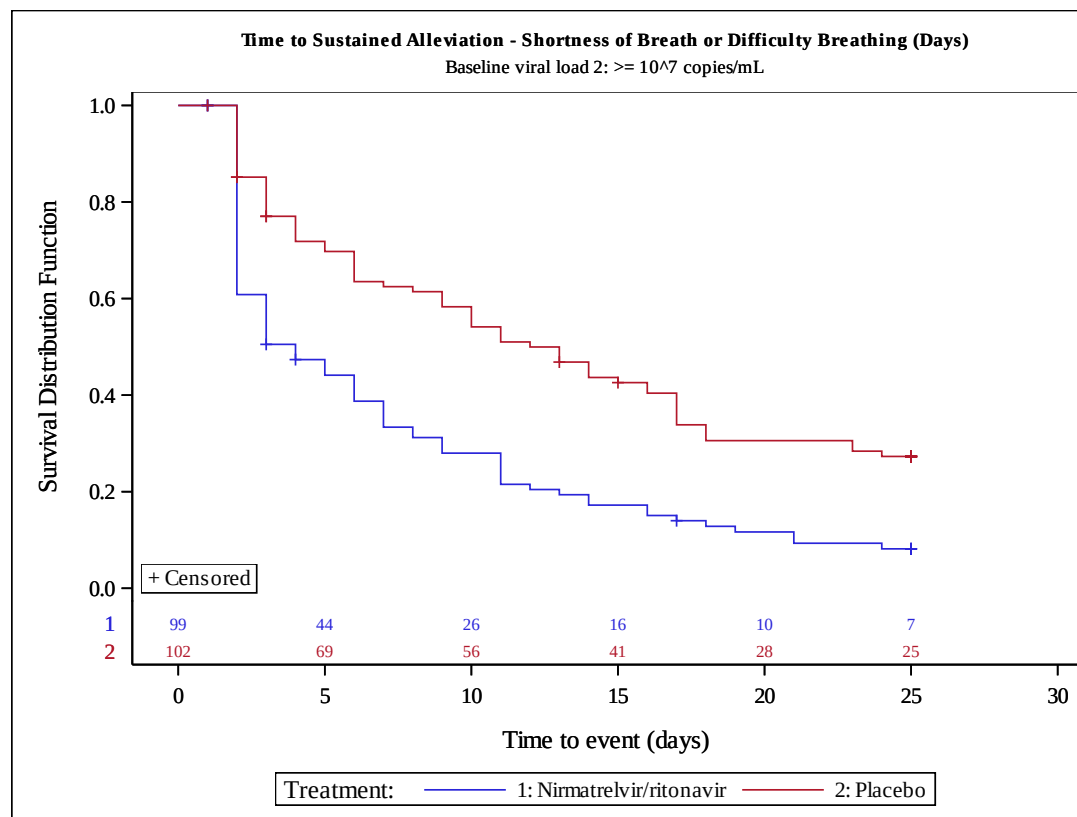
Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Shortness of Breath or Difficulty Breathing

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=425)			Placebo (N=435)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	284/ 365	(77.8)	9.0 (7.0, 10.0)	231/ 366	(63.1)	13.0 (11.0, 16.0)	1.546 (1.292, 1.851)	<.001		0.592	1.534 (1.288, 1.827)	<.001		0.467
>= 65	49/ 60	(81.7)	9.0 (7.0, 11.0)	42/ 69	(60.9)	19.0 (10.0, 24.0)	2.058 (1.315, 3.218)	0.002			1.837 (1.212, 2.784)	0.004		
Gender														
Male	156/ 193	(80.8)	7.0 (7.0, 9.0)	138/ 218	(63.3)	12.0 (10.0, 16.0)	1.648 (1.297, 2.092)	<.001		0.677	1.670 (1.325, 2.104)	<.001		0.500
Female	177/ 232	(76.3)	10.0 (8.0, 11.0)	135/ 217	(62.2)	14.0 (11.0, 18.0)	1.525 (1.210, 1.922)	<.001			1.524 (1.217, 1.909)	<.001		
Geographic region														
United States	150/ 201	(74.6)	9.0 (8.0, 12.0)	118/ 199	(59.3)	16.0 (11.0, 19.0)	1.529 (1.194, 1.959)	<.001		0.711	1.555 (1.220, 1.982)	<.001		0.690
Europe	106/ 132	(80.3)	10.0 (8.0, 11.0)	95/ 146	(65.1)	14.0 (10.0, 17.0)	1.508 (1.131, 2.010)	0.005			1.498 (1.134, 1.979)	0.004		
India	16/ 16	(100.0)	4.5 (3.0, 8.0)	10/ 11	(90.9)	7.0 (3.0, 9.0)	1.728 (0.683, 4.367)	0.248			1.182 (0.526, 2.655)	0.685		
Rest of World	61/ 76	(80.3)	6.0 (4.0, 7.0)	50/ 79	(63.3)	12.0 (8.0, 17.0)	1.964 (1.323, 2.917)	<.001			1.813 (1.242, 2.647)	0.002		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	27/ 33	(81.8)	11.0 (7.0, 18.0)	22/ 33	(66.7)	17.0 (9.0, 21.0)	1.261 (0.691, 2.300)	0.450		0.411	1.485 (0.843, 2.615)	0.171		0.722
No	306/ 392	(78.1)	9.0 (7.0, 10.0)	251/ 402	(62.4)	14.0 (11.0, 16.0)	1.604 (1.350, 1.905)	<.001			1.589 (1.343, 1.879)	<.001		
Baseline viral load 1														
< 10^4 copies/mL	123/ 154	(79.9)	9.0 (7.0, 10.0)	106/ 158	(67.1)	10.0 (8.0, 14.0)	1.394 (1.067, 1.822)	0.015		0.216	1.422 (1.095, 1.847)	0.008		0.379
>= 10^4 copies/mL	197/ 255	(77.3)	9.0 (7.0, 10.0)	161/ 263	(61.2)	15.0 (12.0, 18.0)	1.694 (1.371, 2.094)	<.001			1.657 (1.344, 2.042)	<.001		
Baseline viral load 2														
< 10^7 copies/mL	240/ 310	(77.4)	9.0 (8.0, 10.0)	206/ 319	(64.6)	12.0 (11.0, 15.0)	1.493 (1.235, 1.804)	<.001		0.195	1.497 (1.241, 1.805)	<.001		0.249
>= 10^7 copies/mL	80/ 99	(80.8)	7.0 (5.0, 10.0)	61/ 102	(59.8)	16.0 (10.0, 18.0)	1.880 (1.328, 2.663)	<.001			1.803 (1.290, 2.521)	<.001		
Baseline serology status														
Negative	145/ 186	(78.0)	10.0 (8.0, 11.0)	125/ 211	(59.2)	15.0 (12.0, 20.0)	1.867 (1.459, 2.391)	<.001		0.368	1.731 (1.361, 2.202)	<.001		0.387
Positive	185/ 234	(79.1)	8.0 (7.0, 9.0)	143/ 217	(65.9)	11.0 (9.0, 16.0)	1.464 (1.169, 1.832)	<.001			1.478 (1.186, 1.840)	<.001		
Symptom onset days to first dose date														
<= 3	212/ 270	(78.5)	8.0 (7.0, 9.0)	190/ 278	(68.3)	11.0 (10.0, 14.0)	1.411 (1.153, 1.727)	<.001		0.046	1.429 (1.173, 1.740)	<.001		0.100
> 3	121/ 155	(78.1)	10.0 (7.0, 12.0)	83/ 157	(52.9)	18.0 (14.0, NE)	2.014 (1.504, 2.696)	<.001			1.944 (1.467, 2.575)	<.001		
BMI group														
< 25	74/ 92	(80.4)	7.0 (4.0, 9.0)	55/ 78	(70.5)	11.0 (8.0, 13.0)	1.695 (1.140, 2.521)	0.009		0.945	1.553 (1.094, 2.206)	0.014		0.999
25 - < 30	112/ 137	(81.8)	8.0 (7.0, 10.0)	101/ 157	(64.3)	14.0 (10.0, 17.0)	1.597 (1.208, 2.113)	0.001			1.614 (1.229, 2.118)	<.001		
>= 30	147/ 196	(75.0)	10.0 (8.0, 12.0)	117/ 200	(58.5)	16.0 (12.0, 20.0)	1.615 (1.257, 2.075)	<.001			1.577 (1.236, 2.013)	<.001		
Ethnicity														
White	257/ 334	(76.9)	9.0 (8.0, 10.0)	220/ 352	(62.5)	14.0 (11.0, 16.0)	1.505 (1.250, 1.812)	<.001		0.584	1.533 (1.280, 1.837)	<.001		0.777
Black or African American	13/ 19	(68.4)	11.0 (5.0, 23.0)	8/ 18	(44.4)	NE (4.0, NE)	2.652 (0.874, 8.046)	0.085			2.004 (0.818, 4.907)	0.128		
Asian	34/ 36	(94.4)	3.5 (3.0, 6.0)	27/ 33	(81.8)	7.0 (6.0, 10.0)	1.739 (0.993, 3.045)	0.053			1.697 (1.015, 2.837)	0.044		
Others	29/ 36	(80.6)	8.0 (4.0, 15.0)	18/ 32	(56.3)	17.0 (8.0, NE)	1.933 (1.040, 3.595)	0.037			1.914 (1.055, 3.472)	0.033		
Number of baseline comorbidities present														
0-1	252/ 318	(79.2)		190/ 295	(64.4)									
2-3	80/ 106	(75.5)		80/ 137	(58.4)									
>= 4	1/ 1	(100.0)		3/ 3	(100.0)									
Presence of risk factor: Smoking														
Yes	145/ 180	(80.6)	8.0 (7.0, 9.0)	123/ 199	(61.8)	14.0 (11.0, 18.0)	1.771 (1.375, 2.283)	<.001		0.480	1.746 (1.370, 2.226)	<.001		0.302
No	188/ 244	(77.0)	10.0 (8.0, 11.0)	150/ 236	(63.6)	12.0 (10.0, 16.0)	1.483 (1.190, 1.849)	<.001			1.479 (1.192, 1.835)	<.001		

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=425)			Placebo (N=435)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus										0.364				0.655
Yes	45/ 60	(75.0)	7.0 (5.0, 10.0)	50/ 74	(67.6)	11.0 (9.0, 17.0)	1.477 (0.968, 2.253)	0.071			1.426 (0.952, 2.137)	0.085		
No	288/ 365	(78.9)	9.0 (8.0, 10.0)	223/ 361	(61.8)	14.0 (11.0, 16.0)	1.666 (1.389, 1.998)	<.001			1.621 (1.360, 1.933)	<.001		
Presence of risk factor: Immunosuppression														
Yes	3/ 3	(100.0)		2/ 3	(66.7)									
No	330/ 422	(78.2)		271/ 432	(62.7)									
Presence of risk factor: Chronic lung disease										0.178				0.131
Yes	26/ 33	(78.8)	10.0 (7.0, 13.0)	19/ 24	(79.2)	9.0 (6.0, 16.0)	0.968 (0.492, 1.904)	0.925			1.010 (0.559, 1.826)	0.974		
No	307/ 392	(78.3)	9.0 (7.0, 10.0)	254/ 411	(61.8)	14.0 (11.0, 16.0)	1.609 (1.355, 1.912)	<.001			1.622 (1.372, 1.917)	<.001		
Presence of risk factor: Hypertension										0.979				0.869
Yes	125/ 168	(74.4)	10.0 (8.0, 11.0)	123/ 202	(60.9)	15.0 (11.0, 20.0)	1.516 (1.174, 1.957)	0.001			1.522 (1.185, 1.954)	<.001		
No	208/ 257	(80.9)	8.0 (7.0, 9.0)	150/ 233	(64.4)	12.0 (10.0, 15.0)	1.571 (1.263, 1.955)	<.001			1.594 (1.290, 1.969)	<.001		
Presence of risk factor: Cardiovascular disorder										0.269				0.596
Yes	14/ 19	(73.7)	10.5 (3.0, 15.0)	13/ 24	(54.2)	17.0 (9.0, NE)	1.927 (0.798, 4.650)	0.145			1.880 (0.882, 4.007)	0.102		
No	319/ 406	(78.6)	9.0 (7.0, 10.0)	260/ 411	(63.3)	14.0 (11.0, 16.0)	1.548 (1.308, 1.832)	<.001			1.563 (1.325, 1.842)	<.001		
Presence of risk factor: Chronic kidney disease														
Yes	1/ 2	(50.0)		3/ 5	(60.0)									
No	332/ 423	(78.5)		270/ 430	(62.8)									
Presence of risk factor: HIV Infection														
Yes	0			1/ 1	(100.0)									
No	333/ 425	(78.4)		271/ 433	(62.6)									
Presence of risk factor: Sickle Cell Disease														
No	333/ 425	(78.4)		273/ 435	(62.8)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/ 2	(100.0)		1/ 1	(100.0)									
No	331/ 423	(78.3)		272/ 434	(62.7)									
Presence of risk factor: Cancer														
Yes	0			2/ 2	(100.0)									
No	333/ 425	(78.4)		271/ 433	(62.6)									
Presence of risk factor: Device Dependence														
Yes	0/ 1	(0.0)		0/ 1	(0.0)									
No	330/ 420	(78.6)		272/ 431	(63.1)									

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

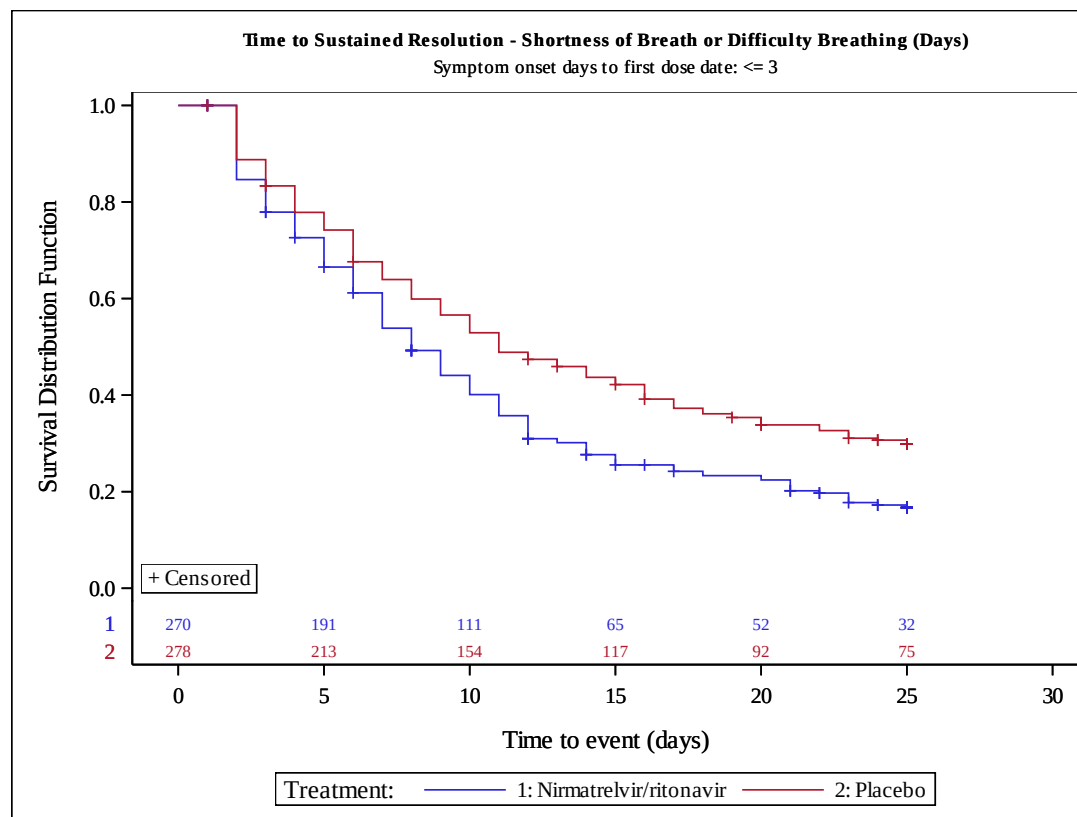
p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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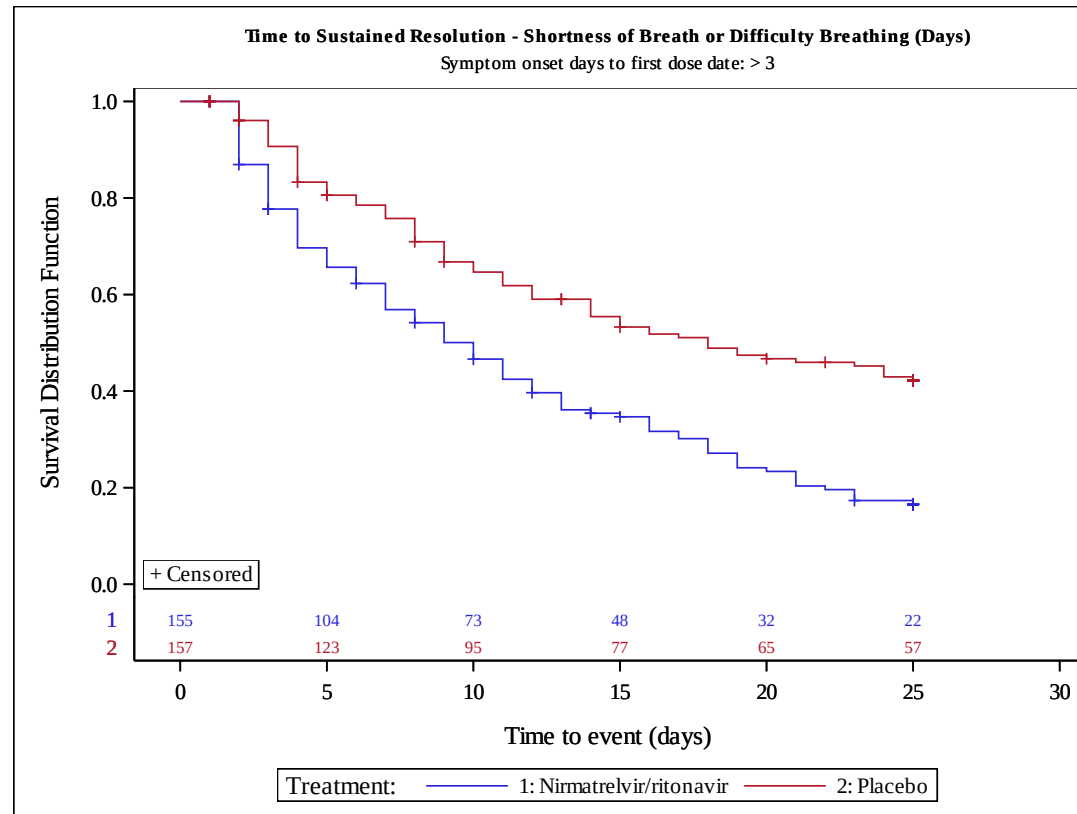
Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Cough - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]		Interaction p-Value	Unadjusted analysis [2]		Interaction p-Value
			Relative Risk (95% CI)	p-Value		Relative Risk (95% CI)	p-Value	
Age								
< 65	178/ 790 (22.5)	199/ 810 (24.6)	0.888 (0.742, 1.062)	0.193	0.382	0.917 (0.768, 1.095)	0.338	0.581
>= 65	30/ 138 (21.7)	30/ 145 (20.7)	1.127 (0.719, 1.766)	0.604		1.051 (0.671, 1.647)	0.829	
Gender								
Male	86/ 463 (18.6)	110/ 507 (21.7)	0.817 (0.631, 1.057)	0.124	0.243	0.856 (0.665, 1.102)	0.228	0.399
Female	122/ 465 (26.2)	119/ 448 (26.6)	0.993 (0.797, 1.238)	0.950		0.988 (0.795, 1.227)	0.911	
Geographic region								
United States	78/ 375 (20.8)	80/ 387 (20.7)	0.993 (0.747, 1.320)	0.962	0.454	1.006 (0.762, 1.328)	0.965	0.324
Europe	92/ 322 (28.6)	91/ 321 (28.3)	0.988 (0.768, 1.270)	0.922		1.008 (0.789, 1.288)	0.950	
India	7/ 74 (9.5)	8/ 78 (10.3)	NE (NE, NE)	NE		0.922 (0.352, 2.417)	0.869	
Rest of World	31/ 157 (19.7)	50/ 169 (29.6)	0.664 (0.448, 0.986)	0.042		0.667 (0.451, 0.988)	0.043	
COVID-19 therapeutic mAb treatment at randomisation								
Yes	12/ 57 (21.1)	15/ 60 (25.0)	0.865 (0.442, 1.693)	0.672	0.766	0.842 (0.432, 1.641)	0.614	0.752
No	196/ 871 (22.5)	214/ 895 (23.9)	0.924 (0.778, 1.099)	0.372		0.941 (0.794, 1.115)	0.484	
Baseline viral load 1								
< 10 ⁴ copies/mL	64/ 335 (19.1)	71/ 354 (20.1)	0.934 (0.690, 1.264)	0.657	0.881	0.953 (0.704, 1.290)	0.753	0.867
>= 10 ⁴ copies/mL	138/ 569 (24.3)	151/ 575 (26.3)	0.912 (0.746, 1.114)	0.367		0.924 (0.756, 1.128)	0.435	
Baseline viral load 2								
< 10 ⁷ copies/mL	126/ 652 (19.3)	150/ 699 (21.5)	0.879 (0.711, 1.086)	0.232	0.535	0.901 (0.729, 1.113)	0.332	0.699
>= 10 ⁷ copies/mL	76/ 252 (30.2)	72/ 230 (31.3)	0.996 (0.758, 1.308)	0.975		0.963 (0.737, 1.260)	0.785	
Baseline serology status								
Negative	114/ 435 (26.2)	130/ 456 (28.5)	0.927 (0.746, 1.151)	0.491	0.981	0.919 (0.742, 1.139)	0.442	0.965
Positive	88/ 482 (18.3)	96/ 487 (19.7)	0.913 (0.703, 1.186)	0.494		0.926 (0.714, 1.202)	0.564	
Symptom onset days to first dose date								
<= 3	146/ 624 (23.4)	162/ 624 (26.0)	0.880 (0.722, 1.073)	0.206	0.445	0.901 (0.742, 1.094)	0.294	0.549
> 3	62/ 304 (20.4)	67/ 331 (20.2)	1.036 (0.758, 1.414)	0.826		1.008 (0.740, 1.371)	0.962	
BMI group								
< 25	49/ 215 (22.8)	54/ 213 (25.4)	0.953 (0.676, 1.345)	0.785	0.542	0.899 (0.642, 1.259)	0.536	0.518
25 - < 30	74/ 319 (23.2)	72/ 332 (21.7)	1.020 (0.763, 1.363)	0.896		1.070 (0.804, 1.423)	0.644	
>= 30	85/ 393 (21.6)	103/ 410 (25.1)	0.815 (0.632, 1.051)	0.115		0.861 (0.669, 1.107)	0.244	
Ethnicity								
White	169/ 699 (24.2)	181/ 718 (25.2)	0.954 (0.793, 1.148)	0.619	0.559	0.959 (0.800, 1.150)	0.653	0.756
Black or African American	10/ 43 (23.3)	9/ 40 (22.5)	NE (NE, NE)	NE		1.034 (0.469, 2.280)	0.935	
Asian	13/ 117 (11.1)	16/ 127 (12.6)	NE (NE, NE)	NE		0.882 (0.444, 1.754)	0.720	
Others	16/ 69 (23.2)	23/ 70 (32.9)	NE (NE, NE)	NE		0.706 (0.409, 1.217)	0.210	
Number of baseline comorbidities present								
0-1	163/ 710 (23.0)	182/ 728 (25.0)	0.875 (0.726, 1.055)	0.162	0.294	0.918 (0.764, 1.104)	0.365	0.812
2-3	45/ 214 (21.0)	46/ 221 (20.8)	1.098 (0.758, 1.590)	0.621		1.010 (0.701, 1.456)	0.956	
>= 4	0/ 4 (0.0)	1/ 6 (16.7)	NE (NE, NE)	NE		0.467 (0.024, 9.259)	0.617	
Presence of risk factor: Smoking								
Yes	92/ 417 (22.1)	101/ 438 (23.1)	0.912 (0.708, 1.174)	0.473	0.955	0.957 (0.746, 1.227)	0.727	0.819
No	116/ 509 (22.8)	128/ 517 (24.8)	0.918 (0.735, 1.147)	0.453		0.920 (0.739, 1.146)	0.459	
Presence of risk factor: Diabetes mellitus					0.689			0.540

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochran's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value	
Yes	25/ 130 (19.2)	32/ 136 (23.5)	0.846 (0.541, 1.321)			0.461		0.817 (0.514, 1.301)			0.395	
No	183/ 797 (23.0)	197/ 819 (24.1)	0.935 (0.781, 1.120)			0.467		0.955 (0.801, 1.138)			0.605	
Presence of risk factor: Immunosuppression							0.041					0.213
Yes	2/ 6 (33.3)	0/ 7 (0.0)	NE (NE, NE)			NE		5.714 (0.327, 99.971)			0.233	
No	206/ 921 (22.4)	229/ 948 (24.2)	0.908 (0.768, 1.074)			0.261		0.926 (0.785, 1.092)			0.360	
Presence of risk factor: Chronic lung disease							0.350					0.423
Yes	15/ 62 (24.2)	13/ 39 (33.3)	0.626 (0.329, 1.193)			0.155		0.726 (0.388, 1.357)			0.315	
No	193/ 865 (22.3)	216/ 916 (23.6)	0.932 (0.784, 1.109)			0.428		0.946 (0.798, 1.122)			0.525	
Presence of risk factor: Hypertension							0.071					0.136
Yes	78/ 348 (22.4)	75/ 371 (20.2)	1.106 (0.833, 1.470)			0.487		1.109 (0.837, 1.469)			0.472	
No	130/ 579 (22.5)	154/ 584 (26.4)	0.809 (0.659, 0.992)			0.042		0.851 (0.695, 1.043)			0.121	
Presence of risk factor: Cardiovascular disorder							0.311					0.645
Yes	7/ 42 (16.7)	7/ 49 (14.3)	NE (NE, NE)			NE		1.167 (0.445, 3.057)			0.754	
No	201/ 885 (22.7)	222/ 906 (24.5)	0.901 (0.761, 1.067)			0.228		0.927 (0.784, 1.095)			0.372	
Presence of risk factor: Chronic kidney disease							0.053					0.251
Yes	0/ 6 (0.0)	3/ 8 (37.5)	NE (NE, NE)			NE		0.184 (0.011, 3.002)			0.234	
No	208/ 921 (22.6)	226/ 947 (23.9)	0.930 (0.786, 1.099)			0.394		0.946 (0.802, 1.116)			0.512	
Presence of risk factor: HIV Infection												
Yes	0	0/ 1 (0.0)										
No	208/ 927 (22.4)	229/ 953 (24.0)										
Presence of risk factor: Sickle Cell Disease												
No	208/ 927 (22.4)	229/ 955 (24.0)										
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0/ 2 (0.0)	0/ 1 (0.0)										
No	208/ 925 (22.5)	229/ 954 (24.0)										
Presence of risk factor: Cancer							NE					NE
Yes	0/ 5 (0.0)	0/ 6 (0.0)	NE (NE, NE)			NE		NE (NE, NE)			NE	
No	208/ 922 (22.6)	229/ 949 (24.1)	0.917 (0.776, 1.084)			0.309		0.935 (0.793, 1.102)			0.422	
Presence of risk factor: Device Dependence												
Yes	0/ 4 (0.0)	1/ 3 (33.3)										
No	206/ 914 (22.5)	226/ 944 (23.9)										

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=766)			Placebo (N=798)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	528/ 644	(82.0)	8.0 (8.0, 9.0)	499/ 663	(75.3)	10.0 (10.0, 11.0)	1.248 (1.101, 1.415)	<.001		0.338	1.265 (1.119, 1.430)	<.001		0.228
>= 65	109/ 122	(89.3)	7.0 (5.0, 9.0)	103/ 135	(76.3)	8.0 (6.0, 9.0)	1.392 (1.049, 1.848)	0.022			1.458 (1.110, 1.916)	0.007		
Gender										0.493				0.491
Male	327/ 380	(86.1)	8.0 (7.0, 9.0)	319/ 419	(76.1)	10.0 (8.0, 11.0)	1.322 (1.129, 1.549)	<.001			1.346 (1.153, 1.572)	<.001		
Female	310/ 386	(80.3)	9.0 (7.0, 10.0)	283/ 379	(74.7)	11.0 (9.0, 13.0)	1.216 (1.031, 1.434)	0.020			1.252 (1.065, 1.472)	0.006		
Geographic region										0.225				0.192
United States	259/ 324	(79.9)	8.0 (6.0, 8.0)	252/ 333	(75.7)	8.0 (7.0, 9.0)	1.112 (0.932, 1.327)	0.240			1.152 (0.968, 1.371)	0.110		
Europe	219/ 260	(84.2)	9.0 (7.0, 10.0)	205/ 269	(76.2)	11.0 (10.0, 13.0)	1.354 (1.111, 1.649)	0.003			1.365 (1.127, 1.653)	0.001		
India	52/ 55	(94.5)	10.0 (8.0, 12.0)	54/ 60	(90.0)	11.0 (9.0, 12.0)	1.285 (0.866, 1.905)	0.213			1.217 (0.828, 1.789)	0.318		
Rest of World	107/ 127	(84.3)	8.0 (6.0, 10.0)	91/ 136	(66.9)	12.0 (9.0, 17.0)	1.599 (1.198, 2.135)	0.001			1.625 (1.226, 2.155)	<.001		
COVID-19 therapeutic mAb treatment at randomisation										0.896				0.854
Yes	36/ 47	(76.6)	8.0 (5.0, 13.0)	40/ 56	(71.4)	12.0 (7.0, 17.0)	1.218 (0.767, 1.933)	0.403			1.216 (0.774, 1.909)	0.396		
No	601/ 719	(83.6)	8.0 (7.0, 9.0)	562/ 742	(75.7)	10.0 (9.0, 11.0)	1.268 (1.127, 1.426)	<.001			1.298 (1.157, 1.457)	<.001		
Baseline viral load 1										0.156				0.216
< 10^4 copies/mL	230/ 266	(86.5)	8.0 (7.0, 9.0)	233/ 285	(81.8)	9.0 (7.0, 10.0)	1.155 (0.959, 1.390)	0.128			1.166 (0.972, 1.400)	0.099		
>= 10^4 copies/mL	388/ 478	(81.2)	8.0 (7.0, 9.0)	355/ 489	(72.6)	11.0 (10.0, 13.0)	1.344 (1.162, 1.555)	<.001			1.341 (1.161, 1.550)	<.001		
Baseline viral load 2										0.236				0.203
< 10^7 copies/mL	437/ 525	(83.2)	8.0 (7.0, 9.0)	455/ 586	(77.6)	10.0 (8.0, 10.0)	1.217 (1.065, 1.390)	0.004			1.222 (1.071, 1.394)	0.003		
>= 10^7 copies/mL	181/ 219	(82.6)	9.0 (8.0, 10.0)	133/ 188	(70.7)	13.0 (9.0, 15.0)	1.442 (1.145, 1.817)	0.002			1.457 (1.164, 1.825)	0.001		
Baseline serology status										0.191				0.201
Negative	289/ 357	(81.0)	9.0 (8.0, 10.0)	270/ 389	(69.4)	12.0 (10.0, 13.0)	1.408 (1.186, 1.670)	<.001			1.405 (1.190, 1.660)	<.001		
Positive	343/ 402	(85.3)	7.0 (6.0, 8.0)	322/ 398	(80.9)	8.0 (7.0, 10.0)	1.188 (1.018, 1.386)	0.029			1.207 (1.036, 1.406)	0.016		
Symptom onset days to first dose date										0.838				0.794
<= 3	437/ 510	(85.7)	8.0 (7.0, 9.0)	402/ 513	(78.4)	10.0 (9.0, 11.0)	1.265 (1.102, 1.453)	<.001			1.284 (1.121, 1.471)	<.001		
> 3	200/ 256	(78.1)	8.0 (7.0, 10.0)	200/ 285	(70.2)	11.0 (8.0, 13.0)	1.275 (1.041, 1.561)	0.019			1.307 (1.073, 1.592)	0.008		
BMI group										0.403				0.433
< 25	137/ 165	(83.0)	8.0 (6.0, 10.0)	141/ 177	(79.7)	10.0 (8.0, 11.0)	1.349 (1.049, 1.735)	0.020			1.324 (1.045, 1.676)	0.020		
25 - < 30	225/ 268	(84.0)	8.0 (7.0, 9.0)	214/ 276	(77.5)	8.0 (7.0, 10.0)	1.174 (0.968, 1.425)	0.103			1.165 (0.966, 1.406)	0.111		
>= 30	275/ 333	(82.6)	8.0 (7.0, 10.0)	247/ 345	(71.6)	12.0 (10.0, 13.0)	1.421 (1.186, 1.701)	<.001			1.395 (1.174, 1.657)	<.001		
Ethnicity										0.791				0.736
White	486/ 588	(82.7)	8.0 (7.0, 9.0)	456/ 608	(75.0)	10.0 (9.0, 11.0)	1.266 (1.110, 1.443)	<.001			1.314 (1.156, 1.494)	<.001		
Black or African American	26/ 34	(76.5)	7.0 (4.0, 8.0)	25/ 36	(69.4)	8.0 (4.0, 16.0)	1.156 (0.628, 2.127)	0.641			1.256 (0.722, 2.184)	0.420		
Asian	77/ 85	(90.6)	9.0 (7.0, 10.0)	83/ 95	(87.4)	10.0 (8.0, 11.0)	1.198 (0.870, 1.649)	0.268			1.150 (0.842, 1.570)	0.380		
Others	48/ 59	(81.4)	11.0 (8.0, 13.0)	38/ 59	(64.4)	16.0 (8.0, 19.0)	1.406 (0.897, 2.202)	0.137			1.454 (0.946, 2.234)	0.088		
Number of baseline comorbidities present														
0-1	480/ 580	(82.8)		448/ 593	(75.5)									
2-3	154/ 182	(84.6)		151/ 200	(75.5)									
>= 4	3/ 4	(75.0)		3/ 5	(60.0)									
Presence of risk factor: Smoking										0.485				0.309
Yes	274/ 323	(84.8)	8.0 (7.0, 9.0)	273/ 357	(76.5)	10.0 (9.0, 12.0)	1.363 (1.145, 1.621)	<.001			1.384 (1.169, 1.638)	<.001		
No	361/ 441	(81.9)	9.0 (7.0, 10.0)	329/ 441	(74.6)	10.0 (8.0, 11.0)	1.224 (1.050, 1.426)	0.010			1.232 (1.061, 1.431)	0.006		

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Subgroup Level	Nirmatrelvir/ritonavir (N=766)			Placebo (N=798)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus										0.644				0.562
Yes	91/ 110	(82.7)	7.0 (6.0, 9.0)	92/ 120	(76.7)	9.0 (8.0, 14.0)	1.397 (1.029, 1.898)	0.032			1.377 (1.029, 1.844)	0.032		
No	545/ 655	(83.2)	8.0 (8.0, 9.0)	510/ 678	(75.2)	10.0 (9.0, 11.0)	1.260 (1.113, 1.426)	<.001			1.278 (1.132, 1.443)	<.001		
Presence of risk factor: Immunosuppression										0.003				0.035
Yes	5/ 6	(83.3)	9.5 (3.0, NE)	6/ 6	(100.0)	3.0 (2.0, 11.0)	0.043 (0.002, 0.968)	0.048			0.343 (0.094, 1.258)	0.107		
No	631/ 759	(83.1)	8.0 (7.0, 9.0)	596/ 792	(75.3)	10.0 (9.0, 11.0)	1.278 (1.140, 1.434)	<.001			1.304 (1.165, 1.459)	<.001		
Presence of risk factor: Chronic lung disease										0.918				0.996
Yes	43/ 54	(79.6)	9.0 (6.0, 13.0)	23/ 31	(74.2)	13.0 (6.0, 19.0)	1.155 (0.659, 2.025)	0.615			1.286 (0.774, 2.136)	0.331		
No	593/ 711	(83.4)	8.0 (7.0, 9.0)	579/ 767	(75.5)	10.0 (9.0, 11.0)	1.271 (1.131, 1.430)	<.001			1.299 (1.158, 1.458)	<.001		
Presence of risk factor: Hypertension										0.785				0.828
Yes	251/ 300	(83.7)	8.0 (7.0, 10.0)	250/ 335	(74.6)	8.0 (7.0, 10.0)	1.252 (1.045, 1.501)	0.015			1.288 (1.080, 1.536)	0.005		
No	385/ 465	(82.8)	8.0 (7.0, 9.0)	352/ 463	(76.0)	11.0 (10.0, 12.0)	1.266 (1.092, 1.469)	0.002			1.290 (1.116, 1.491)	<.001		
Presence of risk factor: Cardiovascular disorder										0.610				0.937
Yes	31/ 37	(83.8)	10.0 (6.0, 13.0)	32/ 44	(72.7)	11.0 (6.0, 19.0)	1.427 (0.832, 2.449)	0.196			1.330 (0.808, 2.187)	0.262		
No	605/ 728	(83.1)	8.0 (7.0, 9.0)	570/ 754	(75.6)	10.0 (9.0, 11.0)	1.260 (1.121, 1.417)	<.001			1.291 (1.151, 1.448)	<.001		
Presence of risk factor: Chronic kidney disease										0.834				0.811
Yes	5/ 6	(83.3)	10.0 (2.0, 20.0)	6/ 7	(85.7)	12.0 (2.0, 23.0)	3.513 (0.644, 19.150)	0.146			2.127 (0.566, 7.999)	0.264		
No	631/ 759	(83.1)	8.0 (7.0, 9.0)	596/ 791	(75.3)	10.0 (9.0, 11.0)	1.266 (1.129, 1.420)	<.001			1.291 (1.154, 1.445)	<.001		
Presence of risk factor: HIV Infection														
Yes	0			1/ 1	(100.0)									
No	636/ 765	(83.1)		600/ 796	(75.4)									
Presence of risk factor: Sickel Cell Disease														
No	636/ 765	(83.1)		602/ 798	(75.4)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/ 2	(100.0)		1/ 1	(100.0)									
No	634/ 763	(83.1)		601/ 797	(75.4)									
Presence of risk factor: Cancer														
Yes	2/ 3	(66.7)		5/ 5	(100.0)									
No	634/ 762	(83.2)		597/ 793	(75.3)									
Presence of risk factor: Device Dependence														
Yes	2/ 4	(50.0)		2/ 3	(66.7)									
No	628/ 753	(83.4)		597/ 789	(75.7)									

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

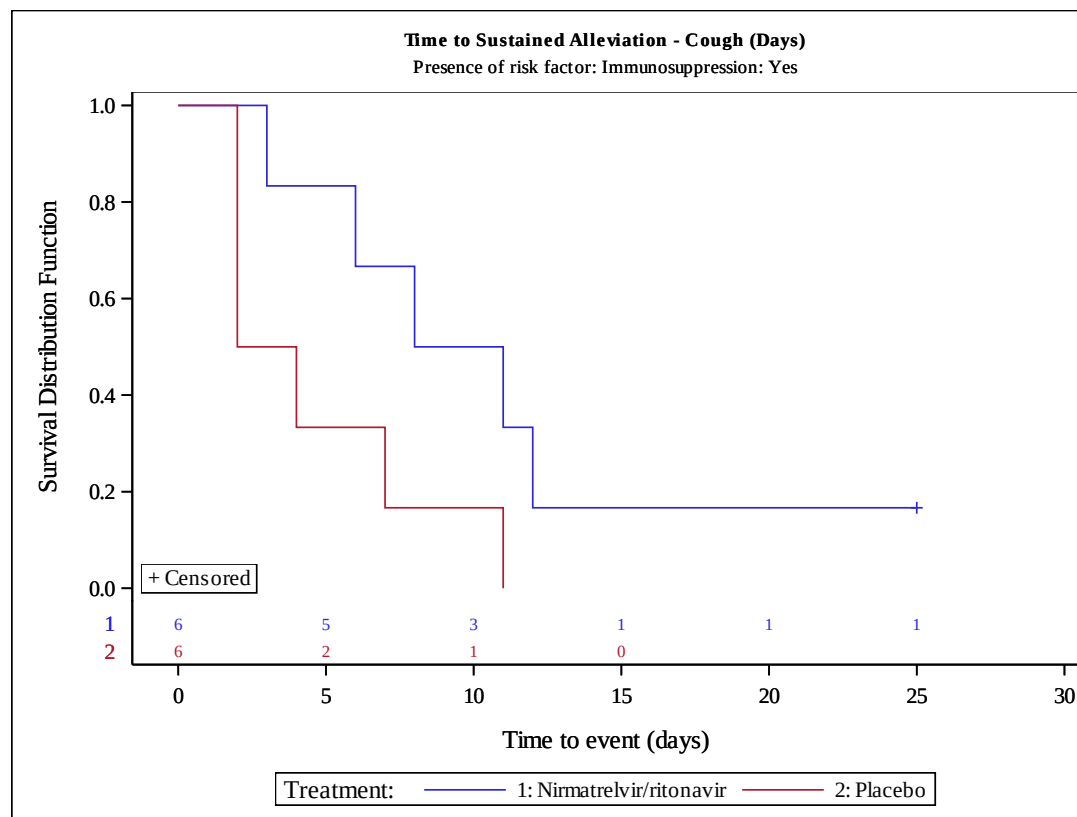
[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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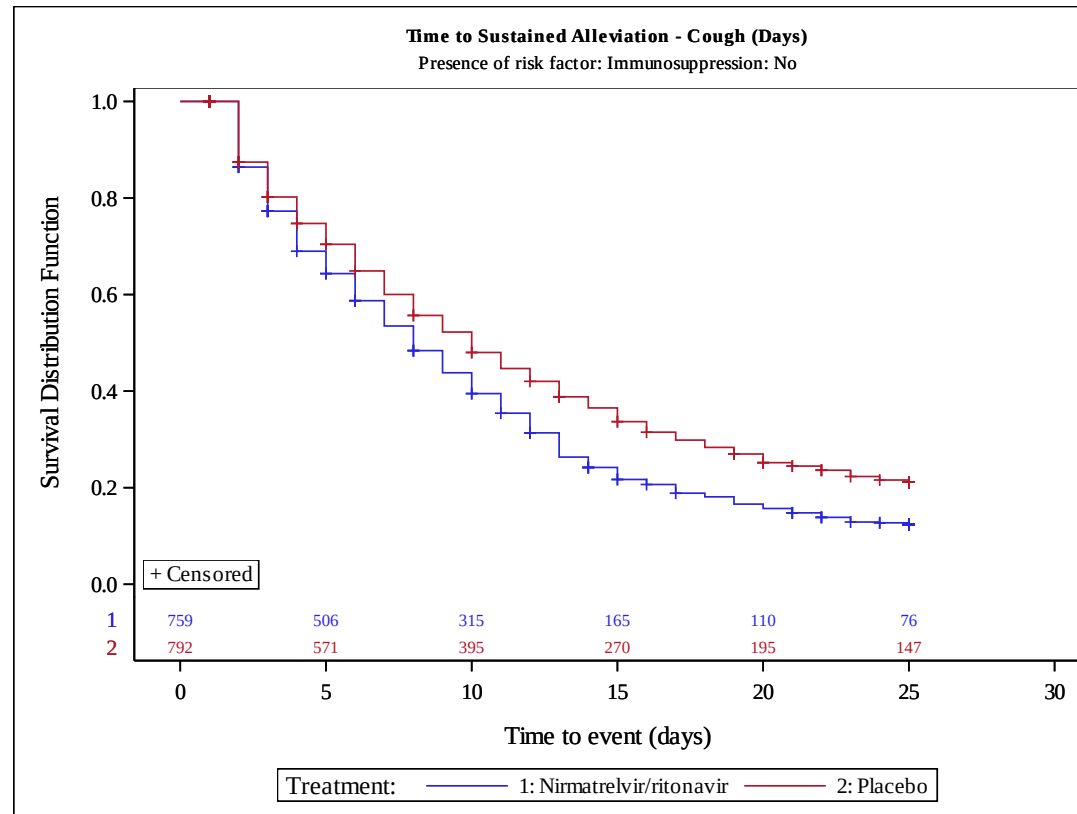
Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Overall Study population
RKI-conform mITT2 Analysis set

Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough - Subgroup analysis

Subgroup Level	Nirmatrelvir/ritonavir (N=48)			Placebo (N=48)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value	
Age													
< 65	37/	44 (84.1)	6.0 (4.0, 10.0)	23/	39 (59.0)	18.0 (12.0, NE)	2.271 (1.274, 4.049)	0.005	0.926	2.417 (1.425, 4.100)	0.001		0.870
>= 65	3/	4 (75.0)	4.5 (2.0, 6.0)	8/	9 (88.9)	6.0 (2.0, 20.0)	1.189 (0.066, 21.420)	0.907		1.643 (0.386, 6.993)	0.502		
Gender													
Male	17/	21 (81.0)	6.0 (4.0, 10.0)	12/	18 (66.7)	8.0 (4.0, NE)	1.616 (0.640, 4.083)	0.310	0.826	1.865 (0.876, 3.969)	0.106		0.846
Female	23/	27 (85.2)	5.0 (3.0, 8.0)	19/	30 (63.3)	18.0 (7.0, NE)	1.906 (0.925, 3.924)	0.080		2.123 (1.147, 3.928)	0.016		
Geographic region													
United States	25/	30 (83.3)		16/	26 (61.5)								
Europe	9/	10 (90.0)		9/	12 (75.0)								
India	0/			0/									
Rest of World	6/	8 (75.0)		6/	10 (60.0)								
COVID-19 therapeutic mAb treatment at randomisation													
Yes	3/	3 (100.0)		4/	5 (80.0)								
No	37/	45 (82.2)		27/	43 (62.8)								
Baseline viral load 1													
< 10^4 copies/mL	7/	12 (58.3)	10.0 (4.0, 22.0)	8/	11 (72.7)	6.0 (2.0, NE)	0.618 (0.164, 2.332)	0.477	0.067	0.885 (0.320, 2.448)	0.814		0.064
>= 10^4 copies/mL	32/	35 (91.4)	5.0 (3.0, 6.0)	23/	37 (62.2)	18.0 (12.0, 22.0)	2.569 (1.429, 4.617)	0.002		2.727 (1.576, 4.720)	<.001		
Baseline viral load 2													
< 10^7 copies/mL	26/	33 (78.8)	6.0 (4.0, 10.0)	23/	37 (62.2)	14.5 (7.0, NE)	1.728 (0.934, 3.197)	0.081	0.981	1.917 (1.086, 3.384)	0.025		0.897
>= 10^7 copies/mL	13/	14 (92.9)	4.5 (3.0, 13.0)	8/	11 (72.7)	17.0 (3.0, 20.0)	2.183 (0.589, 8.085)	0.243		2.187 (0.888, 5.383)	0.089		
Baseline serology status													
Negative	16/	18 (88.9)	5.0 (3.0, 13.0)	18/	31 (58.1)	18.0 (12.0, NE)	2.744 (1.277, 5.894)	0.010	0.233	2.790 (1.401, 5.556)	0.003		0.173
Positive	24/	30 (80.0)	6.0 (4.0, 8.0)	13/	17 (76.5)	8.0 (3.0, 20.0)	1.253 (0.628, 2.501)	0.522		1.340 (0.679, 2.644)	0.400		
Symptom onset days to first dose date													
<= 3	27/	32 (84.4)	5.0 (3.0, 6.0)	22/	26 (84.6)	12.5 (6.0, 18.0)	1.340 (0.734, 2.445)	0.341	0.095	1.400 (0.793, 2.472)	0.246		0.082
> 3	13/	16 (81.3)	7.0 (4.0, 14.0)	9/	22 (40.9)	NE (8.0, NE)	3.663 (1.236, 10.859)	0.019		4.067 (1.677, 9.861)	0.002		
BMI group													
< 25	4/	7 (57.1)	5.0 (3.0, NE)	3/	5 (60.0)	19.0 (3.0, NE)	3.11E8 (0.000, NE)	0.998	0.013	2.063 (0.432, 9.865)	0.364		0.013
25 - < 30	8/	11 (72.7)	7.0 (3.0, 25.0)	18/	22 (81.8)	7.0 (4.0, 14.0)	0.787 (0.309, 2.000)	0.614		0.833 (0.359, 1.930)	0.669		
>= 30	28/	30 (93.3)	5.5 (3.0, 8.0)	10/	21 (47.6)	NE (13.0, NE)	4.794 (2.038, 11.274)	<.001		4.460 (2.110, 9.428)	<.001		
Ethnicity													
White	35/	41 (85.4)		26/	37 (70.3)								
Black or African American	3/	4 (75.0)		2/	4 (50.0)								
Asian	0/	1 (0.0)		0/	1 (0.0)								
Others	2/	2 (100.0)		3/	6 (50.0)								
Number of baseline comorbidities present													
0-1	34/	40 (85.0)		24/	41 (58.5)								
2-3	6/	8 (75.0)		6/	6 (100.0)								
>= 4	0/			1/	1 (100.0)								
Presence of risk factor: Smoking													
Yes	16/	19 (84.2)	6.0 (4.0, 10.0)	13/	17 (76.5)	15.0 (3.0, 18.0)	1.386 (0.500, 3.840)	0.531	0.040	1.250 (0.597, 2.620)	0.554		0.130
No	23/	28 (82.1)	5.5 (3.0, 10.0)	18/	31 (58.1)	19.0 (8.0, NE)	2.865 (1.453, 5.651)	0.002		2.715 (1.445, 5.099)	0.002		

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough - Subgroup analysis

Subgroup Level	Nirmatrelvir/ritonavir (N=48)			Placebo (N=48)			Adjusted Analysis [2]			Unadjusted Analysis [3]		
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus												
Yes	2/	3 (66.7)		6/	6 (100.0)							
No	37/	44 (84.1)		25/	42 (59.5)							
Presence of risk factor: Immunosuppression												
Yes	0			0								
No	39/	47 (83.0)		31/	48 (64.6)							
Presence of risk factor: Chronic lung disease												
Yes	2/	3 (66.7)		0/	1 (0.0)							
No	37/	44 (84.1)		31/	47 (66.0)							
Presence of risk factor: Hypertension												
Yes	13/	17 (76.5)	5.0 (3.0, 14.0)	14/	18 (77.8)	8.0 (6.0, 16.0)	1.742 (0.728, 4.169)	0.212	0.687	1.819 (0.841, 3.933)	0.128	0.595
No	26/	30 (86.7)	6.0 (4.0, 10.0)	17/	30 (56.7)	19.0 (12.0, NE)	2.038 (0.999, 4.160)	0.050		2.222 (1.195, 4.132)	0.012	
Presence of risk factor: Cardiovascular disorder												
Yes	0			2/	2 (100.0)							
No	39/	47 (83.0)		29/	46 (63.0)							
Presence of risk factor: Chronic kidney disease												
Yes	1/	1 (100.0)		1/	1 (100.0)							
No	38/	46 (82.6)		30/	47 (63.8)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	39/	47 (83.0)		31/	48 (64.6)							
Presence of risk factor: Sickle Cell Disease												
No	39/	47 (83.0)		31/	48 (64.6)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0			1/	1 (100.0)							
No	39/	47 (83.0)		30/	47 (63.8)							
Presence of risk factor: Cancer												
Yes	0/	1 (0.0)		1/	1 (100.0)							
No	39/	46 (84.8)		30/	47 (63.8)							
Presence of risk factor: Device Dependence												
Yes	0			0								
No	39/	47 (83.0)		31/	47 (66.0)							

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[3] Estimated by cox regression model assuming proportional hazards.

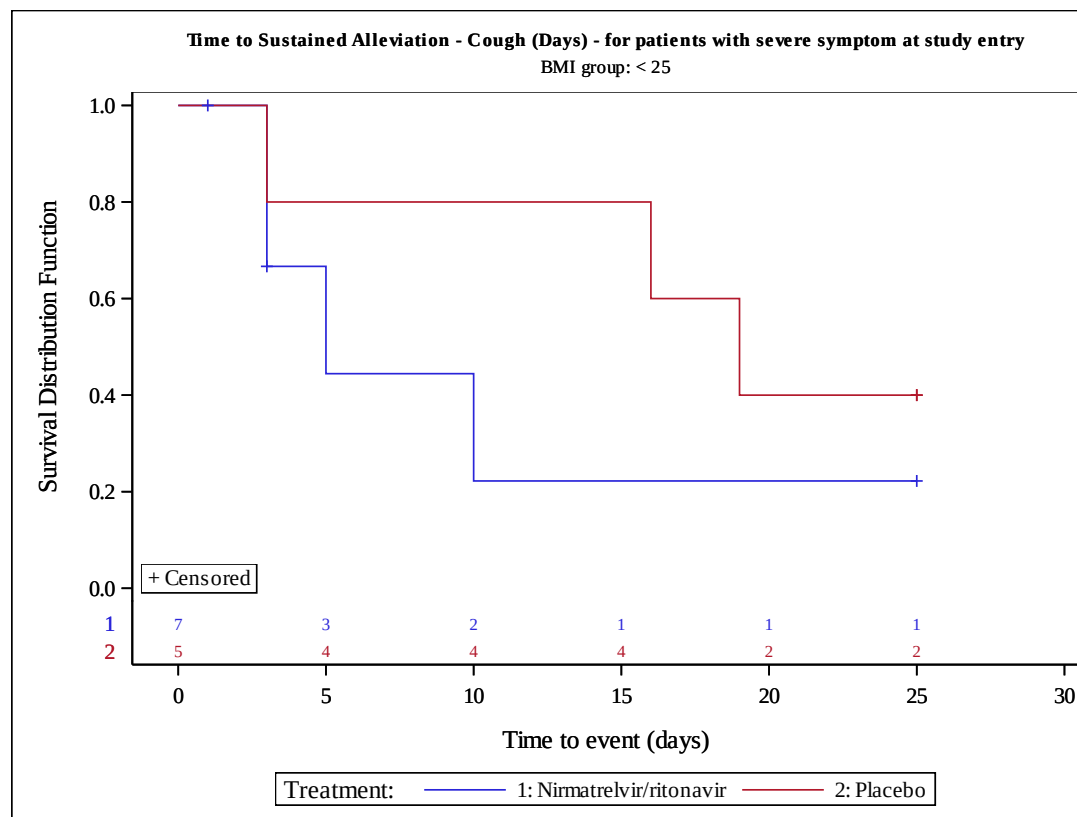
p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough

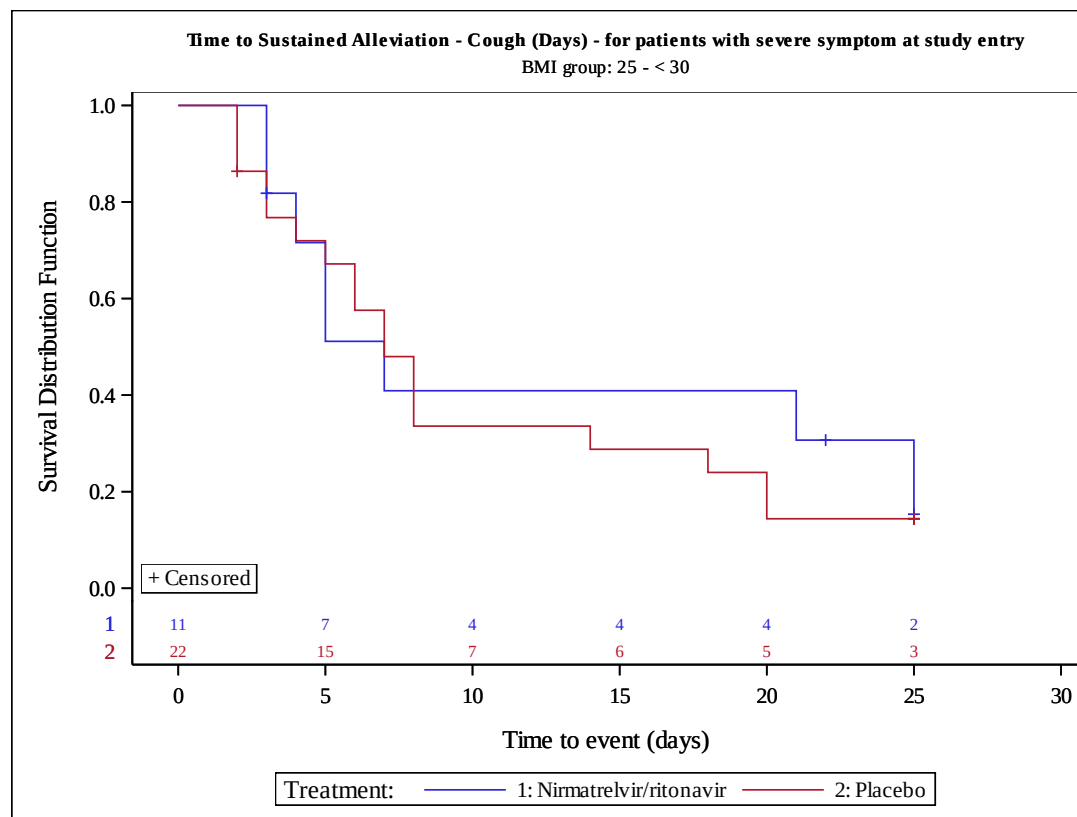
Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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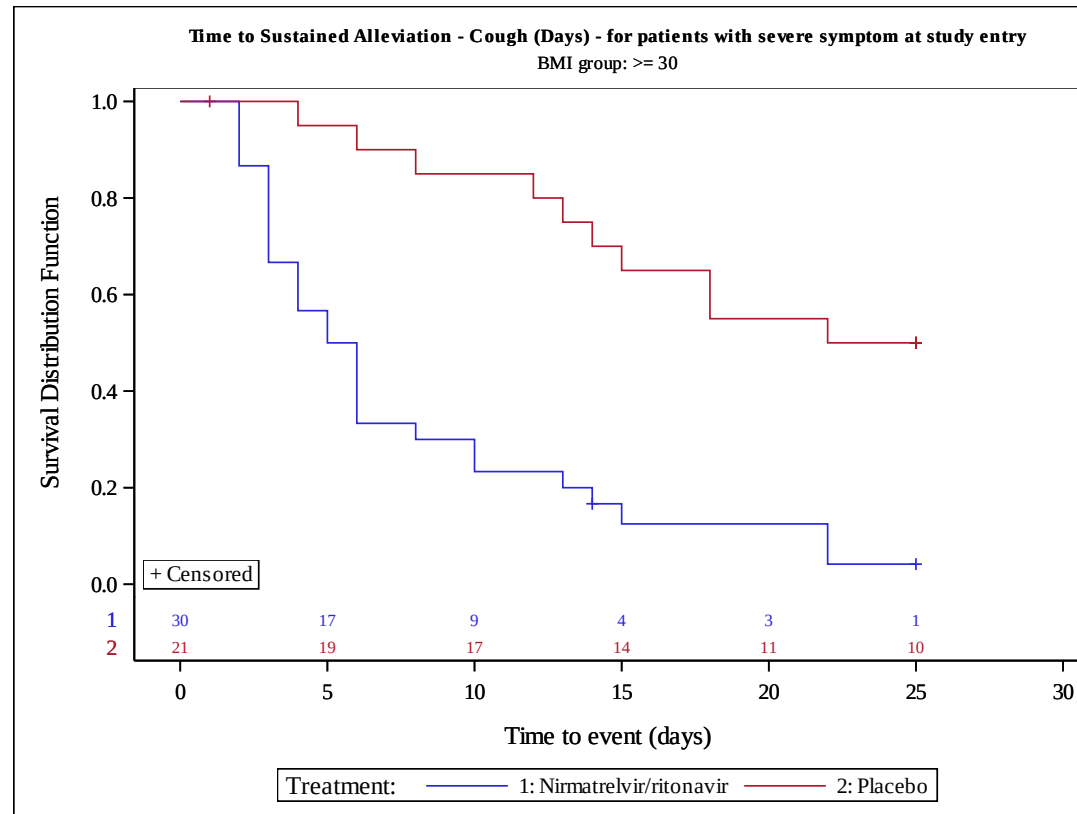
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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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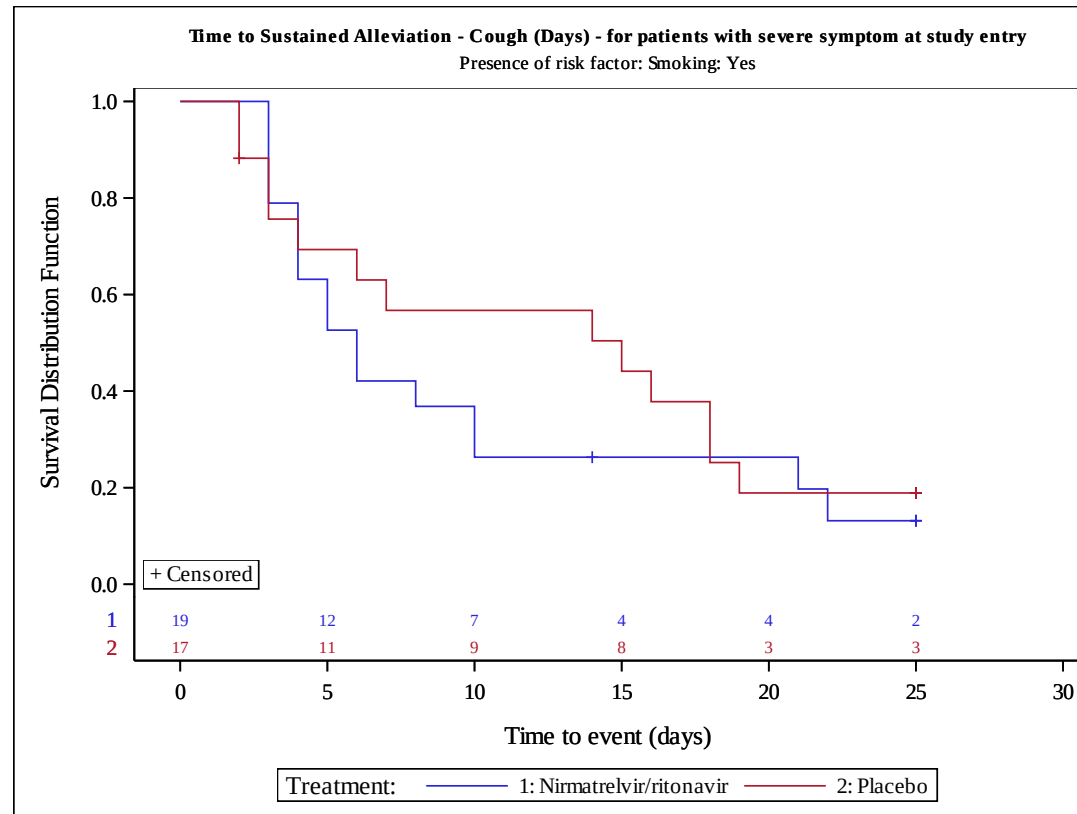
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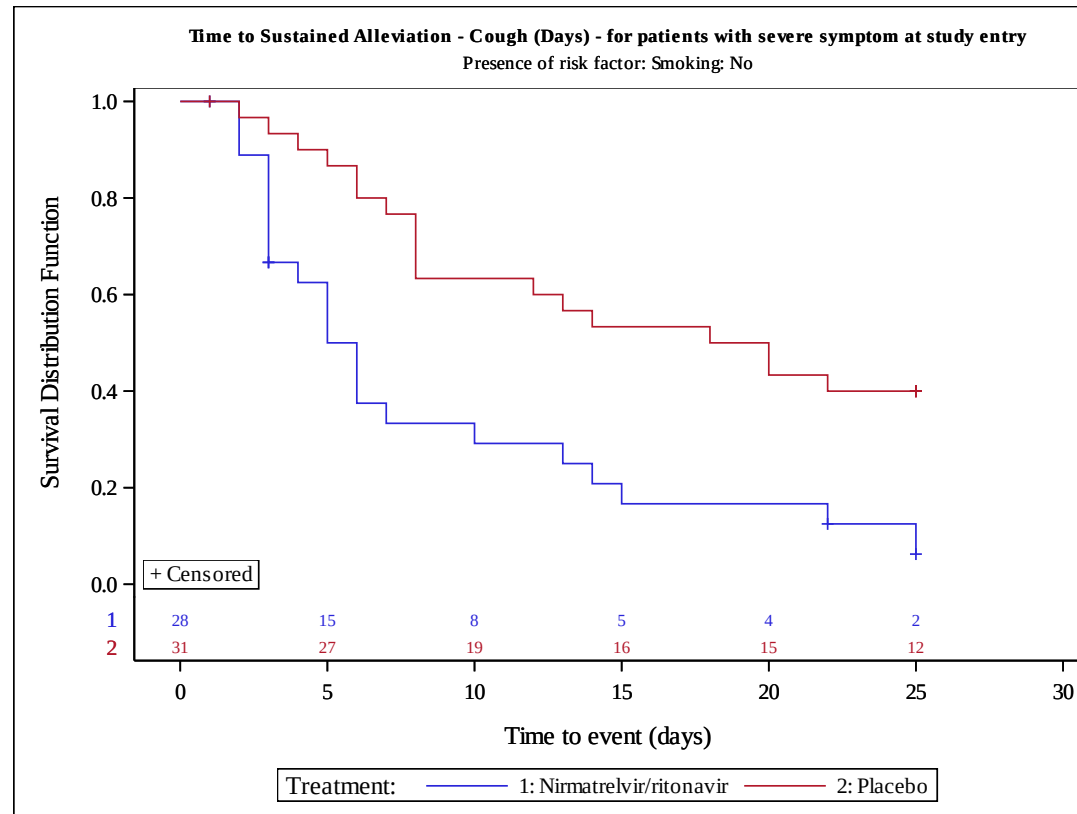


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Subgroup Level	Nirmatrelvir/ritonavir (N=766)			Placebo (N=798)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value	
Age													
< 65	468/ 644	(72.7)	13.0 (12.0, 14.0)	426/ 663	(64.3)	15.0 (14.0, 16.0)	1.265 (1.106, 1.446)	<.001	0.601	1.274 (1.117, 1.453)	<.001		0.508
>= 65	96/ 122	(78.7)	12.0 (10.0, 15.0)	92/ 135	(68.1)	15.0 (14.0, 19.0)	1.387 (1.031, 1.866)	0.031		1.418 (1.065, 1.889)	0.017		
Gender													
Male	300/ 380	(78.9)	12.0 (11.0, 12.0)	284/ 419	(67.8)	13.0 (12.0, 15.0)	1.336 (1.131, 1.578)	<.001	0.412	1.352 (1.149, 1.591)	<.001		0.505
Female	264/ 386	(68.4)	15.0 (13.0, 16.0)	234/ 379	(61.7)	18.0 (16.0, 19.0)	1.215 (1.015, 1.454)	0.033		1.264 (1.060, 1.507)	0.009		
Geographic region													
United States	224/ 324	(69.1)	13.0 (12.0, 15.0)	218/ 333	(65.5)	14.0 (12.0, 16.0)	1.111 (0.918, 1.344)	0.280	0.225	1.133 (0.940, 1.366)	0.189		0.172
Europe	194/ 260	(74.6)	14.0 (13.0, 15.0)	172/ 269	(63.9)	17.0 (15.0, 19.0)	1.383 (1.120, 1.708)	0.003		1.403 (1.143, 1.723)	0.001		
India	51/ 55	(92.7)	11.0 (9.0, 12.0)	53/ 60	(88.3)	11.0 (10.0, 12.0)	1.346 (0.903, 2.006)	0.144		1.252 (0.849, 1.847)	0.256		
Rest of World	95/ 127	(74.8)	12.0 (10.0, 15.0)	75/ 136	(55.1)	19.0 (14.0, 24.0)	1.681 (1.231, 2.295)	0.001		1.643 (1.212, 2.228)	0.001		
COVID-19 therapeutic mAb treatment at randomisation													
Yes	32/ 47	(68.1)	14.0 (11.0, 22.0)	38/ 56	(67.9)	16.0 (13.0, 19.0)	1.110 (0.686, 1.795)	0.671	0.594	1.102 (0.689, 1.765)	0.685		0.472
No	532/ 719	(74.0)	13.0 (12.0, 14.0)	480/ 742	(64.7)	15.0 (14.0, 16.0)	1.291 (1.138, 1.464)	<.001		1.311 (1.158, 1.483)	<.001		
Baseline viral load 1													
< 10^4 copies/mL	213/ 266	(80.1)	12.0 (11.0, 13.0)	204/ 285	(71.6)	13.0 (11.0, 14.0)	1.251 (1.030, 1.519)	0.024	0.757	1.240 (1.023, 1.503)	0.028		0.708
>= 10^4 copies/mL	334/ 478	(69.9)	14.0 (13.0, 15.0)	303/ 489	(62.0)	17.0 (15.0, 19.0)	1.293 (1.105, 1.512)	0.001		1.304 (1.116, 1.524)	<.001		
Baseline viral load 2													
< 10^7 copies/mL	394/ 525	(75.0)	12.0 (12.0, 13.0)	395/ 586	(67.4)	14.0 (13.0, 15.0)	1.268 (1.101, 1.460)	<.001	0.782	1.266 (1.101, 1.456)	<.001		0.628
>= 10^7 copies/mL	153/ 219	(69.9)	14.0 (13.0, 17.0)	112/ 188	(59.6)	19.0 (16.0, 21.0)	1.341 (1.044, 1.721)	0.021		1.372 (1.075, 1.752)	0.011		
Baseline serology status													
Negative	250/ 357	(70.0)	14.0 (13.0, 15.0)	229/ 389	(58.9)	18.0 (16.0, 20.0)	1.373 (1.144, 1.649)	<.001	0.490	1.400 (1.170, 1.675)	<.001		0.291
Positive	310/ 402	(77.1)	12.0 (11.0, 13.0)	282/ 398	(70.9)	13.0 (12.0, 15.0)	1.228 (1.043, 1.447)	0.014		1.215 (1.034, 1.428)	0.018		
Symptom onset days to first dose date													
<= 3	392/ 510	(76.9)	13.0 (12.0, 13.0)	345/ 513	(67.3)	15.0 (14.0, 16.0)	1.293 (1.116, 1.498)	<.001	0.781	1.317 (1.140, 1.523)	<.001		0.707
> 3	172/ 256	(67.2)	13.0 (12.0, 15.0)	173/ 285	(60.7)	17.0 (14.0, 19.0)	1.242 (0.999, 1.544)	0.051		1.246 (1.009, 1.539)	0.041		
BMI group													
< 25	127/ 165	(77.0)	11.0 (10.0, 13.0)	125/ 177	(70.6)	14.0 (12.0, 16.0)	1.444 (1.110, 1.879)	0.006	0.508	1.409 (1.099, 1.805)	0.007		0.547
25 - < 30	201/ 268	(75.0)	12.0 (11.0, 13.0)	192/ 276	(69.6)	15.0 (13.0, 16.0)	1.189 (0.971, 1.456)	0.094		1.198 (0.982, 1.460)	0.074		
>= 30	236/ 333	(70.9)	15.0 (13.0, 17.0)	201/ 345	(58.3)	18.0 (15.0, 21.0)	1.398 (1.149, 1.702)	<.001		1.351 (1.119, 1.631)	0.002		
Ethnicity													
White	425/ 588	(72.3)	14.0 (13.0, 15.0)	384/ 608	(63.2)	16.0 (15.0, 18.0)	1.284 (1.115, 1.479)	<.001	0.629	1.332 (1.160, 1.529)	<.001		0.528
Black or African American	23/ 34	(67.6)	11.0 (7.0, 13.0)	23/ 36	(63.9)	16.0 (8.0, 25.0)	1.113 (0.569, 2.175)	0.755		1.230 (0.689, 2.199)	0.484		
Asian	73/ 85	(85.9)	10.0 (9.0, 12.0)	82/ 95	(86.3)	11.0 (9.0, 12.0)	1.147 (0.830, 1.584)	0.406		1.073 (0.782, 1.473)	0.661		
Others	43/ 59	(72.9)	17.0 (13.0, 19.0)	29/ 59	(49.2)	20.0 (17.0, NE)	1.635 (0.999, 2.677)	0.051		1.616 (1.007, 2.593)	0.047		
Number of baseline comorbidities present													
0-1	426/ 580	(73.4)		394/ 593	(66.4)								
2-3	135/ 182	(74.2)		121/ 200	(60.5)								
>= 4	3/ 4	(75.0)		3/ 5	(60.0)								
Presence of risk factor: Smoking													
Yes	249/ 323	(77.1)	12.0 (11.0, 12.0)	233/ 357	(65.3)	15.0 (13.0, 16.0)	1.450 (1.206, 1.743)	<.001	0.251	1.432 (1.197, 1.714)	<.001		0.148
No	314/ 441	(71.2)	14.0 (13.0, 15.0)	285/ 441	(64.6)	16.0 (14.0, 18.0)	1.213 (1.030, 1.429)	0.021		1.212 (1.032, 1.423)	0.019		

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=766)			Placebo (N=798)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus										0.481				0.297
Yes	86/ 110	(78.2)	11.0 (8.0, 13.0)	81/ 120	(67.5)	14.0 (11.0, 19.0)	1.441 (1.053, 1.972)	0.023			1.480 (1.092, 2.007)	0.012		
No	477/ 655	(72.8)	13.0 (12.0, 14.0)	437/ 678	(64.5)	15.0 (14.0, 17.0)	1.262 (1.105, 1.441)	<.001			1.266 (1.112, 1.442)	<.001		
Presence of risk factor: Immunosuppression										0.156				0.241
Yes	4/ 6	(66.7)	11.5 (6.0, NE)	6/ 6	(100.0)	12.5 (2.0, 24.0)	0.305 (0.026, 3.592)	0.345			0.619 (0.173, 2.215)	0.460		
No	559/ 759	(73.6)	13.0 (12.0, 14.0)	512/ 792	(64.6)	15.0 (14.0, 17.0)	1.285 (1.137, 1.452)	<.001			1.303 (1.156, 1.469)	<.001		
Presence of risk factor: Chronic lung disease										0.608				0.843
Yes	39/ 54	(72.2)	16.0 (13.0, 19.0)	17/ 31	(54.8)	16.0 (12.0, NE)	1.260 (0.671, 2.368)	0.472			1.383 (0.782, 2.445)	0.265		
No	524/ 711	(73.7)	13.0 (12.0, 13.0)	501/ 767	(65.3)	15.0 (14.0, 16.0)	1.276 (1.126, 1.446)	<.001			1.302 (1.151, 1.471)	<.001		
Presence of risk factor: Hypertension										0.782				0.685
Yes	213/ 300	(71.0)	14.0 (13.0, 15.0)	214/ 335	(63.9)	15.0 (14.0, 18.0)	1.235 (1.018, 1.499)	0.032			1.250 (1.034, 1.512)	0.021		
No	350/ 465	(75.3)	12.0 (12.0, 13.0)	304/ 463	(65.7)	15.0 (14.0, 16.0)	1.301 (1.112, 1.523)	0.001			1.322 (1.133, 1.541)	<.001		
Presence of risk factor: Cardiovascular disorder										0.770				0.987
Yes	27/ 37	(73.0)	15.0 (11.0, 19.0)	28/ 44	(63.6)	15.5 (11.0, NE)	1.242 (0.694, 2.223)	0.466			1.291 (0.761, 2.191)	0.344		
No	536/ 728	(73.6)	13.0 (12.0, 14.0)	490/ 754	(65.0)	15.0 (14.0, 17.0)	1.271 (1.122, 1.440)	<.001			1.293 (1.144, 1.462)	<.001		
Presence of risk factor: Chronic kidney disease										0.208				0.380
Yes	4/ 6	(66.7)	10.0 (2.0, NE)	4/ 7	(57.1)	23.0 (7.0, NE)	26.980 (0.742, 981.50)	0.072			2.313 (0.569, 9.409)	0.241		
No	559/ 759	(73.6)	13.0 (12.0, 14.0)	514/ 791	(65.0)	15.0 (14.0, 16.0)	1.268 (1.122, 1.433)	<.001			1.288 (1.142, 1.452)	<.001		
Presence of risk factor: HIV Infection														
Yes	0			1/ 1	(100.0)									
No	563/ 765	(73.6)		516/ 796	(64.8)									
Presence of risk factor: Sickel Cell Disease														
No	563/ 765	(73.6)		518/ 798	(64.9)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/ 2	(100.0)		0/ 1	(0.0)									
No	561/ 763	(73.5)		518/ 797	(65.0)									
Presence of risk factor: Cancer														
Yes	2/ 3	(66.7)		5/ 5	(100.0)									
No	561/ 762	(73.6)		513/ 793	(64.7)									
Presence of risk factor: Device Dependence														
Yes	1/ 4	(25.0)		1/ 3	(33.3)									
No	556/ 753	(73.8)		515/ 789	(65.3)									

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Subgroup Level	Nirmatrelvir/ritonavir (N=48)			Placebo (N=48)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Age												
< 65	28/	44 (63.6)	17.0 (12.0, 23.0)	14/	39 (35.9)	NE (24.0, NE)	2.167 (1.099, 4.275)	0.026	0.351	2.516 (1.320, 4.795)	0.005	0.269
>= 65	3/	4 (75.0)	19.0 (6.0, 22.0)	8/	9 (88.9)	16.0 (6.0, 23.0)	3.735 (0.154, 90.337)	0.418		1.131 (0.289, 4.432)	0.860	
Gender												
Male	15/	21 (71.4)	11.0 (7.0, 21.0)	10/	18 (55.6)	21.0 (12.0, NE)	2.974 (1.119, 7.906)	0.029	0.251	2.133 (0.953, 4.774)	0.065	0.779
Female	16/	27 (59.3)	21.0 (13.0, NE)	12/	30 (40.0)	NE (18.0, NE)	1.285 (0.548, 3.013)	0.564		1.835 (0.864, 3.894)	0.114	
Geographic region												
United States	21/	30 (70.0)		10/	26 (38.5)							
Europe	6/	10 (60.0)		9/	12 (75.0)							
India	0/			0/								
Rest of World	4/	8 (50.0)		3/	10 (30.0)							
COVID-19 therapeutic mAb treatment at randomisation												
Yes	3/	3 (100.0)		4/	5 (80.0)							
No	28/	45 (62.2)		18/	43 (41.9)							
Baseline viral load 1												
< 10^4 copies/mL	7/	12 (58.3)	17.0 (6.0, 22.0)	6/	11 (54.5)	14.0 (6.0, NE)	2.259 (0.506, 10.086)	0.286	0.814	1.574 (0.526, 4.711)	0.418	0.938
>= 10^4 copies/mL	23/	35 (65.7)	20.0 (12.0, 25.0)	16/	37 (43.2)	NE (20.0, NE)	1.628 (0.838, 3.164)	0.151		1.975 (1.042, 3.745)	0.037	
Baseline viral load 2												
< 10^7 copies/mL	23/	33 (69.7)	15.0 (10.0, 21.0)	17/	37 (45.9)	NE (16.0, NE)	2.215 (1.133, 4.329)	0.020	0.162	2.394 (1.271, 4.510)	0.007	0.240
>= 10^7 copies/mL	7/	14 (50.0)	23.0 (14.0, NE)	5/	11 (45.5)	NE (7.0, NE)	0.722 (0.167, 3.130)	0.664		1.133 (0.359, 3.577)	0.832	
Baseline serology status												
Negative	10/	18 (55.6)	21.0 (10.0, NE)	12/	31 (38.7)	NE (21.0, NE)	1.633 (0.681, 3.915)	0.272	0.995	1.856 (0.800, 4.305)	0.150	0.740
Positive	21/	30 (70.0)	17.0 (11.0, 22.0)	10/	17 (58.8)	19.0 (12.0, NE)	1.734 (0.782, 3.844)	0.175		1.531 (0.719, 3.261)	0.270	
Symptom onset days to first dose date												
<= 3	23/	32 (71.9)	14.0 (8.0, 21.0)	16/	26 (61.5)	19.5 (15.0, NE)	1.633 (0.838, 3.182)	0.150	0.765	1.608 (0.847, 3.055)	0.147	0.528
> 3	8/	16 (50.0)	22.0 (11.0, NE)	6/	22 (27.3)	NE (21.0, NE)	3.335 (0.779, 14.274)	0.104		2.460 (0.851, 7.111)	0.096	
BMI group												
< 25	3/	7 (42.9)	8.0 (4.0, NE)	2/	5 (40.0)	NE (15.0, NE)	7.863 (0.408, 151.37)	0.172	0.092	2.423 (0.396, 14.829)	0.338	0.141
25 - < 30	7/	11 (63.6)	13.5 (4.0, NE)	15/	22 (68.2)	17.0 (11.0, 24.0)	1.127 (0.440, 2.885)	0.804		1.112 (0.453, 2.731)	0.817	
>= 30	21/	30 (70.0)	20.0 (12.0, 23.0)	5/	21 (23.8)	NE (23.0, NE)	4.077 (1.418, 11.722)	0.009		4.542 (1.701, 12.125)	0.003	
Ethnicity												
White	27/	41 (65.9)		18/	37 (48.6)							
Black or African American	2/	4 (50.0)		2/	4 (50.0)							
Asian	0/	1 (0.0)		0/	1 (0.0)							
Others	2/	2 (100.0)		2/	6 (33.3)							
Number of baseline comorbidities present												
0-1	26/	40 (65.0)		17/	41 (41.5)							
2-3	5/	8 (62.5)		4/	6 (66.7)							
>= 4	0/			1/	1 (100.0)							
Presence of risk factor: Smoking												
Yes	15/	19 (78.9)	15.0 (7.0, 22.0)	9/	17 (52.9)	21.5 (12.0, NE)	1.958 (0.727, 5.271)	0.184	0.701	1.900 (0.828, 4.360)	0.130	0.869
No	15/	28 (53.6)	20.0 (13.0, NE)	13/	31 (41.9)	NE (20.0, NE)	1.754 (0.796, 3.862)	0.163		1.772 (0.841, 3.735)	0.132	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=48)			Placebo (N=48)			Adjusted Analysis [2]			Unadjusted Analysis [3]		
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus												
Yes	2/	3 (66.7)		4/	6 (66.7)							
No	28/	44 (63.6)		18/	42 (42.9)							
Presence of risk factor: Immunosuppression												
Yes	0			0								
No	30/	47 (63.8)		22/	48 (45.8)							
Presence of risk factor: Chronic lung disease												
Yes	2/	3 (66.7)		0/	1 (0.0)							
No	28/	44 (63.6)		22/	47 (46.8)							
Presence of risk factor: Hypertension									0.071			0.077
Yes	7/	17 (41.2)	20.0 (12.0, NE)	11/	18 (61.1)	20.5 (15.0, NE)	0.808 (0.275, 2.376)	0.699		0.976 (0.376, 2.529)	0.959	
No	23/	30 (76.7)	18.0 (11.0, 22.0)	11/	30 (36.7)	NE (20.0, NE)	2.469 (1.117, 5.459)	0.026		2.776 (1.347, 5.723)	0.006	
Presence of risk factor: Cardiovascular disorder												
Yes	0			2/	2 (100.0)							
No	30/	47 (63.8)		20/	46 (43.5)							
Presence of risk factor: Chronic kidney disease												
Yes	0/	1 (0.0)		1/	1 (100.0)							
No	30/	46 (65.2)		21/	47 (44.7)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	30/	47 (63.8)		22/	48 (45.8)							
Presence of risk factor: Sickle Cell Disease												
No	30/	47 (63.8)		22/	48 (45.8)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0			0/	1 (0.0)							
No	30/	47 (63.8)		22/	47 (46.8)							
Presence of risk factor: Cancer												
Yes	0/	1 (0.0)		1/	1 (100.0)							
No	30/	46 (65.2)		21/	47 (44.7)							
Presence of risk factor: Device Dependence												
Yes	0			0								
No	30/	47 (63.8)		22/	47 (46.8)							

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 [1] Based on the Brookmeyer and Crowley Method.
 [2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.
 p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.
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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)		p-Value	p-Value		Relative Risk (95% CI)		p-Value		
Age							0.549					0.537
< 65	188/ 790 (23.8)	214/ 810 (26.4)	0.896 (0.753, 1.065)		0.212			0.901 (0.760, 1.067)		0.227		
>= 65	29/ 138 (21.0)	29/ 145 (20.0)	1.038 (0.656, 1.643)		0.874			1.051 (0.664, 1.663)		0.833		
Gender							0.391					0.355
Male	101/ 463 (21.8)	130/ 507 (25.6)	0.851 (0.676, 1.070)		0.168			0.851 (0.678, 1.068)		0.164		
Female	116/ 465 (24.9)	113/ 448 (25.2)	0.972 (0.773, 1.223)		0.811			0.989 (0.790, 1.238)		0.923		
Geographic region							0.044					0.052
United States	91/ 375 (24.3)	98/ 387 (25.3)	0.935 (0.726, 1.204)		0.600			0.958 (0.748, 1.227)		0.736		
Europe	75/ 322 (23.3)	81/ 321 (25.2)	0.916 (0.696, 1.207)		0.533			0.923 (0.702, 1.213)		0.566		
India	24/ 74 (32.4)	16/ 78 (20.5)	NE (NE, NE)		NE			1.581 (0.915, 2.732)		0.101		
Rest of World	27/ 157 (17.2)	48/ 169 (28.4)	0.629 (0.415, 0.952)		0.028			0.605 (0.398, 0.920)		0.019		
COVID-19 therapeutic mAb treatment at randomisation							0.243					0.252
Yes	21/ 57 (36.8)	18/ 60 (30.0)	1.256 (0.744, 2.121)		0.393			1.228 (0.734, 2.055)		0.434		
No	196/ 871 (22.5)	225/ 895 (25.1)	0.883 (0.745, 1.048)		0.155			0.895 (0.757, 1.058)		0.194		
Baseline viral load 1							0.534					0.589
< 10^4 copies/mL	70/ 335 (20.9)	76/ 354 (21.5)	0.991 (0.743, 1.323)		0.954			0.973 (0.730, 1.298)		0.854		
>= 10^4 copies/mL	140/ 569 (24.6)	160/ 575 (27.8)	0.869 (0.715, 1.056)		0.159			0.884 (0.728, 1.075)		0.216		
Baseline viral load 2							0.092					0.084
< 10^7 copies/mL	147/ 652 (22.5)	158/ 699 (22.6)	1.004 (0.824, 1.224)		0.967			0.997 (0.819, 1.215)		0.980		
>= 10^7 copies/mL	63/ 252 (25.0)	78/ 230 (33.9)	0.734 (0.555, 0.970)		0.030			0.737 (0.557, 0.975)		0.033		
Baseline serology status							0.617					0.648
Negative	105/ 435 (24.1)	125/ 456 (27.4)	0.876 (0.699, 1.098)		0.250			0.881 (0.704, 1.101)		0.265		
Positive	108/ 482 (22.4)	115/ 487 (23.6)	0.952 (0.755, 1.199)		0.674			0.949 (0.754, 1.195)		0.655		
Symptom onset days to first dose date							0.755					0.780
<= 3	156/ 624 (25.0)	173/ 624 (27.7)	0.894 (0.739, 1.081)		0.249			0.902 (0.749, 1.086)		0.275		
> 3	61/ 304 (20.1)	70/ 331 (21.1)	0.946 (0.695, 1.288)		0.723			0.949 (0.699, 1.288)		0.736		
BMI group							0.184					0.259
< 25	47/ 215 (21.9)	49/ 213 (23.0)	0.977 (0.684, 1.396)		0.898			0.950 (0.668, 1.352)		0.777		
25 - < 30	81/ 319 (25.4)	78/ 332 (23.5)	1.099 (0.832, 1.451)		0.507			1.081 (0.825, 1.416)		0.573		
>= 30	89/ 393 (22.6)	116/ 410 (28.3)	0.793 (0.620, 1.016)		0.066			0.800 (0.630, 1.017)		0.068		
Ethnicity							0.001					0.005
White	160/ 699 (22.9)	190/ 718 (26.5)	0.857 (0.712, 1.031)		0.102			0.865 (0.721, 1.038)		0.120		
Black or African American	11/ 43 (25.6)	5/ 40 (12.5)	2.624 (0.901, 7.644)		0.077			2.047 (0.779, 5.374)		0.146		
Asian	34/ 117 (29.1)	23/ 127 (18.1)	1.669 (1.045, 2.666)		0.032			1.605 (1.007, 2.556)		0.047		
Others	12/ 69 (17.4)	25/ 70 (35.7)	NE (NE, NE)		NE			0.487 (0.267, 0.890)		0.019		
Number of baseline comorbidities present							NE					0.270
0-1	177/ 710 (24.9)	189/ 728 (26.0)	0.936 (0.781, 1.121)		0.470			0.960 (0.804, 1.146)		0.653		
2-3	40/ 214 (18.7)	54/ 221 (24.4)	0.824 (0.571, 1.190)		0.302			0.765 (0.532, 1.100)		0.148		
>= 4	0/ 4 (0.0)	0/ 6 (0.0)	NE (NE, NE)		NE			NE (NE, NE)		NE		
Presence of risk factor: Smoking							0.598					0.817
Yes	94/ 417 (22.5)	105/ 438 (24.0)	0.969 (0.756, 1.243)		0.806			0.940 (0.737, 1.200)		0.621		
No	123/ 509 (24.2)	138/ 517 (26.7)	0.874 (0.707, 1.080)		0.212			0.905 (0.734, 1.117)		0.353		
Presence of risk factor: Diabetes mellitus							0.519					0.426

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928)		Placebo (N=955)		Adjusted analysis [1]				Unadjusted analysis [2]					
	n/N (%)		n/N (%)		Relative Risk (95% CI)			p-Value	Interaction p-Value	Relative Risk (95% CI)			p-Value	Interaction p-Value
Yes	26/ 130	(20.0)	35/ 136	(25.7)	0.777	(0.499,	1.208)	0.263		0.777	(0.497,	1.215)	0.269	
No	191/ 797	(24.0)	208/ 819	(25.4)	0.936	(0.786,	1.114)	0.456		0.944	(0.796,	1.119)	0.505	
Presence of risk factor: Immunosuppression									0.295					0.372
Yes	3/ 6	(50.0)	2/ 7	(28.6)	NE	(NE,	NE)	NE		1.750	(0.424,	7.229)	0.439	
No	214/ 921	(23.2)	241/ 948	(25.4)	0.907	(0.770,	1.067)	0.240		0.914	(0.779,	1.073)	0.271	
Presence of risk factor: Chronic lung disease									0.174					0.415
Yes	11/ 62	(17.7)	5/ 39	(12.8)	NE	(NE,	NE)	NE		1.384	(0.520,	3.681)	0.515	
No	206/ 865	(23.8)	238/ 916	(26.0)	0.902	(0.765,	1.063)	0.217		0.917	(0.780,	1.077)	0.291	
Presence of risk factor: Hypertension									0.691					0.649
Yes	79/ 348	(22.7)	96/ 371	(25.9)	0.877	(0.675,	1.139)	0.324		0.877	(0.677,	1.137)	0.322	
No	138/ 579	(23.8)	147/ 584	(25.2)	0.941	(0.765,	1.156)	0.562		0.947	(0.774,	1.159)	0.596	
Presence of risk factor: Cardiovascular disorder									0.287					0.168
Yes	3/ 42	(7.1)	9/ 49	(18.4)	NE	(NE,	NE)	NE		0.389	(0.113,	1.344)	0.135	
No	214/ 885	(24.2)	234/ 906	(25.8)	0.923	(0.784,	1.086)	0.334		0.936	(0.797,	1.099)	0.421	
Presence of risk factor: Chronic kidney disease									0.602					0.769
Yes	1/ 6	(16.7)	2/ 8	(25.0)	NE	(NE,	NE)	NE		0.667	(0.077,	5.749)	0.712	
No	216/ 921	(23.5)	241/ 947	(25.4)	0.916	(0.778,	1.078)	0.290		0.922	(0.786,	1.081)	0.316	
Presence of risk factor: HIV Infection														
Yes	0		0/ 1	(0.0)										
No	217/ 927	(23.4)	243/ 953	(25.5)										
Presence of risk factor: Sickle Cell Disease														
No	217/ 927	(23.4)	243/ 955	(25.4)										
Presence of risk factor: Neurodevelopmental Disorder														
Yes	0/ 2	(0.0)	0/ 1	(0.0)										
No	217/ 925	(23.5)	243/ 954	(25.5)										
Presence of risk factor: Cancer									0.020					0.200
Yes	2/ 5	(40.0)	0/ 6	(0.0)	NE	(NE,	NE)	NE		5.833	(0.343,	99.226)	0.223	
No	215/ 922	(23.3)	243/ 949	(25.6)	0.902	(0.767,	1.061)	0.213		0.911	(0.776,	1.068)	0.250	
Presence of risk factor: Device Dependence														
Yes	1/ 4	(25.0)	1/ 3	(33.3)										
No	215/ 914	(23.5)	242/ 944	(25.6)										

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

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Overall Study population
RKI-conform mITT2 Analysis set
Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Fatigue (low energy or tiredness) - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=812)			Placebo (N=837)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	564/ 688	(82.0)	8.0 (7.0, 9.0)	531/ 699	(76.0)	9.0 (8.0, 11.0)	1.274 (1.128, 1.439)	<.001	0.370		1.268 (1.126, 1.428)	<.001	0.212	
>= 65	107/ 124	(86.3)	8.0 (7.0, 10.0)	98/ 138	(71.0)	9.0 (8.0, 15.0)	1.466 (1.102, 1.950)	0.009			1.538 (1.165, 2.030)	0.002		
Gender														
Male	324/ 385	(84.2)	8.0 (7.0, 9.0)	323/ 428	(75.5)	9.0 (8.0, 11.0)	1.370 (1.169, 1.606)	<.001	0.426		1.374 (1.177, 1.604)	<.001	0.407	
Female	347/ 427	(81.3)	8.0 (7.0, 9.0)	306/ 409	(74.8)	9.0 (8.0, 12.0)	1.227 (1.047, 1.437)	0.011			1.255 (1.076, 1.465)	0.004		
Geographic region														
United States	268/ 339	(79.1)	8.0 (7.0, 9.0)	259/ 347	(74.6)	9.0 (8.0, 10.0)	1.209 (1.015, 1.440)	0.033	0.376		1.207 (1.017, 1.433)	0.031	0.243	
Europe	262/ 301	(87.0)	8.0 (7.0, 9.0)	228/ 297	(76.8)	10.0 (8.0, 12.0)	1.306 (1.086, 1.572)	0.005			1.342 (1.122, 1.604)	0.001		
India	40/ 43	(93.0)	10.0 (5.0, 14.0)	53/ 55	(96.4)	13.0 (11.0, 14.0)	1.332 (0.855, 2.075)	0.205			1.223 (0.807, 1.855)	0.342		
Rest of World	101/ 129	(78.3)	6.0 (4.0, 7.0)	89/ 138	(64.5)	10.0 (7.0, 15.0)	1.472 (1.099, 1.971)	0.009			1.539 (1.155, 2.050)	0.003		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	39/ 50	(78.0)	7.0 (5.0, 11.0)	39/ 51	(76.5)	10.5 (8.0, 15.0)	1.304 (0.822, 2.070)	0.260	0.988		1.319 (0.846, 2.059)	0.222	0.968	
No	632/ 762	(82.9)	8.0 (7.0, 9.0)	590/ 786	(75.1)	9.0 (8.0, 11.0)	1.304 (1.162, 1.463)	<.001			1.308 (1.168, 1.464)	<.001		
Baseline viral load 1														
< 10^4 copies/mL	240/ 285	(84.2)	8.0 (6.0, 8.0)	246/ 304	(80.9)	8.0 (7.0, 10.0)	1.147 (0.957, 1.375)	0.138	0.138		1.189 (0.995, 1.422)	0.057	0.208	
>= 10^4 copies/mL	410/ 504	(81.3)	8.0 (7.0, 9.0)	369/ 509	(72.5)	11.0 (9.0, 12.0)	1.384 (1.200, 1.596)	<.001			1.364 (1.185, 1.571)	<.001		
Baseline viral load 2														
< 10^7 copies/mL	457/ 561	(81.5)	8.0 (7.0, 9.0)	480/ 616	(77.9)	9.0 (8.0, 10.0)	1.198 (1.052, 1.364)	0.006	0.022		1.206 (1.060, 1.371)	0.004	0.028	
>= 10^7 copies/mL	193/ 228	(84.6)	8.0 (7.0, 9.0)	135/ 197	(68.5)	12.0 (9.0, 15.0)	1.585 (1.261, 1.992)	<.001			1.609 (1.289, 2.008)	<.001		
Baseline serology status														
Negative	323/ 393	(82.2)	9.0 (8.0, 10.0)	284/ 409	(69.4)	10.0 (9.0, 12.0)	1.315 (1.117, 1.549)	<.001	0.808		1.353 (1.153, 1.588)	<.001	0.593	
Positive	339/ 408	(83.1)	7.0 (6.0, 8.0)	335/ 416	(80.5)	9.0 (8.0, 10.0)	1.283 (1.100, 1.497)	0.002			1.285 (1.104, 1.495)	0.001		
Symptom onset days to first dose date														
<= 3	468/ 554	(84.5)	8.0 (7.0, 9.0)	427/ 549	(77.8)	9.0 (8.0, 11.0)	1.318 (1.152, 1.508)	<.001	0.902		1.313 (1.151, 1.498)	<.001	0.997	
> 3	203/ 258	(78.7)	8.0 (7.0, 9.0)	202/ 288	(70.1)	10.0 (8.0, 13.0)	1.261 (1.031, 1.542)	0.024			1.297 (1.067, 1.577)	0.009		
BMI group														
< 25	149/ 180	(82.8)	8.0 (7.0, 9.0)	140/ 173	(80.9)	8.0 (6.0, 11.0)	1.143 (0.895, 1.459)	0.285	0.337		1.196 (0.949, 1.509)	0.129	0.623	
25 - < 30	231/ 275	(84.0)	8.0 (7.0, 9.0)	227/ 303	(74.9)	9.0 (8.0, 11.0)	1.296 (1.074, 1.565)	0.007			1.317 (1.096, 1.583)	0.003		
>= 30	291/ 356	(81.7)	8.0 (7.0, 9.0)	262/ 361	(72.6)	10.0 (9.0, 12.0)	1.418 (1.191, 1.688)	<.001			1.363 (1.152, 1.611)	<.001		
Ethnicity														
White	533/ 644	(82.8)	8.0 (7.0, 9.0)	483/ 656	(73.6)	9.0 (8.0, 11.0)	1.311 (1.155, 1.488)	<.001	0.677		1.325 (1.171, 1.499)	<.001	0.659	
Black or African American	27/ 36	(75.0)	7.0 (4.0, 11.0)	31/ 36	(86.1)	7.0 (4.0, 10.0)	1.039 (0.601, 1.796)	0.891			1.069 (0.636, 1.796)	0.802		
Asian	62/ 68	(91.2)	6.0 (4.0, 10.0)	80/ 86	(93.0)	10.0 (7.0, 13.0)	1.315 (0.924, 1.872)	0.128			1.290 (0.923, 1.802)	0.135		
Others	49/ 64	(76.6)	7.5 (5.0, 11.0)	35/ 59	(59.3)	13.0 (8.0, 21.0)	1.510 (0.959, 2.376)	0.075			1.529 (0.988, 2.364)	0.057		
Number of baseline comorbidities present														
0-1	504/ 613	(82.2)	8.0 (7.0, 9.0)	475/ 623	(76.2)	10.0 (8.0, 11.0)	1.256 (1.104, 1.428)	<.001	0.525		1.261 (1.112, 1.430)	<.001	0.434	
2-3	164/ 195	(84.1)	8.0 (6.0, 9.0)	150/ 208	(72.1)	9.0 (8.0, 12.0)	1.395 (1.108, 1.756)	0.005			1.430 (1.143, 1.787)	0.002		
>= 4	3/ 4	(75.0)	11.5 (2.0, NE)	4/ 6	(66.7)	11.5 (6.0, NE)	0.518 (0.047, 5.683)	0.591			1.149 (0.256, 5.150)	0.856		
Presence of risk factor: Smoking														
Yes	306/ 363	(84.3)	8.0 (7.0, 9.0)	290/ 378	(76.7)	9.0 (8.0, 11.0)	1.280 (1.085, 1.510)	0.003	0.672		1.307 (1.112, 1.536)	0.001	0.930	
No	363/ 447	(81.2)	8.0 (7.0, 9.0)	339/ 459	(73.9)	10.0 (8.0, 11.0)	1.332 (1.144, 1.551)	<.001			1.311 (1.130, 1.521)	<.001		

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=812)			Placebo (N=837)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus										0.630				0.518
Yes	92/ 113	(81.4)	7.0 (6.0, 8.0)	94/ 126	(74.6)	9.0 (8.0, 13.0)	1.453 (1.070, 1.973)	0.017			1.401 (1.049, 1.871)	0.022		
No	578/ 698	(82.8)	8.0 (7.0, 9.0)	535/ 711	(75.2)	10.0 (8.0, 11.0)	1.293 (1.145, 1.458)	<.001			1.291 (1.147, 1.453)	<.001		
Presence of risk factor: Immunosuppression										0.816				0.935
Yes	5/ 6	(83.3)	4.5 (3.0, NE)	5/ 6	(83.3)	4.5 (3.0, NE)	1.263 (0.175, 9.099)	0.816			1.016 (0.290, 3.555)	0.981		
No	665/ 805	(82.6)	8.0 (7.0, 9.0)	624/ 831	(75.1)	9.0 (8.0, 11.0)	1.301 (1.163, 1.456)	<.001			1.308 (1.172, 1.460)	<.001		
Presence of risk factor: Chronic lung disease										0.625				0.615
Yes	47/ 58	(81.0)	9.0 (7.0, 11.0)	24/ 33	(72.7)	8.0 (5.0, 14.0)	1.022 (0.599, 1.746)	0.935			1.135 (0.694, 1.857)	0.614		
No	623/ 753	(82.7)	8.0 (7.0, 8.0)	605/ 804	(75.2)	9.0 (8.0, 11.0)	1.312 (1.170, 1.472)	<.001			1.319 (1.179, 1.476)	<.001		
Presence of risk factor: Hypertension										0.406				0.376
Yes	256/ 310	(82.6)	8.0 (7.0, 9.0)	245/ 340	(72.1)	9.0 (8.0, 12.0)	1.353 (1.128, 1.622)	0.001			1.371 (1.150, 1.636)	<.001		
No	414/ 501	(82.6)	7.0 (7.0, 9.0)	384/ 497	(77.3)	10.0 (8.0, 11.0)	1.249 (1.082, 1.441)	0.002			1.258 (1.095, 1.446)	0.001		
Presence of risk factor: Cardiovascular disorder										0.393				0.602
Yes	32/ 41	(78.0)	8.0 (5.0, 10.0)	32/ 47	(68.1)	10.0 (8.0, 17.0)	1.529 (0.913, 2.560)	0.106			1.441 (0.882, 2.355)	0.145		
No	638/ 770	(82.9)	8.0 (7.0, 9.0)	597/ 790	(75.6)	9.0 (8.0, 11.0)	1.289 (1.149, 1.445)	<.001			1.299 (1.161, 1.453)	<.001		
Presence of risk factor: Chronic kidney disease										0.784				0.572
Yes	4/ 6	(66.7)	10.0 (3.0, NE)	7/ 8	(87.5)	7.0 (5.0, 23.0)	10.065 (0.752, 134.65)	0.081			0.892 (0.255, 3.118)	0.858		
No	666/ 805	(82.7)	8.0 (7.0, 9.0)	622/ 829	(75.0)	10.0 (8.0, 11.0)	1.304 (1.165, 1.458)	<.001			1.311 (1.175, 1.464)	<.001		
Presence of risk factor: HIV Infection														
Yes	0			1/ 1	(100.0)									
No	670/ 811	(82.6)		627/ 835	(75.1)									
Presence of risk factor: Sickie Cell Disease														
No	670/ 811	(82.6)		629/ 837	(75.1)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/ 2	(100.0)		1/ 1	(100.0)									
No	668/ 809	(82.6)		628/ 836	(75.1)									
Presence of risk factor: Cancer														
Yes	3/ 4	(75.0)		5/ 5	(100.0)									
No	667/ 807	(82.7)		624/ 832	(75.0)									
Presence of risk factor: Device Dependence														
Yes	2/ 4	(50.0)		1/ 3	(33.3)									
No	662/ 798	(83.0)		624/ 826	(75.5)									

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

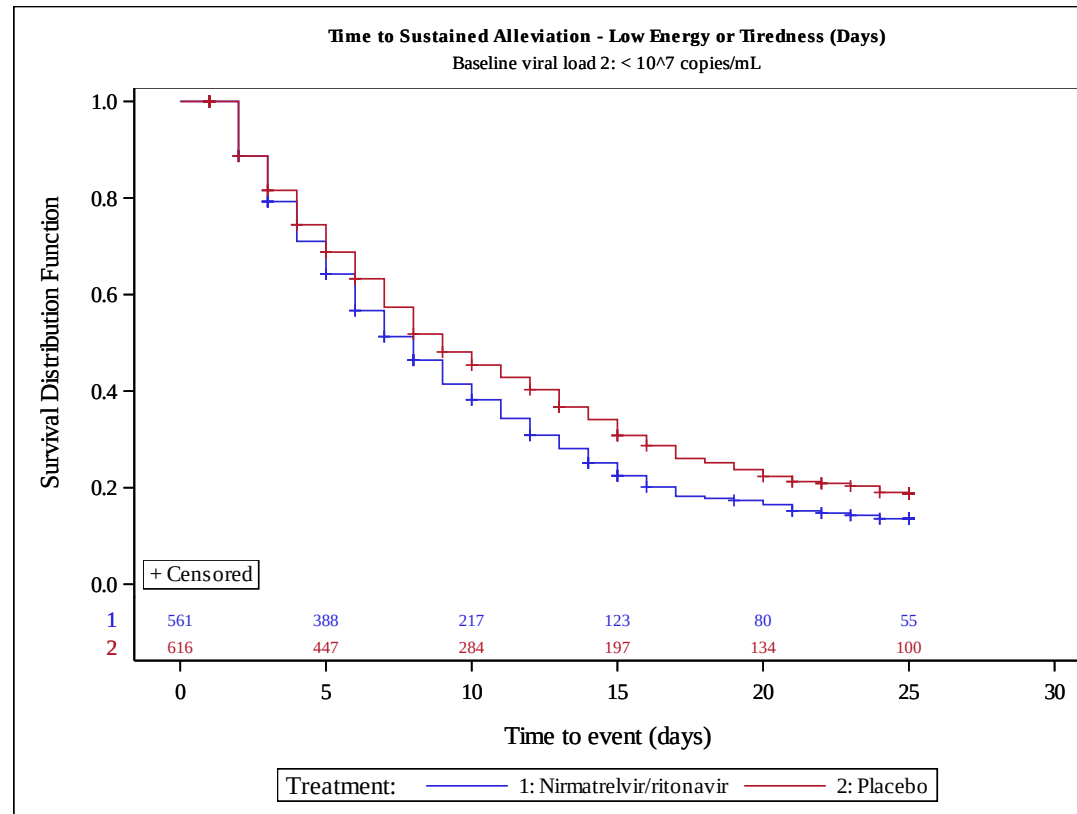
[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

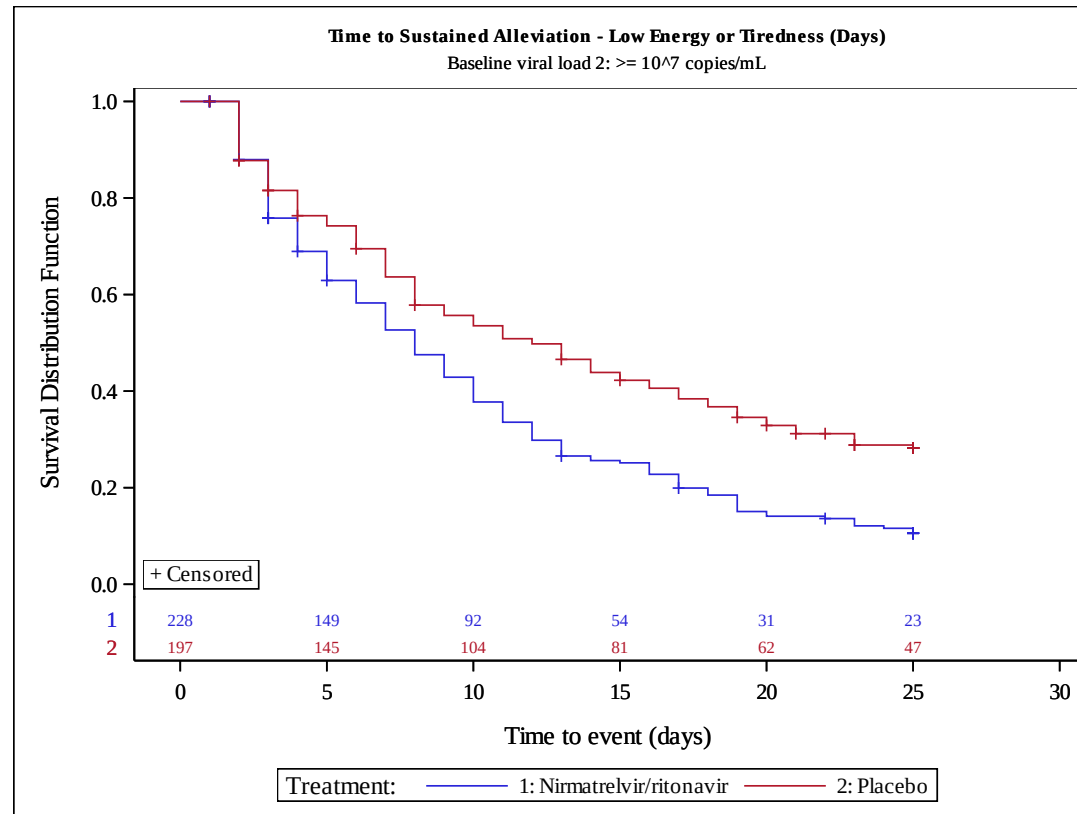


Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Fatigue (low energy or tiredness) - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=96)			Placebo (N=93)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Age												
< 65	70/	86 (81.4)	7.0 (4.0, 10.0)	54/	78 (69.2)	12.0 (8.0, 15.0)	1.616 (1.095, 2.386)	0.016	0.058	1.591 (1.114, 2.273)	0.011	0.119
>= 65	4/	10 (40.0)	NE (4.0, NE)	10/	15 (66.7)	15.0 (7.0, NE)	0.313 (0.064, 1.528)	0.151		0.631 (0.197, 2.025)	0.439	
Gender												
Male	30/	35 (85.7)	6.0 (3.0, 10.0)	21/	30 (70.0)	9.0 (7.0, 12.0)	1.255 (0.689, 2.288)	0.458	0.688	1.439 (0.823, 2.518)	0.202	0.964
Female	44/	61 (72.1)	9.0 (5.0, 12.0)	43/	63 (68.3)	15.0 (9.0, 18.0)	1.424 (0.888, 2.283)	0.142		1.450 (0.951, 2.209)	0.084	
Geographic region												
United States	40/	52 (76.9)		30/	46 (65.2)							
Europe	18/	23 (78.3)		20/	25 (80.0)							
India	0			0								
Rest of World	16/	21 (76.2)		14/	22 (63.6)							
COVID-19 therapeutic mAb treatment at randomisation												
Yes	4/	5 (80.0)	3.0 (2.0, 4.0)	8/	12 (66.7)	9.0 (4.0, NE)	37.187 (2.293, 603.22)	0.011	0.019	7.557 (1.582, 36.098)	0.011	0.015
No	70/	91 (76.9)	8.0 (5.0, 11.0)	56/	81 (69.1)	12.0 (9.0, 16.0)	1.315 (0.905, 1.910)	0.151		1.416 (0.996, 2.014)	0.053	
Baseline viral load 1												
< 10^4 copies/mL	19/	27 (70.4)	11.0 (4.0, 14.0)	15/	19 (78.9)	6.0 (4.0, 15.0)	0.884 (0.403, 1.940)	0.759	0.035	0.897 (0.455, 1.768)	0.753	0.093
>= 10^4 copies/mL	54/	68 (79.4)	6.5 (4.0, 10.0)	48/	72 (66.7)	13.0 (9.0, 18.0)	1.710 (1.115, 2.624)	0.014		1.707 (1.155, 2.522)	0.007	
Baseline viral load 2												
< 10^7 copies/mL	43/	55 (78.2)	9.0 (4.0, 12.0)	46/	69 (66.7)	13.0 (9.0, 18.0)	1.550 (0.970, 2.478)	0.067	0.414	1.605 (1.058, 2.435)	0.026	0.406
>= 10^7 copies/mL	30/	40 (75.0)	7.0 (4.0, 11.0)	17/	22 (77.3)	8.5 (6.0, 18.0)	1.159 (0.585, 2.296)	0.673		1.161 (0.639, 2.108)	0.624	
Baseline serology status												
Negative	40/	53 (75.5)	8.5 (4.0, 12.0)	39/	60 (65.0)	12.0 (8.0, 17.0)	1.407 (0.879, 2.254)	0.155	0.751	1.477 (0.950, 2.298)	0.084	0.998
Positive	34/	43 (79.1)	7.0 (4.0, 11.0)	23/	31 (74.2)	12.0 (6.0, 19.0)	1.496 (0.812, 2.758)	0.196		1.485 (0.872, 2.528)	0.145	
Symptom onset days to first dose date												
<= 3	54/	65 (83.1)	5.5 (4.0, 10.0)	36/	45 (80.0)	10.0 (7.0, 13.0)	1.560 (0.973, 2.501)	0.065	0.973	1.352 (0.886, 2.065)	0.162	0.999
> 3	20/	31 (64.5)	11.0 (8.0, 19.0)	28/	48 (58.3)	15.0 (9.0, NE)	1.419 (0.770, 2.615)	0.262		1.372 (0.772, 2.437)	0.281	
BMI group												
< 25	11/	17 (64.7)	4.5 (3.0, 12.0)	13/	18 (72.2)	14.0 (7.0, 21.0)	1.783 (0.610, 5.216)	0.291	0.304	1.670 (0.741, 3.765)	0.216	0.264
25 - < 30	25/	34 (73.5)	9.0 (5.0, 16.0)	17/	22 (77.3)	8.5 (6.0, 16.0)	0.972 (0.509, 1.853)	0.930		0.995 (0.536, 1.846)	0.987	
>= 30	38/	45 (84.4)	7.0 (4.0, 11.0)	34/	53 (64.2)	13.0 (9.0, 19.0)	1.880 (1.073, 3.295)	0.027		1.821 (1.143, 2.901)	0.012	
Ethnicity												
White	56/	75 (74.7)		52/	76 (68.4)							
Black or African American	5/	6 (83.3)		7/	8 (87.5)							
Asian	4/	4 (100.0)		1/	2 (50.0)							
Others	9/	11 (81.8)		4/	7 (57.1)							
Number of baseline comorbidities present												
0-1	58/	74 (78.4)		50/	72 (69.4)							
2-3	16/	21 (76.2)		13/	20 (65.0)							
>= 4	0/	1 (0.0)		1/	1 (100.0)							
Presence of risk factor: Smoking												
Yes	34/	40 (85.0)	5.0 (4.0, 10.0)	28/	31 (90.3)	9.0 (7.0, 13.0)	1.366 (0.781, 2.389)	0.274	0.597	1.202 (0.726, 1.992)	0.474	0.398
No	40/	56 (71.4)	9.0 (5.0, 12.0)	36/	62 (58.1)	15.0 (9.0, NE)	1.495 (0.883, 2.530)	0.134		1.589 (1.012, 2.495)	0.044	

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Subgroup Level	Nirmatrelvir/ritonavir (N=96)			Placebo (N=93)			Adjusted Analysis [2]			Interaction		Unadjusted Analysis [3]			Interaction	
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	p-Value			Hazard Ratio (95% CI)	p-Value	p-Value		
Presence of risk factor: Diabetes mellitus										0.546					0.536	
Yes	11/	17 (64.7)	8.5 (3.0, NE)	10/	14 (71.4)	12.0 (6.0, 24.0)	1.941 (0.703, 5.360)	0.201				1.222 (0.517, 2.885)	0.648			
No	63/	79 (79.7)	7.0 (5.0, 10.0)	54/	79 (68.4)	12.0 (8.0, 17.0)	1.496 (0.995, 2.249)	0.053				1.543 (1.071, 2.221)	0.020			
Presence of risk factor: Immunosuppression																
Yes	0			1/	1 (100.0)											
No	74/	96 (77.1)		63/	92 (68.5)											
Presence of risk factor: Chronic lung disease										0.964					0.946	
Yes	6/	10 (60.0)	9.0 (2.0, NE)	2/	4 (50.0)	NE (4.0, NE)	5.78E7 (0.000, NE)	0.996				1.437 (0.290, 7.133)	0.657			
No	68/	86 (79.1)	7.0 (4.0, 11.0)	62/	89 (69.7)	12.0 (9.0, 15.0)	1.450 (0.991, 2.121)	0.056				1.504 (1.065, 2.124)	0.020			
Presence of risk factor: Hypertension										0.295					0.434	
Yes	20/	30 (66.7)	11.0 (4.0, 18.0)	21/	34 (61.8)	15.0 (8.0, NE)	0.996 (0.508, 1.955)	0.991				1.175 (0.636, 2.169)	0.607			
No	54/	66 (81.8)	6.0 (4.0, 9.0)	43/	59 (72.9)	11.5 (8.0, 16.0)	1.705 (1.084, 2.681)	0.021				1.621 (1.084, 2.423)	0.019			
Presence of risk factor: Cardiovascular disorder										0.239					0.281	
Yes	1/	5 (20.0)	NE (6.0, NE)	3/	7 (42.9)	NE (4.0, NE)	1.658 (0.102, 27.070)	0.723				0.443 (0.046, 4.268)	0.481			
No	73/	91 (80.2)	7.0 (4.0, 10.0)	61/	86 (70.9)	12.0 (8.0, 15.0)	1.462 (1.005, 2.129)	0.047				1.522 (1.082, 2.141)	0.016			
Presence of risk factor: Chronic kidney disease																
Yes	0			1/	1 (100.0)											
No	74/	96 (77.1)		63/	92 (68.5)											
Presence of risk factor: HIV Infection																
Yes	0			0												
No	74/	96 (77.1)		64/	93 (68.8)											
Presence of risk factor: Sickle Cell Disease																
No	74/	96 (77.1)		64/	93 (68.8)											
Presence of risk factor: Neurodevelopmental Disorder																
Yes	0			0												
No	74/	96 (77.1)		64/	93 (68.8)											
Presence of risk factor: Cancer																
Yes	0			1/	1 (100.0)											
No	74/	96 (77.1)		63/	92 (68.5)											
Presence of risk factor: Device Dependence																
Yes	1/	2 (50.0)		0												
No	73/	93 (78.5)		64/	93 (68.8)											

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

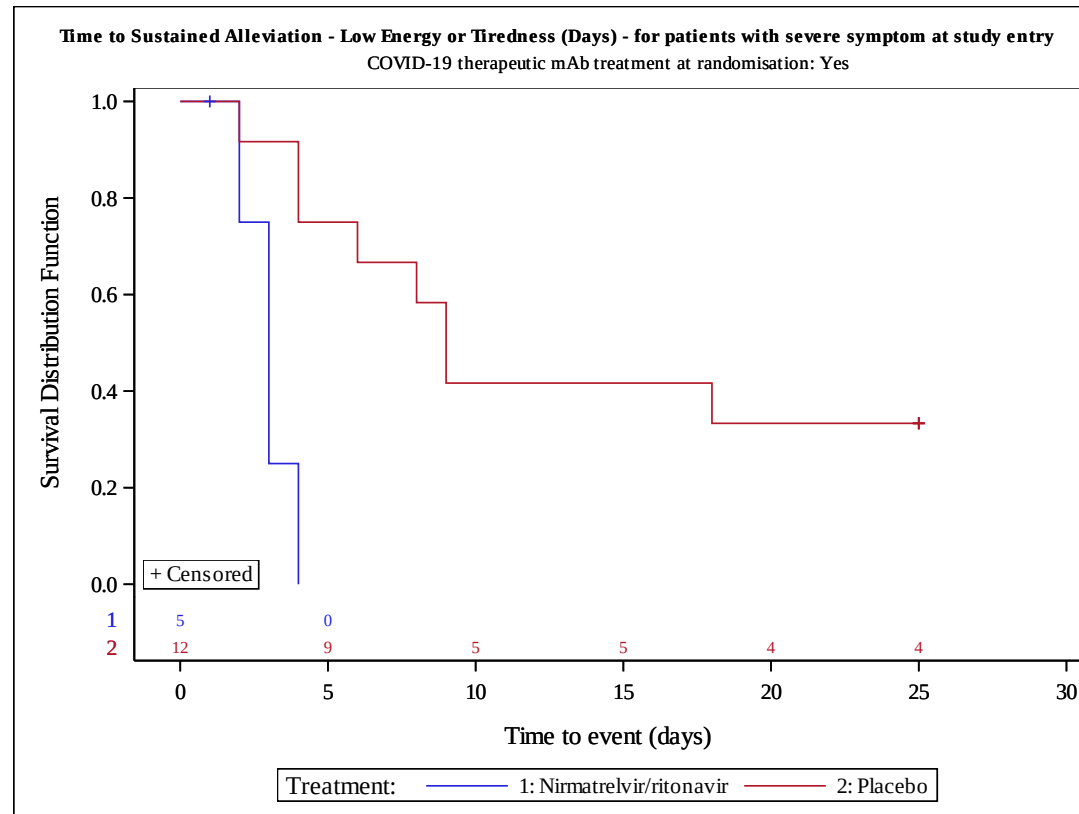
p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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 Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Fatigue (low energy or tiredness)

Final

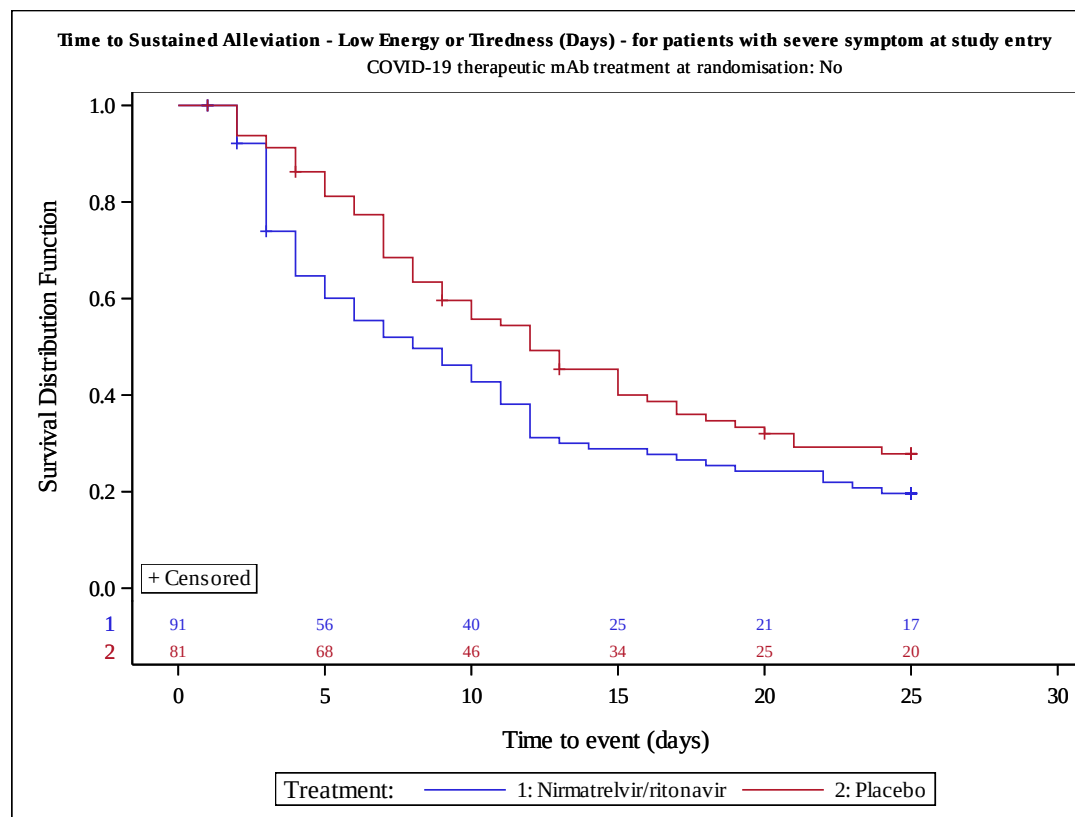


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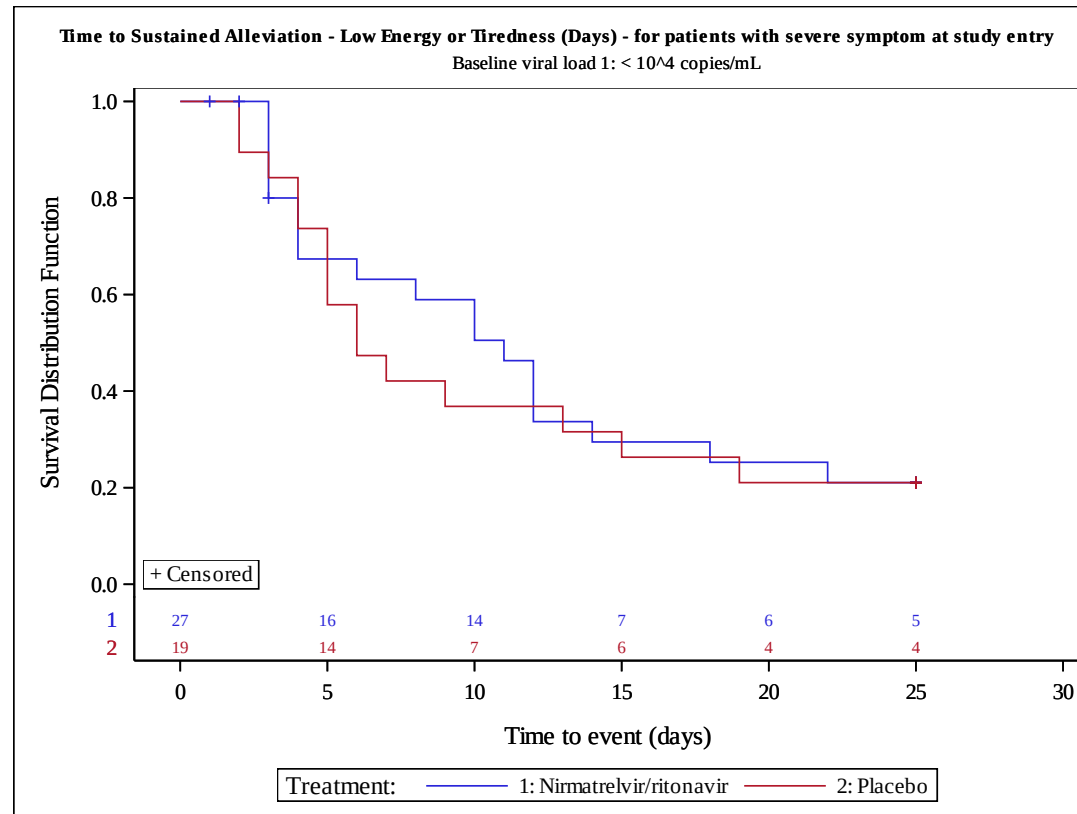
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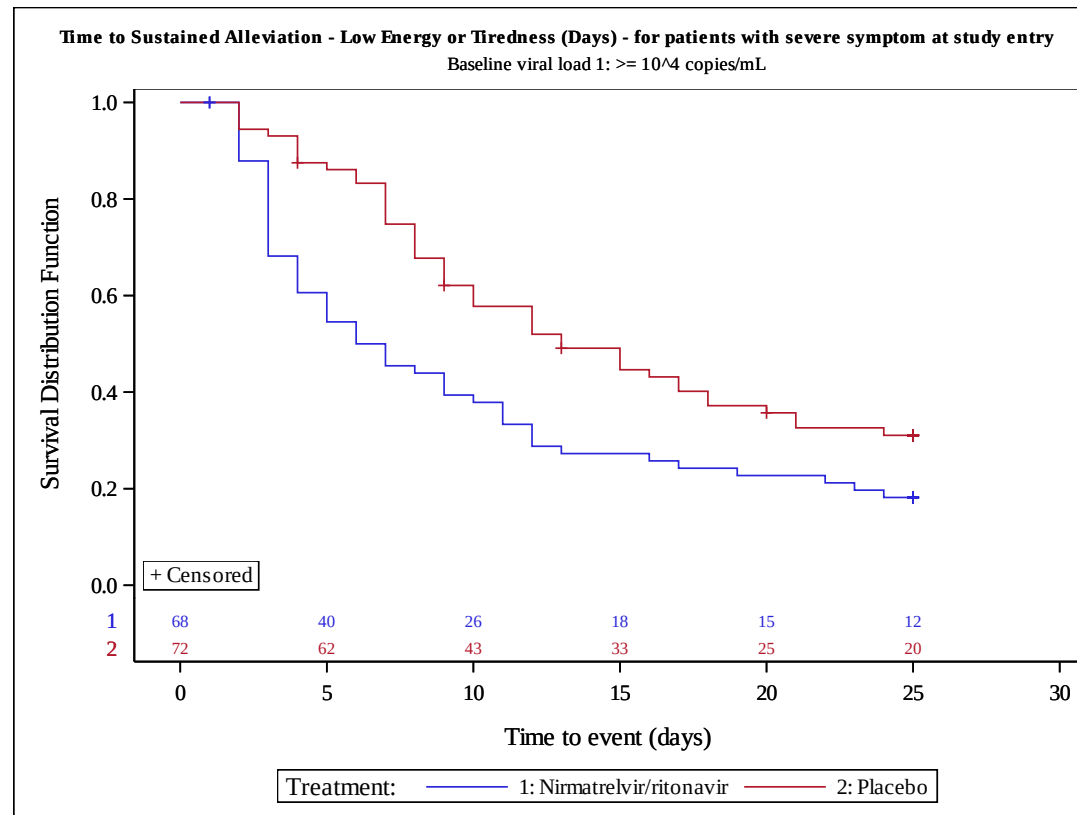
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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=812)			Placebo (N=837)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	480/ 688	(69.8)	13.0 (13.0, 15.0)	438/ 699	(62.7)	16.0 (15.0, 18.0)	1.285 (1.126, 1.468)	<.001		0.901	1.291 (1.134, 1.469)	<.001		0.813
>= 65	82/ 124	(66.1)	16.0 (14.0, 20.0)	79/ 138	(57.2)	21.0 (18.0, 25.0)	1.361 (0.990, 1.870)	0.057			1.380 (1.013, 1.881)	0.041		
Gender														
Male	299/ 385	(77.7)	12.0 (11.0, 13.0)	284/ 428	(66.4)	15.0 (14.0, 16.0)	1.421 (1.203, 1.680)	<.001		0.201	1.439 (1.222, 1.693)	<.001		0.163
Female	263/ 427	(61.6)	17.0 (15.0, 18.0)	233/ 409	(57.0)	20.0 (18.0, 23.0)	1.203 (1.005, 1.441)	0.044			1.229 (1.030, 1.466)	0.022		
Geographic region														
United States	225/ 339	(66.4)	13.0 (12.0, 16.0)	213/ 347	(61.4)	16.0 (14.0, 19.0)	1.201 (0.991, 1.455)	0.062		0.341	1.217 (1.009, 1.468)	0.040		0.225
Europe	211/ 301	(70.1)	15.0 (15.0, 17.0)	181/ 297	(60.9)	20.0 (18.0, 23.0)	1.349 (1.100, 1.655)	0.004			1.385 (1.136, 1.690)	0.001		
India	40/ 43	(93.0)	13.0 (9.0, 15.0)	53/ 55	(96.4)	14.0 (12.0, 15.0)	1.135 (0.727, 1.773)	0.578			1.096 (0.725, 1.656)	0.664		
Rest of World	86/ 129	(66.7)	11.0 (9.0, 14.0)	70/ 138	(50.7)	19.0 (15.0, NE)	1.541 (1.116, 2.127)	0.009			1.611 (1.174, 2.211)	0.003		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	36/ 50	(72.0)	13.0 (9.0, 16.0)	36/ 51	(70.6)	13.5 (11.0, 18.0)	1.068 (0.662, 1.725)	0.787		0.420	1.146 (0.722, 1.820)	0.564		0.590
No	526/ 762	(69.0)	14.0 (13.0, 15.0)	481/ 786	(61.2)	17.0 (16.0, 19.0)	1.314 (1.158, 1.491)	<.001			1.318 (1.165, 1.492)	<.001		
Baseline viral load 1														
< 10^4 copies/mL	200/ 285	(70.2)	14.0 (12.0, 15.0)	207/ 304	(68.1)	15.0 (14.0, 17.0)	1.146 (0.941, 1.394)	0.175		0.151	1.146 (0.943, 1.391)	0.171		0.120
>= 10^4 copies/mL	343/ 504	(68.1)	14.0 (13.0, 16.0)	298/ 509	(58.5)	19.0 (17.0, 21.0)	1.383 (1.183, 1.617)	<.001			1.396 (1.195, 1.630)	<.001		
Baseline viral load 2														
< 10^7 copies/mL	385/ 561	(68.6)	14.0 (13.0, 15.0)	399/ 616	(64.8)	16.0 (15.0, 18.0)	1.210 (1.050, 1.393)	0.008		0.066	1.208 (1.050, 1.390)	0.008		0.043
>= 10^7 copies/mL	158/ 228	(69.3)	14.0 (12.0, 16.0)	106/ 197	(53.8)	22.0 (18.0, NE)	1.518 (1.180, 1.952)	0.001			1.609 (1.257, 2.059)	<.001		
Baseline serology status														
Negative	270/ 393	(68.7)	15.0 (14.0, 16.0)	228/ 409	(55.7)	19.0 (17.0, 23.0)	1.384 (1.156, 1.656)	<.001		0.316	1.447 (1.213, 1.726)	<.001		0.115
Positive	285/ 408	(69.9)	13.0 (12.0, 15.0)	283/ 416	(68.0)	16.0 (15.0, 18.0)	1.215 (1.028, 1.437)	0.022			1.187 (1.007, 1.400)	0.041		
Symptom onset days to first dose date														
<= 3	394/ 554	(71.1)	14.0 (13.0, 15.0)	356/ 549	(64.8)	17.0 (16.0, 19.0)	1.285 (1.110, 1.488)	<.001		0.800	1.296 (1.122, 1.496)	<.001		0.796
> 3	168/ 258	(65.1)	15.0 (13.0, 16.0)	161/ 288	(55.9)	17.0 (15.0, 20.0)	1.299 (1.039, 1.623)	0.022			1.325 (1.068, 1.646)	0.011		
BMI group														
< 25	129/ 180	(71.7)	14.0 (11.0, 16.0)	121/ 173	(69.9)	15.0 (14.0, 18.0)	1.174 (0.904, 1.525)	0.228		0.493	1.227 (0.958, 1.573)	0.106		0.603
25 - < 30	196/ 275	(71.3)	14.0 (13.0, 15.0)	196/ 303	(64.7)	17.0 (16.0, 19.0)	1.270 (1.036, 1.556)	0.021			1.269 (1.041, 1.547)	0.019		
>= 30	237/ 356	(66.6)	14.0 (13.0, 16.0)	200/ 361	(55.4)	19.0 (16.0, 23.0)	1.405 (1.156, 1.708)	<.001			1.395 (1.155, 1.684)	<.001		
Ethnicity														
White	436/ 644	(67.7)	15.0 (14.0, 16.0)	392/ 656	(59.8)	18.0 (17.0, 20.0)	1.279 (1.113, 1.471)	<.001		0.365	1.314 (1.146, 1.506)	<.001		0.502
Black or African American	24/ 36	(66.7)	13.0 (8.0, 14.0)	22/ 36	(61.1)	19.0 (9.0, NE)	1.633 (0.858, 3.107)	0.135			1.517 (0.845, 2.723)	0.163		
Asian	61/ 68	(89.7)	10.0 (8.0, 13.0)	78/ 86	(90.7)	13.0 (10.0, 14.0)	1.295 (0.904, 1.855)	0.158			1.241 (0.886, 1.738)	0.209		
Others	41/ 64	(64.1)	13.0 (11.0, 20.0)	25/ 59	(42.4)	NE (17.0, NE)	1.702 (1.011, 2.868)	0.046			1.765 (1.072, 2.906)	0.025		
Number of baseline comorbidities present														
0-1	423/ 613	(69.0)	14.0 (13.0, 15.0)	401/ 623	(64.4)	17.0 (15.0, 18.0)	1.210 (1.052, 1.393)	0.008		0.193	1.224 (1.068, 1.403)	0.004		0.180
2-3	136/ 195	(69.7)	15.0 (13.0, 16.0)	112/ 208	(53.8)	23.0 (16.0, NE)	1.520 (1.177, 1.964)	0.001			1.579 (1.229, 2.029)	<.001		
>= 4	3/ 4	(75.0)	11.5 (2.0, NE)	4/ 6	(66.7)	18.5 (7.0, NE)	2.238 (0.224, 22.387)	0.493			1.529 (0.339, 6.889)	0.580		
Presence of risk factor: Smoking														
Yes	266/ 363	(73.3)	13.0 (12.0, 15.0)	244/ 378	(64.6)	16.0 (15.0, 18.0)	1.385 (1.159, 1.655)	<.001		0.405	1.373 (1.154, 1.635)	<.001		0.501
No	295/ 447	(66.0)	15.0 (13.0, 17.0)	273/ 459	(59.5)	18.0 (16.0, 21.0)	1.235 (1.044, 1.462)	0.014			1.262 (1.070, 1.488)	0.006		

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=812)			Placebo (N=837)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value	
Presence of risk factor: Diabetes mellitus													
Yes	83/ 113	(73.5)	13.0 (10.0, 15.0)	75/ 126	(59.5)	17.0 (15.0, 24.0)	1.761 (1.268, 2.445)	<.001	0.151	1.626 (1.188, 2.225)	0.002	0.119	
No	478/ 698	(68.5)	14.0 (13.0, 15.0)	442/ 711	(62.2)	17.0 (16.0, 19.0)	1.252 (1.097, 1.429)	<.001		1.256 (1.104, 1.430)	<.001		
Presence of risk factor: Immunosuppression													
Yes	5/ 6	(83.3)	6.5 (3.0, NE)	4/ 6	(66.7)	18.0 (3.0, NE)	2.096 (0.173, 25.364)	0.561	0.278	2.344 (0.592, 9.286)	0.225	0.263	
No	556/ 805	(69.1)	14.0 (13.0, 15.0)	513/ 831	(61.7)	17.0 (16.0, 19.0)	1.287 (1.138, 1.455)	<.001		1.300 (1.153, 1.466)	<.001		
Presence of risk factor: Chronic lung disease													
Yes	38/ 58	(65.5)	16.0 (12.0, 20.0)	16/ 33	(48.5)	24.0 (12.0, NE)	1.506 (0.780, 2.907)	0.222	0.449	1.526 (0.850, 2.740)	0.157	0.572	
No	523/ 753	(69.5)	14.0 (13.0, 15.0)	501/ 804	(62.3)	17.0 (16.0, 18.0)	1.287 (1.135, 1.459)	<.001		1.305 (1.154, 1.475)	<.001		
Presence of risk factor: Hypertension													
Yes	203/ 310	(65.5)	16.0 (15.0, 19.0)	198/ 340	(58.2)	20.0 (17.0, 23.0)	1.236 (1.011, 1.511)	0.039	0.644	1.273 (1.046, 1.548)	0.016	0.733	
No	358/ 501	(71.5)	13.0 (12.0, 14.0)	319/ 497	(64.2)	16.0 (15.0, 17.0)	1.310 (1.122, 1.530)	<.001		1.321 (1.136, 1.537)	<.001		
Presence of risk factor: Cardiovascular disorder													
Yes	25/ 41	(61.0)	18.0 (13.0, NE)	26/ 47	(55.3)	22.0 (15.0, NE)	1.160 (0.654, 2.060)	0.611	0.996	1.290 (0.745, 2.234)	0.363	0.951	
No	536/ 770	(69.6)	14.0 (13.0, 15.0)	491/ 790	(62.2)	17.0 (16.0, 18.0)	1.292 (1.140, 1.464)	<.001		1.304 (1.153, 1.474)	<.001		
Presence of risk factor: Chronic kidney disease													
Yes	3/ 6	(50.0)	13.0 (7.0, NE)	5/ 8	(62.5)	19.0 (7.0, NE)	2.11E8 (0.000, NE)	0.997	0.755	1.119 (0.266, 4.712)	0.878	0.770	
No	558/ 805	(69.3)	14.0 (13.0, 15.0)	512/ 829	(61.8)	17.0 (16.0, 19.0)	1.291 (1.142, 1.459)	<.001		1.307 (1.159, 1.473)	<.001		
Presence of risk factor: HIV Infection													
Yes	0			1/ 1	(100.0)								
No	561/ 811	(69.2)		515/ 835	(61.7)								
Presence of risk factor: Sickle Cell Disease													
No	561/ 811	(69.2)		517/ 837	(61.8)								
Presence of risk factor: Neurodevelopmental Disorder													
Yes	2/ 2	(100.0)		0/ 1	(0.0)								
No	559/ 809	(69.1)		517/ 836	(61.8)								
Presence of risk factor: Cancer													
Yes	2/ 4	(50.0)		4/ 5	(80.0)								
No	559/ 807	(69.3)		513/ 832	(61.7)								
Presence of risk factor: Device Dependence													
Yes	1/ 4	(25.0)		1/ 3	(33.3)								
No	555/ 798	(69.5)		513/ 826	(62.1)								

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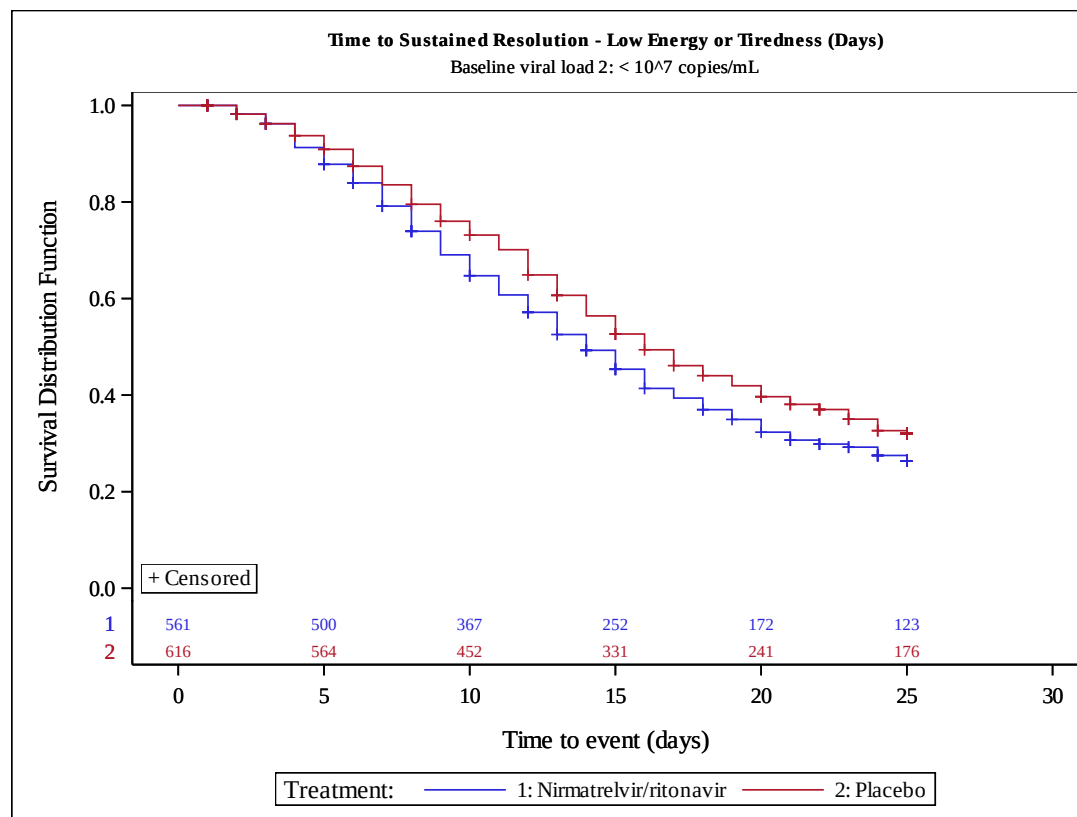
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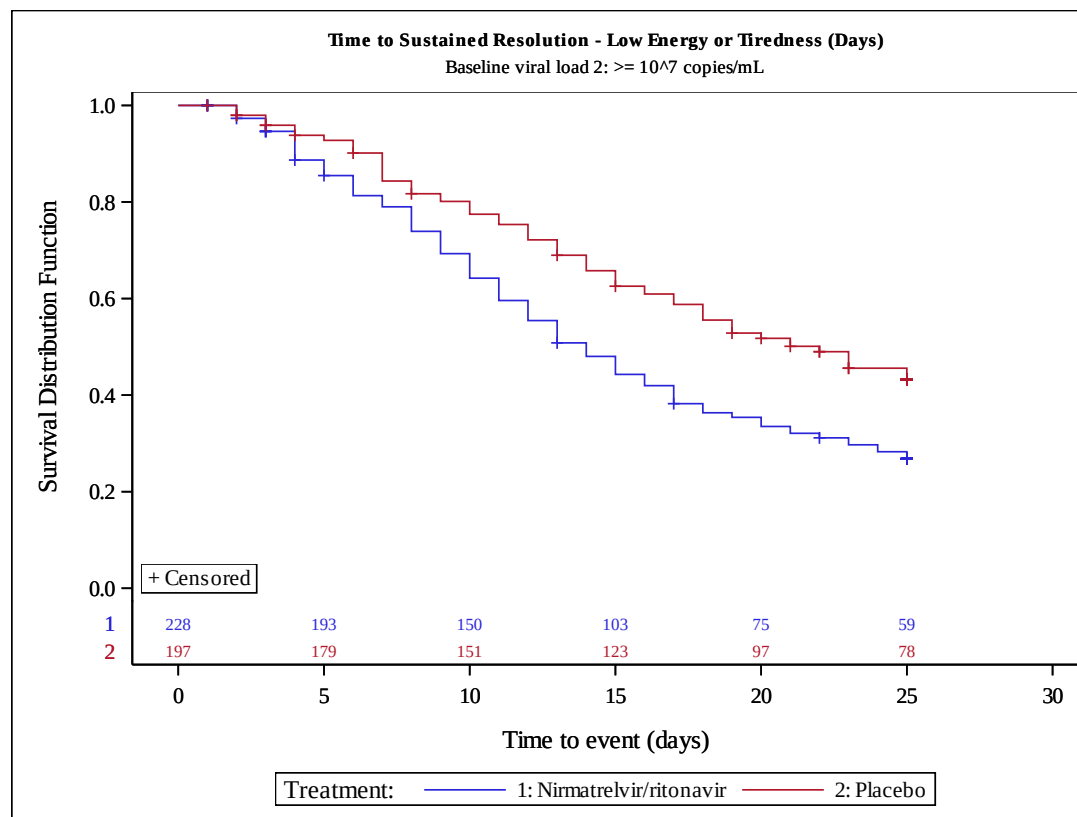


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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=96)			Placebo (N=93)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Age												
< 65	56/	86 (65.1)	16.0 (12.0, 20.0)	31/	78 (39.7)	NE (24.0, NE)	2.519 (1.561, 4.065)	<.001	0.030	2.256 (1.453, 3.503)	<.001	0.046
>= 65	2/	10 (20.0)	NE (13.0, NE)	7/	15 (46.7)	NE (12.0, NE)	0.127 (0.012, 1.371)	0.089		0.425 (0.088, 2.047)	0.286	
Gender												
Male	29/	35 (82.9)	11.0 (9.0, 14.0)	12/	30 (40.0)	NE (15.0, NE)	3.784 (1.751, 8.177)	<.001	0.013	3.058 (1.552, 6.026)	0.001	0.066
Female	29/	61 (47.5)	24.0 (17.0, NE)	26/	63 (41.3)	NE (24.0, NE)	1.482 (0.829, 2.650)	0.185		1.445 (0.851, 2.453)	0.173	
Geographic region												
United States	31/	52 (59.6)		15/	46 (32.6)							
Europe	15/	23 (65.2)		13/	25 (52.0)							
India	0			0								
Rest of World	12/	21 (57.1)		10/	22 (45.5)							
COVID-19 therapeutic mAb treatment at randomisation									0.760			0.755
Yes	3/	5 (60.0)	6.5 (4.0, NE)	7/	12 (58.3)	15.5 (8.0, NE)	8.070 (0.764, 85.199)	0.082		2.468 (0.616, 9.880)	0.202	
No	55/	91 (60.4)	18.0 (12.0, 24.0)	31/	81 (38.3)	NE (25.0, NE)	2.069 (1.302, 3.287)	0.002		2.115 (1.361, 3.288)	<.001	
Baseline viral load 1									0.718			0.932
< 10^4 copies/mL	13/	27 (48.1)	19.0 (12.0, NE)	6/	19 (31.6)	NE (13.0, NE)	2.699 (0.792, 9.196)	0.112		1.901 (0.722, 5.008)	0.193	
>= 10^4 copies/mL	44/	68 (64.7)	16.0 (11.0, 21.0)	31/	72 (43.1)	NE (23.0, NE)	2.197 (1.322, 3.653)	0.002		2.079 (1.311, 3.296)	0.002	
Baseline viral load 2									0.291			0.491
< 10^7 copies/mL	32/	55 (58.2)	16.5 (12.0, NE)	26/	69 (37.7)	NE (24.0, NE)	2.617 (1.473, 4.647)	0.001		2.169 (1.290, 3.645)	0.003	
>= 10^7 copies/mL	25/	40 (62.5)	17.5 (11.0, 25.0)	11/	22 (50.0)	25.0 (15.0, NE)	1.775 (0.783, 4.026)	0.170		1.541 (0.758, 3.134)	0.233	
Baseline serology status									0.944			0.848
Negative	34/	53 (64.2)	17.0 (11.0, 22.0)	26/	60 (43.3)	NE (18.0, NE)	2.095 (1.203, 3.648)	0.009		1.979 (1.187, 3.301)	0.009	
Positive	24/	43 (55.8)	18.0 (12.0, NE)	11/	31 (35.5)	NE (24.0, NE)	2.720 (1.171, 6.321)	0.020		2.176 (1.065, 4.450)	0.033	
Symptom onset days to first dose date									0.853			0.898
<= 3	45/	65 (69.2)	14.0 (11.0, 20.0)	24/	45 (53.3)	24.0 (17.0, NE)	2.204 (1.283, 3.785)	0.004		1.706 (1.038, 2.803)	0.035	
> 3	13/	31 (41.9)	NE (14.0, NE)	14/	48 (29.2)	NE (NE, NE)	2.572 (1.086, 6.092)	0.032		1.840 (0.864, 3.918)	0.114	
BMI group									0.105			0.239
< 25	10/	17 (58.8)	13.5 (5.0, NE)	10/	18 (55.6)	23.0 (12.0, NE)	2.066 (0.651, 6.552)	0.218		1.577 (0.655, 3.798)	0.310	
25 - < 30	17/	34 (50.0)	25.0 (12.0, NE)	10/	22 (45.5)	NE (15.0, NE)	1.289 (0.580, 2.864)	0.533		1.312 (0.601, 2.868)	0.495	
>= 30	31/	45 (68.9)	16.0 (11.0, 22.0)	18/	53 (34.0)	NE (25.0, NE)	5.036 (2.411, 10.516)	<.001		2.857 (1.593, 5.122)	<.001	
Ethnicity												
White	44/	75 (58.7)		32/	76 (42.1)							
Black or African American	4/	6 (66.7)		1/	8 (12.5)							
Asian	4/	4 (100.0)		1/	2 (50.0)							
Others	6/	11 (54.5)		4/	7 (57.1)							
Number of baseline comorbidities present												
0-1	44/	74 (59.5)		32/	72 (44.4)							
2-3	14/	21 (66.7)		5/	20 (25.0)							
>= 4	0/	1 (0.0)		1/	1 (100.0)							
Presence of risk factor: Smoking									0.531			0.440
Yes	27/	40 (67.5)	15.0 (11.0, 21.0)	17/	31 (54.8)	23.0 (15.0, NE)	1.969 (1.013, 3.827)	0.046		1.590 (0.865, 2.922)	0.135	
No	31/	56 (55.4)	20.0 (12.0, NE)	21/	62 (33.9)	NE (NE, NE)	1.966 (1.019, 3.793)	0.044		2.177 (1.250, 3.792)	0.006	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=96)			Placebo (N=93)			Adjusted Analysis [2]			Interaction		Unadjusted Analysis [3]			Interaction	
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	p-Value			Hazard Ratio (95% CI)	p-Value	p-Value		
Presence of risk factor: Diabetes mellitus											0.880					0.680
Yes	9/	17 (52.9)	14.5 (11.0, NE)	6/	14 (42.9)	NE (13.0, NE)	3.631 (0.955, 13.802)	0.058				1.603 (0.569, 4.514)	0.372			
No	49/	79 (62.0)	18.0 (12.0, 22.0)	32/	79 (40.5)	NE (24.0, NE)	2.098 (1.286, 3.424)	0.003				2.033 (1.301, 3.178)	0.002			
Presence of risk factor: Immunosuppression																
Yes	0			1/	1 (100.0)											
No	58/	96 (60.4)		37/	92 (40.2)											
Presence of risk factor: Chronic lung disease											0.984					0.984
Yes	5/	10 (50.0)	16.0 (10.0, NE)	0/	4 (0.0)	NE (NE, NE)	NE (NE, NE)	NE				NE (NE, NE)	NE			
No	53/	86 (61.6)	18.0 (12.0, 22.0)	38/	89 (42.7)	NE (24.0, NE)	2.176 (1.378, 3.436)	<.001				1.898 (1.250, 2.881)	0.003			
Presence of risk factor: Hypertension											0.906					0.988
Yes	15/	30 (50.0)	21.0 (12.0, NE)	11/	34 (32.4)	NE (24.0, NE)	1.929 (0.806, 4.620)	0.140				1.975 (0.906, 4.309)	0.087			
No	43/	66 (65.2)	17.0 (11.0, 20.0)	27/	59 (45.8)	NE (17.0, NE)	2.213 (1.291, 3.794)	0.004				1.909 (1.179, 3.093)	0.009			
Presence of risk factor: Cardiovascular disorder											0.136					0.168
Yes	1/	5 (20.0)	NE (13.0, NE)	3/	7 (42.9)	NE (10.0, NE)	1.414 (0.085, 23.573)	0.809				0.443 (0.046, 4.268)	0.481			
No	57/	91 (62.6)	17.0 (12.0, 20.0)	35/	86 (40.7)	NE (24.0, NE)	2.298 (1.451, 3.640)	<.001				2.105 (1.380, 3.210)	<.001			
Presence of risk factor: Chronic kidney disease																
Yes	0			0/	1 (0.0)											
No	58/	96 (60.4)		38/	92 (41.3)											
Presence of risk factor: HIV Infection																
Yes	0			0												
No	58/	96 (60.4)		38/	93 (40.9)											
Presence of risk factor: Sickle Cell Disease																
No	58/	96 (60.4)		38/	93 (40.9)											
Presence of risk factor: Neurodevelopmental Disorder																
Yes	0			0												
No	58/	96 (60.4)		38/	93 (40.9)											
Presence of risk factor: Cancer																
Yes	0			0/	1 (0.0)											
No	58/	96 (60.4)		38/	92 (41.3)											
Presence of risk factor: Device Dependence																
Yes	1/	2 (50.0)		0												
No	57/	93 (61.3)		38/	93 (40.9)											

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

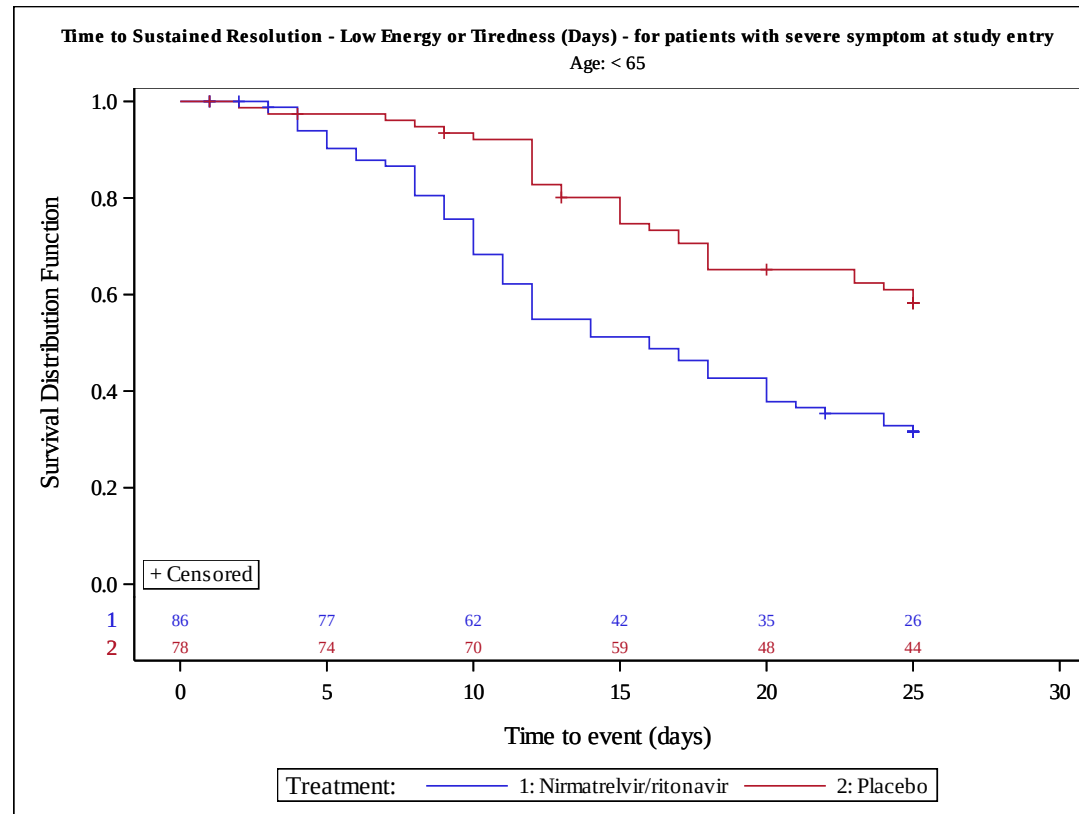
p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

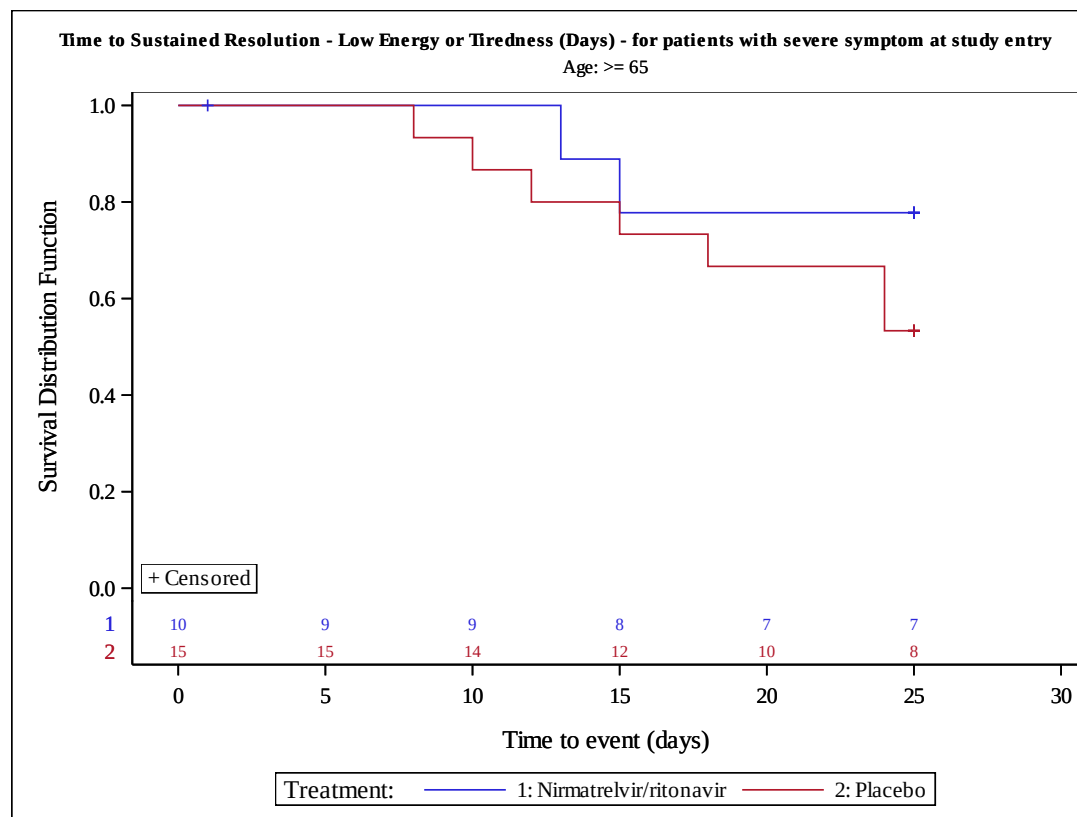


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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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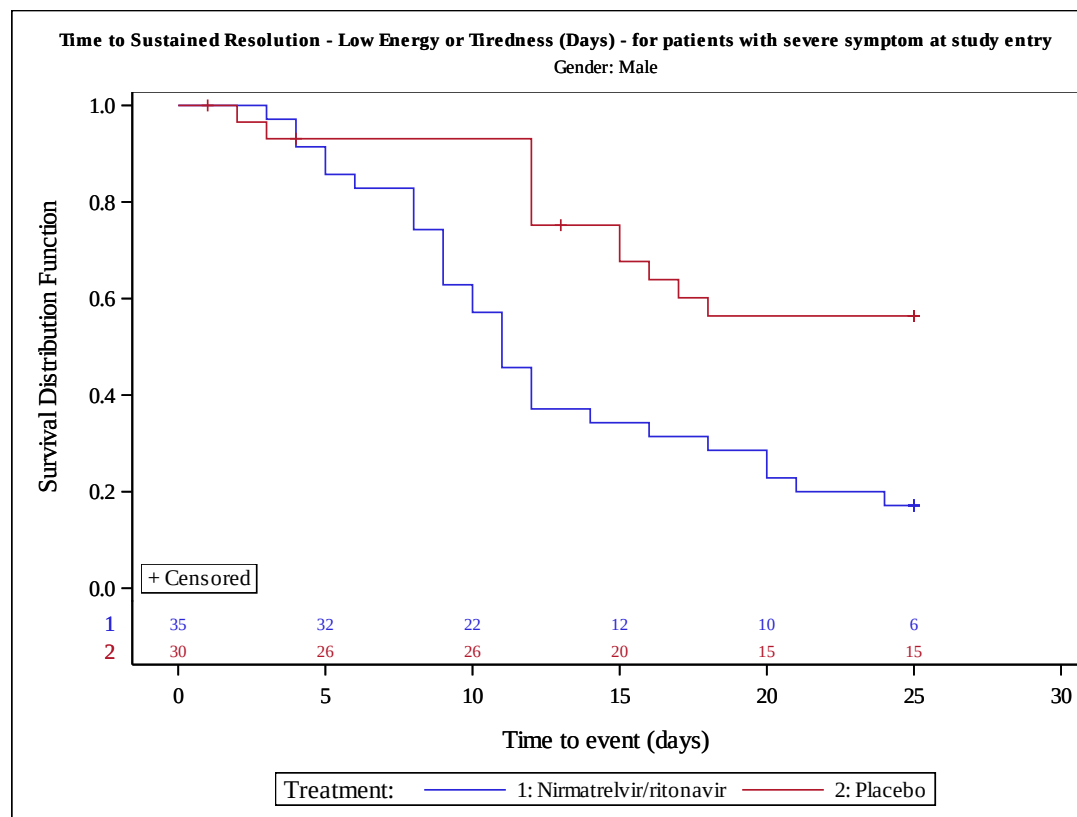


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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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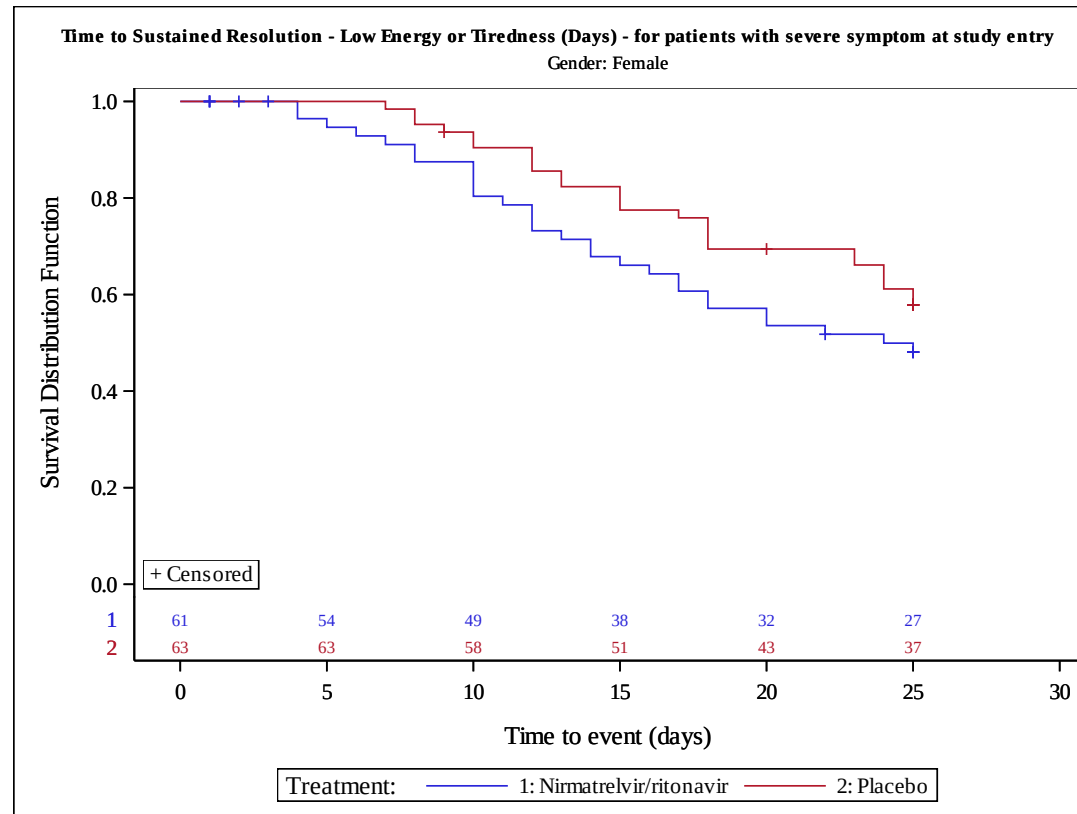


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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Muscle or Body Aches - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]		Interaction p-Value	Unadjusted analysis [2]		Interaction p-Value
			Relative Risk (95% CI)	p-Value		Relative Risk (95% CI)	p-Value	
Age								
< 65	164/ 790 (20.8)	184/ 810 (22.7)	0.915 (0.756, 1.107)	0.360	0.871	0.914 (0.759, 1.101)	0.343	0.888
>= 65	32/ 138 (23.2)	38/ 145 (26.2)	0.957 (0.635, 1.442)	0.834		0.885 (0.588, 1.331)	0.557	
Gender								
Male	84/ 463 (18.1)	106/ 507 (20.9)	0.878 (0.675, 1.142)	0.333	0.646	0.868 (0.671, 1.122)	0.280	0.690
Female	112/ 465 (24.1)	116/ 448 (25.9)	0.947 (0.753, 1.189)	0.637		0.930 (0.743, 1.165)	0.528	
Geographic region								
United States	82/ 375 (21.9)	94/ 387 (24.3)	0.918 (0.701, 1.201)	0.531	0.061	0.900 (0.694, 1.167)	0.428	0.094
Europe	77/ 322 (23.9)	76/ 321 (23.7)	1.072 (0.809, 1.421)	0.627		1.010 (0.766, 1.332)	0.944	
India	11/ 74 (14.9)	6/ 78 (7.7)	1.967 (0.763, 5.074)	0.162		1.932 (0.753, 4.959)	0.171	
Rest of World	26/ 157 (16.6)	46/ 169 (27.2)	0.619 (0.402, 0.953)	0.029		0.608 (0.396, 0.934)	0.023	
COVID-19 therapeutic mAb treatment at randomisation								
Yes	17/ 57 (29.8)	17/ 60 (28.3)	1.086 (0.629, 1.875)	0.766	0.766	1.053 (0.598, 1.854)	0.859	0.598
No	179/ 871 (20.6)	205/ 895 (22.9)	0.908 (0.757, 1.090)	0.301		0.897 (0.751, 1.071)	0.231	
Baseline viral load 1								
< 10 ⁴ copies/mL	73/ 335 (21.8)	67/ 354 (18.9)	1.220 (0.910, 1.637)	0.184	0.027	1.151 (0.856, 1.548)	0.351	0.045
>= 10 ⁴ copies/mL	117/ 569 (20.6)	149/ 575 (25.9)	0.802 (0.647, 0.994)	0.044		0.794 (0.642, 0.981)	0.033	
Baseline viral load 2								
< 10 ⁷ copies/mL	131/ 652 (20.1)	147/ 699 (21.0)	0.987 (0.799, 1.219)	0.902	0.227	0.955 (0.774, 1.179)	0.670	0.277
>= 10 ⁷ copies/mL	59/ 252 (23.4)	69/ 230 (30.0)	0.799 (0.593, 1.078)	0.142		0.780 (0.579, 1.051)	0.103	
Baseline serology status								
Negative	95/ 435 (21.8)	124/ 456 (27.2)	0.805 (0.635, 1.021)	0.073	0.094	0.803 (0.636, 1.014)	0.065	0.085
Positive	98/ 482 (20.3)	91/ 487 (18.7)	1.086 (0.842, 1.401)	0.524		1.088 (0.842, 1.406)	0.518	
Symptom onset days to first dose date								
<= 3	147/ 624 (23.6)	146/ 624 (23.4)	1.021 (0.832, 1.254)	0.840	0.063	1.007 (0.824, 1.230)	0.947	0.063
> 3	49/ 304 (16.1)	76/ 331 (23.0)	0.713 (0.512, 0.994)	0.046		0.702 (0.508, 0.970)	0.032	
BMI group								
< 25	37/ 215 (17.2)	42/ 213 (19.7)	0.959 (0.641, 1.435)	0.838	0.228	0.873 (0.585, 1.301)	0.504	0.239
25 - < 30	79/ 319 (24.8)	75/ 332 (22.6)	1.153 (0.874, 1.522)	0.313		1.096 (0.832, 1.445)	0.514	
>= 30	80/ 393 (20.4)	105/ 410 (25.6)	0.810 (0.621, 1.055)	0.119		0.795 (0.615, 1.027)	0.079	
Ethnicity								
White	162/ 699 (23.2)	178/ 718 (24.8)	0.956 (0.791, 1.156)	0.645	0.069	0.935 (0.776, 1.126)	0.477	0.182
Black or African American	8/ 43 (18.6)	8/ 40 (20.0)	NE (NE, NE)	NE		0.930 (0.386, 2.243)	0.872	
Asian	16/ 117 (13.7)	14/ 127 (11.0)	1.166 (0.593, 2.294)	0.657		1.241 (0.634, 2.429)	0.529	
Others	10/ 69 (14.5)	22/ 70 (31.4)	0.392 (0.194, 0.792)	0.009		0.461 (0.236, 0.901)	0.023	
Number of baseline comorbidities present								
0-1	144/ 710 (20.3)	174/ 728 (23.9)	0.824 (0.674, 1.006)	0.057	0.048	0.849 (0.698, 1.031)	0.099	0.270
2-3	51/ 214 (23.8)	48/ 221 (21.7)	1.255 (0.883, 1.785)	0.205		1.097 (0.776, 1.552)	0.600	
>= 4	1/ 4 (25.0)	0/ 6 (0.0)	NE (NE, NE)	NE		4.200 (0.212, 83.335)	0.346	
Presence of risk factor: Smoking								
Yes	86/ 417 (20.6)	77/ 438 (17.6)	1.162 (0.879, 1.536)	0.293	0.043	1.173 (0.890, 1.547)	0.258	0.019
No	110/ 509 (21.6)	145/ 517 (28.0)	0.797 (0.639, 0.993)	0.043		0.771 (0.621, 0.956)	0.018	
Presence of risk factor: Diabetes mellitus					0.517			0.728

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value	
Yes	29/ 130 (22.3)	31/ 136 (22.8)	0.993 (0.635, 1.554)			0.976		0.979 (0.627, 1.528)			0.924	
No	167/ 797 (21.0)	191/ 819 (23.3)	0.896 (0.743, 1.081)			0.252		0.898 (0.748, 1.079)			0.252	
Presence of risk factor: Immunosuppression							0.523					0.939
Yes	3/ 6 (50.0)	4/ 7 (57.1)	NE (NE, NE)			NE		0.875 (0.314, 2.440)			0.799	
No	193/ 921 (21.0)	218/ 948 (23.0)	0.917 (0.770, 1.092)			0.331		0.911 (0.768, 1.081)			0.287	
Presence of risk factor: Chronic lung disease							0.901					0.894
Yes	11/ 62 (17.7)	8/ 39 (20.5)	0.899 (0.374, 2.165)			0.813		0.865 (0.382, 1.960)			0.728	
No	185/ 865 (21.4)	214/ 916 (23.4)	0.920 (0.771, 1.099)			0.358		0.915 (0.770, 1.089)			0.318	
Presence of risk factor: Hypertension							0.131					0.340
Yes	83/ 348 (23.9)	88/ 371 (23.7)	1.075 (0.822, 1.407)			0.598		1.006 (0.774, 1.306)			0.967	
No	113/ 579 (19.5)	134/ 584 (22.9)	0.827 (0.659, 1.039)			0.103		0.851 (0.681, 1.062)			0.154	
Presence of risk factor: Cardiovascular disorder							0.026					0.084
Yes	16/ 42 (38.1)	12/ 49 (24.5)	NE (NE, NE)			NE		1.556 (0.833, 2.906)			0.166	
No	180/ 885 (20.3)	210/ 906 (23.2)	0.875 (0.731, 1.048)			0.146		0.877 (0.736, 1.047)			0.146	
Presence of risk factor: Chronic kidney disease							0.263					0.302
Yes	1/ 6 (16.7)	4/ 8 (50.0)	NE (NE, NE)			NE		0.333 (0.049, 2.271)			0.262	
No	195/ 921 (21.2)	218/ 947 (23.0)	0.927 (0.779, 1.104)			0.395		0.920 (0.776, 1.091)			0.336	
Presence of risk factor: HIV Infection												
Yes	0	0/ 1 (0.0)										
No	196/ 927 (21.1)	222/ 953 (23.3)										
Presence of risk factor: Sickle Cell Disease												
No	196/ 927 (21.1)	222/ 955 (23.2)										
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0/ 2 (0.0)	0/ 1 (0.0)										
No	196/ 925 (21.2)	222/ 954 (23.3)										
Presence of risk factor: Cancer							0.679					0.828
Yes	1/ 5 (20.0)	1/ 6 (16.7)	NE (NE, NE)			NE		1.200 (0.098, 14.690)			0.887	
No	195/ 922 (21.1)	221/ 949 (23.3)	0.917 (0.771, 1.090)			0.326		0.908 (0.766, 1.076)			0.267	
Presence of risk factor: Device Dependence												
Yes	1/ 4 (25.0)	2/ 3 (66.7)										
No	195/ 914 (21.3)	219/ 944 (23.2)										

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=756)			Placebo (N=760)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	545/ 648	(84.1)	6.0 (5.0, 7.0)	507/ 645	(78.6)	7.0 (6.0, 8.0)	1.262 (1.115, 1.428)	<.001		0.178	1.260 (1.116, 1.422)	<.001		0.143
>= 65	98/ 108	(90.7)	6.0 (4.0, 7.0)	88/ 115	(76.5)	8.0 (6.0, 11.0)	1.638 (1.205, 2.227)	0.002			1.595 (1.192, 2.135)	0.002		
Gender														
Male	311/ 361	(86.1)	6.0 (5.0, 7.0)	305/ 386	(79.0)	7.0 (6.0, 8.0)	1.307 (1.110, 1.539)	0.001		0.969	1.329 (1.133, 1.558)	<.001		0.822
Female	332/ 395	(84.1)	6.0 (5.0, 7.0)	290/ 374	(77.5)	8.0 (7.0, 9.0)	1.294 (1.100, 1.521)	0.002			1.288 (1.100, 1.508)	0.002		
Geographic region														
United States	265/ 328	(80.8)	7.0 (5.0, 8.0)	255/ 325	(78.5)	8.0 (7.0, 9.0)	1.180 (0.990, 1.406)	0.065		0.463	1.186 (0.999, 1.409)	0.052		0.409
Europe	234/ 254	(92.1)	6.0 (5.0, 6.0)	208/ 263	(79.1)	6.0 (6.0, 8.0)	1.435 (1.180, 1.744)	<.001			1.451 (1.202, 1.753)	<.001		
India	45/ 47	(95.7)	7.0 (6.0, 8.0)	45/ 47	(95.7)	9.0 (7.0, 9.0)	1.582 (1.017, 2.459)	0.042			1.456 (0.951, 2.228)	0.084		
Rest of World	99/ 127	(78.0)	4.0 (3.0, 7.0)	87/ 125	(69.6)	8.0 (5.0, 11.0)	1.358 (1.011, 1.825)	0.042			1.352 (1.013, 1.805)	0.041		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	39/ 48	(81.3)	7.0 (4.0, 9.0)	39/ 49	(79.6)	8.0 (6.0, 10.0)	1.168 (0.735, 1.856)	0.512		0.764	1.233 (0.790, 1.924)	0.356		0.829
No	604/ 708	(85.3)	6.0 (5.0, 7.0)	556/ 711	(78.2)	7.0 (6.0, 8.0)	1.312 (1.165, 1.476)	<.001			1.310 (1.167, 1.470)	<.001		
Baseline viral load 1														
< 10^4 copies/mL	231/ 273	(84.6)	7.0 (6.0, 8.0)	226/ 273	(82.8)	7.0 (6.0, 8.0)	1.140 (0.947, 1.374)	0.167		0.038	1.135 (0.944, 1.364)	0.177		0.047
>= 10^4 copies/mL	392/ 461	(85.0)	5.0 (5.0, 6.0)	352/ 464	(75.9)	8.0 (7.0, 9.0)	1.412 (1.220, 1.633)	<.001			1.411 (1.221, 1.631)	<.001		
Baseline viral load 2														
< 10^7 copies/mL	434/ 525	(82.7)	7.0 (6.0, 7.0)	441/ 555	(79.5)	8.0 (7.0, 8.0)	1.182 (1.035, 1.351)	0.014		0.005	1.185 (1.038, 1.353)	0.012		0.006
>= 10^7 copies/mL	189/ 209	(90.4)	4.0 (4.0, 5.0)	137/ 182	(75.3)	7.0 (6.0, 10.0)	1.669 (1.328, 2.097)	<.001			1.683 (1.347, 2.102)	<.001		
Baseline serology status														
Negative	304/ 355	(85.6)	6.0 (5.0, 6.0)	275/ 374	(73.5)	7.0 (6.0, 9.0)	1.396 (1.180, 1.652)	<.001		0.198	1.415 (1.201, 1.667)	<.001		0.137
Positive	330/ 390	(84.6)	6.0 (6.0, 7.0)	318/ 382	(83.2)	8.0 (7.0, 8.0)	1.245 (1.063, 1.457)	0.006			1.220 (1.045, 1.423)	0.012		
Symptom onset days to first dose date														
<= 3	448/ 509	(88.0)	6.0 (5.0, 7.0)	401/ 491	(81.7)	7.0 (6.0, 8.0)	1.308 (1.139, 1.502)	<.001		0.836	1.298 (1.134, 1.486)	<.001		0.812
> 3	195/ 247	(78.9)	6.0 (5.0, 7.0)	194/ 269	(72.1)	8.0 (7.0, 10.0)	1.325 (1.079, 1.627)	0.007			1.312 (1.075, 1.602)	0.008		
BMI group														
< 25	148/ 170	(87.1)	6.0 (5.0, 7.0)	131/ 157	(83.4)	6.0 (5.0, 8.0)	1.318 (1.029, 1.688)	0.029		0.931	1.331 (1.051, 1.687)	0.018		0.923
25 - < 30	227/ 262	(86.6)	6.0 (5.0, 7.0)	208/ 266	(78.2)	8.0 (7.0, 9.0)	1.363 (1.124, 1.654)	0.002			1.350 (1.117, 1.631)	0.002		
>= 30	267/ 323	(82.7)	6.0 (5.0, 7.0)	256/ 337	(76.0)	8.0 (6.0, 9.0)	1.261 (1.057, 1.504)	0.010			1.257 (1.059, 1.493)	0.009		
Ethnicity														
White	497/ 584	(85.1)	6.0 (5.0, 7.0)	466/ 603	(77.3)	7.0 (6.0, 8.0)	1.303 (1.144, 1.483)	<.001		0.666	1.311 (1.155, 1.489)	<.001		0.707
Black or African American	28/ 37	(75.7)	7.0 (3.0, 8.0)	25/ 31	(80.6)	6.0 (3.0, 11.0)	1.171 (0.649, 2.111)	0.601			1.152 (0.669, 1.983)	0.611		
Asian	70/ 76	(92.1)	6.0 (5.0, 7.0)	70/ 75	(93.3)	7.0 (5.0, 9.0)	1.380 (0.972, 1.960)	0.071			1.251 (0.895, 1.747)	0.190		
Others	48/ 59	(81.4)	5.0 (3.0, 9.0)	34/ 51	(66.7)	11.0 (6.0, 16.0)	1.538 (0.976, 2.425)	0.064			1.537 (0.989, 2.389)	0.056		
Number of baseline comorbidities present														
0-1	492/ 576	(85.4)		447/ 564	(79.3)									
2-3	148/ 177	(83.6)		142/ 190	(74.7)									
>= 4	3/ 3	(100.0)		6/ 6	(100.0)									
Presence of risk factor: Smoking														
Yes	292/ 342	(85.4)	7.0 (6.0, 7.0)	267/ 340	(78.5)	7.0 (6.0, 8.0)	1.234 (1.041, 1.464)	0.016		0.355	1.240 (1.049, 1.464)	0.012		0.486
No	349/ 412	(84.7)	6.0 (5.0, 6.0)	328/ 420	(78.1)	8.0 (7.0, 9.0)	1.365 (1.170, 1.594)	<.001			1.350 (1.160, 1.570)	<.001		

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=756)			Placebo (N=760)			Adjusted Analysis [2]				Unadjusted Analysis [3]			
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)		p-Value	Interaction p-Value	Hazard Ratio (95% CI)		p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus										0.904				0.935
Yes	90/ 108	(83.3)	6.0 (5.0, 8.0)	91/ 116	(78.4)	8.0 (6.0, 9.0)	1.379 (1.016, 1.871)	0.039			1.306 (0.975, 1.750)	0.074		
No	552/ 647	(85.3)	6.0 (5.0, 7.0)	504/ 644	(78.3)	8.0 (7.0, 8.0)	1.300 (1.149, 1.472)	<.001			1.304 (1.155, 1.472)	<.001		
Presence of risk factor: Immunosuppression										0.524				0.450
Yes	2/ 3	(66.7)	8.0 (4.0, NE)	5/ 7	(71.4)	5.0 (2.0, NE)	0.486 (0.000, NE)	1.000			0.684 (0.131, 3.582)	0.653		
No	640/ 752	(85.1)	6.0 (5.0, 7.0)	590/ 753	(78.4)	8.0 (7.0, 8.0)	1.306 (1.165, 1.465)	<.001			1.309 (1.170, 1.465)	<.001		
Presence of risk factor: Chronic lung disease										0.861				0.886
Yes	47/ 51	(92.2)	5.0 (4.0, 7.0)	28/ 32	(87.5)	8.0 (4.0, 11.0)	1.441 (0.863, 2.408)	0.163			1.266 (0.792, 2.023)	0.324		
No	595/ 704	(84.5)	6.0 (5.0, 7.0)	567/ 728	(77.9)	7.0 (7.0, 8.0)	1.296 (1.152, 1.458)	<.001			1.299 (1.157, 1.458)	<.001		
Presence of risk factor: Hypertension										0.669				0.828
Yes	239/ 284	(84.2)	6.0 (5.0, 8.0)	238/ 309	(77.0)	8.0 (6.0, 9.0)	1.326 (1.101, 1.597)	0.003			1.316 (1.099, 1.577)	0.003		
No	403/ 471	(85.6)	6.0 (5.0, 7.0)	357/ 451	(79.2)	7.0 (6.0, 8.0)	1.274 (1.101, 1.475)	0.001			1.288 (1.117, 1.486)	<.001		
Presence of risk factor: Cardiovascular disorder										0.667				0.963
Yes	26/ 32	(81.3)	9.0 (5.0, 13.0)	27/ 40	(67.5)	6.0 (4.0, 10.0)	1.354 (0.763, 2.405)	0.301			1.295 (0.754, 2.225)	0.349		
No	616/ 723	(85.2)	6.0 (5.0, 7.0)	568/ 720	(78.9)	8.0 (7.0, 8.0)	1.295 (1.152, 1.455)	<.001			1.304 (1.163, 1.462)	<.001		
Presence of risk factor: Chronic kidney disease										0.926				0.810
Yes	4/ 6	(66.7)	7.0 (2.0, NE)	6/ 7	(85.7)	8.0 (6.0, 25.0)	5.863 (0.700, 49.087)	0.103			1.067 (0.300, 3.788)	0.921		
No	638/ 749	(85.2)	6.0 (5.0, 7.0)	589/ 753	(78.2)	8.0 (7.0, 8.0)	1.304 (1.162, 1.462)	<.001			1.305 (1.166, 1.460)	<.001		
Presence of risk factor: HIV Infection														
Yes	0			0										
No	642/ 755	(85.0)		594/ 759	(78.3)									
Presence of risk factor: Sickie Cell Disease														
No	642/ 755	(85.0)		595/ 760	(78.3)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/ 2	(100.0)		1/ 1	(100.0)									
No	640/ 753	(85.0)		594/ 759	(78.3)									
Presence of risk factor: Cancer										0.942				0.596
Yes	4/ 5	(80.0)	7.0 (2.0, 9.0)	5/ 5	(100.0)	2.0 (2.0, 15.0)	0.896 (0.111, 7.213)	0.918			1.000 (0.250, 3.998)	1.000		
No	638/ 750	(85.1)	6.0 (5.0, 7.0)	590/ 755	(78.1)	8.0 (7.0, 8.0)	1.306 (1.165, 1.465)	<.001			1.308 (1.169, 1.463)	<.001		
Presence of risk factor: Device Dependence														
Yes	2/ 3	(66.7)		2/ 3	(66.7)									
No	634/ 743	(85.3)		589/ 750	(78.5)									

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

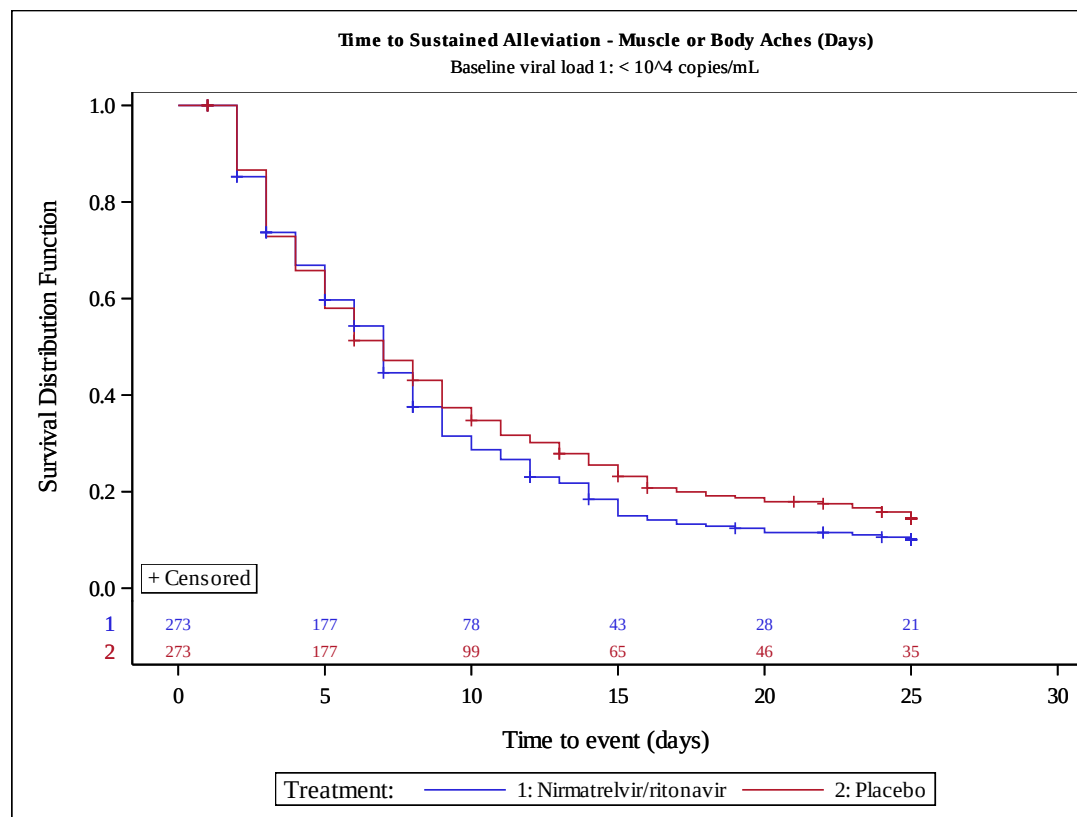
p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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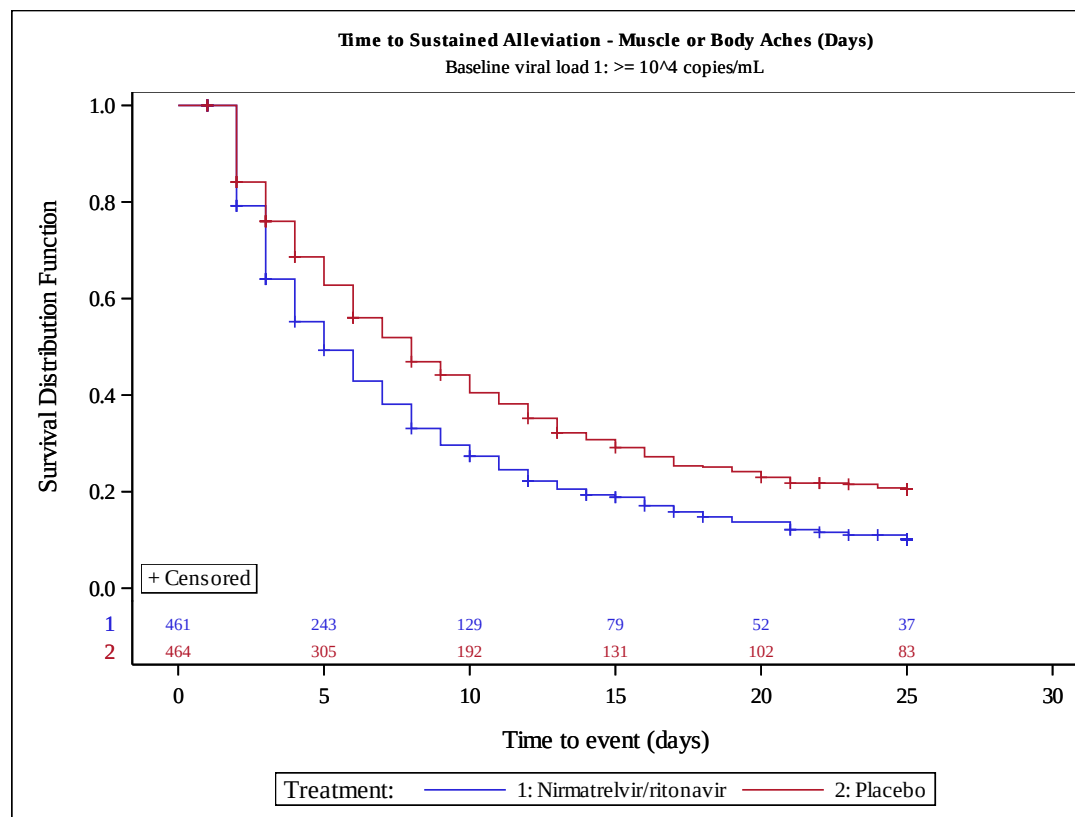


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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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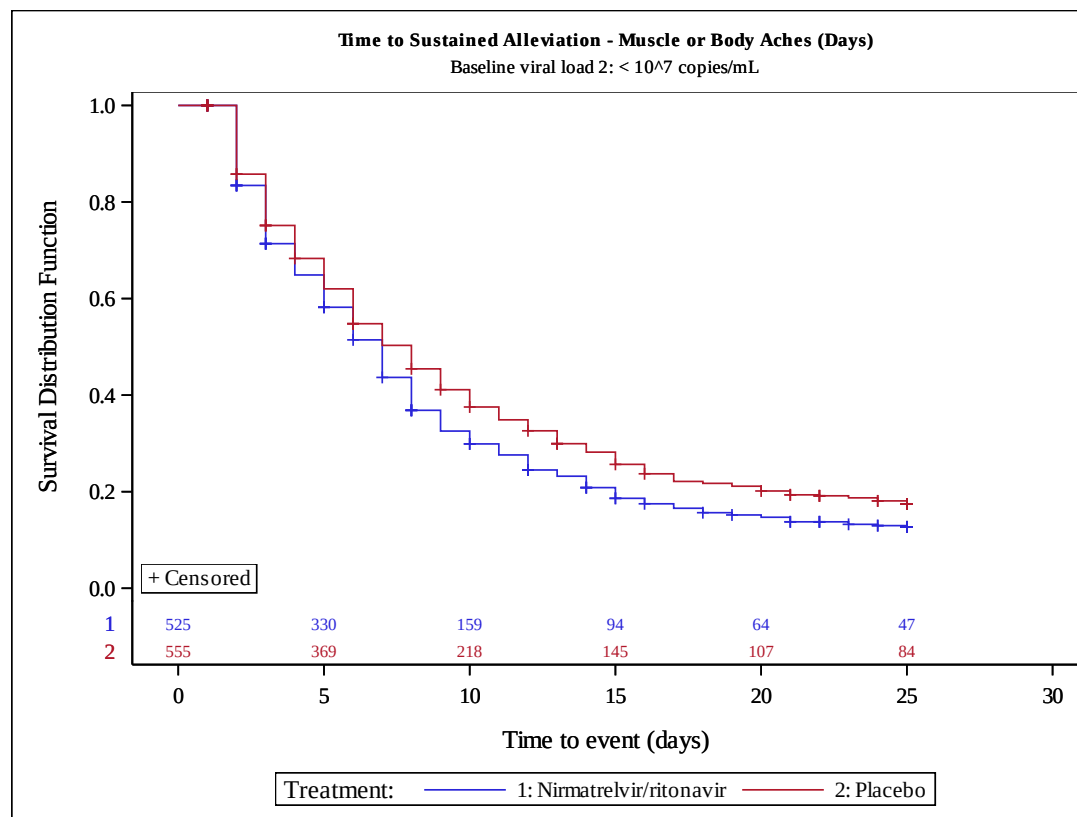


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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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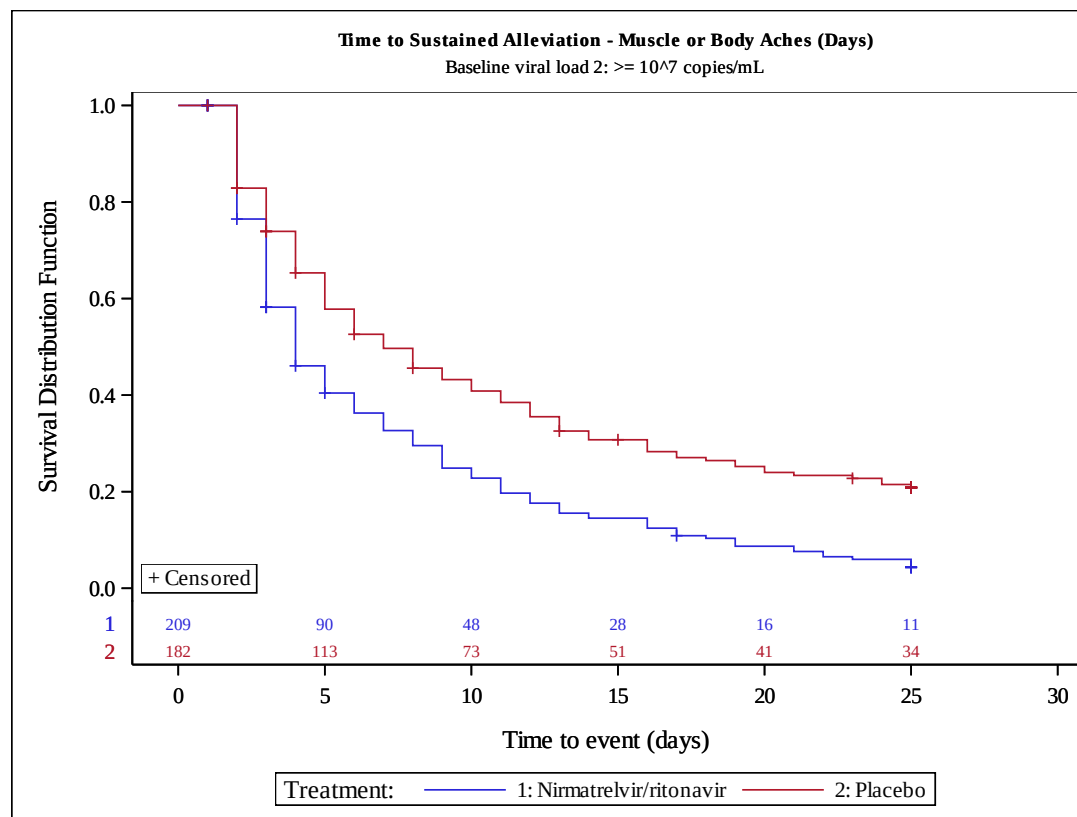


Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=83)			Placebo (N=71)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Age												
< 65	67/	77 (87.0)	4.0 (4.0, 6.0)	51/	65 (78.5)	7.0 (4.0, 10.0)	1.405 (0.954, 2.069)	0.085	0.779	1.495 (1.035, 2.160)	0.032	0.989
>= 65	4/	6 (66.7)	6.0 (2.0, 25.0)	5/	6 (83.3)	8.0 (5.0, NE)	24.726 (0.583, 1049.5)	0.093		1.745 (0.451, 6.745)	0.420	
Gender												
Male	28/	30 (93.3)	4.0 (3.0, 6.0)	19/	25 (76.0)	8.0 (4.0, 13.0)	1.730 (0.887, 3.375)	0.108	0.823	1.796 (0.973, 3.315)	0.061	0.606
Female	43/	53 (81.1)	4.0 (4.0, 7.0)	37/	46 (80.4)	7.5 (5.0, 11.0)	1.441 (0.887, 2.341)	0.140		1.401 (0.901, 2.178)	0.134	
Geographic region												
United States	33/	40 (82.5)		32/	44 (72.7)							
Europe	23/	24 (95.8)		12/	13 (92.3)							
India	0			0								
Rest of World	15/	19 (78.9)		12/	14 (85.7)							
COVID-19 therapeutic mAb treatment at randomisation									0.084			0.109
Yes	8/	9 (88.9)	4.5 (2.0, 7.0)	4/	8 (50.0)	8.0 (2.0, NE)	8.060 (0.819, 79.371)	0.074		3.342 (0.874, 12.777)	0.078	
No	63/	74 (85.1)	4.0 (4.0, 6.0)	52/	63 (82.5)	7.5 (4.0, 10.0)	1.331 (0.907, 1.954)	0.144		1.376 (0.951, 1.991)	0.091	
Baseline viral load 1									0.602			0.459
< 10^4 copies/mL	17/	23 (73.9)	10.0 (3.0, 13.0)	12/	16 (75.0)	10.5 (3.0, 23.0)	1.278 (0.575, 2.841)	0.547		1.263 (0.600, 2.657)	0.538	
>= 10^4 copies/mL	54/	60 (90.0)	4.0 (3.0, 5.0)	42/	52 (80.8)	7.0 (4.0, 10.0)	1.518 (0.993, 2.321)	0.054		1.684 (1.118, 2.537)	0.013	
Baseline viral load 2									0.671			0.504
< 10^7 copies/mL	37/	45 (82.2)	6.0 (4.0, 8.0)	33/	44 (75.0)	10.0 (4.0, 15.0)	1.572 (0.929, 2.661)	0.092		1.648 (1.023, 2.654)	0.040	
>= 10^7 copies/mL	34/	38 (89.5)	4.0 (3.0, 4.0)	21/	24 (87.5)	5.0 (3.0, 7.0)	1.200 (0.661, 2.178)	0.549		1.296 (0.746, 2.252)	0.357	
Baseline serology status									0.469			0.257
Negative	38/	43 (88.4)	4.0 (3.0, 4.0)	32/	43 (74.4)	7.0 (5.0, 8.0)	1.658 (0.990, 2.774)	0.054		1.924 (1.191, 3.107)	0.007	
Positive	32/	39 (82.1)	6.0 (3.0, 9.0)	24/	28 (85.7)	10.5 (4.0, 14.0)	1.172 (0.648, 2.118)	0.600		1.260 (0.738, 2.150)	0.397	
Symptom onset days to first dose date									0.399			0.509
<= 3	51/	58 (87.9)	4.0 (3.0, 5.0)	37/	43 (86.0)	5.5 (4.0, 8.0)	1.338 (0.858, 2.087)	0.199		1.340 (0.875, 2.053)	0.179	
> 3	20/	25 (80.0)	4.0 (3.0, 11.0)	19/	28 (67.9)	13.0 (4.0, 23.0)	1.950 (0.953, 3.989)	0.068		1.785 (0.945, 3.372)	0.074	
BMI group									0.871			0.793
< 25	15/	21 (71.4)	4.0 (2.0, 6.0)	12/	14 (85.7)	7.5 (3.0, 21.0)	1.601 (0.677, 3.787)	0.284		1.754 (0.803, 3.833)	0.159	
25 - < 30	19/	21 (90.5)	6.0 (4.0, 8.0)	19/	25 (76.0)	7.5 (4.0, 13.0)	1.446 (0.700, 2.988)	0.319		1.317 (0.695, 2.495)	0.399	
>= 30	37/	41 (90.2)	4.0 (3.0, 5.0)	25/	32 (78.1)	8.0 (4.0, 11.0)	1.283 (0.719, 2.289)	0.399		1.525 (0.915, 2.544)	0.106	
Ethnicity												
White	54/	66 (81.8)		47/	60 (78.3)							
Black or African American	4/	4 (100.0)		4/	5 (80.0)							
Asian	4/	4 (100.0)		2/	2 (100.0)							
Others	9/	9 (100.0)		3/	4 (75.0)							
Number of baseline comorbidities present												
0-1	57/	66 (86.4)		49/	61 (80.3)							
2-3	13/	16 (81.3)		7/	10 (70.0)							
>= 4	1/	1 (100.0)		0								
Presence of risk factor: Smoking									0.445			0.596
Yes	29/	32 (90.6)	5.0 (4.0, 7.0)	26/	32 (81.3)	7.0 (4.0, 11.0)	1.284 (0.713, 2.312)	0.405		1.419 (0.831, 2.422)	0.200	
No	42/	51 (82.4)	4.0 (3.0, 6.0)	30/	39 (76.9)	8.0 (5.0, 14.0)	1.765 (1.034, 3.013)	0.037		1.608 (1.001, 2.582)	0.049	

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=83)			Placebo (N=71)			Adjusted Analysis [2]		Interaction		Unadjusted Analysis [3]			Interaction	
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)	p-Value	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value		
Presence of risk factor: Diabetes mellitus										0.695				0.387	
Yes	11/	13 (84.6)	11.0 (2.0, 15.0)	5/	6 (83.3)	7.0 (2.0, NE)	3.301 (0.681, 16.008)	0.138			1.013 (0.349, 2.942)	0.981			
No	60/	70 (85.7)	4.0 (4.0, 5.0)	51/	65 (78.5)	8.0 (5.0, 10.0)	1.509 (1.019, 2.234)	0.040			1.685 (1.152, 2.464)	0.007			
Presence of risk factor: Immunosuppression															
Yes	0			0											
No	71/	83 (85.5)		56/	71 (78.9)										
Presence of risk factor: Chronic lung disease										0.645				0.340	
Yes	8/	10 (80.0)	8.0 (2.0, 25.0)	4/	4 (100.0)	7.0 (3.0, 24.0)	4.372 (0.295, 64.908)	0.284			0.758 (0.220, 2.603)	0.659			
No	63/	73 (86.3)	4.0 (4.0, 5.0)	52/	67 (77.6)	8.0 (5.0, 10.0)	1.500 (1.013, 2.222)	0.043			1.612 (1.111, 2.339)	0.012			
Presence of risk factor: Hypertension										0.768				0.894	
Yes	19/	24 (79.2)	7.0 (2.0, 12.0)	18/	24 (75.0)	8.0 (4.0, 23.0)	1.836 (0.908, 3.714)	0.091			1.481 (0.774, 2.835)	0.235			
No	52/	59 (88.1)	4.0 (4.0, 5.0)	38/	47 (80.9)	6.0 (4.0, 10.0)	1.467 (0.921, 2.336)	0.107			1.472 (0.964, 2.248)	0.073			
Presence of risk factor: Cardiovascular disorder															
Yes	1/	3 (33.3)		0/	2 (0.0)										
No	70/	80 (87.5)		56/	69 (81.2)										
Presence of risk factor: Chronic kidney disease															
Yes	0			0											
No	71/	83 (85.5)		56/	71 (78.9)										
Presence of risk factor: HIV Infection															
Yes	0			0											
No	71/	83 (85.5)		56/	71 (78.9)										
Presence of risk factor: Sickle Cell Disease															
No	71/	83 (85.5)		56/	71 (78.9)										
Presence of risk factor: Neurodevelopmental Disorder															
Yes	0			0											
No	71/	83 (85.5)		56/	71 (78.9)										
Presence of risk factor: Cancer															
Yes	0/	1 (0.0)		0											
No	71/	82 (86.6)		56/	71 (78.9)										
Presence of risk factor: Device Dependence															
Yes	1/	1 (100.0)		0											
No	70/	82 (85.4)		56/	71 (78.9)										

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=756)			Placebo (N=760)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value	
Age													
< 65	491/ 648	(75.8)	9.0 (9.0, 10.0)	456/ 645	(70.7)	12.0 (10.0, 13.0)	1.221 (1.072, 1.391)	0.003	0.065	1.227 (1.080, 1.394)	0.002	0.091	
>= 65	88/ 108	(81.5)	9.0 (7.0, 12.0)	78/ 115	(67.8)	13.0 (12.0, 17.0)	1.705 (1.238, 2.347)	0.001		1.645 (1.211, 2.235)	0.001		
Gender													
Male	294/ 361	(81.4)	8.0 (8.0, 9.0)	280/ 386	(72.5)	10.0 (9.0, 12.0)	1.318 (1.113, 1.560)	0.001	0.640	1.361 (1.154, 1.604)	<.001	0.371	
Female	285/ 395	(72.2)	11.0 (9.0, 12.0)	254/ 374	(67.9)	13.0 (12.0, 15.0)	1.258 (1.058, 1.496)	0.009		1.227 (1.036, 1.453)	0.018		
Geographic region													
United States	236/ 328	(72.0)	11.0 (9.0, 12.0)	226/ 325	(69.5)	13.0 (11.0, 14.0)	1.156 (0.959, 1.393)	0.129	0.361	1.163 (0.969, 1.396)	0.104	0.345	
Europe	209/ 254	(82.3)	9.0 (8.0, 11.0)	186/ 263	(70.7)	13.0 (11.0, 15.0)	1.462 (1.191, 1.793)	<.001		1.473 (1.208, 1.797)	<.001		
India	44/ 47	(93.6)	8.0 (7.0, 9.0)	45/ 47	(95.7)	9.0 (8.0, 10.0)	1.505 (0.961, 2.356)	0.074		1.333 (0.870, 2.044)	0.187		
Rest of World	90/ 127	(70.9)	9.0 (7.0, 12.0)	77/ 125	(61.6)	12.0 (8.0, 16.0)	1.309 (0.960, 1.785)	0.089		1.312 (0.968, 1.779)	0.080		
COVID-19 therapeutic mAb treatment at randomisation													
Yes	36/ 48	(75.0)	9.0 (7.0, 12.0)	37/ 49	(75.5)	10.0 (8.0, 14.0)	1.113 (0.687, 1.806)	0.663	0.615	1.170 (0.739, 1.853)	0.503	0.706	
No	543/ 708	(76.7)	9.0 (9.0, 10.0)	497/ 711	(69.9)	12.0 (11.0, 13.0)	1.294 (1.142, 1.465)	<.001		1.291 (1.143, 1.459)	<.001		
Baseline viral load 1													
< 10^4 copies/mL	206/ 273	(75.5)	10.0 (9.0, 12.0)	200/ 273	(73.3)	11.0 (9.0, 13.0)	1.111 (0.912, 1.353)	0.295	0.054	1.115 (0.918, 1.355)	0.272	0.068	
>= 10^4 copies/mL	355/ 461	(77.0)	9.0 (7.0, 10.0)	319/ 464	(68.8)	13.0 (12.0, 14.0)	1.373 (1.178, 1.599)	<.001		1.384 (1.189, 1.610)	<.001		
Baseline viral load 2													
< 10^7 copies/mL	389/ 525	(74.1)	10.0 (9.0, 11.0)	395/ 555	(71.2)	12.0 (11.0, 13.0)	1.201 (1.043, 1.383)	0.011	0.071	1.196 (1.040, 1.376)	0.012	0.071	
>= 10^7 copies/mL	172/ 209	(82.3)	8.0 (7.0, 11.0)	124/ 182	(68.1)	13.0 (10.0, 14.0)	1.472 (1.162, 1.864)	0.001		1.519 (1.205, 1.915)	<.001		
Baseline serology status													
Negative	274/ 355	(77.2)	9.0 (8.0, 11.0)	250/ 374	(66.8)	13.0 (11.0, 14.0)	1.392 (1.168, 1.659)	<.001	0.196	1.421 (1.196, 1.687)	<.001	0.092	
Positive	297/ 390	(76.2)	9.0 (9.0, 11.0)	282/ 382	(73.8)	12.0 (10.0, 13.0)	1.212 (1.026, 1.431)	0.023		1.171 (0.995, 1.379)	0.058		
Symptom onset days to first dose date													
<= 3	399/ 509	(78.4)	9.0 (8.0, 11.0)	357/ 491	(72.7)	12.0 (11.0, 13.0)	1.278 (1.104, 1.479)	0.001	0.885	1.273 (1.103, 1.469)	<.001	0.854	
> 3	180/ 247	(72.9)	9.0 (8.0, 11.0)	177/ 269	(65.8)	12.0 (11.0, 14.0)	1.291 (1.043, 1.598)	0.019		1.301 (1.057, 1.601)	0.013		
BMI group													
< 25	130/ 170	(76.5)	8.0 (7.0, 10.0)	120/ 157	(76.4)	11.0 (9.0, 13.0)	1.198 (0.923, 1.555)	0.175	0.646	1.191 (0.929, 1.526)	0.169	0.705	
25 - < 30	207/ 262	(79.0)	9.0 (8.0, 10.0)	190/ 266	(71.4)	13.0 (10.0, 14.0)	1.378 (1.127, 1.686)	0.002		1.361 (1.117, 1.658)	0.002		
>= 30	241/ 323	(74.6)	11.0 (9.0, 12.0)	224/ 337	(66.5)	13.0 (11.0, 15.0)	1.282 (1.063, 1.547)	0.009		1.271 (1.059, 1.525)	0.010		
Ethnicity													
White	447/ 584	(76.5)	10.0 (9.0, 11.0)	414/ 603	(68.7)	13.0 (12.0, 14.0)	1.299 (1.133, 1.490)	<.001	0.918	1.306 (1.142, 1.493)	<.001	0.916	
Black or African American	23/ 37	(62.2)	8.0 (7.0, 13.0)	22/ 31	(71.0)	15.5 (9.0, 22.0)	1.362 (0.725, 2.560)	0.337		1.213 (0.673, 2.183)	0.521		
Asian	68/ 76	(89.5)	7.0 (7.0, 8.0)	69/ 75	(92.0)	8.0 (7.0, 9.0)	1.355 (0.952, 1.930)	0.092		1.211 (0.864, 1.697)	0.266		
Others	41/ 59	(69.5)	13.0 (9.0, 15.0)	29/ 51	(56.9)	17.0 (11.0, NE)	1.310 (0.802, 2.140)	0.281		1.387 (0.861, 2.235)	0.178		
Number of baseline comorbidities present													
0-1	445/ 576	(77.3)		410/ 564	(72.7)								
2-3	132/ 177	(74.6)		118/ 190	(62.1)								
>= 4	2/ 3	(66.7)		6/ 6	(100.0)								
Presence of risk factor: Smoking													
Yes	266/ 342	(77.8)	9.0 (8.0, 11.0)	237/ 340	(69.7)	12.0 (10.0, 14.0)	1.308 (1.093, 1.566)	0.003	0.892	1.332 (1.117, 1.588)	0.001	0.586	
No	312/ 412	(75.7)	9.0 (8.0, 11.0)	297/ 420	(70.7)	12.0 (11.0, 13.0)	1.261 (1.072, 1.485)	0.005		1.246 (1.063, 1.460)	0.007		

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Subgroup Level	Nirmatrelvir/ritonavir (N=756)			Placebo (N=760)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus										0.591				0.557
Yes	83/ 108	(76.9)	10.0 (8.0, 12.0)	81/ 116	(69.8)	13.0 (10.0, 15.0)	1.494 (1.086, 2.055)	0.014			1.399 (1.029, 1.903)	0.032		
No	495/ 647	(76.5)	9.0 (8.0, 10.0)	453/ 644	(70.3)	12.0 (11.0, 13.0)	1.260 (1.106, 1.436)	<.001			1.260 (1.109, 1.431)	<.001		
Presence of risk factor: Immunosuppression										0.587				0.563
Yes	2/ 3	(66.7)	8.0 (4.0, NE)	5/ 7	(71.4)	5.0 (2.0, NE)	0.564 (0.000, NE)	1.000			0.798 (0.154, 4.148)	0.789		
No	576/ 752	(76.6)	9.0 (9.0, 10.0)	529/ 753	(70.3)	12.0 (11.0, 13.0)	1.283 (1.137, 1.447)	<.001			1.286 (1.142, 1.447)	<.001		
Presence of risk factor: Chronic lung disease										0.470				0.434
Yes	41/ 51	(80.4)	8.5 (6.0, 11.0)	25/ 32	(78.1)	9.0 (8.0, 13.0)	1.124 (0.654, 1.930)	0.673			1.048 (0.637, 1.725)	0.854		
No	537/ 704	(76.3)	9.0 (9.0, 11.0)	509/ 728	(69.9)	12.0 (11.0, 13.0)	1.284 (1.134, 1.453)	<.001			1.289 (1.142, 1.456)	<.001		
Presence of risk factor: Hypertension										0.723				0.966
Yes	207/ 284	(72.9)	11.0 (9.0, 13.0)	209/ 309	(67.6)	14.0 (12.0, 16.0)	1.293 (1.060, 1.576)	0.011			1.272 (1.049, 1.542)	0.014		
No	371/ 471	(78.8)	8.0 (8.0, 9.0)	325/ 451	(72.1)	11.0 (10.0, 12.0)	1.243 (1.067, 1.449)	0.005			1.271 (1.095, 1.476)	0.002		
Presence of risk factor: Cardiovascular disorder										0.494				0.805
Yes	24/ 32	(75.0)	13.0 (6.0, 18.0)	26/ 40	(65.0)	14.5 (8.0, 23.0)	1.422 (0.792, 2.554)	0.238			1.361 (0.781, 2.372)	0.276		
No	554/ 723	(76.6)	9.0 (8.0, 10.0)	508/ 720	(70.6)	12.0 (11.0, 13.0)	1.265 (1.118, 1.430)	<.001			1.275 (1.130, 1.438)	<.001		
Presence of risk factor: Chronic kidney disease										0.973				0.753
Yes	3/ 6	(50.0)	7.0 (2.0, NE)	5/ 7	(71.4)	12.0 (7.0, NE)	1.2E8 (0.000, NE)	0.997			1.032 (0.243, 4.375)	0.966		
No	575/ 749	(76.8)	9.0 (9.0, 10.0)	529/ 753	(70.3)	12.0 (11.0, 13.0)	1.279 (1.134, 1.444)	<.001			1.282 (1.139, 1.443)	<.001		
Presence of risk factor: HIV Infection														
Yes	0			0										
No	578/ 755	(76.6)		533/ 759	(70.2)									
Presence of risk factor: Sickle Cell Disease														
No	578/ 755	(76.6)		534/ 760	(70.3)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/ 2	(100.0)		0/ 1	(0.0)									
No	576/ 753	(76.5)		534/ 759	(70.4)									
Presence of risk factor: Cancer										0.908				0.624
Yes	4/ 5	(80.0)	7.0 (2.0, 9.0)	5/ 5	(100.0)	3.0 (2.0, 15.0)	0.392 (0.027, 5.688)	0.493			0.917 (0.228, 3.682)	0.903		
No	574/ 750	(76.5)	9.0 (9.0, 11.0)	529/ 755	(70.1)	12.0 (11.0, 13.0)	1.284 (1.138, 1.449)	<.001			1.285 (1.141, 1.446)	<.001		
Presence of risk factor: Device Dependence														
Yes	1/ 3	(33.3)		2/ 3	(66.7)									
No	571/ 743	(76.9)		528/ 750	(70.4)									

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	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value	
Age													
< 65	57/	77 (74.0)	10.5 (7.0, 13.0)	42/	65 (64.6)	15.0 (10.0, 20.0)	1.334 (0.878, 2.027)	0.177	0.497	1.405 (0.943, 2.094)	0.095		0.346
>= 65	2/	6 (33.3)	NE (5.0, NE)	5/	6 (83.3)	14.0 (5.0, NE)	2.649 (0.085, 82.865)	0.579		0.661 (0.127, 3.452)	0.624		
Gender													
Male	28/	30 (93.3)	10.0 (6.0, 12.0)	16/	25 (64.0)	16.0 (7.0, 23.0)	1.974 (0.978, 3.986)	0.058	0.318	2.113 (1.119, 3.989)	0.021		0.180
Female	31/	53 (58.5)	12.0 (7.0, 25.0)	31/	46 (67.4)	14.0 (10.0, 21.0)	1.129 (0.661, 1.928)	0.658		1.089 (0.661, 1.793)	0.737		
Geographic region													
United States	26/	40 (65.0)		27/	44 (61.4)								
Europe	21/	24 (87.5)		11/	13 (84.6)								
India	0			0									
Rest of World	12/	19 (63.2)		9/	14 (64.3)								
COVID-19 therapeutic mAb treatment at randomisation													
Yes	7/	9 (77.8)	6.0 (4.0, 15.0)	4/	8 (50.0)	9.0 (3.0, NE)	3.270 (0.449, 23.822)	0.242	0.245	1.779 (0.515, 6.148)	0.363		0.445
No	52/	74 (70.3)	11.0 (7.0, 13.0)	43/	63 (68.3)	14.0 (11.0, 20.0)	1.209 (0.795, 1.838)	0.374		1.275 (0.851, 1.911)	0.238		
Baseline viral load 1													
< 10^4 copies/mL	12/	23 (52.2)	17.0 (10.0, NE)	10/	16 (62.5)	17.0 (9.0, NE)	1.008 (0.391, 2.596)	0.987	0.563	1.018 (0.439, 2.358)	0.967		0.429
>= 10^4 copies/mL	47/	60 (78.3)	8.0 (7.0, 12.0)	35/	52 (67.3)	14.0 (8.0, 20.0)	1.382 (0.877, 2.177)	0.164		1.513 (0.975, 2.346)	0.065		
Baseline viral load 2													
< 10^7 copies/mL	28/	45 (62.2)	12.0 (7.0, 17.0)	26/	44 (59.1)	20.0 (13.0, NE)	1.466 (0.802, 2.680)	0.214	0.405	1.508 (0.883, 2.575)	0.132		0.266
>= 10^7 copies/mL	31/	38 (81.6)	8.0 (6.0, 13.0)	19/	24 (79.2)	8.0 (5.0, 14.0)	0.966 (0.522, 1.789)	0.913		0.972 (0.548, 1.724)	0.922		
Baseline serology status													
Negative	34/	43 (79.1)	10.0 (7.0, 13.0)	29/	43 (67.4)	12.0 (8.0, 15.0)	1.240 (0.726, 2.116)	0.430	0.985	1.418 (0.863, 2.329)	0.168		0.763
Positive	24/	39 (61.5)	11.0 (7.0, NE)	18/	28 (64.3)	20.0 (13.0, NE)	1.269 (0.644, 2.501)	0.492		1.238 (0.670, 2.287)	0.495		
Symptom onset days to first dose date													
<= 3	43/	58 (74.1)	10.0 (6.0, 13.0)	32/	43 (74.4)	11.5 (8.0, 15.0)	1.181 (0.738, 1.888)	0.489	0.396	1.189 (0.752, 1.880)	0.459		0.528
> 3	16/	25 (64.0)	11.0 (7.0, 21.0)	15/	28 (53.6)	21.0 (12.0, NE)	1.857 (0.831, 4.149)	0.132		1.572 (0.776, 3.184)	0.209		
BMI group													
< 25	12/	21 (57.1)	11.0 (5.0, 14.0)	9/	14 (64.3)	12.5 (8.0, NE)	1.513 (0.566, 4.045)	0.409	0.262	1.459 (0.613, 3.472)	0.393		0.128
25 - < 30	13/	21 (61.9)	15.0 (7.0, NE)	19/	25 (76.0)	13.0 (8.0, 18.0)	0.865 (0.392, 1.906)	0.718		0.729 (0.357, 1.485)	0.383		
>= 30	34/	41 (82.9)	9.0 (6.0, 13.0)	19/	32 (59.4)	17.0 (7.0, NE)	1.704 (0.921, 3.154)	0.090		1.844 (1.048, 3.246)	0.034		
Ethnicity													
White	46/	66 (69.7)		41/	60 (68.3)								
Black or African American	3/	4 (75.0)		2/	5 (40.0)								
Asian	4/	4 (100.0)		2/	2 (100.0)								
Others	6/	9 (66.7)		2/	4 (50.0)								
Number of baseline comorbidities present													
0-1	49/	66 (74.2)		41/	61 (67.2)								
2-3	10/	16 (62.5)		6/	10 (60.0)								
>= 4	0/	1 (0.0)		0									
Presence of risk factor: Smoking													
Yes	26/	32 (81.3)	11.0 (7.0, 12.0)	23/	32 (71.9)	13.0 (9.0, 18.0)	1.352 (0.730, 2.503)	0.338	0.939	1.431 (0.815, 2.513)	0.212		0.944
No	33/	51 (64.7)	10.0 (6.0, 14.0)	24/	39 (61.5)	14.0 (8.0, NE)	1.355 (0.757, 2.423)	0.306		1.328 (0.785, 2.248)	0.291		

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RRI-conform mITT2 Analysis set
Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Muscle or Body Aches - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=83)			Placebo (N=71)			Adjusted Analysis [2]				Unadjusted Analysis [3]			
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)		p-Value	Interaction p-Value	Hazard Ratio (95% CI)		p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus										0.441				0.193
Yes	8/	13 (61.5)	14.0 (7.0, NE)	5/	6 (83.3)	14.0 (4.0, NE)	1.179 (0.268, 5.185)	0.827			0.753 (0.246, 2.310)	0.620		
No	51/	70 (72.9)	9.0 (7.0, 12.0)	42/	65 (64.6)	15.0 (10.0, 20.0)	1.370 (0.896, 2.096)	0.147			1.507 (1.001, 2.269)	0.049		
Presence of risk factor: Immunosuppression														
Yes	0			0										
No	59/	83 (71.1)		47/	71 (66.2)									
Presence of risk factor: Chronic lung disease										0.192				0.101
Yes	4/	10 (40.0)	NE (6.0, NE)	3/	4 (75.0)	11.0 (4.0, NE)	1.332 (0.120, 14.833)	0.816			0.396 (0.087, 1.797)	0.230		
No	55/	73 (75.3)	9.0 (7.0, 12.0)	44/	67 (65.7)	15.0 (11.0, 20.0)	1.441 (0.950, 2.185)	0.085			1.527 (1.027, 2.272)	0.037		
Presence of risk factor: Hypertension										0.600				0.583
Yes	14/	24 (58.3)	12.0 (5.0, NE)	16/	24 (66.7)	14.0 (8.0, 24.0)	1.321 (0.614, 2.843)	0.477			1.107 (0.540, 2.271)	0.781		
No	45/	59 (76.3)	10.0 (7.0, 13.0)	31/	47 (66.0)	13.0 (9.0, 20.0)	1.420 (0.874, 2.308)	0.157			1.428 (0.903, 2.258)	0.128		
Presence of risk factor: Cardiovascular disorder														
Yes	0/	3 (0.0)		0/	2 (0.0)									
No	59/	80 (73.8)		47/	69 (68.1)									
Presence of risk factor: Chronic kidney disease														
Yes	0			0										
No	59/	83 (71.1)		47/	71 (66.2)									
Presence of risk factor: HIV Infection														
Yes	0			0										
No	59/	83 (71.1)		47/	71 (66.2)									
Presence of risk factor: Sickle Cell Disease														
No	59/	83 (71.1)		47/	71 (66.2)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	0			0										
No	59/	83 (71.1)		47/	71 (66.2)									
Presence of risk factor: Cancer														
Yes	0/	1 (0.0)		0										
No	59/	82 (72.0)		47/	71 (66.2)									
Presence of risk factor: Device Dependence														
Yes	0/	1 (0.0)		0										
No	59/	82 (72.0)		47/	71 (66.2)									

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

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[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Headache - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Unadjusted analysis [2]			
			Relative Risk (95% CI)		p-Value	Interaction p-Value	Relative Risk (95% CI)		p-Value	Interaction p-Value
Age						0.364				0.367
< 65	195/ 790 (24.7)	214/ 810 (26.4)	0.924 (0.780, 1.095)	0.363			0.934 (0.790, 1.105)	0.426		
>= 65	33/ 138 (23.9)	45/ 145 (31.0)	0.724 (0.491, 1.068)	0.104			0.771 (0.525, 1.131)	0.183		
Gender						0.434				0.377
Male	108/ 463 (23.3)	122/ 507 (24.1)	0.960 (0.762, 1.209)	0.728			0.969 (0.773, 1.215)	0.788		
Female	120/ 465 (25.8)	137/ 448 (30.6)	0.844 (0.685, 1.041)	0.114			0.844 (0.685, 1.039)	0.110		
Geographic region						0.347				0.316
United States	91/ 375 (24.3)	99/ 387 (25.6)	0.932 (0.724, 1.199)	0.584			0.949 (0.741, 1.214)	0.675		
Europe	92/ 322 (28.6)	97/ 321 (30.2)	0.955 (0.748, 1.218)	0.708			0.946 (0.744, 1.202)	0.647		
India	13/ 74 (17.6)	11/ 78 (14.1)	1.082 (0.526, 2.228)	0.830			1.246 (0.596, 2.604)	0.559		
Rest of World	32/ 157 (20.4)	52/ 169 (30.8)	0.668 (0.456, 0.978)	0.038			0.662 (0.452, 0.972)	0.035		
COVID-19 therapeutic mAb treatment at randomisation						0.299				0.255
Yes	16/ 57 (28.1)	13/ 60 (21.7)	1.241 (0.657, 2.342)	0.506			1.296 (0.686, 2.447)	0.425		
No	212/ 871 (24.3)	246/ 895 (27.5)	0.878 (0.747, 1.031)	0.112			0.886 (0.756, 1.037)	0.132		
Baseline viral load 1						0.302				0.239
< 10 ⁴ copies/mL	68/ 335 (20.3)	92/ 354 (26.0)	0.787 (0.598, 1.037)	0.088			0.781 (0.593, 1.029)	0.079		
>= 10 ⁴ copies/mL	153/ 569 (26.9)	162/ 575 (28.2)	0.952 (0.788, 1.150)	0.611			0.954 (0.791, 1.152)	0.627		
Baseline viral load 2						0.226				0.279
< 10 ⁷ copies/mL	156/ 652 (23.9)	178/ 699 (25.5)	0.956 (0.793, 1.153)	0.639			0.940 (0.780, 1.132)	0.513		
>= 10 ⁷ copies/mL	65/ 252 (25.8)	76/ 230 (33.0)	0.775 (0.586, 1.024)	0.073			0.781 (0.591, 1.032)	0.082		
Baseline serology status						0.335				0.248
Negative	122/ 435 (28.0)	129/ 456 (28.3)	0.962 (0.778, 1.189)	0.720			0.991 (0.804, 1.223)	0.936		
Positive	103/ 482 (21.4)	126/ 487 (25.9)	0.830 (0.661, 1.043)	0.110			0.826 (0.658, 1.037)	0.100		
Symptom onset days to first dose date						0.590				0.619
<= 3	155/ 624 (24.8)	176/ 624 (28.2)	0.867 (0.719, 1.046)	0.137			0.881 (0.732, 1.060)	0.179		
> 3	73/ 304 (24.0)	83/ 331 (25.1)	0.945 (0.718, 1.245)	0.690			0.958 (0.729, 1.259)	0.756		
BMI group						0.919				0.818
< 25	45/ 215 (20.9)	50/ 213 (23.5)	0.883 (0.609, 1.279)	0.510			0.892 (0.625, 1.272)	0.527		
25 - < 30	81/ 319 (25.4)	98/ 332 (29.5)	0.873 (0.679, 1.124)	0.292			0.860 (0.669, 1.106)	0.240		
>= 30	102/ 393 (26.0)	111/ 410 (27.1)	0.919 (0.726, 1.163)	0.482			0.959 (0.761, 1.207)	0.720		
Ethnicity						0.537				0.715
White	182/ 699 (26.0)	203/ 718 (28.3)	0.913 (0.767, 1.087)	0.305			0.921 (0.776, 1.092)	0.345		
Black or African American	10/ 43 (23.3)	10/ 40 (25.0)	1.026 (0.428, 2.463)	0.953			0.930 (0.434, 1.996)	0.853		
Asian	21/ 117 (17.9)	23/ 127 (18.1)	1.007 (0.600, 1.691)	0.979			0.991 (0.580, 1.693)	0.974		
Others	15/ 69 (21.7)	23/ 70 (32.9)	NE (NE, NE)	NE			0.662 (0.378, 1.157)	0.148		
Number of baseline comorbidities present						0.231				0.577
0-1	168/ 710 (23.7)	198/ 728 (27.2)	0.849 (0.709, 1.016)	0.074			0.870 (0.728, 1.039)	0.125		
2-3	60/ 214 (28.0)	60/ 221 (27.1)	1.124 (0.824, 1.532)	0.460			1.033 (0.762, 1.400)	0.836		
>= 4	0/ 4 (0.0)	1/ 6 (16.7)	NE (NE, NE)	NE			0.467 (0.024, 9.259)	0.617		
Presence of risk factor: Smoking						0.258				0.367
Yes	95/ 417 (22.8)	101/ 438 (23.1)	0.990 (0.772, 1.270)	0.938			0.988 (0.773, 1.263)	0.923		
No	133/ 509 (26.1)	158/ 517 (30.6)	0.836 (0.685, 1.019)	0.076			0.855 (0.703, 1.040)	0.116		
Presence of risk factor: Diabetes mellitus						0.219				0.236

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

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 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Headache - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value	
Yes	29/ 130 (22.3)	42/ 136 (30.9)	0.707 (0.474, 1.056)			0.090		0.722 (0.481, 1.086)			0.118	
No	199/ 797 (25.0)	217/ 819 (26.5)	0.940 (0.794, 1.113)			0.471		0.942 (0.798, 1.112)			0.483	
Presence of risk factor: Immunosuppression							0.352					0.761
Yes	2/ 6 (33.3)	2/ 7 (28.6)	NE (NE, NE)			NE		1.167 (0.229, 5.946)			0.853	
No	226/ 921 (24.5)	257/ 948 (27.1)	0.892 (0.763, 1.043)			0.153		0.905 (0.776, 1.056)			0.205	
Presence of risk factor: Chronic lung disease							0.014					0.022
Yes	20/ 62 (32.3)	5/ 39 (12.8)	2.372 (0.959, 5.869)			0.062		2.516 (1.029, 6.154)			0.043	
No	208/ 865 (24.0)	254/ 916 (27.7)	0.860 (0.732, 1.009)			0.064		0.867 (0.740, 1.016)			0.077	
Presence of risk factor: Hypertension							0.527					0.754
Yes	93/ 348 (26.7)	106/ 371 (28.6)	0.976 (0.768, 1.241)			0.844		0.935 (0.738, 1.185)			0.580	
No	135/ 579 (23.3)	153/ 584 (26.2)	0.863 (0.704, 1.058)			0.157		0.890 (0.728, 1.088)			0.255	
Presence of risk factor: Cardiovascular disorder							0.239					0.306
Yes	13/ 42 (31.0)	22/ 49 (44.9)	NE (NE, NE)			NE		0.689 (0.399, 1.192)			0.183	
No	215/ 885 (24.3)	237/ 906 (26.2)	0.918 (0.781, 1.079)			0.301		0.929 (0.792, 1.089)			0.364	
Presence of risk factor: Chronic kidney disease							0.071					0.260
Yes	0/ 6 (0.0)	3/ 8 (37.5)	NE (NE, NE)			NE		0.184 (0.011, 3.002)			0.234	
No	228/ 921 (24.8)	256/ 947 (27.0)	0.906 (0.775, 1.059)			0.214		0.916 (0.785, 1.068)			0.262	
Presence of risk factor: HIV Infection												
Yes	0	0/ 1 (0.0)										
No	228/ 927 (24.6)	259/ 953 (27.2)										
Presence of risk factor: Sickle Cell Disease												
No	228/ 927 (24.6)	259/ 955 (27.1)										
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0/ 2 (0.0)	0/ 1 (0.0)										
No	228/ 925 (24.6)	259/ 954 (27.1)										
Presence of risk factor: Cancer							0.004					0.116
Yes	3/ 5 (60.0)	0/ 6 (0.0)	NE (NE, NE)			NE		8.167 (0.519, 128.422)			0.135	
No	225/ 922 (24.4)	259/ 949 (27.3)	0.883 (0.755, 1.032)			0.118		0.894 (0.767, 1.043)			0.154	
Presence of risk factor: Device Dependence												
Yes	2/ 4 (50.0)	1/ 3 (33.3)										
No	224/ 914 (24.5)	255/ 944 (27.0)										

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

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If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochran's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Headache - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=691)						Placebo (N=693)				Adjusted Analysis [2]		Unadjusted Analysis [3]						
	n/N	(%)	Median	(95% CI)	[1]		n/N	(%)	Median	(95% CI)	[1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value		
Age																			
< 65	502/ 92	591 100	(84.9) (92.0)	5.0	(5.0, 4.0, 6.0 7.0)		471/ 82	589 104	(80.0) (78.8)	7.0	(6.0, 8.0 10.0)	1.200 (1.055, 1.365)	0.005	0.108	1.210 (1.067, 1.372)	0.003	0.065		
>= 65												1.593 (1.157, 2.192)	0.004			1.666 (1.230, 2.257)		<.001	
Gender																			
Male	280/ 314	323 368	(86.7) (85.3)	5.0	(4.0, 5.0, 6.0 7.0)		282/ 271	353 340	(79.9) (79.7)	7.0	(6.0, 8.0 8.0)	1.272 (1.073, 1.508)	0.006	0.896	1.287 (1.090, 1.519)	0.003	0.815		
Female												1.242 (1.052, 1.467)	0.011			1.255 (1.067, 1.478)		0.006	
Geographic region																			
United States	242/ 242	294 294	(82.3)	6.0	(5.0, 5.0, 8.0 8.0)		252/ 178	314 223	(80.3) (79.8)	7.0	(6.0, 8.0 8.0)	1.070 (0.893, 1.281)	0.464	0.111	1.093 (0.916, 1.304)	0.325	0.131		
Europe	209/ 209	231 231	(90.5)	5.0	(4.0, 4.0, 6.0 6.0)		178/ 178	223 223	(79.8)	7.0	(6.0, 8.0 8.0)	1.382 (1.122, 1.703)	0.002			1.421 (1.161, 1.738)		<.001	
India	46/ 46	50 50	(92.0)	5.0	(3.0, 3.0, 9.0 9.0)		42/ 42	44 44	(95.5)	8.0	(6.0, 11.0 11.0)	1.544 (0.986, 2.416)	0.057			1.474 (0.957, 2.272)		0.079	
Rest of World	97/ 97	116 116	(83.6)	5.0	(3.0, 3.0, 6.0 6.0)		81/ 81	112 112	(72.3)	7.0	(5.0, 9.0 9.0)	1.413 (1.046, 1.909)	0.024			1.422 (1.057, 1.914)		0.020	
COVID-19 therapeutic mAb treatment at randomisation																			
Yes	35/ 35	45 45	(77.8)	8.0	(5.0, 5.0, 14.0 14.0)		41/ 41	47 47	(87.2)	7.0	(4.0, 9.0 9.0)	0.720 (0.451, 1.149)	0.168	0.016	0.739 (0.470, 1.161)	0.189	0.016		
No	559/ 559	646 646	(86.5)	5.0	(4.0, 4.0, 6.0 6.0)		512/ 512	646 646	(79.3)	7.0	(6.0, 8.0 8.0)	1.301 (1.151, 1.471)	<.001			1.321 (1.171, 1.490)		<.001	
Baseline viral load 1																			
< 10^4 copies/mL	216/ 216	249 249	(86.7)	6.0	(5.0, 5.0, 7.0 7.0)		215/ 215	254 254	(84.6)	7.0	(5.0, 8.0 8.0)	1.122 (0.927, 1.358)	0.237	0.142	1.148 (0.950, 1.387)	0.153	0.201		
>= 10^4 copies/mL	360/ 360	423 423	(85.1)	5.0	(4.0, 4.0, 6.0 6.0)		325/ 325	417 417	(77.9)	7.0	(6.0, 8.0 8.0)	1.323 (1.136, 1.540)	<.001			1.311 (1.128, 1.524)		<.001	
Baseline viral load 2																			
< 10^7 copies/mL	399/ 399	478 478	(83.5)	6.0	(5.0, 5.0, 7.0 7.0)		411/ 411	507 507	(81.1)	7.0	(6.0, 8.0 8.0)	1.180 (1.027, 1.356)	0.020	0.127	1.181 (1.029, 1.356)	0.018	0.138		
>= 10^7 copies/mL	177/ 177	194 194	(91.2)	4.0	(3.0, 3.0, 5.0 5.0)		129/ 129	164 164	(78.7)	6.0	(5.0, 8.0 8.0)	1.451 (1.144, 1.840)	0.002			1.434 (1.142, 1.801)		0.002	
Baseline serology status																			
Negative	274/ 274	324 324	(84.6)	5.0	(4.0, 4.0, 6.0 6.0)		244/ 244	330 330	(73.9)	8.0	(7.0, 9.0 9.0)	1.367 (1.145, 1.631)	<.001	0.136	1.391 (1.170, 1.653)	<.001	0.112		
Positive	314/ 314	360 360	(87.2)	5.0	(5.0, 5.0, 6.0 6.0)		303/ 303	356 356	(85.1)	6.0	(6.0, 8.0 8.0)	1.164 (0.991, 1.367)	0.064			1.180 (1.007, 1.382)		0.041	
Symptom onset days to first dose date																			
<= 3	419/ 419	473 473	(88.6)	5.0	(4.0, 4.0, 6.0 6.0)		365/ 365	438 438	(83.3)	7.0	(6.0, 8.0 8.0)	1.292 (1.119, 1.491)	<.001	0.627	1.278 (1.110, 1.471)	<.001	0.811		
> 3	175/ 175	218 218	(80.3)	6.0	(5.0, 5.0, 8.0 8.0)		188/ 188	255 255	(73.7)	8.0	(6.0, 9.0 9.0)	1.198 (0.970, 1.480)	0.093			1.229 (1.000, 1.511)		0.050	
BMI group																			
< 25	135/ 135	155 155	(87.1)	5.0	(4.0, 4.0, 6.0 6.0)		125/ 125	147 147	(85.0)	6.0	(5.0, 7.0 7.0)	1.172 (0.911, 1.509)	0.218	0.709	1.218 (0.954, 1.555)	0.113	0.804		
25 - < 30	205/ 205	237 237	(86.5)	6.0	(5.0, 5.0, 7.0 7.0)		191/ 191	236 236	(80.9)	8.0	(6.0, 8.0 8.0)	1.226 (1.000, 1.504)	0.050			1.241 (1.018, 1.513)		0.032	
>= 30	253/ 253	298 298	(84.9)	5.0	(4.0, 4.0, 6.0 6.0)		237/ 237	310 310	(76.5)	8.0	(6.0, 8.0 8.0)	1.314 (1.094, 1.577)	0.003			1.318 (1.104, 1.575)		0.002	
Ethnicity																			
White	448/ 448	527 527	(85.0)	5.0	(5.0, 5.0, 6.0 6.0)		426/ 426	540 540	(78.9)	7.0	(6.0, 8.0 8.0)	1.207 (1.054, 1.383)	0.007	0.346	1.237 (1.083, 1.413)	0.002	0.478		
Black or African American	28/ 28	34 34	(82.4)	4.0	(3.0, 3.0, 8.0 8.0)		29/ 29	36 36	(80.6)	8.0	(3.0, 16.0 16.0)	1.251 (0.706, 2.216)	0.443			1.374 (0.809, 2.334)		0.240	
Asian	70/ 70	76 76	(92.1)	4.0	(3.0, 3.0, 6.0 6.0)		63/ 63	67 67	(94.0)	6.0	(4.0, 8.0 8.0)	1.158 (0.809, 1.658)	0.422			1.215 (0.860, 1.715)		0.269	
Others	48/ 48	54 54	(88.9)	5.0	(3.0, 3.0, 9.0 9.0)		35/ 35	50 50	(70.0)	9.0	(5.0, 16.0 16.0)	1.821 (1.146, 2.893)	0.011			1.770 (1.134, 2.761)		0.012	
Number of baseline comorbidities present																			
0-1	458/ 458	533 533	(85.9)				416/ 416	523 523	(79.5)					0.930			0.809		
2-3	133/ 133	155 155	(85.8)				132/ 132	165 165	(80.0)										
>= 4	3/ 3	3 3	(100.0)				5/ 5	5 5	(100.0)										
Presence of risk factor: Smoking																			
Yes	258/ 258	297 297	(86.9)	5.0	(4.0, 4.0, 6.0 6.0)		251/ 251	311 311	(80.7)	6.0	(5.0, 7.0 7.0)	1.258 (1.052, 1.505)	0.012	0.930	1.279 (1.074, 1.523)	0.006	0.809		
No	334/ 334	392 392	(85.2)	5.0	(5.0, 5.0, 7.0 7.0)		302/ 302	382 382	(79.1)	8.0	(7.0, 8.0 8.0)	1.249 (1.065, 1.464)	0.006			1.259 (1.077, 1.471)		0.004	

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[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=691)			Placebo (N=693)			Adjusted Analysis [2]				Unadjusted Analysis [3]			
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)		p-Value	Interaction p-Value	Hazard Ratio (95% CI)		p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus										0.273				0.337
Yes	91/ 103	(88.3)	5.0 (4.0, 6.0)	81/ 100	(81.0)	7.0 (6.0, 8.0)	1.543 (1.125, 2.117)	0.007			1.452 (1.074, 1.965)	0.015		
No	502/ 587	(85.5)	5.0 (5.0, 6.0)	472/ 593	(79.6)	7.0 (6.0, 8.0)	1.221 (1.073, 1.389)	0.002			1.237 (1.090, 1.403)	<.001		
Presence of risk factor: Immunosuppression														
Yes	4/ 4	(100.0)		5/ 5	(100.0)									
No	589/ 686	(85.9)		548/ 688	(79.7)									
Presence of risk factor: Chronic lung disease										0.077				0.064
Yes	42/ 49	(85.7)	7.0 (4.0, 9.0)	28/ 33	(84.8)	5.0 (3.0, 7.0)	0.820 (0.497, 1.352)	0.437			0.818 (0.505, 1.326)	0.415		
No	551/ 641	(86.0)	5.0 (5.0, 6.0)	525/ 660	(79.5)	7.0 (6.0, 8.0)	1.282 (1.134, 1.449)	<.001			1.300 (1.153, 1.466)	<.001		
Presence of risk factor: Hypertension										0.301				0.444
Yes	220/ 259	(84.9)	5.0 (4.0, 7.0)	213/ 270	(78.9)	8.0 (7.0, 9.0)	1.353 (1.113, 1.645)	0.002			1.334 (1.104, 1.612)	0.003		
No	373/ 431	(86.5)	5.0 (4.0, 6.0)	340/ 423	(80.4)	6.0 (6.0, 7.0)	1.196 (1.029, 1.390)	0.020			1.220 (1.053, 1.413)	0.008		
Presence of risk factor: Cardiovascular disorder										0.801				0.981
Yes	24/ 28	(85.7)	9.0 (3.0, 13.0)	22/ 29	(75.9)	8.0 (3.0, 13.0)	1.394 (0.729, 2.666)	0.315			1.262 (0.704, 2.262)	0.434		
No	569/ 662	(86.0)	5.0 (5.0, 6.0)	531/ 664	(80.0)	7.0 (6.0, 8.0)	1.250 (1.107, 1.411)	<.001			1.268 (1.126, 1.427)	<.001		
Presence of risk factor: Chronic kidney disease										0.198				0.087
Yes	5/ 6	(83.3)	4.0 (2.0, 7.0)	6/ 8	(75.0)	8.0 (4.0, NE)	13.762 (1.520, 124.57)	0.020			5.996 (1.356, 26.510)	0.018		
No	588/ 684	(86.0)	5.0 (5.0, 6.0)	547/ 685	(79.9)	7.0 (6.0, 8.0)	1.243 (1.104, 1.401)	<.001			1.256 (1.117, 1.411)	<.001		
Presence of risk factor: HIV Infection														
Yes	0			0										
No	593/ 690	(85.9)		552/ 692	(79.8)									
Presence of risk factor: Sickle Cell Disease														
No	593/ 690	(85.9)		553/ 693	(79.8)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/ 2	(100.0)		0/ 1	(0.0)									
No	591/ 688	(85.9)		553/ 692	(79.9)									
Presence of risk factor: Cancer														
Yes	1/ 1	(100.0)		5/ 5	(100.0)									
No	592/ 689	(85.9)		548/ 688	(79.7)									
Presence of risk factor: Device Dependence														
Yes	2/ 3	(66.7)		2/ 3	(66.7)									
No	586/ 679	(86.3)		550/ 687	(80.1)									

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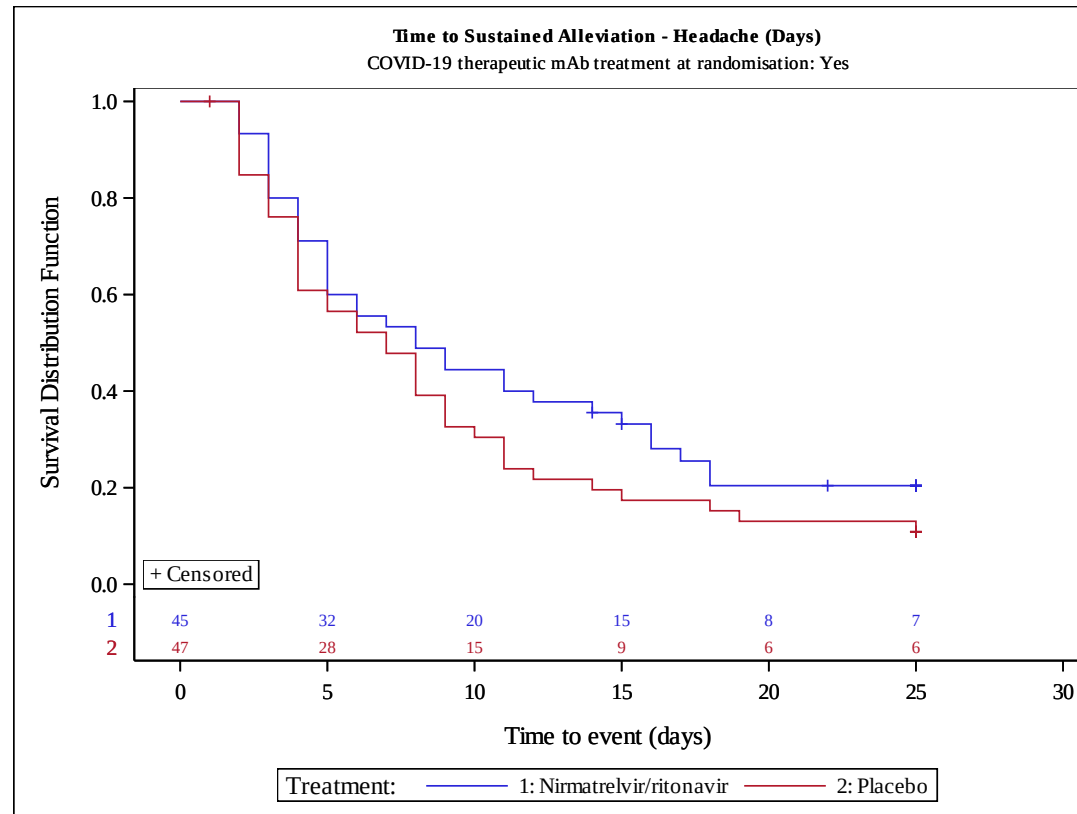
[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Final

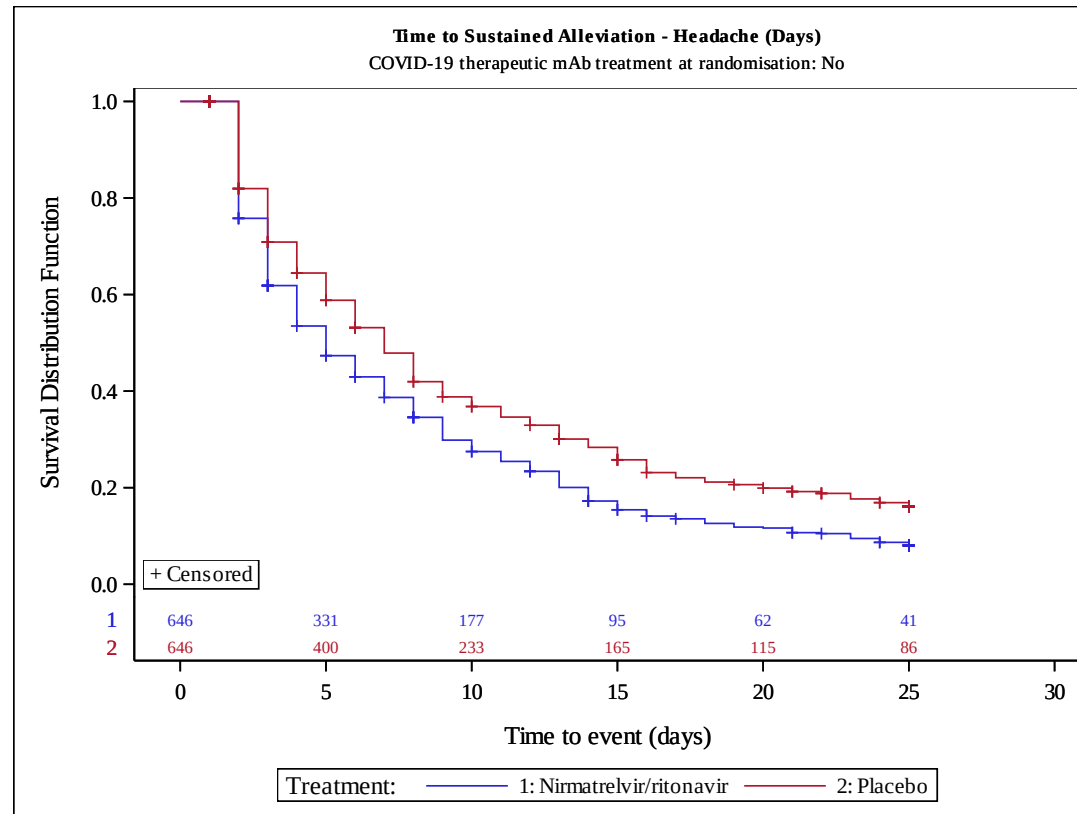


Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=79)			Placebo (N=70)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value	
Age													
< 65	66/	74 (89.2)	3.0 (3.0, 4.0)	52/	64 (81.3)	7.0 (5.0, 12.0)	1.467 (0.986, 2.181)	0.058	0.982	1.542 (1.069, 2.225)	0.021		0.946
>= 65	5/	5 (100.0)	10.0 (2.0, 25.0)	4/	6 (66.7)	7.5 (2.0, NE)	1.023 (0.116, 8.985)	0.984		1.464 (0.389, 5.519)	0.573		
Gender													
Male	27/	29 (93.1)	3.0 (2.0, 5.0)	16/	23 (69.6)	8.0 (3.0, 12.0)	1.452 (0.688, 3.068)	0.328	0.934	1.740 (0.930, 3.255)	0.083		0.662
Female	44/	50 (88.0)	3.5 (3.0, 5.0)	40/	47 (85.1)	7.0 (5.0, 13.0)	1.483 (0.930, 2.364)	0.098		1.459 (0.949, 2.244)	0.085		
Geographic region													
United States	30/	36 (83.3)		30/	38 (78.9)								
Europe	21/	21 (100.0)		13/	15 (86.7)								
India	0			0									
Rest of World	20/	22 (90.9)		13/	17 (76.5)								
COVID-19 therapeutic mAb treatment at randomisation									0.793				0.961
Yes	4/	4 (100.0)	4.0 (3.0, 9.0)	6/	7 (85.7)	7.0 (3.0, 19.0)	4.552 (0.189, 109.63)	0.351		2.114 (0.519, 8.619)	0.296		
No	67/	75 (89.3)	3.0 (3.0, 4.0)	50/	63 (79.4)	7.0 (5.0, 12.0)	1.432 (0.970, 2.116)	0.071		1.539 (1.065, 2.225)	0.022		
Baseline viral load 1									0.467				0.429
< 10^4 copies/mL	15/	19 (78.9)	4.0 (2.0, 14.0)	8/	10 (80.0)	9.0 (2.0, 14.0)	1.316 (0.486, 3.566)	0.589		1.139 (0.480, 2.700)	0.768		
>= 10^4 copies/mL	54/	58 (93.1)	3.0 (3.0, 4.0)	44/	55 (80.0)	7.0 (4.0, 11.0)	1.598 (1.052, 2.429)	0.028		1.681 (1.124, 2.514)	0.011		
Baseline viral load 2									0.485				0.789
< 10^7 copies/mL	35/	41 (85.4)	4.0 (3.0, 8.0)	34/	43 (79.1)	8.0 (5.0, 14.0)	1.501 (0.863, 2.612)	0.151		1.475 (0.918, 2.371)	0.108		
>= 10^7 copies/mL	34/	36 (94.4)	3.0 (2.0, 4.0)	18/	22 (81.8)	5.0 (3.0, 9.0)	1.275 (0.690, 2.356)	0.439		1.394 (0.783, 2.480)	0.259		
Baseline serology status									0.279				0.293
Negative	38/	42 (90.5)	3.0 (3.0, 4.0)	39/	50 (78.0)	8.0 (6.0, 12.0)	1.830 (1.126, 2.975)	0.015		1.902 (1.208, 2.995)	0.006		
Positive	33/	37 (89.2)	4.0 (2.0, 8.0)	17/	20 (85.0)	6.0 (3.0, 13.0)	1.154 (0.595, 2.241)	0.672		1.208 (0.671, 2.175)	0.528		
Symptom onset days to first dose date									0.772				0.743
<= 3	53/	57 (93.0)	3.0 (3.0, 4.0)	39/	42 (92.9)	7.0 (4.0, 8.0)	1.389 (0.894, 2.157)	0.144		1.443 (0.950, 2.193)	0.086		
> 3	18/	22 (81.8)	4.0 (2.0, 14.0)	17/	28 (60.7)	12.0 (5.0, NE)	2.147 (0.991, 4.653)	0.053		1.580 (0.813, 3.072)	0.177		
BMI group									0.649				0.657
< 25	11/	13 (84.6)	3.0 (2.0, 8.0)	13/	16 (81.3)	9.0 (4.0, 14.0)	2.512 (1.017, 6.203)	0.046		2.365 (1.034, 5.412)	0.041		
25 - < 30	22/	23 (95.7)	4.0 (3.0, 8.0)	15/	20 (75.0)	7.0 (3.0, 8.0)	0.921 (0.420, 2.017)	0.837		1.262 (0.653, 2.437)	0.489		
>= 30	38/	43 (88.4)	3.0 (2.0, 4.0)	28/	34 (82.4)	9.0 (4.0, 14.0)	1.408 (0.810, 2.448)	0.225		1.468 (0.896, 2.404)	0.128		
Ethnicity													
White	50/	57 (87.7)		44/	54 (81.5)								
Black or African American	6/	7 (85.7)		5/	6 (83.3)								
Asian	4/	4 (100.0)		2/	3 (66.7)								
Others	11/	11 (100.0)		5/	7 (71.4)								
Number of baseline comorbidities present													
0-1	61/	68 (89.7)		51/	64 (79.7)								
2-3	9/	10 (90.0)		5/	6 (83.3)								
>= 4	1/	1 (100.0)		0									
Presence of risk factor: Smoking									0.615				0.494
Yes	30/	33 (90.9)	3.0 (2.0, 5.0)	26/	33 (78.8)	7.0 (4.0, 12.0)	1.768 (0.942, 3.321)	0.076		1.874 (1.100, 3.192)	0.021		
No	40/	45 (88.9)	3.5 (3.0, 8.0)	30/	37 (81.1)	8.0 (4.0, 13.0)	1.341 (0.810, 2.218)	0.254		1.364 (0.848, 2.194)	0.200		

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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Headache - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=79)			Placebo (N=70)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Presence of risk factor: Diabetes mellitus									0.852			0.627
Yes	7/	9 (77.8)	3.0 (2.0, NE)	3/	3 (100.0)	14.0 (13.0, 22.0)	2.223 (0.216, 22.840)	0.501		0.876 (0.217, 3.538)	0.853	
No	63/	69 (91.3)	3.0 (3.0, 4.0)	53/	67 (79.1)	7.0 (5.0, 11.0)	1.505 (0.996, 2.272)	0.052		1.647 (1.140, 2.382)	0.008	
Presence of risk factor: Immunosuppression												
Yes	0			1/	1 (100.0)							
No	70/	78 (89.7)		55/	69 (79.7)							
Presence of risk factor: Chronic lung disease												
Yes	5/	6 (83.3)		1/	2 (50.0)							
No	65/	72 (90.3)		55/	68 (80.9)							
Presence of risk factor: Hypertension									0.825			0.755
Yes	17/	20 (85.0)	4.0 (2.0, 13.0)	13/	17 (76.5)	8.0 (4.0, 14.0)	1.178 (0.527, 2.633)	0.690		1.371 (0.663, 2.833)	0.395	
No	53/	58 (91.4)	3.0 (3.0, 4.0)	43/	53 (81.1)	7.0 (4.0, 12.0)	1.689 (1.052, 2.713)	0.030		1.611 (1.073, 2.420)	0.021	
Presence of risk factor: Cardiovascular disorder												
Yes	2/	2 (100.0)		0/	1 (0.0)							
No	68/	76 (89.5)		56/	69 (81.2)							
Presence of risk factor: Chronic kidney disease												
Yes	1/	1 (100.0)		0								
No	69/	77 (89.6)		56/	70 (80.0)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	70/	78 (89.7)		56/	70 (80.0)							
Presence of risk factor: Sickle Cell Disease												
No	70/	78 (89.7)		56/	70 (80.0)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0			0								
No	70/	78 (89.7)		56/	70 (80.0)							
Presence of risk factor: Cancer												
Yes	0			0								
No	70/	78 (89.7)		56/	70 (80.0)							
Presence of risk factor: Device Dependence												
Yes	1/	1 (100.0)		0								
No	69/	77 (89.6)		56/	70 (80.0)							

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

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p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=691)			Placebo (N=693)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	467/ 591	(79.0)	9.0 (8.0, 10.0)	427/ 589	(72.5)	11.0 (9.0, 13.0)	1.185 (1.036, 1.355)	0.013		0.051	1.214 (1.065, 1.385)	0.004		0.038
>= 65	84/ 100	(84.0)	8.0 (7.0, 10.0)	72/ 104	(69.2)	13.0 (10.0, 16.0)	1.662 (1.192, 2.318)	0.003			1.756 (1.279, 2.412)	<.001		
Gender														
Male	272/ 323	(84.2)	8.0 (7.0, 9.0)	260/ 353	(73.7)	10.0 (9.0, 12.0)	1.308 (1.098, 1.557)	0.003		0.528	1.361 (1.148, 1.614)	<.001		0.397
Female	279/ 368	(75.8)	10.0 (9.0, 12.0)	239/ 340	(70.3)	13.0 (11.0, 15.0)	1.215 (1.019, 1.449)	0.030			1.234 (1.038, 1.467)	0.017		
Geographic region														
United States	226/ 294	(76.9)	10.0 (9.0, 12.0)	229/ 314	(72.9)	11.0 (9.0, 14.0)	1.089 (0.903, 1.314)	0.373		0.217	1.129 (0.939, 1.357)	0.197		0.263
Europe	191/ 231	(82.7)	9.0 (8.0, 10.0)	156/ 223	(70.0)	12.0 (10.0, 15.0)	1.436 (1.155, 1.785)	0.001			1.472 (1.190, 1.820)	<.001		
India	46/ 50	(92.0)	7.0 (4.0, 9.0)	42/ 44	(95.5)	8.0 (6.0, 12.0)	1.422 (0.904, 2.235)	0.127			1.450 (0.940, 2.236)	0.093		
Rest of World	88/ 116	(75.9)	8.0 (7.0, 10.0)	72/ 112	(64.3)	11.0 (9.0, 16.0)	1.356 (0.989, 1.858)	0.058			1.355 (0.991, 1.852)	0.057		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	34/ 45	(75.6)	11.0 (8.0, 17.0)	38/ 47	(80.9)	10.0 (8.0, 11.0)	0.800 (0.500, 1.281)	0.353		0.050	0.828 (0.521, 1.317)	0.426		0.052
No	517/ 646	(80.0)	9.0 (8.0, 10.0)	461/ 646	(71.4)	12.0 (10.0, 13.0)	1.294 (1.138, 1.471)	<.001			1.326 (1.169, 1.504)	<.001		
Baseline viral load 1														
< 10^4 copies/mL	200/ 249	(80.3)	9.0 (8.0, 10.0)	196/ 254	(77.2)	10.0 (8.0, 11.0)	1.137 (0.933, 1.387)	0.204		0.205	1.140 (0.936, 1.388)	0.194		0.204
>= 10^4 copies/mL	335/ 423	(79.2)	9.0 (8.0, 10.0)	293/ 417	(70.3)	12.0 (10.0, 14.0)	1.324 (1.130, 1.551)	<.001			1.334 (1.140, 1.561)	<.001		
Baseline viral load 2														
< 10^7 copies/mL	374/ 478	(78.2)	9.0 (8.0, 10.0)	375/ 507	(74.0)	11.0 (9.0, 13.0)	1.202 (1.040, 1.389)	0.013		0.277	1.200 (1.040, 1.385)	0.013		0.223
>= 10^7 copies/mL	161/ 194	(83.0)	9.0 (7.0, 11.0)	114/ 164	(69.5)	11.0 (9.0, 16.0)	1.382 (1.081, 1.767)	0.010			1.423 (1.119, 1.810)	0.004		
Baseline serology status														
Negative	257/ 324	(79.3)	9.0 (8.0, 11.0)	215/ 330	(65.2)	13.0 (11.0, 15.0)	1.399 (1.163, 1.682)	<.001		0.116	1.466 (1.222, 1.758)	<.001		0.045
Positive	289/ 360	(80.3)	9.0 (8.0, 10.0)	279/ 356	(78.4)	10.0 (9.0, 12.0)	1.153 (0.975, 1.363)	0.096			1.150 (0.976, 1.356)	0.095		
Symptom onset days to first dose date														
<= 3	387/ 473	(81.8)	9.0 (8.0, 10.0)	328/ 438	(74.9)	11.0 (9.0, 12.0)	1.243 (1.070, 1.445)	0.004		0.899	1.278 (1.102, 1.481)	0.001		0.996
> 3	164/ 218	(75.2)	10.0 (8.0, 12.0)	171/ 255	(67.1)	13.0 (10.0, 14.0)	1.250 (1.004, 1.558)	0.046			1.275 (1.029, 1.580)	0.027		
BMI group														
< 25	124/ 155	(80.0)	8.0 (6.0, 9.0)	115/ 147	(78.2)	9.0 (7.0, 12.0)	1.179 (0.905, 1.537)	0.223		0.596	1.204 (0.934, 1.552)	0.153		0.693
25 - < 30	194/ 237	(81.9)	9.0 (8.0, 11.0)	177/ 236	(75.0)	11.0 (9.0, 14.0)	1.248 (1.011, 1.539)	0.039			1.247 (1.016, 1.529)	0.034		
>= 30	232/ 298	(77.9)	10.0 (9.0, 11.0)	207/ 310	(66.8)	13.0 (11.0, 15.0)	1.332 (1.098, 1.616)	0.004			1.359 (1.126, 1.640)	0.001		
Ethnicity														
White	412/ 527	(78.2)	10.0 (9.0, 11.0)	382/ 540	(70.7)	11.0 (10.0, 13.0)	1.206 (1.046, 1.390)	0.010		0.578	1.248 (1.085, 1.434)	0.002		0.629
Black or African American	27/ 34	(79.4)	7.0 (5.0, 15.0)	26/ 36	(72.2)	16.0 (6.0, 21.0)	1.518 (0.822, 2.805)	0.183			1.547 (0.895, 2.676)	0.118		
Asian	70/ 76	(92.1)	6.0 (4.0, 8.0)	63/ 67	(94.0)	6.0 (5.0, 11.0)	1.287 (0.898, 1.842)	0.169			1.330 (0.939, 1.883)	0.108		
Others	42/ 54	(77.8)	12.0 (8.0, 14.0)	28/ 50	(56.0)	18.0 (9.0, NE)	1.580 (0.961, 2.599)	0.071			1.692 (1.045, 2.740)	0.032		
Number of baseline comorbidities present														
0-1	427/ 533	(80.1)		383/ 523	(73.2)									
2-3	121/ 155	(78.1)		111/ 165	(67.3)									
>= 4	3/ 3	(100.0)		5/ 5	(100.0)									
Presence of risk factor: Smoking														
Yes	242/ 297	(81.5)	8.0 (7.0, 9.0)	226/ 311	(72.7)	11.0 (9.0, 13.0)	1.357 (1.127, 1.634)	0.001		0.288	1.389 (1.158, 1.666)	<.001		0.250
No	308/ 392	(78.6)	10.0 (9.0, 11.0)	273/ 382	(71.5)	11.0 (10.0, 13.0)	1.178 (0.998, 1.392)	0.053			1.214 (1.031, 1.429)	0.020		

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Subgroup Level	Nirmatrelvir/ritonavir (N=691)			Placebo (N=693)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N (%)	Median	(95% CI) [1]	n/N (%)	Median	(95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value	
Presence of risk factor: Diabetes mellitus													
Yes	86/ 103 (83.5)	8.0	(6.0, 9.0)	75/ 100 (75.0)	9.0	(8.0, 13.0)	1.521 (1.100, 2.103)	0.011	0.403	1.437 (1.051, 1.963)	0.023		0.354
No	464/ 587 (79.0)	9.0	(8.0, 10.0)	424/ 593 (71.5)	11.0	(10.0, 13.0)	1.228 (1.074, 1.405)	0.003		1.255 (1.100, 1.432)	<.001		
Presence of risk factor: Immunosuppression													
Yes	4/ 4 (100.0)			4/ 5 (80.0)									
No	546/ 686 (79.6)			495/ 688 (71.9)									
Presence of risk factor: Chronic lung disease													
Yes	39/ 49 (79.6)	9.0	(6.0, 14.0)	25/ 33 (75.8)	8.0	(6.0, 15.0)	0.981 (0.574, 1.676)	0.944	0.310	0.980 (0.593, 1.620)	0.937		0.268
No	511/ 641 (79.7)	9.0	(8.0, 10.0)	474/ 660 (71.8)	11.0	(10.0, 13.0)	1.267 (1.115, 1.440)	<.001		1.303 (1.149, 1.477)	<.001		
Presence of risk factor: Hypertension													
Yes	201/ 259 (77.6)	10.0	(9.0, 12.0)	187/ 270 (69.3)	13.0	(11.0, 15.0)	1.327 (1.082, 1.628)	0.007	0.342	1.331 (1.090, 1.625)	0.005		0.599
No	349/ 431 (81.0)	9.0	(7.0, 10.0)	312/ 423 (73.8)	11.0	(9.0, 12.0)	1.188 (1.016, 1.388)	0.030		1.244 (1.067, 1.449)	0.005		
Presence of risk factor: Cardiovascular disorder													
Yes	21/ 28 (75.0)	14.0	(7.0, 15.0)	21/ 29 (72.4)	10.0	(5.0, 21.0)	1.056 (0.541, 2.060)	0.873	0.831	1.100 (0.599, 2.018)	0.759		0.599
No	529/ 662 (79.9)	9.0	(8.0, 10.0)	478/ 664 (72.0)	11.0	(10.0, 13.0)	1.254 (1.105, 1.422)	<.001		1.291 (1.140, 1.461)	<.001		
Presence of risk factor: Chronic kidney disease													
Yes	5/ 6 (83.3)	9.0	(2.0, 19.0)	5/ 8 (62.5)	18.0	(7.0, NE)	17.389 (1.396, 216.66)	0.026	0.244	3.000 (0.786, 11.440)	0.108		0.174
No	545/ 684 (79.7)	9.0	(8.0, 10.0)	494/ 685 (72.1)	11.0	(10.0, 13.0)	1.242 (1.096, 1.406)	<.001		1.270 (1.124, 1.435)	<.001		
Presence of risk factor: HIV Infection													
Yes	0			0									
No	550/ 690 (79.7)			498/ 692 (72.0)									
Presence of risk factor: Sick Cell Disease													
No	550/ 690 (79.7)			499/ 693 (72.0)									
Presence of risk factor: Neurodevelopmental Disorder													
Yes	2/ 2 (100.0)			0/ 1 (0.0)									
No	548/ 688 (79.7)			499/ 692 (72.1)									
Presence of risk factor: Cancer													
Yes	1/ 1 (100.0)			5/ 5 (100.0)									
No	549/ 689 (79.7)			494/ 688 (71.8)									
Presence of risk factor: Device Dependence													
Yes	2/ 3 (66.7)			2/ 3 (66.7)									
No	543/ 679 (80.0)			496/ 687 (72.2)									

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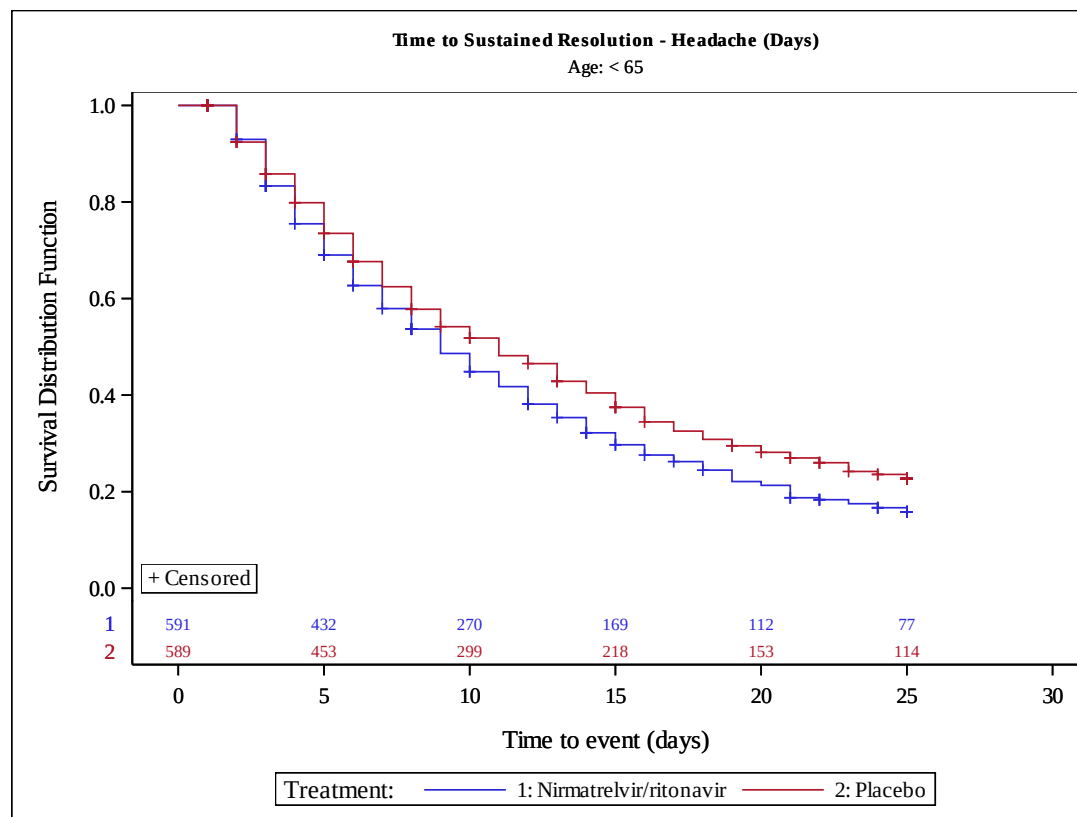
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Final

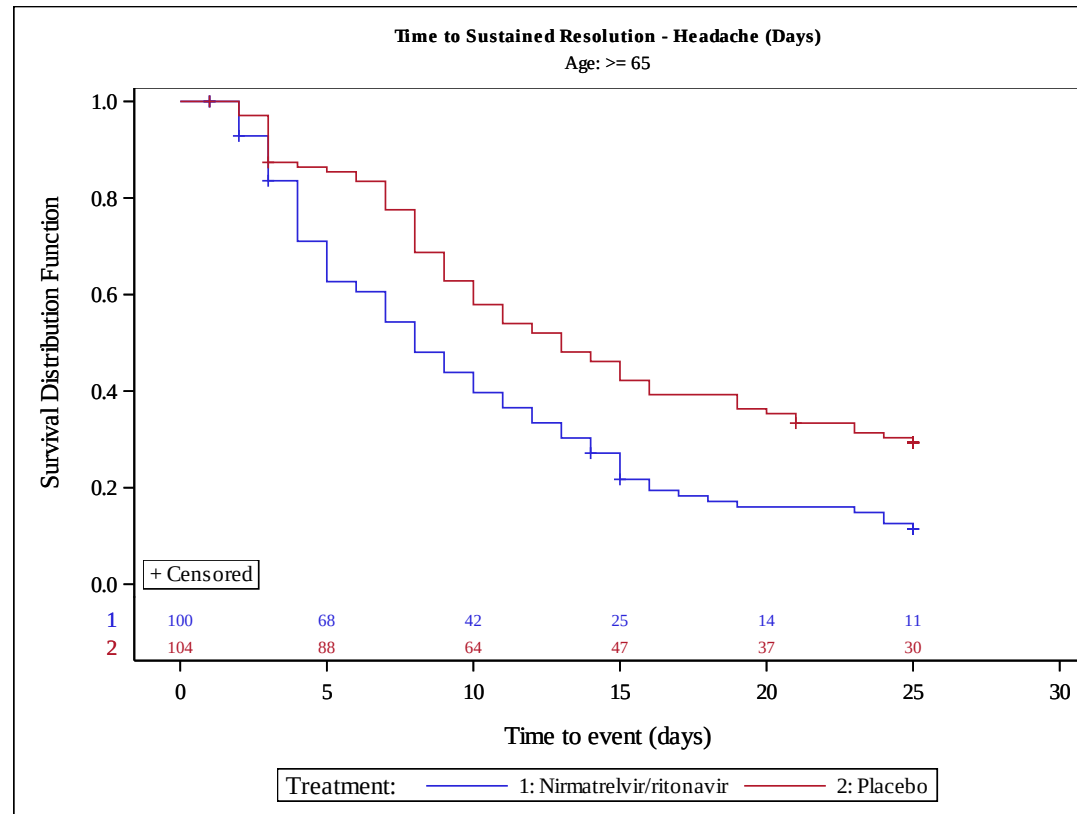


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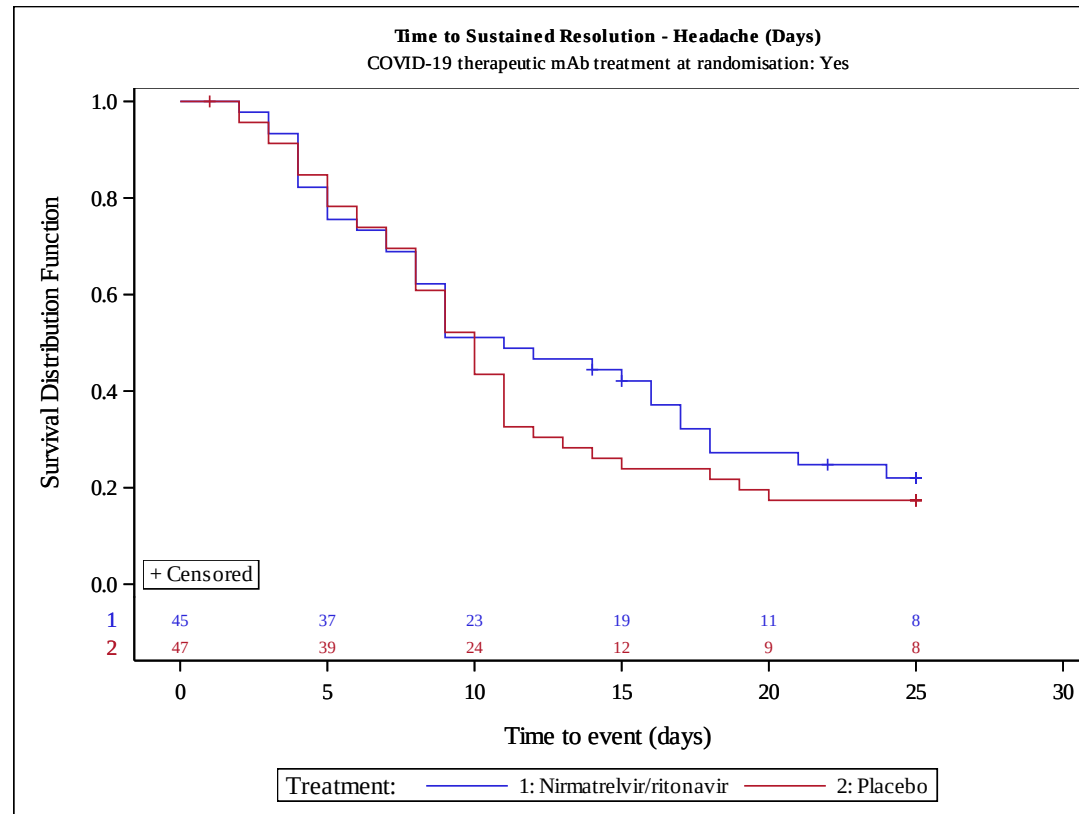


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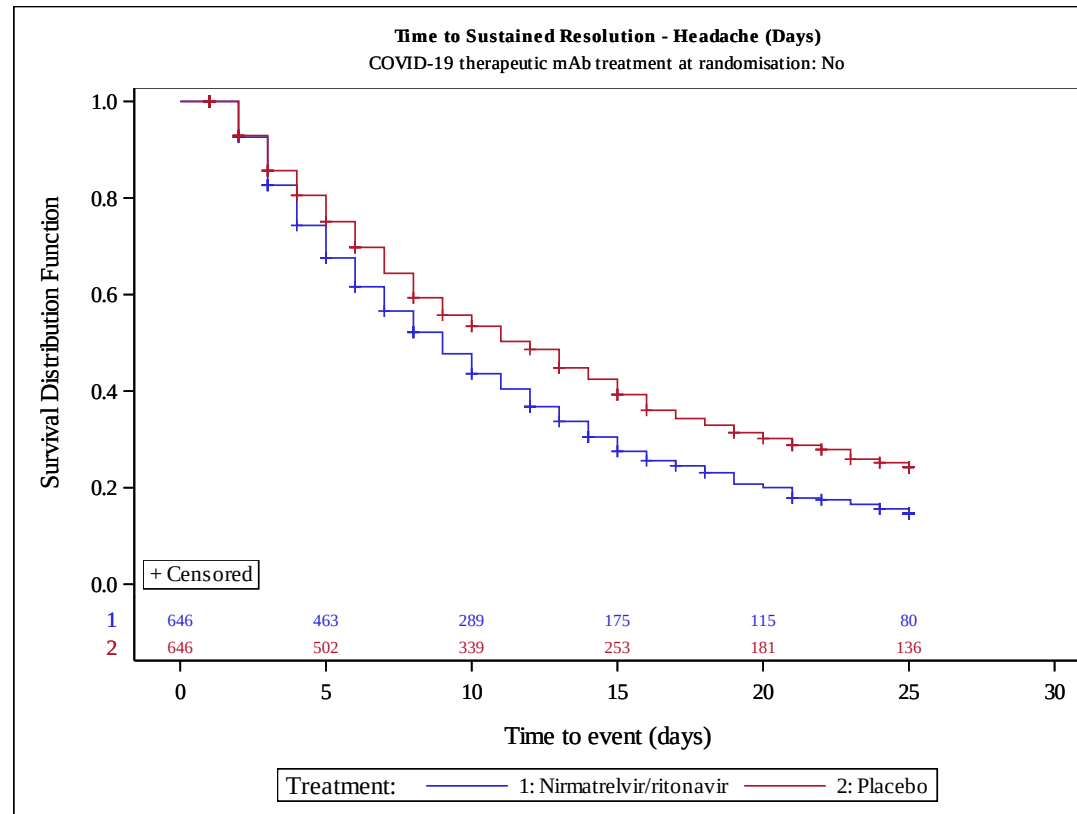
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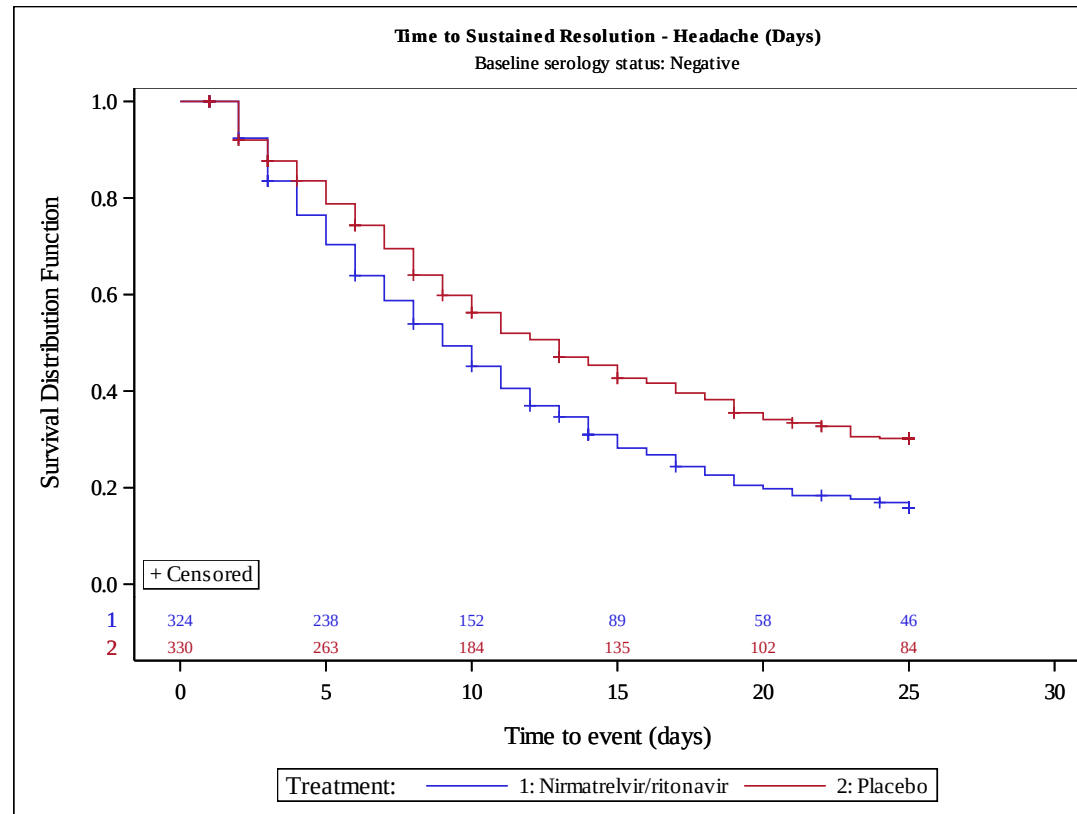
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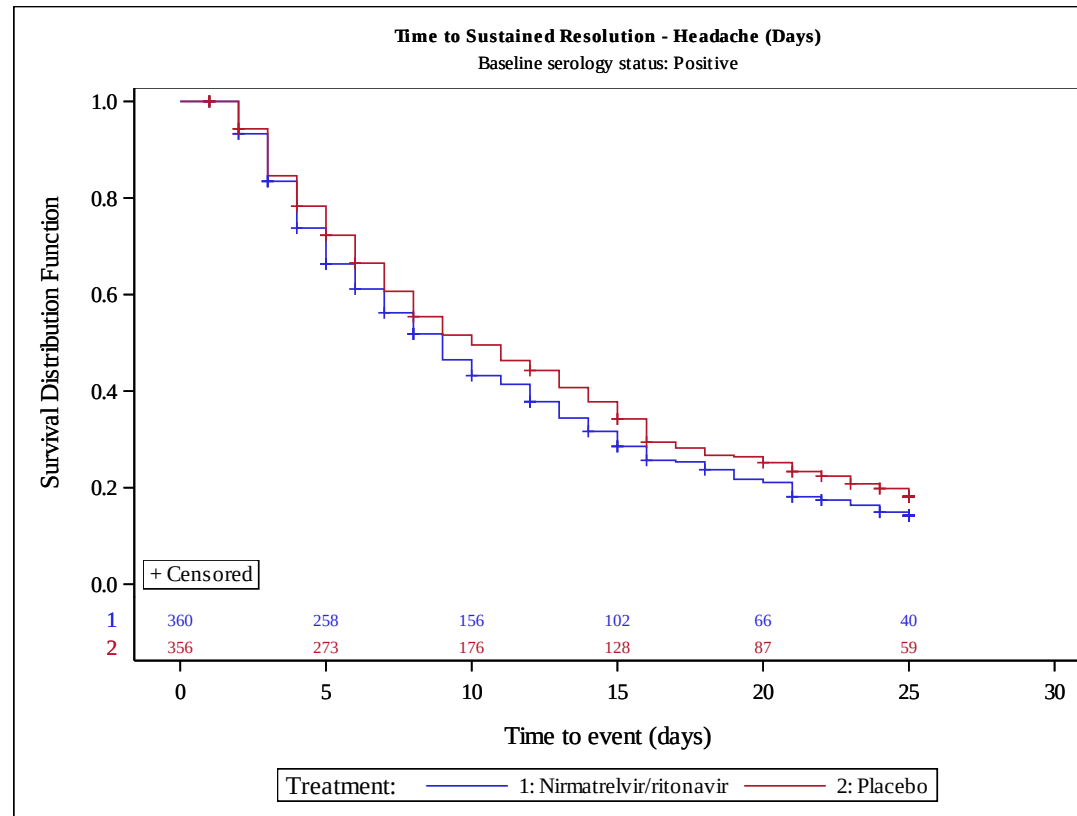
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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=79)			Placebo (N=70)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Age												
< 65	56/	74 (75.7)	10.0 (7.0, 12.0)	41/	64 (64.1)	17.0 (13.0, 19.0)	1.545 (1.006, 2.373)	0.047	0.655	1.544 (1.031, 2.312)	0.035	0.558
>= 65	5/	5 (100.0)	10.0 (5.0, 25.0)	3/	6 (50.0)	NE (8.0, NE)	2.545 (0.205, 31.630)	0.467		2.458 (0.575, 10.504)	0.225	
Gender												
Male	25/	29 (86.2)	8.0 (5.0, 11.0)	13/	23 (56.5)	17.0 (12.0, NE)	1.733 (0.839, 3.581)	0.138	0.710	2.175 (1.104, 4.287)	0.025	0.242
Female	36/	50 (72.0)	12.0 (9.0, 18.0)	31/	47 (66.0)	17.0 (13.0, 22.0)	1.441 (0.861, 2.413)	0.164		1.351 (0.835, 2.184)	0.220	
Geographic region												
United States	26/	36 (72.2)		22/	38 (57.9)							
Europe	19/	21 (90.5)		11/	15 (73.3)							
India	0			0								
Rest of World	16/	22 (72.7)		11/	17 (64.7)							
COVID-19 therapeutic mAb treatment at randomisation												
Yes	4/	4 (100.0)	8.0 (5.0, 9.0)	6/	7 (85.7)	7.0 (5.0, 19.0)	1.029 (0.088, 11.996)	0.982	0.645	1.270 (0.316, 5.109)	0.737	0.879
No	57/	75 (76.0)	11.0 (7.0, 12.0)	38/	63 (60.3)	17.0 (14.0, 23.0)	1.598 (1.040, 2.455)	0.032		1.677 (1.111, 2.531)	0.014	
Baseline viral load 1												
< 10^4 copies/mL	11/	19 (57.9)	12.0 (3.0, NE)	6/	10 (60.0)	13.0 (3.0, NE)	1.071 (0.366, 3.130)	0.901	0.334	1.127 (0.415, 3.059)	0.814	0.328
>= 10^4 copies/mL	48/	58 (82.8)	9.5 (7.0, 12.0)	35/	55 (63.6)	17.0 (13.0, 22.0)	1.753 (1.123, 2.735)	0.013		1.788 (1.154, 2.769)	0.009	
Baseline viral load 2												
< 10^7 copies/mL	30/	41 (73.2)	10.0 (5.0, 17.0)	30/	43 (69.8)	15.0 (13.0, 21.0)	1.782 (1.002, 3.168)	0.049	0.944	1.455 (0.876, 2.416)	0.148	0.503
>= 10^7 copies/mL	29/	36 (80.6)	10.5 (7.0, 12.0)	11/	22 (50.0)	19.0 (9.0, NE)	1.791 (0.876, 3.661)	0.110		1.869 (0.931, 3.752)	0.079	
Baseline serology status												
Negative	33/	42 (78.6)	10.5 (6.0, 12.0)	31/	50 (62.0)	17.0 (12.0, 21.0)	1.743 (1.040, 2.920)	0.035	0.779	1.707 (1.044, 2.792)	0.033	0.787
Positive	28/	37 (75.7)	10.0 (7.0, 18.0)	13/	20 (65.0)	16.5 (7.0, NE)	1.686 (0.769, 3.697)	0.192		1.527 (0.789, 2.956)	0.209	
Symptom onset days to first dose date												
<= 3	49/	57 (86.0)	9.0 (7.0, 11.0)	30/	42 (71.4)	15.0 (9.0, 19.0)	1.759 (1.093, 2.829)	0.020	0.361	1.719 (1.088, 2.716)	0.020	0.390
> 3	12/	22 (54.5)	18.0 (4.0, NE)	14/	28 (50.0)	18.0 (13.0, NE)	1.854 (0.724, 4.747)	0.198		1.182 (0.545, 2.563)	0.673	
BMI group												
< 25	9/	13 (69.2)	7.0 (3.0, 14.0)	9/	16 (56.3)	19.0 (13.0, NE)	2.025 (0.710, 5.774)	0.187	0.183	2.818 (1.102, 7.207)	0.031	0.124
25 - < 30	19/	23 (82.6)	12.0 (8.0, 18.0)	14/	20 (70.0)	10.0 (6.0, 17.0)	0.685 (0.308, 1.523)	0.353		0.866 (0.432, 1.735)	0.684	
>= 30	33/	43 (76.7)	9.0 (6.0, 12.0)	21/	34 (61.8)	18.0 (14.0, NE)	1.812 (0.984, 3.334)	0.056		1.770 (1.021, 3.068)	0.042	
Ethnicity												
White	43/	57 (75.4)		34/	54 (63.0)							
Black or African American	6/	7 (85.7)		4/	6 (66.7)							
Asian	4/	4 (100.0)		2/	3 (66.7)							
Others	8/	11 (72.7)		4/	7 (57.1)							
Number of baseline comorbidities present												
0-1	54/	68 (79.4)		42/	64 (65.6)							
2-3	6/	10 (60.0)		2/	6 (33.3)							
>= 4	1/	1 (100.0)		0								
Presence of risk factor: Smoking												
Yes	26/	33 (78.8)	8.0 (5.0, 12.0)	24/	33 (72.7)	13.0 (10.0, 18.0)	1.465 (0.773, 2.775)	0.241	0.434	1.470 (0.842, 2.566)	0.176	0.544
No	34/	45 (75.6)	11.0 (8.0, 18.0)	20/	37 (54.1)	19.0 (14.0, NE)	1.961 (1.097, 3.506)	0.023		1.798 (1.033, 3.129)	0.038	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Headache - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=79)			Placebo (N=70)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Presence of risk factor: Diabetes mellitus									0.982			0.982
Yes	5/	9 (55.6)	25.0 (4.0, NE)	0/	3 (0.0)	NE (NE, NE)	NE (NE, NE)	NE		NE (NE, NE)	NE	
No	55/	69 (79.7)	9.0 (7.0, 12.0)	44/	67 (65.7)	15.0 (13.0, 19.0)	1.562 (1.015, 2.404)	0.043		1.633 (1.097, 2.431)	0.016	
Presence of risk factor: Immunosuppression												
Yes	0			0/	1 (0.0)							
No	60/	78 (76.9)		44/	69 (63.8)							
Presence of risk factor: Chronic lung disease												
Yes	3/	6 (50.0)		0/	2 (0.0)							
No	57/	72 (79.2)		44/	68 (64.7)							
Presence of risk factor: Hypertension									0.429			0.452
Yes	16/	20 (80.0)	11.0 (4.0, 19.0)	9/	17 (52.9)	23.0 (8.0, NE)	1.947 (0.791, 4.793)	0.147		2.027 (0.892, 4.607)	0.092	
No	44/	58 (75.9)	10.0 (7.0, 12.0)	35/	53 (66.0)	15.0 (12.0, 19.0)	1.638 (0.990, 2.709)	0.055		1.486 (0.952, 2.320)	0.081	
Presence of risk factor: Cardiovascular disorder												
Yes	1/	2 (50.0)		0/	1 (0.0)							
No	59/	76 (77.6)		44/	69 (63.8)							
Presence of risk factor: Chronic kidney disease												
Yes	1/	1 (100.0)		0								
No	59/	77 (76.6)		44/	70 (62.9)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	60/	78 (76.9)		44/	70 (62.9)							
Presence of risk factor: Sick Cell Disease												
No	60/	78 (76.9)		44/	70 (62.9)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0			0								
No	60/	78 (76.9)		44/	70 (62.9)							
Presence of risk factor: Cancer												
Yes	0			0								
No	60/	78 (76.9)		44/	70 (62.9)							
Presence of risk factor: Device Dependence												
Yes	1/	1 (100.0)		0								
No	59/	77 (76.6)		44/	70 (62.9)							

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value	
Age							0.273					0.357
< 65	130/ 790 (16.5)	152/ 810 (18.8)	0.897 (0.722, 1.114)			0.325		0.877 (0.709, 1.085)			0.226	
>= 65	17/ 138 (12.3)	27/ 145 (18.6)	NE (NE, NE)			NE		0.662 (0.378, 1.159)			0.148	
Gender							0.160					0.130
Male	69/ 463 (14.9)	76/ 507 (15.0)	1.007 (0.741, 1.368)			0.967		0.994 (0.736, 1.343)			0.970	
Female	78/ 465 (16.8)	103/ 448 (23.0)	0.747 (0.571, 0.978)			0.034		0.730 (0.560, 0.950)			0.019	
Geographic region							0.402					0.381
United States	68/ 375 (18.1)	68/ 387 (17.6)	1.056 (0.770, 1.448)			0.735		1.032 (0.761, 1.400)			0.839	
Europe	54/ 322 (16.8)	73/ 321 (22.7)	0.771 (0.559, 1.064)			0.113		0.737 (0.538, 1.011)			0.059	
India	5/ 74 (6.8)	9/ 78 (11.5)	NE (NE, NE)			NE		0.586 (0.206, 1.667)			0.316	
Rest of World	20/ 157 (12.7)	29/ 169 (17.2)	0.755 (0.444, 1.284)			0.300		0.742 (0.438, 1.257)			0.268	
COVID-19 therapeutic mAb treatment at randomisation							0.347					0.507
Yes	11/ 57 (19.3)	17/ 60 (28.3)	0.627 (0.326, 1.204)			0.161		0.681 (0.350, 1.326)			0.259	
No	136/ 871 (15.6)	162/ 895 (18.1)	0.885 (0.715, 1.094)			0.259		0.863 (0.701, 1.062)			0.164	
Baseline viral load 1							0.093					0.087
< 10^4 copies/mL	50/ 335 (14.9)	47/ 354 (13.3)	1.097 (0.756, 1.591)			0.626		1.124 (0.777, 1.626)			0.534	
>= 10^4 copies/mL	93/ 569 (16.3)	123/ 575 (21.4)	0.765 (0.601, 0.974)			0.030		0.764 (0.599, 0.974)			0.030	
Baseline viral load 2							0.235					0.242
< 10^7 copies/mL	98/ 652 (15.0)	113/ 699 (16.2)	0.928 (0.723, 1.191)			0.557		0.930 (0.725, 1.192)			0.566	
>= 10^7 copies/mL	45/ 252 (17.9)	57/ 230 (24.8)	0.719 (0.509, 1.014)			0.060		0.721 (0.509, 1.020)			0.065	
Baseline serology status							0.236					0.152
Negative	70/ 435 (16.1)	100/ 456 (21.9)	0.763 (0.578, 1.007)			0.056		0.734 (0.557, 0.967)			0.028	
Positive	75/ 482 (15.6)	77/ 487 (15.8)	0.993 (0.739, 1.334)			0.961		0.984 (0.735, 1.318)			0.914	
Symptom onset days to first dose date							0.864					0.992
<= 3	102/ 624 (16.3)	121/ 624 (19.4)	0.866 (0.678, 1.105)			0.247		0.843 (0.664, 1.071)			0.161	
> 3	45/ 304 (14.8)	58/ 331 (17.5)	0.833 (0.580, 1.197)			0.323		0.845 (0.591, 1.207)			0.354	
BMI group							0.250					0.210
< 25	23/ 215 (10.7)	39/ 213 (18.3)	0.663 (0.409, 1.076)			0.096		0.584 (0.362, 0.943)			0.028	
25 - < 30	53/ 319 (16.6)	56/ 332 (16.9)	1.031 (0.728, 1.461)			0.862		0.985 (0.699, 1.388)			0.931	
>= 30	71/ 393 (18.1)	84/ 410 (20.5)	0.829 (0.617, 1.113)			0.213		0.882 (0.664, 1.171)			0.385	
Ethnicity							0.546					0.508
White	119/ 699 (17.0)	145/ 718 (20.2)	0.854 (0.682, 1.068)			0.166		0.843 (0.677, 1.049)			0.126	
Black or African American	10/ 43 (23.3)	6/ 40 (15.0)	1.854 (0.631, 5.450)			0.262		1.550 (0.620, 3.875)			0.348	
Asian	9/ 117 (7.7)	15/ 127 (11.8)	NE (NE, NE)			NE		0.651 (0.296, 1.431)			0.286	
Others	9/ 69 (13.0)	13/ 70 (18.6)	NE (NE, NE)			NE		0.702 (0.321, 1.535)			0.376	
Number of baseline comorbidities present							0.043					0.326
0-1	109/ 710 (15.4)	136/ 728 (18.7)	0.814 (0.644, 1.030)			0.087		0.822 (0.653, 1.034)			0.094	
2-3	36/ 214 (16.8)	43/ 221 (19.5)	0.887 (0.593, 1.325)			0.557		0.865 (0.579, 1.291)			0.477	
>= 4	2/ 4 (50.0)	0/ 6 (0.0)	NE (NE, NE)			NE		7.000 (0.421, 116.400)			0.175	
Presence of risk factor: Smoking							0.229					0.246
Yes	59/ 417 (14.1)	63/ 438 (14.4)	1.005 (0.718, 1.406)			0.977		0.984 (0.708, 1.367)			0.922	
No	88/ 509 (17.3)	116/ 517 (22.4)	0.772 (0.600, 0.992)			0.043		0.771 (0.601, 0.988)			0.040	
Presence of risk factor: Diabetes mellitus							0.081					0.065

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochran's Q statistic.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928)		Placebo (N=955)		Adjusted analysis [1]				Interaction		Unadjusted analysis [2]				Interaction	
	n/N (%)		n/N (%)		Relative Risk (95% CI)			p-Value	p-Value	Relative Risk (95% CI)			p-Value	p-Value		
Yes	14/	130 (10.8)	29/	136 (21.3)	0.539 (	0.299,	0.971)	0.040		0.505 (	0.280,	0.912)	0.023			
No	133/	797 (16.7)	150/	819 (18.3)	0.918 (	0.739,	1.140)	0.440		0.911 (	0.737,	1.126)	0.390			
Presence of risk factor: Immunosuppression									0.350						0.698	
Yes	2/	6 (33.3)	2/	7 (28.6)	NE (	NE,	NE)	NE		1.167 (	0.229,	5.946)	0.853			
No	145/	921 (15.7)	177/	948 (18.7)	0.849 (	0.693,	1.041)	0.115		0.843 (	0.690,	1.030)	0.095			
Presence of risk factor: Chronic lung disease									0.099						0.232	
Yes	15/	62 (24.2)	7/	39 (17.9)	1.602 (	0.661,	3.887)	0.297		1.348 (	0.604,	3.008)	0.466			
No	132/	865 (15.3)	172/	916 (18.8)	0.813 (	0.659,	1.004)	0.055		0.813 (	0.661,	0.999)	0.049			
Presence of risk factor: Hypertension									0.359						0.325	
Yes	66/	348 (19.0)	74/	371 (19.9)	0.975 (	0.723,	1.313)	0.865		0.951 (	0.706,	1.281)	0.740			
No	81/	579 (14.0)	105/	584 (18.0)	0.798 (	0.606,	1.050)	0.107		0.778 (	0.596,	1.015)	0.065			
Presence of risk factor: Cardiovacular disorder									0.740						0.706	
Yes	10/	42 (23.8)	12/	49 (24.5)	NE (	NE,	NE)	NE		0.972 (	0.468,	2.020)	0.940			
No	137/	885 (15.5)	167/	906 (18.4)	0.849 (	0.688,	1.048)	0.128		0.840 (	0.683,	1.032)	0.097			
Presence of risk factor: Chronic kidney disease									0.205						0.727	
Yes	1/	6 (16.7)	1/	8 (12.5)	NE (	NE,	NE)	NE		1.333 (	0.103,	17.278)	0.826			
No	146/	921 (15.9)	178/	947 (18.8)	0.851 (	0.695,	1.042)	0.119		0.843 (	0.691,	1.029)	0.094			
Presence of risk factor: HIV Infection																
Yes	0		0/	1 (0.0)												
No	147/	927 (15.9)	179/	953 (18.8)												
Presence of risk factor: Sickle Cell Disease																
No	147/	927 (15.9)	179/	955 (18.7)												
Presence of risk factor: Neurodevelopmental Disorder																
Yes	0/	2 (0.0)	0/	1 (0.0)												
No	147/	925 (15.9)	179/	954 (18.8)												
Presence of risk factor: Cancer									0.136						0.353	
Yes	1/	5 (20.0)	0/	6 (0.0)	NE (	NE,	NE)	NE		3.500 (	0.173,	70.944)	0.415			
No	146/	922 (15.8)	179/	949 (18.9)	0.849 (	0.693,	1.040)	0.114		0.840 (	0.688,	1.024)	0.085			
Presence of risk factor: Device Dependence																
Yes	2/	4 (50.0)	2/	3 (66.7)												
No	145/	914 (15.9)	174/	944 (18.4)												

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

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[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

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RKI-conform mITT2 Analysis set
Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Chills or Shivering - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=579)			Placebo (N=558)			Adjusted Analysis [2]				Interaction p-Value	Unadjusted Analysis [3]				Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value				Hazard Ratio (95% CI)	p-Value			
Age																
< 65	428/ 494	(86.6)	3.0 (3.0, 4.0)	384/ 471	(81.5)	4.0 (4.0, 5.0)	1.228 (1.066, 1.414)	0.005		0.334		1.247 (1.086, 1.432)	0.002			0.269
>= 65	80/ 85	(94.1)	3.0 (3.0, 4.0)	71/ 87	(81.6)	5.0 (3.0, 6.0)	1.588 (1.135, 2.222)	0.007				1.582 (1.144, 2.188)	0.006			
Gender																
Male	246/ 278	(88.5)	3.0 (3.0, 4.0)	231/ 287	(80.5)	4.0 (3.0, 5.0)	1.312 (1.088, 1.582)	0.004		0.551		1.340 (1.118, 1.606)	0.002			0.454
Female	262/ 301	(87.0)	3.0 (3.0, 4.0)	224/ 271	(82.7)	5.0 (4.0, 6.0)	1.232 (1.026, 1.479)	0.025				1.234 (1.032, 1.475)	0.021			
Geographic region																
United States	204/ 245	(83.3)	4.0 (3.0, 4.0)	198/ 240	(82.5)	4.0 (3.0, 6.0)	1.117 (0.916, 1.363)	0.275		0.164		1.136 (0.934, 1.382)	0.202			0.098
Europe	208/ 221	(94.1)	3.0 (3.0, 4.0)	175/ 214	(81.8)	5.0 (4.0, 6.0)	1.523 (1.233, 1.881)	<.001				1.576 (1.285, 1.933)	<.001			
India	22/ 23	(95.7)	3.0 (3.0, 4.0)	19/ 20	(95.0)	3.0 (2.0, 5.0)	0.694 (0.329, 1.467)	0.339				0.772 (0.406, 1.467)	0.430			
Rest of World	74/ 90	(82.2)	3.0 (2.0, 4.0)	63/ 84	(75.0)	4.0 (3.0, 7.0)	1.167 (0.828, 1.646)	0.378				1.197 (0.855, 1.676)	0.295			
COVID-19 therapeutic mAb treatment at randomisation																
Yes	34/ 40	(85.0)	3.0 (2.0, 5.0)	34/ 39	(87.2)	3.0 (3.0, 5.0)	1.018 (0.615, 1.686)	0.945		0.278		1.021 (0.634, 1.644)	0.932			0.310
No	474/ 539	(87.9)	3.0 (3.0, 4.0)	421/ 519	(81.1)	4.0 (4.0, 5.0)	1.293 (1.130, 1.481)	<.001				1.312 (1.150, 1.497)	<.001			
Baseline viral load 1																
< 10^4 copies/mL	148/ 175	(84.6)	4.0 (3.0, 5.0)	161/ 186	(86.6)	3.0 (3.0, 4.0)	1.004 (0.800, 1.260)	0.970		0.008		0.994 (0.795, 1.243)	0.959			0.009
>= 10^4 copies/mL	343/ 387	(88.6)	3.0 (NE, NE)	284/ 357	(79.6)	5.0 (4.0, 6.0)	1.414 (1.205, 1.660)	<.001				1.422 (1.213, 1.666)	<.001			
Baseline viral load 2																
< 10^7 copies/mL	317/ 376	(84.3)	4.0 (3.0, 4.0)	336/ 406	(82.8)	4.0 (3.0, 5.0)	1.139 (0.975, 1.331)	0.100		0.022		1.141 (0.978, 1.330)	0.094			0.024
>= 10^7 copies/mL	174/ 186	(93.5)	3.0 (NE, NE)	109/ 137	(79.6)	5.0 (4.0, 6.0)	1.565 (1.218, 2.010)	<.001				1.602 (1.257, 2.041)	<.001			
Baseline serology status																
Negative	275/ 308	(89.3)	3.0 (NE, NE)	228/ 293	(77.8)	5.0 (4.0, 6.0)	1.460 (1.218, 1.750)	<.001		0.032		1.493 (1.251, 1.782)	<.001			0.017
Positive	225/ 262	(85.9)	3.0 (3.0, 4.0)	221/ 257	(86.0)	4.0 (3.0, 4.0)	1.103 (0.912, 1.333)	0.311				1.094 (0.908, 1.317)	0.346			
Symptom onset days to first dose date																
<= 3	368/ 406	(90.6)	3.0 (NE, NE)	308/ 370	(83.2)	4.0 (3.0, 5.0)	1.311 (1.122, 1.532)	<.001		0.375		1.315 (1.130, 1.532)	<.001			0.540
> 3	140/ 173	(80.9)	4.0 (3.0, 5.0)	147/ 188	(78.2)	6.0 (4.0, 7.0)	1.123 (0.882, 1.430)	0.346				1.203 (0.954, 1.518)	0.119			
BMI group																
< 25	110/ 124	(88.7)	3.0 (2.0, 4.0)	101/ 117	(86.3)	5.0 (4.0, 6.0)	1.376 (1.034, 1.831)	0.029		0.359		1.429 (1.088, 1.876)	0.010			0.337
25 - < 30	177/ 201	(88.1)	4.0 (3.0, 4.0)	168/ 203	(82.8)	4.0 (3.0, 5.0)	1.125 (0.906, 1.397)	0.288				1.136 (0.919, 1.404)	0.238			
>= 30	220/ 253	(87.0)	3.0 (3.0, 4.0)	186/ 238	(78.2)	4.0 (3.0, 6.0)	1.341 (1.096, 1.640)	0.004				1.362 (1.119, 1.658)	0.002			
Ethnicity																
White	405/ 460	(88.0)	3.0 (3.0, 4.0)	374/ 457	(81.8)	4.0 (4.0, 5.0)	1.283 (1.110, 1.483)	<.001		0.509		1.311 (1.138, 1.510)	<.001			0.420
Black or African American	23/ 30	(76.7)	4.0 (3.0, 7.0)	21/ 26	(80.8)	5.0 (2.0, 9.0)	1.096 (0.581, 2.065)	0.777				1.093 (0.603, 1.981)	0.770			
Asian	37/ 40	(92.5)	3.0 (3.0, 4.0)	40/ 43	(93.0)	3.0 (2.0, 4.0)	0.997 (0.620, 1.603)	0.991				0.980 (0.626, 1.536)	0.930			
Others	43/ 49	(87.8)	3.0 (2.0, 8.0)	20/ 32	(62.5)	7.0 (3.0, NE)	1.550 (0.887, 2.706)	0.124				1.693 (0.992, 2.889)	0.054			
Number of baseline comorbidities present																
0-1	393/ 443	(88.7)		320/ 395	(81.0)											
2-3	113/ 134	(84.3)		131/ 159	(82.4)											
>= 4	2/ 2	(100.0)		4/ 4	(100.0)											
Presence of risk factor: Smoking																
Yes	229/ 266	(86.1)	3.0 (3.0, 4.0)	215/ 263	(81.7)	4.0 (3.0, 5.0)	1.206 (0.995, 1.461)	0.057		0.565		1.230 (1.020, 1.483)	0.030			0.589
No	277/ 311	(89.1)	3.0 (3.0, 4.0)	240/ 295	(81.4)	5.0 (4.0, 5.0)	1.313 (1.100, 1.568)	0.003				1.332 (1.120, 1.585)	0.001			

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=579)			Placebo (N=558)			Adjusted Analysis [2]			Interaction		Unadjusted Analysis [3]			Interaction	
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	p-Value			Hazard Ratio (95% CI)	p-Value	p-Value		
Presence of risk factor: Diabetes mellitus										0.883					0.952	
Yes	66/	77 (85.7)	3.0 (3.0, 5.0)	70/	85 (82.4)	5.0 (4.0, 7.0)	1.332 (0.934, 1.899)	0.114				1.280 (0.913, 1.795)	0.152			
No	441/	501 (88.0)	3.0 (3.0, 4.0)	385/	473 (81.4)	4.0 (4.0, 5.0)	1.251 (1.087, 1.439)	0.002				1.284 (1.119, 1.473)	<.001			
Presence of risk factor: Immunosuppression																
Yes	3/	3 (100.0)		4/	4 (100.0)											
No	504/	575 (87.7)		451/	554 (81.4)											
Presence of risk factor: Chronic lung disease										0.504					0.488	
Yes	40/	43 (93.0)	3.0 (3.0, 4.0)	23/	25 (92.0)	4.0 (3.0, 6.0)	1.201 (0.697, 2.070)	0.510				1.089 (0.651, 1.822)	0.745			
No	467/	535 (87.3)	3.0 (3.0, 4.0)	432/	533 (81.1)	4.0 (4.0, 5.0)	1.266 (1.107, 1.449)	<.001				1.290 (1.131, 1.472)	<.001			
Presence of risk factor: Hypertension										0.426					0.743	
Yes	185/	211 (87.7)	4.0 (3.0, 4.0)	187/	233 (80.3)	4.5 (4.0, 5.0)	1.341 (1.085, 1.658)	0.007				1.310 (1.068, 1.608)	0.010			
No	322/	367 (87.7)	3.0 (NE, NE)	268/	325 (82.5)	4.0 (3.0, 5.0)	1.210 (1.024, 1.431)	0.025				1.261 (1.072, 1.484)	0.005			
Presence of risk factor: Cardiovascular disorder										0.612					0.680	
Yes	22/	24 (91.7)	5.0 (2.0, 7.0)	23/	29 (79.3)	5.0 (2.0, 12.0)	1.674 (0.851, 3.294)	0.135				1.451 (0.804, 2.620)	0.217			
No	485/	554 (87.5)	3.0 (3.0, 4.0)	432/	529 (81.7)	4.0 (4.0, 5.0)	1.253 (1.097, 1.431)	<.001				1.275 (1.119, 1.453)	<.001			
Presence of risk factor: Chronic kidney disease										0.256					0.251	
Yes	4/	5 (80.0)	3.0 (2.0, 4.0)	5/	6 (83.3)	7.0 (3.0, NE)	6.881 (0.885, 53.502)	0.065				5.356 (0.937, 30.613)	0.059			
No	503/	573 (87.8)	3.0 (3.0, 4.0)	450/	552 (81.5)	4.0 (4.0, 5.0)	1.255 (1.101, 1.430)	<.001				1.277 (1.124, 1.451)	<.001			
Presence of risk factor: HIV Infection																
Yes	0			0												
No	507/	578 (87.7)		454/	557 (81.5)											
Presence of risk factor: Sick Cell Disease																
No	507/	578 (87.7)		455/	558 (81.5)											
Presence of risk factor: Neurodevelopmental Disorder																
Yes	2/	2 (100.0)		1/	1 (100.0)											
No	505/	576 (87.7)		454/	557 (81.5)											
Presence of risk factor: Cancer																
Yes	0/	1 (0.0)		4/	4 (100.0)											
No	507/	577 (87.9)		451/	554 (81.4)											
Presence of risk factor: Device Dependence																
Yes	2/	3 (66.7)		1/	1 (100.0)											
No	500/	568 (88.0)		452/	554 (81.6)											

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[3] Estimated by cox regression model assuming proportional hazards.

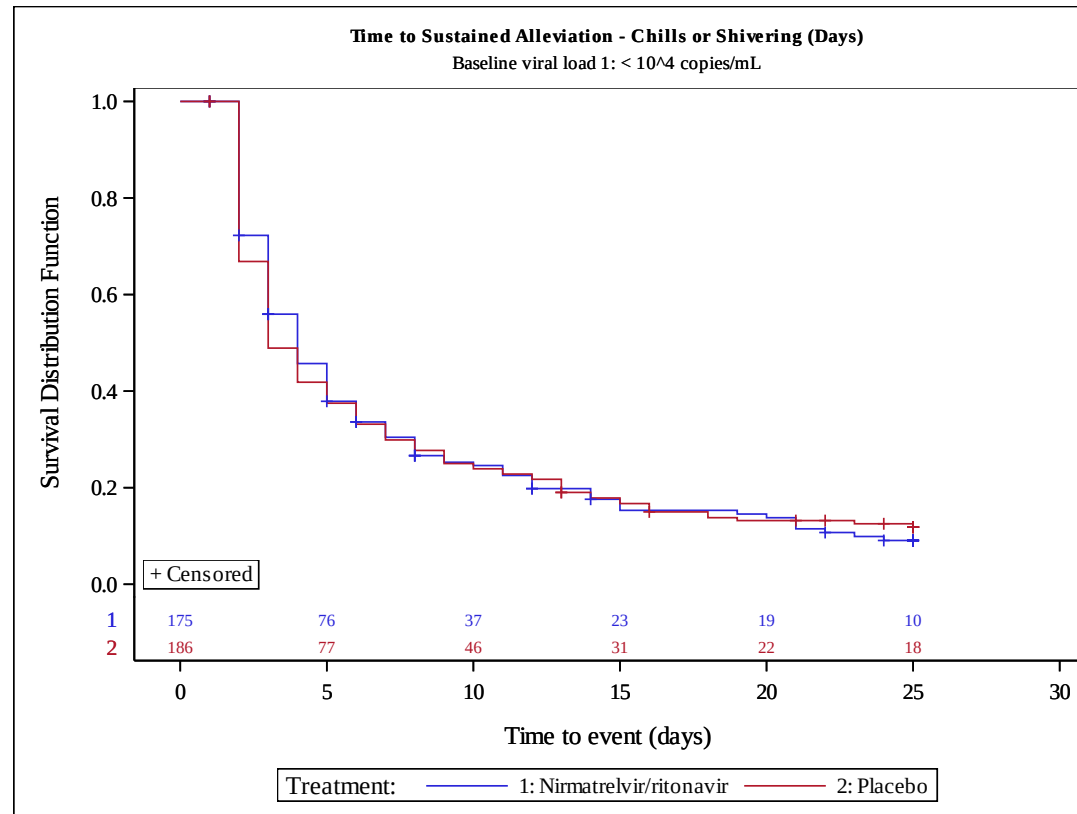
p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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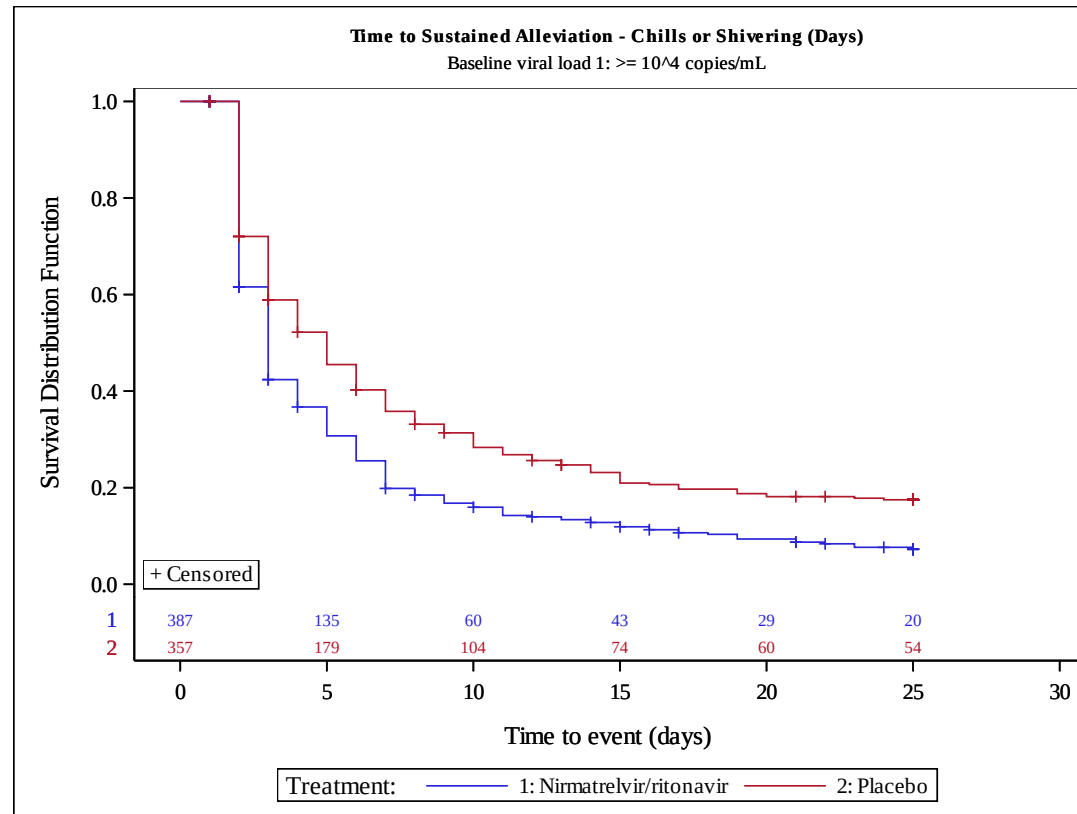
Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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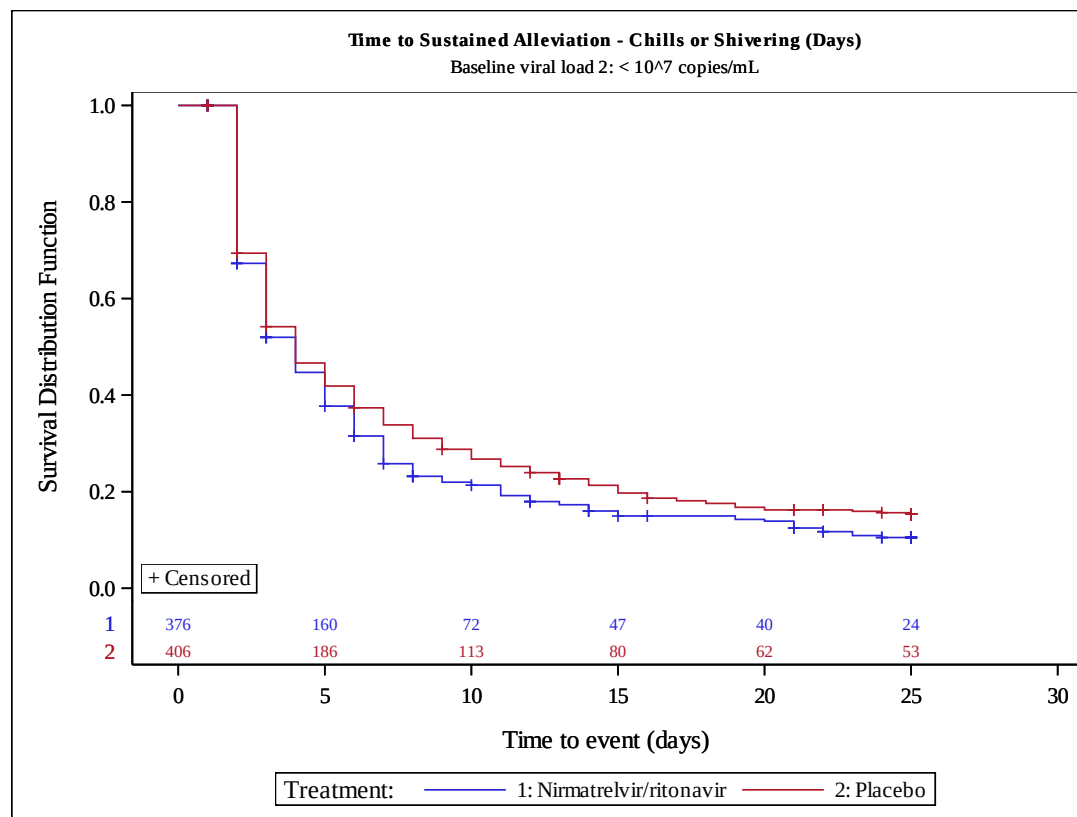


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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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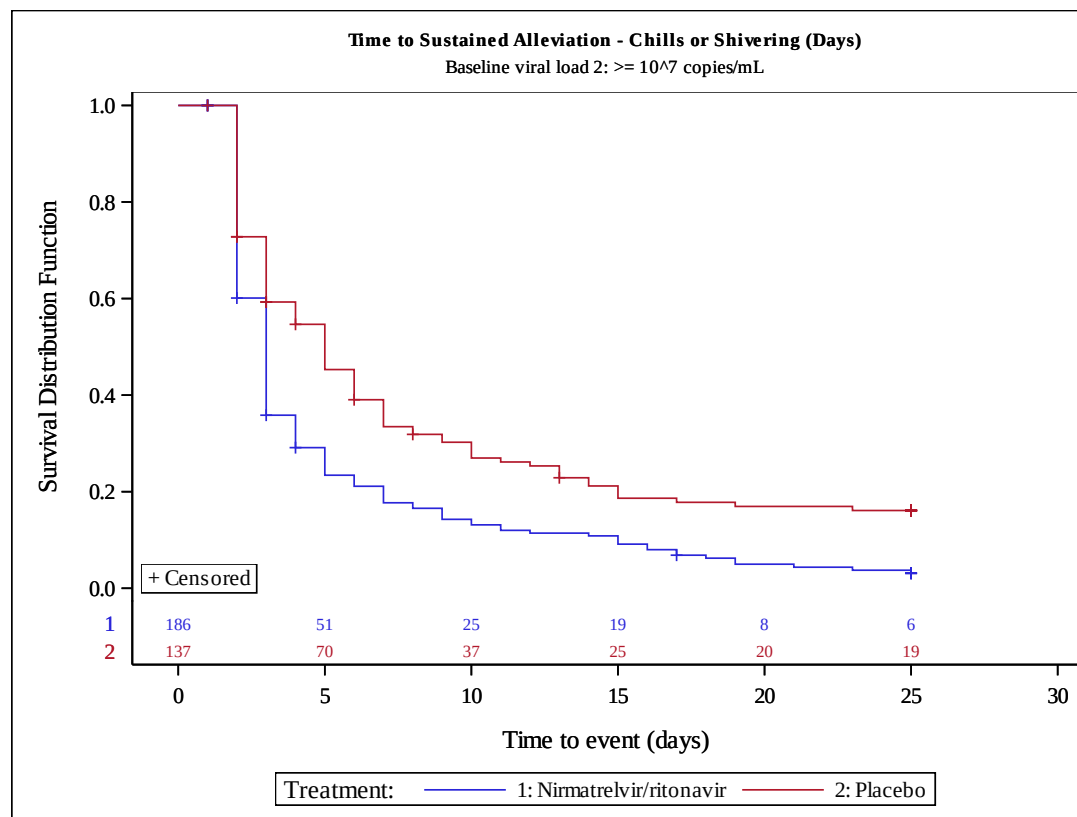


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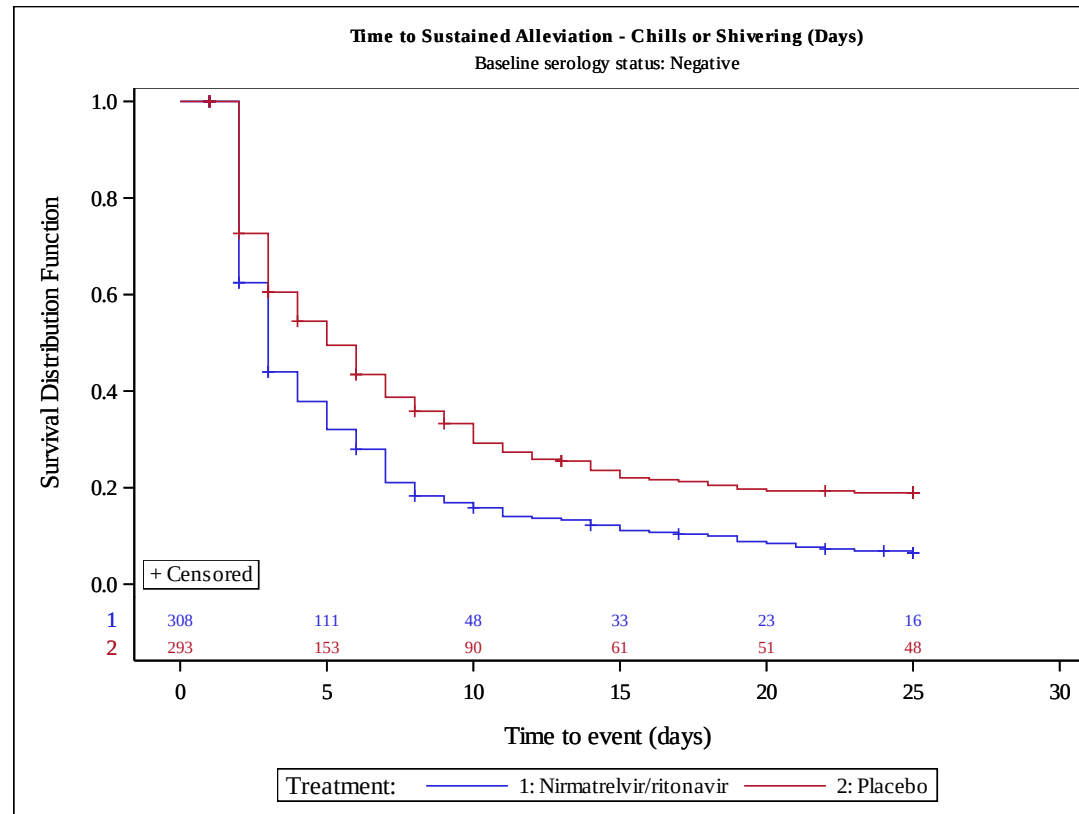
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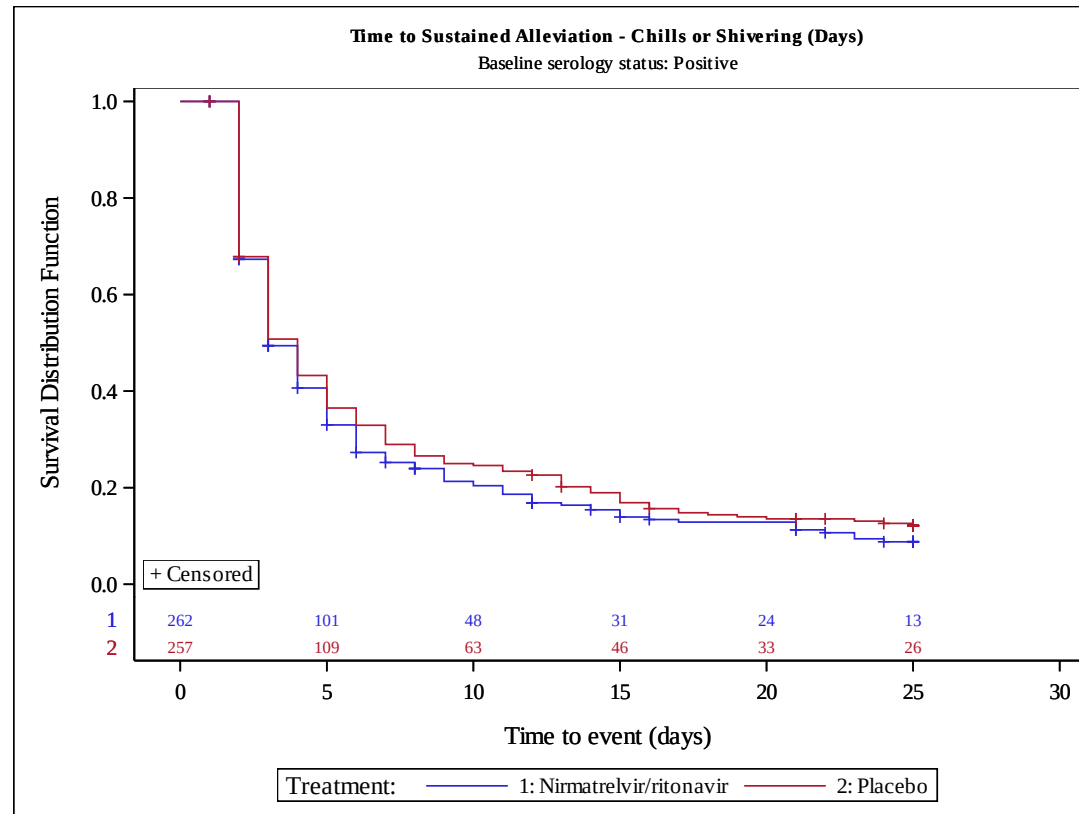


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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=47)				Placebo (N=37)				Adjusted Analysis [2]		Interaction	Unadjusted Analysis [3]		Interaction
	n/N	(%)	Median	(95% CI)[1]	n/N	(%)	Median	(95% CI)[1]	Hazard Ratio (95% CI)	p-Value	p-Value	Hazard Ratio (95% CI)	p-Value	p-Value
Age														
< 65	40/	45 (88.9)			29/	36 (80.6)								
>= 65	2/	2 (100.0)			0/	1 (0.0)								
Gender											0.712			0.681
Male	15/	16 (93.8)	3.0 (2.0, 5.0)		13/	18 (72.2)	2.5 (2.0, 7.0)		1.133 (0.477, 2.690)	0.777		1.166 (0.548, 2.484)	0.690	
Female	27/	31 (87.1)	3.0 (2.0, 3.0)		16/	19 (84.2)	4.0 (3.0, 9.0)		1.600 (0.831, 3.082)	0.160		1.598 (0.856, 2.982)	0.141	
Geographic region														
United States	17/	21 (81.0)			18/	24 (75.0)								
Europe	12/	12 (100.0)			5/	6 (83.3)								
India	0				0									
Rest of World	13/	14 (92.9)			6/	7 (85.7)								
COVID-19 therapeutic mAb treatment at randomisation														
Yes	4/	5 (80.0)			1/	2 (50.0)								
No	38/	42 (90.5)			28/	35 (80.0)								
Baseline viral load 1											0.685			0.527
< 10^4 copies/mL	8/	11 (72.7)	3.0 (2.0, 12.0)		9/	11 (81.8)	3.0 (2.0, 18.0)		0.547 (0.145, 2.063)	0.373		1.055 (0.404, 2.752)	0.913	
>= 10^4 copies/mL	33/	35 (94.3)	3.0 (2.0, 3.0)		20/	25 (80.0)	3.5 (3.0, 7.0)		1.564 (0.876, 2.789)	0.130		1.573 (0.896, 2.763)	0.115	
Baseline viral load 2											0.627			0.452
< 10^7 copies/mL	22/	25 (88.0)	3.0 (2.0, 5.0)		27/	32 (84.4)	3.0 (2.0, 6.0)		1.455 (0.769, 2.753)	0.250		1.344 (0.760, 2.377)	0.309	
>= 10^7 copies/mL	19/	21 (90.5)	3.0 (2.0, 4.0)		2/	4 (50.0)	7.0 (3.0, NE)		3.000 (0.592, 15.191)	0.184		2.547 (0.582, 11.145)	0.214	
Baseline serology status											0.076			0.073
Negative	26/	29 (89.7)	3.0 (2.0, 3.0)		16/	23 (69.6)	6.0 (3.0, 18.0)		2.116 (1.061, 4.221)	0.033		2.188 (1.142, 4.191)	0.018	
Positive	16/	18 (88.9)	3.0 (2.0, 5.0)		12/	13 (92.3)	3.0 (2.0, 4.0)		0.643 (0.270, 1.532)	0.319		0.852 (0.401, 1.808)	0.676	
Symptom onset days to first dose date											0.943			0.949
<= 3	28/	31 (90.3)	3.0 (2.0, 3.0)		19/	22 (86.4)	3.0 (2.0, 6.0)		1.417 (0.753, 2.666)	0.280		1.424 (0.788, 2.575)	0.241	
> 3	14/	16 (87.5)	4.0 (2.0, 6.0)		10/	15 (66.7)	3.0 (2.0, NE)		1.416 (0.521, 3.852)	0.495		1.320 (0.584, 2.982)	0.505	
BMI group											0.027			0.043
< 25	7/	10 (70.0)	3.0 (2.0, 6.0)		2/	4 (50.0)	NE (7.0, NE)		87.441 (2.686, 2847.0)	0.012		10.856 (1.233, 95.602)	0.032	
25 - < 30	8/	9 (88.9)	3.0 (2.0, 25.0)		11/	12 (91.7)	3.0 (2.0, 6.0)		0.364 (0.113, 1.172)	0.090		0.524 (0.200, 1.371)	0.188	
>= 30	27/	28 (96.4)	3.0 (2.0, 3.0)		16/	21 (76.2)	3.0 (2.0, 9.0)		1.477 (0.732, 2.980)	0.276		1.567 (0.837, 2.934)	0.160	
Ethnicity														
White	29/	34 (85.3)			24/	29 (82.8)								
Black or African American	4/	4 (100.0)			4/	5 (80.0)								
Asian	1/	1 (100.0)			1/	1 (100.0)								
Others	8/	8 (100.0)			0/	2 (0.0)								
Number of baseline comorbidities present														
0-1	35/	40 (87.5)			26/	34 (76.5)								
2-3	6/	6 (100.0)			3/	3 (100.0)								
>= 4	1/	1 (100.0)			0									
Presence of risk factor: Smoking											0.986			0.731
Yes	15/	17 (88.2)	2.5 (2.0, 5.0)		14/	16 (87.5)	3.0 (2.0, 7.0)		1.632 (0.605, 4.401)	0.333		1.339 (0.639, 2.803)	0.439	
No	26/	29 (89.7)	3.0 (3.0, 4.0)		15/	21 (71.4)	3.5 (2.0, 20.0)		1.391 (0.673, 2.873)	0.372		1.513 (0.796, 2.877)	0.206	

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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Chills or Shivering - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=47)			Placebo (N=37)			Adjusted Analysis [2]			Unadjusted Analysis [3]		
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus												
Yes	5/	5 (100.0)		2/	2 (100.0)							
No	36/	41 (87.8)		27/	35 (77.1)							
Presence of risk factor: Immunosuppression												
Yes	0			0								
No	41/	46 (89.1)		29/	37 (78.4)							
Presence of risk factor: Chronic lung disease												
Yes	4/	6 (66.7)		1/	1 (100.0)							
No	37/	40 (92.5)		28/	36 (77.8)							
Presence of risk factor: Hypertension									0.335			0.556
Yes	13/	14 (92.9)	3.0 (2.0, 7.0)	7/	9 (77.8)	3.0 (2.0, NE)	0.753 (0.252, 2.245)	0.611		1.098 (0.436, 2.768)	0.842	
No	28/	32 (87.5)	3.0 (2.0, 3.0)	22/	28 (78.6)	3.5 (3.0, 7.0)	1.637 (0.882, 3.039)	0.118		1.543 (0.872, 2.730)	0.136	
Presence of risk factor: Cardiovascular disorder												
Yes	1/	1 (100.0)		0								
No	40/	45 (88.9)		29/	37 (78.4)							
Presence of risk factor: Chronic kidney disease												
Yes	1/	1 (100.0)		0								
No	40/	45 (88.9)		29/	37 (78.4)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	41/	46 (89.1)		29/	37 (78.4)							
Presence of risk factor: Sickle Cell Disease												
No	41/	46 (89.1)		29/	37 (78.4)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0			0								
No	41/	46 (89.1)		29/	37 (78.4)							
Presence of risk factor: Cancer												
Yes	0			0								
No	41/	46 (89.1)		29/	37 (78.4)							
Presence of risk factor: Device Dependence												
Yes	1/	1 (100.0)		0								
No	40/	45 (88.9)		29/	37 (78.4)							

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

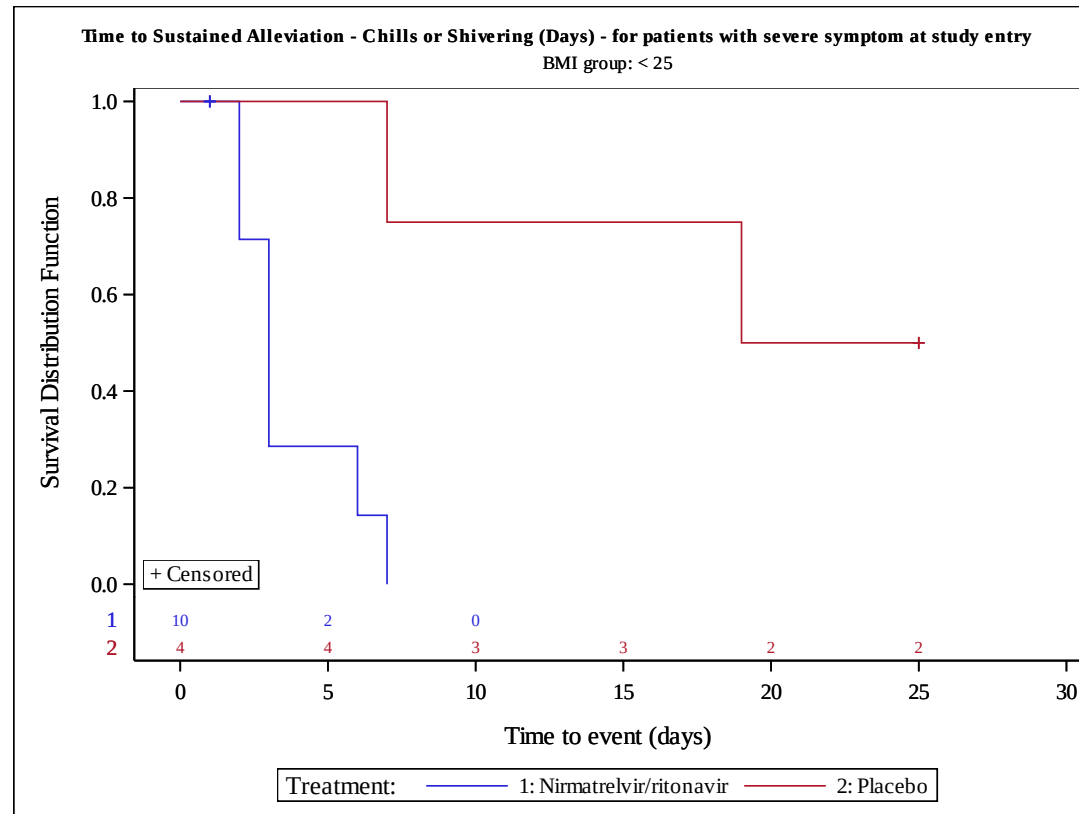
[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

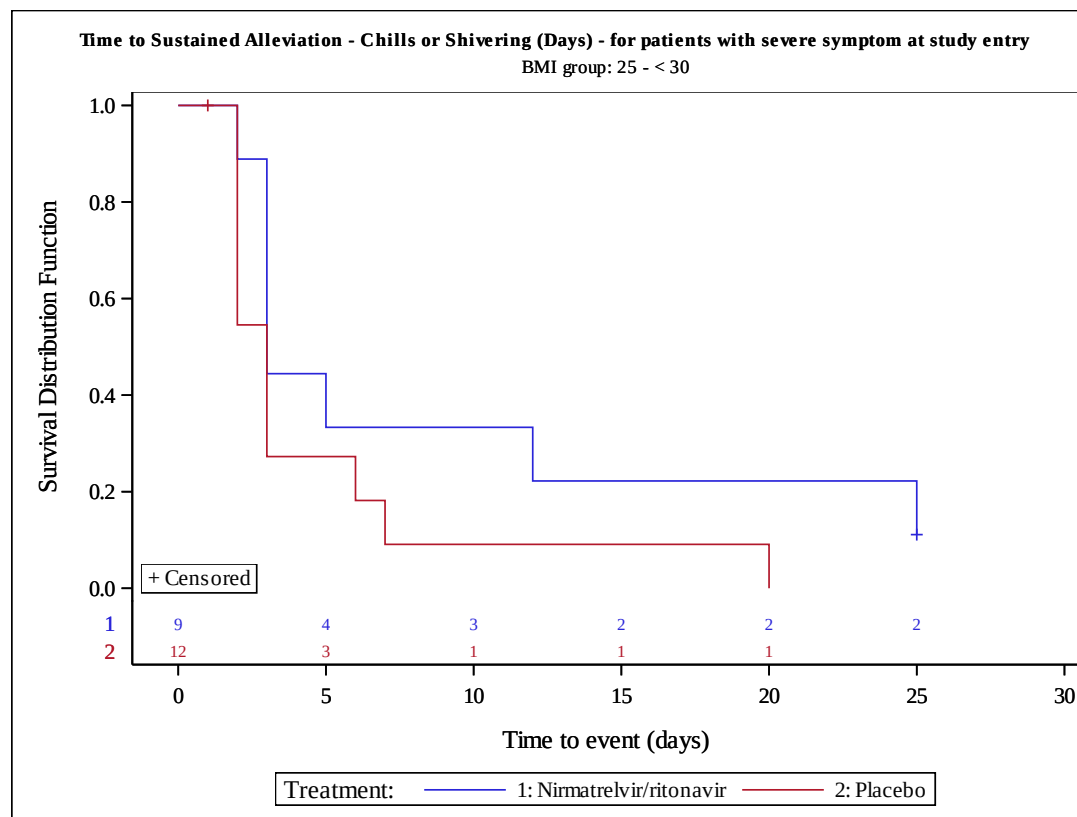


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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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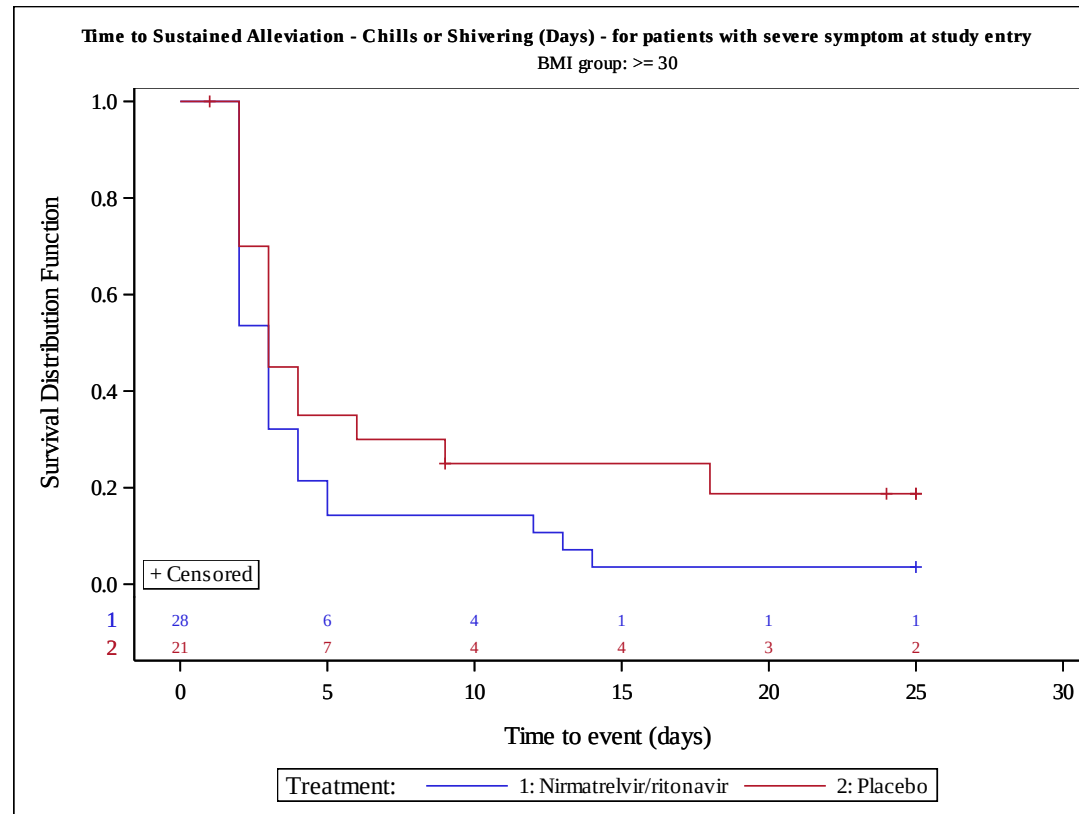
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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Chills or Shivering - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=579)					Placebo (N=558)				Adjusted Analysis [2]		Interaction	Unadjusted Analysis [3]			Interaction
	n/N	(%)	Median	(95% CI)	[1]	n/N	(%)	Median	(95% CI)	[1]	Hazard Ratio (95% CI)	p-Value	p-Value	Hazard Ratio (95% CI)	p-Value	p-Value
Age													0.387			0.289
< 65	419/ 75	494/ 85	(84.8)	5.0 (4.0, 5.0)	360/ 64	471/ 87	(76.4)	6.0 (5.0, 7.0)	7.0 (5.0, 9.0)	1.313 (1.136, 1.517)	<.001			1.338 (1.161, 1.542)	<.001	
>= 65										1.620 (1.144, 2.293)	0.007			1.651 (1.178, 2.313)	0.004	
Gender													0.972			0.563
Male	242/ 252	278/ 301	(87.1)	5.0 (4.0, 5.0)	218/ 206	287/ 271	(76.0)	6.0 (5.0, 8.0)	7.0 (5.0, 8.0)	1.345 (1.112, 1.627)	0.002			1.429 (1.188, 1.719)	<.001	
Female										1.361 (1.127, 1.643)	0.001			1.335 (1.109, 1.606)	0.002	
Geographic region													0.193			0.133
United States	202/ 197	245/ 221	(82.4)	5.0 (4.0, 5.0)	182/ 160	240/ 214	(75.8)	7.0 (5.0, 9.0)	7.0 (6.0, 9.0)	1.272 (1.036, 1.561)	0.022			1.296 (1.059, 1.586)	0.012	
Europe										1.611 (1.296, 2.003)	<.001			1.630 (1.320, 2.012)	<.001	
India	22/ 73	23/ 90	(95.7)	4.0 (3.0, 6.0)	19/ 63	20/ 84	(95.0)	4.0 (2.0, 6.0)	6.0 (4.0, 7.0)	0.553 (0.255, 1.197)	0.133			0.712 (0.375, 1.352)	0.299	
Rest of World										1.156 (0.819, 1.634)	0.410			1.185 (0.846, 1.661)	0.323	
COVID-19 therapeutic mAb treatment at randomisation													0.362			0.436
Yes	34/ 460	40/ 539	(85.0)	4.0 (3.0, 5.0)	32/ 392	39/ 519	(82.1)	4.0 (3.0, 8.0)	7.0 (6.0, 8.0)	1.128 (0.679, 1.873)	0.643			1.140 (0.702, 1.853)	0.595	
No										1.372 (1.195, 1.576)	<.001			1.401 (1.223, 1.604)	<.001	
Baseline viral load 1													0.039			0.044
< 10^4 copies/mL	145/ 334	175/ 387	(82.9)	5.0 (4.0, 5.0)	147/ 269	186/ 357	(79.0)	5.0 (4.0, 6.0)	7.0 (6.0, 8.0)	1.110 (0.878, 1.403)	0.383			1.114 (0.885, 1.403)	0.357	
>= 10^4 copies/mL										1.474 (1.252, 1.735)	<.001			1.491 (1.269, 1.753)	<.001	
Baseline viral load 2													0.180			0.159
< 10^7 copies/mL	309/ 170	376/ 186	(82.2)	5.0 (5.0, 4.0)	310/ 106	406/ 137	(76.4)	6.0 (5.0, 7.0)	7.0 (5.0, 8.0)	1.250 (1.065, 1.467)	0.006			1.253 (1.070, 1.468)	0.005	
>= 10^7 copies/mL										1.525 (1.185, 1.964)	0.001			1.582 (1.238, 2.021)	<.001	
Baseline serology status													0.043			0.020
Negative	269/ 219	308/ 262	(87.3)	5.0 (4.0, 5.0)	213/ 205	293/ 257	(72.7)	8.0 (6.0, 7.0)	5.0 (4.0, 6.0)	1.570 (1.305, 1.888)	<.001			1.640 (1.368, 1.967)	<.001	
Positive										1.161 (0.956, 1.411)	0.133			1.164 (0.961, 1.409)	0.121	
Symptom onset days to first dose date													0.671			0.672
<= 3	358/ 136	406/ 173	(88.2)	4.0 (4.0, 7.0)	288/ 136	370/ 188	(77.8)	6.0 (5.0, 7.0)	8.0 (6.0, 11.0)	1.367 (1.165, 1.603)	<.001			1.397 (1.195, 1.634)	<.001	
> 3										1.236 (0.964, 1.584)	0.095			1.313 (1.034, 1.667)	0.025	
BMI group													0.091			0.098
< 25	103/ 175	124/ 201	(83.1)	4.0 (4.0, 6.0)	97/ 160	117/ 203	(82.9)	6.0 (5.0, 7.0)	6.0 (4.0, 7.0)	1.249 (0.931, 1.676)	0.137			1.272 (0.963, 1.681)	0.090	
25 - < 30										1.192 (0.956, 1.486)	0.119			1.210 (0.975, 1.501)	0.083	
>= 30	215/ 215	253/ 253	(85.0)	4.0 (4.0, 5.0)	167/ 167	238/ 238	(70.2)	8.0 (5.0, 11.0)		1.578 (1.280, 1.946)	<.001			1.602 (1.306, 1.965)	<.001	
Ethnicity													0.538			0.569
White	392/ 23	460/ 30	(85.2)	5.0 (4.0, 8.0)	345/ 20	457/ 26	(75.5)	7.0 (6.0, 6.0)	8.0 (4.0, 10.0)	1.390 (1.197, 1.613)	<.001			1.418 (1.226, 1.640)	<.001	
Black or African American										1.130 (0.592, 2.157)	0.710			1.153 (0.629, 2.113)	0.645	
Asian	37/ 42	40/ 49	(92.5)	4.0 (3.0, 9.0)	39/ 20	43/ 32	(90.7)	4.0 (3.0, 6.0)	7.0 (3.0, NE)	0.980 (0.606, 1.583)	0.933			1.042 (0.663, 1.637)	0.860	
Others										1.429 (0.814, 2.508)	0.214			1.569 (0.918, 2.683)	0.100	
Number of baseline comorbidities present																
0-1	387/ 105	443/ 134	(87.4)		307/ 113	395/ 159	(77.7)									
2-3																
>= 4	2/ 2	2/ 2	(100.0)		4/ 4	4/ 4	(100.0)									
Presence of risk factor: Smoking													0.897			0.854
Yes	224/ 269	266/ 311	(84.2)	5.0 (4.0, 5.0)	195/ 229	263/ 295	(74.1)	6.0 (5.0, 8.0)	7.0 (5.0, 8.0)	1.329 (1.089, 1.622)	0.005			1.390 (1.145, 1.687)	<.001	
No										1.363 (1.137, 1.633)	<.001			1.371 (1.148, 1.637)	<.001	

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	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus												
Yes	64/	77 (83.1)	5.0 (4.0, 7.0)	67/	85 (78.8)	6.5 (4.0, 10.0)	1.180 (0.825, 1.686)	0.365	0.416	1.218 (0.863, 1.718)	0.261	0.465
No	429/	501 (85.6)	5.0 (4.0, 5.0)	357/	473 (75.5)	6.0 (6.0, 8.0)	1.373 (1.188, 1.587)	<.001		1.405 (1.219, 1.618)	<.001	
Presence of risk factor: Immunosuppression												
Yes	3/	3 (100.0)		4/	4 (100.0)							
No	490/	575 (85.2)		420/	554 (75.8)							
Presence of risk factor: Chronic lung disease												
Yes	39/	43 (90.7)	4.5 (3.0, 6.0)	22/	25 (88.0)	5.0 (3.0, 8.0)	1.045 (0.608, 1.797)	0.873	0.300	1.058 (0.627, 1.785)	0.834	0.286
No	454/	535 (84.9)	5.0 (4.0, 5.0)	402/	533 (75.4)	7.0 (6.0, 8.0)	1.353 (1.178, 1.553)	<.001		1.389 (1.213, 1.590)	<.001	
Presence of risk factor: Hypertension												
Yes	173/	211 (82.0)	5.0 (4.0, 6.0)	167/	233 (71.7)	8.0 (6.0, 10.0)	1.444 (1.160, 1.799)	0.001	0.236	1.408 (1.137, 1.743)	0.002	0.555
No	320/	367 (87.2)	5.0 (4.0, 5.0)	257/	325 (79.1)	6.0 (5.0, 7.0)	1.257 (1.060, 1.490)	0.008		1.331 (1.128, 1.570)	<.001	
Presence of risk factor: Cardiovascular disorder												
Yes	21/	24 (87.5)	5.0 (3.0, 11.0)	22/	29 (75.9)	8.0 (4.0, 13.0)	1.847 (0.945, 3.610)	0.073	0.450	1.473 (0.807, 2.690)	0.207	0.854
No	472/	554 (85.2)	5.0 (4.0, 5.0)	402/	529 (76.0)	6.0 (5.0, 7.0)	1.324 (1.155, 1.518)	<.001		1.369 (1.197, 1.565)	<.001	
Presence of risk factor: Chronic kidney disease												
Yes	3/	5 (60.0)	3.0 (3.0, NE)	5/	6 (83.3)	7.0 (3.0, NE)	2.880 (0.415, 19.984)	0.285	0.989	1.339 (0.308, 5.819)	0.697	0.907
No	490/	573 (85.5)	5.0 (4.0, 5.0)	419/	552 (75.9)	6.0 (5.0, 8.0)	1.343 (1.174, 1.536)	<.001		1.378 (1.208, 1.571)	<.001	
Presence of risk factor: HIV Infection												
Yes	0			0								
No	493/	578 (85.3)		423/	557 (75.9)							
Presence of risk factor: Sickle Cell Disease												
No	493/	578 (85.3)		424/	558 (76.0)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	2/	2 (100.0)		1/	1 (100.0)							
No	491/	576 (85.2)		423/	557 (75.9)							
Presence of risk factor: Cancer												
Yes	0/	1 (0.0)		4/	4 (100.0)							
No	493/	577 (85.4)		420/	554 (75.8)							
Presence of risk factor: Device Dependence												
Yes	2/	3 (66.7)		1/	1 (100.0)							
No	486/	568 (85.6)		421/	554 (76.0)							

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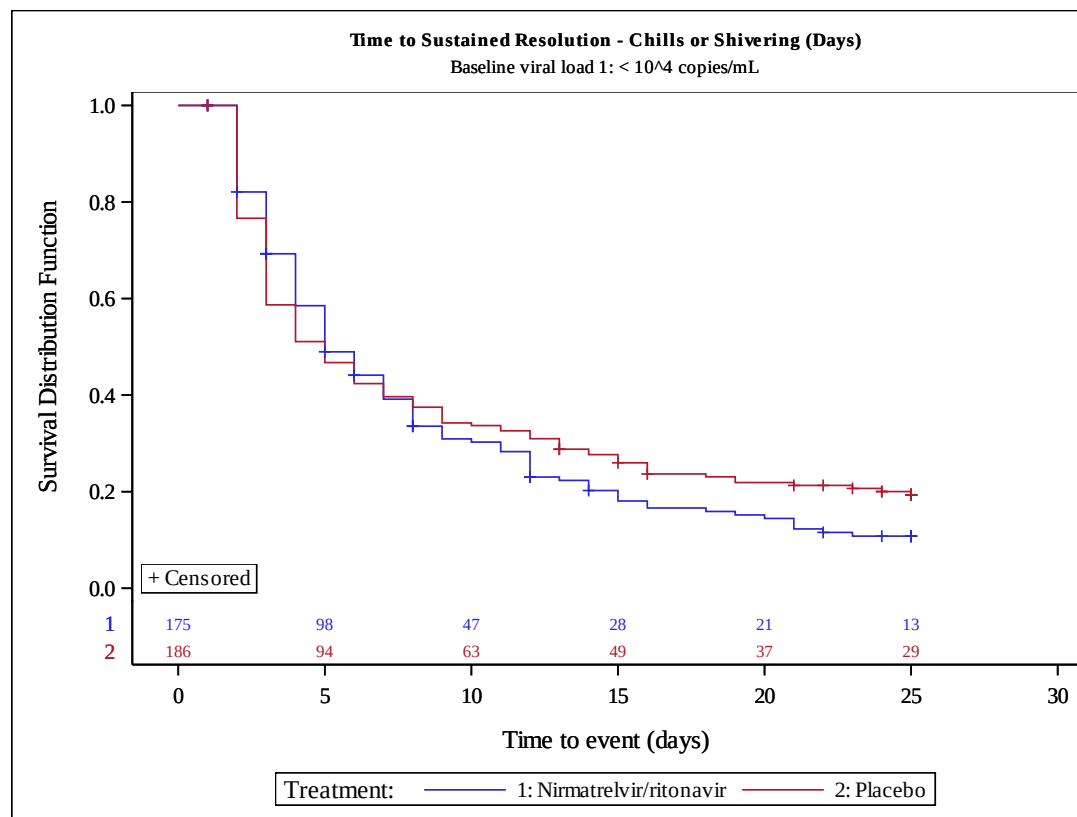
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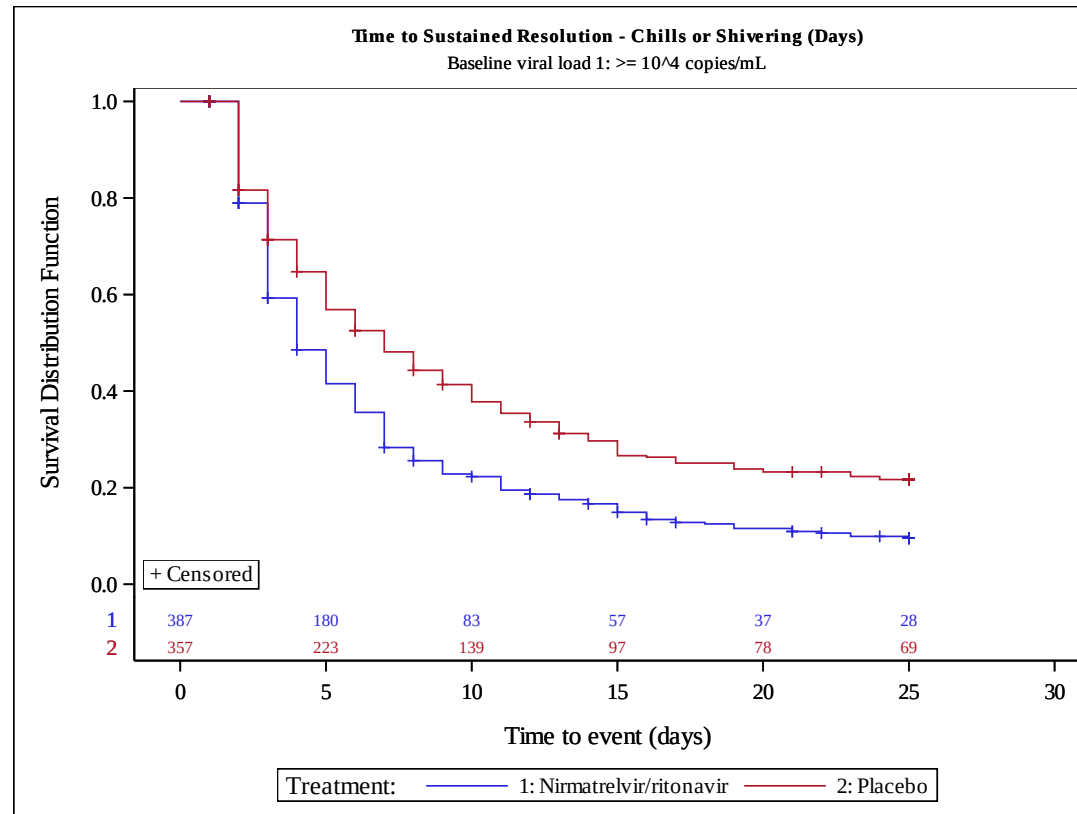
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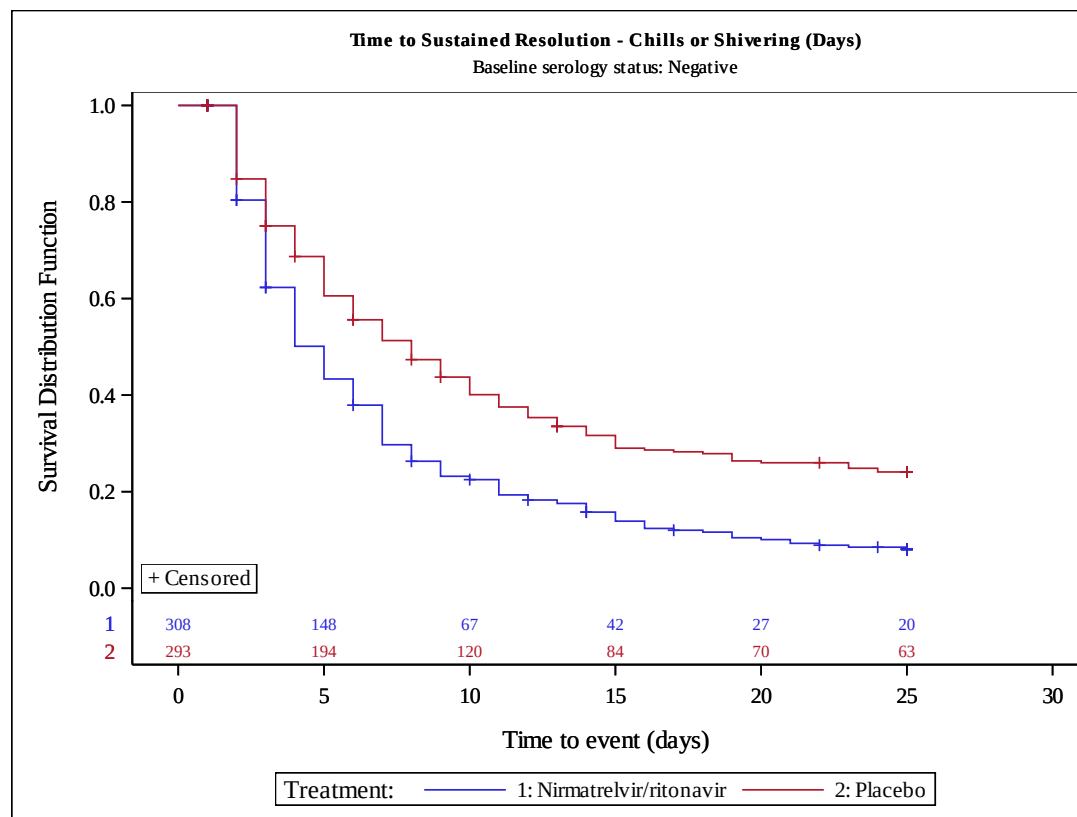


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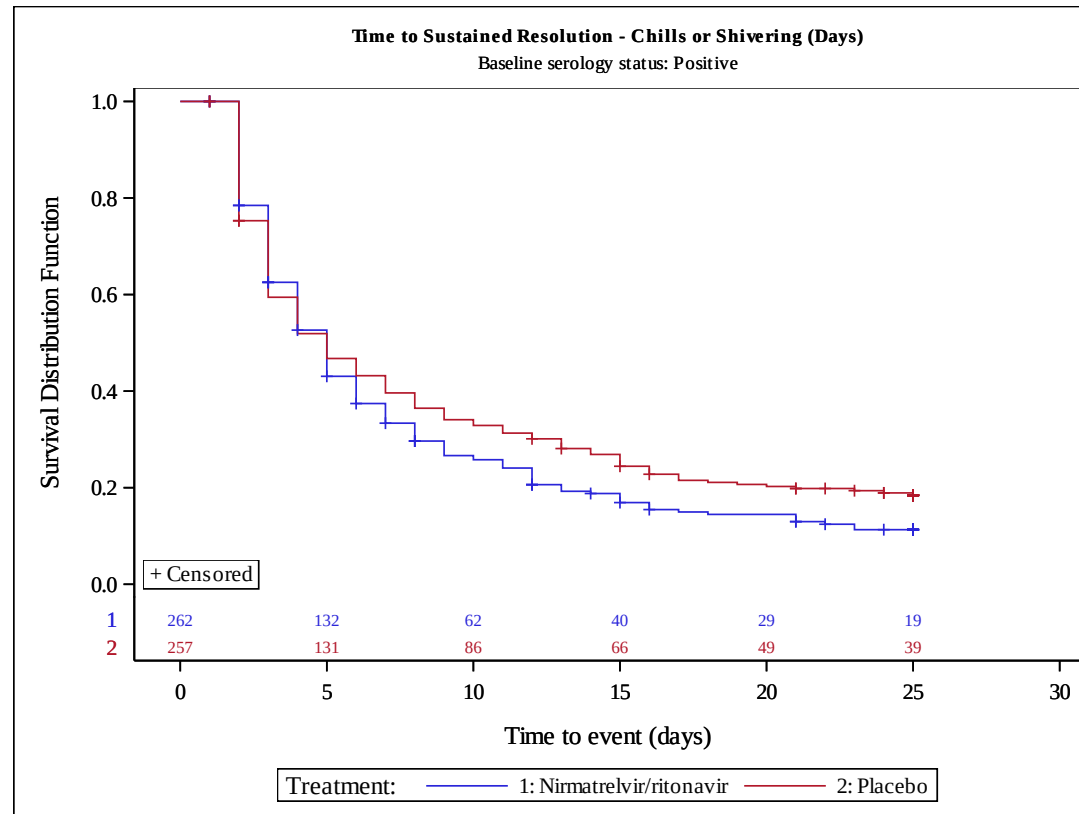
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Subgroup Level	Nirmatrelvir/ritonavir (N=47)			Placebo (N=37)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Age												
< 65	39/	45 (86.7)		27/	36 (75.0)							
>= 65	2/	2 (100.0)		0/	1 (0.0)							
Gender									0.860			0.812
Male	15/	16 (93.8)	4.5 (3.0, 7.0)	12/	18 (66.7)	5.5 (3.0, 20.0)	1.525 (0.633, 3.677)	0.347		1.474 (0.682, 3.185)	0.324	
Female	26/	31 (83.9)	4.0 (3.0, 6.0)	15/	19 (78.9)	9.0 (7.0, 17.0)	1.962 (1.008, 3.816)	0.047		1.827 (0.962, 3.470)	0.066	
Geographic region												
United States	17/	21 (81.0)		16/	24 (66.7)							
Europe	11/	12 (91.7)		5/	6 (83.3)							
India	0			0								
Rest of World	13/	14 (92.9)		6/	7 (85.7)							
COVID-19 therapeutic mAb treatment at randomisation												
Yes	4/	5 (80.0)		1/	2 (50.0)							
No	37/	42 (88.1)		26/	35 (74.3)							
Baseline viral load 1									0.508			0.751
< 10^4 copies/mL	8/	11 (72.7)	4.0 (2.0, 12.0)	7/	11 (63.6)	8.0 (3.0, NE)	0.750 (0.180, 3.127)	0.693		1.607 (0.582, 4.441)	0.360	
>= 10^4 copies/mL	32/	35 (91.4)	4.0 (3.0, 6.0)	20/	25 (80.0)	7.0 (5.0, 15.0)	1.666 (0.935, 2.971)	0.083		1.714 (0.975, 3.012)	0.061	
Baseline viral load 2									0.903			0.755
< 10^7 copies/mL	22/	25 (88.0)	5.0 (3.0, 6.0)	25/	32 (78.1)	7.5 (4.0, 15.0)	1.814 (0.939, 3.508)	0.076		1.779 (0.990, 3.197)	0.054	
>= 10^7 copies/mL	18/	21 (85.7)	4.0 (3.0, 8.0)	2/	4 (50.0)	7.0 (6.0, NE)	1.874 (0.396, 8.865)	0.428		2.070 (0.477, 8.986)	0.332	
Baseline serology status									0.438			0.419
Negative	25/	29 (86.2)	4.0 (3.0, 6.0)	15/	23 (65.2)	7.0 (5.0, 24.0)	1.910 (0.964, 3.781)	0.064		2.154 (1.127, 4.117)	0.020	
Positive	16/	18 (88.9)	4.0 (3.0, 12.0)	11/	13 (84.6)	9.0 (3.0, 17.0)	1.049 (0.437, 2.523)	0.914		1.384 (0.637, 3.009)	0.412	
Symptom onset days to first dose date									0.339			0.375
<= 3	28/	31 (90.3)	4.0 (3.0, 5.0)	17/	22 (77.3)	7.0 (5.0, 17.0)	2.016 (1.035, 3.925)	0.039		2.080 (1.120, 3.861)	0.020	
> 3	13/	16 (81.3)	6.0 (3.0, 12.0)	10/	15 (66.7)	7.5 (3.0, NE)	1.467 (0.529, 4.067)	0.461		1.265 (0.553, 2.892)	0.577	
BMI group									0.009			0.026
< 25	7/	10 (70.0)	4.0 (3.0, 7.0)	2/	4 (50.0)	NE (7.0, NE)	46.808 (1.912, 1145.9)	0.018		8.922 (1.049, 75.871)	0.045	
25 - < 30	8/	9 (88.9)	8.0 (3.0, 25.0)	11/	12 (91.7)	6.0 (2.0, 10.0)	0.304 (0.087, 1.065)	0.063		0.568 (0.218, 1.476)	0.246	
>= 30	26/	28 (92.9)	4.0 (3.0, 5.0)	14/	21 (66.7)	8.0 (4.0, 17.0)	2.102 (1.014, 4.357)	0.046		2.110 (1.093, 4.074)	0.026	
Ethnicity												
White	28/	34 (82.4)		23/	29 (79.3)							
Black or African American	4/	4 (100.0)		3/	5 (60.0)							
Asian	1/	1 (100.0)		1/	1 (100.0)							
Others	8/	8 (100.0)		0/	2 (0.0)							
Number of baseline comorbidities present												
0-1	35/	40 (87.5)		25/	34 (73.5)							
2-3	5/	6 (83.3)		2/	3 (66.7)							
>= 4	1/	1 (100.0)		0								
Presence of risk factor: Smoking									0.460			0.776
Yes	15/	17 (88.2)	4.5 (3.0, 5.0)	12/	16 (75.0)	7.0 (3.0, 15.0)	2.882 (0.980, 8.481)	0.055		1.889 (0.866, 4.119)	0.110	
No	25/	29 (86.2)	4.0 (3.0, 8.0)	15/	21 (71.4)	7.5 (4.0, 17.0)	1.492 (0.732, 3.041)	0.271		1.625 (0.853, 3.095)	0.140	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=47)			Placebo (N=37)			Adjusted Analysis [2]			Unadjusted Analysis [3]			
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	
Presence of risk factor: Diabetes mellitus													
Yes	5/	5 (100.0)		2/	2 (100.0)								
No	35/	41 (85.4)		25/	35 (71.4)								
Presence of risk factor: Immunosuppression													
Yes	0			0									
No	40/	46 (87.0)		27/	37 (73.0)								
Presence of risk factor: Chronic lung disease													
Yes	4/	6 (66.7)		1/	1 (100.0)								
No	36/	40 (90.0)		26/	36 (72.2)								
Presence of risk factor: Hypertension									0.540			0.832	
Yes	12/	14 (85.7)	4.0 (3.0, 12.0)	6/	9 (66.7)	8.0 (2.0, NE)	1.451 (0.473, 4.448)	0.515		1.519 (0.566, 4.073)	0.406		
No	28/	32 (87.5)	4.0 (3.0, 6.0)	21/	28 (75.0)	7.0 (5.0, 10.0)	1.928 (1.038, 3.581)	0.038		1.870 (1.052, 3.323)	0.033		
Presence of risk factor: Cardiovascular disorder													
Yes	1/	1 (100.0)		0									
No	39/	45 (86.7)		27/	37 (73.0)								
Presence of risk factor: Chronic kidney disease													
Yes	0/	1 (0.0)		0									
No	40/	45 (88.9)		27/	37 (73.0)								
Presence of risk factor: HIV Infection													
Yes	0			0									
No	40/	46 (87.0)		27/	37 (73.0)								
Presence of risk factor: Sickle Cell Disease													
No	40/	46 (87.0)		27/	37 (73.0)								
Presence of risk factor: Neurodevelopmental Disorder													
Yes	0			0									
No	40/	46 (87.0)		27/	37 (73.0)								
Presence of risk factor: Cancer													
Yes	0			0									
No	40/	46 (87.0)		27/	37 (73.0)								
Presence of risk factor: Device Dependence													
Yes	1/	1 (100.0)		0									
No	39/	45 (86.7)		27/	37 (73.0)								

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

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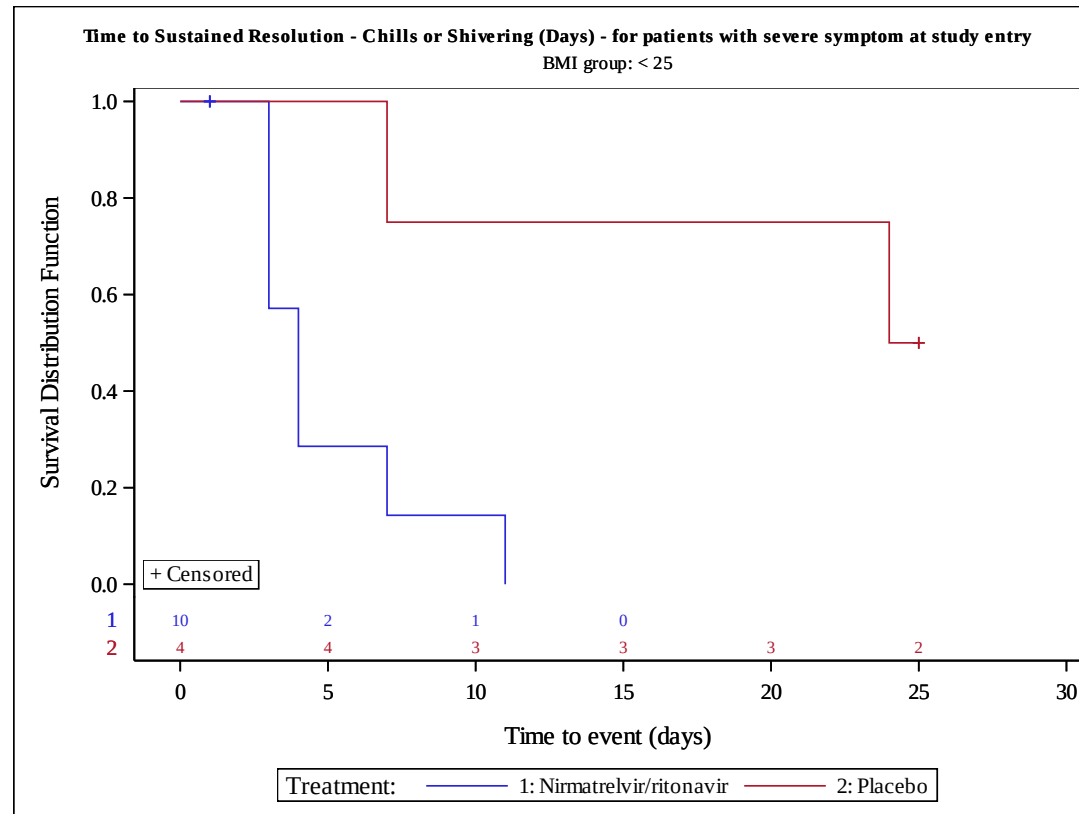
p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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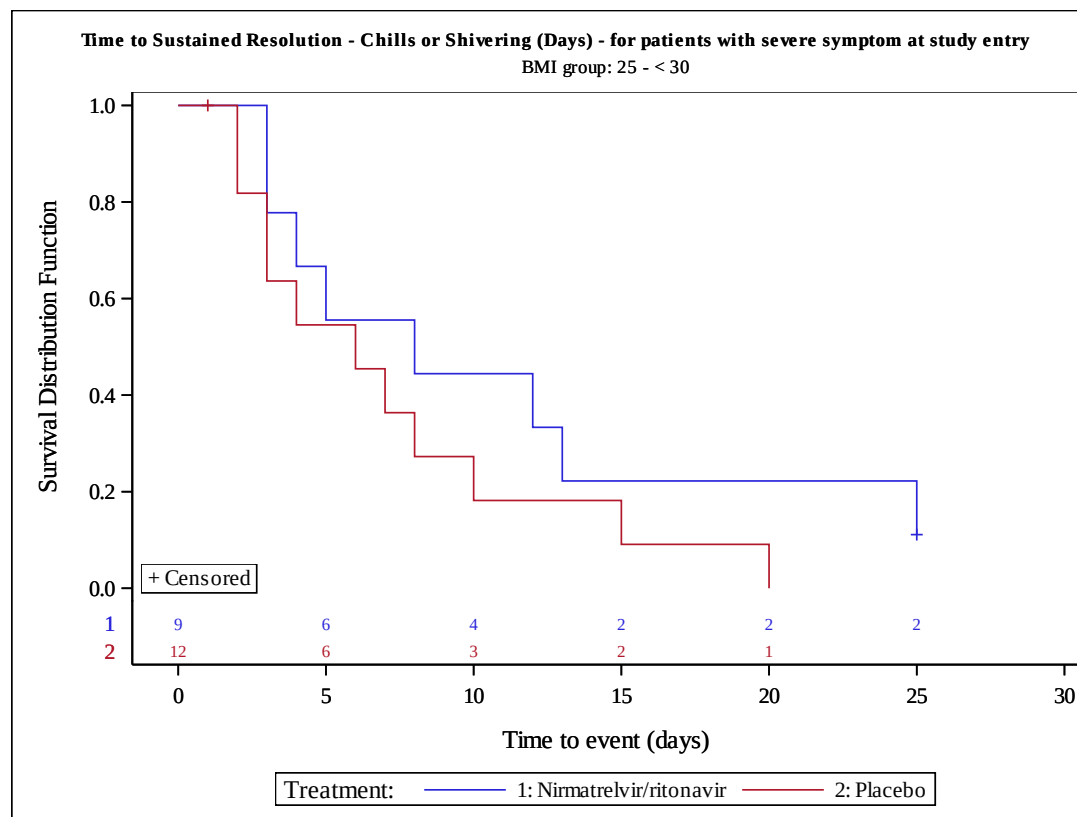


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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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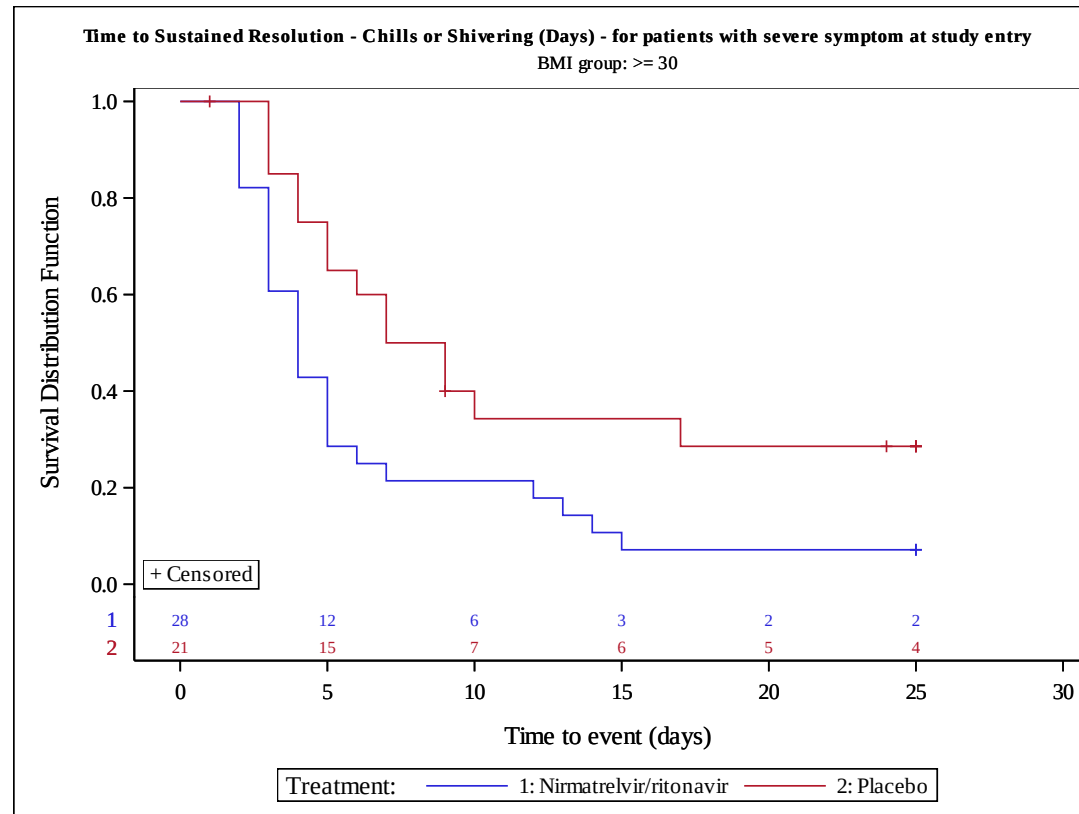
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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Unadjusted analysis [2]			
			Relative Risk (95% CI)		p-Value	Interaction p-Value	Relative Risk (95% CI)		p-Value	Interaction p-Value
Age										
< 65	149/ 790 (18.9)	174/ 810 (21.5)	0.879 (0.721, 1.071)	0.202		0.051	0.878 (0.722, 1.068)	0.192		0.076
>= 65	17/ 138 (12.3)	34/ 145 (23.4)	0.445 (0.257, 0.768)	0.004			0.525 (0.308, 0.896)	0.018		
Gender										
Male	70/ 463 (15.1)	96/ 507 (18.9)	0.784 (0.589, 1.044)	0.096		0.722	0.798 (0.603, 1.058)	0.117		0.858
Female	96/ 465 (20.6)	112/ 448 (25.0)	0.836 (0.656, 1.066)	0.149			0.826 (0.650, 1.050)	0.118		
Geographic region										
United States	74/ 375 (19.7)	80/ 387 (20.7)	0.961 (0.721, 1.282)	0.789		0.185	0.955 (0.720, 1.266)	0.747		0.203
Europe	55/ 322 (17.1)	77/ 321 (24.0)	0.707 (0.516, 0.968)	0.031			0.712 (0.522, 0.970)	0.032		
India	10/ 74 (13.5)	7/ 78 (9.0)	NE (NE, NE)	NE			1.506 (0.605, 3.748)	0.379		
Rest of World	27/ 157 (17.2)	44/ 169 (26.0)	0.677 (0.441, 1.040)	0.075			0.661 (0.431, 1.012)	0.057		
COVID-19 therapeutic mAb treatment at randomisation										
Yes	16/ 57 (28.1)	17/ 60 (28.3)	0.935 (0.523, 1.673)	0.822		0.574	0.991 (0.556, 1.767)	0.975		0.510
No	150/ 871 (17.2)	191/ 895 (21.3)	0.802 (0.660, 0.975)	0.027			0.807 (0.666, 0.978)	0.029		
Baseline viral load 1										
< 10 ⁴ copies/mL	55/ 335 (16.4)	59/ 354 (16.7)	1.004 (0.713, 1.414)	0.982		0.168	0.985 (0.704, 1.378)	0.930		0.186
>= 10 ⁴ copies/mL	107/ 569 (18.8)	144/ 575 (25.0)	0.752 (0.603, 0.937)	0.011			0.751 (0.602, 0.937)	0.011		
Baseline viral load 2										
< 10 ⁷ copies/mL	114/ 652 (17.5)	124/ 699 (17.7)	0.999 (0.792, 1.259)	0.990		0.004	0.986 (0.782, 1.242)	0.902		0.004
>= 10 ⁷ copies/mL	48/ 252 (19.0)	79/ 230 (34.3)	0.564 (0.413, 0.770)	<.001			0.555 (0.406, 0.757)	<.001		
Baseline serology status										
Negative	84/ 435 (19.3)	116/ 456 (25.4)	0.762 (0.594, 0.978)	0.033		0.436	0.759 (0.592, 0.973)	0.030		0.378
Positive	79/ 482 (16.4)	89/ 487 (18.3)	0.884 (0.671, 1.165)	0.382			0.897 (0.681, 1.181)	0.439		
Symptom onset days to first dose date										
<= 3	114/ 624 (18.3)	130/ 624 (20.8)	0.859 (0.684, 1.079)	0.192		0.452	0.877 (0.700, 1.099)	0.254		0.338
> 3	52/ 304 (17.1)	78/ 331 (23.6)	0.754 (0.548, 1.039)	0.085			0.726 (0.530, 0.994)	0.046		
BMI group										
< 25	23/ 215 (10.7)	48/ 213 (22.5)	0.499 (0.314, 0.791)	0.003		0.054	0.475 (0.300, 0.752)	0.001		0.027
25 - < 30	61/ 319 (19.1)	64/ 332 (19.3)	0.949 (0.689, 1.308)	0.751			0.992 (0.724, 1.360)	0.960		
>= 30	82/ 393 (20.9)	96/ 410 (23.4)	0.871 (0.667, 1.138)	0.312			0.891 (0.687, 1.156)	0.385		
Ethnicity										
White	123/ 699 (17.6)	161/ 718 (22.4)	0.774 (0.626, 0.957)	0.018		0.308	0.785 (0.636, 0.968)	0.024		0.585
Black or African American	10/ 43 (23.3)	9/ 40 (22.5)	NE (NE, NE)	NE			1.034 (0.469, 2.280)	0.935		
Asian	19/ 117 (16.2)	18/ 127 (14.2)	1.313 (0.728, 2.370)	0.366			1.146 (0.633, 2.075)	0.653		
Others	14/ 69 (20.3)	20/ 70 (28.6)	NE (NE, NE)	NE			0.710 (0.391, 1.290)	0.261		
Number of baseline comorbidities present										
0-1	122/ 710 (17.2)	155/ 728 (21.3)	0.791 (0.637, 0.982)	0.033		0.256	0.807 (0.652, 0.999)	0.049		0.553
2-3	43/ 214 (20.1)	53/ 221 (24.0)	0.849 (0.590, 1.222)	0.378			0.838 (0.587, 1.196)	0.330		
>= 4	1/ 4 (25.0)	0/ 6 (0.0)	NE (NE, NE)	NE			4.200 (0.212, 83.335)	0.346		
Presence of risk factor: Smoking										
Yes	60/ 417 (14.4)	68/ 438 (15.5)	0.926 (0.667, 1.285)	0.646		0.332	0.927 (0.673, 1.277)	0.642		0.347
No	106/ 509 (20.8)	140/ 517 (27.1)	0.767 (0.615, 0.958)	0.019			0.769 (0.617, 0.959)	0.020		
Presence of risk factor: Diabetes mellitus										
						0.430				0.495

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928)		Placebo (N=955)		Adjusted analysis [1]			Interaction p-Value	Unadjusted analysis [2]			Interaction p-Value
	n/N (%)		n/N (%)		Relative Risk (95% CI)		p-Value		Relative Risk (95% CI)		p-Value	
Yes	26/ 130 (20.0)		38/ 136 (27.9)		0.691 (0.445, 1.074)		0.101		0.716 (0.462, 1.108)		0.134	
No	140/ 797 (17.6)		170/ 819 (20.8)		0.847 (0.691, 1.038)		0.110		0.846 (0.692, 1.035)		0.104	
Presence of risk factor: Immunosuppression								0.093			0.150	
Yes	3/ 6 (50.0)		1/ 7 (14.3)		NE (NE, NE)		NE		3.500 (0.482, 25.430)		0.216	
No	163/ 921 (17.7)		207/ 948 (21.8)		0.805 (0.668, 0.970)		0.022		0.811 (0.674, 0.974)		0.025	
Presence of risk factor: Chronic lung disease								0.049			0.126	
Yes	15/ 62 (24.2)		6/ 39 (15.4)		1.869 (0.705, 4.959)		0.209		1.573 (0.667, 3.708)		0.301	
No	151/ 865 (17.5)		202/ 916 (22.1)		0.781 (0.645, 0.946)		0.011		0.792 (0.655, 0.957)		0.016	
Presence of risk factor: Hypertension								0.986			0.776	
Yes	69/ 348 (19.8)		92/ 371 (24.8)		0.830 (0.629, 1.096)		0.188		0.800 (0.607, 1.053)		0.112	
No	97/ 579 (16.8)		116/ 584 (19.9)		0.825 (0.643, 1.058)		0.129		0.843 (0.661, 1.076)		0.171	
Presence of risk factor: Cardiovascular disorder								0.243			0.245	
Yes	6/ 42 (14.3)		14/ 49 (28.6)		NE (NE, NE)		NE		0.500 (0.211, 1.185)		0.115	
No	160/ 885 (18.1)		194/ 906 (21.4)		0.839 (0.694, 1.015)		0.070		0.844 (0.700, 1.019)		0.077	
Presence of risk factor: Chronic kidney disease								0.601			0.353	
Yes	1/ 6 (16.7)		4/ 8 (50.0)		NE (NE, NE)		NE		0.333 (0.049, 2.271)		0.262	
No	165/ 921 (17.9)		204/ 947 (21.5)		0.821 (0.682, 0.988)		0.037		0.832 (0.692, 1.000)		0.050	
Presence of risk factor: HIV Infection												
Yes	0		0/ 1 (0.0)									
No	166/ 927 (17.9)		208/ 953 (21.8)									
Presence of risk factor: Sickle Cell Disease												
No	166/ 927 (17.9)		208/ 955 (21.8)									
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0/ 2 (0.0)		0/ 1 (0.0)									
No	166/ 925 (17.9)		208/ 954 (21.8)									
Presence of risk factor: Cancer								0.592			0.767	
Yes	1/ 5 (20.0)		1/ 6 (16.7)		NE (NE, NE)		NE		1.200 (0.098, 14.690)		0.887	
No	165/ 922 (17.9)		207/ 949 (21.8)		0.814 (0.676, 0.981)		0.030		0.820 (0.683, 0.986)		0.034	
Presence of risk factor: Device Dependence												
Yes	2/ 4 (50.0)		2/ 3 (66.7)									
No	163/ 914 (17.8)		204/ 944 (21.6)									

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=580)			Placebo (N=591)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	439/ 78	496 (88.5)	3.0 (3.0, 4.0)	400/ 75	497 (80.5)	4.0 (4.0, 5.0)	1.299 (1.130, 1.494)	<.001		0.375	1.316 (1.148, 1.508)	<.001		0.233
>= 65		84 (92.9)	3.0 (2.0, 4.0)		94 (79.8)	4.0 (3.0, 7.0)	1.558 (1.120, 2.168)	0.008			1.660 (1.201, 2.295)	0.002		
Gender														
Male	256/ 261	284 (90.1)	3.0 (3.0, 4.0)	245/ 230	314 (78.0)	4.0 (4.0, 5.0)	1.393 (1.162, 1.670)	<.001		0.447	1.420 (1.189, 1.695)	<.001		0.370
Female		296 (88.2)	3.0 (3.0, 4.0)		277 (83.0)	5.0 (4.0, 6.0)	1.273 (1.059, 1.529)	0.010			1.289 (1.079, 1.541)	0.005		
Geographic region														
United States	193/ 201	226 (85.4)	3.0 (3.0, 4.0)	175/ 182	215 (81.4)	4.0 (3.0, 6.0)	1.135 (0.921, 1.399)	0.236		0.265	1.180 (0.961, 1.449)	0.114		0.261
Europe		214 (93.9)	3.0 (3.0, 4.0)		227 (80.2)	4.0 (4.0, 6.0)	1.533 (1.242, 1.891)	<.001			1.579 (1.288, 1.936)	<.001		
India	34/ 34	36 (94.4)	4.0 (3.0, 5.0)	33/ 33	35 (94.3)	5.0 (4.0, 7.0)	1.805 (1.056, 3.086)	0.031			1.271 (0.785, 2.059)	0.330		
Rest of World	89/ 89	104 (85.6)	3.0 (2.0, 4.0)	85/ 85	114 (74.6)	4.0 (3.0, 7.0)	1.360 (1.004, 1.842)	0.047			1.368 (1.015, 1.845)	0.040		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	38/ 479	43 (88.4)	3.5 (2.0, 5.0)	33/ 442	39 (84.6)	4.0 (3.0, 6.0)	1.174 (0.726, 1.898)	0.513		0.580	1.203 (0.753, 1.922)	0.439		0.586
No		537 (89.2)	3.0 (NE, NE)		552 (80.1)	5.0 (4.0, 5.0)	1.342 (1.174, 1.533)	<.001			1.370 (1.203, 1.561)	<.001		
Baseline viral load 1														
< 10^4 copies/mL	149/ 353	170 (87.6)	3.0 (3.0, 4.0)	158/ 308	181 (87.3)	4.0 (3.0, 4.0)	1.077 (0.857, 1.352)	0.526		0.018	1.069 (0.855, 1.338)	0.557		0.019
>= 10^4 copies/mL		395 (89.4)	3.0 (NE, NE)		395 (78.0)	5.0 (4.0, 6.0)	1.466 (1.254, 1.713)	<.001			1.469 (1.259, 1.714)	<.001		
Baseline viral load 2														
< 10^7 copies/mL	323/ 179	373 (86.6)	4.0 (3.0, 4.0)	343/ 123	415 (82.7)	4.0 (4.0, 5.0)	1.169 (1.002, 1.364)	0.047		0.003	1.172 (1.007, 1.366)	0.041		0.003
>= 10^7 copies/mL		192 (93.2)	3.0 (NE, NE)		161 (76.4)	6.0 (4.0, 7.0)	1.746 (1.372, 2.221)	<.001			1.781 (1.410, 2.251)	<.001		
Baseline serology status														
Negative	268/ 241	300 (89.3)	3.0 (3.0, 4.0)	239/ 228	317 (75.4)	5.0 (4.0, 6.0)	1.517 (1.267, 1.816)	<.001		0.061	1.539 (1.290, 1.835)	<.001		0.032
Positive		271 (88.9)	3.0 (3.0, 4.0)		265 (86.0)	4.0 (3.0, 5.0)	1.196 (0.994, 1.439)	0.058			1.184 (0.987, 1.420)	0.070		
Symptom onset days to first dose date														
<= 3	369/ 148	401 (92.0)	3.0 (NE, NE)	316/ 159	381 (82.9)	4.0 (4.0, 5.0)	1.365 (1.169, 1.593)	<.001		0.544	1.387 (1.191, 1.614)	<.001		0.566
> 3		179 (82.7)	4.0 (3.0, 5.0)		210 (75.7)	6.0 (4.0, 7.0)	1.243 (0.986, 1.568)	0.066			1.275 (1.019, 1.597)	0.034		
BMI group														
< 25	115/ 179	129 (89.1)	3.0 (2.0, 3.0)	110/ 173	130 (84.6)	5.0 (4.0, 6.0)	1.512 (1.145, 1.995)	0.004		0.230	1.591 (1.219, 2.076)	<.001		0.242
25 - < 30		201 (89.1)	3.0 (3.0, 4.0)		211 (82.0)	4.0 (3.0, 5.0)	1.168 (0.942, 1.448)	0.156			1.184 (0.960, 1.460)	0.115		
>= 30	222/ 222	249 (89.2)	3.0 (3.0, 4.0)	192/ 192	250 (76.8)	4.0 (4.0, 6.0)	1.438 (1.175, 1.759)	<.001			1.418 (1.167, 1.722)	<.001		
Ethnicity														
White	400/ 17	446 (89.7)	3.0 (NE, NE)	365/ 19	456 (80.0)	4.0 (4.0, 5.0)	1.349 (1.165, 1.562)	<.001		0.881	1.389 (1.203, 1.602)	<.001		0.783
Black or African American		22 (77.3)	4.0 (2.0, 8.0)		22 (86.4)	4.0 (2.0, 11.0)	1.023 (0.498, 2.102)	0.950			1.070 (0.550, 2.083)	0.842		
Asian	54/ 46	59 (91.5)	3.0 (3.0, 4.0)	59/ 32	65 (90.8)	5.0 (4.0, 6.0)	1.587 (1.067, 2.361)	0.023			1.344 (0.927, 1.950)	0.119		
Others		53 (86.8)	3.0 (2.0, 7.0)		48 (66.7)	4.0 (2.0, 10.0)	1.442 (0.909, 2.287)	0.120			1.399 (0.890, 2.201)	0.146		
Number of baseline comorbidities present														
0-1	410/ 105	457 (89.7)		347/ 125	432 (80.3)									
2-3		121 (86.8)			156 (80.1)									
>= 4	2/ 2	2 (100.0)		3/ 3	3 (100.0)									
Presence of risk factor: Smoking														
Yes	234/ 282	263 (89.0)	3.0 (3.0, 4.0)	222/ 253	268 (82.8)	4.0 (3.0, 5.0)	1.219 (1.008, 1.474)	0.041		0.182	1.250 (1.039, 1.504)	0.018		0.230
No		316 (89.2)	3.0 (NE, NE)		323 (78.3)	5.0 (4.0, 6.0)	1.425 (1.196, 1.698)	<.001			1.454 (1.225, 1.726)	<.001		

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=580)			Placebo (N=591)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus										0.459				0.463
Yes	65/ 74	(87.8)	3.0 (3.0, 4.0)	72/ 89	(80.9)	6.0 (5.0, 8.0)	1.618 (1.137, 2.301)	0.007			1.566 (1.115, 2.199)	0.010		
No	452/ 506	(89.3)	3.0 (3.0, 4.0)	403/ 502	(80.3)	4.0 (4.0, 5.0)	1.298 (1.130, 1.491)	<.001			1.321 (1.154, 1.513)	<.001		
Presence of risk factor: Immunosuppression														
Yes	3/ 3	(100.0)		6/ 6	(100.0)									
No	514/ 577	(89.1)		469/ 585	(80.2)									
Presence of risk factor: Chronic lung disease										0.723				0.698
Yes	39/ 42	(92.9)	3.0 (2.0, 5.0)	21/ 24	(87.5)	4.0 (3.0, 6.0)	1.232 (0.716, 2.120)	0.452			1.243 (0.731, 2.116)	0.422		
No	478/ 538	(88.8)	3.0 (3.0, 4.0)	454/ 567	(80.1)	4.0 (4.0, 5.0)	1.329 (1.164, 1.517)	<.001			1.358 (1.193, 1.546)	<.001		
Presence of risk factor: Hypertension										0.600				0.616
Yes	178/ 203	(87.7)	3.0 (3.0, 4.0)	189/ 242	(78.1)	4.0 (4.0, 6.0)	1.356 (1.096, 1.677)	0.005			1.389 (1.130, 1.707)	0.002		
No	339/ 377	(89.9)	3.0 (3.0, 4.0)	286/ 349	(81.9)	4.0 (4.0, 5.0)	1.302 (1.106, 1.532)	0.002			1.324 (1.130, 1.551)	<.001		
Presence of risk factor: Cardiovascular disorder										0.220				0.251
Yes	23/ 25	(92.0)	3.0 (2.0, 5.0)	24/ 31	(77.4)	6.0 (4.0, 9.0)	2.256 (1.178, 4.321)	0.014			1.933 (1.077, 3.467)	0.027		
No	494/ 555	(89.0)	3.0 (3.0, 4.0)	451/ 560	(80.5)	4.0 (4.0, 5.0)	1.306 (1.146, 1.490)	<.001			1.334 (1.173, 1.517)	<.001		
Presence of risk factor: Chronic kidney disease														
Yes	3/ 3	(100.0)		5/ 6	(83.3)									
No	514/ 577	(89.1)		470/ 585	(80.3)									
Presence of risk factor: HIV Infection														
Yes	0			0										
No	517/ 580	(89.1)		474/ 590	(80.3)									
Presence of risk factor: Sick Cell Disease														
No	517/ 580	(89.1)		475/ 591	(80.4)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	1/ 1	(100.0)		1/ 1	(100.0)									
No	516/ 579	(89.1)		474/ 590	(80.3)									
Presence of risk factor: Cancer														
Yes	0/ 1	(0.0)		6/ 6	(100.0)									
No	517/ 579	(89.3)		469/ 585	(80.2)									
Presence of risk factor: Device Dependence														
Yes	2/ 2	(100.0)		1/ 2	(50.0)									
No	509/ 569	(89.5)		471/ 582	(80.9)									

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[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

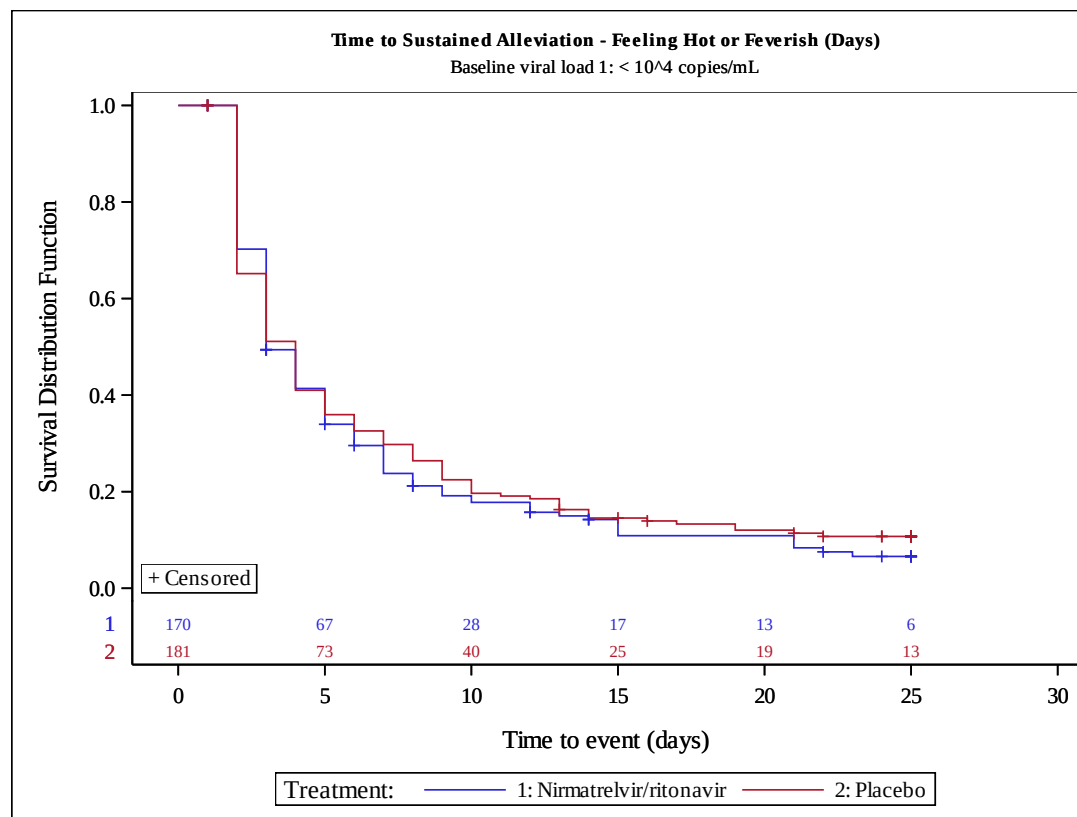
p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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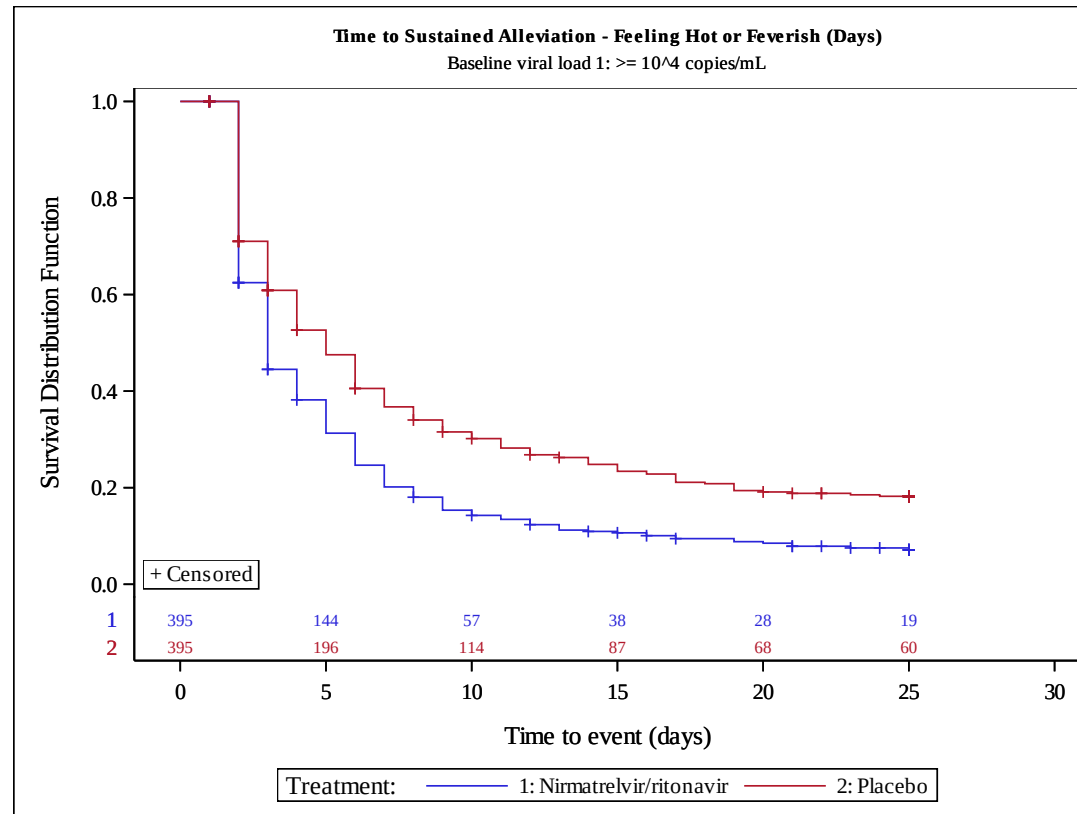
Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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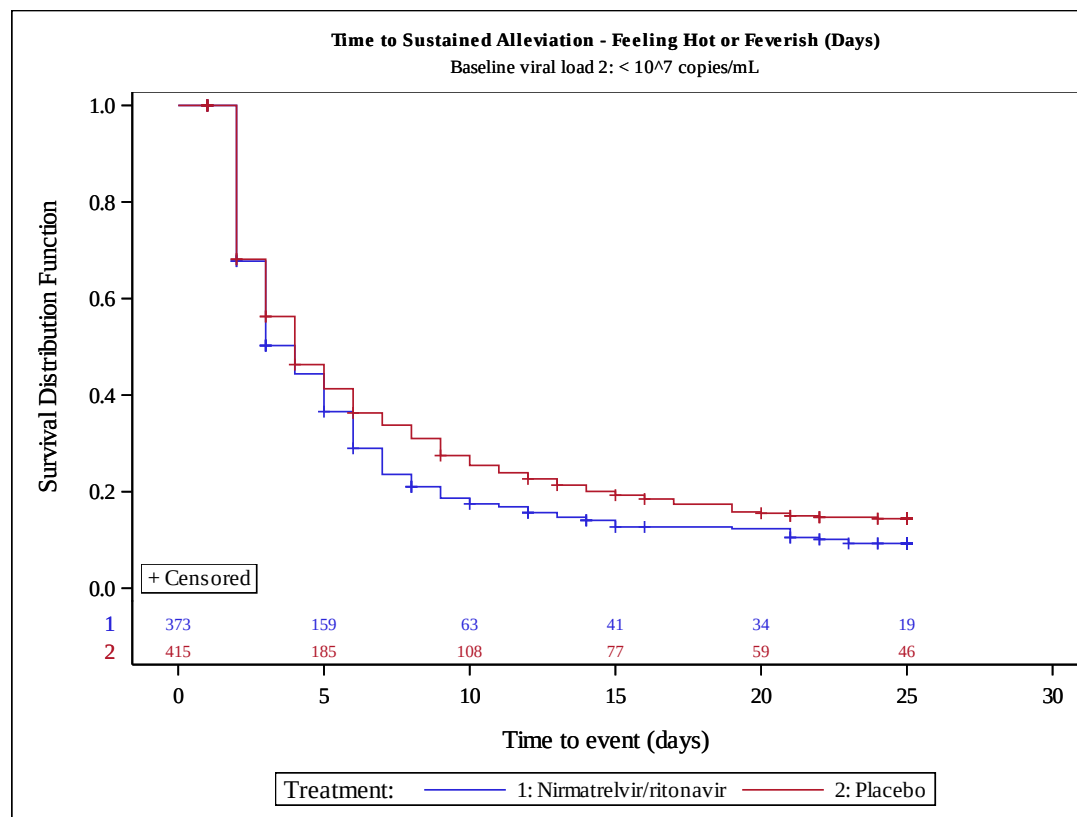


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Final

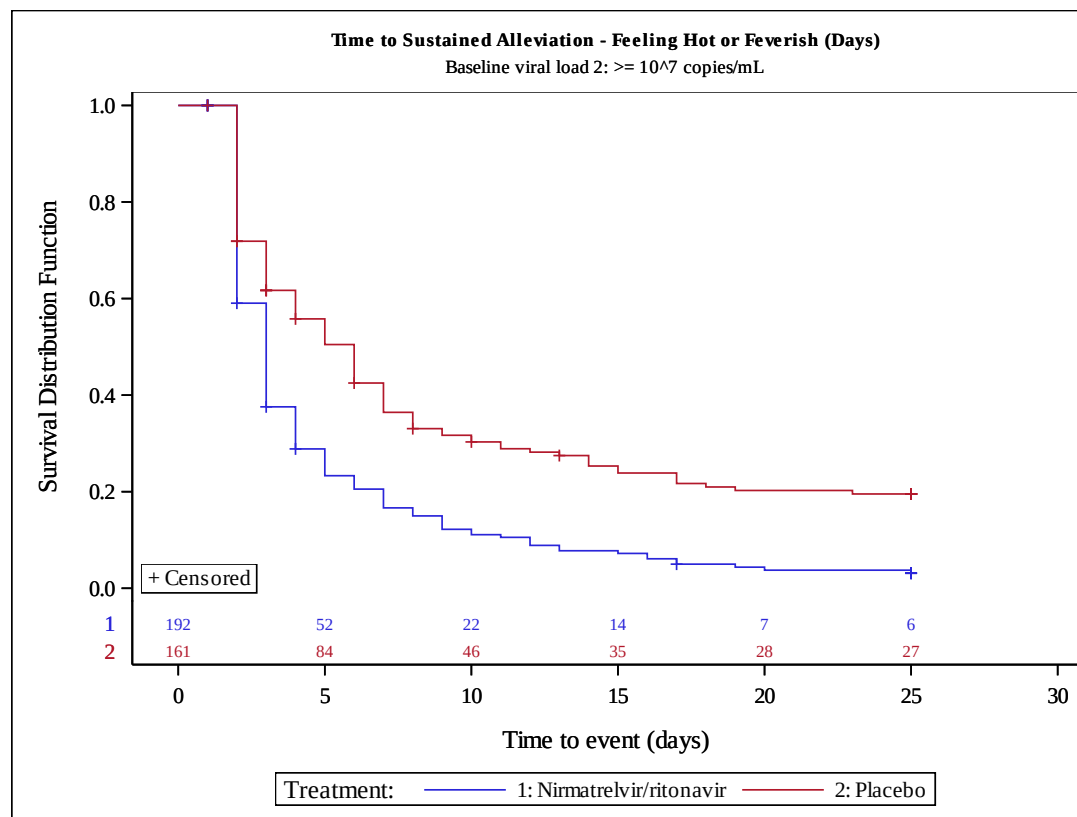


Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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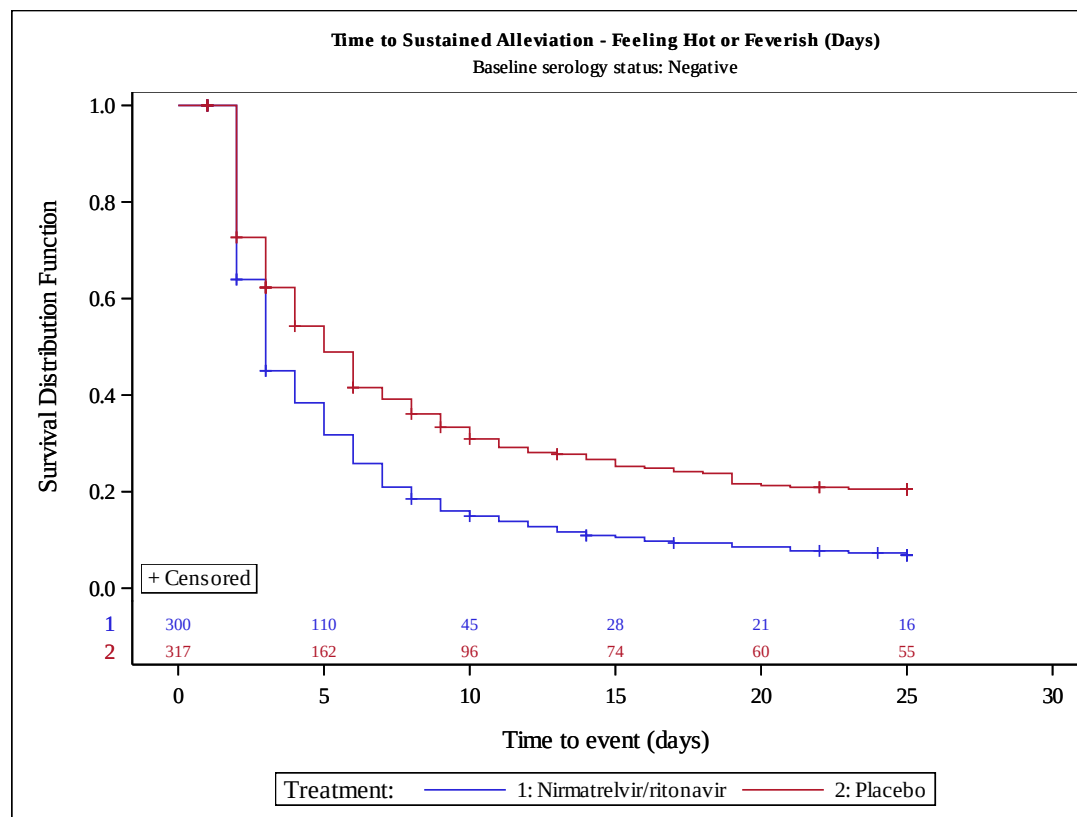


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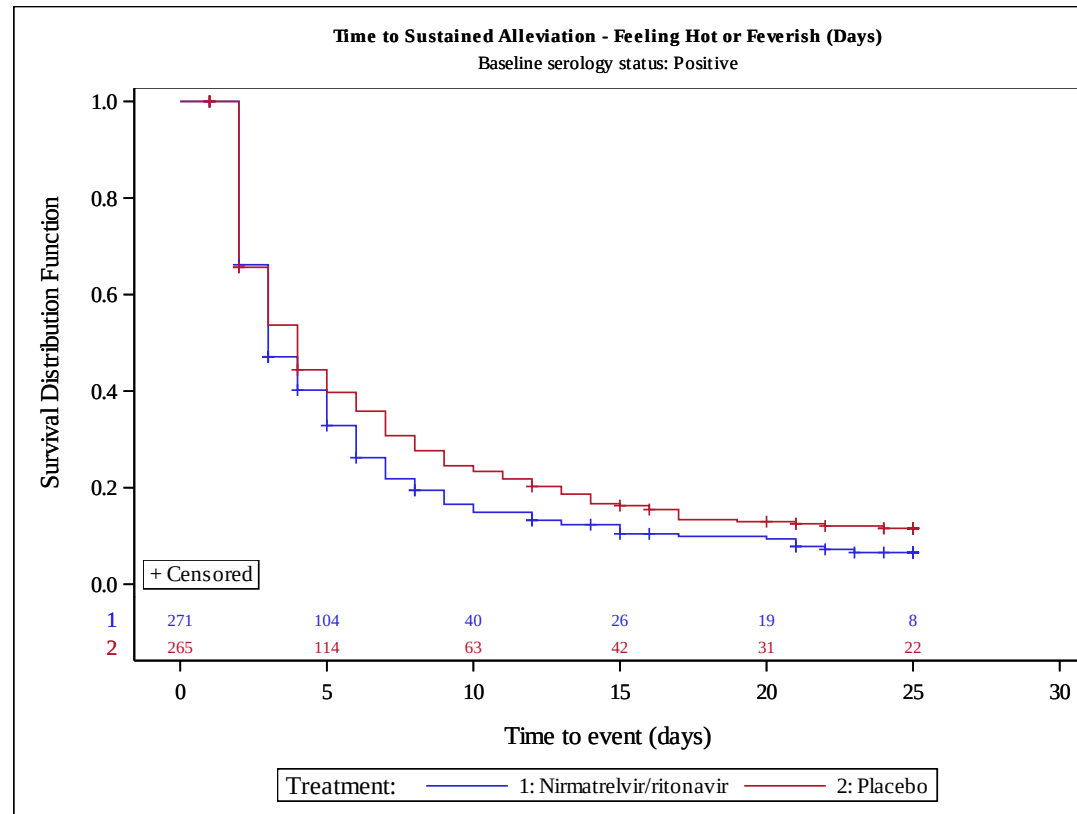


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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=44)			Placebo (N=42)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Age												
< 65	37/	41 (90.2)		29/	39 (74.4)							
>= 65	3/	3 (100.0)		3/	3 (100.0)							
Gender									0.615			0.438
Male	19/	21 (90.5)	3.0 (2.0, 5.0)	11/	13 (84.6)	3.0 (2.0, 7.0)	1.617 (0.707, 3.699)	0.255		1.348 (0.635, 2.863)	0.436	
Female	21/	23 (91.3)	3.0 (2.0, 4.0)	21/	29 (72.4)	6.0 (3.0, 17.0)	2.254 (1.066, 4.767)	0.033		2.275 (1.186, 4.365)	0.013	
Geographic region												
United States	19/	23 (82.6)		17/	20 (85.0)							
Europe	11/	11 (100.0)		7/	10 (70.0)							
India	0			0								
Rest of World	10/	10 (100.0)		8/	12 (66.7)							
COVID-19 therapeutic mAb treatment at randomisation												
Yes	3/	4 (75.0)		4/	5 (80.0)							
No	37/	40 (92.5)		28/	37 (75.7)							
Baseline viral load 1									0.437			0.399
< 10^4 copies/mL	4/	6 (66.7)	4.0 (2.0, NE)	3/	4 (75.0)	3.0 (2.0, NE)	0.724 (0.104, 5.037)	0.745		0.864 (0.190, 3.923)	0.850	
>= 10^4 copies/mL	36/	38 (94.7)	3.0 (2.0, 3.0)	27/	36 (75.0)	6.0 (3.0, 8.0)	1.875 (1.093, 3.215)	0.022		2.032 (1.212, 3.408)	0.007	
Baseline viral load 2									0.385			0.428
< 10^7 copies/mL	17/	21 (81.0)	3.5 (2.0, 5.0)	25/	34 (73.5)	4.0 (3.0, 8.0)	1.086 (0.520, 2.268)	0.826		1.376 (0.740, 2.560)	0.313	
>= 10^7 copies/mL	23/	23 (100.0)	3.0 (2.0, 3.0)	5/	6 (83.3)	6.0 (2.0, 17.0)	3.807 (0.968, 14.972)	0.056		2.971 (0.990, 8.918)	0.052	
Baseline serology status									0.027			0.044
Negative	25/	28 (89.3)	3.0 (2.0, 3.0)	19/	28 (67.9)	6.0 (3.0, 21.0)	2.519 (1.316, 4.823)	0.005		2.330 (1.254, 4.329)	0.007	
Positive	15/	16 (93.8)	3.5 (2.0, 5.0)	12/	13 (92.3)	3.0 (2.0, 7.0)	0.799 (0.344, 1.853)	0.601		0.936 (0.434, 2.017)	0.865	
Symptom onset days to first dose date									0.697			0.838
<= 3	29/	30 (96.7)	3.0 (2.0, 3.0)	23/	28 (82.1)	3.5 (3.0, 7.0)	1.978 (1.073, 3.645)	0.029		1.887 (1.072, 3.322)	0.028	
> 3	11/	14 (78.6)	3.0 (2.0, 6.0)	9/	14 (64.3)	6.0 (2.0, NE)	1.728 (0.536, 5.573)	0.360		1.806 (0.731, 4.460)	0.200	
BMI group									0.398			0.436
< 25	8/	9 (88.9)	3.0 (2.0, 6.0)	5/	6 (83.3)	14.0 (3.0, NE)	13.951 (1.213, 160.41)	0.034		5.953 (1.210, 29.286)	0.028	
25 - < 30	13/	14 (92.9)	3.0 (2.0, 5.0)	9/	10 (90.0)	3.5 (2.0, 5.0)	1.144 (0.410, 3.194)	0.798		1.121 (0.478, 2.630)	0.793	
>= 30	19/	21 (90.5)	3.0 (2.0, 4.0)	18/	26 (69.2)	6.0 (3.0, 19.0)	1.456 (0.704, 3.015)	0.311		1.799 (0.930, 3.483)	0.081	
Ethnicity												
White	29/	33 (87.9)		26/	34 (76.5)							
Black or African American	5/	5 (100.0)		2/	2 (100.0)							
Asian	2/	2 (100.0)		0								
Others	4/	4 (100.0)		4/	6 (66.7)							
Number of baseline comorbidities present												
0-1	35/	39 (89.7)		29/	38 (76.3)							
2-3	5/	5 (100.0)		2/	3 (66.7)							
>= 4	0			1/	1 (100.0)							
Presence of risk factor: Smoking									0.409			0.226
Yes	14/	16 (87.5)	3.0 (2.0, 5.0)	16/	18 (88.9)	3.5 (3.0, 6.0)	1.637 (0.680, 3.940)	0.272		1.257 (0.607, 2.604)	0.538	
No	26/	28 (92.9)	3.0 (2.0, 3.0)	16/	24 (66.7)	6.0 (3.0, 19.0)	2.215 (1.092, 4.490)	0.027		2.317 (1.213, 4.424)	0.011	

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=44)			Placebo (N=42)			Adjusted Analysis [2]			Unadjusted Analysis [3]			
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	
Presence of risk factor: Diabetes mellitus													
Yes	4/	4 (100.0)		2/	3 (66.7)								
No	36/	40 (90.0)		30/	39 (76.9)								
Presence of risk factor: Immunosuppression													
Yes	0			1/	1 (100.0)								
No	40/	44 (90.9)		31/	41 (75.6)								
Presence of risk factor: Chronic lung disease													
Yes	4/	4 (100.0)		1/	1 (100.0)								
No	36/	40 (90.0)		31/	41 (75.6)								
Presence of risk factor: Hypertension													
Yes	13/	14 (92.9)	3.0 (2.0, 3.0)	7/	10 (70.0)	5.0 (2.0, NE)	2.888 (0.992, 8.411)	0.052	0.280	2.534 (0.924, 6.952)	0.071	0.334	
No	27/	30 (90.0)	3.0 (2.0, 5.0)	25/	32 (78.1)	5.0 (3.0, 8.0)	1.521 (0.831, 2.785)	0.174		1.578 (0.908, 2.744)	0.106		
Presence of risk factor: Cardiovascular disorder													
Yes	1/	1 (100.0)		1/	2 (50.0)								
No	39/	43 (90.7)		31/	40 (77.5)								
Presence of risk factor: Chronic kidney disease													
Yes	0			0									
No	40/	44 (90.9)		32/	42 (76.2)								
Presence of risk factor: HIV Infection													
Yes	0			0									
No	40/	44 (90.9)		32/	42 (76.2)								
Presence of risk factor: Sickle Cell Disease													
No	40/	44 (90.9)		32/	42 (76.2)								
Presence of risk factor: Neurodevelopmental Disorder													
Yes	0			0									
No	40/	44 (90.9)		32/	42 (76.2)								
Presence of risk factor: Cancer													
Yes	0			0									
No	40/	44 (90.9)		32/	42 (76.2)								
Presence of risk factor: Device Dependence													
Yes	0			0									
No	40/	44 (90.9)		32/	41 (78.0)								

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum (last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

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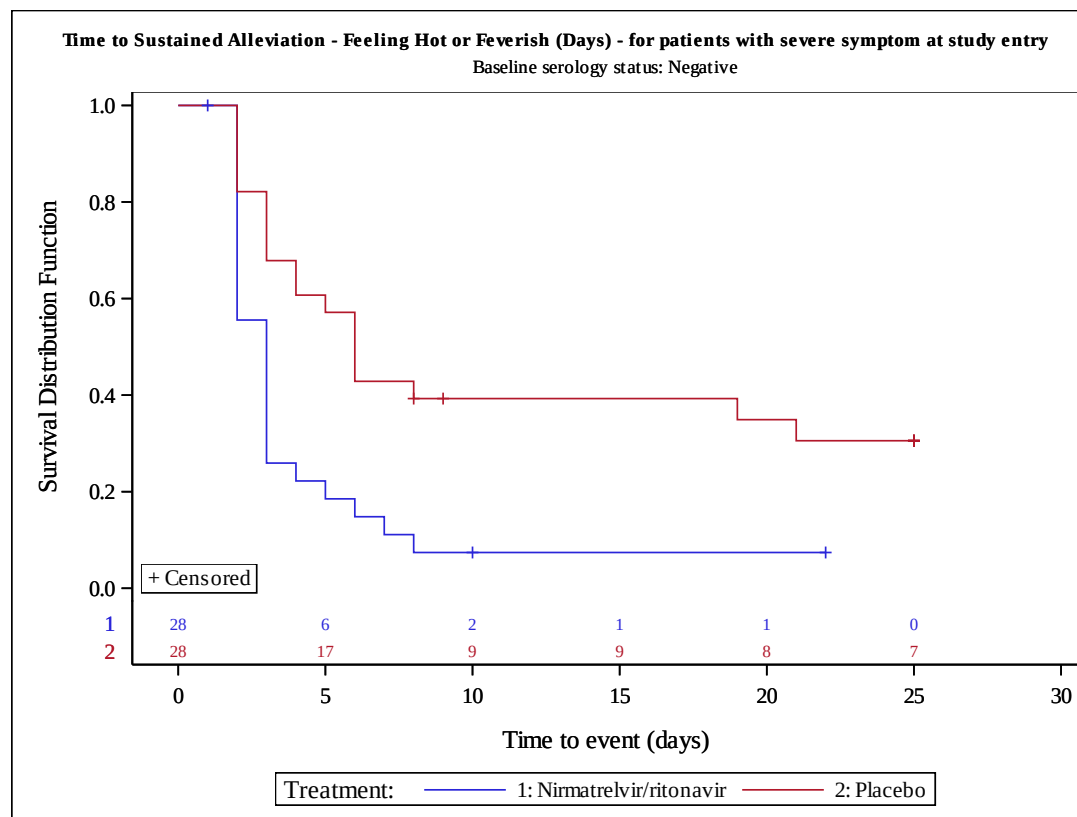
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Final

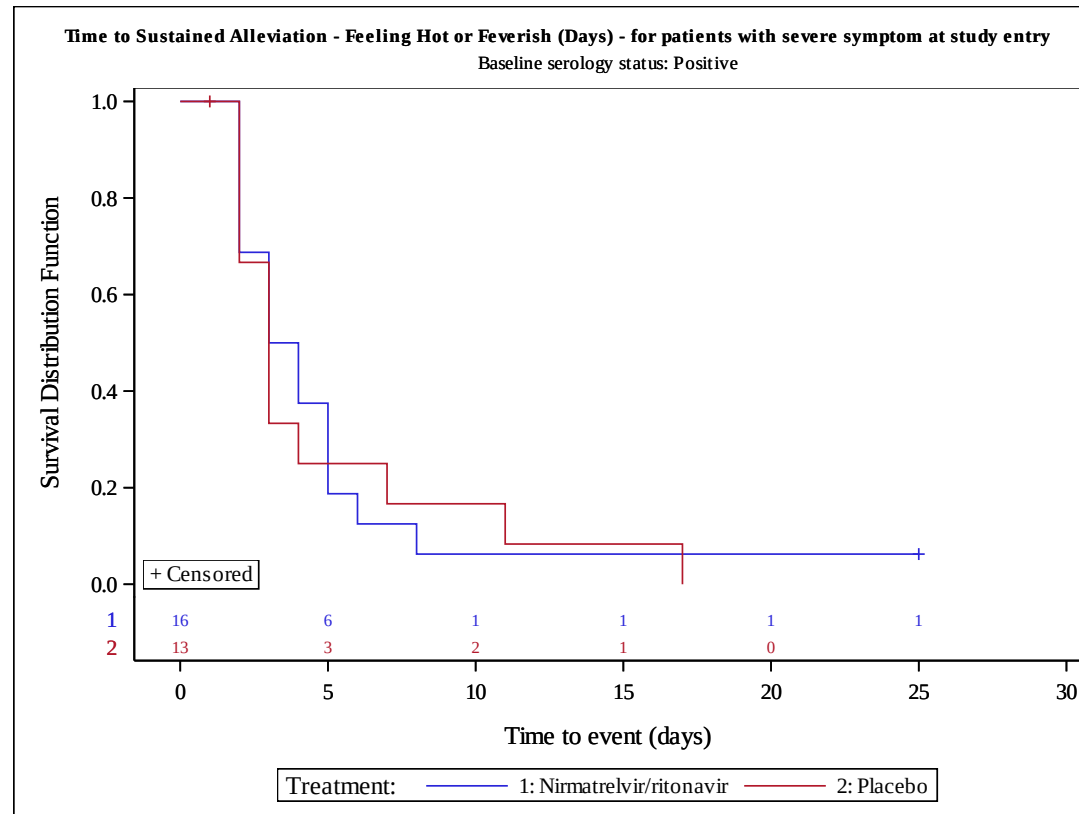


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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=580)			Placebo (N=591)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	432/ 496	(87.1)	5.0 (4.0, 5.0)	378/ 497	(76.1)	7.0 (6.0, 7.0)	1.392 (1.207, 1.604)	<.001		0.344	1.407 (1.224, 1.616)	<.001		0.227
>= 65	73/ 84	(86.9)	5.0 (4.0, 5.0)	67/ 94	(71.3)	7.0 (5.0, 10.0)	1.601 (1.137, 2.256)	0.007			1.734 (1.239, 2.427)	0.001		
Gender														
Male	251/ 284	(88.4)	5.0 (4.0, 5.0)	232/ 314	(73.9)	7.0 (6.0, 8.0)	1.476 (1.227, 1.776)	<.001		0.538	1.529 (1.277, 1.831)	<.001		0.414
Female	254/ 296	(85.8)	5.0 (4.0, 6.0)	213/ 277	(76.9)	7.0 (6.0, 8.0)	1.368 (1.133, 1.651)	0.001			1.382 (1.151, 1.660)	<.001		
Geographic region														
United States	190/ 226	(84.1)	5.0 (4.0, 6.0)	160/ 215	(74.4)	7.0 (6.0, 9.0)	1.308 (1.054, 1.623)	0.015		0.493	1.361 (1.101, 1.682)	0.004		0.470
Europe	192/ 214	(89.7)	5.0 (4.0, 5.0)	169/ 227	(74.4)	7.0 (6.0, 9.0)	1.616 (1.303, 2.004)	<.001			1.636 (1.328, 2.016)	<.001		
India	34/ 36	(94.4)	5.0 (3.0, 5.0)	33/ 35	(94.3)	6.0 (5.0, 7.0)	1.629 (0.961, 2.763)	0.070			1.212 (0.749, 1.961)	0.435		
Rest of World	89/ 104	(85.6)	5.0 (4.0, 6.0)	83/ 114	(72.8)	6.0 (5.0, 9.0)	1.382 (1.018, 1.876)	0.038			1.396 (1.034, 1.885)	0.029		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	38/ 43	(88.4)	5.5 (4.0, 7.0)	30/ 39	(76.9)	6.5 (4.0, 10.0)	1.318 (0.800, 2.170)	0.279		0.777	1.400 (0.865, 2.265)	0.171		0.870
No	467/ 537	(87.0)	5.0 (4.0, 5.0)	415/ 552	(75.2)	7.0 (6.0, 8.0)	1.430 (1.248, 1.639)	<.001			1.457 (1.275, 1.665)	<.001		
Baseline viral load 1														
< 10^4 copies/mL	145/ 170	(85.3)	5.0 (4.0, 7.0)	148/ 181	(81.8)	5.0 (4.0, 7.0)	1.112 (0.881, 1.404)	0.370		0.011	1.114 (0.885, 1.401)	0.359		0.009
>= 10^4 copies/mL	347/ 395	(87.8)	5.0 (4.0, 5.0)	289/ 395	(73.2)	7.0 (6.0, 9.0)	1.593 (1.359, 1.867)	<.001			1.609 (1.374, 1.883)	<.001		
Baseline viral load 2														
< 10^7 copies/mL	316/ 373	(84.7)	5.0 (5.0, 6.0)	319/ 415	(76.9)	6.0 (6.0, 7.0)	1.286 (1.098, 1.507)	0.002		0.038	1.298 (1.110, 1.518)	0.001		0.039
>= 10^7 copies/mL	176/ 192	(91.7)	4.0 (4.0, 5.0)	118/ 161	(73.3)	7.0 (6.0, 9.0)	1.770 (1.389, 2.255)	<.001			1.779 (1.405, 2.253)	<.001		
Baseline serology status														
Negative	265/ 300	(88.3)	5.0 (4.0, 5.0)	225/ 317	(71.0)	7.0 (6.0, 9.0)	1.647 (1.372, 1.977)	<.001		0.048	1.700 (1.421, 2.035)	<.001		0.018
Positive	233/ 271	(86.0)	5.0 (4.0, 6.0)	212/ 265	(80.0)	6.0 (5.0, 7.0)	1.243 (1.028, 1.503)	0.024			1.236 (1.025, 1.490)	0.026		
Symptom onset days to first dose date														
<= 3	359/ 401	(89.5)	5.0 (4.0, 5.0)	296/ 381	(77.7)	6.0 (6.0, 7.0)	1.436 (1.226, 1.682)	<.001		0.846	1.462 (1.252, 1.708)	<.001		0.841
> 3	146/ 179	(81.6)	5.0 (4.0, 7.0)	149/ 210	(71.0)	7.0 (7.0, 9.0)	1.377 (1.087, 1.744)	0.008			1.415 (1.125, 1.779)	0.003		
BMI group														
< 25	109/ 129	(84.5)	4.0 (4.0, 5.0)	105/ 130	(80.8)	6.0 (5.0, 7.0)	1.356 (1.021, 1.802)	0.036		0.123	1.426 (1.089, 1.867)	0.010		0.147
25 - < 30	177/ 201	(88.1)	6.0 (5.0, 7.0)	166/ 211	(78.7)	6.0 (5.0, 7.0)	1.274 (1.024, 1.584)	0.029			1.253 (1.012, 1.550)	0.038		
>= 30	218/ 249	(87.6)	5.0 (4.0, 5.0)	174/ 250	(69.6)	8.0 (7.0, 10.0)	1.691 (1.372, 2.082)	<.001			1.669 (1.365, 2.042)	<.001		
Ethnicity														
White	388/ 446	(87.0)	5.0 (4.0, 5.0)	339/ 456	(74.3)	7.0 (6.0, 8.0)	1.474 (1.268, 1.714)	<.001		0.813	1.511 (1.304, 1.750)	<.001		0.754
Black or African American	17/ 22	(77.3)	7.0 (4.0, 12.0)	16/ 22	(72.7)	8.0 (2.0, 19.0)	1.099 (0.509, 2.374)	0.810			1.284 (0.634, 2.601)	0.488		
Asian	54/ 59	(91.5)	4.0 (4.0, 5.0)	58/ 65	(89.2)	6.0 (5.0, 7.0)	1.485 (1.002, 2.202)	0.049			1.345 (0.927, 1.953)	0.119		
Others	46/ 53	(86.8)	7.0 (4.0, 9.0)	32/ 48	(66.7)	8.0 (4.0, 11.0)	1.354 (0.855, 2.144)	0.196			1.363 (0.867, 2.143)	0.180		
Number of baseline comorbidities present														
0-1	402/ 457	(88.0)		333/ 432	(77.1)									
2-3	101/ 121	(83.5)		109/ 156	(69.9)									
>= 4	2/ 2	(100.0)		3/ 3	(100.0)									
Presence of risk factor: Smoking														
Yes	228/ 263	(86.7)	5.0 (4.0, 6.0)	205/ 268	(76.5)	7.0 (6.0, 8.0)	1.362 (1.121, 1.655)	0.002		0.377	1.388 (1.147, 1.678)	<.001		0.433
No	277/ 316	(87.7)	5.0 (4.0, 5.0)	240/ 323	(74.3)	7.0 (6.0, 8.0)	1.478 (1.236, 1.766)	<.001			1.525 (1.281, 1.815)	<.001		

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=580)			Placebo (N=591)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus										0.983				0.798
Yes	63/ 74	(85.1)	5.0 (4.0, 6.0)	67/ 89	(75.3)	7.0 (6.0, 9.0)	1.477 (1.036, 2.105)	0.031			1.510 (1.068, 2.136)	0.020		
No	442/ 506	(87.4)	5.0 (4.0, 5.0)	378/ 502	(75.3)	7.0 (6.0, 8.0)	1.431 (1.242, 1.649)	<.001			1.443 (1.256, 1.657)	<.001		
Presence of risk factor: Immunosuppression														
Yes	3/ 3	(100.0)		6/ 6	(100.0)									
No	502/ 577	(87.0)		439/ 585	(75.0)									
Presence of risk factor: Chronic lung disease										0.934				0.877
Yes	39/ 42	(92.9)	5.0 (3.0, 7.0)	19/ 24	(79.2)	6.0 (3.0, 10.0)	1.352 (0.766, 2.385)	0.298			1.394 (0.805, 2.416)	0.236		
No	466/ 538	(86.6)	5.0 (4.0, 5.0)	426/ 567	(75.1)	7.0 (6.0, 8.0)	1.418 (1.238, 1.623)	<.001			1.451 (1.271, 1.656)	<.001		
Presence of risk factor: Hypertension										0.404				0.467
Yes	169/ 203	(83.3)	5.0 (4.0, 6.0)	172/ 242	(71.1)	7.0 (6.0, 10.0)	1.444 (1.160, 1.798)	0.001			1.490 (1.203, 1.845)	<.001		
No	336/ 377	(89.1)	5.0 (4.0, 5.0)	273/ 349	(78.2)	6.0 (6.0, 7.0)	1.376 (1.166, 1.623)	<.001			1.406 (1.197, 1.652)	<.001		
Presence of risk factor: Cardiovascular disorder										0.173				0.191
Yes	23/ 25	(92.0)	3.0 (2.0, 6.0)	23/ 31	(74.2)	7.0 (4.0, 13.0)	2.363 (1.234, 4.526)	0.010			2.129 (1.180, 3.842)	0.012		
No	482/ 555	(86.8)	5.0 (4.0, 5.0)	422/ 560	(75.4)	7.0 (6.0, 8.0)	1.396 (1.221, 1.597)	<.001			1.427 (1.251, 1.628)	<.001		
Presence of risk factor: Chronic kidney disease														
Yes	3/ 3	(100.0)		5/ 6	(83.3)									
No	502/ 577	(87.0)		440/ 585	(75.2)									
Presence of risk factor: HIV Infection														
Yes	0			0										
No	505/ 580	(87.1)		444/ 590	(75.3)									
Presence of risk factor: Sickle Cell Disease														
No	505/ 580	(87.1)		445/ 591	(75.3)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	1/ 1	(100.0)		1/ 1	(100.0)									
No	504/ 579	(87.0)		444/ 590	(75.3)									
Presence of risk factor: Cancer														
Yes	0/ 1	(0.0)		6/ 6	(100.0)									
No	505/ 579	(87.2)		439/ 585	(75.0)									
Presence of risk factor: Device Dependence														
Yes	2/ 2	(100.0)		1/ 2	(50.0)									
No	497/ 569	(87.3)		441/ 582	(75.8)									

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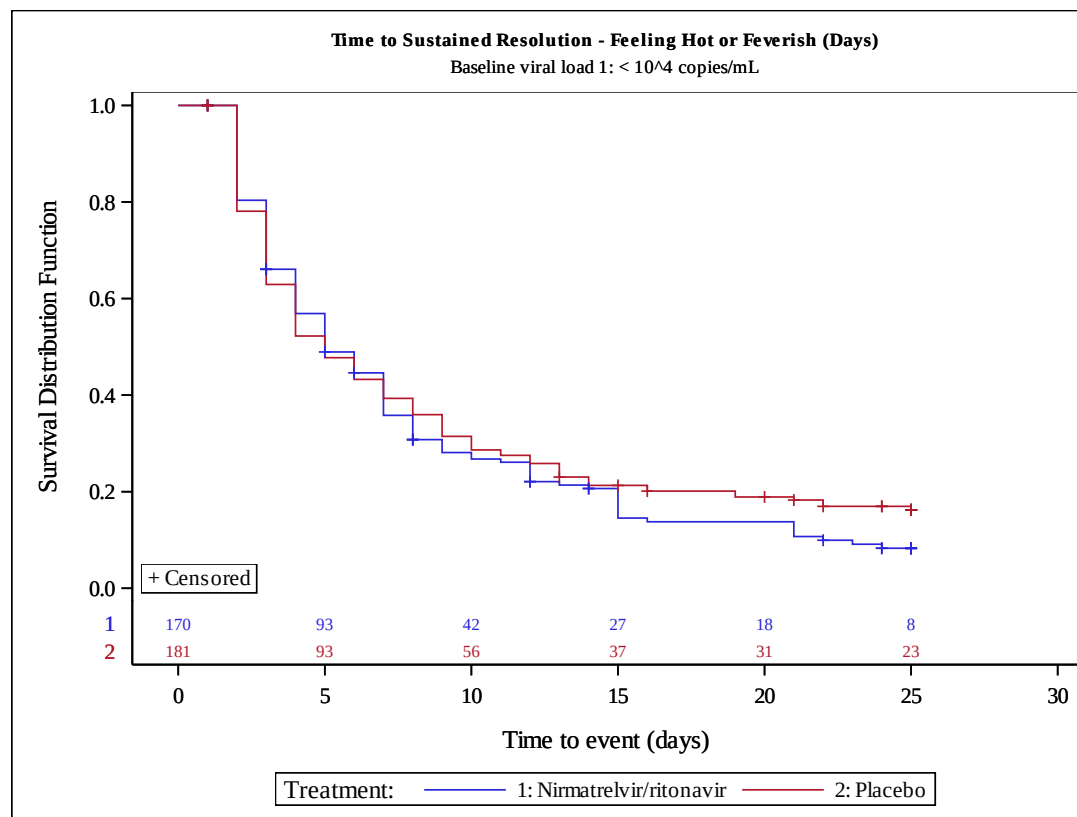
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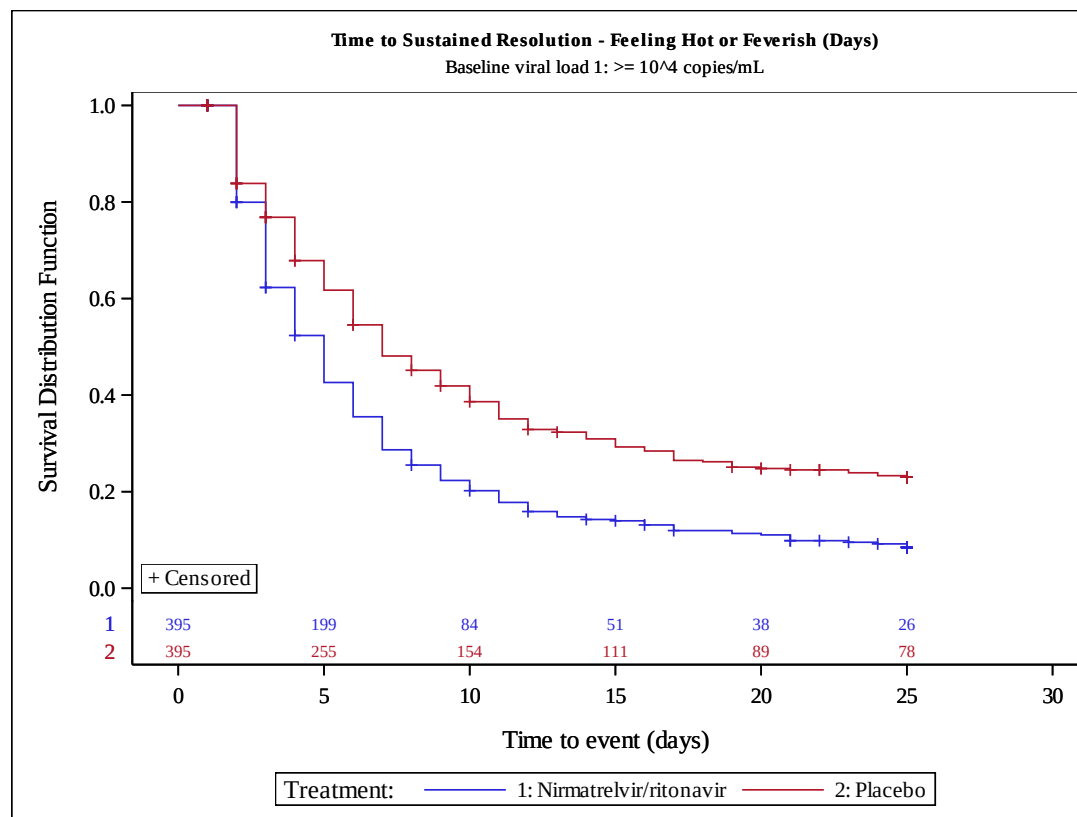


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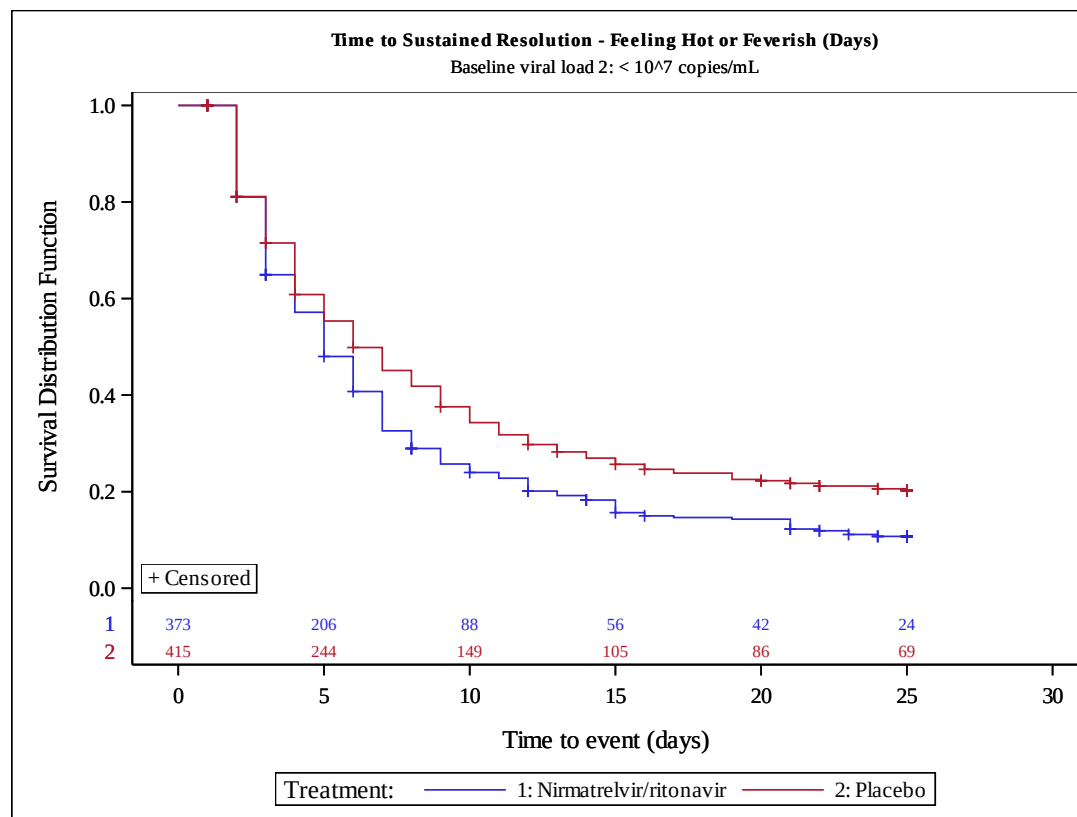


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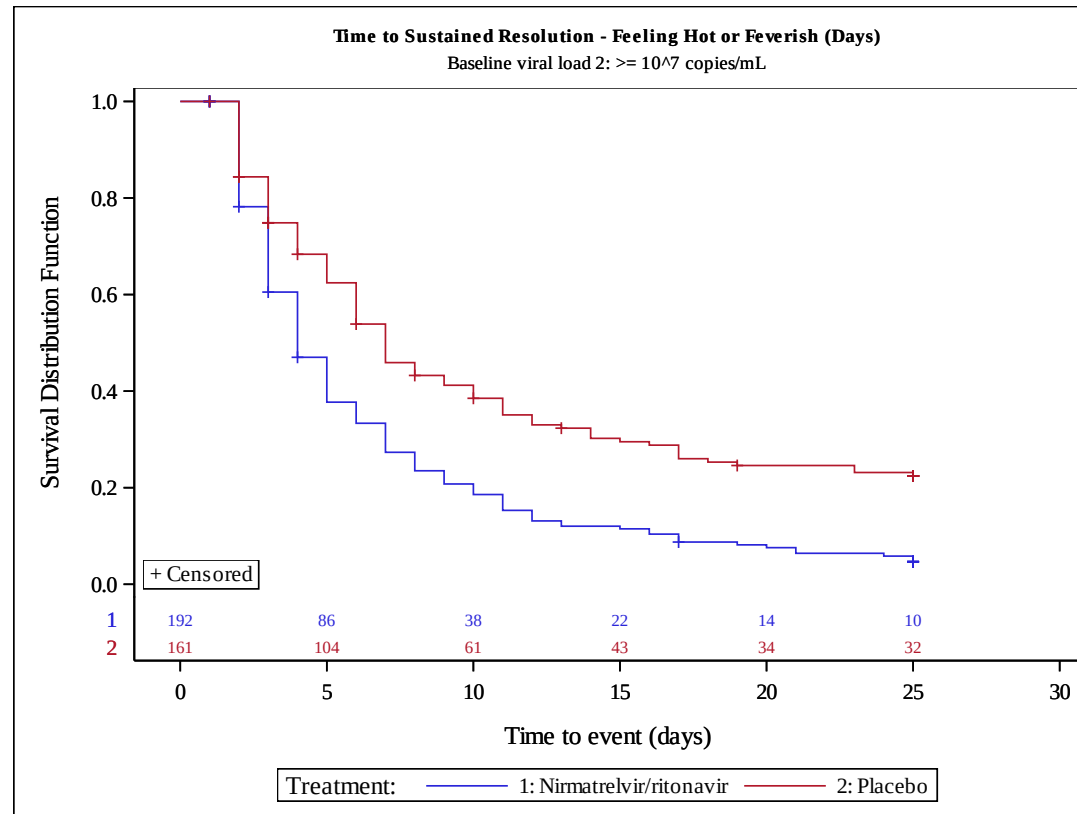


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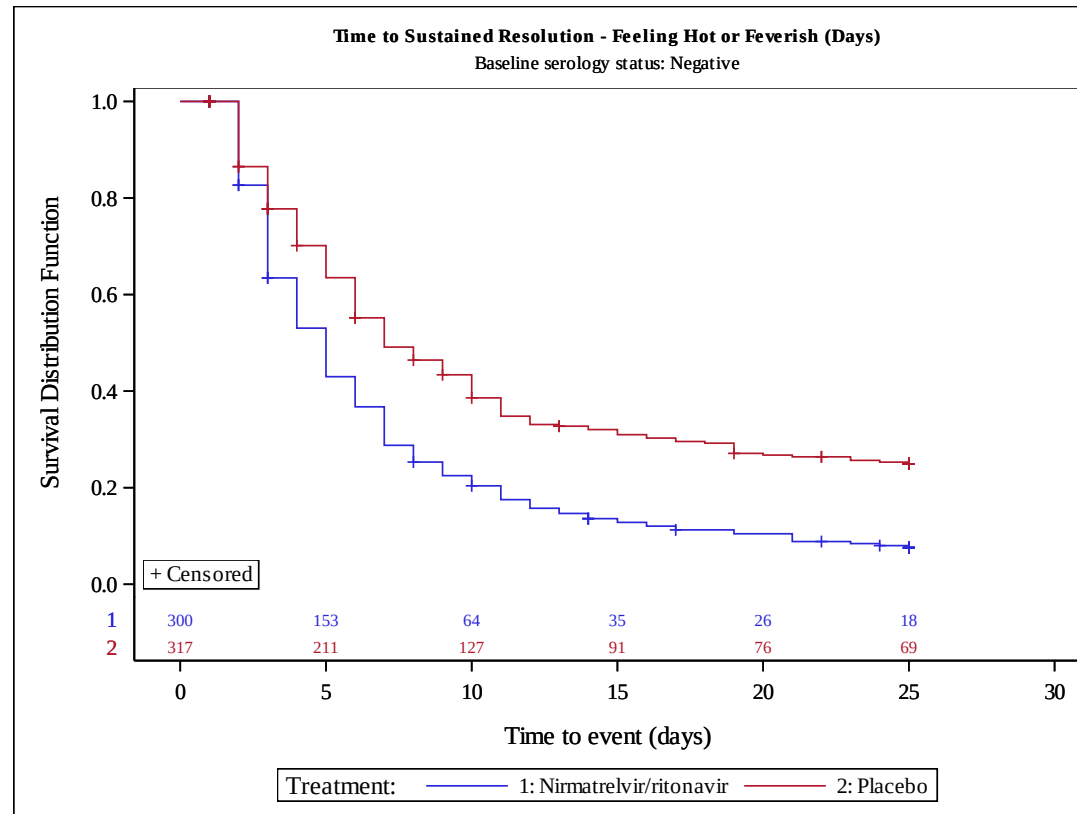


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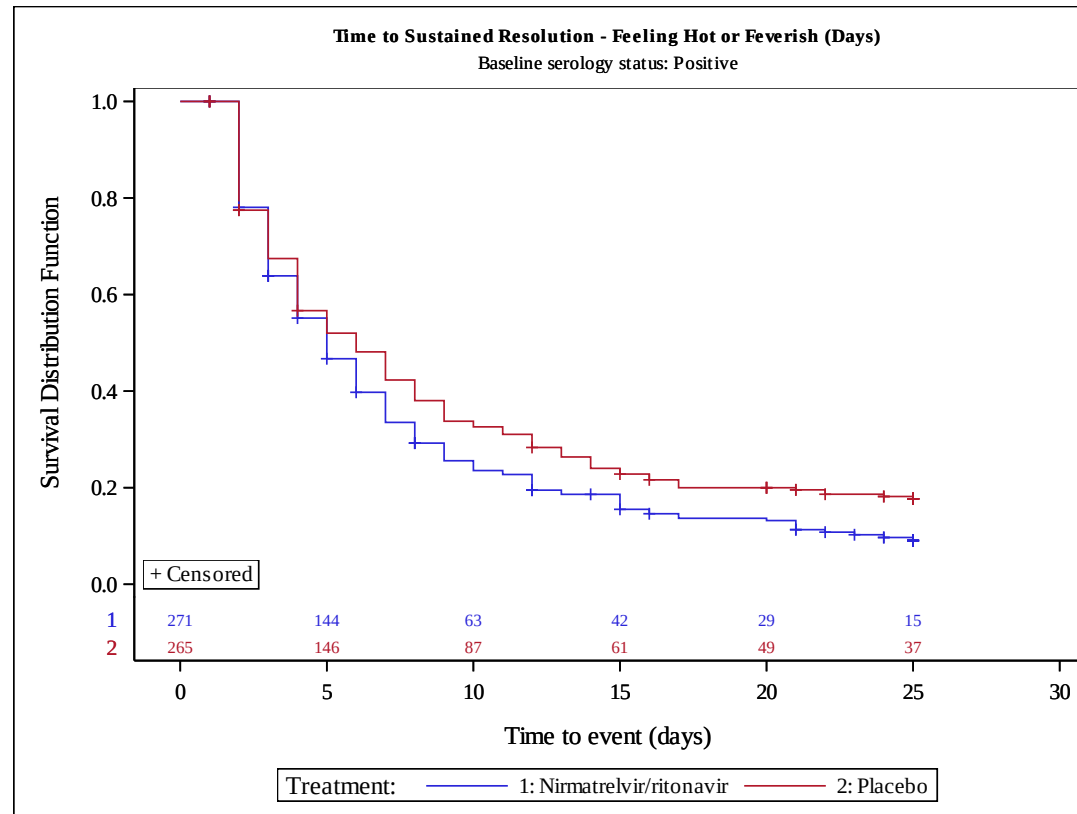
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Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=44)			Placebo (N=42)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Age												
< 65	37/	41 (90.2)		28/	39 (71.8)							
>= 65	3/	3 (100.0)		1/	3 (33.3)							
Gender									0.278			0.326
Male	19/	21 (90.5)	4.0 (3.0, 6.0)	11/	13 (84.6)	9.0 (4.0, 15.0)	1.786 (0.781, 4.083)	0.169		1.588 (0.748, 3.373)	0.229	
Female	21/	23 (91.3)	4.0 (3.0, 8.0)	18/	29 (62.1)	11.0 (7.0, NE)	3.249 (1.438, 7.338)	0.005		2.921 (1.463, 5.830)	0.002	
Geographic region												
United States	19/	23 (82.6)		14/	20 (70.0)							
Europe	11/	11 (100.0)		7/	10 (70.0)							
India	0			0								
Rest of World	10/	10 (100.0)		8/	12 (66.7)							
COVID-19 therapeutic mAb treatment at randomisation												
Yes	3/	4 (75.0)		2/	5 (40.0)							
No	37/	40 (92.5)		27/	37 (73.0)							
Baseline viral load 1									0.373			0.285
< 10^4 copies/mL	4/	6 (66.7)	5.0 (4.0, NE)	3/	4 (75.0)	14.0 (2.0, NE)	1.012 (0.075, 13.617)	0.993		0.974 (0.208, 4.569)	0.973	
>= 10^4 copies/mL	36/	38 (94.7)	4.0 (3.0, 7.0)	24/	36 (66.7)	10.0 (7.0, 17.0)	2.523 (1.448, 4.397)	0.001		2.669 (1.549, 4.601)	<.001	
Baseline viral load 2									0.605			0.503
< 10^7 copies/mL	17/	21 (81.0)	5.0 (3.0, 11.0)	23/	34 (67.6)	10.0 (7.0, 24.0)	1.823 (0.873, 3.803)	0.110		1.798 (0.952, 3.396)	0.071	
>= 10^7 copies/mL	23/	23 (100.0)	4.0 (3.0, 6.0)	4/	6 (66.7)	12.0 (2.0, NE)	3.993 (0.892, 17.870)	0.070		3.169 (0.929, 10.811)	0.065	
Baseline serology status									0.157			0.129
Negative	25/	28 (89.3)	4.0 (3.0, 7.0)	17/	28 (60.7)	9.0 (7.0, NE)	2.894 (1.458, 5.744)	0.002		2.605 (1.385, 4.901)	0.003	
Positive	15/	16 (93.8)	4.5 (3.0, 9.0)	11/	13 (84.6)	10.0 (2.0, 17.0)	1.696 (0.631, 4.555)	0.295		1.251 (0.568, 2.758)	0.578	
Symptom onset days to first dose date									0.901			0.839
<= 3	29/	30 (96.7)	4.0 (3.0, 7.0)	22/	28 (78.6)	9.0 (7.0, 17.0)	2.511 (1.348, 4.678)	0.004		2.398 (1.329, 4.328)	0.004	
> 3	11/	14 (78.6)	5.0 (3.0, 8.0)	7/	14 (50.0)	11.0 (5.0, NE)	1.738 (0.496, 6.086)	0.387		2.223 (0.852, 5.799)	0.102	
BMI group									0.063			0.063
< 25	8/	9 (88.9)	5.5 (3.0, 11.0)	5/	6 (83.3)	16.0 (7.0, NE)	68.333 (2.122, 2200.2)	0.017		5.932 (1.228, 28.664)	0.027	
25 - < 30	13/	14 (92.9)	6.5 (3.0, 12.0)	9/	10 (90.0)	6.0 (2.0, 11.0)	0.995 (0.357, 2.771)	0.992		0.923 (0.393, 2.166)	0.854	
>= 30	19/	21 (90.5)	4.0 (3.0, 5.0)	15/	26 (57.7)	10.0 (7.0, NE)	2.656 (1.219, 5.786)	0.014		2.961 (1.452, 6.039)	0.003	
Ethnicity												
White	29/	33 (87.9)		23/	34 (67.6)							
Black or African American	5/	5 (100.0)		2/	2 (100.0)							
Asian	2/	2 (100.0)		0								
Others	4/	4 (100.0)		4/	6 (66.7)							
Number of baseline comorbidities present												
0-1	35/	39 (89.7)		26/	38 (68.4)							
2-3	5/	5 (100.0)		2/	3 (66.7)							
>= 4	0			1/	1 (100.0)							
Presence of risk factor: Smoking									0.086			0.041
Yes	14/	16 (87.5)	5.5 (4.0, 11.0)	16/	18 (88.9)	8.5 (4.0, 15.0)	1.916 (0.837, 4.384)	0.124		1.380 (0.668, 2.848)	0.384	
No	26/	28 (92.9)	4.0 (3.0, 7.0)	13/	24 (54.2)	11.0 (7.0, NE)	2.780 (1.309, 5.907)	0.008		3.076 (1.544, 6.125)	0.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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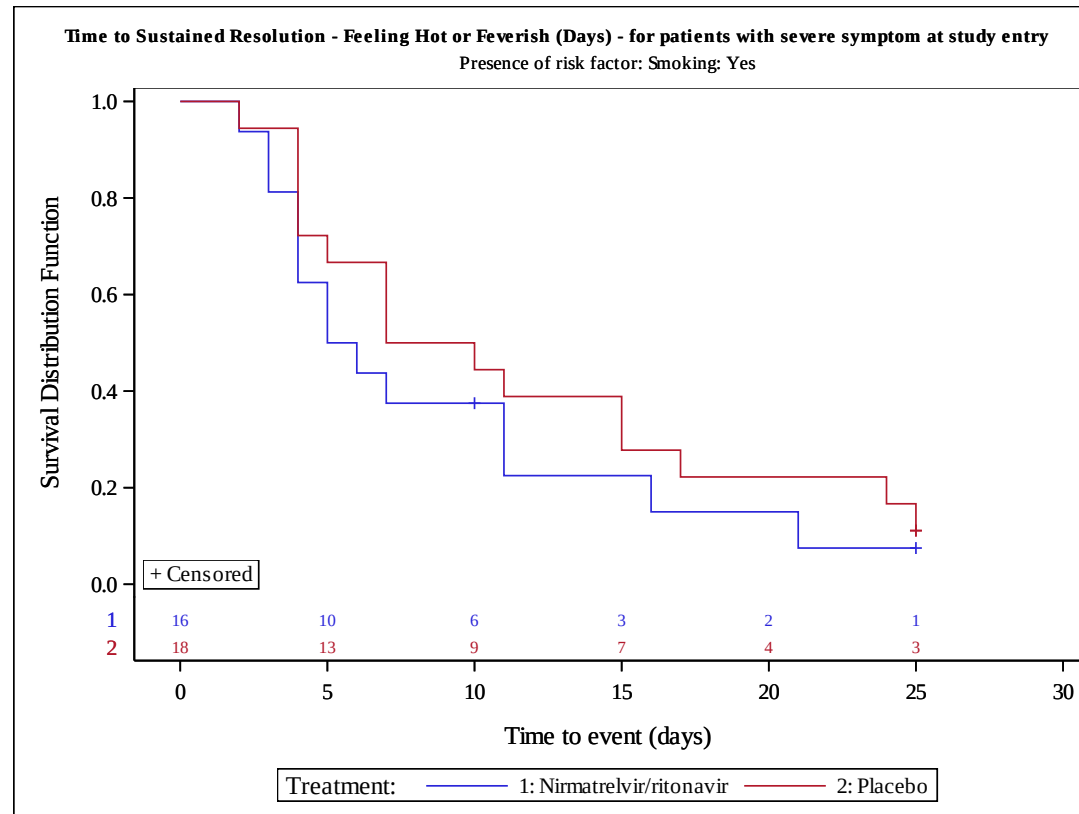
Final

Subgroup Level	Nirmatrelvir/ritonavir (N=44)			Placebo (N=42)			Adjusted Analysis [2]			Unadjusted Analysis [3]		
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus												
Yes	4/	4 (100.0)		2/	3 (66.7)							
No	36/	40 (90.0)		27/	39 (69.2)							
Presence of risk factor: Immunosuppression												
Yes	0			1/	1 (100.0)							
No	40/	44 (90.9)		28/	41 (68.3)							
Presence of risk factor: Chronic lung disease												
Yes	4/	4 (100.0)		1/	1 (100.0)							
No	36/	40 (90.0)		28/	41 (68.3)							
Presence of risk factor: Hypertension									0.327			0.370
Yes	13/	14 (92.9)	4.0 (3.0, 7.0)	7/	10 (70.0)	11.0 (2.0, NE)	4.913 (1.456, 16.576)	0.010		3.700 (1.262, 10.847)	0.017	
No	27/	30 (90.0)	4.5 (4.0, 8.0)	22/	32 (68.8)	8.0 (5.0, 17.0)	2.312 (1.230, 4.346)	0.009		1.960 (1.105, 3.475)	0.021	
Presence of risk factor: Cardiovascular disorder												
Yes	1/	1 (100.0)		1/	2 (50.0)							
No	39/	43 (90.7)		28/	40 (70.0)							
Presence of risk factor: Chronic kidney disease												
Yes	0			0								
No	40/	44 (90.9)		29/	42 (69.0)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	40/	44 (90.9)		29/	42 (69.0)							
Presence of risk factor: Sickle Cell Disease												
No	40/	44 (90.9)		29/	42 (69.0)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0			0								
No	40/	44 (90.9)		29/	42 (69.0)							
Presence of risk factor: Cancer												
Yes	0			0								
No	40/	44 (90.9)		29/	42 (69.0)							
Presence of risk factor: Device Dependence												
Yes	0			0								
No	40/	44 (90.9)		29/	41 (70.7)							

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish

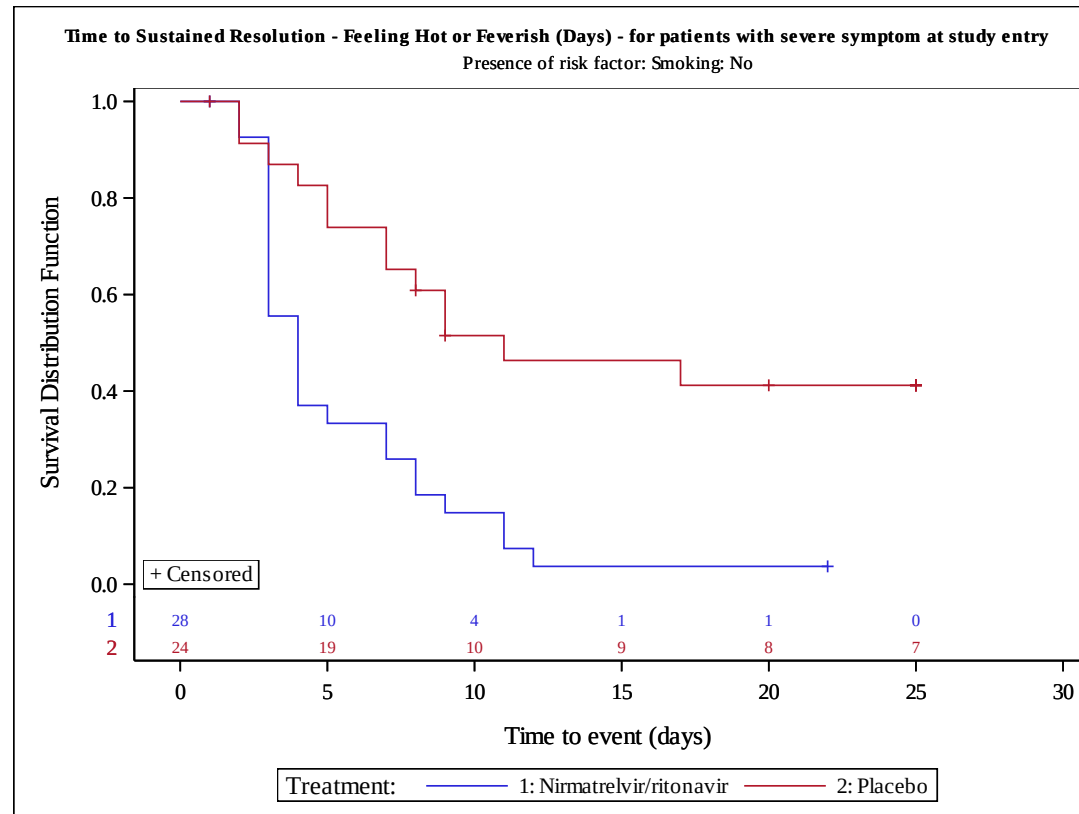
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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Nausea - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]		Interaction p-Value	Unadjusted analysis [2]		Interaction p-Value
			Relative Risk (95% CI)	p-Value		Relative Risk (95% CI)	p-Value	
Age								
< 65	169/ 790 (21.4)	183/ 810 (22.6)	0.948 (0.786, 1.143)	0.574	0.803	0.947 (0.787, 1.139)	0.562	0.829
>= 65	35/ 138 (25.4)	37/ 145 (25.5)	0.948 (0.640, 1.406)	0.791		0.994 (0.667, 1.481)	0.976	
Gender								
Male	73/ 463 (15.8)	97/ 507 (19.1)	0.800 (0.604, 1.059)	0.119	0.113	0.824 (0.625, 1.086)	0.170	0.215
Female	131/ 465 (28.2)	123/ 448 (27.5)	1.060 (0.858, 1.309)	0.588		1.026 (0.832, 1.265)	0.809	
Geographic region								
United States	100/ 375 (26.7)	81/ 387 (20.9)	1.282 (0.987, 1.666)	0.063	0.020	1.274 (0.986, 1.646)	0.064	0.028
Europe	68/ 322 (21.1)	85/ 321 (26.5)	0.811 (0.614, 1.072)	0.142		0.798 (0.603, 1.054)	0.112	
India	7/ 74 (9.5)	8/ 78 (10.3)	NE (NE, NE)	NE		0.922 (0.352, 2.417)	0.869	
Rest of World	29/ 157 (18.5)	46/ 169 (27.2)	0.652 (0.430, 0.990)	0.045		0.679 (0.450, 1.023)	0.064	
COVID-19 therapeutic mAb treatment at randomisation								
Yes	19/ 57 (33.3)	12/ 60 (20.0)	1.402 (0.759, 2.590)	0.281	0.112	1.667 (0.892, 3.114)	0.109	0.070
No	185/ 871 (21.2)	208/ 895 (23.2)	0.917 (0.768, 1.095)	0.338		0.914 (0.767, 1.088)	0.313	
Baseline viral load 1								
< 10 ⁴ copies/mL	68/ 335 (20.3)	60/ 354 (16.9)	1.230 (0.899, 1.683)	0.197	0.055	1.198 (0.875, 1.638)	0.259	0.088
>= 10 ⁴ copies/mL	131/ 569 (23.0)	153/ 575 (26.6)	0.863 (0.706, 1.056)	0.152		0.865 (0.707, 1.059)	0.161	
Baseline viral load 2								
< 10 ⁷ copies/mL	134/ 652 (20.6)	138/ 699 (19.7)	1.052 (0.850, 1.302)	0.640	0.111	1.041 (0.842, 1.287)	0.711	0.126
>= 10 ⁷ copies/mL	65/ 252 (25.8)	75/ 230 (32.6)	0.787 (0.596, 1.039)	0.091		0.791 (0.598, 1.047)	0.101	
Baseline serology status								
Negative	108/ 435 (24.8)	130/ 456 (28.5)	0.873 (0.702, 1.086)	0.223	0.209	0.871 (0.700, 1.084)	0.215	0.243
Positive	93/ 482 (19.3)	88/ 487 (18.1)	1.076 (0.826, 1.402)	0.586		1.068 (0.821, 1.389)	0.625	
Symptom onset days to first dose date								
<= 3	147/ 624 (23.6)	145/ 624 (23.2)	1.022 (0.835, 1.251)	0.833	0.214	1.014 (0.829, 1.239)	0.894	0.278
> 3	57/ 304 (18.8)	75/ 331 (22.7)	0.804 (0.588, 1.100)	0.173		0.828 (0.609, 1.125)	0.227	
BMI group								
< 25	35/ 215 (16.3)	50/ 213 (23.5)	0.725 (0.492, 1.068)	0.103	0.281	0.693 (0.470, 1.022)	0.065	0.183
25 - < 30	69/ 319 (21.6)	71/ 332 (21.4)	1.001 (0.745, 1.346)	0.992		1.011 (0.754, 1.357)	0.939	
>= 30	100/ 393 (25.4)	99/ 410 (24.1)	0.993 (0.777, 1.269)	0.954		1.054 (0.828, 1.341)	0.670	
Ethnicity								
White	165/ 699 (23.6)	176/ 718 (24.5)	0.961 (0.797, 1.159)	0.677	0.052	0.963 (0.800, 1.159)	0.690	0.123
Black or African American	14/ 43 (32.6)	8/ 40 (20.0)	2.496 (1.008, 6.179)	0.048		1.628 (0.766, 3.462)	0.206	
Asian	14/ 117 (12.0)	14/ 127 (11.0)	NE (NE, NE)	NE		1.085 (0.541, 2.179)	0.818	
Others	11/ 69 (15.9)	22/ 70 (31.4)	NE (NE, NE)	NE		0.507 (0.267, 0.965)	0.039	
Number of baseline comorbidities present								
0-1	153/ 710 (21.5)	168/ 728 (23.1)	0.910 (0.749, 1.106)	0.343	NE	0.934 (0.770, 1.133)	0.487	0.682
2-3	51/ 214 (23.8)	52/ 221 (23.5)	1.097 (0.776, 1.550)	0.600		1.013 (0.723, 1.419)	0.941	
>= 4	0/ 4 (0.0)	0/ 6 (0.0)	NE (NE, NE)	NE		NE (NE, NE)	NE	
Presence of risk factor: Smoking								
Yes	71/ 417 (17.0)	91/ 438 (20.8)	0.815 (0.614, 1.083)	0.159	0.155	0.820 (0.619, 1.084)	0.163	0.169
No	133/ 509 (26.1)	129/ 517 (25.0)	1.046 (0.849, 1.290)	0.672		1.047 (0.850, 1.291)	0.665	
Presence of risk factor: Diabetes mellitus					0.633			0.929

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value	
Yes	27/ 130 (20.8)	29/ 136 (21.3)	0.956 (0.600, 1.526)			0.852		0.974 (0.611, 1.552)			0.912	
No	177/ 797 (22.2)	191/ 819 (23.3)	0.941 (0.785, 1.128)			0.511		0.952 (0.796, 1.140)			0.594	
Presence of risk factor: Immunosuppression							0.721					0.738
Yes	3/ 6 (50.0)	3/ 7 (42.9)	NE (NE, NE)			NE		1.167 (0.362, 3.764)			0.796	
No	201/ 921 (21.8)	217/ 948 (22.9)	0.954 (0.804, 1.131)			0.585		0.953 (0.805, 1.129)			0.580	
Presence of risk factor: Chronic lung disease							0.818					0.891
Yes	13/ 62 (21.0)	9/ 39 (23.1)	0.968 (0.445, 2.106)			0.934		0.909 (0.429, 1.923)			0.802	
No	191/ 865 (22.1)	211/ 916 (23.0)	0.963 (0.809, 1.146)			0.671		0.959 (0.807, 1.139)			0.630	
Presence of risk factor: Hypertension							0.412					0.708
Yes	83/ 348 (23.9)	89/ 371 (24.0)	1.044 (0.801, 1.361)			0.748		0.994 (0.766, 1.291)			0.965	
No	121/ 579 (20.9)	131/ 584 (22.4)	0.916 (0.735, 1.142)			0.435		0.932 (0.749, 1.159)			0.526	
Presence of risk factor: Cardiovascular disorder							0.866					0.780
Yes	10/ 42 (23.8)	11/ 49 (22.4)	NE (NE, NE)			NE		1.061 (0.501, 2.247)			0.878	
No	194/ 885 (21.9)	209/ 906 (23.1)	0.952 (0.801, 1.133)			0.580		0.950 (0.800, 1.129)			0.561	
Presence of risk factor: Chronic kidney disease							0.086					0.348
Yes	2/ 6 (33.3)	1/ 8 (12.5)	NE (NE, NE)			NE		2.667 (0.309, 22.996)			0.372	
No	202/ 921 (21.9)	219/ 947 (23.1)	0.948 (0.800, 1.123)			0.534		0.948 (0.801, 1.122)			0.537	
Presence of risk factor: HIV Infection												
Yes	0	0/ 1 (0.0)										
No	204/ 927 (22.0)	220/ 953 (23.1)										
Presence of risk factor: Sickie Cell Disease												
No	204/ 927 (22.0)	220/ 955 (23.0)										
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0/ 2 (0.0)	0/ 1 (0.0)										
No	204/ 925 (22.1)	220/ 954 (23.1)										
Presence of risk factor: Cancer							0.134					0.328
Yes	0/ 5 (0.0)	2/ 6 (33.3)	NE (NE, NE)			NE		0.233 (0.014, 3.969)			0.314	
No	204/ 922 (22.1)	218/ 949 (23.0)	0.962 (0.812, 1.141)			0.659		0.963 (0.814, 1.139)			0.662	
Presence of risk factor: Device Dependence												
Yes	2/ 4 (50.0)	3/ 3 (100.0)										
No	202/ 914 (22.1)	216/ 944 (22.9)										

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

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[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=339)			Placebo (N=344)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	238/ 292	(81.5)	5.0 (4.0, 6.0)	224/ 287	(78.0)	5.0 (4.0, 7.0)	1.114 (0.924, 1.344)	0.258		0.523	1.115 (0.929, 1.338)	0.244		0.435
>= 65	43/ 47	(91.5)	4.0 (3.0, 7.0)	47/ 57	(82.5)	6.0 (4.0, 9.0)	1.406 (0.907, 2.180)	0.127			1.379 (0.909, 2.094)	0.131		
Gender														
Male	109/ 136	(80.1)	3.0 (3.0, 5.0)	120/ 153	(78.4)	5.0 (3.0, 6.0)	1.114 (0.851, 1.460)	0.432		0.936	1.121 (0.864, 1.454)	0.390		0.868
Female	172/ 203	(84.7)	6.0 (4.0, 7.0)	151/ 191	(79.1)	6.0 (5.0, 8.0)	1.177 (0.940, 1.473)	0.155			1.181 (0.949, 1.470)	0.137		
Geographic region														
United States	128/ 159	(80.5)	5.0 (4.0, 7.0)	127/ 166	(76.5)	5.0 (4.0, 7.0)	1.067 (0.830, 1.372)	0.614		0.691	1.117 (0.873, 1.428)	0.378		0.788
Europe	94/ 105	(89.5)	4.0 (3.0, 6.0)	88/ 109	(80.7)	5.0 (3.0, 7.0)	1.314 (0.967, 1.785)	0.081			1.294 (0.965, 1.734)	0.085		
India	17/ 20	(85.0)	4.0 (3.0, 9.0)	18/ 19	(94.7)	7.0 (4.0, 10.0)	1.663 (0.750, 3.688)	0.211			1.135 (0.577, 2.230)	0.714		
Rest of World	42/ 55	(76.4)	6.0 (2.0, 9.0)	38/ 50	(76.0)	7.0 (3.0, 9.0)	1.017 (0.651, 1.587)	0.942			1.053 (0.678, 1.634)	0.819		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	15/ 22	(68.2)	6.0 (3.0, 14.0)	21/ 25	(84.0)	6.0 (4.0, 10.0)	0.684 (0.339, 1.381)	0.290		0.237	0.799 (0.411, 1.554)	0.508		0.211
No	266/ 317	(83.9)	5.0 (4.0, 6.0)	250/ 319	(78.4)	6.0 (4.0, 7.0)	1.186 (0.993, 1.416)	0.060			1.187 (0.998, 1.412)	0.052		
Baseline viral load 1														
< 10^4 copies/mL	96/ 115	(83.5)	6.0 (4.0, 7.0)	90/ 112	(80.4)	4.5 (3.0, 6.0)	1.000 (0.746, 1.340)	1.000		0.225	1.018 (0.763, 1.358)	0.905		0.311
>= 10^4 copies/mL	177/ 216	(81.9)	4.0 (3.0, 6.0)	171/ 219	(78.1)	6.0 (5.0, 7.0)	1.230 (0.995, 1.521)	0.055			1.213 (0.983, 1.498)	0.072		
Baseline viral load 2														
< 10^7 copies/mL	190/ 236	(80.5)	6.0 (4.0, 7.0)	203/ 259	(78.4)	6.0 (4.0, 7.0)	1.085 (0.888, 1.326)	0.425		0.328	1.076 (0.882, 1.311)	0.471		0.324
>= 10^7 copies/mL	83/ 95	(87.4)	3.0 (3.0, 5.0)	58/ 72	(80.6)	6.0 (4.0, 8.0)	1.353 (0.955, 1.917)	0.089			1.329 (0.949, 1.861)	0.097		
Baseline serology status														
Negative	141/ 167	(84.4)	5.0 (3.0, 7.0)	134/ 180	(74.4)	6.0 (5.0, 9.0)	1.335 (1.045, 1.705)	0.021		0.110	1.330 (1.049, 1.687)	0.019		0.089
Positive	137/ 168	(81.5)	5.0 (4.0, 6.0)	135/ 161	(83.9)	4.0 (4.0, 6.0)	1.008 (0.790, 1.285)	0.951			0.995 (0.785, 1.263)	0.970		
Symptom onset days to first dose date														
<= 3	183/ 210	(87.1)	4.0 (3.0, 5.0)	167/ 206	(81.1)	5.0 (3.0, 6.0)	1.235 (0.995, 1.534)	0.055		0.278	1.232 (0.997, 1.521)	0.053		0.310
> 3	98/ 129	(76.0)	6.0 (5.0, 9.0)	104/ 138	(75.4)	7.0 (5.0, 8.0)	0.994 (0.748, 1.321)	0.969			1.026 (0.778, 1.352)	0.856		
BMI group														
< 25	61/ 74	(82.4)	4.0 (3.0, 6.0)	47/ 57	(82.5)	7.0 (4.0, 11.0)	1.534 (1.006, 2.341)	0.047		0.250	1.471 (1.000, 2.163)	0.050		0.170
25 - < 30	100/ 119	(84.0)	5.0 (3.0, 7.0)	116/ 143	(81.1)	4.0 (3.0, 6.0)	0.972 (0.738, 1.280)	0.840			0.952 (0.728, 1.245)	0.719		
>= 30	120/ 146	(82.2)	5.0 (4.0, 6.0)	108/ 144	(75.0)	6.0 (4.0, 8.0)	1.198 (0.917, 1.566)	0.185			1.235 (0.952, 1.603)	0.112		
Ethnicity														
White	215/ 259	(83.0)	5.0 (4.0, 6.0)	219/ 280	(78.2)	6.0 (4.0, 6.0)	1.177 (0.970, 1.428)	0.098		0.942	1.190 (0.985, 1.437)	0.071		0.925
Black or African American	13/ 17	(76.5)	7.0 (3.0, 11.0)	10/ 13	(76.9)	7.5 (2.0, 11.0)	1.393 (0.519, 3.742)	0.511			1.031 (0.451, 2.358)	0.942		
Asian	25/ 29	(86.2)	3.0 (3.0, 5.0)	27/ 29	(93.1)	4.0 (3.0, 7.0)	0.996 (0.554, 1.793)	0.990			1.047 (0.607, 1.807)	0.868		
Others	28/ 34	(82.4)	8.0 (2.0, 12.0)	15/ 22	(68.2)	7.0 (3.0, 10.0)	0.988 (0.517, 1.891)	0.971			1.061 (0.565, 1.993)	0.854		
Number of baseline comorbidities present														
0-1	210/ 253	(83.0)		195/ 243	(80.2)									
2-3	69/ 84	(82.1)		72/ 97	(74.2)									
>= 4	2/ 2	(100.0)		4/ 4	(100.0)									
Presence of risk factor: Smoking														
Yes	119/ 145	(82.1)	5.0 (3.0, 6.0)	116/ 151	(76.8)	5.0 (3.0, 7.0)	1.178 (0.900, 1.543)	0.233		0.487	1.200 (0.927, 1.552)	0.166		0.493
No	161/ 193	(83.4)	5.0 (4.0, 7.0)	155/ 193	(80.3)	6.0 (4.0, 7.0)	1.084 (0.865, 1.357)	0.484			1.096 (0.879, 1.366)	0.417		

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=339)			Placebo (N=344)			Adjusted Analysis [2]			Interaction		Unadjusted Analysis [3]			Interaction	
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	p-Value			Hazard Ratio (95% CI)	p-Value	p-Value		
Presence of risk factor: Diabetes mellitus										0.631					0.697	
Yes	36/ 44	(81.8)	3.0 (3.0, 9.0)	46/ 56	(82.1)	6.0 (5.0, 10.0)	1.499 (0.939, 2.395)	0.090				1.263 (0.815, 1.958)	0.295			
No	245/ 295	(83.1)	5.0 (4.0, 6.0)	225/ 288	(78.1)	5.0 (4.0, 7.0)	1.120 (0.930, 1.348)	0.233				1.129 (0.942, 1.353)	0.190			
Presence of risk factor: Immunosuppression																
Yes	3/ 3	(100.0)		5/ 5	(100.0)											
No	278/ 336	(82.7)		266/ 339	(78.5)											
Presence of risk factor: Chronic lung disease										0.172					0.149	
Yes	24/ 28	(85.7)	5.0 (3.0, 9.0)	17/ 18	(94.4)	3.5 (2.0, 6.0)	0.737 (0.361, 1.502)	0.400				0.710 (0.379, 1.332)	0.286			
No	257/ 311	(82.6)	5.0 (4.0, 6.0)	254/ 326	(77.9)	6.0 (4.0, 7.0)	1.174 (0.982, 1.403)	0.078				1.178 (0.990, 1.402)	0.064			
Presence of risk factor: Hypertension										0.347					0.568	
Yes	109/ 130	(83.8)	6.0 (3.0, 8.0)	109/ 145	(75.2)	6.0 (4.0, 8.0)	1.273 (0.969, 1.672)	0.083				1.225 (0.938, 1.599)	0.135			
No	172/ 209	(82.3)	5.0 (3.0, 6.0)	162/ 199	(81.4)	6.0 (4.0, 7.0)	1.056 (0.847, 1.317)	0.629				1.105 (0.891, 1.370)	0.362			
Presence of risk factor: Cardiovascular disorder										0.624					0.909	
Yes	16/ 19	(84.2)	11.0 (3.0, 13.0)	16/ 22	(72.7)	6.0 (3.0, 15.0)	1.559 (0.734, 3.312)	0.248				1.214 (0.606, 2.433)	0.584			
No	265/ 320	(82.8)	5.0 (4.0, 6.0)	255/ 322	(79.2)	6.0 (4.0, 7.0)	1.135 (0.951, 1.354)	0.161				1.147 (0.965, 1.363)	0.119			
Presence of risk factor: Chronic kidney disease																
Yes	1/ 2	(50.0)		6/ 6	(100.0)											
No	280/ 337	(83.1)		265/ 338	(78.4)											
Presence of risk factor: HIV Infection																
Yes	0			0												
No	281/ 339	(82.9)		270/ 343	(78.7)											
Presence of risk factor: Sick Cell Disease																
No	281/ 339	(82.9)		271/ 344	(78.8)											
Presence of risk factor: Neurodevelopmental Disorder																
Yes	2/ 2	(100.0)		0												
No	279/ 337	(82.8)		271/ 344	(78.8)											
Presence of risk factor: Cancer																
Yes	1/ 1	(100.0)		3/ 3	(100.0)											
No	280/ 338	(82.8)		268/ 341	(78.6)											
Presence of risk factor: Device Dependence																
Yes	2/ 3	(66.7)		0												
No	277/ 331	(83.7)		270/ 341	(79.2)											

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Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Nausea - Subgroup analysis

Subgroup Level	Nirmatrelvir/ritonavir (N=16)			Placebo (N=18)			Adjusted Analysis [2]		Interaction		Unadjusted Analysis [3]				Interaction	
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value		p-Value	
Age																
< 65	12/	13 (92.3)		10/	14 (71.4)											
>= 65	2/	3 (66.7)		3/	4 (75.0)											
Gender																
Male	3/	3 (100.0)		2/	4 (50.0)											
Female	11/	13 (84.6)		11/	14 (78.6)											
Geographic region																
United States	6/	7 (85.7)		7/	8 (87.5)											
Europe	3/	3 (100.0)		1/	1 (100.0)											
India	0			0												
Rest of World	5/	6 (83.3)		5/	9 (55.6)											
COVID-19 therapeutic mAb treatment at randomisation																
Yes	1/	2 (50.0)		3/	3 (100.0)											
No	13/	14 (92.9)		10/	15 (66.7)											
Baseline viral load 1																
< 10^4 copies/mL	3/	3 (100.0)		3/	3 (100.0)											
>= 10^4 copies/mL	11/	13 (84.6)		9/	14 (64.3)											
Baseline viral load 2																
< 10^7 copies/mL	8/	8 (100.0)		11/	16 (68.8)											
>= 10^7 copies/mL	6/	8 (75.0)		1/	1 (100.0)											
Baseline serology status										0.050					0.171	
Negative	7/	9 (77.8)	11.0 (3.0, 15.0)	7/	11 (63.6)	10.0 (4.0, NE)	3.954 (0.797, 19.608)	0.092			1.247 (0.432, 3.604)	0.683				
Positive	7/	7 (100.0)	5.0 (2.0, 13.0)	6/	7 (85.7)	5.0 (2.0, 9.0)	0.554 (0.119, 2.581)	0.452			0.488 (0.136, 1.754)	0.272				
Symptom onset days to first dose date										0.222					0.512	
<= 3	8/	9 (88.9)	11.0 (2.0, 15.0)	6/	8 (75.0)	9.5 (2.0, NE)	5.746 (0.868, 38.043)	0.070			1.164 (0.399, 3.395)	0.781				
> 3	6/	7 (85.7)	7.0 (3.0, 18.0)	7/	10 (70.0)	7.0 (2.0, 9.0)	1.140 (0.228, 5.691)	0.873			0.834 (0.243, 2.857)	0.772				
BMI group																
< 25	6/	8 (75.0)		1/	2 (50.0)											
25 - < 30	5/	5 (100.0)		3/	4 (75.0)											
>= 30	3/	3 (100.0)		9/	12 (75.0)											
Ethnicity																
White	9/	10 (90.0)		10/	13 (76.9)											
Black or African American	1/	1 (100.0)		2/	2 (100.0)											
Asian	0			1/	1 (100.0)											
Others	4/	5 (80.0)		0/	2 (0.0)											
Number of baseline comorbidities present																
0-1	10/	12 (83.3)		10/	13 (76.9)											
2-3	3/	3 (100.0)		3/	5 (60.0)											
>= 4	1/	1 (100.0)		0												
Presence of risk factor: Smoking																
Yes	4/	4 (100.0)		3/	3 (100.0)											
No	10/	12 (83.3)		10/	15 (66.7)											

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Subgroup Level	Nirmatrelvir/ritonavir (N=16)			Placebo (N=18)			Adjusted Analysis [2]			Unadjusted Analysis [3]			
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	
Presence of risk factor: Diabetes mellitus													
Yes	2/	3 (66.7)		1/	2 (50.0)								
No	12/	13 (92.3)		12/	16 (75.0)								
Presence of risk factor: Immunosuppression													
Yes	0			2/	2 (100.0)								
No	14/	16 (87.5)		11/	16 (68.8)								
Presence of risk factor: Chronic lung disease													
Yes	5/	6 (83.3)		0									
No	9/	10 (90.0)		13/	18 (72.2)								
Presence of risk factor: Hypertension													
Yes	6/	6 (100.0)	13.5 (3.0, 25.0)	1/	4 (25.0)	NE (9.0, NE)	3.090 (0.275, 34.726)	0.361	0.232	5.382 (0.629, 46.037)	0.124	0.083	
No	8/	10 (80.0)	7.0 (2.0, 11.0)	12/	14 (85.7)	7.0 (2.0, 9.0)	0.793 (0.230, 2.741)	0.714		0.616 (0.234, 1.623)	0.327		
Presence of risk factor: Cardiovascular disorder													
Yes	2/	2 (100.0)		1/	3 (33.3)								
No	12/	14 (85.7)		12/	15 (80.0)								
Presence of risk factor: Chronic kidney disease													
Yes	0			1/	1 (100.0)								
No	14/	16 (87.5)		12/	17 (70.6)								
Presence of risk factor: HIV Infection													
Yes	0			0									
No	14/	16 (87.5)		13/	18 (72.2)								
Presence of risk factor: Sickle Cell Disease													
No	14/	16 (87.5)		13/	18 (72.2)								
Presence of risk factor: Neurodevelopmental Disorder													
Yes	0			0									
No	14/	16 (87.5)		13/	18 (72.2)								
Presence of risk factor: Cancer													
Yes	0			1/	1 (100.0)								
No	14/	16 (87.5)		12/	17 (70.6)								
Presence of risk factor: Device Dependence													
Yes	1/	1 (100.0)		0									
No	13/	14 (92.9)		13/	16 (81.3)								

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Subgroup Level	Nirmatrelvir/ritonavir (N=339)			Placebo (N=344)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value	
Age													
< 65	230/ 38	292 (78.8)	7.0 (6.0, 8.0)	210/ 43	287 (73.2)	7.0 (6.0, 8.0)	1.169 (0.965, 1.415)	0.111	0.905	1.166 (0.967, 1.406)	0.108	0.857	
>= 65	38/ 47	(80.9)	8.0 (4.0, 12.0)	57 (75.4)	9.0 (6.0, 13.0)		1.268 (0.807, 1.993)	0.303		1.245 (0.804, 1.930)	0.326		
Gender													
Male	106/ 162	136 (77.9)	5.0 (4.0, 7.0)	111/ 142	153 (72.5)	7.0 (5.0, 8.0)	1.179 (0.894, 1.555)	0.242	0.801	1.208 (0.925, 1.578)	0.165	0.745	
Female	162/ 203	(79.8)	8.0 (7.0, 9.0)	191 (74.3)	8.0 (6.0, 10.0)		1.172 (0.931, 1.476)	0.175		1.172 (0.935, 1.469)	0.168		
Geographic region													
United States	124/ 86	159 (78.0)	7.0 (6.0, 9.0)	121/ 78	166 (72.9)	7.0 (5.0, 9.0)	1.052 (0.814, 1.358)	0.699	0.396	1.109 (0.863, 1.425)	0.419	0.532	
Europe	17/ 17	20 (81.9)	6.0 (4.0, 8.0)	18/ 19	109 (71.6)	7.0 (6.0, 12.0)	1.477 (1.073, 2.032)	0.017		1.417 (1.041, 1.928)	0.027		
India	17/ 17	20 (85.0)	4.0 (3.0, 9.0)	18/ 19	19 (94.7)	7.0 (4.0, 10.0)	1.918 (0.876, 4.200)	0.103		1.177 (0.599, 2.314)	0.637		
Rest of World	41/ 41	55 (74.5)	8.0 (5.0, 12.0)	36/ 50	(72.0)	8.0 (4.0, 10.0)	1.024 (0.651, 1.610)	0.920		1.054 (0.674, 1.650)	0.817		
COVID-19 therapeutic mAb treatment at randomisation													
Yes	15/ 253	22 (68.2)	6.0 (4.0, 14.0)	21/ 319	25 (84.0)	8.0 (4.0, 13.0)	0.761 (0.377, 1.536)	0.445	0.244	0.833 (0.429, 1.617)	0.589	0.257	
No	253/ 317	(79.8)	7.0 (6.0, 8.0)	319 (72.7)	7.0 (6.0, 9.0)		1.216 (1.013, 1.459)	0.036		1.216 (1.017, 1.453)	0.032		
Baseline viral load 1													
< 10^4 copies/mL	94/ 168	115 (81.7)	7.0 (6.0, 9.0)	83/ 163	112 (74.1)	6.0 (4.0, 9.0)	1.116 (0.827, 1.504)	0.473	0.599	1.115 (0.829, 1.500)	0.471	0.669	
>= 10^4 copies/mL	168/ 216	(77.8)	6.0 (5.0, 8.0)	219 (74.4)	7.0 (6.0, 9.0)		1.215 (0.978, 1.510)	0.079		1.196 (0.964, 1.485)	0.103		
Baseline viral load 2													
< 10^7 copies/mL	183/ 79	236 (77.5)	7.0 (6.0, 8.0)	188/ 58	259 (72.6)	7.0 (6.0, 9.0)	1.163 (0.946, 1.429)	0.151	0.914	1.152 (0.939, 1.413)	0.174	0.945	
>= 10^7 copies/mL	79/ 95	(83.2)	5.0 (3.0, 8.0)	72 (80.6)	6.0 (5.0, 9.0)		1.144 (0.806, 1.623)	0.452		1.153 (0.821, 1.619)	0.410		
Baseline serology status													
Negative	135/ 131	167 (80.8)	7.0 (5.0, 8.0)	126/ 125	180 (70.0)	9.0 (6.0, 10.0)	1.344 (1.048, 1.724)	0.020	0.232	1.377 (1.080, 1.757)	0.010	0.112	
Positive	131/ 168	(78.0)	7.0 (6.0, 8.0)	161 (77.6)	6.0 (5.0, 8.0)		1.057 (0.823, 1.358)	0.664		1.029 (0.805, 1.315)	0.822		
Symptom onset days to first dose date													
<= 3	176/ 92	210 (83.8)	6.0 (4.0, 7.0)	152/ 101	206 (73.8)	7.0 (6.0, 9.0)	1.330 (1.065, 1.661)	0.012	0.060	1.363 (1.096, 1.695)	0.005	0.036	
> 3	92/ 129	(71.3)	9.0 (7.0, 11.0)	138 (73.2)	8.0 (6.0, 10.0)		0.929 (0.695, 1.240)	0.617		0.932 (0.703, 1.237)	0.628		
BMI group													
< 25	55/ 97	74 (74.3)	6.0 (4.0, 8.0)	46/ 108	57 (80.7)	8.0 (5.0, 12.0)	1.208 (0.791, 1.845)	0.381	0.567	1.198 (0.809, 1.774)	0.368	0.398	
25 - < 30	97/ 116	(81.5)	7.0 (5.0, 9.0)	143 (75.5)	6.0 (5.0, 8.0)		1.062 (0.800, 1.410)	0.677		1.031 (0.784, 1.357)	0.826		
>= 30	116/ 146	(79.5)	7.0 (5.0, 8.0)	144 (68.8)	8.0 (6.0, 11.0)		1.311 (0.995, 1.727)	0.054		1.346 (1.029, 1.762)	0.030		
Ethnicity													
White	204/ 12	259 (78.8)	7.0 (6.0, 8.0)	202/ 9	280 (72.1)	7.0 (6.0, 10.0)	1.226 (1.005, 1.495)	0.045	0.808	1.239 (1.020, 1.506)	0.031	0.817	
Black or African American	12/ 17	(70.6)	8.0 (3.0, 15.0)	13 (69.2)	9.0 (2.0, NE)		1.358 (0.476, 3.870)	0.567		1.080 (0.453, 2.576)	0.863		
Asian	25/ 27	29 (86.2)	3.5 (3.0, 5.0)	27/ 15	29 (93.1)	5.0 (4.0, 8.0)	1.212 (0.677, 2.170)	0.518		1.131 (0.655, 1.954)	0.659		
Others	27/ 34	(79.4)	8.0 (6.0, 13.0)	22 (68.2)	8.0 (3.0, 10.0)		0.869 (0.450, 1.678)	0.676		0.923 (0.489, 1.742)	0.805		
Number of baseline comorbidities present													
0-1	201/ 65	253 (79.4)		189/ 60	243 (77.8)								
2-3	65/ 2	84 (77.4)		97 (61.9)									
>= 4	2/ 2	(100.0)		4/ 4	(100.0)								
Presence of risk factor: Smoking													
Yes	115/ 153	145 (79.3)	6.0 (5.0, 7.0)	104/ 149	151 (68.9)	8.0 (5.0, 12.0)	1.360 (1.029, 1.799)	0.031	0.102	1.383 (1.058, 1.807)	0.018	0.091	
No	153/ 193	(79.3)	7.0 (6.0, 9.0)	193 (77.2)	7.0 (6.0, 8.0)		1.037 (0.824, 1.304)	0.758		1.048 (0.836, 1.313)	0.686		

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=339)			Placebo (N=344)			Adjusted Analysis [2]			Interaction		Unadjusted Analysis [3]			Interaction	
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	p-Value			Hazard Ratio (95% CI)	p-Value	p-Value		
Presence of risk factor: Diabetes mellitus										0.941					0.933	
Yes	34/ 44	(77.3)	5.0 (3.0, 12.0)	43/ 56	(76.8)	6.5 (5.0, 11.0)	1.323 (0.823, 2.128)	0.248				1.195 (0.761, 1.875)	0.439			
No	234/ 295	(79.3)	7.0 (6.0, 8.0)	210/ 288	(72.9)	7.0 (6.0, 9.0)	1.188 (0.982, 1.438)	0.077				1.181 (0.980, 1.424)	0.080			
Presence of risk factor: Immunosuppression																
Yes	3/ 3	(100.0)		5/ 5	(100.0)											
No	265/ 336	(78.9)		248/ 339	(73.2)											
Presence of risk factor: Chronic lung disease										0.019					0.040	
Yes	22/ 28	(78.6)	8.0 (3.0, 13.0)	16/ 18	(88.9)	4.0 (3.0, 6.0)	0.561 (0.265, 1.187)	0.131				0.612 (0.315, 1.190)	0.148			
No	246/ 311	(79.1)	7.0 (6.0, 8.0)	237/ 326	(72.7)	8.0 (6.0, 9.0)	1.225 (1.020, 1.470)	0.029				1.226 (1.025, 1.466)	0.025			
Presence of risk factor: Hypertension										0.190					0.304	
Yes	102/ 130	(78.5)	8.0 (5.0, 11.0)	97/ 145	(66.9)	8.0 (6.0, 11.0)	1.327 (1.001, 1.761)	0.050				1.311 (0.992, 1.732)	0.057			
No	166/ 209	(79.4)	6.0 (5.0, 7.0)	156/ 199	(78.4)	7.0 (6.0, 8.0)	1.055 (0.843, 1.321)	0.639				1.099 (0.883, 1.368)	0.396			
Presence of risk factor: Cardiovascular disorder										0.345					0.538	
Yes	16/ 19	(84.2)	11.0 (3.0, 13.0)	15/ 22	(68.2)	9.5 (5.0, NE)	1.928 (0.895, 4.152)	0.093				1.507 (0.742, 3.059)	0.257			
No	252/ 320	(78.8)	7.0 (6.0, 8.0)	238/ 322	(73.9)	7.0 (6.0, 8.0)	1.152 (0.961, 1.380)	0.125				1.164 (0.975, 1.390)	0.094			
Presence of risk factor: Chronic kidney disease																
Yes	1/ 2	(50.0)		6/ 6	(100.0)											
No	267/ 337	(79.2)		247/ 338	(73.1)											
Presence of risk factor: HIV Infection																
Yes	0			0												
No	268/ 339	(79.1)		252/ 343	(73.5)											
Presence of risk factor: Sick Cell Disease																
No	268/ 339	(79.1)		253/ 344	(73.5)											
Presence of risk factor: Neurodevelopmental Disorder																
Yes	2/ 2	(100.0)		0												
No	266/ 337	(78.9)		253/ 344	(73.5)											
Presence of risk factor: Cancer																
Yes	1/ 1	(100.0)		3/ 3	(100.0)											
No	267/ 338	(79.0)		250/ 341	(73.3)											
Presence of risk factor: Device Dependence																
Yes	2/ 3	(66.7)		0												
No	264/ 331	(79.8)		252/ 341	(73.9)											

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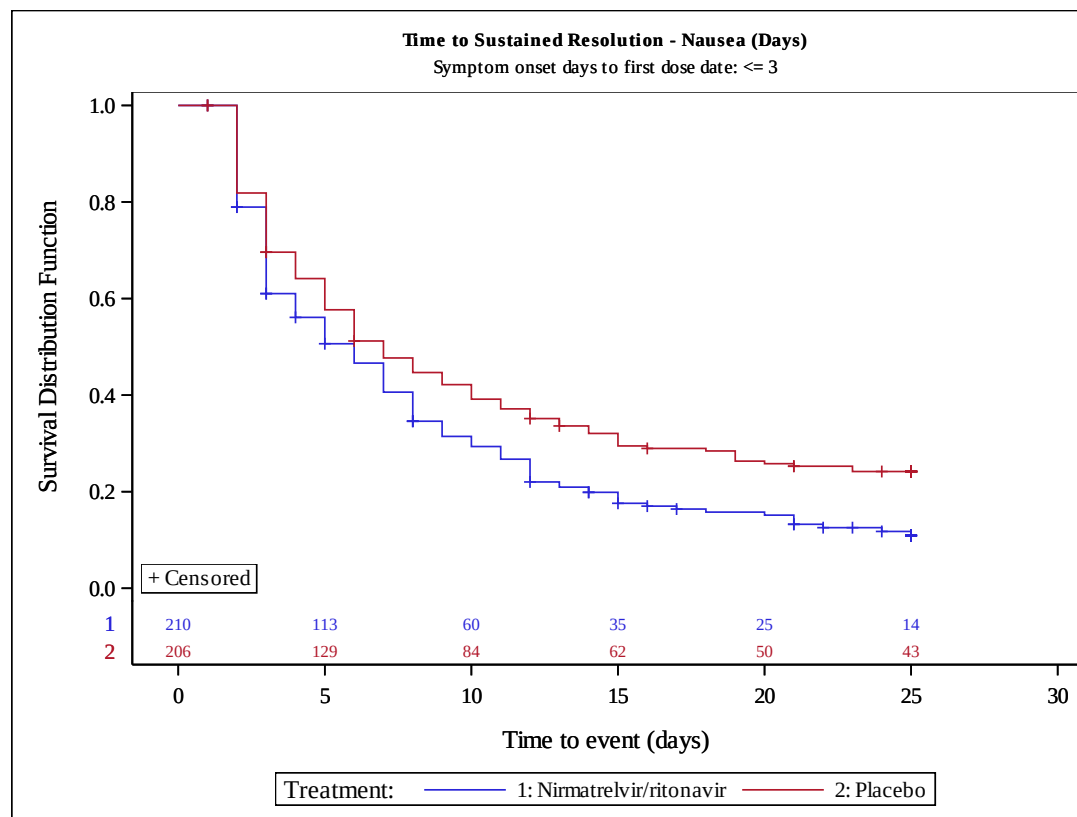
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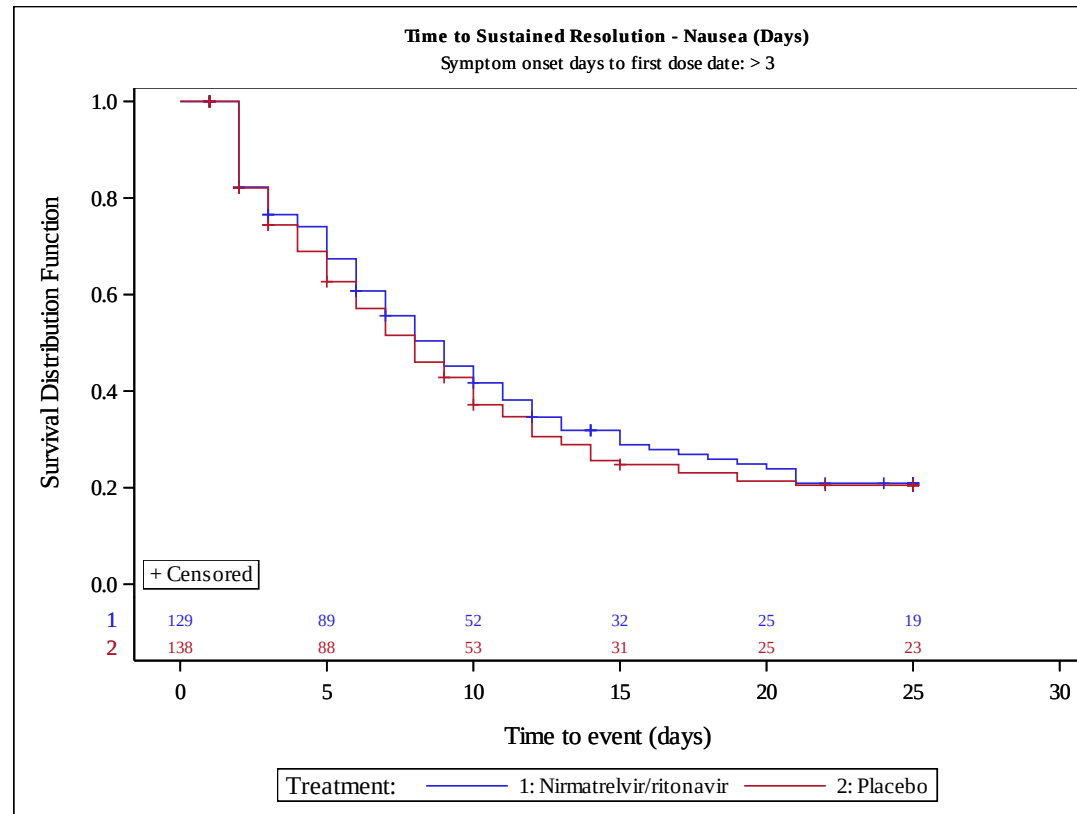
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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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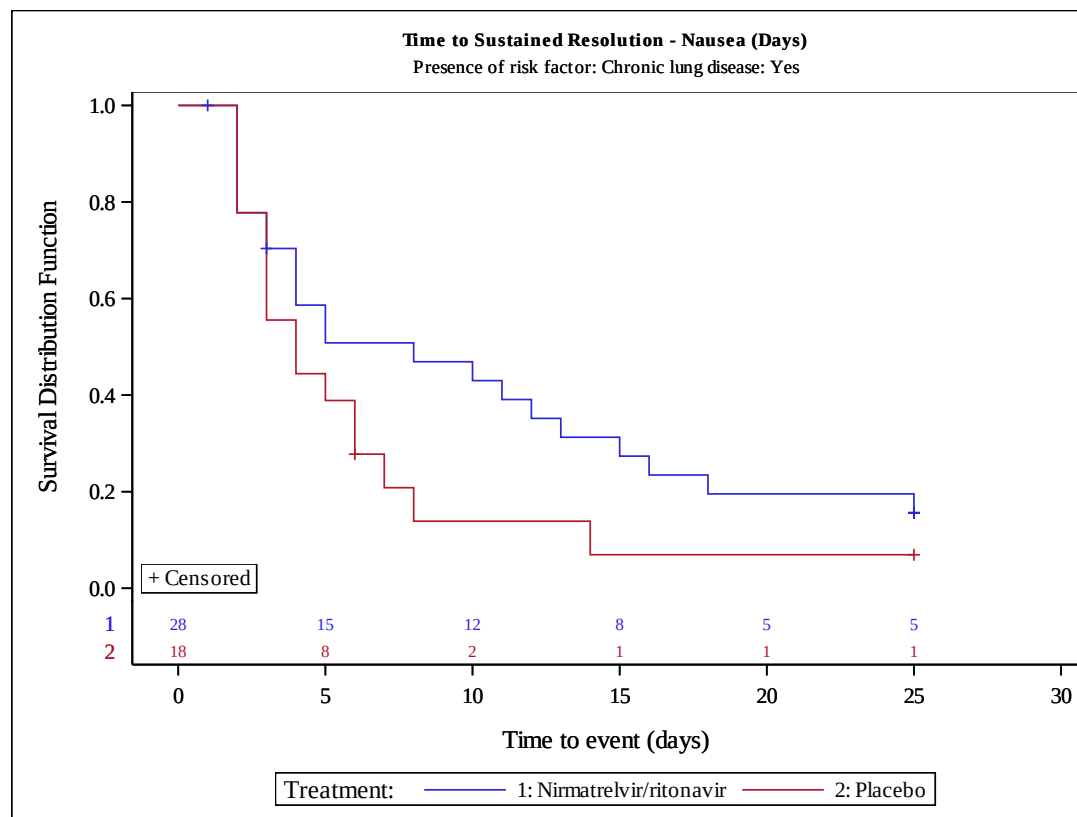


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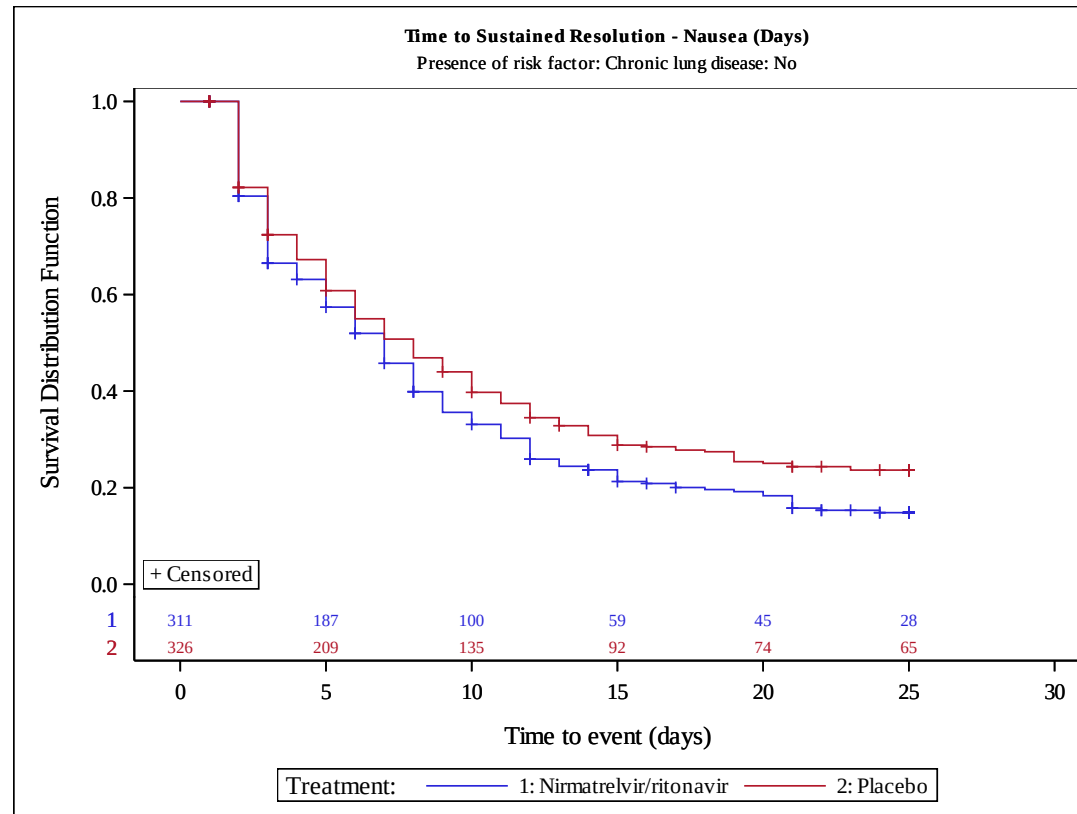
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Overall Study population

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Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Nausea - Subgroup analysis

Subgroup Level	Nirmatrelvir/ritonavir (N=16)						Placebo (N=18)						Adjusted Analysis [2]		Interaction		Unadjusted Analysis [3]				Interaction	
	n/N	(%)	Median	(95% CI)	[1]		n/N	(%)	Median	(95% CI)	[1]		Hazard Ratio (95% CI)	p-Value	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value		p-Value	p-Value
Age																						
< 65	10/	13	(76.9)				8/	14	(57.1)													
>= 65	2/	3	(66.7)				3/	4	(75.0)													
Gender																						
Male	3/	3	(100.0)				2/	4	(50.0)													
Female	9/	13	(69.2)				9/	14	(64.3)													
Geographic region																						
United States	5/	7	(71.4)				6/	8	(75.0)													
Europe	3/	3	(100.0)				1/	1	(100.0)													
India	0/						0/															
Rest of World	4/	6	(66.7)				4/	9	(44.4)													
COVID-19 therapeutic mAb treatment at randomisation																						
Yes	1/	2	(50.0)				3/	3	(100.0)													
No	11/	14	(78.6)				8/	15	(53.3)													
Baseline viral load 1																						
< 10^4 copies/mL	2/	3	(66.7)				3/	3	(100.0)													
>= 10^4 copies/mL	10/	13	(76.9)				7/	14	(50.0)													
Baseline viral load 2																						
< 10^7 copies/mL	7/	8	(87.5)				9/	16	(56.3)													
>= 10^7 copies/mL	5/	8	(62.5)				1/	1	(100.0)													
Baseline serology status															0.493							0.783
Negative	6/	9	(66.7)	15.0	(3.0, 25.0)		6/	11	(54.5)	19.0	(6.0, NE)	3.119	(0.469, 20.729)	0.239		1.614	(0.517, 5.040)	0.410				
Positive	6/	7	(85.7)	8.0	(5.0, 18.0)		5/	7	(71.4)	12.0	(7.0, NE)	1.243	(0.233, 6.641)	0.799		1.294	(0.389, 4.308)	0.674				
Symptom onset days to first dose date															0.109							0.200
<= 3	8/	9	(88.9)	11.5	(3.0, 18.0)		5/	8	(62.5)	17.0	(6.0, NE)	6.691	(0.790, 56.701)	0.081		2.542	(0.814, 7.936)	0.108				
> 3	4/	7	(57.1)	13.0	(5.0, NE)		6/	10	(60.0)	10.0	(7.0, 19.0)	0.436	(0.069, 2.742)	0.377		0.934	(0.258, 3.376)	0.917				
BMI group																						
< 25	5/	8	(62.5)				1/	2	(50.0)													
25 - < 30	4/	5	(80.0)				3/	4	(75.0)													
>= 30	3/	3	(100.0)				7/	12	(58.3)													
Ethnicity																						
White	8/	10	(80.0)				8/	13	(61.5)													
Black or African American	1/	1	(100.0)				2/	2	(100.0)													
Asian	0/						1/	1	(100.0)													
Others	3/	5	(60.0)				0/	2	(0.0)													
Number of baseline comorbidities present																						
0-1	9/	12	(75.0)				8/	13	(61.5)													
2-3	2/	3	(66.7)				3/	5	(60.0)													
>= 4	1/	1	(100.0)				0/															
Presence of risk factor: Smoking																						
Yes	3/	4	(75.0)				3/	3	(100.0)													
No	9/	12	(75.0)				8/	15	(53.3)													

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=16)			Placebo (N=18)			Adjusted Analysis [2]			Unadjusted Analysis [3]		
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus												
Yes	2/	3 (66.7)		1/	2 (50.0)							
No	10/	13 (76.9)		10/	16 (62.5)							
Presence of risk factor: Immunosuppression												
Yes	0			2/	2 (100.0)							
No	12/	16 (75.0)		9/	16 (56.3)							
Presence of risk factor: Chronic lung disease												
Yes	3/	6 (50.0)		0								
No	9/	10 (90.0)		11/	18 (61.1)							
Presence of risk factor: Hypertension												
Yes	6/	6 (100.0)	13.5 (5.0, 25.0)	1/	4 (25.0)	NE (11.0, NE)	3.090 (0.275, 34.726)	0.361	0.540	5.284 (0.618, 45.191)	0.128	0.202
No	6/	10 (60.0)	8.5 (3.0, NE)	10/	14 (71.4)	12.5 (7.0, 19.0)	1.452 (0.409, 5.151)	0.564		1.188 (0.430, 3.283)	0.740	
Presence of risk factor: Cardiovascular disorder												
Yes	2/	2 (100.0)		1/	3 (33.3)							
No	10/	14 (71.4)		10/	15 (66.7)							
Presence of risk factor: Chronic kidney disease												
Yes	0			1/	1 (100.0)							
No	12/	16 (75.0)		10/	17 (58.8)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	12/	16 (75.0)		11/	18 (61.1)							
Presence of risk factor: Sickle Cell Disease												
No	12/	16 (75.0)		11/	18 (61.1)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0			0								
No	12/	16 (75.0)		11/	18 (61.1)							
Presence of risk factor: Cancer												
Yes	0			1/	1 (100.0)							
No	12/	16 (75.0)		10/	17 (58.8)							
Presence of risk factor: Device Dependence												
Yes	1/	1 (100.0)		0								
No	11/	14 (78.6)		11/	16 (68.8)							

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Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]		Interaction p-Value	Unadjusted analysis [2]		Interaction p-Value
			Relative Risk (95% CI)	p-Value		Relative Risk (95% CI)	p-Value	
Age								
< 65	66/ 790 (8.4)	69/ 810 (8.5)	0.991 (0.716, 1.372)	0.957	0.059	0.981 (0.710, 1.355)	0.906	0.077
>= 65	7/ 138 (5.1)	17/ 145 (11.7)	0.412 (0.166, 1.023)	0.056		0.433 (0.185, 1.011)	0.053	
Gender								
Male	29/ 463 (6.3)	37/ 507 (7.3)	0.847 (0.528, 1.358)	0.491	0.755	0.858 (0.537, 1.373)	0.523	0.980
Female	44/ 465 (9.5)	49/ 448 (10.9)	0.921 (0.621, 1.365)	0.681		0.865 (0.588, 1.272)	0.462	
Geographic region								
United States	36/ 375 (9.6)	34/ 387 (8.8)	1.054 (0.667, 1.665)	0.821	0.054	1.093 (0.699, 1.708)	0.697	0.043
Europe	17/ 322 (5.3)	36/ 321 (11.2)	0.488 (0.279, 0.852)	0.012		0.471 (0.270, 0.821)	0.008	
India	2/ 74 (2.7)	3/ 78 (3.8)	NE (NE, NE)	NE		0.703 (0.121, 4.087)	0.695	
Rest of World	18/ 157 (11.5)	13/ 169 (7.7)	1.423 (0.720, 2.814)	0.311		1.490 (0.755, 2.940)	0.250	
COVID-19 therapeutic mAb treatment at randomisation								
Yes	7/ 57 (12.3)	4/ 60 (6.7)	1.714 (0.525, 5.596)	0.372	0.204	1.842 (0.570, 5.958)	0.308	0.196
No	66/ 871 (7.6)	82/ 895 (9.2)	0.835 (0.610, 1.144)	0.262		0.827 (0.606, 1.128)	0.231	
Baseline viral load 1								
< 10^4 copies/mL	20/ 335 (6.0)	24/ 354 (6.8)	0.843 (0.471, 1.508)	0.564	0.886	0.881 (0.496, 1.564)	0.664	0.974
>= 10^4 copies/mL	52/ 569 (9.1)	59/ 575 (10.3)	0.888 (0.623, 1.265)	0.512		0.891 (0.625, 1.269)	0.522	
Baseline viral load 2								
< 10^7 copies/mL	48/ 652 (7.4)	55/ 699 (7.9)	0.927 (0.638, 1.346)	0.689	0.582	0.936 (0.645, 1.357)	0.726	0.581
>= 10^7 copies/mL	24/ 252 (9.5)	28/ 230 (12.2)	0.749 (0.447, 1.257)	0.274		0.782 (0.467, 1.309)	0.350	
Baseline serology status								
Negative	40/ 435 (9.2)	50/ 456 (11.0)	0.833 (0.561, 1.237)	0.365	0.775	0.839 (0.565, 1.244)	0.382	0.906
Positive	31/ 482 (6.4)	36/ 487 (7.4)	0.918 (0.574, 1.466)	0.719		0.870 (0.547, 1.383)	0.556	
Symptom onset days to first dose date								
<= 3	47/ 624 (7.5)	55/ 624 (8.8)	0.838 (0.576, 1.218)	0.353	0.667	0.855 (0.588, 1.241)	0.409	0.834
> 3	26/ 304 (8.6)	31/ 331 (9.4)	0.934 (0.561, 1.555)	0.794		0.913 (0.555, 1.502)	0.721	
BMI group								
< 25	14/ 215 (6.5)	25/ 213 (11.7)	NE (NE, NE)	NE	0.322	0.555 (0.297, 1.038)	0.065	0.157
25 - < 30	22/ 319 (6.9)	28/ 332 (8.4)	0.846 (0.491, 1.456)	0.546		0.818 (0.478, 1.399)	0.463	
>= 30	37/ 393 (9.4)	33/ 410 (8.0)	1.063 (0.670, 1.687)	0.795		1.170 (0.747, 1.832)	0.493	
Ethnicity								
White	52/ 699 (7.4)	70/ 718 (9.7)	0.759 (0.535, 1.076)	0.121	0.385	0.763 (0.541, 1.076)	0.123	0.475
Black or African American	6/ 43 (14.0)	4/ 40 (10.0)	NE (NE, NE)	NE		1.395 (0.425, 4.585)	0.583	
Asian	6/ 117 (5.1)	4/ 127 (3.1)	NE (NE, NE)	NE		1.628 (0.471, 5.626)	0.441	
Others	9/ 69 (13.0)	8/ 70 (11.4)	NE (NE, NE)	NE		1.141 (0.468, 2.786)	0.772	
Number of baseline comorbidities present								
0-1	58/ 710 (8.2)	65/ 728 (8.9)	0.908 (0.645, 1.279)	0.582	0.920	0.915 (0.652, 1.284)	0.607	0.558
2-3	15/ 214 (7.0)	21/ 221 (9.5)	NE (NE, NE)	NE		0.738 (0.391, 1.392)	0.348	
>= 4	0/ 4 (0.0)	0/ 6 (0.0)	NE (NE, NE)	NE		NE (NE, NE)	NE	
Presence of risk factor: Smoking								
Yes	37/ 417 (8.9)	33/ 438 (7.5)	1.153 (0.734, 1.810)	0.537	0.123	1.178 (0.751, 1.846)	0.476	0.083
No	36/ 509 (7.1)	53/ 517 (10.3)	0.705 (0.467, 1.064)	0.096		0.690 (0.460, 1.035)	0.073	
Presence of risk factor: Diabetes mellitus					0.476			0.298

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF) / last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

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[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Vomit - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928)		Placebo (N=955)		Adjusted analysis [1]				Interaction		Unadjusted analysis [2]				Interaction	
	n/N (%)		n/N (%)		Relative Risk (95% CI)			p-Value	p-Value	Relative Risk (95% CI)			p-Value	p-Value		
Yes	7/ 130 (5.4)		13/ 136 (9.6)		NE (	NE,	NE)	NE			0.563 (	0.232,	1.367)	0.205		
No	66/ 797 (8.3)		73/ 819 (8.9)		0.914 (	0.662,	1.261)	0.584			0.929 (	0.676,	1.277)	0.651		
Presence of risk factor: Immunosuppression									NE						0.375	
Yes	1/ 6 (16.7)		0/ 7 (0.0)		NE (	NE,	NE)	NE			3.429 (	0.165,	71.361)	0.426		
No	72/ 921 (7.8)		86/ 948 (9.1)		0.869 (	0.642,	1.177)	0.364			0.862 (	0.639,	1.163)	0.330		
Presence of risk factor: Chronic lung disease										0.495					0.463	
Yes	5/ 62 (8.1)		2/ 39 (5.1)		NE (	NE,	NE)	NE			1.573 (	0.321,	7.713)	0.577		
No	68/ 865 (7.9)		84/ 916 (9.2)		0.866 (	0.635,	1.181)	0.363			0.857 (	0.631,	1.164)	0.324		
Presence of risk factor: Hypertension										0.058					0.044	
Yes	22/ 348 (6.3)		40/ 371 (10.8)		0.592 (	0.355,	0.987)	0.045			0.586 (	0.356,	0.966)	0.036		
No	51/ 579 (8.8)		46/ 584 (7.9)		1.118 (	0.762,	1.640)	0.568			1.118 (	0.764,	1.638)	0.566		
Presence of risk factor: Cardiovacular disorder										0.067					0.146	
Yes	1/ 42 (2.4)		6/ 49 (12.2)		NE (	NE,	NE)	NE			0.194 (	0.024,	1.551)	0.122		
No	72/ 885 (8.1)		80/ 906 (8.8)		0.933 (	0.685,	1.271)	0.661			0.921 (	0.679,	1.249)	0.598		
Presence of risk factor: Chronic kidney disease										0.231					0.398	
Yes	0/ 6 (0.0)		2/ 8 (25.0)		NE (	NE,	NE)	NE			0.257 (	0.015,	4.541)	0.354		
No	73/ 921 (7.9)		84/ 947 (8.9)		0.892 (	0.659,	1.208)	0.462			0.894 (	0.662,	1.206)	0.463		
Presence of risk factor: HIV Infection																
Yes	0		0/ 1 (0.0)													
No	73/ 927 (7.9)		86/ 953 (9.0)													
Presence of risk factor: Sickie Cell Disease																
No	73/ 927 (7.9)		86/ 955 (9.0)													
Presence of risk factor: Neurodevelopmental Disorder																
Yes	0/ 2 (0.0)		0/ 1 (0.0)													
No	73/ 925 (7.9)		86/ 954 (9.0)													
Presence of risk factor: Cancer										0.331					0.595	
Yes	0/ 5 (0.0)		1/ 6 (16.7)		NE (	NE,	NE)	NE			0.389 (	0.019,	7.883)	0.538		
No	73/ 922 (7.9)		85/ 949 (9.0)		0.890 (	0.657,	1.205)	0.450			0.884 (	0.655,	1.192)	0.419		
Presence of risk factor: Device Dependence																
Yes	1/ 4 (25.0)		0/ 3 (0.0)													
No	71/ 914 (7.8)		86/ 944 (9.1)													

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

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[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=119)			Placebo (N=121)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value	
Age													
< 65	87/ 105	(82.9)	3.0 (3.0, 4.0)	77/ 96	(80.2)	3.0 (2.0, 5.0)	1.118 (0.809, 1.546)	0.500	0.991	1.114 (0.819, 1.515)	0.492	0.831	
>= 65	12/ 14	(85.7)	2.5 (2.0, 4.0)	21/ 25	(84.0)	3.0 (2.0, 5.0)	1.218 (0.556, 2.670)	0.622		1.144 (0.561, 2.333)	0.711		
Gender													
Male	36/ 44	(81.8)	3.0 (2.0, 5.0)	43/ 53	(81.1)	3.0 (2.0, 5.0)	1.046 (0.643, 1.700)	0.858	0.489	1.023 (0.656, 1.595)	0.922	0.688	
Female	63/ 75	(84.0)	3.0 (2.0, 4.0)	55/ 68	(80.9)	3.0 (2.0, 6.0)	1.207 (0.826, 1.765)	0.330		1.165 (0.810, 1.674)	0.410		
Geographic region													
United States	60/ 73	(82.2)	3.0 (3.0, 4.0)	51/ 65	(78.5)	3.0 (2.0, 7.0)	1.101 (0.744, 1.628)	0.630	0.644	1.167 (0.801, 1.700)	0.421	0.714	
Europe	19/ 22	(86.4)	2.0 (2.0, 4.0)	23/ 28	(82.1)	2.0 (2.0, 4.0)	1.192 (0.625, 2.272)	0.594		1.259 (0.682, 2.327)	0.462		
India	10/ 10	(100.0)	2.0 (2.0, 3.0)	12/ 12	(100.0)	4.0 (2.0, 5.0)	3.187 (0.922, 11.014)	0.067		1.327 (0.547, 3.217)	0.532		
Rest of World	10/ 14	(71.4)	10.5 (2.0, 20.0)	12/ 16	(75.0)	6.0 (2.0, 12.0)	0.669 (0.281, 1.596)	0.365		0.710 (0.305, 1.654)	0.428		
COVID-19 therapeutic mAb treatment at randomisation													
Yes	10/ 13	(76.9)	4.5 (2.0, 14.0)	14/ 18	(77.8)	4.0 (2.0, 14.0)	0.849 (0.340, 2.119)	0.725	0.739	0.986 (0.436, 2.234)	0.974	0.796	
No	89/ 106	(84.0)	3.0 (2.0, 4.0)	84/ 103	(81.6)	3.0 (2.0, 5.0)	1.149 (0.837, 1.577)	0.389		1.121 (0.831, 1.512)	0.453		
Baseline viral load 1													
< 10^4 copies/mL	41/ 48	(85.4)	3.0 (2.0, 6.0)	37/ 43	(86.0)	3.0 (2.0, 5.0)	1.052 (0.669, 1.654)	0.828	0.605	1.029 (0.659, 1.608)	0.899	0.710	
>= 10^4 copies/mL	52/ 65	(80.0)	3.0 (2.0, 4.0)	58/ 74	(78.4)	3.0 (2.0, 7.0)	1.168 (0.790, 1.727)	0.436		1.138 (0.782, 1.656)	0.501		
Baseline viral load 2													
< 10^7 copies/mL	73/ 92	(79.3)	3.0 (3.0, 4.0)	77/ 97	(79.4)	4.0 (2.0, 5.0)	1.084 (0.783, 1.501)	0.629	0.867	1.083 (0.786, 1.493)	0.626	0.924	
>= 10^7 copies/mL	20/ 21	(95.2)	2.5 (2.0, 5.0)	18/ 20	(90.0)	2.0 (2.0, 4.0)	1.126 (0.537, 2.359)	0.754		1.235 (0.641, 2.379)	0.528		
Baseline serology status													
Negative	37/ 45	(82.2)	4.0 (3.0, 7.0)	39/ 54	(72.2)	4.0 (2.0, 9.0)	1.269 (0.787, 2.047)	0.328	0.479	1.268 (0.806, 1.995)	0.304	0.434	
Positive	60/ 72	(83.3)	3.0 (2.0, 3.0)	58/ 66	(87.9)	3.0 (2.0, 4.0)	1.059 (0.724, 1.549)	0.766		0.988 (0.688, 1.418)	0.947		
Symptom onset days to first dose date													
<= 3	60/ 72	(83.3)	3.0 (2.0, 4.0)	62/ 76	(81.6)	3.0 (2.0, 5.0)	1.117 (0.768, 1.626)	0.563	0.919	1.117 (0.781, 1.596)	0.545	0.955	
> 3	39/ 47	(83.0)	3.0 (2.0, 4.0)	36/ 45	(80.0)	4.0 (2.0, 8.0)	1.111 (0.688, 1.796)	0.667		1.099 (0.698, 1.730)	0.684		
BMI group													
< 25	24/ 28	(85.7)	2.0 (2.0, 5.0)	14/ 17	(82.4)	5.0 (2.0, 13.0)	1.735 (0.795, 3.788)	0.166	0.043	1.465 (0.752, 2.856)	0.262	0.032	
25 - < 30	30/ 41	(73.2)	4.0 (2.0, 9.0)	45/ 52	(86.5)	2.0 (2.0, 4.0)	0.709 (0.430, 1.171)	0.179		0.697 (0.438, 1.109)	0.128		
>= 30	45/ 50	(90.0)	3.0 (2.0, 4.0)	39/ 52	(75.0)	4.0 (2.0, 8.0)	1.585 (0.987, 2.547)	0.057		1.560 (1.006, 2.421)	0.047		
Ethnicity													
White	74/ 91	(81.3)	3.0 (2.0, 4.0)	80/ 99	(80.8)	3.0 (2.0, 5.0)	1.080 (0.777, 1.502)	0.647	0.932	1.125 (0.819, 1.545)	0.468	0.952	
Black or African American	6/ 7	(85.7)	4.0 (2.0, 7.0)	2/ 3	(66.7)	15.0 (11.0, 19.0)	9.13E7 (0.000, NE)	0.998		6.99E7 (0.000, NE)	0.996		
Asian	11/ 11	(100.0)	2.0 (2.0, 3.0)	14/ 14	(100.0)	4.0 (2.0, 5.0)	3.296 (0.950, 11.432)	0.060		1.220 (0.534, 2.790)	0.637		
Others	8/ 10	(80.0)	3.5 (2.0, 20.0)	2/ 5	(40.0)	6.0 (2.0, 6.0)	0.510 (0.083, 3.133)	0.467		0.852 (0.171, 4.235)	0.845		
Number of baseline comorbidities present													
0-1	76/ 90	(84.4)		68/ 81	(84.0)				0.872			0.777	
2-3	22/ 28	(78.6)		28/ 38	(73.7)								
>= 4	1/ 1	(100.0)		2/ 2	(100.0)								
Presence of risk factor: Smoking													
Yes	42/ 53	(79.2)	3.0 (2.0, 5.0)	37/ 48	(77.1)	4.0 (2.0, 7.0)	1.159 (0.715, 1.881)	0.549	0.872	1.144 (0.734, 1.783)	0.554	0.777	
No	56/ 65	(86.2)	3.0 (2.0, 4.0)	61/ 73	(83.6)	3.0 (2.0, 4.0)	1.125 (0.766, 1.653)	0.547		1.086 (0.755, 1.562)	0.658		

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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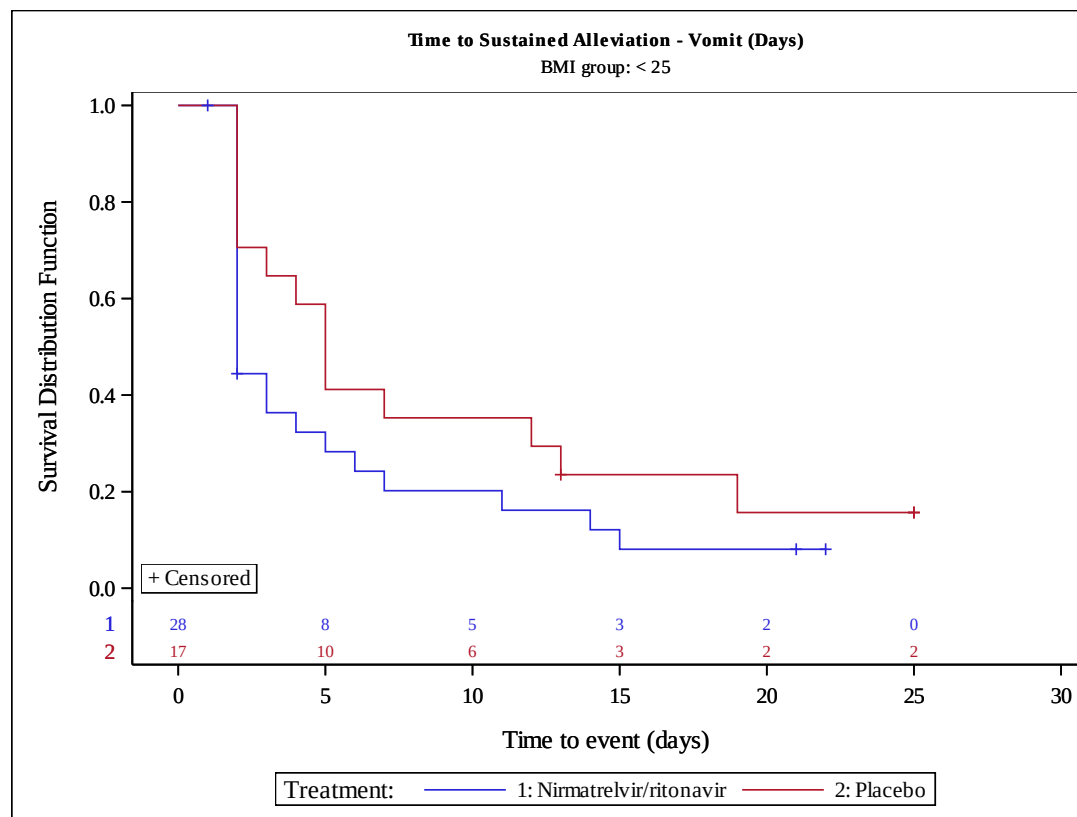
Subgroup Level	Nirmatrelvir/ritonavir (N=119)			Placebo (N=121)			Adjusted Analysis [2]			Unadjusted Analysis [3]		
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus									0.937			0.975
Yes	12/	15 (80.0)	3.0 (2.0, 6.0)	21/	25 (84.0)	3.0 (2.0, 8.0)	1.189 (0.473, 2.991)	0.713		1.090 (0.530, 2.244)	0.814	
No	87/	104 (83.7)	3.0 (2.0, 4.0)	77/	96 (80.2)	3.0 (2.0, 5.0)	1.098 (0.797, 1.511)	0.568		1.112 (0.818, 1.512)	0.500	
Presence of risk factor: Immunosuppression												
Yes	2/	2 (100.0)		3/	3 (100.0)							
No	97/	117 (82.9)		95/	118 (80.5)							
Presence of risk factor: Chronic lung disease									0.931			0.882
Yes	13/	14 (92.9)	3.0 (2.0, 7.0)	5/	5 (100.0)	3.0 (2.0, 8.0)	1.910 (0.446, 8.189)	0.384		0.834 (0.283, 2.455)	0.742	
No	86/	105 (81.9)	3.0 (2.0, 4.0)	93/	116 (80.2)	3.0 (2.0, 5.0)	1.096 (0.804, 1.494)	0.561		1.089 (0.812, 1.462)	0.568	
Presence of risk factor: Hypertension									0.575			0.692
Yes	37/	44 (84.1)	3.0 (2.0, 5.0)	42/	54 (77.8)	4.0 (2.0, 5.0)	1.333 (0.831, 2.139)	0.233		1.184 (0.760, 1.847)	0.455	
No	62/	75 (82.7)	3.0 (2.0, 4.0)	56/	67 (83.6)	3.0 (2.0, 5.0)	1.046 (0.713, 1.534)	0.819		1.066 (0.742, 1.533)	0.728	
Presence of risk factor: Cardiovascular disorder									0.358			0.531
Yes	4/	5 (80.0)	5.0 (2.0, 15.0)	7/	11 (63.6)	2.0 (2.0, NE)	0.736 (0.059, 9.238)	0.812		1.391 (0.403, 4.805)	0.602	
No	95/	114 (83.3)	3.0 (2.0, 4.0)	91/	110 (82.7)	3.0 (2.0, 5.0)	1.068 (0.791, 1.442)	0.668		1.072 (0.804, 1.430)	0.636	
Presence of risk factor: Chronic kidney disease												
Yes	0/	1 (0.0)		3/	3 (100.0)							
No	99/	118 (83.9)		95/	118 (80.5)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	99/	119 (83.2)		97/	120 (80.8)							
Presence of risk factor: Sickle Cell Disease												
No	99/	119 (83.2)		98/	121 (81.0)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	1/	1 (100.0)		0								
No	98/	118 (83.1)		98/	121 (81.0)							
Presence of risk factor: Cancer												
Yes	0			1/	1 (100.0)							
No	99/	119 (83.2)		97/	120 (80.8)							
Presence of risk factor: Device Dependence												
Yes	0			0								
No	99/	118 (83.9)		98/	119 (82.4)							

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 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Vomit

Final

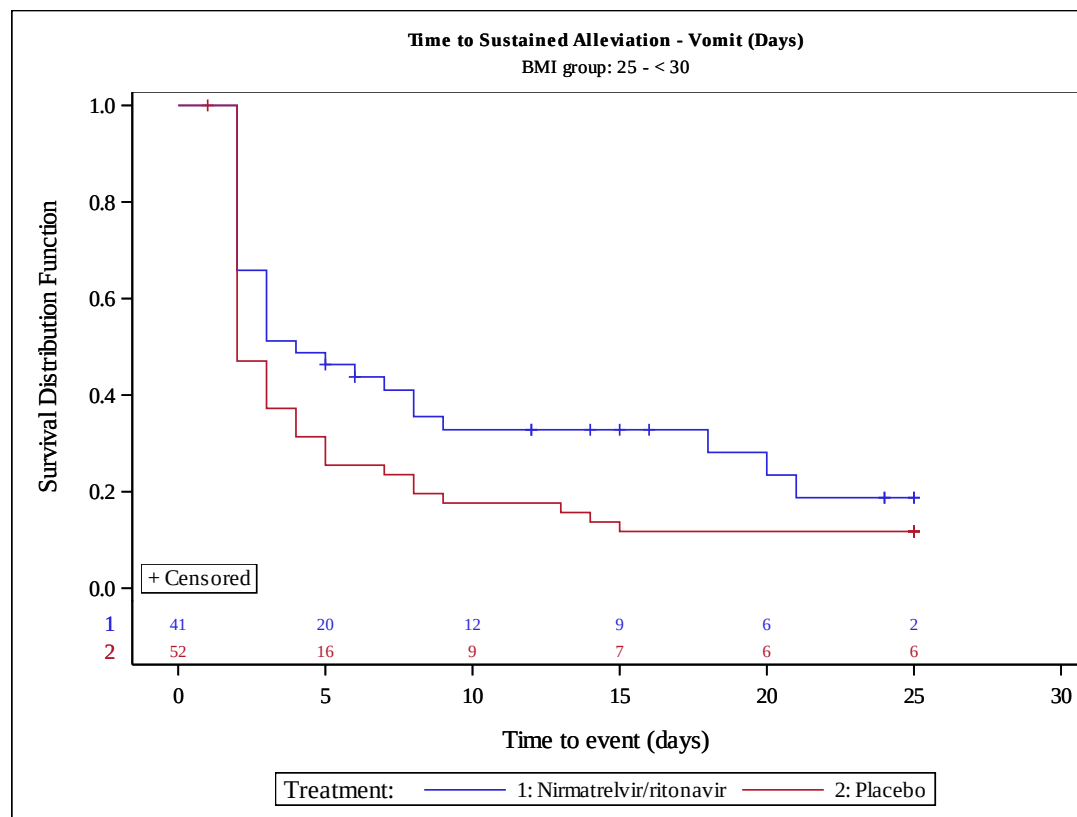


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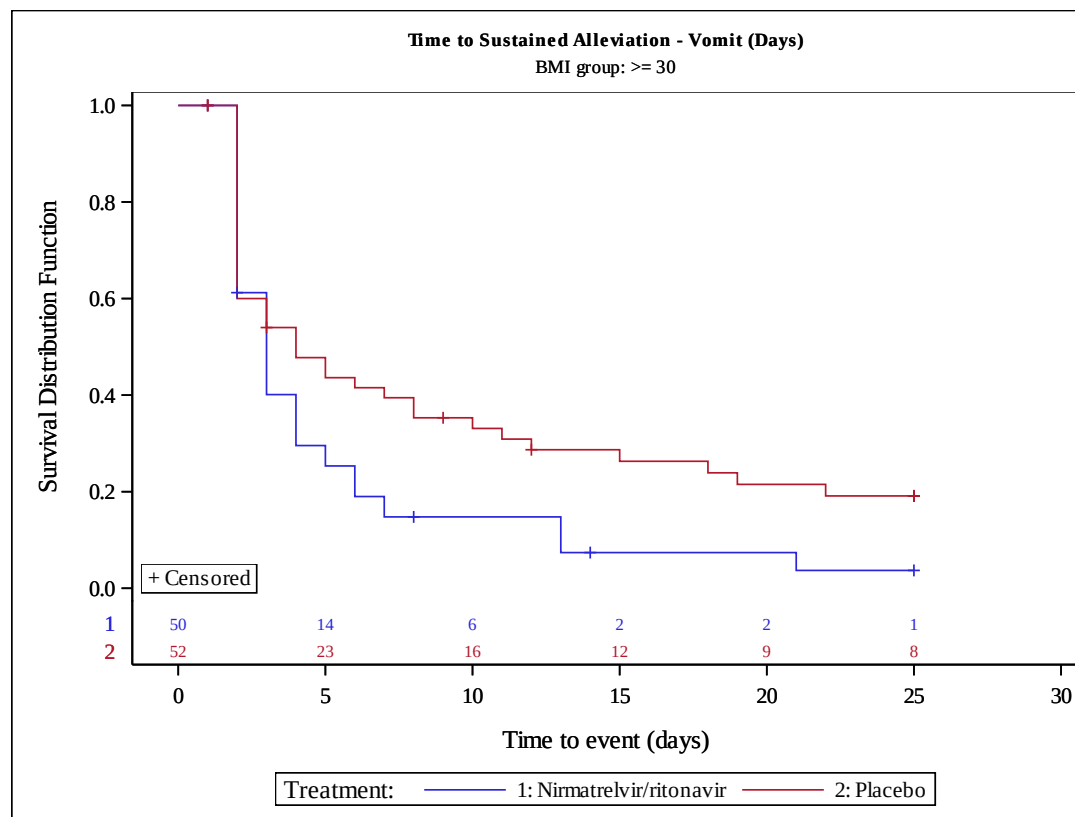


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Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Vomit - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=3)				Placebo (N=2)				Adjusted Analysis [2]		Interaction		Unadjusted Analysis [3]		Interaction	
	n/N	(%)	Median	(95% CI) [1]	n/N	(%)	Median	(95% CI) [1]	Hazard Ratio (95% CI)	p-Value	p-Value	Hazard Ratio (95% CI)	p-Value	p-Value		
Age																
< 65	2/	3 (66.7)			1/	2 (50.0)										
>= 65	0				0											
Gender																
Male	0				0											
Female	2/	3 (66.7)			1/	2 (50.0)										
Geographic region																
United States	0				1/	1 (100.0)										
Europe	1/	1 (100.0)			0											
India	0				0											
Rest of World	1/	2 (50.0)			0/	1 (0.0)										
COVID-19 therapeutic mAb treatment at randomisation																
Yes	0				0											
No	2/	3 (66.7)			1/	2 (50.0)										
Baseline viral load 1																
< 10^4 copies/mL	0				0											
>= 10^4 copies/mL	2/	3 (66.7)			1/	2 (50.0)										
Baseline viral load 2																
< 10^7 copies/mL	1/	2 (50.0)			1/	2 (50.0)										
>= 10^7 copies/mL	1/	1 (100.0)			0											
Baseline serology status																
Negative	2/	3 (66.7)			0/	1 (0.0)										
Positive	0				1/	1 (100.0)										
Symptom onset days to first dose date																
<= 3	2/	2 (100.0)			1/	2 (50.0)										
> 3	0/	1 (0.0)			0											
BMI group																
< 25	2/	2 (100.0)			0											
25 - < 30	0/	1 (0.0)			0/	1 (0.0)										
>= 30	0				1/	1 (100.0)										
Ethnicity																
White	2/	3 (66.7)			1/	2 (50.0)										
Black or African American	0				0											
Asian	0				0											
Others	0				0											
Number of baseline comorbidities present																
0-1	1/	2 (50.0)			1/	1 (100.0)										
2-3	1/	1 (100.0)			0/	1 (0.0)										
>= 4	0				0											
Presence of risk factor: Smoking																
Yes	0/	1 (0.0)			0											
No	2/	2 (100.0)			1/	2 (50.0)										

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Subgroup Level	Nirmatrelvir/ritonavir (N=3)			Placebo (N=2)			Adjusted Analysis [2]			Unadjusted Analysis [3]			
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	
Presence of risk factor: Diabetes mellitus													
Yes	0			0/	1 (0.0)								
No	2/	3 (66.7)		1/	1 (100.0)								
Presence of risk factor: Immunosuppression													
Yes	0			0									
No	2/	3 (66.7)		1/	2 (50.0)								
Presence of risk factor: Chronic lung disease													
Yes	1/	1 (100.0)		0									
No	1/	2 (50.0)		1/	2 (50.0)								
Presence of risk factor: Hypertension													
Yes	1/	1 (100.0)		0/	1 (0.0)								
No	1/	2 (50.0)		1/	1 (100.0)								
Presence of risk factor: Cardiovascular disorder													
Yes	1/	1 (100.0)		0/	1 (0.0)								
No	1/	2 (50.0)		1/	1 (100.0)								
Presence of risk factor: Chronic kidney disease													
Yes	0			0									
No	2/	3 (66.7)		1/	2 (50.0)								
Presence of risk factor: HIV Infection													
Yes	0			0									
No	2/	3 (66.7)		1/	2 (50.0)								
Presence of risk factor: Sickle Cell Disease													
No	2/	3 (66.7)		1/	2 (50.0)								
Presence of risk factor: Neurodevelopmental Disorder													
Yes	0			0									
No	2/	3 (66.7)		1/	2 (50.0)								
Presence of risk factor: Cancer													
Yes	0			0									
No	2/	3 (66.7)		1/	2 (50.0)								
Presence of risk factor: Device Dependence													
Yes	0			0									
No	2/	3 (66.7)		1/	2 (50.0)								

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Subgroup Level	Nirmatrelvir/ritonavir (N=119)			Placebo (N=121)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	87/ 105	(82.9)	3.0 (3.0, 5.0)	77/ 96	(80.2)	4.0 (2.0, 5.0)	1.108 (0.801, 1.533)	0.535		0.943	1.103 (0.811, 1.500)	0.534		0.766
>= 65	12/ 14	(85.7)	2.5 (2.0, 4.0)	21/ 25	(84.0)	3.0 (2.0, 5.0)	1.232 (0.559, 2.714)	0.606			1.182 (0.579, 2.412)	0.646		
Gender														
Male	36/ 44	(81.8)	3.0 (2.0, 5.0)	43/ 53	(81.1)	3.0 (2.0, 5.0)	1.029 (0.632, 1.676)	0.907		0.478	1.008 (0.646, 1.573)	0.971		0.675
Female	63/ 75	(84.0)	3.0 (3.0, 5.0)	55/ 68	(80.9)	4.0 (3.0, 7.0)	1.207 (0.825, 1.767)	0.332			1.165 (0.811, 1.674)	0.409		
Geographic region														
United States	60/ 73	(82.2)	3.0 (3.0, 6.0)	51/ 65	(78.5)	4.0 (2.0, 8.0)	1.085 (0.734, 1.605)	0.683		0.661	1.153 (0.792, 1.678)	0.458		0.758
Europe	19/ 22	(86.4)	2.0 (2.0, 4.0)	23/ 28	(82.1)	2.0 (2.0, 4.0)	1.178 (0.618, 2.247)	0.619			1.246 (0.674, 2.302)	0.483		
India	10/ 10	(100.0)	2.0 (2.0, 3.0)	12/ 12	(100.0)	4.0 (2.0, 5.0)	3.187 (0.922, 11.014)	0.067			1.327 (0.547, 3.217)	0.532		
Rest of World	10/ 14	(71.4)	10.5 (2.0, 20.0)	12/ 16	(75.0)	7.0 (2.0, 12.0)	0.775 (0.327, 1.835)	0.562			0.742 (0.319, 1.725)	0.488		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	10/ 13	(76.9)	4.5 (2.0, 14.0)	14/ 18	(77.8)	4.0 (2.0, 14.0)	1.020 (0.420, 2.478)	0.965		0.866	1.106 (0.489, 2.502)	0.809		0.977
No	89/ 106	(84.0)	3.0 (2.0, 4.0)	84/ 103	(81.6)	3.0 (2.0, 5.0)	1.129 (0.823, 1.550)	0.452			1.095 (0.812, 1.477)	0.551		
Baseline viral load 1														
< 10^4 copies/mL	41/ 48	(85.4)	3.0 (2.0, 7.0)	37/ 43	(86.0)	4.0 (2.0, 5.0)	1.021 (0.649, 1.606)	0.930		0.499	0.993 (0.635, 1.551)	0.974		0.599
>= 10^4 copies/mL	52/ 65	(80.0)	3.0 (2.0, 5.0)	58/ 74	(78.4)	4.0 (2.0, 7.0)	1.174 (0.794, 1.736)	0.421			1.147 (0.788, 1.670)	0.473		
Baseline viral load 2														
< 10^7 copies/mL	73/ 92	(79.3)	4.0 (3.0, 6.0)	77/ 97	(79.4)	4.0 (3.0, 5.0)	1.062 (0.766, 1.470)	0.719		0.681	1.060 (0.769, 1.460)	0.724		0.717
>= 10^7 copies/mL	20/ 21	(95.2)	2.5 (2.0, 5.0)	18/ 20	(90.0)	2.0 (2.0, 7.0)	1.263 (0.603, 2.649)	0.536			1.342 (0.695, 2.590)	0.381		
Baseline serology status														
Negative	37/ 45	(82.2)	4.0 (3.0, 7.0)	39/ 54	(72.2)	5.0 (2.0, 9.0)	1.267 (0.786, 2.041)	0.331		0.422	1.280 (0.814, 2.011)	0.285		0.361
Positive	60/ 72	(83.3)	3.0 (2.0, 4.0)	58/ 66	(87.9)	3.0 (2.0, 4.0)	1.043 (0.712, 1.526)	0.830			0.959 (0.668, 1.377)	0.822		
Symptom onset days to first dose date														
<= 3	60/ 72	(83.3)	3.0 (2.0, 6.0)	62/ 76	(81.6)	3.0 (2.0, 5.0)	1.113 (0.765, 1.620)	0.577		0.918	1.106 (0.774, 1.582)	0.579		0.991
> 3	39/ 47	(83.0)	3.0 (2.0, 5.0)	36/ 45	(80.0)	4.0 (2.0, 8.0)	1.098 (0.678, 1.780)	0.703			1.092 (0.694, 1.720)	0.703		
BMI group														
< 25	24/ 28	(85.7)	2.0 (2.0, 5.0)	14/ 17	(82.4)	5.0 (2.0, 13.0)	1.757 (0.805, 3.836)	0.157		0.046	1.401 (0.721, 2.724)	0.320		0.030
25 - < 30	30/ 41	(73.2)	5.0 (3.0, 9.0)	45/ 52	(86.5)	2.0 (2.0, 4.0)	0.707 (0.429, 1.165)	0.173			0.688 (0.432, 1.094)	0.114		
>= 30	45/ 50	(90.0)	3.0 (2.0, 4.0)	39/ 52	(75.0)	4.0 (3.0, 9.0)	1.576 (0.982, 2.529)	0.060			1.574 (1.016, 2.439)	0.042		
Ethnicity														
White	74/ 91	(81.3)	3.0 (2.0, 4.0)	80/ 99	(80.8)	3.0 (2.0, 5.0)	1.085 (0.780, 1.509)	0.628		0.861	1.128 (0.821, 1.549)	0.458		0.945
Black or African American	6/ 7	(85.7)	7.0 (3.0, 17.0)	2/ 3	(66.7)	15.0 (11.0, 19.0)	1.448 (0.072, 29.144)	0.809			4.368 (0.497, 38.427)	0.184		
Asian	11/ 11	(100.0)	2.0 (2.0, 3.0)	14/ 14	(100.0)	4.0 (2.0, 5.0)	3.329 (0.989, 11.211)	0.052			1.345 (0.585, 3.090)	0.485		
Others	8/ 10	(80.0)	8.0 (2.0, 20.0)	2/ 5	(40.0)	6.0 (2.0, 6.0)	0.440 (0.069, 2.804)	0.385			0.658 (0.127, 3.420)	0.619		
Number of baseline comorbidities present														
0-1	76/ 90	(84.4)		68/ 81	(84.0)									
2-3	22/ 28	(78.6)		28/ 38	(73.7)									
>= 4	1/ 1	(100.0)		2/ 2	(100.0)									
Presence of risk factor: Smoking														
Yes	42/ 53	(79.2)	3.5 (3.0, 6.0)	37/ 48	(77.1)	5.0 (2.0, 7.0)	1.152 (0.709, 1.871)	0.568		0.862	1.132 (0.726, 1.764)	0.584		0.780
No	56/ 65	(86.2)	3.0 (2.0, 4.0)	61/ 73	(83.6)	3.0 (2.0, 5.0)	1.105 (0.751, 1.624)	0.613			1.078 (0.749, 1.551)	0.687		

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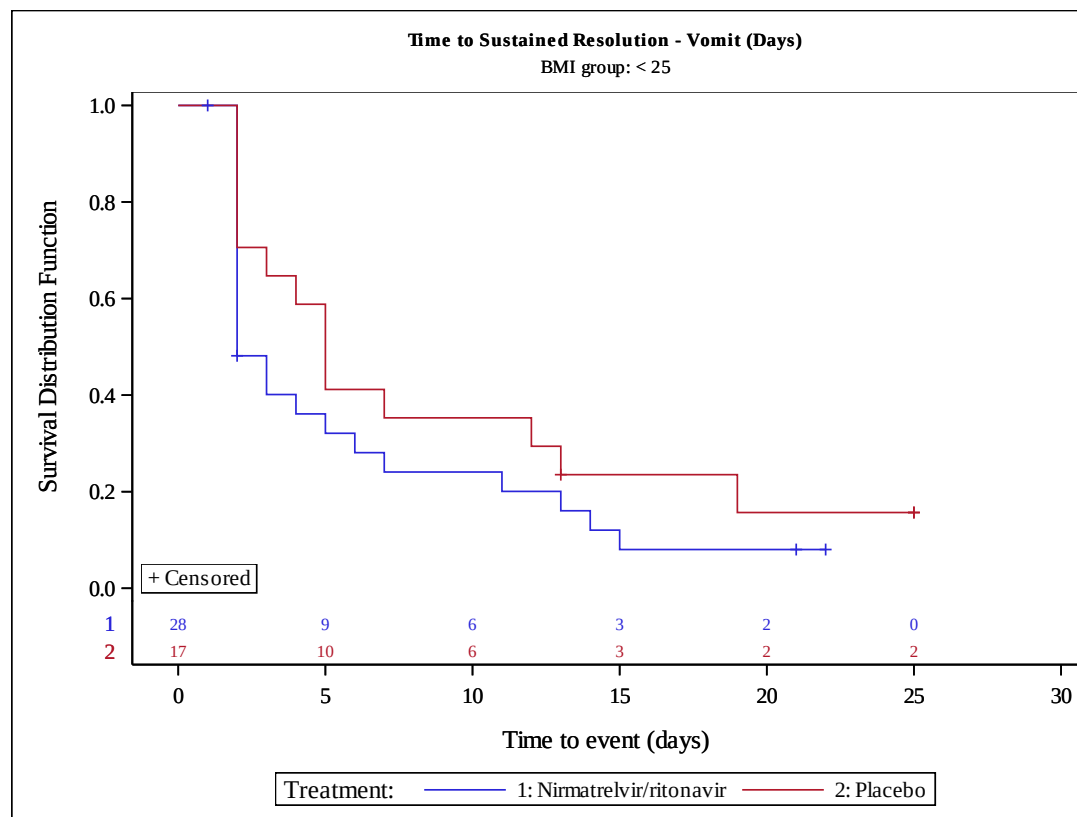
Subgroup Level	Nirmatrelvir/ritonavir (N=119)			Placebo (N=121)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Presence of risk factor: Diabetes mellitus									0.856			0.980
Yes	12/	15 (80.0)	3.0 (2.0, 6.0)	21/	25 (84.0)	3.0 (2.0, 8.0)	1.189 (0.473, 2.991)	0.713		1.090 (0.530, 2.244)	0.814	
No	87/	104 (83.7)	3.0 (3.0, 5.0)	77/	96 (80.2)	4.0 (2.0, 5.0)	1.088 (0.789, 1.499)	0.607		1.103 (0.811, 1.499)	0.533	
Presence of risk factor: Immunosuppression												
Yes	2/	2 (100.0)		3/	3 (100.0)							
No	97/	117 (82.9)		95/	118 (80.5)							
Presence of risk factor: Chronic lung disease									0.747			0.722
Yes	13/	14 (92.9)	3.0 (2.0, 9.0)	5/	5 (100.0)	3.0 (2.0, 8.0)	1.602 (0.324, 7.914)	0.563		0.683 (0.227, 2.055)	0.498	
No	86/	105 (81.9)	3.0 (3.0, 4.0)	93/	116 (80.2)	4.0 (2.0, 5.0)	1.098 (0.806, 1.497)	0.552		1.091 (0.813, 1.464)	0.562	
Presence of risk factor: Hypertension									0.551			0.678
Yes	37/	44 (84.1)	3.0 (2.0, 5.0)	42/	54 (77.8)	4.0 (2.0, 5.0)	1.340 (0.835, 2.150)	0.225		1.177 (0.755, 1.836)	0.471	
No	62/	75 (82.7)	3.0 (2.0, 5.0)	56/	67 (83.6)	3.0 (2.0, 6.0)	1.029 (0.700, 1.513)	0.884		1.053 (0.733, 1.513)	0.780	
Presence of risk factor: Cardiovascular disorder									0.267			0.418
Yes	4/	5 (80.0)	5.0 (2.0, 15.0)	7/	11 (63.6)	9.0 (2.0, NE)	0.708 (0.055, 9.153)	0.791		1.564 (0.450, 5.434)	0.482	
No	95/	114 (83.3)	3.0 (3.0, 4.0)	91/	110 (82.7)	4.0 (2.0, 5.0)	1.048 (0.776, 1.416)	0.760		1.052 (0.789, 1.403)	0.731	
Presence of risk factor: Chronic kidney disease												
Yes	0/	1 (0.0)		3/	3 (100.0)							
No	99/	118 (83.9)		95/	118 (80.5)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	99/	119 (83.2)		97/	120 (80.8)							
Presence of risk factor: Sickel Cell Disease												
No	99/	119 (83.2)		98/	121 (81.0)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	1/	1 (100.0)		0								
No	98/	118 (83.1)		98/	121 (81.0)							
Presence of risk factor: Cancer												
Yes	0			1/	1 (100.0)							
No	99/	119 (83.2)		97/	120 (80.8)							
Presence of risk factor: Device Dependence												
Yes	0			0								
No	99/	118 (83.9)		98/	119 (82.4)							

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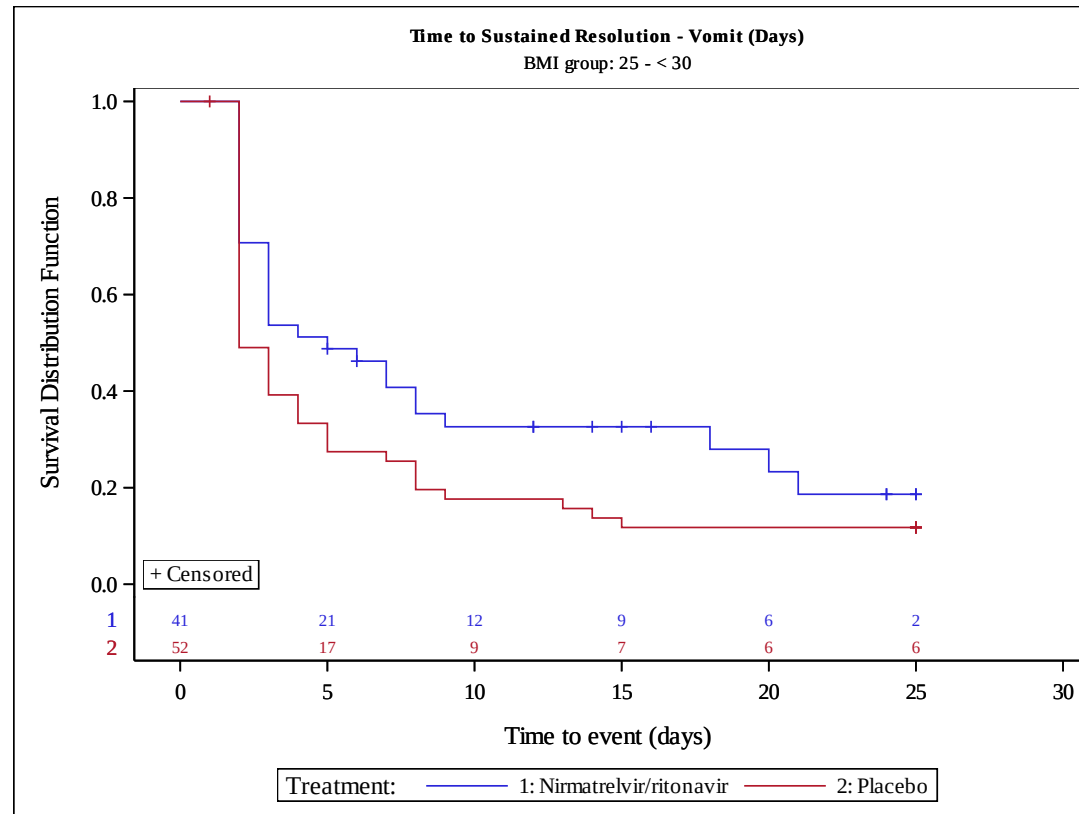
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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Vomit

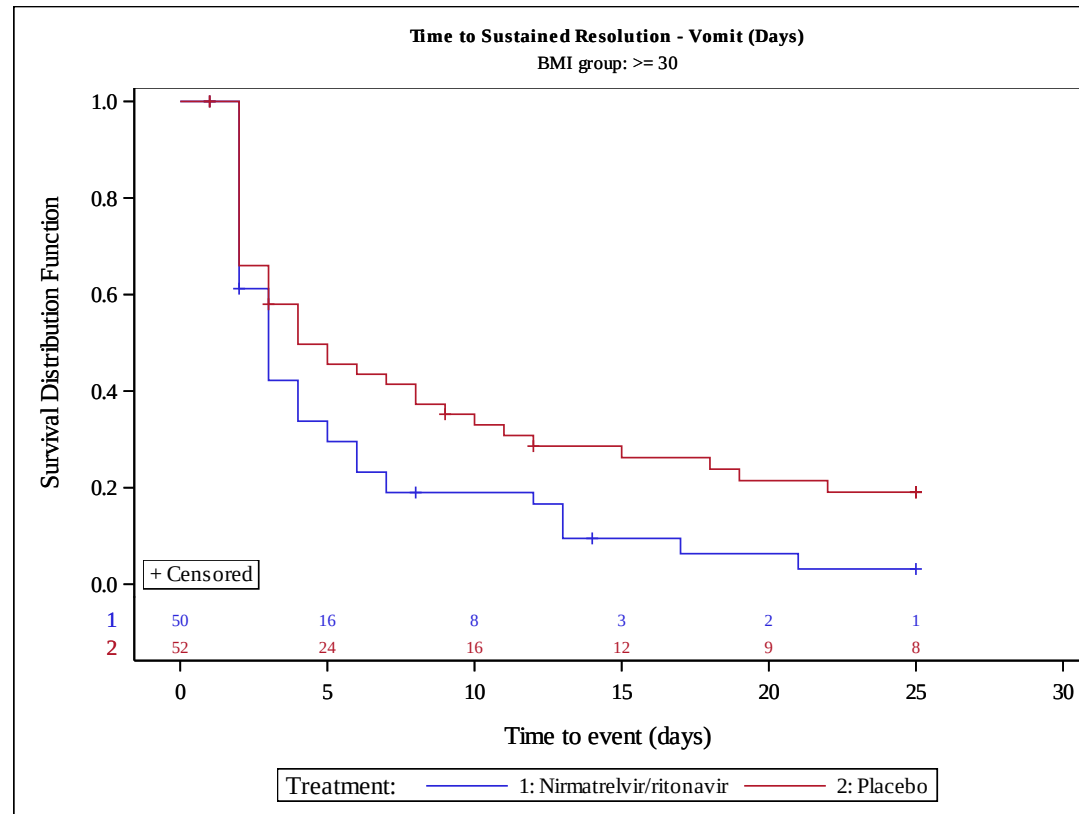
Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Vomit

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Vomit - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=3)			Placebo (N=2)			Adjusted Analysis [2]			Unadjusted Analysis [3]		
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value
Age												
< 65	2/	3 (66.7)		1/	2 (50.0)							
>= 65	0			0								
Gender												
Male	0			0								
Female	2/	3 (66.7)		1/	2 (50.0)							
Geographic region												
United States	0			1/	1 (100.0)							
Europe	1/	1 (100.0)		0								
India	0			0								
Rest of World	1/	2 (50.0)		0/	1 (0.0)							
COVID-19 therapeutic mAb treatment at randomisation												
Yes	0			0								
No	2/	3 (66.7)		1/	2 (50.0)							
Baseline viral load 1												
< 10^4 copies/mL	0			0								
>= 10^4 copies/mL	2/	3 (66.7)		1/	2 (50.0)							
Baseline viral load 2												
< 10^7 copies/mL	1/	2 (50.0)		1/	2 (50.0)							
>= 10^7 copies/mL	1/	1 (100.0)		0								
Baseline serology status												
Negative	2/	3 (66.7)		0/	1 (0.0)							
Positive	0			1/	1 (100.0)							
Symptom onset days to first dose date												
<= 3	2/	2 (100.0)		1/	2 (50.0)							
> 3	0/	1 (0.0)		0								
BMI group												
< 25	2/	2 (100.0)		0								
25 - < 30	0/	1 (0.0)		0/	1 (0.0)							
>= 30	0			1/	1 (100.0)							
Ethnicity												
White	2/	3 (66.7)		1/	2 (50.0)							
Black or African American	0			0								
Asian	0			0								
Others	0			0								
Number of baseline comorbidities present												
0-1	1/	2 (50.0)		1/	1 (100.0)							
2-3	1/	1 (100.0)		0/	1 (0.0)							
>= 4	0			0								
Presence of risk factor: Smoking												
Yes	0/	1 (0.0)		0								
No	2/	2 (100.0)		1/	2 (50.0)							

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=3)			Placebo (N=2)			Adjusted Analysis [2]			Unadjusted Analysis [3]			
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	
Presence of risk factor: Diabetes mellitus													
Yes	0			0/	1 (0.0)								
No	2/	3 (66.7)		1/	1 (100.0)								
Presence of risk factor: Immunosuppression													
Yes	0			0									
No	2/	3 (66.7)		1/	2 (50.0)								
Presence of risk factor: Chronic lung disease													
Yes	1/	1 (100.0)		0									
No	1/	2 (50.0)		1/	2 (50.0)								
Presence of risk factor: Hypertension													
Yes	1/	1 (100.0)		0/	1 (0.0)								
No	1/	2 (50.0)		1/	1 (100.0)								
Presence of risk factor: Cardiovascular disorder													
Yes	1/	1 (100.0)		0/	1 (0.0)								
No	1/	2 (50.0)		1/	1 (100.0)								
Presence of risk factor: Chronic kidney disease													
Yes	0			0									
No	2/	3 (66.7)		1/	2 (50.0)								
Presence of risk factor: HIV Infection													
Yes	0			0									
No	2/	3 (66.7)		1/	2 (50.0)								
Presence of risk factor: Sickle Cell Disease													
No	2/	3 (66.7)		1/	2 (50.0)								
Presence of risk factor: Neurodevelopmental Disorder													
Yes	0			0									
No	2/	3 (66.7)		1/	2 (50.0)								
Presence of risk factor: Cancer													
Yes	0			0									
No	2/	3 (66.7)		1/	2 (50.0)								
Presence of risk factor: Device Dependence													
Yes	0			0									
No	2/	3 (66.7)		1/	2 (50.0)								

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Diarrhea - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Unadjusted analysis [2]			
			Relative Risk (95% CI)		p-Value	Interaction p-Value	Relative Risk (95% CI)		p-Value	Interaction p-Value
Age						0.677				0.707
< 65	202/ 790 (25.6)	184/ 810 (22.7)	1.112 (0.936, 1.321)		0.225		1.126 (0.946, 1.340)		0.183	
>= 65	34/ 138 (24.6)	29/ 145 (20.0)	1.217 (0.785, 1.886)		0.381		1.232 (0.796, 1.907)		0.350	
Gender						0.854				0.516
Male	114/ 463 (24.6)	104/ 507 (20.5)	1.149 (0.910, 1.450)		0.243		1.200 (0.950, 1.517)		0.126	
Female	122/ 465 (26.2)	109/ 448 (24.3)	1.107 (0.890, 1.378)		0.361		1.078 (0.862, 1.348)		0.508	
Geographic region						0.647				0.672
United States	96/ 375 (25.6)	80/ 387 (20.7)	1.214 (0.939, 1.568)		0.139		1.238 (0.954, 1.607)		0.108	
Europe	77/ 322 (23.9)	69/ 321 (21.5)	1.102 (0.822, 1.476)		0.516		1.112 (0.836, 1.480)		0.465	
India	9/ 74 (12.2)	6/ 78 (7.7)	1.636 (0.657, 4.072)		0.290		1.581 (0.592, 4.225)		0.361	
Rest of World	54/ 157 (34.4)	58/ 169 (34.3)	1.023 (0.756, 1.383)		0.883		1.002 (0.742, 1.353)		0.989	
COVID-19 therapeutic mAb treatment at randomisation						0.965				0.877
Yes	17/ 57 (29.8)	15/ 60 (25.0)	1.185 (0.674, 2.084)		0.555		1.193 (0.660, 2.157)		0.559	
No	219/ 871 (25.1)	198/ 895 (22.1)	1.129 (0.956, 1.334)		0.153		1.137 (0.961, 1.345)		0.136	
Baseline viral load 1						0.118				0.118
< 10 ⁴ copies/mL	45/ 335 (13.4)	54/ 354 (15.3)	0.869 (0.599, 1.261)		0.460		0.881 (0.611, 1.270)		0.496	
>= 10 ⁴ copies/mL	187/ 569 (32.9)	155/ 575 (27.0)	1.204 (1.007, 1.439)		0.042		1.219 (1.020, 1.458)		0.030	
Baseline viral load 2						0.124				0.088
< 10 ⁷ copies/mL	137/ 652 (21.0)	145/ 699 (20.7)	1.022 (0.834, 1.253)		0.835		1.013 (0.823, 1.247)		0.903	
>= 10 ⁷ copies/mL	95/ 252 (37.7)	64/ 230 (27.8)	1.307 (1.007, 1.696)		0.044		1.355 (1.043, 1.760)		0.023	
Baseline serology status						0.967				0.743
Negative	133/ 435 (30.6)	121/ 456 (26.5)	1.128 (0.916, 1.390)		0.256		1.152 (0.936, 1.419)		0.182	
Positive	96/ 482 (19.9)	89/ 487 (18.3)	1.140 (0.891, 1.458)		0.297		1.090 (0.841, 1.413)		0.516	
Symptom onset days to first dose date						0.523				0.465
<= 3	154/ 624 (24.7)	141/ 624 (22.6)	1.088 (0.893, 1.326)		0.402		1.092 (0.894, 1.334)		0.387	
> 3	82/ 304 (27.0)	72/ 331 (21.8)	1.225 (0.933, 1.607)		0.144		1.240 (0.941, 1.634)		0.126	
BMI group						0.352				0.209
< 25	36/ 215 (16.7)	42/ 213 (19.7)	0.938 (0.626, 1.406)		0.758		0.849 (0.568, 1.270)		0.426	
25 - < 30	77/ 319 (24.1)	60/ 332 (18.1)	1.322 (0.976, 1.790)		0.072		1.336 (0.989, 1.804)		0.059	
>= 30	123/ 393 (31.3)	111/ 410 (27.1)	1.074 (0.866, 1.331)		0.517		1.156 (0.931, 1.435)		0.188	
Ethnicity						0.966				0.950
White	179/ 699 (25.6)	159/ 718 (22.1)	1.151 (0.956, 1.386)		0.137		1.156 (0.960, 1.393)		0.127	
Black or African American	9/ 43 (20.9)	8/ 40 (20.0)	1.032 (0.420, 2.532)		0.946		1.047 (0.448, 2.447)		0.916	
Asian	20/ 117 (17.1)	22/ 127 (17.3)	NE (NE, NE)		NE		0.987 (0.569, 1.712)		0.962	
Others	28/ 69 (40.6)	24/ 70 (34.3)	NE (NE, NE)		NE		1.184 (0.768, 1.823)		0.445	
Number of baseline comorbidities present						0.387				0.169
0-1	187/ 710 (26.3)	157/ 728 (21.6)	1.179 (0.982, 1.417)		0.078		1.221 (1.015, 1.470)		0.034	
2-3	47/ 214 (22.0)	55/ 221 (24.9)	0.930 (0.666, 1.299)		0.670		0.882 (0.628, 1.241)		0.472	
>= 4	2/ 4 (50.0)	1/ 6 (16.7)	NE (NE, NE)		NE		3.000 (0.390, 23.072)		0.291	
Presence of risk factor: Smoking						0.028				0.052
Yes	79/ 417 (18.9)	90/ 438 (20.5)	0.889 (0.679, 1.164)		0.394		0.922 (0.703, 1.209)		0.557	
No	156/ 509 (30.6)	123/ 517 (23.8)	1.295 (1.060, 1.583)		0.011		1.288 (1.052, 1.577)		0.014	
Presence of risk factor: Diabetes mellitus						0.007				0.003

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928)		Placebo (N=955)		Adjusted analysis [1]			Interaction p-Value	Unadjusted analysis [2]			Interaction p-Value
	n/N (%)		n/N (%)		Relative Risk (95% CI)		p-Value		Relative Risk (95% CI)		p-Value	
Yes	20/ 130 (15.4)		37/ 136 (27.2)		0.608 (0.381, 0.970)		0.037		0.565 (0.347, 0.921)		0.022	
No	215/ 797 (27.0)		176/ 819 (21.5)		1.225 (1.031, 1.456)		0.021		1.255 (1.055, 1.493)		0.010	
Presence of risk factor: Immunosuppression								0.699			0.540	
Yes	1/ 6 (16.7)		2/ 7 (28.6)		NE (NE, NE)		NE		0.583 (0.069, 4.951)		0.621	
No	234/ 921 (25.4)		211/ 948 (22.3)		1.128 (0.960, 1.324)		0.143		1.142 (0.970, 1.343)		0.110	
Presence of risk factor: Chronic lung disease								0.452			0.353	
Yes	20/ 62 (32.3)		8/ 39 (20.5)		1.363 (0.652, 2.849)		0.411		1.573 (0.769, 3.216)		0.215	
No	215/ 865 (24.9)		205/ 916 (22.4)		1.106 (0.937, 1.305)		0.233		1.111 (0.940, 1.313)		0.219	
Presence of risk factor: Hypertension								0.012			0.050	
Yes	96/ 348 (27.6)		73/ 371 (19.7)		1.430 (1.097, 1.864)		0.008		1.402 (1.074, 1.831)		0.013	
No	139/ 579 (24.0)		140/ 584 (24.0)		0.966 (0.789, 1.182)		0.736		1.001 (0.816, 1.229)		0.989	
Presence of risk factor: Cardiovascular disorder								0.756			0.530	
Yes	12/ 42 (28.6)		15/ 49 (30.6)		NE (NE, NE)		NE		0.933 (0.493, 1.766)		0.832	
No	223/ 885 (25.2)		198/ 906 (21.9)		1.134 (0.962, 1.337)		0.135		1.153 (0.975, 1.363)		0.096	
Presence of risk factor: Chronic kidney disease								0.424			0.427	
Yes	2/ 6 (33.3)		4/ 8 (50.0)		NE (NE, NE)		NE		0.667 (0.177, 2.513)		0.549	
No	233/ 921 (25.3)		209/ 947 (22.1)		1.132 (0.963, 1.330)		0.133		1.146 (0.974, 1.350)		0.101	
Presence of risk factor: HIV Infection												
Yes	0		1/ 1 (100.0)									
No	235/ 927 (25.4)		212/ 953 (22.2)									
Presence of risk factor: Sickle Cell Disease												
No	235/ 927 (25.4)		213/ 955 (22.3)									
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0/ 2 (0.0)		0/ 1 (0.0)									
No	235/ 925 (25.4)		213/ 954 (22.3)									
Presence of risk factor: Cancer								0.831			0.946	
Yes	2/ 5 (40.0)		2/ 6 (33.3)		NE (NE, NE)		NE		1.200 (0.252, 5.709)		0.819	
No	233/ 922 (25.3)		211/ 949 (22.2)		1.128 (0.960, 1.325)		0.143		1.137 (0.966, 1.337)		0.123	
Presence of risk factor: Device Dependence												
Yes	1/ 4 (25.0)		0/ 3 (0.0)									
No	230/ 914 (25.2)		213/ 944 (22.6)									

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[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=254)			Placebo (N=242)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	190/ 225	(84.4)	5.0 (4.0, 6.0)	176/ 212	(83.0)	4.0 (3.0, 5.0)	1.008 (0.816, 1.245)	0.941		0.390	1.022 (0.832, 1.255)	0.836		0.339
>= 65	26/ 29	(89.7)	3.0 (2.0, 6.0)	23/ 30	(76.7)	4.0 (2.0, 9.0)	1.417 (0.776, 2.586)	0.256			1.277 (0.726, 2.245)	0.396		
Gender														
Male	97/ 112	(86.6)	5.0 (3.0, 6.0)	101/ 118	(85.6)	4.0 (3.0, 6.0)	1.132 (0.844, 1.518)	0.407		0.817	1.139 (0.860, 1.508)	0.365		0.635
Female	119/ 142	(83.8)	4.0 (3.0, 6.0)	98/ 124	(79.0)	4.0 (3.0, 5.0)	1.021 (0.774, 1.348)	0.882			1.017 (0.778, 1.329)	0.901		
Geographic region														
United States	123/ 149	(82.6)	6.0 (4.0, 7.0)	112/ 139	(80.6)	5.0 (4.0, 7.0)	0.997 (0.767, 1.294)	0.979		0.811	1.026 (0.794, 1.326)	0.843		0.867
Europe	44/ 48	(91.7)	3.0 (3.0, 5.0)	44/ 54	(81.5)	3.0 (2.0, 5.0)	1.130 (0.729, 1.752)	0.584			1.145 (0.753, 1.743)	0.526		
India	13/ 14	(92.9)	3.0 (2.0, 4.0)	11/ 11	(100.0)	3.0 (2.0, 4.0)	0.879 (0.308, 2.512)	0.810			0.859 (0.379, 1.951)	0.717		
Rest of World	36/ 43	(83.7)	4.0 (3.0, 6.0)	32/ 38	(84.2)	4.0 (3.0, 7.0)	1.063 (0.637, 1.775)	0.814			1.088 (0.674, 1.756)	0.730		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	19/ 24	(79.2)	6.0 (3.0, 8.0)	22/ 26	(84.6)	4.0 (2.0, 10.0)	0.817 (0.427, 1.563)	0.542		0.471	0.836 (0.452, 1.547)	0.568		0.502
No	197/ 230	(85.7)	4.0 (3.0, 6.0)	177/ 216	(81.9)	4.0 (3.0, 5.0)	1.072 (0.870, 1.322)	0.514			1.079 (0.880, 1.322)	0.466		
Baseline viral load 1														
< 10^4 copies/mL	79/ 97	(81.4)	4.0 (3.0, 6.0)	82/ 96	(85.4)	3.0 (2.0, 4.0)	0.832 (0.603, 1.148)	0.263		0.070	0.885 (0.649, 1.206)	0.438		0.170
>= 10^4 copies/mL	126/ 146	(86.3)	5.0 (4.0, 6.0)	111/ 138	(80.4)	6.0 (4.0, 7.0)	1.217 (0.939, 1.577)	0.137			1.175 (0.909, 1.517)	0.218		
Baseline viral load 2														
< 10^7 copies/mL	147/ 179	(82.1)	5.0 (3.0, 6.0)	152/ 184	(82.6)	4.0 (3.0, 5.0)	0.939 (0.746, 1.181)	0.589		0.094	0.959 (0.764, 1.203)	0.715		0.152
>= 10^7 copies/mL	58/ 64	(90.6)	4.0 (3.0, 6.0)	41/ 50	(82.0)	7.0 (3.0, 10.0)	1.476 (0.955, 2.281)	0.079			1.409 (0.941, 2.110)	0.096		
Baseline serology status														
Negative	104/ 119	(87.4)	5.0 (4.0, 6.0)	95/ 118	(80.5)	5.0 (3.0, 7.0)	1.165 (0.870, 1.559)	0.306		0.304	1.157 (0.875, 1.529)	0.306		0.401
Positive	110/ 133	(82.7)	4.0 (3.0, 6.0)	102/ 121	(84.3)	4.0 (2.0, 4.0)	0.945 (0.716, 1.247)	0.689			0.974 (0.743, 1.275)	0.847		
Symptom onset days to first dose date														
<= 3	134/ 155	(86.5)	4.0 (3.0, 6.0)	115/ 137	(83.9)	4.0 (3.0, 6.0)	1.054 (0.814, 1.365)	0.690		0.887	1.087 (0.847, 1.395)	0.514		0.742
> 3	82/ 99	(82.8)	6.0 (3.0, 6.0)	84/ 105	(80.0)	4.0 (3.0, 5.0)	1.025 (0.748, 1.405)	0.879			1.006 (0.742, 1.364)	0.969		
BMI group														
< 25	48/ 55	(87.3)	3.0 (2.0, 4.0)	24/ 29	(82.8)	4.0 (2.0, 10.0)	1.393 (0.814, 2.382)	0.226		0.029	1.410 (0.859, 2.313)	0.174		0.049
25 - < 30	63/ 82	(76.8)	6.0 (4.0, 7.0)	76/ 90	(84.4)	3.0 (3.0, 4.0)	0.739 (0.519, 1.051)	0.092			0.740 (0.529, 1.035)	0.079		
>= 30	105/ 117	(89.7)	6.0 (4.0, 6.0)	99/ 123	(80.5)	6.0 (4.0, 7.0)	1.312 (0.981, 1.754)	0.067			1.171 (0.889, 1.542)	0.261		
Ethnicity														
White	161/ 192	(83.9)	5.0 (4.0, 6.0)	156/ 191	(81.7)	4.0 (3.0, 6.0)	1.032 (0.822, 1.294)	0.787		0.080	1.064 (0.853, 1.326)	0.584		0.091
Black or African American	12/ 16	(75.0)	6.0 (2.0, 13.0)	10/ 12	(83.3)	3.0 (2.0, 9.0)	0.553 (0.195, 1.567)	0.265			0.601 (0.255, 1.413)	0.243		
Asian	23/ 24	(95.8)	3.0 (2.0, 4.0)	25/ 25	(100.0)	3.0 (2.0, 3.0)	0.766 (0.373, 1.572)	0.467			0.813 (0.454, 1.455)	0.485		
Others	20/ 22	(90.9)	5.0 (3.0, 9.0)	8/ 14	(57.1)	11.0 (7.0, NE)	2.319 (0.899, 5.985)	0.082			2.531 (1.102, 5.813)	0.029		
Number of baseline comorbidities present														
0-1	166/ 195	(85.1)		149/ 183	(81.4)									
2-3	49/ 58	(84.5)		49/ 58	(84.5)									
>= 4	1/ 1	(100.0)		1/ 1	(100.0)									
Presence of risk factor: Smoking														
Yes	98/ 118	(83.1)	4.0 (3.0, 6.0)	91/ 108	(84.3)	3.0 (3.0, 5.0)	1.006 (0.738, 1.372)	0.971		0.584	1.040 (0.781, 1.385)	0.788		0.967
No	117/ 135	(86.7)	5.0 (4.0, 6.0)	108/ 134	(80.6)	5.0 (3.0, 6.0)	1.119 (0.854, 1.466)	0.414			1.060 (0.816, 1.378)	0.661		

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=254)			Placebo (N=242)			Adjusted Analysis [2]			Unadjusted Analysis [3]		
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus									0.884			0.969
Yes	28/ 34	(82.4)	4.5 (3.0, 6.0)	26/ 31	(83.9)	3.0 (2.0, 7.0)	1.044 (0.590, 1.846)	0.882		0.996 (0.581, 1.706)	0.989	
No	188/ 220	(85.5)	5.0 (4.0, 6.0)	173/ 211	(82.0)	4.0 (3.0, 5.0)	1.038 (0.839, 1.284)	0.732		1.059 (0.861, 1.302)	0.587	
Presence of risk factor: Immunosuppression												
Yes	4/ 4	(100.0)		5/ 5	(100.0)							
No	212/ 250	(84.8)		194/ 237	(81.9)							
Presence of risk factor: Chronic lung disease									0.907			0.945
Yes	25/ 26	(96.2)	3.0 (2.0, 10.0)	11/ 12	(91.7)	5.0 (2.0, 10.0)	0.899 (0.347, 2.328)	0.827		1.120 (0.537, 2.336)	0.762	
No	191/ 228	(83.8)	5.0 (4.0, 6.0)	188/ 230	(81.7)	4.0 (3.0, 5.0)	1.029 (0.836, 1.268)	0.785		1.038 (0.849, 1.271)	0.714	
Presence of risk factor: Hypertension									0.687			0.829
Yes	69/ 81	(85.2)	4.0 (3.0, 6.0)	83/ 102	(81.4)	3.0 (2.0, 5.0)	1.130 (0.811, 1.574)	0.471		1.077 (0.782, 1.484)	0.649	
No	147/ 173	(85.0)	5.0 (4.0, 6.0)	116/ 140	(82.9)	4.0 (3.0, 7.0)	1.031 (0.802, 1.327)	0.810		1.044 (0.819, 1.332)	0.727	
Presence of risk factor: Cardiovascular disorder									0.868			0.598
Yes	6/ 7	(85.7)	5.0 (3.0, 15.0)	8/ 9	(88.9)	5.0 (2.0, 10.0)	0.790 (0.188, 3.313)	0.747		0.727 (0.247, 2.140)	0.563	
No	210/ 247	(85.0)	4.0 (4.0, 6.0)	191/ 233	(82.0)	4.0 (3.0, 5.0)	1.047 (0.856, 1.282)	0.652		1.065 (0.875, 1.296)	0.530	
Presence of risk factor: Chronic kidney disease												
Yes	1/ 1	(100.0)		3/ 3	(100.0)							
No	215/ 253	(85.0)		196/ 239	(82.0)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	216/ 254	(85.0)		198/ 241	(82.2)							
Presence of risk factor: Sickle Cell Disease												
No	216/ 254	(85.0)		199/ 242	(82.2)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	1/ 1	(100.0)		0								
No	215/ 253	(85.0)		199/ 242	(82.2)							
Presence of risk factor: Cancer												
Yes	1/ 2	(50.0)		1/ 1	(100.0)							
No	215/ 252	(85.3)		198/ 241	(82.2)							
Presence of risk factor: Device Dependence												
Yes	1/ 1	(100.0)		0								
No	213/ 250	(85.2)		199/ 241	(82.6)							

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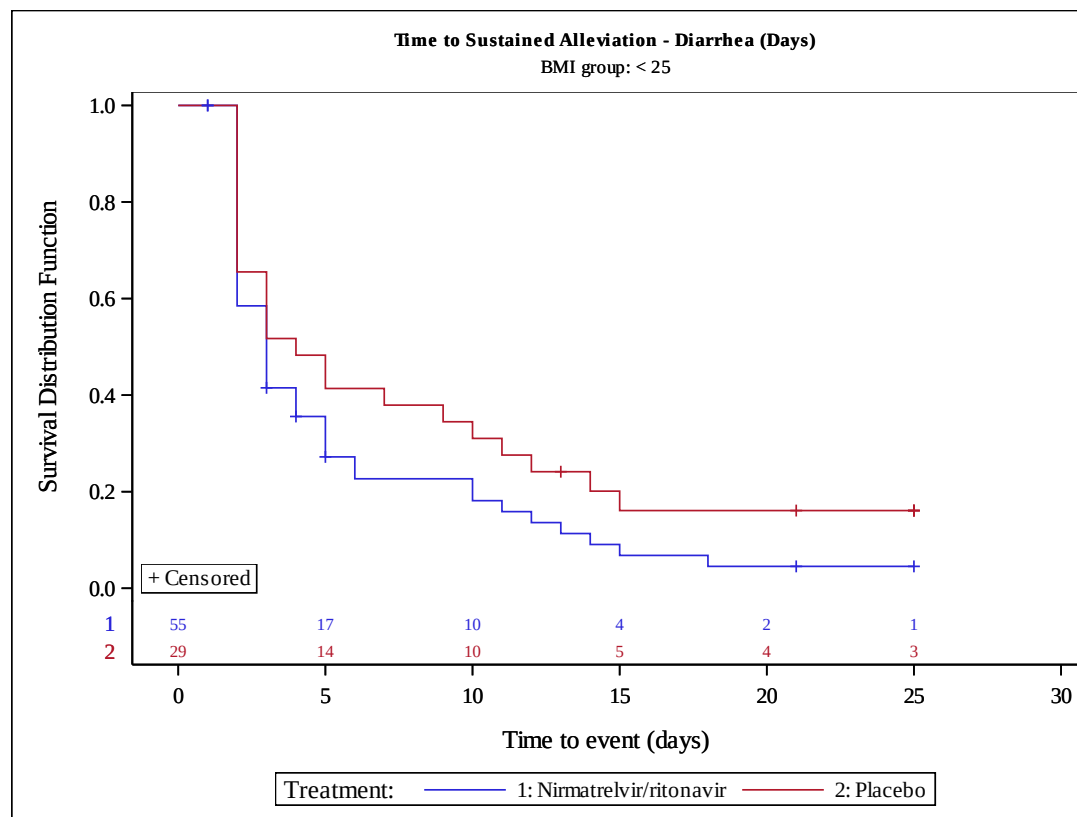
[3] Estimated by cox regression model assuming proportional hazards.

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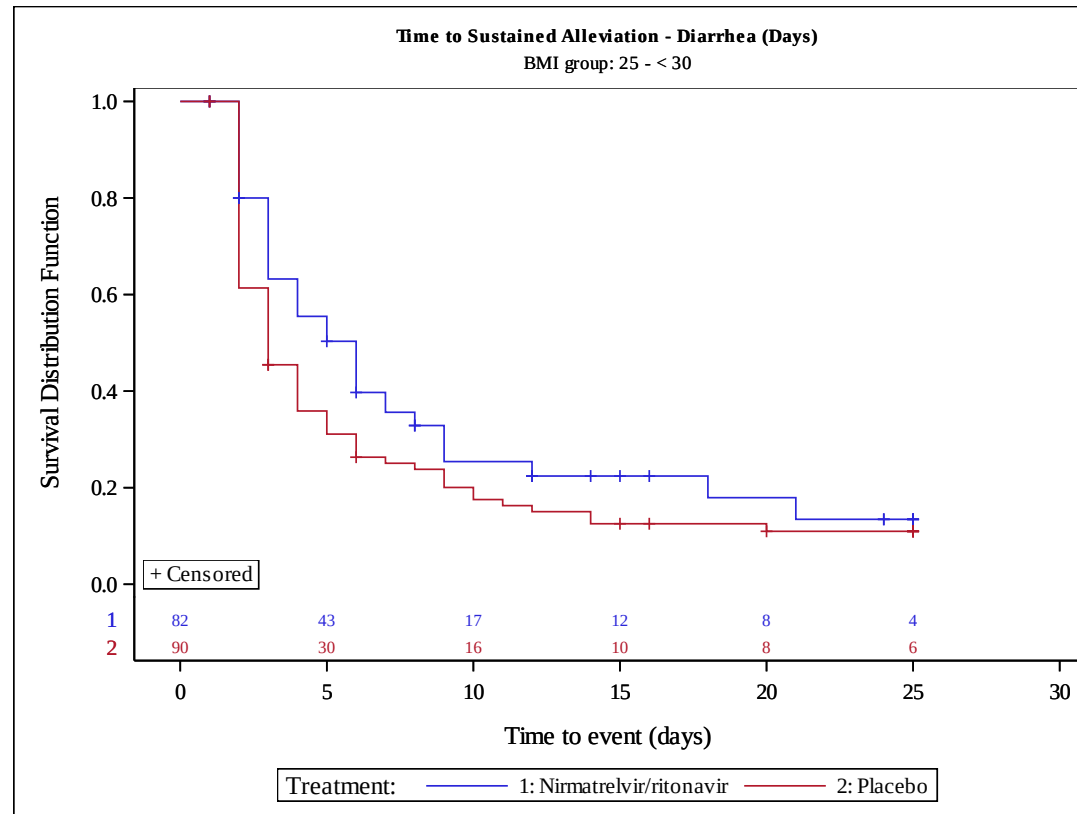
Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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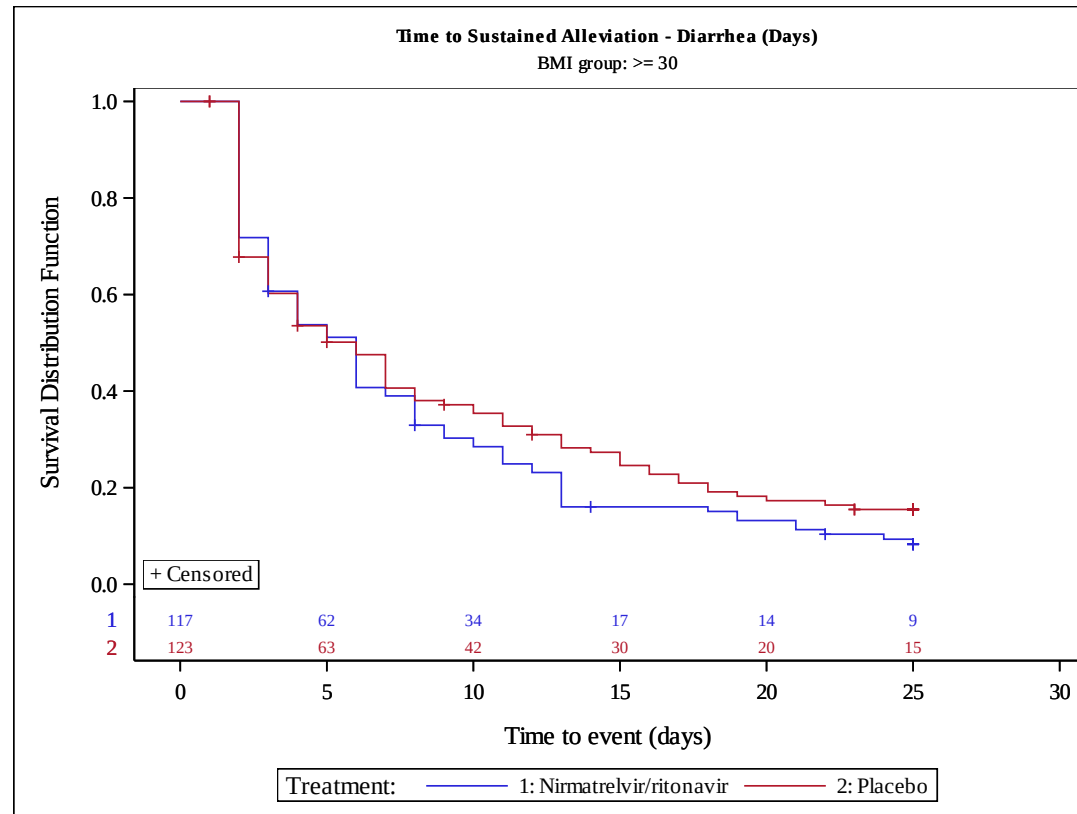
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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea - Subgroup analysis

Subgroup Level	Nirmatrelvir/ritonavir (N=17)			Placebo (N=10)			Adjusted Analysis [2]		Interaction		Unadjusted Analysis [3]			
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)	p-Value	p-Value	Hazard Ratio (95% CI)	p-Value	p-Value	p-Value	
Age														
< 65	14/	17 (82.4)		9/	10 (90.0)									
>= 65	0			0										
Gender									0.610				0.574	
Male	6/	6 (100.0)	3.5 (2.0, 13.0)	4/	4 (100.0)	2.5 (2.0, 17.0)	1.659 (0.153, 17.986)	0.677		1.268 (0.314, 5.123)	0.739			
Female	8/	11 (72.7)	6.0 (2.0, 22.0)	5/	6 (83.3)	14.0 (3.0, 15.0)	0.757 (0.199, 2.875)	0.682		0.841 (0.253, 2.791)	0.777			
Geographic region														
United States	12/	14 (85.7)		6/	7 (85.7)									
Europe	1/	1 (100.0)		0										
India	0			0										
Rest of World	1/	2 (50.0)		3/	3 (100.0)									
COVID-19 therapeutic mAb treatment at randomisation														
Yes	1/	1 (100.0)		0										
No	13/	16 (81.3)		9/	10 (90.0)									
Baseline viral load 1									0.558				0.358	
< 10^4 copies/mL	8/	9 (88.9)	2.0 (2.0, 19.0)	3/	3 (100.0)	15.0 (7.0, 17.0)	1.321 (0.152, 11.510)	0.801		0.991 (0.240, 4.101)	0.990			
>= 10^4 copies/mL	6/	8 (75.0)	5.5 (2.0, NE)	5/	6 (83.3)	8.5 (2.0, 15.0)	0.382 (0.066, 2.224)	0.284		0.761 (0.230, 2.514)	0.654			
Baseline viral load 2														
< 10^7 copies/mL	11/	13 (84.6)		5/	6 (83.3)									
>= 10^7 copies/mL	3/	4 (75.0)		3/	3 (100.0)									
Baseline serology status									0.779				0.867	
Negative	6/	8 (75.0)	9.5 (2.0, NE)	7/	8 (87.5)	14.0 (2.0, 15.0)	1.001 (0.213, 4.704)	0.999		0.629 (0.197, 2.013)	0.435			
Positive	8/	9 (88.9)	2.0 (2.0, 10.0)	2/	2 (100.0)	4.5 (2.0, 7.0)	0.637 (0.035, 11.495)	0.760		0.791 (0.157, 3.975)	0.776			
Symptom onset days to first dose date									0.359				0.234	
<= 3	11/	11 (100.0)	2.0 (2.0, 6.0)	6/	6 (100.0)	5.0 (2.0, 17.0)	1.490 (0.400, 5.552)	0.552		1.306 (0.465, 3.668)	0.613			
> 3	3/	6 (50.0)	19.0 (4.0, NE)	3/	4 (75.0)	14.0 (2.0, 15.0)	0.000 (0.000, NE)	0.999		0.356 (0.059, 2.161)	0.262			
BMI group														
< 25	2/	2 (100.0)		1/	1 (100.0)									
25 - < 30	2/	4 (50.0)		0										
>= 30	10/	11 (90.9)		8/	9 (88.9)									
Ethnicity														
White	11/	14 (78.6)		5/	6 (83.3)									
Black or African American	2/	2 (100.0)		1/	1 (100.0)									
Asian	0			2/	2 (100.0)									
Others	1/	1 (100.0)		1/	1 (100.0)									
Number of baseline comorbidities present														
0-1	11/	14 (78.6)		6/	7 (85.7)									
2-3	3/	3 (100.0)		3/	3 (100.0)									
>= 4	0			0										
Presence of risk factor: Smoking									0.167				0.301	
Yes	4/	6 (66.7)	10.0 (2.0, NE)	5/	5 (100.0)	7.0 (2.0, 17.0)	0.150 (0.013, 1.793)	0.134		0.479 (0.114, 2.024)	0.317			
No	10/	11 (90.9)	4.0 (2.0, 13.0)	4/	5 (80.0)	15.0 (2.0, 15.0)	0.628 (0.129, 3.056)	0.565		1.330 (0.405, 4.366)	0.639			

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Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea - Subgroup analysis

Subgroup Level	Nirmatrelvir/ritonavir (N=17)			Placebo (N=10)			Adjusted Analysis [2]			Unadjusted Analysis [3]			
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	
Presence of risk factor: Diabetes mellitus													
Yes	1/	1 (100.0)		2/	2 (100.0)								
No	13/	16 (81.3)		7/	8 (87.5)								
Presence of risk factor: Immunosuppression													
Yes	1/	1 (100.0)		0									
No	13/	16 (81.3)		9/	10 (90.0)								
Presence of risk factor: Chronic lung disease													
Yes	2/	2 (100.0)		0									
No	12/	15 (80.0)		9/	10 (90.0)								
Presence of risk factor: Hypertension													
Yes	3/	4 (75.0)		4/	5 (80.0)								
No	11/	13 (84.6)		5/	5 (100.0)								
Presence of risk factor: Cardiovascular disorder													
Yes	1/	1 (100.0)		0									
No	13/	16 (81.3)		9/	10 (90.0)								
Presence of risk factor: Chronic kidney disease													
Yes	0			0									
No	14/	17 (82.4)		9/	10 (90.0)								
Presence of risk factor: HIV Infection													
Yes	0			0									
No	14/	17 (82.4)		9/	10 (90.0)								
Presence of risk factor: Sickle Cell Disease													
No	14/	17 (82.4)		9/	10 (90.0)								
Presence of risk factor: Neurodevelopmental Disorder													
Yes	0			0									
No	14/	17 (82.4)		9/	10 (90.0)								
Presence of risk factor: Cancer													
Yes	0			0									
No	14/	17 (82.4)		9/	10 (90.0)								
Presence of risk factor: Device Dependence													
Yes	0			0									
No	14/	17 (82.4)		9/	10 (90.0)								

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=254)			Placebo (N=242)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value	
Age													
< 65	185/ 225	(82.2)	6.0 (6.0, 7.0)	165/ 212	(77.8)	6.0 (4.0, 8.0)	1.087 (0.874, 1.351)	0.455	0.482	1.087 (0.881, 1.342)	0.436	0.362	
>= 65	26/ 29	(89.7)	5.0 (2.0, 7.0)	22/ 30	(73.3)	4.0 (2.0, 9.0)	1.393 (0.760, 2.555)	0.283		1.295 (0.731, 2.296)	0.376		
Gender													
Male	94/ 112	(83.9)	6.0 (5.0, 7.0)	97/ 118	(82.2)	6.0 (4.0, 8.0)	1.187 (0.878, 1.605)	0.264	0.738	1.173 (0.881, 1.562)	0.275	0.922	
Female	117/ 142	(82.4)	6.0 (5.0, 8.0)	90/ 124	(72.6)	5.0 (4.0, 8.0)	1.130 (0.848, 1.506)	0.404		1.095 (0.831, 1.443)	0.518		
Geographic region													
United States	119/ 149	(79.9)	8.0 (6.0, 9.0)	103/ 139	(74.1)	7.0 (5.0, 9.0)	1.042 (0.795, 1.365)	0.764	0.750	1.071 (0.822, 1.395)	0.613	0.783	
Europe	44/ 48	(91.7)	4.0 (3.0, 6.0)	44/ 54	(81.5)	4.0 (2.0, 6.0)	1.168 (0.751, 1.817)	0.491		1.180 (0.774, 1.800)	0.441		
India	13/ 14	(92.9)	3.0 (2.0, 4.0)	11/ 11	(100.0)	3.0 (2.0, 4.0)	1.166 (0.418, 3.251)	0.769		0.931 (0.410, 2.114)	0.864		
Rest of World	35/ 43	(81.4)	5.0 (4.0, 7.0)	29/ 38	(76.3)	7.0 (3.0, 11.0)	1.299 (0.764, 2.210)	0.334		1.315 (0.799, 2.163)	0.281		
COVID-19 therapeutic mAb treatment at randomisation													
Yes	18/ 24	(75.0)	8.0 (4.0, 16.0)	21/ 26	(80.8)	4.0 (2.0, 11.0)	0.693 (0.357, 1.347)	0.280	0.127	0.714 (0.380, 1.343)	0.296	0.151	
No	193/ 230	(83.9)	6.0 (5.0, 7.0)	166/ 216	(76.9)	6.0 (4.0, 8.0)	1.175 (0.947, 1.457)	0.142		1.172 (0.951, 1.443)	0.137		
Baseline viral load 1													
< 10^4 copies/mL	76/ 97	(78.4)	7.0 (5.0, 9.0)	76/ 96	(79.2)	4.0 (3.0, 5.0)	0.850 (0.609, 1.185)	0.338	0.057	0.905 (0.657, 1.245)	0.538	0.142	
>= 10^4 copies/mL	124/ 146	(84.9)	6.0 (5.0, 7.0)	105/ 138	(76.1)	7.0 (5.0, 10.0)	1.318 (1.011, 1.718)	0.041		1.246 (0.960, 1.618)	0.099		
Baseline viral load 2													
< 10^7 copies/mL	143/ 179	(79.9)	6.0 (6.0, 8.0)	143/ 184	(77.7)	5.0 (4.0, 7.0)	0.981 (0.775, 1.243)	0.876	0.067	0.992 (0.786, 1.252)	0.947	0.114	
>= 10^7 copies/mL	57/ 64	(89.1)	6.0 (4.0, 7.0)	38/ 50	(76.0)	9.0 (4.0, 11.0)	1.555 (1.006, 2.406)	0.047		1.525 (1.006, 2.311)	0.047		
Baseline serology status													
Negative	102/ 119	(85.7)	6.0 (6.0, 8.0)	89/ 118	(75.4)	7.0 (5.0, 11.0)	1.253 (0.931, 1.687)	0.137	0.337	1.233 (0.927, 1.641)	0.150	0.387	
Positive	107/ 133	(80.5)	6.0 (5.0, 7.0)	96/ 121	(79.3)	4.0 (3.0, 7.0)	0.991 (0.746, 1.317)	0.950		1.012 (0.767, 1.335)	0.933		
Symptom onset days to first dose date													
<= 3	129/ 155	(83.2)	6.0 (5.0, 7.0)	107/ 137	(78.1)	6.0 (4.0, 9.0)	1.111 (0.850, 1.452)	0.442	0.922	1.143 (0.883, 1.480)	0.309	0.808	
> 3	82/ 99	(82.8)	6.0 (5.0, 8.0)	80/ 105	(76.2)	5.0 (4.0, 8.0)	1.136 (0.824, 1.566)	0.437		1.072 (0.787, 1.460)	0.658		
BMI group													
< 25	48/ 55	(87.3)	4.0 (3.0, 6.0)	22/ 29	(75.9)	5.0 (3.0, 14.0)	1.682 (0.959, 2.950)	0.069	0.051	1.716 (1.025, 2.872)	0.040	0.055	
25 - < 30	62/ 82	(75.6)	6.0 (5.0, 7.0)	73/ 90	(81.1)	4.0 (3.0, 5.0)	0.840 (0.589, 1.198)	0.336		0.812 (0.578, 1.139)	0.228		
>= 30	101/ 117	(86.3)	7.0 (6.0, 9.0)	92/ 123	(74.8)	8.0 (5.0, 11.0)	1.306 (0.968, 1.764)	0.081		1.205 (0.907, 1.601)	0.199		
Ethnicity													
White	158/ 192	(82.3)	6.0 (6.0, 8.0)	148/ 191	(77.5)	6.0 (4.0, 8.0)	1.094 (0.868, 1.379)	0.447	0.078	1.119 (0.893, 1.402)	0.330	0.075	
Black or African American	11/ 16	(68.8)	7.0 (4.0, NE)	9/ 12	(75.0)	3.0 (2.0, 9.0)	0.545 (0.195, 1.525)	0.248		0.543 (0.222, 1.332)	0.183		
Asian	23/ 24	(95.8)	3.0 (2.0, 4.0)	24/ 25	(96.0)	3.0 (2.0, 4.0)	1.202 (0.605, 2.388)	0.600		1.149 (0.647, 2.039)	0.635		
Others	19/ 22	(86.4)	5.5 (3.0, 12.0)	6/ 14	(42.9)	NE (7.0, NE)	1.945 (0.700, 5.403)	0.202		2.758 (1.094, 6.957)	0.032		
Number of baseline comorbidities present													
0-1	161/ 195	(82.6)		140/ 183	(76.5)								
2-3	49/ 58	(84.5)		46/ 58	(79.3)								
>= 4	1/ 1	(100.0)		1/ 1	(100.0)								
Presence of risk factor: Smoking													
Yes	94/ 118	(79.7)	6.0 (4.0, 7.0)	82/ 108	(75.9)	5.0 (3.0, 7.0)	1.079 (0.779, 1.495)	0.647	0.624	1.100 (0.817, 1.482)	0.529	0.894	
No	116/ 135	(85.9)	6.0 (6.0, 8.0)	105/ 134	(78.4)	7.0 (4.0, 9.0)	1.199 (0.910, 1.579)	0.197		1.117 (0.857, 1.456)	0.414		

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

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p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=254)			Placebo (N=242)			Adjusted Analysis [2]			Unadjusted Analysis [3]		
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus									0.337			0.485
Yes	28/ 34	(82.4)	5.0 (3.0, 6.0)	24/ 31	(77.4)	5.0 (2.0, 13.0)	1.293 (0.720, 2.325)	0.390		1.229 (0.707, 2.135)	0.465	
No	183/ 220	(83.2)	6.0 (6.0, 7.0)	163/ 211	(77.3)	5.0 (4.0, 7.0)	1.071 (0.860, 1.334)	0.540		1.092 (0.883, 1.349)	0.418	
Presence of risk factor: Immunosuppression												
Yes	4/ 4	(100.0)		5/ 5	(100.0)							
No	207/ 250	(82.8)		182/ 237	(76.8)							
Presence of risk factor: Chronic lung disease									0.387			0.497
Yes	24/ 26	(92.3)	7.0 (3.0, 10.0)	11/ 12	(91.7)	5.0 (2.0, 10.0)	0.805 (0.318, 2.040)	0.648		0.844 (0.411, 1.734)	0.645	
No	187/ 228	(82.0)	6.0 (5.0, 7.0)	176/ 230	(76.5)	5.0 (4.0, 7.0)	1.116 (0.901, 1.383)	0.315		1.117 (0.908, 1.373)	0.296	
Presence of risk factor: Hypertension									0.471			0.664
Yes	69/ 81	(85.2)	6.0 (4.0, 8.0)	79/ 102	(77.5)	4.0 (3.0, 8.0)	1.258 (0.900, 1.759)	0.179		1.185 (0.856, 1.640)	0.307	
No	142/ 173	(82.1)	6.0 (6.0, 7.0)	108/ 140	(77.1)	6.0 (4.0, 8.0)	1.073 (0.827, 1.393)	0.596		1.085 (0.844, 1.395)	0.524	
Presence of risk factor: Cardiovascular disorder									0.889			0.561
Yes	6/ 7	(85.7)	9.0 (3.0, 15.0)	8/ 9	(88.9)	9.0 (2.0, 11.0)	0.903 (0.212, 3.842)	0.891		0.746 (0.253, 2.201)	0.596	
No	205/ 247	(83.0)	6.0 (6.0, 7.0)	179/ 233	(76.8)	5.0 (4.0, 7.0)	1.116 (0.907, 1.373)	0.301		1.127 (0.921, 1.378)	0.246	
Presence of risk factor: Chronic kidney disease												
Yes	1/ 1	(100.0)		3/ 3	(100.0)							
No	210/ 253	(83.0)		184/ 239	(77.0)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	211/ 254	(83.1)		186/ 241	(77.2)							
Presence of risk factor: Sickle Cell Disease												
No	211/ 254	(83.1)		187/ 242	(77.3)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	1/ 1	(100.0)		0								
No	210/ 253	(83.0)		187/ 242	(77.3)							
Presence of risk factor: Cancer												
Yes	1/ 2	(50.0)		1/ 1	(100.0)							
No	210/ 252	(83.3)		186/ 241	(77.2)							
Presence of risk factor: Device Dependence												
Yes	1/ 1	(100.0)		0								
No	209/ 250	(83.6)		187/ 241	(77.6)							

N: Number of participants, CI: Confidence Interval, NE: Not estimable
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 [2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.
 p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.
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Final

Overall Study population

RKI-conform mITT2 Analysis set

Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea - Subgroup analysis

Subgroup Level	Nirmatrelvir/ritonavir (N=17)				Placebo (N=10)				Adjusted Analysis [2]		Interaction		Unadjusted Analysis [3]		Interaction	
	n/N	(%)	Median	(95% CI) [1]	n/N	(%)	Median	(95% CI) [1]	Hazard Ratio (95% CI)	p-Value	p-Value	Hazard Ratio (95% CI)	p-Value	p-Value		
Age																
< 65	13/	17 (76.5)			6/	10 (60.0)										
>= 65	0				0											
Gender											0.939					0.620
Male	6/	6 (100.0)	9.5 (7.0, 13.0)		3/	4 (75.0)	17.5 (8.0, NE)		0.849 (0.049, 14.574)	0.910		6.976 (0.803, 60.583)	0.078			
Female	7/	11 (63.6)	9.5 (5.0, NE)		3/	6 (50.0)	15.0 (8.0, NE)		2.524 (0.472, 13.504)	0.279		1.818 (0.466, 7.097)	0.389			
Geographic region																
United States	11/	14 (78.6)			5/	7 (71.4)										
Europe	1/	1 (100.0)			0											
India	0				0											
Rest of World	1/	2 (50.0)			1/	3 (33.3)										
COVID-19 therapeutic mAb treatment at randomisation																
Yes	1/	1 (100.0)			0											
No	12/	16 (75.0)			6/	10 (60.0)										
Baseline viral load 1											0.804					0.324
< 10^4 copies/mL	7/	9 (77.8)	11.0 (5.0, 19.0)		1/	3 (33.3)	NE (17.0, NE)		2.372 (0.210, 26.809)	0.485		4.960 (0.595, 41.348)	0.139			
>= 10^4 copies/mL	6/	8 (75.0)	8.0 (5.0, NE)		4/	6 (66.7)	14.0 (8.0, NE)		4.273 (0.674, 27.102)	0.123		1.635 (0.457, 5.845)	0.450			
Baseline viral load 2																
< 10^7 copies/mL	10/	13 (76.9)			3/	6 (50.0)										
>= 10^7 copies/mL	3/	4 (75.0)			2/	3 (66.7)										
Baseline serology status											0.964					0.479
Negative	6/	8 (75.0)	12.5 (6.0, NE)		5/	8 (62.5)	17.0 (8.0, NE)		3.233 (0.585, 17.881)	0.179		1.460 (0.441, 4.841)	0.536			
Positive	7/	9 (77.8)	7.0 (5.0, 12.0)		1/	2 (50.0)	NE (8.0, NE)		6.510 (0.228, 186.22)	0.274		2.586 (0.314, 21.296)	0.377			
Symptom onset days to first dose date											0.853					0.253
<= 3	10/	11 (90.9)	7.0 (6.0, 12.0)		4/	6 (66.7)	17.5 (8.0, NE)		3.381 (0.650, 17.588)	0.148		3.446 (1.010, 11.759)	0.048			
> 3	3/	6 (50.0)	19.0 (5.0, NE)		2/	4 (50.0)	14.0 (8.0, NE)		0.870 (0.100, 7.534)	0.899		0.939 (0.152, 5.792)	0.946			
BMI group																
< 25	2/	2 (100.0)			1/	1 (100.0)										
25 - < 30	2/	4 (50.0)			0											
>= 30	9/	11 (81.8)			5/	9 (55.6)										
Ethnicity																
White	10/	14 (71.4)			5/	6 (83.3)										
Black or African American	2/	2 (100.0)			0/	1 (0.0)										
Asian	0				1/	2 (50.0)										
Others	1/	1 (100.0)			0/	1 (0.0)										
Number of baseline comorbidities present																
0-1	10/	14 (71.4)			4/	7 (57.1)										
2-3	3/	3 (100.0)			2/	3 (66.7)										
>= 4	0				0											
Presence of risk factor: Smoking											0.281					0.759
Yes	3/	6 (50.0)	10.0 (7.0, NE)		3/	5 (60.0)	18.0 (14.0, NE)		0.679 (0.000, NE)	1.000		1.581 (0.314, 7.973)	0.579			
No	10/	11 (90.9)	7.0 (5.0, 13.0)		3/	5 (60.0)	15.0 (8.0, NE)		1.727 (0.357, 8.357)	0.497		2.103 (0.571, 7.737)	0.264			

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[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=17)			Placebo (N=10)			Adjusted Analysis [2]			Unadjusted Analysis [3]			
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	
Presence of risk factor: Diabetes mellitus													
Yes	1/	1 (100.0)		1/	2 (50.0)								
No	12/	16 (75.0)		5/	8 (62.5)								
Presence of risk factor: Immunosuppression													
Yes	1/	1 (100.0)		0									
No	12/	16 (75.0)		6/	10 (60.0)								
Presence of risk factor: Chronic lung disease													
Yes	2/	2 (100.0)		0									
No	11/	15 (73.3)		6/	10 (60.0)								
Presence of risk factor: Hypertension													
Yes	3/	4 (75.0)		3/	5 (60.0)								
No	10/	13 (76.9)		3/	5 (60.0)								
Presence of risk factor: Cardiovascular disorder													
Yes	1/	1 (100.0)		0									
No	12/	16 (75.0)		6/	10 (60.0)								
Presence of risk factor: Chronic kidney disease													
Yes	0			0									
No	13/	17 (76.5)		6/	10 (60.0)								
Presence of risk factor: HIV Infection													
Yes	0			0									
No	13/	17 (76.5)		6/	10 (60.0)								
Presence of risk factor: Sickle Cell Disease													
No	13/	17 (76.5)		6/	10 (60.0)								
Presence of risk factor: Neurodevelopmental Disorder													
Yes	0			0									
No	13/	17 (76.5)		6/	10 (60.0)								
Presence of risk factor: Cancer													
Yes	0			0									
No	13/	17 (76.5)		6/	10 (60.0)								
Presence of risk factor: Device Dependence													
Yes	0			0									
No	13/	17 (76.5)		6/	10 (60.0)								

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Analysis of Participants with Worsening of Signs and Symptoms - Loss of smell - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value	
Age							0.740					0.606
< 65	204/ 790 (25.8)	210/ 810 (25.9)	0.975 (0.824, 1.152)		0.764			0.996 (0.844, 1.176)		0.962		
>= 65	24/ 138 (17.4)	29/ 145 (20.0)	0.920 (0.560, 1.511)		0.743			0.870 (0.534, 1.417)		0.575		
Gender							0.673					0.952
Male	103/ 463 (22.2)	115/ 507 (22.7)	0.923 (0.729, 1.169)		0.506			0.981 (0.776, 1.240)		0.871		
Female	125/ 465 (26.9)	124/ 448 (27.7)	0.977 (0.788, 1.211)		0.829			0.971 (0.786, 1.200)		0.787		
Geographic region							0.737					0.831
United States	88/ 375 (23.5)	97/ 387 (25.1)	0.907 (0.702, 1.172)		0.456			0.936 (0.728, 1.204)		0.607		
Europe	86/ 322 (26.7)	79/ 321 (24.6)	1.111 (0.848, 1.454)		0.445			1.085 (0.834, 1.412)		0.543		
India	9/ 74 (12.2)	10/ 78 (12.8)	NE (NE, NE)		NE			0.949 (0.409, 2.203)		0.902		
Rest of World	45/ 157 (28.7)	53/ 169 (31.4)	0.900 (0.647, 1.253)		0.534			0.914 (0.655, 1.275)		0.596		
COVID-19 therapeutic mAb treatment at randomisation							0.459					0.379
Yes	17/ 57 (29.8)	14/ 60 (23.3)	1.372 (0.736, 2.558)		0.319			1.278 (0.696, 2.346)		0.428		
No	211/ 871 (24.2)	225/ 895 (25.1)	0.950 (0.806, 1.120)		0.544			0.964 (0.819, 1.134)		0.656		
Baseline viral load 1							0.416					0.420
< 10^4 copies/mL	50/ 335 (14.9)	62/ 354 (17.5)	0.858 (0.611, 1.204)		0.376			0.852 (0.606, 1.199)		0.358		
>= 10^4 copies/mL	167/ 569 (29.3)	169/ 575 (29.4)	1.004 (0.838, 1.202)		0.969			0.999 (0.834, 1.195)		0.988		
Baseline viral load 2							0.993					0.892
< 10^7 copies/mL	119/ 652 (18.3)	137/ 699 (19.6)	0.949 (0.761, 1.184)		0.646			0.931 (0.746, 1.162)		0.528		
>= 10^7 copies/mL	98/ 252 (38.9)	94/ 230 (40.9)	0.940 (0.755, 1.171)		0.583			0.952 (0.764, 1.185)		0.657		
Baseline serology status							0.440					0.459
Negative	132/ 435 (30.3)	133/ 456 (29.2)	1.022 (0.833, 1.255)		0.833			1.040 (0.850, 1.273)		0.701		
Positive	93/ 482 (19.3)	102/ 487 (20.9)	0.897 (0.697, 1.154)		0.399			0.921 (0.717, 1.184)		0.522		
Symptom onset days to first dose date							0.483					0.417
<= 3	165/ 624 (26.4)	176/ 624 (28.2)	0.935 (0.778, 1.124)		0.475			0.938 (0.782, 1.124)		0.485		
> 3	63/ 304 (20.7)	63/ 331 (19.0)	1.081 (0.791, 1.477)		0.626			1.089 (0.797, 1.488)		0.594		
BMI group							0.081					0.056
< 25	41/ 215 (19.1)	58/ 213 (27.2)	0.657 (0.460, 0.939)		0.021			0.700 (0.492, 0.996)		0.047		
25 - < 30	74/ 319 (23.2)	81/ 332 (24.4)	0.944 (0.715, 1.245)		0.682			0.951 (0.722, 1.252)		0.719		
>= 30	112/ 393 (28.5)	100/ 410 (24.4)	1.132 (0.891, 1.437)		0.309			1.168 (0.927, 1.473)		0.187		
Ethnicity							0.492					0.707
White	183/ 699 (26.2)	186/ 718 (25.9)	1.023 (0.856, 1.222)		0.802			1.011 (0.848, 1.204)		0.906		
Black or African American	7/ 43 (16.3)	8/ 40 (20.0)	0.567 (0.231, 1.390)		0.215			0.814 (0.325, 2.039)		0.660		
Asian	23/ 117 (19.7)	24/ 127 (18.9)	NE (NE, NE)		NE			1.040 (0.622, 1.739)		0.880		
Others	15/ 69 (21.7)	21/ 70 (30.0)	NE (NE, NE)		NE			0.725 (0.409, 1.285)		0.271		
Number of baseline comorbidities present							0.762					0.563
0-1	189/ 710 (26.6)	191/ 728 (26.2)	0.985 (0.828, 1.173)		0.868			1.015 (0.854, 1.206)		0.869		
2-3	37/ 214 (17.3)	46/ 221 (20.8)	0.840 (0.560, 1.259)		0.398			0.831 (0.562, 1.227)		0.351		
>= 4	2/ 4 (50.0)	2/ 6 (33.3)	NE (NE, NE)		NE			1.500 (0.336, 6.702)		0.596		
Presence of risk factor: Smoking							0.663					0.873
Yes	94/ 417 (22.5)	102/ 438 (23.3)	0.915 (0.716, 1.169)		0.478			0.968 (0.757, 1.238)		0.795		
No	134/ 509 (26.3)	137/ 517 (26.5)	0.998 (0.811, 1.229)		0.987			0.993 (0.810, 1.219)		0.950		
Presence of risk factor: Diabetes mellitus							0.061					0.076

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value	
Yes	22/ 130 (16.9)	35/ 136 (25.7)	0.631 (0.391, 1.018)			0.059		0.658 (0.409, 1.058)			0.084	
No	206/ 797 (25.8)	204/ 819 (24.9)	1.024 (0.864, 1.213)			0.784		1.038 (0.878, 1.227)			0.665	
Presence of risk factor: Immunosuppression							0.181					0.418
Yes	1/ 6 (16.7)	0/ 7 (0.0)	NE (NE, NE)			NE		3.429 (0.165, 71.361)			0.426	
No	227/ 921 (24.6)	239/ 948 (25.2)	0.962 (0.821, 1.128)			0.635		0.978 (0.835, 1.144)			0.778	
Presence of risk factor: Chronic lung disease							0.315					0.185
Yes	8/ 62 (12.9)	9/ 39 (23.1)	NE (NE, NE)			NE		0.559 (0.236, 1.327)			0.187	
No	220/ 865 (25.4)	230/ 916 (25.1)	0.997 (0.849, 1.171)			0.971		1.013 (0.863, 1.188)			0.875	
Presence of risk factor: Hypertension							0.386					0.388
Yes	80/ 348 (23.0)	95/ 371 (25.6)	0.854 (0.654, 1.117)			0.249		0.898 (0.693, 1.163)			0.414	
No	148/ 579 (25.6)	144/ 584 (24.7)	1.008 (0.826, 1.230)			0.937		1.037 (0.850, 1.264)			0.722	
Presence of risk factor: Cardiovascular disorder							0.981					0.942
Yes	9/ 42 (21.4)	11/ 49 (22.4)	NE (NE, NE)			NE		0.955 (0.438, 2.079)			0.907	
No	219/ 885 (24.7)	228/ 906 (25.2)	0.968 (0.823, 1.138)			0.695		0.983 (0.837, 1.155)			0.837	
Presence of risk factor: Chronic kidney disease							0.401					0.435
Yes	1/ 6 (16.7)	3/ 8 (37.5)	NE (NE, NE)			NE		0.444 (0.060, 3.285)			0.427	
No	227/ 921 (24.6)	236/ 947 (24.9)	0.974 (0.830, 1.142)			0.742		0.989 (0.844, 1.158)			0.891	
Presence of risk factor: HIV Infection												
Yes	0	0/ 1 (0.0)										
No	228/ 927 (24.6)	239/ 953 (25.1)										
Presence of risk factor: Sickie Cell Disease												
No	228/ 927 (24.6)	239/ 955 (25.0)										
Presence of risk factor: Neurodevelopmental Disorder												
Yes	1/ 2 (50.0)	0/ 1 (0.0)										
No	227/ 925 (24.5)	239/ 954 (25.1)										
Presence of risk factor: Cancer							NE					0.400
Yes	2/ 5 (40.0)	1/ 6 (16.7)	NE (NE, NE)			NE		2.400 (0.298, 19.337)			0.411	
No	226/ 922 (24.5)	238/ 949 (25.1)	0.961 (0.819, 1.127)			0.623		0.977 (0.835, 1.145)			0.776	
Presence of risk factor: Device Dependence												
Yes	2/ 4 (50.0)	1/ 3 (33.3)										
No	224/ 914 (24.5)	235/ 944 (24.9)										

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[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=511)			Placebo (N=539)			Adjusted Analysis [2]				Interaction p-Value	Unadjusted Analysis [3]				Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)		p-Value			Hazard Ratio (95% CI)		p-Value		
Age																
< 65	322/ 447	(72.0)	11.0 (9.0, 12.0)	300/ 472	(63.6)	13.0 (12.0, 15.0)	1.276 (1.085, 1.499)		0.003		0.278	1.258 (1.075, 1.473)		0.004		0.174
>= 65	48/ 64	(75.0)	10.0 (7.0, 13.0)	40/ 67	(59.7)	15.0 (9.0, NE)	1.566 (1.009, 2.432)		0.046			1.685 (1.104, 2.571)		0.015		
Gender																
Male	189/ 241	(78.4)	9.0 (8.0, 11.0)	170/ 270	(63.0)	13.0 (11.0, 15.0)	1.550 (1.250, 1.921)		<.001		0.057	1.468 (1.192, 1.808)		<.001		0.148
Female	181/ 270	(67.0)	11.0 (10.0, 13.0)	170/ 269	(63.2)	14.0 (12.0, 16.0)	1.151 (0.928, 1.427)		0.202			1.179 (0.956, 1.453)		0.124		
Geographic region																
United States	174/ 246	(70.7)	10.0 (9.0, 11.0)	157/ 236	(66.5)	12.0 (10.0, 15.0)	1.143 (0.916, 1.426)		0.238		0.406	1.154 (0.929, 1.432)		0.195		0.462
Europe	103/ 146	(70.5)	13.0 (11.0, 14.0)	90/ 166	(54.2)	19.0 (15.0, NE)	1.612 (1.204, 2.157)		0.001			1.547 (1.165, 2.054)		0.003		
India	32/ 34	(94.1)	5.0 (3.0, 6.0)	31/ 32	(96.9)	8.5 (6.0, 12.0)	1.850 (1.064, 3.214)		0.029			1.594 (0.966, 2.630)		0.068		
Rest of World	61/ 85	(71.8)	9.0 (7.0, 13.0)	62/ 105	(59.0)	11.0 (8.0, 18.0)	1.277 (0.886, 1.840)		0.189			1.325 (0.929, 1.889)		0.120		
COVID-19 therapeutic mAb treatment at randomisation																
Yes	24/ 36	(66.7)	11.0 (8.0, 16.0)	27/ 37	(73.0)	10.5 (3.0, 18.0)	0.809 (0.455, 1.438)		0.470		0.185	0.850 (0.490, 1.475)		0.563		0.117
No	346/ 475	(72.8)	10.0 (9.0, 11.0)	313/ 502	(62.4)	14.0 (12.0, 15.0)	1.353 (1.157, 1.583)		<.001			1.351 (1.159, 1.574)		<.001		
Baseline viral load 1																
< 10^4 copies/mL	149/ 192	(77.6)	9.0 (8.0, 11.0)	136/ 201	(67.7)	11.0 (8.0, 14.0)	1.325 (1.047, 1.677)		0.019		0.979	1.316 (1.042, 1.661)		0.021		0.914
>= 10^4 copies/mL	209/ 303	(69.0)	11.0 (10.0, 12.0)	196/ 324	(60.5)	15.0 (12.0, 17.0)	1.318 (1.081, 1.608)		0.006			1.305 (1.073, 1.586)		0.008		
Baseline viral load 2																
< 10^7 copies/mL	290/ 398	(72.9)	10.0 (9.0, 11.0)	273/ 418	(65.3)	12.0 (11.0, 14.0)	1.261 (1.067, 1.490)		0.007		0.278	1.258 (1.066, 1.485)		0.007		0.349
>= 10^7 copies/mL	68/ 97	(70.1)	11.0 (10.0, 14.0)	59/ 107	(55.1)	18.0 (14.0, NE)	1.541 (1.068, 2.223)		0.021			1.533 (1.081, 2.175)		0.017		
Baseline serology status																
Negative	160/ 233	(68.7)	11.0 (10.0, 13.0)	140/ 251	(55.8)	16.0 (13.0, 21.0)	1.423 (1.125, 1.798)		0.003		0.595	1.413 (1.126, 1.774)		0.003		0.399
Positive	205/ 272	(75.4)	9.0 (8.0, 10.0)	197/ 281	(70.1)	11.0 (9.0, 14.0)	1.256 (1.029, 1.535)		0.025			1.223 (1.006, 1.488)		0.044		
Symptom onset days to first dose date																
<= 3	233/ 320	(72.8)	11.0 (10.0, 12.0)	201/ 317	(63.4)	14.0 (12.0, 16.0)	1.313 (1.082, 1.592)		0.006		0.928	1.307 (1.081, 1.578)		0.006		0.873
> 3	137/ 191	(71.7)	9.0 (8.0, 11.0)	139/ 222	(62.6)	12.0 (10.0, 16.0)	1.315 (1.030, 1.679)		0.028			1.318 (1.040, 1.670)		0.022		
BMI group																
< 25	83/ 109	(76.1)	9.0 (8.0, 10.0)	69/ 103	(67.0)	12.0 (9.0, 18.0)	1.528 (1.094, 2.135)		0.013		0.651	1.424 (1.034, 1.962)		0.030		0.825
25 - < 30	118/ 166	(71.1)	10.0 (8.0, 13.0)	115/ 183	(62.8)	14.0 (11.0, 17.0)	1.312 (1.009, 1.707)		0.043			1.290 (0.997, 1.669)		0.052		
>= 30	169/ 236	(71.6)	11.0 (10.0, 12.0)	156/ 253	(61.7)	14.0 (11.0, 16.0)	1.285 (1.026, 1.609)		0.029			1.266 (1.018, 1.575)		0.034		
Ethnicity																
White	268/ 385	(69.6)	12.0 (10.0, 13.0)	246/ 406	(60.6)	15.0 (13.0, 17.0)	1.248 (1.045, 1.490)		0.015		0.592	1.275 (1.072, 1.516)		0.006		0.778
Black or African American	23/ 29	(79.3)	8.0 (6.0, 11.0)	15/ 24	(62.5)	10.0 (3.0, NE)	1.545 (0.734, 3.255)		0.252			1.444 (0.746, 2.794)		0.276		
Asian	50/ 56	(89.3)	5.0 (4.0, 8.0)	52/ 60	(86.7)	8.5 (6.0, 12.0)	1.582 (1.050, 2.384)		0.028			1.446 (0.977, 2.141)		0.065		
Others	29/ 41	(70.7)	8.0 (4.0, 13.0)	27/ 49	(55.1)	12.0 (8.0, NE)	1.477 (0.848, 2.570)		0.168			1.531 (0.905, 2.589)		0.112		
Number of baseline comorbidities present																
0-1	281/ 392	(71.7)		252/ 402	(62.7)											
2-3	88/ 118	(74.6)		86/ 135	(63.7)											
>= 4	1/ 1	(100.0)		2/ 2	(100.0)											
Presence of risk factor: Smoking																
Yes	175/ 235	(74.5)	11.0 (9.0, 12.0)	165/ 255	(64.7)	13.0 (11.0, 16.0)	1.377 (1.105, 1.717)		0.004		0.697	1.356 (1.095, 1.679)		0.005		0.764
No	195/ 275	(70.9)	10.0 (9.0, 11.0)	175/ 284	(61.6)	14.0 (11.0, 16.0)	1.279 (1.038, 1.575)		0.021			1.280 (1.043, 1.570)		0.018		

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Subgroup Level	Nirmatrelvir/ritonavir (N=511)			Placebo (N=539)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus										0.625				0.615
Yes	57/ 74	(77.0)	9.0 (7.0, 11.0)	58/ 77	(75.3)	11.0 (8.0, 14.0)	1.194 (0.812, 1.757)	0.368			1.211 (0.840, 1.746)	0.306		
No	313/ 437	(71.6)	11.0 (10.0, 12.0)	282/ 462	(61.0)	14.0 (12.0, 16.0)	1.338 (1.133, 1.579)	<.001			1.329 (1.131, 1.562)	<.001		
Presence of risk factor: Immunosuppression										0.063				0.133
Yes	3/ 4	(75.0)	12.0 (2.0, NE)	7/ 7	(100.0)	5.0 (2.0, 10.0)	0.000 (0.000, NE)	0.998			0.422 (0.084, 2.118)	0.295		
No	367/ 507	(72.4)	10.0 (9.0, 11.0)	333/ 532	(62.6)	14.0 (12.0, 15.0)	1.332 (1.144, 1.551)	<.001			1.326 (1.143, 1.539)	<.001		
Presence of risk factor: Chronic lung disease										0.039				0.060
Yes	35/ 43	(81.4)	9.0 (7.0, 13.0)	11/ 24	(45.8)	NE (12.0, NE)	2.428 (1.055, 5.589)	0.037			2.476 (1.252, 4.896)	0.009		
No	335/ 468	(71.6)	10.0 (9.0, 11.0)	329/ 515	(63.9)	13.0 (12.0, 15.0)	1.258 (1.076, 1.471)	0.004			1.262 (1.083, 1.470)	0.003		
Presence of risk factor: Hypertension										0.950				0.745
Yes	135/ 185	(73.0)	10.0 (9.0, 12.0)	132/ 209	(63.2)	15.0 (12.0, 17.0)	1.315 (1.028, 1.683)	0.029			1.358 (1.068, 1.728)	0.013		
No	235/ 326	(72.1)	10.0 (9.0, 12.0)	208/ 330	(63.0)	13.0 (11.0, 15.0)	1.329 (1.096, 1.612)	0.004			1.277 (1.060, 1.540)	0.010		
Presence of risk factor: Cardiovascular disorder										0.330				0.704
Yes	10/ 15	(66.7)	14.0 (4.0, NE)	12/ 23	(52.2)	21.0 (7.0, NE)	1.832 (0.684, 4.901)	0.228			1.494 (0.643, 3.470)	0.350		
No	360/ 496	(72.6)	10.0 (9.0, 11.0)	328/ 516	(63.6)	13.0 (12.0, 15.0)	1.298 (1.113, 1.513)	<.001			1.299 (1.118, 1.509)	<.001		
Presence of risk factor: Chronic kidney disease														
Yes	2/ 3	(66.7)		3/ 4	(75.0)									
No	368/ 508	(72.4)		337/ 535	(63.0)									
Presence of risk factor: HIV Infection														
Yes	0			0										
No	370/ 511	(72.4)		339/ 538	(63.0)									
Presence of risk factor: Sickel Cell Disease														
No	370/ 511	(72.4)		340/ 539	(63.1)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/ 2	(100.0)		1/ 1	(100.0)									
No	368/ 509	(72.3)		339/ 538	(63.0)									
Presence of risk factor: Cancer														
Yes	0			4/ 4	(100.0)									
No	370/ 511	(72.4)		336/ 535	(62.8)									
Presence of risk factor: Device Dependence														
Yes	0/ 1	(0.0)		0/ 1	(0.0)									
No	367/ 503	(73.0)		338/ 534	(63.3)									

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

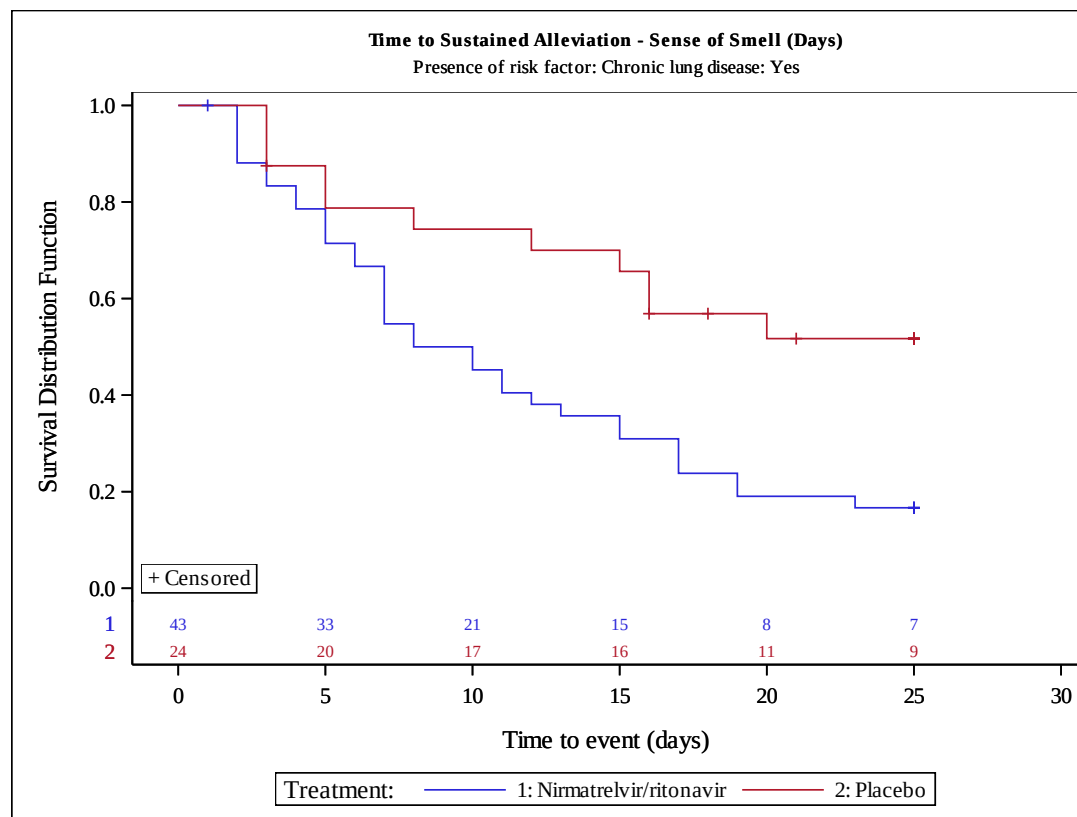
[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Final

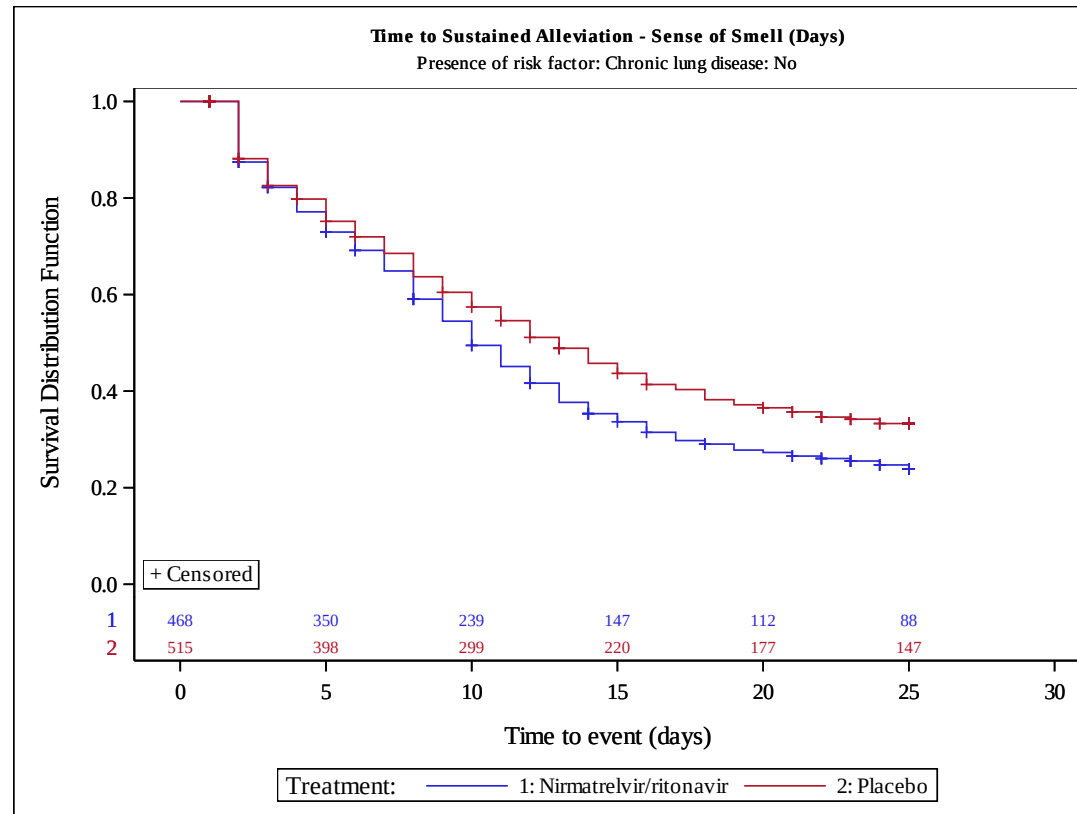


Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=240)						Placebo (N=232)				Adjusted Analysis [2]				Unadjusted Analysis [3]			
	n/N	(%)	Median	(95% CI)	[1]		n/N	(%)	Median	(95% CI)	[1]		Hazard Ratio (95% CI)	p-Value	p-Value	Hazard Ratio (95% CI)	p-Value	p-Value
Age																		
< 65	172/ 15/	221 19	(77.8) (78.9)	8.0 7.0	(7.0, 10.0) (3.0, 10.0)		150/ 10/	213 19	(70.4) (52.6)	10.0 16.5	(7.0, 12.0) (5.0, NE)		1.237 1.869	(0.985, 0.705,	1.554) 4.952)	0.067 0.209		
>= 65																		
Gender																		
Male	91/ 96/	106 134	(85.8) (71.6)	8.0 8.0	(6.0, 9.0) (7.0, 11.0)		70/ 90/	105 127	(66.7) (70.9)	9.0 10.0	(7.0, 14.0) (8.0, 12.0)		1.528 1.017	(1.102, 0.747,	2.119) 1.385)	0.011 0.913		
Female																		
Geographic region																		
United States	95/ 49/	129 59	(73.6) (83.1)	8.0 8.0	(7.0, 10.0) (6.0, 12.0)		71/ 42/	100 70	(71.0) (60.0)	9.0 14.0	(5.0, 13.0) (10.0, 21.0)		1.101 1.949	(0.801, 1.250,	1.512) 3.040)	0.553 0.003		
Europe																		
India	14/ 29/	14 38	(100.0) (76.3)	3.0 8.0	(2.0, 4.0) (7.0, 13.0)		10/ 37/	11 51	(90.9) (72.5)	4.0 8.0	(2.0, 7.0) (6.0, 11.0)		1.639 1.066	(0.647, 0.638,	4.152) 1.782)	0.298 0.807		
Rest of World																		
COVID-19 therapeutic mAb treatment at randomisation																		
Yes	11/ 176/	15 225	(73.3) (78.2)	9.5 8.0	(4.0, 23.0) (7.0, 9.0)		7/ 153/	10 222	(70.0) (68.9)	18.5 9.0	(3.0, NE) (8.0, 12.0)		1.892 1.248	(0.488, 0.997,	7.339) 1.562)	0.357 0.053		
No																		
Baseline viral load 1																		
< 10^4 copies/mL	69/ 113/	85 150	(81.2) (75.3)	7.0 8.0	(4.0, 8.0) (7.0, 10.0)		52/ 104/	73 153	(71.2) (68.0)	6.5 10.0	(4.0, 13.0) (8.0, 13.0)		1.337 1.216	(0.919, 0.924,	1.944) 1.600)	0.129 0.163		
>= 10^4 copies/mL																		
Baseline viral load 2																		
< 10^7 copies/mL	154/ 28/	198 37	(77.8) (75.7)	8.0 11.0	(7.0, 9.0) (6.0, 12.0)		125/ 31/	185 41	(67.6) (75.6)	9.0 10.0	(7.0, 13.0) (6.0, 14.0)		1.342 0.828	(1.054, 0.469,	1.709) 1.463)	0.017 0.516		
>= 10^7 copies/mL																		
Baseline serology status																		
Negative	81/ 103/	109 127	(74.3) (81.1)	9.0 7.0	(8.0, 11.0) (5.0, 8.0)		72/ 86/	113 115	(63.7) (74.8)	12.0 7.0	(9.0, 17.0) (5.0, 11.0)		1.355 1.212	(0.963, 0.903,	1.905) 1.628)	0.081 0.201		
Positive																		
Symptom onset days to first dose date																		
<= 3	115/ 72/	147 93	(78.2) (77.4)	8.0 8.0	(7.0, 10.0) (5.0, 9.0)		92/ 68/	130 102	(70.8) (66.7)	9.0 10.0	(8.0, 13.0) (7.0, 13.0)		1.247 1.262	(0.937, 0.887,	1.658) 1.795)	0.130 0.196		
> 3																		
BMI group																		
< 25	34/ 60/	43 76	(79.1) (78.9)	7.5 8.0	(5.0, 8.0) (6.0, 10.0)		28/ 52/	41 71	(68.3) (73.2)	8.0 8.0	(5.0, 22.0) (5.0, 12.0)		1.505 1.070	(0.856, 0.721,	2.647) 1.587)	0.156 0.738		
25 - < 30																		
>= 30	93/	121	(76.9)	9.0	(7.0, 11.0)		80/	120	(66.7)	11.0	(8.0, 14.0)		1.375	(1.006,	1.879)	0.046		
Ethnicity																		
White	140/ 12/	183 14	(76.5) (85.7)	9.0 6.0	(8.0, 11.0) (2.0, 8.0)		115/ 8/	172 11	(66.9) (72.7)	11.0 5.0	(9.0, 14.0) (2.0, NE)		1.248 1.995	(0.965, 0.491,	1.615) 8.108)	0.091 0.334		
Black or African American																		
Asian	17/ 18/	19 24	(89.5) (75.0)	4.0 8.0	(2.0, 5.0) (4.0, 13.0)		17/ 20/	19 30	(89.5) (66.7)	5.0 8.0	(2.0, 7.0) (6.0, 12.0)		1.369 1.138	(0.634, 0.544,	2.955) 2.380)	0.424 0.731		
Others																		
Number of baseline comorbidities present																		
0-1	152/	193	(78.8)				122/	187	(65.2)									
2-3	35/	47	(74.5)				38/	45	(84.4)									
>= 4	0						0											
Presence of risk factor: Smoking																		
Yes	90/ 97/	112 128	(80.4) (75.8)	8.0 8.0	(6.0, 11.0) (7.0, 10.0)		81/ 79/	107 125	(75.7) (63.2)	9.0 10.0	(6.0, 12.0) (8.0, 14.0)		1.149 1.371	(0.836, 1.009,	1.580) 1.864)	0.392 0.044		
No																		

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p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of smell - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=240)			Placebo (N=232)			Adjusted Analysis [2]			Unadjusted Analysis [3]		
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus									0.308			0.423
Yes	19/	26 (73.1)	5.0 (3.0, 8.0)	24/	27 (88.9)	7.0 (5.0, 9.0)	0.753 (0.372, 1.524)	0.430		1.013 (0.553, 1.855)	0.967	
No	168/	214 (78.5)	8.0 (7.0, 10.0)	136/	205 (66.3)	10.0 (8.0, 13.0)	1.336 (1.054, 1.692)	0.016		1.298 (1.035, 1.628)	0.024	
Presence of risk factor: Immunosuppression												
Yes	1/	2 (50.0)		4/	4 (100.0)							
No	186/	238 (78.2)		156/	228 (68.4)							
Presence of risk factor: Chronic lung disease									0.162			0.221
Yes	16/	22 (72.7)	8.0 (5.0, 17.0)	4/	10 (40.0)	NE (3.0, NE)	5.646 (0.978, 32.601)	0.053		2.428 (0.806, 7.314)	0.115	
No	171/	218 (78.4)	8.0 (7.0, 9.0)	156/	222 (70.3)	9.0 (7.0, 12.0)	1.230 (0.982, 1.540)	0.071		1.222 (0.984, 1.519)	0.070	
Presence of risk factor: Hypertension									0.830			0.676
Yes	62/	77 (80.5)	8.0 (6.0, 10.0)	52/	77 (67.5)	11.0 (7.0, 15.0)	1.093 (0.725, 1.648)	0.671		1.333 (0.921, 1.930)	0.128	
No	125/	163 (76.7)	8.0 (7.0, 10.0)	108/	155 (69.7)	9.0 (7.0, 12.0)	1.222 (0.934, 1.597)	0.144		1.205 (0.931, 1.559)	0.157	
Presence of risk factor: Cardiovascular disorder									0.961			0.968
Yes	0/	3 (0.0)	NE (NE, NE)	5/	8 (62.5)	15.0 (2.0, NE)	NE (NE, NE)	NE		NE (NE, NE)	NE	
No	187/	237 (78.9)	8.0 (7.0, 9.0)	155/	224 (69.2)	10.0 (8.0, 12.0)	1.295 (1.038, 1.615)	0.022		1.268 (1.024, 1.569)	0.029	
Presence of risk factor: Chronic kidney disease												
Yes	2/	3 (66.7)		2/	2 (100.0)							
No	185/	237 (78.1)		158/	230 (68.7)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	187/	240 (77.9)		160/	232 (69.0)							
Presence of risk factor: Sick Cell Disease												
No	187/	240 (77.9)		160/	232 (69.0)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	1/	1 (100.0)		0								
No	186/	239 (77.8)		160/	232 (69.0)							
Presence of risk factor: Cancer												
Yes	0			1/	1 (100.0)							
No	187/	240 (77.9)		159/	231 (68.8)							
Presence of risk factor: Device Dependence												
Yes	0			0								
No	186/	236 (78.8)		158/	228 (69.3)							

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=511)			Placebo (N=539)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	269/ 447	(60.2)	16.0 (14.0, 19.0)	235/ 472	(49.8)	22.0 (18.0, NE)	1.324 (1.107, 1.584)	0.002		0.452	1.332 (1.118, 1.587)	0.001		0.357
>= 65	46/ 64	(71.9)	13.0 (10.0, 16.0)	38/ 67	(56.7)	18.0 (12.0, NE)	1.486 (0.948, 2.330)	0.084			1.640 (1.065, 2.526)	0.025		
Gender														
Male	164/ 241	(68.0)	14.0 (12.0, 16.0)	142/ 270	(52.6)	18.0 (16.0, NE)	1.585 (1.258, 1.997)	<.001		0.093	1.468 (1.172, 1.838)	<.001		0.410
Female	151/ 270	(55.9)	18.0 (15.0, 21.0)	131/ 269	(48.7)	23.0 (20.0, NE)	1.201 (0.944, 1.528)	0.137			1.286 (1.017, 1.625)	0.035		
Geographic region														
United States	144/ 246	(58.5)	16.0 (13.0, 19.0)	131/ 236	(55.5)	18.0 (16.0, 23.0)	1.075 (0.843, 1.370)	0.560		0.078	1.121 (0.884, 1.420)	0.346		0.119
Europe	92/ 146	(63.0)	18.0 (15.0, 21.0)	66/ 166	(39.8)	NE (NE, NE)	1.983 (1.435, 2.741)	<.001			1.831 (1.334, 2.514)	<.001		
India	31/ 34	(91.2)	9.0 (6.0, 11.0)	31/ 32	(96.9)	11.5 (8.0, 13.0)	1.719 (0.997, 2.964)	0.051			1.512 (0.914, 2.500)	0.107		
Rest of World	48/ 85	(56.5)	15.0 (11.0, NE)	45/ 105	(42.9)	NE (22.0, NE)	1.363 (0.894, 2.077)	0.150			1.508 (1.003, 2.268)	0.048		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	19/ 36	(52.8)	14.0 (10.0, NE)	24/ 37	(64.9)	13.0 (3.0, 22.0)	0.717 (0.384, 1.340)	0.297		0.078	0.724 (0.396, 1.322)	0.293		0.037
No	296/ 475	(62.3)	15.0 (14.0, 17.0)	249/ 502	(49.6)	23.0 (19.0, NE)	1.414 (1.190, 1.679)	<.001			1.435 (1.212, 1.699)	<.001		
Baseline viral load 1														
< 10^4 copies/mL	133/ 192	(69.3)	13.0 (11.0, 16.0)	121/ 201	(60.2)	15.0 (13.0, 18.0)	1.296 (1.010, 1.665)	0.042		0.588	1.273 (0.995, 1.628)	0.055		0.545
>= 10^4 copies/mL	172/ 303	(56.8)	17.0 (14.0, 20.0)	148/ 324	(45.7)	NE (22.0, NE)	1.410 (1.128, 1.763)	0.003			1.416 (1.136, 1.765)	0.002		
Baseline viral load 2														
< 10^7 copies/mL	247/ 398	(62.1)	15.0 (13.0, 17.0)	226/ 418	(54.1)	18.0 (16.0, 23.0)	1.252 (1.043, 1.503)	0.016		0.043	1.250 (1.043, 1.497)	0.016		0.070
>= 10^7 copies/mL	58/ 97	(59.8)	17.0 (12.0, 23.0)	43/ 107	(40.2)	NE (23.0, NE)	1.896 (1.259, 2.855)	0.002			1.895 (1.276, 2.814)	0.002		
Baseline serology status														
Negative	135/ 233	(57.9)	17.0 (15.0, 20.0)	107/ 251	(42.6)	NE (23.0, NE)	1.513 (1.167, 1.963)	0.002		0.399	1.549 (1.201, 1.997)	<.001		0.243
Positive	176/ 272	(64.7)	13.0 (12.0, 16.0)	163/ 281	(58.0)	16.0 (14.0, 21.0)	1.271 (1.023, 1.580)	0.030			1.249 (1.009, 1.545)	0.041		
Symptom onset days to first dose date														
<= 3	197/ 320	(61.6)	16.0 (14.0, 19.0)	166/ 317	(52.4)	22.0 (16.0, NE)	1.290 (1.045, 1.592)	0.018		0.508	1.297 (1.055, 1.595)	0.014		0.378
> 3	118/ 191	(61.8)	14.0 (12.0, 17.0)	107/ 222	(48.2)	23.0 (18.0, NE)	1.446 (1.103, 1.895)	0.008			1.488 (1.144, 1.934)	0.003		
BMI group														
< 25	79/ 109	(72.5)	13.0 (11.0, 15.0)	58/ 103	(56.3)	19.0 (13.0, NE)	1.617 (1.134, 2.306)	0.008		0.426	1.620 (1.153, 2.277)	0.005		0.496
25 - < 30	98/ 166	(59.0)	17.0 (14.0, 21.0)	96/ 183	(52.5)	22.0 (17.0, NE)	1.253 (0.940, 1.672)	0.124			1.250 (0.943, 1.657)	0.120		
>= 30	138/ 236	(58.5)	18.0 (14.0, 20.0)	119/ 253	(47.0)	24.0 (18.0, NE)	1.351 (1.049, 1.741)	0.020			1.339 (1.048, 1.712)	0.020		
Ethnicity														
White	226/ 385	(58.7)	17.0 (15.0, 20.0)	192/ 406	(47.3)	NE (21.0, NE)	1.299 (1.067, 1.581)	0.009		0.740	1.348 (1.112, 1.634)	0.002		0.852
Black or African American	19/ 29	(65.5)	11.0 (7.0, 17.0)	13/ 24	(54.2)	16.0 (9.0, NE)	1.663 (0.718, 3.852)	0.235			1.477 (0.727, 3.002)	0.281		
Asian	48/ 56	(85.7)	9.0 (7.0, 11.0)	50/ 60	(83.3)	12.0 (9.0, 15.0)	1.664 (1.095, 2.529)	0.017			1.554 (1.040, 2.321)	0.032		
Others	22/ 41	(53.7)	19.0 (10.0, NE)	18/ 49	(36.7)	NE (23.0, NE)	1.586 (0.812, 3.100)	0.177			1.700 (0.911, 3.172)	0.096		
Number of baseline comorbidities present														
0-1	235/ 392	(59.9)		203/ 402	(50.5)									
2-3	79/ 118	(66.9)		68/ 135	(50.4)									
>= 4	1/ 1	(100.0)		2/ 2	(100.0)									
Presence of risk factor: Smoking														
Yes	149/ 235	(63.4)	16.0 (14.0, 18.0)	132/ 255	(51.8)	22.0 (18.0, NE)	1.420 (1.115, 1.808)	0.005		0.699	1.418 (1.122, 1.794)	0.004		0.820
No	166/ 275	(60.4)	15.0 (12.0, 18.0)	141/ 284	(49.6)	22.0 (16.0, NE)	1.315 (1.046, 1.653)	0.019			1.334 (1.066, 1.670)	0.012		

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	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value		
Presence of risk factor: Diabetes mellitus														
Yes	53/ 74	(71.6)	11.0 (9.0, 15.0)	45/ 77	(58.4)	17.0 (13.0, NE)	1.739 (1.143, 2.647)	0.010	0.443	1.596 (1.070, 2.379)	0.022	0.443		
No	262/ 437	(60.0)	16.0 (14.0, 19.0)	228/ 462	(49.4)	23.0 (19.0, NE)	1.326 (1.105, 1.592)	0.002		1.336 (1.119, 1.596)	0.001			
Presence of risk factor: Immunosuppression														
Yes	3/ 4	(75.0)	16.5 (2.0, NE)	6/ 7	(85.7)	19.0 (2.0, 23.0)	0.000 (0.000, NE)	0.998	0.078	0.914 (0.227, 3.679)	0.899	0.505		
No	312/ 507	(61.5)	15.0 (14.0, 17.0)	267/ 532	(50.2)	22.0 (18.0, NE)	1.375 (1.163, 1.625)	<.001		1.379 (1.171, 1.624)	<.001			
Presence of risk factor: Chronic lung disease														
Yes	29/ 43	(67.4)	16.5 (12.0, 21.0)	10/ 24	(41.7)	NE (15.0, NE)	1.770 (0.730, 4.291)	0.207	0.318	1.776 (0.865, 3.647)	0.118	0.478		
No	286/ 468	(61.1)	15.0 (13.0, 17.0)	263/ 515	(51.1)	22.0 (18.0, NE)	1.324 (1.115, 1.572)	0.001		1.349 (1.141, 1.595)	<.001			
Presence of risk factor: Hypertension														
Yes	117/ 185	(63.2)	15.0 (13.0, 18.0)	108/ 209	(51.7)	22.0 (17.0, NE)	1.289 (0.984, 1.688)	0.065	0.747	1.385 (1.066, 1.800)	0.015	0.927		
No	198/ 326	(60.7)	16.0 (13.0, 19.0)	165/ 330	(50.0)	22.0 (18.0, NE)	1.385 (1.121, 1.711)	0.003		1.358 (1.105, 1.671)	0.004			
Presence of risk factor: Cardiovascular disorder														
Yes	10/ 15	(66.7)	14.0 (4.0, NE)	10/ 23	(43.5)	NE (9.0, NE)	3.960 (1.276, 12.297)	0.017	0.059	2.060 (0.853, 4.976)	0.108	0.267		
No	305/ 496	(61.5)	16.0 (14.0, 17.0)	263/ 516	(51.0)	22.0 (18.0, NE)	1.320 (1.115, 1.562)	0.001		1.346 (1.141, 1.587)	<.001			
Presence of risk factor: Chronic kidney disease														
Yes	1/ 3	(33.3)		1/ 4	(25.0)									
No	314/ 508	(61.8)		272/ 535	(50.8)									
Presence of risk factor: HIV Infection														
Yes	0			0										
No	315/ 511	(61.6)		272/ 538	(50.6)									
Presence of risk factor: Sickel Cell Disease														
No	315/ 511	(61.6)		273/ 539	(50.6)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/ 2	(100.0)		1/ 1	(100.0)									
No	313/ 509	(61.5)		272/ 538	(50.6)									
Presence of risk factor: Cancer														
Yes	0			4/ 4	(100.0)									
No	315/ 511	(61.6)		269/ 535	(50.3)									
Presence of risk factor: Device Dependence														
Yes	0/ 1	(0.0)		0/ 1	(0.0)									
No	312/ 503	(62.0)		272/ 534	(50.9)									

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

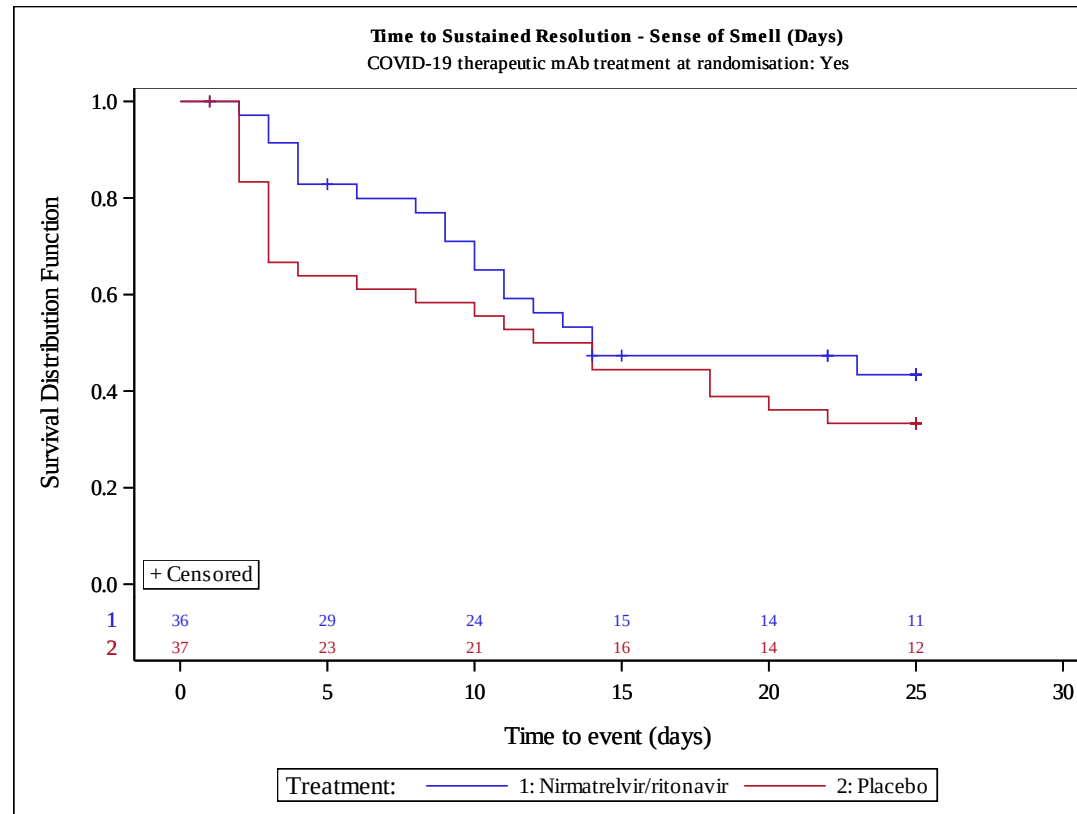
p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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 Overall Study population
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 Kaplan-Meier Plot of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Loss of smell

Final

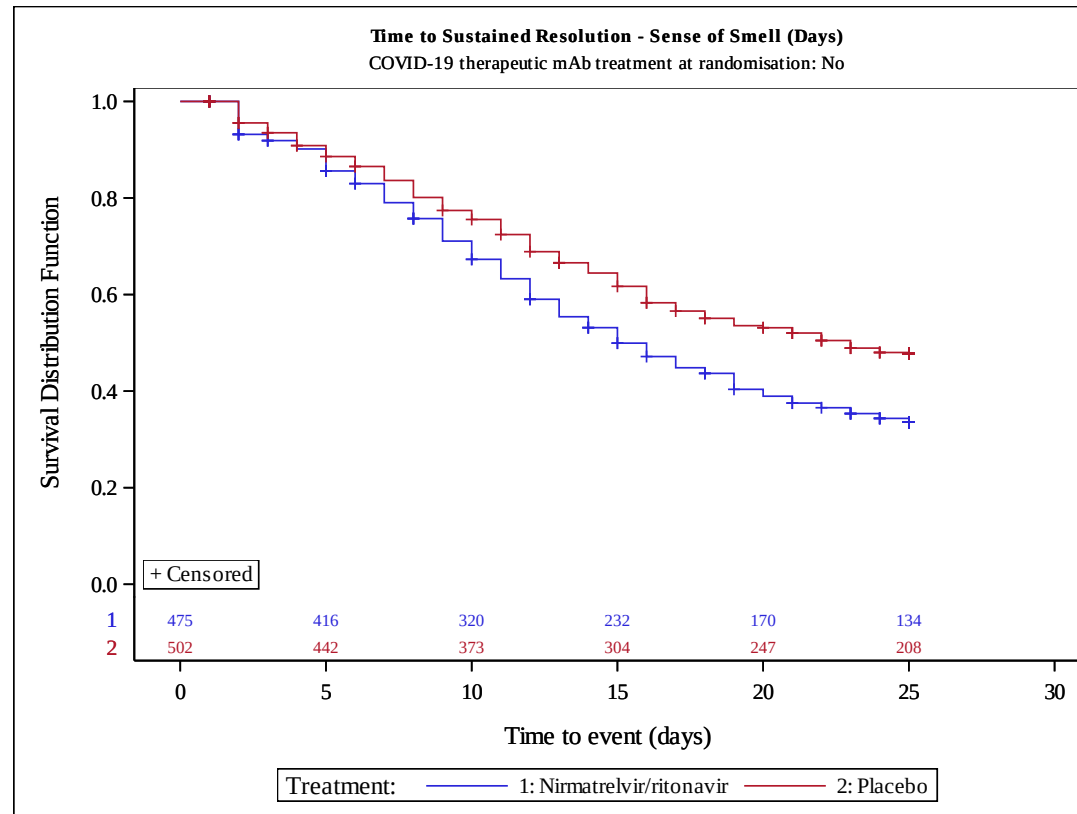


Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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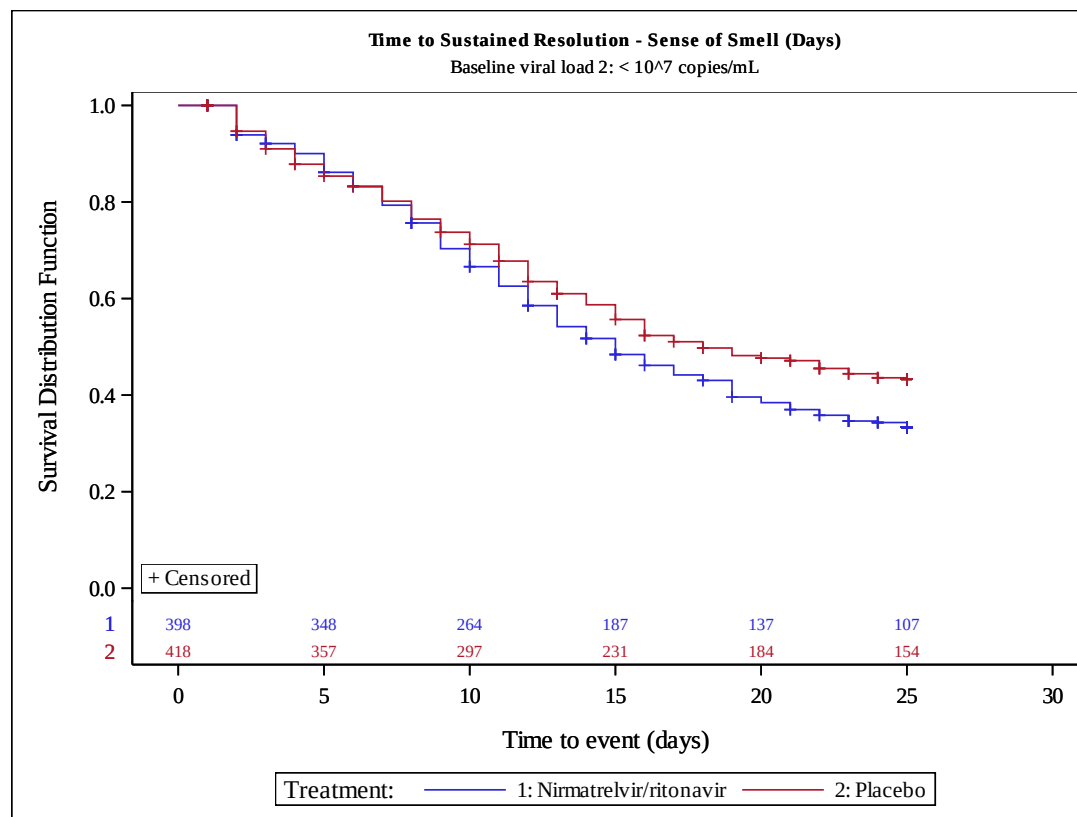


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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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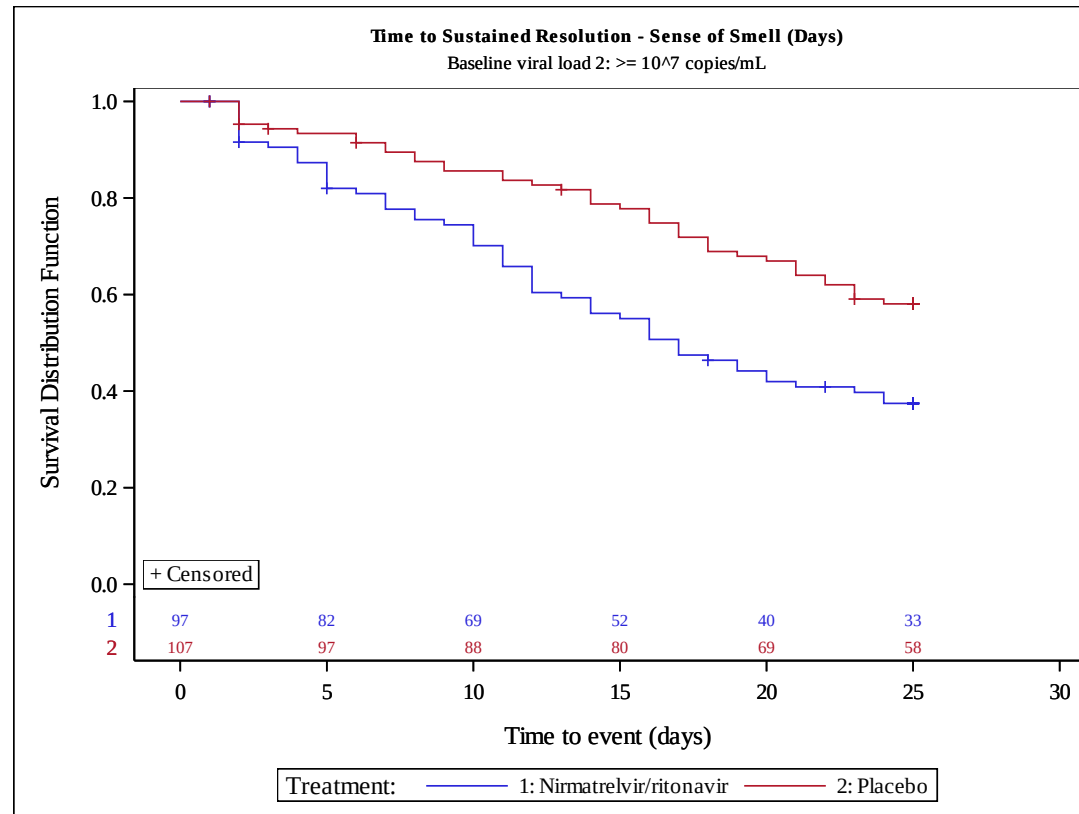
Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of smell - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=240)			Placebo (N=232)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value	
Age													
< 65	119/ 221	(53.8)	20.0 (18.0, 25.0)	85/ 213	(39.9)	NE (25.0, NE)	1.511 (1.134, 2.012)	0.005	0.572	1.493 (1.130, 1.973)	0.005		0.477
>= 65	13/ 19	(68.4)	16.0 (11.0, 23.0)	8/ 19	(42.1)	NE (17.0, NE)	2.296 (0.714, 7.389)	0.163		2.314 (0.949, 5.639)	0.065		
Gender													
Male	66/ 106	(62.3)	18.0 (14.0, 22.0)	42/ 105	(40.0)	NE (22.0, NE)	1.982 (1.326, 2.963)	<.001	0.076	1.803 (1.223, 2.657)	0.003		0.275
Female	66/ 134	(49.3)	22.0 (19.0, NE)	51/ 127	(40.2)	NE (23.0, NE)	1.245 (0.845, 1.835)	0.269		1.338 (0.928, 1.929)	0.119		
Geographic region													
United States	65/ 129	(50.4)	19.0 (16.0, NE)	45/ 100	(45.0)	NE (19.0, NE)	1.193 (0.806, 1.767)	0.378	0.052	1.227 (0.839, 1.795)	0.291		0.076
Europe	38/ 59	(64.4)	20.5 (16.0, 24.0)	18/ 70	(25.7)	NE (NE, NE)	3.755 (2.060, 6.845)	<.001		2.977 (1.695, 5.230)	<.001		
India	13/ 14	(92.9)	9.5 (7.0, 11.0)	10/ 11	(90.9)	12.0 (7.0, 15.0)	2.300 (0.777, 6.806)	0.132		1.820 (0.771, 4.294)	0.171		
Rest of World	16/ 38	(42.1)	NE (16.0, NE)	20/ 51	(39.2)	NE (23.0, NE)	1.282 (0.628, 2.617)	0.496		1.090 (0.565, 2.105)	0.796		
COVID-19 therapeutic mAb treatment at randomisation													
Yes	6/ 15	(40.0)	NE (4.0, NE)	4/ 10	(40.0)	NE (6.0, NE)	1.087 (0.173, 6.846)	0.929	0.999	1.258 (0.355, 4.465)	0.722		0.805
No	126/ 225	(56.0)	19.0 (16.0, 23.0)	89/ 222	(40.1)	NE (25.0, NE)	1.532 (1.160, 2.023)	0.003		1.555 (1.185, 2.040)	0.001		
Baseline viral load 1													
< 10^4 copies/mL	53/ 85	(62.4)	19.0 (14.0, 21.0)	37/ 73	(50.7)	21.0 (15.0, NE)	1.627 (1.049, 2.524)	0.030	0.755	1.378 (0.905, 2.098)	0.135		0.693
>= 10^4 copies/mL	76/ 150	(50.7)	22.0 (18.0, NE)	56/ 153	(36.6)	NE (NE, NE)	1.466 (1.027, 2.092)	0.035		1.552 (1.099, 2.193)	0.013		
Baseline viral load 2													
< 10^7 copies/mL	111/ 198	(56.1)	19.0 (16.0, 22.0)	78/ 185	(42.2)	NE (23.0, NE)	1.543 (1.147, 2.075)	0.004	0.899	1.490 (1.115, 1.991)	0.007		0.955
>= 10^7 copies/mL	18/ 37	(48.6)	24.0 (16.0, NE)	15/ 41	(36.6)	NE (23.0, NE)	1.573 (0.743, 3.327)	0.236		1.491 (0.751, 2.960)	0.253		
Baseline serology status													
Negative	56/ 109	(51.4)	21.0 (18.0, NE)	39/ 113	(34.5)	NE (NE, NE)	1.667 (1.087, 2.557)	0.019	0.639	1.703 (1.130, 2.565)	0.011		0.600
Positive	74/ 127	(58.3)	19.0 (15.0, 23.0)	52/ 115	(45.2)	NE (20.0, NE)	1.487 (1.036, 2.133)	0.031		1.442 (1.011, 2.057)	0.043		
Symptom onset days to first dose date													
<= 3	79/ 147	(53.7)	21.0 (19.0, NE)	57/ 130	(43.8)	NE (22.0, NE)	1.344 (0.947, 1.909)	0.098	0.364	1.327 (0.944, 1.867)	0.103		0.170
> 3	53/ 93	(57.0)	17.0 (13.0, 23.0)	36/ 102	(35.3)	NE (25.0, NE)	1.883 (1.205, 2.944)	0.005		1.925 (1.260, 2.943)	0.002		
BMI group													
< 25	30/ 43	(69.8)	14.5 (12.0, 16.0)	17/ 41	(41.5)	NE (15.0, NE)	1.873 (0.971, 3.614)	0.061	0.204	2.166 (1.190, 3.944)	0.011		0.202
25 - < 30	40/ 76	(52.6)	21.0 (16.0, NE)	33/ 71	(46.5)	25.0 (17.0, NE)	1.210 (0.746, 1.963)	0.439		1.148 (0.724, 1.821)	0.557		
>= 30	62/ 121	(51.2)	22.0 (19.0, NE)	43/ 120	(35.8)	NE (NE, NE)	1.682 (1.119, 2.528)	0.012		1.609 (1.090, 2.374)	0.017		
Ethnicity													
White	98/ 183	(53.6)	21.0 (19.0, NE)	61/ 172	(35.5)	NE (NE, NE)	1.611 (1.161, 2.237)	0.004	0.869	1.666 (1.209, 2.294)	0.002		0.952
Black or African American	8/ 14	(57.1)	11.0 (4.0, NE)	6/ 11	(54.5)	19.0 (5.0, NE)	1.817 (0.336, 9.822)	0.488		1.397 (0.483, 4.036)	0.537		
Asian	15/ 19	(78.9)	11.0 (7.0, 12.0)	15/ 19	(78.9)	15.0 (9.0, 22.0)	1.586 (0.674, 3.729)	0.291		1.598 (0.773, 3.302)	0.206		
Others	11/ 24	(45.8)	23.0 (15.0, NE)	11/ 30	(36.7)	NE (23.0, NE)	1.148 (0.429, 3.069)	0.784		1.277 (0.553, 2.950)	0.567		
Number of baseline comorbidities present													
0-1	106/ 193	(54.9)		73/ 187	(39.0)								
2-3	26/ 47	(55.3)		20/ 45	(44.4)								
>= 4	0			0									
Presence of risk factor: Smoking													
Yes	64/ 112	(57.1)	20.0 (16.0, 25.0)	48/ 107	(44.9)	NE (21.0, NE)	1.458 (0.982, 2.164)	0.061	0.799	1.418 (0.975, 2.062)	0.068		0.502
No	68/ 128	(53.1)	19.0 (15.0, NE)	45/ 125	(36.0)	NE (NE, NE)	1.650 (1.121, 2.428)	0.011		1.655 (1.135, 2.414)	0.009		

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[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=240)			Placebo (N=232)			Adjusted Analysis [2]			Interaction		Unadjusted Analysis [3]			Interaction	
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	p-Value			Hazard Ratio (95% CI)	p-Value	p-Value		
Presence of risk factor: Diabetes mellitus										0.471					0.358	
Yes	15/	26 (57.7)	15.0 (9.0, NE)	11/	27 (40.7)	NE (22.0, NE)	2.631 (1.054, 6.567)	0.038				2.262 (1.027, 4.986)	0.043			
No	117/	214 (54.7)	20.0 (18.0, 24.0)	82/	205 (40.0)	NE (25.0, NE)	1.483 (1.108, 1.986)	0.008				1.476 (1.113, 1.957)	0.007			
Presence of risk factor: Immunosuppression																
Yes	1/	2 (50.0)		3/	4 (75.0)											
No	131/	238 (55.0)		90/	228 (39.5)											
Presence of risk factor: Chronic lung disease										0.989					0.827	
Yes	10/	22 (45.5)	NE (16.0, NE)	3/	10 (30.0)	NE (6.0, NE)	5.209 (0.511, 53.090)	0.164				1.340 (0.369, 4.874)	0.656			
No	122/	218 (56.0)	19.0 (16.0, 23.0)	90/	222 (40.5)	NE (24.0, NE)	1.566 (1.184, 2.072)	0.002				1.580 (1.203, 2.075)	0.001			
Presence of risk factor: Hypertension										0.845					0.558	
Yes	44/	77 (57.1)	21.0 (16.0, NE)	28/	77 (36.4)	NE (24.0, NE)	1.668 (0.986, 2.821)	0.056				1.764 (1.097, 2.837)	0.019			
No	88/	163 (54.0)	19.0 (15.0, NE)	65/	155 (41.9)	NE (22.0, NE)	1.464 (1.051, 2.040)	0.024				1.452 (1.054, 2.002)	0.023			
Presence of risk factor: Cardiovascular disorder										0.974					0.966	
Yes	0/	3 (0.0)	NE (NE, NE)	3/	8 (37.5)	NE (9.0, NE)	NE (NE, NE)	NE				NE (NE, NE)	NE			
No	132/	237 (55.7)	19.0 (16.0, 23.0)	90/	224 (40.2)	NE (25.0, NE)	1.549 (1.177, 2.039)	0.002				1.557 (1.191, 2.037)	0.001			
Presence of risk factor: Chronic kidney disease																
Yes	1/	3 (33.3)		0/	2 (0.0)											
No	131/	237 (55.3)		93/	230 (40.4)											
Presence of risk factor: HIV Infection																
Yes	0			0												
No	132/	240 (55.0)		93/	232 (40.1)											
Presence of risk factor: Sickle Cell Disease																
No	132/	240 (55.0)		93/	232 (40.1)											
Presence of risk factor: Neurodevelopmental Disorder																
Yes	1/	1 (100.0)		0												
No	131/	239 (54.8)		93/	232 (40.1)											
Presence of risk factor: Cancer																
Yes	0			1/	1 (100.0)											
No	132/	240 (55.0)		92/	231 (39.8)											
Presence of risk factor: Device Dependence																
Yes	0			0												
No	131/	236 (55.5)		92/	228 (40.4)											

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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Analysis of Participants with Worsening of Signs and Symptoms - Loss of taste - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]		Interaction p-Value	Unadjusted analysis [2]		Interaction p-Value
			Relative Risk (95% CI)	p-Value		Relative Risk (95% CI)	p-Value	
Age								
< 65	202/ 790 (25.6)	198/ 810 (24.4)	1.031 (0.868, 1.223)	0.731	0.430	1.046 (0.883, 1.240)	0.603	0.332
>= 65	24/ 138 (17.4)	31/ 145 (21.4)	0.860 (0.530, 1.393)	0.539		0.813 (0.504, 1.314)	0.398	
Gender								
Male	103/ 463 (22.2)	108/ 507 (21.3)	1.043 (0.820, 1.327)	0.733	0.715	1.044 (0.823, 1.326)	0.722	0.695
Female	123/ 465 (26.5)	121/ 448 (27.0)	0.983 (0.791, 1.221)	0.874		0.979 (0.790, 1.214)	0.849	
Geographic region								
United States	91/ 375 (24.3)	93/ 387 (24.0)	0.981 (0.760, 1.267)	0.884	0.944	1.010 (0.785, 1.299)	0.939	0.970
Europe	88/ 322 (27.3)	83/ 321 (25.9)	1.090 (0.837, 1.419)	0.522		1.057 (0.817, 1.367)	0.673	
India	5/ 74 (6.8)	6/ 78 (7.7)	NE (NE, NE)	NE		0.878 (0.280, 2.756)	0.824	
Rest of World	42/ 157 (26.8)	47/ 169 (27.8)	0.964 (0.677, 1.371)	0.838		0.962 (0.674, 1.372)	0.830	
COVID-19 therapeutic mAb treatment at randomisation								
Yes	16/ 57 (28.1)	13/ 60 (21.7)	1.395 (0.733, 2.654)	0.311	0.601	1.296 (0.686, 2.447)	0.425	0.438
No	210/ 871 (24.1)	216/ 895 (24.1)	0.995 (0.842, 1.176)	0.952		0.999 (0.847, 1.179)	0.991	
Baseline viral load 1								
< 10^4 copies/mL	52/ 335 (15.5)	62/ 354 (17.5)	0.922 (0.659, 1.291)	0.637	0.537	0.886 (0.633, 1.241)	0.482	0.426
>= 10^4 copies/mL	164/ 569 (28.8)	160/ 575 (27.8)	1.036 (0.862, 1.246)	0.706		1.036 (0.861, 1.246)	0.708	
Baseline viral load 2								
< 10^7 copies/mL	120/ 652 (18.4)	142/ 699 (20.3)	0.927 (0.745, 1.153)	0.496	0.317	0.906 (0.728, 1.127)	0.376	0.248
>= 10^7 copies/mL	96/ 252 (38.1)	80/ 230 (34.8)	1.082 (0.856, 1.368)	0.511		1.095 (0.864, 1.388)	0.452	
Baseline serology status								
Negative	129/ 435 (29.7)	126/ 456 (27.6)	1.060 (0.860, 1.307)	0.584	0.452	1.073 (0.872, 1.321)	0.504	0.501
Positive	93/ 482 (19.3)	98/ 487 (20.1)	0.939 (0.729, 1.210)	0.628		0.959 (0.744, 1.236)	0.746	
Symptom onset days to first dose date								
<= 3	171/ 624 (27.4)	164/ 624 (26.3)	1.049 (0.871, 1.264)	0.611	0.389	1.043 (0.868, 1.252)	0.655	0.514
> 3	55/ 304 (18.1)	65/ 331 (19.6)	0.905 (0.653, 1.254)	0.548		0.921 (0.667, 1.273)	0.620	
BMI group								
< 25	38/ 215 (17.7)	50/ 213 (23.5)	0.696 (0.475, 1.019)	0.063	0.058	0.753 (0.517, 1.098)	0.140	0.082
25 - < 30	72/ 319 (22.6)	80/ 332 (24.1)	0.943 (0.712, 1.250)	0.685		0.937 (0.709, 1.238)	0.646	
>= 30	115/ 393 (29.3)	99/ 410 (24.1)	1.197 (0.944, 1.519)	0.138		1.212 (0.963, 1.526)	0.102	
Ethnicity								
White	178/ 699 (25.5)	184/ 718 (25.6)	1.004 (0.838, 1.204)	0.962	0.986	0.994 (0.832, 1.187)	0.944	0.957
Black or African American	10/ 43 (23.3)	8/ 40 (20.0)	0.848 (0.373, 1.931)	0.695		1.163 (0.510, 2.651)	0.720	
Asian	18/ 117 (15.4)	17/ 127 (13.4)	NE (NE, NE)	NE		1.149 (0.622, 2.123)	0.657	
Others	20/ 69 (29.0)	20/ 70 (28.6)	NE (NE, NE)	NE		1.014 (0.601, 1.712)	0.957	
Number of baseline comorbidities present								
0-1	183/ 710 (25.8)	178/ 728 (24.5)	1.030 (0.860, 1.233)	0.748	0.732	1.054 (0.882, 1.260)	0.563	0.560
2-3	41/ 214 (19.2)	49/ 221 (22.2)	0.879 (0.599, 1.290)	0.511		0.864 (0.597, 1.251)	0.439	
>= 4	2/ 4 (50.0)	2/ 6 (33.3)	NE (NE, NE)	NE		1.500 (0.336, 6.702)	0.596	
Presence of risk factor: Smoking								
Yes	96/ 417 (23.0)	103/ 438 (23.5)	0.958 (0.749, 1.224)	0.730	0.608	0.979 (0.767, 1.249)	0.864	0.680
No	130/ 509 (25.5)	126/ 517 (24.4)	1.048 (0.846, 1.298)	0.669		1.048 (0.848, 1.296)	0.665	
Presence of risk factor: Diabetes mellitus					0.018			0.010

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF) / last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochran's Q statistic.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with Worsening of Signs and Symptoms - Loss of taste - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]			Interaction p-Value	Unadjusted analysis [2]			Interaction p-Value
			Relative Risk (95% CI)		p-Value		Relative Risk (95% CI)		p-Value	
Yes	19/ 130 (14.6)	36/ 136 (26.5)	0.576 (0.351, 0.947)		0.030		0.552 (0.335, 0.911)		0.020	
No	207/ 797 (26.0)	193/ 819 (23.6)	1.083 (0.911, 1.287)		0.367		1.102 (0.930, 1.307)		0.263	
Presence of risk factor: Immunosuppression						0.189				0.431
Yes	1/ 6 (16.7)	0/ 7 (0.0)	NE (NE, NE)		NE		3.429 (0.165, 71.361)		0.426	
No	225/ 921 (24.4)	229/ 948 (24.2)	1.002 (0.852, 1.178)		0.982		1.011 (0.862, 1.187)		0.890	
Presence of risk factor: Chronic lung disease						0.959				0.964
Yes	10/ 62 (16.1)	6/ 39 (15.4)	1.250 (0.487, 3.210)		0.642		1.048 (0.414, 2.656)		0.921	
No	216/ 865 (25.0)	223/ 916 (24.3)	1.018 (0.864, 1.200)		0.829		1.026 (0.872, 1.207)		0.759	
Presence of risk factor: Hypertension						0.766				0.670
Yes	84/ 348 (24.1)	92/ 371 (24.8)	0.955 (0.733, 1.243)		0.732		0.973 (0.753, 1.259)		0.837	
No	142/ 579 (24.5)	137/ 584 (23.5)	1.014 (0.826, 1.246)		0.893		1.045 (0.852, 1.283)		0.670	
Presence of risk factor: Cardiovascular disorder						0.656				0.930
Yes	11/ 42 (26.2)	13/ 49 (26.5)	NE (NE, NE)		NE		0.987 (0.496, 1.966)		0.971	
No	215/ 885 (24.3)	216/ 906 (23.8)	1.016 (0.861, 1.200)		0.848		1.019 (0.864, 1.201)		0.823	
Presence of risk factor: Chronic kidney disease						0.846				0.854
Yes	2/ 6 (33.3)	3/ 8 (37.5)	NE (NE, NE)		NE		0.889 (0.210, 3.761)		0.873	
No	224/ 921 (24.3)	226/ 947 (23.9)	1.009 (0.858, 1.187)		0.915		1.019 (0.868, 1.197)		0.818	
Presence of risk factor: HIV Infection										
Yes	0	0/ 1 (0.0)								
No	226/ 927 (24.4)	229/ 953 (24.0)								
Presence of risk factor: Sickle Cell Disease										
No	226/ 927 (24.4)	229/ 955 (24.0)								
Presence of risk factor: Neurodevelopmental Disorder										
Yes	1/ 2 (50.0)	0/ 1 (0.0)								
No	225/ 925 (24.3)	229/ 954 (24.0)								
Presence of risk factor: Cancer						NE				0.418
Yes	2/ 5 (40.0)	1/ 6 (16.7)	NE (NE, NE)		NE		2.400 (0.298, 19.337)		0.411	
No	224/ 922 (24.3)	228/ 949 (24.0)	1.000 (0.850, 1.177)		0.998		1.011 (0.861, 1.187)		0.892	
Presence of risk factor: Device Dependence										
Yes	2/ 4 (50.0)	2/ 3 (66.7)								
No	221/ 914 (24.2)	224/ 944 (23.7)								

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

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[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

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RKI-conform mITT2 Analysis set
Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Loss of taste - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=492)						Placebo (N=517)				Adjusted Analysis [2]		Unadjusted Analysis [3]				
	n/N	(%)	Median	(95% CI)	[1]		n/N	(%)	Median	(95% CI)	[1]	Hazard Ratio (95% CI)	p-Value	p-Value	Hazard Ratio (95% CI)	p-Value	p-Value
Age														0.439			0.322
< 65	318/ 432	(73.6)	10.0	(9.0, 11.0)			288/ 449	(64.1)	14.0	(13.0, 16.0)		1.371 (1.164, 1.616)	<.001		1.376 (1.173, 1.615)	<.001	
>= 65	49/ 60	(81.7)	9.0	(7.0, 12.0)			44/ 68	(64.7)	13.0	(9.0, 22.0)		1.721 (1.119, 2.646)	0.013		1.699 (1.126, 2.564)	0.012	
Gender														0.094			0.099
Male	178/ 229	(77.7)	9.0	(8.0, 11.0)			154/ 249	(61.8)	14.0	(12.0, 17.0)		1.607 (1.286, 2.008)	<.001		1.610 (1.296, 2.000)	<.001	
Female	189/ 263	(71.9)	11.0	(9.0, 12.0)			178/ 268	(66.4)	13.0	(12.0, 16.0)		1.254 (1.016, 1.548)	0.035		1.258 (1.025, 1.545)	0.028	
Geographic region														0.329			0.337
United States	180/ 245	(73.5)	10.0	(8.0, 11.0)			164/ 237	(69.2)	13.0	(11.0, 16.0)		1.248 (1.003, 1.553)	0.047		1.249 (1.010, 1.544)	0.040	
Europe	103/ 137	(75.2)	11.0	(9.0, 13.0)			87/ 153	(56.9)	18.0	(13.0, 23.0)		1.743 (1.299, 2.339)	<.001		1.691 (1.270, 2.253)	<.001	
India	32/ 35	(91.4)	6.0	(4.0, 14.0)			29/ 32	(90.6)	9.0	(6.0, 14.0)		1.241 (0.723, 2.131)	0.433		1.183 (0.715, 1.957)	0.513	
Rest of World	52/ 75	(69.3)	10.0	(8.0, 13.0)			52/ 95	(54.7)	16.0	(11.0, NE)		1.414 (0.951, 2.101)	0.087		1.487 (1.010, 2.188)	0.044	
COVID-19 therapeutic mAb treatment at randomisation														0.267			0.197
Yes	25/ 35	(71.4)	11.0	(6.0, 16.0)			28/ 38	(73.7)	11.0	(5.0, 18.0)		0.918 (0.523, 1.610)	0.765		0.984 (0.573, 1.689)	0.954	
No	342/ 457	(74.8)	10.0	(9.0, 11.0)			304/ 479	(63.5)	14.0	(13.0, 16.0)		1.436 (1.225, 1.684)	<.001		1.454 (1.245, 1.697)	<.001	
Baseline viral load 1														0.987			0.965
< 10^4 copies/mL	149/ 186	(80.1)	9.0	(8.0, 11.0)			130/ 191	(68.1)	12.0	(10.0, 15.0)		1.413 (1.111, 1.797)	0.005		1.428 (1.128, 1.809)	0.003	
>= 10^4 copies/mL	206/ 290	(71.0)	10.0	(9.0, 12.0)			192/ 310	(61.9)	15.0	(13.0, 18.0)		1.382 (1.133, 1.687)	0.001		1.415 (1.161, 1.724)	<.001	
Baseline viral load 2														0.494			0.508
< 10^7 copies/mL	287/ 379	(75.7)	9.0	(8.0, 11.0)			264/ 398	(66.3)	13.0	(12.0, 15.0)		1.363 (1.151, 1.615)	<.001		1.383 (1.169, 1.636)	<.001	
>= 10^7 copies/mL	68/ 97	(70.1)	11.0	(9.0, 13.0)			58/ 103	(56.3)	20.0	(14.0, NE)		1.562 (1.080, 2.260)	0.018		1.594 (1.121, 2.267)	0.009	
Baseline serology status														0.224			0.185
Negative	160/ 224	(71.4)	11.0	(9.0, 12.0)			140/ 243	(57.6)	17.0	(14.0, 21.0)		1.593 (1.259, 2.015)	<.001		1.588 (1.264, 1.994)	<.001	
Positive	203/ 263	(77.2)	9.0	(8.0, 12.0)			189/ 269	(70.3)	13.0	(10.0, 14.0)		1.292 (1.056, 1.581)	0.013		1.279 (1.049, 1.560)	0.015	
Symptom onset days to first dose date														0.334			0.350
<= 3	230/ 310	(74.2)	11.0	(9.0, 12.0)			201/ 310	(64.8)	13.0	(12.0, 15.0)		1.327 (1.093, 1.610)	0.004		1.338 (1.107, 1.618)	0.003	
> 3	137/ 182	(75.3)	9.0	(8.0, 11.0)			131/ 207	(63.3)	16.0	(13.0, 18.0)		1.553 (1.209, 1.995)	<.001		1.546 (1.214, 1.968)	<.001	
BMI group														0.596			0.591
< 25	83/ 106	(78.3)	10.0	(8.0, 11.0)			66/ 101	(65.3)	13.0	(11.0, 19.0)		1.609 (1.141, 2.269)	0.007		1.607 (1.161, 2.226)	0.004	
25 - < 30	115/ 156	(73.7)	10.0	(8.0, 13.0)			122/ 184	(66.3)	14.0	(12.0, 16.0)		1.309 (1.006, 1.702)	0.045		1.285 (0.996, 1.659)	0.054	
>= 30	169/ 230	(73.5)	10.0	(9.0, 12.0)			144/ 232	(62.1)	14.0	(12.0, 18.0)		1.438 (1.141, 1.811)	0.002		1.433 (1.147, 1.791)	0.002	
Ethnicity														0.903			0.976
White	275/ 374	(73.5)	11.0	(9.0, 12.0)			244/ 393	(62.1)	15.0	(13.0, 17.0)		1.412 (1.182, 1.687)	<.001		1.423 (1.197, 1.692)	<.001	
Black or African American	23/ 28	(82.1)	7.0	(6.0, 11.0)			17/ 23	(73.9)	9.0	(3.0, 19.0)		1.510 (0.706, 3.230)	0.288		1.505 (0.782, 2.897)	0.221	
Asian	45/ 53	(84.9)	7.0	(4.0, 11.0)			46/ 56	(82.1)	9.0	(6.0, 15.0)		1.321 (0.851, 2.049)	0.214		1.326 (0.876, 2.006)	0.182	
Others	24/ 37	(64.9)	10.0	(4.0, 13.0)			25/ 45	(55.6)	14.0	(10.0, NE)		1.412 (0.783, 2.547)	0.252		1.439 (0.820, 2.524)	0.204	
Number of baseline comorbidities present																	
0-1	281/ 378	(74.3)					244/ 384	(63.5)									
2-3	85/ 113	(75.2)					86/ 131	(65.6)									
>= 4	1/ 1	(100.0)					2/ 2	(100.0)									
Presence of risk factor: Smoking														0.937			0.806
Yes	170/ 227	(74.9)	11.0	(9.0, 13.0)			149/ 234	(63.7)	15.0	(13.0, 18.0)		1.458 (1.162, 1.830)	0.001		1.470 (1.179, 1.834)	<.001	
No	197/ 264	(74.6)	9.0	(8.0, 11.0)			183/ 283	(64.7)	13.0	(12.0, 15.0)		1.385 (1.126, 1.703)	0.002		1.385 (1.132, 1.695)	0.002	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=492)			Placebo (N=517)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus										0.337				0.397
Yes	53/ 68	(77.9)	9.0 (7.0, 11.0)	57/ 74	(77.0)	11.0 (9.0, 15.0)	1.169 (0.794, 1.723)	0.429			1.241 (0.852, 1.806)	0.260		
No	314/ 424	(74.1)	10.0 (9.0, 12.0)	275/ 443	(62.1)	14.0 (13.0, 17.0)	1.452 (1.228, 1.716)	<.001			1.453 (1.235, 1.710)	<.001		
Presence of risk factor: Immunosuppression										0.016				0.080
Yes	4/ 4	(100.0)	16.0 (2.0, 21.0)	6/ 6	(100.0)	5.5 (2.0, 12.0)	517E16 (0.000, NE)	0.999			0.268 (0.051, 1.421)	0.122		
No	363/ 488	(74.4)	10.0 (9.0, 11.0)	326/ 511	(63.8)	14.0 (13.0, 16.0)	1.419 (1.216, 1.654)	<.001			1.431 (1.231, 1.662)	<.001		
Presence of risk factor: Chronic lung disease										0.069				0.127
Yes	34/ 40	(85.0)	8.0 (5.0, 13.0)	14/ 27	(51.9)	20.0 (8.0, NE)	2.395 (1.048, 5.474)	0.038			2.237 (1.196, 4.184)	0.012		
No	333/ 452	(73.7)	10.0 (9.0, 11.0)	318/ 490	(64.9)	14.0 (13.0, 16.0)	1.341 (1.144, 1.571)	<.001			1.370 (1.174, 1.598)	<.001		
Presence of risk factor: Hypertension										0.709				0.769
Yes	133/ 180	(73.9)	10.0 (9.0, 12.0)	137/ 207	(66.2)	15.0 (12.0, 17.0)	1.353 (1.060, 1.729)	0.015			1.381 (1.087, 1.754)	0.008		
No	234/ 312	(75.0)	10.0 (9.0, 11.0)	195/ 310	(62.9)	13.0 (12.0, 16.0)	1.435 (1.179, 1.746)	<.001			1.429 (1.181, 1.730)	<.001		
Presence of risk factor: Cardiovascular disorder										0.516				0.928
Yes	10/ 15	(66.7)	14.0 (4.0, NE)	13/ 23	(56.5)	19.0 (6.0, NE)	2.196 (0.808, 5.969)	0.123			1.450 (0.633, 3.323)	0.380		
No	357/ 477	(74.8)	10.0 (9.0, 11.0)	319/ 494	(64.6)	14.0 (12.0, 16.0)	1.389 (1.189, 1.622)	<.001			1.409 (1.211, 1.640)	<.001		
Presence of risk factor: Chronic kidney disease														
Yes	2/ 3	(66.7)		2/ 4	(50.0)									
No	365/ 489	(74.6)		330/ 513	(64.3)									
Presence of risk factor: HIV Infection														
Yes	0			0										
No	367/ 492	(74.6)		331/ 516	(64.1)									
Presence of risk factor: Sickle Cell Disease														
No	367/ 492	(74.6)		332/ 517	(64.2)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/ 2	(100.0)		1/ 1	(100.0)									
No	365/ 490	(74.5)		331/ 516	(64.1)									
Presence of risk factor: Cancer														
Yes	0			4/ 4	(100.0)									
No	367/ 492	(74.6)		328/ 513	(63.9)									
Presence of risk factor: Device Dependence														
Yes	0/ 1	(0.0)		0/ 1	(0.0)									
No	365/ 485	(75.3)		330/ 511	(64.6)									

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=208)			Placebo (N=194)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	154/ 193	(79.8)	8.0 (6.0, 8.0)	122/ 178	(68.5)	12.0 (9.0, 13.0)	1.400 (1.088, 1.803)	0.009		0.708	1.397 (1.100, 1.773)	0.006		0.644
>= 65	13/ 15	(86.7)	6.5 (2.0, 8.0)	12/ 16	(75.0)	8.0 (2.0, 23.0)	1.456 (0.544, 3.900)	0.455			1.691 (0.735, 3.888)	0.217		
Gender														
Male	75/ 87	(86.2)	6.5 (4.0, 8.0)	58/ 91	(63.7)	12.0 (8.0, 15.0)	1.562 (1.083, 2.253)	0.017		0.198	1.737 (1.229, 2.455)	0.002		0.101
Female	92/ 121	(76.0)	8.0 (6.0, 10.0)	76/ 103	(73.8)	11.0 (6.0, 13.0)	1.191 (0.857, 1.655)	0.298			1.202 (0.886, 1.630)	0.237		
Geographic region														
United States	97/ 126	(77.0)	8.0 (6.0, 9.0)	66/ 91	(72.5)	10.0 (6.0, 13.0)	1.210 (0.874, 1.676)	0.251		0.595	1.196 (0.874, 1.636)	0.264		0.357
Europe	29/ 32	(90.6)	6.0 (3.0, 8.0)	39/ 58	(67.2)	13.0 (10.0, 20.0)	2.146 (1.233, 3.735)	0.007			2.208 (1.347, 3.619)	0.002		
India	12/ 12	(100.0)	3.5 (2.0, 5.0)	8/ 9	(88.9)	4.0 (2.0, 11.0)	1.204 (0.422, 3.433)	0.729			1.636 (0.635, 4.213)	0.308		
Rest of World	29/ 38	(76.3)	9.0 (7.0, 13.0)	21/ 36	(58.3)	10.0 (5.0, NE)	1.511 (0.845, 2.703)	0.164			1.391 (0.791, 2.444)	0.252		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	13/ 16	(81.3)	8.0 (3.0, 11.0)	4/ 9	(44.4)	NE (7.0, NE)	7.575 (1.679, 34.175)	0.008		0.075	3.510 (1.118, 11.020)	0.031		0.151
No	154/ 192	(80.2)	7.0 (6.0, 8.0)	130/ 185	(70.3)	11.0 (8.0, 13.0)	1.320 (1.030, 1.692)	0.028			1.353 (1.070, 1.711)	0.011		
Baseline viral load 1														
< 10^4 copies/mL	65/ 79	(82.3)	6.0 (4.0, 8.0)	41/ 61	(67.2)	11.5 (6.0, 16.0)	1.639 (1.091, 2.463)	0.017		0.233	1.541 (1.040, 2.284)	0.031		0.424
>= 10^4 copies/mL	97/ 124	(78.2)	8.0 (6.0, 9.0)	88/ 126	(69.8)	11.0 (8.0, 14.0)	1.270 (0.935, 1.724)	0.126			1.320 (0.988, 1.764)	0.060		
Baseline viral load 2														
< 10^7 copies/mL	137/ 173	(79.2)	8.0 (6.0, 8.0)	103/ 154	(66.9)	12.0 (9.0, 14.0)	1.472 (1.129, 1.920)	0.004		0.338	1.466 (1.134, 1.895)	0.004		0.330
>= 10^7 copies/mL	25/ 30	(83.3)	8.0 (5.0, 11.0)	26/ 33	(78.8)	8.0 (3.0, 14.0)	0.890 (0.469, 1.689)	0.722			1.156 (0.665, 2.011)	0.607		
Baseline serology status														
Negative	71/ 93	(76.3)	8.0 (6.0, 10.0)	62/ 95	(65.3)	12.0 (9.0, 19.0)	1.449 (0.989, 2.123)	0.057		0.993	1.440 (1.021, 2.029)	0.037		0.944
Positive	93/ 112	(83.0)	6.0 (4.0, 8.0)	70/ 96	(72.9)	10.0 (6.0, 13.0)	1.392 (1.013, 1.914)	0.042			1.361 (0.997, 1.858)	0.052		
Symptom onset days to first dose date														
<= 3	107/ 131	(81.7)	7.0 (6.0, 8.0)	86/ 118	(72.9)	9.0 (7.0, 13.0)	1.323 (0.981, 1.785)	0.067		0.600	1.301 (0.978, 1.729)	0.071		0.393
> 3	60/ 77	(77.9)	8.0 (6.0, 9.0)	48/ 76	(63.2)	13.0 (9.0, 18.0)	1.563 (1.014, 2.410)	0.043			1.605 (1.095, 2.354)	0.015		
BMI group														
< 25	30/ 35	(85.7)	6.0 (4.0, 8.0)	23/ 34	(67.6)	11.0 (5.0, 24.0)	1.862 (0.987, 3.513)	0.055		0.144	1.994 (1.139, 3.490)	0.016		0.107
25 - < 30	53/ 67	(79.1)	8.0 (6.0, 11.0)	48/ 66	(72.7)	9.0 (5.0, 13.0)	1.027 (0.679, 1.554)	0.898			1.036 (0.701, 1.531)	0.860		
>= 30	84/ 106	(79.2)	7.0 (5.0, 9.0)	63/ 94	(67.0)	13.0 (9.0, 18.0)	1.567 (1.093, 2.245)	0.014			1.531 (1.102, 2.127)	0.011		
Ethnicity														
White	125/ 155	(80.6)	8.0 (6.0, 9.0)	102/ 148	(68.9)	13.0 (10.0, 14.0)	1.445 (1.090, 1.915)	0.011		0.989	1.453 (1.117, 1.889)	0.005		0.958
Black or African American	12/ 14	(85.7)	6.0 (2.0, 8.0)	7/ 9	(77.8)	6.0 (2.0, 19.0)	1.049 (0.314, 3.513)	0.938			1.141 (0.445, 2.927)	0.784		
Asian	13/ 16	(81.3)	4.0 (2.0, 7.0)	11/ 13	(84.6)	5.0 (2.0, 11.0)	0.902 (0.348, 2.343)	0.833			1.119 (0.500, 2.504)	0.785		
Others	17/ 23	(73.9)	8.0 (3.0, 12.0)	14/ 24	(58.3)	9.0 (3.0, NE)	1.544 (0.712, 3.345)	0.271			1.295 (0.636, 2.637)	0.476		
Number of baseline comorbidities present														
0-1	140/ 169	(82.8)		103/ 158	(65.2)									
2-3	27/ 39	(69.2)		31/ 36	(86.1)									
>= 4	0			0										
Presence of risk factor: Smoking														
Yes	71/ 89	(79.8)	8.0 (6.0, 11.0)	65/ 89	(73.0)	11.0 (7.0, 13.0)	1.214 (0.850, 1.735)	0.287		0.175	1.192 (0.851, 1.671)	0.307		0.168
No	96/ 119	(80.7)	6.0 (5.0, 8.0)	69/ 105	(65.7)	12.0 (8.0, 17.0)	1.563 (1.122, 2.177)	0.008			1.617 (1.184, 2.209)	0.003		

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=208)			Placebo (N=194)			Adjusted Analysis [2]				Unadjusted Analysis [3]			
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)		p-Value	Interaction p-Value	Hazard Ratio (95% CI)		p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus										0.253				0.136
Yes	17/ 24	(70.8)	6.5 (3.0, 8.0)	20/ 22	(90.9)	6.5 (3.0, 10.0)	0.746 (0.341, 1.633)	0.464			0.874 (0.457, 1.673)	0.685		
No	150/ 184	(81.5)	8.0 (6.0, 8.0)	114/ 172	(66.3)	12.0 (9.0, 14.0)	1.482 (1.140, 1.926)	0.003			1.504 (1.177, 1.922)	0.001		
Presence of risk factor: Immunosuppression														
Yes	1/ 1	(100.0)		3/ 3	(100.0)									
No	166/ 207	(80.2)		131/ 191	(68.6)									
Presence of risk factor: Chronic lung disease										0.267				0.678
Yes	15/ 21	(71.4)	7.5 (3.0, 19.0)	3/ 7	(42.9)	NE (2.0, NE)	8.041 (0.993, 65.132)	0.051			1.796 (0.519, 6.218)	0.355		
No	152/ 187	(81.3)	7.0 (6.0, 8.0)	131/ 187	(70.1)	11.0 (8.0, 13.0)	1.384 (1.081, 1.771)	0.010			1.431 (1.131, 1.810)	0.003		
Presence of risk factor: Hypertension										0.828				0.875
Yes	52/ 65	(80.0)	7.0 (5.0, 8.0)	45/ 62	(72.6)	12.0 (7.0, 15.0)	1.194 (0.756, 1.884)	0.447			1.370 (0.917, 2.047)	0.124		
No	115/ 143	(80.4)	8.0 (6.0, 9.0)	89/ 132	(67.4)	11.0 (7.0, 13.0)	1.407 (1.051, 1.884)	0.022			1.424 (1.078, 1.880)	0.013		
Presence of risk factor: Cardiovascular disorder														
Yes	0/ 1	(0.0)		2/ 4	(50.0)									
No	167/ 207	(80.7)		132/ 190	(69.5)									
Presence of risk factor: Chronic kidney disease														
Yes	1/ 2	(50.0)		1/ 1	(100.0)									
No	166/ 206	(80.6)		133/ 193	(68.9)									
Presence of risk factor: HIV Infection														
Yes	0			0										
No	167/ 208	(80.3)		134/ 194	(69.1)									
Presence of risk factor: Sickle Cell Disease														
No	167/ 208	(80.3)		134/ 194	(69.1)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	1/ 1	(100.0)		0										
No	166/ 207	(80.2)		134/ 194	(69.1)									
Presence of risk factor: Cancer														
Yes	0			1/ 1	(100.0)									
No	167/ 208	(80.3)		133/ 193	(68.9)									
Presence of risk factor: Device Dependence														
Yes	0			0										
No	165/ 203	(81.3)		132/ 190	(69.5)									

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=492)			Placebo (N=517)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	268/ 432	(62.0)	16.0 (14.0, 17.0)	234/ 449	(52.1)	20.0 (17.0, 25.0)	1.305 (1.090, 1.562)	0.004		0.239	1.338 (1.123, 1.595)	0.001		0.200
>= 65	47/ 60	(78.3)	12.0 (9.0, 15.0)	40/ 68	(58.8)	16.0 (12.0, NE)	1.693 (1.086, 2.638)	0.020			1.772 (1.158, 2.712)	0.008		
Gender														
Male	157/ 229	(68.6)	14.0 (12.0, 16.0)	135/ 249	(54.2)	18.0 (16.0, 25.0)	1.530 (1.206, 1.940)	<.001		0.160	1.506 (1.196, 1.897)	<.001		0.340
Female	158/ 263	(60.1)	16.0 (13.0, 18.0)	139/ 268	(51.9)	21.0 (17.0, NE)	1.221 (0.966, 1.542)	0.095			1.284 (1.022, 1.614)	0.032		
Geographic region														
United States	151/ 245	(61.6)	16.0 (13.0, 18.0)	137/ 237	(57.8)	18.0 (16.0, 21.0)	1.130 (0.890, 1.433)	0.315		0.011	1.162 (0.922, 1.465)	0.202		0.016
Europe	95/ 137	(69.3)	14.0 (12.0, 17.0)	64/ 153	(41.8)	NE (23.0, NE)	2.189 (1.576, 3.039)	<.001			2.097 (1.525, 2.883)	<.001		
India	31/ 35	(88.6)	10.0 (7.0, 14.0)	29/ 32	(90.6)	13.0 (8.0, 15.0)	1.206 (0.706, 2.060)	0.493			1.162 (0.700, 1.931)	0.562		
Rest of World	38/ 75	(50.7)	19.0 (12.0, NE)	44/ 95	(46.3)	24.0 (17.0, NE)	1.042 (0.664, 1.635)	0.858			1.153 (0.747, 1.780)	0.521		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	21/ 35	(60.0)	14.0 (10.0, NE)	24/ 38	(63.2)	12.0 (5.0, NE)	0.861 (0.469, 1.581)	0.628		0.247	0.877 (0.488, 1.577)	0.662		0.146
No	294/ 457	(64.3)	15.0 (13.0, 17.0)	250/ 479	(52.2)	21.0 (17.0, 24.0)	1.384 (1.164, 1.646)	<.001			1.434 (1.211, 1.698)	<.001		
Baseline viral load 1														
< 10^4 copies/mL	130/ 186	(69.9)	15.0 (12.0, 17.0)	118/ 191	(61.8)	16.0 (13.0, 18.0)	1.241 (0.962, 1.603)	0.097		0.279	1.229 (0.958, 1.577)	0.105		0.288
>= 10^4 copies/mL	174/ 290	(60.0)	15.0 (13.0, 18.0)	150/ 310	(48.4)	24.0 (20.0, NE)	1.444 (1.157, 1.802)	0.001			1.468 (1.179, 1.827)	<.001		
Baseline viral load 2														
< 10^7 copies/mL	245/ 379	(64.6)	15.0 (13.0, 16.0)	223/ 398	(56.0)	18.0 (16.0, 22.0)	1.267 (1.055, 1.523)	0.012		0.127	1.288 (1.074, 1.544)	0.006		0.156
>= 10^7 copies/mL	59/ 97	(60.8)	16.0 (13.0, 21.0)	45/ 103	(43.7)	NE (21.0, NE)	1.689 (1.126, 2.532)	0.011			1.766 (1.197, 2.604)	0.004		
Baseline serology status														
Negative	135/ 224	(60.3)	15.0 (14.0, 19.0)	113/ 243	(46.5)	25.0 (21.0, NE)	1.541 (1.192, 1.993)	<.001		0.235	1.555 (1.211, 1.998)	<.001		0.212
Positive	176/ 263	(66.9)	15.0 (12.0, 17.0)	158/ 269	(58.7)	16.0 (14.0, 19.0)	1.244 (1.000, 1.549)	0.050			1.245 (1.004, 1.544)	0.046		
Symptom onset days to first dose date														
<= 3	195/ 310	(62.9)	16.0 (14.0, 18.0)	168/ 310	(54.2)	18.0 (16.0, 24.0)	1.243 (1.007, 1.534)	0.043		0.200	1.271 (1.034, 1.562)	0.023		0.168
> 3	120/ 182	(65.9)	14.0 (11.0, 15.0)	106/ 207	(51.2)	21.0 (18.0, NE)	1.570 (1.195, 2.062)	0.001			1.597 (1.228, 2.076)	<.001		
BMI group														
< 25	78/ 106	(73.6)	13.0 (10.0, 15.0)	57/ 101	(56.4)	18.0 (13.0, NE)	1.470 (1.023, 2.111)	0.037		0.625	1.612 (1.144, 2.271)	0.006		0.539
25 - < 30	98/ 156	(62.8)	16.0 (13.0, 19.0)	104/ 184	(56.5)	18.0 (16.0, 24.0)	1.280 (0.965, 1.700)	0.087			1.264 (0.959, 1.666)	0.096		
>= 30	139/ 230	(60.4)	15.0 (13.0, 19.0)	113/ 232	(48.7)	22.0 (17.0, NE)	1.359 (1.051, 1.758)	0.019			1.380 (1.077, 1.770)	0.011		
Ethnicity														
White	233/ 374	(62.3)	16.0 (14.0, 18.0)	194/ 393	(49.4)	23.0 (18.0, NE)	1.393 (1.145, 1.695)	<.001		0.880	1.423 (1.176, 1.722)	<.001		0.938
Black or African American	20/ 28	(71.4)	9.0 (7.0, 14.0)	15/ 23	(65.2)	16.0 (6.0, 25.0)	1.388 (0.624, 3.088)	0.422			1.413 (0.717, 2.784)	0.318		
Asian	44/ 53	(83.0)	10.0 (7.0, 12.0)	45/ 56	(80.4)	13.0 (8.0, 16.0)	1.339 (0.859, 2.086)	0.197			1.359 (0.894, 2.066)	0.151		
Others	18/ 37	(48.6)	22.0 (13.0, NE)	20/ 45	(44.4)	24.0 (14.0, NE)	1.112 (0.566, 2.185)	0.759			1.160 (0.614, 2.194)	0.648		
Number of baseline comorbidities present														
0-1	237/ 378	(62.7)		202/ 384	(52.6)									
2-3	77/ 113	(68.1)		70/ 131	(53.4)									
>= 4	1/ 1	(100.0)		2/ 2	(100.0)									
Presence of risk factor: Smoking														
Yes	148/ 227	(65.2)	16.0 (14.0, 18.0)	128/ 234	(54.7)	20.0 (17.0, 25.0)	1.404 (1.099, 1.793)	0.007		0.997	1.416 (1.117, 1.795)	0.004		0.961
No	167/ 264	(63.3)	14.0 (12.0, 16.0)	146/ 283	(51.6)	18.0 (16.0, NE)	1.342 (1.069, 1.685)	0.011			1.364 (1.092, 1.704)	0.006		

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	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus										0.784				0.736
Yes	48/ 68	(70.6)	11.0 (9.0, 14.0)	47/ 74	(63.5)	16.0 (13.0, 24.0)	1.563 (1.029, 2.374)	0.036			1.509 (1.007, 2.261)	0.046		
No	267/ 424	(63.0)	16.0 (14.0, 17.0)	227/ 443	(51.2)	21.0 (18.0, NE)	1.349 (1.124, 1.620)	0.001			1.378 (1.154, 1.645)	<.001		
Presence of risk factor: Immunosuppression										0.040				0.359
Yes	3/ 4	(75.0)	16.5 (2.0, NE)	5/ 6	(83.3)	9.5 (2.0, NE)	1.32E8 (0.000, NE)	0.999			0.752 (0.176, 3.204)	0.699		
No	312/ 488	(63.9)	15.0 (13.0, 17.0)	269/ 511	(52.6)	20.0 (17.0, 24.0)	1.366 (1.155, 1.615)	<.001			1.396 (1.186, 1.644)	<.001		
Presence of risk factor: Chronic lung disease										0.412				0.558
Yes	28/ 40	(70.0)	15.0 (10.0, 19.0)	12/ 27	(44.4)	NE (9.0, NE)	1.459 (0.630, 3.376)	0.378			1.665 (0.846, 3.278)	0.140		
No	287/ 452	(63.5)	15.0 (13.0, 17.0)	262/ 490	(53.5)	19.0 (17.0, 24.0)	1.315 (1.107, 1.562)	0.002			1.367 (1.156, 1.617)	<.001		
Presence of risk factor: Hypertension										0.948				0.922
Yes	117/ 180	(65.0)	15.0 (13.0, 18.0)	112/ 207	(54.1)	20.0 (17.0, NE)	1.346 (1.032, 1.755)	0.029			1.403 (1.082, 1.819)	0.011		
No	198/ 312	(63.5)	14.0 (13.0, 17.0)	162/ 310	(52.3)	20.0 (16.0, 25.0)	1.339 (1.081, 1.659)	0.007			1.371 (1.114, 1.688)	0.003		
Presence of risk factor: Cardiovascular disorder										0.146				0.460
Yes	10/ 15	(66.7)	14.0 (4.0, NE)	11/ 23	(47.8)	NE (6.0, NE)	3.284 (1.046, 10.316)	0.042			1.727 (0.729, 4.092)	0.214		
No	305/ 477	(63.9)	15.0 (13.0, 17.0)	263/ 494	(53.2)	20.0 (17.0, 24.0)	1.323 (1.117, 1.566)	0.001			1.371 (1.163, 1.618)	<.001		
Presence of risk factor: Chronic kidney disease														
Yes	1/ 3	(33.3)		1/ 4	(25.0)									
No	314/ 489	(64.2)		273/ 513	(53.2)									
Presence of risk factor: HIV Infection														
Yes	0			0										
No	315/ 492	(64.0)		273/ 516	(52.9)									
Presence of risk factor: Sickle Cell Disease														
No	315/ 492	(64.0)		274/ 517	(53.0)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/ 2	(100.0)		1/ 1	(100.0)									
No	313/ 490	(63.9)		273/ 516	(52.9)									
Presence of risk factor: Cancer														
Yes	0			4/ 4	(100.0)									
No	315/ 492	(64.0)		270/ 513	(52.6)									
Presence of risk factor: Device Dependence														
Yes	0/ 1	(0.0)		0/ 1	(0.0)									
No	313/ 485	(64.5)		273/ 511	(53.4)									

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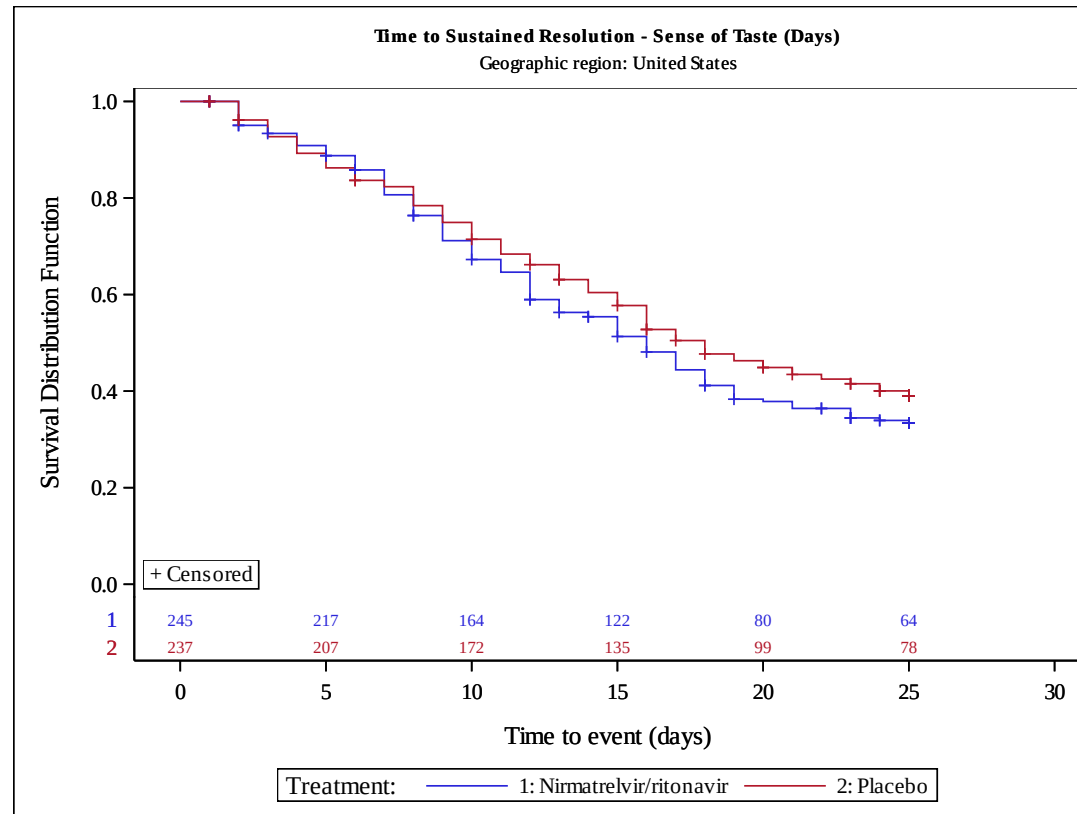
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Final

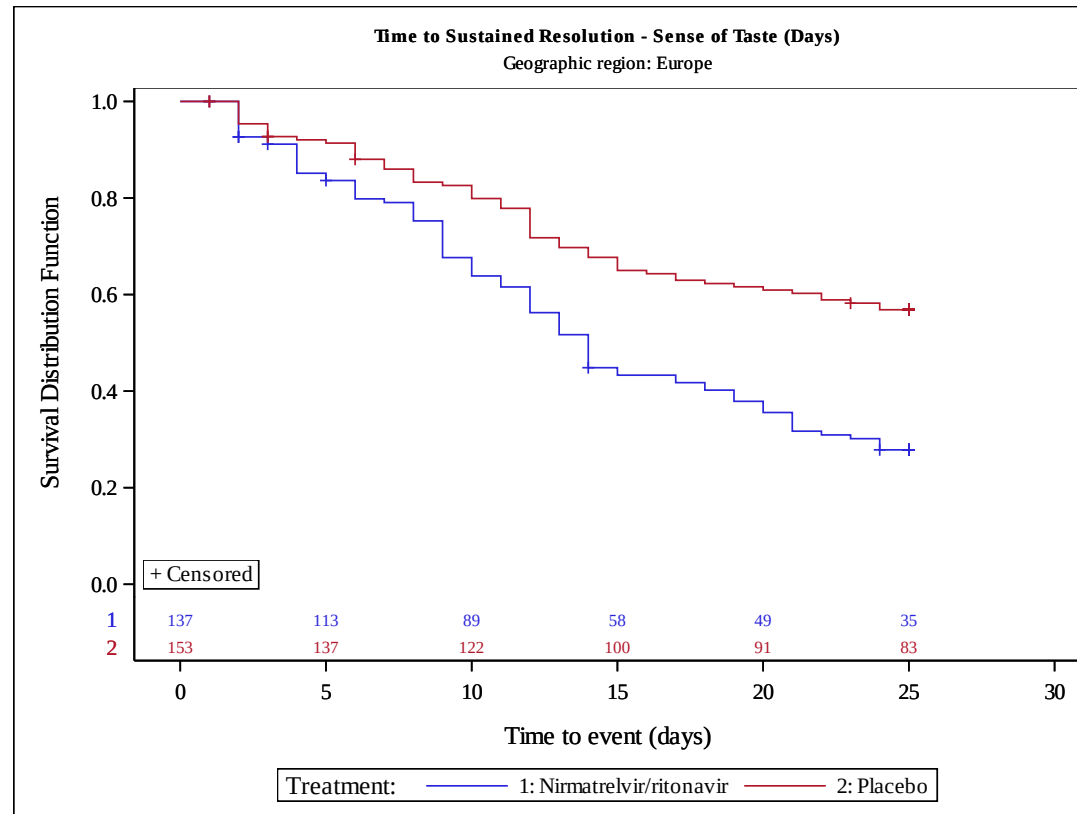


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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Loss of taste

Final

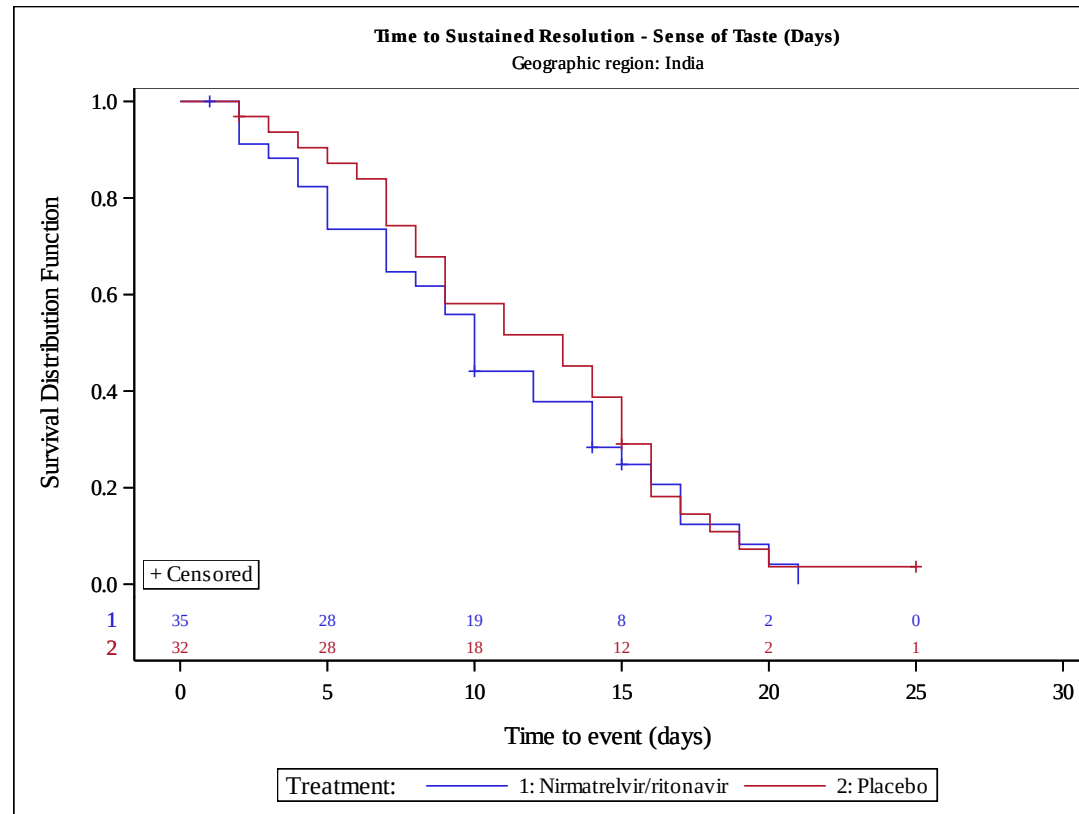


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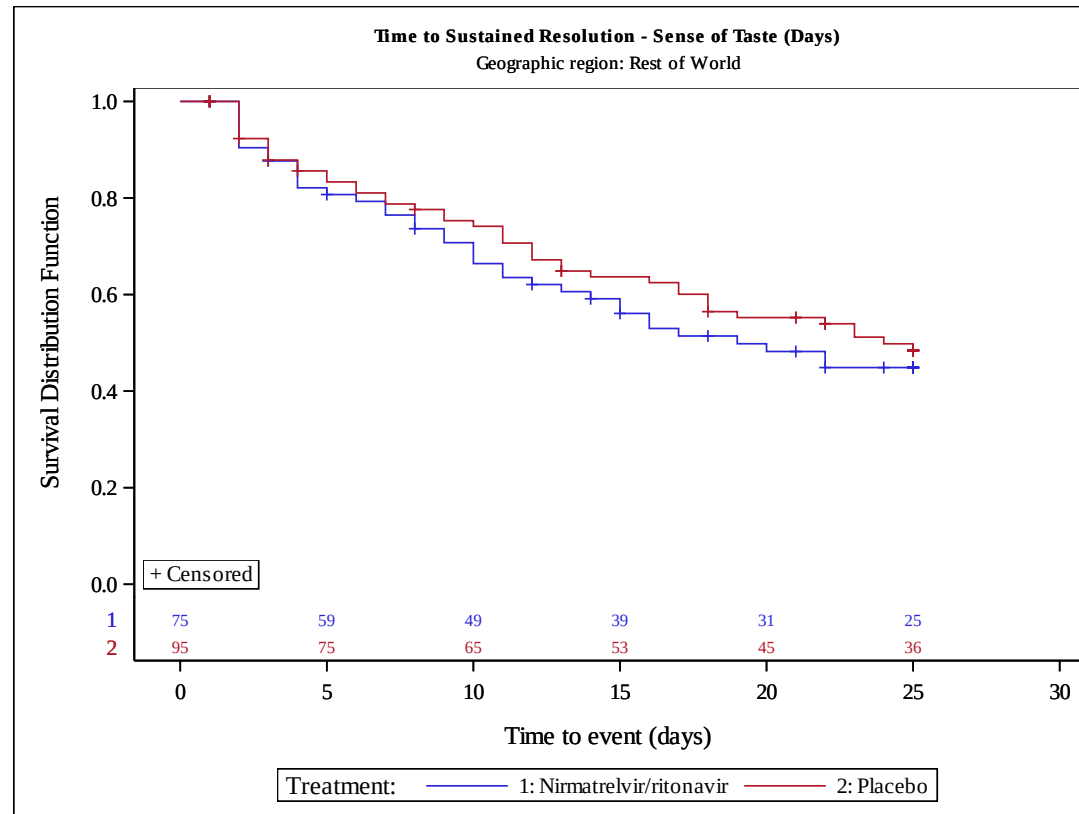


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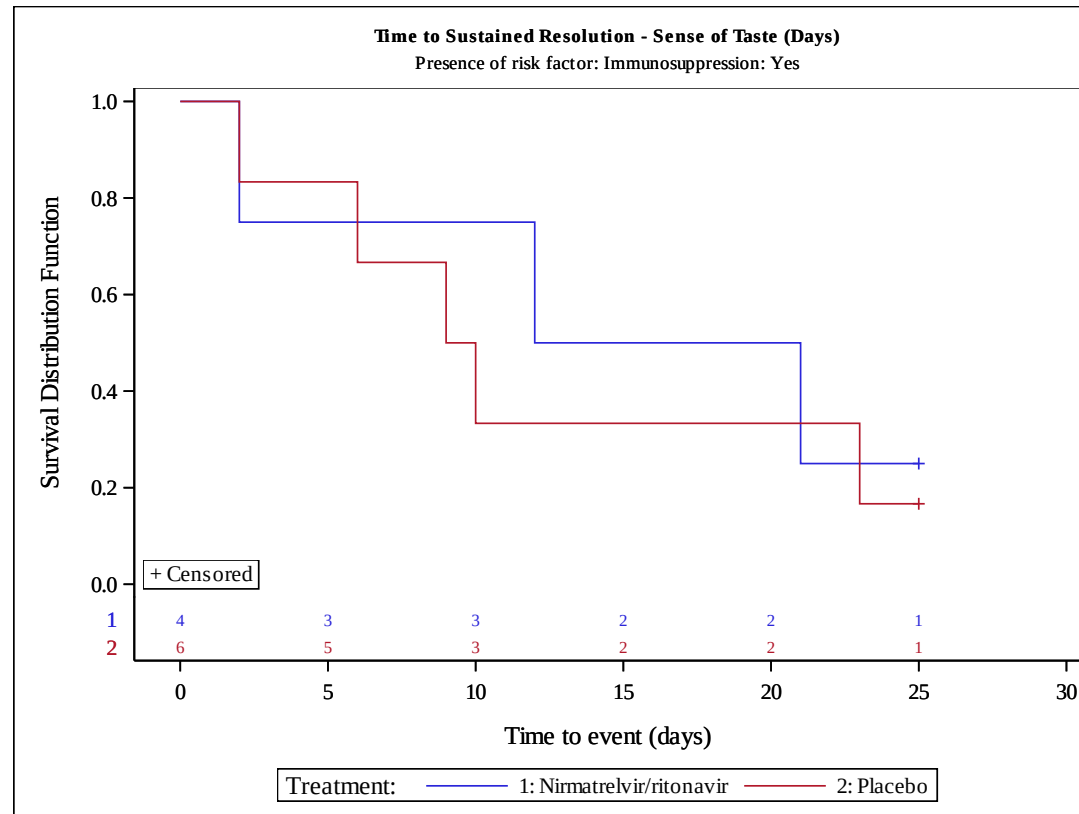
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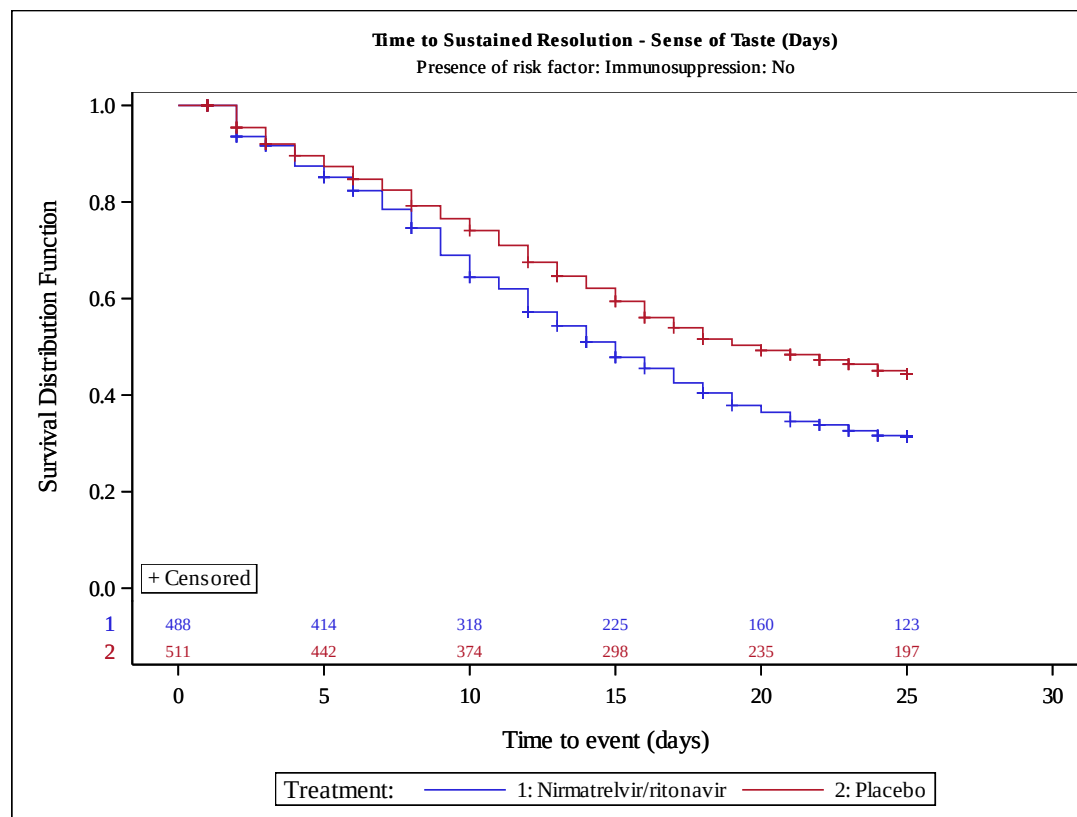


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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=208)				Placebo (N=194)				Adjusted Analysis [2]				Unadjusted Analysis [3]			
	n/N	(%)	Median	(95% CI) [1]	n/N	(%)	Median	(95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value		
Age																
< 65	104/ 193	(53.9)	19.0	(18.0, 24.0)	68/ 178	(38.2)	NE	(25.0, NE)	1.440 (1.045, 1.984)	0.026	0.242	1.550 (1.142, 2.105)	0.005	0.537		
>= 65	11/ 15	(73.3)	13.5	(7.0, 21.0)	8/ 16	(50.0)	24.0	(7.0, NE)	2.808 (0.868, 9.087)	0.085		2.176 (0.860, 5.503)	0.100			
Gender																
Male	54/ 87	(62.1)	19.0	(14.0, 22.0)	39/ 91	(42.9)	NE	(17.0, NE)	1.467 (0.946, 2.275)	0.087	0.761	1.574 (1.042, 2.378)	0.031	0.947		
Female	61/ 121	(50.4)	20.0	(17.0, NE)	37/ 103	(35.9)	NE	(NE, NE)	1.418 (0.918, 2.190)	0.115		1.606 (1.067, 2.417)	0.023			
Geographic region																
United States	68/ 126	(54.0)	19.0	(16.0, NE)	39/ 91	(42.9)	NE	(18.0, NE)	1.337 (0.890, 2.008)	0.163	0.344	1.401 (0.945, 2.078)	0.093	0.255		
Europe	21/ 32	(65.6)	20.0	(14.0, 24.0)	16/ 58	(27.6)	NE	(NE, NE)	2.872 (1.331, 6.195)	0.007		2.779 (1.444, 5.348)	0.002			
India	11/ 12	(91.7)	8.5	(3.0, 10.0)	8/ 9	(88.9)	11.0	(6.0, 16.0)	2.650 (0.889, 7.897)	0.080		1.804 (0.678, 4.798)	0.237			
Rest of World	15/ 38	(39.5)	NE	(19.0, NE)	13/ 36	(36.1)	NE	(23.0, NE)	1.238 (0.554, 2.766)	0.602		1.048 (0.499, 2.203)	0.901			
COVID-19 therapeutic mAb treatment at randomisation																
Yes	9/ 16	(56.3)	13.0	(4.0, NE)	0/ 9	(0.0)	NE	(NE, NE)	NE (NE, NE)	NE	0.978	NE (NE, NE)	NE	0.976		
No	106/ 192	(55.2)	19.0	(18.0, 23.0)	76/ 185	(41.1)	NE	(24.0, NE)	1.351 (0.991, 1.840)	0.057		1.460 (1.087, 1.961)	0.012			
Baseline viral load 1																
< 10^4 copies/mL	46/ 79	(58.2)	19.0	(15.0, 23.0)	29/ 61	(47.5)	NE	(16.0, NE)	1.614 (0.988, 2.638)	0.056	0.916	1.368 (0.859, 2.179)	0.186	0.602		
>= 10^4 copies/mL	65/ 124	(52.4)	20.0	(17.0, NE)	46/ 126	(36.5)	NE	(25.0, NE)	1.412 (0.954, 2.091)	0.084		1.606 (1.100, 2.344)	0.014			
Baseline viral load 2																
< 10^7 copies/mL	95/ 173	(54.9)	19.0	(16.0, 23.0)	62/ 154	(40.3)	NE	(24.0, NE)	1.500 (1.078, 2.086)	0.016	0.883	1.535 (1.114, 2.114)	0.009	0.847		
>= 10^7 copies/mL	16/ 30	(53.3)	20.0	(14.0, NE)	13/ 33	(39.4)	NE	(17.0, NE)	1.071 (0.461, 2.488)	0.874		1.421 (0.683, 2.955)	0.347			
Baseline serology status																
Negative	46/ 93	(49.5)	21.0	(18.0, NE)	35/ 95	(36.8)	NE	(24.0, NE)	1.325 (0.826, 2.126)	0.243	0.525	1.474 (0.949, 2.290)	0.084	0.661		
Positive	66/ 112	(58.9)	18.0	(15.0, 23.0)	39/ 96	(40.6)	NE	(23.0, NE)	1.624 (1.086, 2.428)	0.018		1.636 (1.101, 2.432)	0.015			
Symptom onset days to first dose date																
<= 3	72/ 131	(55.0)	20.0	(18.0, NE)	53/ 118	(44.9)	NE	(18.0, NE)	1.241 (0.856, 1.798)	0.254	0.167	1.279 (0.897, 1.825)	0.174	0.061		
> 3	43/ 77	(55.8)	18.0	(14.0, NE)	23/ 76	(30.3)	NE	(NE, NE)	2.363 (1.332, 4.192)	0.003		2.283 (1.374, 3.793)	0.001			
BMI group																
< 25	25/ 35	(71.4)	15.0	(10.0, 19.0)	14/ 34	(41.2)	NE	(12.0, NE)	1.300 (0.627, 2.693)	0.481	0.675	2.116 (1.096, 4.085)	0.026	0.341		
25 - < 30	36/ 67	(53.7)	19.0	(16.0, NE)	30/ 66	(45.5)	24.0	(17.0, NE)	1.308 (0.778, 2.200)	0.311		1.237 (0.762, 2.009)	0.390			
>= 30	54/ 106	(50.9)	20.0	(18.0, NE)	32/ 94	(34.0)	NE	(NE, NE)	1.608 (0.999, 2.589)	0.050		1.695 (1.094, 2.626)	0.018			
Ethnicity																
White	83/ 155	(53.5)	20.0	(18.0, NE)	52/ 148	(35.1)	NE	(NE, NE)	1.516 (1.051, 2.188)	0.026	0.931	1.689 (1.193, 2.389)	0.003	0.916		
Black or African American	9/ 14	(64.3)	10.0	(4.0, NE)	5/ 9	(55.6)	20.5	(4.0, NE)	1.281 (0.260, 6.300)	0.761		1.395 (0.466, 4.176)	0.552			
Asian	12/ 16	(75.0)	9.5	(7.0, 12.0)	10/ 13	(76.9)	13.0	(7.0, 19.0)	2.634 (0.943, 7.361)	0.065		1.345 (0.577, 3.134)	0.492			
Others	11/ 23	(47.8)	22.0	(13.0, NE)	9/ 24	(37.5)	NE	(12.0, NE)	1.275 (0.478, 3.404)	0.628		1.212 (0.501, 2.929)	0.670			
Number of baseline comorbidities present																
0-1	96/ 169	(56.8)			61/ 158	(38.6)										
2-3	19/ 39	(48.7)			15/ 36	(41.7)										
>= 4	0				0											
Presence of risk factor: Smoking																
Yes	49/ 89	(55.1)	20.0	(18.0, NE)	44/ 89	(49.4)	24.0	(17.0, NE)	1.156 (0.745, 1.792)	0.519	0.072	1.104 (0.735, 1.659)	0.634	0.017		
No	66/ 119	(55.5)	18.0	(13.0, 23.0)	32/ 105	(30.5)	NE	(NE, NE)	1.913 (1.232, 2.971)	0.004		2.174 (1.424, 3.321)	<.001			

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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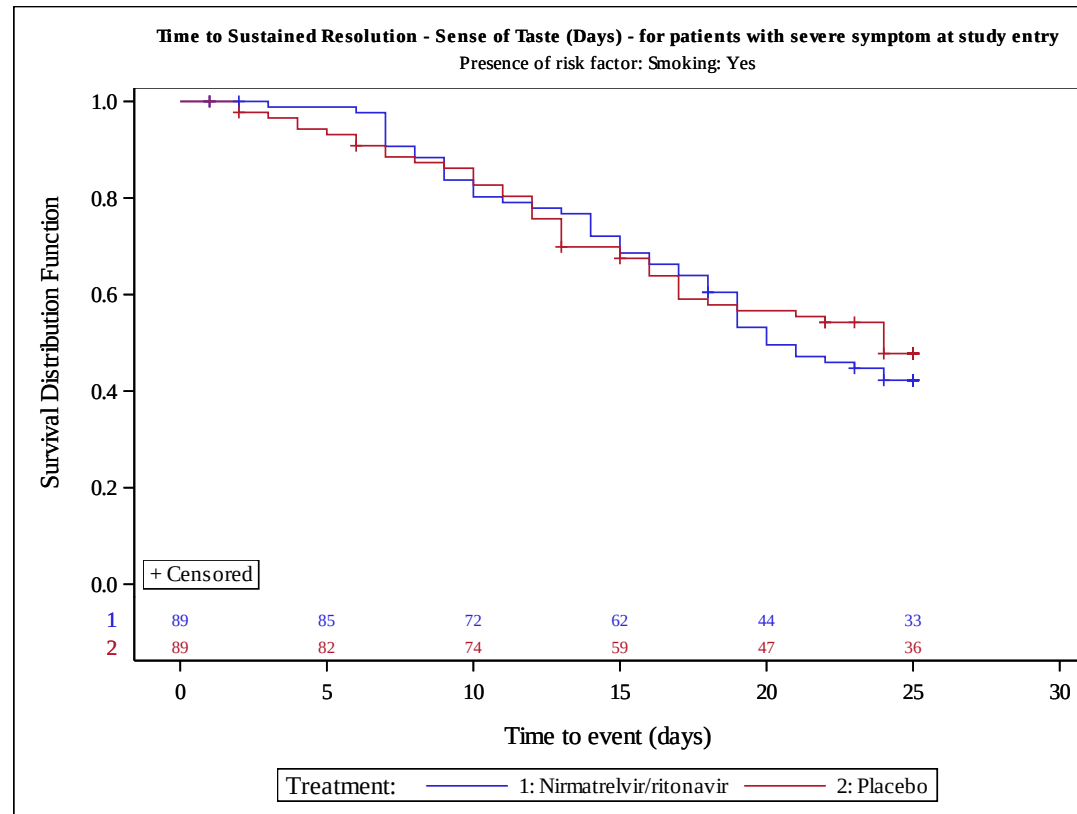
Final

Subgroup Level	Nirmatrelvir/ritonavir (N=208)			Placebo (N=194)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]		Interaction p-Value
	n/N (%)	Median	(95% CI) [1]	n/N (%)	Median	(95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Presence of risk factor: Diabetes mellitus									0.303			0.701
Yes	12/ 24 (50.0)	12.0	(9.0, NE)	10/ 22 (45.5)	NE (16.0, NE)		4.526 (1.489, 13.758)	0.008		1.823 (0.782, 4.251)	0.164	
No	103/ 184 (56.0)	19.0	(18.0, 23.0)	66/ 172 (38.4)	NE (25.0, NE)		1.375 (0.992, 1.907)	0.056		1.548 (1.136, 2.110)	0.006	
Presence of risk factor: Immunosuppression												
Yes	0/ 1 (0.0)			2/ 3 (66.7)								
No	115/ 207 (55.6)			74/ 191 (38.7)								
Presence of risk factor: Chronic lung disease									0.541			0.715
Yes	9/ 21 (42.9)	NE (15.0, NE)		1/ 7 (14.3)	NE (7.0, NE)		4.741 (0.211, 106.35)	0.327		2.217 (0.281, 17.520)	0.450	
No	106/ 187 (56.7)	19.0	(16.0, 22.0)	75/ 187 (40.1)	NE (24.0, NE)		1.495 (1.097, 2.038)	0.011		1.620 (1.204, 2.178)	0.001	
Presence of risk factor: Hypertension									0.413			0.276
Yes	36/ 65 (55.4)	20.0	(17.0, NE)	20/ 62 (32.3)	NE (NE, NE)		1.946 (1.050, 3.607)	0.034		2.093 (1.209, 3.626)	0.008	
No	79/ 143 (55.2)	19.0	(15.0, 24.0)	56/ 132 (42.4)	NE (19.0, NE)		1.362 (0.952, 1.950)	0.091		1.407 (0.999, 1.981)	0.051	
Presence of risk factor: Cardiovascular disorder												
Yes	0/ 1 (0.0)			0/ 4 (0.0)								
No	115/ 207 (55.6)			76/ 190 (40.0)								
Presence of risk factor: Chronic kidney disease												
Yes	0/ 2 (0.0)			0/ 1 (0.0)								
No	115/ 206 (55.8)			76/ 193 (39.4)								
Presence of risk factor: HIV Infection												
Yes	0			0								
No	115/ 208 (55.3)			76/ 194 (39.2)								
Presence of risk factor: Sickle Cell Disease												
No	115/ 208 (55.3)			76/ 194 (39.2)								
Presence of risk factor: Neurodevelopmental Disorder												
Yes	1/ 1 (100.0)			0								
No	114/ 207 (55.1)			76/ 194 (39.2)								
Presence of risk factor: Cancer												
Yes	0			1/ 1 (100.0)								
No	115/ 208 (55.3)			75/ 193 (38.9)								
Presence of risk factor: Device Dependence												
Yes	0			0								
No	113/ 203 (55.7)			75/ 190 (39.5)								

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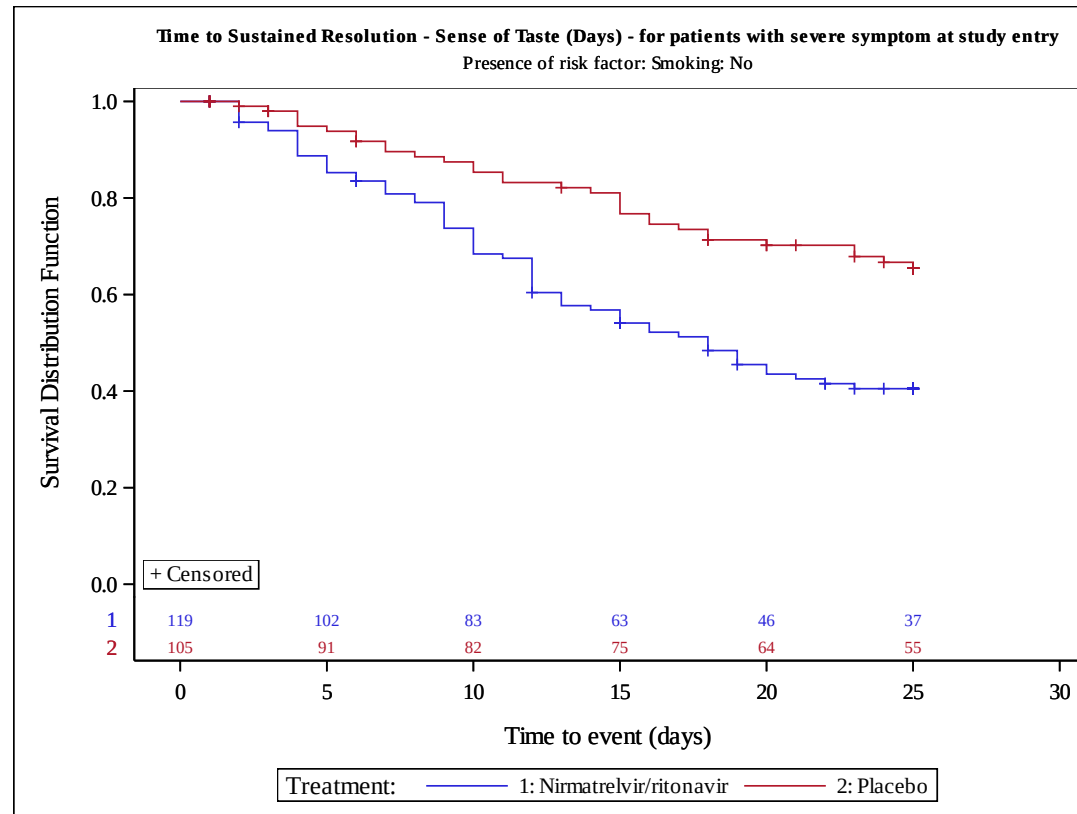


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Analysis of Participants with Any Severe Targeted Signs and Symptoms - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]		Interaction p-Value	Unadjusted analysis [2]		Interaction p-Value
			Relative Risk (95% CI)	p-Value		Relative Risk (95% CI)	p-Value	
Age								
< 65	167/ 790 (21.1)	170/ 810 (21.0)	1.028 (0.853, 1.239)	0.769	0.143	1.007 (0.833, 1.218)	0.941	0.106
>= 65	18/ 138 (13.0)	30/ 145 (20.7)	0.685 (0.403, 1.166)	0.163		0.630 (0.369, 1.077)	0.092	
Gender								
Male	67/ 463 (14.5)	88/ 507 (17.4)	0.829 (0.619, 1.110)	0.207	0.130	0.834 (0.623, 1.116)	0.222	0.294
Female	118/ 465 (25.4)	112/ 448 (25.0)	1.080 (0.872, 1.336)	0.482		1.015 (0.812, 1.269)	0.896	
Geographic region								
United States	96/ 375 (25.6)	94/ 387 (24.3)	1.064 (0.843, 1.344)	0.600	0.452	1.054 (0.824, 1.348)	0.676	0.580
Europe	57/ 322 (17.7)	61/ 321 (19.0)	0.960 (0.690, 1.336)	0.810		0.932 (0.672, 1.291)	0.670	
India	0/ 74 (0.0)	1/ 78 (1.3)	NE (NE, NE)	NE		0.351 (0.015, 8.485)	0.520	
Rest of World	32/ 157 (20.4)	44/ 169 (26.0)	0.775 (0.518, 1.159)	0.215		0.783 (0.525, 1.168)	0.231	
COVID-19 therapeutic mAb treatment at randomisation								
Yes	20/ 57 (35.1)	17/ 60 (28.3)	NE (NE, NE)	NE	0.255	1.238 (0.725, 2.115)	0.434	0.316
No	165/ 871 (18.9)	183/ 895 (20.4)	0.943 (0.782, 1.137)	0.537		0.926 (0.767, 1.119)	0.427	
Baseline viral load 1								
< 10^4 copies/mL	42/ 335 (12.5)	40/ 354 (11.3)	1.185 (0.792, 1.775)	0.409	0.333	1.110 (0.739, 1.666)	0.616	0.463
>= 10^4 copies/mL	139/ 569 (24.4)	150/ 575 (26.1)	0.943 (0.778, 1.143)	0.551		0.936 (0.767, 1.143)	0.519	
Baseline viral load 2								
< 10^7 copies/mL	109/ 652 (16.7)	124/ 699 (17.7)	0.988 (0.789, 1.238)	0.918	0.924	0.942 (0.746, 1.191)	0.619	0.769
>= 10^7 copies/mL	72/ 252 (28.6)	66/ 230 (28.7)	0.961 (0.729, 1.266)	0.777		0.996 (0.751, 1.320)	0.976	
Baseline serology status								
Negative	119/ 435 (27.4)	129/ 456 (28.3)	0.978 (0.798, 1.200)	0.834	0.948	0.967 (0.783, 1.195)	0.756	0.804
Positive	62/ 482 (12.9)	68/ 487 (14.0)	0.989 (0.720, 1.359)	0.947		0.921 (0.669, 1.269)	0.616	
Symptom onset days to first dose date								
<= 3	122/ 624 (19.6)	124/ 624 (19.9)	0.987 (0.790, 1.232)	0.906	0.804	0.984 (0.786, 1.231)	0.887	0.648
> 3	63/ 304 (20.7)	76/ 331 (23.0)	0.940 (0.710, 1.245)	0.666		0.903 (0.672, 1.213)	0.496	
BMI group								
< 25	31/ 215 (14.4)	34/ 213 (16.0)	1.051 (0.680, 1.624)	0.823	0.764	0.903 (0.577, 1.414)	0.657	0.940
25 - < 30	56/ 319 (17.6)	62/ 332 (18.7)	0.962 (0.696, 1.331)	0.816		0.940 (0.678, 1.304)	0.711	
>= 30	98/ 393 (24.9)	104/ 410 (25.4)	0.912 (0.722, 1.152)	0.439		0.983 (0.774, 1.248)	0.889	
Ethnicity								
White	155/ 699 (22.2)	161/ 718 (22.4)	1.013 (0.838, 1.225)	0.891	0.739	0.989 (0.814, 1.201)	0.910	0.758
Black or African American	10/ 43 (23.3)	11/ 40 (27.5)	NE (NE, NE)	NE		0.846 (0.403, 1.773)	0.657	
Asian	6/ 117 (5.1)	10/ 127 (7.9)	NE (NE, NE)	NE		0.651 (0.244, 1.736)	0.391	
Others	14/ 69 (20.3)	18/ 70 (25.7)	NE (NE, NE)	NE		0.789 (0.427, 1.458)	0.450	
Number of baseline comorbidities present								
0-1	144/ 710 (20.3)	162/ 728 (22.3)	0.939 (0.775, 1.138)	0.523	NE	0.911 (0.747, 1.112)	0.362	0.378
2-3	41/ 214 (19.2)	38/ 221 (17.2)	1.202 (0.804, 1.796)	0.370		1.114 (0.747, 1.661)	0.595	
>= 4	0/ 4 (0.0)	0/ 6 (0.0)	NE (NE, NE)	NE		NE (NE, NE)	NE	
Presence of risk factor: Smoking								
Yes	72/ 417 (17.3)	73/ 438 (16.7)	1.051 (0.779, 1.418)	0.746	0.498	1.036 (0.770, 1.394)	0.815	0.470
No	113/ 509 (22.2)	127/ 517 (24.6)	0.933 (0.755, 1.152)	0.518		0.904 (0.724, 1.128)	0.371	
Presence of risk factor: Diabetes mellitus								
					0.928			0.733

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 Analysis of Participants with Any Severe Targeted Signs and Symptoms - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value	
Yes	20/ 130 (15.4)	24/ 136 (17.6)	0.916 (0.542, 1.548)			0.743		0.872 (0.507, 1.500)			0.620	
No	165/ 797 (20.7)	176/ 819 (21.5)	0.981 (0.818, 1.177)			0.839		0.963 (0.798, 1.163)			0.698	
Presence of risk factor: Immunosuppression							0.169					0.876
Yes	1/ 6 (16.7)	1/ 7 (14.3)	NE (NE, NE)			NE		1.167 (0.091, 14.916)			0.906	
No	184/ 921 (20.0)	199/ 948 (21.0)	0.971 (0.816, 1.156)			0.741		0.952 (0.796, 1.138)			0.588	
Presence of risk factor: Chronic lung disease							0.172					0.239
Yes	15/ 62 (24.2)	6/ 39 (15.4)	NE (NE, NE)			NE		1.573 (0.667, 3.708)			0.301	
No	170/ 865 (19.7)	194/ 916 (21.2)	0.952 (0.795, 1.140)			0.592		0.928 (0.772, 1.115)			0.425	
Presence of risk factor: Hypertension							0.768					0.935
Yes	64/ 348 (18.4)	71/ 371 (19.1)	1.014 (0.748, 1.374)			0.929		0.961 (0.709, 1.303)			0.798	
No	121/ 579 (20.9)	129/ 584 (22.1)	0.967 (0.781, 1.197)			0.757		0.946 (0.759, 1.179)			0.621	
Presence of risk factor: Cardiovascular disorder							0.708					0.997
Yes	9/ 42 (21.4)	11/ 49 (22.4)	NE (NE, NE)			NE		0.955 (0.438, 2.079)			0.907	
No	176/ 885 (19.9)	189/ 906 (20.9)	0.987 (0.825, 1.179)			0.882		0.953 (0.794, 1.145)			0.609	
Presence of risk factor: Chronic kidney disease							0.839					0.923
Yes	2/ 6 (33.3)	3/ 8 (37.5)	NE (NE, NE)			NE		0.889 (0.210, 3.761)			0.873	
No	183/ 921 (19.9)	197/ 947 (20.8)	0.977 (0.820, 1.164)			0.792		0.955 (0.798, 1.143)			0.617	
Presence of risk factor: HIV Infection												
Yes	0	0/ 1 (0.0)										
No	185/ 927 (20.0)	200/ 953 (21.0)										
Presence of risk factor: Sickle Cell Disease												
No	185/ 927 (20.0)	200/ 955 (20.9)										
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0/ 2 (0.0)	0/ 1 (0.0)										
No	185/ 925 (20.0)	200/ 954 (21.0)										
Presence of risk factor: Cancer							0.683					0.856
Yes	1/ 5 (20.0)	1/ 6 (16.7)	NE (NE, NE)			NE		1.200 (0.098, 14.690)			0.887	
No	184/ 922 (20.0)	199/ 949 (21.0)	0.975 (0.819, 1.161)			0.779		0.952 (0.796, 1.138)			0.587	
Presence of risk factor: Device Dependence												
Yes	2/ 4 (50.0)	1/ 3 (33.3)										
No	182/ 914 (19.9)	198/ 944 (21.0)										

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				
			Relative Risk (95% CI)			p-Value		p-Value	Relative Risk (95% CI)			p-Value
Age								0.918				0.966
< 65	602/ 790 (76.2)	603/ 810 (74.4)	1.008 (0.956, 1.064)		0.758				1.024 (0.968, 1.083)		0.415	
>= 65	100/ 138 (72.5)	103/ 145 (71.0)	NE (NE, NE)		NE				1.020 (0.881, 1.181)		0.789	
Gender								0.732				0.491
Male	335/ 463 (72.4)	353/ 507 (69.6)	1.019 (0.943, 1.100)		0.638				1.039 (0.959, 1.126)		0.349	
Female	367/ 465 (78.9)	353/ 448 (78.8)	1.006 (0.941, 1.074)		0.866				1.002 (0.937, 1.071)		0.962	
Geographic region								0.500				0.410
United States	279/ 375 (74.4)	288/ 387 (74.4)	1.004 (0.924, 1.092)		0.917				1.000 (0.920, 1.087)		0.995	
Europe	258/ 322 (80.1)	247/ 321 (76.9)	1.034 (0.952, 1.123)		0.425				1.041 (0.960, 1.129)		0.327	
India	40/ 74 (54.1)	33/ 78 (42.3)	1.204 (0.853, 1.699)		0.292				1.278 (0.915, 1.784)		0.150	
Rest of World	125/ 157 (79.6)	138/ 169 (81.7)	NE (NE, NE)		NE				0.975 (0.876, 1.085)		0.642	
COVID-19 therapeutic mAb treatment at randomisation								0.886				0.571
Yes	48/ 57 (84.2)	47/ 60 (78.3)	NE (NE, NE)		NE				1.075 (0.903, 1.280)		0.416	
No	654/ 871 (75.1)	659/ 895 (73.6)	1.015 (0.962, 1.070)		0.596				1.020 (0.965, 1.077)		0.484	
Baseline viral load 1								0.103				0.190
< 10^4 copies/mL	244/ 335 (72.8)	240/ 354 (67.8)	1.065 (0.973, 1.166)		0.174				1.074 (0.975, 1.184)		0.148	
>= 10^4 copies/mL	443/ 569 (77.9)	450/ 575 (78.3)	0.986 (0.928, 1.047)		0.641				0.995 (0.936, 1.058)		0.869	
Baseline viral load 2								0.290				0.409
< 10^7 copies/mL	476/ 652 (73.0)	495/ 699 (70.8)	1.031 (0.967, 1.100)		0.349				1.031 (0.964, 1.102)		0.370	
>= 10^7 copies/mL	211/ 252 (83.7)	195/ 230 (84.8)	0.986 (0.911, 1.067)		0.721				0.988 (0.914, 1.067)		0.751	
Baseline serology status								0.649				0.622
Negative	341/ 435 (78.4)	354/ 456 (77.6)	0.997 (0.931, 1.068)		0.938				1.010 (0.942, 1.083)		0.784	
Positive	351/ 482 (72.8)	342/ 487 (70.2)	NE (NE, NE)		NE				1.037 (0.958, 1.123)		0.371	
Symptom onset days to first dose date								0.421				0.349
<= 3	481/ 624 (77.1)	462/ 624 (74.0)	1.027 (0.967, 1.092)		0.386				1.041 (0.977, 1.109)		0.211	
> 3	221/ 304 (72.7)	244/ 331 (73.7)	NE (NE, NE)		NE				0.986 (0.897, 1.084)		0.772	
BMI group								NE				0.052
< 25	147/ 215 (68.4)	154/ 213 (72.3)	NE (NE, NE)		NE				0.946 (0.836, 1.070)		0.374	
25 - < 30	256/ 319 (80.3)	239/ 332 (72.0)	1.095 (1.009, 1.188)		0.031				1.115 (1.023, 1.215)		0.014	
>= 30	298/ 393 (75.8)	313/ 410 (76.3)	0.964 (0.896, 1.037)		0.327				0.993 (0.919, 1.073)		0.864	
Ethnicity								0.952				0.884
White	541/ 699 (77.4)	545/ 718 (75.9)	1.013 (0.956, 1.074)		0.652				1.020 (0.963, 1.080)		0.507	
Black or African American	32/ 43 (74.4)	31/ 40 (77.5)	NE (NE, NE)		NE				0.960 (0.754, 1.223)		0.743	
Asian	71/ 117 (60.7)	71/ 127 (55.9)	NE (NE, NE)		NE				1.085 (0.878, 1.342)		0.449	
Others	58/ 69 (84.1)	59/ 70 (84.3)	NE (NE, NE)		NE				0.997 (0.863, 1.152)		0.971	
Number of baseline comorbidities present								0.925				0.819
0-1	545/ 710 (76.8)	543/ 728 (74.6)	1.011 (0.957, 1.069)		0.689				1.029 (0.971, 1.091)		0.337	
2-3	155/ 214 (72.4)	159/ 221 (71.9)	1.061 (0.944, 1.193)		0.323				1.007 (0.896, 1.131)		0.910	
>= 4	2/ 4 (50.0)	4/ 6 (66.7)	NE (NE, NE)		NE				0.750 (0.242, 2.325)		0.618	
Presence of risk factor: Smoking								0.462				0.461
Yes	305/ 417 (73.1)	306/ 438 (69.9)	1.038 (0.957, 1.126)		0.372				1.047 (0.962, 1.139)		0.288	
No	396/ 509 (77.8)	400/ 517 (77.4)	0.999 (0.936, 1.066)		0.968				1.006 (0.942, 1.074)		0.869	
Presence of risk factor: Diabetes mellitus								0.159				0.079

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Subgroup Level	Nirmatrelvir/ritonavir (N=928)		Placebo (N=955)		Adjusted analysis [1]				Unadjusted analysis [2]					
	n/N (%)		n/N (%)		Relative Risk (95% CI)			p-Value	Interaction p-Value	Relative Risk (95% CI)			p-Value	Interaction p-Value
Yes	90/ 130	(69.2)	104/ 136	(76.5)	0.918 (0.792,	1.064)	0.257			0.905 (0.781,	1.049)	0.187		
No	611/ 797	(76.7)	602/ 819	(73.5)	1.024 (0.971,	1.081)	0.381			1.043 (0.986,	1.103)	0.142		
Presence of risk factor: Immunosuppression									NE					0.189
Yes	6/ 6	(100.0)	5/ 7	(71.4)	NE (NE,	NE)	NE			1.400 (0.876,	2.237)	0.159		
No	695/ 921	(75.5)	701/ 948	(73.9)	1.008 (0.958,	1.061)	0.752			1.021 (0.968,	1.076)	0.451		
Presence of risk factor: Chronic lung disease									0.558					0.977
Yes	47/ 62	(75.8)	29/ 39	(74.4)	NE (NE,	NE)	NE			1.019 (0.809,	1.285)	0.871		
No	654/ 865	(75.6)	677/ 916	(73.9)	1.016 (0.965,	1.070)	0.545			1.023 (0.969,	1.080)	0.409		
Presence of risk factor: Hypertension									0.419					0.586
Yes	261/ 348	(75.0)	267/ 371	(72.0)	1.039 (0.952,	1.133)	0.392			1.042 (0.955,	1.138)	0.357		
No	440/ 579	(76.0)	439/ 584	(75.2)	NE (NE,	NE)	NE			1.011 (0.947,	1.079)	0.744		
Presence of risk factor: Cardiovascular disorder									0.353					0.268
Yes	31/ 42	(73.8)	40/ 49	(81.6)	NE (NE,	NE)	NE			0.904 (0.723,	1.131)	0.378		
No	670/ 885	(75.7)	666/ 906	(73.5)	1.016 (0.965,	1.071)	0.545			1.030 (0.976,	1.087)	0.286		
Presence of risk factor: Chronic kidney disease									0.313					0.173
Yes	3/ 6	(50.0)	7/ 8	(87.5)	NE (NE,	NE)	NE			0.571 (0.246,	1.326)	0.193		
No	698/ 921	(75.8)	699/ 947	(73.8)	1.014 (0.963,	1.067)	0.601			1.027 (0.974,	1.082)	0.326		
Presence of risk factor: HIV Infection														
Yes	0		1/ 1	(100.0)										
No	701/ 927	(75.6)	705/ 953	(74.0)										
Presence of risk factor: Sickle Cell Disease														
No	701/ 927	(75.6)	706/ 955	(73.9)										
Presence of risk factor: Neurodevelopmental Disorder														
Yes	1/ 2	(50.0)	0/ 1	(0.0)										
No	700/ 925	(75.7)	706/ 954	(74.0)										
Presence of risk factor: Cancer									NE					0.184
Yes	5/ 5	(100.0)	4/ 6	(66.7)	NE (NE,	NE)	NE			1.500 (0.852,	2.641)	0.160		
No	696/ 922	(75.5)	702/ 949	(74.0)	1.009 (0.959,	1.061)	0.738			1.020 (0.968,	1.076)	0.451		
Presence of risk factor: Device Dependence														
Yes	3/ 4	(75.0)	3/ 3	(100.0)										
No	691/ 914	(75.6)	698/ 944	(73.9)										

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Final

Overall Study population
RKI-conform mITT2 Analysis set

Analysis of Time to Sustained Alleviation of All Targeted Signs and Symptoms Through Day 28 - Subgroup analysis

Subgroup Level	Nirmatrelvir/ritonavir (N=928)			Placebo (N=955)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	570/ 790	(72.2)	13.0 (12.0, 13.0)	527/ 810	(65.1)	15.0 (14.0, 17.0)	1.238 (1.097, 1.397)	<.001		0.070	1.253 (1.113, 1.411)	<.001		0.067
>= 65	114/ 138	(82.6)	12.0 (10.0, 13.0)	94/ 145	(64.8)	16.0 (13.0, 19.0)	1.664 (1.255, 2.207)	<.001			1.667 (1.266, 2.194)	<.001		
Gender														
Male	369/ 463	(79.7)	11.0 (11.0, 12.0)	338/ 507	(66.7)	14.0 (13.0, 15.0)	1.418 (1.219, 1.650)	<.001		0.080	1.424 (1.227, 1.651)	<.001		0.125
Female	315/ 465	(67.7)	14.0 (13.0, 16.0)	283/ 448	(63.2)	17.0 (16.0, 19.0)	1.159 (0.984, 1.366)	0.077			1.213 (1.033, 1.424)	0.018		
Geographic region														
United States	261/ 375	(69.6)	13.0 (12.0, 15.0)	246/ 387	(63.6)	16.0 (13.0, 17.0)	1.186 (0.993, 1.417)	0.059		0.365	1.210 (1.016, 1.440)	0.032		0.319
Europe	248/ 322	(77.0)	13.0 (12.0, 14.0)	217/ 321	(67.6)	17.0 (15.0, 18.0)	1.347 (1.116, 1.626)	0.002			1.360 (1.133, 1.633)	<.001		
India	70/ 74	(94.6)	11.0 (9.0, 12.0)	72/ 78	(92.3)	11.0 (10.0, 13.0)	1.310 (0.936, 1.835)	0.116			1.237 (0.888, 1.723)	0.209		
Rest of World	105/ 157	(66.9)	12.0 (10.0, 15.0)	86/ 169	(50.9)	21.0 (15.0, NE)	1.573 (1.175, 2.107)	0.002			1.570 (1.180, 2.090)	0.002		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	37/ 57	(64.9)	13.0 (10.0, 19.0)	39/ 60	(65.0)	16.0 (13.0, 20.0)	1.095 (0.691, 1.737)	0.698		0.617	1.109 (0.707, 1.740)	0.653		0.482
No	647/ 871	(74.3)	13.0 (12.0, 13.0)	582/ 895	(65.0)	15.0 (14.0, 17.0)	1.302 (1.161, 1.459)	<.001			1.322 (1.181, 1.479)	<.001		
Baseline viral load 1														
< 10^4 copies/mL	262/ 335	(78.2)	12.0 (11.0, 13.0)	252/ 354	(71.2)	13.0 (11.0, 14.0)	1.224 (1.028, 1.459)	0.024		0.416	1.218 (1.025, 1.449)	0.025		0.434
>= 10^4 copies/mL	401/ 569	(70.5)	13.0 (12.0, 14.0)	356/ 575	(61.9)	17.0 (16.0, 19.0)	1.341 (1.161, 1.548)	<.001			1.342 (1.164, 1.549)	<.001		
Baseline viral load 2														
< 10^7 copies/mL	485/ 652	(74.4)	12.0 (12.0, 13.0)	482/ 699	(69.0)	14.0 (13.0, 15.0)	1.221 (1.075, 1.386)	0.002		0.059	1.221 (1.076, 1.385)	0.002		0.060
>= 10^7 copies/mL	178/ 252	(70.6)	13.0 (12.0, 16.0)	126/ 230	(54.8)	20.0 (17.0, 24.0)	1.612 (1.277, 2.034)	<.001			1.589 (1.264, 1.997)	<.001		
Baseline serology status														
Negative	310/ 435	(71.3)	13.0 (12.0, 14.0)	272/ 456	(59.6)	17.0 (16.0, 19.0)	1.379 (1.168, 1.629)	<.001		0.455	1.390 (1.180, 1.636)	<.001		0.358
Positive	365/ 482	(75.7)	12.0 (11.0, 13.0)	341/ 487	(70.0)	14.0 (13.0, 15.0)	1.246 (1.073, 1.447)	0.004			1.246 (1.075, 1.444)	0.004		
Symptom onset days to first dose date														
<= 3	474/ 624	(76.0)	12.0 (12.0, 13.0)	426/ 624	(68.3)	15.0 (13.0, 16.0)	1.274 (1.115, 1.456)	<.001		0.674	1.276 (1.119, 1.455)	<.001		0.551
> 3	210/ 304	(69.1)	14.0 (12.0, 15.0)	195/ 331	(58.9)	17.0 (15.0, 20.0)	1.336 (1.093, 1.634)	0.005			1.363 (1.121, 1.656)	0.002		
BMI group														
< 25	169/ 215	(78.6)	11.0 (10.0, 12.0)	155/ 213	(72.8)	13.0 (12.0, 16.0)	1.352 (1.073, 1.703)	0.010		0.620	1.370 (1.101, 1.706)	0.005		0.582
25 - < 30	240/ 319	(75.2)	13.0 (12.0, 14.0)	228/ 332	(68.7)	15.0 (13.0, 16.0)	1.240 (1.030, 1.494)	0.023			1.214 (1.012, 1.455)	0.037		
>= 30	274/ 393	(69.7)	14.0 (13.0, 15.0)	238/ 410	(58.0)	18.0 (16.0, 21.0)	1.416 (1.183, 1.696)	<.001			1.371 (1.152, 1.631)	<.001		
Ethnicity														
White	509/ 699	(72.8)	13.0 (12.0, 14.0)	456/ 718	(63.5)	16.0 (15.0, 17.0)	1.277 (1.122, 1.454)	<.001		0.530	1.316 (1.159, 1.493)	<.001		0.548
Black or African American	29/ 43	(67.4)	10.0 (7.0, 15.0)	24/ 40	(60.0)	19.0 (10.0, NE)	1.548 (0.860, 2.786)	0.145			1.521 (0.881, 2.628)	0.132		
Asian	103/ 117	(88.0)	10.0 (9.0, 11.0)	111/ 127	(87.4)	11.0 (10.0, 13.0)	1.287 (0.976, 1.698)	0.074			1.207 (0.922, 1.580)	0.171		
Others	43/ 69	(62.3)	18.0 (13.0, 23.0)	30/ 70	(42.9)	NE (18.0, NE)	1.519 (0.936, 2.463)	0.090			1.657 (1.038, 2.644)	0.034		
Number of baseline comorbidities present														
0-1	520/ 710	(73.2)	12.0 (12.0, 13.0)	482/ 728	(66.2)	15.0 (14.0, 16.0)	1.247 (1.098, 1.415)	<.001		0.340	1.260 (1.113, 1.427)	<.001		0.307
2-3	161/ 214	(75.2)	13.0 (12.0, 14.0)	135/ 221	(61.1)	16.0 (14.0, 21.0)	1.415 (1.117, 1.792)	0.004			1.492 (1.185, 1.877)	<.001		
>= 4	3/ 4	(75.0)	20.0 (10.0, NE)	4/ 6	(66.7)	11.5 (3.0, NE)	0.000 (0.000, NE)	0.997			0.785 (0.174, 3.533)	0.753		
Presence of risk factor: Smoking														
Yes	325/ 417	(77.9)	12.0 (11.0, 12.0)	301/ 438	(68.7)	14.0 (13.0, 15.0)	1.332 (1.134, 1.565)	<.001		0.852	1.340 (1.145, 1.568)	<.001		0.724
No	358/ 509	(70.3)	13.0 (13.0, 15.0)	320/ 517	(61.9)	17.0 (16.0, 19.0)	1.292 (1.108, 1.506)	0.001			1.297 (1.115, 1.508)	<.001		

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928)			Placebo (N=955)			Adjusted Analysis [2]				Unadjusted Analysis [3]			
	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)		p-Value	Interaction p-Value	Hazard Ratio (95% CI)		p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus										0.291				0.241
Yes	97/ 130	(74.6)	11.0 (9.0, 13.0)	86/ 136	(63.2)	16.0 (14.0, 21.0)	1.603	(1.185, 2.170)	0.002		1.489	(1.112, 1.993)	0.007	
No	586/ 797	(73.5)	13.0 (12.0, 13.0)	535/ 819	(65.3)	15.0 (14.0, 17.0)	1.270	(1.126, 1.431)	<.001		1.278	(1.137, 1.438)	<.001	
Presence of risk factor: Immunosuppression										0.666				0.776
Yes	5/ 6	(83.3)	11.5 (6.0, NE)	5/ 7	(71.4)	11.0 (2.0, NE)	15.855	(0.061, 4133.7)	0.330		1.077	(0.311, 3.729)	0.907	
No	678/ 921	(73.6)	13.0 (12.0, 13.0)	616/ 948	(65.0)	15.0 (15.0, 17.0)	1.292	(1.156, 1.445)	<.001		1.309	(1.174, 1.461)	<.001	
Presence of risk factor: Chronic lung disease										0.851				0.737
Yes	43/ 62	(69.4)	15.0 (13.0, 20.0)	22/ 39	(56.4)	16.0 (12.0, NE)	1.268	(0.710, 2.266)	0.422		1.220	(0.730, 2.041)	0.448	
No	640/ 865	(74.0)	12.0 (12.0, 13.0)	599/ 916	(65.4)	15.0 (14.0, 17.0)	1.301	(1.161, 1.458)	<.001		1.323	(1.183, 1.479)	<.001	
Presence of risk factor: Hypertension										0.830				0.768
Yes	252/ 348	(72.4)	13.0 (12.0, 15.0)	233/ 371	(62.8)	17.0 (15.0, 19.0)	1.297	(1.081, 1.556)	0.005		1.333	(1.115, 1.593)	0.002	
No	431/ 579	(74.4)	12.0 (11.0, 13.0)	388/ 584	(66.4)	15.0 (13.0, 16.0)	1.282	(1.114, 1.476)	<.001		1.291	(1.126, 1.482)	<.001	
Presence of risk factor: Cardiovascular disorder										0.886				0.778
Yes	29/ 42	(69.0)	14.0 (11.0, 19.0)	31/ 49	(63.3)	15.0 (11.0, 22.0)	1.251	(0.731, 2.141)	0.415		1.212	(0.730, 2.012)	0.458	
No	654/ 885	(73.9)	13.0 (12.0, 13.0)	590/ 906	(65.1)	15.0 (14.0, 17.0)	1.288	(1.150, 1.443)	<.001		1.311	(1.173, 1.466)	<.001	
Presence of risk factor: Chronic kidney disease										0.535				0.517
Yes	4/ 6	(66.7)	14.0 (7.0, NE)	4/ 8	(50.0)	25.0 (8.0, NE)	16.179	(0.838, 312.31)	0.065		2.005	(0.500, 8.042)	0.326	
No	679/ 921	(73.7)	13.0 (12.0, 13.0)	617/ 947	(65.2)	15.0 (14.0, 16.0)	1.286	(1.150, 1.437)	<.001		1.301	(1.167, 1.451)	<.001	
Presence of risk factor: HIV Infection														
Yes	0			1/ 1	(100.0)									
No	683/ 927	(73.7)		619/ 953	(65.0)									
Presence of risk factor: Sickle Cell Disease														
No	683/ 927	(73.7)		621/ 955	(65.0)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/ 2	(100.0)		0/ 1	(0.0)									
No	681/ 925	(73.6)		621/ 954	(65.1)									
Presence of risk factor: Cancer										0.218				0.375
Yes	3/ 5	(60.0)	14.0 (9.0, NE)	5/ 6	(83.3)	12.5 (2.0, NE)	0.000	(0.000, NE)	0.999		0.654	(0.153, 2.804)	0.568	
No	680/ 922	(73.8)	13.0 (12.0, 13.0)	616/ 949	(64.9)	15.0 (14.0, 17.0)	1.297	(1.161, 1.450)	<.001		1.312	(1.177, 1.464)	<.001	
Presence of risk factor: Device Dependence														
Yes	2/ 4	(50.0)		1/ 3	(33.3)									
No	676/ 914	(74.0)		617/ 944	(65.4)									

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=188)			Placebo (N=178)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value	
Age													
< 65	152/ 97	175 (86.9)	4.0 (4.0, 5.0)	117/ 19	155 (75.5)	9.0 (6.0, 11.0)	1.449 (1.127, 1.862)	0.004	0.476	1.521 (1.194, 1.938)	<.001		0.693
>= 65	9/ 13	(69.2)	4.0 (2.0, 25.0)	23 (82.6)	8.0 (5.0, 14.0)		0.963 (0.381, 2.435)	0.936		1.304 (0.585, 2.906)	0.516		
Gender													
Male	68/ 93	78 (87.2)	5.0 (3.0, 5.0)	54/ 82	73 (74.0)	8.0 (4.0, 9.0)	1.330 (0.912, 1.939)	0.139	0.560	1.399 (0.976, 2.005)	0.067		0.692
Female	93/ 110	(84.5)	4.0 (4.0, 6.0)	105 (78.1)	9.0 (7.0, 13.0)		1.522 (1.116, 2.076)	0.008		1.566 (1.162, 2.111)	0.003		
Geographic region													
United States	77/ 48	95 (81.1)		68/ 36	92 (73.9)				0.885				0.708
Europe	0/ 50	(96.0)		0/ 42	(85.7)								
India	0/ 0			0/ 0									
Rest of World	36/ 43	(83.7)		32/ 44	(72.7)								
COVID-19 therapeutic mAb treatment at randomisation													
Yes	11/ 14	(78.6)	5.0 (3.0, 8.0)	12/ 16	(75.0)	18.0 (4.0, 19.0)	1.453 (0.559, 3.775)	0.443	0.421	1.871 (0.806, 4.345)	0.145		0.272
No	150/ 174	(86.2)	4.0 (4.0, 5.0)	124/ 162	(76.5)	8.0 (6.0, 9.0)	1.411 (1.103, 1.805)	0.006		1.474 (1.160, 1.871)	0.001		
Baseline viral load 1													
< 10^4 copies/mL	38/ 121	48 (79.2)	5.0 (4.0, 12.0)	33/ 97	41 (80.5)	7.0 (4.0, 13.0)	1.181 (0.722, 1.932)	0.508	0.381	1.193 (0.747, 1.904)	0.460		0.601
>= 10^4 copies/mL	121/ 138	(87.7)	4.0 (4.0, 5.0)	130 (74.6)	8.0 (7.0, 11.0)		1.493 (1.134, 1.966)	0.004		1.633 (1.248, 2.138)	<.001		
Baseline viral load 2													
< 10^7 copies/mL	92/ 67	112 (82.1)	5.0 (4.0, 6.0)	87/ 43	119 (73.1)	9.0 (7.0, 13.0)	1.443 (1.064, 1.957)	0.018	0.370	1.526 (1.136, 2.049)	0.005		0.348
>= 10^7 copies/mL	67/ 74	(90.5)	4.0 (3.0, 5.0)	52 (82.7)	7.0 (4.0, 9.0)		1.248 (0.831, 1.873)	0.286		1.354 (0.921, 1.990)	0.123		
Baseline serology status													
Negative	84/ 76	98 (85.7)	4.0 (3.0, 5.0)	81/ 53	110 (73.6)	9.0 (7.0, 12.0)	1.563 (1.138, 2.147)	0.006	0.808	1.655 (1.217, 2.251)	0.001		0.578
Positive	76/ 89	(85.4)	5.0 (4.0, 6.0)	66 (80.3)	7.0 (4.0, 11.0)		1.262 (0.879, 1.814)	0.208		1.318 (0.927, 1.875)	0.124		
Symptom onset days to first dose date													
<= 3	118/ 43	132 (89.4)	4.0 (3.0, 5.0)	92/ 44	106 (86.8)	7.0 (5.0, 8.0)	1.393 (1.050, 1.848)	0.021	0.105	1.376 (1.046, 1.811)	0.022		0.100
> 3	43/ 56	(76.8)	8.0 (4.0, 12.0)	72 (61.1)	13.0 (9.0, 18.0)		1.507 (0.964, 2.356)	0.072		1.611 (1.057, 2.456)	0.027		
BMI group													
< 25	27/ 42	35 (77.1)	4.0 (3.0, 5.0)	25/ 45	32 (78.1)	8.5 (5.0, 16.0)	1.816 (0.988, 3.340)	0.055	0.167	2.032 (1.163, 3.553)	0.013		0.350
25 - < 30	42/ 50	(84.0)	6.0 (4.0, 8.0)	56 (80.4)	7.0 (4.0, 8.0)		1.056 (0.678, 1.644)	0.810		1.048 (0.688, 1.597)	0.827		
>= 30	92/ 103	(89.3)	4.0 (3.0, 5.0)	66/ 90	(73.3)	10.0 (7.0, 14.0)	1.566 (1.114, 2.200)	0.010		1.688 (1.227, 2.323)	0.001		
Ethnicity													
White	122/ 13	145 (84.1)	4.0 (4.0, 6.0)	109/ 9	140 (77.9)	8.0 (7.0, 11.0)	1.367 (1.046, 1.785)	0.022	0.843	1.440 (1.111, 1.866)	0.006		0.739
Black or African American	13/ 6	(86.7)	4.0 (2.0, 6.0)	12 (75.0)	10.0 (3.0, 19.0)		3.139 (0.873, 11.289)	0.080		2.209 (0.902, 5.410)	0.083		
Asian	6/ 20	(85.7)	4.0 (2.0, 6.0)	9/ 16	(90.0)	4.0 (2.0, 5.0)	0.836 (0.152, 4.595)	0.837		0.739 (0.261, 2.096)	0.569		
Others	20/ 21	(95.2)	5.0 (3.0, 11.0)	9/ 16	(56.3)	17.0 (4.0, NE)	2.109 (0.896, 4.961)	0.087		2.744 (1.202, 6.266)	0.017		
Number of baseline comorbidities present													
0-1	137/ 23	158 (86.7)		112/ 23	149 (75.2)				0.843				0.739
2-3	23/ 1	(79.3)		28 (82.1)									
>= 4	1/ 1	(100.0)		1 (100.0)									
Presence of risk factor: Smoking													
Yes	66/ 94	75 (88.0)	4.0 (4.0, 5.0)	59/ 77	72 (81.9)	7.0 (5.0, 10.0)	1.471 (1.003, 2.158)	0.048	0.843	1.455 (1.021, 2.073)	0.038		0.739
No	94/ 112	(83.9)	5.0 (4.0, 6.0)	106 (72.6)	9.0 (7.0, 13.0)		1.452 (1.061, 1.988)	0.020		1.539 (1.137, 2.083)	0.005		

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Subgroup Level	Nirmatrelvir/ritonavir (N=188)			Placebo (N=178)			Adjusted Analysis [2]			Unadjusted Analysis [3]		
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus												
Yes	15/ 19	(78.9)	5.0 (3.0, 14.0)	17/ 19	(89.5)	9.0 (6.0, 13.0)	1.484 (0.685, 3.216)	0.317	0.400	0.958 (0.475, 1.934)	0.905	0.248
No	145/ 168	(86.3)	4.0 (4.0, 5.0)	119/ 159	(74.8)	8.0 (6.0, 10.0)	1.466 (1.137, 1.889)	0.003		1.559 (1.221, 1.990)	<.001	
Presence of risk factor: Immunosuppression												
Yes	1/ 1	(100.0)		3/ 3	(100.0)				0.988			0.904
No	159/ 186	(85.5)		133/ 175	(76.0)							
Presence of risk factor: Chronic lung disease												
Yes	13/ 16	(81.3)	8.0 (3.0, 10.0)	4/ 6	(66.7)	9.5 (4.0, NE)	3.425 (0.802, 14.631)	0.097	0.988	1.599 (0.520, 4.912)	0.412	0.904
No	147/ 171	(86.0)	4.0 (4.0, 5.0)	132/ 172	(76.7)	8.0 (6.0, 10.0)	1.430 (1.120, 1.826)	0.004		1.512 (1.194, 1.915)	<.001	
Presence of risk factor: Hypertension												
Yes	43/ 55	(78.2)	5.0 (3.0, 10.0)	41/ 54	(75.9)	8.0 (6.0, 14.0)	1.231 (0.795, 1.906)	0.351	0.620	1.274 (0.830, 1.956)	0.269	0.477
No	117/ 132	(88.6)	4.0 (4.0, 5.0)	95/ 124	(76.6)	8.0 (6.0, 11.0)	1.507 (1.130, 2.012)	0.005		1.585 (1.206, 2.082)	<.001	
Presence of risk factor: Cardiovascular disorder												
Yes	4/ 6	(66.7)	5.0 (2.0, NE)	6/ 9	(66.7)	6.0 (3.0, NE)	3.349 (0.640, 17.526)	0.152	0.874	1.369 (0.383, 4.896)	0.630	0.839
No	156/ 181	(86.2)	4.0 (4.0, 5.0)	130/ 169	(76.9)	8.0 (7.0, 10.0)	1.411 (1.107, 1.798)	0.005		1.497 (1.184, 1.892)	<.001	
Presence of risk factor: Chronic kidney disease												
Yes	1/ 1	(100.0)		1/ 1	(100.0)							
No	159/ 186	(85.5)		135/ 177	(76.3)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	160/ 187	(85.6)		136/ 178	(76.4)							
Presence of risk factor: Sickie Cell Disease												
No	160/ 187	(85.6)		136/ 178	(76.4)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	0			1/ 1	(100.0)							
No	160/ 187	(85.6)		135/ 177	(76.3)							
Presence of risk factor: Cancer												
Yes	0/ 1	(0.0)		1/ 1	(100.0)							
No	160/ 186	(86.0)		135/ 177	(76.3)							
Presence of risk factor: Device Dependence												
Yes	1/ 2	(50.0)		0								
No	158/ 183	(86.3)		136/ 176	(77.3)							

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	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	
Age												
< 65	504/ 790	(63.8)	17.0 (15.0, 18.0)	470/ 810	(58.0)	18.0 (17.0, 20.0)	1.169 (1.028, 1.329)	0.017	0.261	1.180 (1.040, 1.338)	0.010	0.229
>= 65	98/ 138	(71.0)	16.0 (14.0, 19.0)	86/ 145	(59.3)	21.0 (17.0, 24.0)	1.445 (1.075, 1.944)	0.015		1.464 (1.095, 1.956)	0.010	
Gender												
Male	331/ 463	(71.5)	14.0 (13.0, 15.0)	318/ 507	(62.7)	16.0 (15.0, 17.0)	1.251 (1.068, 1.464)	0.005	0.511	1.255 (1.076, 1.464)	0.004	0.674
Female	271/ 465	(58.3)	20.0 (18.0, 21.0)	238/ 448	(53.1)	22.0 (20.0, 25.0)	1.160 (0.972, 1.386)	0.100		1.207 (1.014, 1.437)	0.034	
Geographic region												
United States	225/ 375	(60.0)	18.0 (16.0, 20.0)	224/ 387	(57.9)	19.0 (17.0, 21.0)	1.069 (0.885, 1.290)	0.490	0.325	1.097 (0.912, 1.320)	0.327	0.350
Europe	221/ 322	(68.6)	17.0 (16.0, 20.0)	191/ 321	(59.5)	20.0 (18.0, 23.0)	1.275 (1.045, 1.556)	0.017		1.295 (1.067, 1.572)	0.009	
India	70/ 74	(94.6)	11.0 (9.0, 12.0)	71/ 78	(91.0)	12.0 (10.0, 13.0)	1.339 (0.954, 1.881)	0.092		1.284 (0.920, 1.793)	0.141	
Rest of World	86/ 157	(54.8)	19.0 (15.0, 25.0)	70/ 169	(41.4)	NE (23.0, NE)	1.486 (1.076, 2.053)	0.016		1.470 (1.072, 2.016)	0.017	
COVID-19 therapeutic mAb treatment at randomisation												
Yes	34/ 57	(59.6)	18.0 (14.0, 24.0)	36/ 60	(60.0)	19.0 (15.0, NE)	1.045 (0.645, 1.693)	0.858	0.720	1.065 (0.666, 1.702)	0.793	0.548
No	568/ 871	(65.2)	17.0 (15.0, 18.0)	520/ 895	(58.1)	19.0 (17.0, 20.0)	1.213 (1.074, 1.369)	0.002		1.230 (1.092, 1.386)	<.001	
Baseline viral load 1												
< 10 ⁴ copies/mL	244/ 335	(72.8)	14.0 (13.0, 16.0)	235/ 354	(66.4)	15.0 (13.0, 17.0)	1.188 (0.992, 1.424)	0.062	0.780	1.182 (0.988, 1.414)	0.067	0.807
>= 10 ⁴ copies/mL	339/ 569	(59.6)	19.0 (17.0, 20.0)	309/ 575	(53.7)	21.0 (19.0, 23.0)	1.219 (1.044, 1.424)	0.012		1.221 (1.047, 1.425)	0.011	
Baseline viral load 2												
< 10 ⁷ copies/mL	440/ 652	(67.5)	16.0 (14.0, 17.0)	435/ 699	(62.2)	17.0 (16.0, 19.0)	1.185 (1.037, 1.355)	0.013	0.474	1.189 (1.042, 1.358)	0.010	0.503
>= 10 ⁷ copies/mL	143/ 252	(56.7)	19.0 (17.0, 23.0)	109/ 230	(47.4)	25.0 (20.0, NE)	1.304 (1.012, 1.680)	0.040		1.312 (1.023, 1.684)	0.033	
Baseline serology status												
Negative	265/ 435	(60.9)	19.0 (17.0, 20.0)	236/ 456	(51.8)	23.0 (19.0, 25.0)	1.253 (1.048, 1.499)	0.013	0.647	1.294 (1.086, 1.543)	0.004	0.381
Positive	330/ 482	(68.5)	15.0 (13.0, 16.0)	314/ 487	(64.5)	16.0 (15.0, 18.0)	1.176 (1.006, 1.376)	0.042		1.162 (0.995, 1.356)	0.057	
Symptom onset days to first dose date												
<= 3	416/ 624	(66.7)	16.0 (15.0, 18.0)	383/ 624	(61.4)	18.0 (17.0, 20.0)	1.185 (1.028, 1.365)	0.019	0.605	1.184 (1.031, 1.361)	0.017	0.482
> 3	186/ 304	(61.2)	18.0 (16.0, 20.0)	173/ 331	(52.3)	20.0 (18.0, 25.0)	1.270 (1.026, 1.572)	0.028		1.287 (1.046, 1.584)	0.017	
BMI group												
< 25	158/ 215	(73.5)	13.0 (12.0, 15.0)	146/ 213	(68.5)	16.0 (14.0, 18.0)	1.273 (1.003, 1.615)	0.047	0.920	1.290 (1.030, 1.616)	0.027	0.838
25 - < 30	215/ 319	(67.4)	15.0 (13.0, 17.0)	209/ 332	(63.0)	17.0 (16.0, 19.0)	1.195 (0.983, 1.452)	0.073		1.179 (0.974, 1.426)	0.090	
>= 30	228/ 393	(58.0)	20.0 (19.0, 21.0)	201/ 410	(49.0)	24.0 (20.0, NE)	1.285 (1.056, 1.564)	0.012		1.238 (1.024, 1.496)	0.028	
Ethnicity												
White	445/ 699	(63.7)	18.0 (17.0, 19.0)	411/ 718	(57.2)	20.0 (18.0, 22.0)	1.164 (1.015, 1.335)	0.030	0.238	1.204 (1.052, 1.376)	0.007	0.300
Black or African American	25/ 43	(58.1)	13.0 (9.0, 19.0)	20/ 40	(50.0)	22.0 (15.0, NE)	1.504 (0.798, 2.834)	0.207		1.515 (0.839, 2.736)	0.168	
Asian	99/ 117	(84.6)	11.0 (9.0, 12.0)	107/ 127	(84.3)	12.0 (10.0, 13.0)	1.292 (0.975, 1.712)	0.075		1.214 (0.923, 1.598)	0.166	
Others	33/ 69	(47.8)	25.0 (19.0, NE)	18/ 70	(25.7)	NE (NE, NE)	1.815 (0.997, 3.303)	0.051		1.955 (1.100, 3.475)	0.022	
Number of baseline comorbidities present												
0-1	458/ 710	(64.5)	16.0 (15.0, 18.0)	435/ 728	(59.8)	18.0 (17.0, 19.0)	1.151 (1.006, 1.316)	0.040	0.278	1.158 (1.015, 1.320)	0.029	0.195
2-3	142/ 214	(66.4)	17.0 (15.0, 19.0)	117/ 221	(52.9)	23.0 (18.0, NE)	1.373 (1.068, 1.766)	0.013		1.464 (1.146, 1.870)	0.002	
>= 4	2/ 4	(50.0)	NE (11.0, NE)	4/ 6	(66.7)	15.5 (5.0, NE)	0.851 (0.066, 10.944)	0.901		0.711 (0.130, 3.888)	0.694	
Presence of risk factor: Smoking												
Yes	296/ 417	(71.0)	14.0 (13.0, 16.0)	270/ 438	(61.6)	16.0 (15.0, 19.0)	1.266 (1.069, 1.499)	0.006	0.563	1.291 (1.094, 1.523)	0.002	0.364
No	305/ 509	(59.9)	19.0 (18.0, 20.0)	286/ 517	(55.3)	20.0 (19.0, 23.0)	1.174 (0.996, 1.384)	0.056		1.166 (0.992, 1.370)	0.062	

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p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928)			Placebo (N=955)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus														
Yes	93/ 130	(71.5)	13.0 (11.0, 16.0)	80/ 136	(58.8)	19.0 (16.0, 24.0)	1.622 (1.190, 2.209)	0.002		0.105	1.579 (1.170, 2.131)	0.003		0.058
No	508/ 797	(63.7)	17.0 (16.0, 19.0)	476/ 819	(58.1)	19.0 (17.0, 20.0)	1.162 (1.022, 1.320)	0.021			1.166 (1.029, 1.322)	0.016		
Presence of risk factor: Immunosuppression														
Yes	3/ 6	(50.0)	NE (7.0, NE)	3/ 7	(42.9)	NE (2.0, NE)	0.828 (0.000, NE)	1.000		0.984	1.159 (0.232, 5.781)	0.857		0.981
No	598/ 921	(64.9)	17.0 (15.0, 18.0)	553/ 948	(58.3)	19.0 (17.0, 20.0)	1.205 (1.071, 1.356)	0.002			1.219 (1.086, 1.368)	<.001		
Presence of risk factor: Chronic lung disease														
Yes	35/ 62	(56.5)	20.0 (16.0, NE)	17/ 39	(43.6)	NE (14.0, NE)	1.210 (0.632, 2.314)	0.566		0.675	1.227 (0.687, 2.191)	0.489		0.982
No	566/ 865	(65.4)	16.0 (15.0, 18.0)	539/ 916	(58.8)	19.0 (17.0, 20.0)	1.207 (1.070, 1.362)	0.002			1.231 (1.094, 1.386)	<.001		
Presence of risk factor: Hypertension														
Yes	217/ 348	(62.4)	18.0 (17.0, 21.0)	210/ 371	(56.6)	21.0 (18.0, 23.0)	1.172 (0.966, 1.422)	0.107		0.826	1.213 (1.003, 1.466)	0.047		0.924
No	384/ 579	(66.3)	15.0 (14.0, 17.0)	346/ 584	(59.2)	18.0 (16.0, 19.0)	1.208 (1.041, 1.402)	0.013			1.218 (1.053, 1.409)	0.008		
Presence of risk factor: Cardiovascular disorder														
Yes	25/ 42	(59.5)	21.0 (13.0, NE)	28/ 49	(57.1)	20.0 (16.0, NE)	1.200 (0.675, 2.134)	0.535		0.873	1.128 (0.658, 1.935)	0.662		0.784
No	576/ 885	(65.1)	17.0 (15.0, 18.0)	528/ 906	(58.3)	19.0 (17.0, 20.0)	1.200 (1.064, 1.353)	0.003			1.221 (1.085, 1.374)	<.001		
Presence of risk factor: Chronic kidney disease														
Yes	3/ 6	(50.0)	25.0 (7.0, NE)	3/ 8	(37.5)	NE (12.0, NE)	684E14 (0.000, NE)	0.997		0.482	1.951 (0.391, 9.739)	0.415		0.570
No	598/ 921	(64.9)	17.0 (15.0, 18.0)	553/ 947	(58.4)	19.0 (17.0, 20.0)	1.199 (1.066, 1.349)	0.003			1.213 (1.081, 1.362)	0.001		
Presence of risk factor: HIV Infection														
Yes	0			1/ 1	(100.0)									
No	601/ 927	(64.8)		554/ 953	(58.1)									
Presence of risk factor: Sickle Cell Disease														
No	601/ 927	(64.8)		556/ 955	(58.2)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/ 2	(100.0)		0/ 1	(0.0)									
No	599/ 925	(64.8)		556/ 954	(58.3)									
Presence of risk factor: Cancer														
Yes	3/ 5	(60.0)	14.0 (9.0, NE)	5/ 6	(83.3)	12.5 (2.0, NE)	0.000 (0.000, NE)	0.999		0.229	0.654 (0.153, 2.804)	0.568		0.411
No	598/ 922	(64.9)	17.0 (15.0, 18.0)	551/ 949	(58.1)	19.0 (17.0, 20.0)	1.211 (1.076, 1.363)	0.001			1.224 (1.090, 1.374)	<.001		
Presence of risk factor: Device Dependence														
Yes	0/ 4	(0.0)		1/ 3	(33.3)									
No	597/ 914	(65.3)		553/ 944	(58.6)									

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=188)			Placebo (N=178)			Adjusted Analysis [2]		Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value		Hazard Ratio (95% CI)	p-Value	p-Value	
Age													
< 65	121/ 75	(69.1)	12.0 (10.0, 15.0)	85/ 155	(54.8)	18.0 (16.0, 24.0)	1.469 (1.101, 1.960)	0.009	0.388	1.548 (1.172, 2.044)	0.002		0.481
>= 65	7/ 13	(53.8)	19.0 (6.0, NE)	16/ 23	(69.6)	16.0 (11.0, 24.0)	0.905 (0.333, 2.460)	0.844		1.099 (0.451, 2.676)	0.836		
Gender													
Male	60/ 78	(76.9)	11.0 (8.0, 12.0)	44/ 73	(60.3)	17.0 (12.0, 21.0)	1.358 (0.909, 2.029)	0.135	0.783	1.522 (1.030, 2.249)	0.035		0.885
Female	68/ 110	(61.8)	13.0 (11.0, 20.0)	57/ 105	(54.3)	19.0 (16.0, NE)	1.439 (0.997, 2.077)	0.052		1.463 (1.028, 2.080)	0.034		
Geographic region													
United States	63/ 95	(66.3)		46/ 92	(50.0)								
Europe	39/ 50	(78.0)		32/ 42	(76.2)								
India	0			0									
Rest of World	26/ 43	(60.5)		23/ 44	(52.3)								
COVID-19 therapeutic mAb treatment at randomisation													
Yes	10/ 14	(71.4)	11.0 (5.0, 23.0)	9/ 16	(56.3)	18.0 (7.0, NE)	1.096 (0.356, 3.375)	0.873	0.953	1.654 (0.668, 4.095)	0.277		0.827
No	118/ 174	(67.8)	12.0 (11.0, 15.0)	92/ 162	(56.8)	18.0 (15.0, 23.0)	1.423 (1.074, 1.885)	0.014		1.485 (1.130, 1.951)	0.005		
Baseline viral load 1													
< 10 ⁴ copies/mL	31/ 48	(64.6)	12.0 (9.0, 21.0)	25/ 41	(61.0)	14.0 (11.0, NE)	1.390 (0.803, 2.408)	0.240	0.704	1.278 (0.754, 2.167)	0.361		0.512
>= 10 ⁴ copies/mL	95/ 138	(68.8)	11.0 (9.0, 15.0)	71/ 130	(54.6)	19.0 (17.0, 24.0)	1.439 (1.052, 1.968)	0.023		1.580 (1.161, 2.150)	0.004		
Baseline viral load 2													
< 10 ⁷ copies/mL	78/ 112	(69.6)	12.0 (9.0, 15.0)	67/ 119	(56.3)	20.0 (15.0, 24.0)	1.620 (1.156, 2.270)	0.005	0.323	1.657 (1.195, 2.299)	0.002		0.406
>= 10 ⁷ copies/mL	48/ 74	(64.9)	11.5 (10.0, 19.0)	29/ 52	(55.8)	18.0 (11.0, NE)	1.188 (0.741, 1.906)	0.474		1.268 (0.800, 2.012)	0.312		
Baseline serology status													
Negative	65/ 98	(66.3)	12.0 (10.0, 16.0)	58/ 110	(52.7)	19.0 (16.0, NE)	1.502 (1.043, 2.162)	0.029	0.724	1.584 (1.111, 2.258)	0.011		0.583
Positive	62/ 89	(69.7)	12.0 (9.0, 18.0)	41/ 66	(62.1)	17.0 (14.0, 23.0)	1.361 (0.905, 2.048)	0.139		1.375 (0.926, 2.041)	0.114		
Symptom onset days to first dose date													
<= 3	98/ 132	(74.2)	11.0 (8.0, 12.0)	70/ 106	(66.0)	16.0 (12.0, 18.0)	1.473 (1.074, 2.022)	0.016	0.671	1.438 (1.057, 1.955)	0.021		0.957
> 3	30/ 56	(53.6)	20.0 (12.0, NE)	31/ 72	(43.1)	NE (18.0, NE)	1.219 (0.713, 2.085)	0.468		1.424 (0.862, 2.354)	0.167		
BMI group													
< 25	23/ 35	(65.7)	8.0 (5.0, 12.0)	21/ 32	(65.6)	15.0 (12.0, 24.0)	1.642 (0.856, 3.151)	0.136	0.005	1.917 (1.054, 3.487)	0.033		0.004
25 - < 30	30/ 50	(60.0)	16.0 (11.0, NE)	39/ 56	(69.6)	13.0 (9.0, 18.0)	0.741 (0.450, 1.223)	0.241		0.786 (0.488, 1.267)	0.323		
>= 30	75/ 103	(72.8)	12.0 (10.0, 17.0)	41/ 90	(45.6)	NE (18.0, NE)	2.096 (1.388, 3.165)	<.001		2.122 (1.448, 3.111)	<.001		
Ethnicity													
White	99/ 145	(68.3)	12.0 (10.0, 16.0)	83/ 140	(59.3)	18.0 (15.0, 23.0)	1.365 (1.010, 1.844)	0.043	0.284	1.450 (1.083, 1.942)	0.013		0.570
Black or African American	11/ 15	(73.3)	11.0 (4.0, 17.0)	5/ 12	(41.7)	NE (7.0, NE)	7.098 (1.406, 35.829)	0.018		2.367 (0.813, 6.890)	0.114		
Asian	5/ 7	(71.4)	9.0 (4.0, NE)	8/ 10	(80.0)	14.5 (3.0, 19.0)	2.557 (0.401, 16.291)	0.321		1.050 (0.341, 3.233)	0.932		
Others	13/ 21	(61.9)	12.5 (5.0, NE)	5/ 16	(31.3)	NE (11.0, NE)	2.047 (0.629, 6.662)	0.234		2.065 (0.735, 5.799)	0.169		
Number of baseline comorbidities present													
0-1	111/ 158	(70.3)		82/ 149	(55.0)								
2-3	17/ 29	(58.6)		18/ 28	(64.3)								
>= 4	0/ 1	(0.0)		1/ 1	(100.0)								
Presence of risk factor: Smoking													
Yes	56/ 75	(74.7)	11.0 (7.0, 14.0)	45/ 72	(62.5)	15.0 (12.0, 19.0)	1.555 (1.022, 2.364)	0.039	0.846	1.496 (1.010, 2.217)	0.045		0.995
No	71/ 112	(63.4)	12.0 (11.0, 19.0)	56/ 106	(52.8)	21.0 (17.0, NE)	1.405 (0.976, 2.022)	0.067		1.490 (1.049, 2.116)	0.026		

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	n/N	(%)	Median (95% CI)[1]	n/N	(%)	Median (95% CI)[1]	Hazard Ratio (95% CI)		p-Value	Interaction p-Value	Hazard Ratio (95% CI)		p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus										0.121				0.055
Yes	9/ 19	(47.4)	NE (11.0, NE)	13/ 19	(68.4)	15.0 (11.0, 24.0)	0.998	(0.399, 2.499)	0.997		0.700	(0.298, 1.641)	0.412	
No	118/ 168	(70.2)	12.0 (9.0, 14.0)	88/ 159	(55.3)	18.0 (16.0, 24.0)	1.529	(1.146, 2.039)	0.004		1.619	(1.227, 2.135)	<.001	
Presence of risk factor: Immunosuppression														
Yes	1/ 1	(100.0)		2/ 3	(66.7)									
No	126/ 186	(67.7)		99/ 175	(56.6)									
Presence of risk factor: Chronic lung disease										0.661				0.629
Yes	8/ 16	(50.0)	22.0 (7.0, NE)	3/ 6	(50.0)	NE (5.0, NE)	1.208	(0.249, 5.863)	0.814		1.132	(0.300, 4.270)	0.855	
No	119/ 171	(69.6)	12.0 (10.0, 14.0)	98/ 172	(57.0)	18.0 (15.0, 23.0)	1.470	(1.115, 1.939)	0.006		1.549	(1.185, 2.025)	0.001	
Presence of risk factor: Hypertension										0.155				0.098
Yes	30/ 55	(54.5)	14.0 (10.0, NE)	34/ 54	(63.0)	18.0 (14.0, 24.0)	1.034	(0.628, 1.702)	0.895		1.039	(0.635, 1.698)	0.879	
No	97/ 132	(73.5)	11.0 (9.0, 14.0)	67/ 124	(54.0)	18.0 (15.0, NE)	1.669	(1.198, 2.324)	0.002		1.718	(1.257, 2.347)	<.001	
Presence of risk factor: Cardiovascular disorder										0.741				0.621
Yes	3/ 6	(50.0)	11.0 (2.0, NE)	6/ 9	(66.7)	15.0 (6.0, NE)	2.700	(0.413, 17.638)	0.300		1.062	(0.264, 4.271)	0.932	
No	124/ 181	(68.5)	12.0 (11.0, 15.0)	95/ 169	(56.2)	18.0 (16.0, 23.0)	1.422	(1.078, 1.877)	0.013		1.507	(1.153, 1.970)	0.003	
Presence of risk factor: Chronic kidney disease														
Yes	0/ 1	(0.0)		1/ 1	(100.0)									
No	127/ 186	(68.3)		100/ 177	(56.5)									
Presence of risk factor: HIV Infection														
Yes	0			0										
No	127/ 187	(67.9)		101/ 178	(56.7)									
Presence of risk factor: Sickle Cell Disease														
No	127/ 187	(67.9)		101/ 178	(56.7)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	0			0/ 1	(0.0)									
No	127/ 187	(67.9)		101/ 177	(57.1)									
Presence of risk factor: Cancer														
Yes	0/ 1	(0.0)		1/ 1	(100.0)									
No	127/ 186	(68.3)		100/ 177	(56.5)									
Presence of risk factor: Device Dependence														
Yes	0/ 2	(0.0)		0										
No	126/ 183	(68.9)		101/ 176	(57.4)									

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

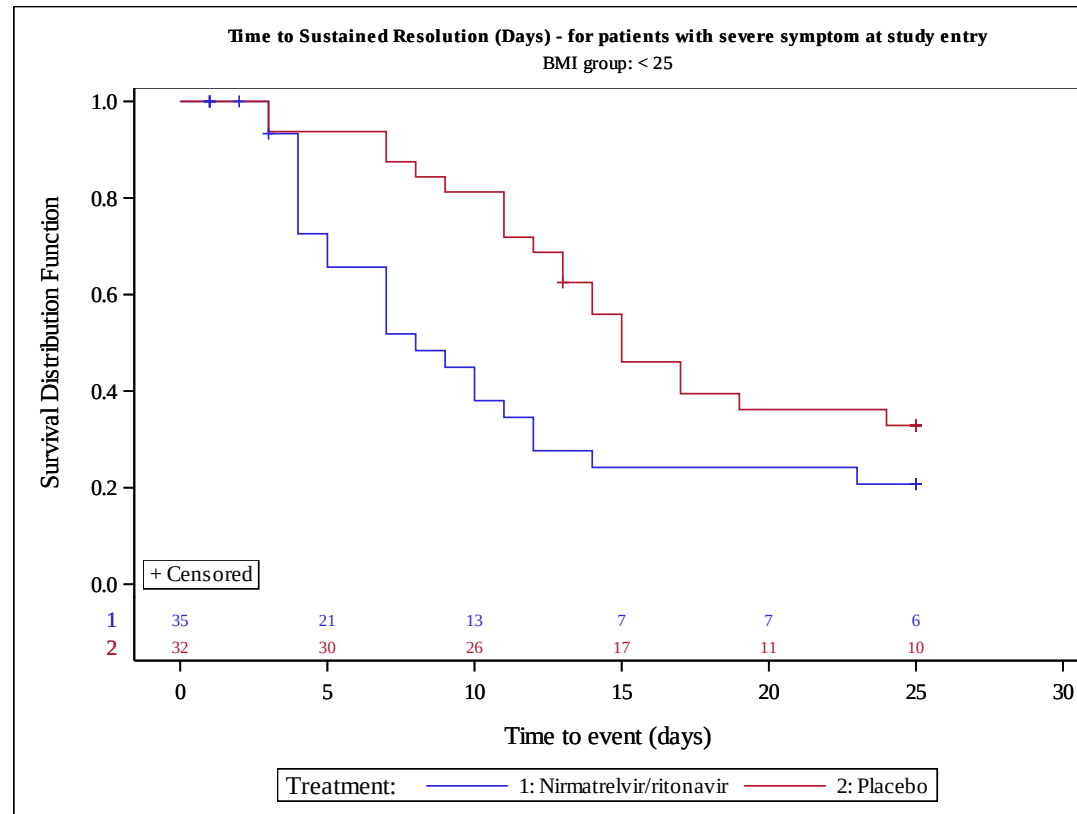
p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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 Overall Study population
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Final

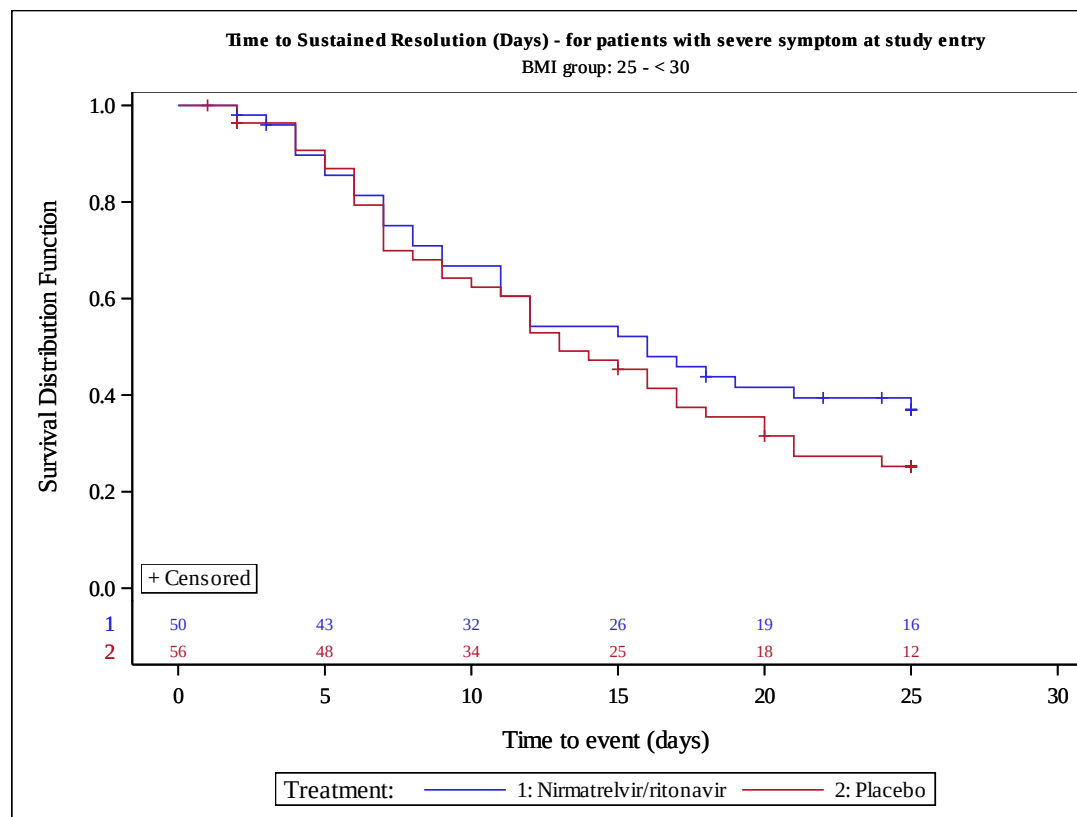


Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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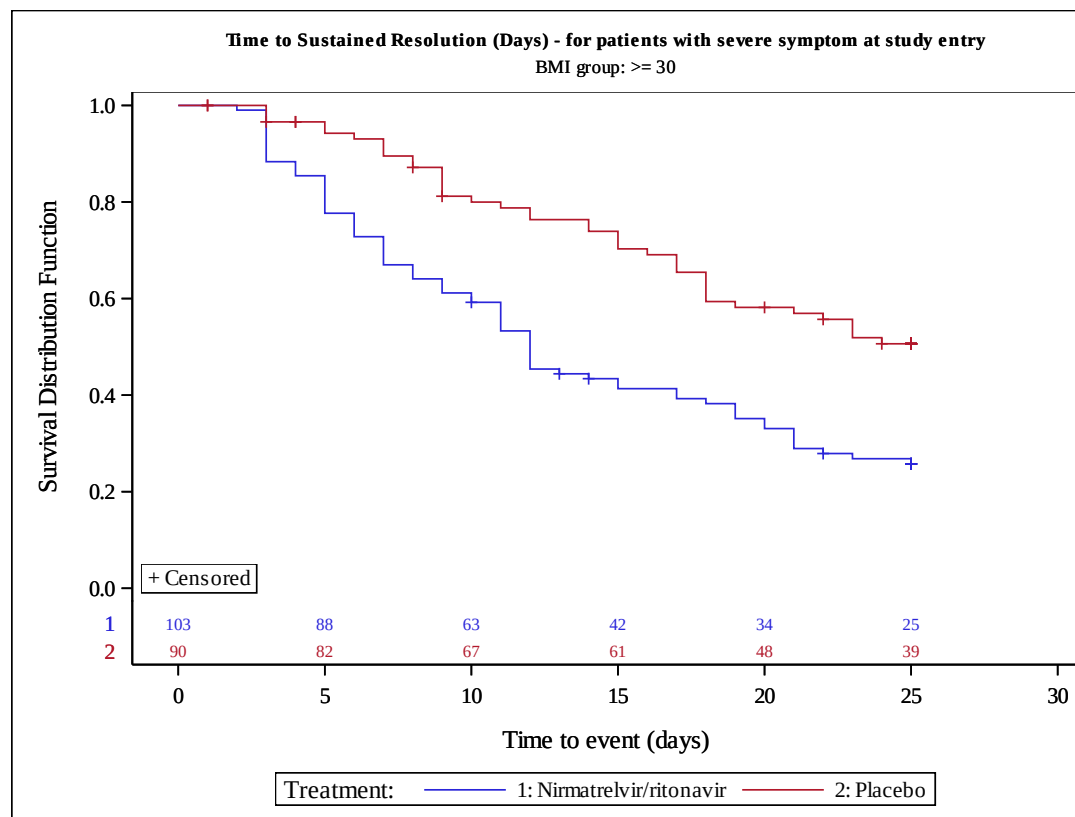


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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Analysis of Participants with Any Severe Signs and Symptoms - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)		p-Value	Relative Risk (95% CI)		p-Value				
Age							0.559				0.397	
< 65	401/ 790 (50.8)	399/ 810 (49.3)	1.018 (0.926, 1.119)		0.711			1.030 (0.934, 1.137)		0.548		
>= 65	44/ 138 (31.9)	52/ 145 (35.9)	0.973 (0.700, 1.351)		0.869			0.889 (0.641, 1.233)		0.481		
Gender							0.704				0.791	
Male	194/ 463 (41.9)	208/ 507 (41.0)	0.980 (0.847, 1.134)		0.786			1.021 (0.879, 1.186)		0.782		
Female	251/ 465 (54.0)	243/ 448 (54.2)	1.020 (0.911, 1.141)		0.734			0.995 (0.883, 1.121)		0.937		
Geographic region							0.250				0.293	
United States	208/ 375 (55.5)	194/ 387 (50.1)	1.097 (0.962, 1.251)		0.165			1.106 (0.967, 1.266)		0.140		
Europe	142/ 322 (44.1)	144/ 321 (44.9)	1.017 (0.855, 1.208)		0.853			0.983 (0.827, 1.168)		0.846		
India	15/ 74 (20.3)	15/ 78 (19.2)	NE (NE, NE)		NE			1.054 (0.555, 2.001)		0.872		
Rest of World	80/ 157 (51.0)	98/ 169 (58.0)	0.881 (0.726, 1.070)		0.201			0.879 (0.719, 1.073)		0.205		
COVID-19 therapeutic mAb treatment at randomisation							0.163				0.120	
Yes	36/ 57 (63.2)	29/ 60 (48.3)	NE (NE, NE)		NE			1.307 (0.941, 1.814)		0.110		
No	409/ 871 (47.0)	422/ 895 (47.2)	0.991 (0.901, 1.090)		0.856			0.996 (0.902, 1.099)		0.935		
Baseline viral load 1							0.297				0.571	
< 10^4 copies/mL	123/ 335 (36.7)	122/ 354 (34.5)	1.126 (0.925, 1.370)		0.236			1.065 (0.871, 1.303)		0.537		
>= 10^4 copies/mL	310/ 569 (54.5)	314/ 575 (54.6)	0.984 (0.888, 1.090)		0.759			0.998 (0.898, 1.109)		0.966		
Baseline viral load 2							0.457				0.590	
< 10^7 copies/mL	293/ 652 (44.9)	305/ 699 (43.6)	1.053 (0.940, 1.180)		0.371			1.030 (0.914, 1.161)		0.629		
>= 10^7 copies/mL	140/ 252 (55.6)	131/ 230 (57.0)	0.964 (0.828, 1.121)		0.632			0.975 (0.833, 1.142)		0.757		
Baseline serology status							0.970				0.725	
Negative	243/ 435 (55.9)	246/ 456 (53.9)	1.017 (0.907, 1.141)		0.771			1.035 (0.919, 1.166)		0.566		
Positive	196/ 482 (40.7)	198/ 487 (40.7)	1.016 (0.878, 1.176)		0.828			1.000 (0.859, 1.165)		0.998		
Symptom onset days to first dose date							0.194				0.233	
<= 3	300/ 624 (48.1)	283/ 624 (45.4)	1.065 (0.948, 1.197)		0.286			1.060 (0.942, 1.194)		0.335		
> 3	145/ 304 (47.7)	168/ 331 (50.8)	0.933 (0.806, 1.079)		0.350			0.940 (0.802, 1.101)		0.442		
BMI group							0.225				0.180	
< 25	79/ 215 (36.7)	91/ 213 (42.7)	0.916 (0.728, 1.153)		0.456			0.860 (0.680, 1.087)		0.207		
25 - < 30	153/ 319 (48.0)	141/ 332 (42.5)	1.130 (0.963, 1.325)		0.135			1.129 (0.953, 1.338)		0.160		
>= 30	213/ 393 (54.2)	219/ 410 (53.4)	NE (NE, NE)		NE			1.015 (0.893, 1.153)		0.824		
Ethnicity							0.545				0.764	
White	353/ 699 (50.5)	351/ 718 (48.9)	1.024 (0.926, 1.133)		0.640			1.033 (0.930, 1.147)		0.543		
Black or African American	22/ 43 (51.2)	19/ 40 (47.5)	NE (NE, NE)		NE			1.077 (0.695, 1.668)		0.739		
Asian	29/ 117 (24.8)	36/ 127 (28.3)	NE (NE, NE)		NE			0.874 (0.575, 1.330)		0.531		
Others	41/ 69 (59.4)	45/ 70 (64.3)	NE (NE, NE)		NE			0.924 (0.711, 1.201)		0.556		
Number of baseline comorbidities present							NE				0.690	
0-1	357/ 710 (50.3)	358/ 728 (49.2)	1.026 (0.929, 1.134)		0.608			1.022 (0.922, 1.134)		0.675		
2-3	85/ 214 (39.7)	90/ 221 (40.7)	1.006 (0.805, 1.257)		0.959			0.975 (0.776, 1.227)		0.831		
>= 4	3/ 4 (75.0)	3/ 6 (50.0)	NE (NE, NE)		NE			1.500 (0.563, 3.997)		0.417		
Presence of risk factor: Smoking							0.969				0.904	
Yes	192/ 417 (46.0)	197/ 438 (45.0)	1.006 (0.870, 1.163)		0.937			1.024 (0.884, 1.185)		0.754		
No	253/ 509 (49.7)	254/ 517 (49.1)	1.002 (0.891, 1.127)		0.967			1.012 (0.894, 1.145)		0.854		
Presence of risk factor: Diabetes mellitus							0.669				0.647	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928)		Placebo (N=955)		Adjusted analysis [1]		Interaction p-Value	Unadjusted analysis [2]		Interaction p-Value
	n/N (%)	n/N (%)	n/N (%)	Relative Risk (95% CI)	p-Value	Relative Risk (95% CI)		p-Value		
Yes	52/ 130 (40.0)	57/ 136 (41.9)	1.017 (0.780, 1.325)	0.904	0.954 (0.715, 1.274)	0.751				
No	393/ 797 (49.3)	394/ 819 (48.1)	1.027 (0.934, 1.129)	0.585	1.025 (0.927, 1.133)	0.629				
Presence of risk factor: Immunosuppression				0.997		0.774				
Yes	3/ 6 (50.0)	4/ 7 (57.1)	NE (NE, NE)	NE	0.875 (0.314, 2.440)	0.799				
No	442/ 921 (48.0)	447/ 948 (47.2)	1.012 (0.924, 1.109)	0.795	1.018 (0.925, 1.119)	0.716				
Presence of risk factor: Chronic lung disease				0.600		0.592				
Yes	34/ 62 (54.8)	19/ 39 (48.7)	NE (NE, NE)	NE	1.126 (0.760, 1.668)	0.555				
No	411/ 865 (47.5)	432/ 916 (47.2)	1.005 (0.914, 1.104)	0.924	1.007 (0.913, 1.111)	0.881				
Presence of risk factor: Hypertension				0.455		0.459				
Yes	158/ 348 (45.4)	158/ 371 (42.6)	1.073 (0.916, 1.258)	0.380	1.066 (0.904, 1.257)	0.447				
No	287/ 579 (49.6)	293/ 584 (50.2)	0.998 (0.893, 1.116)	0.977	0.988 (0.880, 1.109)	0.837				
Presence of risk factor: Cardiovascular disorder				0.191		0.445				
Yes	15/ 42 (35.7)	21/ 49 (42.9)	NE (NE, NE)	NE	0.833 (0.496, 1.400)	0.491				
No	430/ 885 (48.6)	430/ 906 (47.5)	1.025 (0.934, 1.125)	0.600	1.024 (0.930, 1.127)	0.633				
Presence of risk factor: Chronic kidney disease				0.917		0.363				
Yes	4/ 6 (66.7)	7/ 8 (87.5)	NE (NE, NE)	NE	0.762 (0.408, 1.421)	0.393				
No	441/ 921 (47.9)	444/ 947 (46.9)	1.014 (0.925, 1.111)	0.766	1.021 (0.928, 1.124)	0.666				
Presence of risk factor: HIV Infection										
Yes	0	0/ 1 (0.0)								
No	445/ 927 (48.0)	451/ 953 (47.3)								
Presence of risk factor: Sickle Cell Disease										
No	445/ 927 (48.0)	451/ 955 (47.2)								
Presence of risk factor: Neurodevelopmental Disorder										
Yes	2/ 2 (100.0)	0/ 1 (0.0)								
No	443/ 925 (47.9)	451/ 954 (47.3)								
Presence of risk factor: Cancer				0.461		0.342				
Yes	1/ 5 (20.0)	3/ 6 (50.0)	NE (NE, NE)	NE	0.400 (0.058, 2.748)	0.351				
No	444/ 922 (48.2)	448/ 949 (47.2)	1.014 (0.926, 1.111)	0.764	1.020 (0.928, 1.122)	0.681				
Presence of risk factor: Device Dependence										
Yes	4/ 4 (100.0)	2/ 3 (66.7)								
No	436/ 914 (47.7)	446/ 944 (47.2)								

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value	
Age							0.502					0.496
< 65	655/ 790 (82.9)	644/ 810 (79.5)	1.027 (0.981, 1.076)			0.257		1.043 (0.995, 1.093)			0.081	
>= 65	105/ 138 (76.1)	111/ 145 (76.6)	NE (NE, NE)			NE		0.994 (0.873, 1.132)			0.927	
Gender							0.491					0.307
Male	369/ 463 (79.7)	382/ 507 (75.3)	1.033 (0.966, 1.104)			0.341		1.058 (0.988, 1.132)			0.104	
Female	391/ 465 (84.1)	373/ 448 (83.3)	NE (NE, NE)			NE		1.010 (0.954, 1.070)			0.735	
Geographic region							0.081					0.116
United States	301/ 375 (80.3)	305/ 387 (78.8)	1.023 (0.951, 1.101)			0.538		1.018 (0.948, 1.095)			0.619	
Europe	270/ 322 (83.9)	261/ 321 (81.3)	NE (NE, NE)			NE		1.031 (0.961, 1.107)			0.396	
India	57/ 74 (77.0)	45/ 78 (57.7)	NE (NE, NE)			NE		1.335 (1.064, 1.676)			0.013	
Rest of World	132/ 157 (84.1)	144/ 169 (85.2)	NE (NE, NE)			NE		0.987 (0.899, 1.082)			0.777	
COVID-19 therapeutic mAb treatment at randomisation							0.833					0.620
Yes	51/ 57 (89.5)	50/ 60 (83.3)	NE (NE, NE)			NE		1.074 (0.930, 1.240)			0.333	
No	709/ 871 (81.4)	705/ 895 (78.8)	1.022 (0.975, 1.071)			0.363		1.033 (0.986, 1.083)			0.167	
Baseline viral load 1							0.138					0.193
< 10 ⁴ copies/mL	270/ 335 (80.6)	266/ 354 (75.1)	1.063 (0.981, 1.153)			0.136		1.073 (0.990, 1.162)			0.085	
>= 10 ⁴ copies/mL	470/ 569 (82.6)	472/ 575 (82.1)	1.002 (0.950, 1.057)			0.927		1.006 (0.954, 1.062)			0.820	
Baseline viral load 2							0.170					0.242
< 10 ⁷ copies/mL	520/ 652 (79.8)	535/ 699 (76.5)	1.045 (0.988, 1.106)			0.120		1.042 (0.985, 1.102)			0.152	
>= 10 ⁷ copies/mL	220/ 252 (87.3)	203/ 230 (88.3)	0.992 (0.925, 1.064)			0.821		0.989 (0.925, 1.057)			0.748	
Baseline serology status							0.720					0.762
Negative	364/ 435 (83.7)	371/ 456 (81.4)	1.018 (0.958, 1.082)			0.557		1.028 (0.968, 1.093)			0.362	
Positive	385/ 482 (79.9)	373/ 487 (76.6)	NE (NE, NE)			NE		1.043 (0.976, 1.115)			0.216	
Symptom onset days to first dose date							0.197					0.134
<= 3	523/ 624 (83.8)	493/ 624 (79.0)	1.040 (0.987, 1.096)			0.142		1.061 (1.006, 1.119)			0.029	
> 3	237/ 304 (78.0)	262/ 331 (79.2)	NE (NE, NE)			NE		0.985 (0.908, 1.068)			0.715	
BMI group							0.384					0.435
< 25	167/ 215 (77.7)	168/ 213 (78.9)	0.981 (0.887, 1.085)			0.708		0.985 (0.891, 1.088)			0.764	
25 - < 30	268/ 319 (84.0)	261/ 332 (78.6)	1.043 (0.970, 1.121)			0.259		1.069 (0.993, 1.150)			0.078	
>= 30	324/ 393 (82.4)	326/ 410 (79.5)	NE (NE, NE)			NE		1.037 (0.970, 1.109)			0.290	
Ethnicity							0.290					0.299
White	574/ 699 (82.1)	579/ 718 (80.6)	1.014 (0.964, 1.067)			0.580		1.018 (0.969, 1.070)			0.475	
Black or African American	34/ 43 (79.1)	31/ 40 (77.5)	NE (NE, NE)			NE		1.020 (0.813, 1.280)			0.863	
Asian	92/ 117 (78.6)	84/ 127 (66.1)	NE (NE, NE)			NE		1.189 (1.017, 1.390)			0.030	
Others	60/ 69 (87.0)	61/ 70 (87.1)	NE (NE, NE)			NE		0.998 (0.878, 1.134)			0.974	
Number of baseline comorbidities present							0.950					0.978
0-1	589/ 710 (83.0)	583/ 728 (80.1)	1.017 (0.969, 1.067)			0.492		1.036 (0.986, 1.088)			0.160	
2-3	168/ 214 (78.5)	168/ 221 (76.0)	NE (NE, NE)			NE		1.033 (0.933, 1.144)			0.536	
>= 4	3/ 4 (75.0)	4/ 6 (66.7)	NE (NE, NE)			NE		1.125 (0.505, 2.504)			0.773	
Presence of risk factor: Smoking							0.463					0.384
Yes	338/ 417 (81.1)	335/ 438 (76.5)	1.042 (0.971, 1.119)			0.254		1.060 (0.988, 1.136)			0.102	
No	421/ 509 (82.7)	420/ 517 (81.2)	1.011 (0.954, 1.072)			0.704		1.018 (0.961, 1.078)			0.539	
Presence of risk factor: Diabetes mellitus							0.160					0.108

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with Progression of Worsening Status in 1 or More Signs and Symptoms - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928) n/N (%)	Placebo (N=955) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value	
Yes	99/ 130 (76.2)	110/ 136 (80.9)	NE (	NE,	NE)	NE		0.942 (	0.830,	1.068)	0.350	
No	660/ 797 (82.8)	645/ 819 (78.8)	1.032 (	0.985,	1.082)	0.189		1.052 (	1.003,	1.103)	0.039	
Presence of risk factor: Immunosuppression							NE					0.206
Yes	6/ 6 (100.0)	5/ 7 (71.4)	NE (	NE,	NE)	NE		1.400 (	0.876,	2.237)	0.159	
No	753/ 921 (81.8)	750/ 948 (79.1)	1.018 (	0.974,	1.064)	0.423		1.033 (	0.988,	1.081)	0.150	
Presence of risk factor: Chronic lung disease							0.879					0.911
Yes	50/ 62 (80.6)	30/ 39 (76.9)	1.038 (	0.820,	1.315)	0.755		1.048 (	0.849,	1.294)	0.660	
No	709/ 865 (82.0)	725/ 916 (79.1)	1.025 (	0.980,	1.072)	0.288		1.036 (	0.989,	1.084)	0.133	
Presence of risk factor: Hypertension							0.583					0.785
Yes	279/ 348 (80.2)	285/ 371 (76.8)	1.041 (	0.966,	1.122)	0.297		1.044 (	0.967,	1.127)	0.274	
No	480/ 579 (82.9)	470/ 584 (80.5)	1.005 (	0.952,	1.060)	0.859		1.030 (	0.976,	1.088)	0.286	
Presence of risk factor: Cardiovascular disorder							0.262					0.217
Yes	32/ 42 (76.2)	41/ 49 (83.7)	NE (	NE,	NE)	NE		0.911 (	0.738,	1.123)	0.381	
No	727/ 885 (82.1)	714/ 906 (78.8)	1.027 (	0.982,	1.075)	0.240		1.042 (	0.996,	1.091)	0.075	
Presence of risk factor: Chronic kidney disease							0.280					0.164
Yes	3/ 6 (50.0)	7/ 8 (87.5)	NE (	NE,	NE)	NE		0.571 (	0.246,	1.326)	0.193	
No	756/ 921 (82.1)	748/ 947 (79.0)	1.024 (	0.980,	1.070)	0.294		1.039 (	0.994,	1.087)	0.091	
Presence of risk factor: HIV Infection												
Yes	0	1/ 1 (100.0)										
No	759/ 927 (81.9)	754/ 953 (79.1)										
Presence of risk factor: Sickle Cell Disease												
No	759/ 927 (81.9)	755/ 955 (79.1)										
Presence of risk factor: Neurodevelopmental Disorder												
Yes	2/ 2 (100.0)	0/ 1 (0.0)										
No	757/ 925 (81.8)	755/ 954 (79.1)										
Presence of risk factor: Cancer							NE					0.198
Yes	5/ 5 (100.0)	4/ 6 (66.7)	NE (	NE,	NE)	NE		1.500 (	0.852,	2.641)	0.160	
No	754/ 922 (81.8)	751/ 949 (79.1)	1.019 (	0.975,	1.065)	0.413		1.033 (	0.988,	1.081)	0.149	
Presence of risk factor: Device Dependence												
Yes	3/ 4 (75.0)	3/ 3 (100.0)										
No	749/ 914 (81.9)	747/ 944 (79.1)										

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RKI-conform mITT2 Analysis set
Analysis of Time to Sustained Alleviation of All Signs and Symptoms Through Day 28 - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928)			Placebo (N=955)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	489/ 790	(61.9)	16.0 (15.0, 17.0)	441/ 810	(54.4)	20.0 (18.0, 22.0)	1.253 (1.099, 1.429)	<.001		0.124	1.261 (1.109, 1.434)	<.001		0.096
>= 65	99/ 138	(71.7)	14.0 (13.0, 18.0)	81/ 145	(55.9)	22.0 (18.0, NE)	1.641 (1.215, 2.217)	0.001			1.675 (1.247, 2.249)	<.001		
Gender														
Male	325/ 463	(70.2)	14.0 (13.0, 16.0)	288/ 507	(56.8)	18.0 (16.0, 20.0)	1.435 (1.220, 1.687)	<.001		0.108	1.435 (1.224, 1.682)	<.001		0.144
Female	263/ 465	(56.6)	19.0 (16.0, 21.0)	234/ 448	(52.2)	23.0 (20.0, 25.0)	1.175 (0.981, 1.406)	0.079			1.213 (1.017, 1.446)	0.032		
Geographic region														
United States	220/ 375	(58.7)	17.0 (15.0, 20.0)	208/ 387	(53.7)	20.0 (18.0, 24.0)	1.178 (0.970, 1.429)	0.098		0.281	1.193 (0.987, 1.442)	0.068		0.241
Europe	213/ 322	(66.1)	17.0 (15.0, 18.0)	174/ 321	(54.2)	22.0 (19.0, 25.0)	1.429 (1.164, 1.754)	<.001			1.434 (1.173, 1.752)	<.001		
India	68/ 74	(91.9)	13.0 (12.0, 14.0)	71/ 78	(91.0)	14.0 (13.0, 15.0)	1.169 (0.834, 1.637)	0.365			1.128 (0.808, 1.573)	0.479		
Rest of World	87/ 157	(55.4)	16.0 (13.0, 22.0)	69/ 169	(40.8)	NE (25.0, NE)	1.553 (1.123, 2.149)	0.008			1.565 (1.140, 2.147)	0.006		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	33/ 57	(57.9)	15.0 (12.0, NE)	32/ 60	(53.3)	20.0 (15.0, NE)	1.254 (0.761, 2.068)	0.374		0.930	1.238 (0.760, 2.014)	0.391		0.879
No	555/ 871	(63.7)	16.0 (15.0, 17.0)	490/ 895	(54.7)	20.0 (19.0, 22.0)	1.303 (1.152, 1.475)	<.001			1.320 (1.169, 1.491)	<.001		
Baseline viral load 1														
< 10 ⁴ copies/mL	241/ 335	(71.9)	15.0 (13.0, 16.0)	222/ 354	(62.7)	16.0 (15.0, 19.0)	1.273 (1.058, 1.530)	0.010		0.679	1.293 (1.077, 1.552)	0.006		0.811
>= 10 ⁴ copies/mL	332/ 569	(58.3)	18.0 (16.0, 19.0)	289/ 575	(50.3)	24.0 (21.0, NE)	1.331 (1.135, 1.560)	<.001			1.333 (1.138, 1.560)	<.001		
Baseline viral load 2														
< 10 ⁷ copies/mL	433/ 652	(66.4)	15.0 (14.0, 16.0)	410/ 699	(58.7)	19.0 (17.0, 20.0)	1.273 (1.111, 1.458)	<.001		0.351	1.297 (1.133, 1.485)	<.001		0.465
>= 10 ⁷ copies/mL	140/ 252	(55.6)	20.0 (18.0, 24.0)	101/ 230	(43.9)	NE (23.0, NE)	1.498 (1.154, 1.945)	0.002			1.447 (1.120, 1.869)	0.005		
Baseline serology status														
Negative	258/ 435	(59.3)	18.0 (16.0, 19.0)	214/ 456	(46.9)	NE (23.0, NE)	1.453 (1.208, 1.748)	<.001		0.161	1.454 (1.213, 1.743)	<.001		0.146
Positive	322/ 482	(66.8)	15.0 (13.0, 16.0)	302/ 487	(62.0)	17.0 (16.0, 19.0)	1.212 (1.034, 1.420)	0.018			1.212 (1.036, 1.418)	0.017		
Symptom onset days to first dose date														
<= 3	402/ 624	(64.4)	16.0 (15.0, 17.0)	361/ 624	(57.9)	19.0 (18.0, 22.0)	1.274 (1.103, 1.473)	0.001		0.539	1.256 (1.089, 1.447)	0.002		0.250
> 3	186/ 304	(61.2)	16.0 (15.0, 18.0)	161/ 331	(48.6)	22.0 (19.0, NE)	1.366 (1.100, 1.698)	0.005			1.447 (1.172, 1.788)	<.001		
BMI group														
< 25	158/ 215	(73.5)	13.0 (12.0, 15.0)	131/ 213	(61.5)	18.0 (15.0, 20.0)	1.480 (1.158, 1.892)	0.002		0.621	1.488 (1.179, 1.878)	<.001		0.309
25 - < 30	203/ 319	(63.6)	17.0 (14.0, 18.0)	197/ 332	(59.3)	19.0 (17.0, 20.0)	1.239 (1.014, 1.513)	0.036			1.183 (0.973, 1.440)	0.093		
>= 30	227/ 393	(57.8)	19.0 (16.0, 20.0)	194/ 410	(47.3)	25.0 (22.0, NE)	1.428 (1.170, 1.743)	<.001			1.359 (1.122, 1.647)	0.002		
Ethnicity														
White	431/ 699	(61.7)	17.0 (16.0, 19.0)	375/ 718	(52.2)	22.0 (19.0, 24.0)	1.297 (1.126, 1.493)	<.001		0.347	1.325 (1.154, 1.522)	<.001		0.447
Black or African American	26/ 43	(60.5)	11.0 (8.0, 17.0)	21/ 40	(52.5)	22.0 (11.0, NE)	1.592 (0.853, 2.974)	0.144			1.502 (0.842, 2.681)	0.169		
Asian	97/ 117	(82.9)	13.0 (11.0, 14.0)	104/ 127	(81.9)	14.0 (13.0, 16.0)	1.221 (0.919, 1.624)	0.169			1.198 (0.908, 1.581)	0.202		
Others	34/ 69	(49.3)	23.0 (16.0, NE)	22/ 70	(31.4)	NE (NE, NE)	1.622 (0.938, 2.804)	0.083			1.760 (1.028, 3.011)	0.039		
Number of baseline comorbidities present														
0-1	447/ 710	(63.0)	16.0 (15.0, 17.0)	402/ 728	(55.2)	20.0 (19.0, 22.0)	1.267 (1.104, 1.455)	<.001		0.196	1.277 (1.116, 1.461)	<.001		0.160
2-3	140/ 214	(65.4)	15.0 (13.0, 17.0)	116/ 221	(52.5)	23.0 (18.0, NE)	1.416 (1.100, 1.822)	0.007			1.493 (1.166, 1.910)	0.001		
>= 4	1/ 4	(25.0)	NE (15.0, NE)	4/ 6	(66.7)	15.5 (6.0, NE)	0.914 (0.071, 11.799)	0.945			0.281 (0.031, 2.527)	0.257		
Presence of risk factor: Smoking														
Yes	287/ 417	(68.8)	15.0 (14.0, 16.0)	250/ 438	(57.1)	19.0 (17.0, 21.0)	1.405 (1.181, 1.672)	<.001		0.437	1.404 (1.184, 1.664)	<.001		0.372
No	300/ 509	(58.9)	18.0 (16.0, 20.0)	272/ 517	(52.6)	22.0 (20.0, 25.0)	1.253 (1.060, 1.481)	0.008			1.251 (1.062, 1.475)	0.007		

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928)						Placebo (N=955)		Adjusted Analysis [2]				Unadjusted Analysis [3]					
	n/N	(%)	Median (95% CI)[1]			n/N	(%)	Median (95% CI)[1]		Hazard Ratio (95% CI)		p-Value	Interaction p-Value	Hazard Ratio (95% CI)		p-Value	Interaction p-Value	
Presence of risk factor: Diabetes mellitus																		
Yes	89/	130	(68.5)	13.0	(11.0, 15.0)	78/	136	(57.4)	20.0	(16.0, 25.0)	1.561	(1.137, 2.141)	0.006	0.396	1.498	(1.104, 2.033)	0.009	0.284
No	498/	797	(62.5)	17.0	(16.0, 18.0)	444/	819	(54.2)	20.0	(19.0, 22.0)	1.284	(1.126, 1.463)	<.001		1.286	(1.131, 1.462)	<.001	
Presence of risk factor: Immunosuppression																		
Yes	3/	6	(50.0)	NE	(6.0, NE)	5/	7	(71.4)	13.0	(5.0, NE)	1.052	(0.000, NE)	1.000	0.261	0.643	(0.153, 2.693)	0.545	0.269
No	584/	921	(63.4)	16.0	(15.0, 17.0)	517/	948	(54.5)	20.0	(19.0, 22.0)	1.309	(1.160, 1.477)	<.001		1.323	(1.175, 1.489)	<.001	
Presence of risk factor: Chronic lung disease																		
Yes	35/	62	(56.5)	19.0	(15.0, NE)	17/	39	(43.6)	NE	(16.0, NE)	1.196	(0.622, 2.300)	0.591	0.899	1.241	(0.695, 2.216)	0.465	0.801
No	552/	865	(63.8)	16.0	(15.0, 17.0)	505/	916	(55.1)	20.0	(19.0, 22.0)	1.313	(1.161, 1.485)	<.001		1.331	(1.180, 1.502)	<.001	
Presence of risk factor: Hypertension																		
Yes	214/	348	(61.5)	17.0	(15.0, 19.0)	202/	371	(54.4)	22.0	(19.0, 25.0)	1.253	(1.031, 1.524)	0.024	0.714	1.283	(1.059, 1.556)	0.011	0.755
No	373/	579	(64.4)	16.0	(14.0, 17.0)	320/	584	(54.8)	19.0	(18.0, 22.0)	1.320	(1.133, 1.538)	<.001		1.333	(1.148, 1.548)	<.001	
Presence of risk factor: Cardiovascular disorder																		
Yes	25/	42	(59.5)	19.0	(13.0, NE)	25/	49	(51.0)	22.0	(14.0, NE)	1.461	(0.805, 2.654)	0.213	0.704	1.345	(0.772, 2.341)	0.295	0.915
No	562/	885	(63.5)	16.0	(15.0, 17.0)	497/	906	(54.9)	20.0	(19.0, 22.0)	1.296	(1.146, 1.465)	<.001		1.313	(1.163, 1.481)	<.001	
Presence of risk factor: Chronic kidney disease																		
Yes	3/	6	(50.0)	25.0	(7.0, NE)	3/	8	(37.5)	NE	(8.0, NE)	5.894	(0.240, 144.92)	0.278	0.881	1.773	(0.357, 8.800)	0.483	0.618
No	584/	921	(63.4)	16.0	(15.0, 17.0)	519/	947	(54.8)	20.0	(19.0, 22.0)	1.301	(1.153, 1.467)	<.001		1.310	(1.164, 1.474)	<.001	
Presence of risk factor: HIV Infection																		
Yes	0					1/	1	(100.0)										
No	587/	927	(63.3)			520/	953	(54.6)										
Presence of risk factor: Sickel Cell Disease																		
No	587/	927	(63.3)			522/	955	(54.7)										
Presence of risk factor: Neurodevelopmental Disorder																		
Yes	2/	2	(100.0)			0/	1	(0.0)										
No	585/	925	(63.2)			522/	954	(54.7)										
Presence of risk factor: Cancer																		
Yes	2/	5	(40.0)	NE	(9.0, NE)	5/	6	(83.3)	13.5	(5.0, NE)	0.000	(0.000, NE)	0.999	0.098	0.528	(0.101, 2.742)	0.447	0.175
No	585/	922	(63.4)	16.0	(15.0, 17.0)	517/	949	(54.5)	20.0	(19.0, 22.0)	1.313	(1.164, 1.481)	<.001		1.324	(1.176, 1.490)	<.001	
Presence of risk factor: Device Dependence																		
Yes	1/	4	(25.0)			1/	3	(33.3)										
No	582/	914	(63.7)			518/	944	(54.9)										

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=392)			Placebo (N=377)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Age														
< 65	284/ 359	(79.1)	7.0 (6.0, 8.0)	240/ 333	(72.1)	10.0 (8.0, 12.0)	1.289 (1.080, 1.539)	0.005		0.396	1.267 (1.066, 1.504)	0.007		0.631
>= 65	22/ 33	(66.7)	8.0 (6.0, 22.0)	30/ 44	(68.2)	9.0 (7.0, 15.0)	0.944 (0.511, 1.744)	0.855			1.099 (0.633, 1.906)	0.738		
Gender														
Male	149/ 177	(84.2)	6.0 (5.0, 8.0)	115/ 164	(70.1)	9.0 (7.0, 11.0)	1.357 (1.054, 1.748)	0.018		0.254	1.388 (1.087, 1.771)	0.009		0.227
Female	157/ 215	(73.0)	8.0 (7.0, 11.0)	155/ 213	(72.8)	11.0 (9.0, 13.0)	1.155 (0.917, 1.454)	0.222			1.147 (0.919, 1.433)	0.225		
Geographic region														
United States	140/ 193	(72.5)	9.0 (7.0, 10.0)	121/ 168	(72.0)	12.0 (9.0, 13.0)	1.141 (0.887, 1.466)	0.305		0.346	1.157 (0.907, 1.476)	0.240		0.381
Europe	89/ 105	(84.8)	6.0 (5.0, 10.0)	78/ 112	(69.6)	11.0 (8.0, 14.0)	1.555 (1.132, 2.136)	0.006			1.533 (1.130, 2.079)	0.006		
India	16/ 16	(100.0)	3.0 (2.0, 4.0)	13/ 14	(92.9)	3.5 (2.0, 7.0)	1.301 (0.565, 2.994)	0.536			1.613 (0.739, 3.520)	0.230		
Rest of World	61/ 78	(78.2)	7.0 (5.0, 9.0)	58/ 83	(69.9)	8.0 (6.0, 10.0)	1.080 (0.746, 1.563)	0.685			1.109 (0.774, 1.589)	0.573		
COVID-19 therapeutic mAb treatment at randomisation														
Yes	19/ 24	(79.2)	8.0 (4.0, 11.0)	16/ 24	(66.7)	18.0 (9.0, 21.0)	1.432 (0.651, 3.150)	0.372		0.339	1.815 (0.927, 3.555)	0.082		0.381
No	287/ 368	(78.0)	7.0 (6.0, 8.0)	254/ 353	(72.0)	9.0 (8.0, 11.0)	1.234 (1.038, 1.468)	0.017			1.226 (1.035, 1.451)	0.018		
Baseline viral load 1														
< 10^4 copies/mL	97/ 127	(76.4)	7.0 (5.0, 10.0)	81/ 109	(74.3)	8.5 (6.0, 13.0)	1.242 (0.916, 1.683)	0.162		0.858	1.184 (0.881, 1.591)	0.263		0.716
>= 10^4 copies/mL	203/ 259	(78.4)	7.0 (6.0, 8.0)	180/ 257	(70.0)	10.0 (9.0, 12.0)	1.278 (1.041, 1.567)	0.019			1.289 (1.054, 1.575)	0.013		
Baseline viral load 2														
< 10^7 copies/mL	214/ 282	(75.9)	8.0 (6.0, 9.0)	191/ 279	(68.5)	11.0 (9.0, 13.0)	1.318 (1.081, 1.608)	0.006		0.276	1.312 (1.079, 1.596)	0.006		0.264
>= 10^7 copies/mL	86/ 104	(82.7)	7.0 (5.0, 9.0)	70/ 87	(80.5)	8.0 (6.0, 10.0)	1.025 (0.737, 1.426)	0.883			1.049 (0.764, 1.439)	0.768		
Baseline serology status														
Negative	145/ 190	(76.3)	8.0 (6.0, 10.0)	138/ 202	(68.3)	10.0 (9.0, 13.0)	1.257 (0.987, 1.601)	0.064		0.918	1.257 (0.996, 1.588)	0.054		0.965
Positive	158/ 198	(79.8)	7.0 (5.0, 8.0)	129/ 170	(75.9)	9.0 (7.0, 12.0)	1.266 (1.000, 1.605)	0.050			1.234 (0.977, 1.558)	0.077		
Symptom onset days to first dose date														
<= 3	208/ 260	(80.0)	7.0 (5.0, 8.0)	176/ 228	(77.2)	9.0 (7.0, 10.0)	1.194 (0.971, 1.467)	0.092		0.510	1.163 (0.952, 1.422)	0.140		0.322
> 3	98/ 132	(74.2)	8.0 (7.0, 11.0)	94/ 149	(63.1)	12.0 (9.0, 16.0)	1.340 (0.997, 1.802)	0.052			1.394 (1.050, 1.851)	0.022		
BMI group														
< 25	61/ 76	(80.3)	6.0 (4.0, 8.0)	52/ 71	(73.2)	8.0 (6.0, 13.0)	1.673 (1.124, 2.489)	0.011		0.003	1.562 (1.075, 2.267)	0.019		0.006
25 - < 30	89/ 118	(75.4)	8.0 (7.0, 11.0)	96/ 123	(78.0)	7.0 (5.0, 9.0)	0.872 (0.646, 1.177)	0.371			0.856 (0.641, 1.143)	0.291		
>= 30	156/ 198	(78.8)	8.0 (6.0, 10.0)	122/ 183	(66.7)	13.0 (10.0, 15.0)	1.485 (1.159, 1.904)	0.002			1.475 (1.163, 1.871)	0.001		
Ethnicity														
White	232/ 302	(76.8)	8.0 (7.0, 10.0)	204/ 289	(70.6)	11.0 (9.0, 13.0)	1.247 (1.027, 1.513)	0.026		0.806	1.253 (1.038, 1.513)	0.019		0.771
Black or African American	18/ 23	(78.3)	6.0 (3.0, 7.0)	12/ 18	(66.7)	7.0 (3.0, NE)	1.439 (0.539, 3.838)	0.468			1.522 (0.727, 3.183)	0.265		
Asian	23/ 27	(85.2)	4.0 (3.0, 6.0)	27/ 30	(90.0)	4.5 (3.0, 7.0)	1.071 (0.601, 1.909)	0.815			1.049 (0.601, 1.831)	0.867		
Others	33/ 40	(82.5)	8.0 (5.0, 11.0)	27/ 40	(67.5)	9.0 (6.0, 16.0)	1.360 (0.793, 2.331)	0.264			1.347 (0.806, 2.249)	0.256		
Number of baseline comorbidities present														
0-1	256/ 317	(80.8)		213/ 306	(69.6)									
2-3	50/ 74	(67.6)		56/ 70	(80.0)									
>= 4	0/ 1	(0.0)		1/ 1	(100.0)									
Presence of risk factor: Smoking														
Yes	137/ 172	(79.7)	7.0 (6.0, 9.0)	131/ 166	(78.9)	8.0 (6.0, 11.0)	1.155 (0.901, 1.480)	0.255		0.286	1.123 (0.884, 1.428)	0.342		0.219
No	168/ 219	(76.7)	7.0 (6.0, 9.0)	139/ 211	(65.9)	12.0 (9.0, 13.0)	1.385 (1.098, 1.746)	0.006			1.371 (1.095, 1.717)	0.006		

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=392)			Placebo (N=377)			Adjusted Analysis [2]			Unadjusted Analysis [3]		
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value	Interaction p-Value	Hazard Ratio (95% CI)	p-Value	Interaction p-Value
Presence of risk factor: Diabetes mellitus												
Yes	31/ 45	(68.9)	6.0 (4.0, 12.0)	39/ 46	(84.8)	8.0 (6.0, 10.0)	1.004 (0.596, 1.691)	0.987	0.062	0.851 (0.530, 1.367)	0.505	0.072
No	274/ 346	(79.2)	8.0 (6.0, 8.0)	231/ 331	(69.8)	10.0 (9.0, 12.0)	1.344 (1.121, 1.611)	0.001		1.322 (1.109, 1.576)	0.002	
Presence of risk factor: Immunosuppression												
Yes	1/ 2	(50.0)		5/ 5	(100.0)							
No	304/ 389	(78.1)		265/ 372	(71.2)							
Presence of risk factor: Chronic lung disease												
Yes	22/ 31	(71.0)	7.5 (5.0, 17.0)	6/ 14	(42.9)	NE (5.0, NE)	3.944 (1.202, 12.943)	0.024	0.070	2.084 (0.842, 5.153)	0.112	0.228
No	283/ 360	(78.6)	7.0 (6.0, 8.0)	264/ 363	(72.7)	9.0 (8.0, 12.0)	1.229 (1.035, 1.460)	0.019		1.241 (1.049, 1.467)	0.012	
Presence of risk factor: Hypertension												
Yes	93/ 126	(73.8)	8.0 (6.0, 11.0)	85/ 120	(70.8)	11.0 (8.0, 14.0)	1.067 (0.781, 1.458)	0.684	0.452	1.154 (0.860, 1.549)	0.339	0.521
No	212/ 265	(80.0)	7.0 (6.0, 8.0)	185/ 257	(72.0)	9.0 (8.0, 12.0)	1.301 (1.062, 1.594)	0.011		1.301 (1.068, 1.585)	0.009	
Presence of risk factor: Cardiovascular disorder												
Yes	3/ 11	(27.3)	NE (5.0, NE)	8/ 15	(53.3)	21.0 (5.0, NE)	0.559 (0.096, 3.254)	0.518	0.221	0.529 (0.140, 1.996)	0.347	0.192
No	302/ 380	(79.5)	7.0 (6.0, 8.0)	262/ 362	(72.4)	9.0 (8.0, 12.0)	1.268 (1.070, 1.504)	0.006		1.264 (1.071, 1.492)	0.006	
Presence of risk factor: Chronic kidney disease												
Yes	3/ 4	(75.0)		3/ 3	(100.0)							
No	302/ 387	(78.0)		267/ 374	(71.4)							
Presence of risk factor: HIV Infection												
Yes	0			0								
No	305/ 391	(78.0)		270/ 377	(71.6)							
Presence of risk factor: Sickle Cell Disease												
No	305/ 391	(78.0)		270/ 377	(71.6)							
Presence of risk factor: Neurodevelopmental Disorder												
Yes	1/ 1	(100.0)		1/ 1	(100.0)							
No	304/ 390	(77.9)		269/ 376	(71.5)							
Presence of risk factor: Cancer												
Yes	0/ 1	(0.0)		2/ 2	(100.0)							
No	305/ 390	(78.2)		268/ 375	(71.5)							
Presence of risk factor: Device Dependence												
Yes	1/ 3	(33.3)		0								
No	301/ 382	(78.8)		268/ 372	(72.0)							

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[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

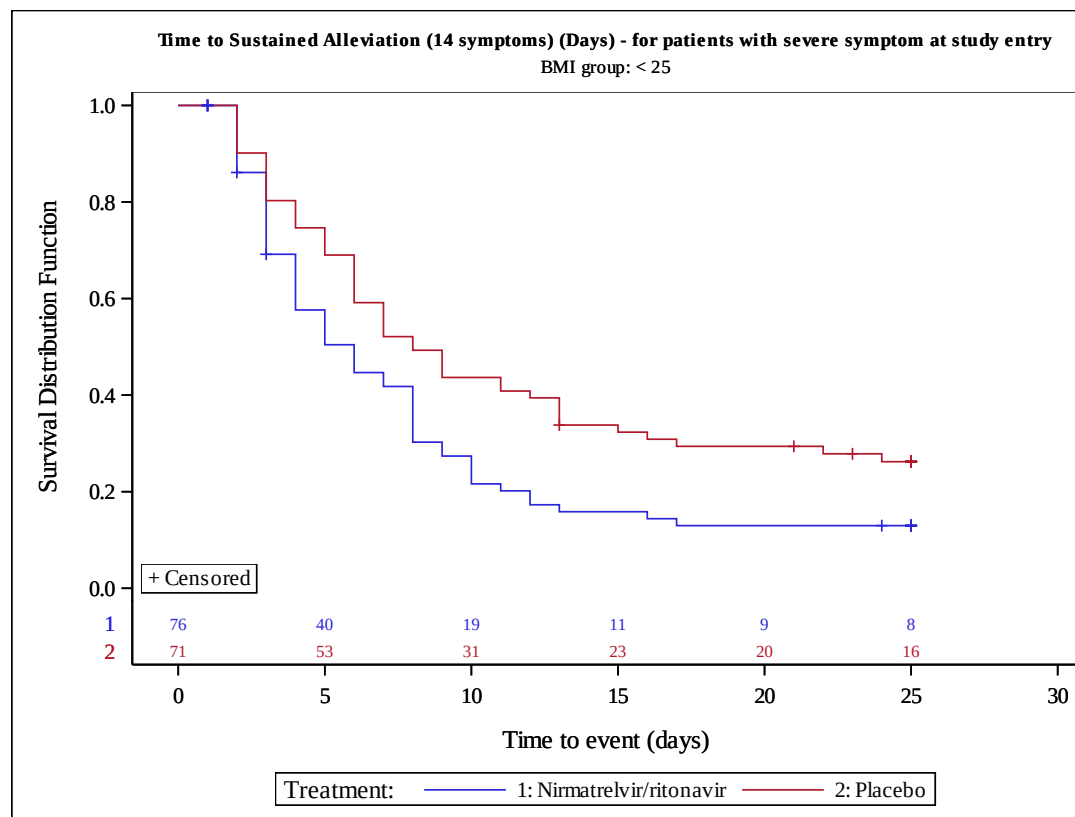
p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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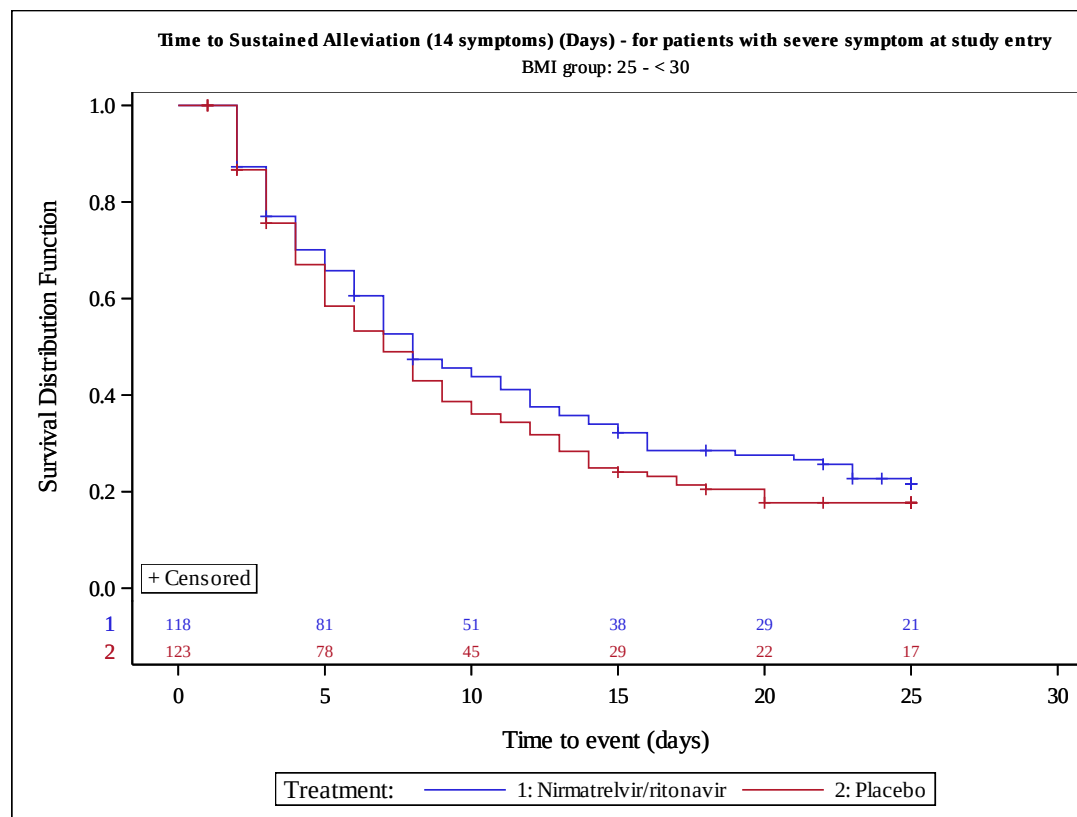


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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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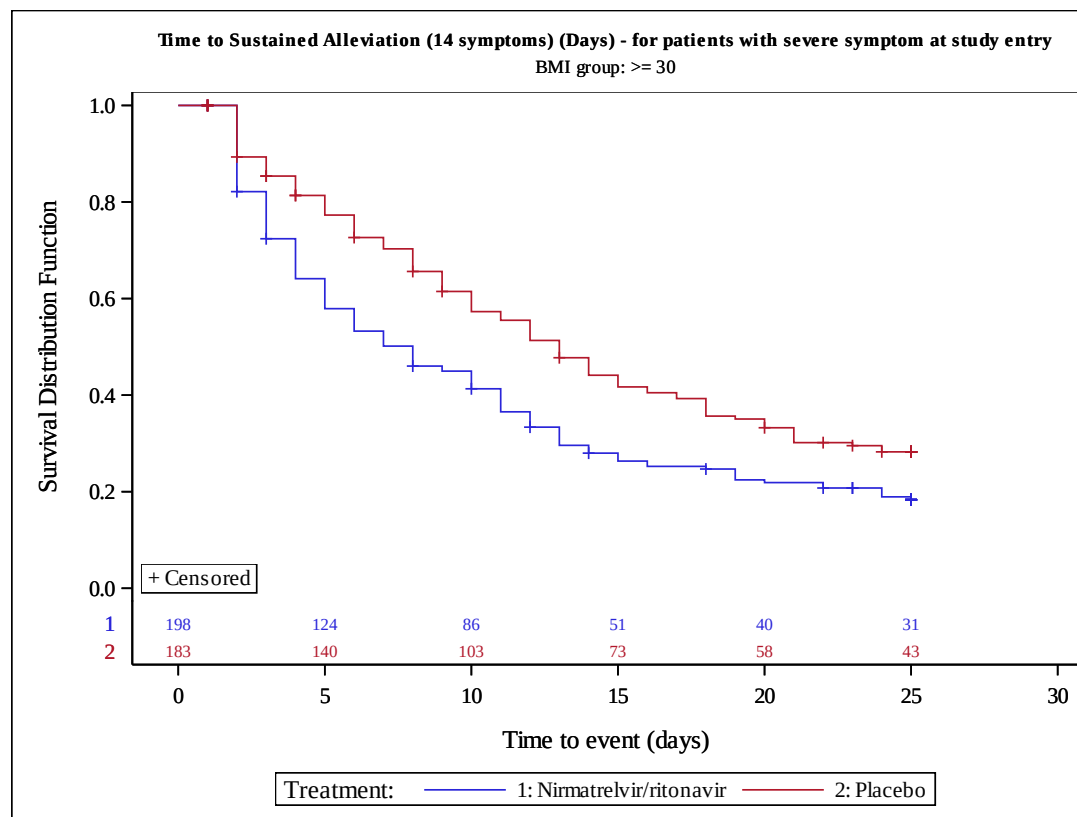


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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=928)			Placebo (N=955)			Adjusted Analysis [2]				Interaction p-Value	Unadjusted Analysis [3]				Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value				Hazard Ratio (95% CI)	p-Value			
Age																
< 65	431/ 790	(54.6)	21.0 (19.0, 23.0)	376/ 810	(46.4)	NE (23.0, NE)	1.245 (1.082, 1.433)	0.002		0.282		1.268 (1.104, 1.456)	<.001			0.233
>= 65	89/ 138	(64.5)	19.0 (15.0, 21.0)	74/ 145	(51.0)	24.0 (22.0, NE)	1.544 (1.126, 2.119)	0.007				1.577 (1.158, 2.147)	0.004			
Gender																
Male	292/ 463	(63.1)	17.0 (16.0, 19.0)	267/ 507	(52.7)	21.0 (19.0, 25.0)	1.328 (1.122, 1.572)	<.001		0.664		1.329 (1.125, 1.569)	<.001			0.950
Female	228/ 465	(49.0)	25.0 (22.0, NE)	183/ 448	(40.8)	NE (NE, NE)	1.256 (1.031, 1.531)	0.024				1.329 (1.094, 1.615)	0.004			
Geographic region																
United States	189/ 375	(50.4)	23.0 (20.0, 25.0)	179/ 387	(46.3)	NE (23.0, NE)	1.110 (0.901, 1.367)	0.326		0.208		1.162 (0.947, 1.425)	0.151			0.228
Europe	190/ 322	(59.0)	21.0 (19.0, 23.0)	144/ 321	(44.9)	NE (24.0, NE)	1.454 (1.167, 1.812)	<.001				1.485 (1.196, 1.845)	<.001			
India	68/ 74	(91.9)	13.0 (12.0, 14.0)	70/ 78	(89.7)	14.0 (13.0, 15.0)	1.212 (0.862, 1.703)	0.268				1.179 (0.844, 1.648)	0.334			
Rest of World	73/ 157	(46.5)	NE (18.0, NE)	57/ 169	(33.7)	NE (NE, NE)	1.562 (1.093, 2.233)	0.014				1.554 (1.099, 2.199)	0.013			
COVID-19 therapeutic mAb treatment at randomisation																
Yes	28/ 57	(49.1)	23.0 (15.0, NE)	27/ 60	(45.0)	NE (18.0, NE)	1.191 (0.689, 2.058)	0.531		0.963		1.176 (0.693, 1.996)	0.548			0.705
No	492/ 871	(56.5)	20.0 (19.0, 22.0)	423/ 895	(47.3)	25.0 (23.0, NE)	1.284 (1.125, 1.465)	<.001				1.319 (1.158, 1.502)	<.001			
Baseline viral load 1																
< 10^4 copies/mL	215/ 335	(64.2)	17.0 (16.0, 19.0)	203/ 354	(57.3)	19.0 (16.0, 22.0)	1.164 (0.960, 1.412)	0.123		0.178		1.186 (0.979, 1.437)	0.082			0.237
>= 10^4 copies/mL	291/ 569	(51.1)	23.0 (20.0, 25.0)	239/ 575	(41.6)	NE (NE, NE)	1.386 (1.167, 1.646)	<.001				1.391 (1.172, 1.650)	<.001			
Baseline viral load 2																
< 10^7 copies/mL	384/ 652	(58.9)	19.0 (18.0, 21.0)	360/ 699	(51.5)	23.0 (21.0, 25.0)	1.228 (1.063, 1.420)	0.005		0.175		1.259 (1.090, 1.454)	0.002			0.228
>= 10^7 copies/mL	122/ 252	(48.4)	25.0 (20.0, NE)	82/ 230	(35.7)	NE (NE, NE)	1.547 (1.164, 2.055)	0.003				1.531 (1.157, 2.025)	0.003			
Baseline serology status																
Negative	224/ 435	(51.5)	22.0 (20.0, 25.0)	180/ 456	(39.5)	NE (NE, NE)	1.446 (1.184, 1.765)	<.001		0.125		1.478 (1.215, 1.799)	<.001			0.081
Positive	290/ 482	(60.2)	19.0 (17.0, 21.0)	268/ 487	(55.0)	20.0 (19.0, 23.0)	1.175 (0.994, 1.390)	0.059				1.171 (0.991, 1.382)	0.063			
Symptom onset days to first dose date																
<= 3	359/ 624	(57.5)	21.0 (19.0, 22.0)	315/ 624	(50.5)	24.0 (22.0, NE)	1.253 (1.074, 1.461)	0.004		0.550		1.248 (1.072, 1.452)	0.004			0.257
> 3	161/ 304	(53.0)	20.0 (18.0, 23.0)	135/ 331	(40.8)	NE (25.0, NE)	1.345 (1.063, 1.700)	0.013				1.446 (1.150, 1.818)	0.002			
BMI group																
< 25	146/ 215	(67.9)	16.0 (14.0, 17.0)	117/ 213	(54.9)	21.0 (18.0, 24.0)	1.458 (1.128, 1.886)	0.004		0.654		1.496 (1.172, 1.909)	0.001			0.257
25 - < 30	180/ 319	(56.4)	21.0 (18.0, 23.0)	175/ 332	(52.7)	23.0 (19.0, 25.0)	1.206 (0.976, 1.490)	0.083				1.160 (0.942, 1.428)	0.163			
>= 30	194/ 393	(49.4)	23.0 (21.0, NE)	158/ 410	(38.5)	NE (NE, NE)	1.423 (1.144, 1.770)	0.002				1.369 (1.109, 1.689)	0.003			
Ethnicity																
White	377/ 699	(53.9)	22.0 (21.0, 24.0)	319/ 718	(44.4)	NE (25.0, NE)	1.269 (1.090, 1.476)	0.002		0.436		1.318 (1.135, 1.530)	<.001			0.427
Black or African American	23/ 43	(53.5)	13.0 (11.0, NE)	16/ 40	(40.0)	NE (22.0, NE)	1.538 (0.781, 3.030)	0.213				1.723 (0.908, 3.271)	0.096			
Asian	95/ 117	(81.2)	13.0 (12.0, 14.0)	101/ 127	(79.5)	15.0 (13.0, 16.0)	1.297 (0.972, 1.732)	0.077				1.265 (0.955, 1.675)	0.101			
Others	25/ 69	(36.2)	NE (23.0, NE)	14/ 70	(20.0)	NE (NE, NE)	1.703 (0.873, 3.321)	0.118				1.928 (1.002, 3.710)	0.049			
Number of baseline comorbidities present																
0-1	393/ 710	(55.4)	21.0 (19.0, 22.0)	347/ 728	(47.7)	25.0 (23.0, NE)	1.243 (1.073, 1.441)	0.004		0.229		1.266 (1.096, 1.463)	0.001			0.182
2-3	126/ 214	(58.9)	20.0 (17.0, 23.0)	99/ 221	(44.8)	NE (24.0, NE)	1.397 (1.067, 1.828)	0.015				1.508 (1.159, 1.963)	0.002			
>= 4	1/ 4	(25.0)	NE (15.0, NE)	4/ 6	(66.7)	18.5 (7.0, NE)	0.914 (0.071, 11.799)	0.945				0.281 (0.031, 2.527)	0.257			
Presence of risk factor: Smoking																
Yes	256/ 417	(61.4)	18.0 (16.0, 20.0)	220/ 438	(50.2)	24.0 (20.0, NE)	1.354 (1.127, 1.626)	0.001		0.673		1.375 (1.148, 1.647)	<.001			0.522
No	263/ 509	(51.7)	22.0 (20.0, 25.0)	230/ 517	(44.5)	NE (25.0, NE)	1.257 (1.050, 1.505)	0.013				1.261 (1.056, 1.505)	0.010			

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p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Subgroup Level	Nirmatrelvir/ritonavir (N=928)			Placebo (N=955)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus										0.045				0.033
Yes	89/ 130	(68.5)	15.0 (13.0, 19.0)	68/ 136	(50.0)	25.0 (22.0, NE)	1.850 (1.331, 2.571)	<.001			1.773 (1.291, 2.434)	<.001		
No	430/ 797	(54.0)	21.0 (20.0, 23.0)	382/ 819	(46.6)	NE (23.0, NE)	1.219 (1.060, 1.403)	0.006			1.242 (1.082, 1.426)	0.002		
Presence of risk factor: Immunosuppression										0.992				0.603
Yes	3/ 6	(50.0)	NE (7.0, NE)	2/ 7	(28.6)	NE (7.0, NE)	0.000 (0.000, NE)	1.000			1.731 (0.289, 10.373)	0.548		
No	516/ 921	(56.0)	20.0 (19.0, 22.0)	448/ 948	(47.3)	25.0 (23.0, NE)	1.280 (1.125, 1.455)	<.001			1.306 (1.150, 1.482)	<.001		
Presence of risk factor: Chronic lung disease										0.510				0.726
Yes	27/ 62	(43.5)	NE (20.0, NE)	11/ 39	(28.2)	NE (NE, NE)	1.472 (0.677, 3.200)	0.329			1.491 (0.740, 3.006)	0.264		
No	492/ 865	(56.9)	20.0 (18.0, 21.0)	439/ 916	(47.9)	25.0 (23.0, NE)	1.282 (1.125, 1.462)	<.001			1.323 (1.163, 1.504)	<.001		
Presence of risk factor: Hypertension										0.320				0.350
Yes	189/ 348	(54.3)	22.0 (20.0, 24.0)	180/ 371	(48.5)	NE (23.0, NE)	1.159 (0.942, 1.427)	0.163			1.216 (0.992, 1.492)	0.060		
No	330/ 579	(57.0)	19.0 (17.0, 21.0)	270/ 584	(46.2)	NE (22.0, NE)	1.339 (1.137, 1.577)	<.001			1.368 (1.165, 1.607)	<.001		
Presence of risk factor: Cardiovascular disorder										0.930				0.927
Yes	22/ 42	(52.4)	23.5 (15.0, NE)	22/ 49	(44.9)	NE (17.0, NE)	1.337 (0.712, 2.511)	0.366			1.272 (0.704, 2.297)	0.425		
No	497/ 885	(56.2)	20.0 (19.0, 22.0)	428/ 906	(47.2)	25.0 (23.0, NE)	1.278 (1.121, 1.458)	<.001			1.310 (1.151, 1.491)	<.001		
Presence of risk factor: Chronic kidney disease										0.549				0.366
Yes	3/ 6	(50.0)	25.0 (7.0, NE)	2/ 8	(25.0)	NE (12.0, NE)	11E25 (0.000, NE)	0.999			2.796 (0.466, 16.762)	0.261		
No	516/ 921	(56.0)	20.0 (19.0, 22.0)	448/ 947	(47.3)	25.0 (23.0, NE)	1.275 (1.121, 1.450)	<.001			1.301 (1.146, 1.477)	<.001		
Presence of risk factor: HIV Infection														
Yes	0			1/ 1	(100.0)									
No	519/ 927	(56.0)		448/ 953	(47.0)									
Presence of risk factor: Sickle Cell Disease														
No	519/ 927	(56.0)		450/ 955	(47.1)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	2/ 2	(100.0)		0/ 1	(0.0)									
No	517/ 925	(55.9)		450/ 954	(47.2)									
Presence of risk factor: Cancer										0.093				0.187
Yes	2/ 5	(40.0)	NE (9.0, NE)	5/ 6	(83.3)	14.0 (7.0, NE)	0.000 (0.000, NE)	0.999			0.581 (0.112, 3.004)	0.517		
No	517/ 922	(56.1)	20.0 (19.0, 22.0)	445/ 949	(46.9)	NE (24.0, NE)	1.292 (1.136, 1.469)	<.001			1.319 (1.162, 1.497)	<.001		
Presence of risk factor: Device Dependence														
Yes	0/ 4	(0.0)		1/ 3	(33.3)									
No	515/ 914	(56.3)		447/ 944	(47.4)									

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

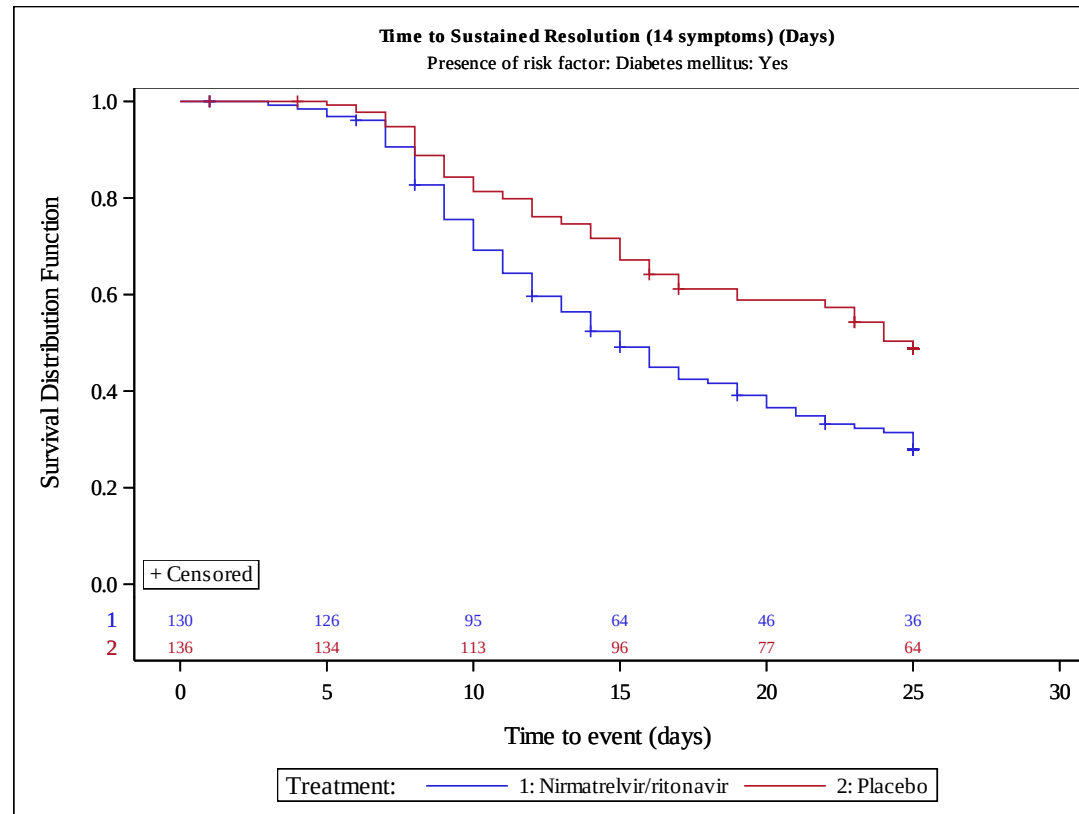
p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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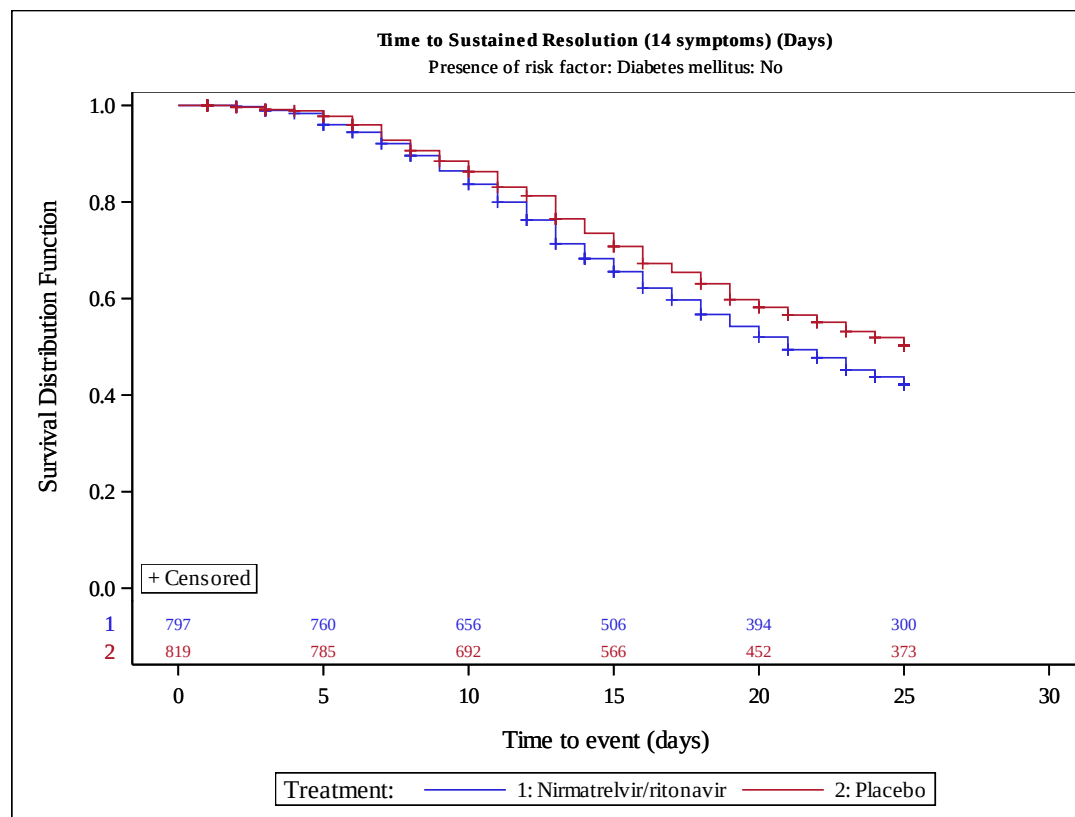


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RKI-conform mITT2 Analysis set

Analysis of Time to Sustained Resolution of All Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Subgroup analysis

Subgroup Level	Nirmatrelvir/ritonavir (N=392)				Placebo (N=377)				Adjusted Analysis [2]				Unadjusted Analysis [3]									
	n/N	(%)	Median	(95% CI) [1]	n/N	(%)	Median	(95% CI) [1]	Hazard Ratio	(95% CI)	p-Value	Interaction p-Value	Hazard Ratio	(95% CI)	p-Value	Interaction p-Value						
Age																						
< 65	204/ 17	359/ 33	(56.8) (51.5)	19.0 21.0	(16.0, 15.0,	22.0) (NE)	143/ 23	333/ 44	(42.9) (52.3)	NE 24.0	(24.0, 14.0,	NE)	1.508 0.969	(1.212, 0.473,	1.876) 1.984)	<.001 0.931	0.230	1.506 1.078	(1.216, 0.576,	1.866) 2.019)	<.001 0.814	0.316
Gender																						
Male	114/ 107	177/ 215	(64.4) (49.8)	16.0 23.0	(13.0, 19.0,	19.0) (NE)	78/ 88	164/ 213	(47.6) (41.3)	24.0 NE	(18.0, 25.0,	NE)	1.625 1.287	(1.206, 0.961,	2.190) 1.723)	0.001 0.090	0.266	1.575 1.340	(1.180, 1.010,	2.102) 1.777)	0.002 0.042	0.436
Female																						
Geographic region																						
United States	100/ 66	193/ 105	(51.8) (62.9)	20.0 19.0	(18.0, 14.0,	23.0) (NE)	71/ 47	168/ 112	(42.3) (42.0)	NE NE	(23.0, 23.0,	NE)	1.330 1.702	(0.971, 1.160,	1.822) 2.497)	0.075 0.007	0.794	1.410 1.684	(1.040, 1.158,	1.912) 2.450)	0.027 0.006	0.844
Europe	15/ 40	16/ 78	(93.8) (51.3)	10.0 22.0	(7.0, 12.0,	11.0) (NE)	13/ 35	14/ 83	(92.9) (42.2)	12.5 NE	(7.0, 19.0,	15.0) (NE)	3.517 1.244	(1.358, 0.779,	9.106) 1.987)	0.010 0.361		2.190 1.312	(0.982, 0.833,	4.883) 2.066)	0.055 0.241	
Rest of World																						
COVID-19 therapeutic mAb treatment at randomisation																						
Yes	14/ 207	24/ 368	(58.3) (56.3)	15.0 19.0	(9.0, 17.0,	22.0) (NE)	9/ 157	24/ 353	(37.5) (44.5)	NE NE	(14.0, 23.0,	NE)	1.875 1.416	(0.687, 1.146,	5.118) 1.749)	0.220 0.001	0.362	1.972 1.423	(0.852, 1.156,	4.567) 1.752)	0.113 <.001	0.437
No																						
Baseline viral load 1																						
< 10^4 copies/mL	77/ 141	127/ 259	(60.6) (54.4)	19.0 20.0	(13.0, 16.0,	21.0) (25.0)	56/ 107	109/ 257	(51.4) (41.6)	22.0 NE	(15.0, 24.0,	NE)	1.559 1.411	(1.089, 1.094,	2.233) 1.820)	0.015 0.008	0.895	1.387 1.459	(0.983, 1.135,	1.958) 1.877)	0.062 0.003	0.809
>= 10^4 copies/mL																						
Baseline viral load 2																						
< 10^7 copies/mL	159/ 59	282/ 104	(56.4) (56.7)	19.0 20.0	(16.0, 14.0,	21.0) (NE)	126/ 37	279/ 87	(45.2) (42.5)	NE NE	(23.0, 21.0,	NE)	1.437 1.524	(1.133, 0.999,	1.823) 2.324)	0.003 0.050	0.736	1.430 1.482	(1.132, 0.982,	1.807) 2.236)	0.003 0.061	0.840
>= 10^7 copies/mL																						
Baseline serology status																						
Negative	102/ 117	190/ 198	(53.7) (59.1)	20.0 19.0	(16.0, 15.0,	21.0) (NE)	84/ 80	202/ 170	(41.6) (47.1)	NE NE	(24.0, 20.0,	NE)	1.414 1.517	(1.052, 1.137,	1.901) 2.024)	0.022 0.005	0.792	1.426 1.467	(1.068, 1.104,	1.904) 1.950)	0.016 0.008	0.897
Positive																						
Symptom onset days to first dose date																						
<= 3	152/ 69	260/ 132	(58.5) (52.3)	19.0 19.0	(15.0, 16.0,	22.0) (NE)	116/ 50	228/ 149	(50.9) (33.6)	23.0 NE	(18.0, NE,	NE)	1.287 1.856	(1.006, 1.273,	1.646) 2.706)	0.045 0.001	0.148	1.247 1.897	(0.979, 1.318,	1.588) 2.732)	0.074 <.001	0.070
> 3																						
BMI group																						
< 25	52/ 62	76/ 118	(68.4) (52.5)	13.0 21.0	(11.0, 17.0,	15.0) (NE)	37/ 66	71/ 123	(52.1) (53.7)	23.0 22.0	(14.0, 16.0,	NE)	1.853 0.946	(1.174, 0.660,	2.924) 1.357)	0.008 0.764	0.016	1.788 0.959	(1.172, 0.678,	2.729) 1.357)	0.007 0.814	0.013
25 - < 30	107/ 63	198/ 183	(54.0) (34.4)	21.0	(19.0, NE)	NE	NE	NE	NE	NE	NE	NE	1.816	(1.312, 2.513)	<.001			1.822	(1.334, 2.488)	<.001		
>= 30																						
Ethnicity																						
White	165/ 14	302/ 23	(54.6) (60.9)	21.0 11.0	(19.0, 6.0,	24.0) (NE)	121/ 6	289/ 18	(41.9) (33.3)	NE NE	(25.0, 11.0,	NE)	1.396 2.427	(1.099, 0.629,	1.773) 9.362)	0.006 0.198	0.346	1.449 2.543	(1.146, 0.972,	1.832) 6.650)	0.002 0.057	0.554
Black or African American	21/ 21	27/ 30	(77.8) (52.5)	10.0 22.0	(8.0, 12.0,	12.0) (NE)	23/ 16	30/ 40	(76.7) (40.0)	15.0 NE	(12.0, 18.0,	19.0) (NE)	1.769 1.297	(0.936, 0.645,	3.342) 2.606)	0.079 0.466		1.571 1.345	(0.863, 0.701,	2.861) 2.580)	0.140 0.372	
Others																						
Number of baseline comorbidities present																						
0-1	184/ 37	317/ 74	(58.0) (50.0)				135/ 30	306/ 70	(44.1) (42.9)													
2-3	0/ 1	1	(0.0)				1/ 1		(100.0)													
>= 4																						
Presence of risk factor: Smoking																						
Yes	104/ 85	172/ 166	(60.5) (51.2)	19.0 24.0	(15.0, 18.0,	21.0) (NE)							1.454	(1.080, 1.959)		0.014	0.893	1.346	(1.010, 1.793)		0.042	0.462
No	116/ 81	219/ 211	(53.0) (38.4)	20.0	(16.0, NE)	NE							1.485	(1.112, 1.982)		0.007		1.548	(1.165, 2.056)		0.003	

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[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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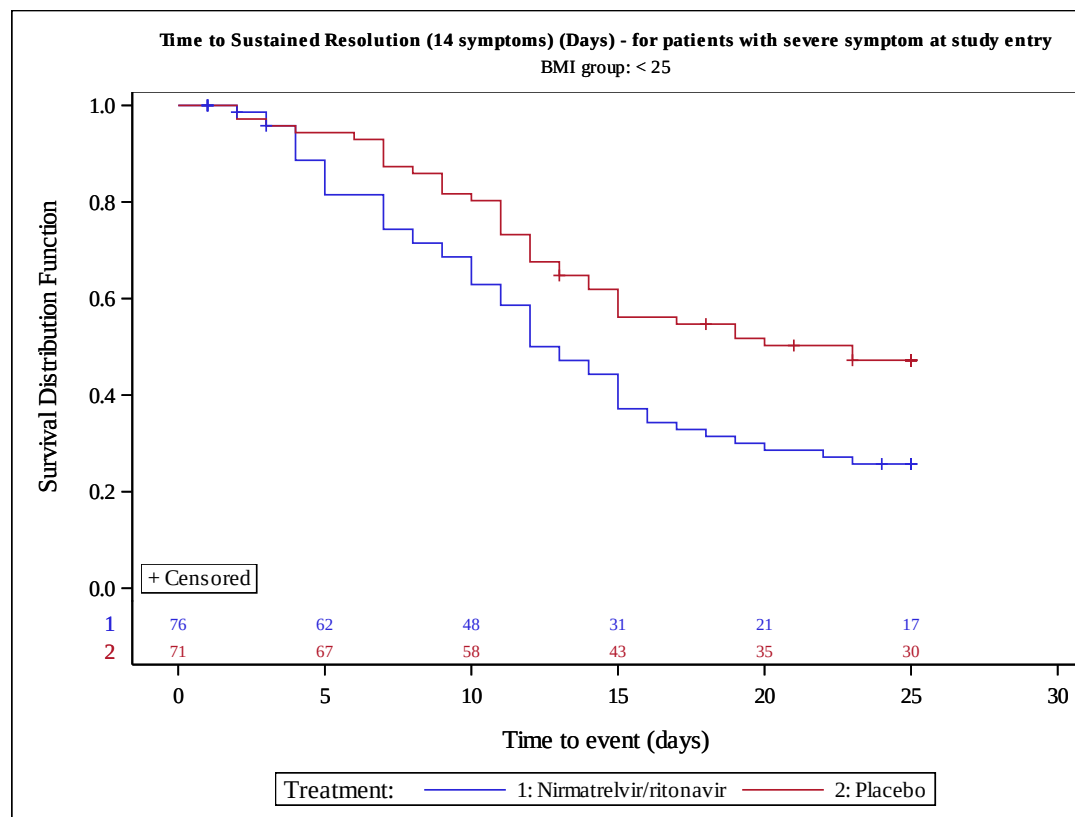
Subgroup Level	Nirmatrelvir/ritonavir (N=392)			Placebo (N=377)			Adjusted Analysis [2]			Interaction p-Value	Unadjusted Analysis [3]			Interaction p-Value
	n/N	(%)	Median (95% CI) [1]	n/N	(%)	Median (95% CI) [1]	Hazard Ratio (95% CI)	p-Value			Hazard Ratio (95% CI)	p-Value		
Presence of risk factor: Diabetes mellitus										0.892				0.854
Yes	24/	45 (53.3)	20.0 (12.0, NE)	22/	46 (47.8)	24.0 (17.0, NE)	2.093 (1.115, 3.930)	0.022			1.415 (0.792, 2.527)	0.241		
No	196/	346 (56.6)	19.0 (17.0, 22.0)	144/	331 (43.5)	NE (23.0, NE)	1.451 (1.163, 1.810)	<.001			1.453 (1.172, 1.803)	<.001		
Presence of risk factor: Immunosuppression														
Yes	1/	2 (50.0)		2/	5 (40.0)									
No	219/	389 (56.3)		164/	372 (44.1)									
Presence of risk factor: Chronic lung disease										0.160				0.276
Yes	14/	31 (45.2)	NE (15.0, NE)	2/	14 (14.3)	NE (14.0, NE)	5.811 (0.975, 34.633)	0.053			3.202 (0.728, 14.092)	0.124		
No	206/	360 (57.2)	19.0 (16.0, 21.0)	164/	363 (45.2)	NE (23.0, NE)	1.424 (1.155, 1.755)	<.001			1.449 (1.180, 1.779)	<.001		
Presence of risk factor: Hypertension										0.124				0.237
Yes	62/	126 (49.2)	23.0 (19.0, NE)	52/	120 (43.3)	NE (23.0, NE)	1.148 (0.780, 1.688)	0.485			1.213 (0.839, 1.754)	0.305		
No	158/	265 (59.6)	18.0 (14.0, 20.0)	114/	257 (44.4)	NE (21.0, NE)	1.599 (1.248, 2.047)	<.001			1.572 (1.235, 2.000)	<.001		
Presence of risk factor: Cardiovascular disorder										0.564				0.515
Yes	3/	11 (27.3)	NE (9.0, NE)	5/	15 (33.3)	NE (9.0, NE)	0.749 (0.125, 4.504)	0.752			0.924 (0.221, 3.872)	0.914		
No	217/	380 (57.1)	19.0 (16.0, 21.0)	161/	362 (44.5)	NE (23.0, NE)	1.445 (1.173, 1.779)	<.001			1.454 (1.185, 1.783)	<.001		
Presence of risk factor: Chronic kidney disease														
Yes	1/	4 (25.0)		0/	3 (0.0)									
No	219/	387 (56.6)		166/	374 (44.4)									
Presence of risk factor: HIV Infection														
Yes	0			0										
No	220/	391 (56.3)		166/	377 (44.0)									
Presence of risk factor: Sickle Cell Disease														
No	220/	391 (56.3)		166/	377 (44.0)									
Presence of risk factor: Neurodevelopmental Disorder														
Yes	1/	1 (100.0)		0/	1 (0.0)									
No	219/	390 (56.2)		166/	376 (44.1)									
Presence of risk factor: Cancer														
Yes	0/	1 (0.0)		1/	2 (50.0)									
No	220/	390 (56.4)		165/	375 (44.0)									
Presence of risk factor: Device Dependence														
Yes	1/	3 (33.3)		0										
No	216/	382 (56.5)		165/	372 (44.4)									

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 p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.
 Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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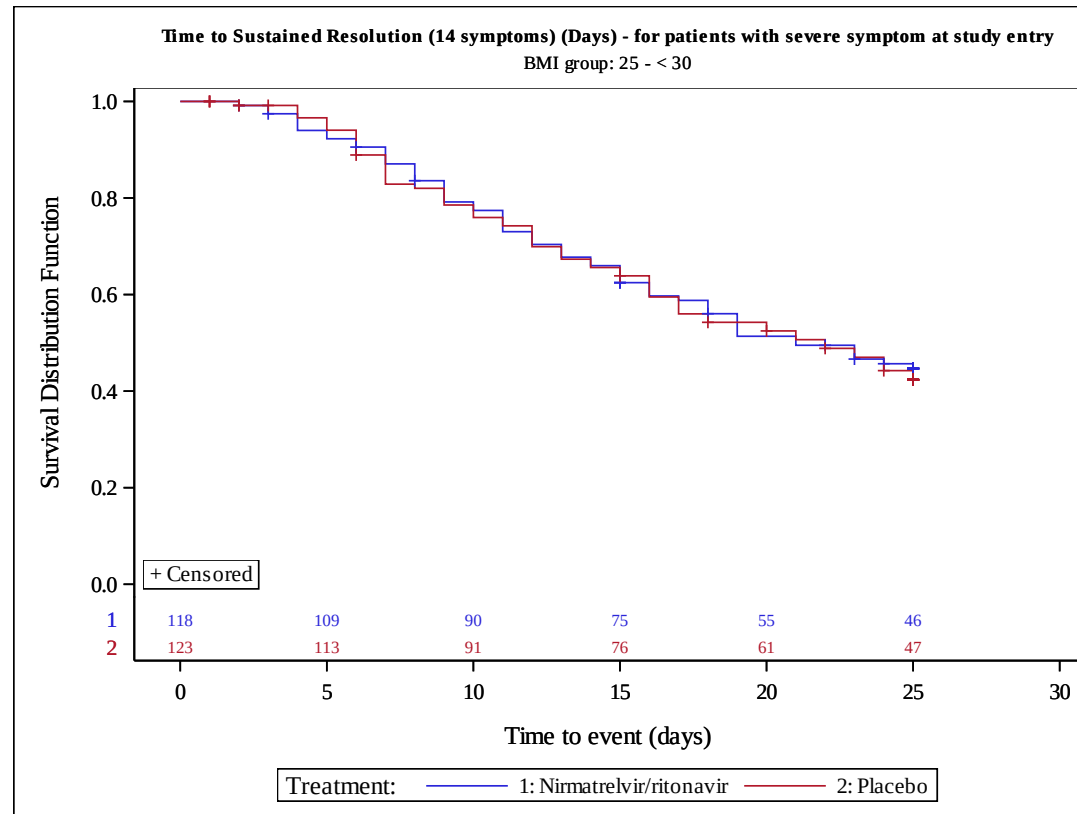
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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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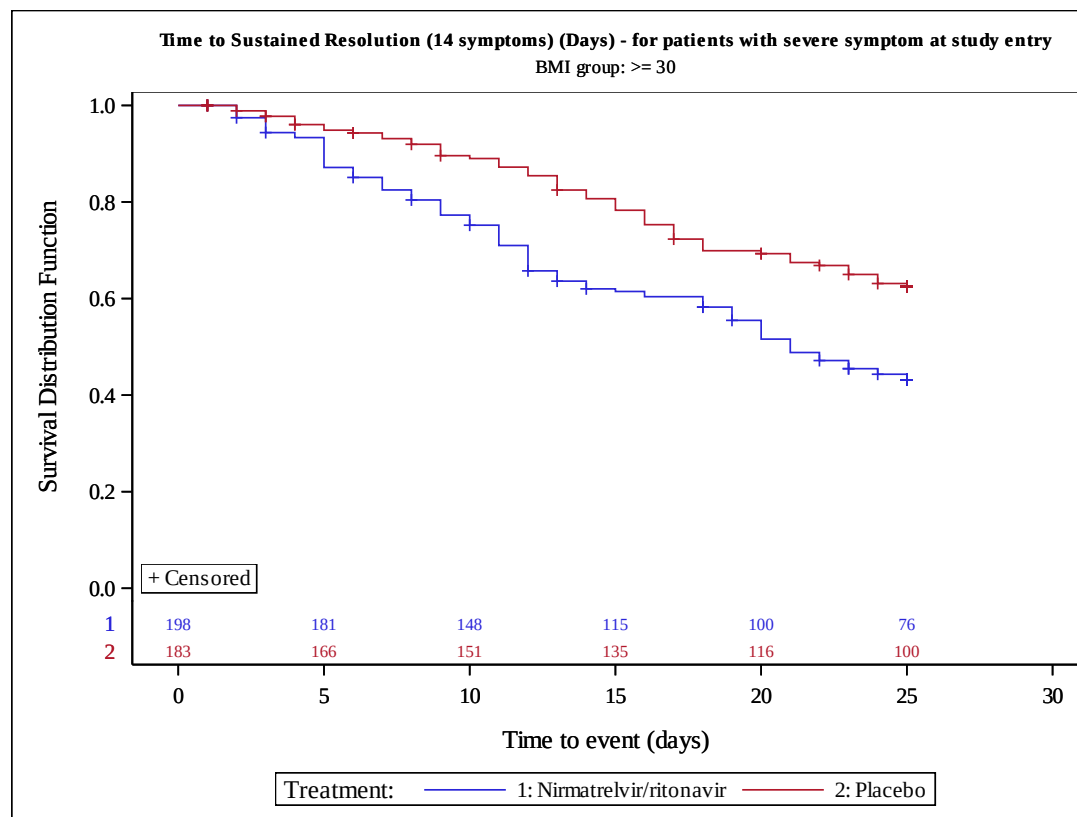


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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Anhang 4-G 1.12: Subgruppenanalysen - Global Impression Questions (Symptomatik)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022) Overall Study population RKI-conform mITT2 Analysis set Analysis of Participants with Global Impression Questionnaire return to usual health 1 point improvement from baseline - Subgroup analysis										Final	
Subgroup Level	Nirmatrelvir/ritonavir (N=944) n/N (%)	Placebo (N=964) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]			Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)		p-Value	
Age							0.746				0.716
< 65	440/ 804 (54.7)	399/ 816 (48.9)	1.111 (1.017, 1.212)			0.019		1.119 (1.019, 1.230)		0.019	
>= 65	85/ 140 (60.7)	77/ 148 (52.0)	1.218 (0.982, 1.511)			0.073		1.167 (0.951, 1.431)		0.138	
Gender							0.134				0.153
Male	288/ 474 (60.8)	259/ 510 (50.8)	1.180 (1.061, 1.312)			0.002		1.196 (1.070, 1.338)		0.002	
Female	237/ 470 (50.4)	217/ 454 (47.8)	1.046 (0.923, 1.184)			0.482		1.055 (0.925, 1.203)		0.425	
Geographic region							0.461				0.497
United States	185/ 387 (47.8)	175/ 395 (44.3)	1.079 (0.925, 1.258)			0.335		1.079 (0.927, 1.256)		0.326	
Europe	215/ 322 (66.8)	188/ 321 (58.6)	1.153 (1.027, 1.296)			0.016		1.140 (1.011, 1.285)		0.032	
India	51/ 74 (68.9)	53/ 78 (67.9)	0.991 (0.826, 1.190)			0.926		1.014 (0.817, 1.259)		0.898	
Rest of World	74/ 161 (46.0)	60/ 170 (35.3)	1.266 (0.976, 1.642)			0.075		1.302 (1.001, 1.695)		0.050	
COVID-19 therapeutic mAb treatment at randomisation							0.806				0.827
Yes	26/ 60 (43.3)	22/ 60 (36.7)	NE (NE, NE)			NE		1.182 (0.761, 1.837)		0.458	
No	499/ 884 (56.4)	454/ 904 (50.2)	1.115 (1.028, 1.210)			0.009		1.124 (1.030, 1.226)		0.008	
Baseline viral load 1							0.395				0.464
< 10^4 copies/mL	200/ 340 (58.8)	194/ 356 (54.5)	1.071 (0.950, 1.207)			0.263		1.079 (0.948, 1.229)		0.249	
>= 10^4 copies/mL	315/ 579 (54.4)	275/ 582 (47.3)	1.144 (1.027, 1.275)			0.015		1.151 (1.028, 1.290)		0.015	
Baseline viral load 2							0.435				0.428
< 10^7 copies/mL	377/ 663 (56.9)	365/ 707 (51.6)	1.103 (1.007, 1.208)			0.036		1.101 (0.999, 1.214)		0.052	
>= 10^7 copies/mL	138/ 256 (53.9)	104/ 231 (45.0)	1.166 (0.979, 1.389)			0.086		1.197 (0.998, 1.436)		0.052	
Baseline serology status							0.035				0.108
Negative	255/ 439 (58.1)	218/ 457 (47.7)	1.209 (1.077, 1.359)			0.001		1.218 (1.075, 1.379)		0.002	
Positive	267/ 494 (54.0)	253/ 495 (51.1)	1.023 (0.915, 1.143)			0.692		1.057 (0.939, 1.190)		0.355	
Symptom onset days to first dose date							0.833				0.677
<= 3	369/ 637 (57.9)	330/ 632 (52.2)	1.118 (1.018, 1.228)			0.019		1.109 (1.004, 1.226)		0.041	
> 3	156/ 307 (50.8)	146/ 332 (44.0)	1.106 (0.942, 1.297)			0.219		1.156 (0.981, 1.361)		0.084	
BMI group							0.028				0.175
< 25	129/ 216 (59.7)	122/ 213 (57.3)	1.018 (0.873, 1.188)			0.817		1.043 (0.889, 1.223)		0.608	
25 - < 30	184/ 324 (56.8)	180/ 336 (53.6)	1.050 (0.926, 1.190)			0.449		1.060 (0.924, 1.216)		0.406	
>= 30	211/ 403 (52.4)	174/ 415 (41.9)	1.297 (1.118, 1.505)			<.001		1.249 (1.078, 1.446)		0.003	
Ethnicity							0.072				0.096
White	401/ 712 (56.3)	361/ 725 (49.8)	1.128 (1.027, 1.239)			0.012		1.131 (1.026, 1.247)		0.013	
Black or African American	21/ 45 (46.7)	22/ 42 (52.4)	0.944 (0.605, 1.474)			0.801		0.891 (0.582, 1.363)		0.594	
Asian	74/ 118 (62.7)	78/ 127 (61.4)	NE (NE, NE)			NE		1.021 (0.839, 1.242)		0.835	
Others	29/ 69 (42.0)	15/ 70 (21.4)	NE (NE, NE)			NE		1.961 (1.158, 3.323)		0.012	
Number of baseline comorbidities present							0.501				0.678
0-1	394/ 720 (54.7)	364/ 734 (49.6)	1.096 (1.002, 1.199)			0.045		1.103 (1.000, 1.218)		0.050	
2-3	129/ 220 (58.6)	109/ 224 (48.7)	1.195 (1.003, 1.425)			0.046		1.205 (1.012, 1.435)		0.036	
>= 4	2/ 4 (50.0)	3/ 6 (50.0)	NE (NE, NE)			NE		1.000 (0.282, 3.544)		1.000	
Presence of risk factor: Smoking							0.411				0.270
Yes	246/ 423 (58.2)	239/ 442 (54.1)	1.086 (0.978, 1.206)			0.121		1.076 (0.956, 1.210)		0.226	
No	279/ 519 (53.8)	237/ 522 (45.4)	1.147 (1.016, 1.295)			0.027		1.184 (1.047, 1.339)		0.007	
Presence of risk factor: Diabetes mellitus							0.437				0.935
Yes	76/ 135 (56.3)	69/ 137 (50.4)	1.153 (0.921, 1.444)			0.213		1.118 (0.894, 1.397)		0.328	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with Global Impression Questionnaire return to usual health 1 point improvement from baseline - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944) n/N (%)	Placebo (N=964) n/N (%)	Adjusted analysis [1]		Interaction p-Value	Unadjusted analysis [2]		Interaction p-Value
			Relative Risk (95% CI)	p-Value		Relative Risk (95% CI)	p-Value	
No	449/ 808 (55.6)	407/ 827 (49.2)	1.135 (1.041, 1.237)	0.004		1.129 (1.029, 1.239)	0.010	
Presence of risk factor: Immunosuppression					0.762			0.627
Yes	3/ 6 (50.0)	4/ 7 (57.1)	NE (NE, NE)	NE		0.875 (0.314, 2.440)	0.799	
No	522/ 937 (55.7)	472/ 957 (49.3)	1.119 (1.032, 1.214)	0.006		1.130 (1.037, 1.231)	0.005	
Presence of risk factor: Chronic lung disease					0.127			0.140
Yes	30/ 62 (48.4)	11/ 39 (28.2)	NE (NE, NE)	NE		1.716 (0.977, 3.012)	0.060	
No	495/ 881 (56.2)	465/ 925 (50.3)	1.109 (1.022, 1.204)	0.013		1.118 (1.025, 1.219)	0.012	
Presence of risk factor: Hypertension					0.634			0.603
Yes	206/ 358 (57.5)	186/ 375 (49.6)	1.135 (0.993, 1.297)	0.064		1.160 (1.013, 1.328)	0.032	
No	319/ 585 (54.5)	290/ 589 (49.2)	1.101 (0.994, 1.219)	0.065		1.108 (0.992, 1.237)	0.070	
Presence of risk factor: Cardiovascular disorder					0.890			0.643
Yes	24/ 42 (57.1)	27/ 49 (55.1)	NE (NE, NE)	NE		1.037 (0.721, 1.492)	0.845	
No	501/ 901 (55.6)	449/ 915 (49.1)	1.120 (1.032, 1.217)	0.007		1.133 (1.038, 1.238)	0.005	
Presence of risk factor: Chronic kidney disease					0.182			0.202
Yes	4/ 6 (66.7)	2/ 8 (25.0)	NE (NE, NE)	NE		2.667 (0.707, 10.052)	0.147	
No	521/ 937 (55.6)	474/ 956 (49.6)	1.115 (1.028, 1.209)	0.008		1.121 (1.029, 1.222)	0.009	
Presence of risk factor: HIV Infection								
Yes	0	1/ 1 (100.0)						
No	525/ 943 (55.7)	475/ 962 (49.4)						
Presence of risk factor: Sickle Cell Disease								
No	525/ 943 (55.7)	476/ 964 (49.4)						
Presence of risk factor: Neurodevelopmental Disorder								
Yes	1/ 2 (50.0)	1/ 1 (100.0)						
No	524/ 941 (55.7)	475/ 963 (49.3)						
Presence of risk factor: Cancer					0.941			0.615
Yes	2/ 5 (40.0)	3/ 6 (50.0)	NE (NE, NE)	NE		0.800 (0.210, 3.052)	0.744	
No	523/ 938 (55.8)	473/ 958 (49.4)	1.119 (1.031, 1.213)	0.007		1.129 (1.036, 1.230)	0.005	
Presence of risk factor: Device Dependence								
Yes	1/ 4 (25.0)	2/ 3 (66.7)						
No	519/ 930 (55.8)	471/ 953 (49.4)						

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022) Overall Study population RKI-conform mITT2 Analysis set Analysis of Participants with Global Impression Questionnaire overall COVID-19-related symptoms >= 1 point improvement from baseline - Subgroup analysis										Final	
Subgroup Level	Nirmatrelvir/ritonavir (N=944) n/N (%)	Placebo (N=964) n/N (%)	Adjusted analysis [1]				Unadjusted analysis [2]				
			Relative Risk (95% CI)			p-Value	Interaction p-Value	Relative Risk (95% CI)			p-Value
Age							0.645				0.723
< 65	511/ 804 (63.6)	491/ 816 (60.2)	1.062 (0.989, 1.140)			0.099		1.056 (0.978, 1.140)		0.161	
>= 65	103/ 140 (73.6)	100/ 148 (67.6)	NE (NE, NE)			NE		1.089 (0.938, 1.264)		0.264	
Gender							0.082				0.174
Male	317/ 474 (66.9)	307/ 510 (60.2)	1.119 (1.026, 1.221)			0.011		1.111 (1.010, 1.222)		0.030	
Female	297/ 470 (63.2)	284/ 454 (62.6)	1.011 (0.923, 1.108)			0.808		1.010 (0.915, 1.115)		0.841	
Geographic region							0.687				0.812
United States	210/ 387 (54.3)	208/ 395 (52.7)	1.030 (0.902, 1.175)			0.662		1.030 (0.904, 1.174)		0.653	
Europe	251/ 322 (78.0)	237/ 321 (73.8)	1.078 (0.987, 1.176)			0.094		1.056 (0.968, 1.152)		0.223	
India	55/ 74 (74.3)	56/ 78 (71.8)	1.031 (0.878, 1.211)			0.708		1.035 (0.853, 1.256)		0.725	
Rest of World	98/ 161 (60.9)	90/ 170 (52.9)	1.126 (0.930, 1.365)			0.224		1.150 (0.953, 1.388)		0.146	
COVID-19 therapeutic mAb treatment at randomisation							0.929				0.887
Yes	30/ 60 (50.0)	29/ 60 (48.3)	NE (NE, NE)			NE		1.034 (0.719, 1.489)		0.855	
No	584/ 884 (66.1)	562/ 904 (62.2)	1.069 (1.002, 1.140)			0.044		1.063 (0.991, 1.139)		0.086	
Baseline viral load 1							0.806				0.782
< 10^4 copies/mL	220/ 340 (64.7)	214/ 356 (60.1)	1.066 (0.964, 1.179)			0.212		1.076 (0.959, 1.208)		0.211	
>= 10^4 copies/mL	383/ 579 (66.1)	365/ 582 (62.7)	1.060 (0.977, 1.149)			0.159		1.055 (0.968, 1.149)		0.222	
Baseline viral load 2							0.698				0.912
< 10^7 copies/mL	430/ 663 (64.9)	431/ 707 (61.0)	1.074 (0.996, 1.157)			0.062		1.064 (0.981, 1.154)		0.136	
>= 10^7 copies/mL	173/ 256 (67.6)	148/ 231 (64.1)	1.053 (0.931, 1.191)			0.412		1.055 (0.928, 1.199)		0.416	
Baseline serology status							0.130				0.275
Negative	301/ 439 (68.6)	283/ 457 (61.9)	1.116 (1.021, 1.221)			0.016		1.107 (1.006, 1.219)		0.037	
Positive	307/ 494 (62.1)	300/ 495 (60.6)	1.011 (0.924, 1.107)			0.810		1.025 (0.929, 1.132)		0.619	
Symptom onset days to first dose date							0.966				0.621
<= 3	429/ 637 (67.3)	407/ 632 (64.4)	1.069 (0.994, 1.149)			0.072		1.046 (0.966, 1.132)		0.268	
> 3	185/ 307 (60.3)	184/ 332 (55.4)	1.061 (0.931, 1.209)			0.378		1.087 (0.952, 1.241)		0.216	
BMI group							0.273				0.467
< 25	149/ 216 (69.0)	138/ 213 (64.8)	1.043 (0.922, 1.180)			0.506		1.065 (0.932, 1.217)		0.357	
25 - < 30	212/ 324 (65.4)	219/ 336 (65.2)	NE (NE, NE)			NE		1.004 (0.898, 1.122)		0.945	
>= 30	252/ 403 (62.5)	234/ 415 (56.4)	1.115 (0.995, 1.250)			0.061		1.109 (0.990, 1.242)		0.074	
Ethnicity							NE				0.176
White	466/ 712 (65.4)	445/ 725 (61.4)	1.069 (0.994, 1.150)			0.071		1.066 (0.986, 1.154)		0.109	
Black or African American	21/ 45 (46.7)	25/ 42 (59.5)	NE (NE, NE)			NE		0.784 (0.526, 1.169)		0.233	
Asian	84/ 118 (71.2)	89/ 127 (70.1)	NE (NE, NE)			NE		1.016 (0.864, 1.194)		0.849	
Others	43/ 69 (62.3)	32/ 70 (45.7)	NE (NE, NE)			NE		1.363 (0.995, 1.867)		0.053	
Number of baseline comorbidities present							0.222				0.411
0-1	464/ 720 (64.4)	436/ 734 (59.4)	1.092 (1.014, 1.176)			0.020		1.085 (1.001, 1.176)		0.048	
2-3	149/ 220 (67.7)	152/ 224 (67.9)	0.999 (0.882, 1.132)			0.990		0.998 (0.878, 1.135)		0.977	
>= 4	1/ 4 (25.0)	3/ 6 (50.0)	NE (NE, NE)			NE		0.500 (0.077, 3.265)		0.469	
Presence of risk factor: Smoking							0.563				0.381
Yes	281/ 423 (66.4)	286/ 442 (64.7)	1.048 (0.962, 1.142)			0.282		1.027 (0.932, 1.131)		0.594	
No	331/ 519 (63.8)	305/ 522 (58.4)	1.084 (0.987, 1.190)			0.093		1.092 (0.990, 1.203)		0.077	
Presence of risk factor: Diabetes mellitus							0.454				0.614
Yes	85/ 135 (63.0)	85/ 137 (62.0)	1.036 (0.863, 1.243)			0.704		1.015 (0.844, 1.220)		0.876	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochran's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with Global Impression Questionnaire overall COVID-19-related symptoms ≥ 1 point improvement from baseline - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944) n/N (%)	Placebo (N=964) n/N (%)	Adjusted analysis [1]		Interaction p-Value	Unadjusted analysis [2]		Interaction p-Value
			Relative Risk (95% CI)	p-Value		Relative Risk (95% CI)	p-Value	
No	528/ 808 (65.3)	506/ 827 (61.2)	1.077 (1.006, 1.153)	0.032		1.068 (0.992, 1.150)	0.081	
Presence of risk factor: Immunosuppression					0.974			0.713
Yes	3/ 6 (50.0)	4/ 7 (57.1)	NE (NE, NE)	NE		0.875 (0.314, 2.440)	0.799	
No	610/ 937 (65.1)	587/ 957 (61.3)	1.066 (1.000, 1.136)	0.050		1.061 (0.991, 1.137)	0.090	
Presence of risk factor: Chronic lung disease					0.588			0.979
Yes	37/ 62 (59.7)	22/ 39 (56.4)	NE (NE, NE)	NE		1.058 (0.750, 1.491)	0.748	
No	576/ 881 (65.4)	569/ 925 (61.5)	1.072 (1.004, 1.144)	0.038		1.063 (0.991, 1.140)	0.088	
Presence of risk factor: Hypertension					0.608			0.757
Yes	243/ 358 (67.9)	243/ 375 (64.8)	1.034 (0.938, 1.139)	0.501		1.047 (0.945, 1.161)	0.378	
No	370/ 585 (63.2)	348/ 589 (59.1)	1.080 (0.992, 1.175)	0.076		1.070 (0.977, 1.173)	0.144	
Presence of risk factor: Cardiovascular disorder					0.726			0.478
Yes	27/ 42 (64.3)	33/ 49 (67.3)	NE (NE, NE)	NE		0.955 (0.709, 1.286)	0.760	
No	586/ 901 (65.0)	558/ 915 (61.0)	1.070 (1.003, 1.141)	0.041		1.066 (0.994, 1.144)	0.074	
Presence of risk factor: Chronic kidney disease					0.205			0.131
Yes	5/ 6 (83.3)	3/ 8 (37.5)	NE (NE, NE)	NE		2.222 (0.848, 5.824)	0.104	
No	608/ 937 (64.9)	588/ 956 (61.5)	1.063 (0.997, 1.133)	0.060		1.055 (0.985, 1.130)	0.127	
Presence of risk factor: HIV Infection								
Yes	0	1/ 1 (100.0)						
No	613/ 943 (65.0)	590/ 962 (61.3)						
Presence of risk factor: Sickle Cell Disease								
No	613/ 943 (65.0)	591/ 964 (61.3)						
Presence of risk factor: Neurodevelopmental Disorder								
Yes	0/ 2 (0.0)	1/ 1 (100.0)						
No	613/ 941 (65.1)	590/ 963 (61.3)						
Presence of risk factor: Cancer					0.386			0.320
Yes	1/ 5 (20.0)	3/ 6 (50.0)	NE (NE, NE)	NE		0.400 (0.058, 2.748)	0.351	
No	612/ 938 (65.2)	588/ 958 (61.4)	1.068 (1.002, 1.138)	0.043		1.063 (0.993, 1.138)	0.081	
Presence of risk factor: Device Dependence								
Yes	2/ 4 (50.0)	1/ 3 (33.3)						
No	606/ 930 (65.2)	587/ 953 (61.6)						

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Anhang 4-G 1.13: Subgruppenanalysen - Gesundheitszustand (EQ-5D VAS)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Analysis of Participants with EQ 5D-VAS >= 15 points improvement from baseline - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944) n/N (%)	Placebo (N=964) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value	
Age							NE					
< 65	18/ 804 (2.2)	13/ 816 (1.6)	NE (NE, NE)			NE		1.405 (0.693, 2.849)			0.345	0.442
>= 65	1/ 140 (0.7)	2/ 148 (1.4)	NE (NE, NE)			NE		0.529 (0.048, 5.765)			0.601	
Gender							NE					
Male	9/ 474 (1.9)	5/ 510 (1.0)	NE (NE, NE)			NE		1.937 (0.654, 5.738)			0.233	0.327
Female	10/ 470 (2.1)	10/ 454 (2.2)	NE (NE, NE)			NE		0.966 (0.406, 2.299)			0.938	
Geographic region							NE					
United States	18/ 387 (4.7)	15/ 395 (3.8)	1.253 (0.645, 2.433)			0.506		1.225 (0.626, 2.395)			0.553	0.568
Europe	0/ 322 (0.0)	0/ 321 (0.0)	NE (NE, NE)			NE		NE (NE, NE)			NE	
India	0/ 74 (0.0)	0/ 78 (0.0)	NE (NE, NE)			NE		NE (NE, NE)			NE	
Rest of World	1/ 161 (0.6)	0/ 170 (0.0)	NE (NE, NE)			NE		3.167 (0.130, 77.174)			0.479	
COVID-19 therapeutic mAb treatment at randomisation							NE					
Yes	0/ 60 (0.0)	1/ 60 (1.7)	NE (NE, NE)			NE		0.333 (0.014, 8.023)			0.498	0.390
No	19/ 884 (2.1)	14/ 904 (1.5)	NE (NE, NE)			NE		1.388 (0.700, 2.751)			0.348	
Baseline viral load 1							NE					
< 10^4 copies/mL	15/ 340 (4.4)	9/ 356 (2.5)	NE (NE, NE)			NE		1.745 (0.774, 3.934)			0.179	0.211
>= 10^4 copies/mL	4/ 579 (0.7)	6/ 582 (1.0)	NE (NE, NE)			NE		0.670 (0.190, 2.362)			0.533	
Baseline viral load 2							NE					
< 10^7 copies/mL	18/ 663 (2.7)	14/ 707 (2.0)	NE (NE, NE)			NE		1.371 (0.687, 2.734)			0.370	0.774
>= 10^7 copies/mL	1/ 256 (0.4)	1/ 231 (0.4)	NE (NE, NE)			NE		0.902 (0.057, 14.344)			0.942	
Baseline serology status							NE					
Negative	5/ 439 (1.1)	6/ 457 (1.3)	NE (NE, NE)			NE		0.868 (0.267, 2.822)			0.813	0.425
Positive	14/ 494 (2.8)	9/ 495 (1.8)	NE (NE, NE)			NE		1.559 (0.681, 3.568)			0.293	
Symptom onset days to first dose date							NE					
<= 3	15/ 637 (2.4)	12/ 632 (1.9)	NE (NE, NE)			NE		1.240 (0.585, 2.628)			0.574	0.859
> 3	4/ 307 (1.3)	3/ 332 (0.9)	NE (NE, NE)			NE		1.442 (0.325, 6.391)			0.630	
BMI group							NE					
< 25	1/ 216 (0.5)	1/ 213 (0.5)	NE (NE, NE)			NE		0.986 (0.062, 15.664)			0.992	0.843
25 - < 30	6/ 324 (1.9)	6/ 336 (1.8)	NE (NE, NE)			NE		1.037 (0.338, 3.182)			0.949	
>= 30	12/ 403 (3.0)	8/ 415 (1.9)	NE (NE, NE)			NE		1.545 (0.638, 3.739)			0.335	
Ethnicity							NE					
White	14/ 712 (2.0)	14/ 725 (1.9)	1.066 (0.520, 2.185)			0.861		1.018 (0.489, 2.120)			0.961	0.181
Black or African American	5/ 45 (11.1)	1/ 42 (2.4)	NE (NE, NE)			NE		4.667 (0.568, 38.317)			0.152	
Asian	0/ 127 (0.0)	0/ 127 (0.0)	NE (NE, NE)			NE		NE (NE, NE)			NE	
Others	0/ 69 (0.0)	0/ 70 (0.0)	NE (NE, NE)			NE		NE (NE, NE)			NE	
Number of baseline comorbidities present							NE					
0-1	16/ 720 (2.2)	12/ 734 (1.6)	NE (NE, NE)			NE		1.359 (0.648, 2.853)			0.417	0.747
2-3	3/ 220 (1.4)	3/ 224 (1.3)	NE (NE, NE)			NE		1.018 (0.208, 4.990)			0.982	
>= 4	0/ 4 (0.0)	0/ 6 (0.0)	NE (NE, NE)			NE		NE (NE, NE)			NE	
Presence of risk factor: Smoking							NE					
Yes	9/ 423 (2.1)	5/ 442 (1.1)	1.915 (0.664, 5.522)			0.229		1.881 (0.636, 5.567)			0.254	0.308
No	9/ 519 (1.7)	10/ 522 (1.9)	NE (NE, NE)			NE		0.905 (0.371, 2.209)			0.827	
Presence of risk factor: Diabetes mellitus							NE					
Yes	2/ 135 (1.5)	2/ 137 (1.5)	NE (NE, NE)			NE		1.015 (0.145, 7.101)			0.988	0.838

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with EQ 5D-VAS >= 15 points improvement from baseline - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944) n/N (%)	Placebo (N=964) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]			
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value
No	16/ 808 (2.0)	13/ 827 (1.6)	NE (	NE,	NE)	NE		1.260 (	0.610,	2.602)	0.533
Presence of risk factor: Immunosuppression							NE				NE
Yes	0/ 6 (0.0)	0/ 7 (0.0)	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE
No	18/ 937 (1.9)	15/ 957 (1.6)	NE (	NE,	NE)	NE		1.226 (	0.621,	2.417)	0.557
Presence of risk factor: Chronic lung disease							NE				0.122
Yes	0/ 62 (0.0)	2/ 39 (5.1)	NE (	NE,	NE)	NE		0.127 (	0.006,	2.577)	0.179
No	18/ 881 (2.0)	13/ 925 (1.4)	NE (	NE,	NE)	NE		1.454 (	0.717,	2.949)	0.300
Presence of risk factor: Hypertension							NE				0.839
Yes	4/ 358 (1.1)	3/ 375 (0.8)	NE (	NE,	NE)	NE		1.397 (	0.315,	6.197)	0.660
No	14/ 585 (2.4)	12/ 589 (2.0)	NE (	NE,	NE)	NE		1.175 (	0.548,	2.518)	0.679
Presence of risk factor: Cardiovascular disorder							NE				NE
Yes	0/ 42 (0.0)	0/ 49 (0.0)	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE
No	18/ 901 (2.0)	15/ 915 (1.6)	NE (	NE,	NE)	NE		1.219 (	0.618,	2.403)	0.568
Presence of risk factor: Chronic kidney disease							NE				NE
Yes	0/ 6 (0.0)	0/ 8 (0.0)	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE
No	18/ 937 (1.9)	15/ 956 (1.6)	NE (	NE,	NE)	NE		1.224 (	0.621,	2.415)	0.559
Presence of risk factor: HIV Infection											
Yes	0	0/ 1 (0.0)									
No	18/ 943 (1.9)	15/ 962 (1.6)									
Presence of risk factor: Sickle Cell Disease											
No	18/ 943 (1.9)	15/ 964 (1.6)									
Presence of risk factor: Neurodevelopmental Disorder											
Yes	0/ 2 (0.0)	0/ 1 (0.0)									
No	18/ 941 (1.9)	15/ 963 (1.6)									
Presence of risk factor: Cancer							NE				NE
Yes	0/ 5 (0.0)	0/ 6 (0.0)	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE
No	18/ 938 (1.9)	15/ 958 (1.6)	NE (	NE,	NE)	NE		1.226 (	0.621,	2.417)	0.557
Presence of risk factor: Device Dependence											
Yes	0/ 4 (0.0)	0/ 3 (0.0)									
No	18/ 930 (1.9)	15/ 953 (1.6)									

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Anhang 4-G 1.14: Subgruppenanalysen - WPAI (Beeinträchtigung täglicher Aktivitäten)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Analysis of Participants with WPAI Question 6 >= 15 points improvement from baseline - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944) n/N (%)	Placebo (N=964) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]				Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value	
Age												
< 65	16/ 804 (2.0)	18/ 816 (2.2)	NE (NE, NE)			NE	NE	0.902 (0.463, 1.757)			0.762	0.397
>= 65	2/ 140 (1.4)	5/ 148 (3.4)	NE (NE, NE)			NE	NE	0.423 (0.083, 2.144)			0.299	
Gender												
Male	8/ 474 (1.7)	8/ 510 (1.6)	NE (NE, NE)			NE	NE	1.076 (0.407, 2.844)			0.883	0.422
Female	10/ 470 (2.1)	15/ 454 (3.3)	NE (NE, NE)			NE	NE	0.644 (0.292, 1.418)			0.275	
Geographic region												
United States	17/ 387 (4.4)	22/ 395 (5.6)	0.789 (0.428, 1.455)			0.448	NE	0.789 (0.425, 1.462)			0.451	0.840
Europe	0/ 322 (0.0)	0/ 321 (0.0)	NE (NE, NE)			NE	NE	NE (NE, NE)			NE	
India	0/ 74 (0.0)	0/ 78 (0.0)	NE (NE, NE)			NE	NE	NE (NE, NE)			NE	
Rest of World	1/ 161 (0.6)	1/ 170 (0.6)	NE (NE, NE)			NE	NE	1.056 (0.067, 16.740)			0.969	
COVID-19 therapeutic mAb treatment at randomisation												
Yes	0/ 60 (0.0)	1/ 60 (1.7)	NE (NE, NE)			NE	NE	0.333 (0.014, 8.023)			0.498	0.578
No	18/ 884 (2.0)	22/ 904 (2.4)	NE (NE, NE)			NE	NE	0.837 (0.452, 1.549)			0.570	
Baseline viral load 1												
< 10 ⁴ copies/mL	11/ 340 (3.2)	13/ 356 (3.7)	NE (NE, NE)			NE	NE	0.886 (0.402, 1.950)			0.764	0.716
>= 10 ⁴ copies/mL	7/ 579 (1.2)	10/ 582 (1.7)	NE (NE, NE)			NE	NE	0.704 (0.270, 1.836)			0.473	
Baseline viral load 2												
< 10 ⁷ copies/mL	16/ 663 (2.4)	22/ 707 (3.1)	NE (NE, NE)			NE	NE	0.776 (0.411, 1.464)			0.433	0.504
>= 10 ⁷ copies/mL	2/ 256 (0.8)	1/ 231 (0.4)	NE (NE, NE)			NE	NE	1.805 (0.165, 19.772)			0.629	
Baseline serology status												
Negative	3/ 439 (0.7)	4/ 457 (0.9)	NE (NE, NE)			NE	NE	0.781 (0.176, 3.468)			0.745	0.987
Positive	15/ 494 (3.0)	19/ 495 (3.8)	NE (NE, NE)			NE	NE	0.791 (0.407, 1.539)			0.490	
Symptom onset days to first dose date												
<= 3	15/ 637 (2.4)	18/ 632 (2.8)	NE (NE, NE)			NE	NE	0.827 (0.420, 1.626)			0.581	0.763
> 3	3/ 307 (1.0)	5/ 332 (1.5)	NE (NE, NE)			NE	NE	0.649 (0.156, 2.692)			0.551	
BMI group												
< 25	1/ 216 (0.5)	2/ 213 (0.9)	NE (NE, NE)			NE	NE	0.493 (0.045, 5.397)			0.562	0.565
25 - < 30	5/ 324 (1.5)	10/ 336 (3.0)	NE (NE, NE)			NE	NE	0.519 (0.179, 1.501)			0.226	
>= 30	11/ 403 (2.7)	11/ 415 (2.7)	NE (NE, NE)			NE	NE	1.030 (0.452, 2.348)			0.944	
Ethnicity												
White	17/ 712 (2.4)	20/ 725 (2.8)	0.883 (0.473, 1.647)			0.695	NE	0.866 (0.457, 1.639)			0.657	0.386
Black or African American	1/ 45 (2.2)	3/ 42 (7.1)	NE (NE, NE)			NE	NE	0.311 (0.034, 2.875)			0.303	
Asian	0/ 118 (0.0)	0/ 127 (0.0)	NE (NE, NE)			NE	NE	NE (NE, NE)			NE	
Others	0/ 69 (0.0)	0/ 70 (0.0)	NE (NE, NE)			NE	NE	NE (NE, NE)			NE	
Number of baseline comorbidities present												
0-1	14/ 720 (1.9)	15/ 734 (2.0)	NE (NE, NE)			NE	NE	0.951 (0.463, 1.957)			0.892	0.738
2-3	4/ 220 (1.8)	7/ 224 (3.1)	NE (NE, NE)			NE	NE	0.582 (0.173, 1.960)			0.382	
>= 4	0/ 4 (0.0)	1/ 6 (16.7)	NE (NE, NE)			NE	NE	0.467 (0.024, 9.259)			0.617	
Presence of risk factor: Smoking												
Yes	8/ 423 (1.9)	9/ 442 (2.0)	NE (NE, NE)			NE	NE	0.929 (0.362, 2.385)			0.878	0.572
No	9/ 519 (1.7)	14/ 522 (2.7)	NE (NE, NE)			NE	NE	0.647 (0.282, 1.481)			0.302	
Presence of risk factor: Diabetes mellitus												
Yes	1/ 135 (0.7)	7/ 137 (5.1)	NE (NE, NE)			NE	NE	0.145 (0.018, 1.162)			0.069	0.081

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with WPAI Question 6 >= 15 points improvement from baseline - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944) n/N (%)	Placebo (N=964) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]			
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)			p-Value
No	16/ 808 (2.0)	16/ 827 (1.9)	NE (	NE,	NE)	NE		1.024 (	0.515,	2.033)	0.947
Presence of risk factor: Immunosuppression							NE				NE
Yes	0/ 6 (0.0)	0/ 7 (0.0)	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE
No	17/ 937 (1.8)	23/ 957 (2.4)	NE (	NE,	NE)	NE		0.755 (	0.406,	1.404)	0.374
Presence of risk factor: Chronic lung disease							NE				0.456
Yes	1/ 62 (1.6)	2/ 39 (5.1)	NE (	NE,	NE)	NE		0.315 (	0.029,	3.354)	0.338
No	16/ 881 (1.8)	21/ 925 (2.3)	NE (	NE,	NE)	NE		0.800 (	0.420,	1.523)	0.497
Presence of risk factor: Hypertension							NE				0.849
Yes	6/ 358 (1.7)	9/ 375 (2.4)	NE (	NE,	NE)	NE		0.698 (	0.251,	1.942)	0.491
No	11/ 585 (1.9)	14/ 589 (2.4)	NE (	NE,	NE)	NE		0.791 (	0.362,	1.728)	0.557
Presence of risk factor: Cardiovascular disorder							NE				0.669
Yes	0/ 42 (0.0)	1/ 49 (2.0)	NE (	NE,	NE)	NE		0.388 (	0.016,	9.270)	0.558
No	17/ 901 (1.9)	22/ 915 (2.4)	NE (	NE,	NE)	NE		0.785 (	0.420,	1.468)	0.448
Presence of risk factor: Chronic kidney disease							NE				NE
Yes	0/ 6 (0.0)	0/ 8 (0.0)	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE
No	17/ 937 (1.8)	23/ 956 (2.4)	NE (	NE,	NE)	NE		0.754 (	0.406,	1.402)	0.373
Presence of risk factor: HIV Infection											
Yes	0	0/ 1 (0.0)									
No	17/ 943 (1.8)	23/ 962 (2.4)									
Presence of risk factor: Sickle Cell Disease											
No	17/ 943 (1.8)	23/ 964 (2.4)									
Presence of risk factor: Neurodevelopmental Disorder											
Yes	0/ 2 (0.0)	0/ 1 (0.0)									
No	17/ 941 (1.8)	23/ 963 (2.4)									
Presence of risk factor: Cancer							NE				NE
Yes	0/ 5 (0.0)	0/ 6 (0.0)	NE (	NE,	NE)	NE		NE (	NE,	NE)	NE
No	17/ 938 (1.8)	23/ 958 (2.4)	NE (	NE,	NE)	NE		0.755 (	0.406,	1.404)	0.374
Presence of risk factor: Device Dependence											
Yes	0/ 4 (0.0)	0/ 3 (0.0)									
No	17/ 930 (1.8)	23/ 953 (2.4)									

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Anhang 4-G 1.15: Subgruppenanalysen - Global Impression Questions (Lebensqualität)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022) Overall Study population RKI-conform mITT2 Analysis set Analysis of Participants with Global Impression Questionnaire return to usual activities 1 point improvement from baseline - Subgroup analysis										Final	
Subgroup Level	Nirmatrelvir/ritonavir (N=944) n/N (%)	Placebo (N=964) n/N (%)	Adjusted analysis [1]				Interaction p-Value	Unadjusted analysis [2]			Interaction p-Value
			Relative Risk (95% CI)			p-Value		Relative Risk (95% CI)		p-Value	
Age							0.681				0.606
< 65	446/ 804 (55.5)	427/ 816 (52.3)	1.056 (0.970, 1.149)	0.207				1.060 (0.969, 1.160)	0.204		
>= 65	89/ 140 (63.6)	84/ 148 (56.8)	1.166 (0.960, 1.417)	0.121				1.120 (0.928, 1.352)	0.238		
Gender							0.797				0.903
Male	277/ 474 (58.4)	277/ 510 (54.3)	1.067 (0.961, 1.184)	0.223				1.076 (0.964, 1.201)	0.192		
Female	258/ 470 (54.9)	234/ 454 (51.5)	1.057 (0.944, 1.184)	0.333				1.065 (0.944, 1.202)	0.308		
Geographic region							0.798				0.836
United States	194/ 387 (50.1)	192/ 395 (48.6)	1.036 (0.898, 1.196)	0.625				1.031 (0.895, 1.189)	0.670		
Europe	222/ 322 (68.9)	204/ 321 (63.6)	1.090 (0.978, 1.214)	0.118				1.085 (0.971, 1.212)	0.149		
India	49/ 74 (66.2)	51/ 78 (65.4)	0.974 (0.799, 1.188)	0.796				1.013 (0.805, 1.274)	0.914		
Rest of World	70/ 161 (43.5)	64/ 170 (37.6)	NE (NE, NE)	NE				1.155 (0.889, 1.500)	0.281		
COVID-19 therapeutic mAb treatment at randomisation							0.793				0.732
Yes	27/ 60 (45.0)	27/ 60 (45.0)	NE (NE, NE)	NE				1.000 (0.673, 1.485)	1.000		
No	508/ 884 (57.5)	484/ 904 (53.5)	1.066 (0.986, 1.153)	0.110				1.073 (0.988, 1.166)	0.095		
Baseline viral load 1							0.359				0.337
< 10^4 copies/mL	197/ 340 (57.9)	203/ 356 (57.0)	1.016 (0.902, 1.143)	0.798				1.016 (0.894, 1.155)	0.806		
>= 10^4 copies/mL	330/ 579 (57.0)	301/ 582 (51.7)	1.084 (0.981, 1.198)	0.114				1.102 (0.992, 1.225)	0.072		
Baseline viral load 2							0.292				0.172
< 10^7 copies/mL	379/ 663 (57.2)	391/ 707 (55.3)	1.044 (0.955, 1.140)	0.345				1.034 (0.941, 1.135)	0.488		
>= 10^7 copies/mL	148/ 256 (57.8)	113/ 231 (48.9)	1.113 (0.946, 1.309)	0.196				1.182 (0.999, 1.398)	0.052		
Baseline serology status							0.028				0.086
Negative	260/ 439 (59.2)	234/ 457 (51.2)	1.150 (1.031, 1.283)	0.012				1.157 (1.027, 1.302)	0.016		
Positive	271/ 494 (54.9)	271/ 495 (54.7)	0.977 (0.877, 1.088)	0.669				1.002 (0.895, 1.122)	0.972		
Symptom onset days to first dose date							0.373				0.234
<= 3	373/ 637 (58.6)	359/ 632 (56.8)	1.046 (0.956, 1.143)	0.326				1.031 (0.938, 1.133)	0.528		
> 3	162/ 307 (52.8)	152/ 332 (45.8)	1.104 (0.947, 1.288)	0.206				1.153 (0.984, 1.350)	0.078		
BMI group							0.413				0.556
< 25	127/ 216 (58.8)	120/ 213 (56.3)	1.022 (0.875, 1.193)	0.782				1.044 (0.887, 1.228)	0.607		
25 - < 30	190/ 324 (58.6)	193/ 336 (57.4)	1.035 (0.916, 1.170)	0.577				1.021 (0.897, 1.162)	0.754		
>= 30	217/ 403 (53.8)	198/ 415 (47.7)	1.134 (0.991, 1.299)	0.068				1.129 (0.986, 1.292)	0.080		
Ethnicity							0.252				0.204
White	418/ 712 (58.7)	392/ 725 (54.1)	1.079 (0.989, 1.178)	0.087				1.086 (0.991, 1.189)	0.077		
Black or African American	20/ 45 (44.4)	24/ 42 (57.1)	NE (NE, NE)	NE				0.778 (0.512, 1.182)	0.239		
Asian	62/ 118 (52.5)	69/ 127 (54.3)	NE (NE, NE)	NE				0.967 (0.765, 1.222)	0.779		
Others	35/ 69 (50.7)	26/ 70 (37.1)	NE (NE, NE)	NE				1.366 (0.931, 2.004)	0.111		
Number of baseline comorbidities present							NE				0.458
0-1	405/ 720 (56.3)	389/ 734 (53.0)	1.057 (0.970, 1.151)	0.208				1.061 (0.966, 1.166)	0.213		
2-3	129/ 220 (58.6)	118/ 224 (52.7)	1.088 (0.922, 1.285)	0.318				1.113 (0.942, 1.315)	0.207		
>= 4	1/ 4 (25.0)	4/ 6 (66.7)	NE (NE, NE)	NE				0.375 (0.063, 2.244)	0.283		
Presence of risk factor: Smoking							0.288				0.117
Yes	243/ 423 (57.4)	254/ 442 (57.5)	1.021 (0.921, 1.132)	0.692				1.000 (0.891, 1.121)	0.995		
No	291/ 519 (56.1)	257/ 522 (49.2)	1.102 (0.984, 1.234)	0.094				1.139 (1.014, 1.279)	0.028		
Presence of risk factor: Diabetes mellitus							0.201				0.450
Yes	72/ 135 (53.3)	74/ 137 (54.0)	1.008 (0.807, 1.259)	0.944				0.987 (0.792, 1.231)	0.910		

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Participants with Global Impression Questionnaire return to usual activities 1 point improvement from baseline - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944) n/N (%)	Placebo (N=964) n/N (%)	Adjusted analysis [1]		Interaction p-Value	Unadjusted analysis [2]		Interaction p-Value
			Relative Risk (95% CI)	p-Value		Relative Risk (95% CI)	p-Value	
No	462/ 808 (57.2)	437/ 827 (52.8)	1.085 (0.999, 1.178)	0.052		1.082 (0.991, 1.181)	0.078	
Presence of risk factor: Immunosuppression					0.777			0.840
Yes	4/ 6 (66.7)	4/ 7 (57.1)	NE (NE, NE)	NE		1.167 (0.496, 2.744)	0.724	
No	530/ 937 (56.6)	507/ 957 (53.0)	1.062 (0.983, 1.148)	0.126		1.068 (0.984, 1.159)	0.117	
Presence of risk factor: Chronic lung disease					0.861			0.755
Yes	31/ 62 (50.0)	17/ 39 (43.6)	1.016 (0.664, 1.556)	0.940		1.147 (0.742, 1.773)	0.537	
No	503/ 881 (57.1)	494/ 925 (53.4)	1.066 (0.985, 1.153)	0.111		1.069 (0.984, 1.162)	0.115	
Presence of risk factor: Hypertension					0.523			0.352
Yes	214/ 358 (59.8)	200/ 375 (53.3)	1.087 (0.960, 1.232)	0.189		1.121 (0.987, 1.273)	0.079	
No	320/ 585 (54.7)	311/ 589 (52.8)	1.040 (0.943, 1.148)	0.431		1.036 (0.932, 1.152)	0.514	
Presence of risk factor: Cardiovascular disorder					0.724			0.569
Yes	25/ 42 (59.5)	30/ 49 (61.2)	NE (NE, NE)	NE		0.972 (0.696, 1.358)	0.869	
No	509/ 901 (56.5)	481/ 915 (52.6)	1.067 (0.986, 1.155)	0.107		1.075 (0.988, 1.169)	0.093	
Presence of risk factor: Chronic kidney disease					0.338			0.194
Yes	3/ 6 (50.0)	1/ 8 (12.5)	NE (NE, NE)	NE		4.000 (0.541, 29.567)	0.174	
No	531/ 937 (56.7)	510/ 956 (53.3)	1.062 (0.983, 1.147)	0.127		1.062 (0.979, 1.153)	0.146	
Presence of risk factor: HIV Infection								
Yes	0	0/ 1 (0.0)						
No	534/ 943 (56.6)	511/ 962 (53.1)						
Presence of risk factor: Sickle Cell Disease								
No	534/ 943 (56.6)	511/ 964 (53.0)						
Presence of risk factor: Neurodevelopmental Disorder								
Yes	1/ 2 (50.0)	1/ 1 (100.0)						
No	533/ 941 (56.6)	510/ 963 (53.0)						
Presence of risk factor: Cancer					0.891			0.671
Yes	2/ 5 (40.0)	3/ 6 (50.0)	NE (NE, NE)	NE		0.800 (0.210, 3.052)	0.744	
No	532/ 938 (56.7)	508/ 958 (53.0)	1.063 (0.984, 1.149)	0.123		1.070 (0.986, 1.161)	0.107	
Presence of risk factor: Device Dependence								
Yes	1/ 4 (25.0)	2/ 3 (66.7)						
No	528/ 930 (56.8)	506/ 953 (53.1)						

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald). p-Value for interaction is computed from a test for heterogeneity of the unadjusted relative risk in the subgroups using Cochrane's Q statistic.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Anhang 4-G 1.16: Subgruppenanalysen - Verträglichkeit

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Analysis of Adverse Events - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/ N (%)	Median	(95% CI) [1]	n/ N (%)	Median	(95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Age									0.1922
< 65	165/ 804 (20.5)	NE (NE , NE)		179/ 816 (21.9)	NE (NE , NE)		0.95 (0.77, 1.17)	0.62	
>= 65	61/ 140 (43.6)	NE (12.0, NE)		55/ 148 (37.2)	NE (NE , NE)		1.24 (0.86, 1.79)	0.23	
Gender									0.5576
Male	101/ 474 (21.3)	NE (NE , NE)		116/ 510 (22.7)	NE (NE , NE)		0.95 (0.72, 1.24)	0.68	
Female	125/ 470 (26.6)	NE (NE , NE)		118/ 454 (26.0)	NE (NE , NE)		1.05 (0.82, 1.35)	0.69	
Geographic region									0.2718
United States	72/ 387 (18.6)	NE (NE , NE)		65/ 395 (16.5)	NE (NE , NE)		1.16 (0.83, 1.63)	0.37	
Europe	93/ 322 (28.9)	NE (NE , NE)		108/ 321 (33.6)	NE (NE , NE)		0.86 (0.65, 1.13)	0.27	
India	18/ 74 (24.3)	NE (NE , NE)		12/ 78 (15.4)	NE (NE , NE)		1.69 (0.81, 3.50)	0.16	
Rest of World	43/ 161 (26.7)	NE (NE , NE)		49/ 170 (28.8)	NE (NE , NE)		0.94 (0.62, 1.41)	0.76	
COVID-19 therapeutic mAb treatment at randomisation									0.8820
Yes	18/ 60 (30.0)	NE (NE , NE)		19/ 60 (31.7)	NE (NE , NE)		0.97 (0.51, 1.84)	0.91	
No	208/ 884 (23.5)	NE (NE , NE)		215/ 904 (23.8)	NE (NE , NE)		1.01 (0.83, 1.22)	0.92	
Baseline viral load 1									0.0303
< 10^4 copies/mL	70/ 340 (20.6)	NE (NE , NE)		54/ 356 (15.2)	NE (NE , NE)		1.42 (0.99, 2.02)	0.05	
>= 10^4 copies/mL	152/ 579 (26.3)	NE (NE , NE)		172/ 582 (29.6)	NE (NE , NE)		0.89 (0.72, 1.11)	0.31	
Baseline viral load 2									0.1207
< 10^7 copies/mL	157/ 663 (23.7)	NE (NE , NE)		154/ 707 (21.8)	NE (NE , NE)		1.12 (0.90, 1.40)	0.32	
>= 10^7 copies/mL	65/ 256 (25.4)	NE (NE , NE)		72/ 231 (31.2)	NE (NE , NE)		0.81 (0.58, 1.14)	0.22	
Baseline serology status									0.0011
Negative	108/ 439 (24.6)	NE (NE , NE)		143/ 457 (31.3)	NE (NE , NE)		0.78 (0.60, 1.00)	0.04	
Positive	116/ 494 (23.5)	NE (NE , NE)		84/ 495 (17.0)	NE (NE , NE)		1.45 (1.09, 1.92)	0.01	
Symptom onset days to first dose date									0.4335
<= 3	143/ 637 (22.4)	NE (NE , NE)		151/ 632 (23.9)	NE (NE , NE)		0.95 (0.76, 1.20)	0.67	
> 3	83/ 307 (27.0)	NE (NE , NE)		83/ 332 (25.0)	NE (NE , NE)		1.12 (0.82, 1.51)	0.48	
BMI group									0.8715
< 25	46/ 216 (21.3)	NE (NE , NE)		50/ 213 (23.5)	NE (NE , NE)		0.92 (0.62, 1.38)	0.69	
25 - < 30	74/ 324 (22.8)	NE (NE , NE)		74/ 336 (22.0)	NE (NE , NE)		1.06 (0.77, 1.46)	0.73	
>= 30	106/ 403 (26.3)	NE (NE , NE)		110/ 415 (26.5)	NE (NE , NE)		1.01 (0.78, 1.32)	0.92	
Ethnicity									0.0858
White	171/ 712 (24.0)	NE (NE , NE)		185/ 725 (25.5)	NE (NE , NE)		0.95 (0.78, 1.17)	0.65	
Black or African American	7/ 45 (15.6)	NE (NE , NE)		9/ 42 (21.4)	NE (NE , NE)		0.74 (0.28, 1.99)	0.55	
Asian	33/ 118 (28.0)	NE (NE , NE)		20/ 127 (15.7)	NE (NE , NE)		1.94 (1.11, 3.38)	0.01	
Others	15/ 69 (21.7)	NE (NE , NE)		20/ 70 (28.6)	NE (NE , NE)		0.72 (0.37, 1.42)	0.34	
Number of baseline comorbidities present									0.8741
0-1	158/ 720 (21.9)	NE (NE , NE)		166/ 734 (22.6)	NE (NE , NE)		0.98 (0.79, 1.22)	0.85	
2-3	68/ 220 (30.9)	NE (NE , NE)		67/ 224 (29.9)	NE (NE , NE)		1.09 (0.78, 1.53)	0.60	
>= 4	0/ 4 (0.0)	NE (NE , NE)		1/ 6 (16.7)	NE (1.0, NE)		NE	NE	
Presence of risk factor: Smoking									0.3685
Yes	76/ 423 (18.0)	NE (NE , NE)		89/ 442 (20.1)	NE (NE , NE)		0.90 (0.66, 1.22)	0.49	
No	150/ 519 (28.9)	NE (NE , NE)		145/ 522 (27.8)	NE (NE , NE)		1.07 (0.85, 1.35)	0.55	

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Analysis of Adverse Events - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/ N (%)	Median	(95% CI) [1]	n/ N (%)	Median	(95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Presence of risk factor: Diabetes mellitus									
Yes	44/ 135 (32.6)	NE (NE , NE)		40/ 137 (29.2)	NE (NE , NE)		1.19 (0.77, 1.82)	0.43	0.4243
No	182/ 808 (22.5)	NE (NE , NE)		194/ 827 (23.5)	NE (NE , NE)		0.97 (0.79, 1.19)	0.79	
Presence of risk factor: Immunosuppression									
Yes	2/ 6 (33.3)	NE (2.0, NE)		1/ 7 (14.3)	NE (3.0, NE)		2.69 (0.24, 29.93)	0.42	0.4282
No	224/ 937 (23.9)	NE (NE , NE)		233/ 957 (24.3)	NE (NE , NE)		1.00 (0.83, 1.20)	1.00	
Presence of risk factor: Chronic lung disease									
Yes	14/ 62 (22.6)	NE (NE , NE)		12/ 39 (30.8)	NE (NE , NE)		0.76 (0.35, 1.64)	0.48	0.4613
No	212/ 881 (24.1)	NE (NE , NE)		222/ 925 (24.0)	NE (NE , NE)		1.02 (0.85, 1.23)	0.82	
Presence of risk factor: Hypertension									
Yes	109/ 358 (30.4)	NE (NE , NE)		111/ 375 (29.6)	NE (NE , NE)		1.07 (0.82, 1.39)	0.61	0.5753
No	117/ 585 (20.0)	NE (NE , NE)		123/ 589 (20.9)	NE (NE , NE)		0.97 (0.75, 1.24)	0.78	
Presence of risk factor: Cardiovascular disorder									
Yes	18/ 42 (42.9)	NE (5.0, NE)		16/ 49 (32.7)	NE (NE , NE)		1.49 (0.76, 2.92)	0.24	0.2513
No	208/ 901 (23.1)	NE (NE , NE)		218/ 915 (23.8)	NE (NE , NE)		0.98 (0.81, 1.19)	0.86	
Presence of risk factor: Chronic kidney disease									
Yes	3/ 6 (50.0)	NE (1.0, NE)		5/ 8 (62.5)	4.0 (1.0, NE)		0.79 (0.19, 3.29)	0.74	0.6966
No	223/ 937 (23.8)	NE (NE , NE)		229/ 956 (24.0)	NE (NE , NE)		1.01 (0.84, 1.22)	0.88	
Presence of risk factor: HIV Infection									
Yes	0			1/ 1 (100.0)					
No	226/ 943 (24.0)			233/ 962 (24.2)					
Presence of risk factor: Sickle Cell Disease									
No	226/ 943 (24.0)			234/ 964 (24.3)					
Presence of risk factor: Neurodevelopmental Disorder									
Yes	2/ 2 (100.0)			1/ 1 (100.0)					
No	224/ 941 (23.8)			233/ 963 (24.2)					
Presence of risk factor: Cancer									
Yes	2/ 5 (40.0)	NE (1.0, NE)		1/ 6 (16.7)	NE (1.0, NE)		2.40 (0.22, 26.47)	0.47	0.3867
No	224/ 938 (23.9)	NE (NE , NE)		233/ 958 (24.3)	NE (NE , NE)		1.00 (0.83, 1.20)	1.00	
Presence of risk factor: Device Dependence									
Yes	2/ 4 (50.0)			0/ 3 (0.0)					
No	220/ 930 (23.7)			230/ 953 (24.1)					

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

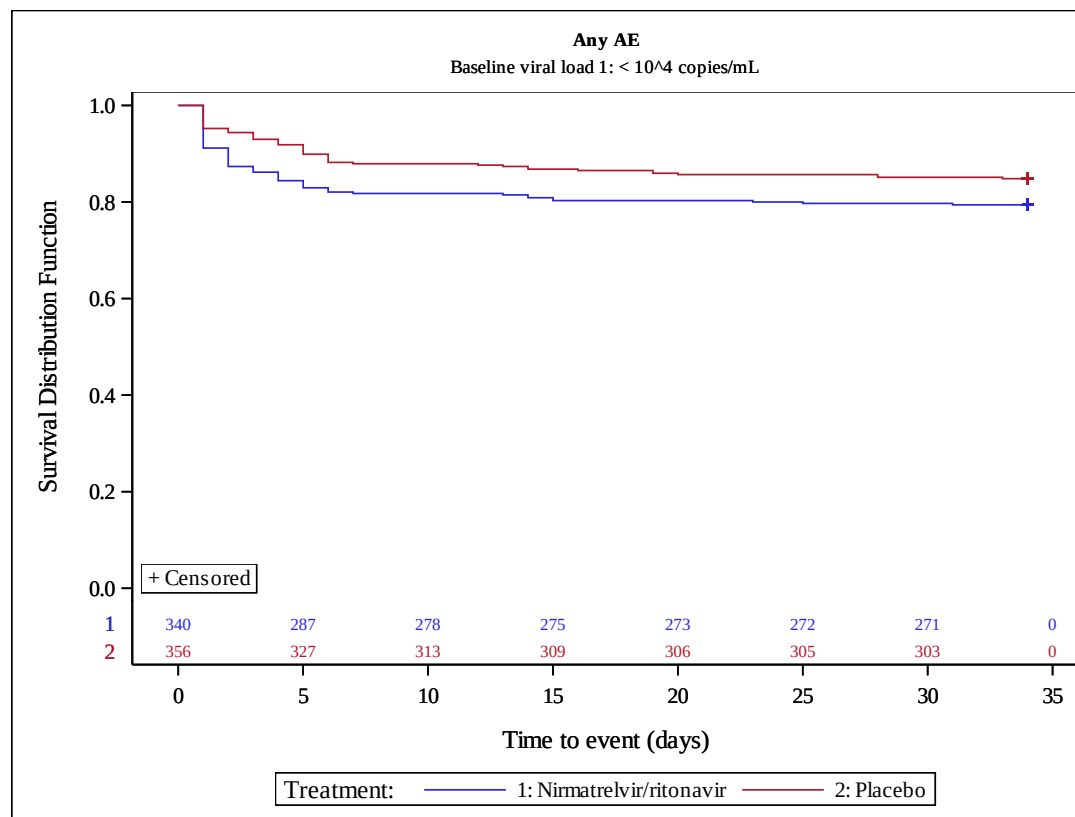
[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Adverse Events

Final

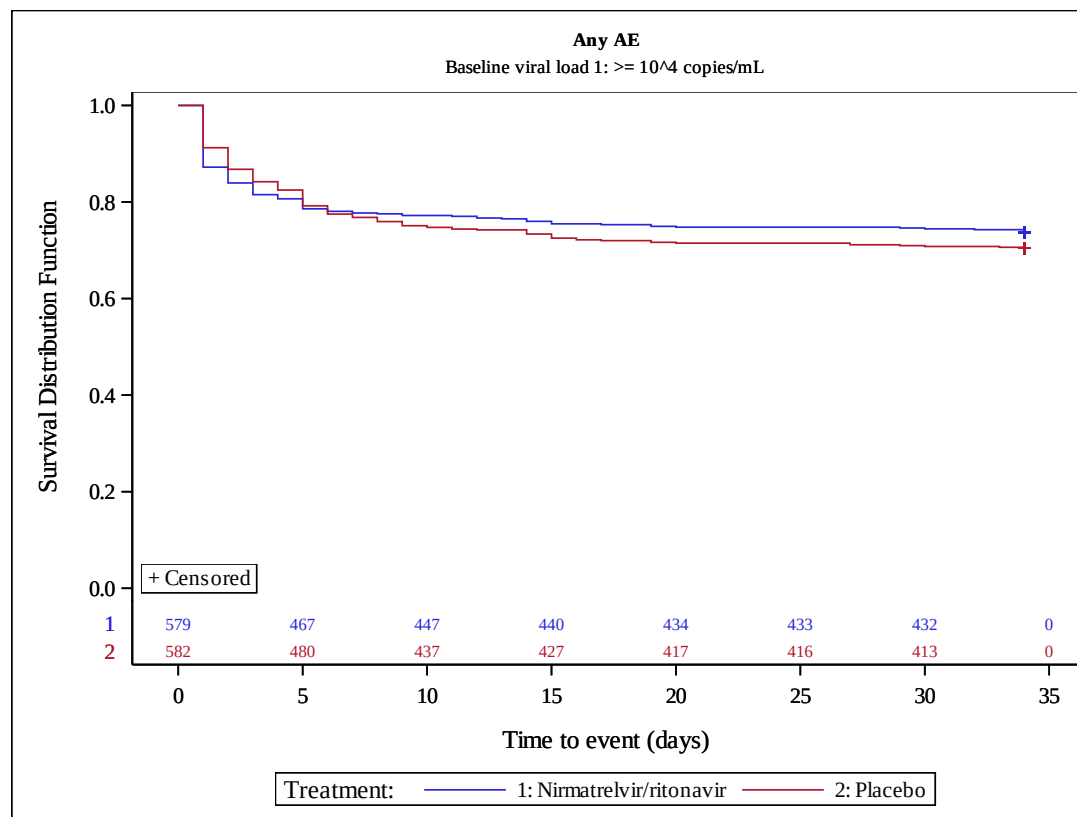


Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Adverse Events

Final

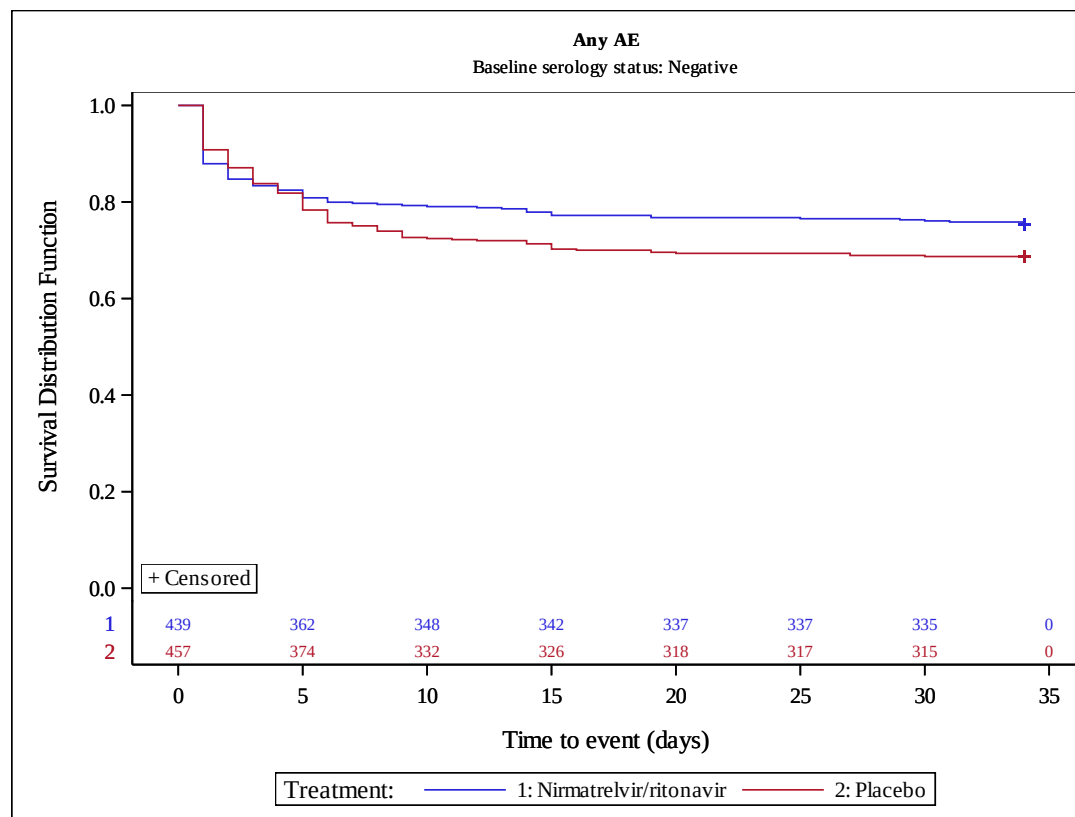


Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Adverse Events

Final

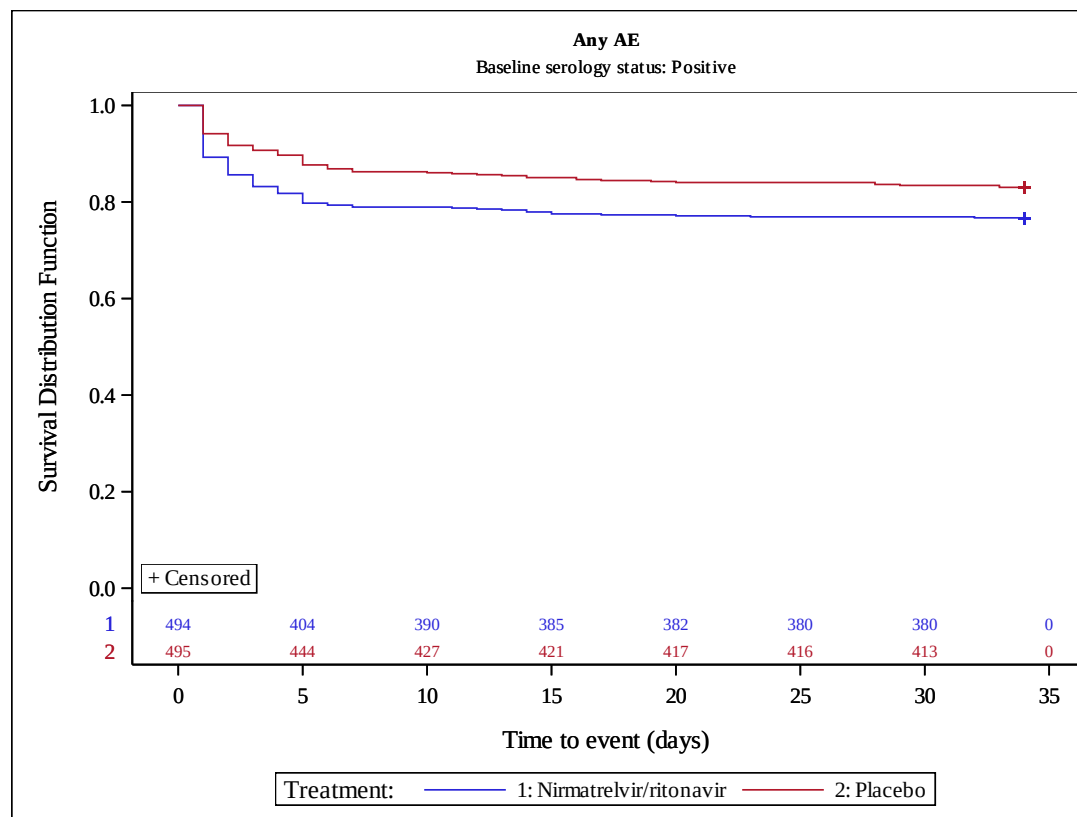


Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Adverse Events

Final



Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Analysis of Severe Adverse Events (DAIDS >=3) - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/ N (%)	Median	(95% CI) [1]	n/ N (%)	Median	(95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Age									
< 65	22/ 804 (2.7)	NE (NE , NE)		59/ 816 (7.2)	NE (NE , NE)		0.37 (0.23, 0.61)	<.001	0.1390
>= 65	21/ 140 (15.0)	NE (NE , NE)		33/ 148 (22.3)	NE (NE , NE)		0.66 (0.38, 1.13)	0.13	
Gender									
Male	18/ 474 (3.8)	NE (NE , NE)		57/ 510 (11.2)	NE (NE , NE)		0.33 (0.19, 0.56)	<.001	0.0535
Female	25/ 470 (5.3)	NE (NE , NE)		35/ 454 (7.7)	NE (NE , NE)		0.68 (0.41, 1.14)	0.14	
Geographic region									
United States	14/ 387 (3.6)	NE (NE , NE)		26/ 395 (6.6)	NE (NE , NE)		0.54 (0.28, 1.04)	0.06	0.9103
Europe	22/ 322 (6.8)	NE (NE , NE)		49/ 321 (15.3)	NE (NE , NE)		0.43 (0.26, 0.72)	0.00	
India	1/ 74 (1.4)	NE (NE , NE)		0/ 78 (0.0)	NE (NE , NE)		NE	NE	
Rest of World	6/ 161 (3.7)	NE (NE , NE)		17/ 170 (10.0)	NE (NE , NE)		0.37 (0.14, 0.93)	0.03	
COVID-19 therapeutic mAb treatment at randomisation									
Yes	1/ 60 (1.7)	NE (NE , NE)		9/ 60 (15.0)	NE (NE , NE)		0.11 (0.01, 0.83)	0.03	0.1446
No	42/ 884 (4.8)	NE (NE , NE)		83/ 904 (9.2)	NE (NE , NE)		0.51 (0.35, 0.74)	<.001	
Baseline viral load 1									
< 10^4 copies/mL	12/ 340 (3.5)	NE (NE , NE)		14/ 356 (3.9)	NE (NE , NE)		0.90 (0.42, 1.94)	0.78	0.0607
>= 10^4 copies/mL	29/ 579 (5.0)	NE (NE , NE)		73/ 582 (12.5)	NE (NE , NE)		0.39 (0.25, 0.59)	<.001	
Baseline viral load 2									
< 10^7 copies/mL	28/ 663 (4.2)	NE (NE , NE)		57/ 707 (8.1)	NE (NE , NE)		0.52 (0.33, 0.81)	0.00	0.4578
>= 10^7 copies/mL	13/ 256 (5.1)	NE (NE , NE)		30/ 231 (13.0)	NE (NE , NE)		0.38 (0.20, 0.73)	0.00	
Baseline serology status									
Negative	25/ 439 (5.7)	NE (NE , NE)		68/ 457 (14.9)	NE (NE , NE)		0.37 (0.23, 0.58)	<.001	0.0695
Positive	18/ 494 (3.6)	NE (NE , NE)		24/ 495 (4.8)	NE (NE , NE)		0.75 (0.41, 1.38)	0.35	
Symptom onset days to first dose date									
<= 3	31/ 637 (4.9)	NE (NE , NE)		60/ 632 (9.5)	NE (NE , NE)		0.50 (0.33, 0.78)	0.00	0.5479
> 3	12/ 307 (3.9)	NE (NE , NE)		32/ 332 (9.6)	NE (NE , NE)		0.40 (0.21, 0.78)	0.00	
BMI group									
< 25	6/ 216 (2.8)	NE (NE , NE)		16/ 213 (7.5)	NE (NE , NE)		0.36 (0.14, 0.92)	0.03	0.3679
25 - < 30	12/ 324 (3.7)	NE (NE , NE)		34/ 336 (10.1)	NE (NE , NE)		0.36 (0.18, 0.69)	0.00	
>= 30	25/ 403 (6.2)	NE (NE , NE)		42/ 415 (10.1)	NE (NE , NE)		0.61 (0.37, 1.00)	0.04	
Ethnicity									
White	37/ 712 (5.2)	NE (NE , NE)		80/ 725 (11.0)	NE (NE , NE)		0.46 (0.31, 0.68)	<.001	0.6320
Black or African American	2/ 45 (4.4)	NE (NE , NE)		1/ 42 (2.4)	NE (NE , NE)		1.85 (0.17, 20.41)	0.61	
Asian	2/ 118 (1.7)	NE (NE , NE)		4/ 127 (3.1)	NE (NE , NE)		0.54 (0.10, 2.92)	0.47	
Others	2/ 69 (2.9)	NE (NE , NE)		7/ 70 (10.0)	NE (NE , NE)		0.28 (0.06, 1.34)	0.11	
Number of baseline comorbidities present									
0-1	26/ 720 (3.6)	NE (NE , NE)		61/ 734 (8.3)	NE (NE , NE)		0.43 (0.27, 0.68)	<.001	0.7658
2-3	17/ 220 (7.7)	NE (NE , NE)		30/ 224 (13.4)	NE (NE , NE)		0.57 (0.31, 1.03)	0.06	
>= 4	0/ 4 (0.0)	NE (NE , NE)		1/ 6 (16.7)	NE (1.0, NE)		NE	NE	
Presence of risk factor: Smoking									
Yes	8/ 423 (1.9)	NE (NE , NE)		30/ 442 (6.8)	NE (NE , NE)		0.27 (0.13, 0.60)	0.00	0.1143
No	35/ 519 (6.7)	NE (NE , NE)		62/ 522 (11.9)	NE (NE , NE)		0.56 (0.37, 0.84)	0.00	

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Severe Adverse Events (DAIDS >=3) - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
	n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Presence of risk factor: Diabetes mellitus							0.2197
Yes	12/ 135 (8.9)	NE (NE , NE)	17/ 137 (12.4)	NE (NE , NE)	0.71 (0.34, 1.48)	0.35	
No	31/ 808 (3.8)	NE (NE , NE)	75/ 827 (9.1)	NE (NE , NE)	0.42 (0.27, 0.63)	<.001	
Presence of risk factor: Immunosuppression							0.9714
Yes	1/ 6 (16.7)	NE (5.0, NE)	0/ 7 (0.0)	NE (NE , NE)	NE	NE	
No	42/ 937 (4.5)	NE (NE , NE)	92/ 957 (9.6)	NE (NE , NE)	0.46 (0.32, 0.66)	<.001	
Presence of risk factor: Chronic lung disease							0.6241
Yes	2/ 62 (3.2)	NE (NE , NE)	4/ 39 (10.3)	NE (NE , NE)	0.31 (0.06, 1.72)	0.18	
No	41/ 881 (4.7)	NE (NE , NE)	88/ 925 (9.5)	NE (NE , NE)	0.48 (0.33, 0.70)	<.001	
Presence of risk factor: Hypertension							0.7003
Yes	26/ 358 (7.3)	NE (NE , NE)	53/ 375 (14.1)	NE (NE , NE)	0.50 (0.31, 0.80)	0.00	
No	17/ 585 (2.9)	NE (NE , NE)	39/ 589 (6.6)	NE (NE , NE)	0.43 (0.24, 0.76)	0.00	
Presence of risk factor: Cardiovascular disorder							0.1855
Yes	8/ 42 (19.0)	NE (NE , NE)	11/ 49 (22.4)	NE (NE , NE)	0.86 (0.34, 2.13)	0.73	
No	35/ 901 (3.9)	NE (NE , NE)	81/ 915 (8.9)	NE (NE , NE)	0.43 (0.29, 0.64)	<.001	
Presence of risk factor: Chronic kidney disease							0.9762
Yes	0/ 6 (0.0)	NE (NE , NE)	2/ 8 (25.0)	NE (1.0, NE)	NE	NE	
No	43/ 937 (4.6)	NE (NE , NE)	90/ 956 (9.4)	NE (NE , NE)	0.48 (0.33, 0.69)	<.001	
Presence of risk factor: HIV Infection							
Yes	0		0/ 1 (0.0)				
No	43/ 943 (4.6)		92/ 962 (9.6)				
Presence of risk factor: Sick Cell Disease							
No	43/ 943 (4.6)		92/ 964 (9.5)				
Presence of risk factor: Neurodevelopmental Disorder							
Yes	0/ 2 (0.0)		1/ 1 (100.0)				
No	43/ 941 (4.6)		91/ 963 (9.4)				
Presence of risk factor: Cancer							0.9994
Yes	0/ 5 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
No	43/ 938 (4.6)	NE (NE , NE)	92/ 958 (9.6)	NE (NE , NE)	0.47 (0.33, 0.67)	<.001	
Presence of risk factor: Device Dependence							
Yes	0/ 4 (0.0)		0/ 3 (0.0)				
No	43/ 930 (4.6)		91/ 953 (9.5)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Analysis of Serious Adverse Events - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/ N (%)	Median	(95% CI) [1]	n/ N (%)	Median	(95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Age									0.3841
< 65	13/ 804 (1.6)	NE (NE , NE)		43/ 816 (5.3)	NE (NE , NE)		0.30 (0.16, 0.56)	<.001	
>= 65	4/ 140 (2.9)	NE (NE , NE)		23/ 148 (15.5)	NE (NE , NE)		0.17 (0.06, 0.50)	0.00	
Gender									0.6189
Male	11/ 474 (2.3)	NE (NE , NE)		40/ 510 (7.8)	NE (NE , NE)		0.29 (0.15, 0.56)	<.001	
Female	6/ 470 (1.3)	NE (NE , NE)		26/ 454 (5.7)	NE (NE , NE)		0.22 (0.09, 0.53)	<.001	
Geographic region									0.6301
United States	5/ 387 (1.3)	NE (NE , NE)		14/ 395 (3.5)	NE (NE , NE)		0.36 (0.13, 1.00)	0.05	
Europe	7/ 322 (2.2)	NE (NE , NE)		38/ 321 (11.8)	NE (NE , NE)		0.18 (0.08, 0.39)	<.001	
India	0/ 74 (0.0)	NE (NE , NE)		0/ 78 (0.0)	NE (NE , NE)		NE	NE	
Rest of World	5/ 161 (3.1)	NE (NE , NE)		14/ 170 (8.2)	NE (NE , NE)		0.37 (0.13, 1.03)	0.05	
COVID-19 therapeutic mAb treatment at randomisation									0.8197
Yes	1/ 60 (1.7)	NE (NE , NE)		3/ 60 (5.0)	NE (NE , NE)		0.33 (0.03, 3.20)	0.34	
No	16/ 884 (1.8)	NE (NE , NE)		63/ 904 (7.0)	NE (NE , NE)		0.25 (0.15, 0.44)	<.001	
Baseline viral load 1									0.2124
< 10 ⁴ copies/mL	2/ 340 (0.6)	NE (NE , NE)		3/ 356 (0.8)	NE (NE , NE)		0.70 (0.12, 4.19)	0.69	
>= 10 ⁴ copies/mL	13/ 579 (2.2)	NE (NE , NE)		60/ 582 (10.3)	NE (NE , NE)		0.21 (0.12, 0.38)	<.001	
Baseline viral load 2									0.1826
< 10 ⁷ copies/mL	11/ 663 (1.7)	NE (NE , NE)		37/ 707 (5.2)	NE (NE , NE)		0.31 (0.16, 0.61)	<.001	
>= 10 ⁷ copies/mL	4/ 256 (1.6)	NE (NE , NE)		26/ 231 (11.3)	NE (NE , NE)		0.13 (0.05, 0.38)	<.001	
Baseline serology status									0.5223
Negative	13/ 439 (3.0)	NE (NE , NE)		55/ 457 (12.0)	NE (NE , NE)		0.24 (0.13, 0.43)	<.001	
Positive	4/ 494 (0.8)	NE (NE , NE)		11/ 495 (2.2)	NE (NE , NE)		0.36 (0.12, 1.14)	0.08	
Symptom onset days to first dose date									0.4539
<= 3	10/ 637 (1.6)	NE (NE , NE)		44/ 632 (7.0)	NE (NE , NE)		0.22 (0.11, 0.44)	<.001	
> 3	7/ 307 (2.3)	NE (NE , NE)		22/ 332 (6.6)	NE (NE , NE)		0.34 (0.14, 0.79)	0.01	
BMI group									0.9206
< 25	3/ 216 (1.4)	NE (NE , NE)		11/ 213 (5.2)	NE (NE , NE)		0.27 (0.07, 0.95)	0.04	
25 - < 30	5/ 324 (1.5)	NE (NE , NE)		23/ 336 (6.8)	NE (NE , NE)		0.22 (0.08, 0.58)	0.00	
>= 30	9/ 403 (2.2)	NE (NE , NE)		32/ 415 (7.7)	NE (NE , NE)		0.28 (0.13, 0.59)	<.001	
Ethnicity									0.8018
White	14/ 712 (2.0)	NE (NE , NE)		55/ 725 (7.6)	NE (NE , NE)		0.25 (0.14, 0.46)	<.001	
Black or African American	1/ 45 (2.2)	NE (NE , NE)		1/ 42 (2.4)	NE (NE , NE)		0.92 (0.06, 14.74)	0.95	
Asian	1/ 118 (0.8)	NE (NE , NE)		4/ 127 (3.1)	NE (NE , NE)		0.27 (0.03, 2.40)	0.23	
Others	1/ 69 (1.4)	NE (NE , NE)		6/ 70 (8.6)	NE (NE , NE)		0.16 (0.02, 1.37)	0.09	
Number of baseline comorbidities present									0.3311
0-1	7/ 720 (1.0)	NE (NE , NE)		40/ 734 (5.4)	NE (NE , NE)		0.18 (0.08, 0.39)	<.001	
2-3	10/ 220 (4.5)	NE (NE , NE)		25/ 224 (11.2)	NE (NE , NE)		0.40 (0.19, 0.83)	0.01	
>= 4	0/ 4 (0.0)	NE (NE , NE)		1/ 6 (16.7)	NE (6.0, NE)		NE	NE	
Presence of risk factor: Smoking									0.2255
Yes	7/ 423 (1.7)	NE (NE , NE)		18/ 442 (4.1)	NE (NE , NE)		0.40 (0.17, 0.97)	0.04	
No	10/ 519 (1.9)	NE (NE , NE)		48/ 522 (9.2)	NE (NE , NE)		0.20 (0.10, 0.40)	<.001	

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RRI-conform mITT2 Analysis set
Analysis of Serious Adverse Events - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
	n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Presence of risk factor: Diabetes mellitus							0.0340
Yes	7/ 135 (5.2)	NE (NE , NE)	11/ 137 (8.0)	NE (NE , NE)	0.64 (0.25, 1.65)	0.35	
No	10/ 808 (1.2)	NE (NE , NE)	55/ 827 (6.7)	NE (NE , NE)	0.18 (0.09, 0.36)	<.001	
Presence of risk factor: Immunosuppression							0.9991
Yes	0/ 6 (0.0)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE	NE	
No	17/ 937 (1.8)	NE (NE , NE)	66/ 957 (6.9)	NE (NE , NE)	0.26 (0.15, 0.44)	<.001	
Presence of risk factor: Chronic lung disease							0.9781
Yes	0/ 62 (0.0)	NE (NE , NE)	2/ 39 (5.1)	NE (NE , NE)	NE	NE	
No	17/ 881 (1.9)	NE (NE , NE)	64/ 925 (6.9)	NE (NE , NE)	0.27 (0.16, 0.47)	<.001	
Presence of risk factor: Hypertension							0.4033
Yes	10/ 358 (2.8)	NE (NE , NE)	46/ 375 (12.3)	NE (NE , NE)	0.22 (0.11, 0.43)	<.001	
No	7/ 585 (1.2)	NE (NE , NE)	20/ 589 (3.4)	NE (NE , NE)	0.35 (0.15, 0.83)	0.01	
Presence of risk factor: Cardiovascular disorder							0.9148
Yes	3/ 42 (7.1)	NE (NE , NE)	13/ 49 (26.5)	NE (NE , NE)	0.24 (0.07, 0.85)	0.02	
No	14/ 901 (1.6)	NE (NE , NE)	53/ 915 (5.8)	NE (NE , NE)	0.26 (0.15, 0.48)	<.001	
Presence of risk factor: Chronic kidney disease							0.9832
Yes	0/ 6 (0.0)	NE (NE , NE)	1/ 8 (12.5)	NE (6.0, NE)	NE	NE	
No	17/ 937 (1.8)	NE (NE , NE)	65/ 956 (6.8)	NE (NE , NE)	0.26 (0.15, 0.45)	<.001	
Presence of risk factor: HIV Infection							
Yes	0		0/ 1 (0.0)				
No	17/ 943 (1.8)		66/ 962 (6.9)				
Presence of risk factor: Sickle Cell Disease							
No	17/ 943 (1.8)		66/ 964 (6.8)				
Presence of risk factor: Neurodevelopmental Disorder							
Yes	0/ 2 (0.0)		0/ 1 (0.0)				
No	17/ 941 (1.8)		66/ 963 (6.9)				
Presence of risk factor: Cancer							0.9991
Yes	0/ 5 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
No	17/ 938 (1.8)	NE (NE , NE)	66/ 958 (6.9)	NE (NE , NE)	0.26 (0.15, 0.44)	<.001	
Presence of risk factor: Device Dependence							
Yes	0/ 4 (0.0)		0/ 3 (0.0)				
No	17/ 930 (1.8)		65/ 953 (6.8)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

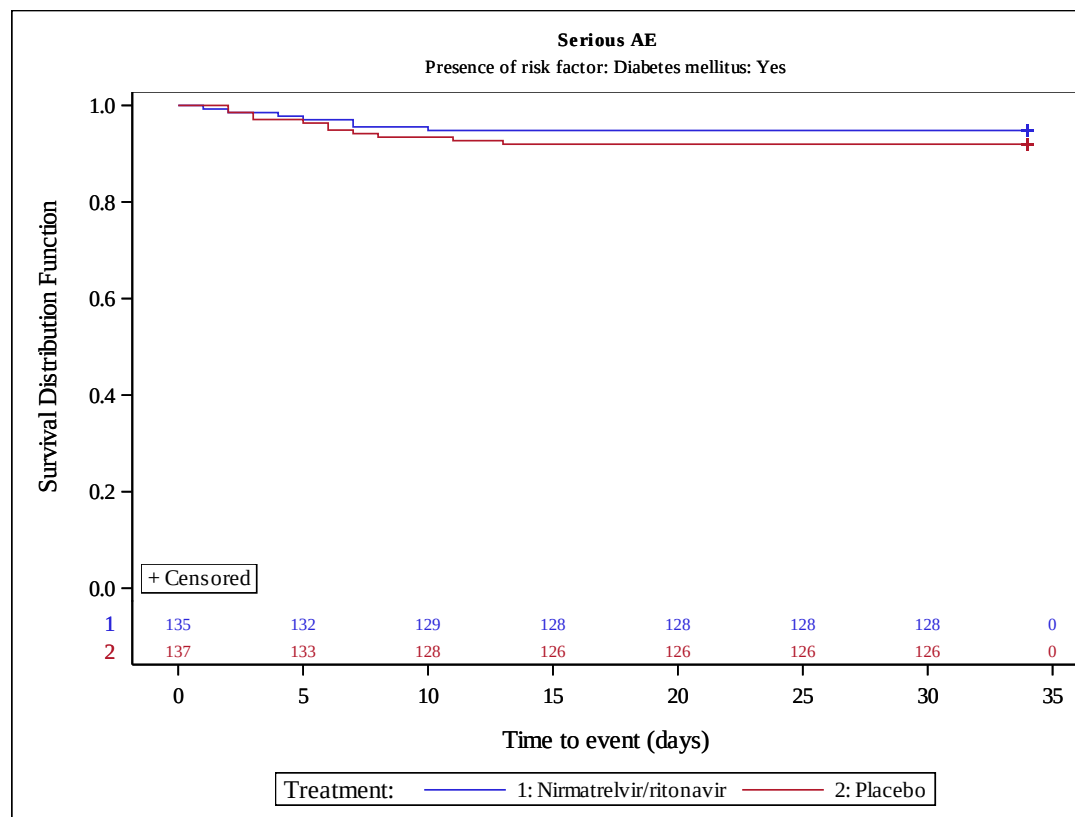
[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Kaplan-Meier Plot of Time to First Serious Adverse Events

Final

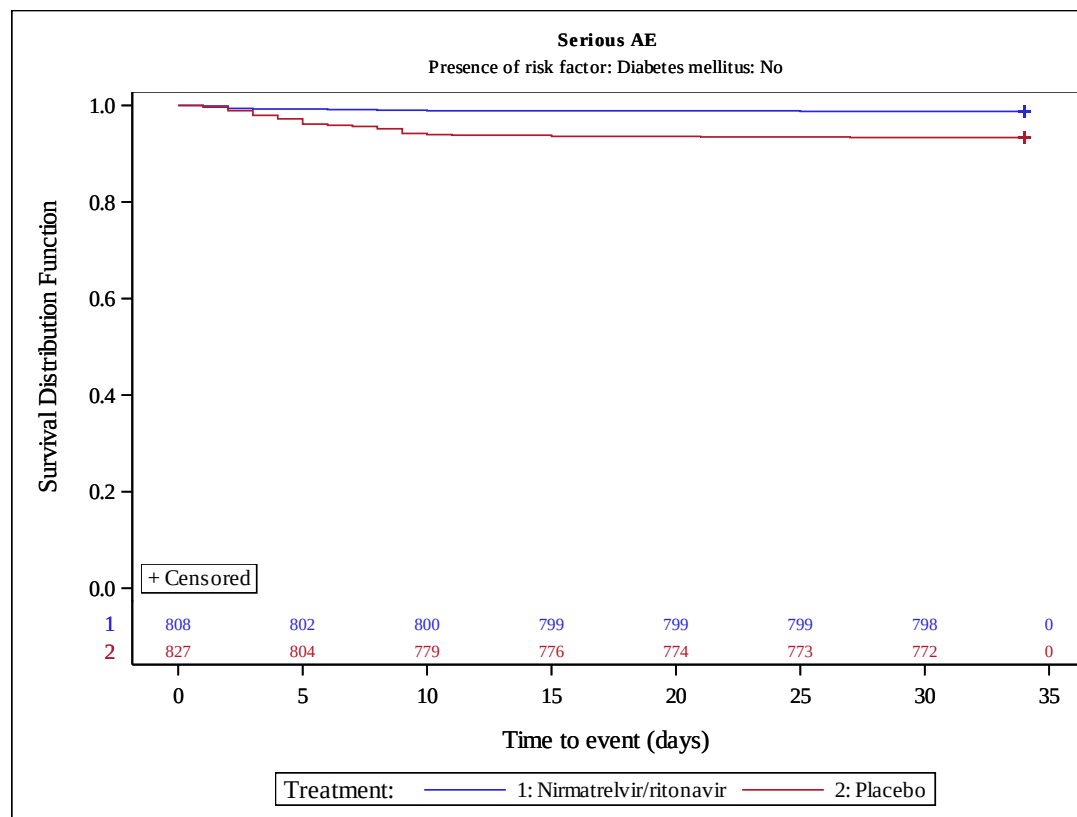


Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Kaplan-Meier Plot of Time to First Serious Adverse Events

Final



Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Analysis of Adverse Events leading to death - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/ N (%)	Median	(95% CI) [1]	n/ N (%)	Median	(95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Age									
< 65	0/ 804 (0.0)			4/ 816 (0.5)					
>= 65	0/ 140 (0.0)			9/ 148 (6.1)					
Gender									
Male	0/ 474 (0.0)			9/ 510 (1.8)					
Female	0/ 470 (0.0)			4/ 454 (0.9)					
Geographic region									
United States	0/ 387 (0.0)			3/ 395 (0.8)					
Europe	0/ 322 (0.0)			9/ 321 (2.8)					
India	0/ 74 (0.0)			0/ 78 (0.0)					
Rest of World	0/ 161 (0.0)			1/ 170 (0.6)					
COVID-19 therapeutic mAb treatment at randomisation									
Yes	0/ 60 (0.0)	NE (NE , NE)		0/ 60 (0.0)	NE (NE , NE)		NE	NE	0.9984
No	0/ 884 (0.0)	NE (NE , NE)		13/ 904 (1.4)	NE (NE , NE)		NE	NE	
Baseline viral load 1									
< 10^4 copies/mL	0/ 340 (0.0)	NE (NE , NE)		0/ 356 (0.0)	NE (NE , NE)		NE	NE	0.9976
>= 10^4 copies/mL	0/ 579 (0.0)	NE (NE , NE)		11/ 582 (1.9)	NE (NE , NE)		NE	NE	
Baseline viral load 2									
< 10^7 copies/mL	0/ 663 (0.0)			4/ 707 (0.6)					
>= 10^7 copies/mL	0/ 256 (0.0)			7/ 231 (3.0)					
Baseline serology status									
Negative	0/ 439 (0.0)	NE (NE , NE)		11/ 457 (2.4)	NE (NE , NE)		NE	NE	0.9995
Positive	0/ 494 (0.0)	NE (NE , NE)		2/ 495 (0.4)	NE (NE , NE)		NE	NE	
Symptom onset days to first dose date									
<= 3	0/ 637 (0.0)			9/ 632 (1.4)					
> 3	0/ 307 (0.0)			4/ 332 (1.2)					
BMI group									
< 25	0/ 216 (0.0)			2/ 213 (0.9)					
25 - < 30	0/ 324 (0.0)			4/ 336 (1.2)					
>= 30	0/ 403 (0.0)			7/ 415 (1.7)					
Ethnicity									
White	0/ 712 (0.0)	NE (NE , NE)		11/ 725 (1.5)	NE (NE , NE)		NE	NE	1.0000
Black or African American	0/ 45 (0.0)	NE (NE , NE)		1/ 42 (2.4)	NE (NE , NE)		NE	NE	
Asian	0/ 118 (0.0)	NE (NE , NE)		0/ 127 (0.0)	NE (NE , NE)		NE	NE	
Others	0/ 69 (0.0)	NE (NE , NE)		1/ 70 (1.4)	NE (NE , NE)		NE	NE	
Number of baseline comorbidities present									
0-1	0/ 720 (0.0)			6/ 734 (0.8)					
2-3	0/ 220 (0.0)			7/ 224 (3.1)					
>= 4	0/ 4 (0.0)			0/ 6 (0.0)					
Presence of risk factor: Smoking									
Yes	0/ 423 (0.0)	NE (NE , NE)		2/ 442 (0.5)	NE (NE , NE)		NE	NE	0.9995
No	0/ 519 (0.0)	NE (NE , NE)		11/ 522 (2.1)	NE (NE , NE)		NE	NE	

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[1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/ N (%)	Median	(95% CI) [1]	n/ N (%)	Median	(95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Presence of risk factor: Diabetes mellitus									
Yes	0/ 135 (0.0)			4/ 137 (2.9)					
No	0/ 808 (0.0)			9/ 827 (1.1)					
Presence of risk factor: Immunosuppression									0.9995
Yes	0/ 6 (0.0)	NE (NE , NE)		0/ 7 (0.0)	NE (NE , NE)		NE	NE	
No	0/ 937 (0.0)	NE (NE , NE)		13/ 957 (1.4)	NE (NE , NE)		NE	NE	
Presence of risk factor: Chronic lung disease									0.9986
Yes	0/ 62 (0.0)	NE (NE , NE)		0/ 39 (0.0)	NE (NE , NE)		NE	NE	
No	0/ 881 (0.0)	NE (NE , NE)		13/ 925 (1.4)	NE (NE , NE)		NE	NE	
Presence of risk factor: Hypertension									0.9989
Yes	0/ 358 (0.0)	NE (NE , NE)		12/ 375 (3.2)	NE (NE , NE)		NE	NE	
No	0/ 585 (0.0)	NE (NE , NE)		1/ 589 (0.2)	NE (NE , NE)		NE	NE	
Presence of risk factor: Cardiovascular disorder									0.9999
Yes	0/ 42 (0.0)	NE (NE , NE)		3/ 49 (6.1)	NE (NE , NE)		NE	NE	
No	0/ 901 (0.0)	NE (NE , NE)		10/ 915 (1.1)	NE (NE , NE)		NE	NE	
Presence of risk factor: Chronic kidney disease									0.9995
Yes	0/ 6 (0.0)	NE (NE , NE)		0/ 8 (0.0)	NE (NE , NE)		NE	NE	
No	0/ 937 (0.0)	NE (NE , NE)		13/ 956 (1.4)	NE (NE , NE)		NE	NE	
Presence of risk factor: HIV Infection									
Yes	0			0/ 1 (0.0)					
No	0/ 943 (0.0)			13/ 962 (1.4)					
Presence of risk factor: Sickle Cell Disease									
No	0/ 943 (0.0)			13/ 964 (1.3)					
Presence of risk factor: Neurodevelopmental Disorder									
Yes	0/ 2 (0.0)			0/ 1 (0.0)					
No	0/ 941 (0.0)			13/ 963 (1.3)					
Presence of risk factor: Cancer									0.9995
Yes	0/ 5 (0.0)	NE (NE , NE)		0/ 6 (0.0)	NE (NE , NE)		NE	NE	
No	0/ 938 (0.0)	NE (NE , NE)		13/ 958 (1.4)	NE (NE , NE)		NE	NE	
Presence of risk factor: Device Dependence									
Yes	0/ 4 (0.0)			0/ 3 (0.0)					
No	0/ 930 (0.0)			12/ 953 (1.3)					

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Analysis of Adverse Events leading to Discontinuation of Study Drug - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/ N (%)	Median	(95% CI) [1]	n/ N (%)	Median	(95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Age									0.5671
< 65	10/ 804 (1.2)	NE (NE , NE)		27/ 816 (3.3)	NE (NE , NE)		0.37 (0.18, 0.77)	0.00	
>= 65	7/ 140 (5.0)	NE (NE , NE)		14/ 148 (9.5)	NE (NE , NE)		0.53 (0.21, 1.30)	0.16	
Gender									0.1550
Male	6/ 474 (1.3)	NE (NE , NE)		24/ 510 (4.7)	NE (NE , NE)		0.27 (0.11, 0.65)	0.00	
Female	11/ 470 (2.3)	NE (NE , NE)		17/ 454 (3.7)	NE (NE , NE)		0.62 (0.29, 1.33)	0.22	
Geographic region									0.9691
United States	5/ 387 (1.3)	NE (NE , NE)		14/ 395 (3.5)	NE (NE , NE)		0.36 (0.13, 1.00)	0.05	
Europe	9/ 322 (2.8)	NE (NE , NE)		18/ 321 (5.6)	NE (NE , NE)		0.50 (0.22, 1.11)	0.08	
India	0/ 74 (0.0)	NE (NE , NE)		1/ 78 (1.3)	NE (NE , NE)		NE	NE	
Rest of World	3/ 161 (1.9)	NE (NE , NE)		8/ 170 (4.7)	NE (NE , NE)		0.40 (0.11, 1.50)	0.17	
COVID-19 therapeutic mAb treatment at randomisation									0.8957
Yes	1/ 60 (1.7)	NE (NE , NE)		2/ 60 (3.3)	NE (NE , NE)		0.49 (0.04, 5.45)	0.56	
No	16/ 884 (1.8)	NE (NE , NE)		39/ 904 (4.3)	NE (NE , NE)		0.42 (0.23, 0.75)	0.00	
Baseline viral load 1									0.0855
< 10 ⁴ copies/mL	5/ 340 (1.5)	NE (NE , NE)		5/ 356 (1.4)	NE (NE , NE)		1.05 (0.30, 3.62)	0.94	
>= 10 ⁴ copies/mL	11/ 579 (1.9)	NE (NE , NE)		36/ 582 (6.2)	NE (NE , NE)		0.30 (0.15, 0.60)	<.001	
Baseline viral load 2									0.9721
< 10 ⁷ copies/mL	10/ 663 (1.5)	NE (NE , NE)		27/ 707 (3.8)	NE (NE , NE)		0.39 (0.19, 0.81)	0.01	
>= 10 ⁷ copies/mL	6/ 256 (2.3)	NE (NE , NE)		14/ 231 (6.1)	NE (NE , NE)		0.38 (0.15, 1.00)	0.05	
Baseline serology status									0.2233
Negative	10/ 439 (2.3)	NE (NE , NE)		31/ 457 (6.8)	NE (NE , NE)		0.33 (0.16, 0.68)	0.00	
Positive	7/ 494 (1.4)	NE (NE , NE)		10/ 495 (2.0)	NE (NE , NE)		0.70 (0.27, 1.84)	0.47	
Symptom onset days to first dose date									0.5082
<= 3	9/ 637 (1.4)	NE (NE , NE)		17/ 632 (2.7)	NE (NE , NE)		0.52 (0.23, 1.18)	0.11	
> 3	8/ 307 (2.6)	NE (NE , NE)		24/ 332 (7.2)	NE (NE , NE)		0.36 (0.16, 0.79)	0.01	
BMI group									0.0785
< 25	7/ 216 (3.2)	NE (NE , NE)		6/ 213 (2.8)	NE (NE , NE)		1.16 (0.39, 3.45)	0.78	
25 - < 30	3/ 324 (0.9)	NE (NE , NE)		17/ 336 (5.1)	NE (NE , NE)		0.18 (0.05, 0.62)	0.00	
>= 30	7/ 403 (1.7)	NE (NE , NE)		18/ 415 (4.3)	NE (NE , NE)		0.40 (0.17, 0.95)	0.03	
Ethnicity									0.9703
White	15/ 712 (2.1)	NE (NE , NE)		33/ 725 (4.6)	NE (NE , NE)		0.46 (0.25, 0.85)	0.01	
Black or African American	1/ 45 (2.2)	NE (NE , NE)		1/ 42 (2.4)	NE (NE , NE)		0.92 (0.06, 14.74)	0.95	
Asian	1/ 118 (0.8)	NE (NE , NE)		2/ 127 (1.6)	NE (NE , NE)		0.54 (0.05, 5.94)	0.61	
Others	0/ 69 (0.0)	NE (NE , NE)		5/ 70 (7.1)	NE (NE , NE)		NE	NE	
Number of baseline comorbidities present									0.9473
0-1	10/ 720 (1.4)	NE (NE , NE)		26/ 734 (3.5)	NE (NE , NE)		0.39 (0.19, 0.81)	0.01	
2-3	7/ 220 (3.2)	NE (NE , NE)		15/ 224 (6.7)	NE (NE , NE)		0.47 (0.19, 1.16)	0.10	
>= 4	0/ 4 (0.0)	NE (NE , NE)		0/ 6 (0.0)	NE (NE , NE)		NE	NE	
Presence of risk factor: Smoking									0.7559
Yes	3/ 423 (0.7)	NE (NE , NE)		9/ 442 (2.0)	NE (NE , NE)		0.35 (0.09, 1.28)	0.11	
No	14/ 519 (2.7)	NE (NE , NE)		32/ 522 (6.1)	NE (NE , NE)		0.44 (0.23, 0.82)	0.01	

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N: Number of participants, CI: Confidence Interval, NE: Not estimable

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 Analysis of Adverse Events leading to Discontinuation of Study Drug - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
	n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Presence of risk factor: Diabetes mellitus							0.8573
Yes	3/ 135 (2.2)	NE (NE , NE)	8/ 137 (5.8)	NE (NE , NE)	0.38 (0.10, 1.43)	0.15	
No	14/ 808 (1.7)	NE (NE , NE)	33/ 827 (4.0)	NE (NE , NE)	0.43 (0.23, 0.81)	0.00	
Presence of risk factor: Immunosuppression							0.9995
Yes	0/ 6 (0.0)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE	NE	
No	17/ 937 (1.8)	NE (NE , NE)	41/ 957 (4.3)	NE (NE , NE)	0.42 (0.24, 0.74)	0.00	
Presence of risk factor: Chronic lung disease							0.9824
Yes	2/ 62 (3.2)	NE (NE , NE)	0/ 39 (0.0)	NE (NE , NE)	NE	NE	
No	15/ 881 (1.7)	NE (NE , NE)	41/ 925 (4.4)	NE (NE , NE)	0.38 (0.21, 0.69)	0.00	
Presence of risk factor: Hypertension							0.2918
Yes	9/ 358 (2.5)	NE (NE , NE)	28/ 375 (7.5)	NE (NE , NE)	0.33 (0.16, 0.70)	0.00	
No	8/ 585 (1.4)	NE (NE , NE)	13/ 589 (2.2)	NE (NE , NE)	0.62 (0.26, 1.49)	0.28	
Presence of risk factor: Cardiovascular disorder							0.1923
Yes	4/ 42 (9.5)	NE (NE , NE)	5/ 49 (10.2)	NE (NE , NE)	0.97 (0.26, 3.62)	0.96	
No	13/ 901 (1.4)	NE (NE , NE)	36/ 915 (3.9)	NE (NE , NE)	0.36 (0.19, 0.69)	0.00	
Presence of risk factor: Chronic kidney disease							0.9850
Yes	0/ 6 (0.0)	NE (NE , NE)	1/ 8 (12.5)	NE (1.0, NE)	NE	NE	
No	17/ 937 (1.8)	NE (NE , NE)	40/ 956 (4.2)	NE (NE , NE)	0.43 (0.24, 0.76)	0.00	
Presence of risk factor: HIV Infection							
Yes	0		0/ 1 (0.0)				
No	17/ 943 (1.8)		41/ 962 (4.3)				
Presence of risk factor: Sickie Cell Disease							
No	17/ 943 (1.8)		41/ 964 (4.3)				
Presence of risk factor: Neurodevelopmental Disorder							
Yes	0/ 2 (0.0)		0/ 1 (0.0)				
No	17/ 941 (1.8)		41/ 963 (4.3)				
Presence of risk factor: Cancer							0.9826
Yes	2/ 5 (40.0)	NE (1.0, NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
No	15/ 938 (1.6)	NE (NE , NE)	41/ 958 (4.3)	NE (NE , NE)	0.37 (0.21, 0.67)	0.00	
Presence of risk factor: Device Dependence							
Yes	0/ 4 (0.0)		0/ 3 (0.0)				
No	17/ 930 (1.8)		40/ 953 (4.2)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/	N (%)	Median (95% CI) [1]	n/	N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Age									
< 65	2/	804 (0.2)		2/	816 (0.2)				
>= 65	1/	140 (0.7)		2/	148 (1.4)				
Gender									
Male	0/	474 (0.0)		0/	510 (0.0)				
Female	3/	470 (0.6)		4/	454 (0.9)				
Geographic region									
United States	2/	387 (0.5)		0/	395 (0.0)				
Europe	1/	322 (0.3)		2/	321 (0.6)				
India	0/	74 (0.0)		0/	78 (0.0)				
Rest of World	0/	161 (0.0)		2/	170 (1.2)				
COVID-19 therapeutic mAb treatment at randomisation									
Yes	1/	60 (1.7)		0/	60 (0.0)				
No	2/	884 (0.2)		4/	904 (0.4)				
Baseline viral load 1									
< 10^4 copies/mL	1/	340 (0.3)		1/	356 (0.3)				
>= 10^4 copies/mL	2/	579 (0.3)		3/	582 (0.5)				
Baseline viral load 2									
< 10^7 copies/mL	2/	663 (0.3)		2/	707 (0.3)				
>= 10^7 copies/mL	1/	256 (0.4)		2/	231 (0.9)				
Baseline serology status									
Negative	1/	439 (0.2)		2/	457 (0.4)				
Positive	2/	494 (0.4)		2/	495 (0.4)				
Symptom onset days to first dose date									
<= 3	2/	637 (0.3)		4/	632 (0.6)				
> 3	1/	307 (0.3)		0/	332 (0.0)				
BMI group									
< 25	1/	216 (0.5)		1/	213 (0.5)				
25 - < 30	1/	324 (0.3)		1/	336 (0.3)				
>= 30	1/	403 (0.2)		2/	415 (0.5)				
Ethnicity									
White	2/	712 (0.3)		2/	725 (0.3)				
Black or African American	1/	45 (2.2)		0/	42 (0.0)				
Asian	0/	118 (0.0)		0/	127 (0.0)				
Others	0/	69 (0.0)		2/	70 (2.9)				
Number of baseline comorbidities present									
0-1	2/	720 (0.3)		3/	734 (0.4)				
2-3	1/	220 (0.5)		1/	224 (0.4)				
>= 4	0/	4 (0.0)		0/	6 (0.0)				
Presence of risk factor: Smoking									
Yes	0/	423 (0.0)		3/	442 (0.7)				
No	3/	519 (0.6)		1/	522 (0.2)				

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/	N (%)	Median (95% CI) [1]	n/	N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Presence of risk factor: Diabetes mellitus									
Yes	0/	135 (0.0)		0/	137 (0.0)				
No	3/	808 (0.4)		4/	827 (0.5)				
Presence of risk factor: Immunosuppression									
Yes	0/	6 (0.0)		0/	7 (0.0)				
No	3/	937 (0.3)		4/	957 (0.4)				
Presence of risk factor: Chronic lung disease									
Yes	1/	62 (1.6)		0/	39 (0.0)				
No	2/	881 (0.2)		4/	925 (0.4)				
Presence of risk factor: Hypertension									
Yes	1/	358 (0.3)		2/	375 (0.5)				
No	2/	585 (0.3)		2/	589 (0.3)				
Presence of risk factor: Cardiovascular disorder									
Yes	1/	42 (2.4)		0/	49 (0.0)				
No	2/	901 (0.2)		4/	915 (0.4)				
Presence of risk factor: Chronic kidney disease									
Yes	0/	6 (0.0)		0/	8 (0.0)				
No	3/	937 (0.3)		4/	956 (0.4)				
Presence of risk factor: HIV Infection									
Yes	0			0/	1 (0.0)				
No	3/	943 (0.3)		4/	962 (0.4)				
Presence of risk factor: Sickle Cell Disease									
No	3/	943 (0.3)		4/	964 (0.4)				
Presence of risk factor: Neurodevelopmental Disorder									
Yes	0/	2 (0.0)		0/	1 (0.0)				
No	3/	941 (0.3)		4/	963 (0.4)				
Presence of risk factor: Cancer									
Yes	0/	5 (0.0)		0/	6 (0.0)				
No	3/	938 (0.3)		4/	958 (0.4)				
Presence of risk factor: Device Dependence									
Yes	0/	4 (0.0)		0/	3 (0.0)				
No	3/	930 (0.3)		4/	953 (0.4)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

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Analysis of Adverse Events of Special Interest: Arrhythmia related Investigations, Signs and Symptoms (SMQ) - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/	N (%)	Median (95% CI) [1]	n/	N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Age									
< 65	0/	804 (0.0)		1/	816 (0.1)				
>= 65	1/	140 (0.7)		1/	148 (0.7)				
Gender									
Male	0/	474 (0.0)		0/	510 (0.0)				
Female	1/	470 (0.2)		2/	454 (0.4)				
Geographic region									
United States	0/	387 (0.0)		2/	395 (0.5)				
Europe	1/	322 (0.3)		0/	321 (0.0)				
India	0/	74 (0.0)		0/	78 (0.0)				
Rest of World	0/	161 (0.0)		0/	170 (0.0)				
COVID-19 therapeutic mAb treatment at randomisation									
Yes	0/	60 (0.0)		0/	60 (0.0)				
No	1/	884 (0.1)		2/	904 (0.2)				
Baseline viral load 1									
< 10^4 copies/mL	1/	340 (0.3)		1/	356 (0.3)				
>= 10^4 copies/mL	0/	579 (0.0)		1/	582 (0.2)				
Baseline viral load 2									
< 10^7 copies/mL	1/	663 (0.2)		2/	707 (0.3)				
>= 10^7 copies/mL	0/	256 (0.0)		0/	231 (0.0)				
Baseline serology status									
Negative	0/	439 (0.0)		1/	457 (0.2)				
Positive	1/	494 (0.2)		1/	495 (0.2)				
Symptom onset days to first dose date									
<= 3	1/	637 (0.2)		2/	632 (0.3)				
> 3	0/	307 (0.0)		0/	332 (0.0)				
BMI group									
< 25	1/	216 (0.5)		0/	213 (0.0)				
25 - < 30	0/	324 (0.0)		1/	336 (0.3)				
>= 30	0/	403 (0.0)		1/	415 (0.2)				
Ethnicity									
White	1/	712 (0.1)		2/	725 (0.3)				
Black or African American	0/	45 (0.0)		0/	42 (0.0)				
Asian	0/	118 (0.0)		0/	127 (0.0)				
Others	0/	69 (0.0)		0/	70 (0.0)				
Number of baseline comorbidities present									
0-1	1/	720 (0.1)		2/	734 (0.3)				
2-3	0/	220 (0.0)		0/	224 (0.0)				
>= 4	0/	4 (0.0)		0/	6 (0.0)				
Presence of risk factor: Smoking									
Yes	0/	423 (0.0)		0/	442 (0.0)				
No	1/	519 (0.2)		2/	522 (0.4)				

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 Analysis of Adverse Events of Special Interest: Arrhythmia related Investigations, Signs and Symptoms (SMQ) - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/	N (%)	Median (95% CI)[1]	n/	N (%)	Median (95% CI)[1]	Hazard Ratio (95% CI)[2]	p-Value[2]	
Presence of risk factor: Diabetes mellitus									
Yes	0/	135 (0.0)		0/	137 (0.0)				
No	1/	808 (0.1)		2/	827 (0.2)				
Presence of risk factor: Immunosuppression									
Yes	0/	6 (0.0)		0/	7 (0.0)				
No	1/	937 (0.1)		2/	957 (0.2)				
Presence of risk factor: Chronic lung disease									
Yes	0/	62 (0.0)		0/	39 (0.0)				
No	1/	881 (0.1)		2/	925 (0.2)				
Presence of risk factor: Hypertension									
Yes	1/	358 (0.3)		1/	375 (0.3)				
No	0/	585 (0.0)		1/	589 (0.2)				
Presence of risk factor: Cardiovascular disorder									
Yes	0/	42 (0.0)		0/	49 (0.0)				
No	1/	901 (0.1)		2/	915 (0.2)				
Presence of risk factor: Chronic kidney disease									
Yes	0/	6 (0.0)		0/	8 (0.0)				
No	1/	937 (0.1)		2/	956 (0.2)				
Presence of risk factor: HIV Infection									
Yes	0			0/	1 (0.0)				
No	1/	943 (0.1)		2/	962 (0.2)				
Presence of risk factor: Sickle Cell Disease									
No	1/	943 (0.1)		2/	964 (0.2)				
Presence of risk factor: Neurodevelopmental Disorder									
Yes	0/	2 (0.0)		0/	1 (0.0)				
No	1/	941 (0.1)		2/	963 (0.2)				
Presence of risk factor: Cancer									
Yes	0/	5 (0.0)		0/	6 (0.0)				
No	1/	938 (0.1)		2/	958 (0.2)				
Presence of risk factor: Device Dependence									
Yes	0/	4 (0.0)		0/	3 (0.0)				
No	1/	930 (0.1)		2/	953 (0.2)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
RKI-conform mITT2 Analysis set
Analysis of Serious Adverse Events of Special Interest: Arrhythmia related Investigations, Signs and Symptoms (SMQ) - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/	N (%)	Median (95% CI) [1]	n/	N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Age									
< 65	0/	804 (0.0)		0/	816 (0.0)				
>= 65	0/	140 (0.0)		0/	148 (0.0)				
Gender									
Male	0/	474 (0.0)		0/	510 (0.0)				
Female	0/	470 (0.0)		0/	454 (0.0)				
Geographic region									
United States	0/	387 (0.0)		0/	395 (0.0)				
Europe	0/	322 (0.0)		0/	321 (0.0)				
India	0/	74 (0.0)		0/	78 (0.0)				
Rest of World	0/	161 (0.0)		0/	170 (0.0)				
COVID-19 therapeutic mAb treatment at randomisation									
Yes	0/	60 (0.0)		0/	60 (0.0)				
No	0/	884 (0.0)		0/	904 (0.0)				
Baseline viral load 1									
< 10^4 copies/mL	0/	340 (0.0)		0/	356 (0.0)				
>= 10^4 copies/mL	0/	579 (0.0)		0/	582 (0.0)				
Baseline viral load 2									
< 10^7 copies/mL	0/	663 (0.0)		0/	707 (0.0)				
>= 10^7 copies/mL	0/	256 (0.0)		0/	231 (0.0)				
Baseline serology status									
Negative	0/	439 (0.0)		0/	457 (0.0)				
Positive	0/	494 (0.0)		0/	495 (0.0)				
Symptom onset days to first dose date									
<= 3	0/	637 (0.0)		0/	632 (0.0)				
> 3	0/	307 (0.0)		0/	332 (0.0)				
BMI group									
< 25	0/	216 (0.0)		0/	213 (0.0)				
25 - < 30	0/	324 (0.0)		0/	336 (0.0)				
>= 30	0/	403 (0.0)		0/	415 (0.0)				
Ethnicity									
White	0/	712 (0.0)		0/	725 (0.0)				
Black or African American	0/	45 (0.0)		0/	42 (0.0)				
Asian	0/	118 (0.0)		0/	127 (0.0)				
Others	0/	69 (0.0)		0/	70 (0.0)				
Number of baseline comorbidities present									
0-1	0/	720 (0.0)		0/	734 (0.0)				
2-3	0/	220 (0.0)		0/	224 (0.0)				
>= 4	0/	4 (0.0)		0/	6 (0.0)				
Presence of risk factor: Smoking									
Yes	0/	423 (0.0)		0/	442 (0.0)				
No	0/	519 (0.0)		0/	522 (0.0)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Serious Adverse Events of Special Interest: Arrhythmia related Investigations, Signs and Symptoms (SMQ) - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/	N (%)	Median (95% CI) [1]	n/	N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Presence of risk factor: Diabetes mellitus									
Yes	0/	135 (0.0)		0/	137 (0.0)				
No	0/	808 (0.0)		0/	827 (0.0)				
Presence of risk factor: Immunosuppression									
Yes	0/	6 (0.0)		0/	7 (0.0)				
No	0/	937 (0.0)		0/	957 (0.0)				
Presence of risk factor: Chronic lung disease									
Yes	0/	62 (0.0)		0/	39 (0.0)				
No	0/	881 (0.0)		0/	925 (0.0)				
Presence of risk factor: Hypertension									
Yes	0/	358 (0.0)		0/	375 (0.0)				
No	0/	585 (0.0)		0/	589 (0.0)				
Presence of risk factor: Cardiovascular disorder									
Yes	0/	42 (0.0)		0/	49 (0.0)				
No	0/	901 (0.0)		0/	915 (0.0)				
Presence of risk factor: Chronic kidney disease									
Yes	0/	6 (0.0)		0/	8 (0.0)				
No	0/	937 (0.0)		0/	956 (0.0)				
Presence of risk factor: HIV Infection									
Yes	0			0/	1 (0.0)				
No	0/	943 (0.0)		0/	962 (0.0)				
Presence of risk factor: Sickle Cell Disease									
No	0/	943 (0.0)		0/	964 (0.0)				
Presence of risk factor: Neurodevelopmental Disorder									
Yes	0/	2 (0.0)		0/	1 (0.0)				
No	0/	941 (0.0)		0/	963 (0.0)				
Presence of risk factor: Cancer									
Yes	0/	5 (0.0)		0/	6 (0.0)				
No	0/	938 (0.0)		0/	958 (0.0)				
Presence of risk factor: Device Dependence									
Yes	0/	4 (0.0)		0/	3 (0.0)				
No	0/	930 (0.0)		0/	953 (0.0)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Analysis of Severe Adverse Events (DAIDS >=3) of Special Interest: Arrhythmia related Investigations, Signs and Symptoms (SMQ) - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/	N (%)	Median (95% CI)[1]	n/	N (%)	Median (95% CI)[1]	Hazard Ratio (95% CI)[2]	p-Value[2]	
Age									
< 65	0/	804 (0.0)		0/	816 (0.0)				
>= 65	0/	140 (0.0)		0/	148 (0.0)				
Gender									
Male	0/	474 (0.0)		0/	510 (0.0)				
Female	0/	470 (0.0)		0/	454 (0.0)				
Geographic region									
United States	0/	387 (0.0)		0/	395 (0.0)				
Europe	0/	322 (0.0)		0/	321 (0.0)				
India	0/	74 (0.0)		0/	78 (0.0)				
Rest of World	0/	161 (0.0)		0/	170 (0.0)				
COVID-19 therapeutic mAb treatment at randomisation									
Yes	0/	60 (0.0)		0/	60 (0.0)				
No	0/	884 (0.0)		0/	904 (0.0)				
Baseline viral load 1									
< 10^4 copies/mL	0/	340 (0.0)		0/	356 (0.0)				
>= 10^4 copies/mL	0/	579 (0.0)		0/	582 (0.0)				
Baseline viral load 2									
< 10^7 copies/mL	0/	663 (0.0)		0/	707 (0.0)				
>= 10^7 copies/mL	0/	256 (0.0)		0/	231 (0.0)				
Baseline serology status									
Negative	0/	439 (0.0)		0/	457 (0.0)				
Positive	0/	494 (0.0)		0/	495 (0.0)				
Symptom onset days to first dose date									
<= 3	0/	637 (0.0)		0/	632 (0.0)				
> 3	0/	307 (0.0)		0/	332 (0.0)				
BMI group									
< 25	0/	216 (0.0)		0/	213 (0.0)				
25 - < 30	0/	324 (0.0)		0/	336 (0.0)				
>= 30	0/	403 (0.0)		0/	415 (0.0)				
Ethnicity									
White	0/	712 (0.0)		0/	725 (0.0)				
Black or African American	0/	45 (0.0)		0/	42 (0.0)				
Asian	0/	118 (0.0)		0/	127 (0.0)				
Others	0/	69 (0.0)		0/	70 (0.0)				
Number of baseline comorbidities present									
0-1	0/	720 (0.0)		0/	734 (0.0)				
2-3	0/	220 (0.0)		0/	224 (0.0)				
>= 4	0/	4 (0.0)		0/	6 (0.0)				
Presence of risk factor: Smoking									
Yes	0/	423 (0.0)		0/	442 (0.0)				
No	0/	519 (0.0)		0/	522 (0.0)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/	N (%)	Median (95% CI)[1]	n/	N (%)	Median (95% CI)[1]	Hazard Ratio (95% CI)[2]	p-Value[2]	
Presence of risk factor: Diabetes mellitus									
Yes	0/	135 (0.0)		0/	137 (0.0)				
No	0/	808 (0.0)		0/	827 (0.0)				
Presence of risk factor: Immunosuppression									
Yes	0/	6 (0.0)		0/	7 (0.0)				
No	0/	937 (0.0)		0/	957 (0.0)				
Presence of risk factor: Chronic lung disease									
Yes	0/	62 (0.0)		0/	39 (0.0)				
No	0/	881 (0.0)		0/	925 (0.0)				
Presence of risk factor: Hypertension									
Yes	0/	358 (0.0)		0/	375 (0.0)				
No	0/	585 (0.0)		0/	589 (0.0)				
Presence of risk factor: Cardiovascular disorder									
Yes	0/	42 (0.0)		0/	49 (0.0)				
No	0/	901 (0.0)		0/	915 (0.0)				
Presence of risk factor: Chronic kidney disease									
Yes	0/	6 (0.0)		0/	8 (0.0)				
No	0/	937 (0.0)		0/	956 (0.0)				
Presence of risk factor: HIV Infection									
Yes	0			0/	1 (0.0)				
No	0/	943 (0.0)		0/	962 (0.0)				
Presence of risk factor: Sickle Cell Disease									
No	0/	943 (0.0)		0/	964 (0.0)				
Presence of risk factor: Neurodevelopmental Disorder									
Yes	0/	2 (0.0)		0/	1 (0.0)				
No	0/	941 (0.0)		0/	963 (0.0)				
Presence of risk factor: Cancer									
Yes	0/	5 (0.0)		0/	6 (0.0)				
No	0/	938 (0.0)		0/	958 (0.0)				
Presence of risk factor: Device Dependence									
Yes	0/	4 (0.0)		0/	3 (0.0)				
No	0/	930 (0.0)		0/	953 (0.0)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Adverse Events of Special Interest: Cardiac Arrhythmia Terms (incl Bradyarrhythmias and Tachyarrhythmias) (SMQ) - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/	N (%)	Median (95% CI) [1]	n/	N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Age									
< 65	0/	804 (0.0)		3/	816 (0.4)				
>= 65	0/	140 (0.0)		0/	148 (0.0)				
Gender									
Male	0/	474 (0.0)		3/	510 (0.6)				
Female	0/	470 (0.0)		0/	454 (0.0)				
Geographic region									
United States	0/	387 (0.0)		1/	395 (0.3)				
Europe	0/	322 (0.0)		1/	321 (0.3)				
India	0/	74 (0.0)		0/	78 (0.0)				
Rest of World	0/	161 (0.0)		1/	170 (0.6)				
COVID-19 therapeutic mAb treatment at randomisation									
Yes	0/	60 (0.0)		0/	60 (0.0)				
No	0/	884 (0.0)		3/	904 (0.3)				
Baseline viral load 1									
< 10^4 copies/mL	0/	340 (0.0)		0/	356 (0.0)				
>= 10^4 copies/mL	0/	579 (0.0)		3/	582 (0.5)				
Baseline viral load 2									
< 10^7 copies/mL	0/	663 (0.0)		1/	707 (0.1)				
>= 10^7 copies/mL	0/	256 (0.0)		2/	231 (0.9)				
Baseline serology status									
Negative	0/	439 (0.0)		3/	457 (0.7)				
Positive	0/	494 (0.0)		0/	495 (0.0)				
Symptom onset days to first dose date									
<= 3	0/	637 (0.0)		2/	632 (0.3)				
> 3	0/	307 (0.0)		1/	332 (0.3)				
BMI group									
< 25	0/	216 (0.0)		0/	213 (0.0)				
25 - < 30	0/	324 (0.0)		2/	336 (0.6)				
>= 30	0/	403 (0.0)		1/	415 (0.2)				
Ethnicity									
White	0/	712 (0.0)		1/	725 (0.1)				
Black or African American	0/	45 (0.0)		1/	42 (2.4)				
Asian	0/	118 (0.0)		0/	127 (0.0)				
Others	0/	69 (0.0)		1/	70 (1.4)				
Number of baseline comorbidities present									
0-1	0/	720 (0.0)		3/	734 (0.4)				
2-3	0/	220 (0.0)		0/	224 (0.0)				
>= 4	0/	4 (0.0)		0/	6 (0.0)				
Presence of risk factor: Smoking									
Yes	0/	423 (0.0)		0/	442 (0.0)				
No	0/	519 (0.0)		3/	522 (0.6)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/	N (%)	Median (95% CI)[1]	n/	N (%)	Median (95% CI)[1]	Hazard Ratio (95% CI)[2]	p-Value[2]	
Presence of risk factor: Diabetes mellitus									
Yes	0/	135 (0.0)		0/	137 (0.0)				
No	0/	808 (0.0)		3/	827 (0.4)				
Presence of risk factor: Immunosuppression									
Yes	0/	6 (0.0)		0/	7 (0.0)				
No	0/	937 (0.0)		3/	957 (0.3)				
Presence of risk factor: Chronic lung disease									
Yes	0/	62 (0.0)		0/	39 (0.0)				
No	0/	881 (0.0)		3/	925 (0.3)				
Presence of risk factor: Hypertension									
Yes	0/	358 (0.0)		1/	375 (0.3)				
No	0/	585 (0.0)		2/	589 (0.3)				
Presence of risk factor: Cardiovascular disorder									
Yes	0/	42 (0.0)		0/	49 (0.0)				
No	0/	901 (0.0)		3/	915 (0.3)				
Presence of risk factor: Chronic kidney disease									
Yes	0/	6 (0.0)		0/	8 (0.0)				
No	0/	937 (0.0)		3/	956 (0.3)				
Presence of risk factor: HIV Infection									
Yes	0			0/	1 (0.0)				
No	0/	943 (0.0)		3/	962 (0.3)				
Presence of risk factor: Sickle Cell Disease									
No	0/	943 (0.0)		3/	964 (0.3)				
Presence of risk factor: Neurodevelopmental Disorder									
Yes	0/	2 (0.0)		0/	1 (0.0)				
No	0/	941 (0.0)		3/	963 (0.3)				
Presence of risk factor: Cancer									
Yes	0/	5 (0.0)		0/	6 (0.0)				
No	0/	938 (0.0)		3/	958 (0.3)				
Presence of risk factor: Device Dependence									
Yes	0/	4 (0.0)		0/	3 (0.0)				
No	0/	930 (0.0)		2/	953 (0.2)				

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Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/	N (%)	Median (95% CI) [1]	n/	N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
Age									
< 65	0/	804 (0.0)		0/	816 (0.0)				
>= 65	0/	140 (0.0)		0/	148 (0.0)				
Gender									
Male	0/	474 (0.0)		0/	510 (0.0)				
Female	0/	470 (0.0)		0/	454 (0.0)				
Geographic region									
United States	0/	387 (0.0)		0/	395 (0.0)				
Europe	0/	322 (0.0)		0/	321 (0.0)				
India	0/	74 (0.0)		0/	78 (0.0)				
Rest of World	0/	161 (0.0)		0/	170 (0.0)				
COVID-19 therapeutic mAb treatment at randomisation									
Yes	0/	60 (0.0)		0/	60 (0.0)				
No	0/	884 (0.0)		0/	904 (0.0)				
Baseline viral load 1									
< 10^4 copies/mL	0/	340 (0.0)		0/	356 (0.0)				
>= 10^4 copies/mL	0/	579 (0.0)		0/	582 (0.0)				
Baseline viral load 2									
< 10^7 copies/mL	0/	663 (0.0)		0/	707 (0.0)				
>= 10^7 copies/mL	0/	256 (0.0)		0/	231 (0.0)				
Baseline serology status									
Negative	0/	439 (0.0)		0/	457 (0.0)				
Positive	0/	494 (0.0)		0/	495 (0.0)				
Symptom onset days to first dose date									
<= 3	0/	637 (0.0)		0/	632 (0.0)				
> 3	0/	307 (0.0)		0/	332 (0.0)				
BMI group									
< 25	0/	216 (0.0)		0/	213 (0.0)				
25 - < 30	0/	324 (0.0)		0/	336 (0.0)				
>= 30	0/	403 (0.0)		0/	415 (0.0)				
Ethnicity									
White	0/	712 (0.0)		0/	725 (0.0)				
Black or African American	0/	45 (0.0)		0/	42 (0.0)				
Asian	0/	118 (0.0)		0/	127 (0.0)				
Others	0/	69 (0.0)		0/	70 (0.0)				
Number of baseline comorbidities present									
0-1	0/	720 (0.0)		0/	734 (0.0)				
2-3	0/	220 (0.0)		0/	224 (0.0)				
>= 4	0/	4 (0.0)		0/	6 (0.0)				
Presence of risk factor: Smoking									
Yes	0/	423 (0.0)		0/	442 (0.0)				
No	0/	519 (0.0)		0/	522 (0.0)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Serious Adverse Events of Special Interest: Cardiac Arrhythmia Terms (incl Bradyarrhythmias and Tachyarrhythmias) (SMQ) - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/	N (%)	Median (95% CI)[1]	n/	N (%)	Median (95% CI)[1]	Hazard Ratio (95% CI)[2]	p-Value[2]	
Presence of risk factor: Diabetes mellitus									
Yes	0/	135 (0.0)		0/	137 (0.0)				
No	0/	808 (0.0)		0/	827 (0.0)				
Presence of risk factor: Immunosuppression									
Yes	0/	6 (0.0)		0/	7 (0.0)				
No	0/	937 (0.0)		0/	957 (0.0)				
Presence of risk factor: Chronic lung disease									
Yes	0/	62 (0.0)		0/	39 (0.0)				
No	0/	881 (0.0)		0/	925 (0.0)				
Presence of risk factor: Hypertension									
Yes	0/	358 (0.0)		0/	375 (0.0)				
No	0/	585 (0.0)		0/	589 (0.0)				
Presence of risk factor: Cardiovascular disorder									
Yes	0/	42 (0.0)		0/	49 (0.0)				
No	0/	901 (0.0)		0/	915 (0.0)				
Presence of risk factor: Chronic kidney disease									
Yes	0/	6 (0.0)		0/	8 (0.0)				
No	0/	937 (0.0)		0/	956 (0.0)				
Presence of risk factor: HIV Infection									
Yes	0			0/	1 (0.0)				
No	0/	943 (0.0)		0/	962 (0.0)				
Presence of risk factor: Sickle Cell Disease									
No	0/	943 (0.0)		0/	964 (0.0)				
Presence of risk factor: Neurodevelopmental Disorder									
Yes	0/	2 (0.0)		0/	1 (0.0)				
No	0/	941 (0.0)		0/	963 (0.0)				
Presence of risk factor: Cancer									
Yes	0/	5 (0.0)		0/	6 (0.0)				
No	0/	938 (0.0)		0/	958 (0.0)				
Presence of risk factor: Device Dependence									
Yes	0/	4 (0.0)		0/	3 (0.0)				
No	0/	930 (0.0)		0/	953 (0.0)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Analysis of Severe Adverse Events (DAIDS >=3) of Special Interest: Cardiac Arrhythmia Terms (incl Bradyarrhythmias and Tachyarrhythmias) (SMQ) - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/	N (%)	Median (95% CI)[1]	n/	N (%)	Median (95% CI)[1]	Hazard Ratio (95% CI)[2]	p-Value[2]	
Age									
< 65	0/	804 (0.0)		1/	816 (0.1)				
>= 65	0/	140 (0.0)		0/	148 (0.0)				
Gender									
Male	0/	474 (0.0)		1/	510 (0.2)				
Female	0/	470 (0.0)		0/	454 (0.0)				
Geographic region									
United States	0/	387 (0.0)		1/	395 (0.3)				
Europe	0/	322 (0.0)		0/	321 (0.0)				
India	0/	74 (0.0)		0/	78 (0.0)				
Rest of World	0/	161 (0.0)		0/	170 (0.0)				
COVID-19 therapeutic mAb treatment at randomisation									
Yes	0/	60 (0.0)		0/	60 (0.0)				
No	0/	884 (0.0)		1/	904 (0.1)				
Baseline viral load 1									
< 10^4 copies/mL	0/	340 (0.0)		0/	356 (0.0)				
>= 10^4 copies/mL	0/	579 (0.0)		1/	582 (0.2)				
Baseline viral load 2									
< 10^7 copies/mL	0/	663 (0.0)		1/	707 (0.1)				
>= 10^7 copies/mL	0/	256 (0.0)		0/	231 (0.0)				
Baseline serology status									
Negative	0/	439 (0.0)		1/	457 (0.2)				
Positive	0/	494 (0.0)		0/	495 (0.0)				
Symptom onset days to first dose date									
<= 3	0/	637 (0.0)		0/	632 (0.0)				
> 3	0/	307 (0.0)		1/	332 (0.3)				
BMI group									
< 25	0/	216 (0.0)		0/	213 (0.0)				
25 - < 30	0/	324 (0.0)		0/	336 (0.0)				
>= 30	0/	403 (0.0)		1/	415 (0.2)				
Ethnicity									
White	0/	712 (0.0)		0/	725 (0.0)				
Black or African American	0/	45 (0.0)		1/	42 (2.4)				
Asian	0/	118 (0.0)		0/	127 (0.0)				
Others	0/	69 (0.0)		0/	70 (0.0)				
Number of baseline comorbidities present									
0-1	0/	720 (0.0)		1/	734 (0.1)				
2-3	0/	220 (0.0)		0/	224 (0.0)				
>= 4	0/	4 (0.0)		0/	6 (0.0)				
Presence of risk factor: Smoking									
Yes	0/	423 (0.0)		0/	442 (0.0)				
No	0/	519 (0.0)		1/	522 (0.2)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Severe Adverse Events (DAIDS >=3) of Special Interest: Cardiac Arrhythmia Terms (incl Bradyarrhythmias and Tachyarrhythmias) (SMQ) - Subgroup analysis

Final

Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
	n/	N (%)	Median (95% CI)[1]	n/	N (%)	Median (95% CI)[1]	Hazard Ratio (95% CI)[2]	p-Value[2]	
Presence of risk factor: Diabetes mellitus									
Yes	0/	135 (0.0)		0/	137 (0.0)				
No	0/	808 (0.0)		1/	827 (0.1)				
Presence of risk factor: Immunosuppression									
Yes	0/	6 (0.0)		0/	7 (0.0)				
No	0/	937 (0.0)		1/	957 (0.1)				
Presence of risk factor: Chronic lung disease									
Yes	0/	62 (0.0)		0/	39 (0.0)				
No	0/	881 (0.0)		1/	925 (0.1)				
Presence of risk factor: Hypertension									
Yes	0/	358 (0.0)		1/	375 (0.3)				
No	0/	585 (0.0)		0/	589 (0.0)				
Presence of risk factor: Cardiovascular disorder									
Yes	0/	42 (0.0)		0/	49 (0.0)				
No	0/	901 (0.0)		1/	915 (0.1)				
Presence of risk factor: Chronic kidney disease									
Yes	0/	6 (0.0)		0/	8 (0.0)				
No	0/	937 (0.0)		1/	956 (0.1)				
Presence of risk factor: HIV Infection									
Yes	0			0/	1 (0.0)				
No	0/	943 (0.0)		1/	962 (0.1)				
Presence of risk factor: Sickle Cell Disease									
No	0/	943 (0.0)		1/	964 (0.1)				
Presence of risk factor: Neurodevelopmental Disorder									
Yes	0/	2 (0.0)		0/	1 (0.0)				
No	0/	941 (0.0)		1/	963 (0.1)				
Presence of risk factor: Cancer									
Yes	0/	5 (0.0)		0/	6 (0.0)				
No	0/	938 (0.0)		1/	958 (0.1)				
Presence of risk factor: Device Dependence									
Yes	0/	4 (0.0)		0/	3 (0.0)				
No	0/	930 (0.0)		1/	953 (0.1)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Adverse Events excluding Progression-related Events

Final

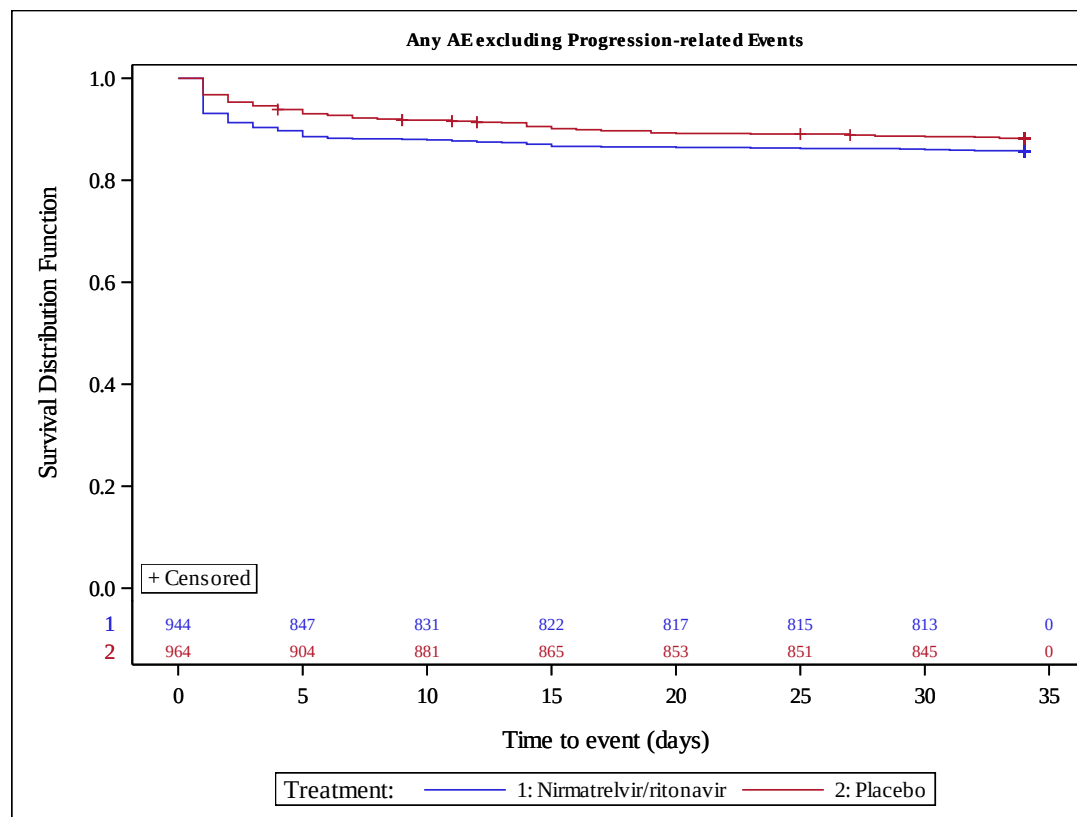
	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)
Number of subjects with events, n (%)	136 (14.4)	113 (11.7)
Number of censored subjects, n (%)	808 (85.6)	851 (88.3)
Kaplan-Meier estimates of Time to Event (days) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unadjusted analysis		
Hazard Ratio (95% CI) [2]	1.26 (0.98, 1.61)	
p-value [2]	0.072	
Relative Risk (95% CI) [3]	1.23 (0.97, 1.55)	
p-value [3]	0.082	
Odds Ratio (95% CI) [3]	1.27 (0.97, 1.66)	
p-value [3]	0.082	
Risk Difference (95% CI) [3]	0.03 (-0.00, 0.06)	
p-value [3]	0.082	

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 Progression-related Events are identified after medical review and are excluded from analysis.
 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Adverse Events excluding Progression-related Events

Final



Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 Progression-related Events are identified after medical review and are excluded from analysis.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Serious Adverse Events excluding Progression-related Events

Final

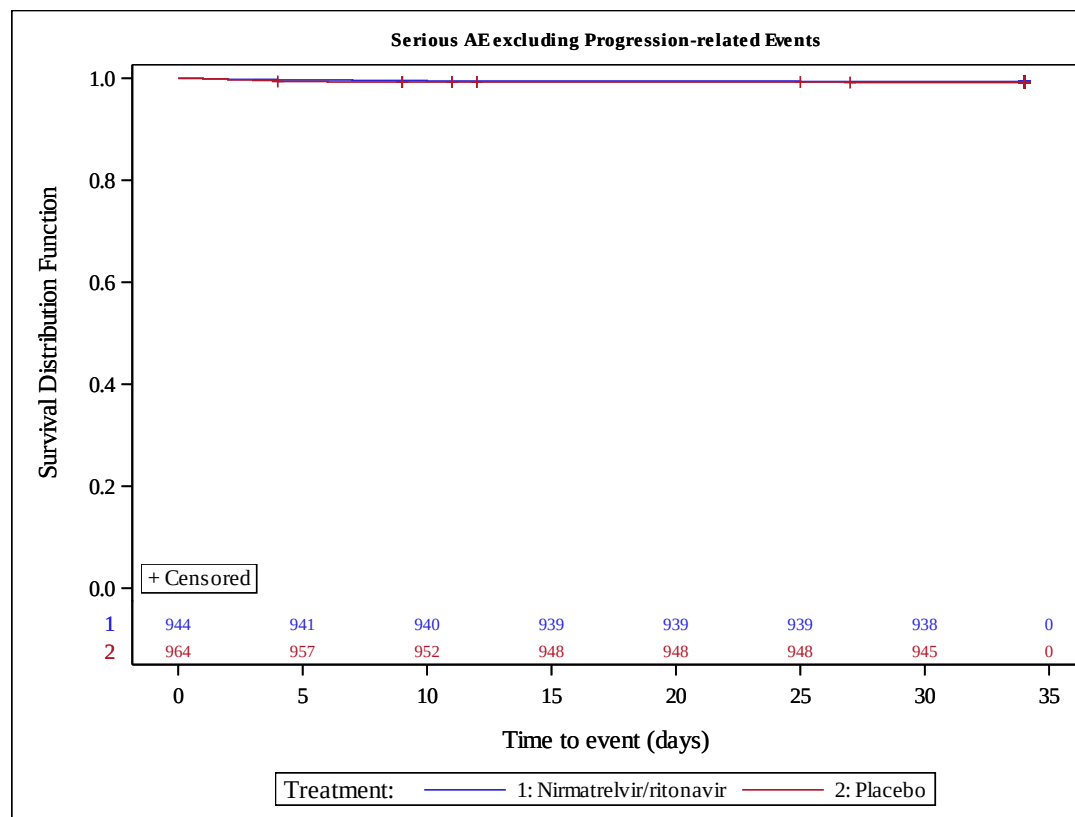
	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)
Number of subjects with events, n (%)	6 (0.6)	8 (0.8)
Number of censored subjects, n (%)	938 (99.4)	956 (99.2)
Kaplan-Meier estimates of Time to Event (days) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unadjusted analysis		
Hazard Ratio (95% CI) [2]	0.76 (0.26, 2.20)	
p-value [2]	0.617	
Relative Risk (95% CI) [3]	0.77 (0.27, 2.20)	
p-value [3]	0.620	
Odds Ratio (95% CI) [3]	0.76 (0.26, 2.21)	
p-value [3]	0.620	
Risk Difference (95% CI) [3]	-0.00 (-0.01, 0.01)	
p-value [3]	0.619	

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 Progression-related Events are identified after medical review and are excluded from analysis.
 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Serious Adverse Events excluding Progression-related Events

Final



Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 Progression-related Events are identified after medical review and are excluded from analysis.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Severe Adverse Events (DAIDS >=3) excluding Progression-related Events

Final

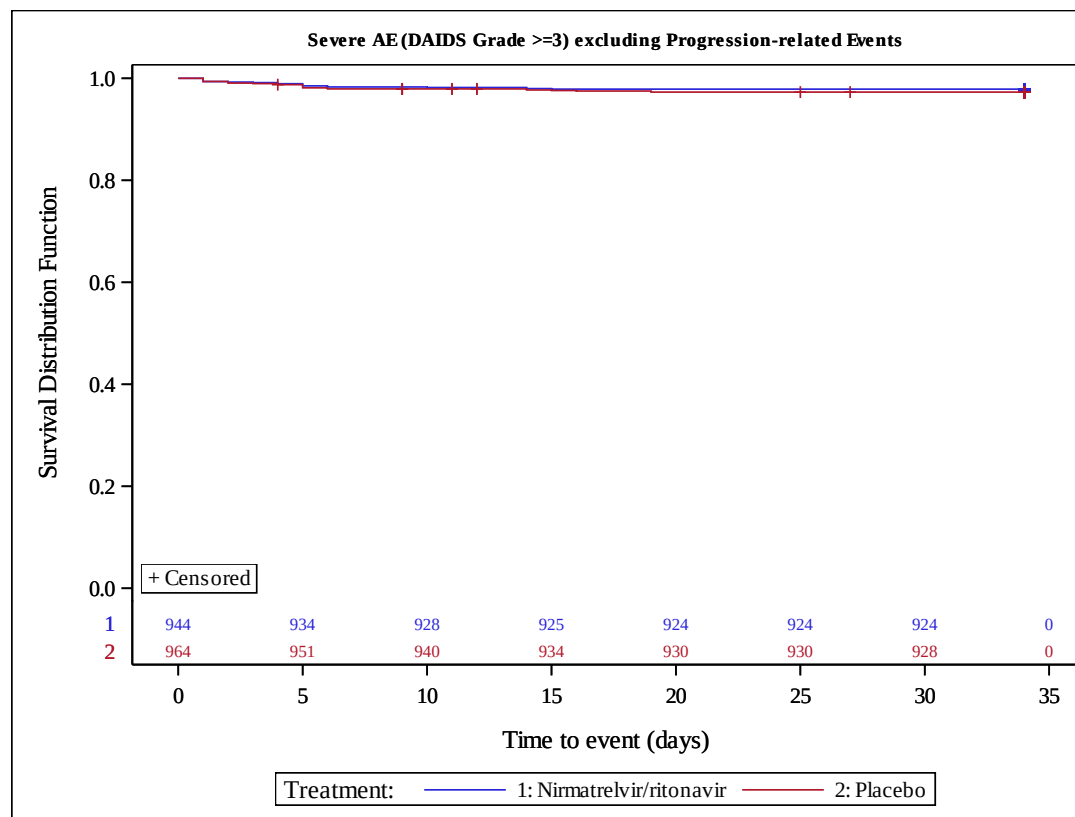
	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)
Number of subjects with events, n (%)	21 (2.2)	26 (2.7)
Number of censored subjects, n (%)	923 (97.8)	938 (97.3)
Kaplan-Meier estimates of Time to Event (days) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unadjusted analysis		
Hazard Ratio (95% CI) [2]	0.82 (0.46, 1.46)	
p-value [2]	0.503	
Relative Risk (95% CI) [3]	0.82 (0.47, 1.46)	
p-value [3]	0.506	
Odds Ratio (95% CI) [3]	0.82 (0.46, 1.47)	
p-value [3]	0.506	
Risk Difference (95% CI) [3]	-0.00 (-0.02, 0.01)	
p-value [3]	0.505	

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 Progression-related Events are identified after medical review and are excluded from analysis.
 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Severe Adverse Events (DAIDS >=3) excluding Progression-related Events

Final



Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 Progression-related Events are identified after medical review and are excluded from analysis.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Non-Severe Adverse Events (DAIDS <3) excluding Progression-related Events

Final

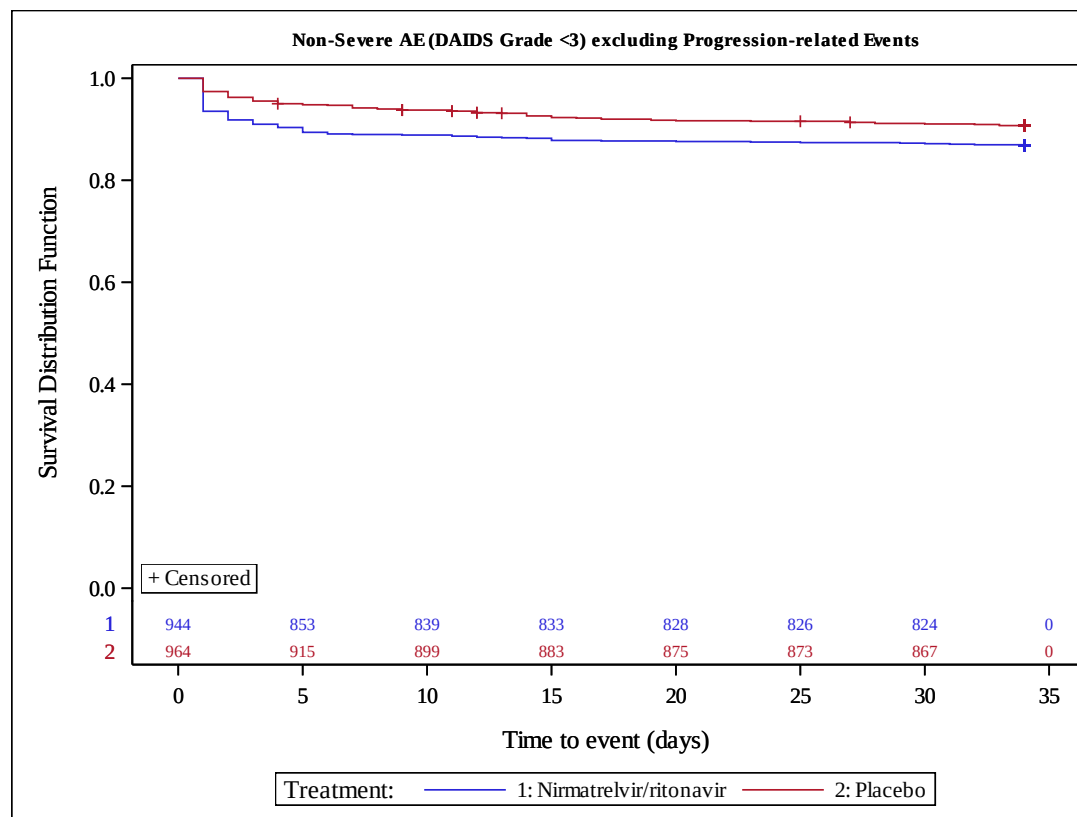
	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)
Number of subjects with events, n (%)	124 (13.1)	89 (9.2)
Number of censored subjects, n (%)	820 (86.9)	875 (90.8)
Kaplan-Meier estimates of Time to Event (days) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unadjusted analysis		
Hazard Ratio (95% CI) [2]	1.46 (1.11, 1.92)	
p-value [2]	0.006	
Relative Risk (95% CI) [3]	1.42 (1.10, 1.84)	
p-value [3]	0.007	
Odds Ratio (95% CI) [3]	1.49 (1.11, 1.98)	
p-value [3]	0.007	
Risk Difference (95% CI) [3]	0.04 (0.01, 0.07)	
p-value [3]	0.007	

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 Progression-related Events are identified after medical review and are excluded from analysis.
 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Non-Severe Adverse Events (DAIDS <3) excluding Progression-related Events

Final



Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 Progression-related Events are identified after medical review and are excluded from analysis.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RKI-conform mITT2 Analysis set
 Analysis of Adverse Events leading to death excluding Progression-related Events

Final

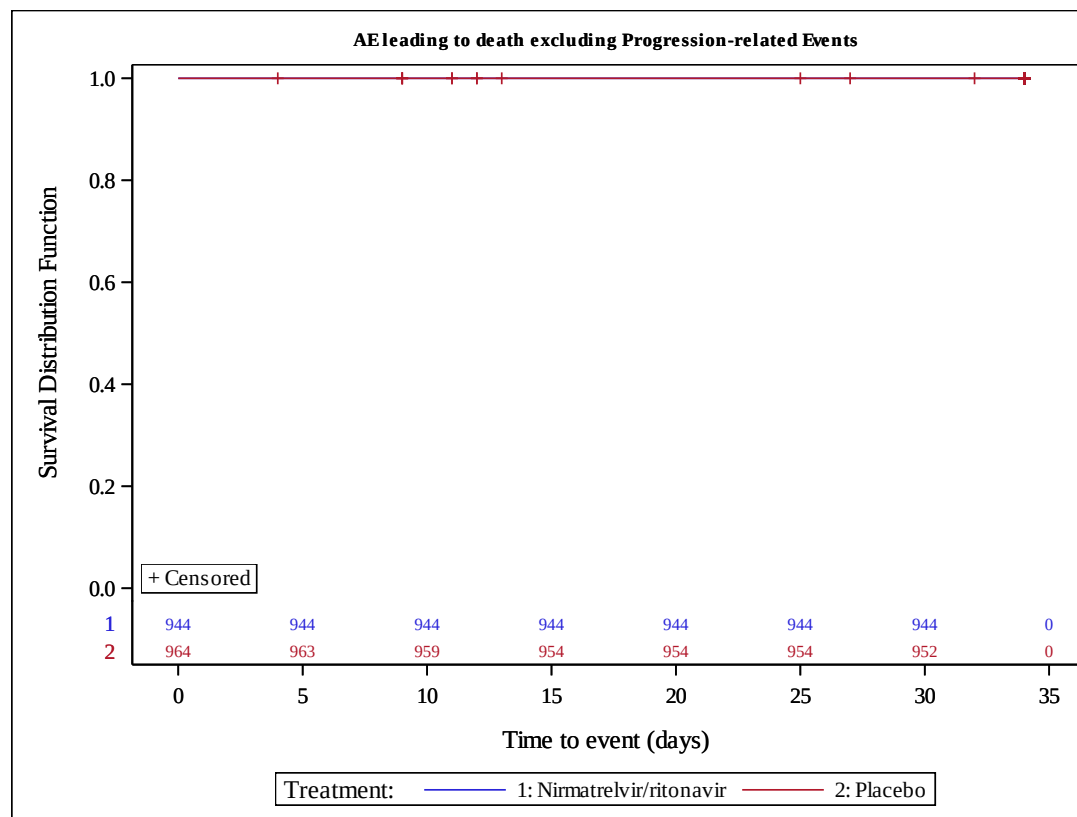
	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)
Number of subjects with events, n (%)	0 (0.0)	0 (0.0)
Number of censored subjects, n (%)	944 (100.0)	964 (100.0)
Kaplan-Meier estimates of Time to Event (days) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unadjusted analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [2]		
Relative Risk (95% CI) [3]	NE	
p-value [3]		
Odds Ratio (95% CI) [3]	NE	
p-value [3]		
Risk Difference (95% CI) [3]	NE	
p-value [3]		

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 Progression-related Events are identified after medical review and are excluded from analysis.
 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

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Pfizer Inc
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 Overall Study population
 RKI-conform mITT2 Analysis set
 Kaplan-Meier Plot of Time to First Adverse Events leading to death excluding Progression-related Events

Final



Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 Progression-related Events are identified after medical review and are excluded from analysis.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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 Overall Study population
 RKI-conform mITT2 Analysis set
 Analysis of Adverse Events leading to Discontinuation of Study Drug excluding Progression-related Events

Final

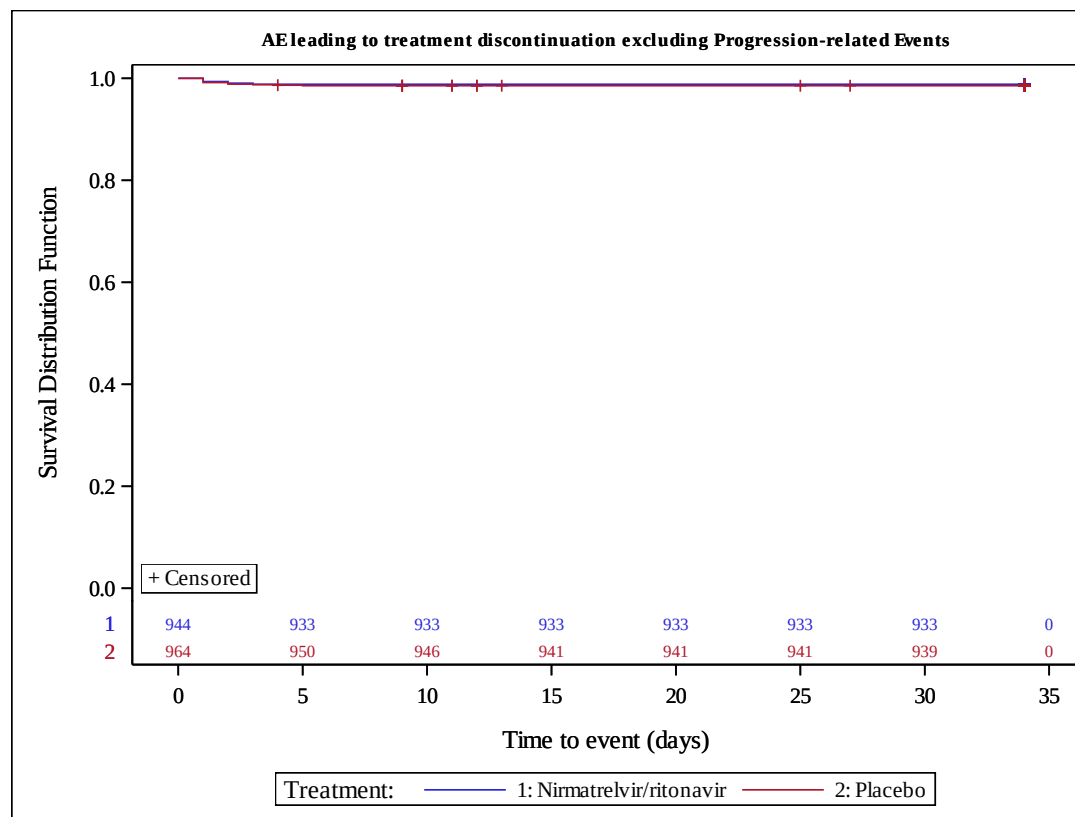
	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)
Number of subjects with events, n (%)	11 (1.2)	14 (1.5)
Number of censored subjects, n (%)	933 (98.8)	950 (98.5)
Kaplan-Meier estimates of Time to Event (days) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unadjusted analysis		
Hazard Ratio (95% CI) [2]	0.80 (0.36, 1.77)	
p-value [2]	0.583	
Relative Risk (95% CI) [3]	0.80 (0.37, 1.76)	
p-value [3]	0.582	
Odds Ratio (95% CI) [3]	0.80 (0.36, 1.77)	
p-value [3]	0.582	
Risk Difference (95% CI) [3]	-0.00 (-0.01, 0.01)	
p-value [3]	0.581	

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 Progression-related Events are identified after medical review and are excluded from analysis.
 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

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Final



Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
MedDRA v24.1 coding dictionary applied.
Progression-related Events are identified after medical review and are excluded from analysis.

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 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Adverse Events leading to temporary Discontinuation of Study Drug excluding Progression-related Events

Final

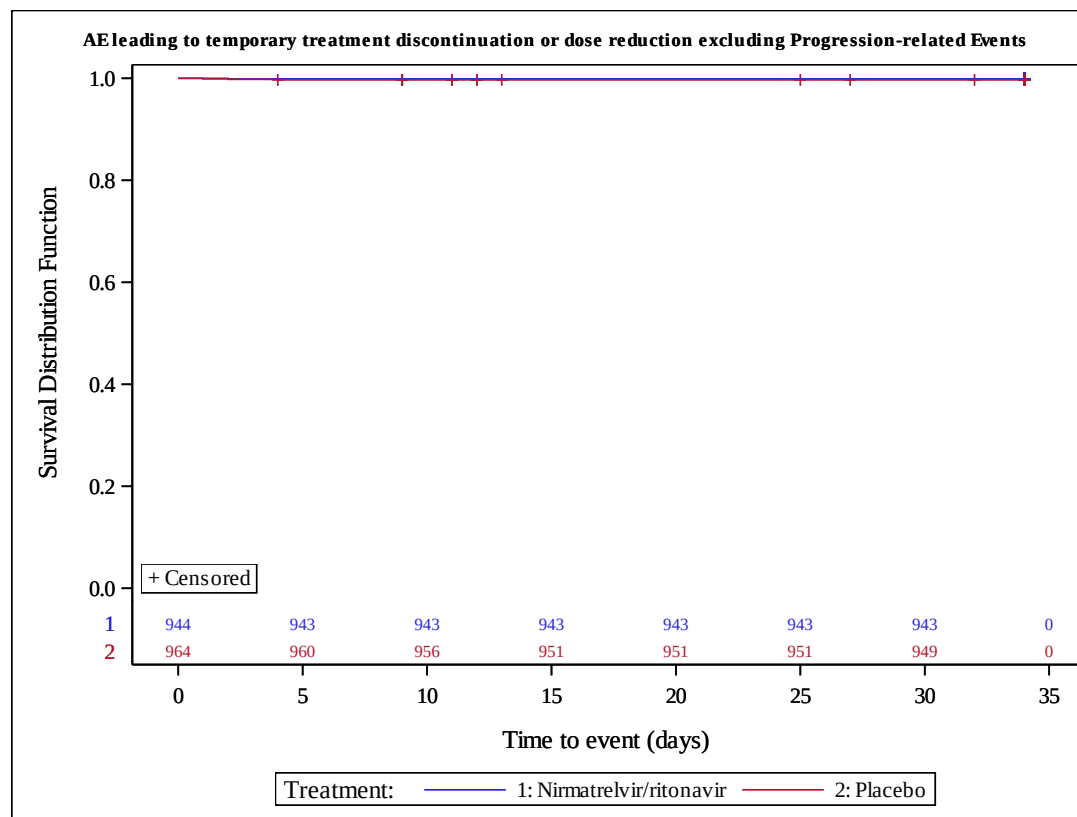
	Nirmatrelvir/ritonavir (N=944)	Placebo (N=964)
Number of subjects with events, n (%)	1 (0.1)	3 (0.3)
Number of censored subjects, n (%)	943 (99.9)	961 (99.7)
Kaplan-Meier estimates of Time to Event (days) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unadjusted analysis		
Hazard Ratio (95% CI) [2]	0.34 (0.04, 3.27)	
p-value [2]	0.351	
Relative Risk (95% CI) [3]	0.34 (0.04, 3.27)	
p-value [3]	0.350	
Odds Ratio (95% CI) [3]	0.34 (0.04, 3.27)	
p-value [3]	0.350	
Risk Difference (95% CI) [3]	-0.00 (-0.01, 0.00)	
p-value [3]	0.324	

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 Progression-related Events are identified after medical review and are excluded from analysis.
 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [1] Based on the Brookmeyer and Crowley Method. [2] Based on the Cox proportional hazards model. [3] Calculated using normal approximation (Wald).

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Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
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 Analysis of Frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or >=10 patients) - Subgroup analysis

Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations	Age							0.1147
	< 65	21/ 804 (2.6)	NE (NE , NE)	48/ 816 (5.9)	NE (NE , NE)	0.44 (0.26, 0.73)	0.00	
	>= 65	3/ 140 (2.1)	NE (NE , NE)	20/ 148 (13.5)	NE (NE , NE)	0.15 (0.04, 0.51)	<.001	
	Gender							0.5616
	Male	13/ 474 (2.7)	NE (NE , NE)	43/ 510 (8.4)	NE (NE , NE)	0.32 (0.17, 0.59)	<.001	
	Female	11/ 470 (2.3)	NE (NE , NE)	25/ 454 (5.5)	NE (NE , NE)	0.42 (0.21, 0.85)	0.01	
	Geographic region							0.5034
	United States	7/ 387 (1.8)	NE (NE , NE)	13/ 395 (3.3)	NE (NE , NE)	0.54 (0.22, 1.36)	0.18	
	Europe	9/ 322 (2.8)	NE (NE , NE)	35/ 321 (10.9)	NE (NE , NE)	0.25 (0.12, 0.51)	<.001	
	India	1/ 74 (1.4)	NE (NE , NE)	1/ 78 (1.3)	NE (NE , NE)	1.05 (0.07, 16.74)	0.97	
	Rest of World	7/ 161 (4.3)	NE (NE , NE)	19/ 170 (11.2)	NE (NE , NE)	0.37 (0.16, 0.89)	0.02	
	COVID-19 therapeutic mAb treatment at randomisation							0.2866
	Yes	2/ 60 (3.3)	NE (NE , NE)	2/ 60 (3.3)	NE (NE , NE)	1.00 (0.14, 7.10)	1.00	
	No	22/ 884 (2.5)	NE (NE , NE)	66/ 904 (7.3)	NE (NE , NE)	0.33 (0.21, 0.54)	<.001	
	Baseline viral load 1							0.8574
	< 10^4 copies/mL	2/ 340 (0.6)	NE (NE , NE)	5/ 356 (1.4)	NE (NE , NE)	0.42 (0.08, 2.15)	0.28	
	>= 10^4 copies/mL	22/ 579 (3.8)	NE (NE , NE)	60/ 582 (10.3)	NE (NE , NE)	0.36 (0.22, 0.58)	<.001	
	Baseline viral load 2							0.7049
	< 10^7 copies/mL	14/ 663 (2.1)	NE (NE , NE)	38/ 707 (5.4)	NE (NE , NE)	0.39 (0.21, 0.71)	0.00	
	>= 10^7 copies/mL	10/ 256 (3.9)	NE (NE , NE)	27/ 231 (11.7)	NE (NE , NE)	0.32 (0.15, 0.66)	0.00	
	Baseline serology status							0.0984
	Negative	15/ 439 (3.4)	NE (NE , NE)	55/ 457 (12.0)	NE (NE , NE)	0.27 (0.15, 0.48)	<.001	
	Positive	8/ 494 (1.6)	NE (NE , NE)	12/ 495 (2.4)	NE (NE , NE)	0.66 (0.27, 1.63)	0.36	
	Symptom onset days to first dose date							0.5155
	<= 3	18/ 637 (2.8)	NE (NE , NE)	45/ 632 (7.1)	NE (NE , NE)	0.39 (0.22, 0.67)	<.001	
	> 3	6/ 307 (2.0)	NE (NE , NE)	23/ 332 (6.9)	NE (NE , NE)	0.28 (0.11, 0.68)	0.00	
	BMI group							0.3481
	< 25	1/ 216 (0.5)	NE (NE , NE)	10/ 213 (4.7)	NE (NE , NE)	0.10 (0.01, 0.76)	0.00	
	25 - < 30	7/ 324 (2.2)	NE (NE , NE)	22/ 336 (6.5)	NE (NE , NE)	0.32 (0.14, 0.76)	0.00	
	>= 30	16/ 403 (4.0)	NE (NE , NE)	36/ 415 (8.7)	NE (NE , NE)	0.45 (0.25, 0.80)	0.00	
	Ethnicity							0.3135
	White	16/ 712 (2.2)	NE (NE , NE)	53/ 725 (7.3)	NE (NE , NE)	0.30 (0.17, 0.52)	<.001	
	Black or African American	2/ 45 (4.4)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	1.85 (0.17, 20.41)	0.61	
	Asian	4/ 118 (3.4)	NE (NE , NE)	6/ 127 (4.7)	NE (NE , NE)	0.71 (0.20, 2.52)	0.59	
	Others	2/ 69 (2.9)	NE (NE , NE)	8/ 70 (11.4)	NE (NE , NE)	0.24 (0.05, 1.14)	0.05	

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.
 Subgroup analysis was done for SOC/PTs with significant overall treatment effect (significant Hazard Ratio).
 Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations	Number of baseline comorbidities present							0.7478
	0-1	13/ 720 (1.8)	NE (NE , NE)	43/ 734 (5.9)	NE (NE , NE)	0.30 (0.16, 0.56)	<.001	
	2-3	11/ 220 (5.0)	NE (NE , NE)	25/ 224 (11.2)	NE (NE , NE)	0.44 (0.21, 0.89)	0.01	
	>= 4	0/ 4 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	Presence of risk factor: Smoking							0.1963
	Yes	9/ 423 (2.1)	NE (NE , NE)	17/ 442 (3.8)	NE (NE , NE)	0.55 (0.24, 1.23)	0.14	
	No	15/ 519 (2.9)	NE (NE , NE)	51/ 522 (9.8)	NE (NE , NE)	0.29 (0.16, 0.51)	<.001	
	Presence of risk factor: Diabetes mellitus							0.3171
	Yes	7/ 135 (5.2)	NE (NE , NE)	13/ 137 (9.5)	NE (NE , NE)	0.53 (0.21, 1.33)	0.17	
	No	17/ 808 (2.1)	NE (NE , NE)	55/ 827 (6.7)	NE (NE , NE)	0.31 (0.18, 0.53)	<.001	
	Presence of risk factor: Immunosuppression							0.9813
	Yes	0/ 6 (0.0)	NE (NE , NE)	1/ 7 (14.3)	NE (3.0, NE)	NE	NE	
	No	24/ 937 (2.6)	NE (NE , NE)	67/ 957 (7.0)	NE (NE , NE)	0.36 (0.22, 0.57)	<.001	
	Presence of risk factor: Chronic lung disease							0.2598
	Yes	3/ 62 (4.8)	NE (NE , NE)	2/ 39 (5.1)	NE (NE , NE)	0.94 (0.16, 5.64)	0.94	
	No	21/ 881 (2.4)	NE (NE , NE)	66/ 925 (7.1)	NE (NE , NE)	0.33 (0.20, 0.53)	<.001	
	Presence of risk factor: Hypertension							0.0613
	Yes	11/ 358 (3.1)	NE (NE , NE)	46/ 375 (12.3)	NE (NE , NE)	0.24 (0.12, 0.46)	<.001	
	No	13/ 585 (2.2)	NE (NE , NE)	22/ 589 (3.7)	NE (NE , NE)	0.59 (0.30, 1.17)	0.12	
	Presence of risk factor: Cardiovascular disorder							0.9789
	Yes	0/ 42 (0.0)	NE (NE , NE)	11/ 49 (22.4)	NE (NE , NE)	NE	NE	
	No	24/ 901 (2.7)	NE (NE , NE)	57/ 915 (6.2)	NE (NE , NE)	0.42 (0.26, 0.68)	<.001	
	Presence of risk factor: Chronic kidney disease							0.9743
	Yes	1/ 6 (16.7)	NE (4.0, NE)	0/ 8 (0.0)	NE (NE , NE)	NE	NE	
	No	23/ 937 (2.5)	NE (NE , NE)	68/ 956 (7.1)	NE (NE , NE)	0.34 (0.21, 0.54)	<.001	
	Presence of risk factor: HIV Infection							
	Yes	0		0/ 1 (0.0)				
	No	24/ 943 (2.5)		68/ 962 (7.1)				
	Presence of risk factor: Sickle Cell Disease							
	No	24/ 943 (2.5)		68/ 964 (7.1)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

MedDRA v24.1 coding dictionary applied.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

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Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations	Presence of risk factor:							
	Neurodevelopmental Disorder							
	Yes	0/ 2 (0.0)		1/ 1 (100.0)				
	No	24/ 941 (2.6)		67/ 963 (7.0)				
	Presence of risk factor: Cancer							0.9993
	Yes	0/ 5 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	No	24/ 938 (2.6)	NE (NE , NE)	68/ 958 (7.1)	NE (NE , NE)	0.35 (0.22, 0.56)	<.001	
	Presence of risk factor: Device Dependence							
	Yes	0/ 4 (0.0)		0/ 3 (0.0)				
	No	24/ 930 (2.6)		66/ 953 (6.9)				

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Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations, PT: COVID-19	Age							0.9901
	< 65	3/ 804 (0.4)	NE (NE , NE)	11/ 816 (1.3)	NE (NE , NE)	0.28 (0.08, 0.99)	0.03	
	>= 65	0/ 140 (0.0)	NE (NE , NE)	3/ 148 (2.0)	NE (NE , NE)	NE	NE	
	Gender							0.4897
	Male	2/ 474 (0.4)	NE (NE , NE)	12/ 510 (2.4)	NE (NE , NE)	0.18 (0.04, 0.80)	0.01	
	Female	1/ 470 (0.2)	NE (NE , NE)	2/ 454 (0.4)	NE (NE , NE)	0.48 (0.04, 5.31)	0.54	
	Geographic region							
	United States	2/ 387 (0.5)		5/ 395 (1.3)				
	Europe	0/ 322 (0.0)		4/ 321 (1.2)				
	India	0/ 74 (0.0)		1/ 78 (1.3)				
	Rest of World	1/ 161 (0.6)		4/ 170 (2.4)				
	COVID-19 therapeutic mAb treatment at randomisation							0.9879
	Yes	1/ 60 (1.7)	NE (NE , NE)	0/ 60 (0.0)	NE (NE , NE)	NE	NE	
	No	2/ 884 (0.2)	NE (NE , NE)	14/ 904 (1.5)	NE (NE , NE)	0.15 (0.03, 0.64)	0.00	
	Baseline viral load 1							0.4640
	< 10^4 copies/mL	1/ 340 (0.3)	NE (NE , NE)	2/ 356 (0.6)	NE (NE , NE)	0.52 (0.05, 5.78)	0.59	
	>= 10^4 copies/mL	2/ 579 (0.3)	NE (NE , NE)	11/ 582 (1.9)	NE (NE , NE)	0.18 (0.04, 0.82)	0.01	
	Baseline viral load 2							0.9916
	< 10^7 copies/mL	3/ 663 (0.5)	NE (NE , NE)	8/ 707 (1.1)	NE (NE , NE)	0.40 (0.11, 1.50)	0.16	
	>= 10^7 copies/mL	0/ 256 (0.0)	NE (NE , NE)	5/ 231 (2.2)	NE (NE , NE)	NE	NE	
	Baseline serology status							0.0881
	Negative	1/ 439 (0.2)	NE (NE , NE)	12/ 457 (2.6)	NE (NE , NE)	0.09 (0.01, 0.66)	0.00	
	Positive	2/ 494 (0.4)	NE (NE , NE)	2/ 495 (0.4)	NE (NE , NE)	1.00 (0.14, 7.12)	0.99	
	Symptom onset days to first dose date							
	<= 3	0/ 637 (0.0)		9/ 632 (1.4)				
	> 3	3/ 307 (1.0)		5/ 332 (1.5)				
	BMI group							0.6029
	< 25	0/ 216 (0.0)	NE (NE , NE)	3/ 213 (1.4)	NE (NE , NE)	NE	NE	
	25 - < 30	1/ 324 (0.3)	NE (NE , NE)	1/ 336 (0.3)	NE (NE , NE)	1.04 (0.06, 16.56)	0.98	
	>= 30	2/ 403 (0.5)	NE (NE , NE)	10/ 415 (2.4)	NE (NE , NE)	0.20 (0.04, 0.93)	0.02	
	Ethnicity							1.0000
	White	3/ 712 (0.4)	NE (NE , NE)	10/ 725 (1.4)	NE (NE , NE)	0.30 (0.08, 1.11)	0.05	
	Black or African American	0/ 45 (0.0)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE	NE	
	Asian	0/ 118 (0.0)	NE (NE , NE)	1/ 127 (0.8)	NE (NE , NE)	NE	NE	
	Others	0/ 69 (0.0)	NE (NE , NE)	3/ 70 (4.3)	NE (NE , NE)	NE	NE	

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 [3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.
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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or >=10 patients) - Subgroup analysis

Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]		n/ N (%)	Median (95% CI) [1]		Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations, PT: COVID-19	Number of baseline comorbidities present									0.9999
	0-1	3/ 720 (0.4)	NE (NE , NE)		7/ 734 (1.0)	NE (NE , NE)		0.44 (0.11, 1.69)	0.21	
	2-3	0/ 220 (0.0)	NE (NE , NE)		7/ 224 (3.1)	NE (NE , NE)		NE	NE	
	>= 4	0/ 4 (0.0)	NE (NE , NE)		0/ 6 (0.0)	NE (NE , NE)		NE	NE	
	Presence of risk factor: Smoking									0.6387
	Yes	1/ 423 (0.2)	NE (NE , NE)		3/ 442 (0.7)	NE (NE , NE)		0.35 (0.04, 3.34)	0.33	
	No	2/ 519 (0.4)	NE (NE , NE)		11/ 522 (2.1)	NE (NE , NE)		0.18 (0.04, 0.82)	0.01	
	Presence of risk factor: Diabetes mellitus									0.9881
	Yes	0/ 135 (0.0)	NE (NE , NE)		7/ 137 (5.1)	NE (NE , NE)		NE	NE	
	No	3/ 808 (0.4)	NE (NE , NE)		7/ 827 (0.8)	NE (NE , NE)		0.44 (0.11, 1.70)	0.21	
	Presence of risk factor: Immunosuppression									0.9995
	Yes	0/ 6 (0.0)	NE (NE , NE)		0/ 7 (0.0)	NE (NE , NE)		NE	NE	
	No	3/ 937 (0.3)	NE (NE , NE)		14/ 957 (1.5)	NE (NE , NE)		0.22 (0.06, 0.76)	0.00	
	Presence of risk factor: Chronic lung disease									0.9996
	Yes	0/ 62 (0.0)	NE (NE , NE)		0/ 39 (0.0)	NE (NE , NE)		NE	NE	
	No	3/ 881 (0.3)	NE (NE , NE)		14/ 925 (1.5)	NE (NE , NE)		0.22 (0.06, 0.78)	0.01	
	Presence of risk factor: Hypertension									0.9865
	Yes	0/ 358 (0.0)	NE (NE , NE)		10/ 375 (2.7)	NE (NE , NE)		NE	NE	
	No	3/ 585 (0.5)	NE (NE , NE)		4/ 589 (0.7)	NE (NE , NE)		0.76 (0.17, 3.38)	0.71	
	Presence of risk factor: Cardiovascular disorder									0.9917
	Yes	0/ 42 (0.0)	NE (NE , NE)		1/ 49 (2.0)	NE (NE , NE)		NE	NE	
	No	3/ 901 (0.3)	NE (NE , NE)		13/ 915 (1.4)	NE (NE , NE)		0.23 (0.07, 0.82)	0.01	
	Presence of risk factor: Chronic kidney disease									0.9995
	Yes	0/ 6 (0.0)	NE (NE , NE)		0/ 8 (0.0)	NE (NE , NE)		NE	NE	
	No	3/ 937 (0.3)	NE (NE , NE)		14/ 956 (1.5)	NE (NE , NE)		0.22 (0.06, 0.76)	0.00	
	Presence of risk factor: HIV Infection									
	Yes	0			0/ 1 (0.0)					
	No	3/ 943 (0.3)			14/ 962 (1.5)					
	Presence of risk factor: Sickle Cell Disease									
	No	3/ 943 (0.3)			14/ 964 (1.5)					

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).
 Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or >=10 patients) - Subgroup analysis

Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations, PT: COVID-19	Presence of risk factor: Neurodevelopmental Disorder							
	Yes	0/ 2 (0.0)		0/ 1 (0.0)				
	No	3/ 941 (0.3)		14/ 963 (1.5)				
	Presence of risk factor: Cancer							0.9996
	Yes	0/ 5 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	No	3/ 938 (0.3)	NE (NE , NE)	14/ 958 (1.5)	NE (NE , NE)	0.22 (0.06, 0.76)	0.00	
	Presence of risk factor: Device Dependence							
	Yes	0/ 4 (0.0)		0/ 3 (0.0)				
	No	3/ 930 (0.3)		13/ 953 (1.4)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
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Pfizer Inc EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022) Overall Study population RKI-conform mITT2 Analysis set Analysis of Frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or >=10 patients) - Subgroup analysis								Final
SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value [2]	p-Value [3]
SOC: Infections and infestations, PT: COVID-19 pneumonia	Age							0.1788
	< 65	7/ 804 (0.9)	NE (NE , NE)	23/ 816 (2.8)	NE (NE , NE)	0.31 (0.13, 0.71)	0.00	
	>= 65	1/ 140 (0.7)	NE (NE , NE)	15/ 148 (10.1)	NE (NE , NE)	0.07 (0.01, 0.51)	<.001	
	Gender							0.6804
	Male	4/ 474 (0.8)	NE (NE , NE)	23/ 510 (4.5)	NE (NE , NE)	0.18 (0.06, 0.53)	<.001	
	Female	4/ 470 (0.9)	NE (NE , NE)	15/ 454 (3.3)	NE (NE , NE)	0.25 (0.08, 0.77)	0.00	
	Geographic region							0.9981
	United States	2/ 387 (0.5)	NE (NE , NE)	9/ 395 (2.3)	NE (NE , NE)	0.22 (0.05, 1.04)	0.03	
	Europe	4/ 322 (1.2)	NE (NE , NE)	20/ 321 (6.2)	NE (NE , NE)	0.20 (0.07, 0.57)	<.001	
	India	0/ 74 (0.0)	NE (NE , NE)	0/ 78 (0.0)	NE (NE , NE)	NE	NE	
	Rest of World	2/ 161 (1.2)	NE (NE , NE)	9/ 170 (5.3)	NE (NE , NE)	0.23 (0.05, 1.07)	0.04	
	COVID-19 therapeutic mAb treatment at randomisation							0.9853
	Yes	0/ 60 (0.0)	NE (NE , NE)	1/ 60 (1.7)	NE (NE , NE)	NE	NE	
	No	8/ 884 (0.9)	NE (NE , NE)	37/ 904 (4.1)	NE (NE , NE)	0.22 (0.10, 0.47)	<.001	
	Baseline viral load 1							0.9882
	< 10^4 copies/mL	0/ 340 (0.0)	NE (NE , NE)	2/ 356 (0.6)	NE (NE , NE)	NE	NE	
	>= 10^4 copies/mL	8/ 579 (1.4)	NE (NE , NE)	34/ 582 (5.8)	NE (NE , NE)	0.23 (0.11, 0.50)	<.001	
	Baseline viral load 2							0.5629
	< 10^7 copies/mL	5/ 663 (0.8)	NE (NE , NE)	20/ 707 (2.8)	NE (NE , NE)	0.26 (0.10, 0.70)	0.00	
	>= 10^7 copies/mL	3/ 256 (1.2)	NE (NE , NE)	16/ 231 (6.9)	NE (NE , NE)	0.16 (0.05, 0.56)	0.00	
	Baseline serology status							0.7787
	Negative	6/ 439 (1.4)	NE (NE , NE)	31/ 457 (6.8)	NE (NE , NE)	0.20 (0.08, 0.47)	<.001	
	Positive	1/ 494 (0.2)	NE (NE , NE)	7/ 495 (1.4)	NE (NE , NE)	0.14 (0.02, 1.16)	0.03	
	Symptom onset days to first dose date							0.7852
	<= 3	6/ 637 (0.9)	NE (NE , NE)	26/ 632 (4.1)	NE (NE , NE)	0.23 (0.09, 0.55)	<.001	
	> 3	2/ 307 (0.7)	NE (NE , NE)	12/ 332 (3.6)	NE (NE , NE)	0.18 (0.04, 0.80)	0.01	
	BMI group							0.9901
	< 25	1/ 216 (0.5)	NE (NE , NE)	5/ 213 (2.3)	NE (NE , NE)	0.20 (0.02, 1.68)	0.09	
	25 - < 30	3/ 324 (0.9)	NE (NE , NE)	15/ 336 (4.5)	NE (NE , NE)	0.20 (0.06, 0.71)	0.00	
	>= 30	4/ 403 (1.0)	NE (NE , NE)	18/ 415 (4.3)	NE (NE , NE)	0.22 (0.08, 0.66)	0.00	
	Ethnicity							0.9722
	White	6/ 712 (0.8)	NE (NE , NE)	30/ 725 (4.1)	NE (NE , NE)	0.20 (0.08, 0.48)	<.001	
	Black or African American	0/ 45 (0.0)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	NE	NE	
	Asian	1/ 118 (0.8)	NE (NE , NE)	3/ 127 (2.4)	NE (NE , NE)	0.36 (0.04, 3.44)	0.35	
	Others	1/ 69 (1.4)	NE (NE , NE)	4/ 70 (5.7)	NE (NE , NE)	0.25 (0.03, 2.24)	0.17	

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Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]		n/ N (%)	Median (95% CI) [1]		Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations, PT: COVID-19 pneumonia	Number of baseline comorbidities present									0.5264
	0-1	4/ 720 (0.6)	NE (NE , NE)		27/ 734 (3.7)	NE (NE , NE)		0.15 (0.05, 0.42)	<.001	
	2-3	4/ 220 (1.8)	NE (NE , NE)		11/ 224 (4.9)	NE (NE , NE)		0.37 (0.12, 1.16)	0.07	
	>= 4	0/ 4 (0.0)	NE (NE , NE)		0/ 6 (0.0)	NE (NE , NE)		NE	NE	
	Presence of risk factor: Smoking									0.2192
	Yes	3/ 423 (0.7)	NE (NE , NE)		7/ 442 (1.6)	NE (NE , NE)		0.45 (0.12, 1.73)	0.23	
	No	5/ 519 (1.0)	NE (NE , NE)		31/ 522 (5.9)	NE (NE , NE)		0.16 (0.06, 0.41)	<.001	
	Presence of risk factor: Diabetes mellitus									0.0699
	Yes	3/ 135 (2.2)	NE (NE , NE)		4/ 137 (2.9)	NE (NE , NE)		0.76 (0.17, 3.40)	0.71	
	No	5/ 808 (0.6)	NE (NE , NE)		34/ 827 (4.1)	NE (NE , NE)		0.15 (0.06, 0.38)	<.001	
	Presence of risk factor: Immunosuppression									0.9992
	Yes	0/ 6 (0.0)	NE (NE , NE)		0/ 7 (0.0)	NE (NE , NE)		NE	NE	
	No	8/ 937 (0.9)	NE (NE , NE)		38/ 957 (4.0)	NE (NE , NE)		0.21 (0.10, 0.45)	<.001	
	Presence of risk factor: Chronic lung disease									0.9844
	Yes	0/ 62 (0.0)	NE (NE , NE)		1/ 39 (2.6)	NE (NE , NE)		NE	NE	
	No	8/ 881 (0.9)	NE (NE , NE)		37/ 925 (4.0)	NE (NE , NE)		0.22 (0.10, 0.48)	<.001	
	Presence of risk factor: Hypertension									0.4318
	Yes	5/ 358 (1.4)	NE (NE , NE)		29/ 375 (7.7)	NE (NE , NE)		0.18 (0.07, 0.45)	<.001	
	No	3/ 585 (0.5)	NE (NE , NE)		9/ 589 (1.5)	NE (NE , NE)		0.33 (0.09, 1.24)	0.08	
	Presence of risk factor: Cardiovascular disorder									0.9871
	Yes	0/ 42 (0.0)	NE (NE , NE)		7/ 49 (14.3)	NE (NE , NE)		NE	NE	
	No	8/ 901 (0.9)	NE (NE , NE)		31/ 915 (3.4)	NE (NE , NE)		0.26 (0.12, 0.56)	<.001	
	Presence of risk factor: Chronic kidney disease									0.9992
	Yes	0/ 6 (0.0)	NE (NE , NE)		0/ 8 (0.0)	NE (NE , NE)		NE	NE	
	No	8/ 937 (0.9)	NE (NE , NE)		38/ 956 (4.0)	NE (NE , NE)		0.21 (0.10, 0.45)	<.001	
	Presence of risk factor: HIV Infection									
	Yes	0			0/ 1 (0.0)					
	No	8/ 943 (0.8)			38/ 962 (4.0)					
	Presence of risk factor: Sickle Cell Disease									
	No	8/ 943 (0.8)			38/ 964 (3.9)					

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

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[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

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Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations, PT: COVID-19 pneumonia	Presence of risk factor: Neurodevelopmental Disorder							
	Yes	0/ 2 (0.0)		0/ 1 (0.0)				
	No	8/ 941 (0.9)		38/ 963 (3.9)				
	Presence of risk factor: Cancer							0.9993
	Yes	0/ 5 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	No	8/ 938 (0.9)	NE (NE , NE)	38/ 958 (4.0)	NE (NE , NE)	0.21 (0.10, 0.45)	<.001	
	Presence of risk factor: Device Dependence							
	Yes	0/ 4 (0.0)		0/ 3 (0.0)				
	No	8/ 930 (0.9)		38/ 953 (4.0)				

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SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations, PT: Pneumonia	Age							
	< 65	1/ 804 (0.1)		8/ 816 (1.0)				
	>= 65	1/ 140 (0.7)		3/ 148 (2.0)				
	Gender							0.9911
	Male	2/ 474 (0.4)	NE (NE , NE)	8/ 510 (1.6)	NE (NE , NE)	0.27 (0.06, 1.26)	0.07	
	Female	0/ 470 (0.0)	NE (NE , NE)	3/ 454 (0.7)	NE (NE , NE)	NE	NE	
	Geographic region							
	United States	1/ 387 (0.3)		2/ 395 (0.5)				
	Europe	1/ 322 (0.3)		8/ 321 (2.5)				
	India	0/ 74 (0.0)		0/ 78 (0.0)				
	Rest of World	0/ 161 (0.0)		1/ 170 (0.6)				
	COVID-19 therapeutic mAb treatment at randomisation							0.9995
	Yes	0/ 60 (0.0)	NE (NE , NE)	0/ 60 (0.0)	NE (NE , NE)	NE	NE	
	No	2/ 884 (0.2)	NE (NE , NE)	11/ 904 (1.2)	NE (NE , NE)	0.18 (0.04, 0.83)	0.01	
	Baseline viral load 1							0.9933
	< 10^4 copies/mL	0/ 340 (0.0)	NE (NE , NE)	1/ 356 (0.3)	NE (NE , NE)	NE	NE	
	>= 10^4 copies/mL	2/ 579 (0.3)	NE (NE , NE)	10/ 582 (1.7)	NE (NE , NE)	0.20 (0.04, 0.91)	0.02	
	Baseline viral load 2							0.9924
	< 10^7 copies/mL	2/ 663 (0.3)	NE (NE , NE)	8/ 707 (1.1)	NE (NE , NE)	0.27 (0.06, 1.25)	0.07	
	>= 10^7 copies/mL	0/ 256 (0.0)	NE (NE , NE)	3/ 231 (1.3)	NE (NE , NE)	NE	NE	
	Baseline serology status							0.9996
	Negative	2/ 439 (0.5)	NE (NE , NE)	11/ 457 (2.4)	NE (NE , NE)	0.19 (0.04, 0.84)	0.01	
	Positive	0/ 494 (0.0)	NE (NE , NE)	0/ 495 (0.0)	NE (NE , NE)	NE	NE	
	Symptom onset days to first dose date							0.9921
	<= 3	2/ 637 (0.3)	NE (NE , NE)	8/ 632 (1.3)	NE (NE , NE)	0.25 (0.05, 1.16)	0.05	
	> 3	0/ 307 (0.0)	NE (NE , NE)	3/ 332 (0.9)	NE (NE , NE)	NE	NE	
	BMI group							
	< 25	0/ 216 (0.0)		3/ 213 (1.4)				
	25 - < 30	1/ 324 (0.3)		3/ 336 (0.9)				
	>= 30	1/ 403 (0.2)		5/ 415 (1.2)				
	Ethnicity							0.6936
	White	1/ 712 (0.1)	NE (NE , NE)	9/ 725 (1.2)	NE (NE , NE)	0.11 (0.01, 0.89)	0.01	
	Black or African American	1/ 45 (2.2)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	0.94 (0.06, 15.09)	0.96	
	Asian	0/ 118 (0.0)	NE (NE , NE)	1/ 127 (0.8)	NE (NE , NE)	NE	NE	
	Others	0/ 69 (0.0)	NE (NE , NE)	0/ 70 (0.0)	NE (NE , NE)	NE	NE	

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SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]		n/ N (%)	Median (95% CI) [1]		Hazard Ratio (95% CI) [2]	p-Value [2]	
SOC: Infections and infestations, PT: Pneumonia	Number of baseline comorbidities present									
	0-1	0/ 720 (0.0)			6/ 734 (0.8)					
	2-3	2/ 220 (0.9)			5/ 224 (2.2)					
	>= 4	0/ 4 (0.0)			0/ 6 (0.0)					
	Presence of risk factor: Smoking									0.9915
	Yes	2/ 423 (0.5)	NE (NE , NE)		8/ 442 (1.8)	NE (NE , NE)		0.26 (0.06, 1.23)	0.06	
	No	0/ 519 (0.0)	NE (NE , NE)		3/ 522 (0.6)	NE (NE , NE)		NE	NE	
	Presence of risk factor: Diabetes mellitus									0.1935
	Yes	1/ 135 (0.7)	NE (NE , NE)		1/ 137 (0.7)	NE (NE , NE)		1.01 (0.06, 16.17)	0.99	
	No	1/ 808 (0.1)	NE (NE , NE)		10/ 827 (1.2)	NE (NE , NE)		0.10 (0.01, 0.79)	0.00	
	Presence of risk factor: Immunosuppression									0.9996
	Yes	0/ 6 (0.0)	NE (NE , NE)		0/ 7 (0.0)	NE (NE , NE)		NE	NE	
	No	2/ 937 (0.2)	NE (NE , NE)		11/ 957 (1.1)	NE (NE , NE)		0.18 (0.04, 0.83)	0.01	
	Presence of risk factor: Chronic lung disease									0.9996
	Yes	0/ 62 (0.0)	NE (NE , NE)		0/ 39 (0.0)	NE (NE , NE)		NE	NE	
	No	2/ 881 (0.2)	NE (NE , NE)		11/ 925 (1.2)	NE (NE , NE)		0.19 (0.04, 0.86)	0.01	
	Presence of risk factor: Hypertension									
	Yes	1/ 358 (0.3)			7/ 375 (1.9)					
	No	1/ 585 (0.2)			4/ 589 (0.7)					
	Presence of risk factor: Cardiovascular disorder									0.9933
	Yes	0/ 42 (0.0)	NE (NE , NE)		2/ 49 (4.1)	NE (NE , NE)		NE	NE	
	No	2/ 901 (0.2)	NE (NE , NE)		9/ 915 (1.0)	NE (NE , NE)		0.22 (0.05, 1.04)	0.03	
	Presence of risk factor: Chronic kidney disease									0.9995
	Yes	0/ 6 (0.0)	NE (NE , NE)		0/ 8 (0.0)	NE (NE , NE)		NE	NE	
	No	2/ 937 (0.2)	NE (NE , NE)		11/ 956 (1.2)	NE (NE , NE)		0.18 (0.04, 0.83)	0.01	
	Presence of risk factor: HIV Infection									
	Yes	0			0/ 1 (0.0)					
	No	2/ 943 (0.2)			11/ 962 (1.1)					
	Presence of risk factor: Sickle Cell Disease									
	No	2/ 943 (0.2)			11/ 964 (1.1)					

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).
 Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Analysis of Frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or >=10 patients) - Subgroup analysis

Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
		n/	N (%)	Median (95% CI) [1]	n/	N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations, PT: Pneumonia	Presence of risk factor: Neurodevelopmental Disorder									
	Yes	0/	2 (0.0)		0/	1 (0.0)				
	No	2/	941 (0.2)		11/	963 (1.1)				
	Presence of risk factor: Cancer									0.9996
	Yes	0/	5 (0.0)	NE (NE , NE)	0/	6 (0.0)	NE (NE , NE)	NE	NE	
	No	2/	938 (0.2)	NE (NE , NE)	11/	958 (1.1)	NE (NE , NE)	0.18 (0.04, 0.83)	0.01	
	Presence of risk factor: Device Dependence									
	Yes	0/	4 (0.0)		0/	3 (0.0)				
	No	2/	930 (0.2)		11/	953 (1.2)				

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Overall Study population
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Analysis of Frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or >=10 patients) - Subgroup analysis

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Nervous system disorders	Age							0.6589
	< 65	53/ 804 (6.6)	NE (NE , NE)	19/ 816 (2.3)	NE (NE , NE)	2.89 (1.71, 4.88)	<.001	
	>= 65	14/ 140 (10.0)	NE (NE , NE)	4/ 148 (2.7)	NE (NE , NE)	3.82 (1.26, 11.62)	0.01	
	Gender							0.5636
	Male	32/ 474 (6.8)	NE (NE , NE)	10/ 510 (2.0)	NE (NE , NE)	3.53 (1.73, 7.17)	<.001	
	Female	35/ 470 (7.4)	NE (NE , NE)	13/ 454 (2.9)	NE (NE , NE)	2.66 (1.41, 5.02)	0.00	
	Geographic region							0.4018
	United States	24/ 387 (6.2)	NE (NE , NE)	12/ 395 (3.0)	NE (NE , NE)	2.08 (1.04, 4.16)	0.03	
	Europe	28/ 322 (8.7)	NE (NE , NE)	5/ 321 (1.6)	NE (NE , NE)	5.73 (2.21, 14.84)	<.001	
	India	3/ 74 (4.1)	NE (NE , NE)	1/ 78 (1.3)	NE (NE , NE)	3.20 (0.33, 30.72)	0.28	
	Rest of World	12/ 161 (7.5)	NE (NE , NE)	5/ 170 (2.9)	NE (NE , NE)	2.60 (0.92, 7.38)	0.06	
	COVID-19 therapeutic mAb treatment at randomisation							0.1012
	Yes	4/ 60 (6.7)	NE (NE , NE)	4/ 60 (6.7)	NE (NE , NE)	1.01 (0.25, 4.04)	0.98	
	No	63/ 884 (7.1)	NE (NE , NE)	19/ 904 (2.1)	NE (NE , NE)	3.47 (2.08, 5.80)	<.001	
	Baseline viral load 1							0.7411
	< 10^4 copies/mL	20/ 340 (5.9)	NE (NE , NE)	8/ 356 (2.2)	NE (NE , NE)	2.67 (1.18, 6.06)	0.01	
	>= 10^4 copies/mL	46/ 579 (7.9)	NE (NE , NE)	15/ 582 (2.6)	NE (NE , NE)	3.16 (1.77, 5.66)	<.001	
	Baseline viral load 2							0.7410
	< 10^7 copies/mL	46/ 663 (6.9)	NE (NE , NE)	16/ 707 (2.3)	NE (NE , NE)	3.15 (1.78, 5.56)	<.001	
	>= 10^7 copies/mL	20/ 256 (7.8)	NE (NE , NE)	7/ 231 (3.0)	NE (NE , NE)	2.62 (1.11, 6.20)	0.02	
	Baseline serology status							0.7974
	Negative	25/ 439 (5.7)	NE (NE , NE)	9/ 457 (2.0)	NE (NE , NE)	2.94 (1.37, 6.30)	0.00	
	Positive	42/ 494 (8.5)	NE (NE , NE)	13/ 495 (2.6)	NE (NE , NE)	3.33 (1.79, 6.20)	<.001	
	Symptom onset days to first dose date							0.7364
	<= 3	42/ 637 (6.6)	NE (NE , NE)	13/ 632 (2.1)	NE (NE , NE)	3.27 (1.75, 6.09)	<.001	
	> 3	25/ 307 (8.1)	NE (NE , NE)	10/ 332 (3.0)	NE (NE , NE)	2.79 (1.34, 5.80)	0.00	
	BMI group							0.3263
	< 25	19/ 216 (8.8)	NE (NE , NE)	6/ 213 (2.8)	NE (NE , NE)	3.22 (1.29, 8.06)	0.00	
	25 - < 30	18/ 324 (5.6)	NE (NE , NE)	3/ 336 (0.9)	NE (NE , NE)	6.32 (1.86, 21.44)	<.001	
	>= 30	30/ 403 (7.4)	NE (NE , NE)	14/ 415 (3.4)	NE (NE , NE)	2.25 (1.20, 4.25)	0.00	
	Ethnicity							0.8323
	White	54/ 712 (7.6)	NE (NE , NE)	17/ 725 (2.3)	NE (NE , NE)	3.31 (1.92, 5.71)	<.001	
	Black or African American	2/ 45 (4.4)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	1.89 (0.17, 20.89)	0.59	
	Asian	6/ 118 (5.1)	NE (NE , NE)	2/ 127 (1.6)	NE (NE , NE)	3.29 (0.66, 16.30)	0.12	
	Others	5/ 69 (7.2)	NE (NE , NE)	3/ 70 (4.3)	NE (NE , NE)	1.71 (0.41, 7.17)	0.45	

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Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Nervous system disorders	Number of baseline comorbidities present							0.8746
	0-1	43/ 720 (6.0)	NE (NE , NE)	16/ 734 (2.2)	NE (NE , NE)	2.79 (1.57, 4.95)	<.001	
	2-3	24/ 220 (10.9)	NE (NE , NE)	7/ 224 (3.1)	NE (NE , NE)	3.60 (1.55, 8.36)	0.00	
	>= 4	0/ 4 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	Presence of risk factor: Smoking							0.7291
	Yes	23/ 423 (5.4)	NE (NE , NE)	9/ 442 (2.0)	NE (NE , NE)	2.72 (1.26, 5.89)	0.00	
	No	44/ 519 (8.5)	NE (NE , NE)	14/ 522 (2.7)	NE (NE , NE)	3.24 (1.78, 5.91)	<.001	
	Presence of risk factor: Diabetes mellitus							0.4161
	Yes	17/ 135 (12.6)	NE (NE , NE)	4/ 137 (2.9)	NE (NE , NE)	4.47 (1.50, 13.29)	0.00	
	No	50/ 808 (6.2)	NE (NE , NE)	19/ 827 (2.3)	NE (NE , NE)	2.75 (1.62, 4.66)	<.001	
	Presence of risk factor: Immunosuppression							0.9802
	Yes	1/ 6 (16.7)	NE (5.0, NE)	0/ 7 (0.0)	NE (NE , NE)	NE	NE	
	No	66/ 937 (7.0)	NE (NE , NE)	23/ 957 (2.4)	NE (NE , NE)	3.00 (1.86, 4.82)	<.001	
	Presence of risk factor: Chronic lung disease							0.1046
	Yes	2/ 62 (3.2)	NE (NE , NE)	2/ 39 (5.1)	NE (NE , NE)	0.62 (0.09, 4.41)	0.63	
	No	65/ 881 (7.4)	NE (NE , NE)	21/ 925 (2.3)	NE (NE , NE)	3.33 (2.03, 5.44)	<.001	
	Presence of risk factor: Hypertension							0.3317
	Yes	36/ 358 (10.1)	NE (NE , NE)	10/ 375 (2.7)	NE (NE , NE)	3.88 (1.93, 7.82)	<.001	
	No	31/ 585 (5.3)	NE (NE , NE)	13/ 589 (2.2)	NE (NE , NE)	2.44 (1.28, 4.67)	0.00	
	Presence of risk factor: Cardiovascular disorder							0.9782
	Yes	6/ 42 (14.3)	NE (NE , NE)	0/ 49 (0.0)	NE (NE , NE)	NE	NE	
	No	61/ 901 (6.8)	NE (NE , NE)	23/ 915 (2.5)	NE (NE , NE)	2.75 (1.70, 4.45)	<.001	
	Presence of risk factor: Chronic kidney disease							0.9814
	Yes	3/ 6 (50.0)	NE (1.0, NE)	0/ 8 (0.0)	NE (NE , NE)	NE	NE	
	No	64/ 937 (6.8)	NE (NE , NE)	23/ 956 (2.4)	NE (NE , NE)	2.90 (1.80, 4.67)	<.001	
	Presence of risk factor: HIV Infection							
	Yes	0		1/ 1 (100.0)				
	No	67/ 943 (7.1)		22/ 962 (2.3)				
	Presence of risk factor: Sickle Cell Disease							
	No	67/ 943 (7.1)		23/ 964 (2.4)				

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SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Nervous system disorders	Presence of risk factor:							
	Neurodevelopmental Disorder							
	Yes	0/ 2 (0.0)		0/ 1 (0.0)				
	No	67/ 941 (7.1)		23/ 963 (2.4)				
	Presence of risk factor: Cancer							0.9817
	Yes	1/ 5 (20.0)	NE (3.0, NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	No	66/ 938 (7.0)	NE (NE , NE)	23/ 958 (2.4)	NE (NE , NE)	3.00 (1.86, 4.82)	<.001	
	Presence of risk factor: Device Dependence							
	Yes	0/ 4 (0.0)		0/ 3 (0.0)				
	No	64/ 930 (6.9)		23/ 953 (2.4)				

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SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Nervous system disorders, PT: Dysgeusia	Age							0.1143
	< 65	43/ 804 (5.3)	NE (NE , NE)	1/ 816 (0.1)	NE (NE , NE)	44.22 (6.09, 320.90)	<.001	
	>= 65	11/ 140 (7.9)	NE (NE , NE)	2/ 148 (1.4)	NE (NE , NE)	5.96 (1.32, 26.90)	0.00	
	Gender							0.5633
	Male	26/ 474 (5.5)	NE (NE , NE)	1/ 510 (0.2)	NE (NE , NE)	28.46 (3.86, 209.74)	<.001	
	Female	28/ 470 (6.0)	NE (NE , NE)	2/ 454 (0.4)	NE (NE , NE)	13.71 (3.27, 57.56)	<.001	
	Geographic region							0.8921
	United States	19/ 387 (4.9)	NE (NE , NE)	2/ 395 (0.5)	NE (NE , NE)	9.79 (2.28, 42.04)	<.001	
	Europe	26/ 322 (8.1)	NE (NE , NE)	1/ 321 (0.3)	NE (NE , NE)	26.54 (3.60, 195.56)	<.001	
	India	0/ 74 (0.0)	NE (NE , NE)	0/ 78 (0.0)	NE (NE , NE)	NE	NE	
	Rest of World	9/ 161 (5.6)	NE (NE , NE)	0/ 170 (0.0)	NE (NE , NE)	NE	NE	
	COVID-19 therapeutic mAb treatment at randomisation							0.1626
	Yes	4/ 60 (6.7)	NE (NE , NE)	1/ 60 (1.7)	NE (NE , NE)	4.08 (0.46, 36.53)	0.16	
	No	50/ 884 (5.7)	NE (NE , NE)	2/ 904 (0.2)	NE (NE , NE)	25.94 (6.31, 106.62)	<.001	
	Baseline viral load 1							0.2832
	< 10^4 copies/mL	18/ 340 (5.3)	NE (NE , NE)	2/ 356 (0.6)	NE (NE , NE)	9.57 (2.22, 41.24)	<.001	
	>= 10^4 copies/mL	36/ 579 (6.2)	NE (NE , NE)	1/ 582 (0.2)	NE (NE , NE)	36.78 (5.04, 268.22)	<.001	
	Baseline viral load 2							0.7903
	< 10^7 copies/mL	38/ 663 (5.7)	NE (NE , NE)	2/ 707 (0.3)	NE (NE , NE)	20.59 (4.97, 85.36)	<.001	
	>= 10^7 copies/mL	16/ 256 (6.3)	NE (NE , NE)	1/ 231 (0.4)	NE (NE , NE)	14.66 (1.95, 110.48)	<.001	
	Baseline serology status							0.9639
	Negative	17/ 439 (3.9)	NE (NE , NE)	1/ 457 (0.2)	NE (NE , NE)	17.90 (2.38, 134.42)	<.001	
	Positive	37/ 494 (7.5)	NE (NE , NE)	2/ 495 (0.4)	NE (NE , NE)	18.89 (4.55, 78.39)	<.001	
	Symptom onset days to first dose date							0.8924
	<= 3	35/ 637 (5.5)	NE (NE , NE)	2/ 632 (0.3)	NE (NE , NE)	17.60 (4.24, 73.12)	<.001	
	> 3	19/ 307 (6.2)	NE (NE , NE)	1/ 332 (0.3)	NE (NE , NE)	20.92 (2.80, 156.30)	<.001	
	BMI group							0.9857
	< 25	12/ 216 (5.6)	NE (NE , NE)	0/ 213 (0.0)	NE (NE , NE)	NE	NE	
	25 - < 30	16/ 324 (4.9)	NE (NE , NE)	1/ 336 (0.3)	NE (NE , NE)	16.79 (2.23, 126.54)	<.001	
	>= 30	26/ 403 (6.5)	NE (NE , NE)	2/ 415 (0.5)	NE (NE , NE)	13.63 (3.23, 57.41)	<.001	
	Ethnicity							1.0000
	White	47/ 712 (6.6)	NE (NE , NE)	3/ 725 (0.4)	NE (NE , NE)	16.23 (5.05, 52.14)	<.001	
	Black or African American	1/ 45 (2.2)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE	NE	
	Asian	2/ 118 (1.7)	NE (NE , NE)	0/ 127 (0.0)	NE (NE , NE)	NE	NE	
	Others	4/ 69 (5.8)	NE (NE , NE)	0/ 70 (0.0)	NE (NE , NE)	NE	NE	

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SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Nervous system disorders, PT: Dysgeusia	Number of baseline comorbidities present							0.6301
	0-1	34/ 720 (4.7)	NE (NE , NE)	1/ 734 (0.1)	NE (NE , NE)	35.21 (4.82, 257.15)	<.001	
	2-3	20/ 220 (9.1)	NE (NE , NE)	2/ 224 (0.9)	NE (NE , NE)	10.30 (2.41, 44.08)	<.001	
	>= 4	0/ 4 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	Presence of risk factor: Smoking							0.9831
	Yes	19/ 423 (4.5)	NE (NE , NE)	0/ 442 (0.0)	NE (NE , NE)	NE	NE	
	No	35/ 519 (6.7)	NE (NE , NE)	3/ 522 (0.6)	NE (NE , NE)	11.96 (3.68, 38.89)	<.001	
	Presence of risk factor: Diabetes mellitus							0.1703
	Yes	14/ 135 (10.4)	NE (NE , NE)	2/ 137 (1.5)	NE (NE , NE)	7.23 (1.64, 31.83)	0.00	
	No	40/ 808 (5.0)	NE (NE , NE)	1/ 827 (0.1)	NE (NE , NE)	41.55 (5.71, 302.14)	<.001	
	Presence of risk factor: Immunosuppression							0.9985
	Yes	0/ 6 (0.0)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE	NE	
	No	54/ 937 (5.8)	NE (NE , NE)	3/ 957 (0.3)	NE (NE , NE)	18.66 (5.84, 59.63)	<.001	
	Presence of risk factor: Chronic lung disease							0.0165
	Yes	1/ 62 (1.6)	NE (NE , NE)	1/ 39 (2.6)	NE (NE , NE)	0.63 (0.04, 10.14)	0.74	
	No	53/ 881 (6.0)	NE (NE , NE)	2/ 925 (0.2)	NE (NE , NE)	28.26 (6.89, 115.95)	<.001	
	Presence of risk factor: Hypertension							0.9818
	Yes	29/ 358 (8.1)	NE (NE , NE)	3/ 375 (0.8)	NE (NE , NE)	10.29 (3.13, 33.77)	<.001	
	No	25/ 585 (4.3)	NE (NE , NE)	0/ 589 (0.0)	NE (NE , NE)	NE	NE	
	Presence of risk factor: Cardiovascular disorder							0.9840
	Yes	6/ 42 (14.3)	NE (NE , NE)	0/ 49 (0.0)	NE (NE , NE)	NE	NE	
	No	48/ 901 (5.3)	NE (NE , NE)	3/ 915 (0.3)	NE (NE , NE)	16.48 (5.13, 52.89)	<.001	
	Presence of risk factor: Chronic kidney disease							0.9869
	Yes	3/ 6 (50.0)	NE (1.0, NE)	0/ 8 (0.0)	NE (NE , NE)	NE	NE	
	No	51/ 937 (5.4)	NE (NE , NE)	3/ 956 (0.3)	NE (NE , NE)	17.59 (5.49, 56.34)	<.001	
	Presence of risk factor: HIV Infection							
	Yes	0		0/ 1 (0.0)				
	No	54/ 943 (5.7)		3/ 962 (0.3)				
	Presence of risk factor: Sickle Cell Disease							
	No	54/ 943 (5.7)		3/ 964 (0.3)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

MedDRA v24.1 coding dictionary applied.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Pfizer Inc
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 Analysis of Frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or >=10 patients) - Subgroup analysis

Final

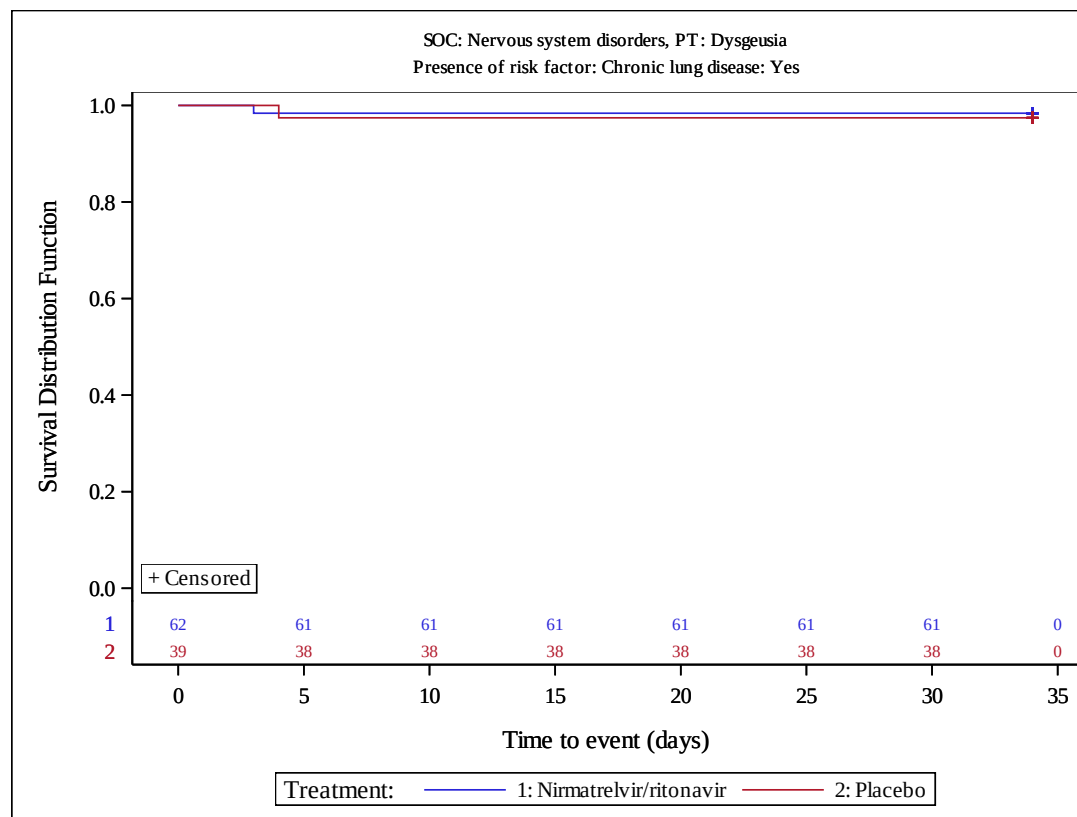
SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Nervous system disorders, PT: Dysgeusia	Presence of risk factor: Neurodevelopmental Disorder							
	Yes	0/ 2 (0.0)		0/ 1 (0.0)				
	No	54/ 941 (5.7)		3/ 963 (0.3)				
	Presence of risk factor: Cancer							0.9866
	Yes	1/ 5 (20.0)	NE (3.0, NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	No	53/ 938 (5.7)	NE (NE , NE)	3/ 958 (0.3)	NE (NE , NE)	18.30 (5.72, 58.53)	<.001	
	Presence of risk factor: Device Dependence							
	Yes	0/ 4 (0.0)		0/ 3 (0.0)				
	No	51/ 930 (5.5)		3/ 953 (0.3)				

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 MedDRA v24.1 coding dictionary applied.
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Final

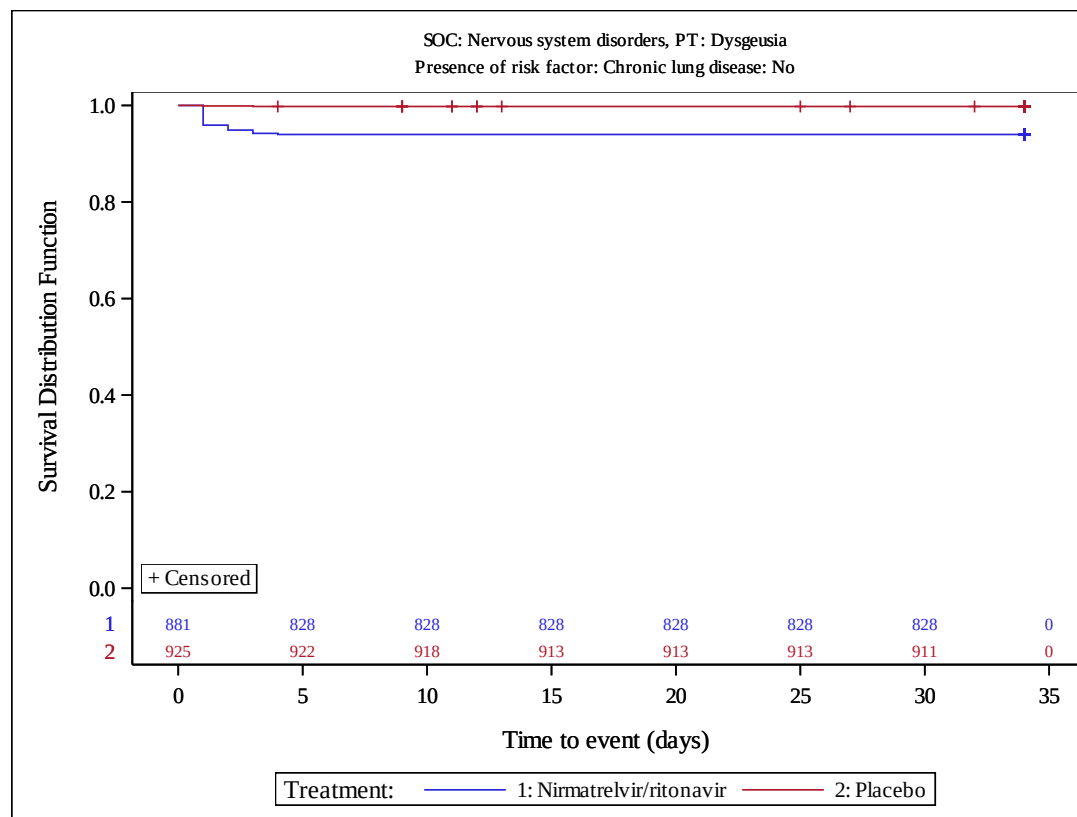


Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

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Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations	Age							0.3888
	< 65	7/ 804 (0.9)	NE (NE , NE)	30/ 816 (3.7)	NE (NE , NE)	0.23 (0.10, 0.53)	<.001	
	>= 65	2/ 140 (1.4)	NE (NE , NE)	18/ 148 (12.2)	NE (NE , NE)	0.11 (0.03, 0.48)	<.001	
	Gender							0.4449
	Male	5/ 474 (1.1)	NE (NE , NE)	34/ 510 (6.7)	NE (NE , NE)	0.15 (0.06, 0.39)	<.001	
	Female	4/ 470 (0.9)	NE (NE , NE)	14/ 454 (3.1)	NE (NE , NE)	0.27 (0.09, 0.83)	0.01	
	Geographic region							0.6089
	United States	4/ 387 (1.0)	NE (NE , NE)	11/ 395 (2.8)	NE (NE , NE)	0.37 (0.12, 1.15)	0.07	
	Europe	4/ 322 (1.2)	NE (NE , NE)	28/ 321 (8.7)	NE (NE , NE)	0.14 (0.05, 0.39)	<.001	
	India	0/ 74 (0.0)	NE (NE , NE)	0/ 78 (0.0)	NE (NE , NE)	NE	NE	
	Rest of World	1/ 161 (0.6)	NE (NE , NE)	9/ 170 (5.3)	NE (NE , NE)	0.11 (0.01, 0.91)	0.01	
	COVID-19 therapeutic mAb treatment at randomisation							0.2257
	Yes	1/ 60 (1.7)	NE (NE , NE)	1/ 60 (1.7)	NE (NE , NE)	1.01 (0.06, 16.12)	0.99	
	No	8/ 884 (0.9)	NE (NE , NE)	47/ 904 (5.2)	NE (NE , NE)	0.17 (0.08, 0.36)	<.001	
	Baseline viral load 1							0.6074
	< 10^4 copies/mL	1/ 340 (0.3)	NE (NE , NE)	3/ 356 (0.8)	NE (NE , NE)	0.35 (0.04, 3.36)	0.34	
	>= 10^4 copies/mL	8/ 579 (1.4)	NE (NE , NE)	42/ 582 (7.2)	NE (NE , NE)	0.19 (0.09, 0.40)	<.001	
	Baseline viral load 2							0.7123
	< 10^7 copies/mL	5/ 663 (0.8)	NE (NE , NE)	24/ 707 (3.4)	NE (NE , NE)	0.22 (0.08, 0.58)	<.001	
	>= 10^7 copies/mL	4/ 256 (1.6)	NE (NE , NE)	21/ 231 (9.1)	NE (NE , NE)	0.17 (0.06, 0.48)	<.001	
	Baseline serology status							0.4545
	Negative	7/ 439 (1.6)	NE (NE , NE)	42/ 457 (9.2)	NE (NE , NE)	0.17 (0.08, 0.37)	<.001	
	Positive	2/ 494 (0.4)	NE (NE , NE)	6/ 495 (1.2)	NE (NE , NE)	0.33 (0.07, 1.65)	0.15	
	Symptom onset days to first dose date							0.7389
	<= 3	7/ 637 (1.1)	NE (NE , NE)	34/ 632 (5.4)	NE (NE , NE)	0.20 (0.09, 0.45)	<.001	
	> 3	2/ 307 (0.7)	NE (NE , NE)	14/ 332 (4.2)	NE (NE , NE)	0.15 (0.03, 0.67)	0.00	
	BMI group							0.5896
	< 25	1/ 216 (0.5)	NE (NE , NE)	7/ 213 (3.3)	NE (NE , NE)	0.14 (0.02, 1.13)	0.03	
	25 - < 30	2/ 324 (0.6)	NE (NE , NE)	18/ 336 (5.4)	NE (NE , NE)	0.11 (0.03, 0.49)	<.001	
	>= 30	6/ 403 (1.5)	NE (NE , NE)	23/ 415 (5.5)	NE (NE , NE)	0.26 (0.11, 0.65)	0.00	
	Ethnicity							0.7245
	White	7/ 712 (1.0)	NE (NE , NE)	41/ 725 (5.7)	NE (NE , NE)	0.17 (0.08, 0.38)	<.001	
	Black or African American	1/ 45 (2.2)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	0.92 (0.06, 14.74)	0.95	
	Asian	0/ 118 (0.0)	NE (NE , NE)	1/ 127 (0.8)	NE (NE , NE)	NE	NE	
	Others	1/ 69 (1.4)	NE (NE , NE)	5/ 70 (7.1)	NE (NE , NE)	0.20 (0.02, 1.70)	0.10	

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SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations	Number of baseline comorbidities present							0.4626
	0-1	4/ 720 (0.6)	NE (NE , NE)	32/ 734 (4.4)	NE (NE , NE)	0.13 (0.04, 0.35)	<.001	
	2-3	5/ 220 (2.3)	NE (NE , NE)	16/ 224 (7.1)	NE (NE , NE)	0.31 (0.11, 0.85)	0.01	
	>= 4	0/ 4 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	Presence of risk factor: Smoking							0.7484
	Yes	3/ 423 (0.7)	NE (NE , NE)	14/ 442 (3.2)	NE (NE , NE)	0.22 (0.06, 0.77)	0.00	
	No	6/ 519 (1.2)	NE (NE , NE)	34/ 522 (6.5)	NE (NE , NE)	0.17 (0.07, 0.41)	<.001	
	Presence of risk factor: Diabetes mellitus							0.0311
	Yes	4/ 135 (3.0)	NE (NE , NE)	6/ 137 (4.4)	NE (NE , NE)	0.67 (0.19, 2.37)	0.53	
	No	5/ 808 (0.6)	NE (NE , NE)	42/ 827 (5.1)	NE (NE , NE)	0.12 (0.05, 0.30)	<.001	
	Presence of risk factor: Immunosuppression							0.9991
	Yes	0/ 6 (0.0)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE	NE	
	No	9/ 937 (1.0)	NE (NE , NE)	48/ 957 (5.0)	NE (NE , NE)	0.19 (0.09, 0.38)	<.001	
	Presence of risk factor: Chronic lung disease							0.3859
	Yes	1/ 62 (1.6)	NE (NE , NE)	1/ 39 (2.6)	NE (NE , NE)	0.62 (0.04, 9.93)	0.73	
	No	8/ 881 (0.9)	NE (NE , NE)	47/ 925 (5.1)	NE (NE , NE)	0.18 (0.08, 0.37)	<.001	
	Presence of risk factor: Hypertension							0.3793
	Yes	5/ 358 (1.4)	NE (NE , NE)	34/ 375 (9.1)	NE (NE , NE)	0.15 (0.06, 0.38)	<.001	
	No	4/ 585 (0.7)	NE (NE , NE)	14/ 589 (2.4)	NE (NE , NE)	0.29 (0.09, 0.87)	0.01	
	Presence of risk factor: Cardiovascular disorder							0.9800
	Yes	0/ 42 (0.0)	NE (NE , NE)	8/ 49 (16.3)	NE (NE , NE)	NE	NE	
	No	9/ 901 (1.0)	NE (NE , NE)	40/ 915 (4.4)	NE (NE , NE)	0.23 (0.11, 0.46)	<.001	
	Presence of risk factor: Chronic kidney disease							0.9990
	Yes	0/ 6 (0.0)	NE (NE , NE)	0/ 8 (0.0)	NE (NE , NE)	NE	NE	
	No	9/ 937 (1.0)	NE (NE , NE)	48/ 956 (5.0)	NE (NE , NE)	0.19 (0.09, 0.38)	<.001	
	Presence of risk factor: HIV Infection							
	Yes	0		0/ 1 (0.0)				
	No	9/ 943 (1.0)		48/ 962 (5.0)				
	Presence of risk factor: Sickle Cell Disease							
	No	9/ 943 (1.0)		48/ 964 (5.0)				

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SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations	Presence of risk factor:							
	Neurodevelopmental Disorder							
	Yes	0/ 2 (0.0)		1/ 1 (100.0)				
	No	9/ 941 (1.0)		47/ 963 (4.9)				
	Presence of risk factor: Cancer							0.9992
	Yes	0/ 5 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	No	9/ 938 (1.0)	NE (NE , NE)	48/ 958 (5.0)	NE (NE , NE)	0.19 (0.09, 0.38)	<.001	
	Presence of risk factor: Device							
	Dependence							
	Yes	0/ 4 (0.0)		0/ 3 (0.0)				
	No	9/ 930 (1.0)		47/ 953 (4.9)				

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SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations, PT: COVID-19 pneumonia	Age							0.3398
	< 65	4/ 804 (0.5)	NE (NE , NE)	18/ 816 (2.2)	NE (NE , NE)	0.22 (0.08, 0.66)	0.00	
	>= 65	1/ 140 (0.7)	NE (NE , NE)	14/ 148 (9.5)	NE (NE , NE)	0.07 (0.01, 0.55)	<.001	
	Gender							0.9988
	Male	3/ 474 (0.6)	NE (NE , NE)	20/ 510 (3.9)	NE (NE , NE)	0.16 (0.05, 0.53)	<.001	
	Female	2/ 470 (0.4)	NE (NE , NE)	12/ 454 (2.6)	NE (NE , NE)	0.16 (0.04, 0.71)	0.00	
	Geographic region							0.9995
	United States	1/ 387 (0.3)	NE (NE , NE)	7/ 395 (1.8)	NE (NE , NE)	0.14 (0.02, 1.18)	0.03	
	Europe	3/ 322 (0.9)	NE (NE , NE)	19/ 321 (5.9)	NE (NE , NE)	0.15 (0.05, 0.52)	<.001	
	India	0/ 74 (0.0)	NE (NE , NE)	0/ 78 (0.0)	NE (NE , NE)	NE	NE	
	Rest of World	1/ 161 (0.6)	NE (NE , NE)	6/ 170 (3.5)	NE (NE , NE)	0.17 (0.02, 1.44)	0.06	
	COVID-19 therapeutic mAb treatment at randomisation							0.9872
	Yes	0/ 60 (0.0)	NE (NE , NE)	1/ 60 (1.7)	NE (NE , NE)	NE	NE	
	No	5/ 884 (0.6)	NE (NE , NE)	31/ 904 (3.4)	NE (NE , NE)	0.16 (0.06, 0.42)	<.001	
	Baseline viral load 1							0.9906
	< 10^4 copies/mL	0/ 340 (0.0)	NE (NE , NE)	1/ 356 (0.3)	NE (NE , NE)	NE	NE	
	>= 10^4 copies/mL	5/ 579 (0.9)	NE (NE , NE)	29/ 582 (5.0)	NE (NE , NE)	0.17 (0.07, 0.44)	<.001	
	Baseline viral load 2							0.7097
	< 10^7 copies/mL	2/ 663 (0.3)	NE (NE , NE)	16/ 707 (2.3)	NE (NE , NE)	0.13 (0.03, 0.58)	0.00	
	>= 10^7 copies/mL	3/ 256 (1.2)	NE (NE , NE)	14/ 231 (6.1)	NE (NE , NE)	0.19 (0.05, 0.66)	0.00	
	Baseline serology status							0.9631
	Negative	4/ 439 (0.9)	NE (NE , NE)	26/ 457 (5.7)	NE (NE , NE)	0.16 (0.05, 0.45)	<.001	
	Positive	1/ 494 (0.2)	NE (NE , NE)	6/ 495 (1.2)	NE (NE , NE)	0.17 (0.02, 1.38)	0.05	
	Symptom onset days to first dose date							0.9869
	<= 3	5/ 637 (0.8)	NE (NE , NE)	23/ 632 (3.6)	NE (NE , NE)	0.21 (0.08, 0.56)	<.001	
	> 3	0/ 307 (0.0)	NE (NE , NE)	9/ 332 (2.7)	NE (NE , NE)	NE	NE	
	BMI group							0.9090
	< 25	1/ 216 (0.5)	NE (NE , NE)	4/ 213 (1.9)	NE (NE , NE)	0.25 (0.03, 2.20)	0.17	
	25 - < 30	2/ 324 (0.6)	NE (NE , NE)	15/ 336 (4.5)	NE (NE , NE)	0.14 (0.03, 0.60)	0.00	
	>= 30	2/ 403 (0.5)	NE (NE , NE)	13/ 415 (3.1)	NE (NE , NE)	0.16 (0.04, 0.69)	0.00	
	Ethnicity							0.9396
	White	4/ 712 (0.6)	NE (NE , NE)	27/ 725 (3.7)	NE (NE , NE)	0.15 (0.05, 0.43)	<.001	
	Black or African American	0/ 45 (0.0)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	NE	NE	
	Asian	0/ 118 (0.0)	NE (NE , NE)	1/ 127 (0.8)	NE (NE , NE)	NE	NE	
	Others	1/ 69 (1.4)	NE (NE , NE)	3/ 70 (4.3)	NE (NE , NE)	0.33 (0.03, 3.22)	0.31	

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Frequent Severe Adverse Events (DAIDS >=3) by SOC and PT (incidence in either arm >= 5% or >=10 patients) - Subgroup analysis

Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]		n/ N (%)	Median (95% CI) [1]		Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations, PT: COVID-19 pneumonia	Number of baseline comorbidities present									0.8672
	0-1	3/ 720 (0.4)	NE (NE , NE)		23/ 734 (3.1)	NE (NE , NE)		0.13 (0.04, 0.44)	<.001	
	2-3	2/ 220 (0.9)	NE (NE , NE)		9/ 224 (4.0)	NE (NE , NE)		0.23 (0.05, 1.04)	0.03	
	>= 4	0/ 4 (0.0)	NE (NE , NE)		0/ 6 (0.0)	NE (NE , NE)		NE	NE	
	Presence of risk factor: Smoking									0.3621
	Yes	2/ 423 (0.5)	NE (NE , NE)		7/ 442 (1.6)	NE (NE , NE)		0.30 (0.06, 1.43)	0.10	
	No	3/ 519 (0.6)	NE (NE , NE)		25/ 522 (4.8)	NE (NE , NE)		0.12 (0.04, 0.39)	<.001	
	Presence of risk factor: Diabetes mellitus									0.4896
	Yes	1/ 135 (0.7)	NE (NE , NE)		3/ 137 (2.2)	NE (NE , NE)		0.34 (0.03, 3.23)	0.32	
	No	4/ 808 (0.5)	NE (NE , NE)		29/ 827 (3.5)	NE (NE , NE)		0.14 (0.05, 0.40)	<.001	
	Presence of risk factor: Immunosuppression									0.9992
	Yes	0/ 6 (0.0)	NE (NE , NE)		0/ 7 (0.0)	NE (NE , NE)		NE	NE	
	No	5/ 937 (0.5)	NE (NE , NE)		32/ 957 (3.3)	NE (NE , NE)		0.16 (0.06, 0.40)	<.001	
	Presence of risk factor: Chronic lung disease									0.9864
	Yes	0/ 62 (0.0)	NE (NE , NE)		1/ 39 (2.6)	NE (NE , NE)		NE	NE	
	No	5/ 881 (0.6)	NE (NE , NE)		31/ 925 (3.4)	NE (NE , NE)		0.17 (0.07, 0.43)	<.001	
	Presence of risk factor: Hypertension									0.3993
	Yes	3/ 358 (0.8)	NE (NE , NE)		25/ 375 (6.7)	NE (NE , NE)		0.12 (0.04, 0.41)	<.001	
	No	2/ 585 (0.3)	NE (NE , NE)		7/ 589 (1.2)	NE (NE , NE)		0.29 (0.06, 1.38)	0.09	
	Presence of risk factor: Cardiovascular disorder									0.9890
	Yes	0/ 42 (0.0)	NE (NE , NE)		6/ 49 (12.2)	NE (NE , NE)		NE	NE	
	No	5/ 901 (0.6)	NE (NE , NE)		26/ 915 (2.8)	NE (NE , NE)		0.19 (0.07, 0.50)	<.001	
	Presence of risk factor: Chronic kidney disease									0.9992
	Yes	0/ 6 (0.0)	NE (NE , NE)		0/ 8 (0.0)	NE (NE , NE)		NE	NE	
	No	5/ 937 (0.5)	NE (NE , NE)		32/ 956 (3.3)	NE (NE , NE)		0.16 (0.06, 0.40)	<.001	
	Presence of risk factor: HIV Infection									
	Yes	0			0/ 1 (0.0)					
	No	5/ 943 (0.5)			32/ 962 (3.3)					
	Presence of risk factor: Sickle Cell Disease									
	No	5/ 943 (0.5)			32/ 964 (3.3)					

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).
 Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value [2]	
SOC: Infections and infestations, PT: COVID-19 pneumonia	Presence of risk factor: Neurodevelopmental Disorder							
	Yes	0/ 2 (0.0)		0/ 1 (0.0)				
	No	5/ 941 (0.5)		32/ 963 (3.3)				
	Presence of risk factor: Cancer							0.9993
	Yes	0/ 5 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	No	5/ 938 (0.5)	NE (NE , NE)	32/ 958 (3.3)	NE (NE , NE)	0.16 (0.06, 0.40)	<.001	
	Presence of risk factor: Device Dependence							
	Yes	0/ 4 (0.0)		0/ 3 (0.0)				
	No	5/ 930 (0.5)		32/ 953 (3.4)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
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SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Respiratory, thoracic and mediastinal disorders	Age							0.9916
	< 65	1/ 804 (0.1)	NE (NE , NE)	13/ 816 (1.6)	NE (NE , NE)	0.08 (0.01, 0.59)	0.00	
	>= 65	0/ 140 (0.0)	NE (NE , NE)	4/ 148 (2.7)	NE (NE , NE)	NE	NE	
	Gender							0.9897
	Male	0/ 474 (0.0)	NE (NE , NE)	12/ 510 (2.4)	NE (NE , NE)	NE	NE	
	Female	1/ 470 (0.2)	NE (NE , NE)	5/ 454 (1.1)	NE (NE , NE)	0.19 (0.02, 1.64)	0.09	
	Geographic region							
	United States	1/ 387 (0.3)		4/ 395 (1.0)				
	Europe	0/ 322 (0.0)		8/ 321 (2.5)				
	India	0/ 74 (0.0)		0/ 78 (0.0)				
	Rest of World	0/ 161 (0.0)		5/ 170 (2.9)				
	COVID-19 therapeutic mAb treatment at randomisation							0.9916
	Yes	0/ 60 (0.0)	NE (NE , NE)	1/ 60 (1.7)	NE (NE , NE)	NE	NE	
	No	1/ 884 (0.1)	NE (NE , NE)	16/ 904 (1.8)	NE (NE , NE)	0.06 (0.01, 0.48)	<.001	
	Baseline viral load 1							0.9991
	< 10^4 copies/mL	0/ 340 (0.0)	NE (NE , NE)	0/ 356 (0.0)	NE (NE , NE)	NE	NE	
	>= 10^4 copies/mL	1/ 579 (0.2)	NE (NE , NE)	16/ 582 (2.7)	NE (NE , NE)	0.06 (0.01, 0.47)	<.001	
	Baseline viral load 2							0.9889
	< 10^7 copies/mL	1/ 663 (0.2)	NE (NE , NE)	10/ 707 (1.4)	NE (NE , NE)	0.11 (0.01, 0.83)	0.00	
	>= 10^7 copies/mL	0/ 256 (0.0)	NE (NE , NE)	6/ 231 (2.6)	NE (NE , NE)	NE	NE	
	Baseline serology status							0.9912
	Negative	1/ 439 (0.2)	NE (NE , NE)	12/ 457 (2.6)	NE (NE , NE)	0.09 (0.01, 0.66)	0.00	
	Positive	0/ 494 (0.0)	NE (NE , NE)	5/ 495 (1.0)	NE (NE , NE)	NE	NE	
	Symptom onset days to first dose date							0.9896
	<= 3	0/ 637 (0.0)	NE (NE , NE)	8/ 632 (1.3)	NE (NE , NE)	NE	NE	
	> 3	1/ 307 (0.3)	NE (NE , NE)	9/ 332 (2.7)	NE (NE , NE)	0.12 (0.02, 0.94)	0.01	
	BMI group							
	< 25	0/ 216 (0.0)		3/ 213 (1.4)				
	25 - < 30	0/ 324 (0.0)		7/ 336 (2.1)				
	>= 30	1/ 403 (0.2)		7/ 415 (1.7)				
	Ethnicity							1.0000
	White	1/ 712 (0.1)	NE (NE , NE)	13/ 725 (1.8)	NE (NE , NE)	0.08 (0.01, 0.59)	0.00	
	Black or African American	0/ 45 (0.0)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE	NE	
	Asian	0/ 118 (0.0)	NE (NE , NE)	2/ 127 (1.6)	NE (NE , NE)	NE	NE	
	Others	0/ 69 (0.0)	NE (NE , NE)	2/ 70 (2.9)	NE (NE , NE)	NE	NE	

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SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]		n/ N (%)	Median (95% CI) [1]		Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Respiratory, thoracic and mediastinal disorders	Number of baseline comorbidities present									0.9999
	0-1	0/ 720 (0.0)	NE (NE , NE)		12/ 734 (1.6)	NE (NE , NE)		NE	NE	
	2-3	1/ 220 (0.5)	NE (NE , NE)		5/ 224 (2.2)	NE (NE , NE)		0.20 (0.02, 1.72)	0.10	
	>= 4	0/ 4 (0.0)	NE (NE , NE)		0/ 6 (0.0)	NE (NE , NE)		NE	NE	
	Presence of risk factor: Smoking									0.9919
	Yes	0/ 423 (0.0)	NE (NE , NE)		4/ 442 (0.9)	NE (NE , NE)		NE	NE	
	No	1/ 519 (0.2)	NE (NE , NE)		13/ 522 (2.5)	NE (NE , NE)		0.08 (0.01, 0.58)	0.00	
	Presence of risk factor: Diabetes mellitus									0.9902
	Yes	1/ 135 (0.7)	NE (NE , NE)		2/ 137 (1.5)	NE (NE , NE)		0.50 (0.05, 5.53)	0.56	
	No	0/ 808 (0.0)	NE (NE , NE)		15/ 827 (1.8)	NE (NE , NE)		NE	NE	
	Presence of risk factor: Immunosuppression									0.9992
	Yes	0/ 6 (0.0)	NE (NE , NE)		0/ 7 (0.0)	NE (NE , NE)		NE	NE	
	No	1/ 937 (0.1)	NE (NE , NE)		17/ 957 (1.8)	NE (NE , NE)		0.06 (0.01, 0.45)	<.001	
	Presence of risk factor: Chronic lung disease									0.9912
	Yes	0/ 62 (0.0)	NE (NE , NE)		1/ 39 (2.6)	NE (NE , NE)		NE	NE	
	No	1/ 881 (0.1)	NE (NE , NE)		16/ 925 (1.7)	NE (NE , NE)		0.07 (0.01, 0.49)	<.001	
	Presence of risk factor: Hypertension									0.9892
	Yes	1/ 358 (0.3)	NE (NE , NE)		9/ 375 (2.4)	NE (NE , NE)		0.12 (0.01, 0.91)	0.01	
	No	0/ 585 (0.0)	NE (NE , NE)		8/ 589 (1.4)	NE (NE , NE)		NE	NE	
	Presence of risk factor: Cardiovascular disorder									0.9929
	Yes	0/ 42 (0.0)	NE (NE , NE)		1/ 49 (2.0)	NE (NE , NE)		NE	NE	
	No	1/ 901 (0.1)	NE (NE , NE)		16/ 915 (1.7)	NE (NE , NE)		0.06 (0.01, 0.48)	<.001	
	Presence of risk factor: Chronic kidney disease									0.9992
	Yes	0/ 6 (0.0)	NE (NE , NE)		0/ 8 (0.0)	NE (NE , NE)		NE	NE	
	No	1/ 937 (0.1)	NE (NE , NE)		17/ 956 (1.8)	NE (NE , NE)		0.06 (0.01, 0.45)	<.001	
	Presence of risk factor: HIV Infection									
	Yes	0			0/ 1 (0.0)					
	No	1/ 943 (0.1)			17/ 962 (1.8)					
	Presence of risk factor: Sickle Cell Disease									
	No	1/ 943 (0.1)			17/ 964 (1.8)					

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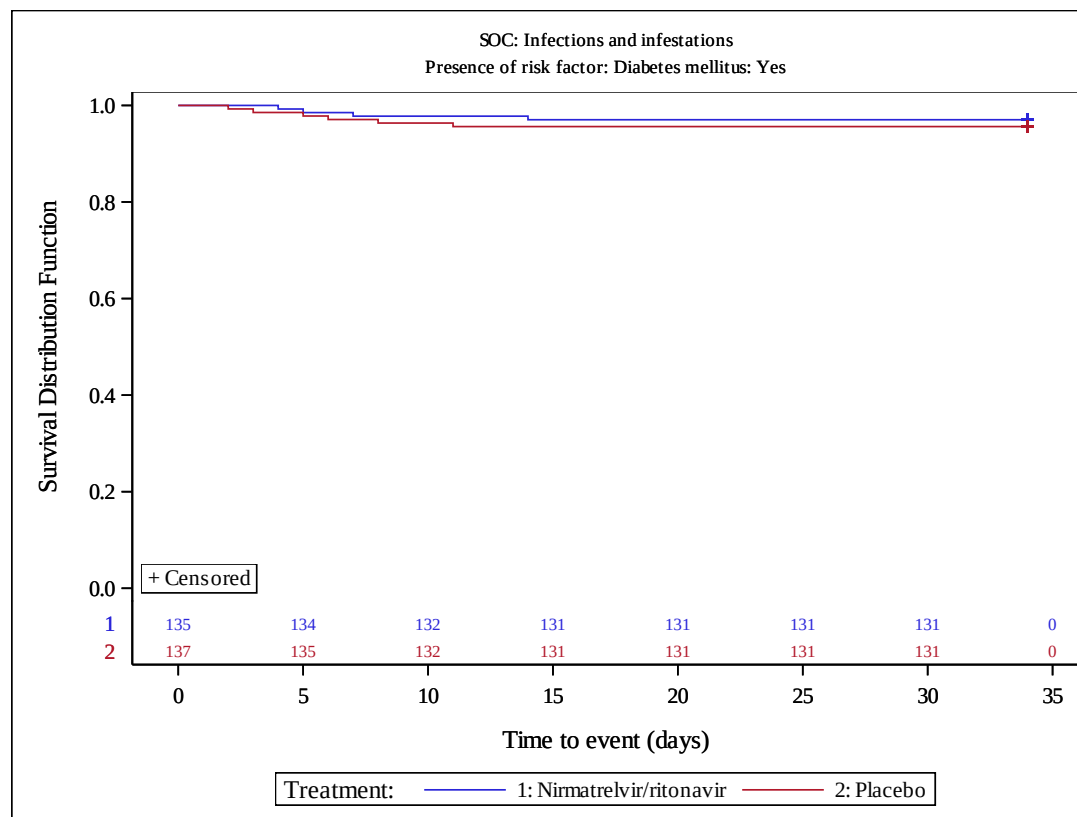
SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Respiratory, thoracic and mediastinal disorders	Presence of risk factor: Neurodevelopmental Disorder							
	Yes	0/ 2 (0.0)		0/ 1 (0.0)				
	No	1/ 941 (0.1)		17/ 963 (1.8)				
	Presence of risk factor: Cancer							0.9988
	Yes	0/ 5 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	No	1/ 938 (0.1)	NE (NE , NE)	17/ 958 (1.8)	NE (NE , NE)	0.06 (0.01, 0.45)	<.001	
	Presence of risk factor: Device Dependence							
	Yes	0/ 4 (0.0)		0/ 3 (0.0)				
	No	1/ 930 (0.1)		16/ 953 (1.7)				

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 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.
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 Kaplan-Meier Plot of Time to First Frequent Severe Adverse Events (DAIDS >=3) by SOC and PT (incidence in either arm >= 5% or >=10 patients)

Final

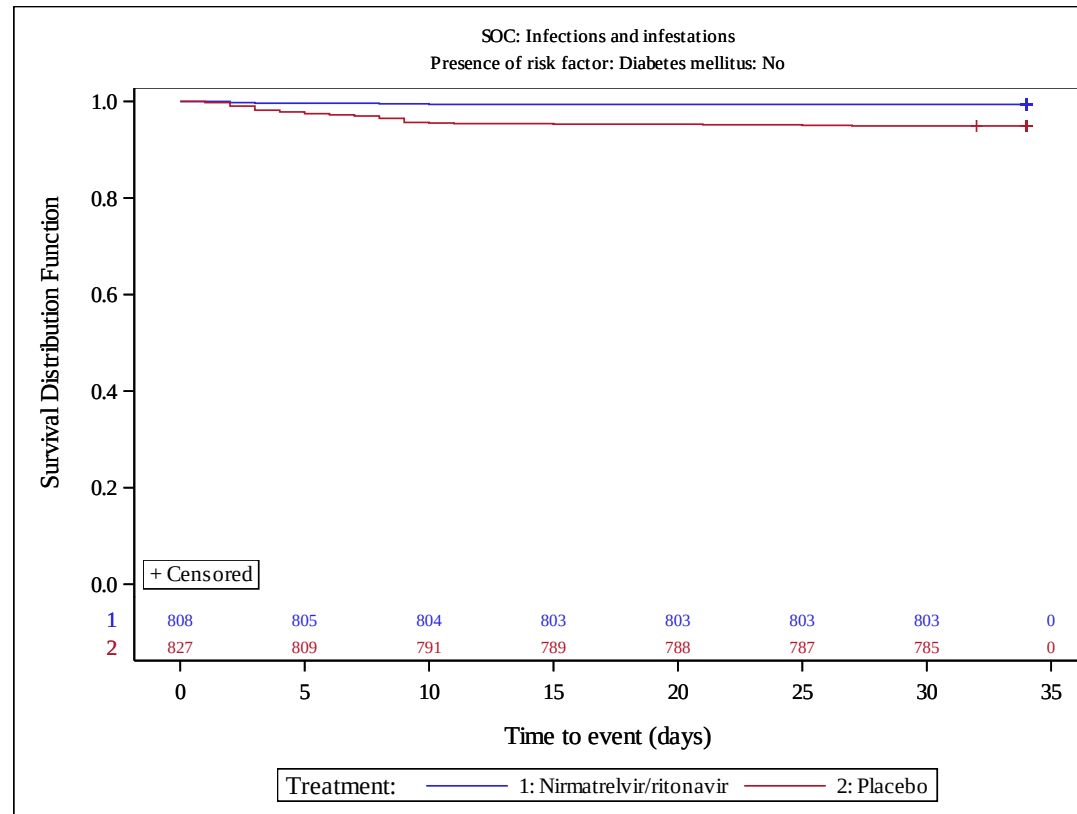


Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)
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SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations	Age							0.2721
	< 65	9/ 804 (1.1)	NE (NE , NE)	32/ 816 (3.9)	NE (NE , NE)	0.28 (0.13, 0.59)	<.001	
	>= 65	2/ 140 (1.4)	NE (NE , NE)	18/ 148 (12.2)	NE (NE , NE)	0.11 (0.03, 0.49)	<.001	
	Gender							0.5646
	Male	8/ 474 (1.7)	NE (NE , NE)	33/ 510 (6.5)	NE (NE , NE)	0.26 (0.12, 0.56)	<.001	
	Female	3/ 470 (0.6)	NE (NE , NE)	17/ 454 (3.7)	NE (NE , NE)	0.17 (0.05, 0.57)	0.00	
	Geographic region							0.5381
	United States	4/ 387 (1.0)	NE (NE , NE)	11/ 395 (2.8)	NE (NE , NE)	0.37 (0.12, 1.15)	0.07	
	Europe	4/ 322 (1.2)	NE (NE , NE)	30/ 321 (9.3)	NE (NE , NE)	0.13 (0.05, 0.37)	<.001	
	India	0/ 74 (0.0)	NE (NE , NE)	0/ 78 (0.0)	NE (NE , NE)	NE	NE	
	Rest of World	3/ 161 (1.9)	NE (NE , NE)	9/ 170 (5.3)	NE (NE , NE)	0.35 (0.09, 1.29)	0.09	
	COVID-19 therapeutic mAb treatment at randomisation							0.2743
	Yes	1/ 60 (1.7)	NE (NE , NE)	1/ 60 (1.7)	NE (NE , NE)	1.01 (0.06, 16.12)	0.99	
	No	10/ 884 (1.1)	NE (NE , NE)	49/ 904 (5.4)	NE (NE , NE)	0.21 (0.10, 0.40)	<.001	
	Baseline viral load 1							0.6973
	< 10^4 copies/mL	1/ 340 (0.3)	NE (NE , NE)	3/ 356 (0.8)	NE (NE , NE)	0.35 (0.04, 3.36)	0.34	
	>= 10^4 copies/mL	10/ 579 (1.7)	NE (NE , NE)	45/ 582 (7.7)	NE (NE , NE)	0.22 (0.11, 0.43)	<.001	
	Baseline viral load 2							0.2169
	< 10^7 copies/mL	8/ 663 (1.2)	NE (NE , NE)	27/ 707 (3.8)	NE (NE , NE)	0.31 (0.14, 0.69)	0.00	
	>= 10^7 copies/mL	3/ 256 (1.2)	NE (NE , NE)	21/ 231 (9.1)	NE (NE , NE)	0.12 (0.04, 0.42)	<.001	
	Baseline serology status							0.5969
	Negative	9/ 439 (2.1)	NE (NE , NE)	44/ 457 (9.6)	NE (NE , NE)	0.21 (0.10, 0.42)	<.001	
	Positive	2/ 494 (0.4)	NE (NE , NE)	6/ 495 (1.2)	NE (NE , NE)	0.33 (0.07, 1.65)	0.15	
	Symptom onset days to first dose date							0.5053
	<= 3	7/ 637 (1.1)	NE (NE , NE)	36/ 632 (5.7)	NE (NE , NE)	0.19 (0.08, 0.43)	<.001	
	> 3	4/ 307 (1.3)	NE (NE , NE)	14/ 332 (4.2)	NE (NE , NE)	0.31 (0.10, 0.93)	0.02	
	BMI group							0.8929
	< 25	1/ 216 (0.5)	NE (NE , NE)	7/ 213 (3.3)	NE (NE , NE)	0.14 (0.02, 1.13)	0.03	
	25 - < 30	4/ 324 (1.2)	NE (NE , NE)	18/ 336 (5.4)	NE (NE , NE)	0.23 (0.08, 0.67)	0.00	
	>= 30	6/ 403 (1.5)	NE (NE , NE)	25/ 415 (6.0)	NE (NE , NE)	0.24 (0.10, 0.59)	<.001	
	Ethnicity							0.6364
	White	8/ 712 (1.1)	NE (NE , NE)	42/ 725 (5.8)	NE (NE , NE)	0.19 (0.09, 0.41)	<.001	
	Black or African American	1/ 45 (2.2)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	0.92 (0.06, 14.74)	0.95	
	Asian	1/ 118 (0.8)	NE (NE , NE)	2/ 127 (1.6)	NE (NE , NE)	0.54 (0.05, 5.94)	0.60	
	Others	1/ 69 (1.4)	NE (NE , NE)	5/ 70 (7.1)	NE (NE , NE)	0.20 (0.02, 1.71)	0.10	

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.
 Subgroup analysis was done for SOC/ PTs with significant overall treatment effect (significant Hazard Ratio).
 Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 RRI-conform mITT2 Analysis set
 Analysis of Frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or >=10 patients) - Subgroup analysis

Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations	Number of baseline comorbidities present							0.6825
	0-1	5/ 720 (0.7)	NE (NE , NE)	30/ 734 (4.1)	NE (NE , NE)	0.17 (0.06, 0.43)	<.001	
	2-3	6/ 220 (2.7)	NE (NE , NE)	20/ 224 (8.9)	NE (NE , NE)	0.30 (0.12, 0.75)	0.00	
	>= 4	0/ 4 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	Presence of risk factor: Smoking							0.0820
	Yes	6/ 423 (1.4)	NE (NE , NE)	14/ 442 (3.2)	NE (NE , NE)	0.45 (0.17, 1.16)	0.08	
	No	5/ 519 (1.0)	NE (NE , NE)	36/ 522 (6.9)	NE (NE , NE)	0.14 (0.05, 0.35)	<.001	
	Presence of risk factor: Diabetes mellitus							0.1363
	Yes	4/ 135 (3.0)	NE (NE , NE)	8/ 137 (5.8)	NE (NE , NE)	0.50 (0.15, 1.67)	0.25	
	No	7/ 808 (0.9)	NE (NE , NE)	42/ 827 (5.1)	NE (NE , NE)	0.17 (0.08, 0.37)	<.001	
	Presence of risk factor: Immunosuppression							0.9991
	Yes	0/ 6 (0.0)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE	NE	
	No	11/ 937 (1.2)	NE (NE , NE)	50/ 957 (5.2)	NE (NE , NE)	0.22 (0.12, 0.42)	<.001	
	Presence of risk factor: Chronic lung disease							0.9823
	Yes	0/ 62 (0.0)	NE (NE , NE)	1/ 39 (2.6)	NE (NE , NE)	NE	NE	
	No	11/ 881 (1.2)	NE (NE , NE)	49/ 925 (5.3)	NE (NE , NE)	0.23 (0.12, 0.45)	<.001	
	Presence of risk factor: Hypertension							0.0546
	Yes	5/ 358 (1.4)	NE (NE , NE)	38/ 375 (10.1)	NE (NE , NE)	0.13 (0.05, 0.34)	<.001	
	No	6/ 585 (1.0)	NE (NE , NE)	12/ 589 (2.0)	NE (NE , NE)	0.50 (0.19, 1.34)	0.15	
	Presence of risk factor: Cardiovascular disorder							0.9850
	Yes	0/ 42 (0.0)	NE (NE , NE)	10/ 49 (20.4)	NE (NE , NE)	NE	NE	
	No	11/ 901 (1.2)	NE (NE , NE)	40/ 915 (4.4)	NE (NE , NE)	0.28 (0.14, 0.54)	<.001	
	Presence of risk factor: Chronic kidney disease							0.9991
	Yes	0/ 6 (0.0)	NE (NE , NE)	0/ 8 (0.0)	NE (NE , NE)	NE	NE	
	No	11/ 937 (1.2)	NE (NE , NE)	50/ 956 (5.2)	NE (NE , NE)	0.22 (0.11, 0.42)	<.001	
	Presence of risk factor: HIV Infection							
	Yes	0		0/ 1 (0.0)				
	No	11/ 943 (1.2)		50/ 962 (5.2)				
	Presence of risk factor: Sickle Cell Disease							
	No	11/ 943 (1.2)		50/ 964 (5.2)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

MedDRA v24.1 coding dictionary applied.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations	Presence of risk factor:							
	Neurodevelopmental Disorder							
	Yes	0/ 2 (0.0)		0/ 1 (0.0)				
	No	11/ 941 (1.2)		50/ 963 (5.2)				
	Presence of risk factor: Cancer							0.9992
	Yes	0/ 5 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	No	11/ 938 (1.2)	NE (NE , NE)	50/ 958 (5.2)	NE (NE , NE)	0.22 (0.12, 0.42)	<.001	
	Presence of risk factor: Device Dependence							
	Yes	0/ 4 (0.0)		0/ 3 (0.0)				
	No	11/ 930 (1.2)		49/ 953 (5.1)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.
 Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).
 Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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 Analysis of Frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or >=10 patients) - Subgroup analysis

Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations, PT: COVID-19 pneumonia	Age							0.2113
	< 65	6/ 804 (0.7)	NE (NE , NE)	20/ 816 (2.5)	NE (NE , NE)	0.30 (0.12, 0.75)	0.00	
	>= 65	1/ 140 (0.7)	NE (NE , NE)	14/ 148 (9.5)	NE (NE , NE)	0.07 (0.01, 0.55)	<.001	
	Gender							0.9640
	Male	4/ 474 (0.8)	NE (NE , NE)	20/ 510 (3.9)	NE (NE , NE)	0.21 (0.07, 0.62)	0.00	
	Female	3/ 470 (0.6)	NE (NE , NE)	14/ 454 (3.1)	NE (NE , NE)	0.20 (0.06, 0.71)	0.00	
	Geographic region							0.8783
	United States	2/ 387 (0.5)	NE (NE , NE)	7/ 395 (1.8)	NE (NE , NE)	0.29 (0.06, 1.39)	0.09	
	Europe	3/ 322 (0.9)	NE (NE , NE)	20/ 321 (6.2)	NE (NE , NE)	0.15 (0.04, 0.49)	<.001	
	India	0/ 74 (0.0)	NE (NE , NE)	0/ 78 (0.0)	NE (NE , NE)	NE	NE	
	Rest of World	2/ 161 (1.2)	NE (NE , NE)	7/ 170 (4.1)	NE (NE , NE)	0.30 (0.06, 1.44)	0.10	
	COVID-19 therapeutic mAb treatment at randomisation							0.9860
	Yes	0/ 60 (0.0)	NE (NE , NE)	1/ 60 (1.7)	NE (NE , NE)	NE	NE	
	No	7/ 884 (0.8)	NE (NE , NE)	33/ 904 (3.7)	NE (NE , NE)	0.21 (0.09, 0.48)	<.001	
	Baseline viral load 1							0.9887
	< 10^4 copies/mL	0/ 340 (0.0)	NE (NE , NE)	2/ 356 (0.6)	NE (NE , NE)	NE	NE	
	>= 10^4 copies/mL	7/ 579 (1.2)	NE (NE , NE)	31/ 582 (5.3)	NE (NE , NE)	0.22 (0.10, 0.51)	<.001	
	Baseline viral load 2							0.7383
	< 10^7 copies/mL	4/ 663 (0.6)	NE (NE , NE)	18/ 707 (2.5)	NE (NE , NE)	0.24 (0.08, 0.70)	0.00	
	>= 10^7 copies/mL	3/ 256 (1.2)	NE (NE , NE)	15/ 231 (6.5)	NE (NE , NE)	0.18 (0.05, 0.61)	0.00	
	Baseline serology status							0.8132
	Negative	6/ 439 (1.4)	NE (NE , NE)	28/ 457 (6.1)	NE (NE , NE)	0.22 (0.09, 0.53)	<.001	
	Positive	1/ 494 (0.2)	NE (NE , NE)	6/ 495 (1.2)	NE (NE , NE)	0.17 (0.02, 1.38)	0.05	
	Symptom onset days to first dose date							0.9159
	<= 3	5/ 637 (0.8)	NE (NE , NE)	23/ 632 (3.6)	NE (NE , NE)	0.21 (0.08, 0.56)	<.001	
	> 3	2/ 307 (0.7)	NE (NE , NE)	11/ 332 (3.3)	NE (NE , NE)	0.19 (0.04, 0.88)	0.01	
	BMI group							0.8350
	< 25	1/ 216 (0.5)	NE (NE , NE)	4/ 213 (1.9)	NE (NE , NE)	0.25 (0.03, 2.20)	0.17	
	25 - < 30	2/ 324 (0.6)	NE (NE , NE)	14/ 336 (4.2)	NE (NE , NE)	0.15 (0.03, 0.64)	0.00	
	>= 30	4/ 403 (1.0)	NE (NE , NE)	16/ 415 (3.9)	NE (NE , NE)	0.25 (0.08, 0.76)	0.00	
	Ethnicity							0.8823
	White	5/ 712 (0.7)	NE (NE , NE)	27/ 725 (3.7)	NE (NE , NE)	0.19 (0.07, 0.48)	<.001	
	Black or African American	0/ 45 (0.0)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	NE	NE	
	Asian	1/ 118 (0.8)	NE (NE , NE)	2/ 127 (1.6)	NE (NE , NE)	0.54 (0.05, 5.94)	0.60	
	Others	1/ 69 (1.4)	NE (NE , NE)	4/ 70 (5.7)	NE (NE , NE)	0.25 (0.03, 2.24)	0.17	

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

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N: Number of participants, CI: Confidence Interval, NE: Not estimable

[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

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Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)			Placebo (N=964)			Unadjusted Analysis		Interaction p-Value[3]
		n/ N (%)	Median (95% CI) [1]		n/ N (%)	Median (95% CI) [1]		Hazard Ratio (95% CI) [2]	p-Value[2]	
SOC: Infections and infestations, PT: COVID-19 pneumonia	Number of baseline comorbidities present									0.4811
	0-1	3/ 720 (0.4)	NE (NE , NE)		23/ 734 (3.1)	NE (NE , NE)		0.13 (0.04, 0.44)	<.001	
	2-3	4/ 220 (1.8)	NE (NE , NE)		11/ 224 (4.9)	NE (NE , NE)		0.37 (0.12, 1.16)	0.07	
	>= 4	0/ 4 (0.0)	NE (NE , NE)		0/ 6 (0.0)	NE (NE , NE)		NE	NE	
	Presence of risk factor: Smoking									0.1401
	Yes	3/ 423 (0.7)	NE (NE , NE)		6/ 442 (1.4)	NE (NE , NE)		0.52 (0.13, 2.09)	0.34	
	No	4/ 519 (0.8)	NE (NE , NE)		28/ 522 (5.4)	NE (NE , NE)		0.14 (0.05, 0.40)	<.001	
	Presence of risk factor: Diabetes mellitus									0.0631
	Yes	3/ 135 (2.2)	NE (NE , NE)		4/ 137 (2.9)	NE (NE , NE)		0.76 (0.17, 3.40)	0.71	
	No	4/ 808 (0.5)	NE (NE , NE)		30/ 827 (3.6)	NE (NE , NE)		0.13 (0.05, 0.38)	<.001	
	Presence of risk factor: Immunosuppression									0.9993
	Yes	0/ 6 (0.0)	NE (NE , NE)		0/ 7 (0.0)	NE (NE , NE)		NE	NE	
	No	7/ 937 (0.7)	NE (NE , NE)		34/ 957 (3.6)	NE (NE , NE)		0.21 (0.09, 0.47)	<.001	
	Presence of risk factor: Chronic lung disease									0.9852
	Yes	0/ 62 (0.0)	NE (NE , NE)		1/ 39 (2.6)	NE (NE , NE)		NE	NE	
	No	7/ 881 (0.8)	NE (NE , NE)		33/ 925 (3.6)	NE (NE , NE)		0.22 (0.10, 0.50)	<.001	
	Presence of risk factor: Hypertension									0.1624
	Yes	4/ 358 (1.1)	NE (NE , NE)		28/ 375 (7.5)	NE (NE , NE)		0.15 (0.05, 0.41)	<.001	
	No	3/ 585 (0.5)	NE (NE , NE)		6/ 589 (1.0)	NE (NE , NE)		0.50 (0.13, 2.01)	0.32	
	Presence of risk factor: Cardiovascular disorder									0.9879
	Yes	0/ 42 (0.0)	NE (NE , NE)		7/ 49 (14.3)	NE (NE , NE)		NE	NE	
	No	7/ 901 (0.8)	NE (NE , NE)		27/ 915 (3.0)	NE (NE , NE)		0.26 (0.11, 0.60)	<.001	
	Presence of risk factor: Chronic kidney disease									0.9992
	Yes	0/ 6 (0.0)	NE (NE , NE)		0/ 8 (0.0)	NE (NE , NE)		NE	NE	
	No	7/ 937 (0.7)	NE (NE , NE)		34/ 956 (3.6)	NE (NE , NE)		0.21 (0.09, 0.47)	<.001	
	Presence of risk factor: HIV Infection									
	Yes	0			0/ 1 (0.0)					
	No	7/ 943 (0.7)			34/ 962 (3.5)					
	Presence of risk factor: Sickle Cell Disease									
	No	7/ 943 (0.7)			34/ 964 (3.5)					

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.

MedDRA v24.1 coding dictionary applied.

N: Number of participants, CI: Confidence Interval, NE: Not estimable

[3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.

Subgroup analysis was done for SOC / PTs with significant overall treatment effect (significant Hazard Ratio).

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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 RRI-conform mITT2 Analysis set
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Final

SOC/PT	Subgroup Level	Nirmatrelvir/ritonavir (N=944)		Placebo (N=964)		Unadjusted Analysis		Interaction
		n/ N (%)	Median (95% CI) [1]	n/ N (%)	Median (95% CI) [1]	Hazard Ratio (95% CI) [2]	p-Value [2]	p-Value [3]
SOC: Infections and infestations, PT: COVID-19 pneumonia	Presence of risk factor: Neurodevelopmental Disorder							
	Yes	0/ 2 (0.0)		0/ 1 (0.0)				
	No	7/ 941 (0.7)		34/ 963 (3.5)				
	Presence of risk factor: Cancer							0.9993
	Yes	0/ 5 (0.0)	NE (NE , NE)	0/ 6 (0.0)	NE (NE , NE)	NE	NE	
	No	7/ 938 (0.7)	NE (NE , NE)	34/ 958 (3.5)	NE (NE , NE)	0.21 (0.09, 0.47)	<.001	
	Presence of risk factor: Device Dependence							
	Yes	0/ 4 (0.0)		0/ 3 (0.0)				
	No	7/ 930 (0.8)		34/ 953 (3.6)				

Analysis based Treatment-Emergent Adverse Events (TEAEs) that started on or prior to Day 34 visit. TEAEs are those events that started on or after the study medication start date and time.
 MedDRA v24.1 coding dictionary applied.
 N: Number of participants, CI: Confidence Interval, NE: Not estimable
 [3] p-Value for interaction from cox proportional hazard model with treatment, subgroup and treatment by subgroup interaction as covariates.
 Subgroup analysis was done for SOC/PTs with significant overall treatment effect (significant Hazard Ratio).
 Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Anhang 4-G 2: mITT2-Population

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Observation Time per Endpoint

Final

		Nirmatrelvir/ritonavir (N=1109)	Placebo (N=1115)	Total (N=2224)
Observation Time for Time to Death (Days) through Day 28[1]	n (missing)	1109 (0)	1115 (0)	2224 (0)
	Mean (SD)	27.23 (4.09)	27.13 (4.16)	27.18 (4.13)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Time to Death (Days) through Week 24[1]	n (missing)	1109 (0)	1115 (0)	2224 (0)
	Mean (SD)	159.10 (32.59)	157.26 (35.62)	158.18 (34.15)
	Median	168.00	168.00	168.00
	Q1, Q3	164.00, 168.00	163.00, 168.00	163.50, 168.00
	Min, Max	1.00, 168.00	1.00, 168.00	1.00, 168.00
Observation Time for Time to COVID-19 related Hospitalization (Days)[2]	n (missing)	1109 (0)	1115 (0)	2224 (0)
	Mean (SD)	27.04 (4.58)	26.04 (6.36)	26.54 (5.57)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Stuffy or Runny Nose (Days)[3]	n (missing)	1093 (16)	1105 (10)	2198 (26)
	Mean (SD)	26.07 (5.76)	25.66 (6.44)	25.86 (6.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Sore Throat (Days)[3]	n (missing)	1093 (16)	1105 (10)	2198 (26)
	Mean (SD)	26.07 (5.76)	25.66 (6.44)	25.86 (6.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Shortness of Breath or Difficulty Breathing (Days)[3]	n (missing)	1093 (16)	1105 (10)	2198 (26)
	Mean (SD)	26.07 (5.76)	25.66 (6.44)	25.86 (6.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Cough (Days)[3]	n (missing)	1093 (16)	1105 (10)	2198 (26)
	Mean (SD)	26.07 (5.76)	25.66 (6.44)	25.86 (6.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Low Energy or Tiredness (Days)[3]	n (missing)	1093 (16)	1105 (10)	2198 (26)
	Mean (SD)	26.07 (5.76)	25.66 (6.44)	25.86 (6.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Muscle or Body Aches (Days)[3]	n (missing)	1093 (16)	1105 (10)	2198 (26)
	Mean (SD)	26.07 (5.76)	25.66 (6.44)	25.86 (6.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00

N: Number of participants, n: Number of participants with non-missing values, SD: Standard Deviation, Q1: 25%-Quartile, Q3: 75%-Quartile, Min: Minimum, Max: Maximum

[1] date of first administration of study drug until death date + 1. Participants without event are censored at minimum(last known alive date, Day 28) or minimum(last known alive date, Day 168) for Week 24.

[2] date of first administration of study drug until minimum(death date, hospitalization date) + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[3] date of first administration of study drug until hospitalization date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[4] date of first administration of study drug until date of last non-missing measurement through Day 28 + 1

[5] date of first administration of study drug until date of last non-missing measurement through Week 24 + 1

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		Nirmatrelvir/ritonavir (N=1109)	Placebo (N=1115)	Total (N=2224)
Observation Time for Headache (Days) [3]	n (missing)	1093 (16)	1105 (10)	2198 (26)
	Mean (SD)	26.07 (5.76)	25.66 (6.44)	25.86 (6.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Chills or Shivering (Days) [3]	n (missing)	1093 (16)	1105 (10)	2198 (26)
	Mean (SD)	26.07 (5.76)	25.66 (6.44)	25.86 (6.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Feeling Hot or Feverish (Days) [3]	n (missing)	1093 (16)	1105 (10)	2198 (26)
	Mean (SD)	26.07 (5.76)	25.66 (6.44)	25.86 (6.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Nausea (Days) [3]	n (missing)	1093 (16)	1105 (10)	2198 (26)
	Mean (SD)	26.07 (5.76)	25.66 (6.44)	25.86 (6.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Vomit (Days) [3]	n (missing)	1093 (16)	1105 (10)	2198 (26)
	Mean (SD)	26.07 (5.76)	25.66 (6.44)	25.86 (6.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Diarrhea (Days) [3]	n (missing)	1093 (16)	1105 (10)	2198 (26)
	Mean (SD)	26.07 (5.76)	25.66 (6.44)	25.86 (6.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Sense of Smell (Days) [3]	n (missing)	1093 (16)	1105 (10)	2198 (26)
	Mean (SD)	26.07 (5.76)	25.66 (6.44)	25.86 (6.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Sense of Taste (Days) [3]	n (missing)	1093 (16)	1105 (10)	2198 (26)
	Mean (SD)	26.07 (5.76)	25.66 (6.44)	25.86 (6.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00

N: Number of participants, n: Number of participants with non-missing values, SD: Standard Deviation, Q1: 25%-Quartile, Q3: 75%-Quartile, Min: Minimum, Max: Maximum

[1] date of first administration of study drug until death date + 1. Participants without event are censored at minimum(last known alive date, Day 28) or minimum(last known alive date, Day 168) for Week 24.

[2] date of first administration of study drug until minimum(death date, hospitalization date) + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[3] date of first administration of study drug until hospitalization date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[4] date of first administration of study drug until date of last non-missing measurement through Day 28 + 1

[5] date of first administration of study drug until date of last non-missing measurement through Week 24 + 1

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		Nirmatrelvir/ritonavir (N=1109)	Placebo (N=1115)	Total (N=2224)
Observation Time for EQ-5D VAS Score (Days) [4]	n (missing)	539 (570)	539 (576)	1078 (1146)
	Mean (SD)	154.46 (34.02)	154.68 (32.87)	154.57 (33.44)
	Median	164.00	164.00	164.00
	Q1, Q3	161.00, 169.00	161.00, 169.00	161.00, 169.00
	Min, Max	4.00, 175.00	1.00, 175.00	1.00, 175.00
Observation Time for GIQ c) overall COVID-19-related (Days) [3]	n (missing)	1059 (50)	1072 (43)	2131 (93)
	Mean (SD)	26.08 (5.75)	25.68 (6.37)	25.88 (6.07)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for GIQ b) return to usual activities (Days) [3]	n (missing)	1059 (50)	1072 (43)	2131 (93)
	Mean (SD)	26.08 (5.75)	25.68 (6.37)	25.88 (6.07)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for GIQ a) return to usual health(Days) [3]	n (missing)	1059 (50)	1072 (43)	2131 (93)
	Mean (SD)	26.08 (5.75)	25.68 (6.37)	25.88 (6.07)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for WPAI-COVID-19 Question 6 (Days) [4]	n (missing)	523 (586)	524 (591)	1047 (1177)
	Mean (SD)	157.67 (28.65)	156.92 (28.70)	157.30 (28.66)
	Median	164.00	164.00	164.00
	Q1, Q3	162.00, 169.00	162.00, 169.00	162.00, 169.00
	Min, Max	4.00, 175.00	12.00, 175.00	4.00, 175.00

N: Number of participants, n: Number of participants with non-missing values, SD: Standard Deviation, Q1: 25%-Quartile, Q3: 75%-Quartile, Min: Minimum, Max: Maximum

[1] date of first administration of study drug until death date + 1. Participants without event are censored at minimum(last known alive date, Day 28) or minimum(last known alive date, Day 168) for Week 24.

[2] date of first administration of study drug until minimum(death date, hospitalization date) + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[3] date of first administration of study drug until hospitalization date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[4] date of first administration of study drug until date of last non-missing measurement through Day 28 + 1

[5] date of first administration of study drug until date of last non-missing measurement through Week 24 + 1

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 Analysis of Time to Death through Day 28

Final

	Nirmatrelvir/ritonavir (N=1109)	Placebo (N=1115)
Number of subjects with events, n (%)	0 (0.0)	12 (1.1)
Number of censored subjects, n (%)	1109 (100.0)	1103 (98.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	NE (NE, NE)	
p-value [3]	NE	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	NE (NE, NE)	
p-value [3]	NE	
Cumulative Proportion and Difference of the Proportions [4]		
Estimated Proportion (95% CI), %	0.000 (0.000, 0.000)	1.103 (0.628, 1.934)
Difference (SE)	-1.103 (0.317)	
95% CI	-1.724, -0.482	
p-value	<.001	

N: Number of subjects, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last known alive date, Day 28).

[1] Based on the Brookmeyer and Crowley Method.

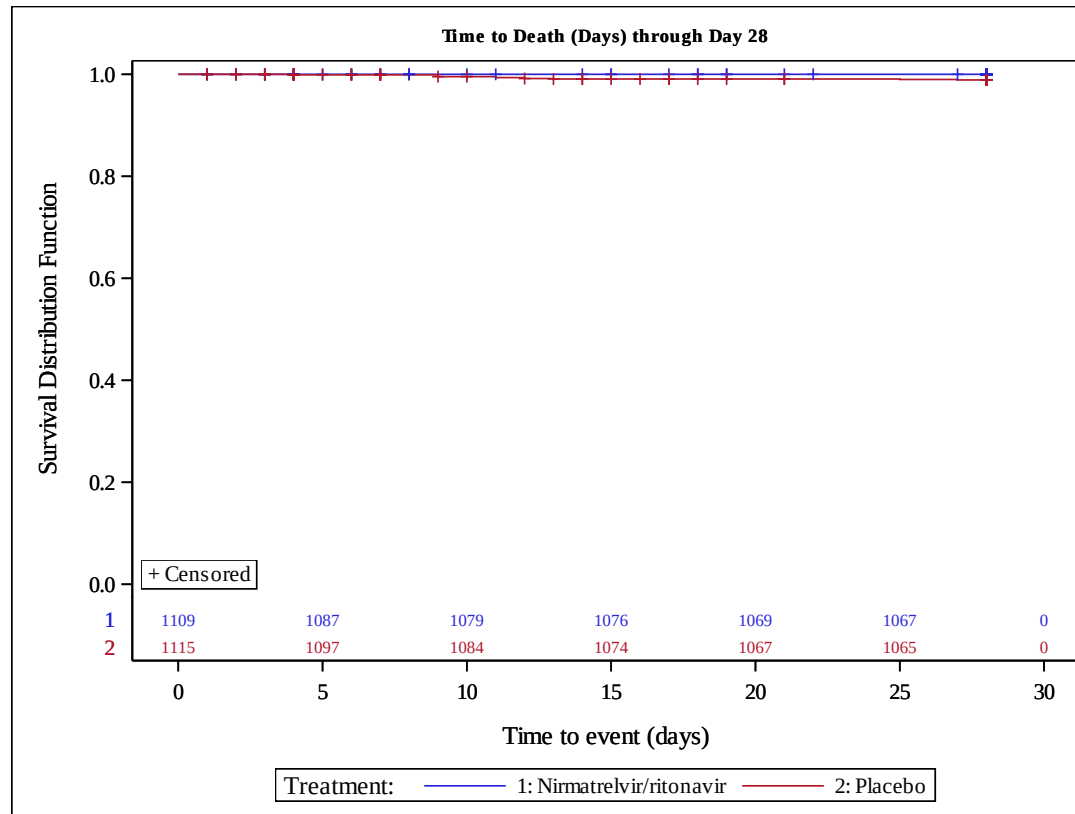
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

[4] The cumulative proportion was estimated using the Kaplan-Meier method. The difference of the proportions in the 2 treatment groups and its 95% confidence interval, and p-value based on Normal approximation.

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 Kaplan-Meier Plot of Time to Death through Day 28

Final



Participants without event are censored at minimum(last known alive date, Day 28).
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Analysis of Participants with Death from any Cause through Day 28

Final

	Nirmatrelvir/ritonavir (N=1109)	Placebo (N=1115)
Number of subjects with Death, n (%)	0 (0.0)	12 (1.1)
Adjusted Analysis [1]		
Odds Ratio (95% CI)	NE (NE, NE)	
p-value	NE	
Relative Risk (95% CI)	NE (NE, NE)	
p-value	NE	
Risk Difference (95% CI)	NE (NE, NE)	
p-value	NE	
Unadjusted Analysis [2]		
Odds Ratio (95% CI)	0.040 (0.002, 0.673)	
p-value	0.025	
Relative Risk (95% CI)	0.040 (0.002, 0.678)	
p-value	0.026	
Risk Difference (95% CI)	-0.011 (-0.017, -0.005)	
p-value	<.001	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Analysis of Time to Death through Week 24

Final

	Nirmatrelvir/ritonavir (N=1109)	Placebo (N=1115)
Number of subjects with events, n (%)	0 (0.0)	15 (1.3)
Number of censored subjects, n (%)	1109 (100.0)	1100 (98.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	NE (NE, NE)	
p-value [3]	NE	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	NE (NE, NE)	
p-value [3]	NE	
Cumulative Proportion and Difference of the Proportions [4]		
Estimated Proportion (95% CI), %	0.000 (0.000, 0.000)	1.384 (0.837, 2.285)
Difference (SE)	-1.384 (0.355)	
95% CI	-2.080, -0.688	
p-value	<.001	

N: Number of subjects, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last known alive date, Week 24 = Day 168).

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

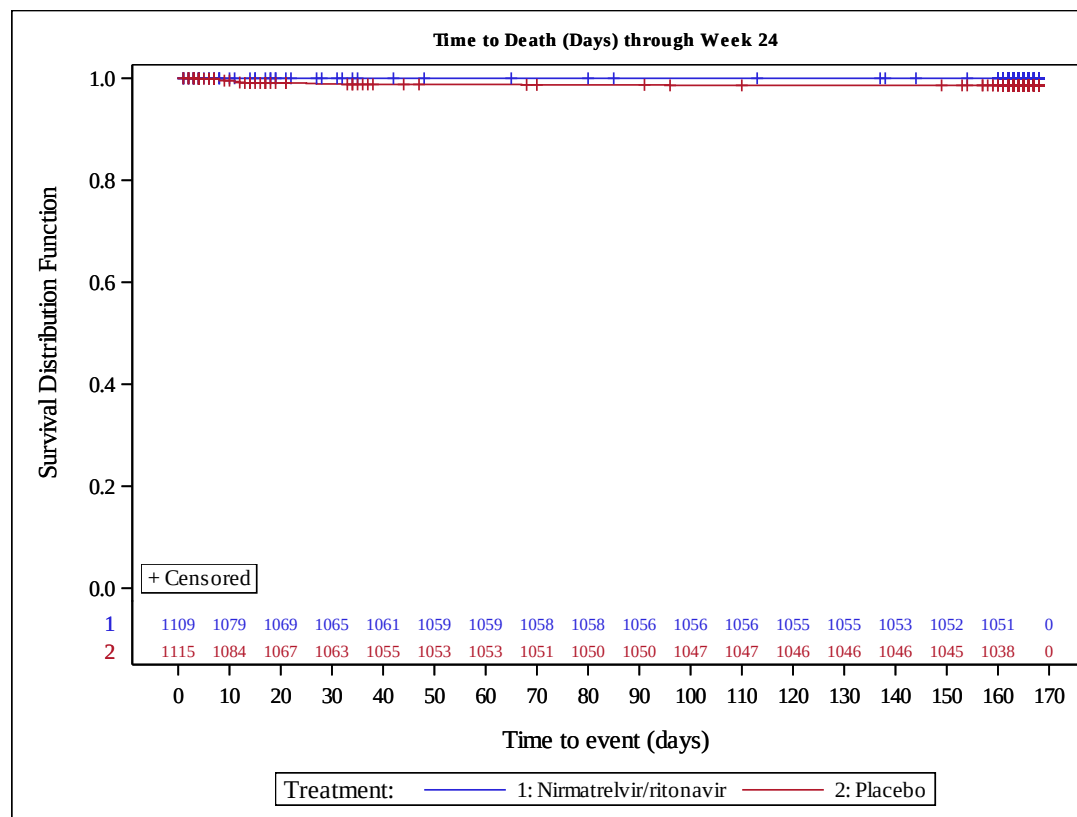
[3] Estimated by cox regression model assuming proportional hazards.

[4] The cumulative proportion was estimated using the Kaplan-Meier method. The difference of the proportions in the 2 treatment groups and its 95% confidence interval, and p-value based on Normal approximation.

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Participants without event are censored at minimum(last known alive date, Week 24 = Day 168).
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Analysis of Participants with Death from any Cause through Week 24

Final

	Nirmatrelvir/ritonavir (N=1109)	Placebo (N=1115)
Number of subjects with Death, n (%)	0 (0.0)	15 (1.3)
Adjusted Analysis [1]		
Odds Ratio (95% CI)	NE (NE, NE)	
p-value	NE	
Relative Risk (95% CI)	NE (NE, NE)	
p-value	NE	
Risk Difference (95% CI)	NE (NE, NE)	
p-value	NE	
Unadjusted Analysis [2]		
Odds Ratio (95% CI)	0.032 (0.002, 0.535)	
p-value	0.017	
Relative Risk (95% CI)	0.032 (0.002, 0.541)	
p-value	0.017	
Risk Difference (95% CI)	-0.013 (-0.020, -0.007)	
p-value	<.001	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Analysis of Number of COVID-19 related hospitalizations

Final

	Nirmatrelvir/ritonavir (N=1109)	Placebo (N=1115)
Number of subjects with at least one event	10	67
Number of events	10	68
Mean of events	0.009	0.061
Mean of events per day	0.0004	0.0026
Adjusted Analysis [1]		
LS mean (95% CI)	NE (NE, NE)	NE (NE, NE)
LS mean Ratio (95% CI)	NE (NE, NE)	
p-value	NE	
Unadjusted Analysis [2]		
LS mean (95% CI)	NE (NE, NE)	NE (NE, NE)
LS mean Ratio (95% CI)	NE (NE, NE)	
p-value	NE	

N: Number of participants, CI: Confidence Interval, NE: Not estimable, I: Infinity, LS: Least Squares

Medical Visits and Hospitalization events are limited through Day 34 visit. Number of events per day = Number of events/Number of days follow up limited to Day 37.

Stratification factors: geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[1] Negative binomial regression model includes main effects of treatment, stratification factors and the log number of days follow up as the participant offset variable.

[2] Negative binomial regression model includes main effects of treatment and the log number of days follow up as the participant offset variable.

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=1109)		Placebo (N=1115)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Stuffy or Runny Nose	Baseline	1109	1033 (93.1)	1115	1061 (95.2)
	DAY 2	1109	1009 (91.0)	1115	1024 (91.8)
	DAY 3	1109	1008 (90.9)	1115	1014 (90.9)
	DAY 4	1109	994 (89.6)	1115	993 (89.1)
	DAY 5	1109	988 (89.1)	1114	978 (87.8)
	DAY 6	1109	919 (82.9)	1114	907 (81.4)
	DAY 7	1109	885 (79.8)	1114	882 (79.2)
	DAY 8	1109	891 (80.3)	1114	876 (78.6)
	DAY 9	1109	892 (80.4)	1114	877 (78.7)
	DAY 10	1109	883 (79.6)	1110	916 (82.5)
	DAY 11	1109	896 (80.8)	1110	911 (82.1)
	DAY 12	1109	900 (81.2)	1108	880 (79.4)
	DAY 13	1109	908 (81.9)	1106	901 (81.5)
	DAY 14	1109	910 (82.1)	1105	913 (82.6)
	DAY 15	1109	898 (81.0)	1105	911 (82.4)
	DAY 16	1109	907 (81.8)	1105	870 (78.7)
	DAY 17	1109	889 (80.2)	1105	882 (79.8)
	DAY 18	1109	884 (79.7)	1105	871 (78.8)
	DAY 19	1109	882 (79.5)	1105	900 (81.4)
	DAY 20	1109	871 (78.5)	1105	903 (81.7)
	DAY 21	1109	903 (81.4)	1105	888 (80.4)
	DAY 22	1109	892 (80.4)	1105	885 (80.1)
	DAY 23	1109	880 (79.4)	1105	863 (78.1)
	DAY 24	1109	870 (78.4)	1105	872 (78.9)
	DAY 25	1109	854 (77.0)	1105	876 (79.3)
	DAY 26	1109	857 (77.3)	1104	863 (78.2)
	DAY 27	1109	871 (78.5)	1104	877 (79.4)
	DAY 28	1109	847 (76.4)	1103	832 (75.4)
COVID-19 Signs and Symptoms: Sore Throat	Baseline	1109	1033 (93.1)	1115	1061 (95.2)
	DAY 2	1109	1009 (91.0)	1115	1024 (91.8)
	DAY 3	1109	1008 (90.9)	1115	1014 (90.9)
	DAY 4	1109	994 (89.6)	1115	993 (89.1)
	DAY 5	1109	988 (89.1)	1114	978 (87.8)
	DAY 6	1109	919 (82.9)	1114	907 (81.4)
	DAY 7	1109	885 (79.8)	1114	882 (79.2)
	DAY 8	1109	891 (80.3)	1114	876 (78.6)
	DAY 9	1109	892 (80.4)	1114	877 (78.7)
	DAY 10	1109	883 (79.6)	1110	916 (82.5)
	DAY 11	1109	896 (80.8)	1110	911 (82.1)
	DAY 12	1109	900 (81.2)	1108	880 (79.4)
	DAY 13	1109	908 (81.9)	1106	901 (81.5)
	DAY 14	1109	910 (82.1)	1105	913 (82.6)
	DAY 15	1109	898 (81.0)	1105	911 (82.4)
	DAY 16	1109	907 (81.8)	1105	870 (78.7)
	DAY 17	1109	889 (80.2)	1105	882 (79.8)
	DAY 18	1109	884 (79.7)	1105	871 (78.8)
	DAY 19	1109	882 (79.5)	1105	900 (81.4)
	DAY 20	1109	871 (78.5)	1105	903 (81.7)
	DAY 21	1109	903 (81.4)	1105	888 (80.4)
	DAY 22	1109	892 (80.4)	1105	885 (80.1)
	DAY 23	1109	880 (79.4)	1105	863 (78.1)
	DAY 24	1109	870 (78.4)	1105	872 (78.9)
	DAY 25	1109	854 (77.0)	1105	876 (79.3)
	DAY 26	1109	857 (77.3)	1104	863 (78.2)
	DAY 27	1109	871 (78.5)	1104	877 (79.4)
	DAY 28	1109	847 (76.4)	1103	832 (75.4)

N: Number of participants, n: Number of participants with non missing values

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Final

Endpoint	Visit	Nirmatrelvir/ritonavir (N=1109)		Placebo (N=1115)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Shortness of Breath or Difficulty Breathing	Baseline	1109	1033 (93.1)	1115	1061 (95.2)
	DAY 2	1109	1009 (91.0)	1115	1024 (91.8)
	DAY 3	1109	1008 (90.9)	1115	1014 (90.9)
	DAY 4	1109	994 (89.6)	1115	993 (89.1)
	DAY 5	1109	988 (89.1)	1114	978 (87.8)
	DAY 6	1109	919 (82.9)	1114	907 (81.4)
	DAY 7	1109	885 (79.8)	1114	882 (79.2)
	DAY 8	1109	891 (80.3)	1114	876 (78.6)
	DAY 9	1109	892 (80.4)	1114	877 (78.7)
	DAY 10	1109	883 (79.6)	1110	916 (82.5)
	DAY 11	1109	896 (80.8)	1110	911 (82.1)
	DAY 12	1109	900 (81.2)	1108	880 (79.4)
	DAY 13	1109	908 (81.9)	1106	901 (81.5)
	DAY 14	1109	910 (82.1)	1105	913 (82.6)
	DAY 15	1109	898 (81.0)	1105	911 (82.4)
	DAY 16	1109	907 (81.8)	1105	870 (78.7)
	DAY 17	1109	889 (80.2)	1105	882 (79.8)
	DAY 18	1109	884 (79.7)	1105	871 (78.8)
	DAY 19	1109	882 (79.5)	1105	900 (81.4)
	DAY 20	1109	871 (78.5)	1105	903 (81.7)
	DAY 21	1109	903 (81.4)	1105	888 (80.4)
	DAY 22	1109	892 (80.4)	1105	885 (80.1)
	DAY 23	1109	880 (79.4)	1105	863 (78.1)
	DAY 24	1109	870 (78.4)	1105	872 (78.9)
	DAY 25	1109	854 (77.0)	1105	876 (79.3)
	DAY 26	1109	857 (77.3)	1104	863 (78.2)
	DAY 27	1109	871 (78.5)	1104	877 (79.4)
	DAY 28	1109	847 (76.4)	1103	832 (75.4)
COVID-19 Signs and Symptoms: Cough	Baseline	1109	1033 (93.1)	1115	1061 (95.2)
	DAY 2	1109	1009 (91.0)	1115	1024 (91.8)
	DAY 3	1109	1008 (90.9)	1115	1014 (90.9)
	DAY 4	1109	994 (89.6)	1115	993 (89.1)
	DAY 5	1109	988 (89.1)	1114	978 (87.8)
	DAY 6	1109	919 (82.9)	1114	907 (81.4)
	DAY 7	1109	885 (79.8)	1114	882 (79.2)
	DAY 8	1109	891 (80.3)	1114	876 (78.6)
	DAY 9	1109	892 (80.4)	1114	877 (78.7)
	DAY 10	1109	883 (79.6)	1110	916 (82.5)
	DAY 11	1109	896 (80.8)	1110	911 (82.1)
	DAY 12	1109	900 (81.2)	1108	880 (79.4)
	DAY 13	1109	908 (81.9)	1106	901 (81.5)
	DAY 14	1109	910 (82.1)	1105	913 (82.6)
	DAY 15	1109	898 (81.0)	1105	911 (82.4)
	DAY 16	1109	907 (81.8)	1105	870 (78.7)
	DAY 17	1109	889 (80.2)	1105	882 (79.8)
	DAY 18	1109	884 (79.7)	1105	871 (78.8)
	DAY 19	1109	882 (79.5)	1105	900 (81.4)
	DAY 20	1109	871 (78.5)	1105	903 (81.7)
	DAY 21	1109	903 (81.4)	1105	888 (80.4)
	DAY 22	1109	892 (80.4)	1105	885 (80.1)
	DAY 23	1109	880 (79.4)	1105	863 (78.1)
	DAY 24	1109	870 (78.4)	1105	872 (78.9)
	DAY 25	1109	854 (77.0)	1105	876 (79.3)
	DAY 26	1109	857 (77.3)	1104	863 (78.2)
	DAY 27	1109	871 (78.5)	1104	877 (79.4)
	DAY 28	1109	847 (76.4)	1103	832 (75.4)

N: Number of participants, n: Number of participants with non missing values

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Final

Endpoint	Visit	Nirmatrelvir/ritonavir (N=1109)		Placebo (N=1115)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Low Energy or Tiredness	Baseline	1109	1033 (93.1)	1115	1061 (95.2)
	DAY 2	1109	1009 (91.0)	1115	1024 (91.8)
	DAY 3	1109	1008 (90.9)	1115	1014 (90.9)
	DAY 4	1109	994 (89.6)	1115	993 (89.1)
	DAY 5	1109	988 (89.1)	1114	978 (87.8)
	DAY 6	1109	919 (82.9)	1114	907 (81.4)
	DAY 7	1109	885 (79.8)	1114	882 (79.2)
	DAY 8	1109	891 (80.3)	1114	876 (78.6)
	DAY 9	1109	892 (80.4)	1114	877 (78.7)
	DAY 10	1109	883 (79.6)	1110	916 (82.5)
	DAY 11	1109	896 (80.8)	1110	911 (82.1)
	DAY 12	1109	900 (81.2)	1108	880 (79.4)
	DAY 13	1109	908 (81.9)	1106	901 (81.5)
	DAY 14	1109	910 (82.1)	1105	913 (82.6)
	DAY 15	1109	898 (81.0)	1105	911 (82.4)
	DAY 16	1109	907 (81.8)	1105	870 (78.7)
	DAY 17	1109	889 (80.2)	1105	882 (79.8)
	DAY 18	1109	884 (79.7)	1105	871 (78.8)
	DAY 19	1109	882 (79.5)	1105	900 (81.4)
	DAY 20	1109	871 (78.5)	1105	903 (81.7)
	DAY 21	1109	903 (81.4)	1105	888 (80.4)
	DAY 22	1109	892 (80.4)	1105	885 (80.1)
	DAY 23	1109	880 (79.4)	1105	863 (78.1)
	DAY 24	1109	870 (78.4)	1105	872 (78.9)
	DAY 25	1109	854 (77.0)	1105	876 (79.3)
	DAY 26	1109	857 (77.3)	1104	863 (78.2)
	DAY 27	1109	871 (78.5)	1104	877 (79.4)
	DAY 28	1109	847 (76.4)	1103	832 (75.4)
COVID-19 Signs and Symptoms: Muscle or Body Aches	Baseline	1109	1033 (93.1)	1115	1061 (95.2)
	DAY 2	1109	1009 (91.0)	1115	1024 (91.8)
	DAY 3	1109	1008 (90.9)	1115	1014 (90.9)
	DAY 4	1109	994 (89.6)	1115	993 (89.1)
	DAY 5	1109	988 (89.1)	1114	978 (87.8)
	DAY 6	1109	919 (82.9)	1114	907 (81.4)
	DAY 7	1109	885 (79.8)	1114	882 (79.2)
	DAY 8	1109	891 (80.3)	1114	876 (78.6)
	DAY 9	1109	892 (80.4)	1114	877 (78.7)
	DAY 10	1109	883 (79.6)	1110	916 (82.5)
	DAY 11	1109	896 (80.8)	1110	911 (82.1)
	DAY 12	1109	900 (81.2)	1108	880 (79.4)
	DAY 13	1109	908 (81.9)	1106	901 (81.5)
	DAY 14	1109	910 (82.1)	1105	913 (82.6)
	DAY 15	1109	898 (81.0)	1105	911 (82.4)
	DAY 16	1109	907 (81.8)	1105	870 (78.7)
	DAY 17	1109	889 (80.2)	1105	882 (79.8)
	DAY 18	1109	884 (79.7)	1105	871 (78.8)
	DAY 19	1109	882 (79.5)	1105	900 (81.4)
	DAY 20	1109	871 (78.5)	1105	903 (81.7)
	DAY 21	1109	903 (81.4)	1105	888 (80.4)
	DAY 22	1109	892 (80.4)	1105	885 (80.1)
	DAY 23	1109	880 (79.4)	1105	863 (78.1)
	DAY 24	1109	870 (78.4)	1105	872 (78.9)
	DAY 25	1109	854 (77.0)	1105	876 (79.3)
	DAY 26	1109	857 (77.3)	1104	863 (78.2)
	DAY 27	1109	871 (78.5)	1104	877 (79.4)
	DAY 28	1109	847 (76.4)	1103	832 (75.4)

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=1109)		Placebo (N=1115)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Headache	Baseline	1109	1033 (93.1)	1115	1061 (95.2)
	DAY 2	1109	1009 (91.0)	1115	1024 (91.8)
	DAY 3	1109	1008 (90.9)	1115	1014 (90.9)
	DAY 4	1109	994 (89.6)	1115	993 (89.1)
	DAY 5	1109	988 (89.1)	1114	978 (87.8)
	DAY 6	1109	919 (82.9)	1114	907 (81.4)
	DAY 7	1109	885 (79.8)	1114	882 (79.2)
	DAY 8	1109	891 (80.3)	1114	876 (78.6)
	DAY 9	1109	892 (80.4)	1114	877 (78.7)
	DAY 10	1109	883 (79.6)	1110	916 (82.5)
	DAY 11	1109	896 (80.8)	1110	911 (82.1)
	DAY 12	1109	900 (81.2)	1108	880 (79.4)
	DAY 13	1109	908 (81.9)	1106	901 (81.5)
	DAY 14	1109	910 (82.1)	1105	913 (82.6)
	DAY 15	1109	898 (81.0)	1105	911 (82.4)
	DAY 16	1109	907 (81.8)	1105	870 (78.7)
	DAY 17	1109	889 (80.2)	1105	882 (79.8)
	DAY 18	1109	884 (79.7)	1105	871 (78.8)
	DAY 19	1109	882 (79.5)	1105	900 (81.4)
	DAY 20	1109	871 (78.5)	1105	903 (81.7)
	DAY 21	1109	903 (81.4)	1105	888 (80.4)
	DAY 22	1109	892 (80.4)	1105	885 (80.1)
	DAY 23	1109	880 (79.4)	1105	863 (78.1)
	DAY 24	1109	870 (78.4)	1105	872 (78.9)
	DAY 25	1109	854 (77.0)	1105	876 (79.3)
	DAY 26	1109	857 (77.3)	1104	863 (78.2)
	DAY 27	1109	871 (78.5)	1104	877 (79.4)
	DAY 28	1109	847 (76.4)	1103	832 (75.4)
COVID-19 Signs and Symptoms: Chills or Shivering	Baseline	1109	1033 (93.1)	1115	1061 (95.2)
	DAY 2	1109	1009 (91.0)	1115	1024 (91.8)
	DAY 3	1109	1008 (90.9)	1115	1014 (90.9)
	DAY 4	1109	994 (89.6)	1115	993 (89.1)
	DAY 5	1109	988 (89.1)	1114	978 (87.8)
	DAY 6	1109	919 (82.9)	1114	907 (81.4)
	DAY 7	1109	885 (79.8)	1114	882 (79.2)
	DAY 8	1109	891 (80.3)	1114	876 (78.6)
	DAY 9	1109	892 (80.4)	1114	877 (78.7)
	DAY 10	1109	883 (79.6)	1110	916 (82.5)
	DAY 11	1109	896 (80.8)	1110	911 (82.1)
	DAY 12	1109	900 (81.2)	1108	880 (79.4)
	DAY 13	1109	908 (81.9)	1106	901 (81.5)
	DAY 14	1109	910 (82.1)	1105	913 (82.6)
	DAY 15	1109	898 (81.0)	1105	911 (82.4)
	DAY 16	1109	907 (81.8)	1105	870 (78.7)
	DAY 17	1109	889 (80.2)	1105	882 (79.8)
	DAY 18	1109	884 (79.7)	1105	871 (78.8)
	DAY 19	1109	882 (79.5)	1105	900 (81.4)
	DAY 20	1109	871 (78.5)	1105	903 (81.7)
	DAY 21	1109	903 (81.4)	1105	888 (80.4)
	DAY 22	1109	892 (80.4)	1105	885 (80.1)
	DAY 23	1109	880 (79.4)	1105	863 (78.1)
	DAY 24	1109	870 (78.4)	1105	872 (78.9)
	DAY 25	1109	854 (77.0)	1105	876 (79.3)
	DAY 26	1109	857 (77.3)	1104	863 (78.2)
	DAY 27	1109	871 (78.5)	1104	877 (79.4)
	DAY 28	1109	847 (76.4)	1103	832 (75.4)

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=1109)		Placebo (N=1115)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Feeling Hot or Feverish	Baseline	1109	1033 (93.1)	1115	1061 (95.2)
	DAY 2	1109	1009 (91.0)	1115	1024 (91.8)
	DAY 3	1109	1008 (90.9)	1115	1014 (90.9)
	DAY 4	1109	994 (89.6)	1115	993 (89.1)
	DAY 5	1109	988 (89.1)	1114	978 (87.8)
	DAY 6	1109	919 (82.9)	1114	907 (81.4)
	DAY 7	1109	885 (79.8)	1114	882 (79.2)
	DAY 8	1109	891 (80.3)	1114	876 (78.6)
	DAY 9	1109	892 (80.4)	1114	877 (78.7)
	DAY 10	1109	883 (79.6)	1110	916 (82.5)
	DAY 11	1109	896 (80.8)	1110	911 (82.1)
	DAY 12	1109	900 (81.2)	1108	880 (79.4)
	DAY 13	1109	908 (81.9)	1106	901 (81.5)
	DAY 14	1109	910 (82.1)	1105	913 (82.6)
	DAY 15	1109	898 (81.0)	1105	911 (82.4)
	DAY 16	1109	907 (81.8)	1105	870 (78.7)
	DAY 17	1109	889 (80.2)	1105	882 (79.8)
	DAY 18	1109	884 (79.7)	1105	871 (78.8)
	DAY 19	1109	882 (79.5)	1105	900 (81.4)
	DAY 20	1109	871 (78.5)	1105	903 (81.7)
	DAY 21	1109	903 (81.4)	1105	888 (80.4)
	DAY 22	1109	892 (80.4)	1105	885 (80.1)
	DAY 23	1109	880 (79.4)	1105	863 (78.1)
	DAY 24	1109	870 (78.4)	1105	872 (78.9)
	DAY 25	1109	854 (77.0)	1105	876 (79.3)
	DAY 26	1109	857 (77.3)	1104	863 (78.2)
	DAY 27	1109	871 (78.5)	1104	877 (79.4)
	DAY 28	1109	847 (76.4)	1103	832 (75.4)
COVID-19 Signs and Symptoms: Nausea	Baseline	1109	1033 (93.1)	1115	1061 (95.2)
	DAY 2	1109	1009 (91.0)	1115	1024 (91.8)
	DAY 3	1109	1008 (90.9)	1115	1014 (90.9)
	DAY 4	1109	994 (89.6)	1115	993 (89.1)
	DAY 5	1109	988 (89.1)	1114	978 (87.8)
	DAY 6	1109	919 (82.9)	1114	907 (81.4)
	DAY 7	1109	885 (79.8)	1114	882 (79.2)
	DAY 8	1109	891 (80.3)	1114	876 (78.6)
	DAY 9	1109	892 (80.4)	1114	877 (78.7)
	DAY 10	1109	883 (79.6)	1110	916 (82.5)
	DAY 11	1109	896 (80.8)	1110	911 (82.1)
	DAY 12	1109	900 (81.2)	1108	880 (79.4)
	DAY 13	1109	908 (81.9)	1106	901 (81.5)
	DAY 14	1109	910 (82.1)	1105	913 (82.6)
	DAY 15	1109	898 (81.0)	1105	911 (82.4)
	DAY 16	1109	907 (81.8)	1105	870 (78.7)
	DAY 17	1109	889 (80.2)	1105	882 (79.8)
	DAY 18	1109	884 (79.7)	1105	871 (78.8)
	DAY 19	1109	882 (79.5)	1105	900 (81.4)
	DAY 20	1109	871 (78.5)	1105	903 (81.7)
	DAY 21	1109	903 (81.4)	1105	888 (80.4)
	DAY 22	1109	892 (80.4)	1105	885 (80.1)
	DAY 23	1109	880 (79.4)	1105	863 (78.1)
	DAY 24	1109	870 (78.4)	1105	872 (78.9)
	DAY 25	1109	854 (77.0)	1105	876 (79.3)
	DAY 26	1109	857 (77.3)	1104	863 (78.2)
	DAY 27	1109	871 (78.5)	1104	877 (79.4)
	DAY 28	1109	847 (76.4)	1103	832 (75.4)

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Final

Endpoint	Visit	Nirmatrelvir/ritonavir (N=1109)		Placebo (N=1115)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Vomit	Baseline	1109	1033 (93.1)	1115	1061 (95.2)
	DAY 2	1109	1009 (91.0)	1115	1024 (91.8)
	DAY 3	1109	1008 (90.9)	1115	1014 (90.9)
	DAY 4	1109	994 (89.6)	1115	993 (89.1)
	DAY 5	1109	988 (89.1)	1114	978 (87.8)
	DAY 6	1109	919 (82.9)	1114	907 (81.4)
	DAY 7	1109	885 (79.8)	1114	882 (79.2)
	DAY 8	1109	891 (80.3)	1114	876 (78.6)
	DAY 9	1109	892 (80.4)	1114	877 (78.7)
	DAY 10	1109	883 (79.6)	1110	916 (82.5)
	DAY 11	1109	896 (80.8)	1110	911 (82.1)
	DAY 12	1109	900 (81.2)	1108	880 (79.4)
	DAY 13	1109	908 (81.9)	1106	901 (81.5)
	DAY 14	1109	910 (82.1)	1105	913 (82.6)
	DAY 15	1109	898 (81.0)	1105	911 (82.4)
	DAY 16	1109	907 (81.8)	1105	870 (78.7)
	DAY 17	1109	889 (80.2)	1105	882 (79.8)
	DAY 18	1109	884 (79.7)	1105	871 (78.8)
	DAY 19	1109	882 (79.5)	1105	900 (81.4)
	DAY 20	1109	871 (78.5)	1105	903 (81.7)
	DAY 21	1109	903 (81.4)	1105	888 (80.4)
	DAY 22	1109	892 (80.4)	1105	885 (80.1)
	DAY 23	1109	880 (79.4)	1105	863 (78.1)
	DAY 24	1109	870 (78.4)	1105	872 (78.9)
	DAY 25	1109	854 (77.0)	1105	876 (79.3)
	DAY 26	1109	857 (77.3)	1104	863 (78.2)
	DAY 27	1109	871 (78.5)	1104	877 (79.4)
	DAY 28	1109	847 (76.4)	1103	832 (75.4)
COVID-19 Signs and Symptoms: Diarrhea	Baseline	1109	1033 (93.1)	1115	1061 (95.2)
	DAY 2	1109	1009 (91.0)	1115	1024 (91.8)
	DAY 3	1109	1008 (90.9)	1115	1014 (90.9)
	DAY 4	1109	994 (89.6)	1115	993 (89.1)
	DAY 5	1109	988 (89.1)	1114	978 (87.8)
	DAY 6	1109	919 (82.9)	1114	907 (81.4)
	DAY 7	1109	885 (79.8)	1114	882 (79.2)
	DAY 8	1109	891 (80.3)	1114	876 (78.6)
	DAY 9	1109	892 (80.4)	1114	877 (78.7)
	DAY 10	1109	883 (79.6)	1110	916 (82.5)
	DAY 11	1109	896 (80.8)	1110	911 (82.1)
	DAY 12	1109	900 (81.2)	1108	880 (79.4)
	DAY 13	1109	908 (81.9)	1106	901 (81.5)
	DAY 14	1109	910 (82.1)	1105	913 (82.6)
	DAY 15	1109	898 (81.0)	1105	911 (82.4)
	DAY 16	1109	907 (81.8)	1105	870 (78.7)
	DAY 17	1109	889 (80.2)	1105	882 (79.8)
	DAY 18	1109	884 (79.7)	1105	871 (78.8)
	DAY 19	1109	882 (79.5)	1105	900 (81.4)
	DAY 20	1109	871 (78.5)	1105	903 (81.7)
	DAY 21	1109	903 (81.4)	1105	888 (80.4)
	DAY 22	1109	892 (80.4)	1105	885 (80.1)
	DAY 23	1109	880 (79.4)	1105	863 (78.1)
	DAY 24	1109	870 (78.4)	1105	872 (78.9)
	DAY 25	1109	854 (77.0)	1105	876 (79.3)
	DAY 26	1109	857 (77.3)	1104	863 (78.2)
	DAY 27	1109	871 (78.5)	1104	877 (79.4)
	DAY 28	1109	847 (76.4)	1103	832 (75.4)

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Final

Endpoint	Visit	Nirmatrelvir/ritonavir (N=1109)		Placebo (N=1115)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Sense of Smell	Baseline	1109	1033 (93.1)	1115	1061 (95.2)
	DAY 2	1109	1009 (91.0)	1115	1024 (91.8)
	DAY 3	1109	1008 (90.9)	1115	1014 (90.9)
	DAY 4	1109	994 (89.6)	1115	993 (89.1)
	DAY 5	1109	988 (89.1)	1114	978 (87.8)
	DAY 6	1109	919 (82.9)	1114	907 (81.4)
	DAY 7	1109	885 (79.8)	1114	882 (79.2)
	DAY 8	1109	891 (80.3)	1114	876 (78.6)
	DAY 9	1109	892 (80.4)	1114	877 (78.7)
	DAY 10	1109	883 (79.6)	1110	916 (82.5)
	DAY 11	1109	896 (80.8)	1110	911 (82.1)
	DAY 12	1109	900 (81.2)	1108	880 (79.4)
	DAY 13	1109	908 (81.9)	1106	901 (81.5)
	DAY 14	1109	910 (82.1)	1105	913 (82.6)
	DAY 15	1109	898 (81.0)	1105	911 (82.4)
	DAY 16	1109	907 (81.8)	1105	870 (78.7)
	DAY 17	1109	889 (80.2)	1105	882 (79.8)
	DAY 18	1109	884 (79.7)	1105	871 (78.8)
	DAY 19	1109	882 (79.5)	1105	900 (81.4)
	DAY 20	1109	871 (78.5)	1105	903 (81.7)
	DAY 21	1109	903 (81.4)	1105	888 (80.4)
	DAY 22	1109	892 (80.4)	1105	885 (80.1)
	DAY 23	1109	880 (79.4)	1105	863 (78.1)
	DAY 24	1109	870 (78.4)	1105	872 (78.9)
	DAY 25	1109	854 (77.0)	1105	876 (79.3)
	DAY 26	1109	857 (77.3)	1104	863 (78.2)
	DAY 27	1109	871 (78.5)	1104	877 (79.4)
	DAY 28	1109	847 (76.4)	1103	832 (75.4)
COVID-19 Signs and Symptoms: Sense of Taste	Baseline	1109	1033 (93.1)	1115	1061 (95.2)
	DAY 2	1109	1009 (91.0)	1115	1024 (91.8)
	DAY 3	1109	1008 (90.9)	1115	1014 (90.9)
	DAY 4	1109	994 (89.6)	1115	993 (89.1)
	DAY 5	1109	988 (89.1)	1114	978 (87.8)
	DAY 6	1109	919 (82.9)	1114	907 (81.4)
	DAY 7	1109	885 (79.8)	1114	882 (79.2)
	DAY 8	1109	891 (80.3)	1114	876 (78.6)
	DAY 9	1109	892 (80.4)	1114	877 (78.7)
	DAY 10	1109	883 (79.6)	1110	916 (82.5)
	DAY 11	1109	896 (80.8)	1110	911 (82.1)
	DAY 12	1109	900 (81.2)	1108	880 (79.4)
	DAY 13	1109	908 (81.9)	1106	901 (81.5)
	DAY 14	1109	910 (82.1)	1105	913 (82.6)
	DAY 15	1109	898 (81.0)	1105	911 (82.4)
	DAY 16	1109	907 (81.8)	1105	870 (78.7)
	DAY 17	1109	889 (80.2)	1105	882 (79.8)
	DAY 18	1109	884 (79.7)	1105	871 (78.8)
	DAY 19	1109	882 (79.5)	1105	900 (81.4)
	DAY 20	1109	871 (78.5)	1105	903 (81.7)
	DAY 21	1109	903 (81.4)	1105	888 (80.4)
	DAY 22	1109	892 (80.4)	1105	885 (80.1)
	DAY 23	1109	880 (79.4)	1105	863 (78.1)
	DAY 24	1109	870 (78.4)	1105	872 (78.9)
	DAY 25	1109	854 (77.0)	1105	876 (79.3)
	DAY 26	1109	857 (77.3)	1104	863 (78.2)
	DAY 27	1109	871 (78.5)	1104	877 (79.4)
	DAY 28	1109	847 (76.4)	1103	832 (75.4)

N: Number of participants, n: Number of participants with non missing values

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=1109)		Placebo (N=1115)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
5-level European Quality of Life Five Dimension (EQ-5D-5L): EQ-VAS Score	Day 1	1109	33 (3.0)	1115	38 (3.4)
	Day 5	1109	37 (3.3)	1114	43 (3.9)
	Day 14	1109	57 (5.1)	1105	70 (6.3)
	Day 34	1109	116 (10.5)	1102	121 (11.0)
	Week 12	1109	236 (21.3)	1101	250 (22.7)
	Week 24	1109	480 (43.3)	1100	478 (43.5)
Global Impression Questionnaire: return to usual health	Baseline	1109	1007 (90.8)	1115	1035 (92.8)
	DAY 2	1109	980 (88.4)	1115	997 (89.4)
	DAY 3	1109	979 (88.3)	1115	989 (88.7)
	DAY 4	1109	962 (86.7)	1115	967 (86.7)
	DAY 5	1109	958 (86.4)	1114	952 (85.5)
	DAY 6	1109	892 (80.4)	1114	879 (78.9)
	DAY 7	1109	861 (77.6)	1114	859 (77.1)
	DAY 8	1109	868 (78.3)	1114	855 (76.8)
	DAY 9	1109	868 (78.3)	1114	855 (76.8)
	DAY 10	1109	860 (77.5)	1110	893 (80.5)
	DAY 11	1109	872 (78.6)	1110	885 (79.7)
	DAY 12	1109	871 (78.5)	1108	855 (77.2)
	DAY 13	1109	882 (79.5)	1106	877 (79.3)
	DAY 14	1109	884 (79.7)	1105	887 (80.3)
	DAY 15	1109	869 (78.4)	1105	883 (79.9)
	DAY 16	1109	882 (79.5)	1105	846 (76.6)
	DAY 17	1109	864 (77.9)	1105	855 (77.4)
	DAY 18	1109	858 (77.4)	1105	845 (76.5)
	DAY 19	1109	856 (77.2)	1105	874 (79.1)
	DAY 20	1109	848 (76.5)	1105	877 (79.4)
	DAY 21	1109	875 (78.9)	1105	863 (78.1)
	DAY 22	1109	862 (77.7)	1105	859 (77.7)
	DAY 23	1109	852 (76.8)	1105	835 (75.6)
	DAY 24	1109	842 (75.9)	1105	845 (76.5)
	DAY 25	1109	829 (74.8)	1105	849 (76.8)
	DAY 26	1109	832 (75.0)	1104	838 (75.9)
	DAY 27	1109	841 (75.8)	1104	848 (76.8)
	DAY 28	1109	820 (73.9)	1103	805 (73.0)

N: Number of participants, n: Number of participants with non missing values

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=1109)		Placebo (N=1115)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
Global Impression Questionnaire: overall COVID-19-related symptoms	Baseline	1109	1007 (90.8)	1115	1035 (92.8)
	DAY 2	1109	980 (88.4)	1115	997 (89.4)
	DAY 3	1109	979 (88.3)	1115	989 (88.7)
	DAY 4	1109	962 (86.7)	1115	967 (86.7)
	DAY 5	1109	958 (86.4)	1114	952 (85.5)
	DAY 6	1109	892 (80.4)	1114	879 (78.9)
	DAY 7	1109	861 (77.6)	1114	859 (77.1)
	DAY 8	1109	868 (78.3)	1114	855 (76.8)
	DAY 9	1109	868 (78.3)	1114	855 (76.8)
	DAY 10	1109	860 (77.5)	1110	893 (80.5)
	DAY 11	1109	872 (78.6)	1110	885 (79.7)
	DAY 12	1109	871 (78.5)	1108	855 (77.2)
	DAY 13	1109	882 (79.5)	1106	877 (79.3)
	DAY 14	1109	884 (79.7)	1105	887 (80.3)
	DAY 15	1109	869 (78.4)	1105	883 (79.9)
	DAY 16	1109	882 (79.5)	1105	846 (76.6)
	DAY 17	1109	864 (77.9)	1105	855 (77.4)
	DAY 18	1109	858 (77.4)	1105	845 (76.5)
	DAY 19	1109	856 (77.2)	1105	874 (79.1)
	DAY 20	1109	848 (76.5)	1105	877 (79.4)
	DAY 21	1109	875 (78.9)	1105	863 (78.1)
	DAY 22	1109	862 (77.7)	1105	859 (77.7)
	DAY 23	1109	852 (76.8)	1105	835 (75.6)
	DAY 24	1109	842 (75.9)	1105	845 (76.5)
	DAY 25	1109	829 (74.8)	1105	849 (76.8)
	DAY 26	1109	832 (75.0)	1104	838 (75.9)
	DAY 27	1109	841 (75.8)	1104	848 (76.8)
	DAY 28	1109	820 (73.9)	1103	805 (73.0)
Global Impression Questionnaire: return to usual activities	Baseline	1109	1007 (90.8)	1115	1035 (92.8)
	DAY 2	1109	980 (88.4)	1115	997 (89.4)
	DAY 3	1109	979 (88.3)	1115	989 (88.7)
	DAY 4	1109	962 (86.7)	1115	967 (86.7)
	DAY 5	1109	958 (86.4)	1114	952 (85.5)
	DAY 6	1109	892 (80.4)	1114	879 (78.9)
	DAY 7	1109	861 (77.6)	1114	859 (77.1)
	DAY 8	1109	868 (78.3)	1114	855 (76.8)
	DAY 9	1109	868 (78.3)	1114	855 (76.8)
	DAY 10	1109	860 (77.5)	1110	893 (80.5)
	DAY 11	1109	872 (78.6)	1110	885 (79.7)
	DAY 12	1109	871 (78.5)	1108	855 (77.2)
	DAY 13	1109	882 (79.5)	1106	877 (79.3)
	DAY 14	1109	884 (79.7)	1105	887 (80.3)
	DAY 15	1109	869 (78.4)	1105	883 (79.9)
	DAY 16	1109	882 (79.5)	1105	846 (76.6)
	DAY 17	1109	864 (77.9)	1105	855 (77.4)
	DAY 18	1109	858 (77.4)	1105	845 (76.5)
	DAY 19	1109	856 (77.2)	1105	874 (79.1)
	DAY 20	1109	848 (76.5)	1105	877 (79.4)
	DAY 21	1109	875 (78.9)	1105	863 (78.1)
	DAY 22	1109	862 (77.7)	1105	859 (77.7)
	DAY 23	1109	852 (76.8)	1105	835 (75.6)
	DAY 24	1109	842 (75.9)	1105	845 (76.5)
	DAY 25	1109	829 (74.8)	1105	849 (76.8)
	DAY 26	1109	832 (75.0)	1104	838 (75.9)
	DAY 27	1109	841 (75.8)	1104	848 (76.8)
	DAY 28	1109	820 (73.9)	1103	805 (73.0)

N: Number of participants, n: Number of participants with non missing values

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Final

Endpoint	Visit	Nirmatrelvir/ritonavir (N=1109)		Placebo (N=1115)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
Work Productivity and Activity Impairment (WPAI): WPAI Question 6	Baseline (Day 5)	1109	34 (3.1)	1114	42 (3.8)
	Day 14	1109	56 (5.0)	1105	69 (6.2)
	Week 12	1109	234 (21.1)	1101	247 (22.4)
	Week 24	1109	479 (43.2)	1100	473 (43.0)

N: Number of participants, n: Number of participants with non missing values

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Stuffy or Runny Nose

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	240 (22.0)	271 (24.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.867 (0.706, 1.065) 0.174	
Relative Risk (95% CI)	0.893 (0.765, 1.043) 0.153	
Risk Difference (95% CI)	-0.020 (-0.054, 0.014) 0.251	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.866 (0.710, 1.056) 0.154	
Relative Risk (95% CI)	0.895 (0.769, 1.043) 0.155	
Risk Difference (95% CI)	-0.026 (-0.061, 0.010) 0.154	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Stuffy or Runny Nose

Final

	Nirmatrelvir/ritonavir (N=773)	Placebo (N=762)
Number of subjects with events, n (%)	675 (87.3)	606 (79.5)
Number of censored subjects, n (%)	98 (12.7)	156 (20.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	6.0 (5.0, 6.0)	7.0 (7.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.332 (1.190, 1.492)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.324 (1.186, 1.479)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

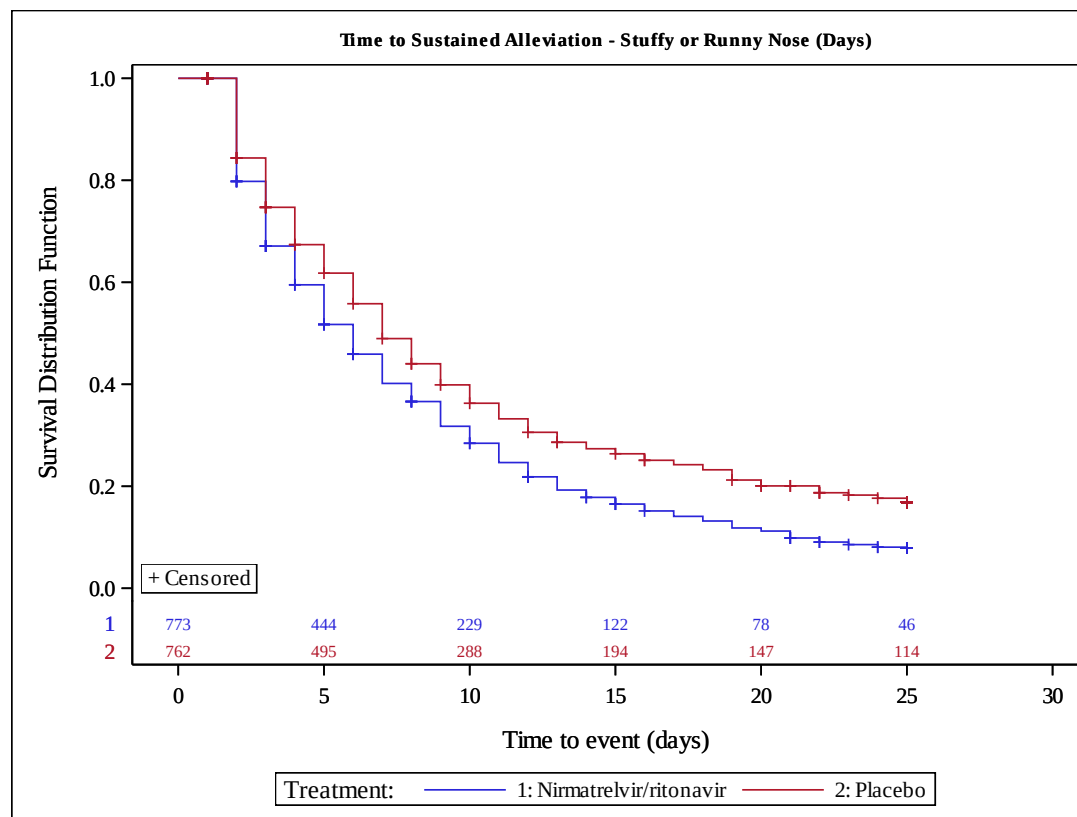
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Stuffy or Runny Nose

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Stuffy or Runny Nose

Final

	Nirmatrelvir/ritonavir (N=33)	Placebo (N=34)
Number of subjects with events, n (%)	28 (84.8)	30 (88.2)
Number of censored subjects, n (%)	5 (15.2)	4 (11.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (3.0, 10.0)	9.0 (5.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	0.941 (0.526, 1.683)	
p-value [3]	0.837	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	0.961 (0.567, 1.629)	
p-value [3]	0.882	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

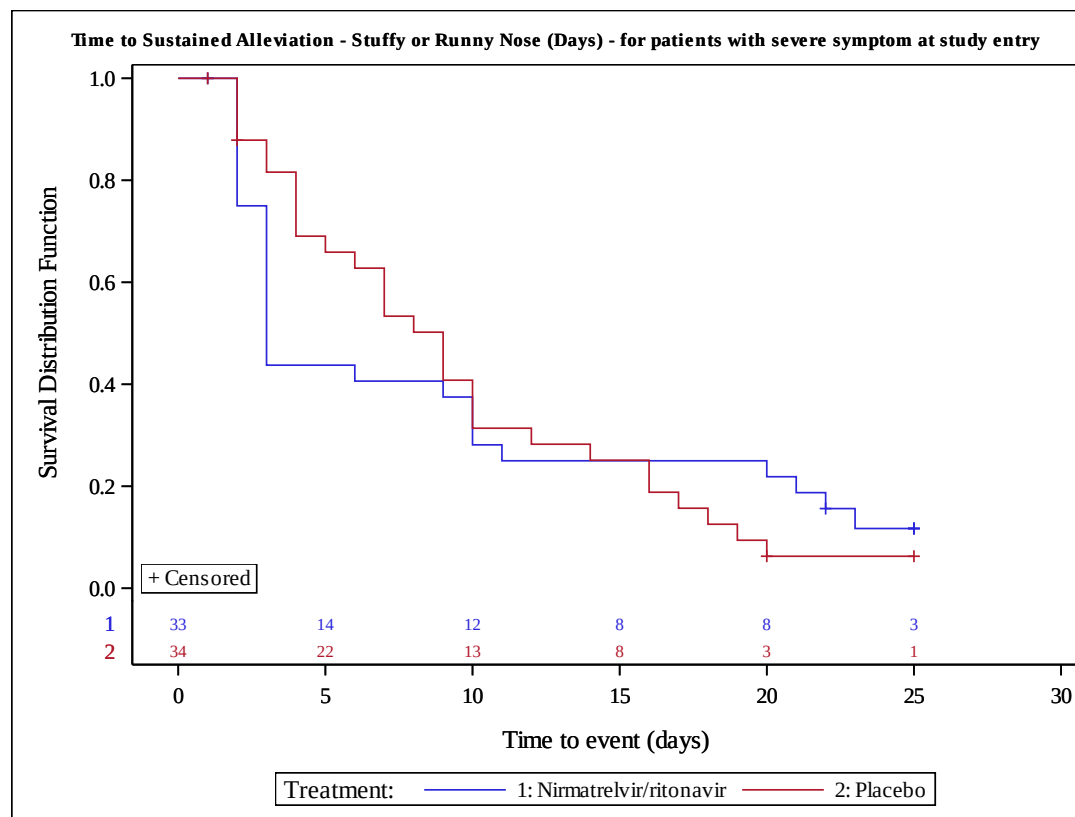
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Stuffy or Runny Nose

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Stuffy or Runny Nose

Final

	Nirmatrelvir/ritonavir (N=773)	Placebo (N=762)
Number of subjects with events, n (%)	620 (80.2)	546 (71.7)
Number of censored subjects, n (%)	153 (19.8)	216 (28.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	9.0 (9.0, 10.0)	11.0 (10.0, 12.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.328 (1.180, 1.494)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.312 (1.169, 1.472)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

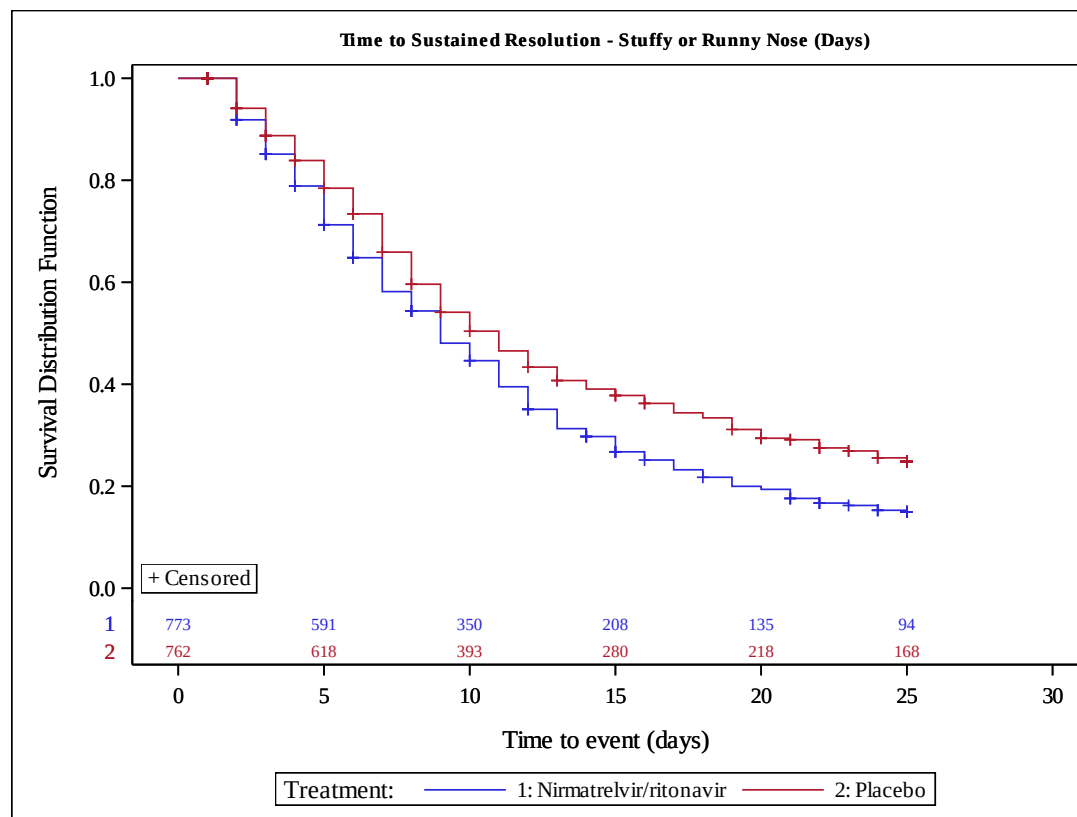
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Stuffy or Runny Nose

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Stuffy or Runny Nose

Final

	Nirmatrelvir/ritonavir (N=33)	Placebo (N=34)
Number of subjects with events, n (%)	21 (63.6)	20 (58.8)
Number of censored subjects, n (%)	12 (36.4)	14 (41.2)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	12.5 (7.0, NE)	18.5 (10.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.163 (0.584, 2.318)	
p-value [3]	0.667	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.225 (0.663, 2.261)	
p-value [3]	0.517	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

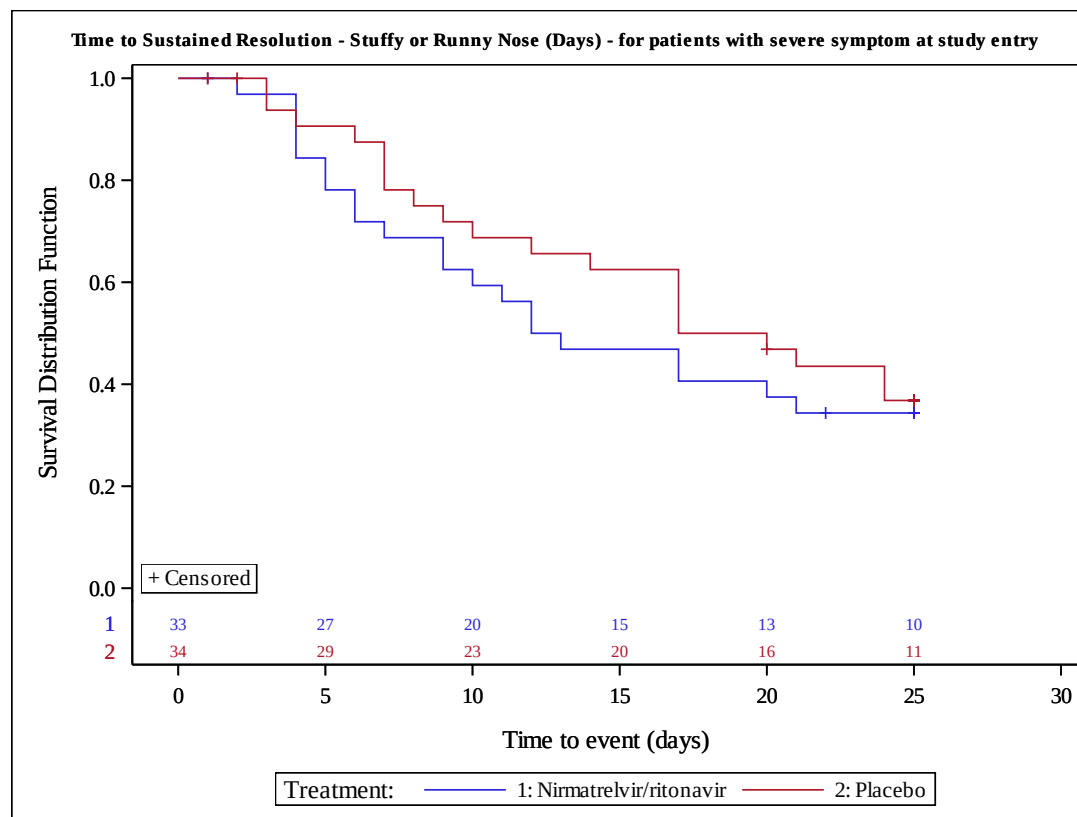
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Stuffy or Runny Nose

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Sore Throat

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	221 (20.2)	258 (23.3)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.816 (0.662, 1.005) 0.055	
Relative Risk (95% CI)	0.855 (0.728, 1.004) 0.055	
Risk Difference (95% CI)	-0.027 (-0.061, 0.007) 0.123	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.832 (0.679, 1.019) 0.076	
Relative Risk (95% CI)	0.866 (0.739, 1.015) 0.076	
Risk Difference (95% CI)	-0.031 (-0.066, 0.003) 0.075	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Sore Throat

Final

	Nirmatrelvir/ritonavir (N=610)	Placebo (N=627)
Number of subjects with events, n (%)	535 (87.7)	506 (80.7)
Number of censored subjects, n (%)	75 (12.3)	121 (19.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 5.0)	6.0 (5.0, 7.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.344 (1.186, 1.523)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.327 (1.174, 1.500)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

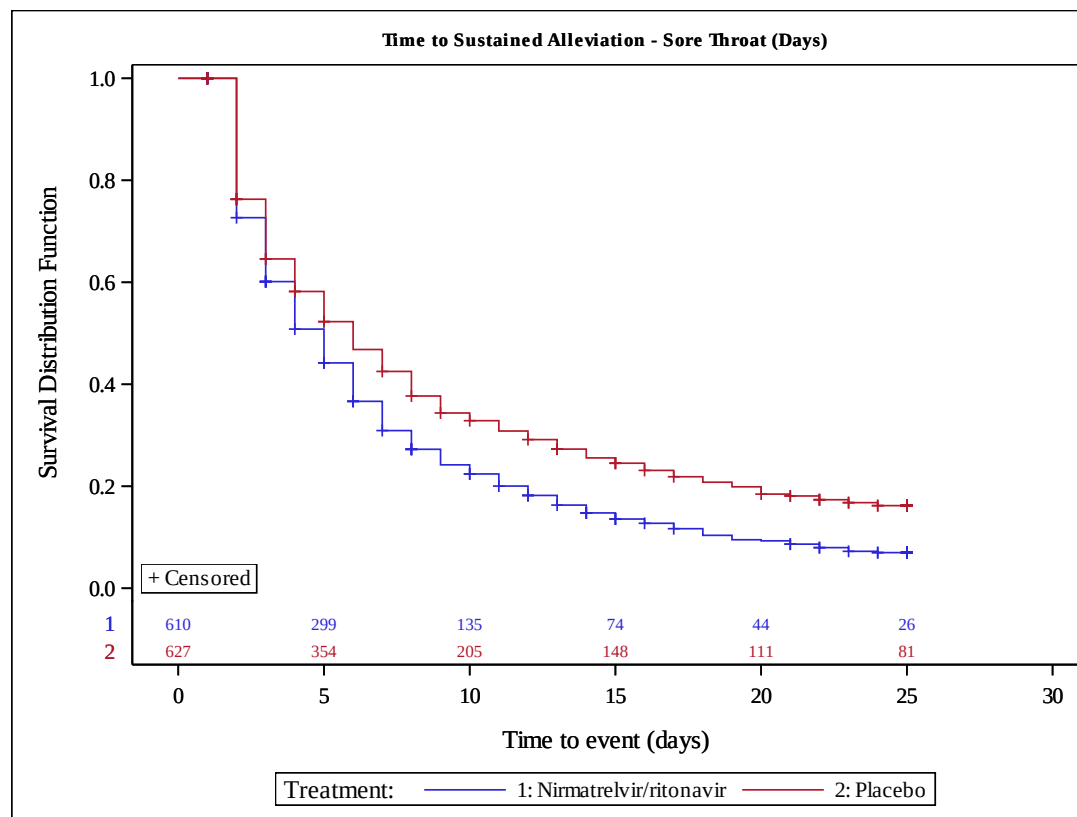
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Sore Throat

Final

	Nirmatrelvir/ritonavir (N=29)	Placebo (N=31)
Number of subjects with events, n (%)	22 (75.9)	24 (77.4)
Number of censored subjects, n (%)	7 (24.1)	7 (22.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (2.0, 7.0)	6.0 (4.0, 12.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.492 (0.773, 2.878)	
p-value [3]	0.233	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.398 (0.782, 2.499)	
p-value [3]	0.258	

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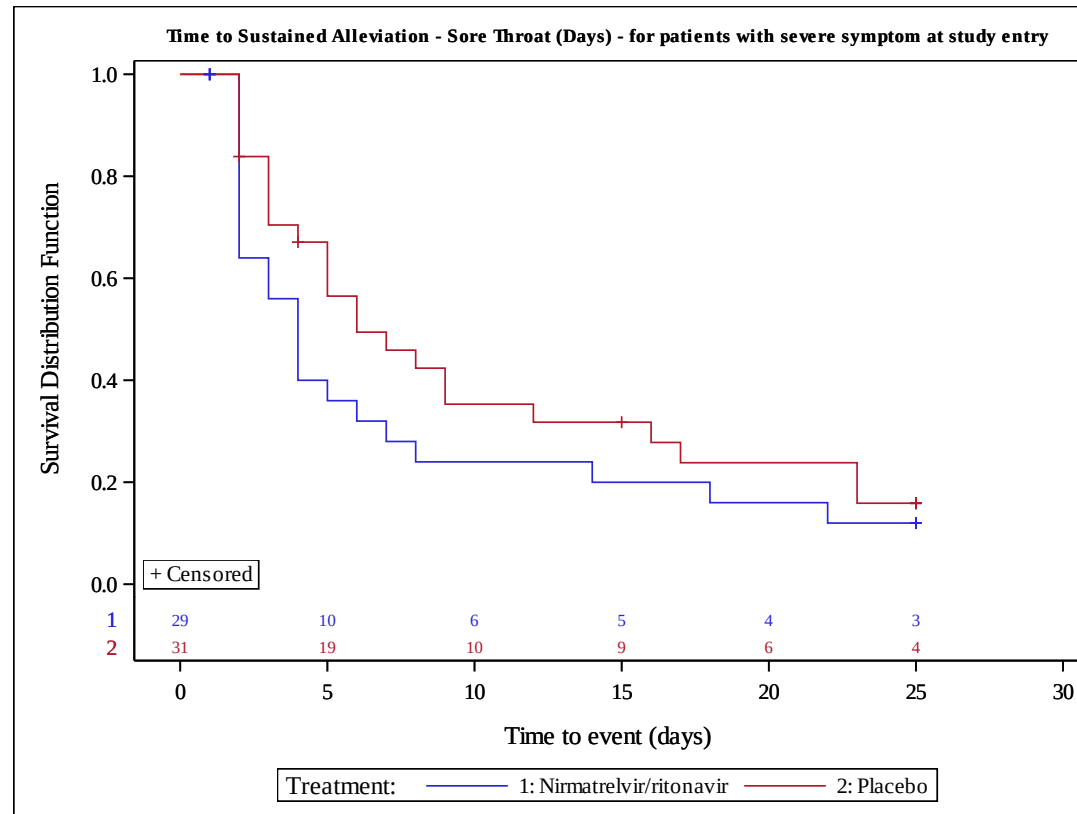
[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

	Nirmatrelvir/ritonavir (N=610)	Placebo (N=627)
Number of subjects with events, n (%)	502 (82.3)	474 (75.6)
Number of censored subjects, n (%)	108 (17.7)	153 (24.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	7.0 (6.0, 8.0)	9.0 (8.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.300 (1.143, 1.479)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.308 (1.153, 1.484)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

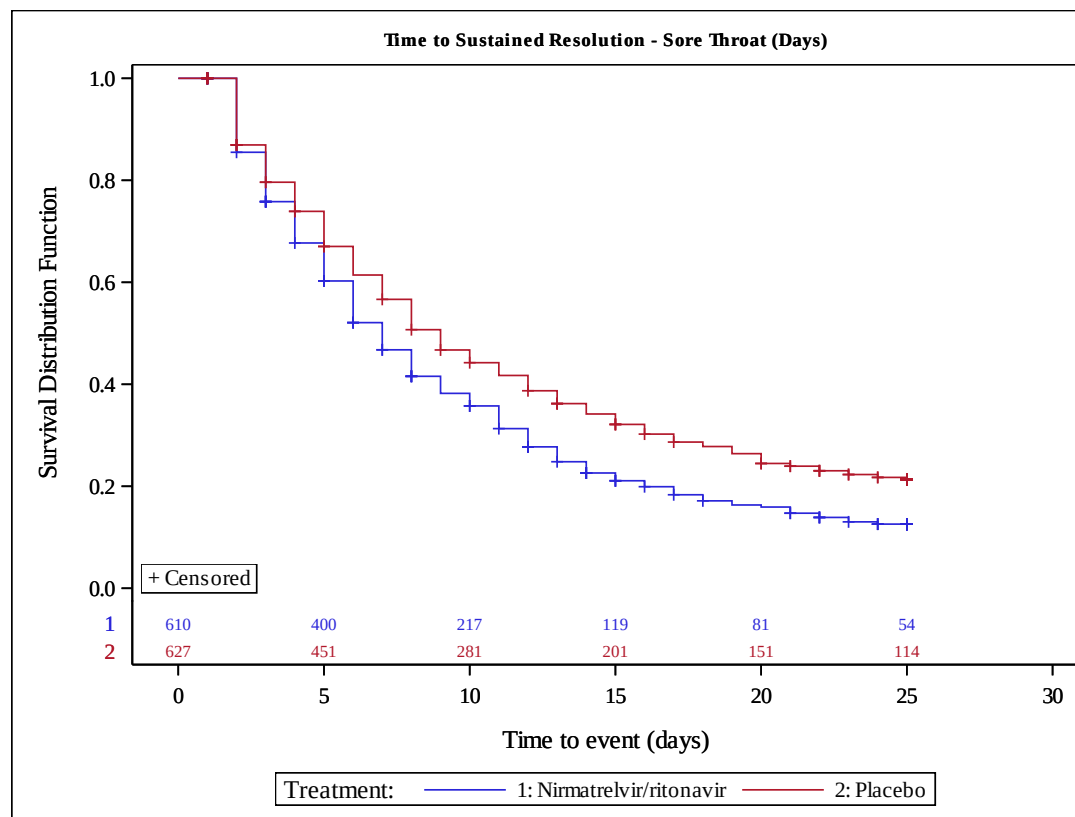
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Final

	Nirmatrelvir/ritonavir (N=29)	Placebo (N=31)
Number of subjects with events, n (%)	18 (62.1)	20 (64.5)
Number of censored subjects, n (%)	11 (37.9)	11 (35.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	14.0 (8.0, 23.0)	13.0 (8.0, 25.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.152 (0.571, 2.324)	
p-value [3]	0.694	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.087 (0.575, 2.056)	
p-value [3]	0.798	

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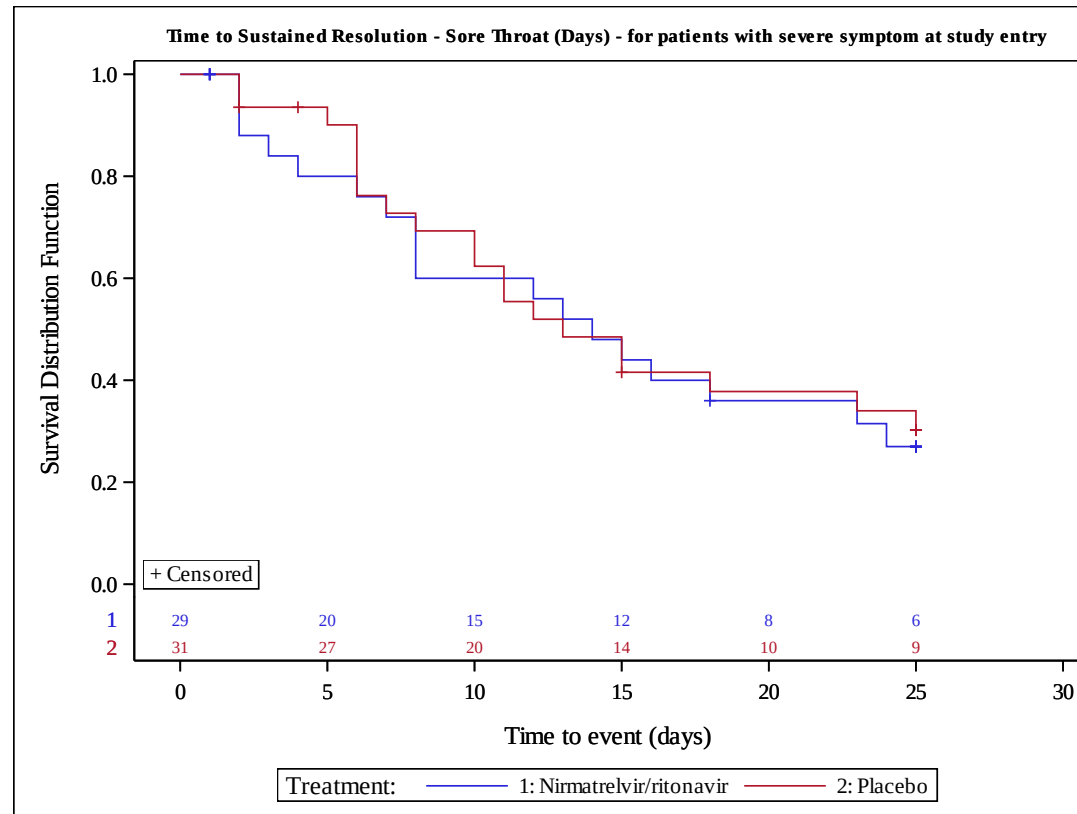
[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Shortness of Breath or Difficulty Breathing

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	242 (22.1)	316 (28.6)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.687 (0.562, 0.839) <.001	
Relative Risk (95% CI)	0.755 (0.653, 0.874) <.001	
Risk Difference (95% CI)	NE (NE, NE)	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.710 (0.585, 0.862) <.001	
Relative Risk (95% CI)	0.774 (0.670, 0.895) <.001	
Risk Difference (95% CI)	-0.065 (-0.101, -0.028) <.001	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Final

	Nirmatrelvir/ritonavir (N=492)	Placebo (N=507)
Number of subjects with events, n (%)	411 (83.5)	375 (74.0)
Number of censored subjects, n (%)	81 (16.5)	132 (26.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	6.0 (5.0, 7.0)	8.0 (7.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.409 (1.219, 1.628)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.399 (1.215, 1.610)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

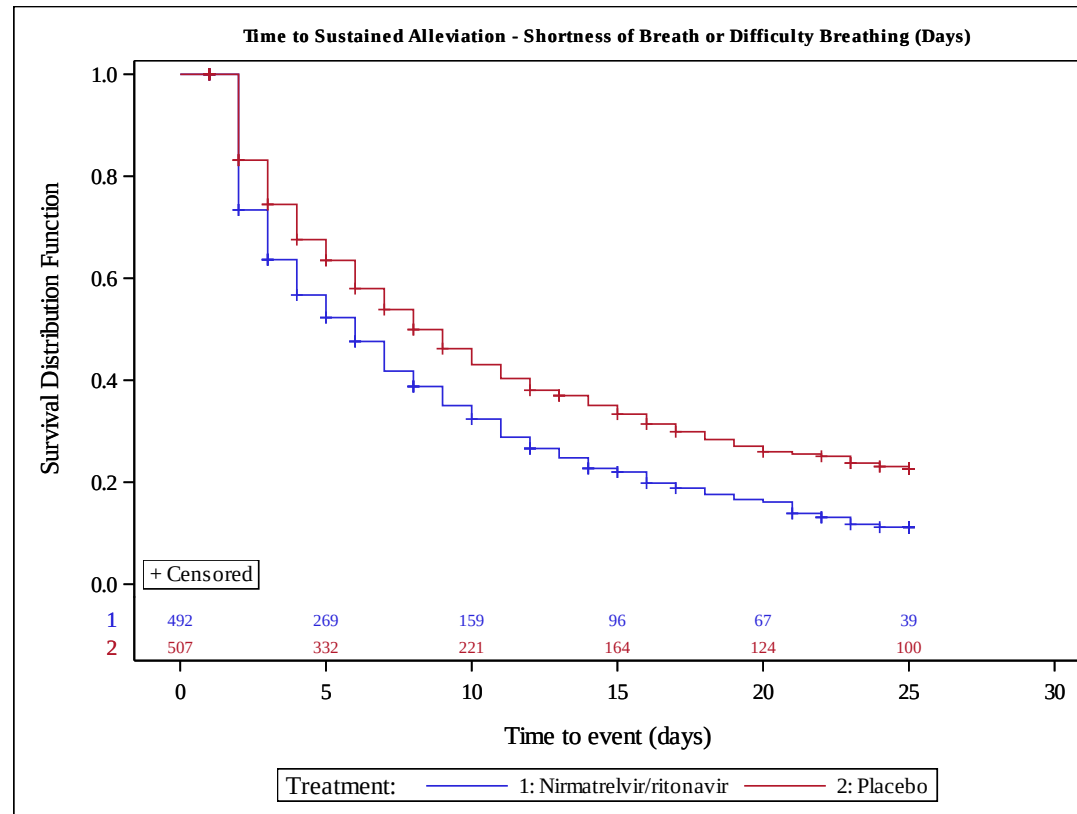
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

	Nirmatrelvir/ritonavir (N=12)	Placebo (N=11)
Number of subjects with events, n (%)	7 (58.3)	4 (36.4)
Number of censored subjects, n (%)	5 (41.7)	7 (63.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	9.0 (2.0, 22.0)	NE (3.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	9.605 (0.485, 190.07)	
p-value [3]	0.137	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	3.006 (0.854, 10.579)	
p-value [3]	0.087	

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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

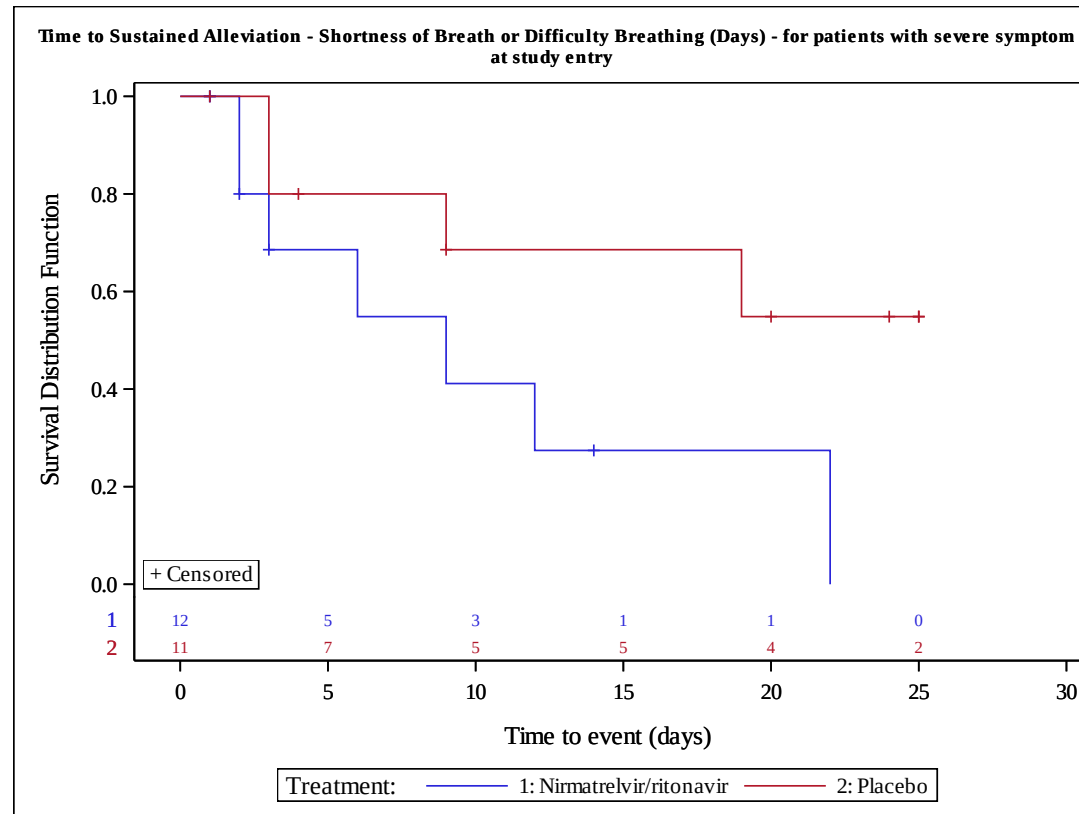
[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Final

	Nirmatrelvir/ritonavir (N=492)	Placebo (N=507)
Number of subjects with events, n (%)	385 (78.3)	326 (64.3)
Number of censored subjects, n (%)	107 (21.7)	181 (35.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	9.0 (7.0, 10.0)	13.0 (11.0, 15.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.547 (1.329, 1.801)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.547 (1.334, 1.795)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

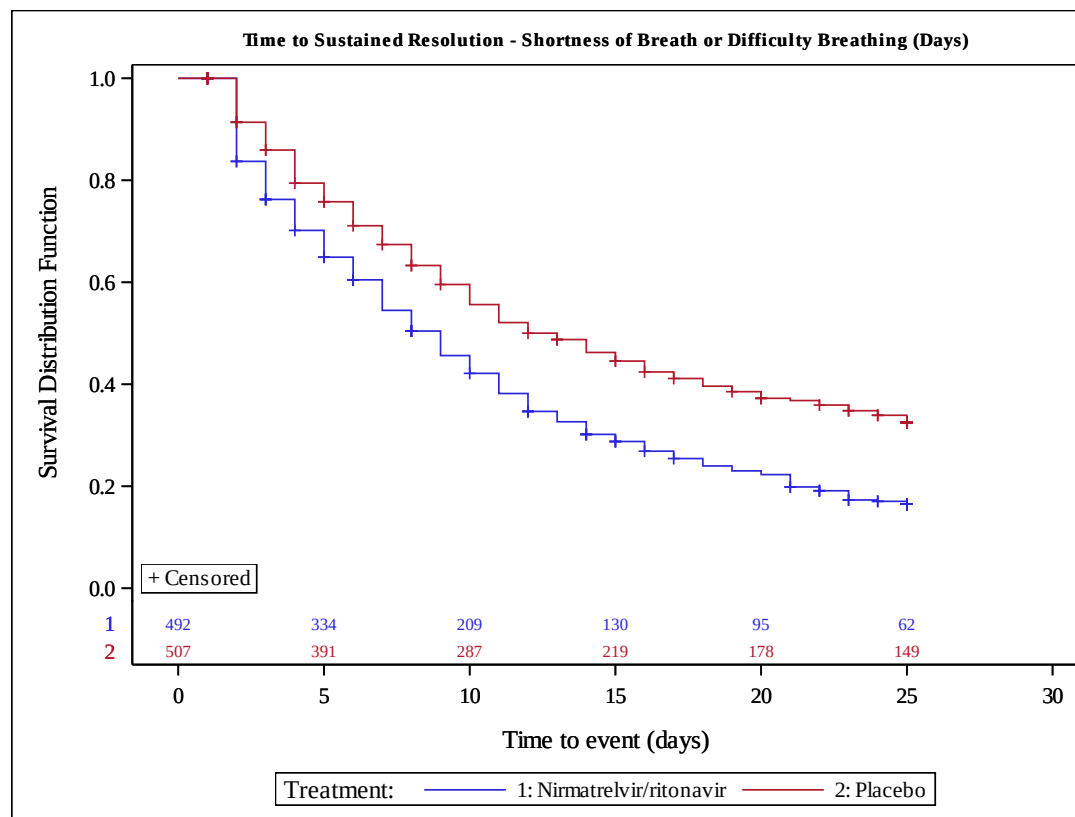
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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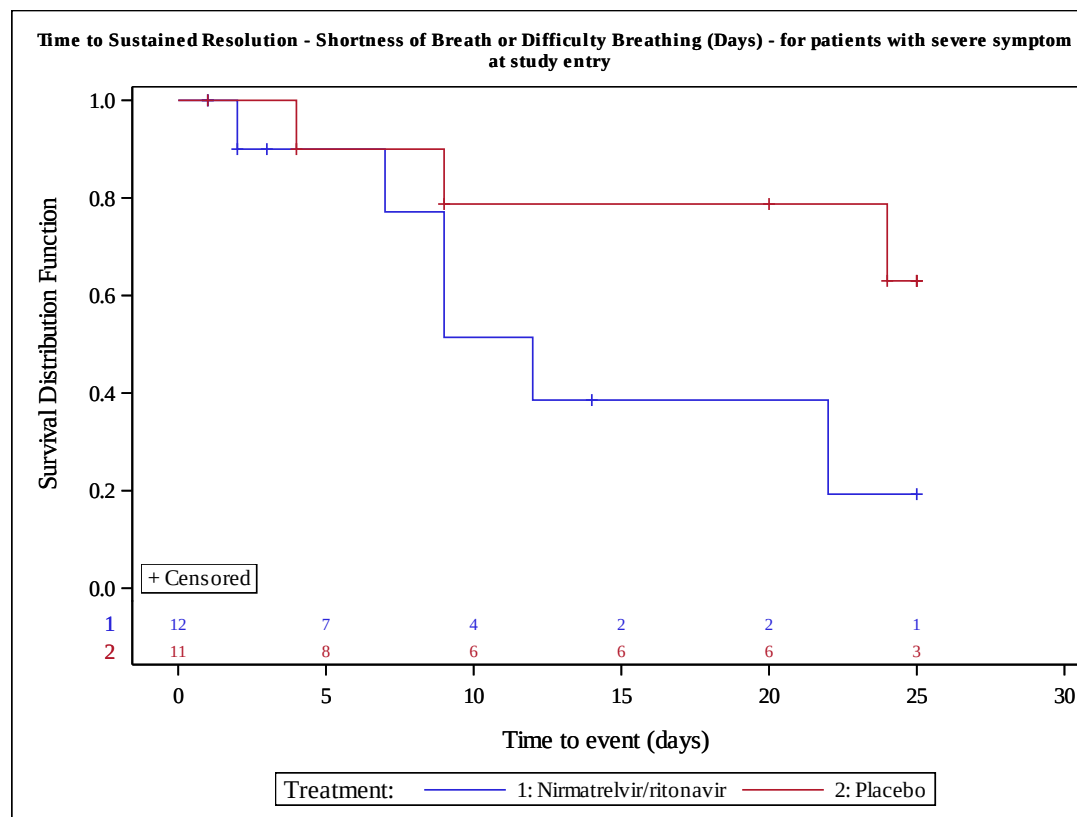
	Nirmatrelvir/ritonavir (N=12)	Placebo (N=11)
Number of subjects with events, n (%)	6 (50.0)	3 (27.3)
Number of censored subjects, n (%)	6 (50.0)	8 (72.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	12.0 (2.0, NE)	NE (4.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	11.563 (0.304, 439.95)	
p-value [3]	0.187	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	3.302 (0.795, 13.715)	
p-value [3]	0.100	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
[1] Based on the Brookmeyer and Crowley Method.
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.
[3] Estimated by cox regression model assuming proportional hazards.

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 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Cough

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	238 (21.8)	273 (24.7)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.826 (0.673, 1.014) 0.068	
Relative Risk (95% CI)	0.864 (0.740, 1.008) 0.063	
Risk Difference (95% CI)	-0.030 (-0.065, 0.004) 0.087	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.848 (0.696, 1.034) 0.104	
Relative Risk (95% CI)	0.881 (0.757, 1.026) 0.104	
Risk Difference (95% CI)	-0.029 (-0.065, 0.006) 0.104	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Final

	Nirmatrelvir/ritonavir (N=892)	Placebo (N=917)
Number of subjects with events, n (%)	737 (82.6)	693 (75.6)
Number of censored subjects, n (%)	155 (17.4)	224 (24.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	8.0 (8.0, 9.0)	10.0 (9.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.249 (1.123, 1.389)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.272 (1.147, 1.412)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

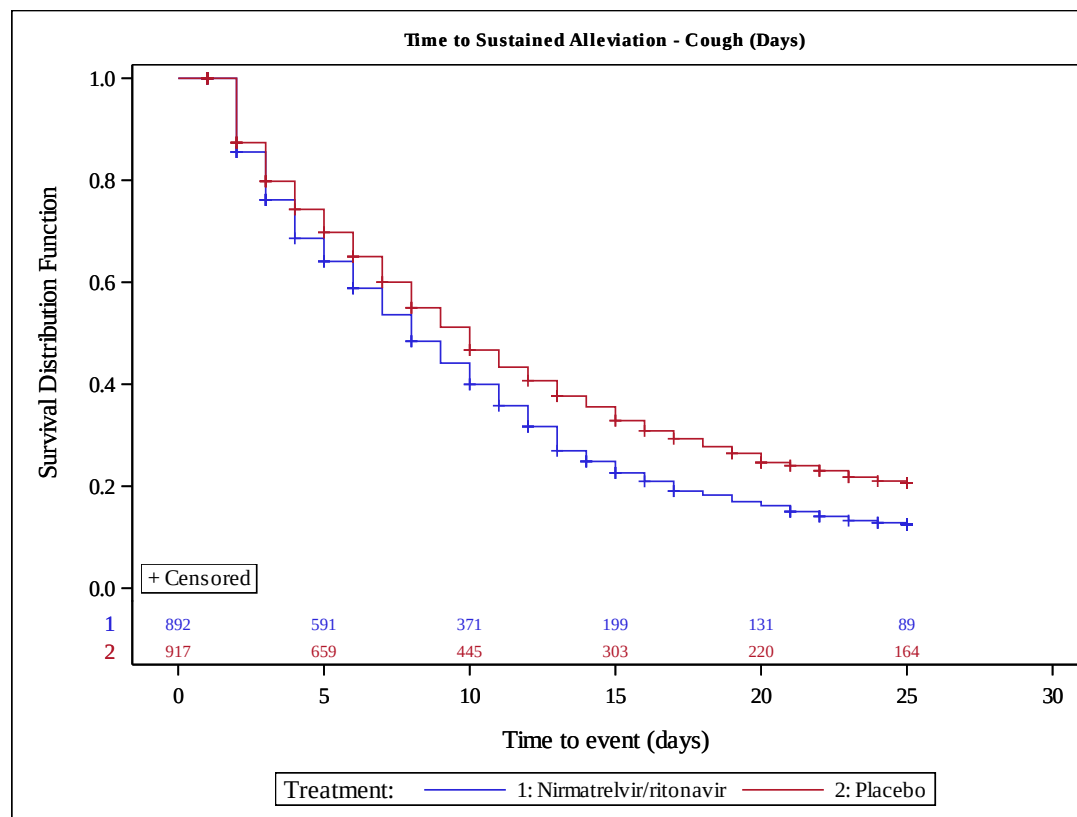
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Cough

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough

Final

	Nirmatrelvir/ritonavir (N=60)	Placebo (N=54)
Number of subjects with events, n (%)	49 (81.7)	35 (64.8)
Number of censored subjects, n (%)	11 (18.3)	19 (35.2)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 7.0)	15.0 (8.0, 20.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.871 (1.167, 2.998)	
p-value [3]	0.009	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	2.162 (1.390, 3.361)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

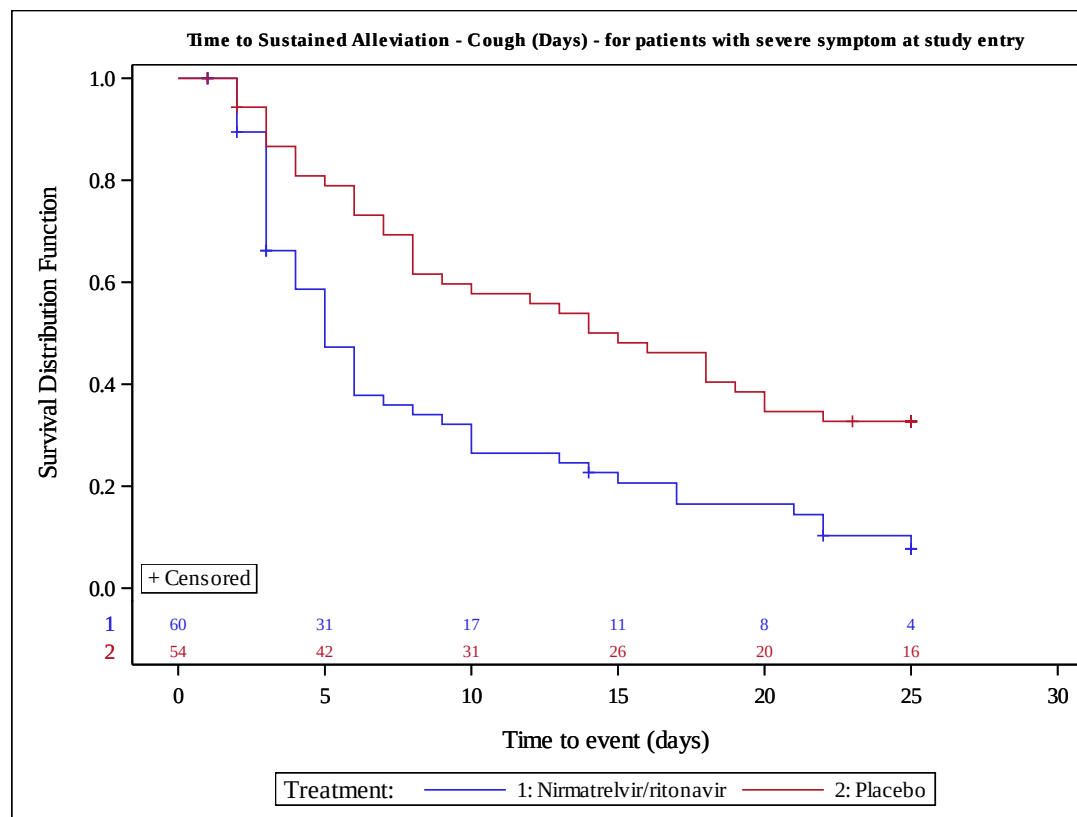
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Cough

Final

	Nirmatrelvir/ritonavir (N=892)	Placebo (N=917)
Number of subjects with events, n (%)	660 (74.0)	600 (65.4)
Number of censored subjects, n (%)	232 (26.0)	317 (34.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	13.0 (12.0, 13.0)	15.0 (14.0, 16.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.268 (1.132, 1.419)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.299 (1.163, 1.452)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

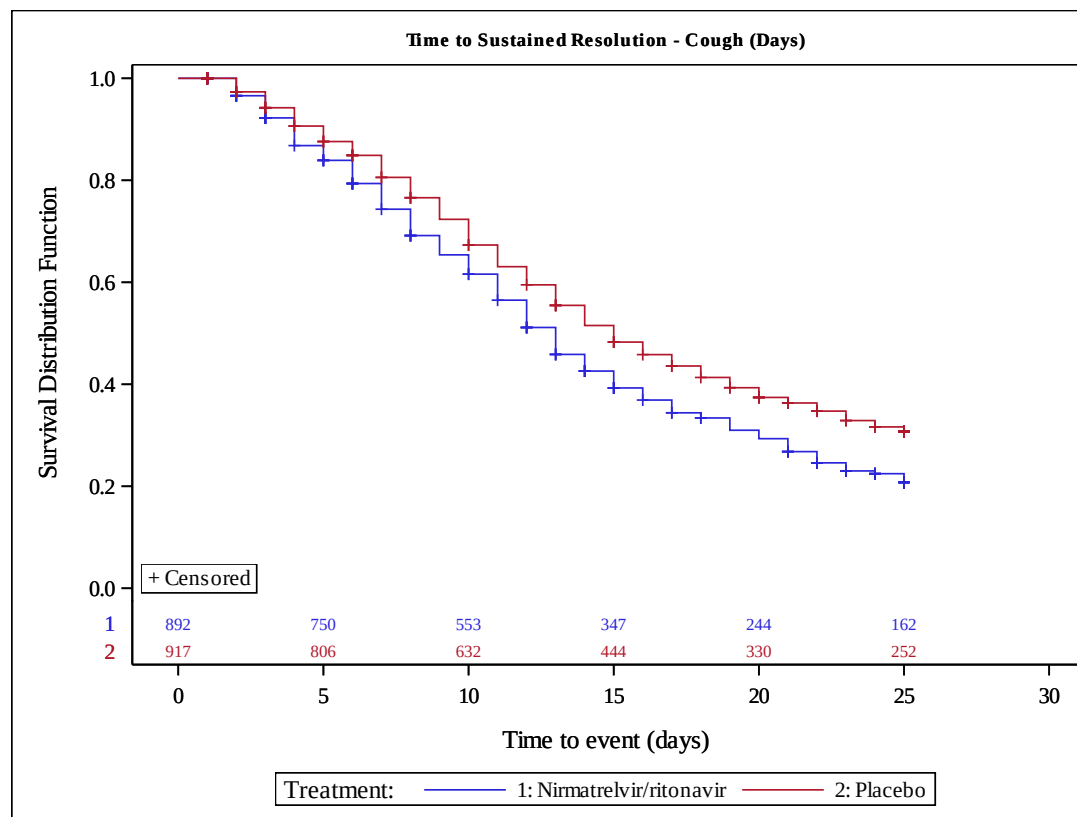
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough

Final

	Nirmatrelvir/ritonavir (N=60)	Placebo (N=54)
Number of subjects with events, n (%)	39 (65.0)	26 (48.1)
Number of censored subjects, n (%)	21 (35.0)	28 (51.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	15.0 (12.0, 22.0)	24.0 (18.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.655 (0.982, 2.789)	
p-value [3]	0.058	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.906 (1.158, 3.136)	
p-value [3]	0.011	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

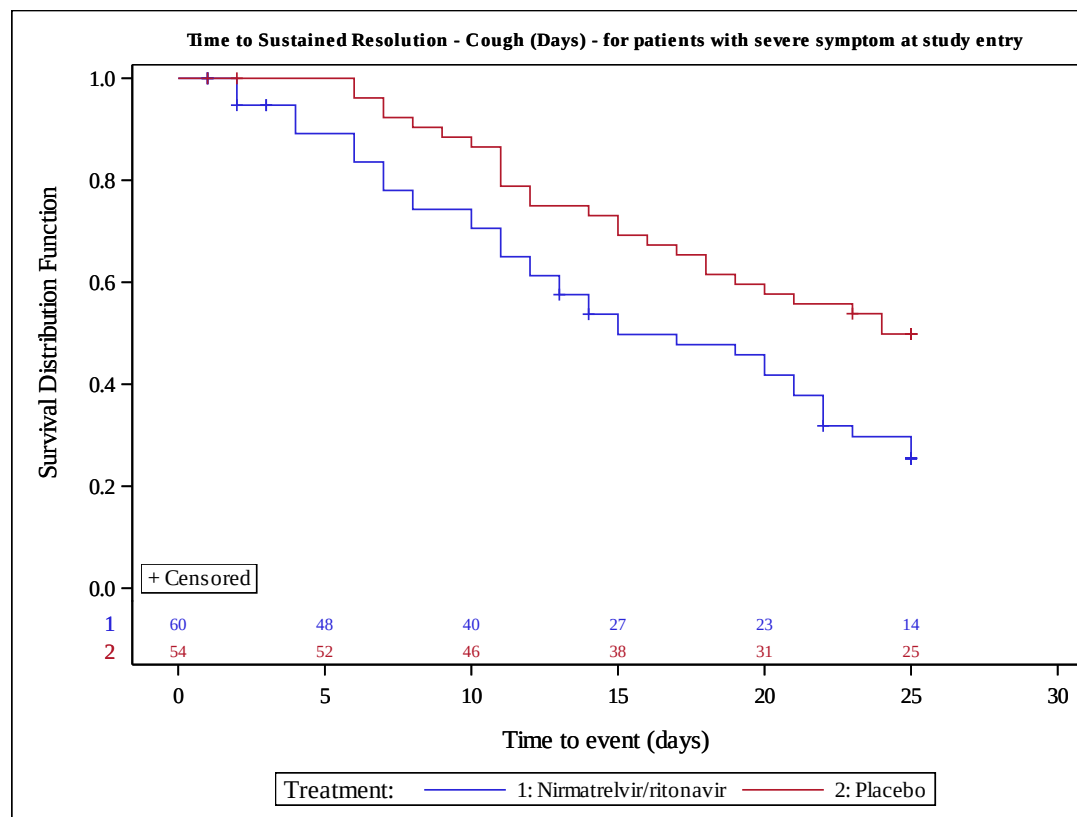
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Worsening of Signs and Symptoms - Fatigue (low energy or tiredness)

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	244 (22.3)	279 (25.2)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.832 (0.680, 1.019) 0.075	
Relative Risk (95% CI)	0.874 (0.750, 1.018) 0.084	
Risk Difference (95% CI)	-0.034 (-0.070, 0.001) 0.058	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.851 (0.699, 1.036) 0.108	
Relative Risk (95% CI)	0.884 (0.761, 1.027) 0.108	
Risk Difference (95% CI)	-0.029 (-0.065, 0.006) 0.107	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Fatigue (low energy or tiredness)

Final

	Nirmatrelvir/ritonavir (N=951)	Placebo (N=965)
Number of subjects with events, n (%)	785 (82.5)	735 (76.2)
Number of censored subjects, n (%)	166 (17.5)	230 (23.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	8.0 (7.0, 8.0)	9.0 (8.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.271 (1.146, 1.409)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.272 (1.150, 1.407)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

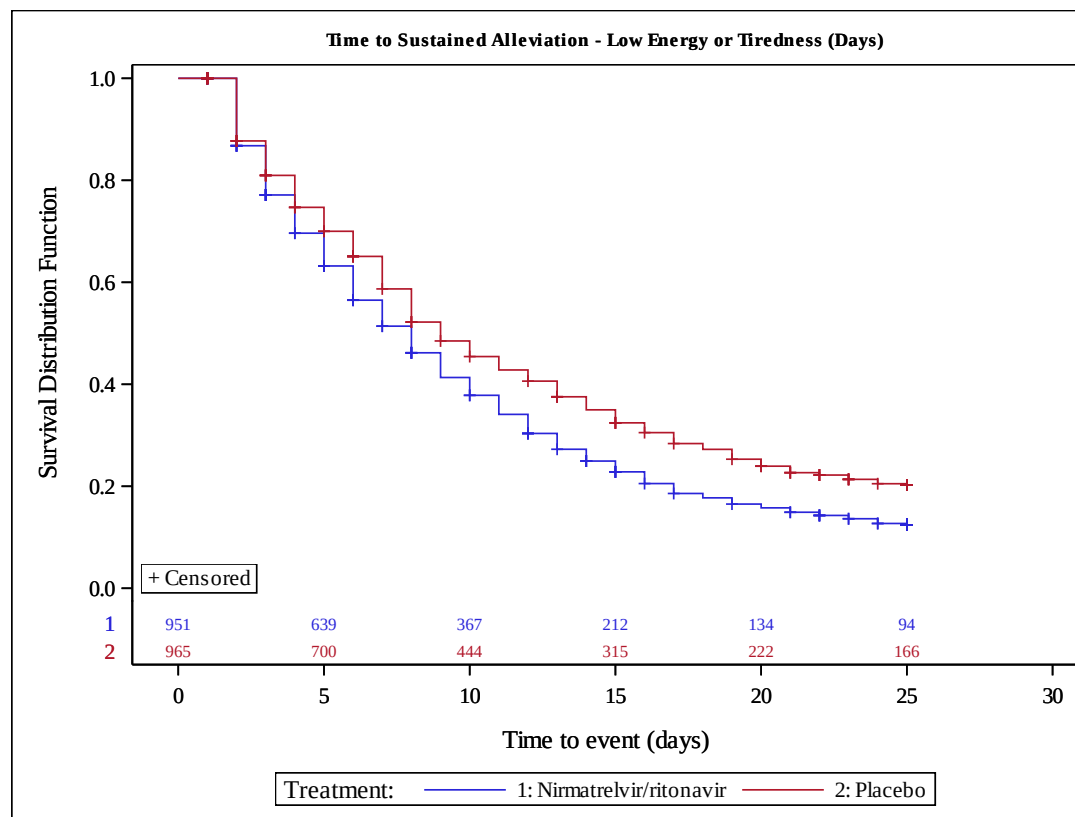
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Fatigue (low energy or tiredness)

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Overall Study population
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 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Fatigue (low energy or tiredness)

Final

	Nirmatrelvir/ritonavir (N=120)	Placebo (N=108)
Number of subjects with events, n (%)	88 (73.3)	73 (67.6)
Number of censored subjects, n (%)	32 (26.7)	35 (32.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	8.0 (5.0, 11.0)	12.0 (9.0, 15.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.436 (1.018, 2.025)	
p-value [3]	0.039	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.438 (1.053, 1.962)	
p-value [3]	0.022	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

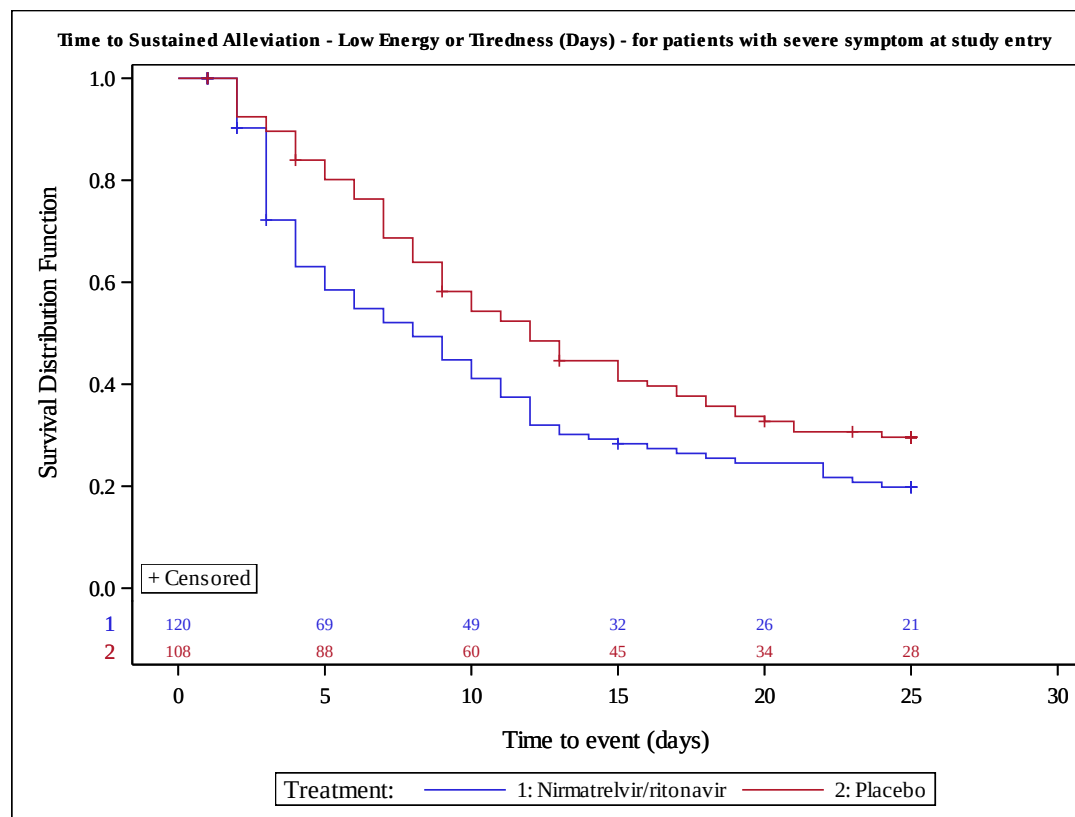
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Overall Study population
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Fatigue (low energy or tiredness)

Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Fatigue (low energy or tiredness)

Final

	Nirmatrelvir/ritonavir (N=951)	Placebo (N=965)
Number of subjects with events, n (%)	661 (69.5)	608 (63.0)
Number of censored subjects, n (%)	290 (30.5)	357 (37.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	14.0 (13.0, 15.0)	17.0 (16.0, 18.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.266 (1.131, 1.417)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.281 (1.148, 1.431)	
p-value [3]	<.001	

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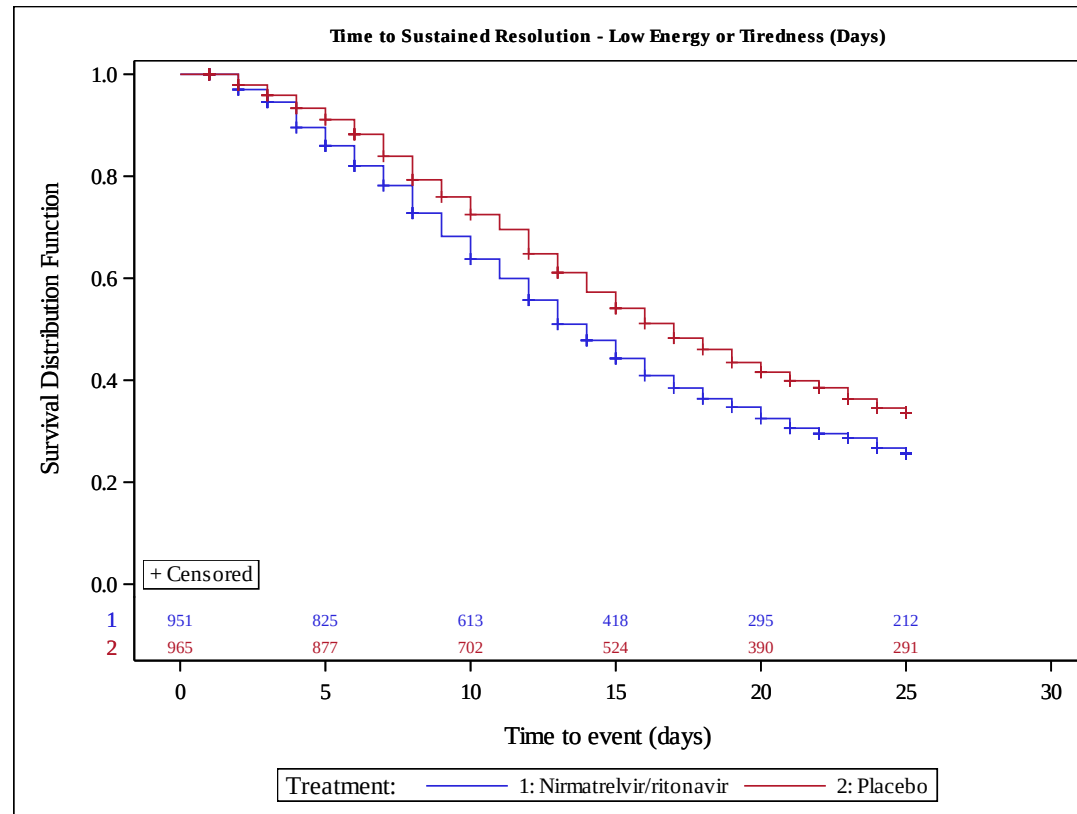
[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Kaplan-Meier Plot of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Fatigue (low energy or tiredness)

Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Fatigue (low energy or tiredness)

Final

	Nirmatrelvir/ritonavir (N=120)	Placebo (N=108)
Number of subjects with events, n (%)	69 (57.5)	45 (41.7)
Number of censored subjects, n (%)	51 (42.5)	63 (58.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	17.0 (14.0, 22.0)	NE (24.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.945 (1.292, 2.929)	
p-value [3]	0.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.819 (1.249, 2.650)	
p-value [3]	0.002	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

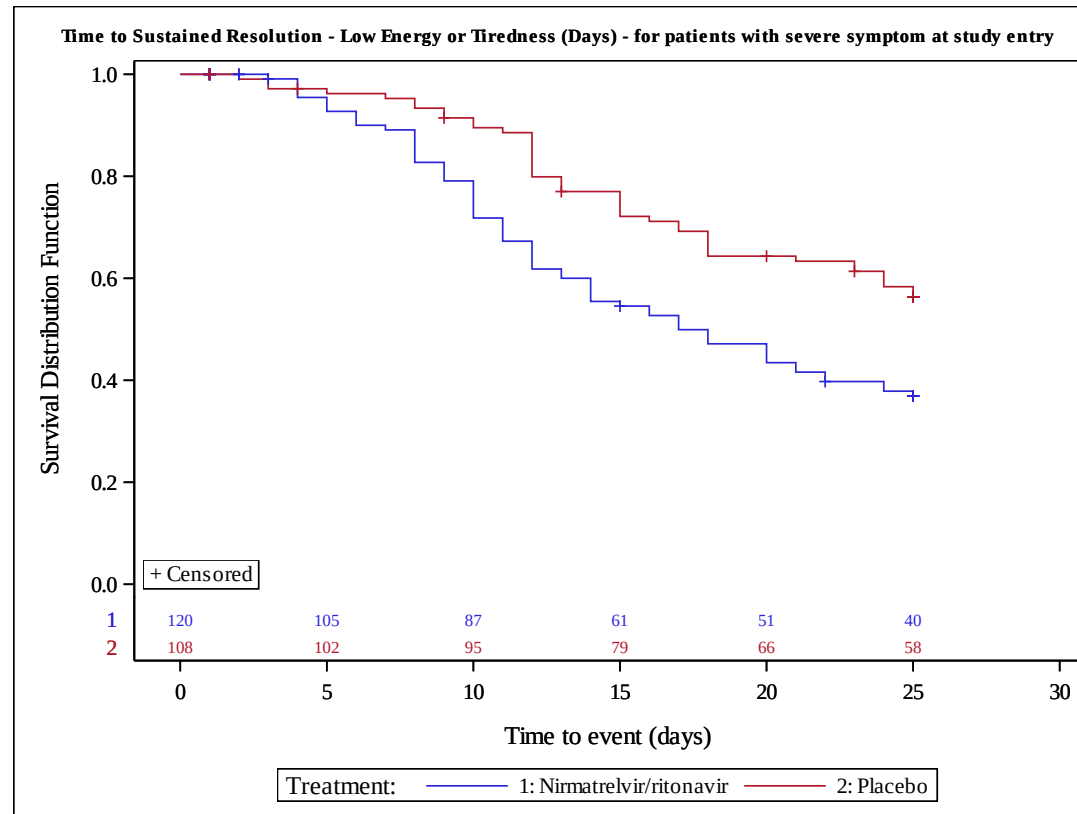
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Pfizer Inc
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 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Muscle or Body Aches

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	224 (20.5)	256 (23.2)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.866 (0.703, 1.067) 0.176	
Relative Risk (95% CI)	0.891 (0.758, 1.047) 0.162	
Risk Difference (95% CI)	-0.021 (-0.055, 0.014) 0.236	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.855 (0.698, 1.047) 0.130	
Relative Risk (95% CI)	0.885 (0.755, 1.037) 0.130	
Risk Difference (95% CI)	-0.027 (-0.061, 0.008) 0.129	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Muscle or Body Aches

Final

	Nirmatrelvir/ritonavir (N=880)	Placebo (N=879)
Number of subjects with events, n (%)	746 (84.8)	691 (78.6)
Number of censored subjects, n (%)	134 (15.2)	188 (21.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	6.0 (5.0, 7.0)	8.0 (7.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.297 (1.166, 1.442)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.292 (1.165, 1.434)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

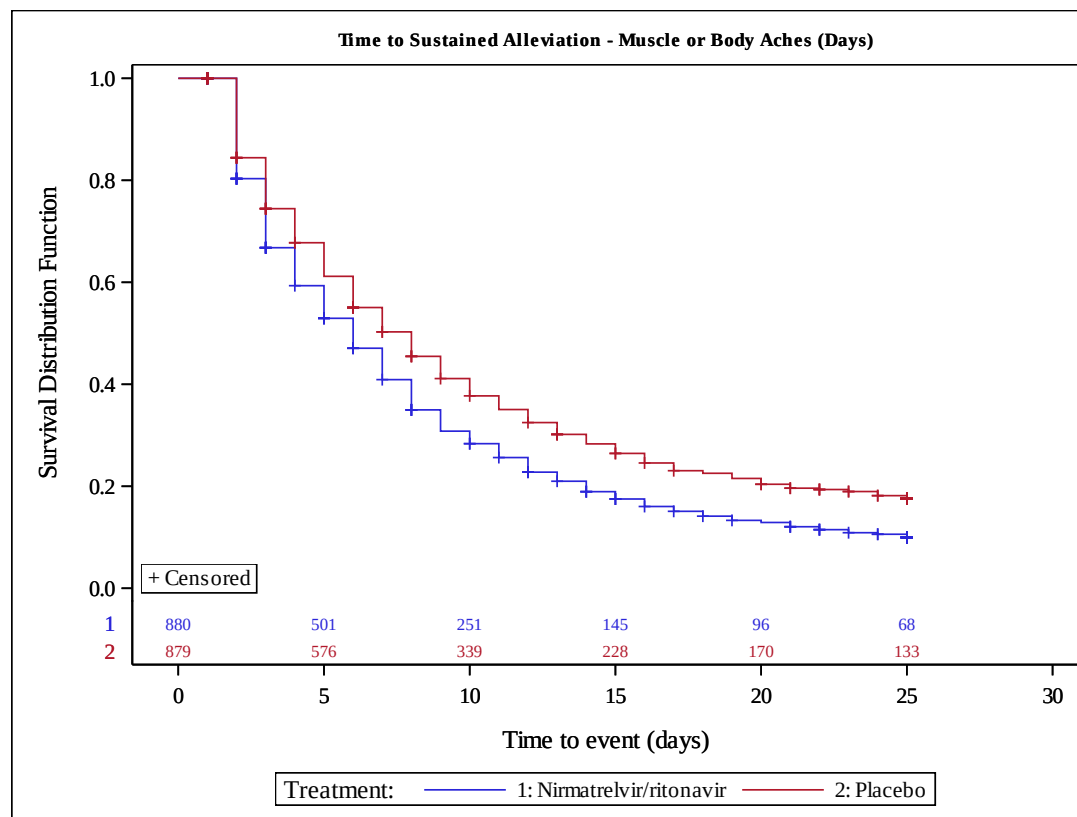
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Muscle or Body Aches

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Overall Study population
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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Muscle or Body Aches

Final

	Nirmatrelvir/ritonavir (N=101)	Placebo (N=87)
Number of subjects with events, n (%)	85 (84.2)	66 (75.9)
Number of censored subjects, n (%)	16 (15.8)	21 (24.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (4.0, 5.0)	8.0 (5.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.536 (1.083, 2.179)	
p-value [3]	0.016	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.608 (1.161, 2.225)	
p-value [3]	0.004	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

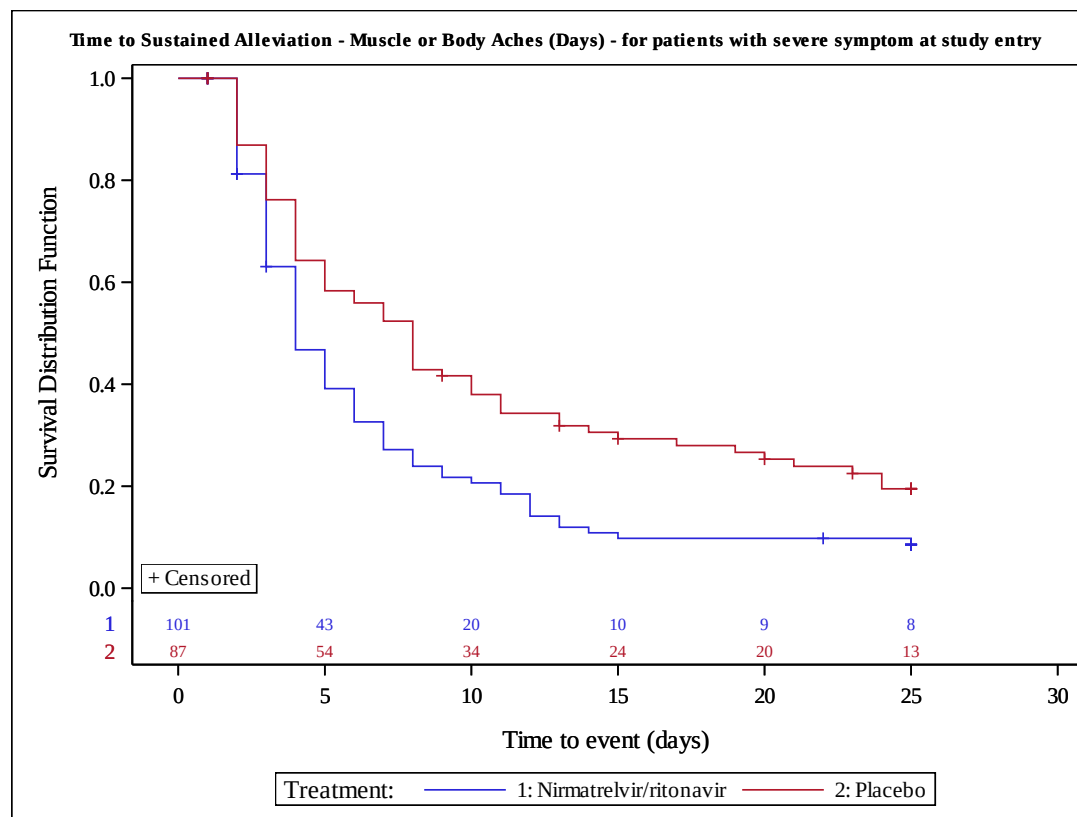
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Muscle or Body Aches

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Muscle or Body Aches

Final

	Nirmatrelvir/ritonavir (N=880)	Placebo (N=879)
Number of subjects with events, n (%)	677 (76.9)	624 (71.0)
Number of censored subjects, n (%)	203 (23.1)	255 (29.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	9.0 (8.0, 10.0)	12.0 (11.0, 13.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.297 (1.160, 1.449)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.285 (1.152, 1.432)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

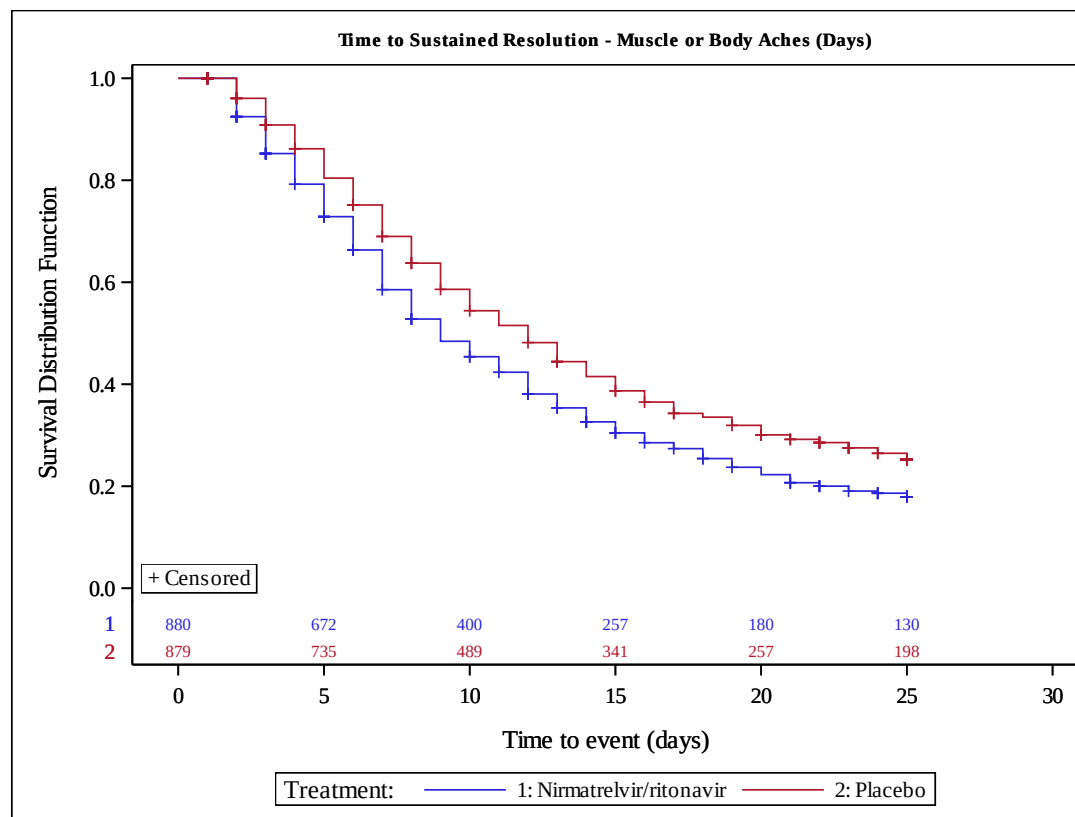
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
Modified Intent-To-Treat (mITT2) set
Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Muscle or Body Aches

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Muscle or Body Aches

Final

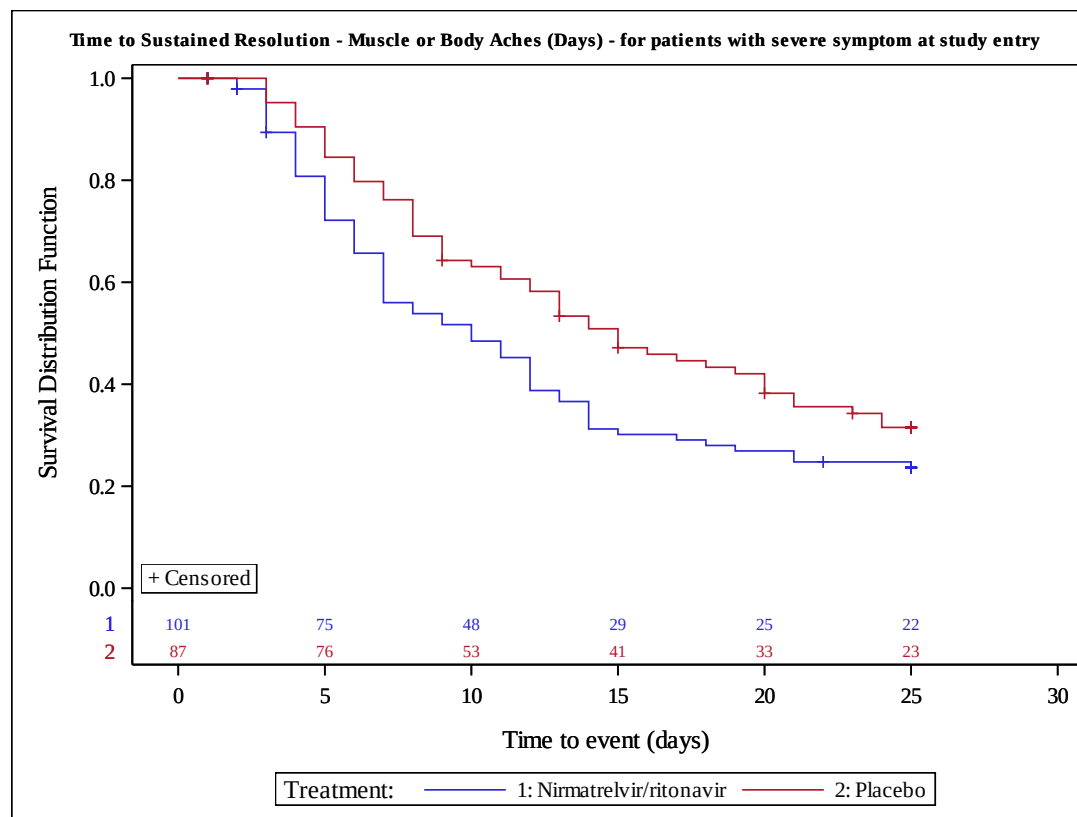
	Nirmatrelvir/ritonavir (N=101)	Placebo (N=87)
Number of subjects with events, n (%)	71 (70.3)	56 (64.4)
Number of censored subjects, n (%)	30 (29.7)	31 (35.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	10.0 (7.0, 12.0)	15.0 (11.0, 20.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.431 (0.986, 2.078)	
p-value [3]	0.060	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.413 (0.995, 2.007)	
p-value [3]	0.054	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 [1] Based on the Brookmeyer and Crowley Method.
 [2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Muscle or Body Aches

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Headache

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	264 (24.2)	304 (27.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.835 (0.687, 1.016) 0.072	
Relative Risk (95% CI)	0.872 (0.755, 1.008) 0.063	
Risk Difference (95% CI)	-0.030 (-0.067, 0.007) 0.108	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.839 (0.693, 1.016) 0.072	
Relative Risk (95% CI)	0.878 (0.762, 1.012) 0.073	
Risk Difference (95% CI)	-0.034 (-0.070, 0.003) 0.072	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Headache

Final

	Nirmatrelvir/ritonavir (N=809)	Placebo (N=806)
Number of subjects with events, n (%)	694 (85.8)	648 (80.4)
Number of censored subjects, n (%)	115 (14.2)	158 (19.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (5.0, 6.0)	7.0 (7.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.257 (1.127, 1.403)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.265 (1.137, 1.409)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

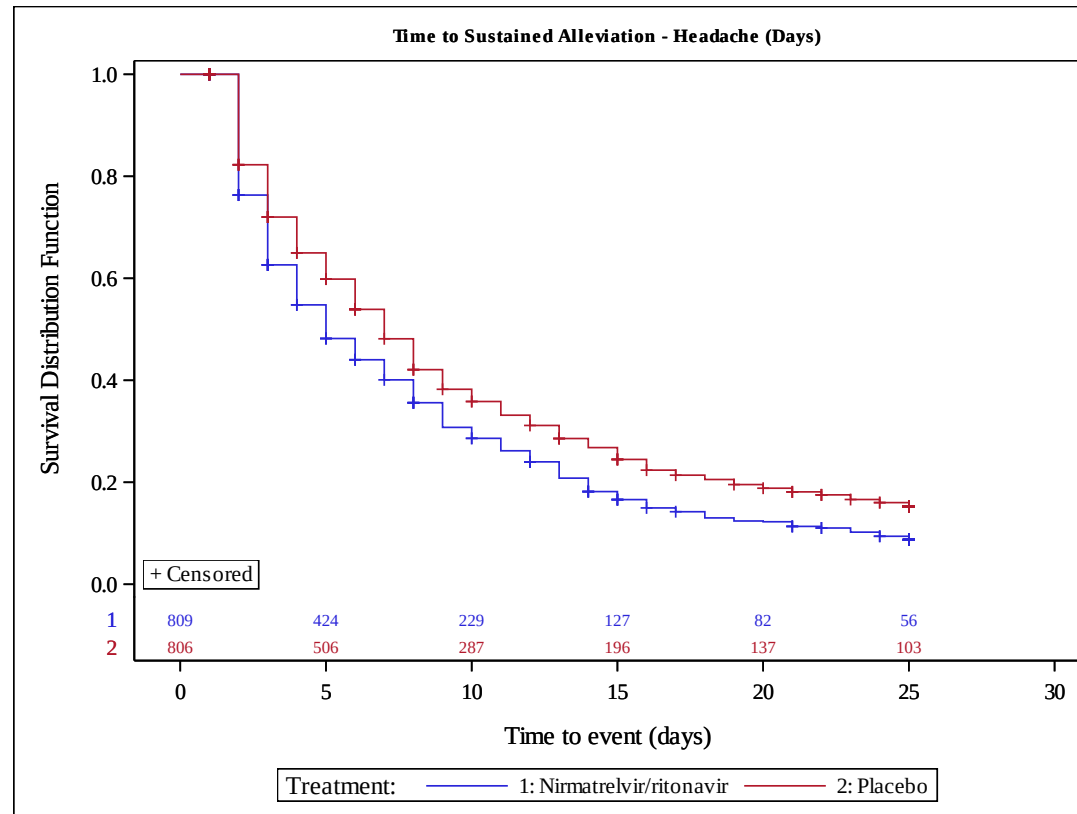
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Headache

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Headache

Final

	Nirmatrelvir/ritonavir (N=102)	Placebo (N=81)
Number of subjects with events, n (%)	88 (86.3)	64 (79.0)
Number of censored subjects, n (%)	14 (13.7)	17 (21.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (3.0, 5.0)	8.0 (6.0, 12.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.419 (1.002, 2.011)	
p-value [3]	0.049	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.483 (1.073, 2.050)	
p-value [3]	0.017	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

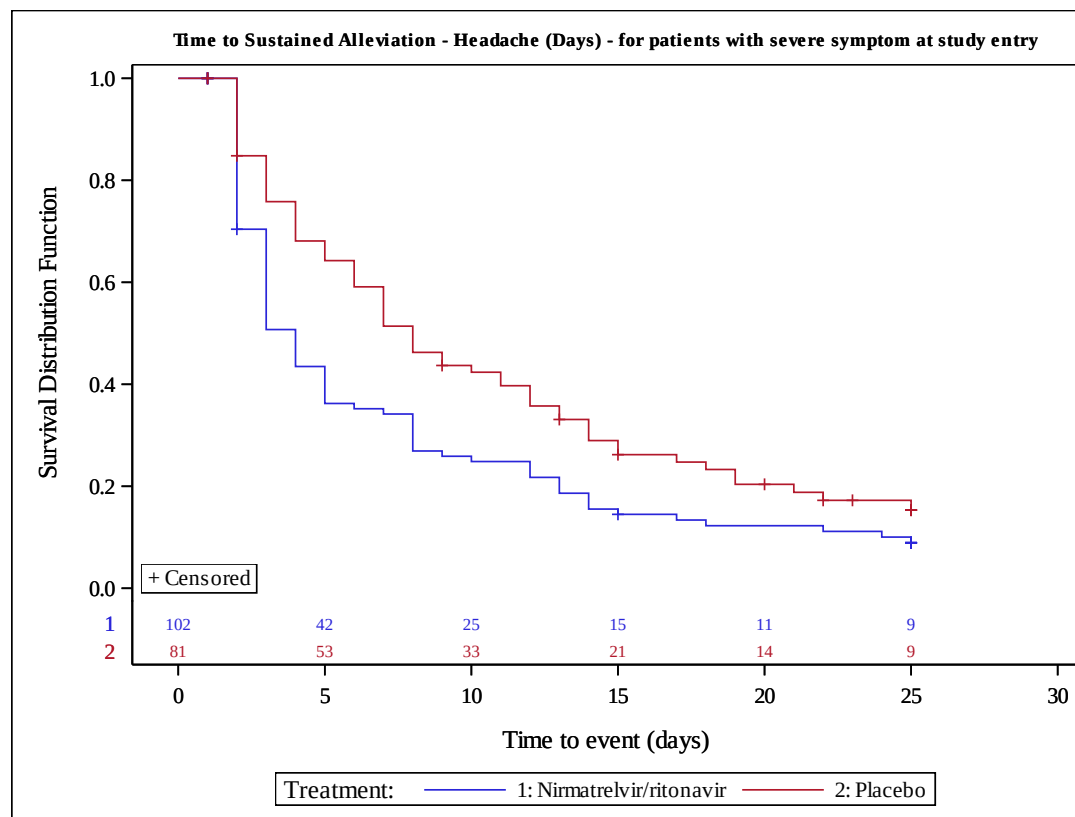
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Headache

Final

	Nirmatrelvir/ritonavir (N=809)	Placebo (N=806)
Number of subjects with events, n (%)	646 (79.9)	590 (73.2)
Number of censored subjects, n (%)	163 (20.1)	216 (26.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	9.0 (8.0, 10.0)	11.0 (10.0, 12.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.265 (1.129, 1.418)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.288 (1.151, 1.440)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

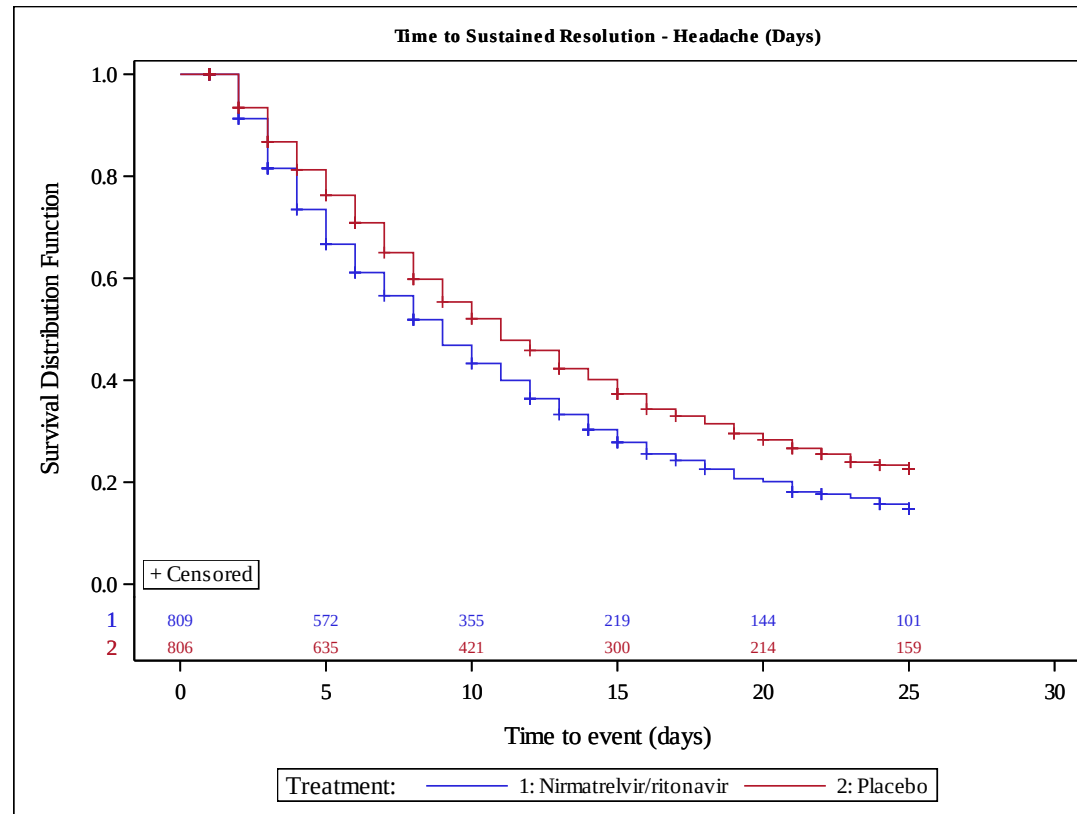
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Headache

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Headache

Final

	Nirmatrelvir/ritonavir (N=102)	Placebo (N=81)
Number of subjects with events, n (%)	77 (75.5)	52 (64.2)
Number of censored subjects, n (%)	25 (24.5)	29 (35.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	11.0 (8.0, 12.0)	17.0 (13.0, 19.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.503 (1.036, 2.182)	
p-value [3]	0.032	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.554 (1.092, 2.212)	
p-value [3]	0.014	

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[1] Based on the Brookmeyer and Crowley Method.

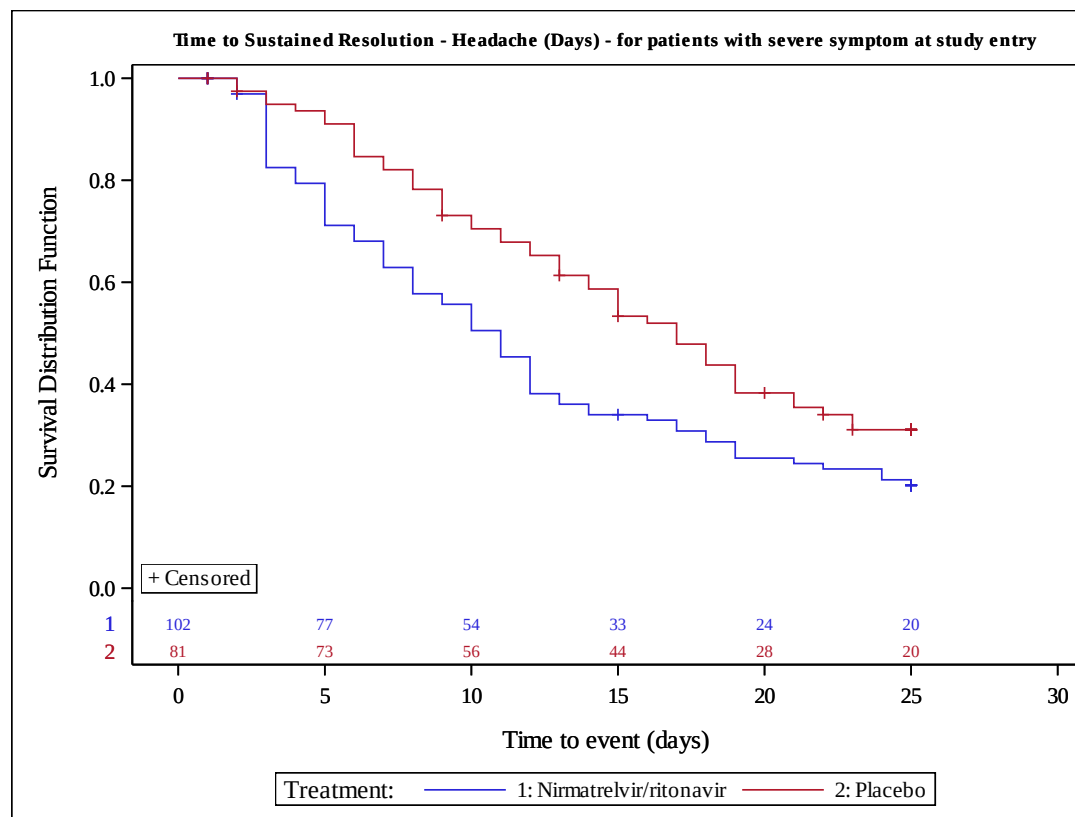
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Chills or Shivering

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	165 (15.1)	199 (18.0)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.835 (0.662, 1.054) 0.129	
Relative Risk (95% CI)	0.857 (0.707, 1.038) 0.115	
Risk Difference (95% CI)	-0.023 (-0.054, 0.007) 0.134	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.809 (0.646, 1.015) 0.067	
Relative Risk (95% CI)	0.838 (0.694, 1.012) 0.067	
Risk Difference (95% CI)	-0.029 (-0.060, 0.002) 0.066	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Chills or Shivering

Final

	Nirmatrelvir/ritonavir (N=664)	Placebo (N=657)
Number of subjects with events, n (%)	580 (87.3)	541 (82.3)
Number of censored subjects, n (%)	84 (12.7)	116 (17.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (3.0, 4.0)	4.0 (4.0, 5.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.239 (1.098, 1.397)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.257 (1.117, 1.414)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

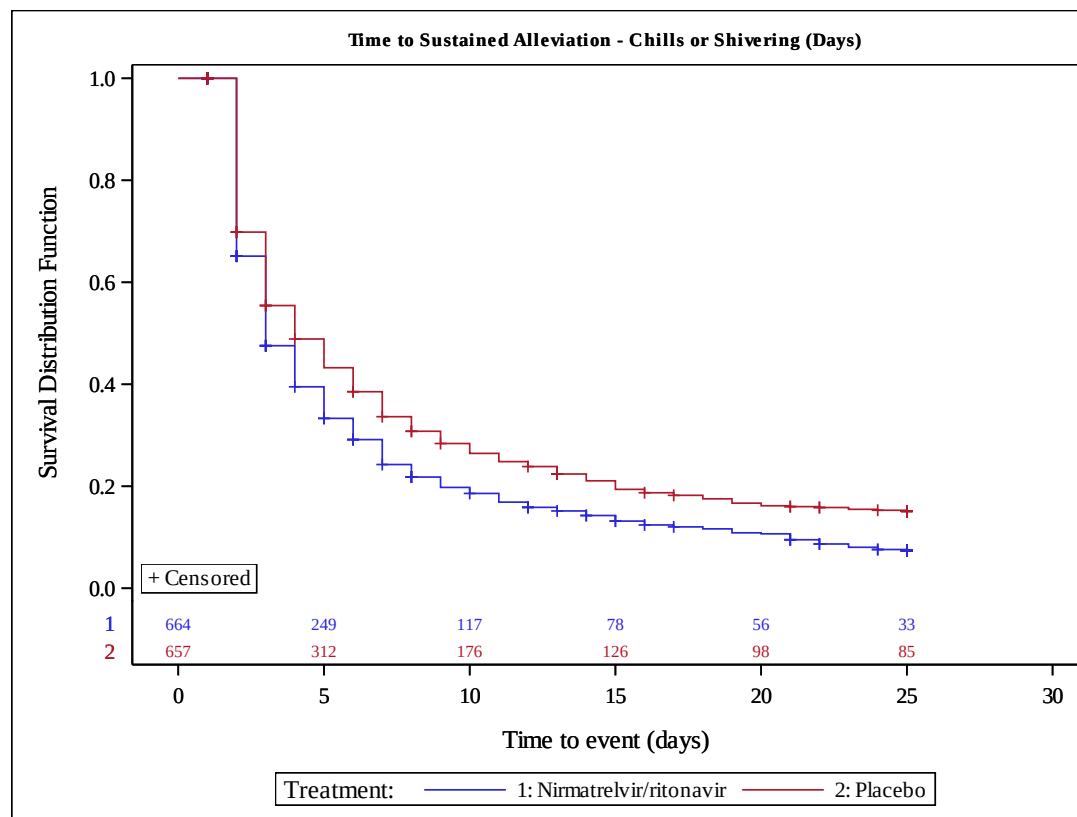
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Chills or Shivering

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Chills or Shivering

Final

	Nirmatrelvir/ritonavir (N=57)	Placebo (N=43)
Number of subjects with events, n (%)	50 (87.7)	35 (81.4)
Number of censored subjects, n (%)	7 (12.3)	8 (18.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (2.0, 3.0)	4.0 (3.0, 6.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.388 (0.867, 2.222)	
p-value [3]	0.172	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.353 (0.876, 2.089)	
p-value [3]	0.173	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

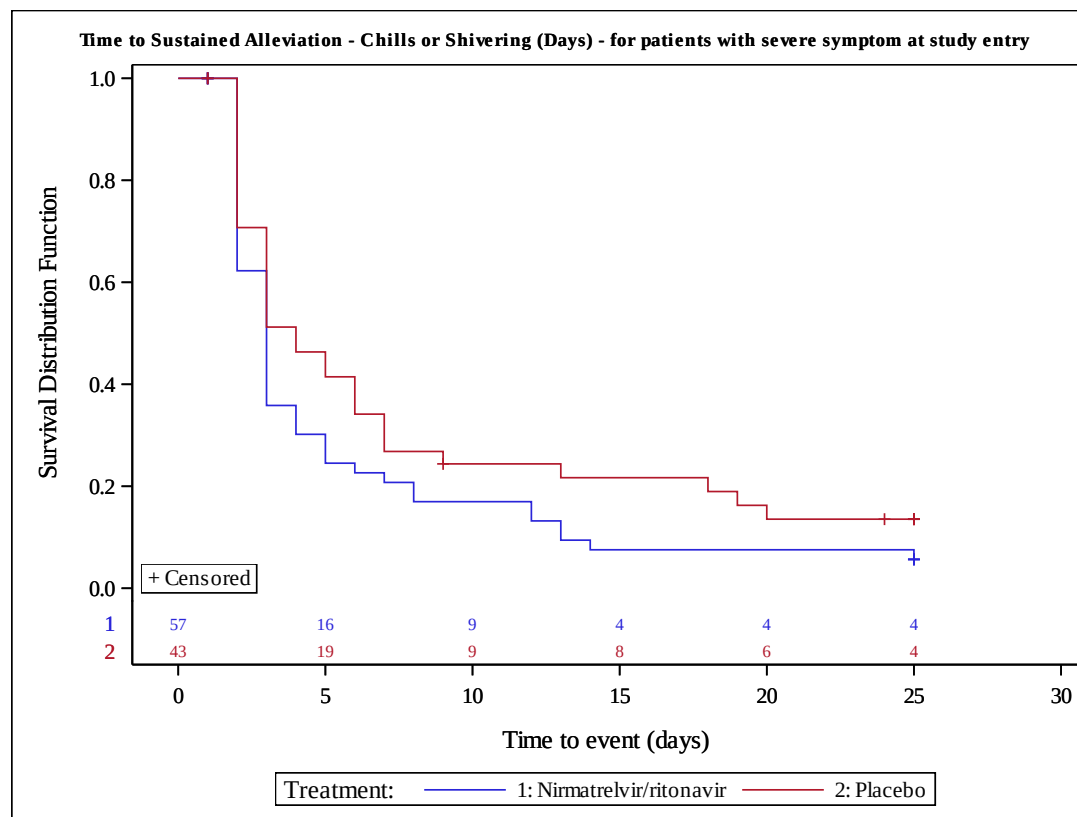
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Overall Study population
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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Chills or Shivering

Final

	Nirmatrelvir/ritonavir (N=664)	Placebo (N=657)
Number of subjects with events, n (%)	566 (85.2)	510 (77.6)
Number of censored subjects, n (%)	98 (14.8)	147 (22.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 5.0)	6.0 (6.0, 7.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.304 (1.153, 1.474)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.327 (1.176, 1.497)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

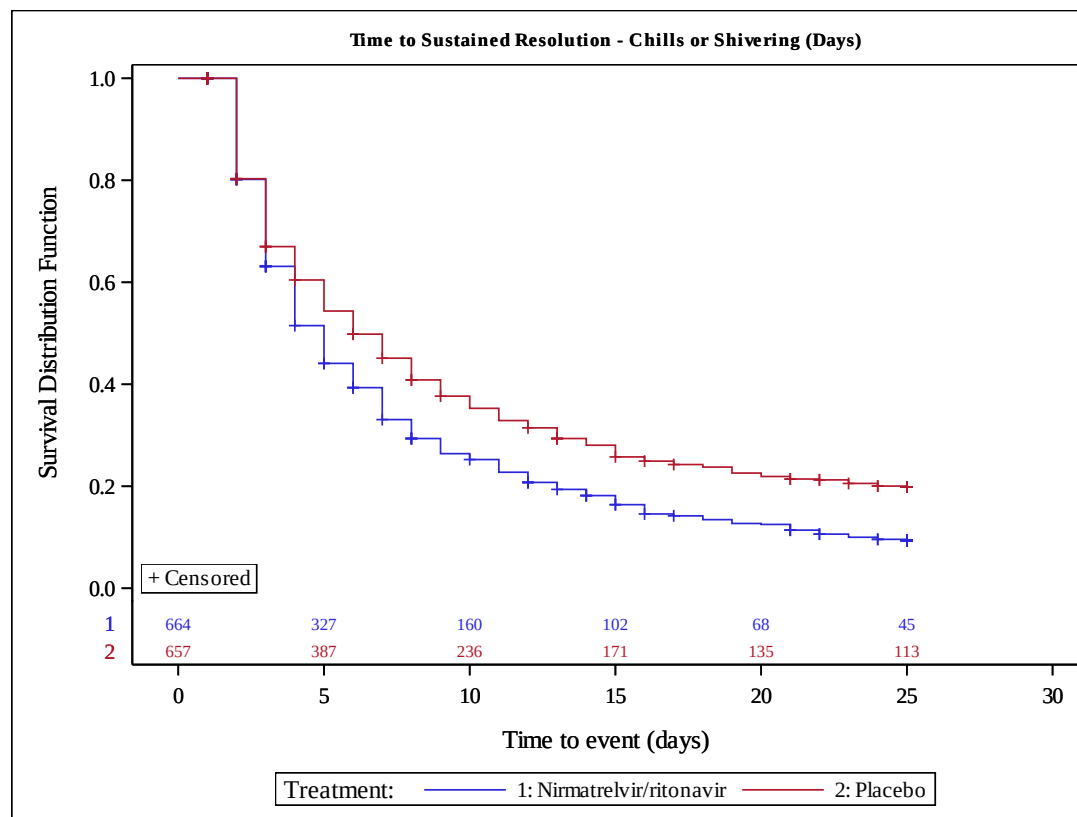
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Chills or Shivering

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Chills or Shivering

Final

	Nirmatrelvir/ritonavir (N=57)	Placebo (N=43)
Number of subjects with events, n (%)	49 (86.0)	33 (76.7)
Number of censored subjects, n (%)	8 (14.0)	10 (23.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (3.0, 6.0)	7.0 (6.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.507 (0.938, 2.421)	
p-value [3]	0.090	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.519 (0.974, 2.369)	
p-value [3]	0.065	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

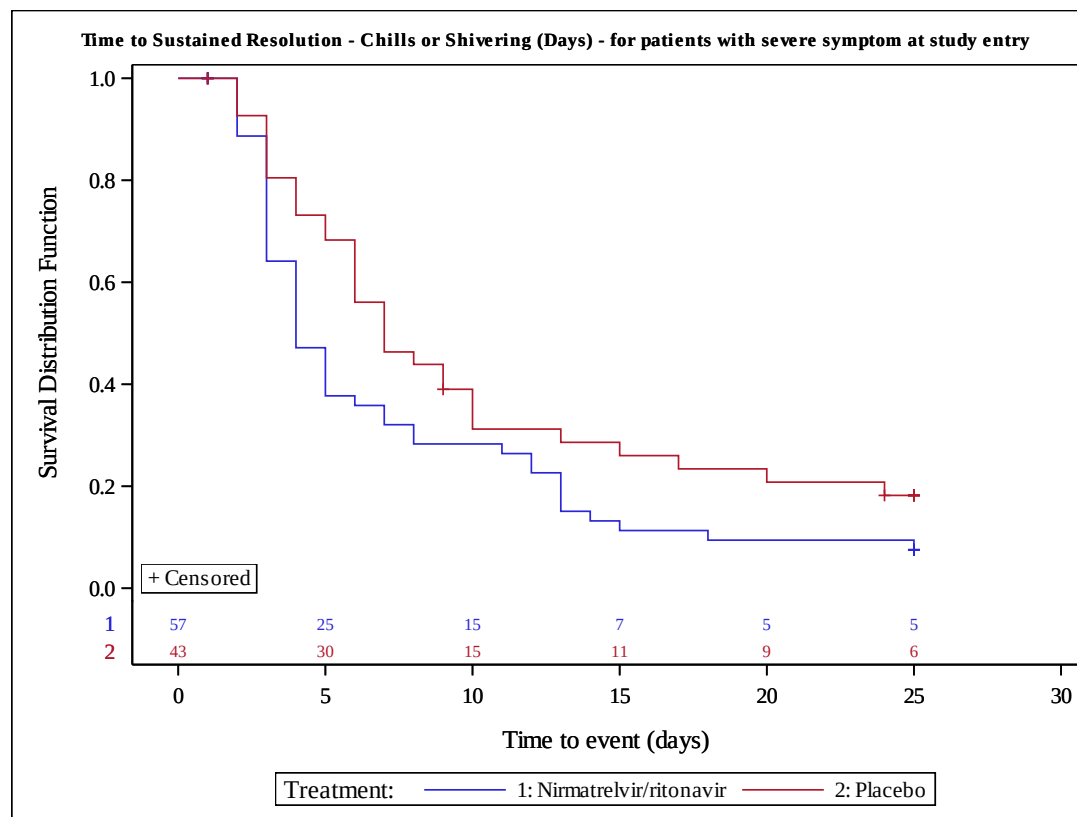
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Chills or Shivering

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Feeling Hot or Feverish

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	188 (17.2)	238 (21.5)
Adjusted analysis [1] Odds Ratio (95% CI)	0.750 (0.603, 0.933) 0.010	
Relative Risk (95% CI)	0.791 (0.665, 0.941) 0.008	
Risk Difference (95% CI)	-0.037 (-0.070, -0.003) 0.030	
Unadjusted analysis [2] Odds Ratio (95% CI)	0.757 (0.612, 0.936) 0.010	
Relative Risk (95% CI)	0.799 (0.672, 0.948) 0.010	
Risk Difference (95% CI)	-0.043 (-0.076, -0.010) 0.010	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Feeling Hot or Feverish

Final

	Nirmatrelvir/ritonavir (N=683)	Placebo (N=686)
Number of subjects with events, n (%)	606 (88.7)	556 (81.0)
Number of censored subjects, n (%)	77 (11.3)	130 (19.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (3.0, 4.0)	4.0 (4.0, 5.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.323 (1.175, 1.490)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.339 (1.192, 1.503)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

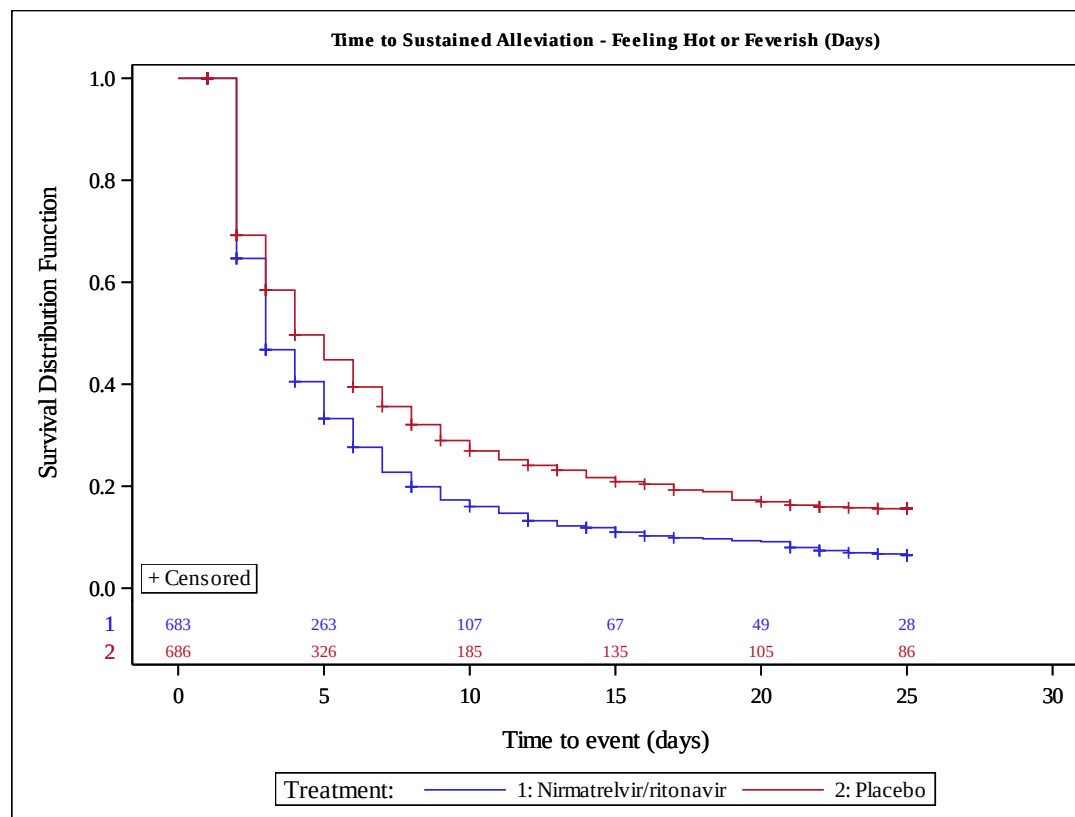
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Feeling Hot or Feverish

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish

Final

	Nirmatrelvir/ritonavir (N=59)	Placebo (N=50)
Number of subjects with events, n (%)	52 (88.1)	36 (72.0)
Number of censored subjects, n (%)	7 (11.9)	14 (28.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (2.0, 3.0)	6.0 (3.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.938 (1.208, 3.110)	
p-value [3]	0.006	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	2.037 (1.313, 3.159)	
p-value [3]	0.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

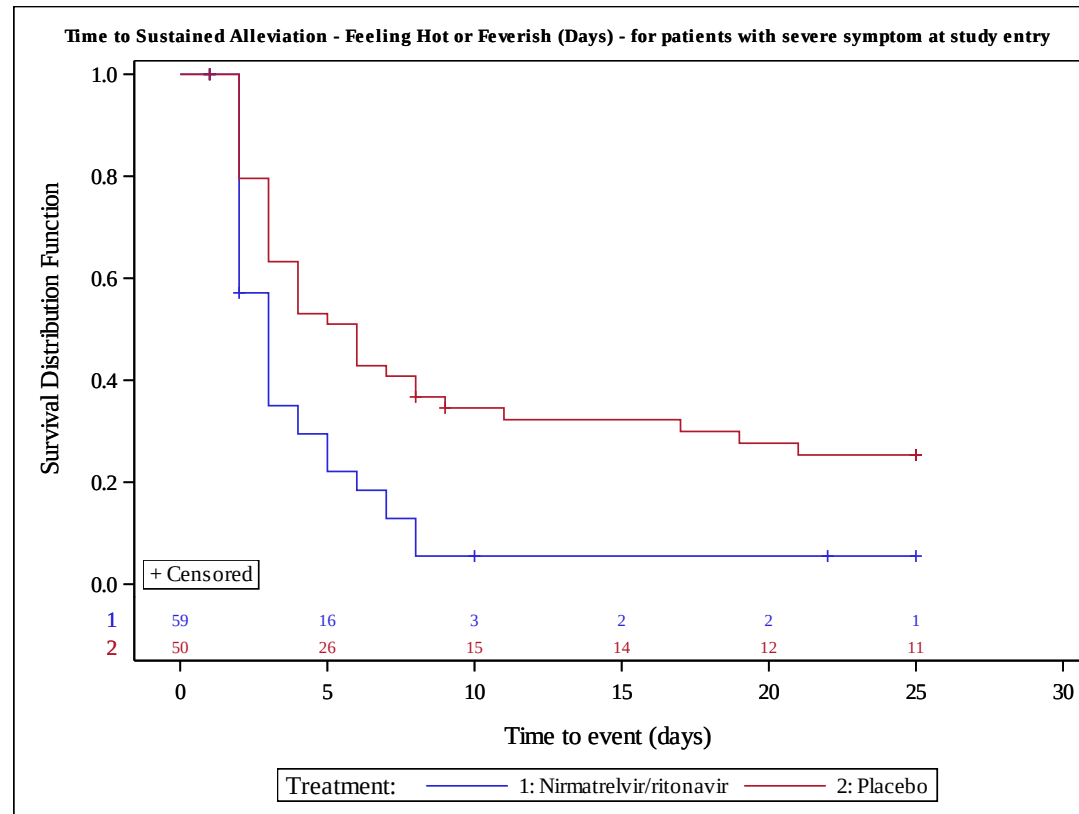
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Feeling Hot or Feverish

Final

	Nirmatrelvir/ritonavir (N=683)	Placebo (N=686)
Number of subjects with events, n (%)	592 (86.7)	526 (76.7)
Number of censored subjects, n (%)	91 (13.3)	160 (23.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (NE, NE)	7.0 (6.0, 7.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.387 (1.229, 1.566)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.407 (1.250, 1.584)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

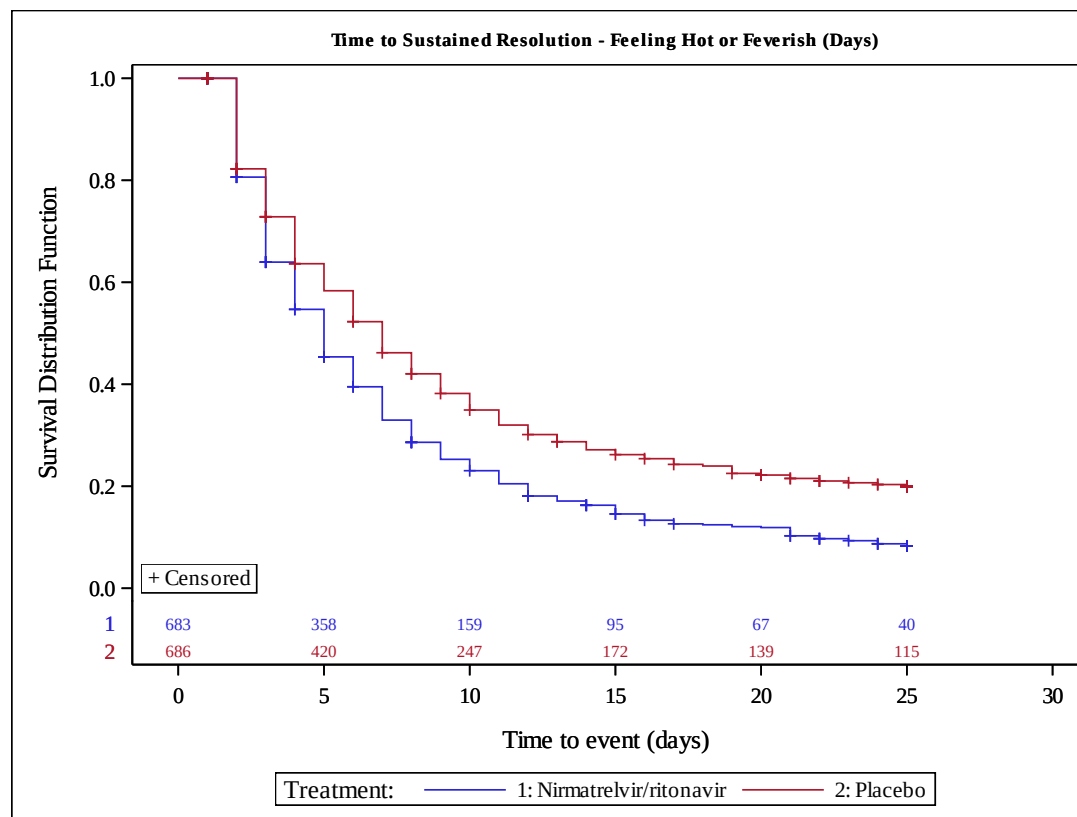
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Feeling Hot or Feverish

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish

Final

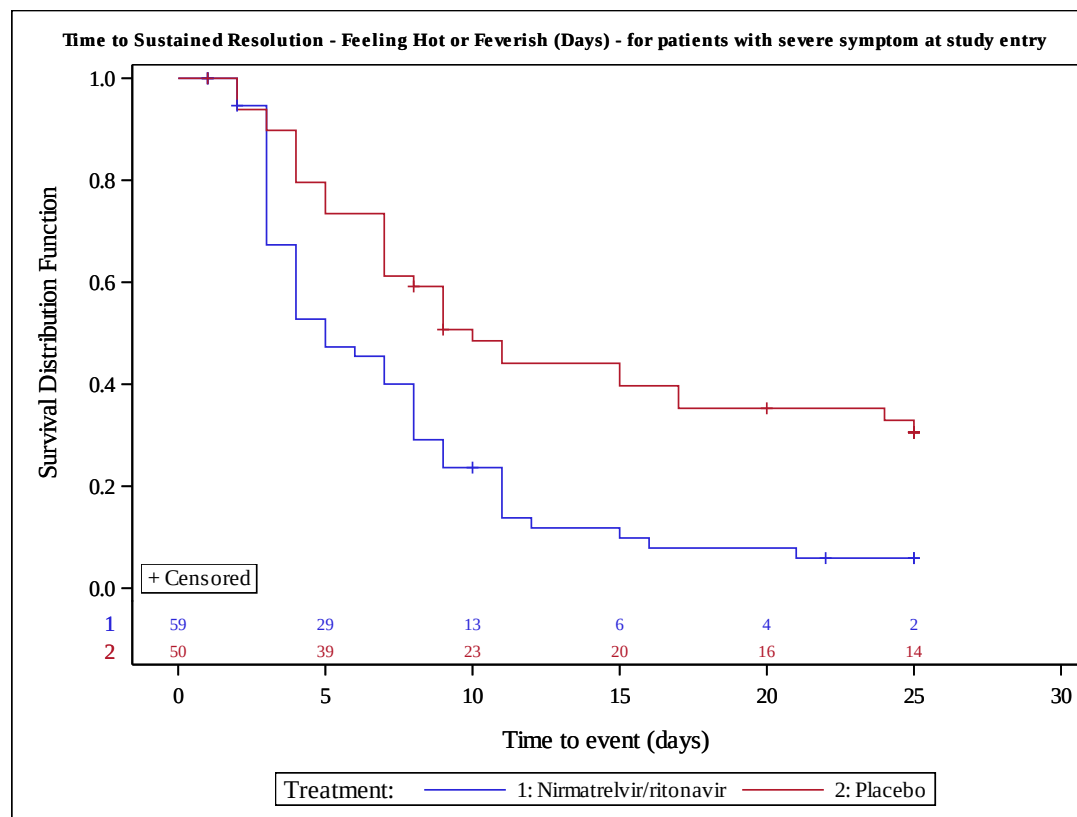
	Nirmatrelvir/ritonavir (N=59)	Placebo (N=50)
Number of subjects with events, n (%)	51 (86.4)	33 (66.0)
Number of censored subjects, n (%)	8 (13.6)	17 (34.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 8.0)	10.0 (7.0, 17.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	2.164 (1.343, 3.487)	
p-value [3]	0.002	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	2.232 (1.424, 3.499)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 [1] Based on the Brookmeyer and Crowley Method.
 [2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish

Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Nausea

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	236 (21.6)	263 (23.8)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.880 (0.717, 1.081) 0.225	
Relative Risk (95% CI)	0.908 (0.777, 1.061) 0.225	
Risk Difference (95% CI)	-0.020 (-0.055, 0.015) 0.257	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.882 (0.722, 1.077) 0.217	
Relative Risk (95% CI)	0.907 (0.777, 1.059) 0.217	
Risk Difference (95% CI)	-0.022 (-0.057, 0.013) 0.216	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Nausea

Final

	Nirmatrelvir/ritonavir (N=397)	Placebo (N=402)
Number of subjects with events, n (%)	329 (82.9)	320 (79.6)
Number of censored subjects, n (%)	68 (17.1)	82 (20.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 6.0)	6.0 (5.0, 7.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.148 (0.980, 1.344)	
p-value [3]	0.088	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.153 (0.988, 1.345)	
p-value [3]	0.071	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

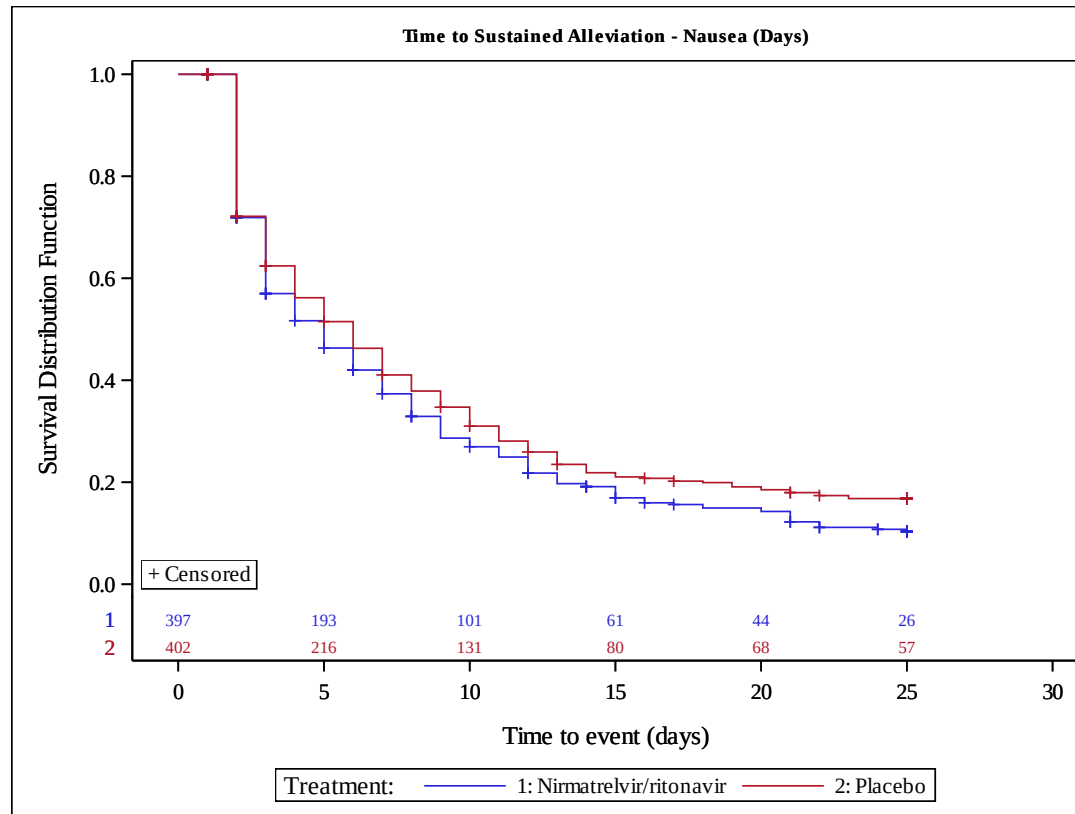
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Nausea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Nausea

Final

	Nirmatrelvir/ritonavir (N=22)	Placebo (N=21)
Number of subjects with events, n (%)	17 (77.3)	16 (76.2)
Number of censored subjects, n (%)	5 (22.7)	5 (23.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	11.0 (3.0, 13.0)	7.0 (3.0, 9.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	0.822 (0.372, 1.814)	
p-value [3]	0.627	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	0.838 (0.416, 1.687)	
p-value [3]	0.621	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

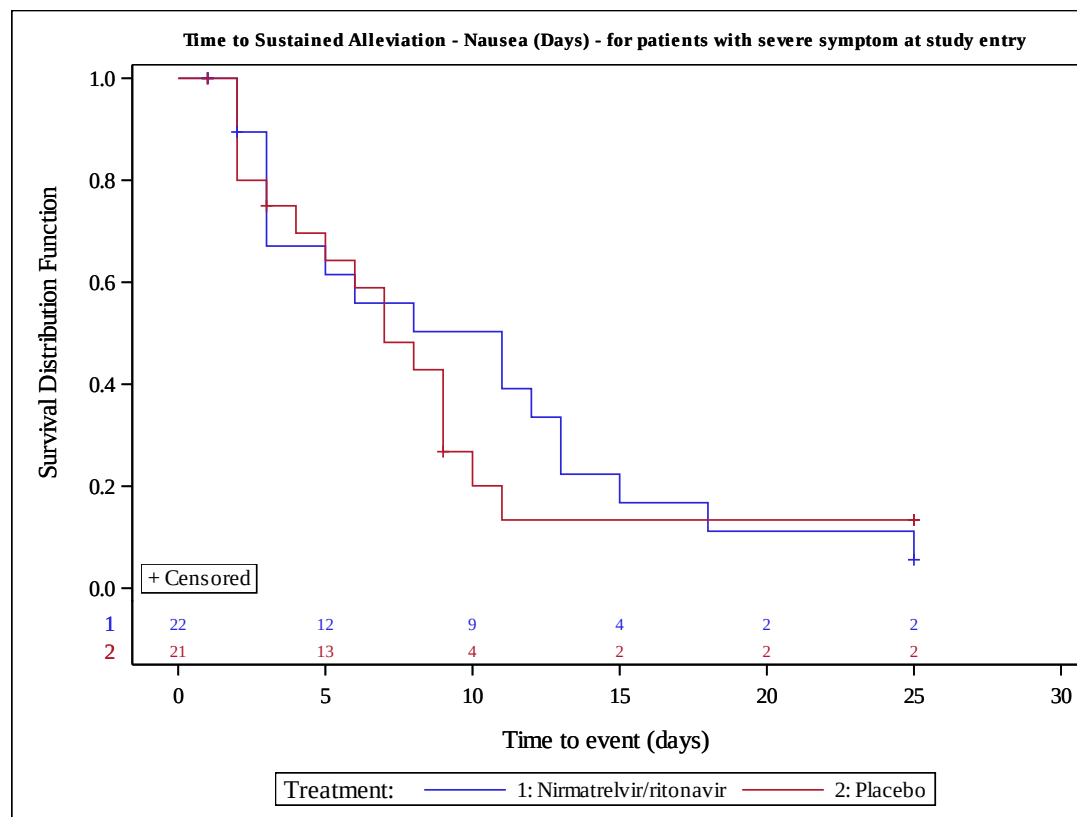
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Nausea

Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Nausea

Final

	Nirmatrelvir/ritonavir (N=397)	Placebo (N=402)
Number of subjects with events, n (%)	316 (79.6)	302 (75.1)
Number of censored subjects, n (%)	81 (20.4)	100 (24.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	7.0 (6.0, 8.0)	7.0 (6.0, 9.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.172 (0.997, 1.377)	
p-value [3]	0.054	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.174 (1.003, 1.375)	
p-value [3]	0.046	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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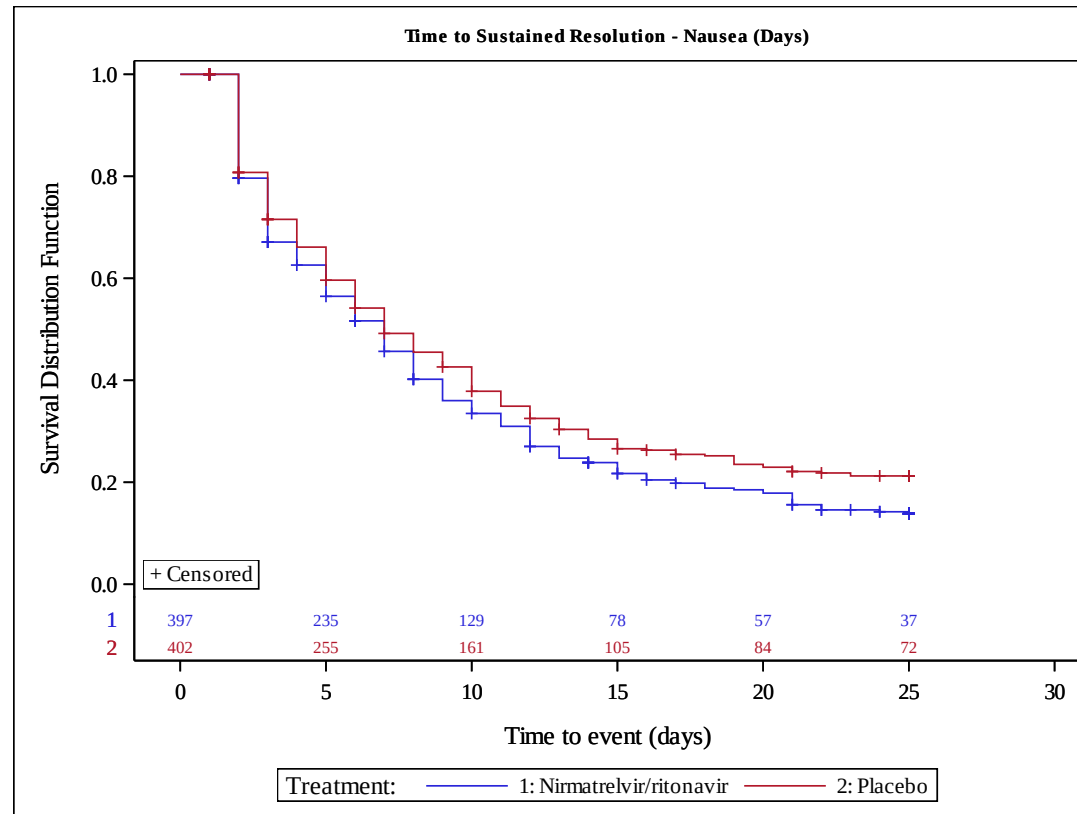
[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Nausea

Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Nausea

Final

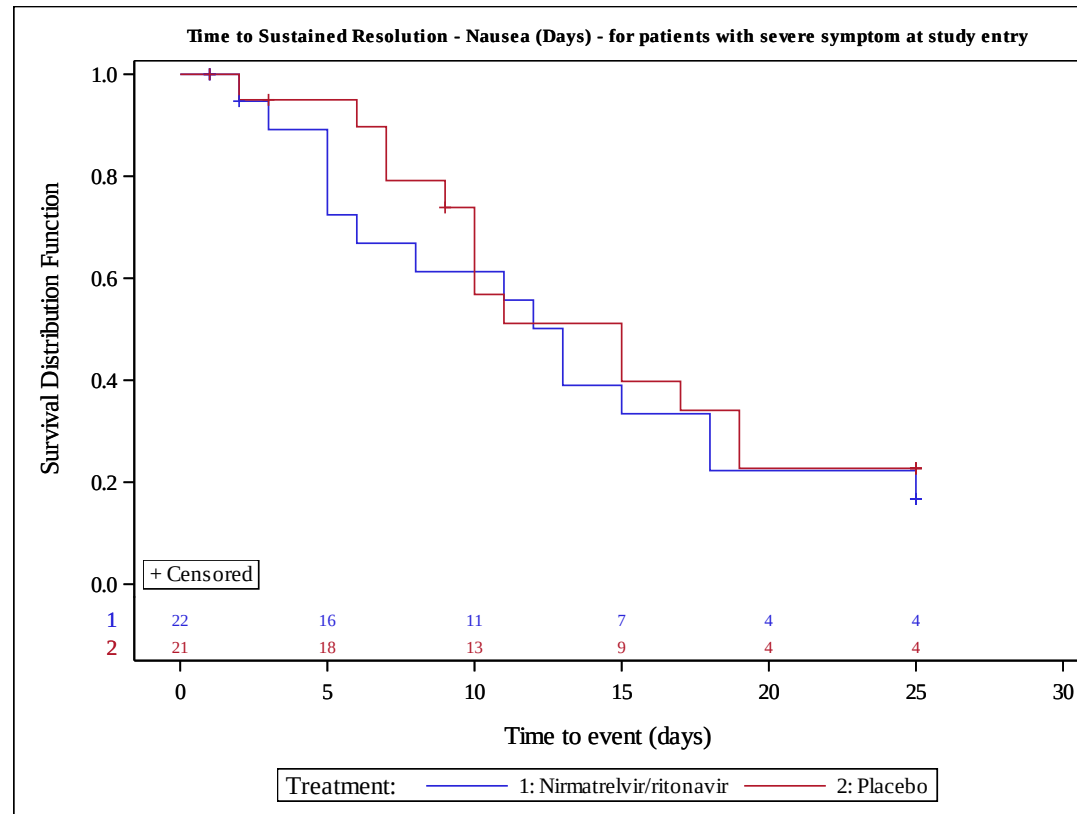
	Nirmatrelvir/ritonavir (N=22)	Placebo (N=21)
Number of subjects with events, n (%)	15 (68.2)	14 (66.7)
Number of censored subjects, n (%)	7 (31.8)	7 (33.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	13.0 (5.0, 18.0)	15.0 (9.0, 19.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.621 (0.668, 3.933)	
p-value [3]	0.286	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.246 (0.600, 2.587)	
p-value [3]	0.555	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 [1] Based on the Brookmeyer and Crowley Method.
 [2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Nausea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Vomit

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	89 (8.1)	106 (9.6)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.824 (0.609, 1.114) 0.209	
Relative Risk (95% CI)	0.838 (0.639, 1.100) 0.203	
Risk Difference (95% CI)	-0.014 (-0.037, 0.009) 0.244	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.835 (0.622, 1.122) 0.232	
Relative Risk (95% CI)	0.849 (0.649, 1.111) 0.233	
Risk Difference (95% CI)	-0.015 (-0.038, 0.009) 0.232	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Vomit

Final

	Nirmatrelvir/ritonavir (N=141)	Placebo (N=138)
Number of subjects with events, n (%)	119 (84.4)	114 (82.6)
Number of censored subjects, n (%)	22 (15.6)	24 (17.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (2.0, 4.0)	3.0 (2.0, 5.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.142 (0.872, 1.495)	
p-value [3]	0.334	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.131 (0.874, 1.463)	
p-value [3]	0.351	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

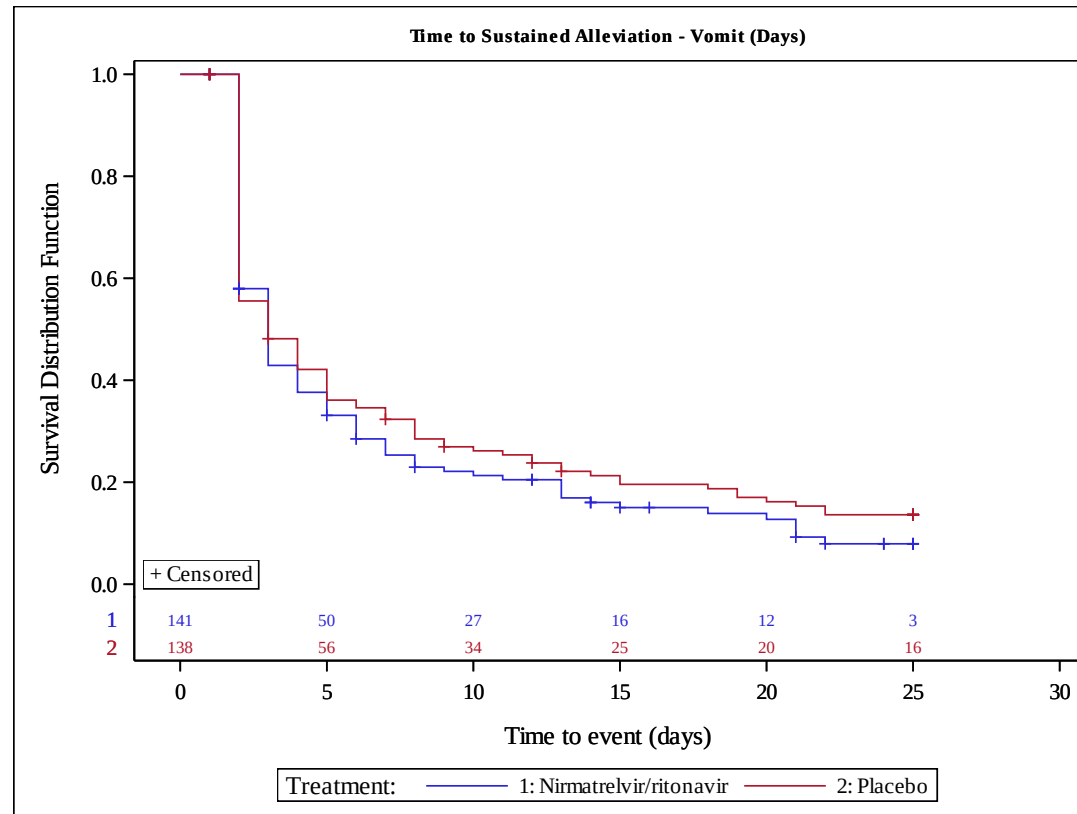
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Vomit

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Vomit

Final

	Nirmatrelvir/ritonavir (N=5)	Placebo (N=3)
Number of subjects with events, n (%)	4 (80.0)	2 (66.7)
Number of censored subjects, n (%)	1 (20.0)	1 (33.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	11.0 (2.0, NE)	8.0 (2.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.386 (0.085, 22.650)	
p-value [3]	0.819	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.051 (0.191, 5.791)	
p-value [3]	0.954	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

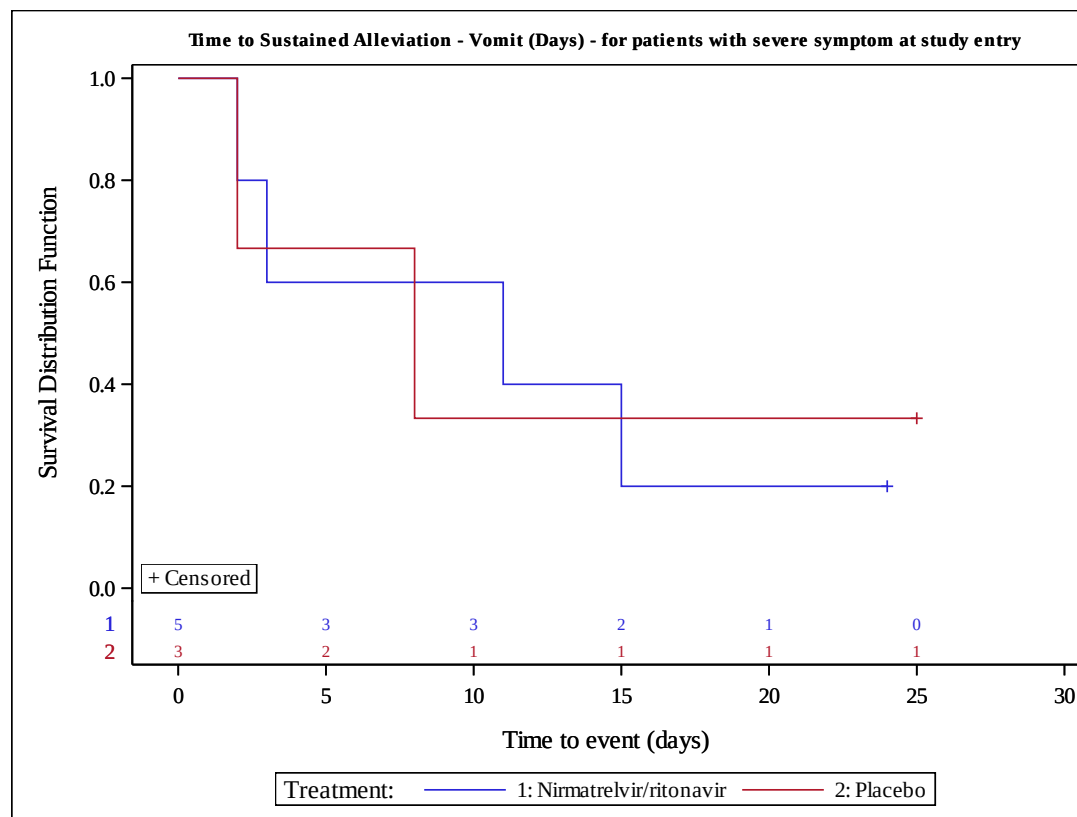
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Vomit

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Vomit

Final

	Nirmatrelvir/ritonavir (N=141)	Placebo (N=138)
Number of subjects with events, n (%)	119 (84.4)	114 (82.6)
Number of censored subjects, n (%)	22 (15.6)	24 (17.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (3.0, 5.0)	4.0 (2.0, 5.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.124 (0.858, 1.472)	
p-value [3]	0.397	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.108 (0.856, 1.434)	
p-value [3]	0.435	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

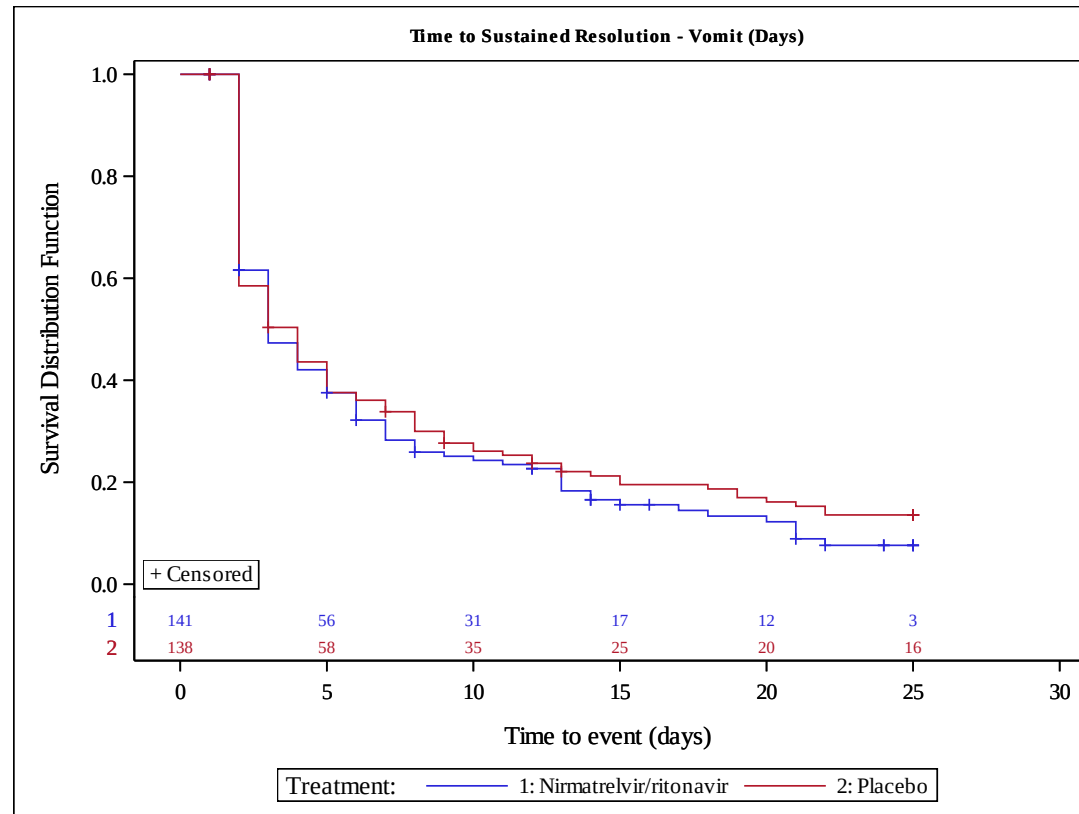
[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Vomit

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Vomit

Final

	Nirmatrelvir/ritonavir (N=5)	Placebo (N=3)
Number of subjects with events, n (%)	4 (80.0)	2 (66.7)
Number of censored subjects, n (%)	1 (20.0)	1 (33.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	14.0 (4.0, NE)	10.0 (3.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.249 (0.077, 20.278)	
p-value [3]	0.876	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	0.839 (0.151, 4.652)	
p-value [3]	0.841	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

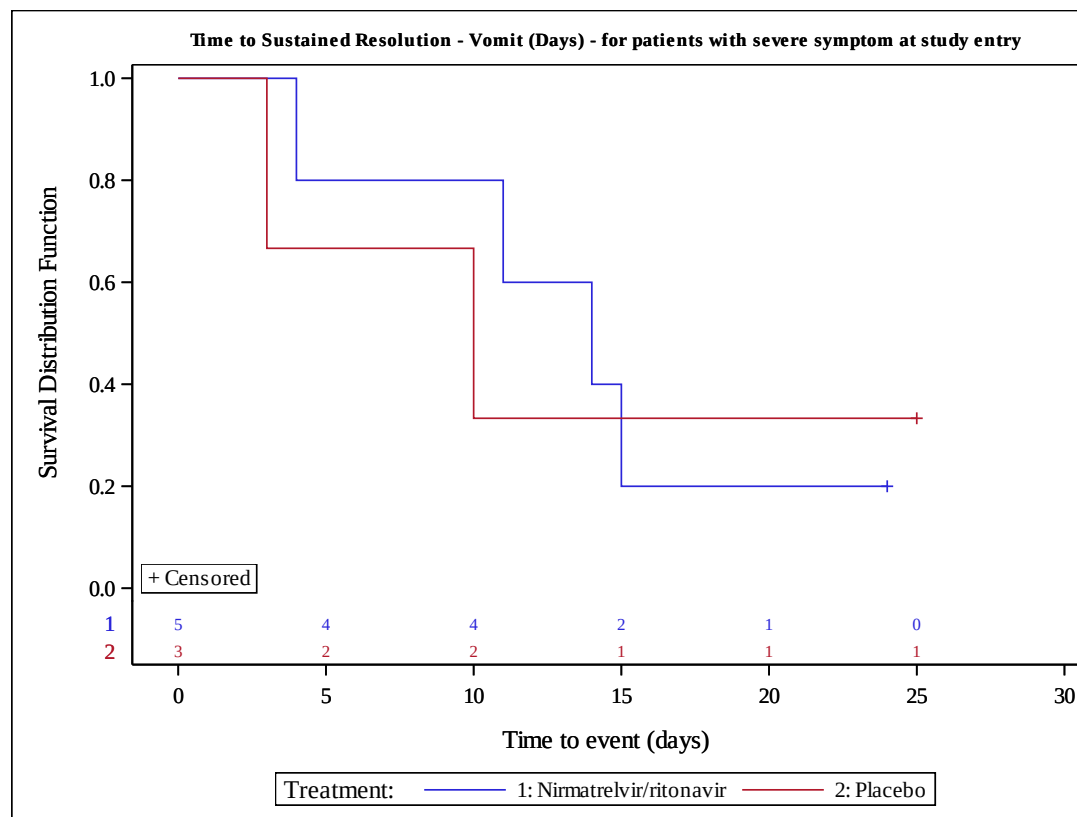
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Vomit

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Diarrhea

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	288 (26.3)	242 (21.9)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.260 (1.027, 1.546) 0.027	
Relative Risk (95% CI)	1.189 (1.026, 1.377) 0.022	
Risk Difference (95% CI)	0.027 (-0.006, 0.061) 0.110	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.276 (1.049, 1.552) 0.015	
Relative Risk (95% CI)	1.203 (1.037, 1.397) 0.015	
Risk Difference (95% CI)	0.044 (0.009, 0.080) 0.015	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Diarrhea

Final

	Nirmatrelvir/ritonavir (N=305)	Placebo (N=290)
Number of subjects with events, n (%)	261 (85.6)	238 (82.1)
Number of censored subjects, n (%)	44 (14.4)	52 (17.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 6.0)	4.0 (3.0, 5.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.034 (0.862, 1.240)	
p-value [3]	0.720	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.040 (0.873, 1.241)	
p-value [3]	0.658	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

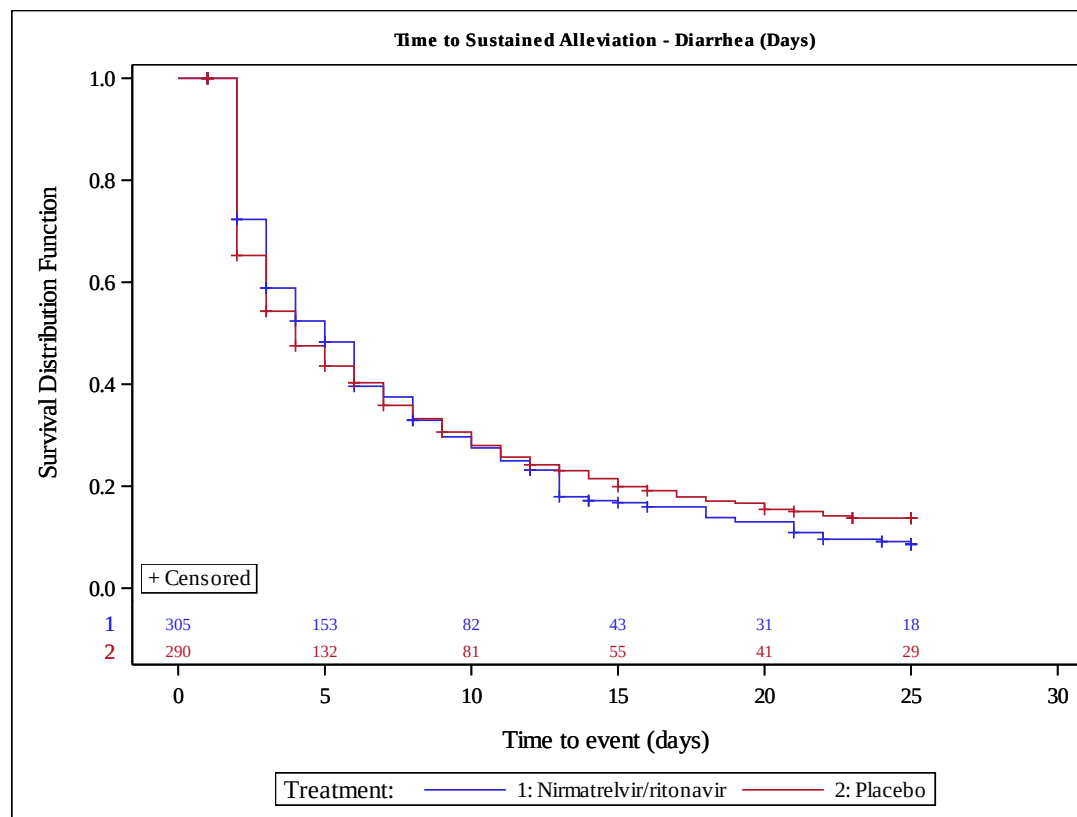
[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Diarrhea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea

Final

	Nirmatrelvir/ritonavir (N=19)	Placebo (N=12)
Number of subjects with events, n (%)	16 (84.2)	10 (83.3)
Number of censored subjects, n (%)	3 (15.8)	2 (16.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (2.0, 11.0)	11.0 (2.0, 15.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.007 (0.400, 2.533)	
p-value [3]	0.988	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.181 (0.531, 2.627)	
p-value [3]	0.684	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

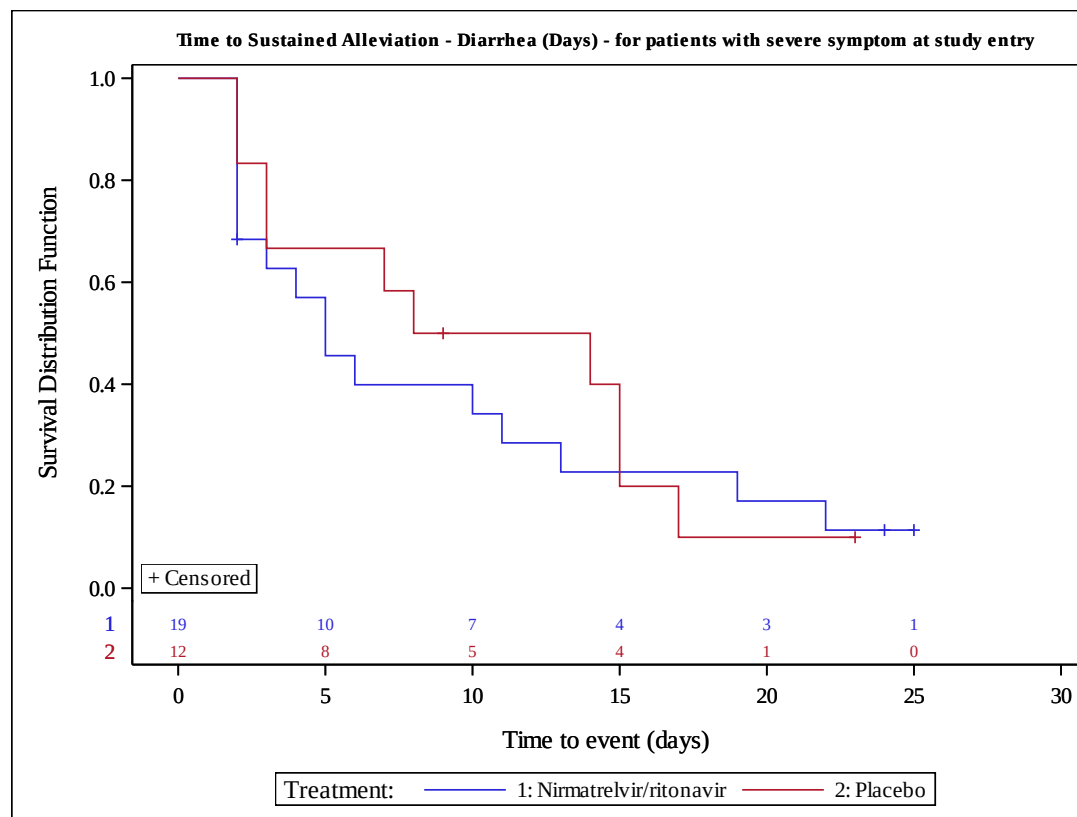
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Diarrhea

Final

	Nirmatrelvir/ritonavir (N=305)	Placebo (N=290)
Number of subjects with events, n (%)	256 (83.9)	222 (76.6)
Number of censored subjects, n (%)	49 (16.1)	68 (23.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	6.0 (6.0, 7.0)	6.0 (5.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.135 (0.942, 1.368)	
p-value [3]	0.184	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.135 (0.947, 1.359)	
p-value [3]	0.170	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

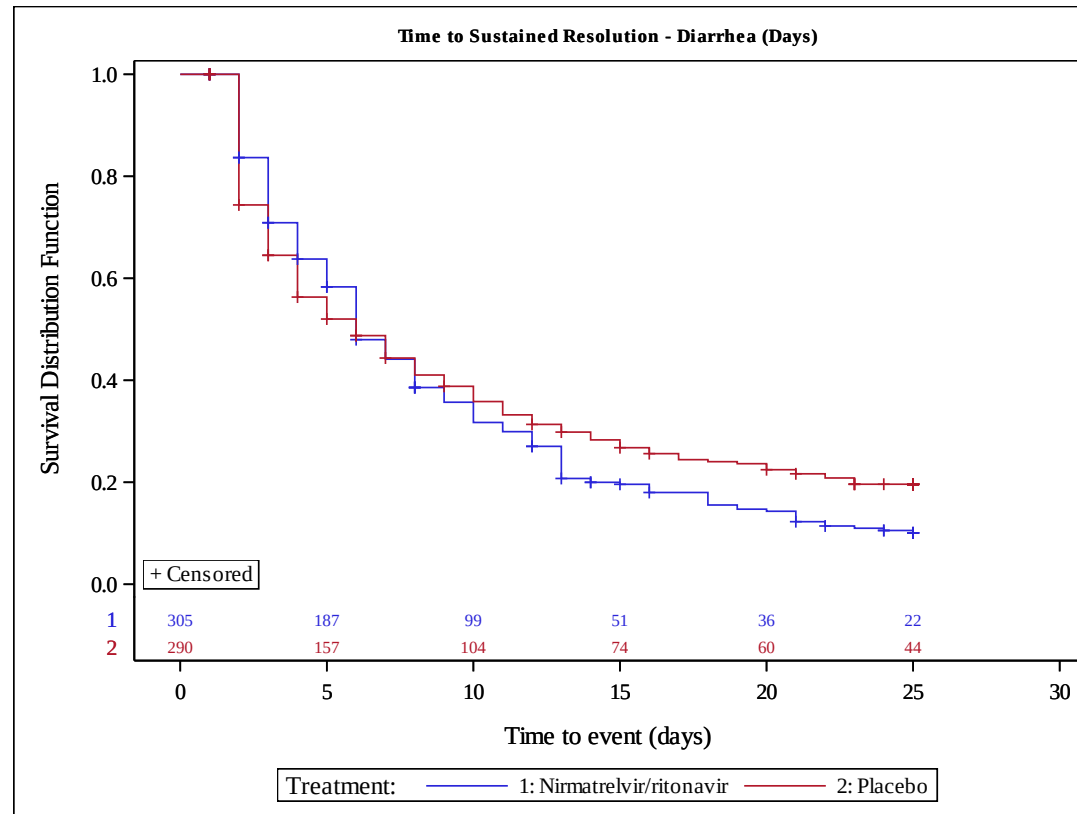
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Diarrhea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea

Final

	Nirmatrelvir/ritonavir (N=19)	Placebo (N=12)
Number of subjects with events, n (%)	15 (78.9)	6 (50.0)
Number of censored subjects, n (%)	4 (21.1)	6 (50.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	11.0 (7.0, 13.0)	18.0 (8.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	2.781 (0.900, 8.589)	
p-value [3]	0.076	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	2.613 (1.007, 6.781)	
p-value [3]	0.048	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

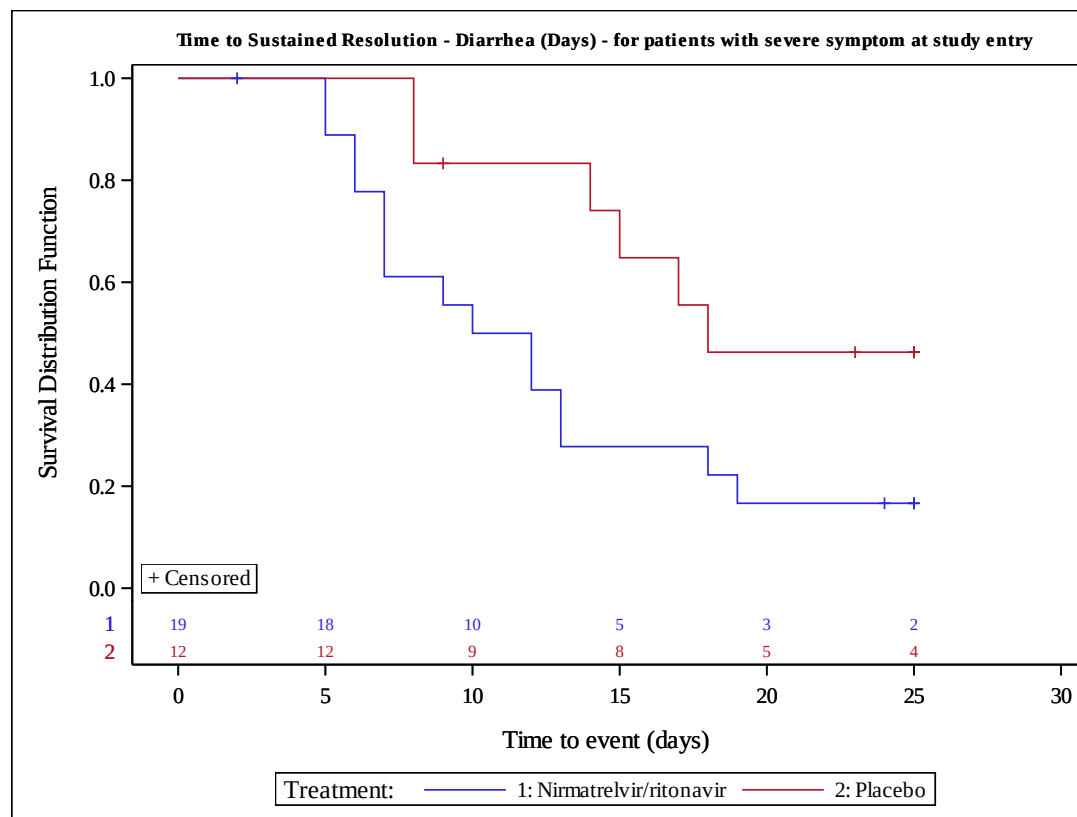
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Worsening of Signs and Symptoms - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	268 (24.5)	280 (25.3)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.926 (0.756, 1.133) 0.455	
Relative Risk (95% CI)	0.946 (0.818, 1.094) 0.455	
Risk Difference (95% CI)	-0.016 (-0.050, 0.019) 0.373	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.957 (0.789, 1.161) 0.657	
Relative Risk (95% CI)	0.968 (0.837, 1.119) 0.657	
Risk Difference (95% CI)	-0.008 (-0.044, 0.028) 0.657	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=609)	Placebo (N=623)
Number of subjects with events, n (%)	440 (72.2)	399 (64.0)
Number of censored subjects, n (%)	169 (27.8)	224 (36.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	10.0 (9.0, 11.0)	13.0 (12.0, 15.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.298 (1.129, 1.491)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.281 (1.118, 1.467)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

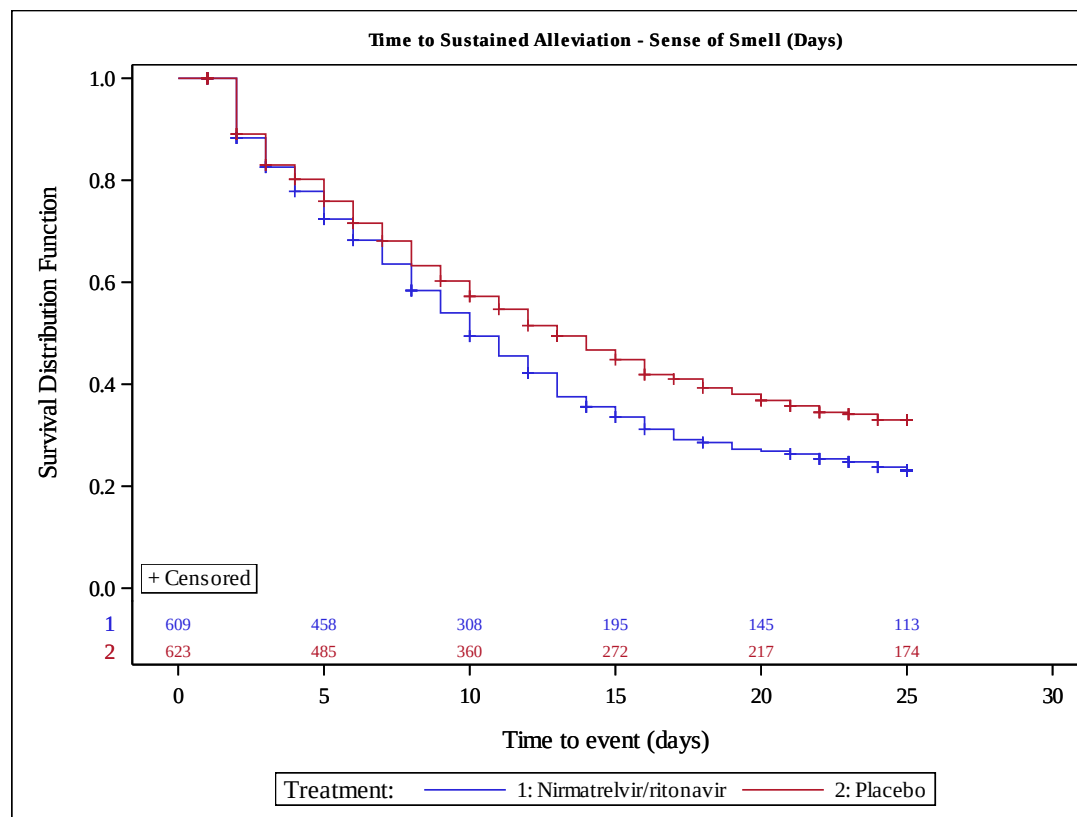
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Loss of smell

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=280)	Placebo (N=277)
Number of subjects with events, n (%)	221 (78.9)	191 (69.0)
Number of censored subjects, n (%)	59 (21.1)	86 (31.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	8.0 (7.0, 9.0)	9.0 (8.0, 12.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.335 (1.093, 1.630)	
p-value [3]	0.005	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.286 (1.059, 1.561)	
p-value [3]	0.011	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

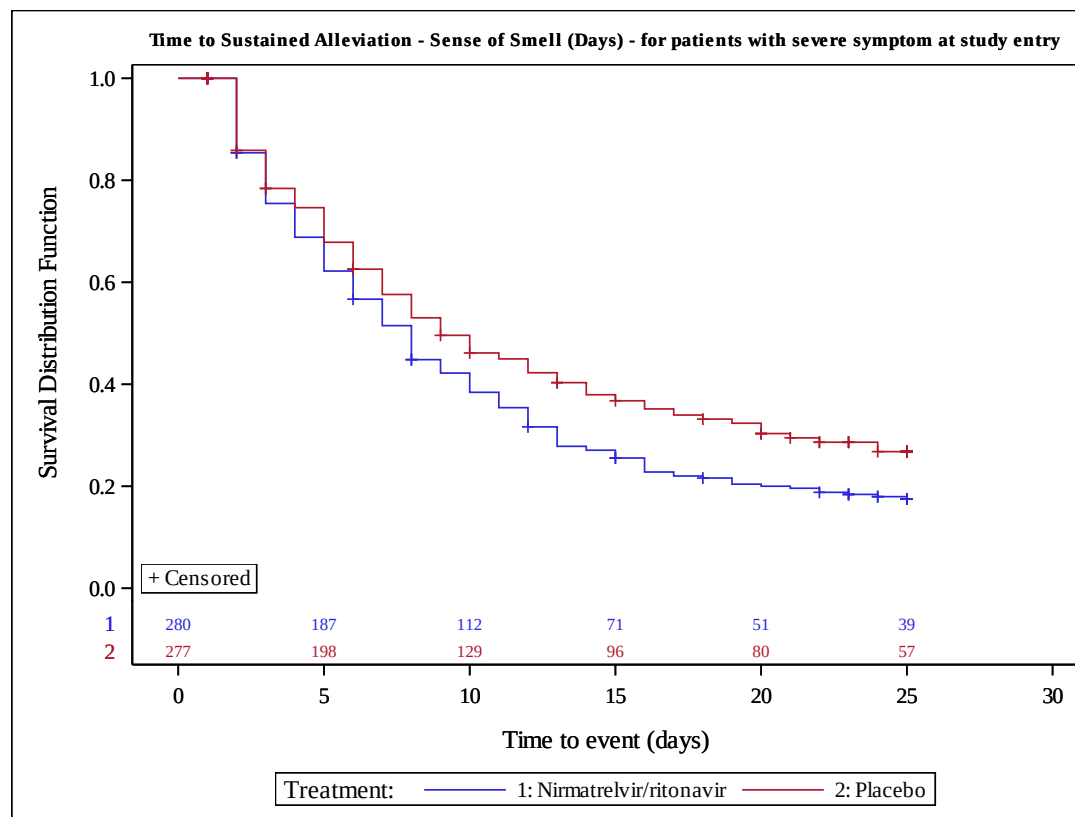
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of smell

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=609)	Placebo (N=623)
Number of subjects with events, n (%)	372 (61.1)	322 (51.7)
Number of censored subjects, n (%)	237 (38.9)	301 (48.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	15.0 (14.0, 17.0)	22.0 (18.0, 24.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.311 (1.126, 1.527)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.313 (1.131, 1.525)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

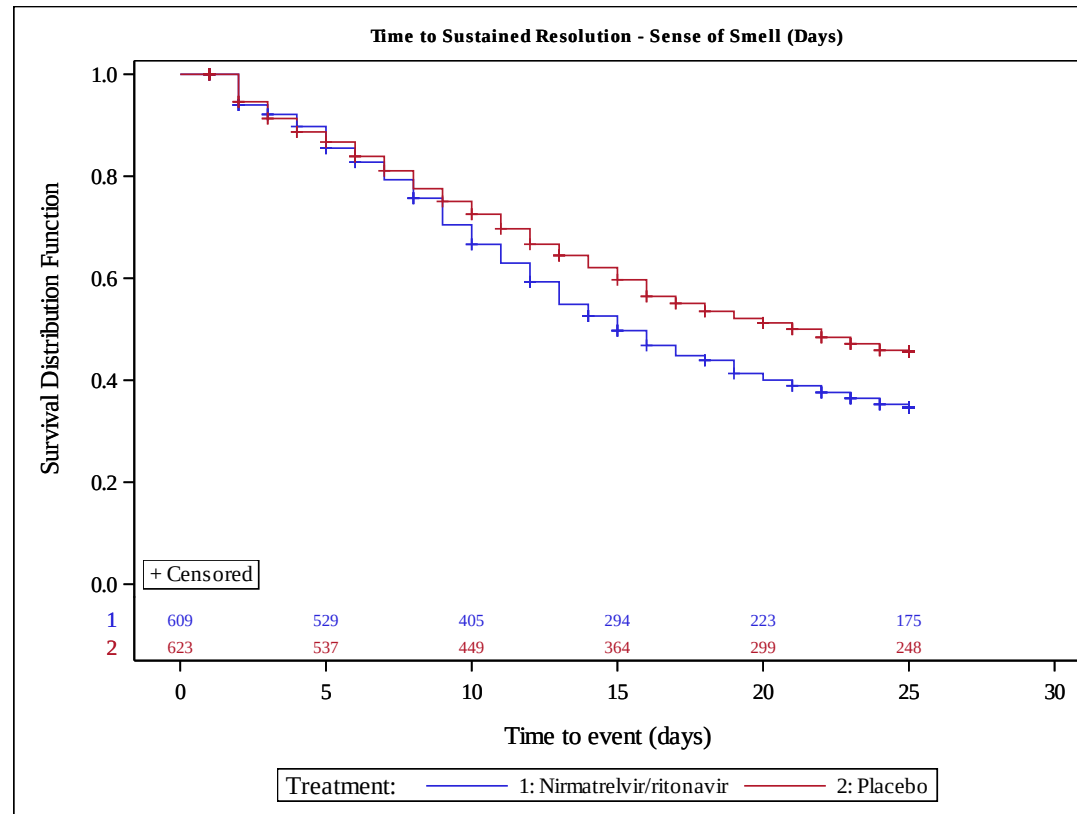
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Loss of smell

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=280)	Placebo (N=277)
Number of subjects with events, n (%)	153 (54.6)	114 (41.2)
Number of censored subjects, n (%)	127 (45.4)	163 (58.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	20.0 (17.0, 23.0)	NE (24.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.466 (1.143, 1.879)	
p-value [3]	0.003	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.455 (1.141, 1.854)	
p-value [3]	0.002	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

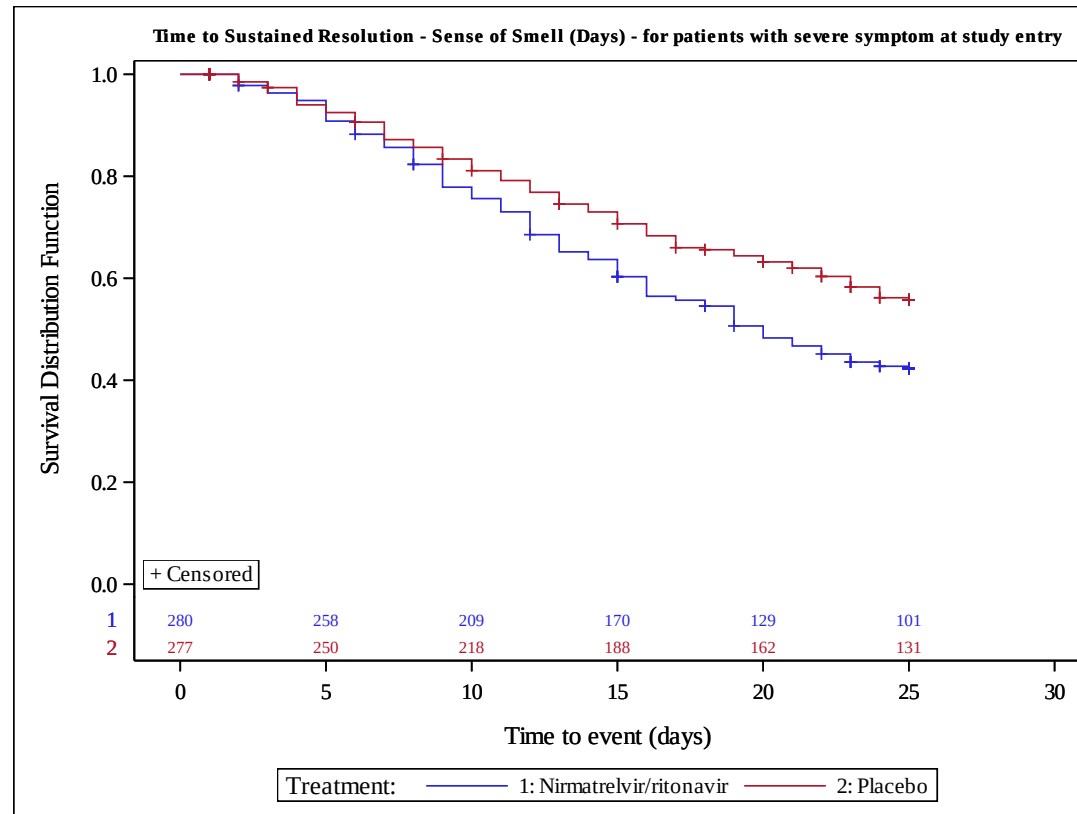
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of smell

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Worsening of Signs and Symptoms - Loss of taste

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	264 (24.2)	271 (24.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.949 (0.774, 1.163) 0.612	
Relative Risk (95% CI)	0.968 (0.834, 1.123) 0.666	
Risk Difference (95% CI)	-0.016 (-0.050, 0.019) 0.371	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.980 (0.807, 1.191) 0.839	
Relative Risk (95% CI)	0.985 (0.850, 1.141) 0.839	
Risk Difference (95% CI)	-0.004 (-0.040, 0.032) 0.839	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Loss of taste

Final

	Nirmatrelvir/ritonavir (N=591)	Placebo (N=600)
Number of subjects with events, n (%)	436 (73.8)	389 (64.8)
Number of censored subjects, n (%)	155 (26.2)	211 (35.2)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	10.0 (9.0, 11.0)	14.0 (12.0, 15.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.351 (1.174, 1.554)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.347 (1.174, 1.544)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

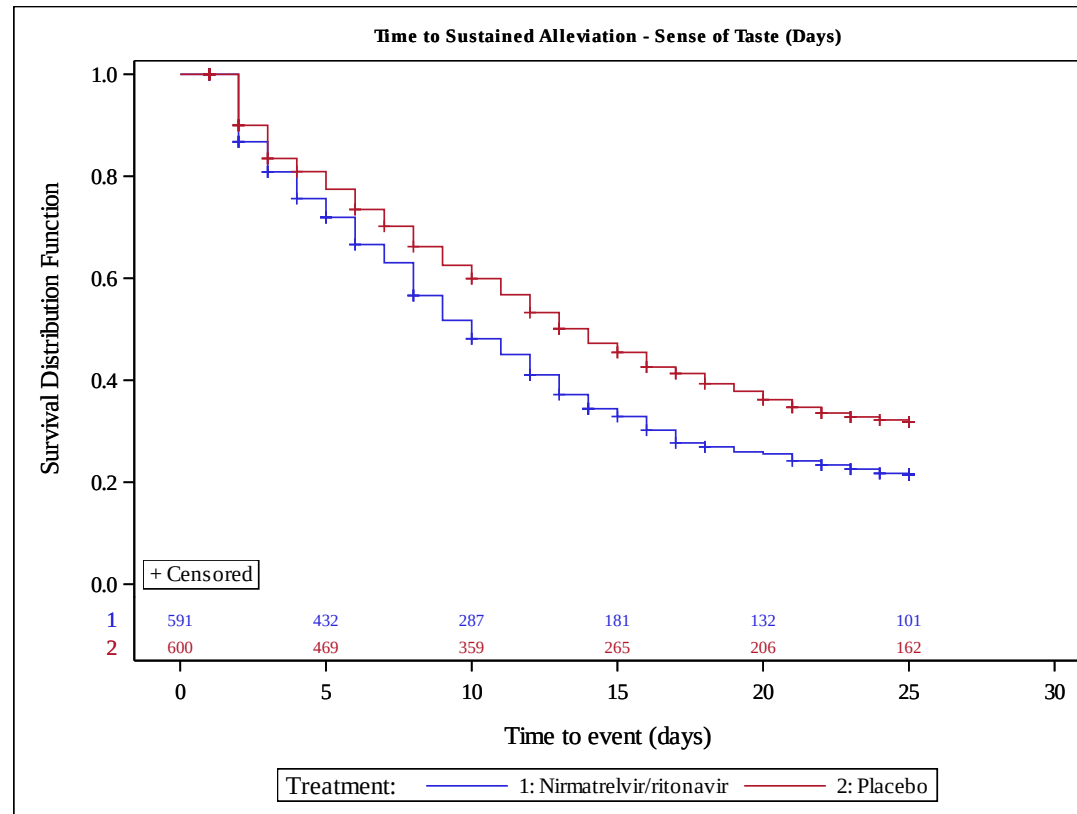
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Loss of taste

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of taste

Final

	Nirmatrelvir/ritonavir (N=245)	Placebo (N=233)
Number of subjects with events, n (%)	198 (80.8)	161 (69.1)
Number of censored subjects, n (%)	47 (19.2)	72 (30.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	7.0 (6.0, 8.0)	10.0 (8.0, 13.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.456 (1.169, 1.815)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.428 (1.158, 1.760)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

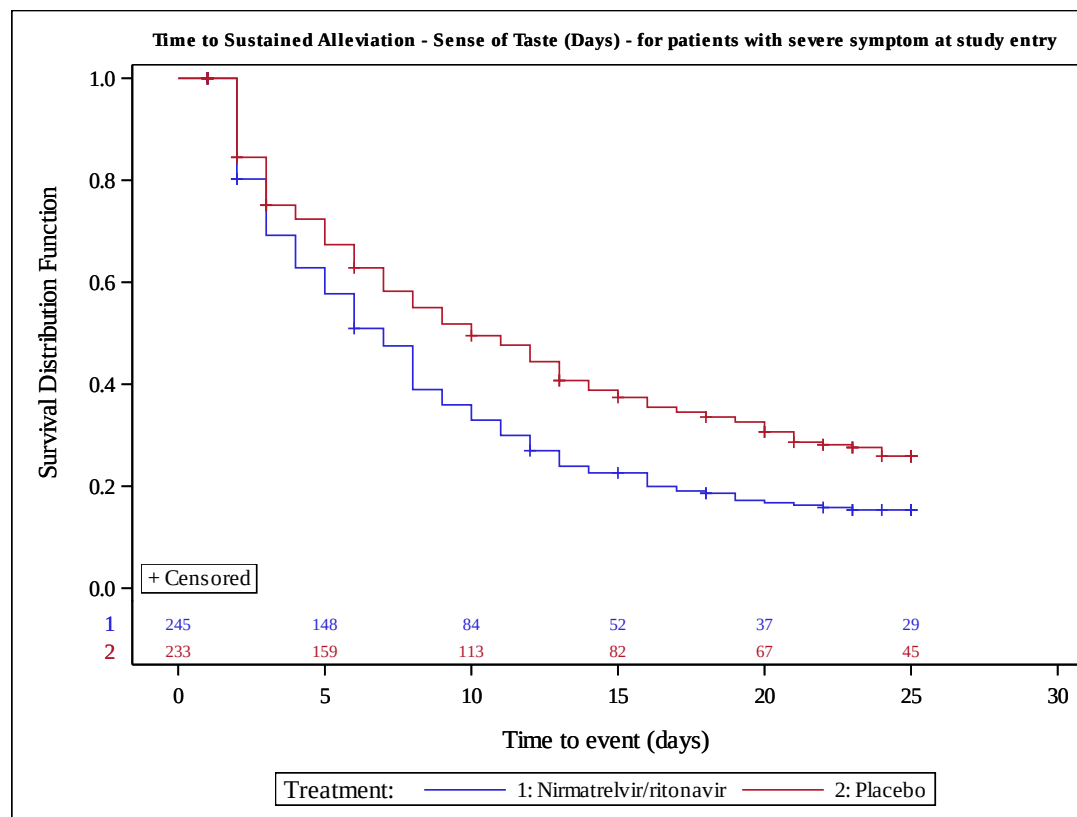
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of taste

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Loss of taste

Final

	Nirmatrelvir/ritonavir (N=591)	Placebo (N=600)
Number of subjects with events, n (%)	375 (63.5)	325 (54.2)
Number of censored subjects, n (%)	216 (36.5)	275 (45.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	15.0 (14.0, 16.0)	19.0 (17.0, 22.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.292 (1.109, 1.504)	
p-value [3]	0.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.308 (1.127, 1.518)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

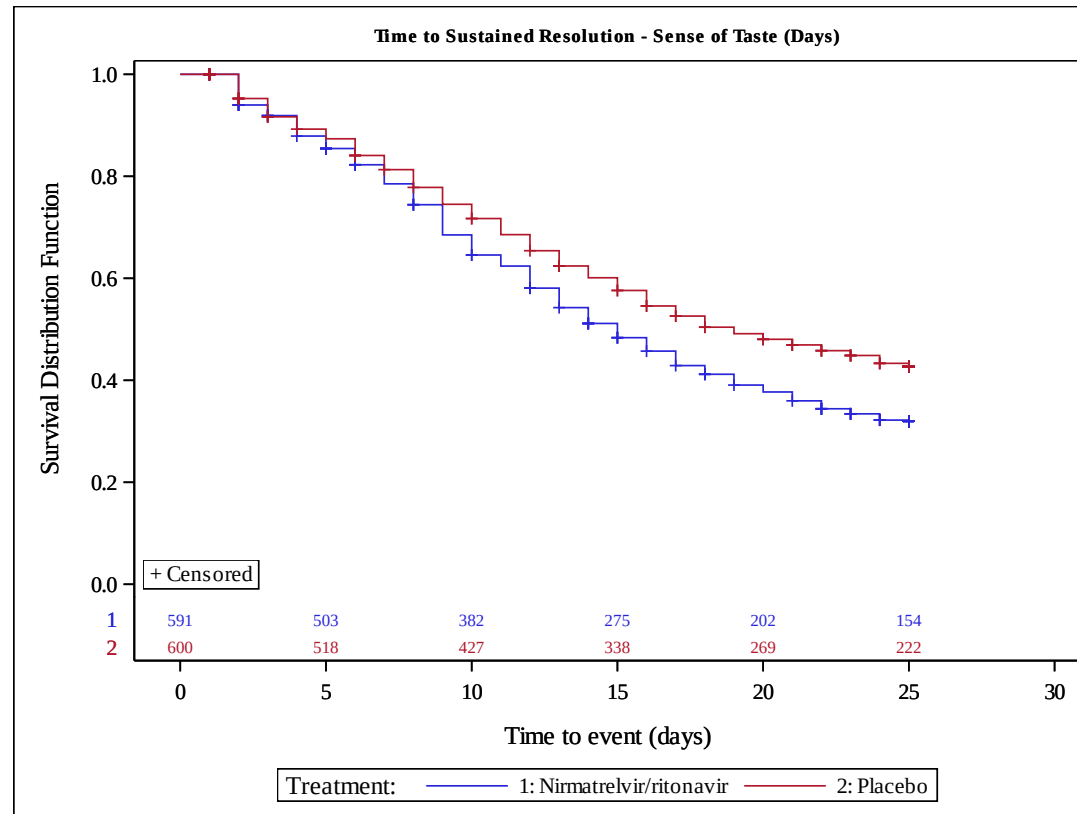
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Loss of taste

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of taste

Final

	Nirmatrelvir/ritonavir (N=245)	Placebo (N=233)
Number of subjects with events, n (%)	137 (55.9)	97 (41.6)
Number of censored subjects, n (%)	108 (44.1)	136 (58.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	19.0 (17.0, 22.0)	NE (24.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.420 (1.082, 1.863)	
p-value [3]	0.012	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.471 (1.134, 1.909)	
p-value [3]	0.004	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

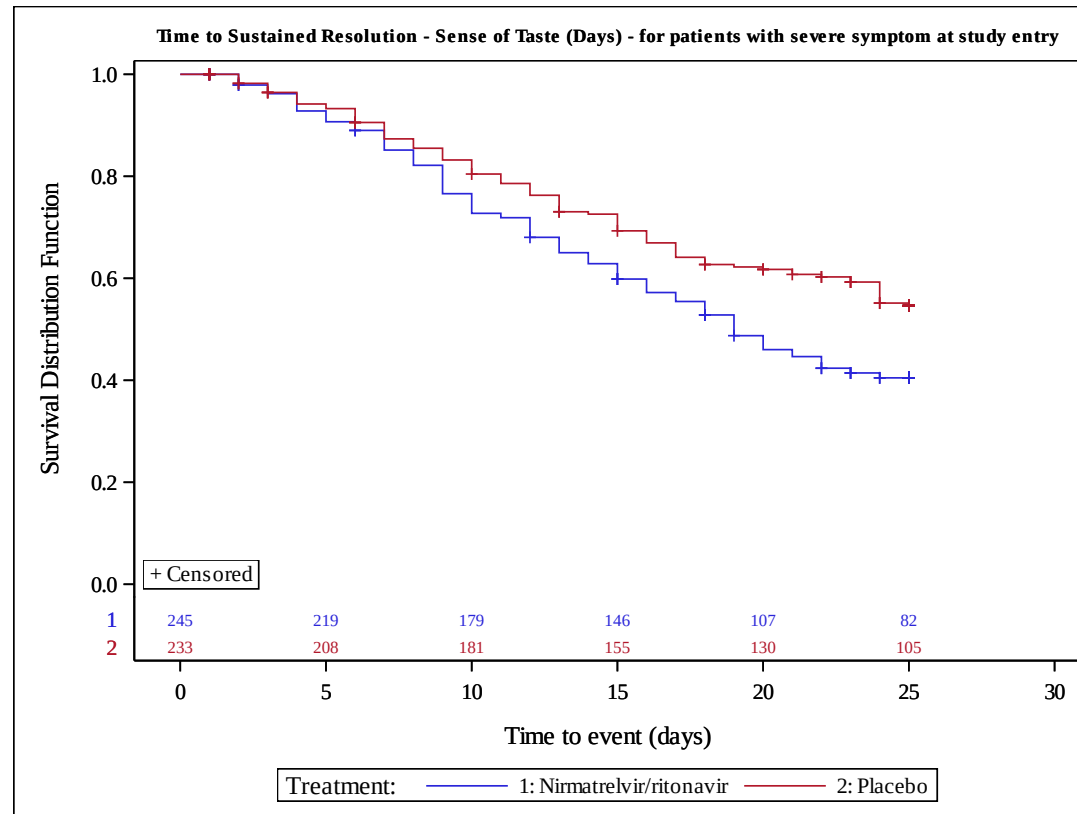
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of taste

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Any Severe Targeted Signs and Symptoms

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	217 (19.9)	235 (21.3)
Adjusted analysis [1] Odds Ratio (95% CI)	0.944 (0.757, 1.178) 0.610	
Relative Risk (95% CI)	0.950 (0.809, 1.114) 0.527	
Risk Difference (95% CI)	NE (NE, NE) NE	
Unadjusted analysis [2] Odds Ratio (95% CI)	0.917 (0.746, 1.128) 0.412	
Relative Risk (95% CI)	0.934 (0.792, 1.100) 0.413	
Risk Difference (95% CI)	-0.014 (-0.048, 0.020) 0.412	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Any Severe Signs and Symptoms

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	530 (48.5)	533 (48.2)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.019 (0.854, 1.217) 0.832	
Relative Risk (95% CI)	0.997 (0.918, 1.083) 0.952	
Risk Difference (95% CI)	0.001 (-0.039, 0.042) 0.945	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.010 (0.855, 1.194) 0.905	
Relative Risk (95% CI)	1.005 (0.922, 1.096) 0.905	
Risk Difference (95% CI)	0.003 (-0.039, 0.044) 0.905	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Progression of Worsening Status in 1 or More Targeted Signs and Symptoms

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	819 (74.9)	822 (74.4)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.012 (0.828, 1.236) 0.907	
Relative Risk (95% CI)	0.995 (0.949, 1.043) 0.839	
Risk Difference (95% CI)	-0.002 (-0.037, 0.034) 0.934	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.029 (0.849, 1.247) 0.770	
Relative Risk (95% CI)	1.007 (0.959, 1.058) 0.770	
Risk Difference (95% CI)	0.005 (-0.031, 0.042) 0.770	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Pfizer Inc
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 Analysis of Participants with Progression of Worsening Status in 1 or More Signs and Symptoms

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with Response, n (%)	889 (81.3)	879 (79.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.085 (0.874, 1.347) 0.460	
Relative Risk (95% CI)	1.008 (0.967, 1.050) 0.703	
Risk Difference (95% CI)	0.008 (-0.025, 0.041) 0.633	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.120 (0.907, 1.384) 0.291	
Relative Risk (95% CI)	1.022 (0.981, 1.066) 0.291	
Risk Difference (95% CI)	0.018 (-0.015, 0.051) 0.290	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of All Targeted Signs and Symptoms Through Day 28

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with events, n (%)	802 (73.4)	728 (65.9)
Number of censored subjects, n (%)	291 (26.6)	377 (34.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	13.0 (12.0, 13.0)	15.0 (14.0, 16.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.264 (1.141, 1.400)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.280 (1.157, 1.415)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

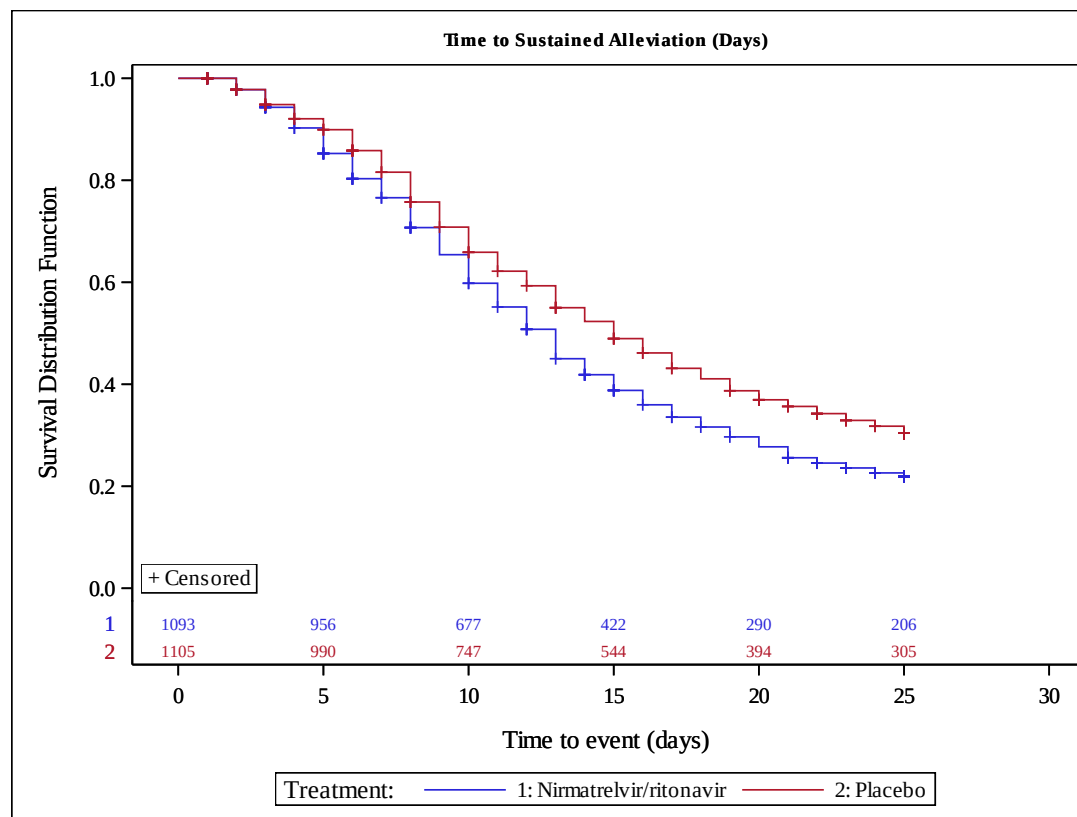
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of All Targeted Signs and Symptoms Through Day 28

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of All Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry

Final

	Nirmatrelvir/ritonavir (N=229)	Placebo (N=207)
Number of subjects with events, n (%)	193 (84.3)	157 (75.8)
Number of censored subjects, n (%)	36 (15.7)	50 (24.2)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 5.0)	8.0 (7.0, 9.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.409 (1.130, 1.758)	
p-value [3]	0.002	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.493 (1.208, 1.845)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

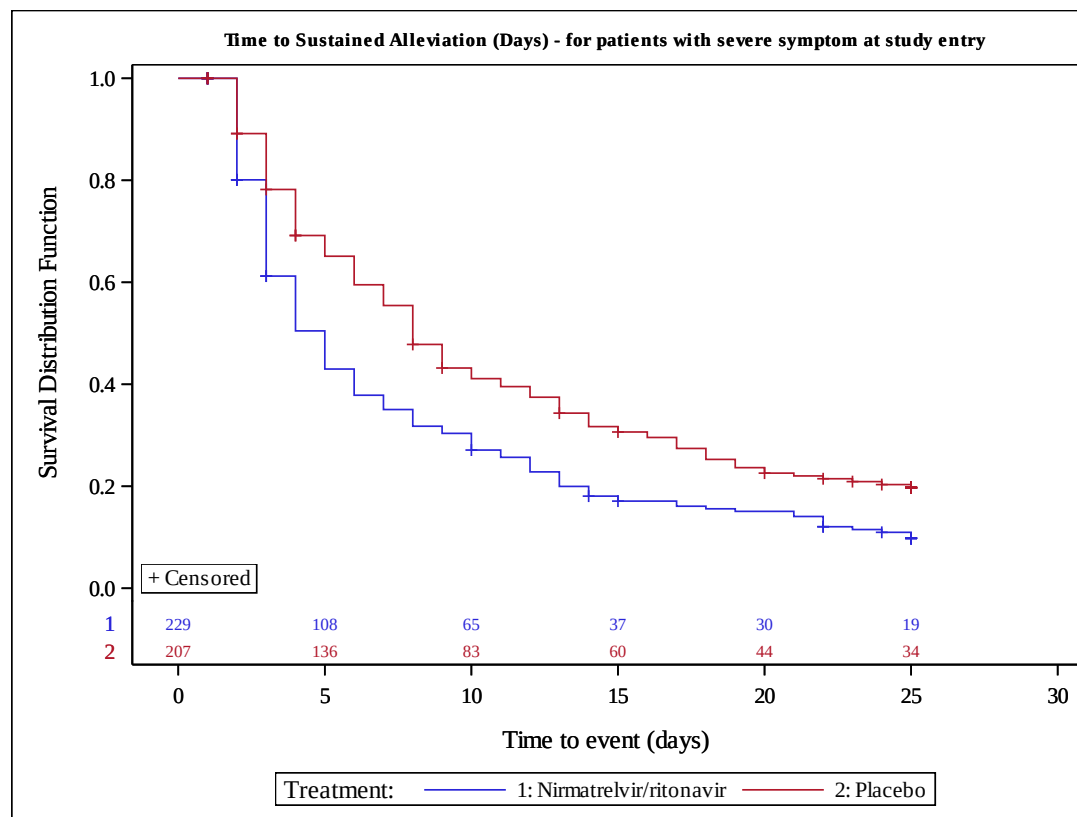
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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 Modified Intent-To-Treat (mITT2) set
 Analysis of Time to Sustained Alleviation of All Signs and Symptoms Through Day 28

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with events, n (%)	690 (63.1)	611 (55.3)
Number of censored subjects, n (%)	403 (36.9)	494 (44.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	16.0 (15.0, 17.0)	20.0 (19.0, 22.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.286 (1.151, 1.437)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.295 (1.161, 1.444)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

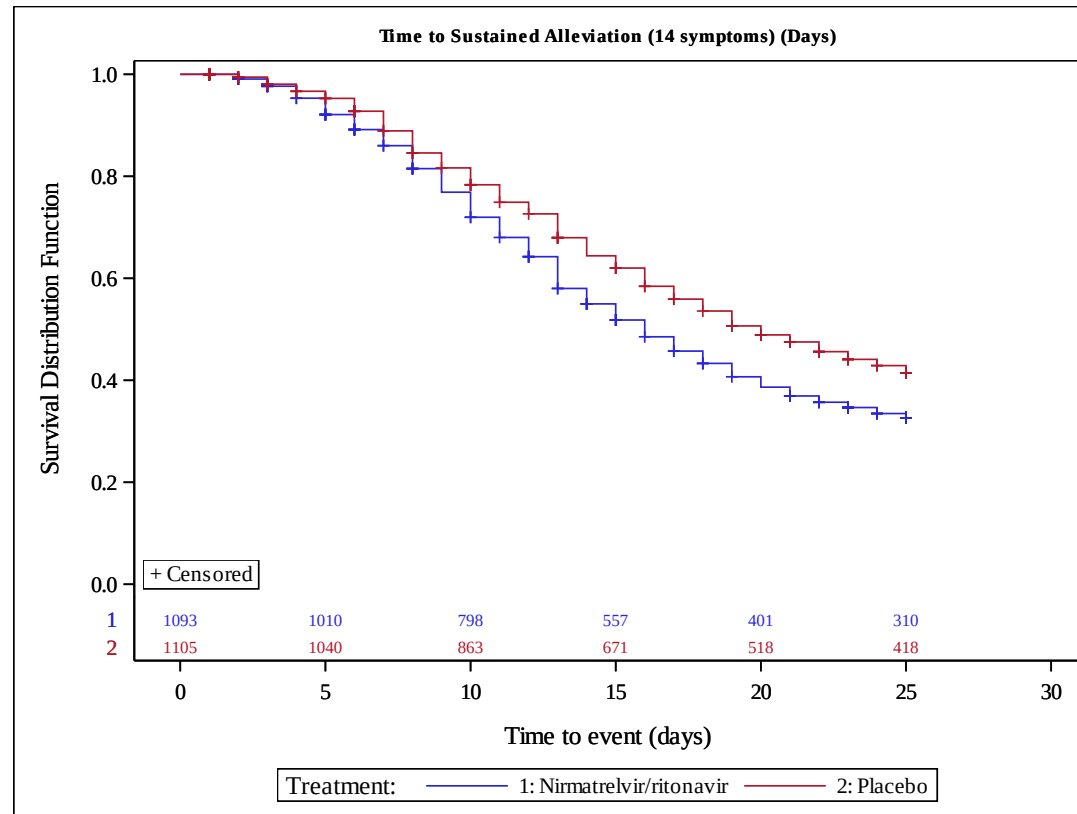
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

	Nirmatrelvir/ritonavir (N=464)	Placebo (N=444)
Number of subjects with events, n (%)	363 (78.2)	318 (71.6)
Number of censored subjects, n (%)	101 (21.8)	126 (28.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	7.0 (6.0, 8.0)	9.0 (8.0, 11.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.285 (1.100, 1.499)	
p-value [3]	0.002	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.277 (1.099, 1.485)	
p-value [3]	0.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

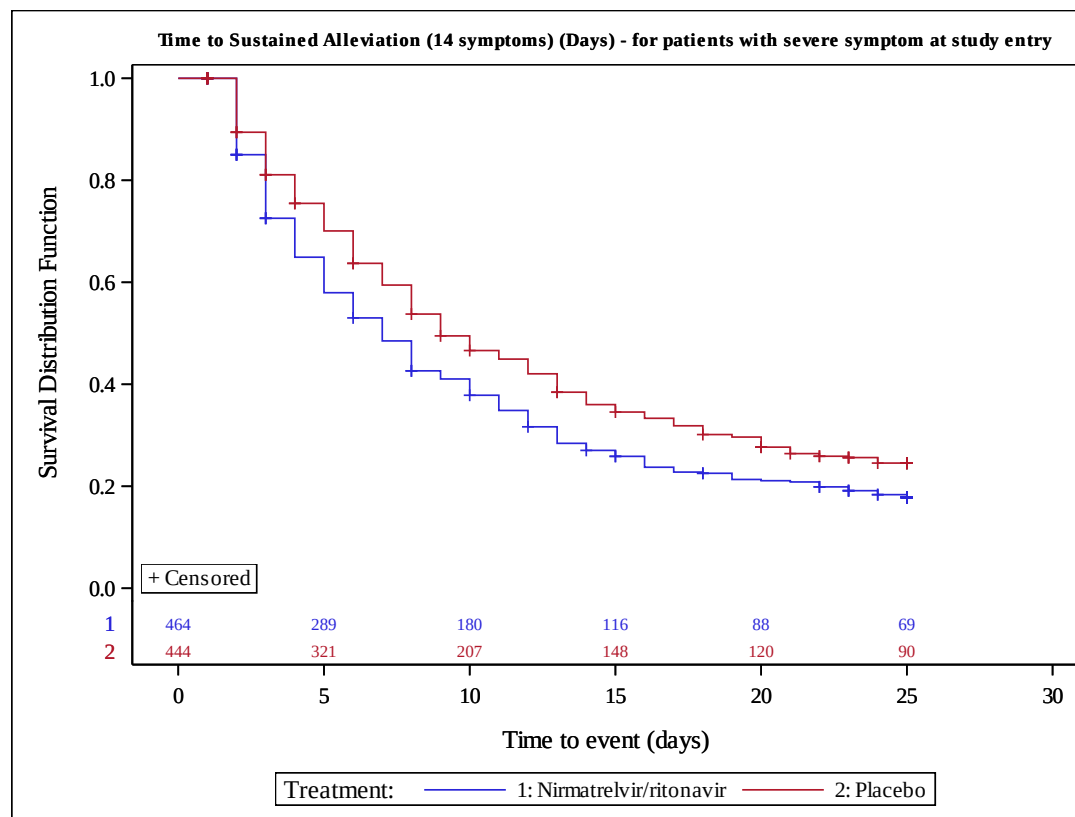
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Analysis of Time to Sustained Resolution of All Targeted Signs and Symptoms Through Day 28

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with events, n (%)	712 (65.1)	650 (58.8)
Number of censored subjects, n (%)	381 (34.9)	455 (41.2)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	16.0 (15.0, 17.0)	19.0 (17.0, 20.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.206 (1.082, 1.344)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.228 (1.104, 1.366)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

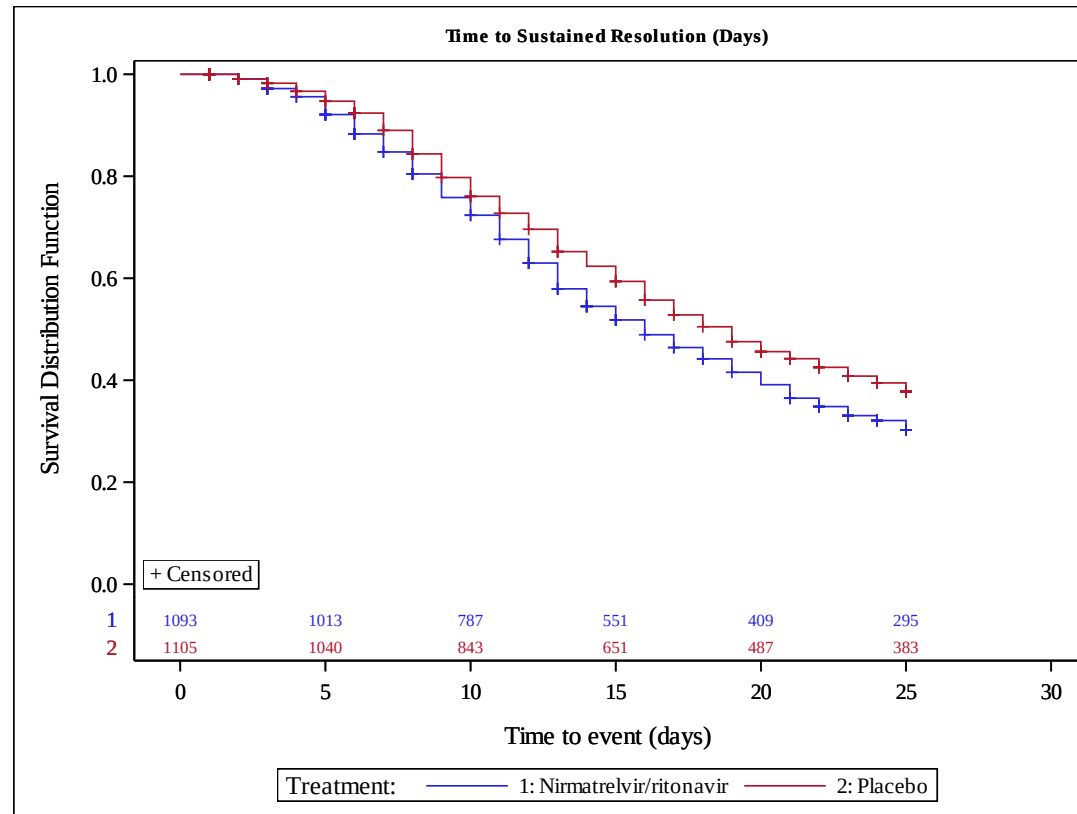
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Kaplan-Meier Plot of Time to Sustained Resolution of All Targeted Signs and Symptoms Through Day 28

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

	Nirmatrelvir/ritonavir (N=229)	Placebo (N=207)
Number of subjects with events, n (%)	157 (68.6)	120 (58.0)
Number of censored subjects, n (%)	72 (31.4)	87 (42.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	12.0 (11.0, 14.0)	18.0 (16.0, 21.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.425 (1.113, 1.824)	
p-value [3]	0.005	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.484 (1.169, 1.882)	
p-value [3]	0.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

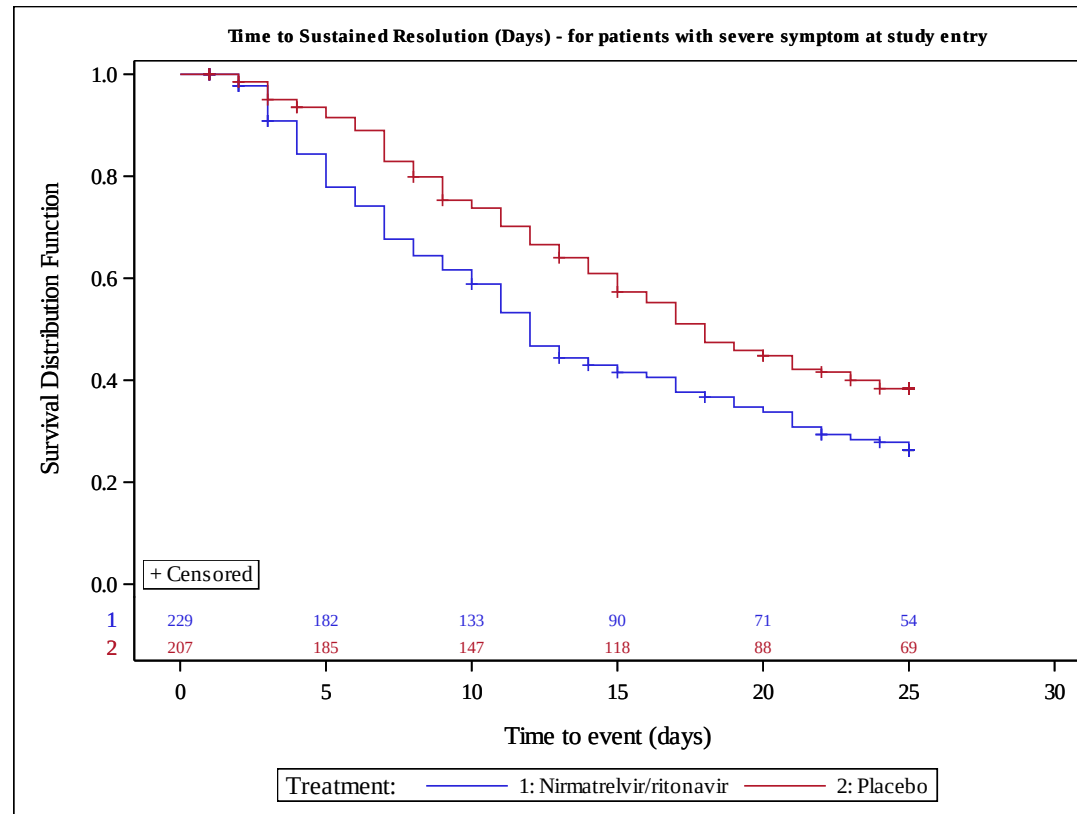
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Analysis of Time to Sustained Resolution of All Signs and Symptoms Through Day 28

Final

	Nirmatrelvir/ritonavir (N=1093)	Placebo (N=1105)
Number of subjects with events, n (%)	613 (56.1)	525 (47.5)
Number of censored subjects, n (%)	480 (43.9)	580 (52.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	20.0 (19.0, 21.0)	25.0 (23.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.285 (1.141, 1.446)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.312 (1.168, 1.475)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

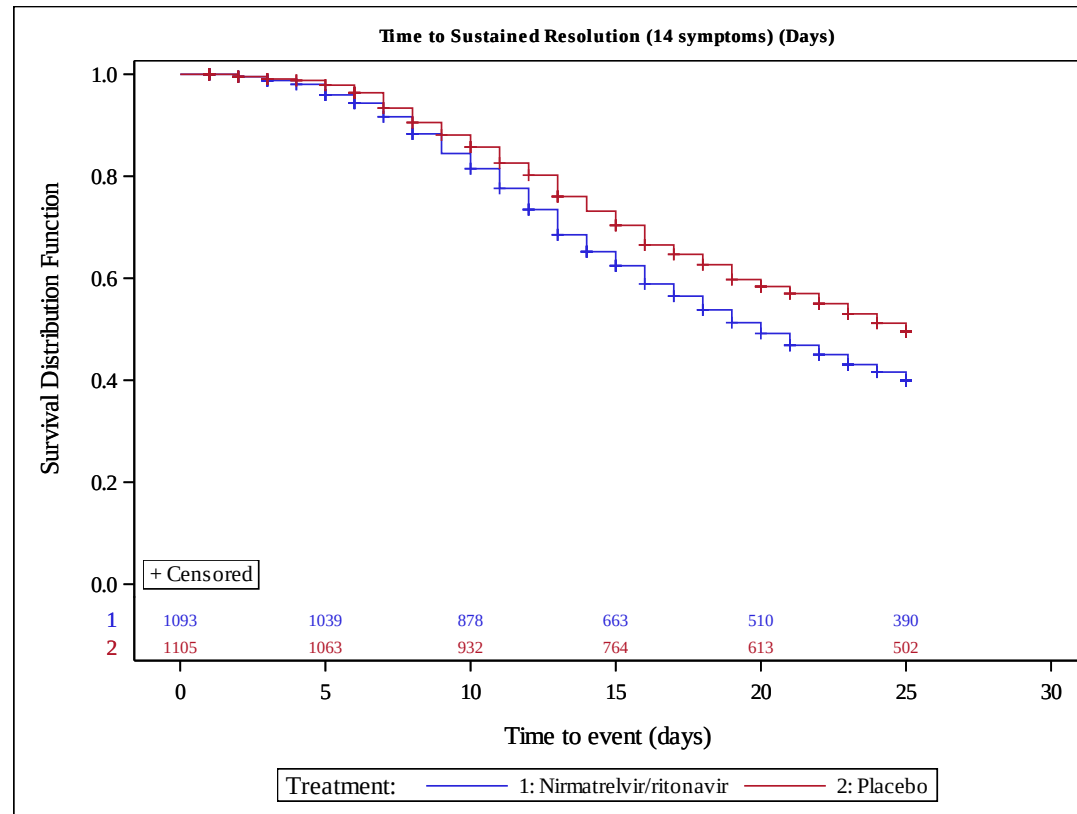
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Analysis of Time to Sustained Resolution of All Signs and Symptoms Through Day 28 for patients with severe symptom at study entry

Final

	Nirmatrelvir/ritonavir (N=464)	Placebo (N=444)
Number of subjects with events, n (%)	263 (56.7)	201 (45.3)
Number of censored subjects, n (%)	201 (43.3)	243 (54.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	19.0 (16.0, 21.0)	NE (23.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.394 (1.156, 1.682)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.410 (1.173, 1.694)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

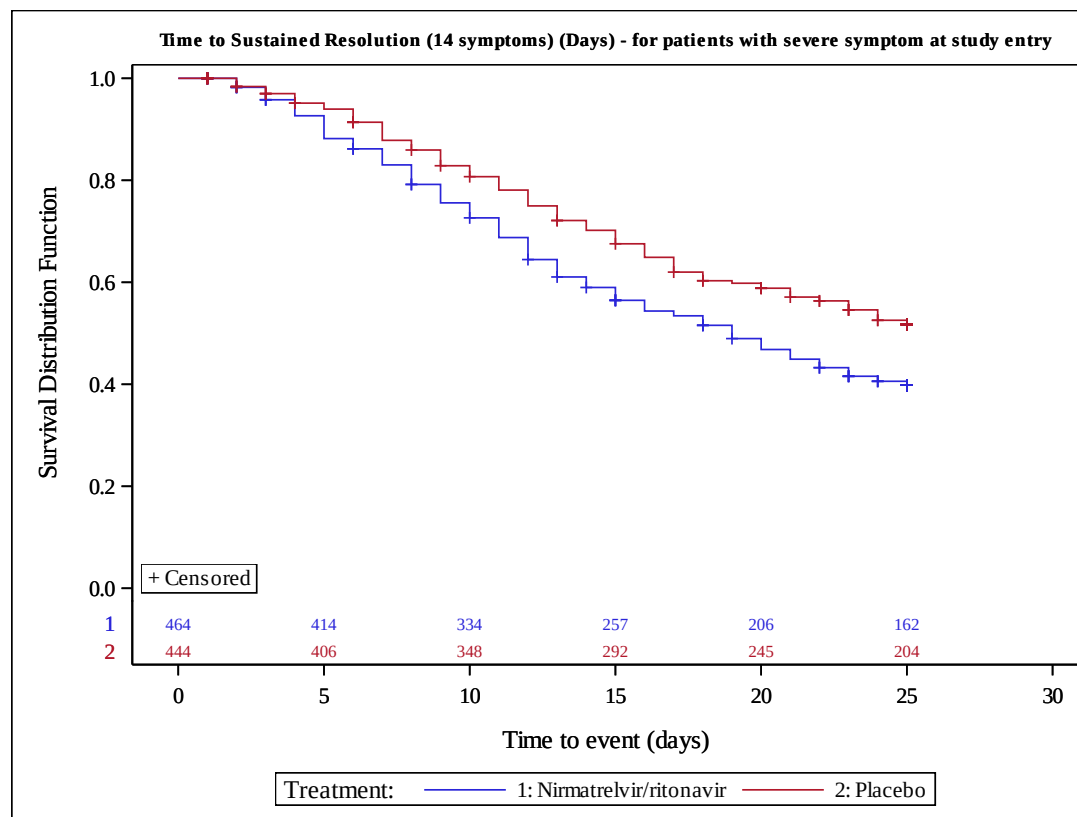
[2] Adjusted by geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with EQ 5D-VAS >= 15 points improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=1109)	Placebo (N=1115)
Number of subjects with Response, n (%)	23 (2.1)	17 (1.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	NE (NE, NE)	
Relative Risk (95% CI)	NE (NE, NE)	
Risk Difference (95% CI)	NE (NE, NE)	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.368 (0.727, 2.575) 0.332	
Relative Risk (95% CI)	1.360 (0.731, 2.532) 0.332	
Risk Difference (95% CI)	0.005 (-0.006, 0.017) 0.330	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Global Impression Questionnaire overall COVID-19-related symptoms ≥ 1 point improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=1109)	Placebo (N=1115)
Number of subjects with Response, n (%)	711 (64.1)	679 (60.9)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.180 (0.985, 1.413) 0.073	
Relative Risk (95% CI)	1.062 (1.000, 1.127) 0.051	
Risk Difference (95% CI)	0.038 (-0.001, 0.077) 0.057	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.147 (0.966, 1.362) 0.117	
Relative Risk (95% CI)	1.053 (0.987, 1.123) 0.118	
Risk Difference (95% CI)	0.032 (-0.008, 0.072) 0.117	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Global Impression Questionnaire return to usual health 1 point improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=1109)	Placebo (N=1115)
Number of subjects with Response, n (%)	606 (54.6)	552 (49.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.247 (1.048, 1.485) 0.013	
Relative Risk (95% CI)	1.107 (1.026, 1.194) 0.009	
Risk Difference (95% CI)	0.054 (0.013, 0.095) 0.010	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.229 (1.040, 1.452) 0.015	
Relative Risk (95% CI)	1.104 (1.019, 1.196) 0.015	
Risk Difference (95% CI)	0.051 (0.010, 0.093) 0.015	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with Global Impression Questionnaire return to usual activities 1 point improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=1109)	Placebo (N=1115)
Number of subjects with Response, n (%)	622 (56.1)	589 (52.8)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.156 (0.971, 1.376) 0.104	
Relative Risk (95% CI)	1.064 (0.990, 1.144) 0.091	
Risk Difference (95% CI)	0.035 (-0.006, 0.076) 0.093	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.141 (0.965, 1.348) 0.123	
Relative Risk (95% CI)	1.062 (0.984, 1.146) 0.123	
Risk Difference (95% CI)	0.033 (-0.009, 0.074) 0.122	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Overall Study population
 Modified Intent-To-Treat (mITT2) set
 Analysis of Participants with WPAI Question 6 >= 15 points improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=1109)	Placebo (N=1115)
Number of subjects with Response, n (%)	21 (1.9)	29 (2.6)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.705 (0.394, 1.263) 0.240	
Relative Risk (95% CI)	NE (NE, NE) NE	
Risk Difference (95% CI)	NE (NE, NE) NE	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.723 (0.410, 1.275) 0.263	
Relative Risk (95% CI)	0.728 (0.418, 1.269) 0.263	
Risk Difference (95% CI)	-0.007 (-0.019, 0.005) 0.260	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, COVID-19 mAb treatment, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Anhang 4-G 3: mITT1-Population

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 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Observation Time per Endpoint

Final

		Nirmatrelvir/ritonavir (N=1039)	Placebo (N=1046)	Total (N=2085)
Observation Time for Time to Death (Days) through Day 28[1]	n (missing)	1039 (0)	1046 (0)	2085 (0)
	Mean (SD)	27.21 (4.14)	27.10 (4.23)	27.15 (4.19)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Time to Death (Days) through Week 24[1]	n (missing)	1039 (0)	1046 (0)	2085 (0)
	Mean (SD)	159.11 (32.56)	156.99 (36.17)	158.05 (34.43)
	Median	168.00	168.00	168.00
	Q1, Q3	164.00, 168.00	163.00, 168.00	163.00, 168.00
	Min, Max	1.00, 168.00	1.00, 168.00	1.00, 168.00
Observation Time for Time to COVID-19 related Hospitalization (Days)[2]	n (missing)	1039 (0)	1046 (0)	2085 (0)
	Mean (SD)	27.03 (4.60)	25.97 (6.46)	26.50 (5.64)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Stuffy or Runny Nose (Days)[3]	n (missing)	1026 (13)	1037 (9)	2063 (22)
	Mean (SD)	26.07 (5.77)	25.55 (6.58)	25.81 (6.20)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Sore Throat (Days)[3]	n (missing)	1026 (13)	1037 (9)	2063 (22)
	Mean (SD)	26.07 (5.77)	25.55 (6.58)	25.81 (6.20)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Shortness of Breath or Difficulty Breathing (Days)[3]	n (missing)	1026 (13)	1037 (9)	2063 (22)
	Mean (SD)	26.07 (5.77)	25.55 (6.58)	25.81 (6.20)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Cough (Days)[3]	n (missing)	1026 (13)	1037 (9)	2063 (22)
	Mean (SD)	26.07 (5.77)	25.55 (6.58)	25.81 (6.20)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Low Energy or Tiredness (Days)[3]	n (missing)	1026 (13)	1037 (9)	2063 (22)
	Mean (SD)	26.07 (5.77)	25.55 (6.58)	25.81 (6.20)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Muscle or Body Aches (Days)[3]	n (missing)	1026 (13)	1037 (9)	2063 (22)
	Mean (SD)	26.07 (5.77)	25.55 (6.58)	25.81 (6.20)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00

N: Number of participants, n: Number of participants with non-missing values, SD: Standard Deviation, Q1: 25%-Quartile, Q3: 75%-Quartile, Min: Minimum, Max: Maximum

[1] date of first administration of study drug until death date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[2] date of first administration of study drug until hospitalization date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[3] date of first administration of study drug until date of last non-missing measurement through Day 28 + 1

[4] date of first administration of study drug until date of last non-missing measurement through Week 24 + 1

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		Nirmatrelvir/ritonavir (N=1039)	Placebo (N=1046)	Total (N=2085)
Observation Time for Headache (Days) [3]	n (missing)	1026 (13)	1037 (9)	2063 (22)
	Mean (SD)	26.07 (5.77)	25.55 (6.58)	25.81 (6.20)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Chills or Shivering (Days) [3]	n (missing)	1026 (13)	1037 (9)	2063 (22)
	Mean (SD)	26.07 (5.77)	25.55 (6.58)	25.81 (6.20)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Feeling Hot or Feverish (Days) [3]	n (missing)	1026 (13)	1037 (9)	2063 (22)
	Mean (SD)	26.07 (5.77)	25.55 (6.58)	25.81 (6.20)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Nausea (Days) [3]	n (missing)	1026 (13)	1037 (9)	2063 (22)
	Mean (SD)	26.07 (5.77)	25.55 (6.58)	25.81 (6.20)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Vomit (Days) [3]	n (missing)	1026 (13)	1037 (9)	2063 (22)
	Mean (SD)	26.07 (5.77)	25.55 (6.58)	25.81 (6.20)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Diarrhea (Days) [3]	n (missing)	1026 (13)	1037 (9)	2063 (22)
	Mean (SD)	26.07 (5.77)	25.55 (6.58)	25.81 (6.20)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Sense of Smell (Days) [3]	n (missing)	1026 (13)	1037 (9)	2063 (22)
	Mean (SD)	26.07 (5.77)	25.55 (6.58)	25.81 (6.20)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Sense of Taste (Days) [3]	n (missing)	1026 (13)	1037 (9)	2063 (22)
	Mean (SD)	26.07 (5.77)	25.55 (6.58)	25.81 (6.20)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00

N: Number of participants, n: Number of participants with non-missing values, SD: Standard Deviation, Q1: 25%-Quartile, Q3: 75%-Quartile, Min: Minimum, Max: Maximum

[1] date of first administration of study drug until death date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[2] date of first administration of study drug until hospitalization date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[3] date of first administration of study drug until date of last non-missing measurement through Day 28 + 1

[4] date of first administration of study drug until date of last non-missing measurement through Week 24 + 1

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		Nirmatrelvir/ritonavir (N=1039)	Placebo (N=1046)	Total (N=2085)
Observation Time for EQ-5D VAS Score (Days)[4]	n (missing)	498 (541)	493 (553)	991 (1094)
	Mean (SD)	154.54 (34.35)	154.85 (33.07)	154.70 (33.70)
	Median	164.00	164.00	164.00
	Q1, Q3	161.00, 169.00	162.00, 169.00	161.00, 169.00
	Min, Max	4.00, 175.00	1.00, 175.00	1.00, 175.00
Observation Time for GIQ c) overall COVID-19-related (Days)[3]	n (missing)	1003 (36)	1015 (31)	2018 (67)
	Mean (SD)	26.08 (5.74)	25.57 (6.53)	25.83 (6.15)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	27.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for GIQ b) return to usual activities (Days)[3]	n (missing)	1003 (36)	1015 (31)	2018 (67)
	Mean (SD)	26.08 (5.74)	25.57 (6.53)	25.83 (6.15)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	27.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for GIQ a) return to usual health(Days)[3]	n (missing)	1003 (36)	1015 (31)	2018 (67)
	Mean (SD)	26.08 (5.74)	25.57 (6.53)	25.83 (6.15)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	27.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for WPAI-COVID-19 Question 6 (Days)[4]	n (missing)	483 (556)	479 (567)	962 (1123)
	Mean (SD)	157.79 (28.98)	157.04 (29.01)	157.42 (28.98)
	Median	164.00	164.00	164.00
	Q1, Q3	162.00, 169.00	162.00, 169.00	162.00, 169.00
	Min, Max	4.00, 175.00	12.00, 175.00	4.00, 175.00

N: Number of participants, n: Number of participants with non-missing values, SD: Standard Deviation, Q1: 25%-Quartile, Q3: 75%-Quartile, Min: Minimum, Max: Maximum

[1] date of first administration of study drug until death date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[2] date of first administration of study drug until hospitalization date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[3] date of first administration of study drug until date of last non-missing measurement through Day 28 + 1

[4] date of first administration of study drug until date of last non-missing measurement through Week 24 + 1

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 Analysis of Time to Death through Day 28

Final

	Nirmatrelvir/ritonavir (N=1039)	Placebo (N=1046)
Number of subjects with events, n (%)	0 (0.0)	12 (1.1)
Number of censored subjects, n (%)	1039 (100.0)	1034 (98.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	NE (NE, NE)	
p-value [3]	NE	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	NE (NE, NE)	
p-value [3]	NE	
Cumulative Proportion and Difference of the Proportions [4]		
Estimated Proportion (95% CI), %	0.000 (0.000, 0.000)	1.177 (0.670, 2.063)
Difference (SE)	-1.177 (0.338)	
95% CI	-1.839, -0.515	
p-value	<.001	

N: Number of subjects, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last known alive date, Day 28).

[1] Based on the Brookmeyer and Crowley Method.

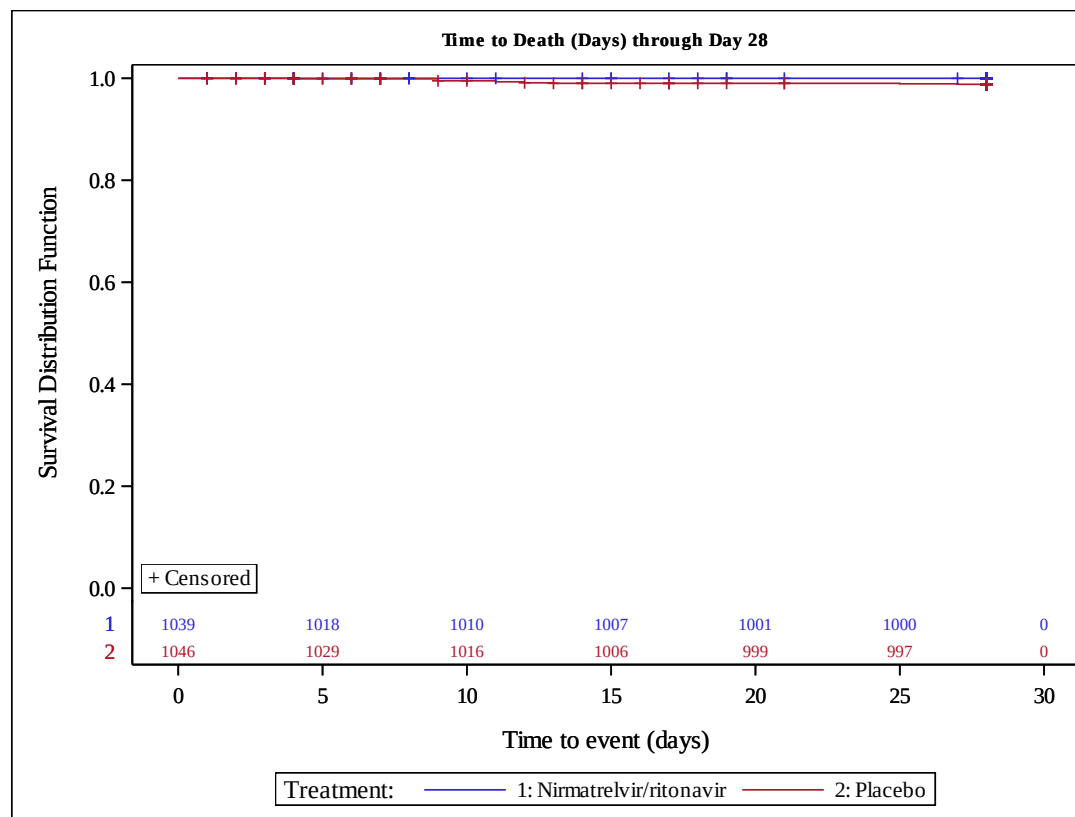
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

[4] The cumulative proportion was estimated using the Kaplan-Meier method. The difference of the proportions in the 2 treatment groups and its 95% confidence interval, and p-value based on Normal approximation.

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Kaplan-Meier Plot of Time to Death through Day 28

Final



Participants without event are censored at minimum(last known alive date, Day 28).
Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Death from any Cause through Day 28

Final

	Nirmatrelvir/ritonavir (N=1039)	Placebo (N=1046)
Number of subjects with Death, n (%)	0 (0.0)	12 (1.1)
Adjusted Analysis [1]		
Odds Ratio (95% CI)	NE (NE, NE)	
p-value	NE	
Relative Risk (95% CI)	NE (NE, NE)	
p-value	NE	
Risk Difference (95% CI)	NE (NE, NE)	
p-value	NE	
Unadjusted Analysis [2]		
Odds Ratio (95% CI)	0.040 (0.002, 0.673)	
p-value	0.025	
Relative Risk (95% CI)	0.040 (0.002, 0.679)	
p-value	0.026	
Risk Difference (95% CI)	-0.011 (-0.018, -0.005)	
p-value	<.001	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Death through Week 24

Final

	Nirmatrelvir/ritonavir (N=1039)	Placebo (N=1046)
Number of subjects with events, n (%)	0 (0.0)	15 (1.4)
Number of censored subjects, n (%)	1039 (100.0)	1031 (98.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	NE (NE, NE)	
p-value [3]	NE	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	NE (NE, NE)	
p-value [3]	NE	
Cumulative Proportion and Difference of the Proportions [4]		
Estimated Proportion (95% CI), %	0.000 (0.000, 0.000)	1.477 (0.893, 2.438)
Difference (SE)	-1.477 (0.378)	
95% CI	-2.218, -0.735	
p-value	<.001	

N: Number of subjects, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last known alive date, Week 24 = Day 168).

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

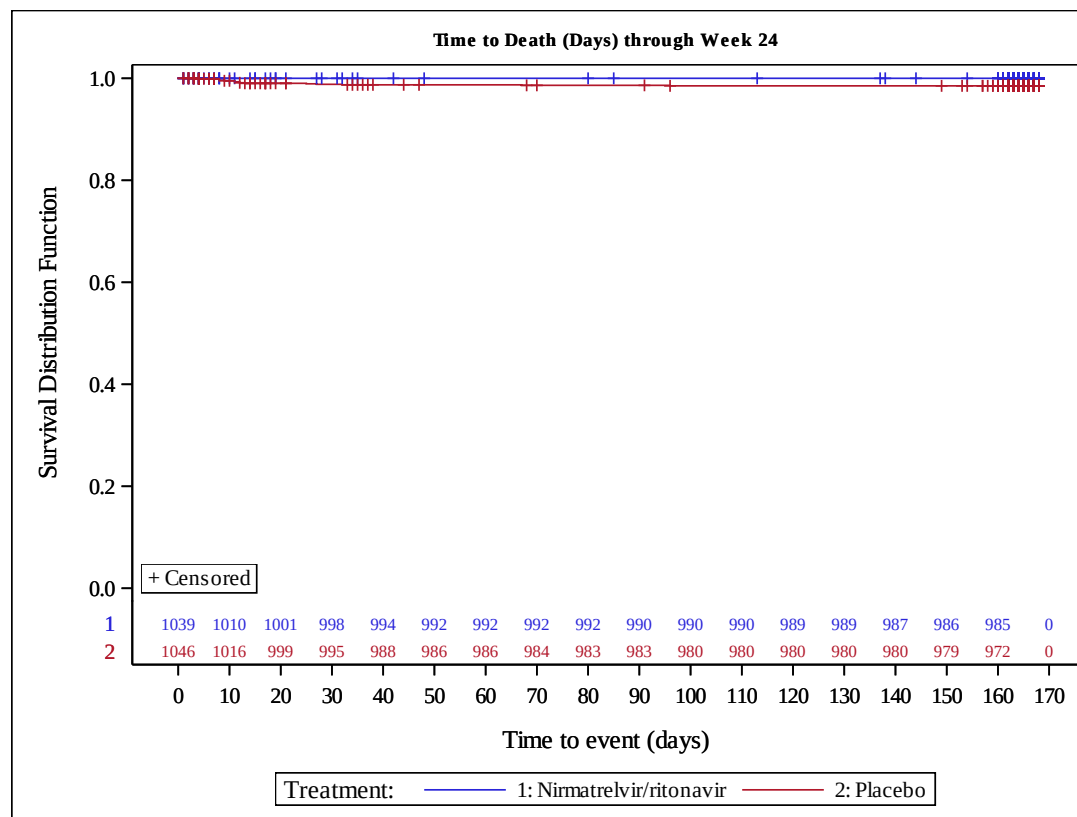
[3] Estimated by cox regression model assuming proportional hazards.

[4] The cumulative proportion was estimated using the Kaplan-Meier method. The difference of the proportions in the 2 treatment groups and its 95% confidence interval, and p-value based on Normal approximation.

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 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Death through Week 24

Final



Participants without event are censored at minimum(last known alive date, Week 24 = Day 168).
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Death from any Cause through Week 24

Final

	Nirmatrelvir/ritonavir (N=1039)	Placebo (N=1046)
Number of subjects with Death, n (%)	0 (0.0)	15 (1.4)
Adjusted Analysis [1]		
Odds Ratio (95% CI)	NE (NE, NE)	
p-value	NE	
Relative Risk (95% CI)	NE (NE, NE)	
p-value	NE	
Risk Difference (95% CI)	NE (NE, NE)	
p-value	NE	
Unadjusted Analysis [2]		
Odds Ratio (95% CI)	0.032 (0.002, 0.536)	
p-value	0.017	
Relative Risk (95% CI)	0.032 (0.002, 0.542)	
p-value	0.017	
Risk Difference (95% CI)	-0.014 (-0.022, -0.007)	
p-value	<.001	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Analysis of Number of COVID-19 related hospitalizations

Final

	Nirmatrelvir/ritonavir (N=1039)	Placebo (N=1046)
Number of subjects with at least one event	9	65
Number of events	9	66
Mean of events	0.009	0.063
Mean of events per day	0.0003	0.0027
Adjusted Analysis [1]		
LS mean (95% CI)	NE (NE, NE)	NE (NE, NE)
LS mean Ratio (95% CI)	NE (NE, NE)	
p-value	NE	
Unadjusted Analysis [2]		
LS mean (95% CI)	NE (NE, NE)	NE (NE, NE)
LS mean Ratio (95% CI)	NE (NE, NE)	
p-value	NE	

N: Number of participants, CI: Confidence Interval, NE: Not estimable, I: Infinity, LS: Least Squares

Medical Visits and Hospitalization events are limited through Day 34 visit. Number of events per day = Number of events/Number of days follow up limited to Day 37.

Stratification factors: geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[1] Negative binomial regression model includes main effects of treatment, stratification factors and the log number of days follow up as the participant offset variable.

[2] Negative binomial regression model includes main effects of treatment and the log number of days follow up as the participant offset variable.

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Final

Endpoint	Visit	Nirmatrelvir/ritonavir (N=1039)		Placebo (N=1046)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Stuffy or Runny Nose	Baseline	1039	972 (93.6)	1046	1005 (96.1)
	DAY 2	1039	951 (91.5)	1046	967 (92.4)
	DAY 3	1039	949 (91.3)	1046	955 (91.3)
	DAY 4	1039	932 (89.7)	1046	934 (89.3)
	DAY 5	1039	931 (89.6)	1045	922 (88.2)
	DAY 6	1039	867 (83.4)	1045	852 (81.5)
	DAY 7	1039	834 (80.3)	1045	829 (79.3)
	DAY 8	1039	842 (81.0)	1045	823 (78.8)
	DAY 9	1039	840 (80.8)	1045	828 (79.2)
	DAY 10	1039	832 (80.1)	1041	859 (82.5)
	DAY 11	1039	839 (80.8)	1041	850 (81.7)
	DAY 12	1039	844 (81.2)	1039	824 (79.3)
	DAY 13	1039	856 (82.4)	1037	844 (81.4)
	DAY 14	1039	854 (82.2)	1036	856 (82.6)
	DAY 15	1039	845 (81.3)	1036	853 (82.3)
	DAY 16	1039	850 (81.8)	1036	820 (79.2)
	DAY 17	1039	840 (80.8)	1036	825 (79.6)
	DAY 18	1039	829 (79.8)	1036	814 (78.6)
	DAY 19	1039	827 (79.6)	1036	842 (81.3)
	DAY 20	1039	820 (78.9)	1036	845 (81.6)
	DAY 21	1039	849 (81.7)	1036	834 (80.5)
	DAY 22	1039	840 (80.8)	1036	822 (79.3)
	DAY 23	1039	828 (79.7)	1036	804 (77.6)
	DAY 24	1039	816 (78.5)	1036	812 (78.4)
	DAY 25	1039	807 (77.7)	1036	817 (78.9)
	DAY 26	1039	807 (77.7)	1035	806 (77.9)
	DAY 27	1039	823 (79.2)	1035	817 (78.9)
	DAY 28	1039	795 (76.5)	1034	779 (75.3)
COVID-19 Signs and Symptoms: Sore Throat	Baseline	1039	972 (93.6)	1046	1005 (96.1)
	DAY 2	1039	951 (91.5)	1046	967 (92.4)
	DAY 3	1039	949 (91.3)	1046	955 (91.3)
	DAY 4	1039	932 (89.7)	1046	934 (89.3)
	DAY 5	1039	931 (89.6)	1045	922 (88.2)
	DAY 6	1039	867 (83.4)	1045	852 (81.5)
	DAY 7	1039	834 (80.3)	1045	829 (79.3)
	DAY 8	1039	842 (81.0)	1045	823 (78.8)
	DAY 9	1039	840 (80.8)	1045	828 (79.2)
	DAY 10	1039	832 (80.1)	1041	859 (82.5)
	DAY 11	1039	839 (80.8)	1041	850 (81.7)
	DAY 12	1039	844 (81.2)	1039	824 (79.3)
	DAY 13	1039	856 (82.4)	1037	844 (81.4)
	DAY 14	1039	854 (82.2)	1036	856 (82.6)
	DAY 15	1039	845 (81.3)	1036	853 (82.3)
	DAY 16	1039	850 (81.8)	1036	820 (79.2)
	DAY 17	1039	840 (80.8)	1036	825 (79.6)
	DAY 18	1039	829 (79.8)	1036	814 (78.6)
	DAY 19	1039	827 (79.6)	1036	842 (81.3)
	DAY 20	1039	820 (78.9)	1036	845 (81.6)
	DAY 21	1039	849 (81.7)	1036	834 (80.5)
	DAY 22	1039	840 (80.8)	1036	822 (79.3)
	DAY 23	1039	828 (79.7)	1036	804 (77.6)
	DAY 24	1039	816 (78.5)	1036	812 (78.4)
	DAY 25	1039	807 (77.7)	1036	817 (78.9)
	DAY 26	1039	807 (77.7)	1035	806 (77.9)
	DAY 27	1039	823 (79.2)	1035	817 (78.9)
	DAY 28	1039	795 (76.5)	1034	779 (75.3)

N: Number of participants, n: Number of participants with non missing values

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=1039)		Placebo (N=1046)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Shortness of Breath or Difficulty Breathing	Baseline	1039	972 (93.6)	1046	1005 (96.1)
	DAY 2	1039	951 (91.5)	1046	967 (92.4)
	DAY 3	1039	949 (91.3)	1046	955 (91.3)
	DAY 4	1039	932 (89.7)	1046	934 (89.3)
	DAY 5	1039	931 (89.6)	1045	922 (88.2)
	DAY 6	1039	867 (83.4)	1045	852 (81.5)
	DAY 7	1039	834 (80.3)	1045	829 (79.3)
	DAY 8	1039	842 (81.0)	1045	823 (78.8)
	DAY 9	1039	840 (80.8)	1045	828 (79.2)
	DAY 10	1039	832 (80.1)	1041	859 (82.5)
	DAY 11	1039	839 (80.8)	1041	850 (81.7)
	DAY 12	1039	844 (81.2)	1039	824 (79.3)
	DAY 13	1039	856 (82.4)	1037	844 (81.4)
	DAY 14	1039	854 (82.2)	1036	856 (82.6)
	DAY 15	1039	845 (81.3)	1036	853 (82.3)
	DAY 16	1039	850 (81.8)	1036	820 (79.2)
	DAY 17	1039	840 (80.8)	1036	825 (79.6)
	DAY 18	1039	829 (79.8)	1036	814 (78.6)
	DAY 19	1039	827 (79.6)	1036	842 (81.3)
	DAY 20	1039	820 (78.9)	1036	845 (81.6)
	DAY 21	1039	849 (81.7)	1036	834 (80.5)
	DAY 22	1039	840 (80.8)	1036	822 (79.3)
	DAY 23	1039	828 (79.7)	1036	804 (77.6)
	DAY 24	1039	816 (78.5)	1036	812 (78.4)
	DAY 25	1039	807 (77.7)	1036	817 (78.9)
	DAY 26	1039	807 (77.7)	1035	806 (77.9)
	DAY 27	1039	823 (79.2)	1035	817 (78.9)
	DAY 28	1039	795 (76.5)	1034	779 (75.3)
COVID-19 Signs and Symptoms: Cough	Baseline	1039	972 (93.6)	1046	1005 (96.1)
	DAY 2	1039	951 (91.5)	1046	967 (92.4)
	DAY 3	1039	949 (91.3)	1046	955 (91.3)
	DAY 4	1039	932 (89.7)	1046	934 (89.3)
	DAY 5	1039	931 (89.6)	1045	922 (88.2)
	DAY 6	1039	867 (83.4)	1045	852 (81.5)
	DAY 7	1039	834 (80.3)	1045	829 (79.3)
	DAY 8	1039	842 (81.0)	1045	823 (78.8)
	DAY 9	1039	840 (80.8)	1045	828 (79.2)
	DAY 10	1039	832 (80.1)	1041	859 (82.5)
	DAY 11	1039	839 (80.8)	1041	850 (81.7)
	DAY 12	1039	844 (81.2)	1039	824 (79.3)
	DAY 13	1039	856 (82.4)	1037	844 (81.4)
	DAY 14	1039	854 (82.2)	1036	856 (82.6)
	DAY 15	1039	845 (81.3)	1036	853 (82.3)
	DAY 16	1039	850 (81.8)	1036	820 (79.2)
	DAY 17	1039	840 (80.8)	1036	825 (79.6)
	DAY 18	1039	829 (79.8)	1036	814 (78.6)
	DAY 19	1039	827 (79.6)	1036	842 (81.3)
	DAY 20	1039	820 (78.9)	1036	845 (81.6)
	DAY 21	1039	849 (81.7)	1036	834 (80.5)
	DAY 22	1039	840 (80.8)	1036	822 (79.3)
	DAY 23	1039	828 (79.7)	1036	804 (77.6)
	DAY 24	1039	816 (78.5)	1036	812 (78.4)
	DAY 25	1039	807 (77.7)	1036	817 (78.9)
	DAY 26	1039	807 (77.7)	1035	806 (77.9)
	DAY 27	1039	823 (79.2)	1035	817 (78.9)
	DAY 28	1039	795 (76.5)	1034	779 (75.3)

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=1039)		Placebo (N=1046)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Low Energy or Tiredness	Baseline	1039	972 (93.6)	1046	1005 (96.1)
	DAY 2	1039	951 (91.5)	1046	967 (92.4)
	DAY 3	1039	949 (91.3)	1046	955 (91.3)
	DAY 4	1039	932 (89.7)	1046	934 (89.3)
	DAY 5	1039	931 (89.6)	1045	922 (88.2)
	DAY 6	1039	867 (83.4)	1045	852 (81.5)
	DAY 7	1039	834 (80.3)	1045	829 (79.3)
	DAY 8	1039	842 (81.0)	1045	823 (78.8)
	DAY 9	1039	840 (80.8)	1045	828 (79.2)
	DAY 10	1039	832 (80.1)	1041	859 (82.5)
	DAY 11	1039	839 (80.8)	1041	850 (81.7)
	DAY 12	1039	844 (81.2)	1039	824 (79.3)
	DAY 13	1039	856 (82.4)	1037	844 (81.4)
	DAY 14	1039	854 (82.2)	1036	856 (82.6)
	DAY 15	1039	845 (81.3)	1036	853 (82.3)
	DAY 16	1039	850 (81.8)	1036	820 (79.2)
	DAY 17	1039	840 (80.8)	1036	825 (79.6)
	DAY 18	1039	829 (79.8)	1036	814 (78.6)
	DAY 19	1039	827 (79.6)	1036	842 (81.3)
	DAY 20	1039	820 (78.9)	1036	845 (81.6)
	DAY 21	1039	849 (81.7)	1036	834 (80.5)
	DAY 22	1039	840 (80.8)	1036	822 (79.3)
	DAY 23	1039	828 (79.7)	1036	804 (77.6)
	DAY 24	1039	816 (78.5)	1036	812 (78.4)
	DAY 25	1039	807 (77.7)	1036	817 (78.9)
	DAY 26	1039	807 (77.7)	1035	806 (77.9)
	DAY 27	1039	823 (79.2)	1035	817 (78.9)
	DAY 28	1039	795 (76.5)	1034	779 (75.3)
COVID-19 Signs and Symptoms: Muscle or Body Aches	Baseline	1039	972 (93.6)	1046	1005 (96.1)
	DAY 2	1039	951 (91.5)	1046	967 (92.4)
	DAY 3	1039	949 (91.3)	1046	955 (91.3)
	DAY 4	1039	932 (89.7)	1046	934 (89.3)
	DAY 5	1039	931 (89.6)	1045	922 (88.2)
	DAY 6	1039	867 (83.4)	1045	852 (81.5)
	DAY 7	1039	834 (80.3)	1045	829 (79.3)
	DAY 8	1039	842 (81.0)	1045	823 (78.8)
	DAY 9	1039	840 (80.8)	1045	828 (79.2)
	DAY 10	1039	832 (80.1)	1041	859 (82.5)
	DAY 11	1039	839 (80.8)	1041	850 (81.7)
	DAY 12	1039	844 (81.2)	1039	824 (79.3)
	DAY 13	1039	856 (82.4)	1037	844 (81.4)
	DAY 14	1039	854 (82.2)	1036	856 (82.6)
	DAY 15	1039	845 (81.3)	1036	853 (82.3)
	DAY 16	1039	850 (81.8)	1036	820 (79.2)
	DAY 17	1039	840 (80.8)	1036	825 (79.6)
	DAY 18	1039	829 (79.8)	1036	814 (78.6)
	DAY 19	1039	827 (79.6)	1036	842 (81.3)
	DAY 20	1039	820 (78.9)	1036	845 (81.6)
	DAY 21	1039	849 (81.7)	1036	834 (80.5)
	DAY 22	1039	840 (80.8)	1036	822 (79.3)
	DAY 23	1039	828 (79.7)	1036	804 (77.6)
	DAY 24	1039	816 (78.5)	1036	812 (78.4)
	DAY 25	1039	807 (77.7)	1036	817 (78.9)
	DAY 26	1039	807 (77.7)	1035	806 (77.9)
	DAY 27	1039	823 (79.2)	1035	817 (78.9)
	DAY 28	1039	795 (76.5)	1034	779 (75.3)

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=1039)		Placebo (N=1046)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Headache	Baseline	1039	972 (93.6)	1046	1005 (96.1)
	DAY 2	1039	951 (91.5)	1046	967 (92.4)
	DAY 3	1039	949 (91.3)	1046	955 (91.3)
	DAY 4	1039	932 (89.7)	1046	934 (89.3)
	DAY 5	1039	931 (89.6)	1045	922 (88.2)
	DAY 6	1039	867 (83.4)	1045	852 (81.5)
	DAY 7	1039	834 (80.3)	1045	829 (79.3)
	DAY 8	1039	842 (81.0)	1045	823 (78.8)
	DAY 9	1039	840 (80.8)	1045	828 (79.2)
	DAY 10	1039	832 (80.1)	1041	859 (82.5)
	DAY 11	1039	839 (80.8)	1041	850 (81.7)
	DAY 12	1039	844 (81.2)	1039	824 (79.3)
	DAY 13	1039	856 (82.4)	1037	844 (81.4)
	DAY 14	1039	854 (82.2)	1036	856 (82.6)
	DAY 15	1039	845 (81.3)	1036	853 (82.3)
	DAY 16	1039	850 (81.8)	1036	820 (79.2)
	DAY 17	1039	840 (80.8)	1036	825 (79.6)
	DAY 18	1039	829 (79.8)	1036	814 (78.6)
	DAY 19	1039	827 (79.6)	1036	842 (81.3)
	DAY 20	1039	820 (78.9)	1036	845 (81.6)
	DAY 21	1039	849 (81.7)	1036	834 (80.5)
	DAY 22	1039	840 (80.8)	1036	822 (79.3)
	DAY 23	1039	828 (79.7)	1036	804 (77.6)
	DAY 24	1039	816 (78.5)	1036	812 (78.4)
	DAY 25	1039	807 (77.7)	1036	817 (78.9)
	DAY 26	1039	807 (77.7)	1035	806 (77.9)
	DAY 27	1039	823 (79.2)	1035	817 (78.9)
	DAY 28	1039	795 (76.5)	1034	779 (75.3)
COVID-19 Signs and Symptoms: Chills or Shivering	Baseline	1039	972 (93.6)	1046	1005 (96.1)
	DAY 2	1039	951 (91.5)	1046	967 (92.4)
	DAY 3	1039	949 (91.3)	1046	955 (91.3)
	DAY 4	1039	932 (89.7)	1046	934 (89.3)
	DAY 5	1039	931 (89.6)	1045	922 (88.2)
	DAY 6	1039	867 (83.4)	1045	852 (81.5)
	DAY 7	1039	834 (80.3)	1045	829 (79.3)
	DAY 8	1039	842 (81.0)	1045	823 (78.8)
	DAY 9	1039	840 (80.8)	1045	828 (79.2)
	DAY 10	1039	832 (80.1)	1041	859 (82.5)
	DAY 11	1039	839 (80.8)	1041	850 (81.7)
	DAY 12	1039	844 (81.2)	1039	824 (79.3)
	DAY 13	1039	856 (82.4)	1037	844 (81.4)
	DAY 14	1039	854 (82.2)	1036	856 (82.6)
	DAY 15	1039	845 (81.3)	1036	853 (82.3)
	DAY 16	1039	850 (81.8)	1036	820 (79.2)
	DAY 17	1039	840 (80.8)	1036	825 (79.6)
	DAY 18	1039	829 (79.8)	1036	814 (78.6)
	DAY 19	1039	827 (79.6)	1036	842 (81.3)
	DAY 20	1039	820 (78.9)	1036	845 (81.6)
	DAY 21	1039	849 (81.7)	1036	834 (80.5)
	DAY 22	1039	840 (80.8)	1036	822 (79.3)
	DAY 23	1039	828 (79.7)	1036	804 (77.6)
	DAY 24	1039	816 (78.5)	1036	812 (78.4)
	DAY 25	1039	807 (77.7)	1036	817 (78.9)
	DAY 26	1039	807 (77.7)	1035	806 (77.9)
	DAY 27	1039	823 (79.2)	1035	817 (78.9)
	DAY 28	1039	795 (76.5)	1034	779 (75.3)

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=1039)		Placebo (N=1046)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Feeling Hot or Feverish	Baseline	1039	972 (93.6)	1046	1005 (96.1)
	DAY 2	1039	951 (91.5)	1046	967 (92.4)
	DAY 3	1039	949 (91.3)	1046	955 (91.3)
	DAY 4	1039	932 (89.7)	1046	934 (89.3)
	DAY 5	1039	931 (89.6)	1045	922 (88.2)
	DAY 6	1039	867 (83.4)	1045	852 (81.5)
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	DAY 9	1039	840 (80.8)	1045	828 (79.2)
	DAY 10	1039	832 (80.1)	1041	859 (82.5)
	DAY 11	1039	839 (80.8)	1041	850 (81.7)
	DAY 12	1039	844 (81.2)	1039	824 (79.3)
	DAY 13	1039	856 (82.4)	1037	844 (81.4)
	DAY 14	1039	854 (82.2)	1036	856 (82.6)
	DAY 15	1039	845 (81.3)	1036	853 (82.3)
	DAY 16	1039	850 (81.8)	1036	820 (79.2)
	DAY 17	1039	840 (80.8)	1036	825 (79.6)
	DAY 18	1039	829 (79.8)	1036	814 (78.6)
	DAY 19	1039	827 (79.6)	1036	842 (81.3)
	DAY 20	1039	820 (78.9)	1036	845 (81.6)
	DAY 21	1039	849 (81.7)	1036	834 (80.5)
	DAY 22	1039	840 (80.8)	1036	822 (79.3)
	DAY 23	1039	828 (79.7)	1036	804 (77.6)
	DAY 24	1039	816 (78.5)	1036	812 (78.4)
	DAY 25	1039	807 (77.7)	1036	817 (78.9)
	DAY 26	1039	807 (77.7)	1035	806 (77.9)
	DAY 27	1039	823 (79.2)	1035	817 (78.9)
	DAY 28	1039	795 (76.5)	1034	779 (75.3)
COVID-19 Signs and Symptoms: Nausea	Baseline	1039	972 (93.6)	1046	1005 (96.1)
	DAY 2	1039	951 (91.5)	1046	967 (92.4)
	DAY 3	1039	949 (91.3)	1046	955 (91.3)
	DAY 4	1039	932 (89.7)	1046	934 (89.3)
	DAY 5	1039	931 (89.6)	1045	922 (88.2)
	DAY 6	1039	867 (83.4)	1045	852 (81.5)
	DAY 7	1039	834 (80.3)	1045	829 (79.3)
	DAY 8	1039	842 (81.0)	1045	823 (78.8)
	DAY 9	1039	840 (80.8)	1045	828 (79.2)
	DAY 10	1039	832 (80.1)	1041	859 (82.5)
	DAY 11	1039	839 (80.8)	1041	850 (81.7)
	DAY 12	1039	844 (81.2)	1039	824 (79.3)
	DAY 13	1039	856 (82.4)	1037	844 (81.4)
	DAY 14	1039	854 (82.2)	1036	856 (82.6)
	DAY 15	1039	845 (81.3)	1036	853 (82.3)
	DAY 16	1039	850 (81.8)	1036	820 (79.2)
	DAY 17	1039	840 (80.8)	1036	825 (79.6)
	DAY 18	1039	829 (79.8)	1036	814 (78.6)
	DAY 19	1039	827 (79.6)	1036	842 (81.3)
	DAY 20	1039	820 (78.9)	1036	845 (81.6)
	DAY 21	1039	849 (81.7)	1036	834 (80.5)
	DAY 22	1039	840 (80.8)	1036	822 (79.3)
	DAY 23	1039	828 (79.7)	1036	804 (77.6)
	DAY 24	1039	816 (78.5)	1036	812 (78.4)
	DAY 25	1039	807 (77.7)	1036	817 (78.9)
	DAY 26	1039	807 (77.7)	1035	806 (77.9)
	DAY 27	1039	823 (79.2)	1035	817 (78.9)
	DAY 28	1039	795 (76.5)	1034	779 (75.3)

N: Number of participants, n: Number of participants with non missing values

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=1039)		Placebo (N=1046)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Vomit	Baseline	1039	972 (93.6)	1046	1005 (96.1)
	DAY 2	1039	951 (91.5)	1046	967 (92.4)
	DAY 3	1039	949 (91.3)	1046	955 (91.3)
	DAY 4	1039	932 (89.7)	1046	934 (89.3)
	DAY 5	1039	931 (89.6)	1045	922 (88.2)
	DAY 6	1039	867 (83.4)	1045	852 (81.5)
	DAY 7	1039	834 (80.3)	1045	829 (79.3)
	DAY 8	1039	842 (81.0)	1045	823 (78.8)
	DAY 9	1039	840 (80.8)	1045	828 (79.2)
	DAY 10	1039	832 (80.1)	1041	859 (82.5)
	DAY 11	1039	839 (80.8)	1041	850 (81.7)
	DAY 12	1039	844 (81.2)	1039	824 (79.3)
	DAY 13	1039	856 (82.4)	1037	844 (81.4)
	DAY 14	1039	854 (82.2)	1036	856 (82.6)
	DAY 15	1039	845 (81.3)	1036	853 (82.3)
	DAY 16	1039	850 (81.8)	1036	820 (79.2)
	DAY 17	1039	840 (80.8)	1036	825 (79.6)
	DAY 18	1039	829 (79.8)	1036	814 (78.6)
	DAY 19	1039	827 (79.6)	1036	842 (81.3)
	DAY 20	1039	820 (78.9)	1036	845 (81.6)
	DAY 21	1039	849 (81.7)	1036	834 (80.5)
	DAY 22	1039	840 (80.8)	1036	822 (79.3)
	DAY 23	1039	828 (79.7)	1036	804 (77.6)
	DAY 24	1039	816 (78.5)	1036	812 (78.4)
	DAY 25	1039	807 (77.7)	1036	817 (78.9)
	DAY 26	1039	807 (77.7)	1035	806 (77.9)
	DAY 27	1039	823 (79.2)	1035	817 (78.9)
	DAY 28	1039	795 (76.5)	1034	779 (75.3)
COVID-19 Signs and Symptoms: Diarrhea	Baseline	1039	972 (93.6)	1046	1005 (96.1)
	DAY 2	1039	951 (91.5)	1046	967 (92.4)
	DAY 3	1039	949 (91.3)	1046	955 (91.3)
	DAY 4	1039	932 (89.7)	1046	934 (89.3)
	DAY 5	1039	931 (89.6)	1045	922 (88.2)
	DAY 6	1039	867 (83.4)	1045	852 (81.5)
	DAY 7	1039	834 (80.3)	1045	829 (79.3)
	DAY 8	1039	842 (81.0)	1045	823 (78.8)
	DAY 9	1039	840 (80.8)	1045	828 (79.2)
	DAY 10	1039	832 (80.1)	1041	859 (82.5)
	DAY 11	1039	839 (80.8)	1041	850 (81.7)
	DAY 12	1039	844 (81.2)	1039	824 (79.3)
	DAY 13	1039	856 (82.4)	1037	844 (81.4)
	DAY 14	1039	854 (82.2)	1036	856 (82.6)
	DAY 15	1039	845 (81.3)	1036	853 (82.3)
	DAY 16	1039	850 (81.8)	1036	820 (79.2)
	DAY 17	1039	840 (80.8)	1036	825 (79.6)
	DAY 18	1039	829 (79.8)	1036	814 (78.6)
	DAY 19	1039	827 (79.6)	1036	842 (81.3)
	DAY 20	1039	820 (78.9)	1036	845 (81.6)
	DAY 21	1039	849 (81.7)	1036	834 (80.5)
	DAY 22	1039	840 (80.8)	1036	822 (79.3)
	DAY 23	1039	828 (79.7)	1036	804 (77.6)
	DAY 24	1039	816 (78.5)	1036	812 (78.4)
	DAY 25	1039	807 (77.7)	1036	817 (78.9)
	DAY 26	1039	807 (77.7)	1035	806 (77.9)
	DAY 27	1039	823 (79.2)	1035	817 (78.9)
	DAY 28	1039	795 (76.5)	1034	779 (75.3)

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=1039)		Placebo (N=1046)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Sense of Smell	Baseline	1039	972 (93.6)	1046	1005 (96.1)
	DAY 2	1039	951 (91.5)	1046	967 (92.4)
	DAY 3	1039	949 (91.3)	1046	955 (91.3)
	DAY 4	1039	932 (89.7)	1046	934 (89.3)
	DAY 5	1039	931 (89.6)	1045	922 (88.2)
	DAY 6	1039	867 (83.4)	1045	852 (81.5)
	DAY 7	1039	834 (80.3)	1045	829 (79.3)
	DAY 8	1039	842 (81.0)	1045	823 (78.8)
	DAY 9	1039	840 (80.8)	1045	828 (79.2)
	DAY 10	1039	832 (80.1)	1041	859 (82.5)
	DAY 11	1039	839 (80.8)	1041	850 (81.7)
	DAY 12	1039	844 (81.2)	1039	824 (79.3)
	DAY 13	1039	856 (82.4)	1037	844 (81.4)
	DAY 14	1039	854 (82.2)	1036	856 (82.6)
	DAY 15	1039	845 (81.3)	1036	853 (82.3)
	DAY 16	1039	850 (81.8)	1036	820 (79.2)
	DAY 17	1039	840 (80.8)	1036	825 (79.6)
	DAY 18	1039	829 (79.8)	1036	814 (78.6)
	DAY 19	1039	827 (79.6)	1036	842 (81.3)
	DAY 20	1039	820 (78.9)	1036	845 (81.6)
	DAY 21	1039	849 (81.7)	1036	834 (80.5)
	DAY 22	1039	840 (80.8)	1036	822 (79.3)
	DAY 23	1039	828 (79.7)	1036	804 (77.6)
	DAY 24	1039	816 (78.5)	1036	812 (78.4)
	DAY 25	1039	807 (77.7)	1036	817 (78.9)
	DAY 26	1039	807 (77.7)	1035	806 (77.9)
	DAY 27	1039	823 (79.2)	1035	817 (78.9)
	DAY 28	1039	795 (76.5)	1034	779 (75.3)
COVID-19 Signs and Symptoms: Sense of Taste	Baseline	1039	972 (93.6)	1046	1005 (96.1)
	DAY 2	1039	951 (91.5)	1046	967 (92.4)
	DAY 3	1039	949 (91.3)	1046	955 (91.3)
	DAY 4	1039	932 (89.7)	1046	934 (89.3)
	DAY 5	1039	931 (89.6)	1045	922 (88.2)
	DAY 6	1039	867 (83.4)	1045	852 (81.5)
	DAY 7	1039	834 (80.3)	1045	829 (79.3)
	DAY 8	1039	842 (81.0)	1045	823 (78.8)
	DAY 9	1039	840 (80.8)	1045	828 (79.2)
	DAY 10	1039	832 (80.1)	1041	859 (82.5)
	DAY 11	1039	839 (80.8)	1041	850 (81.7)
	DAY 12	1039	844 (81.2)	1039	824 (79.3)
	DAY 13	1039	856 (82.4)	1037	844 (81.4)
	DAY 14	1039	854 (82.2)	1036	856 (82.6)
	DAY 15	1039	845 (81.3)	1036	853 (82.3)
	DAY 16	1039	850 (81.8)	1036	820 (79.2)
	DAY 17	1039	840 (80.8)	1036	825 (79.6)
	DAY 18	1039	829 (79.8)	1036	814 (78.6)
	DAY 19	1039	827 (79.6)	1036	842 (81.3)
	DAY 20	1039	820 (78.9)	1036	845 (81.6)
	DAY 21	1039	849 (81.7)	1036	834 (80.5)
	DAY 22	1039	840 (80.8)	1036	822 (79.3)
	DAY 23	1039	828 (79.7)	1036	804 (77.6)
	DAY 24	1039	816 (78.5)	1036	812 (78.4)
	DAY 25	1039	807 (77.7)	1036	817 (78.9)
	DAY 26	1039	807 (77.7)	1035	806 (77.9)
	DAY 27	1039	823 (79.2)	1035	817 (78.9)
	DAY 28	1039	795 (76.5)	1034	779 (75.3)

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=1039)		Placebo (N=1046)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
5-level European Quality of Life Five Dimension (EQ-5D-5L): EQ-VAS Score	Day 1	1039	33 (3.2)	1046	37 (3.5)
	Day 5	1039	37 (3.6)	1045	42 (4.0)
	Day 14	1039	56 (5.4)	1036	68 (6.6)
	Day 34	1039	107 (10.3)	1033	113 (10.9)
	Week 12	1039	208 (20.0)	1032	212 (20.5)
	Week 24	1039	444 (42.7)	1031	438 (42.5)
Global Impression Questionnaire: return to usual health	Baseline	1039	954 (91.8)	1046	985 (94.2)
	DAY 2	1039	930 (89.5)	1046	948 (90.6)
	DAY 3	1039	929 (89.4)	1046	937 (89.6)
	DAY 4	1039	911 (87.7)	1046	916 (87.6)
	DAY 5	1039	910 (87.6)	1045	904 (86.5)
	DAY 6	1039	848 (81.6)	1045	833 (79.7)
	DAY 7	1039	817 (78.6)	1045	813 (77.8)
	DAY 8	1039	826 (79.5)	1045	809 (77.4)
	DAY 9	1039	824 (79.3)	1045	812 (77.7)
	DAY 10	1039	815 (78.4)	1041	843 (81.0)
	DAY 11	1039	825 (79.4)	1041	833 (80.0)
	DAY 12	1039	825 (79.4)	1039	807 (77.7)
	DAY 13	1039	839 (80.8)	1037	828 (79.8)
	DAY 14	1039	838 (80.7)	1036	839 (81.0)
	DAY 15	1039	826 (79.5)	1036	834 (80.5)
	DAY 16	1039	835 (80.4)	1036	805 (77.7)
	DAY 17	1039	824 (79.3)	1036	808 (78.0)
	DAY 18	1039	811 (78.1)	1036	797 (76.9)
	DAY 19	1039	810 (78.0)	1036	824 (79.5)
	DAY 20	1039	804 (77.4)	1036	828 (79.9)
	DAY 21	1039	831 (80.0)	1036	816 (78.8)
	DAY 22	1039	819 (78.8)	1036	805 (77.7)
	DAY 23	1039	809 (77.9)	1036	786 (75.9)
	DAY 24	1039	798 (76.8)	1036	795 (76.7)
	DAY 25	1039	791 (76.1)	1036	799 (77.1)
	DAY 26	1039	789 (75.9)	1035	789 (76.2)
	DAY 27	1039	803 (77.3)	1035	798 (77.1)
	DAY 28	1039	777 (74.8)	1034	761 (73.6)

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=1039)		Placebo (N=1046)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
Global Impression Questionnaire: overall COVID-19-related symptoms	Baseline	1039	954 (91.8)	1046	985 (94.2)
	DAY 2	1039	930 (89.5)	1046	948 (90.6)
	DAY 3	1039	929 (89.4)	1046	937 (89.6)
	DAY 4	1039	911 (87.7)	1046	916 (87.6)
	DAY 5	1039	910 (87.6)	1045	904 (86.5)
	DAY 6	1039	848 (81.6)	1045	833 (79.7)
	DAY 7	1039	817 (78.6)	1045	813 (77.8)
	DAY 8	1039	826 (79.5)	1045	809 (77.4)
	DAY 9	1039	824 (79.3)	1045	812 (77.7)
	DAY 10	1039	815 (78.4)	1041	843 (81.0)
	DAY 11	1039	825 (79.4)	1041	833 (80.0)
	DAY 12	1039	825 (79.4)	1039	807 (77.7)
	DAY 13	1039	839 (80.8)	1037	828 (79.8)
	DAY 14	1039	838 (80.7)	1036	839 (81.0)
	DAY 15	1039	826 (79.5)	1036	834 (80.5)
	DAY 16	1039	835 (80.4)	1036	805 (77.7)
	DAY 17	1039	824 (79.3)	1036	808 (78.0)
	DAY 18	1039	811 (78.1)	1036	797 (76.9)
	DAY 19	1039	810 (78.0)	1036	824 (79.5)
	DAY 20	1039	804 (77.4)	1036	828 (79.9)
	DAY 21	1039	831 (80.0)	1036	816 (78.8)
	DAY 22	1039	819 (78.8)	1036	805 (77.7)
	DAY 23	1039	809 (77.9)	1036	786 (75.9)
	DAY 24	1039	798 (76.8)	1036	795 (76.7)
	DAY 25	1039	791 (76.1)	1036	799 (77.1)
	DAY 26	1039	789 (75.9)	1035	789 (76.2)
	DAY 27	1039	803 (77.3)	1035	798 (77.1)
	DAY 28	1039	777 (74.8)	1034	761 (73.6)
Global Impression Questionnaire: return to usual activities	Baseline	1039	954 (91.8)	1046	985 (94.2)
	DAY 2	1039	930 (89.5)	1046	948 (90.6)
	DAY 3	1039	929 (89.4)	1046	937 (89.6)
	DAY 4	1039	911 (87.7)	1046	916 (87.6)
	DAY 5	1039	910 (87.6)	1045	904 (86.5)
	DAY 6	1039	848 (81.6)	1045	833 (79.7)
	DAY 7	1039	817 (78.6)	1045	813 (77.8)
	DAY 8	1039	826 (79.5)	1045	809 (77.4)
	DAY 9	1039	824 (79.3)	1045	812 (77.7)
	DAY 10	1039	815 (78.4)	1041	843 (81.0)
	DAY 11	1039	825 (79.4)	1041	833 (80.0)
	DAY 12	1039	825 (79.4)	1039	807 (77.7)
	DAY 13	1039	839 (80.8)	1037	828 (79.8)
	DAY 14	1039	838 (80.7)	1036	839 (81.0)
	DAY 15	1039	826 (79.5)	1036	834 (80.5)
	DAY 16	1039	835 (80.4)	1036	805 (77.7)
	DAY 17	1039	824 (79.3)	1036	808 (78.0)
	DAY 18	1039	811 (78.1)	1036	797 (76.9)
	DAY 19	1039	810 (78.0)	1036	824 (79.5)
	DAY 20	1039	804 (77.4)	1036	828 (79.9)
	DAY 21	1039	831 (80.0)	1036	816 (78.8)
	DAY 22	1039	819 (78.8)	1036	805 (77.7)
	DAY 23	1039	809 (77.9)	1036	786 (75.9)
	DAY 24	1039	798 (76.8)	1036	795 (76.7)
	DAY 25	1039	791 (76.1)	1036	799 (77.1)
	DAY 26	1039	789 (75.9)	1035	789 (76.2)
	DAY 27	1039	803 (77.3)	1035	798 (77.1)
	DAY 28	1039	777 (74.8)	1034	761 (73.6)

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Final

Endpoint	Visit	Nirmatrelvir/ritonavir (N=1039)		Placebo (N=1046)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
Work Productivity and Activity Impairment (WPAI): WPAI Question 6	Baseline (Day 5)	1039	34 (3.3)	1045	41 (3.9)
	Day 14	1039	55 (5.3)	1036	67 (6.5)
	Week 12	1039	206 (19.8)	1032	209 (20.3)
	Week 24	1039	443 (42.6)	1031	433 (42.0)

N: Number of participants, n: Number of participants with non missing values

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 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Stuffy or Runny Nose

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	227 (22.1)	254 (24.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.881 (0.712, 1.089) 0.241	
Relative Risk (95% CI)	0.905 (0.771, 1.061) 0.219	
Risk Difference (95% CI)	-0.019 (-0.053, 0.016) 0.292	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.876 (0.714, 1.074) 0.203	
Relative Risk (95% CI)	0.903 (0.772, 1.057) 0.204	
Risk Difference (95% CI)	-0.024 (-0.060, 0.013) 0.203	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Stuffy or Runny Nose

Final

	Nirmatrelvir/ritonavir (N=719)	Placebo (N=704)
Number of subjects with events, n (%)	630 (87.6)	558 (79.3)
Number of censored subjects, n (%)	89 (12.4)	146 (20.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	6.0 (5.0, 6.0)	7.0 (7.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.346 (1.196, 1.514)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.332 (1.188, 1.493)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

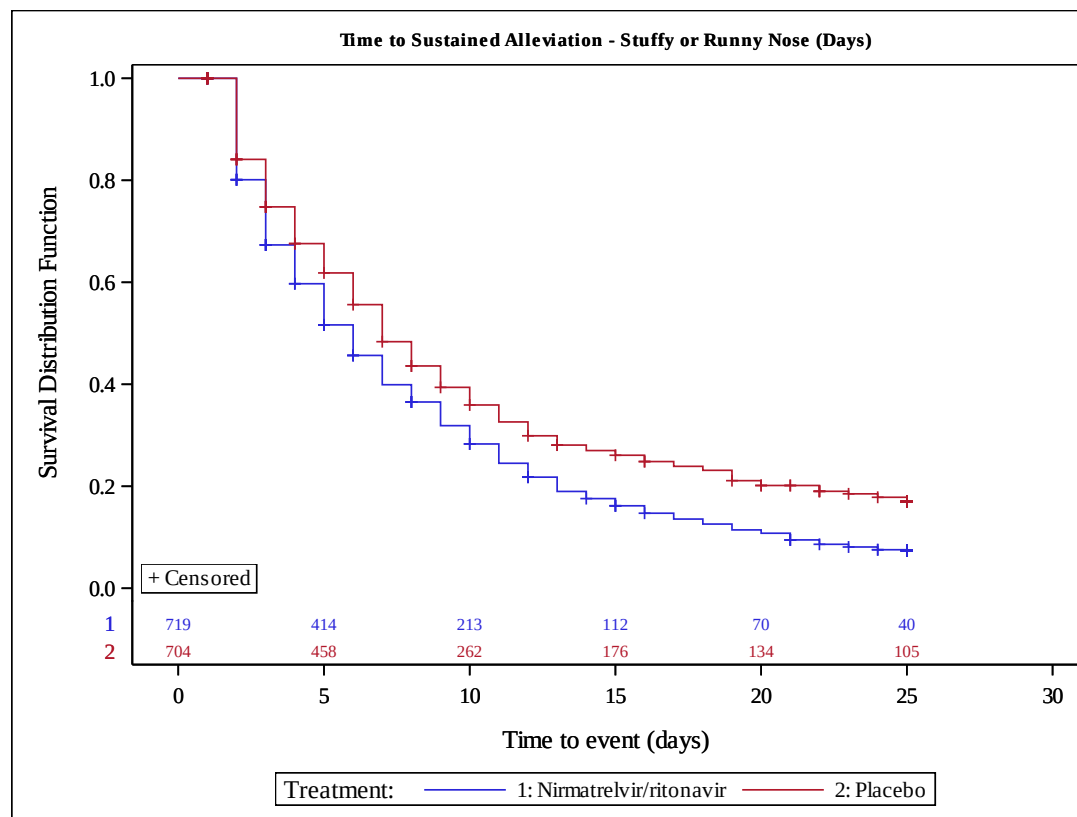
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Stuffy or Runny Nose

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final

	Nirmatrelvir/ritonavir (N=31)	Placebo (N=32)
Number of subjects with events, n (%)	28 (90.3)	28 (87.5)
Number of censored subjects, n (%)	3 (9.7)	4 (12.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (3.0, 10.0)	8.0 (4.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.070 (0.589, 1.943)	
p-value [3]	0.823	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.107 (0.649, 1.889)	
p-value [3]	0.709	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

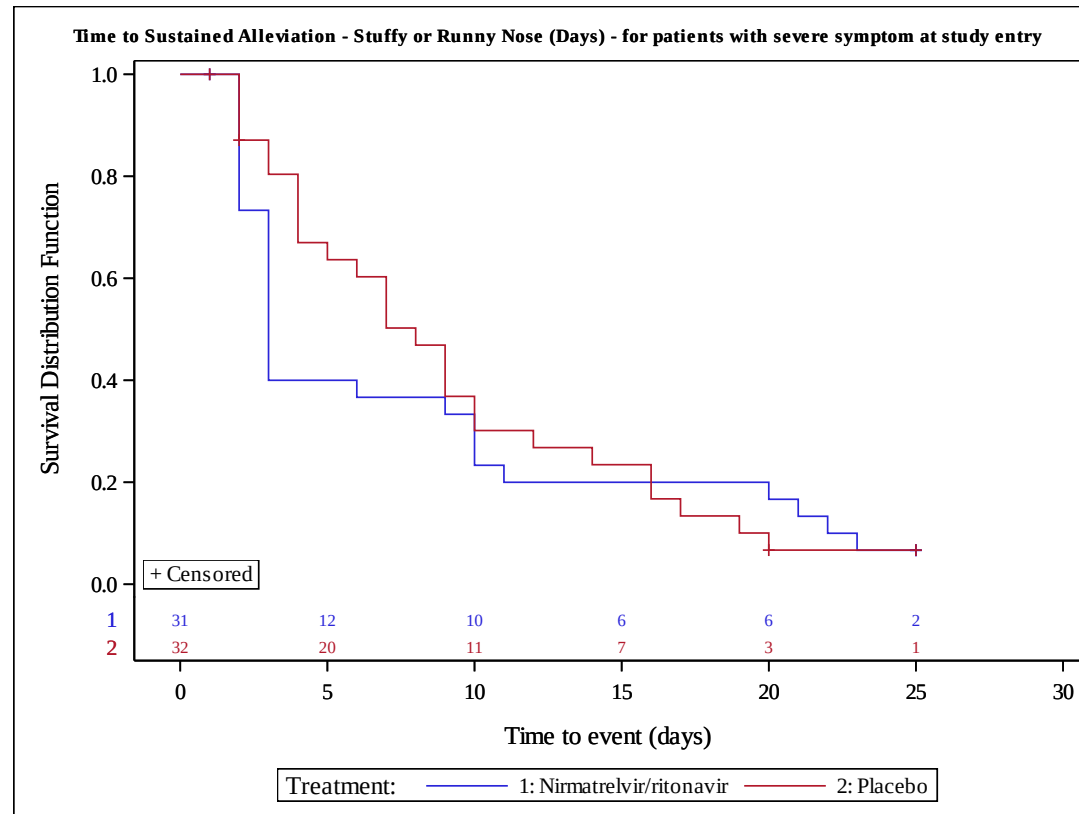
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Stuffy or Runny Nose

Final

	Nirmatrelvir/ritonavir (N=719)	Placebo (N=704)
Number of subjects with events, n (%)	577 (80.3)	502 (71.3)
Number of censored subjects, n (%)	142 (19.7)	202 (28.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	9.0 (9.0, 10.0)	10.0 (9.0, 11.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.339 (1.184, 1.514)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.314 (1.165, 1.481)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

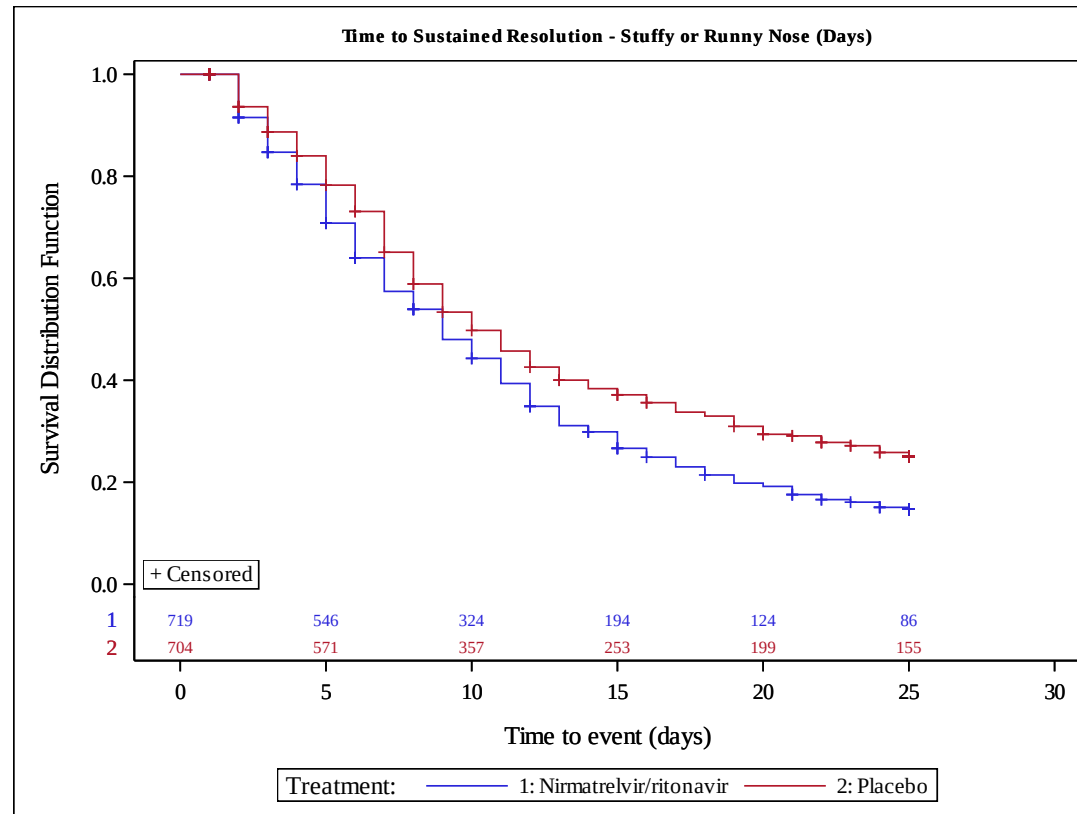
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Stuffy or Runny Nose

Final

	Nirmatrelvir/ritonavir (N=31)	Placebo (N=32)
Number of subjects with events, n (%)	21 (67.7)	20 (62.5)
Number of censored subjects, n (%)	10 (32.3)	12 (37.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	12.0 (7.0, 21.0)	17.0 (10.0, 24.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.163 (0.584, 2.318)	
p-value [3]	0.667	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.242 (0.672, 2.293)	
p-value [3]	0.489	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

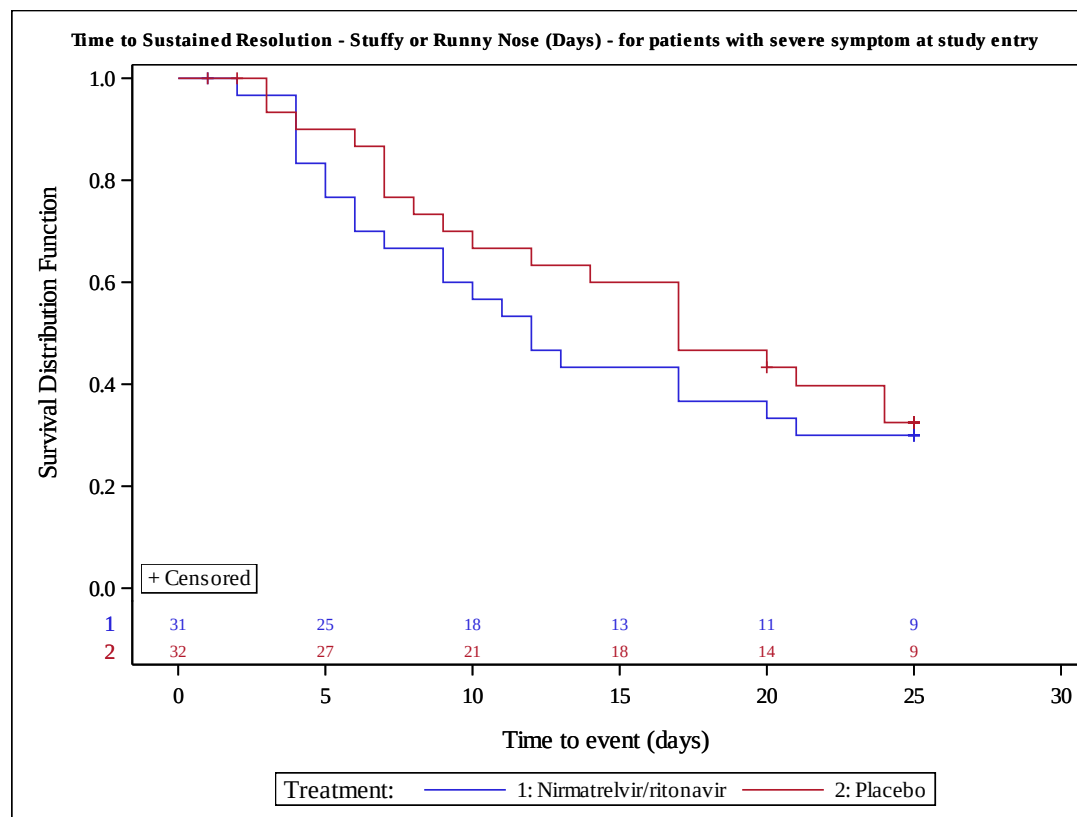
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Sore Throat

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	205 (20.0)	240 (23.1)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.813 (0.655, 1.009) 0.060	
Relative Risk (95% CI)	0.852 (0.721, 1.007) 0.061	
Risk Difference (95% CI)	-0.027 (-0.062, 0.007) 0.124	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.829 (0.672, 1.023) 0.081	
Relative Risk (95% CI)	0.863 (0.732, 1.018) 0.081	
Risk Difference (95% CI)	-0.032 (-0.067, 0.004) 0.080	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Final

	Nirmatrelvir/ritonavir (N=573)	Placebo (N=579)
Number of subjects with events, n (%)	503 (87.8)	464 (80.1)
Number of censored subjects, n (%)	70 (12.2)	115 (19.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 5.0)	6.0 (5.0, 7.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.345 (1.181, 1.532)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.326 (1.168, 1.506)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

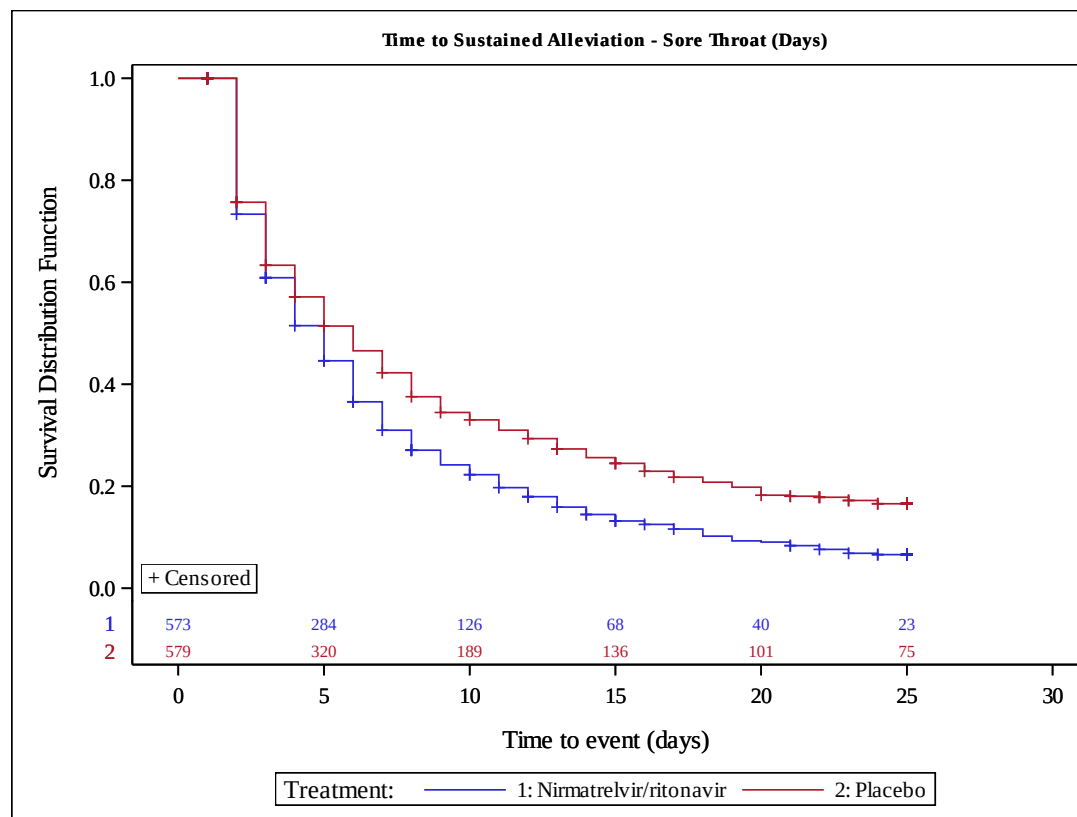
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Sore Throat

Final

	Nirmatrelvir/ritonavir (N=26)	Placebo (N=29)
Number of subjects with events, n (%)	20 (76.9)	23 (79.3)
Number of censored subjects, n (%)	6 (23.1)	6 (20.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (2.0, 7.0)	6.0 (3.0, 12.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.398 (0.697, 2.801)	
p-value [3]	0.345	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.394 (0.764, 2.545)	
p-value [3]	0.279	

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[1] Based on the Brookmeyer and Crowley Method.

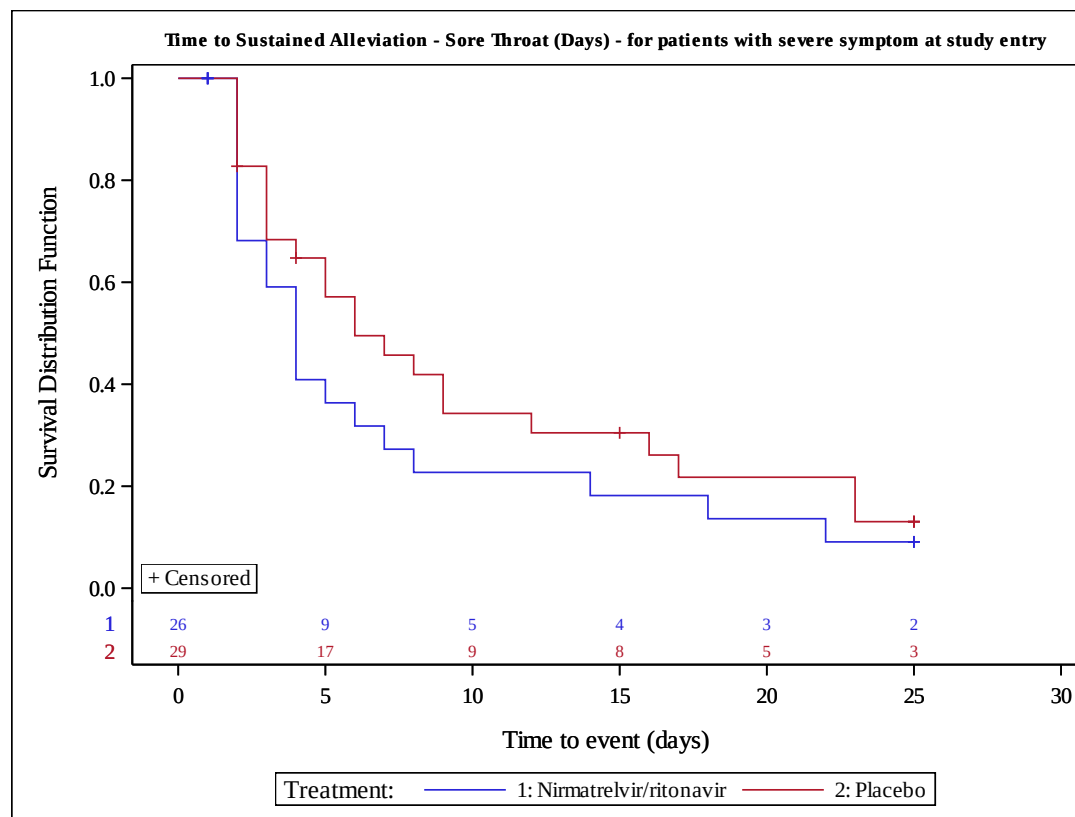
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Sore Throat

Final

	Nirmatrelvir/ritonavir (N=573)	Placebo (N=579)
Number of subjects with events, n (%)	470 (82.0)	432 (74.6)
Number of censored subjects, n (%)	103 (18.0)	147 (25.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	7.0 (6.0, 8.0)	9.0 (8.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.321 (1.155, 1.510)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.327 (1.164, 1.513)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

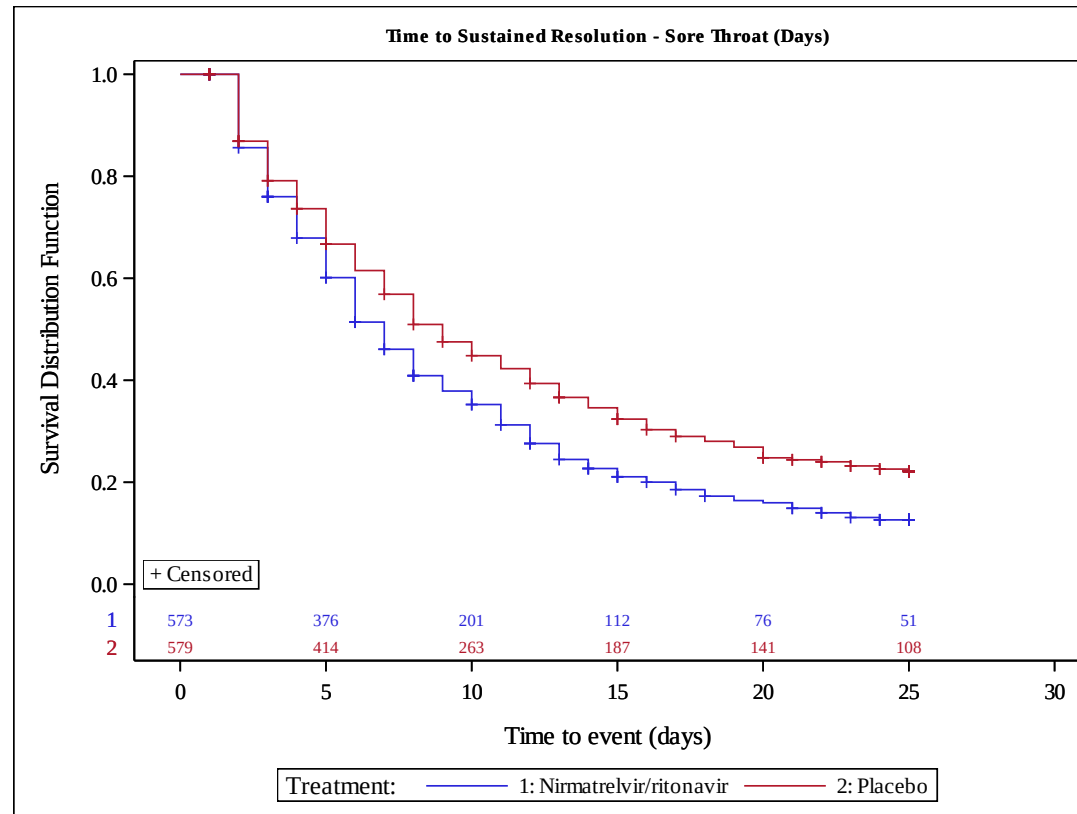
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final

	Nirmatrelvir/ritonavir (N=26)	Placebo (N=29)
Number of subjects with events, n (%)	16 (61.5)	19 (65.5)
Number of censored subjects, n (%)	10 (38.5)	10 (34.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	14.5 (7.0, 24.0)	13.0 (7.0, 25.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.114 (0.522, 2.377)	
p-value [3]	0.780	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.036 (0.532, 2.017)	
p-value [3]	0.917	

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[1] Based on the Brookmeyer and Crowley Method.

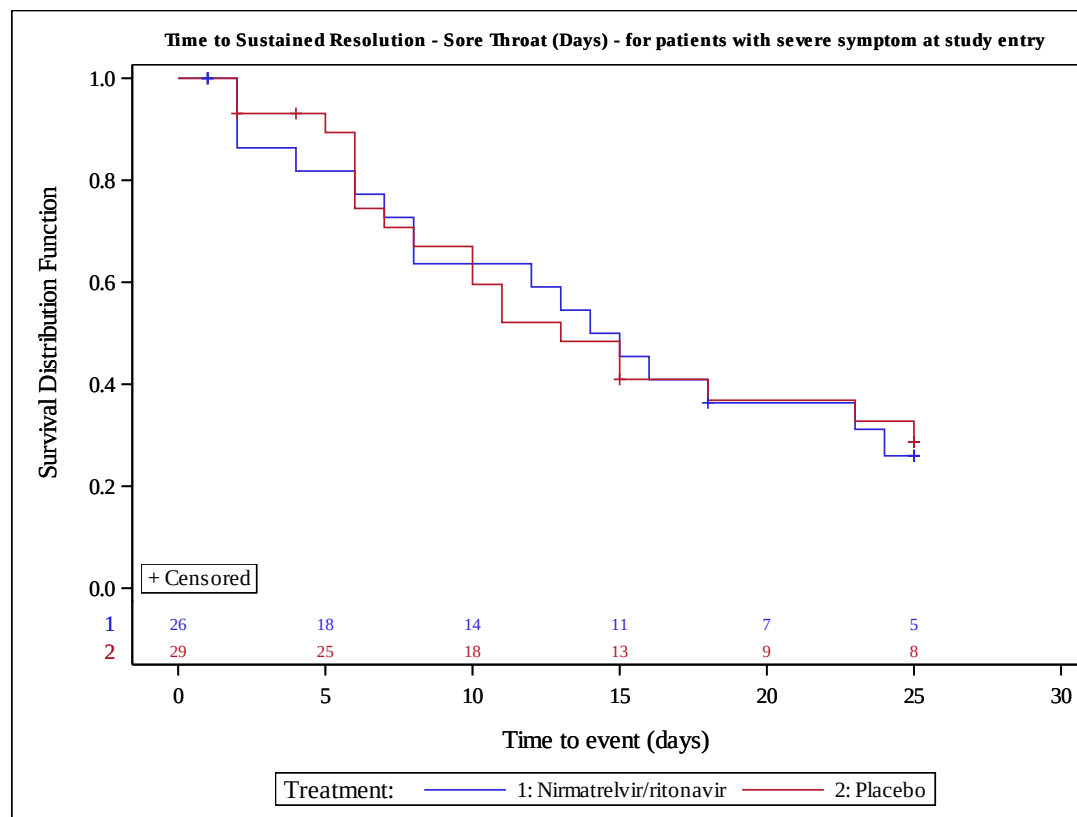
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Shortness of Breath or Difficulty Breathing

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	225 (21.9)	301 (29.0)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.663 (0.539, 0.815) <.001	
Relative Risk (95% CI)	0.738 (0.635, 0.858) <.001	
Risk Difference (95% CI)	-0.068 (-0.105, -0.032) <.001	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.687 (0.563, 0.839) <.001	
Relative Risk (95% CI)	0.756 (0.651, 0.877) <.001	
Risk Difference (95% CI)	-0.071 (-0.108, -0.033) <.001	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

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[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Shortness of Breath or Difficulty Breathing

Final

	Nirmatrelvir/ritonavir (N=454)	Placebo (N=469)
Number of subjects with events, n (%)	379 (83.5)	349 (74.4)
Number of censored subjects, n (%)	75 (16.5)	120 (25.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	6.0 (5.0, 7.0)	8.0 (7.0, 9.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.410 (1.213, 1.638)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.393 (1.203, 1.612)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

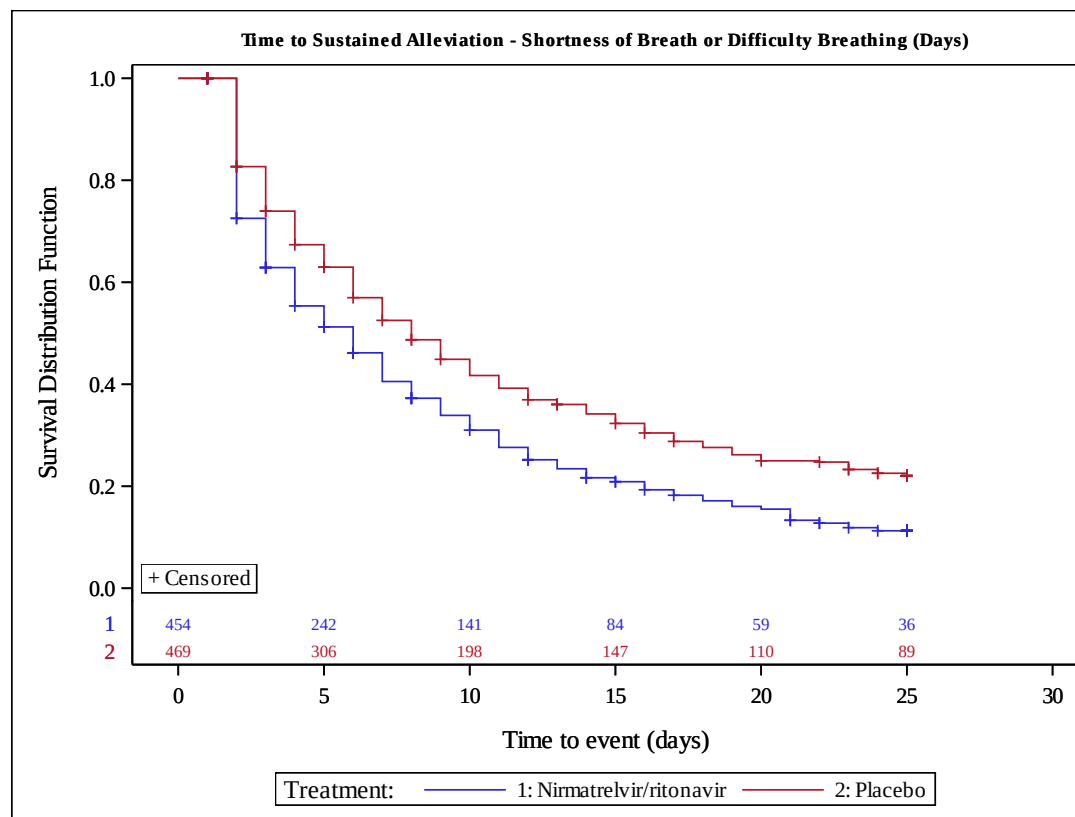
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Shortness of Breath or Difficulty Breathing

Final

	Nirmatrelvir/ritonavir (N=11)	Placebo (N=11)
Number of subjects with events, n (%)	6 (54.5)	4 (36.4)
Number of censored subjects, n (%)	5 (45.5)	7 (63.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	9.0 (2.0, 22.0)	NE (3.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	8.622 (0.488, 152.34)	
p-value [3]	0.141	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	2.737 (0.750, 9.982)	
p-value [3]	0.127	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

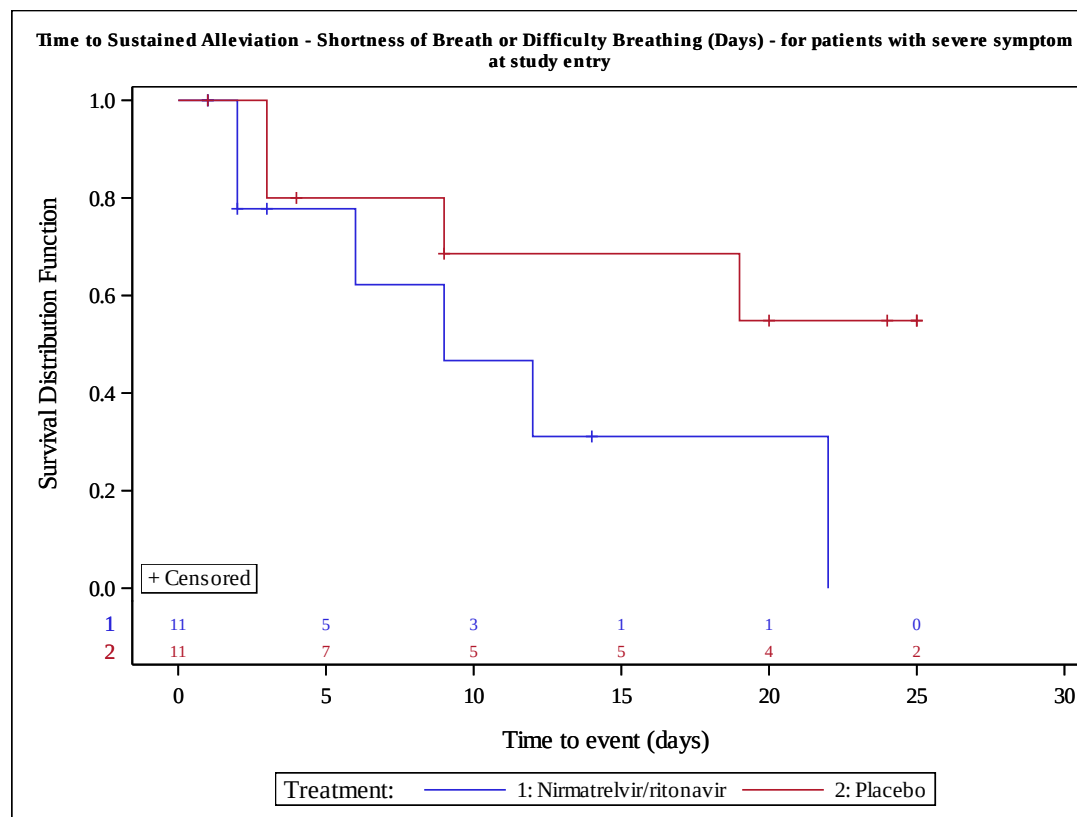
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Shortness of Breath or Difficulty Breathing

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Shortness of Breath or Difficulty Breathing

Final

	Nirmatrelvir/ritonavir (N=454)	Placebo (N=469)
Number of subjects with events, n (%)	353 (77.8)	301 (64.2)
Number of censored subjects, n (%)	101 (22.2)	168 (35.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	8.0 (7.0, 9.0)	12.0 (10.0, 14.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.554 (1.326, 1.820)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.538 (1.318, 1.795)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

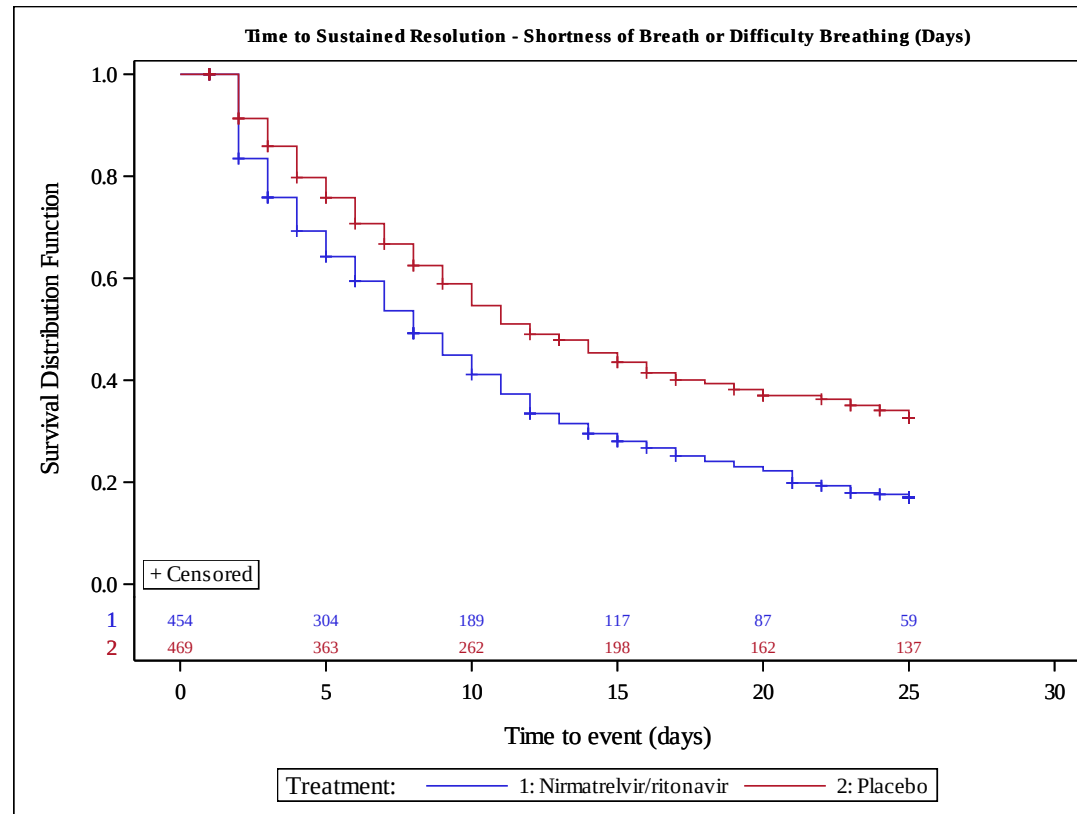
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Shortness of Breath or Difficulty Breathing

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
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Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Shortness of Breath or Difficulty Breathing

Final

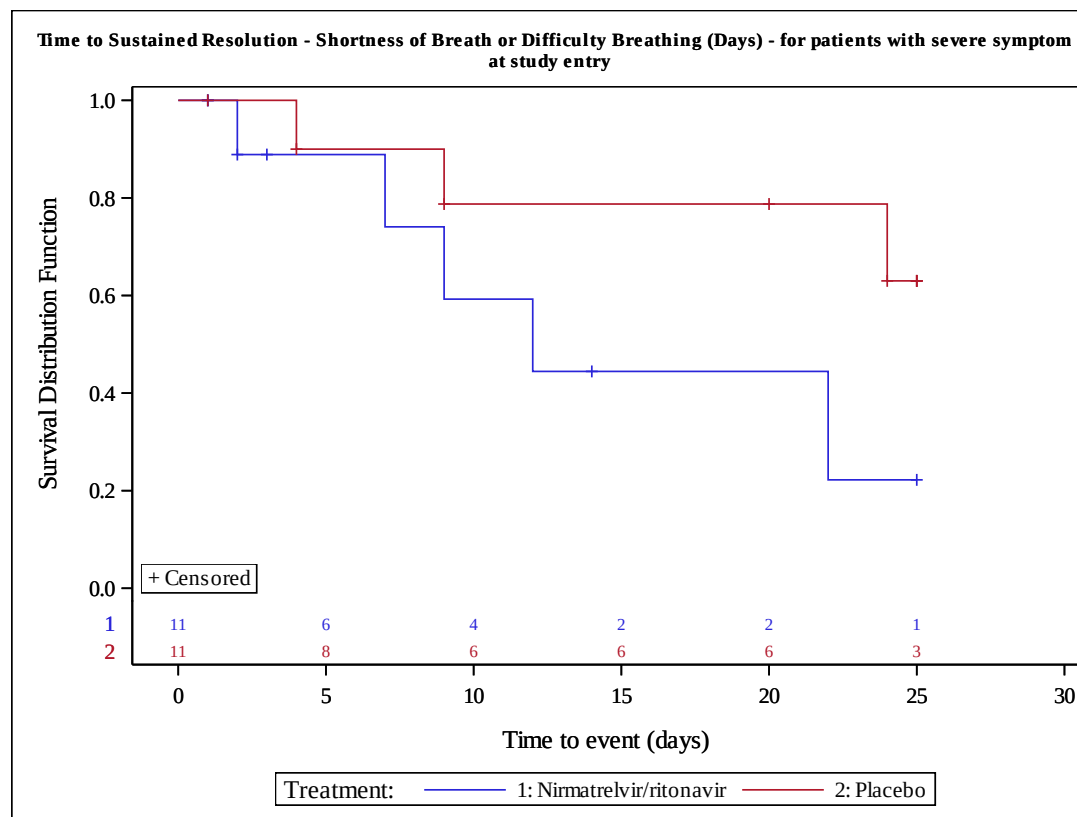
	Nirmatrelvir/ritonavir (N=11)	Placebo (N=11)
Number of subjects with events, n (%)	5 (45.5)	3 (27.3)
Number of censored subjects, n (%)	6 (54.5)	8 (72.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	12.0 (2.0, NE)	NE (4.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	10.753 (0.321, 360.10)	
p-value [3]	0.185	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	3.074 (0.710, 13.314)	
p-value [3]	0.133	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
[1] Based on the Brookmeyer and Crowley Method.
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.
[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Cough

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	224 (21.8)	252 (24.3)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.849 (0.687, 1.050) 0.132	
Relative Risk (95% CI)	0.882 (0.751, 1.035) 0.125	
Risk Difference (95% CI)	-0.026 (-0.061, 0.010) 0.154	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.870 (0.709, 1.068) 0.183	
Relative Risk (95% CI)	0.898 (0.767, 1.052) 0.184	
Risk Difference (95% CI)	-0.025 (-0.061, 0.012) 0.183	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Cough

Final

	Nirmatrelvir/ritonavir (N=837)	Placebo (N=856)
Number of subjects with events, n (%)	694 (82.9)	650 (75.9)
Number of censored subjects, n (%)	143 (17.1)	206 (24.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	8.0 (8.0, 9.0)	10.0 (9.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.239 (1.110, 1.383)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.265 (1.136, 1.408)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

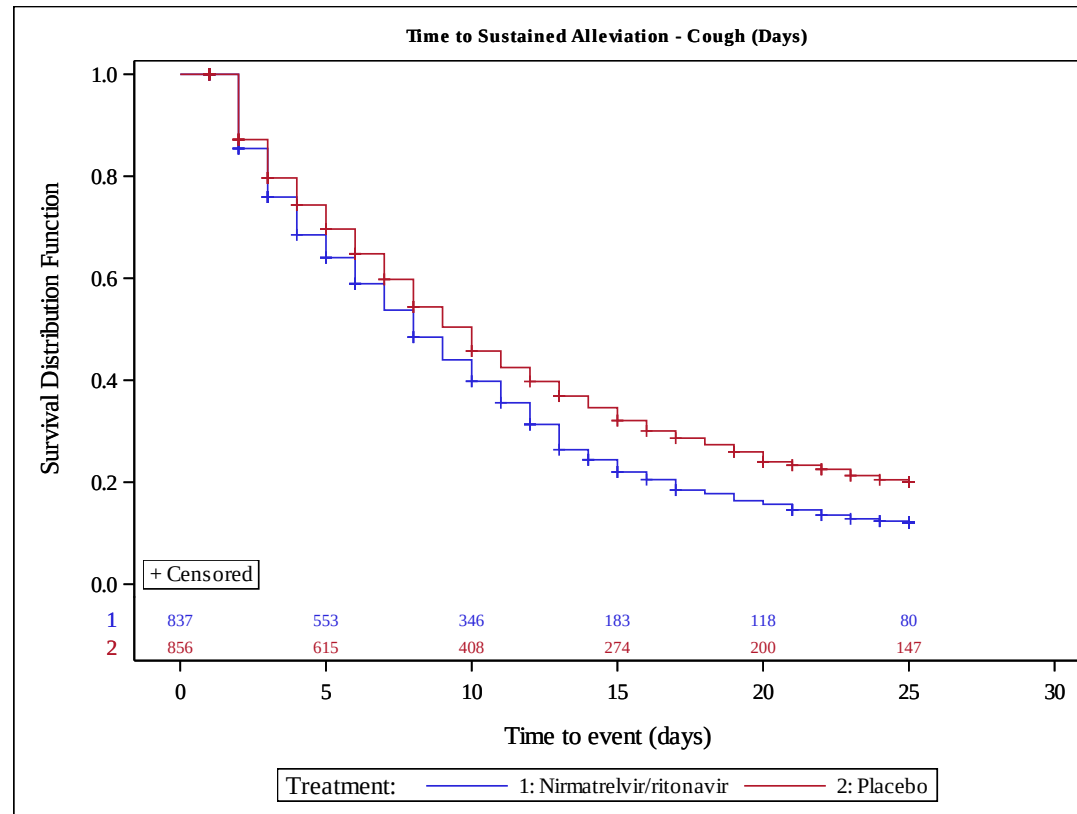
[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Cough

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough

Final

	Nirmatrelvir/ritonavir (N=56)	Placebo (N=49)
Number of subjects with events, n (%)	45 (80.4)	31 (63.3)
Number of censored subjects, n (%)	11 (19.6)	18 (36.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 6.0)	14.0 (8.0, 20.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.784 (1.085, 2.931)	
p-value [3]	0.022	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	2.117 (1.331, 3.367)	
p-value [3]	0.002	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

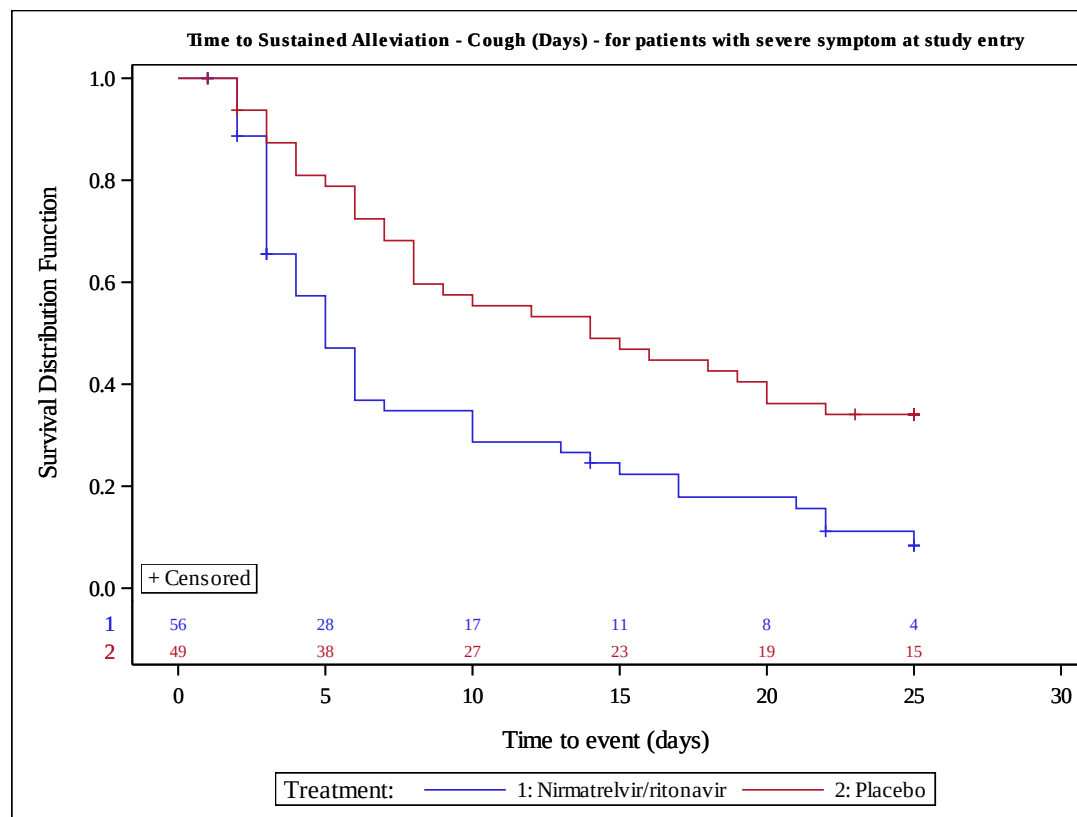
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Cough

Final

	Nirmatrelvir/ritonavir (N=837)	Placebo (N=856)
Number of subjects with events, n (%)	621 (74.2)	559 (65.3)
Number of censored subjects, n (%)	216 (25.8)	297 (34.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	13.0 (12.0, 13.0)	15.0 (14.0, 16.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.269 (1.129, 1.426)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.304 (1.163, 1.462)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

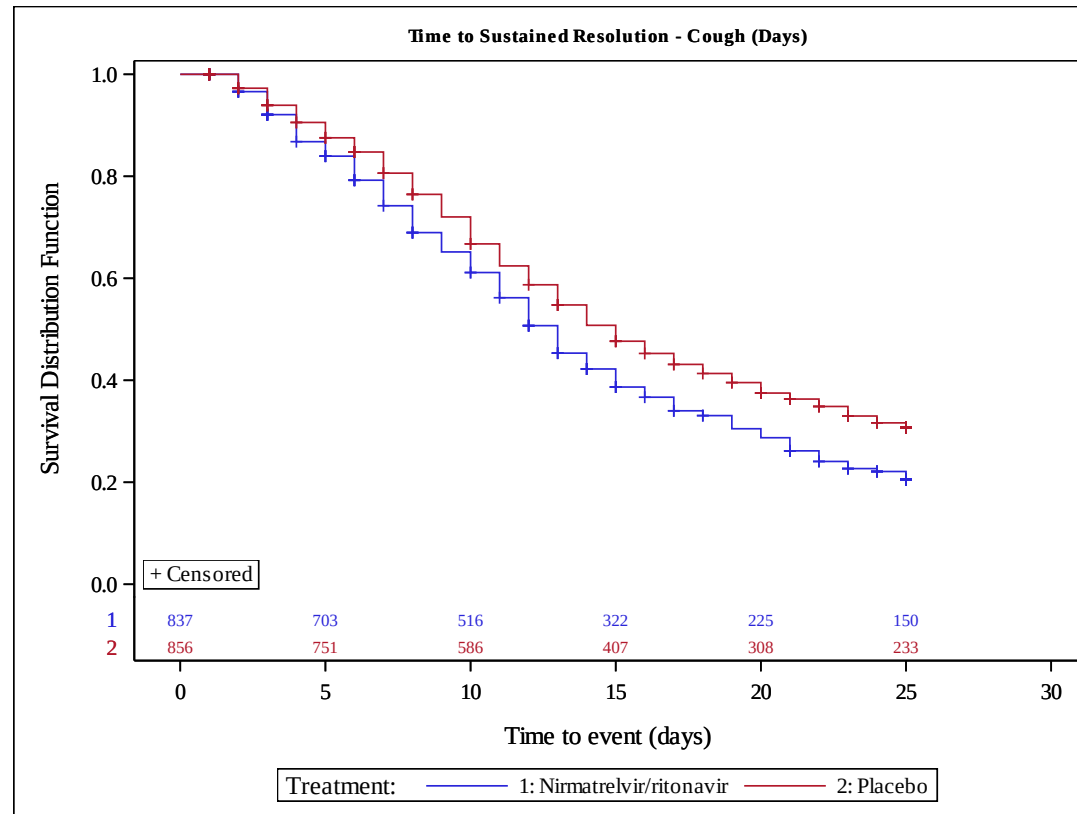
[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Cough

Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough

Final

	Nirmatrelvir/ritonavir (N=56)	Placebo (N=49)
Number of subjects with events, n (%)	35 (62.5)	22 (44.9)
Number of censored subjects, n (%)	21 (37.5)	27 (55.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	17.0 (11.0, 22.0)	NE (18.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.679 (0.954, 2.953)	
p-value [3]	0.072	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.989 (1.164, 3.396)	
p-value [3]	0.012	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

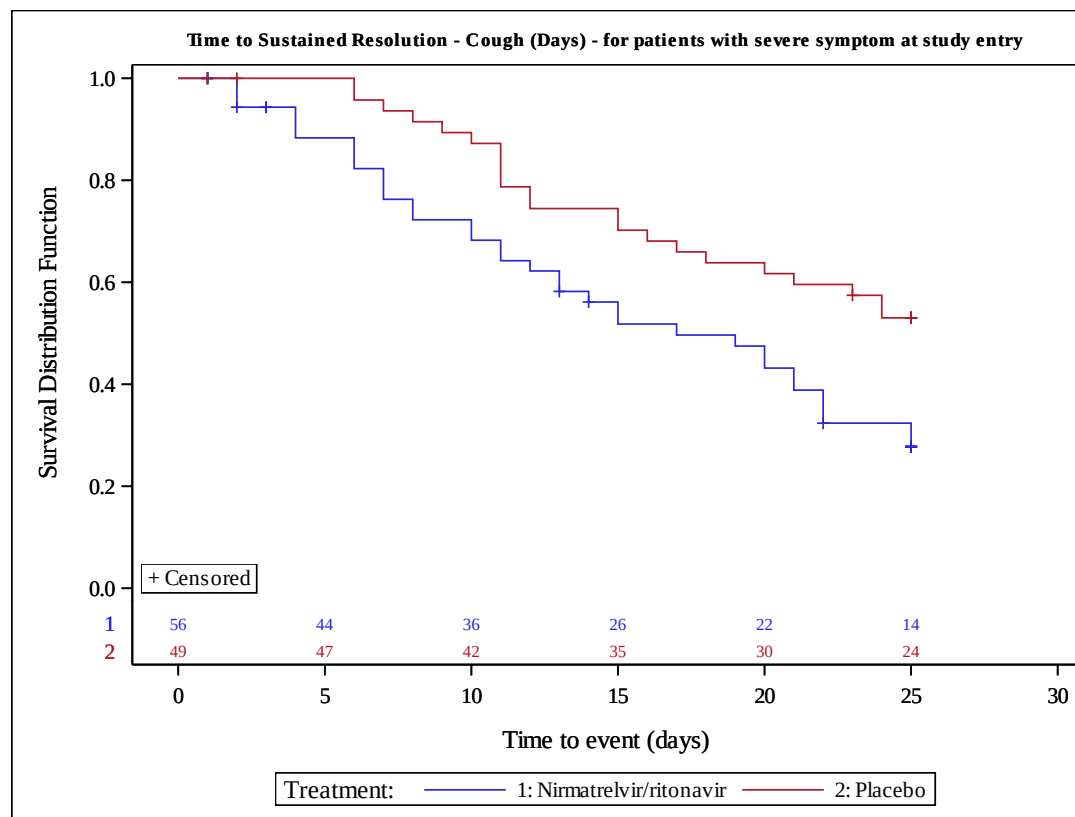
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough

Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Worsening of Signs and Symptoms - Fatigue (low energy or tiredness)

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	221 (21.5)	259 (25.0)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.803 (0.651, 0.992) 0.042	
Relative Risk (95% CI)	0.849 (0.723, 0.997) 0.046	
Risk Difference (95% CI)	-0.039 (-0.076, -0.003) 0.035	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.825 (0.672, 1.012) 0.065	
Relative Risk (95% CI)	0.862 (0.737, 1.009) 0.065	
Risk Difference (95% CI)	-0.034 (-0.071, 0.002) 0.064	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Fatigue (low energy or tiredness)

Final

	Nirmatrelvir/ritonavir (N=892)	Placebo (N=907)
Number of subjects with events, n (%)	738 (82.7)	689 (76.0)
Number of censored subjects, n (%)	154 (17.3)	218 (24.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	8.0 (7.0, 8.0)	9.0 (8.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.271 (1.142, 1.413)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.271 (1.145, 1.410)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

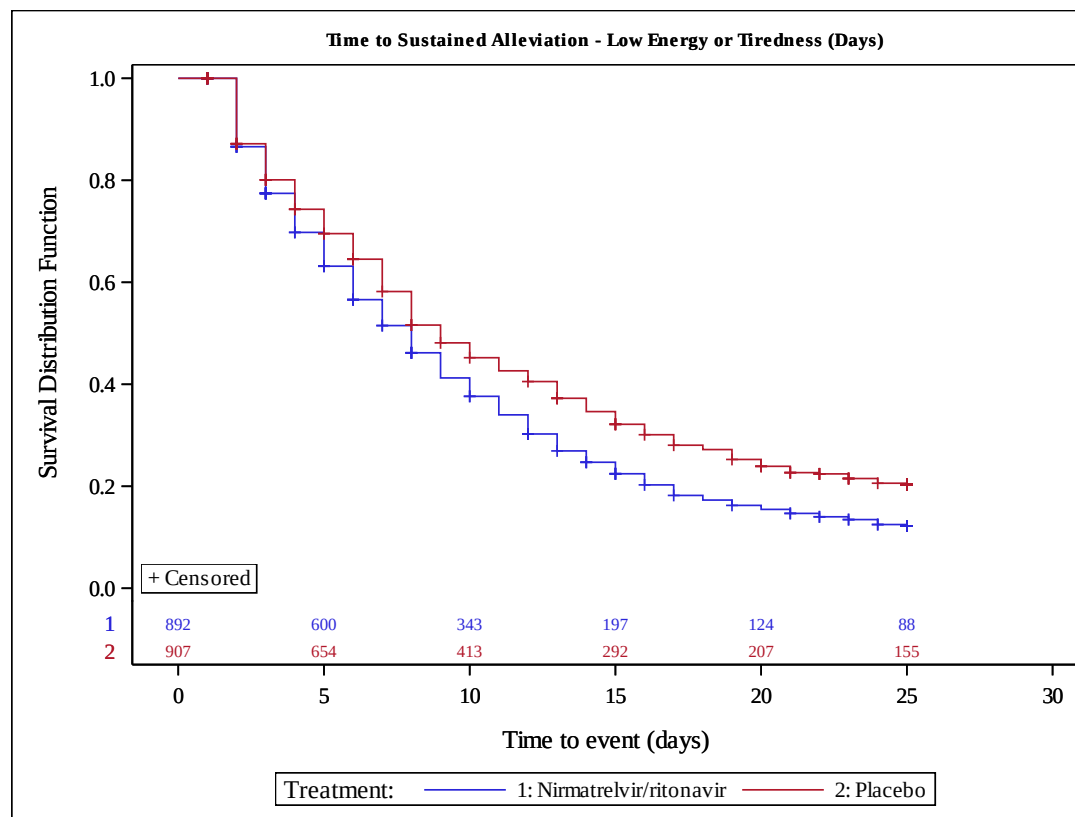
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Fatigue (low energy or tiredness)

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Fatigue (low energy or tiredness)

Final

	Nirmatrelvir/ritonavir (N=114)	Placebo (N=95)
Number of subjects with events, n (%)	83 (72.8)	64 (67.4)
Number of censored subjects, n (%)	31 (27.2)	31 (32.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	9.0 (6.0, 11.0)	12.0 (9.0, 15.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.343 (0.946, 1.907)	
p-value [3]	0.099	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.387 (1.000, 1.923)	
p-value [3]	0.050	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

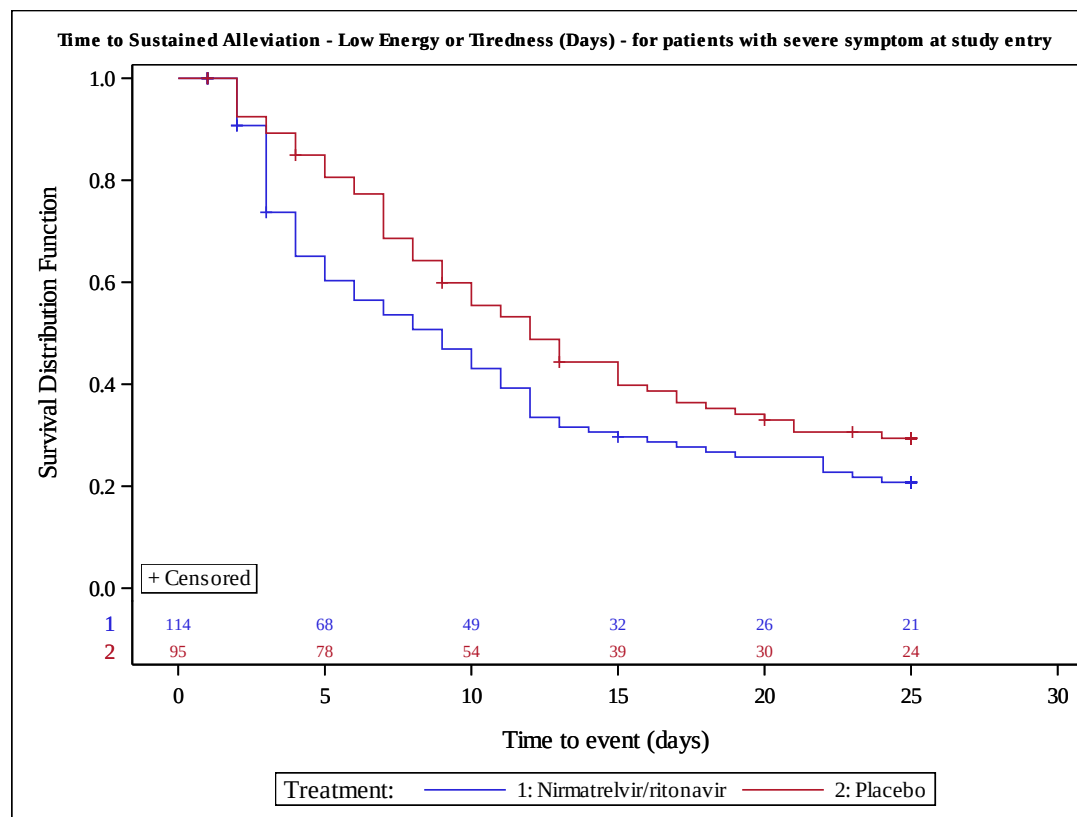
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Fatigue (low energy or tiredness)

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Overall Study population
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 Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Fatigue (low energy or tiredness)

Final

	Nirmatrelvir/ritonavir (N=892)	Placebo (N=907)
Number of subjects with events, n (%)	618 (69.3)	566 (62.4)
Number of censored subjects, n (%)	274 (30.7)	341 (37.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	14.0 (13.0, 15.0)	17.0 (16.0, 19.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.284 (1.143, 1.443)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.293 (1.154, 1.449)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

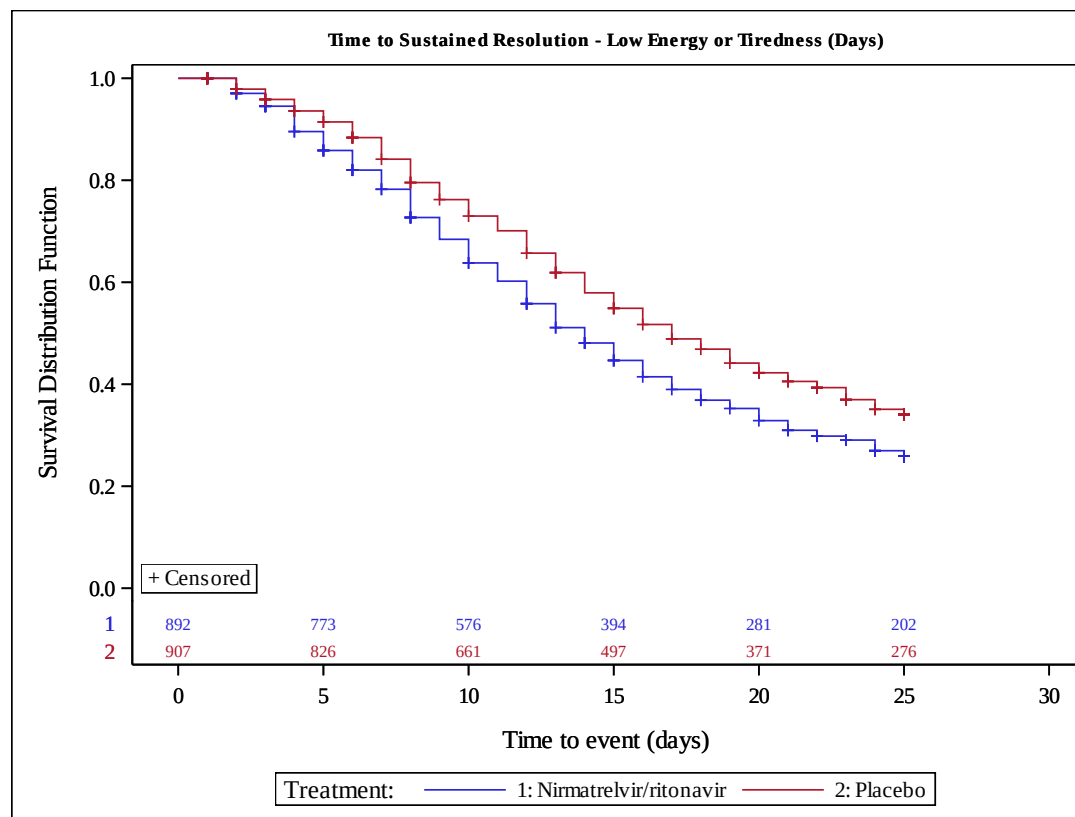
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Fatigue (low energy or tiredness)

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Fatigue (low energy or tiredness)

Final

	Nirmatrelvir/ritonavir (N=114)	Placebo (N=95)
Number of subjects with events, n (%)	65 (57.0)	38 (40.0)
Number of censored subjects, n (%)	49 (43.0)	57 (60.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	18.0 (14.0, 22.0)	NE (24.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.887 (1.234, 2.885)	
p-value [3]	0.003	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.877 (1.257, 2.804)	
p-value [3]	0.002	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

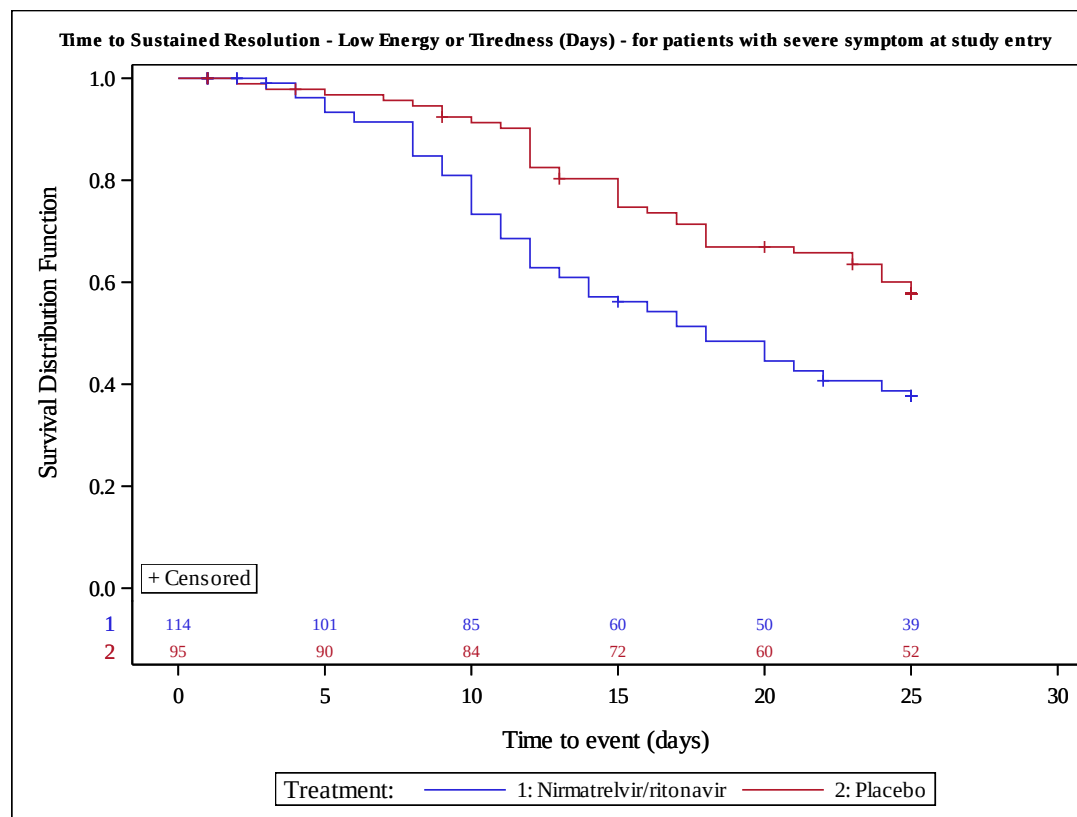
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Fatigue (low energy or tiredness)

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Muscle or Body Aches

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	205 (20.0)	236 (22.8)
Adjusted analysis [1] Odds Ratio (95% CI)	0.862 (0.694, 1.071) 0.180	
Relative Risk (95% CI)	0.887 (0.749, 1.052) 0.168	
Risk Difference (95% CI)	-0.021 (-0.056, 0.014) 0.246	
Unadjusted analysis [2] Odds Ratio (95% CI)	0.847 (0.686, 1.046) 0.124	
Relative Risk (95% CI)	0.878 (0.744, 1.037) 0.124	
Risk Difference (95% CI)	-0.028 (-0.063, 0.008) 0.124	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Muscle or Body Aches

Final

	Nirmatrelvir/ritonavir (N=825)	Placebo (N=823)
Number of subjects with events, n (%)	701 (85.0)	646 (78.5)
Number of censored subjects, n (%)	124 (15.0)	177 (21.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	6.0 (5.0, 6.0)	7.0 (7.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.297 (1.163, 1.448)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.290 (1.159, 1.436)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

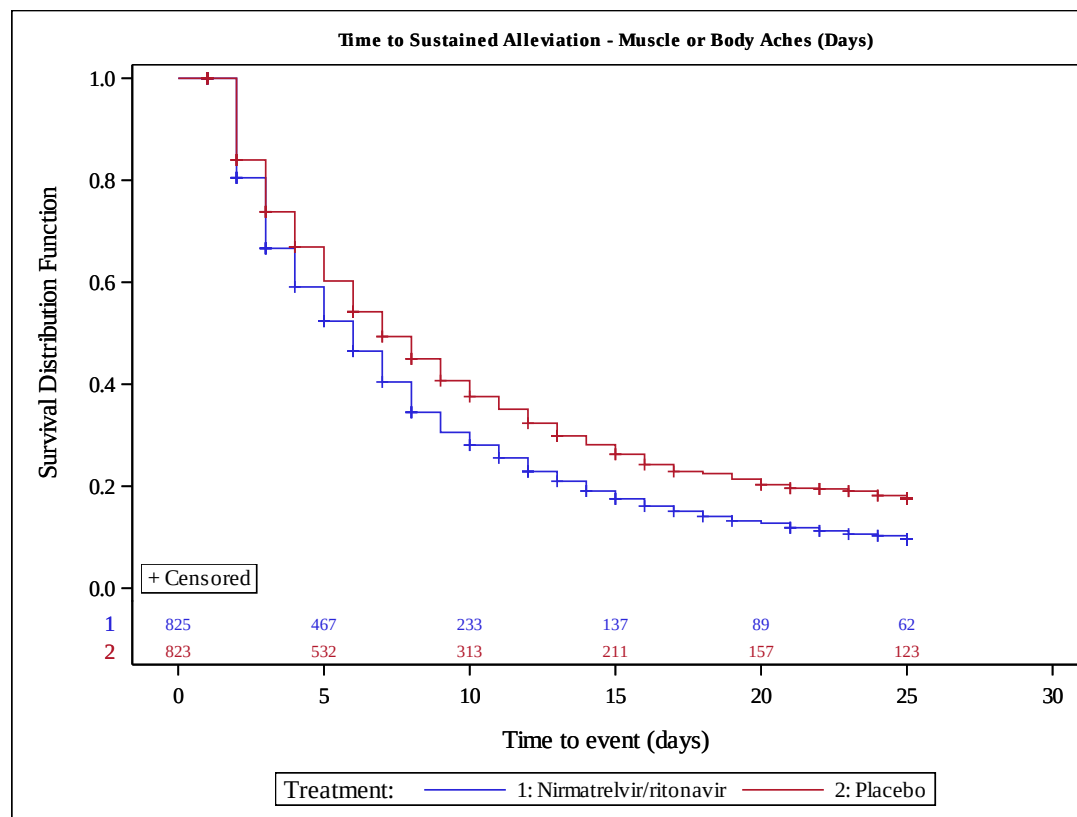
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Muscle or Body Aches

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Muscle or Body Aches

Final

	Nirmatrelvir/ritonavir (N=91)	Placebo (N=78)
Number of subjects with events, n (%)	76 (83.5)	62 (79.5)
Number of censored subjects, n (%)	15 (16.5)	16 (20.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (4.0, 5.0)	8.0 (5.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.416 (0.988, 2.030)	
p-value [3]	0.058	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.465 (1.045, 2.054)	
p-value [3]	0.027	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

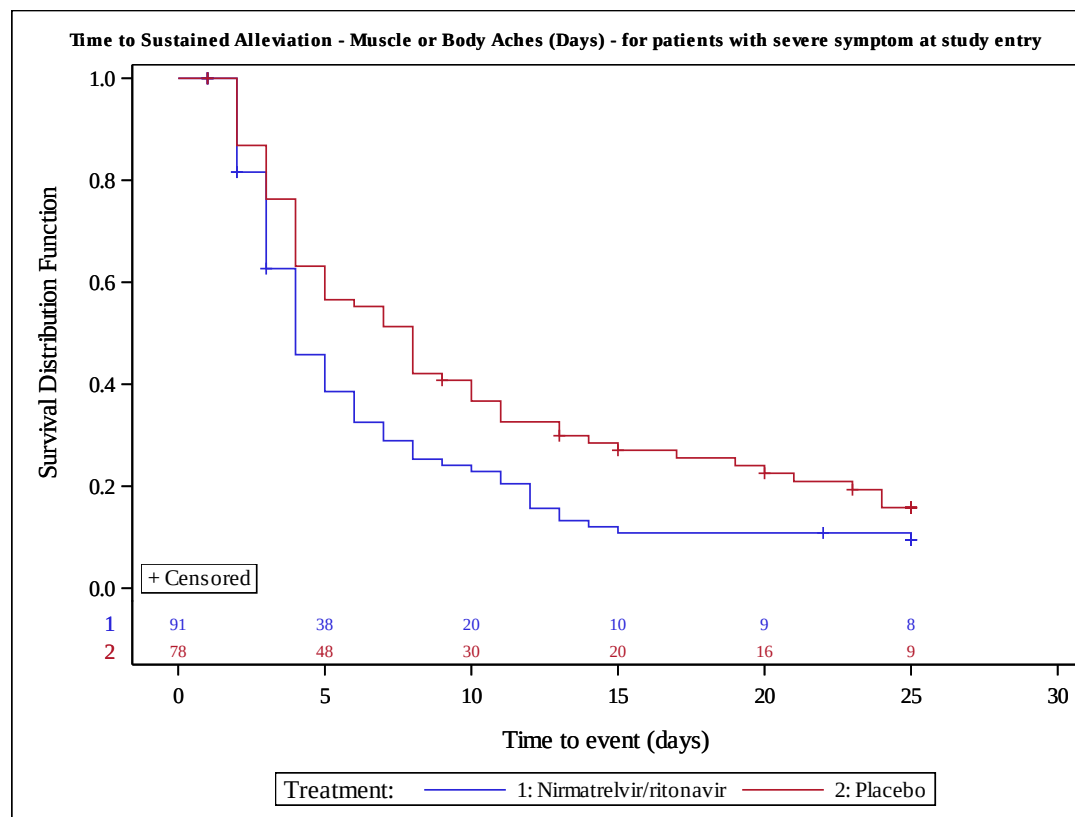
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Muscle or Body Aches

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Muscle or Body Aches

Final

	Nirmatrelvir/ritonavir (N=825)	Placebo (N=823)
Number of subjects with events, n (%)	635 (77.0)	581 (70.6)
Number of censored subjects, n (%)	190 (23.0)	242 (29.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	9.0 (8.0, 10.0)	12.0 (11.0, 13.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.305 (1.163, 1.464)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.289 (1.152, 1.443)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

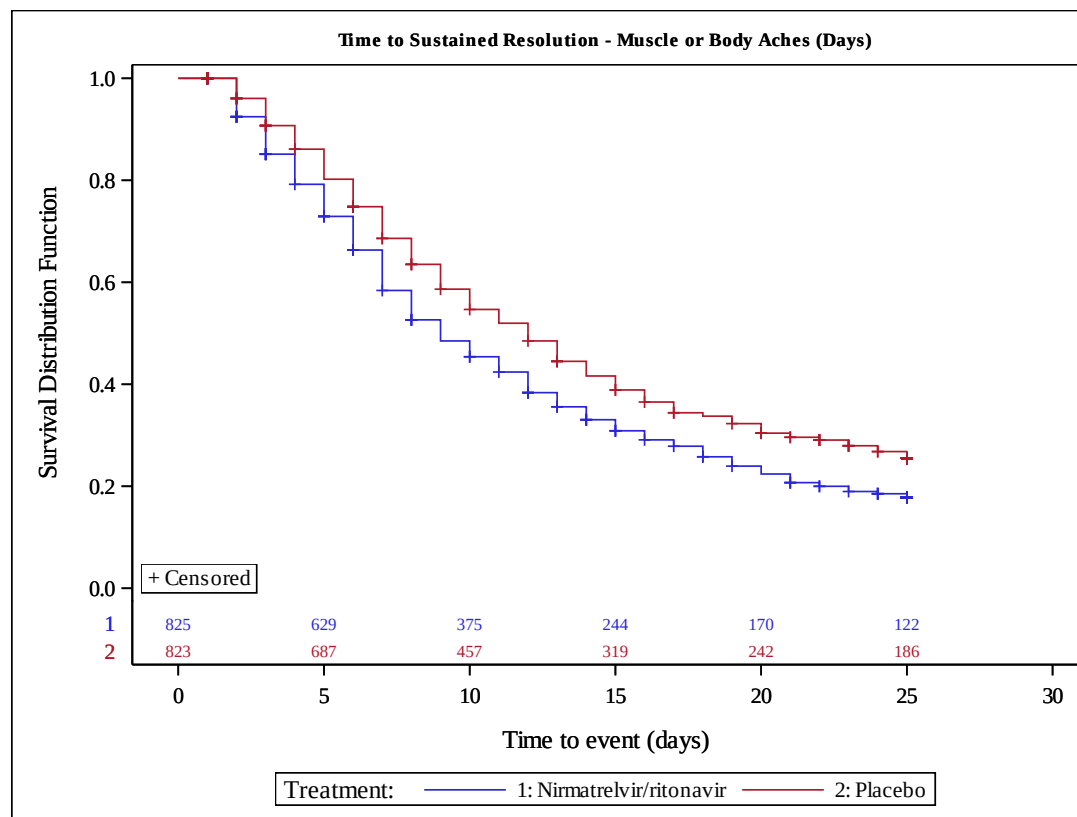
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Muscle or Body Aches

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Muscle or Body Aches

Final

	Nirmatrelvir/ritonavir (N=91)	Placebo (N=78)
Number of subjects with events, n (%)	63 (69.2)	52 (66.7)
Number of censored subjects, n (%)	28 (30.8)	26 (33.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	10.0 (7.0, 12.0)	15.0 (11.0, 20.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.342 (0.909, 1.980)	
p-value [3]	0.139	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.334 (0.924, 1.928)	
p-value [3]	0.124	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

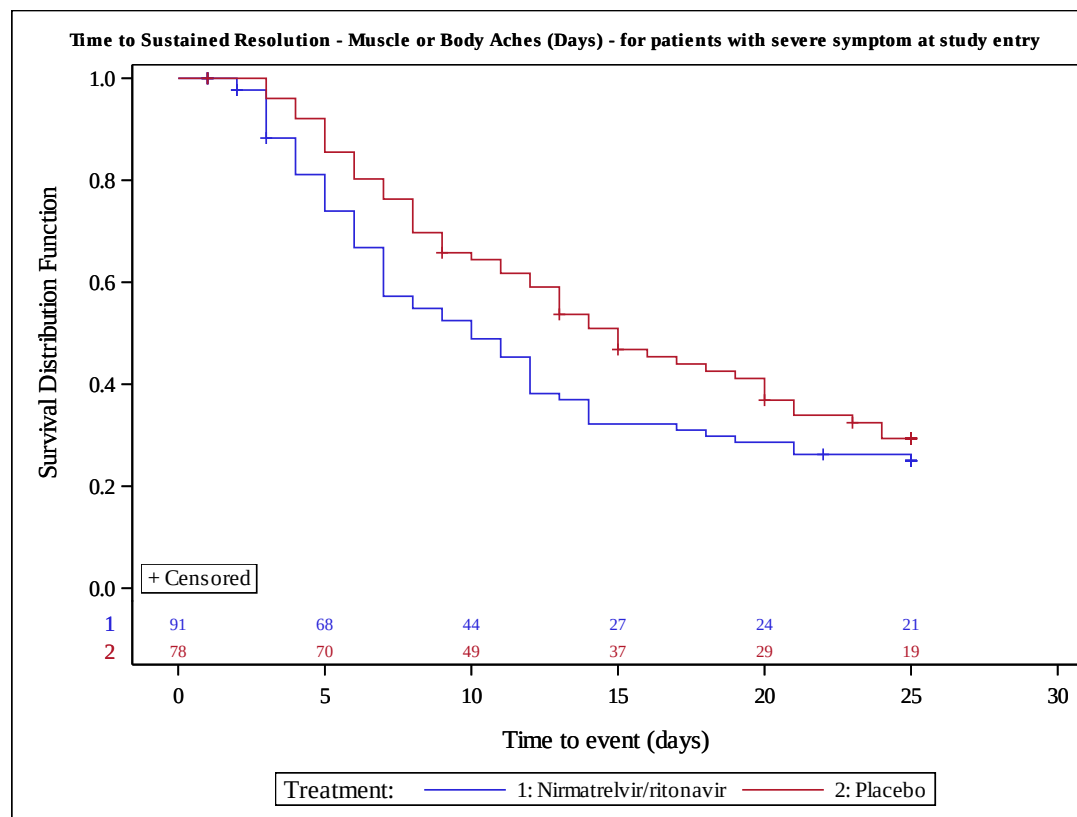
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Muscle or Body Aches

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Headache

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	247 (24.1)	288 (27.8)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.823 (0.672, 1.007) 0.059	
Relative Risk (95% CI)	0.863 (0.744, 1.002) 0.053	
Risk Difference (95% CI)	-0.033 (-0.072, 0.005) 0.086	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.825 (0.677, 1.005) 0.055	
Relative Risk (95% CI)	0.867 (0.749, 1.004) 0.056	
Risk Difference (95% CI)	-0.037 (-0.075, 0.001) 0.055	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Headache

Final

	Nirmatrelvir/ritonavir (N=755)	Placebo (N=751)
Number of subjects with events, n (%)	650 (86.1)	599 (79.8)
Number of censored subjects, n (%)	105 (13.9)	152 (20.2)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (5.0, 6.0)	7.0 (7.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.299 (1.159, 1.456)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.309 (1.171, 1.463)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

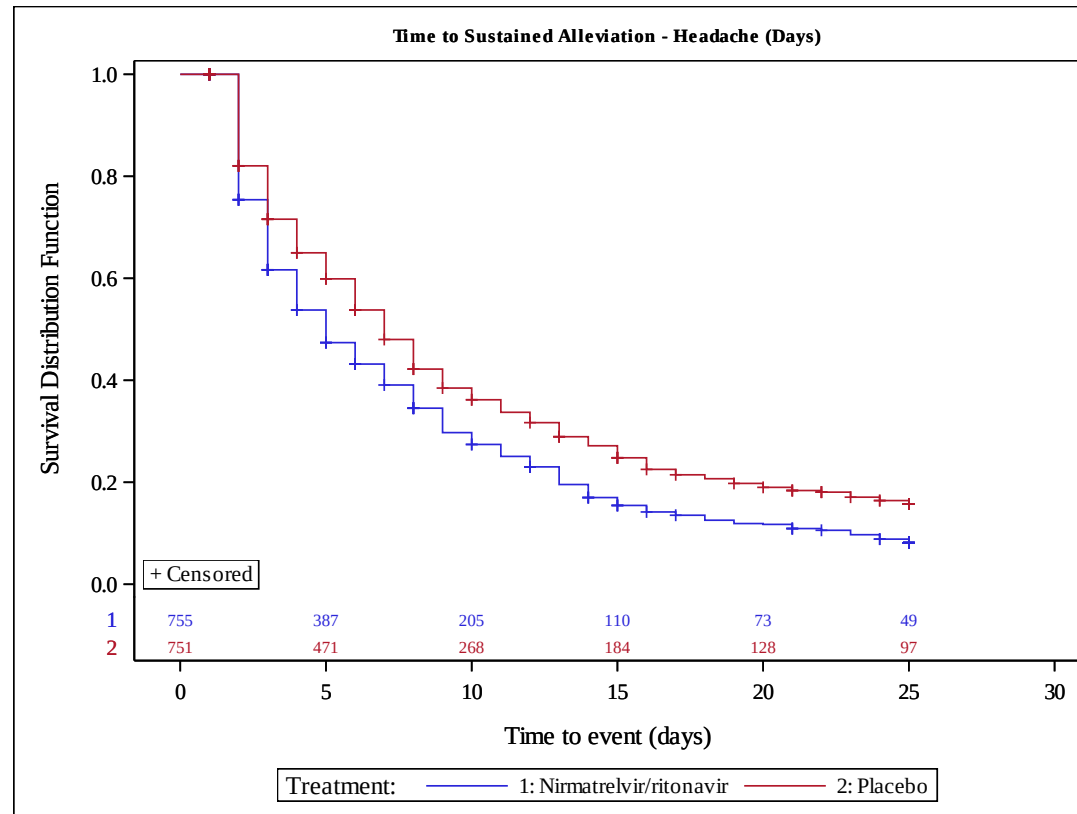
[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Headache

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Headache

Final

	Nirmatrelvir/ritonavir (N=96)	Placebo (N=73)
Number of subjects with events, n (%)	82 (85.4)	57 (78.1)
Number of censored subjects, n (%)	14 (14.6)	16 (21.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (3.0, 5.0)	8.0 (6.0, 12.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.424 (0.991, 2.044)	
p-value [3]	0.056	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.486 (1.058, 2.087)	
p-value [3]	0.022	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

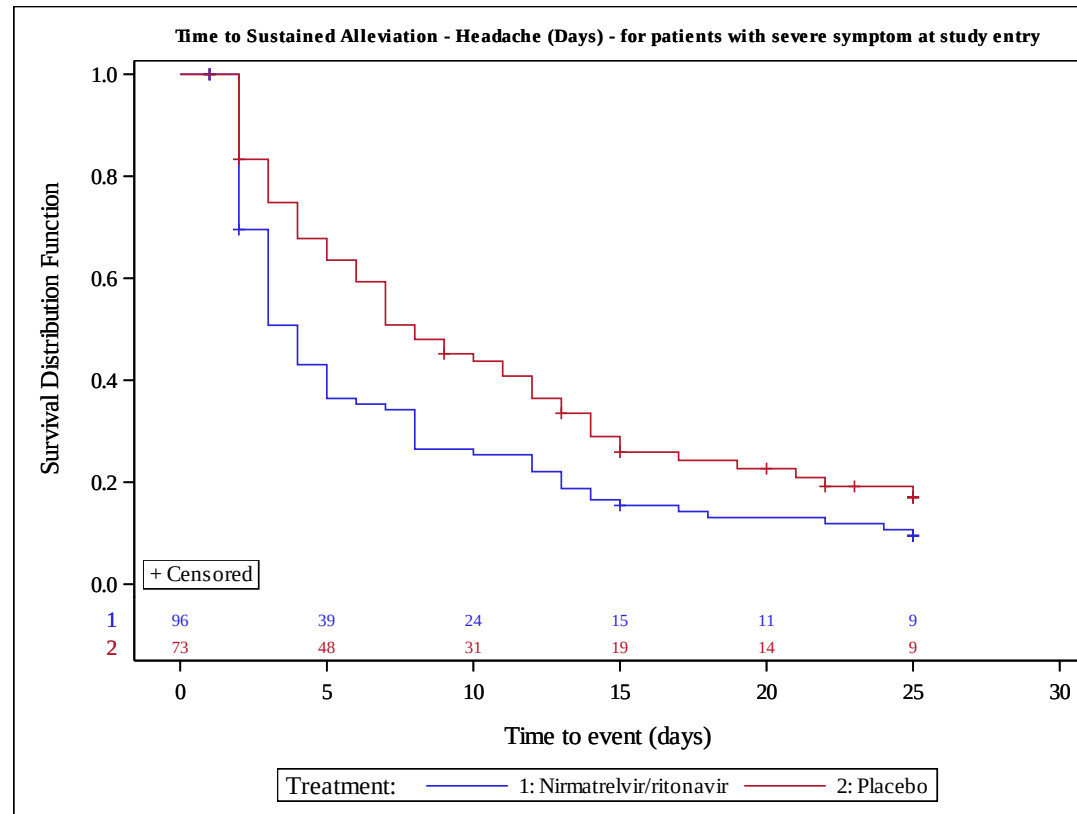
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Headache

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Headache

Final

	Nirmatrelvir/ritonavir (N=755)	Placebo (N=751)
Number of subjects with events, n (%)	604 (80.0)	544 (72.4)
Number of censored subjects, n (%)	151 (20.0)	207 (27.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	9.0 (8.0, 10.0)	11.0 (10.0, 13.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.304 (1.158, 1.467)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.326 (1.181, 1.489)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

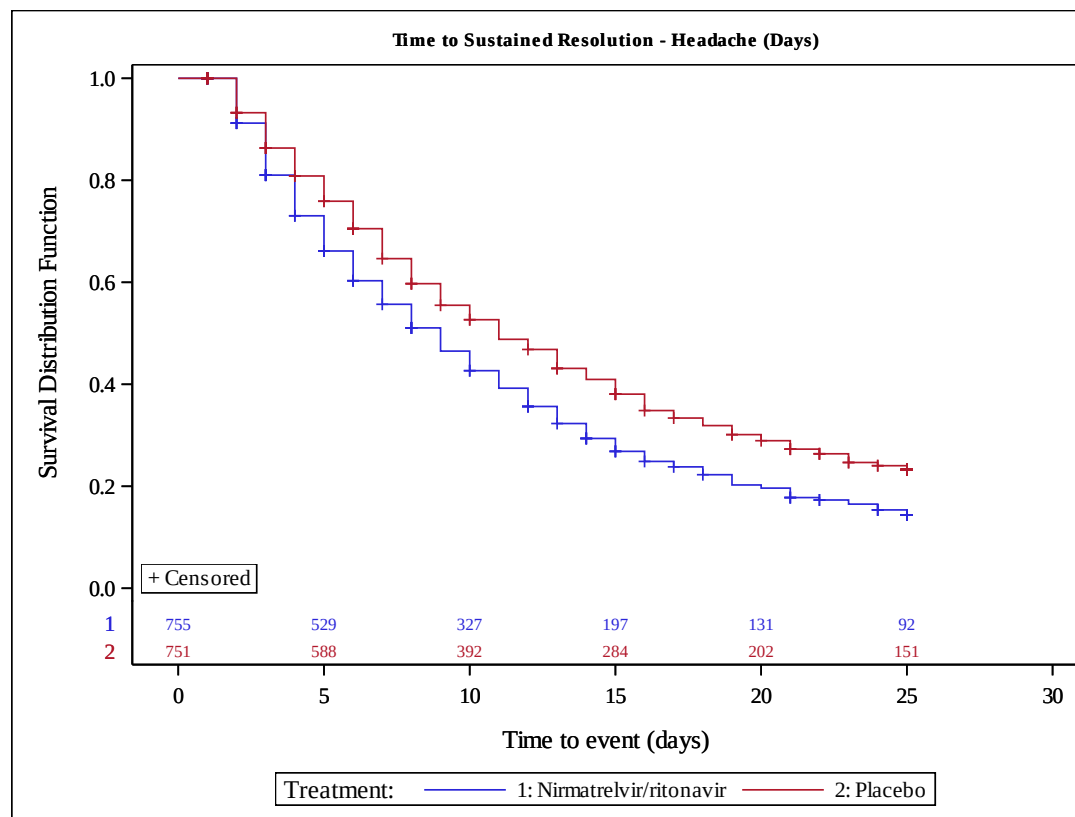
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Headache

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Headache

Final

	Nirmatrelvir/ritonavir (N=96)	Placebo (N=73)
Number of subjects with events, n (%)	71 (74.0)	45 (61.6)
Number of censored subjects, n (%)	25 (26.0)	28 (38.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	11.0 (8.0, 12.0)	17.0 (14.0, 22.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.550 (1.047, 2.295)	
p-value [3]	0.028	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.619 (1.113, 2.355)	
p-value [3]	0.012	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

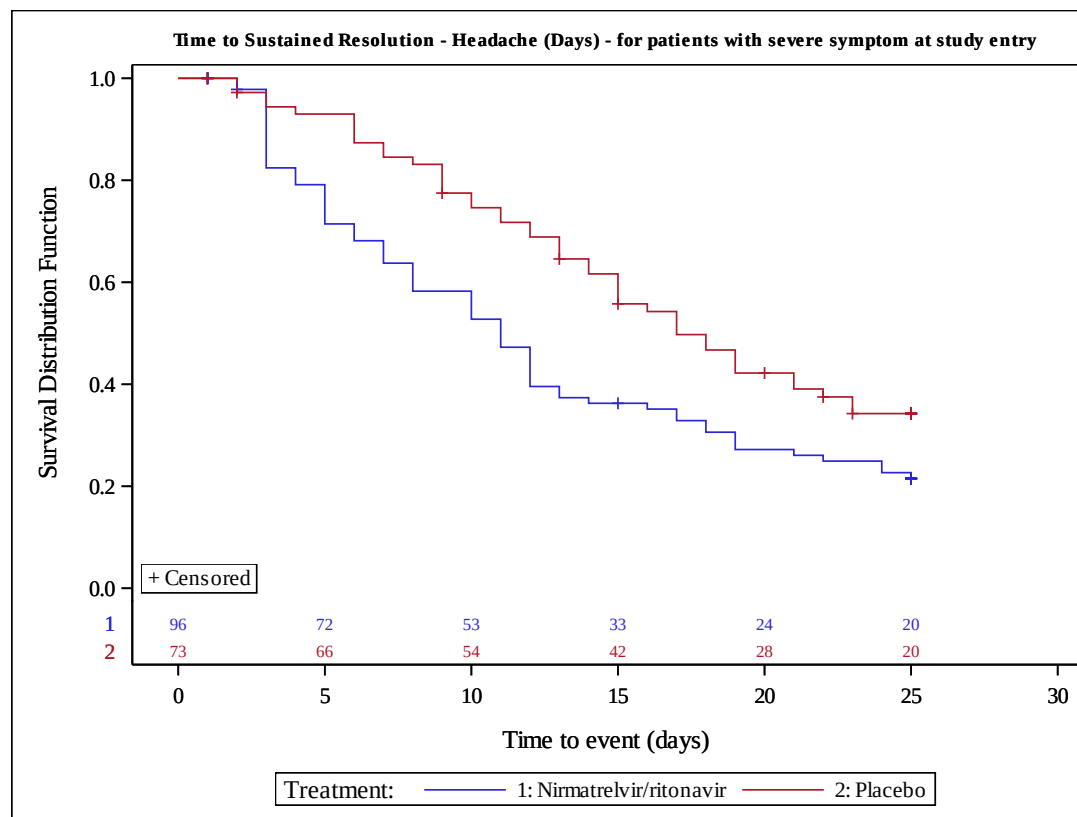
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Headache

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Chills or Shivering

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	153 (14.9)	181 (17.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.862 (0.677, 1.098) 0.228	
Relative Risk (95% CI)	0.884 (0.722, 1.081) 0.228	
Risk Difference (95% CI)	-0.021 (-0.053, 0.010) 0.184	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.829 (0.655, 1.048) 0.117	
Relative Risk (95% CI)	0.854 (0.701, 1.041) 0.118	
Risk Difference (95% CI)	-0.025 (-0.057, 0.006) 0.117	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Chills or Shivering

Final

	Nirmatrelvir/ritonavir (N=616)	Placebo (N=612)
Number of subjects with events, n (%)	538 (87.3)	501 (81.9)
Number of censored subjects, n (%)	78 (12.7)	111 (18.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (3.0, 4.0)	4.0 (4.0, 5.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.263 (1.114, 1.431)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.273 (1.127, 1.439)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

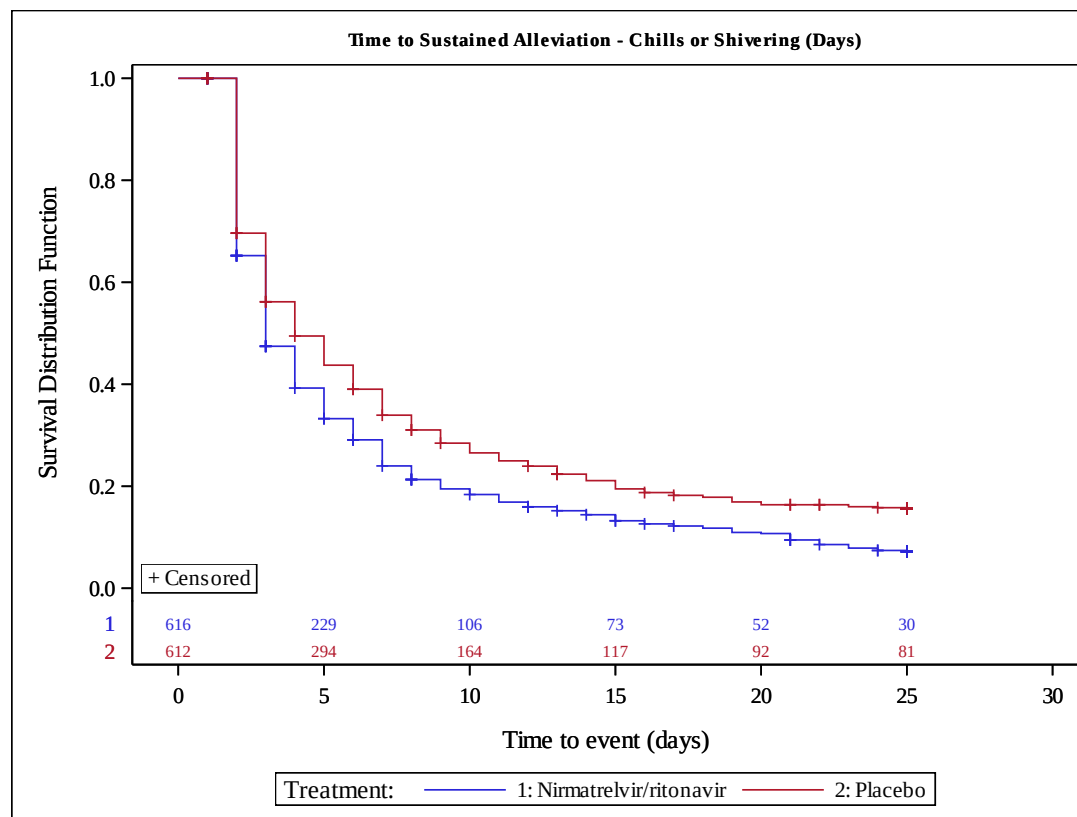
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Chills or Shivering

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Chills or Shivering

Final

	Nirmatrelvir/ritonavir (N=52)	Placebo (N=41)
Number of subjects with events, n (%)	46 (88.5)	34 (82.9)
Number of censored subjects, n (%)	6 (11.5)	7 (17.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (2.0, 3.0)	4.0 (3.0, 6.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.400 (0.863, 2.271)	
p-value [3]	0.173	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.329 (0.851, 2.075)	
p-value [3]	0.211	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

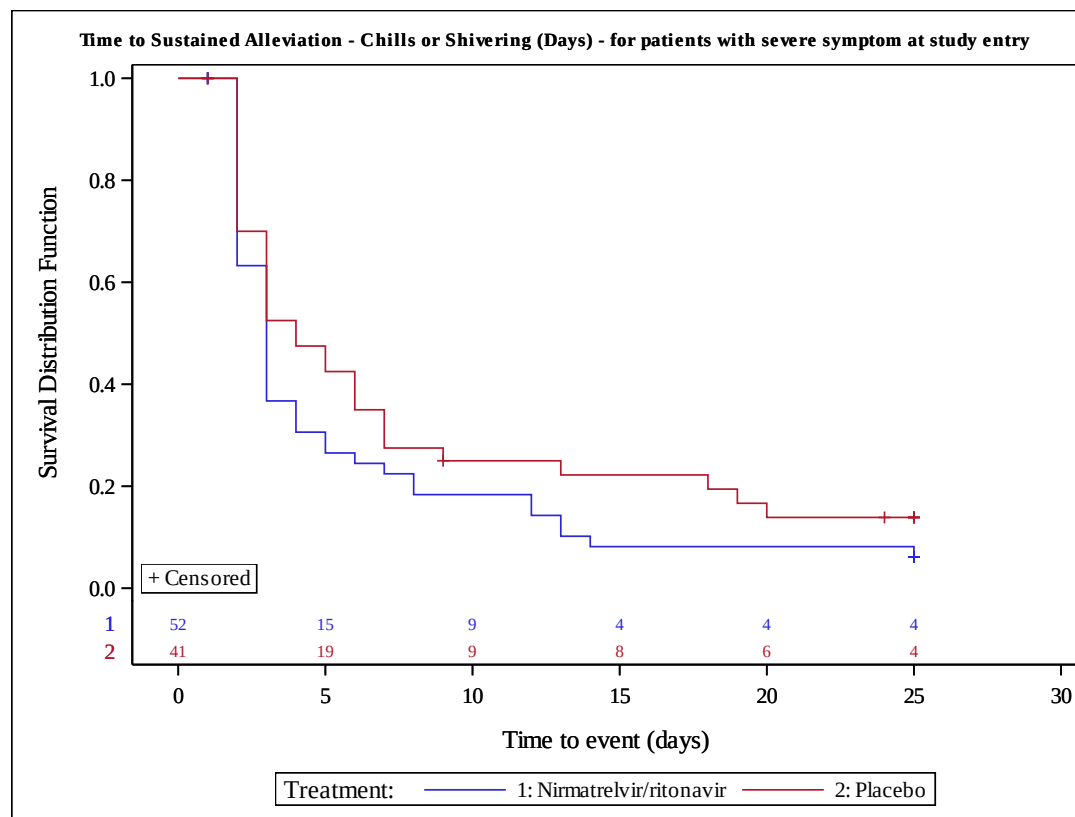
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Chills or Shivering

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Chills or Shivering

Final

	Nirmatrelvir/ritonavir (N=616)	Placebo (N=612)
Number of subjects with events, n (%)	524 (85.1)	472 (77.1)
Number of censored subjects, n (%)	92 (14.9)	140 (22.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 5.0)	7.0 (6.0, 7.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.328 (1.169, 1.509)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.344 (1.186, 1.523)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

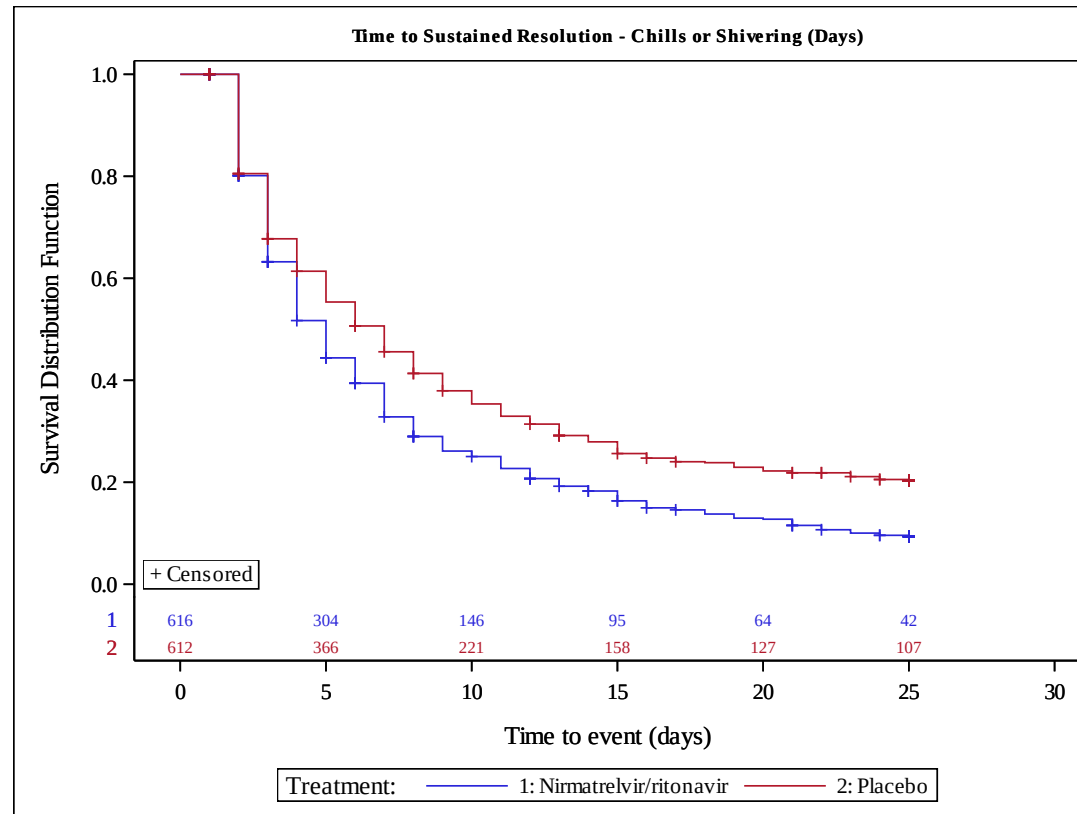
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Chills or Shivering

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Chills or Shivering

Final

	Nirmatrelvir/ritonavir (N=52)	Placebo (N=41)
Number of subjects with events, n (%)	45 (86.5)	32 (78.0)
Number of censored subjects, n (%)	7 (13.5)	9 (22.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (4.0, 7.0)	7.0 (6.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.537 (0.946, 2.497)	
p-value [3]	0.083	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.483 (0.940, 2.339)	
p-value [3]	0.090	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

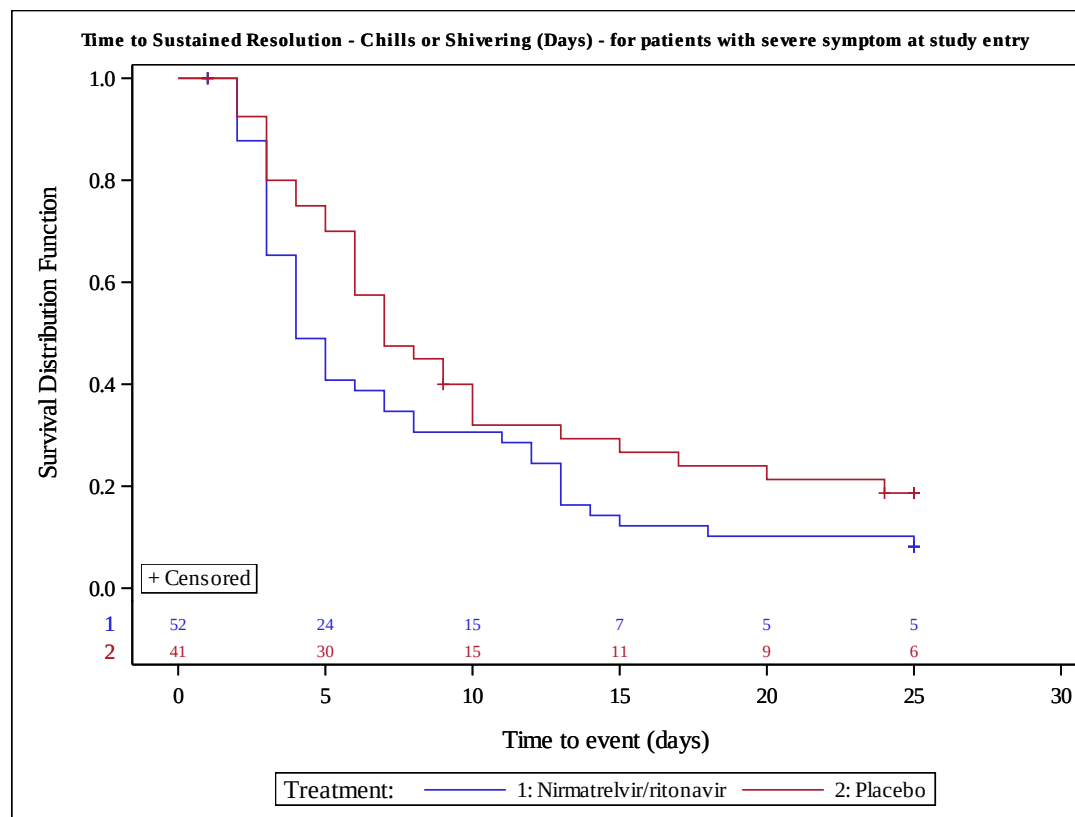
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Chills or Shivering

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Feeling Hot or Feverish

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	171 (16.7)	219 (21.1)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.743 (0.592, 0.933) 0.011	
Relative Risk (95% CI)	0.782 (0.652, 0.940) 0.009	
Risk Difference (95% CI)	-0.037 (-0.071, -0.003) 0.033	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.747 (0.598, 0.933) 0.010	
Relative Risk (95% CI)	0.789 (0.659, 0.945) 0.010	
Risk Difference (95% CI)	-0.045 (-0.078, -0.011) 0.010	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Feeling Hot or Feverish

Final

	Nirmatrelvir/ritonavir (N=631)	Placebo (N=640)
Number of subjects with events, n (%)	559 (88.6)	516 (80.6)
Number of censored subjects, n (%)	72 (11.4)	124 (19.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (3.0, 4.0)	5.0 (4.0, 5.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.333 (1.178, 1.509)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.345 (1.193, 1.518)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

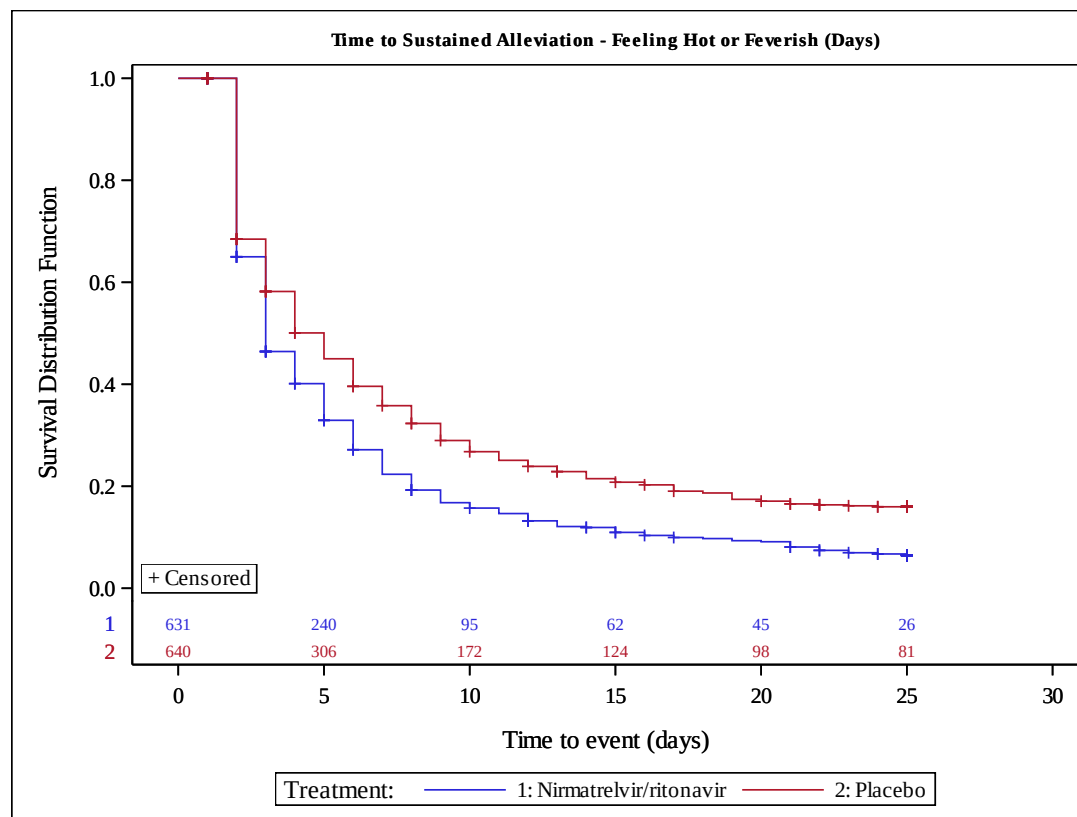
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Feeling Hot or Feverish

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish

Final

	Nirmatrelvir/ritonavir (N=55)	Placebo (N=45)
Number of subjects with events, n (%)	49 (89.1)	32 (71.1)
Number of censored subjects, n (%)	6 (10.9)	13 (28.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (2.0, 3.0)	5.5 (3.0, 9.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	2.092 (1.259, 3.476)	
p-value [3]	0.004	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	2.109 (1.326, 3.353)	
p-value [3]	0.002	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

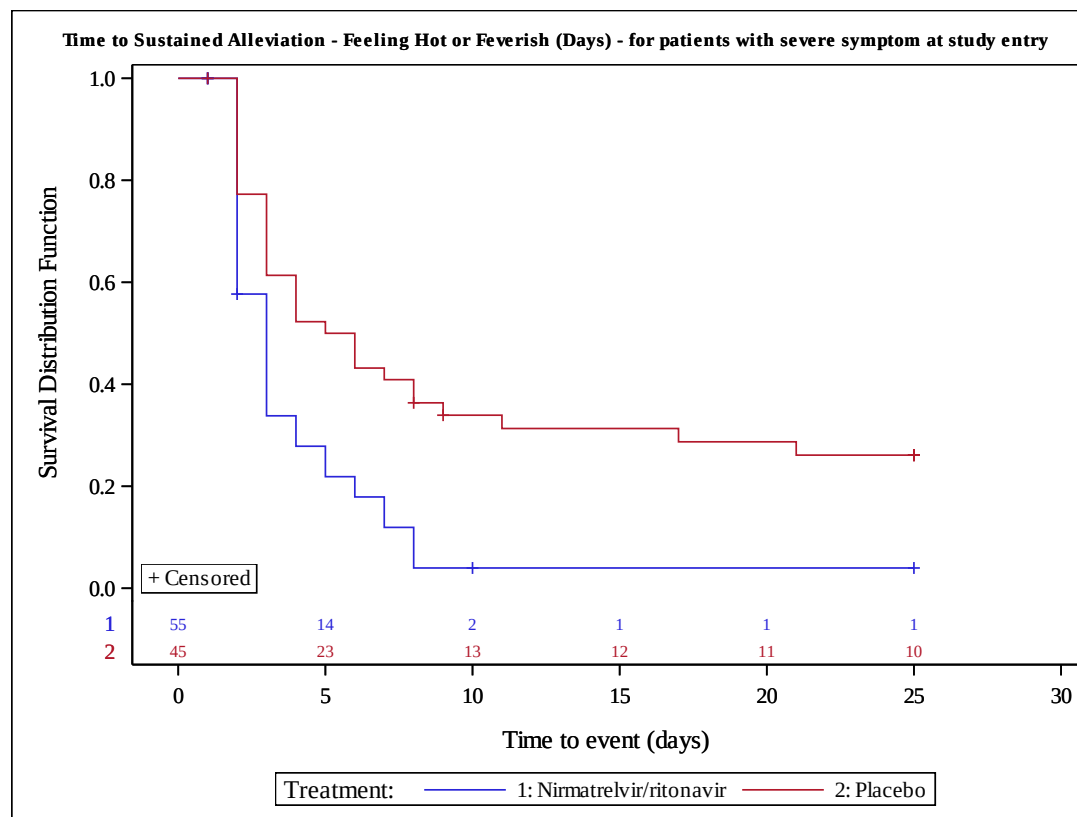
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Feeling Hot or Feverish

Final

	Nirmatrelvir/ritonavir (N=631)	Placebo (N=640)
Number of subjects with events, n (%)	545 (86.4)	489 (76.4)
Number of censored subjects, n (%)	86 (13.6)	151 (23.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (NE, NE)	7.0 (6.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.395 (1.230, 1.582)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.411 (1.248, 1.596)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

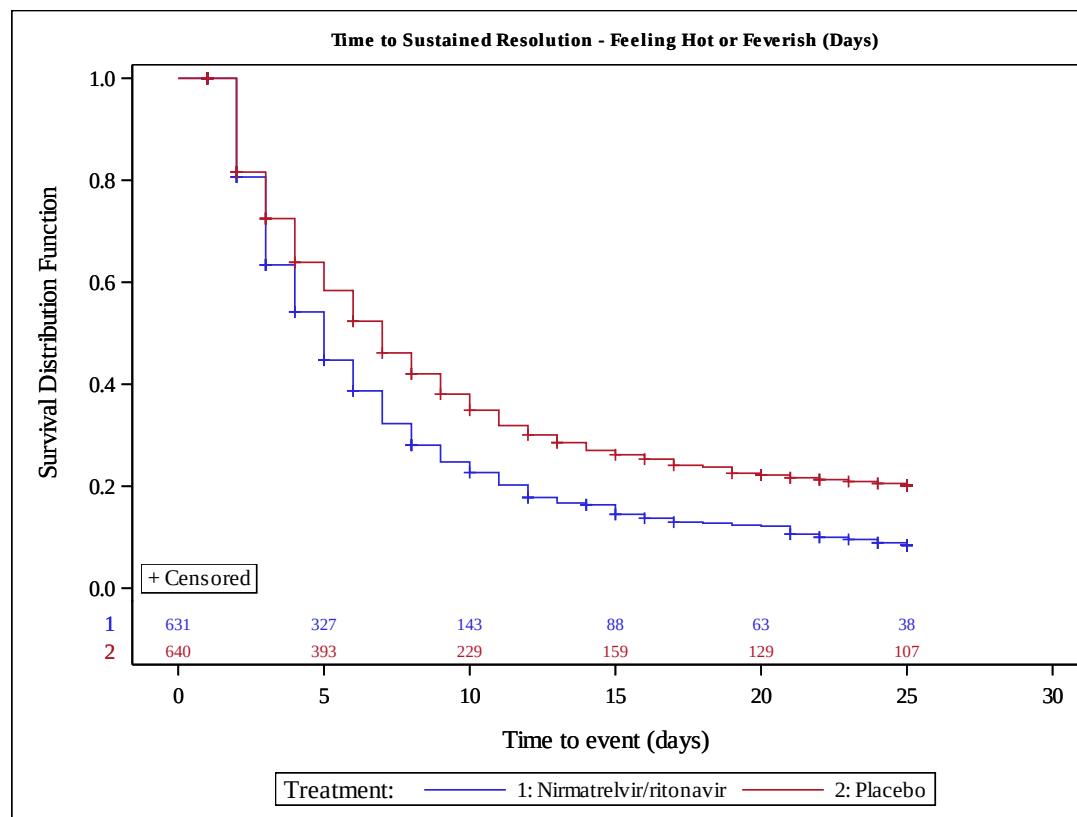
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Feeling Hot or Feverish

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish

Final

	Nirmatrelvir/ritonavir (N=55)	Placebo (N=45)
Number of subjects with events, n (%)	48 (87.3)	31 (68.9)
Number of censored subjects, n (%)	7 (12.7)	14 (31.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 8.0)	9.0 (7.0, 17.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	2.177 (1.323, 3.581)	
p-value [3]	0.002	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	2.178 (1.369, 3.465)	
p-value [3]	0.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

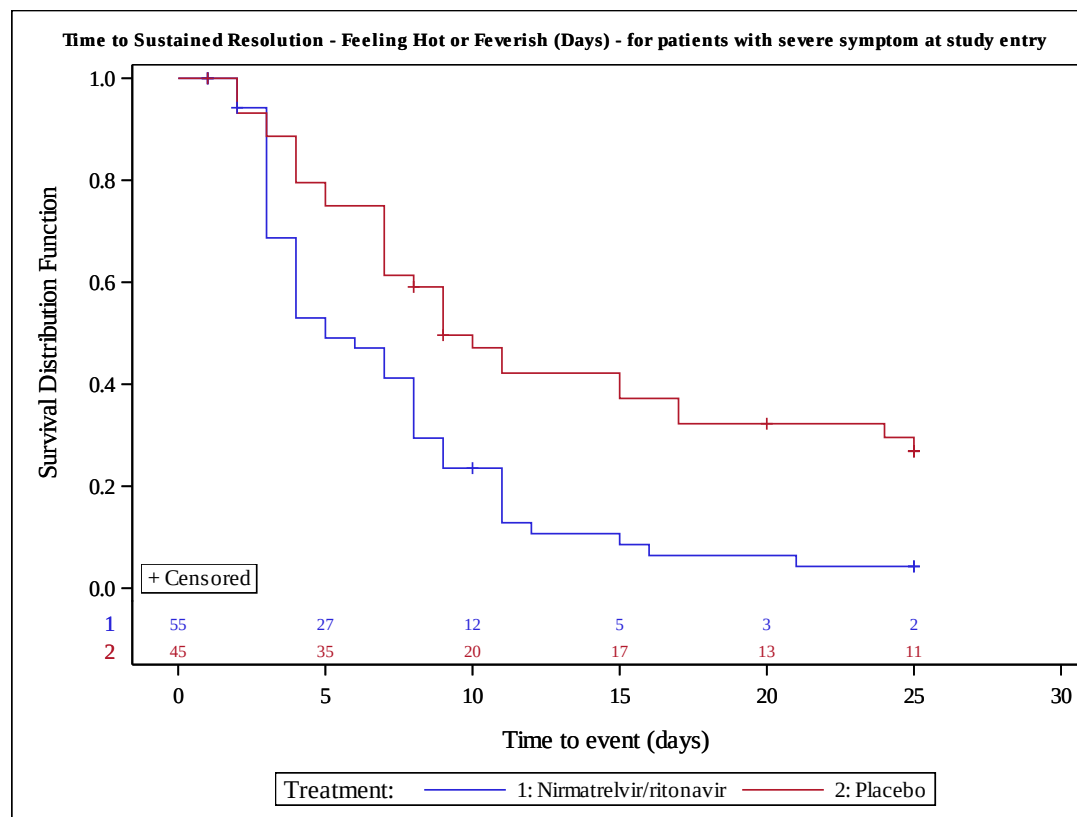
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Nausea

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	214 (20.9)	249 (24.0)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.837 (0.676, 1.036) 0.102	
Relative Risk (95% CI)	0.876 (0.745, 1.031) 0.111	
Risk Difference (95% CI)	-0.029 (-0.064, 0.007) 0.113	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.834 (0.678, 1.026) 0.086	
Relative Risk (95% CI)	0.869 (0.739, 1.020) 0.087	
Risk Difference (95% CI)	-0.032 (-0.068, 0.004) 0.086	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Nausea

Final

	Nirmatrelvir/ritonavir (N=370)	Placebo (N=374)
Number of subjects with events, n (%)	309 (83.5)	296 (79.1)
Number of censored subjects, n (%)	61 (16.5)	78 (20.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 6.0)	6.0 (5.0, 7.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.171 (0.994, 1.380)	
p-value [3]	0.059	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.175 (1.001, 1.378)	
p-value [3]	0.048	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

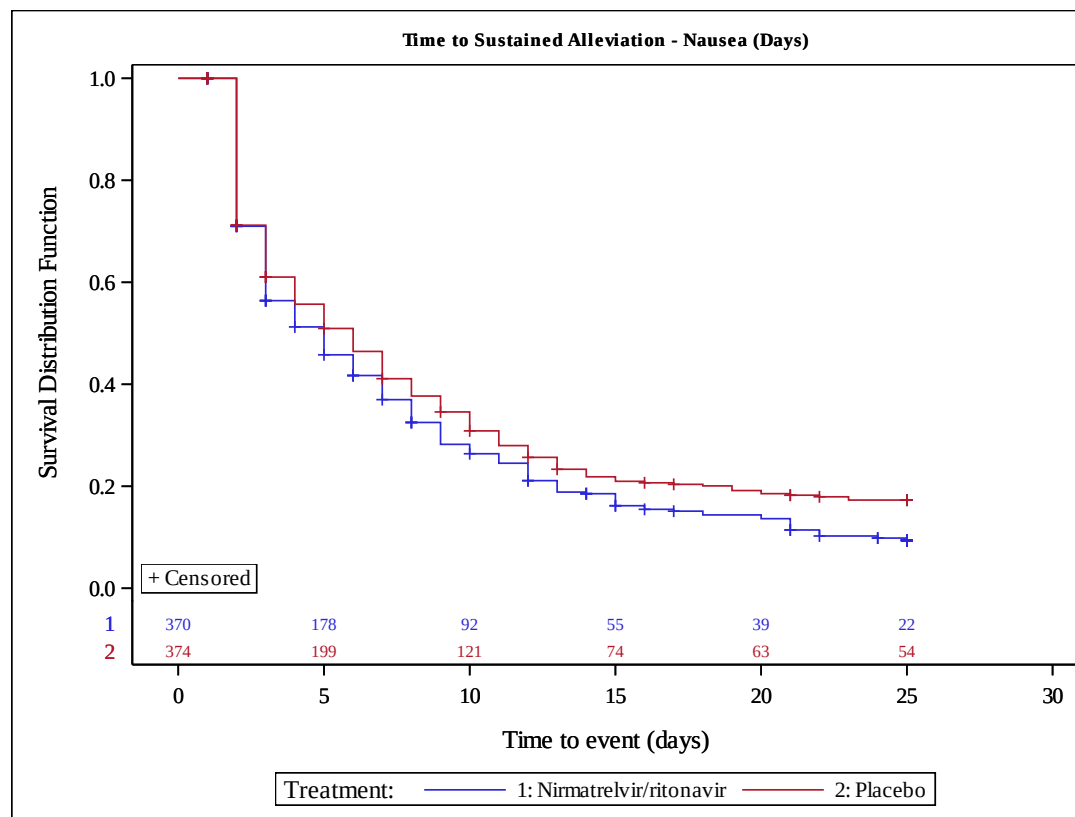
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Nausea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Nausea

Final

	Nirmatrelvir/ritonavir (N=20)	Placebo (N=18)
Number of subjects with events, n (%)	16 (80.0)	13 (72.2)
Number of censored subjects, n (%)	4 (20.0)	5 (27.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	11.0 (3.0, 13.0)	8.0 (2.0, 9.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	0.933 (0.392, 2.219)	
p-value [3]	0.874	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	0.879 (0.417, 1.855)	
p-value [3]	0.736	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

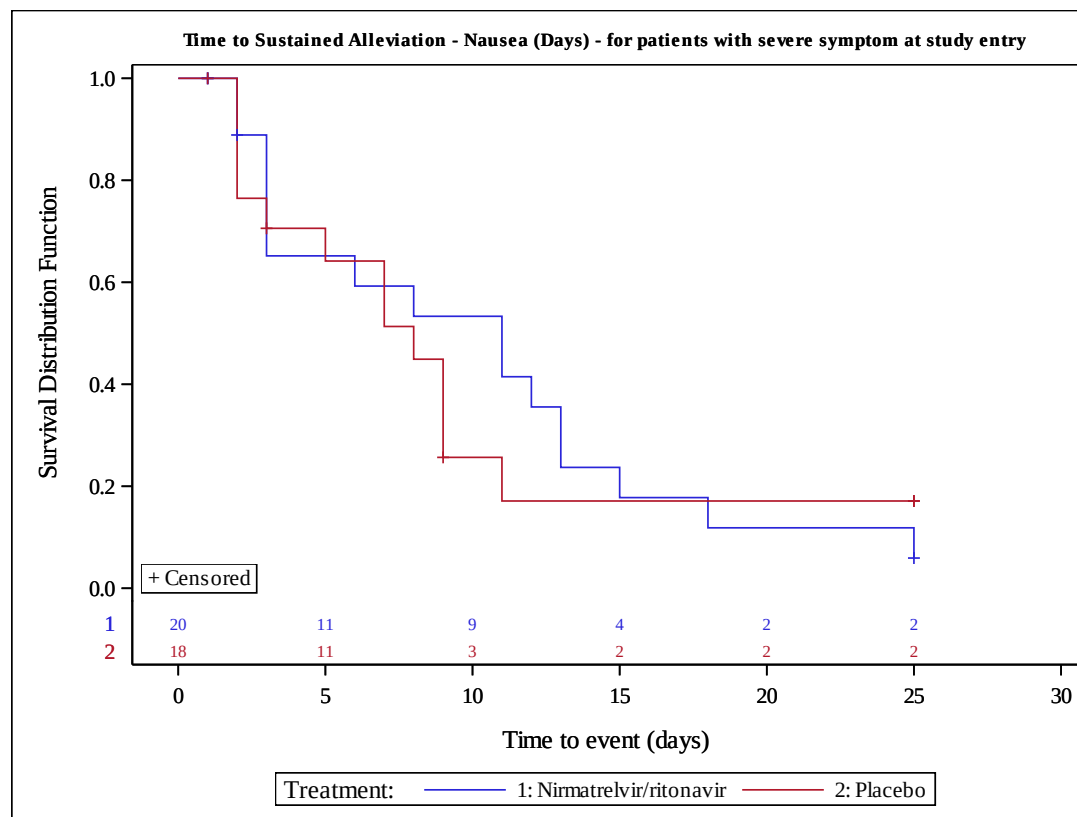
[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Nausea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Nausea

Final

	Nirmatrelvir/ritonavir (N=370)	Placebo (N=374)
Number of subjects with events, n (%)	296 (80.0)	278 (74.3)
Number of censored subjects, n (%)	74 (20.0)	96 (25.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	7.0 (6.0, 8.0)	7.0 (6.0, 9.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.199 (1.014, 1.418)	
p-value [3]	0.034	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.196 (1.015, 1.409)	
p-value [3]	0.033	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

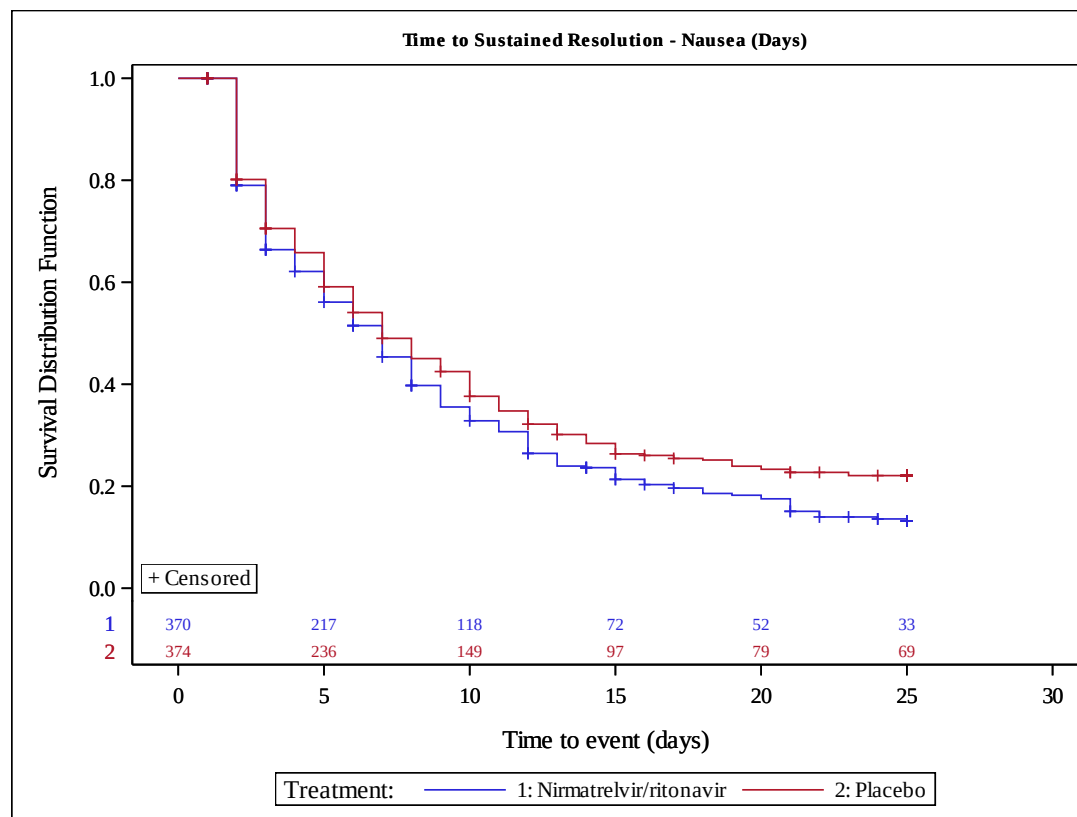
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Nausea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Nausea

Final

	Nirmatrelvir/ritonavir (N=20)	Placebo (N=18)
Number of subjects with events, n (%)	14 (70.0)	11 (61.1)
Number of censored subjects, n (%)	6 (30.0)	7 (38.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	13.0 (5.0, 18.0)	11.0 (7.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.360 (0.498, 3.718)	
p-value [3]	0.549	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.172 (0.530, 2.589)	
p-value [3]	0.695	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

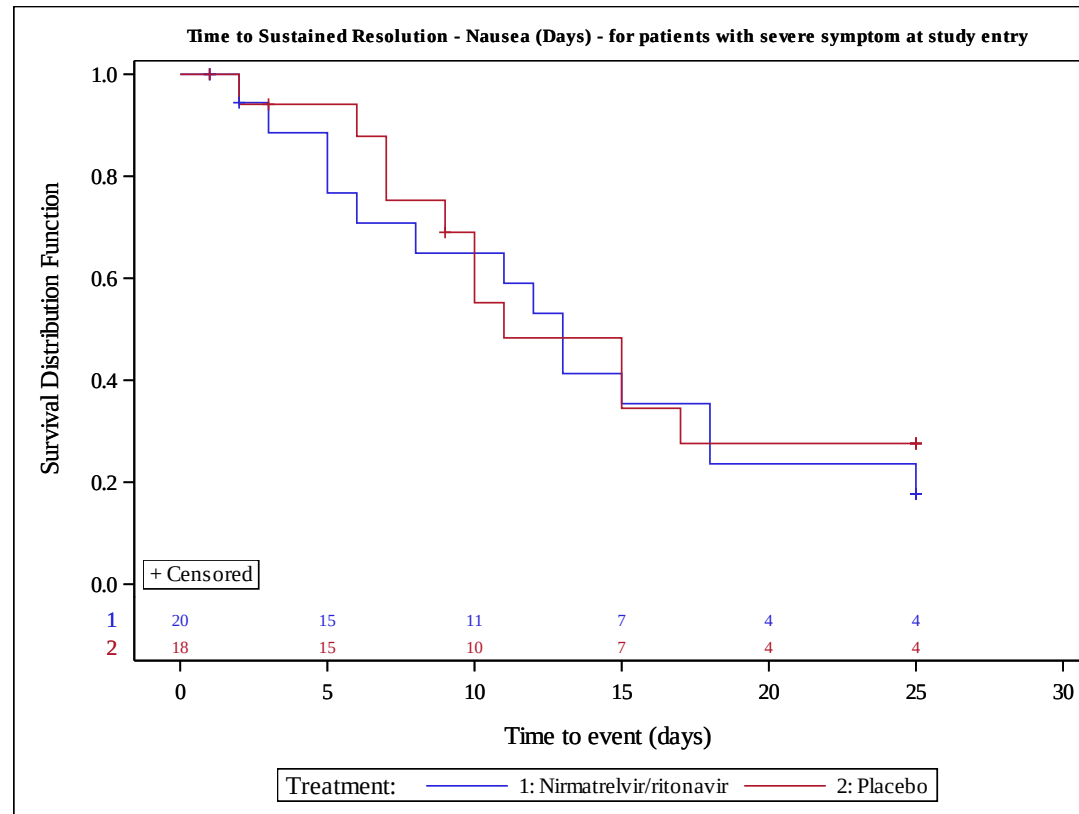
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Nausea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Vomit

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	82 (8.0)	100 (9.6)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.804 (0.588, 1.100) 0.172	
Relative Risk (95% CI)	0.820 (0.619, 1.088) 0.169	
Risk Difference (95% CI)	-0.016 (-0.039, 0.008) 0.198	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.814 (0.600, 1.105) 0.187	
Relative Risk (95% CI)	0.829 (0.627, 1.095) 0.187	
Risk Difference (95% CI)	-0.017 (-0.041, 0.008) 0.186	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Vomit

Final

	Nirmatrelvir/ritonavir (N=124)	Placebo (N=117)
Number of subjects with events, n (%)	105 (84.7)	97 (82.9)
Number of censored subjects, n (%)	19 (15.3)	20 (17.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (2.0, 3.0)	3.0 (2.0, 5.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.140 (0.850, 1.528)	
p-value [3]	0.382	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.113 (0.844, 1.468)	
p-value [3]	0.447	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

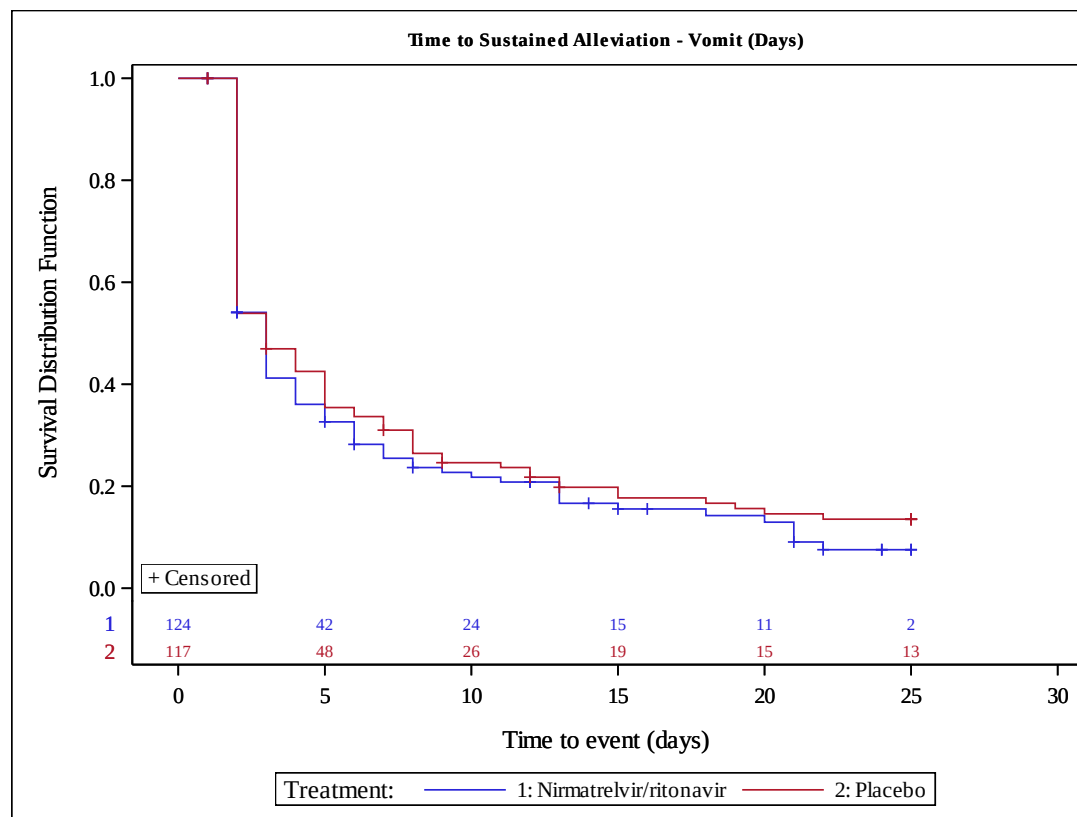
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Vomit

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Vomit

Final

	Nirmatrelvir/ritonavir (N=4)	Placebo (N=3)
Number of subjects with events, n (%)	3 (75.0)	2 (66.7)
Number of censored subjects, n (%)	1 (25.0)	1 (33.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	13.0 (2.0, NE)	8.0 (2.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.375 (0.084, 22.469)	
p-value [3]	0.823	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	0.871 (0.143, 5.316)	
p-value [3]	0.881	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

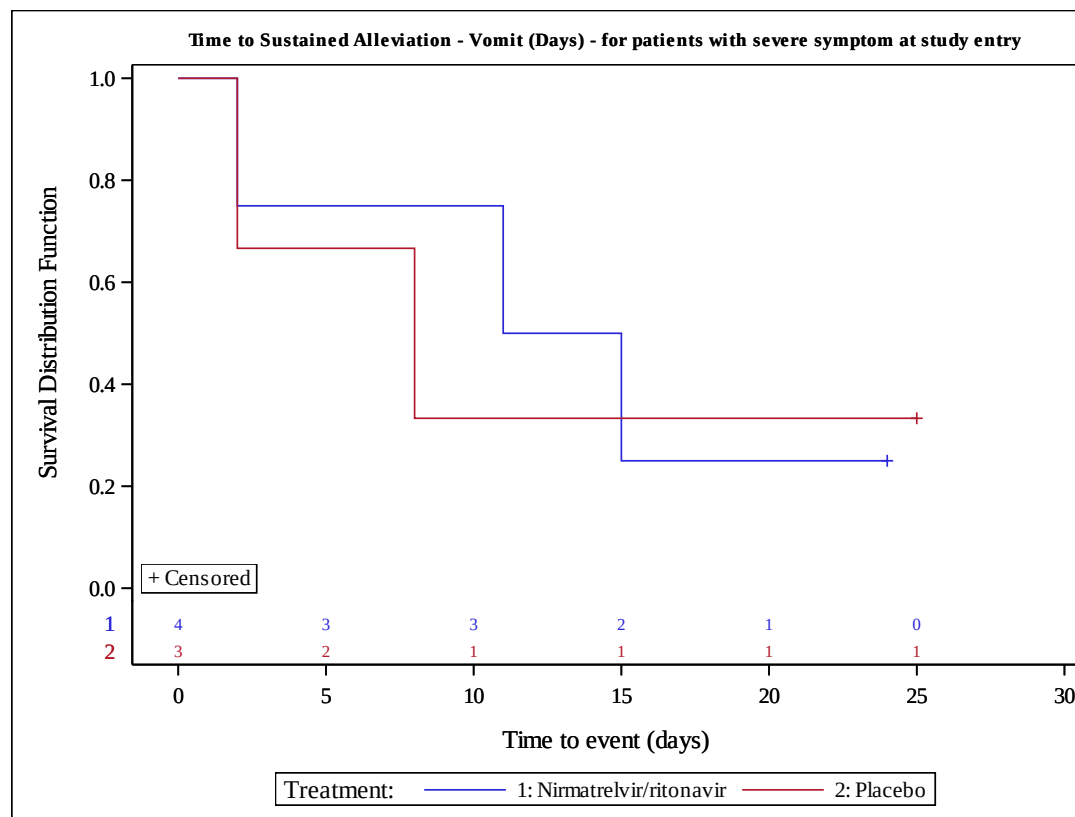
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Vomit

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Vomit

Final

	Nirmatrelvir/ritonavir (N=124)	Placebo (N=117)
Number of subjects with events, n (%)	105 (84.7)	97 (82.9)
Number of censored subjects, n (%)	19 (15.3)	20 (17.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (2.0, 4.0)	3.0 (2.0, 5.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.117 (0.833, 1.499)	
p-value [3]	0.459	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.082 (0.821, 1.427)	
p-value [3]	0.575	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

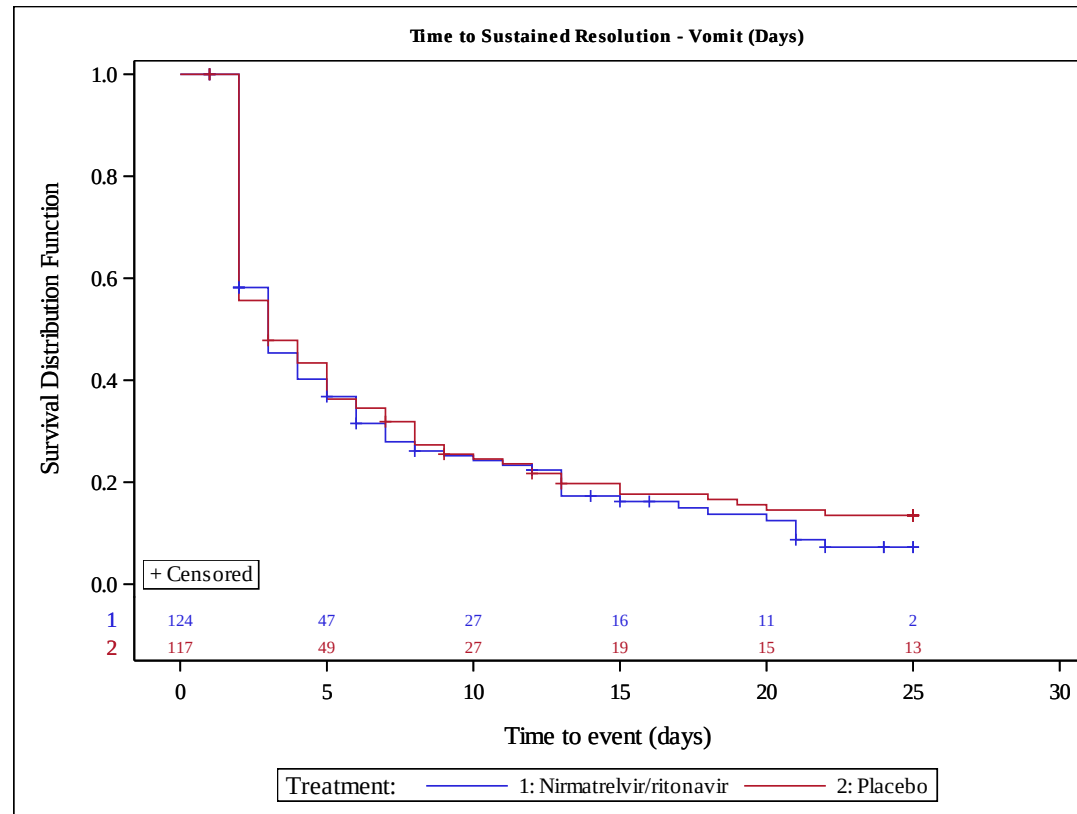
[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Pfizer Inc
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Modified Intent-To-Treat (mITT1) set
Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Vomit

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Vomit

Final

	Nirmatrelvir/ritonavir (N=4)	Placebo (N=3)
Number of subjects with events, n (%)	3 (75.0)	2 (66.7)
Number of censored subjects, n (%)	1 (25.0)	1 (33.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	13.0 (4.0, NE)	10.0 (3.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.375 (0.084, 22.469)	
p-value [3]	0.823	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	0.801 (0.132, 4.874)	
p-value [3]	0.810	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

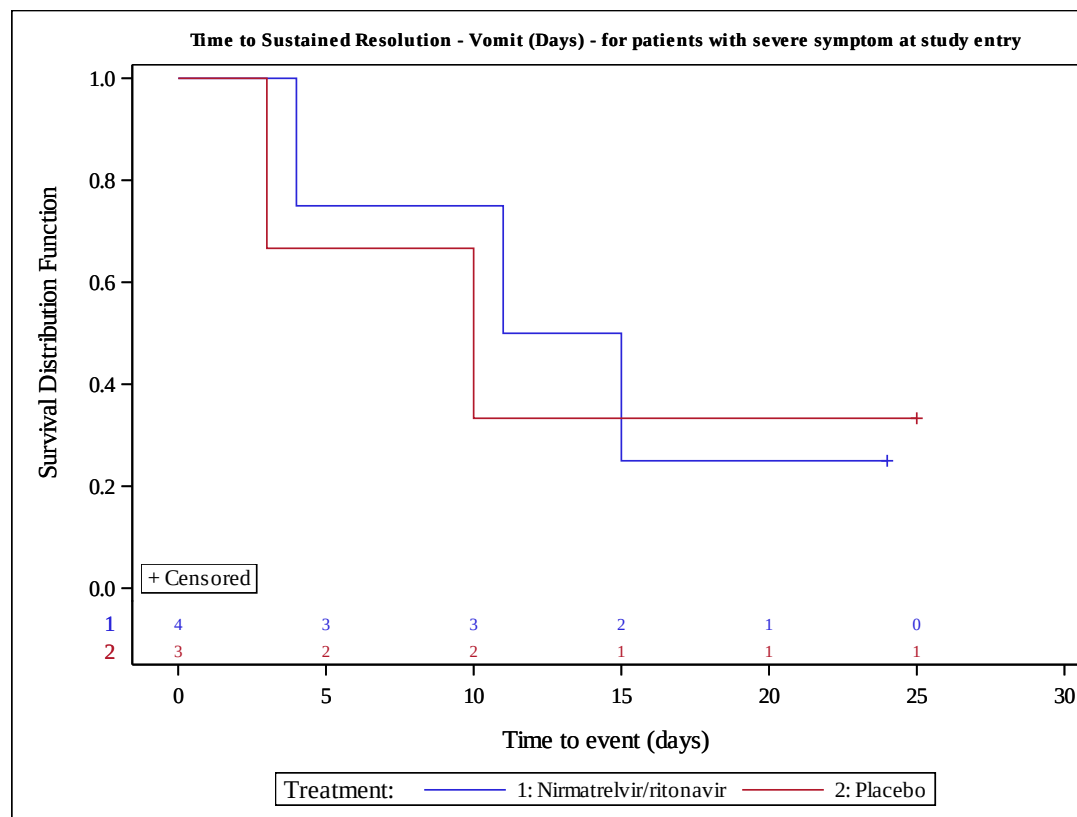
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Vomit

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Diarrhea

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	266 (25.9)	225 (21.7)
Adjusted analysis [1] Odds Ratio (95% CI)	1.251 (1.012, 1.547) 0.039	
Relative Risk (95% CI)	1.183 (1.015, 1.380) 0.032	
Risk Difference (95% CI)	0.026 (-0.008, 0.060) 0.127	
Unadjusted analysis [2] Odds Ratio (95% CI)	1.263 (1.031, 1.548) 0.024	
Relative Risk (95% CI)	1.195 (1.023, 1.395) 0.024	
Risk Difference (95% CI)	0.042 (0.006, 0.079) 0.024	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Diarrhea

Final

	Nirmatrelvir/ritonavir (N=278)	Placebo (N=259)
Number of subjects with events, n (%)	239 (86.0)	211 (81.5)
Number of censored subjects, n (%)	39 (14.0)	48 (18.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 6.0)	4.0 (3.0, 5.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.060 (0.875, 1.284)	
p-value [3]	0.553	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.057 (0.878, 1.272)	
p-value [3]	0.558	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

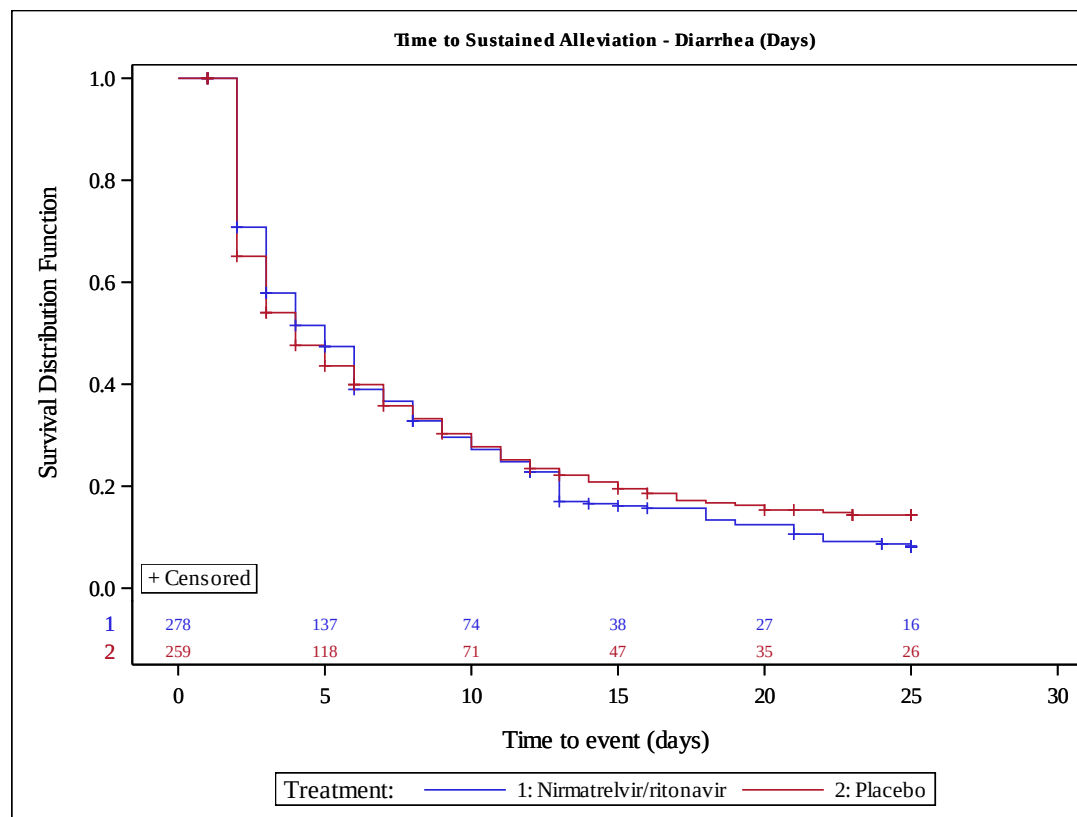
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Diarrhea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea

Final

	Nirmatrelvir/ritonavir (N=18)	Placebo (N=12)
Number of subjects with events, n (%)	15 (83.3)	10 (83.3)
Number of censored subjects, n (%)	3 (16.7)	2 (16.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (2.0, 13.0)	11.0 (2.0, 15.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.007 (0.400, 2.533)	
p-value [3]	0.988	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.129 (0.502, 2.538)	
p-value [3]	0.769	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

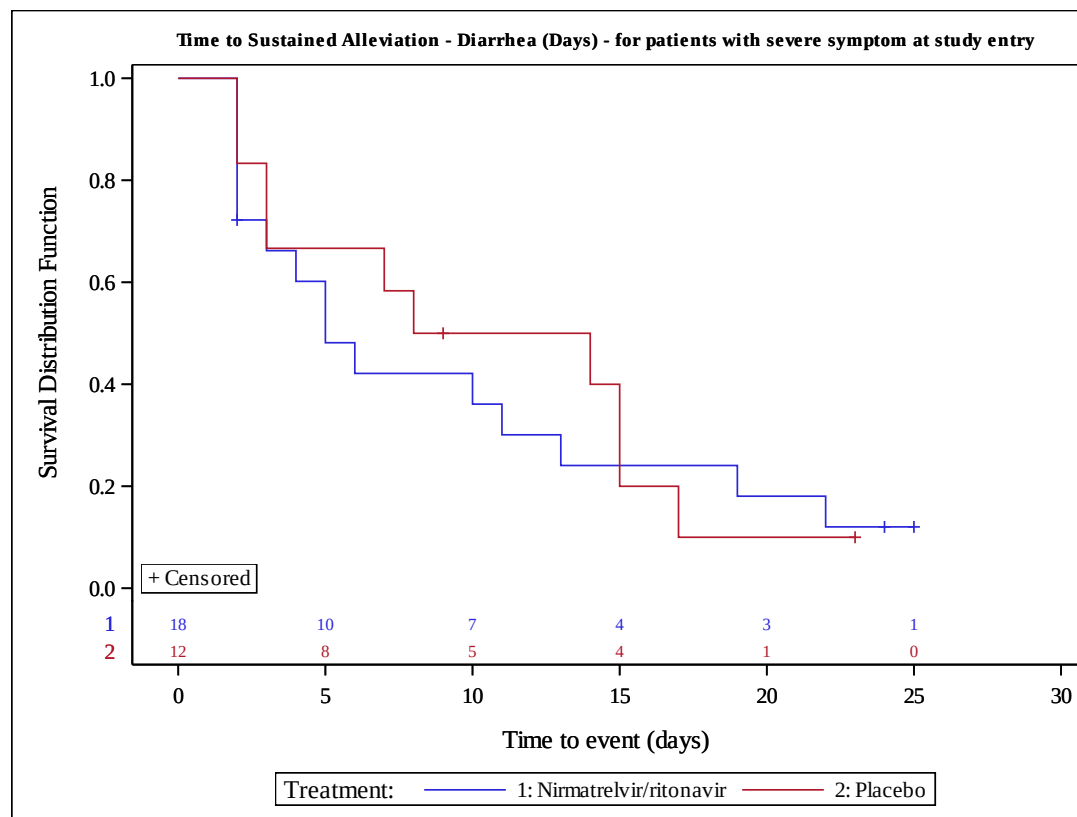
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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 Overall Study population
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Diarrhea

Final

	Nirmatrelvir/ritonavir (N=278)	Placebo (N=259)
Number of subjects with events, n (%)	235 (84.5)	196 (75.7)
Number of censored subjects, n (%)	43 (15.5)	63 (24.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	6.0 (6.0, 7.0)	6.0 (5.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.192 (0.978, 1.452)	
p-value [3]	0.082	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.180 (0.975, 1.427)	
p-value [3]	0.089	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

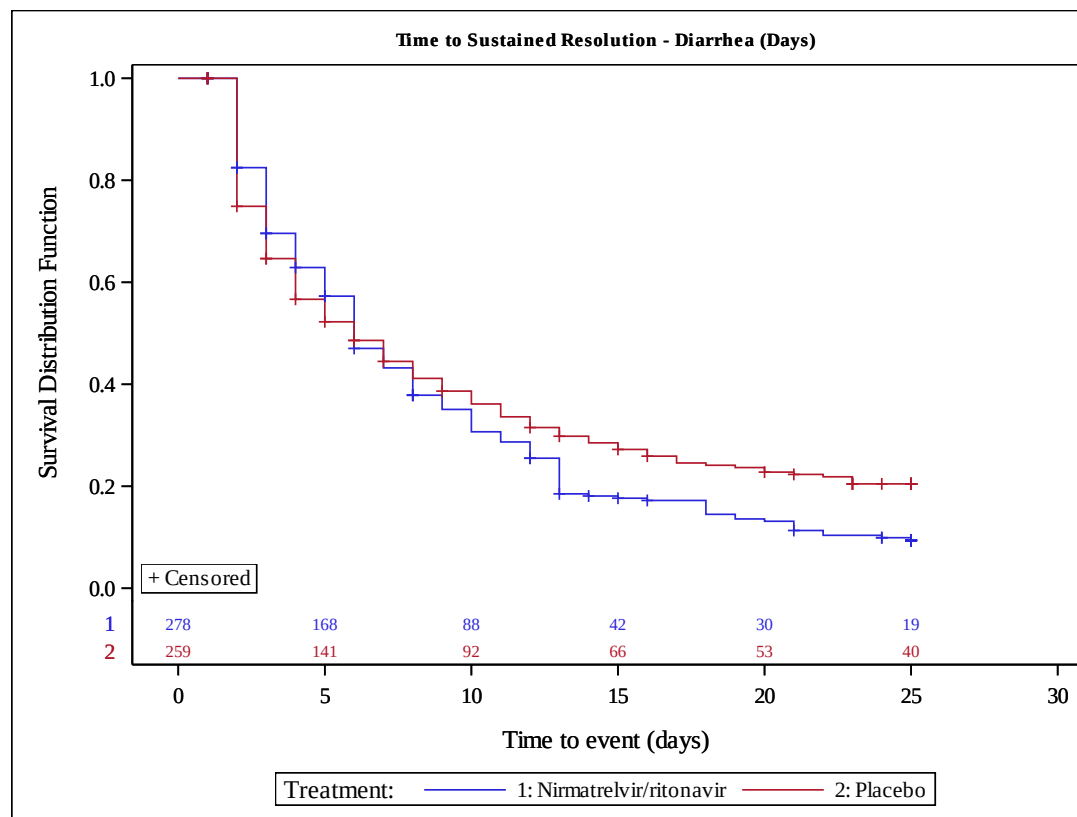
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Diarrhea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea

Final

	Nirmatrelvir/ritonavir (N=18)	Placebo (N=12)
Number of subjects with events, n (%)	14 (77.8)	6 (50.0)
Number of censored subjects, n (%)	4 (22.2)	6 (50.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	12.0 (6.0, 18.0)	18.0 (8.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	2.749 (0.891, 8.483)	
p-value [3]	0.079	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	2.502 (0.956, 6.553)	
p-value [3]	0.062	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

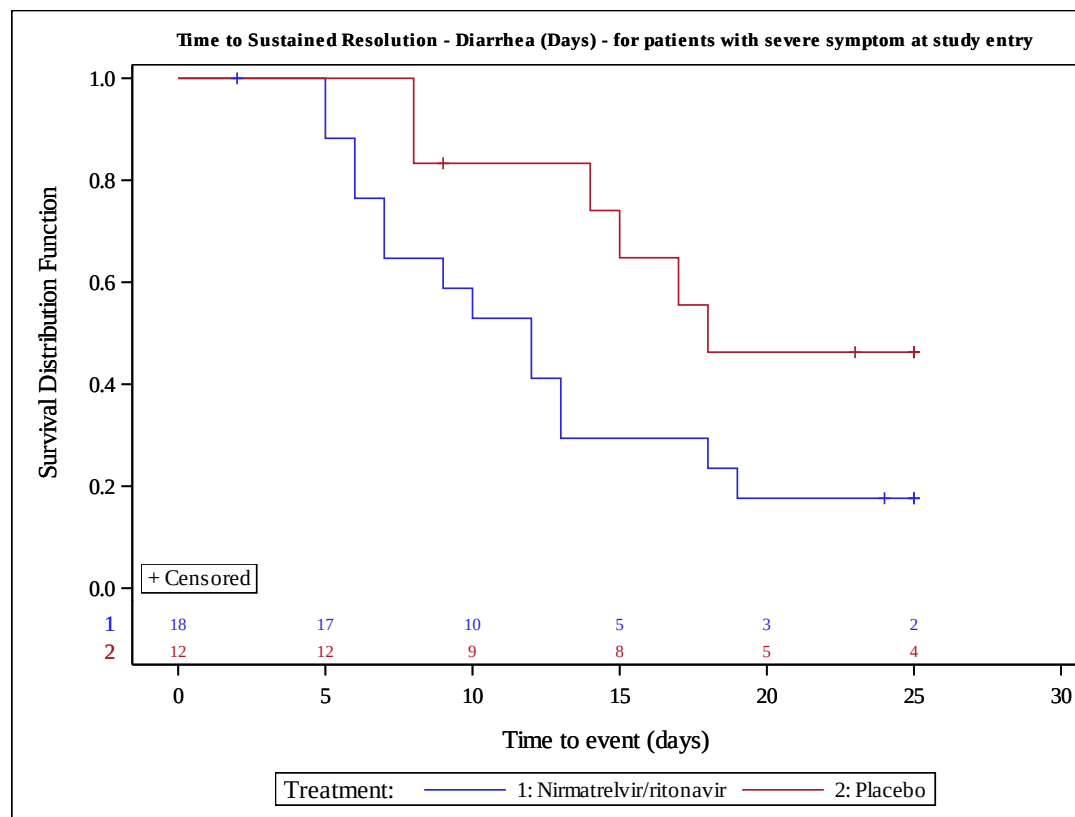
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea

Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Worsening of Signs and Symptoms - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	248 (24.2)	263 (25.4)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.914 (0.741, 1.127) 0.400	
Relative Risk (95% CI)	0.936 (0.805, 1.088) 0.390	
Risk Difference (95% CI)	-0.018 (-0.053, 0.017) 0.313	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.938 (0.768, 1.146) 0.531	
Relative Risk (95% CI)	0.953 (0.820, 1.108) 0.531	
Risk Difference (95% CI)	-0.012 (-0.049, 0.025) 0.531	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=566)	Placebo (N=581)
Number of subjects with events, n (%)	410 (72.4)	368 (63.3)
Number of censored subjects, n (%)	156 (27.6)	213 (36.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	10.0 (9.0, 11.0)	13.0 (12.0, 15.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.321 (1.144, 1.526)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.309 (1.137, 1.507)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

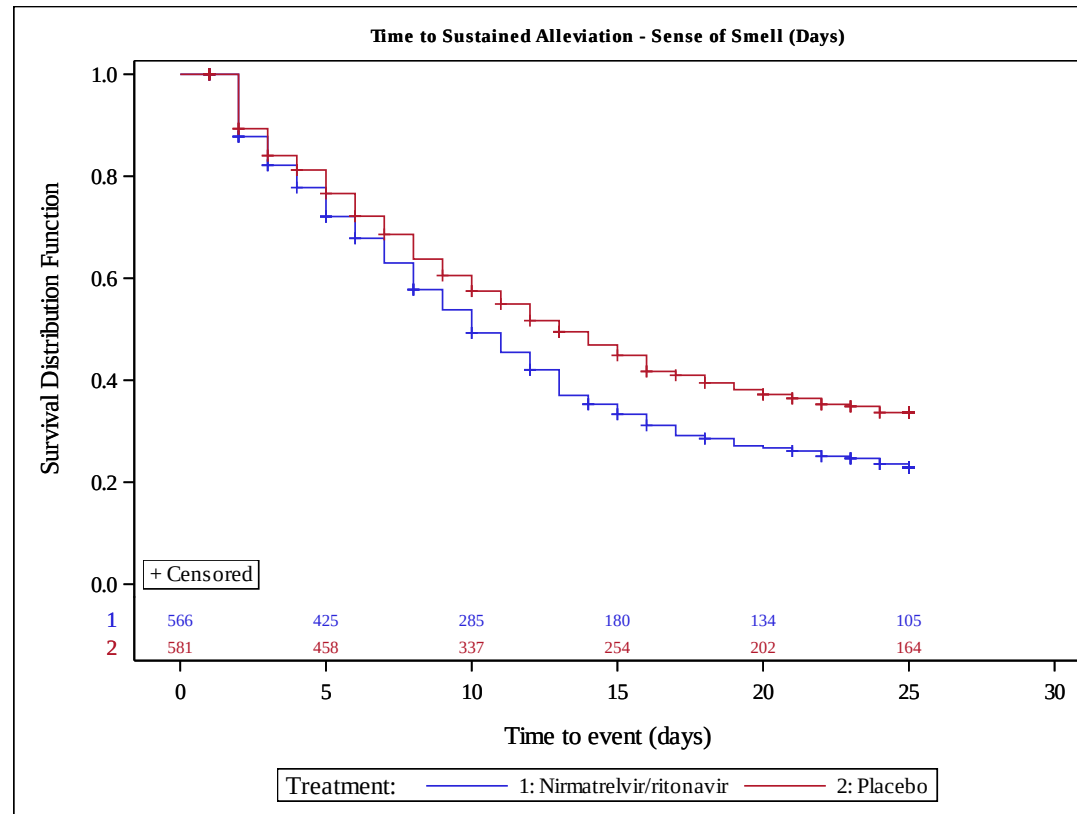
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Loss of smell

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=261)	Placebo (N=266)
Number of subjects with events, n (%)	206 (78.9)	183 (68.8)
Number of censored subjects, n (%)	55 (21.1)	83 (31.2)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	8.0 (7.0, 9.0)	9.0 (8.0, 11.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.305 (1.063, 1.603)	
p-value [3]	0.011	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.272 (1.042, 1.553)	
p-value [3]	0.018	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

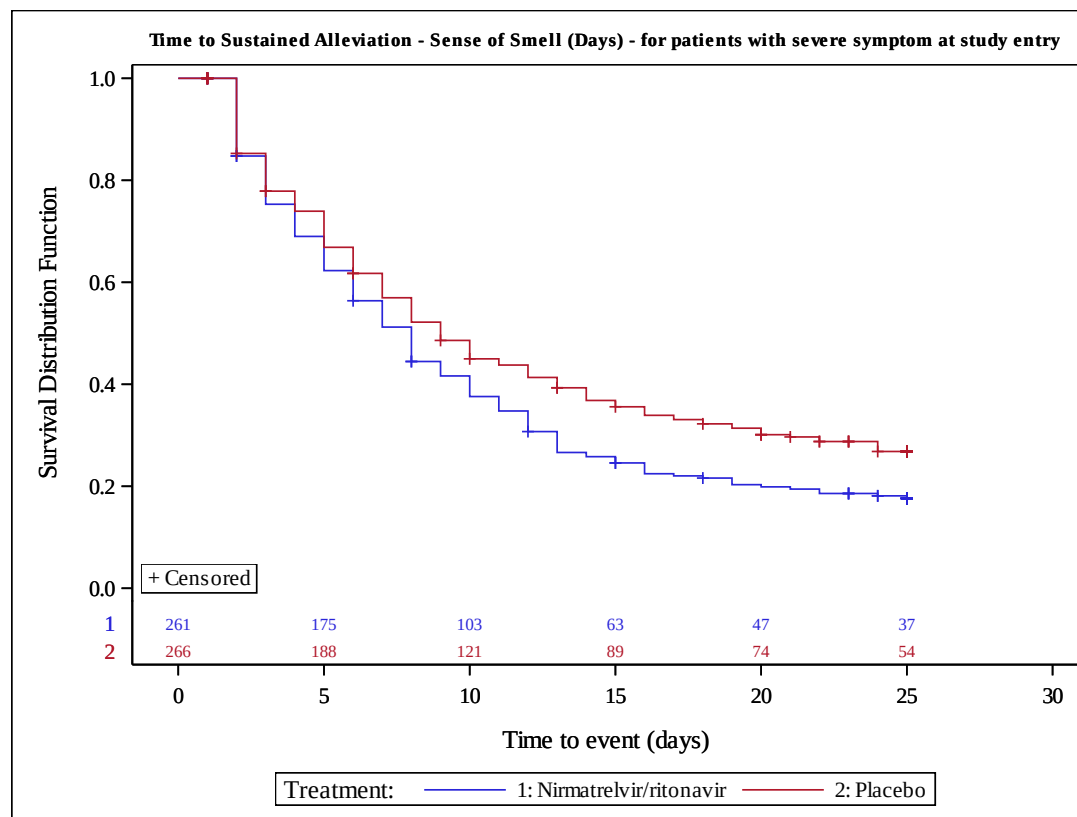
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of smell

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=566)	Placebo (N=581)
Number of subjects with events, n (%)	348 (61.5)	295 (50.8)
Number of censored subjects, n (%)	218 (38.5)	286 (49.2)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	15.0 (14.0, 17.0)	22.0 (18.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.347 (1.150, 1.578)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.359 (1.164, 1.588)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

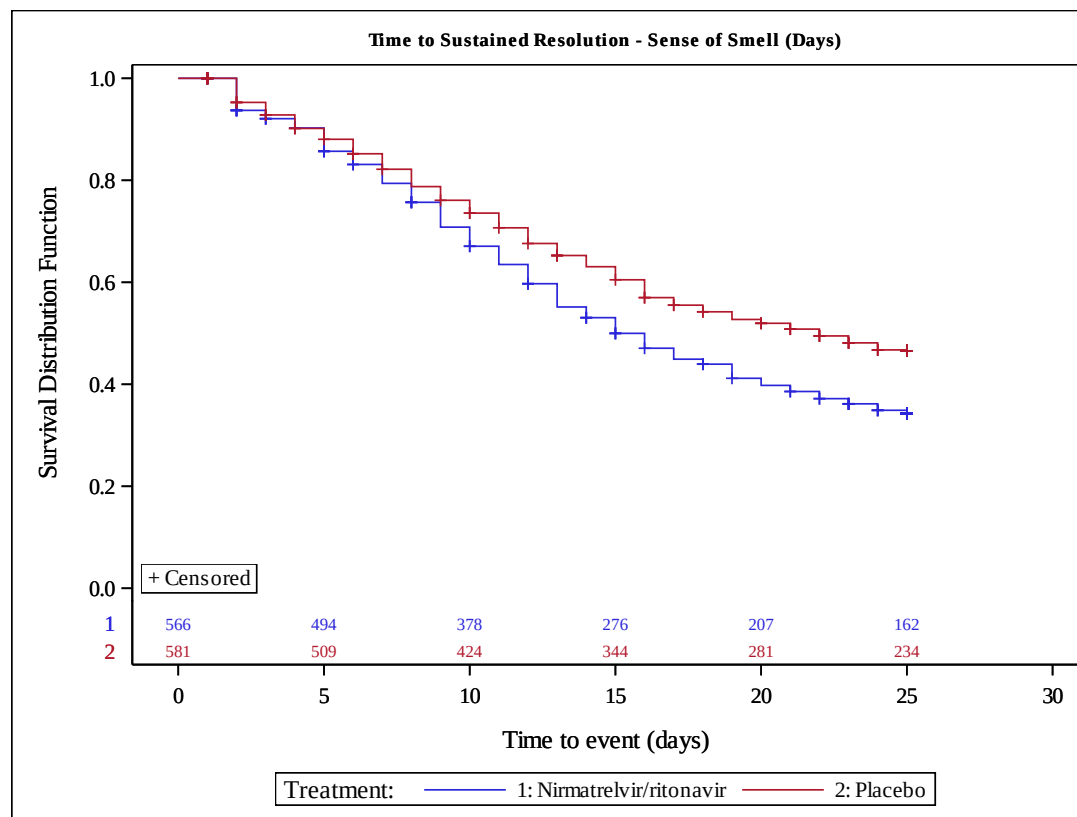
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Modified Intent-To-Treat (mITT1) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Loss of smell

Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=261)	Placebo (N=266)
Number of subjects with events, n (%)	144 (55.2)	110 (41.4)
Number of censored subjects, n (%)	117 (44.8)	156 (58.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	20.0 (17.0, 23.0)	NE (24.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.441 (1.117, 1.857)	
p-value [3]	0.005	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.442 (1.125, 1.849)	
p-value [3]	0.004	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

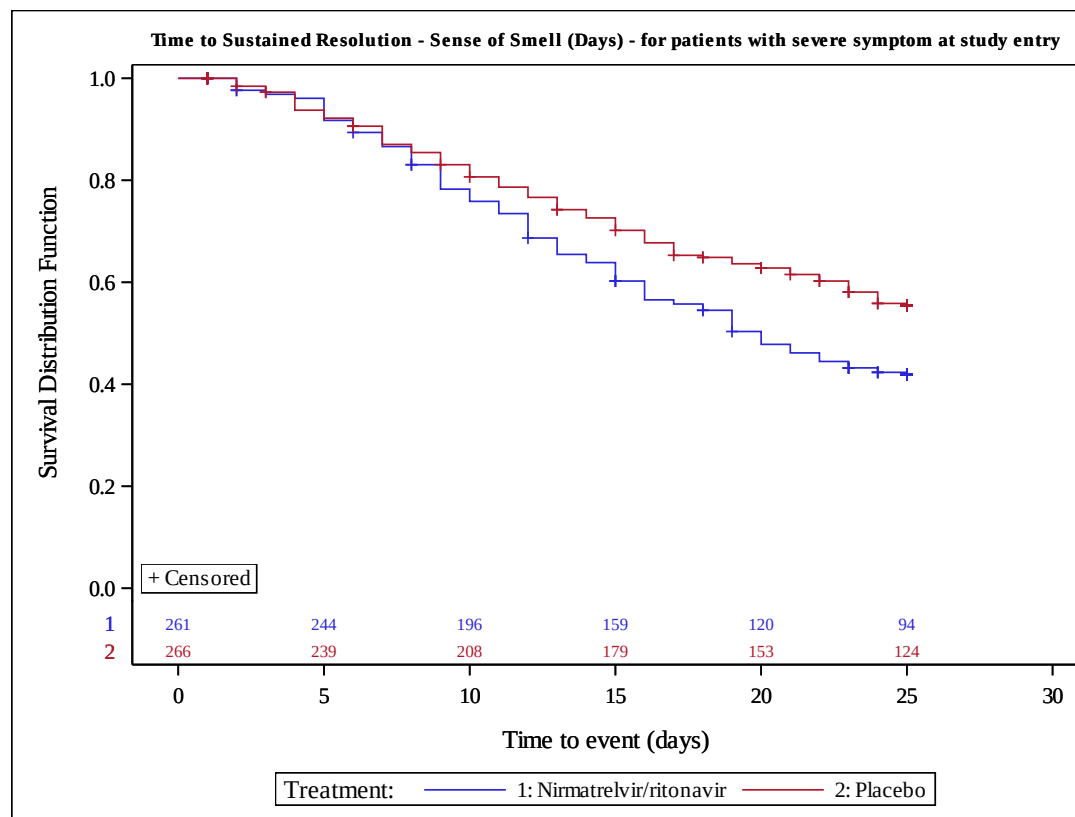
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Kaplan-Meier Plot of Time to Sustained Resolution of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of smell

Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Worsening of Signs and Symptoms - Loss of taste

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	246 (24.0)	255 (24.6)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.942 (0.763, 1.164) 0.581	
Relative Risk (95% CI)	0.966 (0.829, 1.126) 0.660	
Risk Difference (95% CI)	-0.021 (-0.056, 0.014) 0.241	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.967 (0.791, 1.183) 0.745	
Relative Risk (95% CI)	0.975 (0.837, 1.136) 0.745	
Risk Difference (95% CI)	-0.006 (-0.043, 0.031) 0.745	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Loss of taste

Final

	Nirmatrelvir/ritonavir (N=548)	Placebo (N=556)
Number of subjects with events, n (%)	404 (73.7)	357 (64.2)
Number of censored subjects, n (%)	144 (26.3)	199 (35.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	10.0 (9.0, 11.0)	14.0 (12.0, 15.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.367 (1.181, 1.582)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.368 (1.186, 1.578)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

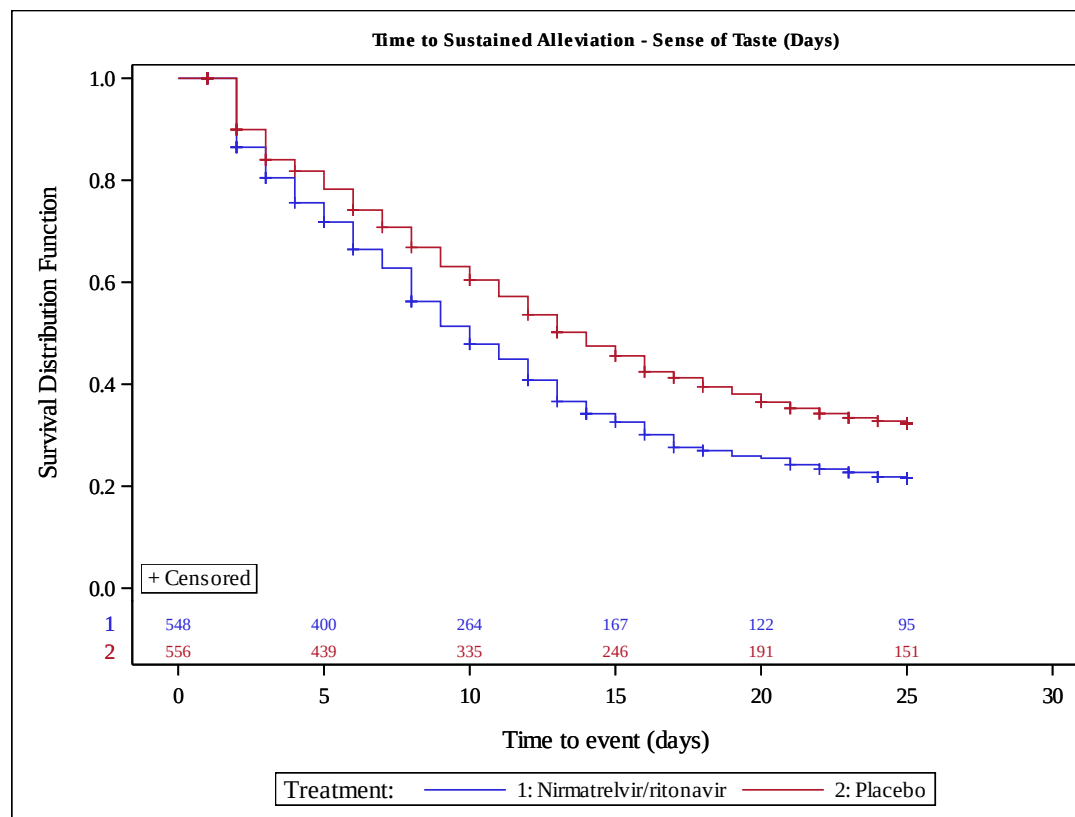
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Loss of taste

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of taste

Final

	Nirmatrelvir/ritonavir (N=225)	Placebo (N=224)
Number of subjects with events, n (%)	181 (80.4)	157 (70.1)
Number of censored subjects, n (%)	44 (19.6)	67 (29.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	7.0 (6.0, 8.0)	10.0 (8.0, 12.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.379 (1.101, 1.729)	
p-value [3]	0.005	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.379 (1.113, 1.709)	
p-value [3]	0.003	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

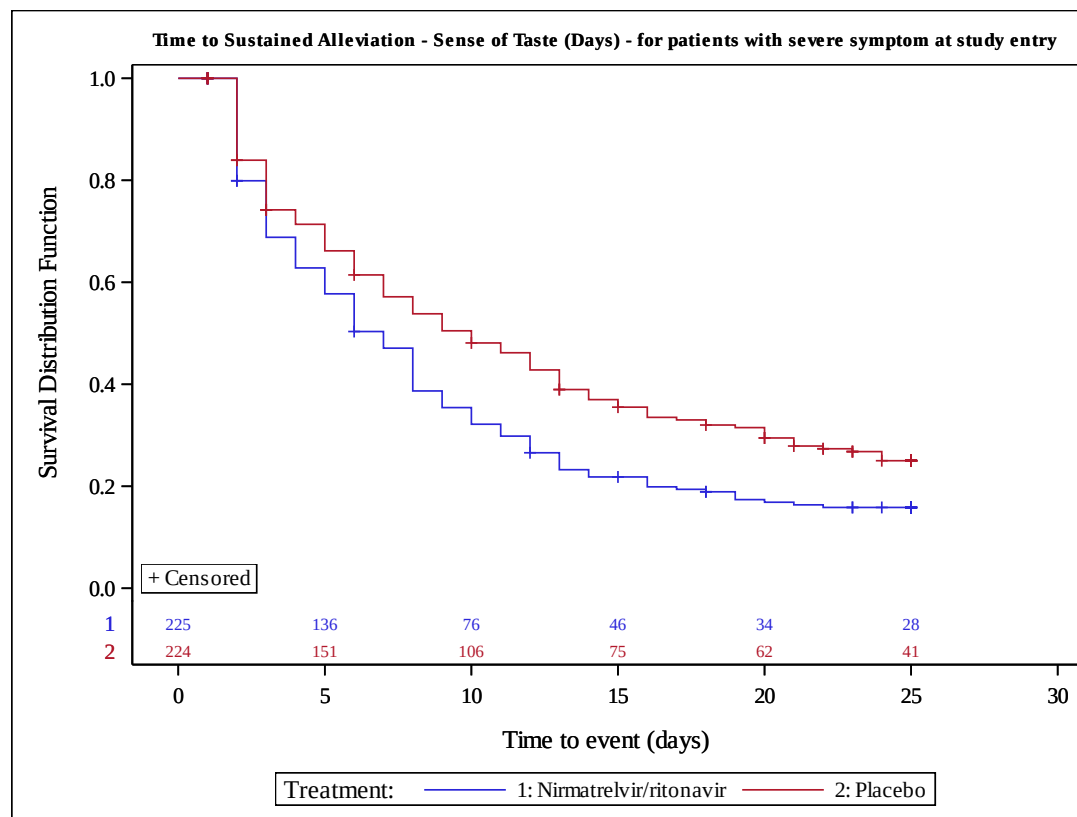
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Pfizer Inc
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Final

	Nirmatrelvir/ritonavir (N=548)	Placebo (N=556)
Number of subjects with events, n (%)	348 (63.5)	297 (53.4)
Number of censored subjects, n (%)	200 (36.5)	259 (46.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	15.0 (14.0, 17.0)	19.0 (17.0, 23.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.311 (1.119, 1.537)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.340 (1.148, 1.565)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

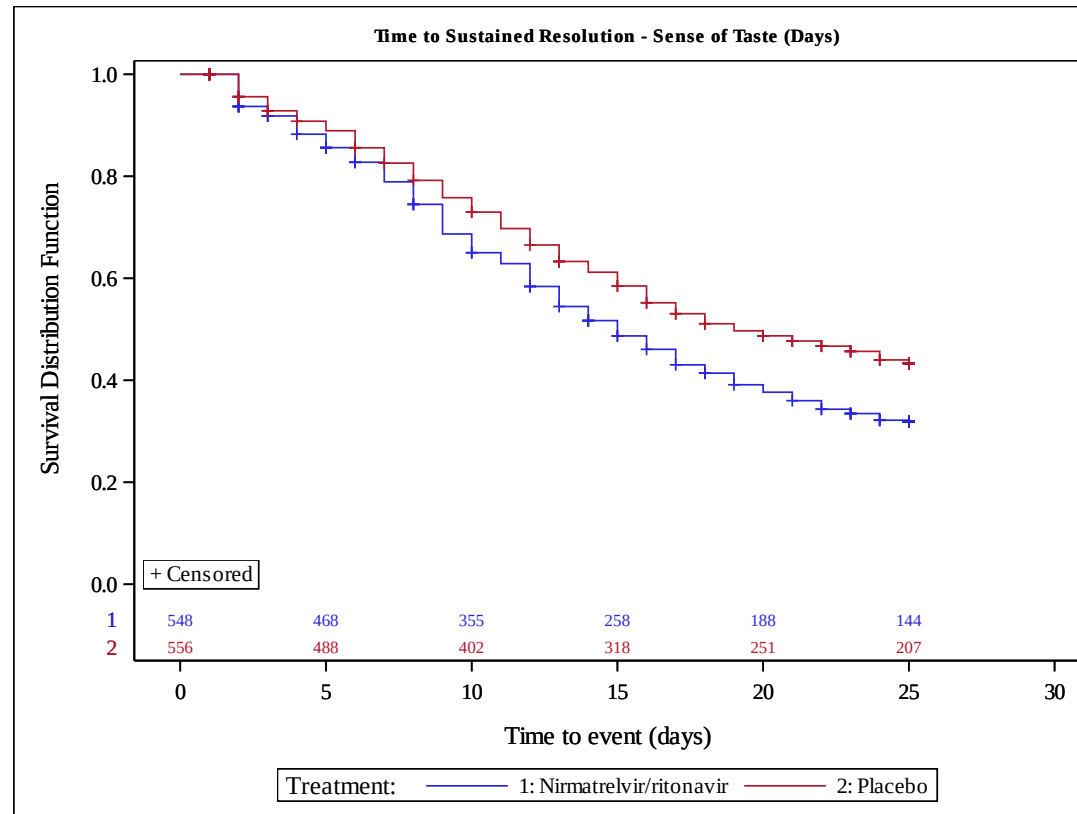
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Final

	Nirmatrelvir/ritonavir (N=225)	Placebo (N=224)
Number of subjects with events, n (%)	125 (55.6)	97 (43.3)
Number of censored subjects, n (%)	100 (44.4)	127 (56.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	19.0 (17.0, 22.0)	NE (24.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.303 (0.987, 1.719)	
p-value [3]	0.062	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.367 (1.049, 1.783)	
p-value [3]	0.021	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

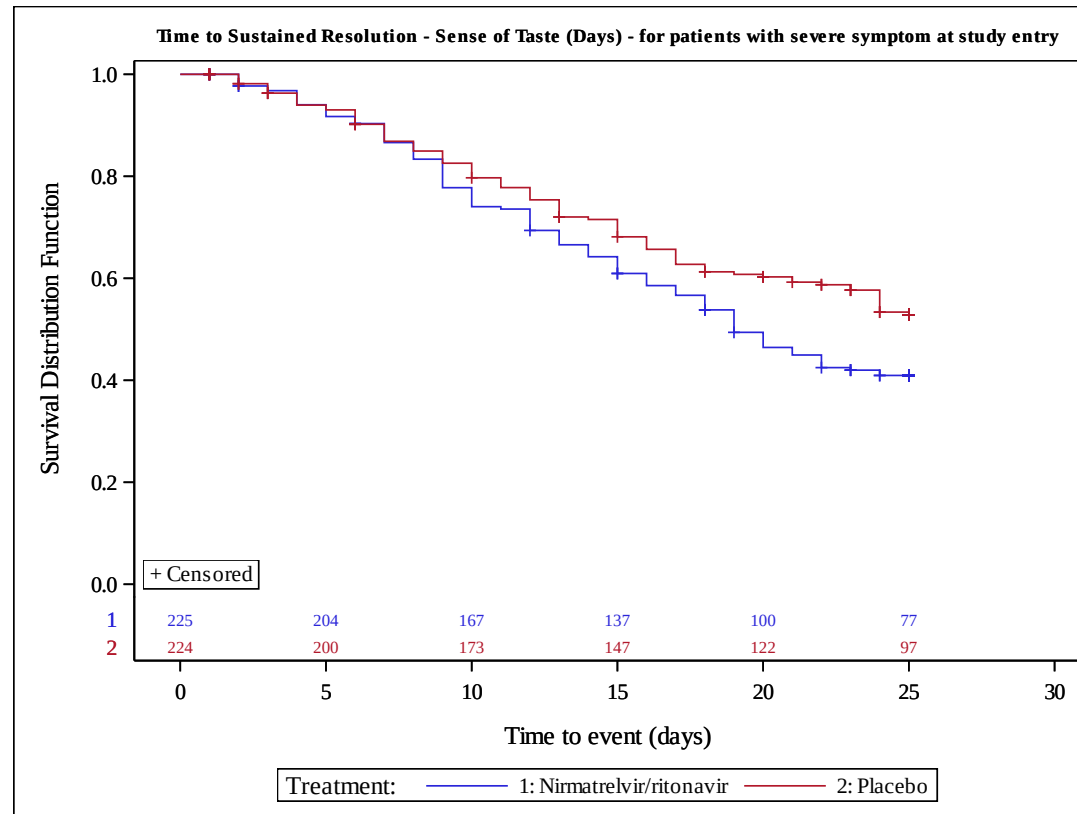
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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 Analysis of Participants with Any Severe Targeted Signs and Symptoms

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	195 (19.0)	216 (20.8)
Adjusted analysis [1] Odds Ratio (95% CI)	0.916 (0.728, 1.152) 0.453	
Relative Risk (95% CI)	0.923 (0.778, 1.096) 0.361	
Risk Difference (95% CI)	NE (NE, NE) NE	
Unadjusted analysis [2] Odds Ratio (95% CI)	0.892 (0.718, 1.107) 0.300	
Relative Risk (95% CI)	0.912 (0.767, 1.085) 0.300	
Risk Difference (95% CI)	-0.018 (-0.053, 0.016) 0.300	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	488 (47.6)	499 (48.1)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.984 (0.818, 1.182) 0.860	
Relative Risk (95% CI)	0.979 (0.898, 1.067) 0.629	
Risk Difference (95% CI)	-0.006 (-0.047, 0.035) 0.774	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.978 (0.823, 1.162) 0.800	
Relative Risk (95% CI)	0.988 (0.903, 1.082) 0.800	
Risk Difference (95% CI)	-0.006 (-0.049, 0.038) 0.800	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

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[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	763 (74.4)	768 (74.1)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.010 (0.823, 1.240) 0.923	
Relative Risk (95% CI)	1.000 (0.951, 1.051) 0.995	
Risk Difference (95% CI)	0.001 (-0.037, 0.038) 0.975	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.016 (0.834, 1.238) 0.874	
Relative Risk (95% CI)	1.004 (0.954, 1.057) 0.874	
Risk Difference (95% CI)	0.003 (-0.035, 0.041) 0.874	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with Response, n (%)	830 (80.9)	821 (79.2)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.084 (0.869, 1.353) 0.474	
Relative Risk (95% CI)	1.012 (0.969, 1.056) 0.597	
Risk Difference (95% CI)	0.010 (-0.024, 0.045) 0.562	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.114 (0.898, 1.383) 0.327	
Relative Risk (95% CI)	1.022 (0.979, 1.067) 0.327	
Risk Difference (95% CI)	0.017 (-0.017, 0.052) 0.327	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with events, n (%)	758 (73.9)	684 (66.0)
Number of censored subjects, n (%)	268 (26.1)	353 (34.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	13.0 (12.0, 13.0)	15.0 (14.0, 16.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.270 (1.143, 1.411)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.289 (1.162, 1.430)	
p-value [3]	<.001	

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[1] Based on the Brookmeyer and Crowley Method.

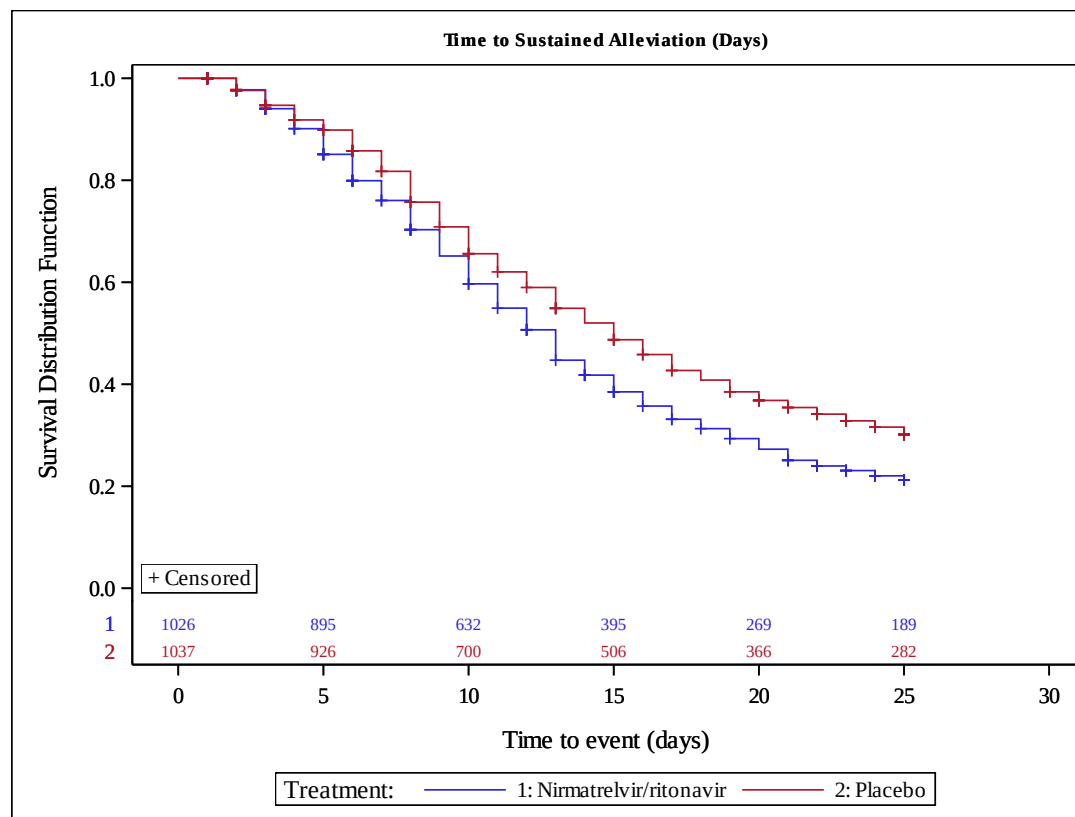
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Final

	Nirmatrelvir/ritonavir (N=213)	Placebo (N=189)
Number of subjects with events, n (%)	180 (84.5)	144 (76.2)
Number of censored subjects, n (%)	33 (15.5)	45 (23.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (4.0, 5.0)	8.0 (7.0, 9.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.394 (1.109, 1.753)	
p-value [3]	0.004	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.454 (1.167, 1.811)	
p-value [3]	<.001	

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[1] Based on the Brookmeyer and Crowley Method.

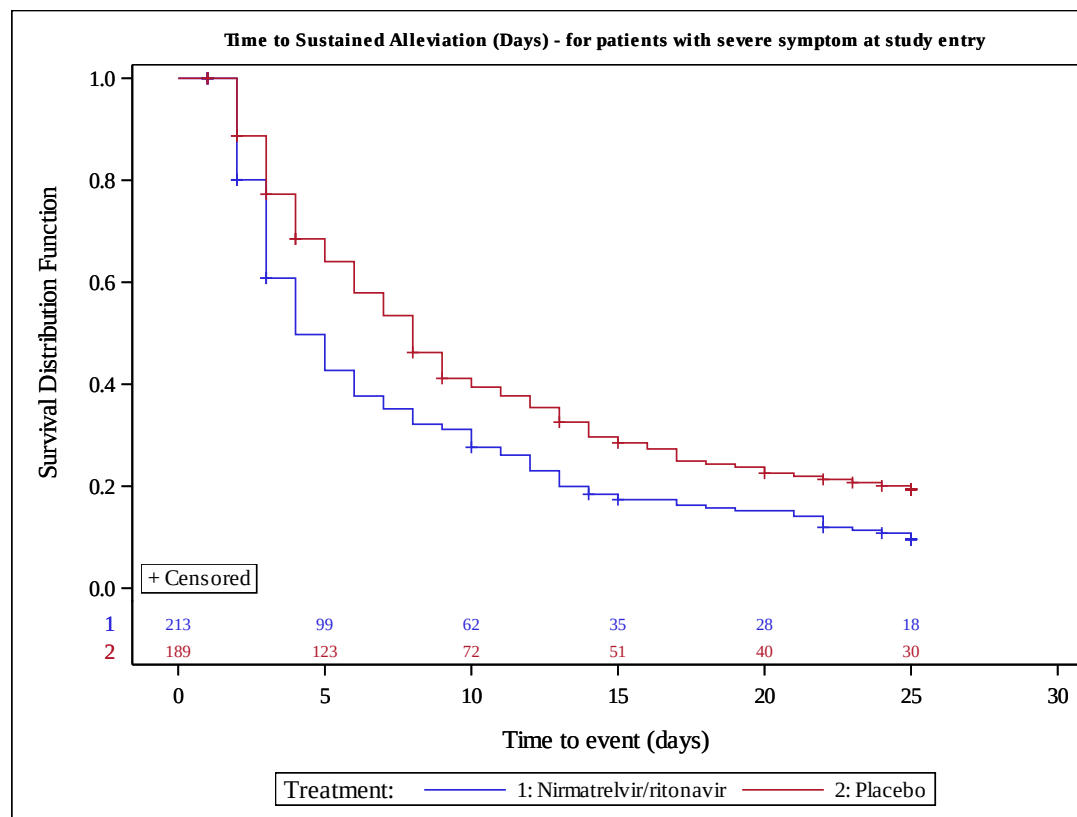
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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with events, n (%)	651 (63.5)	576 (55.5)
Number of censored subjects, n (%)	375 (36.5)	461 (44.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	16.0 (15.0, 17.0)	20.0 (19.0, 22.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.277 (1.139, 1.432)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.292 (1.155, 1.446)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

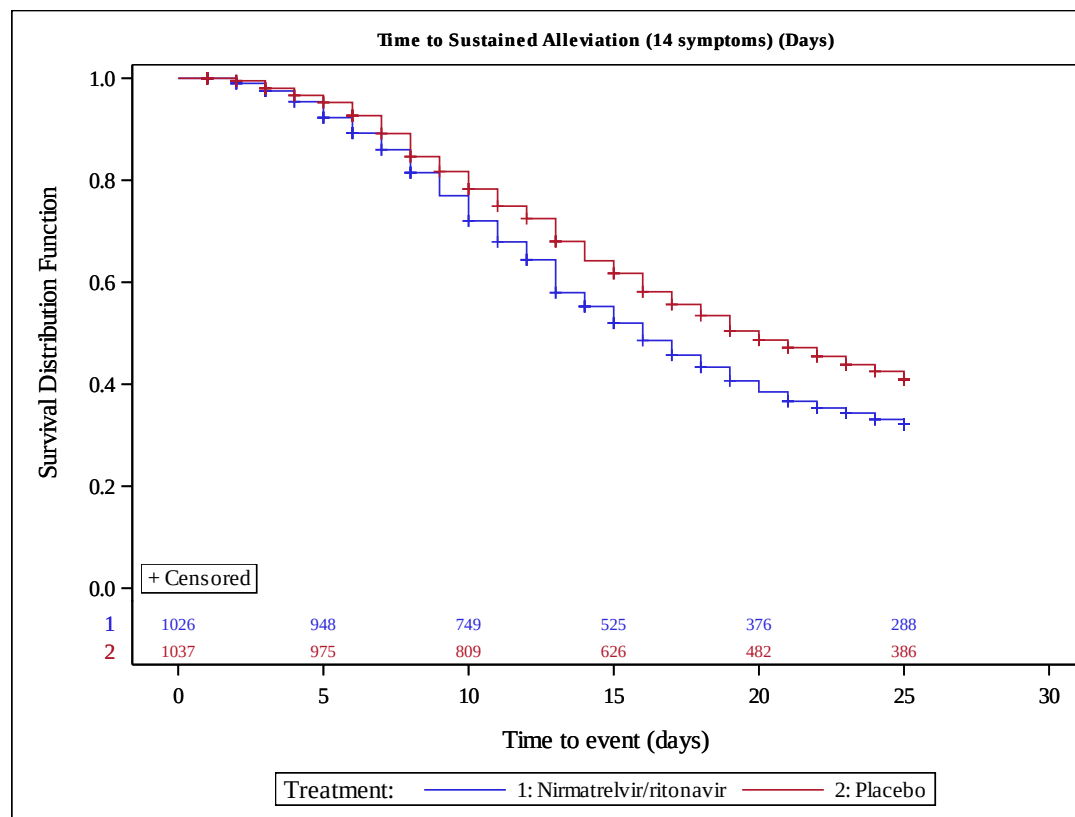
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

	Nirmatrelvir/ritonavir (N=434)	Placebo (N=417)
Number of subjects with events, n (%)	338 (77.9)	300 (71.9)
Number of censored subjects, n (%)	96 (22.1)	117 (28.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	7.0 (6.0, 8.0)	9.0 (8.0, 11.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.252 (1.067, 1.469)	
p-value [3]	0.006	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.244 (1.064, 1.453)	
p-value [3]	0.006	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

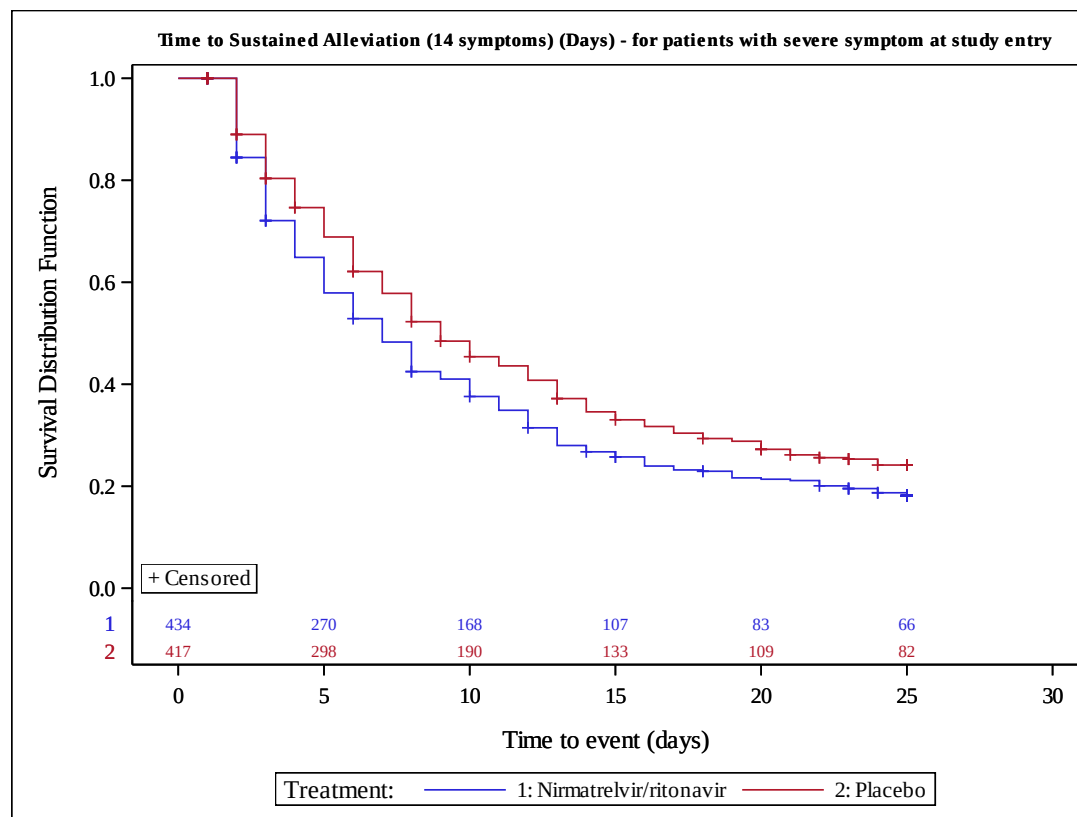
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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with events, n (%)	671 (65.4)	609 (58.7)
Number of censored subjects, n (%)	355 (34.6)	428 (41.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	16.0 (15.0, 17.0)	19.0 (17.0, 20.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.210 (1.082, 1.353)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.236 (1.107, 1.379)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

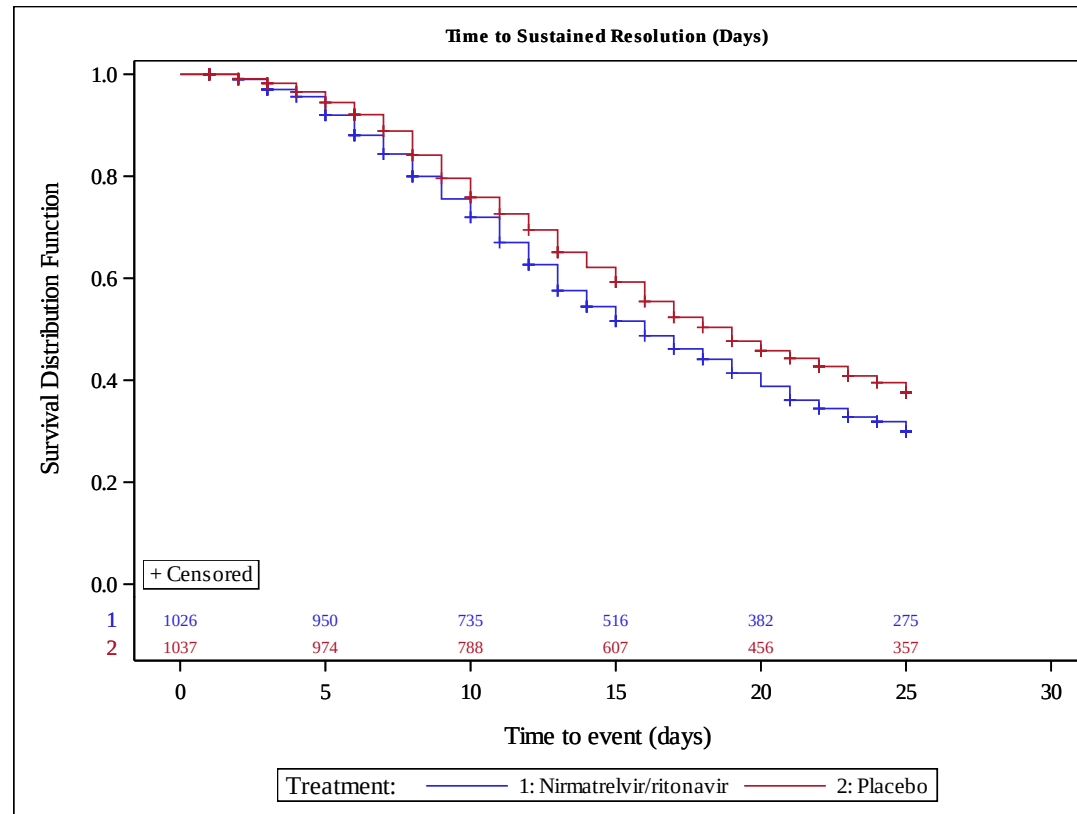
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

	Nirmatrelvir/ritonavir (N=213)	Placebo (N=189)
Number of subjects with events, n (%)	145 (68.1)	110 (58.2)
Number of censored subjects, n (%)	68 (31.9)	79 (41.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	12.0 (11.0, 15.0)	18.0 (15.0, 21.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.413 (1.094, 1.826)	
p-value [3]	0.008	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.458 (1.138, 1.869)	
p-value [3]	0.003	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

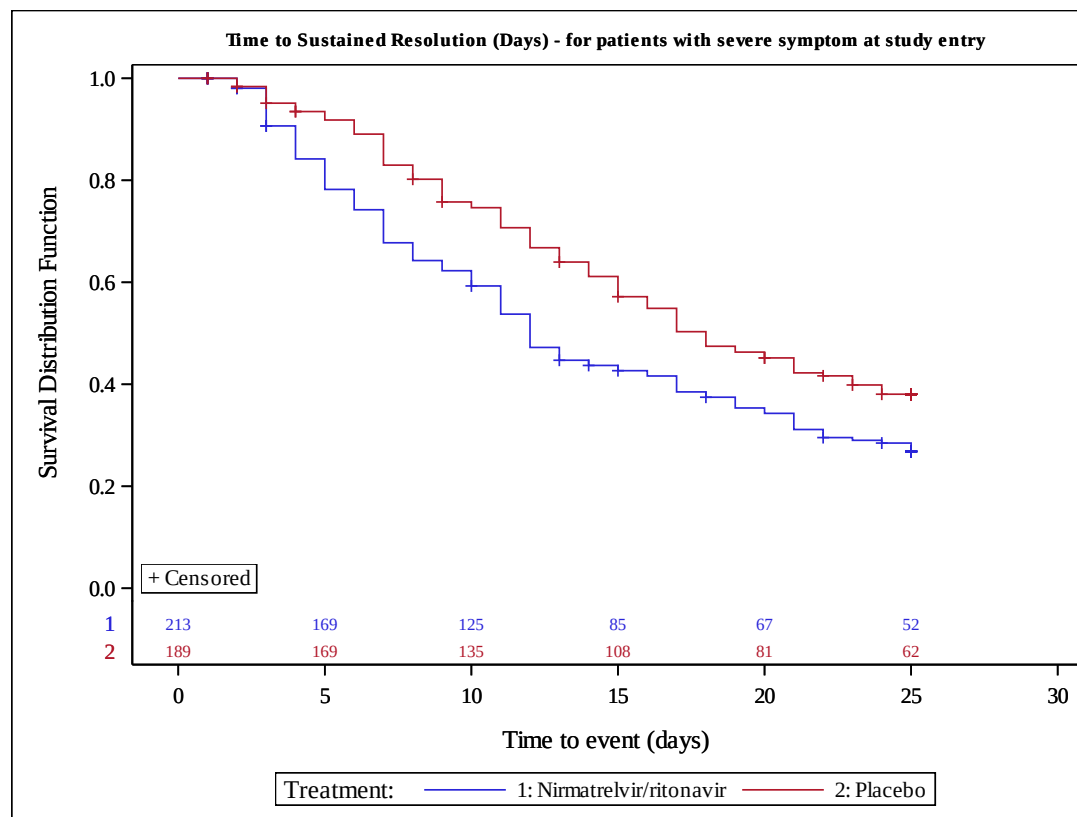
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Kaplan-Meier Plot of Time to Sustained Resolution of All Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Pfizer Inc
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 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of All Signs and Symptoms Through Day 28

Final

	Nirmatrelvir/ritonavir (N=1026)	Placebo (N=1037)
Number of subjects with events, n (%)	580 (56.5)	495 (47.7)
Number of censored subjects, n (%)	446 (43.5)	542 (52.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	20.0 (19.0, 21.0)	25.0 (23.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.281 (1.134, 1.447)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.317 (1.168, 1.484)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

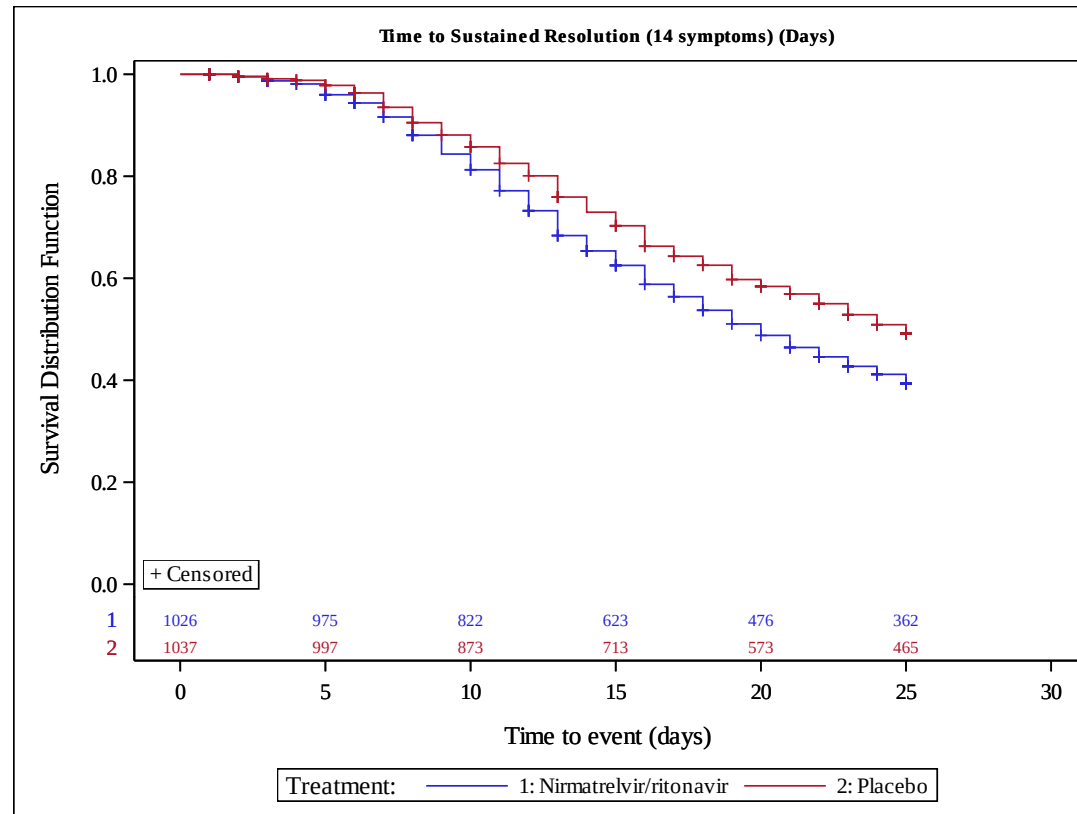
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Kaplan-Meier Plot of Time to Sustained Resolution of All Signs and Symptoms Through Day 28

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Time to Sustained Resolution of All Signs and Symptoms Through Day 28 for patients with severe symptom at study entry

Final

	Nirmatrelvir/ritonavir (N=434)	Placebo (N=417)
Number of subjects with events, n (%)	244 (56.2)	191 (45.8)
Number of censored subjects, n (%)	190 (43.8)	226 (54.2)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	19.0 (17.0, 21.0)	NE (23.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.348 (1.112, 1.635)	
p-value [3]	0.002	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.366 (1.131, 1.651)	
p-value [3]	0.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

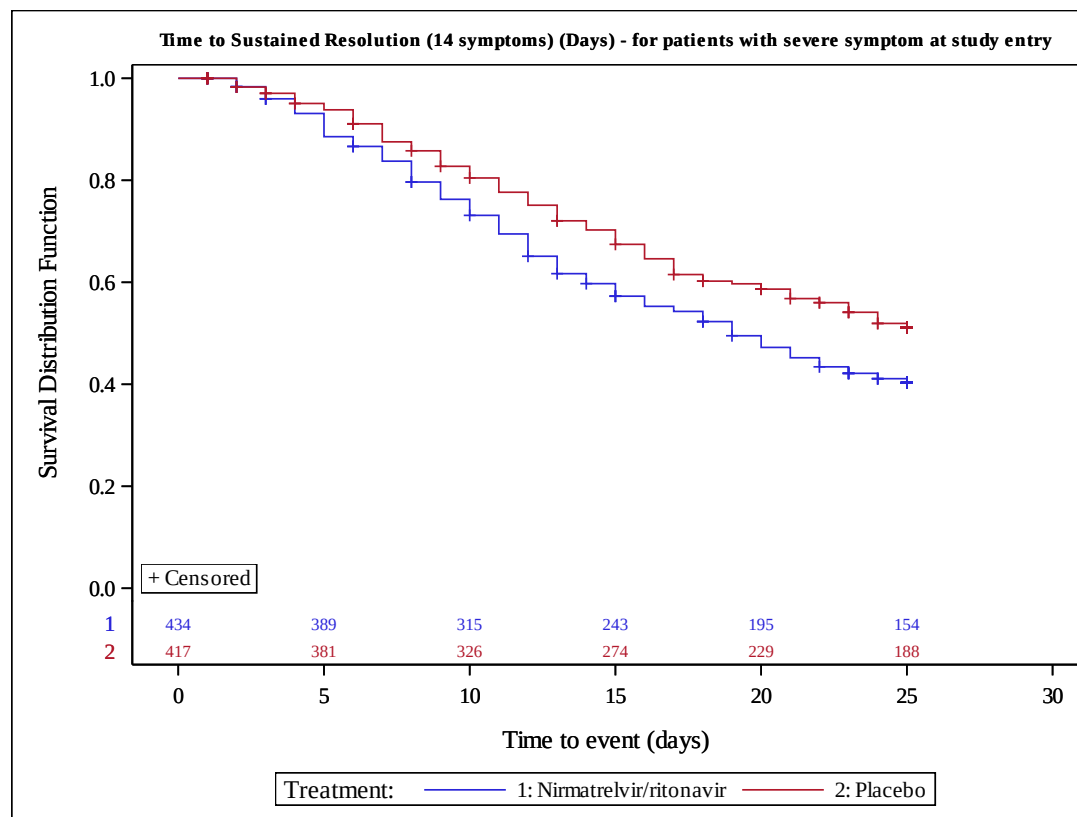
[2] Adjusted by geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with EQ 5D-VAS >= 15 points improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=1039)	Placebo (N=1046)
Number of subjects with Response, n (%)	23 (2.2)	16 (1.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	NE (NE, NE)	
Relative Risk (95% CI)	NE (NE, NE)	
Risk Difference (95% CI)	NE (NE, NE)	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.457 (0.765, 2.775) 0.252	
Relative Risk (95% CI)	1.447 (0.769, 2.723) 0.252	
Risk Difference (95% CI)	0.007 (-0.005, 0.018) 0.249	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Global Impression Questionnaire overall COVID-19-related symptoms ≥ 1 point improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=1039)	Placebo (N=1046)
Number of subjects with Response, n (%)	676 (65.1)	649 (62.0)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.169 (0.969, 1.410) 0.103	
Relative Risk (95% CI)	1.060 (0.998, 1.126) 0.060	
Risk Difference (95% CI)	0.037 (-0.003, 0.077) 0.073	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.139 (0.953, 1.362) 0.153	
Relative Risk (95% CI)	1.049 (0.983, 1.119) 0.153	
Risk Difference (95% CI)	0.030 (-0.011, 0.071) 0.152	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Analysis of Participants with Global Impression Questionnaire return to usual health 1 point improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=1039)	Placebo (N=1046)
Number of subjects with Response, n (%)	577 (55.5)	528 (50.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.238 (1.034, 1.483) 0.020	
Relative Risk (95% CI)	1.103 (1.022, 1.191) 0.012	
Risk Difference (95% CI)	0.053 (0.010, 0.095) 0.015	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.225 (1.031, 1.456) 0.021	
Relative Risk (95% CI)	1.100 (1.015, 1.193) 0.021	
Risk Difference (95% CI)	0.051 (0.008, 0.093) 0.021	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Overall Study population
 Modified Intent-To-Treat (mITT1) set
 Analysis of Participants with Global Impression Questionnaire return to usual activities 1 point improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=1039)	Placebo (N=1046)
Number of subjects with Response, n (%)	591 (56.9)	560 (53.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.157 (0.965, 1.386) 0.115	
Relative Risk (95% CI)	1.064 (0.988, 1.145) 0.099	
Risk Difference (95% CI)	0.036 (-0.007, 0.078) 0.100	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.145 (0.963, 1.361) 0.125	
Relative Risk (95% CI)	1.062 (0.983, 1.148) 0.125	
Risk Difference (95% CI)	0.033 (-0.009, 0.076) 0.124	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Analysis of Participants with WPAI Question 6 >= 15 points improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=1039)	Placebo (N=1046)
Number of subjects with Response, n (%)	21 (2.0)	28 (2.7)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.734 (0.408, 1.321) 0.302	
Relative Risk (95% CI)	NE (NE, NE) NE	
Risk Difference (95% CI)	NE (NE, NE) NE	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.750 (0.423, 1.329) 0.325	
Relative Risk (95% CI)	0.755 (0.432, 1.321) 0.325	
Risk Difference (95% CI)	-0.007 (-0.020, 0.006) 0.323	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, symptom onset duration, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Anhang 4-G 4: mITT-Population

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		Nirmatrelvir/ritonavir (N=697)	Placebo (N=682)	Total (N=1379)
Observation Time for Time to Death (Days) through Day 28[1]	n (missing)	697 (0)	682 (0)	1379 (0)
	Mean (SD)	27.45 (3.40)	27.28 (3.76)	27.37 (3.59)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	2.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Time to Death (Days) through Week 24[1]	n (missing)	697 (0)	682 (0)	1379 (0)
	Mean (SD)	160.98 (27.57)	158.49 (32.85)	159.75 (30.32)
	Median	168.00	168.00	168.00
	Q1, Q3	163.00, 168.00	163.00, 168.00	163.00, 168.00
	Min, Max	2.00, 168.00	1.00, 168.00	1.00, 168.00
Observation Time for Time to COVID-19 related Hospitalization (Days)[2]	n (missing)	697 (0)	682 (0)	1379 (0)
	Mean (SD)	27.30 (3.89)	26.19 (6.07)	26.75 (5.11)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	2.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Stuffy or Runny Nose (Days)[3]	n (missing)	686 (11)	674 (8)	1360 (19)
	Mean (SD)	26.54 (4.81)	26.05 (5.76)	26.30 (5.31)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Sore Throat (Days)[3]	n (missing)	686 (11)	674 (8)	1360 (19)
	Mean (SD)	26.54 (4.81)	26.05 (5.76)	26.30 (5.31)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Shortness of Breath or Difficulty Breathing (Days)[3]	n (missing)	686 (11)	674 (8)	1360 (19)
	Mean (SD)	26.54 (4.81)	26.05 (5.76)	26.30 (5.31)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Cough (Days)[3]	n (missing)	686 (11)	674 (8)	1360 (19)
	Mean (SD)	26.54 (4.81)	26.05 (5.76)	26.30 (5.31)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Low Energy or Tiredness (Days)[3]	n (missing)	686 (11)	674 (8)	1360 (19)
	Mean (SD)	26.54 (4.81)	26.05 (5.76)	26.30 (5.31)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Muscle or Body Aches (Days)[3]	n (missing)	686 (11)	674 (8)	1360 (19)
	Mean (SD)	26.54 (4.81)	26.05 (5.76)	26.30 (5.31)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00

N: Number of participants, n: Number of participants with non-missing values, SD: Standard Deviation, Q1: 25%-Quartile, Q3: 75%-Quartile, Min: Minimum, Max: Maximum

[1] date of first administration of study drug until death date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[2] date of first administration of study drug until hospitalization date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[3] date of first administration of study drug until date of last non-missing measurement through Day 28 + 1

[4] date of first administration of study drug until date of last non-missing measurement through Week 24 + 1

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		Nirmatrelvir/ritonavir (N=697)	Placebo (N=682)	Total (N=1379)
Observation Time for Headache (Days) [3]	n (missing)	686 (11)	674 (8)	1360 (19)
	Mean (SD)	26.54 (4.81)	26.05 (5.76)	26.30 (5.31)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Chills or Shivering (Days) [3]	n (missing)	686 (11)	674 (8)	1360 (19)
	Mean (SD)	26.54 (4.81)	26.05 (5.76)	26.30 (5.31)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Feeling Hot or Feverish (Days) [3]	n (missing)	686 (11)	674 (8)	1360 (19)
	Mean (SD)	26.54 (4.81)	26.05 (5.76)	26.30 (5.31)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Nausea (Days) [3]	n (missing)	686 (11)	674 (8)	1360 (19)
	Mean (SD)	26.54 (4.81)	26.05 (5.76)	26.30 (5.31)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Vomit (Days) [3]	n (missing)	686 (11)	674 (8)	1360 (19)
	Mean (SD)	26.54 (4.81)	26.05 (5.76)	26.30 (5.31)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Diarrhea (Days) [3]	n (missing)	686 (11)	674 (8)	1360 (19)
	Mean (SD)	26.54 (4.81)	26.05 (5.76)	26.30 (5.31)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Sense of Smell (Days) [3]	n (missing)	686 (11)	674 (8)	1360 (19)
	Mean (SD)	26.54 (4.81)	26.05 (5.76)	26.30 (5.31)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for Sense of Taste (Days) [3]	n (missing)	686 (11)	674 (8)	1360 (19)
	Mean (SD)	26.54 (4.81)	26.05 (5.76)	26.30 (5.31)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00

N: Number of participants, n: Number of participants with non-missing values, SD: Standard Deviation, Q1: 25%-Quartile, Q3: 75%-Quartile, Min: Minimum, Max: Maximum

[1] date of first administration of study drug until death date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[2] date of first administration of study drug until hospitalization date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[3] date of first administration of study drug until date of last non-missing measurement through Day 28 + 1

[4] date of first administration of study drug until date of last non-missing measurement through Week 24 + 1

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		Nirmatrelvir/ritonavir (N=697)	Placebo (N=682)	Total (N=1379)
Observation Time for EQ-5D VAS Score (Days)[4]	n (missing)	354 (343)	341 (341)	695 (684)
	Mean (SD)	157.12 (30.91)	155.26 (32.39)	156.20 (31.64)
	Median	164.00	164.00	164.00
	Q1, Q3	162.00, 169.00	162.00, 169.00	162.00, 169.00
	Min, Max	4.00, 175.00	1.00, 175.00	1.00, 175.00
Observation Time for GIQ c) overall COVID-19-related (Days)[3]	n (missing)	667 (30)	664 (18)	1331 (48)
	Mean (SD)	26.58 (4.71)	26.06 (5.75)	26.32 (5.26)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for GIQ b) return to usual activities (Days)[3]	n (missing)	667 (30)	664 (18)	1331 (48)
	Mean (SD)	26.58 (4.71)	26.06 (5.75)	26.32 (5.26)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for GIQ a) return to usual health(Days)[3]	n (missing)	667 (30)	664 (18)	1331 (48)
	Mean (SD)	26.58 (4.71)	26.06 (5.75)	26.32 (5.26)
	Median	28.00	28.00	28.00
	Q1, Q3	28.00, 28.00	28.00, 28.00	28.00, 28.00
	Min, Max	1.00, 28.00	1.00, 28.00	1.00, 28.00
Observation Time for WPAI-COVID-19 Question 6 (Days)[4]	n (missing)	346 (351)	331 (351)	677 (702)
	Mean (SD)	159.75 (25.98)	157.95 (26.64)	158.87 (26.30)
	Median	164.00	164.00	164.00
	Q1, Q3	162.00, 169.00	162.00, 169.00	162.00, 169.00
	Min, Max	4.00, 175.00	12.00, 175.00	4.00, 175.00

N: Number of participants, n: Number of participants with non-missing values, SD: Standard Deviation, Q1: 25%-Quartile, Q3: 75%-Quartile, Min: Minimum, Max: Maximum

[1] date of first administration of study drug until death date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[2] date of first administration of study drug until hospitalization date + 1. Participants without event are censored at minimum(last known alive date, Day 28).

[3] date of first administration of study drug until date of last non-missing measurement through Day 28 + 1

[4] date of first administration of study drug until date of last non-missing measurement through Week 24 + 1

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 Analysis of Time to Death through Day 28

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	Nirmatrelvir/ritonavir (N=697)	Placebo (N=682)
Number of subjects with events, n (%)	0 (0.0)	9 (1.3)
Number of censored subjects, n (%)	697 (100.0)	673 (98.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	NE (NE, NE)	
p-value [3]	NE	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	NE (NE, NE)	
p-value [3]	NE	
Cumulative Proportion and Difference of the Proportions [4]		
Estimated Proportion (95% CI), %	0.000 (0.000, 0.000)	1.345 (0.702, 2.569)
Difference (SE)	-1.345 (0.445)	
95% CI	-2.218, -0.472	
p-value	0.003	

N: Number of subjects, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last known alive date, Day 28).

[1] Based on the Brookmeyer and Crowley Method.

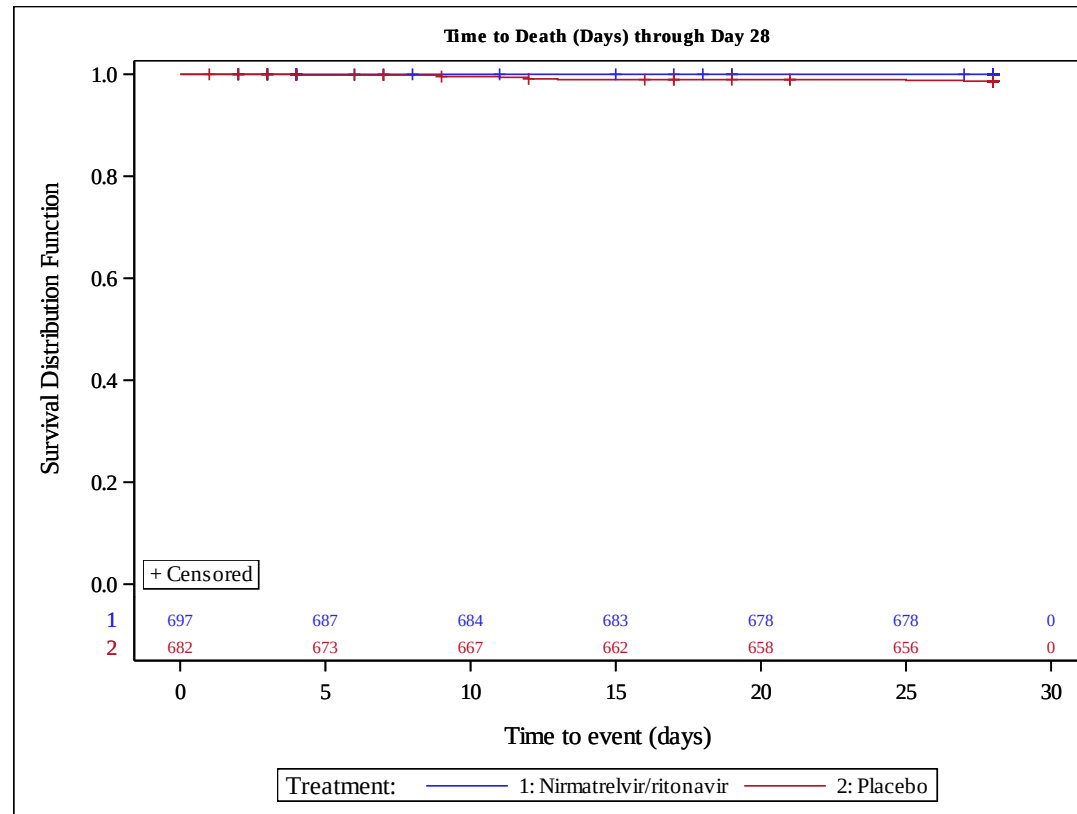
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

[4] The cumulative proportion was estimated using the Kaplan-Meier method. The difference of the proportions in the 2 treatment groups and its 95% confidence interval, and p-value based on Normal approximation.

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Final



Participants without event are censored at minimum(last known alive date, Day 28).
Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Analysis of Participants with Death from any Cause through Day 28

Final

	Nirmatrelvir/ritonavir (N=697)	Placebo (N=682)
Number of subjects with Death, n (%)	0 (0.0)	9 (1.3)
Adjusted Analysis [1]		
Odds Ratio (95% CI)	NE (NE, NE)	
p-value	NE	
Relative Risk (95% CI)	NE (NE, NE)	
p-value	NE	
Risk Difference (95% CI)	NE (NE, NE)	
p-value	NE	
Unadjusted Analysis [2]		
Odds Ratio (95% CI)	0.051 (0.003, 0.875)	
p-value	0.040	
Relative Risk (95% CI)	0.052 (0.003, 0.883)	
p-value	0.041	
Risk Difference (95% CI)	-0.013 (-0.022, -0.005)	
p-value	0.003	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Analysis of Time to Death through Week 24

Final

	Nirmatrelvir/ritonavir (N=697)	Placebo (N=682)
Number of subjects with events, n (%)	0 (0.0)	11 (1.6)
Number of censored subjects, n (%)	697 (100.0)	671 (98.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	NE (NE, NE)	
p-value [3]	NE	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	NE (NE, NE)	
p-value [3]	NE	
Cumulative Proportion and Difference of the Proportions [4]		
Estimated Proportion (95% CI), %	0.000 (0.000, 0.000)	1.649 (0.916, 2.957)
Difference (SE)	-1.649 (0.493)	
95% CI	-2.615, -0.682	
p-value	<.001	

N: Number of subjects, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last known alive date, Week 24 = Day 168).

[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

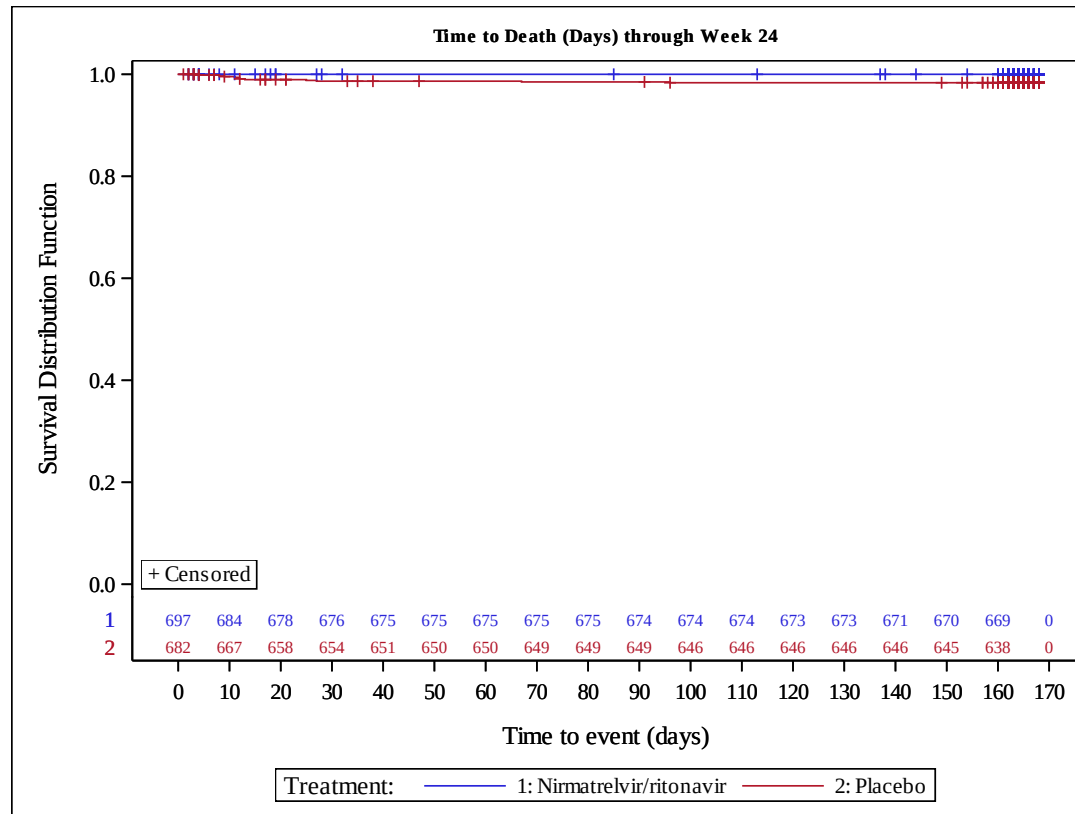
[3] Estimated by cox regression model assuming proportional hazards.

[4] The cumulative proportion was estimated using the Kaplan-Meier method. The difference of the proportions in the 2 treatment groups and its 95% confidence interval, and p-value based on Normal approximation.

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Participants without event are censored at minimum(last known alive date, Week 24 = Day 168).
Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Analysis of Participants with Death from any Cause through Week 24

Final

	Nirmatrelvir/ritonavir (N=697)	Placebo (N=682)
Number of subjects with Death, n (%)	0 (0.0)	11 (1.6)
Adjusted Analysis [1]		
Odds Ratio (95% CI)	NE (NE, NE)	
p-value	NE	
Relative Risk (95% CI)	NE (NE, NE)	
p-value	NE	
Risk Difference (95% CI)	NE (NE, NE)	
p-value	NE	
Unadjusted Analysis [2]		
Odds Ratio (95% CI)	0.042 (0.002, 0.712)	
p-value	0.028	
Relative Risk (95% CI)	0.043 (0.003, 0.721)	
p-value	0.029	
Risk Difference (95% CI)	-0.016 (-0.026, -0.007)	
p-value	<.001	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Analysis of Number of COVID-19 related hospitalizations

Final

	Nirmatrelvir/ritonavir (N=697)	Placebo (N=682)
Number of subjects with at least one event	5	44
Number of events	5	45
Mean of events	0.007	0.066
Mean of events per day	0.0002	0.0029
Adjusted Analysis [1]		
LS mean (95% CI)	NE (NE, NE)	NE (NE, NE)
LS mean Ratio (95% CI)	NE (NE, NE)	
p-value	NE	
Unadjusted Analysis [2]		
LS mean (95% CI)	NE (NE, NE)	NE (NE, NE)
LS mean Ratio (95% CI)	NE (NE, NE)	
p-value	NE	

N: Number of participants, CI: Confidence Interval, NE: Not estimable, I: Infinity, LS: Least Squares

Medical Visits and Hospitalization events are limited through Day 34 visit. Number of events per day = Number of events/Number of days follow up limited to Day 37.

Stratification factors: geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[1] Negative binomial regression model includes main effects of treatment, stratification factors and the log number of days follow up as the participant offset variable.

[2] Negative binomial regression model includes main effects of treatment and the log number of days follow up as the participant offset variable.

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Final

Endpoint	Visit	Nirmatrelvir/ritonavir (N=697)		Placebo (N=682)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Stuffy or Runny Nose	Baseline	697	652 (93.5)	682	654 (95.9)
	DAY 2	697	643 (92.3)	682	637 (93.4)
	DAY 3	697	649 (93.1)	682	630 (92.4)
	DAY 4	697	635 (91.1)	682	622 (91.2)
	DAY 5	697	633 (90.8)	681	615 (90.3)
	DAY 6	697	593 (85.1)	681	575 (84.4)
	DAY 7	697	568 (81.5)	681	568 (83.4)
	DAY 8	697	578 (82.9)	681	558 (81.9)
	DAY 9	697	580 (83.2)	681	560 (82.2)
	DAY 10	697	566 (81.2)	679	584 (86.0)
	DAY 11	697	575 (82.5)	679	573 (84.4)
	DAY 12	697	582 (83.5)	678	552 (81.4)
	DAY 13	697	586 (84.1)	676	568 (84.0)
	DAY 14	697	584 (83.8)	675	567 (84.0)
	DAY 15	697	579 (83.1)	675	567 (84.0)
	DAY 16	697	582 (83.5)	675	553 (81.9)
	DAY 17	697	582 (83.5)	675	553 (81.9)
	DAY 18	697	568 (81.5)	675	545 (80.7)
	DAY 19	697	569 (81.6)	675	566 (83.9)
	DAY 20	697	556 (79.8)	675	566 (83.9)
	DAY 21	697	577 (82.8)	675	559 (82.8)
	DAY 22	697	575 (82.5)	675	547 (81.0)
	DAY 23	697	563 (80.8)	675	541 (80.1)
	DAY 24	697	565 (81.1)	675	556 (82.4)
	DAY 25	697	554 (79.5)	675	554 (82.1)
	DAY 26	697	563 (80.8)	674	539 (80.0)
	DAY 27	697	563 (80.8)	674	558 (82.8)
	DAY 28	697	548 (78.6)	673	534 (79.3)
COVID-19 Signs and Symptoms: Sore Throat	Baseline	697	652 (93.5)	682	654 (95.9)
	DAY 2	697	643 (92.3)	682	637 (93.4)
	DAY 3	697	649 (93.1)	682	630 (92.4)
	DAY 4	697	635 (91.1)	682	622 (91.2)
	DAY 5	697	633 (90.8)	681	615 (90.3)
	DAY 6	697	593 (85.1)	681	575 (84.4)
	DAY 7	697	568 (81.5)	681	568 (83.4)
	DAY 8	697	578 (82.9)	681	558 (81.9)
	DAY 9	697	580 (83.2)	681	560 (82.2)
	DAY 10	697	566 (81.2)	679	584 (86.0)
	DAY 11	697	575 (82.5)	679	573 (84.4)
	DAY 12	697	582 (83.5)	678	552 (81.4)
	DAY 13	697	586 (84.1)	676	568 (84.0)
	DAY 14	697	584 (83.8)	675	567 (84.0)
	DAY 15	697	579 (83.1)	675	567 (84.0)
	DAY 16	697	582 (83.5)	675	553 (81.9)
	DAY 17	697	582 (83.5)	675	553 (81.9)
	DAY 18	697	568 (81.5)	675	545 (80.7)
	DAY 19	697	569 (81.6)	675	566 (83.9)
	DAY 20	697	556 (79.8)	675	566 (83.9)
	DAY 21	697	577 (82.8)	675	559 (82.8)
	DAY 22	697	575 (82.5)	675	547 (81.0)
	DAY 23	697	563 (80.8)	675	541 (80.1)
	DAY 24	697	565 (81.1)	675	556 (82.4)
	DAY 25	697	554 (79.5)	675	554 (82.1)
	DAY 26	697	563 (80.8)	674	539 (80.0)
	DAY 27	697	563 (80.8)	674	558 (82.8)
	DAY 28	697	548 (78.6)	673	534 (79.3)

N: Number of participants, n: Number of participants with non missing values

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=697)		Placebo (N=682)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Shortness of Breath or Difficulty Breathing	Baseline	697	652 (93.5)	682	654 (95.9)
	DAY 2	697	643 (92.3)	682	637 (93.4)
	DAY 3	697	649 (93.1)	682	630 (92.4)
	DAY 4	697	635 (91.1)	682	622 (91.2)
	DAY 5	697	633 (90.8)	681	615 (90.3)
	DAY 6	697	593 (85.1)	681	575 (84.4)
	DAY 7	697	568 (81.5)	681	568 (83.4)
	DAY 8	697	578 (82.9)	681	558 (81.9)
	DAY 9	697	580 (83.2)	681	560 (82.2)
	DAY 10	697	566 (81.2)	679	584 (86.0)
	DAY 11	697	575 (82.5)	679	573 (84.4)
	DAY 12	697	582 (83.5)	678	552 (81.4)
	DAY 13	697	586 (84.1)	676	568 (84.0)
	DAY 14	697	584 (83.8)	675	567 (84.0)
	DAY 15	697	579 (83.1)	675	567 (84.0)
	DAY 16	697	582 (83.5)	675	553 (81.9)
	DAY 17	697	582 (83.5)	675	553 (81.9)
	DAY 18	697	568 (81.5)	675	545 (80.7)
	DAY 19	697	569 (81.6)	675	566 (83.9)
	DAY 20	697	556 (79.8)	675	566 (83.9)
	DAY 21	697	577 (82.8)	675	559 (82.8)
	DAY 22	697	575 (82.5)	675	547 (81.0)
	DAY 23	697	563 (80.8)	675	541 (80.1)
	DAY 24	697	565 (81.1)	675	556 (82.4)
	DAY 25	697	554 (79.5)	675	554 (82.1)
	DAY 26	697	563 (80.8)	674	539 (80.0)
	DAY 27	697	563 (80.8)	674	558 (82.8)
	DAY 28	697	548 (78.6)	673	534 (79.3)
COVID-19 Signs and Symptoms: Cough	Baseline	697	652 (93.5)	682	654 (95.9)
	DAY 2	697	643 (92.3)	682	637 (93.4)
	DAY 3	697	649 (93.1)	682	630 (92.4)
	DAY 4	697	635 (91.1)	682	622 (91.2)
	DAY 5	697	633 (90.8)	681	615 (90.3)
	DAY 6	697	593 (85.1)	681	575 (84.4)
	DAY 7	697	568 (81.5)	681	568 (83.4)
	DAY 8	697	578 (82.9)	681	558 (81.9)
	DAY 9	697	580 (83.2)	681	560 (82.2)
	DAY 10	697	566 (81.2)	679	584 (86.0)
	DAY 11	697	575 (82.5)	679	573 (84.4)
	DAY 12	697	582 (83.5)	678	552 (81.4)
	DAY 13	697	586 (84.1)	676	568 (84.0)
	DAY 14	697	584 (83.8)	675	567 (84.0)
	DAY 15	697	579 (83.1)	675	567 (84.0)
	DAY 16	697	582 (83.5)	675	553 (81.9)
	DAY 17	697	582 (83.5)	675	553 (81.9)
	DAY 18	697	568 (81.5)	675	545 (80.7)
	DAY 19	697	569 (81.6)	675	566 (83.9)
	DAY 20	697	556 (79.8)	675	566 (83.9)
	DAY 21	697	577 (82.8)	675	559 (82.8)
	DAY 22	697	575 (82.5)	675	547 (81.0)
	DAY 23	697	563 (80.8)	675	541 (80.1)
	DAY 24	697	565 (81.1)	675	556 (82.4)
	DAY 25	697	554 (79.5)	675	554 (82.1)
	DAY 26	697	563 (80.8)	674	539 (80.0)
	DAY 27	697	563 (80.8)	674	558 (82.8)
	DAY 28	697	548 (78.6)	673	534 (79.3)

N: Number of participants, n: Number of participants with non missing values

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		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Low Energy or Tiredness	Baseline	697	652 (93.5)	682	654 (95.9)
	DAY 2	697	643 (92.3)	682	637 (93.4)
	DAY 3	697	649 (93.1)	682	630 (92.4)
	DAY 4	697	635 (91.1)	682	622 (91.2)
	DAY 5	697	633 (90.8)	681	615 (90.3)
	DAY 6	697	593 (85.1)	681	575 (84.4)
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	DAY 8	697	578 (82.9)	681	558 (81.9)
	DAY 9	697	580 (83.2)	681	560 (82.2)
	DAY 10	697	566 (81.2)	679	584 (86.0)
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	DAY 16	697	582 (83.5)	675	553 (81.9)
	DAY 17	697	582 (83.5)	675	553 (81.9)
	DAY 18	697	568 (81.5)	675	545 (80.7)
	DAY 19	697	569 (81.6)	675	566 (83.9)
	DAY 20	697	556 (79.8)	675	566 (83.9)
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	DAY 22	697	575 (82.5)	675	547 (81.0)
	DAY 23	697	563 (80.8)	675	541 (80.1)
	DAY 24	697	565 (81.1)	675	556 (82.4)
	DAY 25	697	554 (79.5)	675	554 (82.1)
	DAY 26	697	563 (80.8)	674	539 (80.0)
	DAY 27	697	563 (80.8)	674	558 (82.8)
	DAY 28	697	548 (78.6)	673	534 (79.3)
COVID-19 Signs and Symptoms: Muscle or Body Aches	Baseline	697	652 (93.5)	682	654 (95.9)
	DAY 2	697	643 (92.3)	682	637 (93.4)
	DAY 3	697	649 (93.1)	682	630 (92.4)
	DAY 4	697	635 (91.1)	682	622 (91.2)
	DAY 5	697	633 (90.8)	681	615 (90.3)
	DAY 6	697	593 (85.1)	681	575 (84.4)
	DAY 7	697	568 (81.5)	681	568 (83.4)
	DAY 8	697	578 (82.9)	681	558 (81.9)
	DAY 9	697	580 (83.2)	681	560 (82.2)
	DAY 10	697	566 (81.2)	679	584 (86.0)
	DAY 11	697	575 (82.5)	679	573 (84.4)
	DAY 12	697	582 (83.5)	678	552 (81.4)
	DAY 13	697	586 (84.1)	676	568 (84.0)
	DAY 14	697	584 (83.8)	675	567 (84.0)
	DAY 15	697	579 (83.1)	675	567 (84.0)
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	DAY 17	697	582 (83.5)	675	553 (81.9)
	DAY 18	697	568 (81.5)	675	545 (80.7)
	DAY 19	697	569 (81.6)	675	566 (83.9)
	DAY 20	697	556 (79.8)	675	566 (83.9)
	DAY 21	697	577 (82.8)	675	559 (82.8)
	DAY 22	697	575 (82.5)	675	547 (81.0)
	DAY 23	697	563 (80.8)	675	541 (80.1)
	DAY 24	697	565 (81.1)	675	556 (82.4)
	DAY 25	697	554 (79.5)	675	554 (82.1)
	DAY 26	697	563 (80.8)	674	539 (80.0)
	DAY 27	697	563 (80.8)	674	558 (82.8)
	DAY 28	697	548 (78.6)	673	534 (79.3)

N: Number of participants, n: Number of participants with non missing values

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		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Headache	Baseline	697	652 (93.5)	682	654 (95.9)
	DAY 2	697	643 (92.3)	682	637 (93.4)
	DAY 3	697	649 (93.1)	682	630 (92.4)
	DAY 4	697	635 (91.1)	682	622 (91.2)
	DAY 5	697	633 (90.8)	681	615 (90.3)
	DAY 6	697	593 (85.1)	681	575 (84.4)
	DAY 7	697	568 (81.5)	681	568 (83.4)
	DAY 8	697	578 (82.9)	681	558 (81.9)
	DAY 9	697	580 (83.2)	681	560 (82.2)
	DAY 10	697	566 (81.2)	679	584 (86.0)
	DAY 11	697	575 (82.5)	679	573 (84.4)
	DAY 12	697	582 (83.5)	678	552 (81.4)
	DAY 13	697	586 (84.1)	676	568 (84.0)
	DAY 14	697	584 (83.8)	675	567 (84.0)
	DAY 15	697	579 (83.1)	675	567 (84.0)
	DAY 16	697	582 (83.5)	675	553 (81.9)
	DAY 17	697	582 (83.5)	675	553 (81.9)
	DAY 18	697	568 (81.5)	675	545 (80.7)
	DAY 19	697	569 (81.6)	675	566 (83.9)
	DAY 20	697	556 (79.8)	675	566 (83.9)
	DAY 21	697	577 (82.8)	675	559 (82.8)
	DAY 22	697	575 (82.5)	675	547 (81.0)
	DAY 23	697	563 (80.8)	675	541 (80.1)
	DAY 24	697	565 (81.1)	675	556 (82.4)
	DAY 25	697	554 (79.5)	675	554 (82.1)
	DAY 26	697	563 (80.8)	674	539 (80.0)
	DAY 27	697	563 (80.8)	674	558 (82.8)
	DAY 28	697	548 (78.6)	673	534 (79.3)
COVID-19 Signs and Symptoms: Chills or Shivering	Baseline	697	652 (93.5)	682	654 (95.9)
	DAY 2	697	643 (92.3)	682	637 (93.4)
	DAY 3	697	649 (93.1)	682	630 (92.4)
	DAY 4	697	635 (91.1)	682	622 (91.2)
	DAY 5	697	633 (90.8)	681	615 (90.3)
	DAY 6	697	593 (85.1)	681	575 (84.4)
	DAY 7	697	568 (81.5)	681	568 (83.4)
	DAY 8	697	578 (82.9)	681	558 (81.9)
	DAY 9	697	580 (83.2)	681	560 (82.2)
	DAY 10	697	566 (81.2)	679	584 (86.0)
	DAY 11	697	575 (82.5)	679	573 (84.4)
	DAY 12	697	582 (83.5)	678	552 (81.4)
	DAY 13	697	586 (84.1)	676	568 (84.0)
	DAY 14	697	584 (83.8)	675	567 (84.0)
	DAY 15	697	579 (83.1)	675	567 (84.0)
	DAY 16	697	582 (83.5)	675	553 (81.9)
	DAY 17	697	582 (83.5)	675	553 (81.9)
	DAY 18	697	568 (81.5)	675	545 (80.7)
	DAY 19	697	569 (81.6)	675	566 (83.9)
	DAY 20	697	556 (79.8)	675	566 (83.9)
	DAY 21	697	577 (82.8)	675	559 (82.8)
	DAY 22	697	575 (82.5)	675	547 (81.0)
	DAY 23	697	563 (80.8)	675	541 (80.1)
	DAY 24	697	565 (81.1)	675	556 (82.4)
	DAY 25	697	554 (79.5)	675	554 (82.1)
	DAY 26	697	563 (80.8)	674	539 (80.0)
	DAY 27	697	563 (80.8)	674	558 (82.8)
	DAY 28	697	548 (78.6)	673	534 (79.3)

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=697)		Placebo (N=682)	
		Number of participants		Number of participants	
		alive at planned visit day	n (%)	alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Feeling Hot or Feverish	Baseline	697	652 (93.5)	682	654 (95.9)
	DAY 2	697	643 (92.3)	682	637 (93.4)
	DAY 3	697	649 (93.1)	682	630 (92.4)
	DAY 4	697	635 (91.1)	682	622 (91.2)
	DAY 5	697	633 (90.8)	681	615 (90.3)
	DAY 6	697	593 (85.1)	681	575 (84.4)
	DAY 7	697	568 (81.5)	681	568 (83.4)
	DAY 8	697	578 (82.9)	681	558 (81.9)
	DAY 9	697	580 (83.2)	681	560 (82.2)
	DAY 10	697	566 (81.2)	679	584 (86.0)
	DAY 11	697	575 (82.5)	679	573 (84.4)
	DAY 12	697	582 (83.5)	678	552 (81.4)
	DAY 13	697	586 (84.1)	676	568 (84.0)
	DAY 14	697	584 (83.8)	675	567 (84.0)
	DAY 15	697	579 (83.1)	675	567 (84.0)
	DAY 16	697	582 (83.5)	675	553 (81.9)
	DAY 17	697	582 (83.5)	675	553 (81.9)
	DAY 18	697	568 (81.5)	675	545 (80.7)
	DAY 19	697	569 (81.6)	675	566 (83.9)
	DAY 20	697	556 (79.8)	675	566 (83.9)
	DAY 21	697	577 (82.8)	675	559 (82.8)
	DAY 22	697	575 (82.5)	675	547 (81.0)
	DAY 23	697	563 (80.8)	675	541 (80.1)
	DAY 24	697	565 (81.1)	675	556 (82.4)
	DAY 25	697	554 (79.5)	675	554 (82.1)
	DAY 26	697	563 (80.8)	674	539 (80.0)
	DAY 27	697	563 (80.8)	674	558 (82.8)
	DAY 28	697	548 (78.6)	673	534 (79.3)
COVID-19 Signs and Symptoms: Nausea	Baseline	697	652 (93.5)	682	654 (95.9)
	DAY 2	697	643 (92.3)	682	637 (93.4)
	DAY 3	697	649 (93.1)	682	630 (92.4)
	DAY 4	697	635 (91.1)	682	622 (91.2)
	DAY 5	697	633 (90.8)	681	615 (90.3)
	DAY 6	697	593 (85.1)	681	575 (84.4)
	DAY 7	697	568 (81.5)	681	568 (83.4)
	DAY 8	697	578 (82.9)	681	558 (81.9)
	DAY 9	697	580 (83.2)	681	560 (82.2)
	DAY 10	697	566 (81.2)	679	584 (86.0)
	DAY 11	697	575 (82.5)	679	573 (84.4)
	DAY 12	697	582 (83.5)	678	552 (81.4)
	DAY 13	697	586 (84.1)	676	568 (84.0)
	DAY 14	697	584 (83.8)	675	567 (84.0)
	DAY 15	697	579 (83.1)	675	567 (84.0)
	DAY 16	697	582 (83.5)	675	553 (81.9)
	DAY 17	697	582 (83.5)	675	553 (81.9)
	DAY 18	697	568 (81.5)	675	545 (80.7)
	DAY 19	697	569 (81.6)	675	566 (83.9)
	DAY 20	697	556 (79.8)	675	566 (83.9)
	DAY 21	697	577 (82.8)	675	559 (82.8)
	DAY 22	697	575 (82.5)	675	547 (81.0)
	DAY 23	697	563 (80.8)	675	541 (80.1)
	DAY 24	697	565 (81.1)	675	556 (82.4)
	DAY 25	697	554 (79.5)	675	554 (82.1)
	DAY 26	697	563 (80.8)	674	539 (80.0)
	DAY 27	697	563 (80.8)	674	558 (82.8)
	DAY 28	697	548 (78.6)	673	534 (79.3)

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=697)		Placebo (N=682)	
		Number of participants		Number of participants	
		alive at planned visit day	n (%)	alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Vomit	Baseline	697	652 (93.5)	682	654 (95.9)
	DAY 2	697	643 (92.3)	682	637 (93.4)
	DAY 3	697	649 (93.1)	682	630 (92.4)
	DAY 4	697	635 (91.1)	682	622 (91.2)
	DAY 5	697	633 (90.8)	681	615 (90.3)
	DAY 6	697	593 (85.1)	681	575 (84.4)
	DAY 7	697	568 (81.5)	681	568 (83.4)
	DAY 8	697	578 (82.9)	681	558 (81.9)
	DAY 9	697	580 (83.2)	681	560 (82.2)
	DAY 10	697	566 (81.2)	679	584 (86.0)
	DAY 11	697	575 (82.5)	679	573 (84.4)
	DAY 12	697	582 (83.5)	678	552 (81.4)
	DAY 13	697	586 (84.1)	676	568 (84.0)
	DAY 14	697	584 (83.8)	675	567 (84.0)
	DAY 15	697	579 (83.1)	675	567 (84.0)
	DAY 16	697	582 (83.5)	675	553 (81.9)
	DAY 17	697	582 (83.5)	675	553 (81.9)
	DAY 18	697	568 (81.5)	675	545 (80.7)
	DAY 19	697	569 (81.6)	675	566 (83.9)
	DAY 20	697	556 (79.8)	675	566 (83.9)
	DAY 21	697	577 (82.8)	675	559 (82.8)
	DAY 22	697	575 (82.5)	675	547 (81.0)
	DAY 23	697	563 (80.8)	675	541 (80.1)
	DAY 24	697	565 (81.1)	675	556 (82.4)
	DAY 25	697	554 (79.5)	675	554 (82.1)
	DAY 26	697	563 (80.8)	674	539 (80.0)
	DAY 27	697	563 (80.8)	674	558 (82.8)
	DAY 28	697	548 (78.6)	673	534 (79.3)
COVID-19 Signs and Symptoms: Diarrhea	Baseline	697	652 (93.5)	682	654 (95.9)
	DAY 2	697	643 (92.3)	682	637 (93.4)
	DAY 3	697	649 (93.1)	682	630 (92.4)
	DAY 4	697	635 (91.1)	682	622 (91.2)
	DAY 5	697	633 (90.8)	681	615 (90.3)
	DAY 6	697	593 (85.1)	681	575 (84.4)
	DAY 7	697	568 (81.5)	681	568 (83.4)
	DAY 8	697	578 (82.9)	681	558 (81.9)
	DAY 9	697	580 (83.2)	681	560 (82.2)
	DAY 10	697	566 (81.2)	679	584 (86.0)
	DAY 11	697	575 (82.5)	679	573 (84.4)
	DAY 12	697	582 (83.5)	678	552 (81.4)
	DAY 13	697	586 (84.1)	676	568 (84.0)
	DAY 14	697	584 (83.8)	675	567 (84.0)
	DAY 15	697	579 (83.1)	675	567 (84.0)
	DAY 16	697	582 (83.5)	675	553 (81.9)
	DAY 17	697	582 (83.5)	675	553 (81.9)
	DAY 18	697	568 (81.5)	675	545 (80.7)
	DAY 19	697	569 (81.6)	675	566 (83.9)
	DAY 20	697	556 (79.8)	675	566 (83.9)
	DAY 21	697	577 (82.8)	675	559 (82.8)
	DAY 22	697	575 (82.5)	675	547 (81.0)
	DAY 23	697	563 (80.8)	675	541 (80.1)
	DAY 24	697	565 (81.1)	675	556 (82.4)
	DAY 25	697	554 (79.5)	675	554 (82.1)
	DAY 26	697	563 (80.8)	674	539 (80.0)
	DAY 27	697	563 (80.8)	674	558 (82.8)
	DAY 28	697	548 (78.6)	673	534 (79.3)

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=697)		Placebo (N=682)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
COVID-19 Signs and Symptoms: Sense of Smell	Baseline	697	652 (93.5)	682	654 (95.9)
	DAY 2	697	643 (92.3)	682	637 (93.4)
	DAY 3	697	649 (93.1)	682	630 (92.4)
	DAY 4	697	635 (91.1)	682	622 (91.2)
	DAY 5	697	633 (90.8)	681	615 (90.3)
	DAY 6	697	593 (85.1)	681	575 (84.4)
	DAY 7	697	568 (81.5)	681	568 (83.4)
	DAY 8	697	578 (82.9)	681	558 (81.9)
	DAY 9	697	580 (83.2)	681	560 (82.2)
	DAY 10	697	566 (81.2)	679	584 (86.0)
	DAY 11	697	575 (82.5)	679	573 (84.4)
	DAY 12	697	582 (83.5)	678	552 (81.4)
	DAY 13	697	586 (84.1)	676	568 (84.0)
	DAY 14	697	584 (83.8)	675	567 (84.0)
	DAY 15	697	579 (83.1)	675	567 (84.0)
	DAY 16	697	582 (83.5)	675	553 (81.9)
	DAY 17	697	582 (83.5)	675	553 (81.9)
	DAY 18	697	568 (81.5)	675	545 (80.7)
	DAY 19	697	569 (81.6)	675	566 (83.9)
	DAY 20	697	556 (79.8)	675	566 (83.9)
	DAY 21	697	577 (82.8)	675	559 (82.8)
	DAY 22	697	575 (82.5)	675	547 (81.0)
	DAY 23	697	563 (80.8)	675	541 (80.1)
	DAY 24	697	565 (81.1)	675	556 (82.4)
	DAY 25	697	554 (79.5)	675	554 (82.1)
	DAY 26	697	563 (80.8)	674	539 (80.0)
	DAY 27	697	563 (80.8)	674	558 (82.8)
	DAY 28	697	548 (78.6)	673	534 (79.3)
COVID-19 Signs and Symptoms: Sense of Taste	Baseline	697	652 (93.5)	682	654 (95.9)
	DAY 2	697	643 (92.3)	682	637 (93.4)
	DAY 3	697	649 (93.1)	682	630 (92.4)
	DAY 4	697	635 (91.1)	682	622 (91.2)
	DAY 5	697	633 (90.8)	681	615 (90.3)
	DAY 6	697	593 (85.1)	681	575 (84.4)
	DAY 7	697	568 (81.5)	681	568 (83.4)
	DAY 8	697	578 (82.9)	681	558 (81.9)
	DAY 9	697	580 (83.2)	681	560 (82.2)
	DAY 10	697	566 (81.2)	679	584 (86.0)
	DAY 11	697	575 (82.5)	679	573 (84.4)
	DAY 12	697	582 (83.5)	678	552 (81.4)
	DAY 13	697	586 (84.1)	676	568 (84.0)
	DAY 14	697	584 (83.8)	675	567 (84.0)
	DAY 15	697	579 (83.1)	675	567 (84.0)
	DAY 16	697	582 (83.5)	675	553 (81.9)
	DAY 17	697	582 (83.5)	675	553 (81.9)
	DAY 18	697	568 (81.5)	675	545 (80.7)
	DAY 19	697	569 (81.6)	675	566 (83.9)
	DAY 20	697	556 (79.8)	675	566 (83.9)
	DAY 21	697	577 (82.8)	675	559 (82.8)
	DAY 22	697	575 (82.5)	675	547 (81.0)
	DAY 23	697	563 (80.8)	675	541 (80.1)
	DAY 24	697	565 (81.1)	675	556 (82.4)
	DAY 25	697	554 (79.5)	675	554 (82.1)
	DAY 26	697	563 (80.8)	674	539 (80.0)
	DAY 27	697	563 (80.8)	674	558 (82.8)
	DAY 28	697	548 (78.6)	673	534 (79.3)

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		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
5-level European Quality of Life Five Dimension (EQ-5D-5L): EQ-VAS Score	Day 1	697	25 (3.6)	682	31 (4.5)
	Day 5	697	28 (4.0)	681	32 (4.7)
	Day 14	697	38 (5.5)	675	49 (7.3)
	Day 34	697	71 (10.2)	673	80 (11.9)
	Week 12	697	132 (18.9)	672	133 (19.8)
	Week 24	697	326 (46.8)	671	305 (45.5)
Global Impression Questionnaire: return to usual health	Baseline	697	636 (91.2)	682	645 (94.6)
	DAY 2	697	626 (89.8)	682	628 (92.1)
	DAY 3	697	633 (90.8)	682	621 (91.1)
	DAY 4	697	617 (88.5)	682	612 (89.7)
	DAY 5	697	616 (88.4)	681	606 (89.0)
	DAY 6	697	577 (82.8)	681	565 (83.0)
	DAY 7	697	555 (79.6)	681	561 (82.4)
	DAY 8	697	566 (81.2)	681	551 (80.9)
	DAY 9	697	567 (81.3)	681	553 (81.2)
	DAY 10	697	552 (79.2)	679	577 (85.0)
	DAY 11	697	564 (80.9)	679	565 (83.2)
	DAY 12	697	567 (81.3)	678	544 (80.2)
	DAY 13	697	573 (82.2)	676	561 (83.0)
	DAY 14	697	571 (81.9)	675	559 (82.8)
	DAY 15	697	563 (80.8)	675	558 (82.7)
	DAY 16	697	570 (81.8)	675	545 (80.7)
	DAY 17	697	569 (81.6)	675	545 (80.7)
	DAY 18	697	554 (79.5)	675	538 (79.7)
	DAY 19	697	555 (79.6)	675	558 (82.7)
	DAY 20	697	543 (77.9)	675	558 (82.7)
	DAY 21	697	562 (80.6)	675	551 (81.6)
	DAY 22	697	558 (80.1)	675	539 (79.9)
	DAY 23	697	548 (78.6)	675	533 (79.0)
	DAY 24	697	549 (78.8)	675	547 (81.0)
	DAY 25	697	541 (77.6)	675	545 (80.7)
	DAY 26	697	548 (78.6)	674	530 (78.6)
	DAY 27	697	546 (78.3)	674	549 (81.5)
	DAY 28	697	533 (76.5)	673	525 (78.0)

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Endpoint	Visit	Nirmatrelvir/ritonavir (N=697)		Placebo (N=682)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
Global Impression Questionnaire: overall COVID-19-related symptoms	Baseline	697	636 (91.2)	682	645 (94.6)
	DAY 2	697	626 (89.8)	682	628 (92.1)
	DAY 3	697	633 (90.8)	682	621 (91.1)
	DAY 4	697	617 (88.5)	682	612 (89.7)
	DAY 5	697	616 (88.4)	681	606 (89.0)
	DAY 6	697	577 (82.8)	681	565 (83.0)
	DAY 7	697	555 (79.6)	681	561 (82.4)
	DAY 8	697	566 (81.2)	681	551 (80.9)
	DAY 9	697	567 (81.3)	681	553 (81.2)
	DAY 10	697	552 (79.2)	679	577 (85.0)
	DAY 11	697	564 (80.9)	679	565 (83.2)
	DAY 12	697	567 (81.3)	678	544 (80.2)
	DAY 13	697	573 (82.2)	676	561 (83.0)
	DAY 14	697	571 (81.9)	675	559 (82.8)
	DAY 15	697	563 (80.8)	675	558 (82.7)
	DAY 16	697	570 (81.8)	675	545 (80.7)
	DAY 17	697	569 (81.6)	675	545 (80.7)
	DAY 18	697	554 (79.5)	675	538 (79.7)
	DAY 19	697	555 (79.6)	675	558 (82.7)
	DAY 20	697	543 (77.9)	675	558 (82.7)
	DAY 21	697	562 (80.6)	675	551 (81.6)
	DAY 22	697	558 (80.1)	675	539 (79.9)
	DAY 23	697	548 (78.6)	675	533 (79.0)
	DAY 24	697	549 (78.8)	675	547 (81.0)
	DAY 25	697	541 (77.6)	675	545 (80.7)
	DAY 26	697	548 (78.6)	674	530 (78.6)
	DAY 27	697	546 (78.3)	674	549 (81.5)
	DAY 28	697	533 (76.5)	673	525 (78.0)
Global Impression Questionnaire: return to usual activities	Baseline	697	636 (91.2)	682	645 (94.6)
	DAY 2	697	626 (89.8)	682	628 (92.1)
	DAY 3	697	633 (90.8)	682	621 (91.1)
	DAY 4	697	617 (88.5)	682	612 (89.7)
	DAY 5	697	616 (88.4)	681	606 (89.0)
	DAY 6	697	577 (82.8)	681	565 (83.0)
	DAY 7	697	555 (79.6)	681	561 (82.4)
	DAY 8	697	566 (81.2)	681	551 (80.9)
	DAY 9	697	567 (81.3)	681	553 (81.2)
	DAY 10	697	552 (79.2)	679	577 (85.0)
	DAY 11	697	564 (80.9)	679	565 (83.2)
	DAY 12	697	567 (81.3)	678	544 (80.2)
	DAY 13	697	573 (82.2)	676	561 (83.0)
	DAY 14	697	571 (81.9)	675	559 (82.8)
	DAY 15	697	563 (80.8)	675	558 (82.7)
	DAY 16	697	570 (81.8)	675	545 (80.7)
	DAY 17	697	569 (81.6)	675	545 (80.7)
	DAY 18	697	554 (79.5)	675	538 (79.7)
	DAY 19	697	555 (79.6)	675	558 (82.7)
	DAY 20	697	543 (77.9)	675	558 (82.7)
	DAY 21	697	562 (80.6)	675	551 (81.6)
	DAY 22	697	558 (80.1)	675	539 (79.9)
	DAY 23	697	548 (78.6)	675	533 (79.0)
	DAY 24	697	549 (78.8)	675	547 (81.0)
	DAY 25	697	541 (77.6)	675	545 (80.7)
	DAY 26	697	548 (78.6)	674	530 (78.6)
	DAY 27	697	546 (78.3)	674	549 (81.5)
	DAY 28	697	533 (76.5)	673	525 (78.0)

N: Number of participants, n: Number of participants with non missing values

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
Overall Study population
Modified Intent-To-Treat (mITT) set
Overview Completion Rates

Final

Endpoint	Visit	Nirmatrelvir/ritonavir (N=697)		Placebo (N=682)	
		Number of participants alive at planned visit day	n (%)	Number of participants alive at planned visit day	n (%)
Work Productivity and Activity Impairment (WPAI): WPAI Question 6	Baseline (Day 5)	697	25 (3.6)	681	31 (4.6)
	Day 14	697	37 (5.3)	675	48 (7.1)
	Week 12	697	131 (18.8)	672	131 (19.5)
	Week 24	697	326 (46.8)	671	302 (45.0)

N: Number of participants, n: Number of participants with non missing values

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Stuffy or Runny Nose

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	161 (23.5)	178 (26.4)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.856 (0.662, 1.106) 0.233	
Relative Risk (95% CI)	0.887 (0.735, 1.071) 0.213	
Risk Difference (95% CI)	-0.025 (-0.068, 0.019) 0.268	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.855 (0.668, 1.093) 0.210	
Relative Risk (95% CI)	0.889 (0.739, 1.069) 0.211	
Risk Difference (95% CI)	-0.029 (-0.075, 0.017) 0.210	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Stuffy or Runny Nose

Final

	Nirmatrelvir/ritonavir (N=477)	Placebo (N=452)
Number of subjects with events, n (%)	429 (89.9)	372 (82.3)
Number of censored subjects, n (%)	48 (10.1)	80 (17.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	6.0 (5.0, 7.0)	7.0 (6.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.302 (1.129, 1.502)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.294 (1.126, 1.488)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

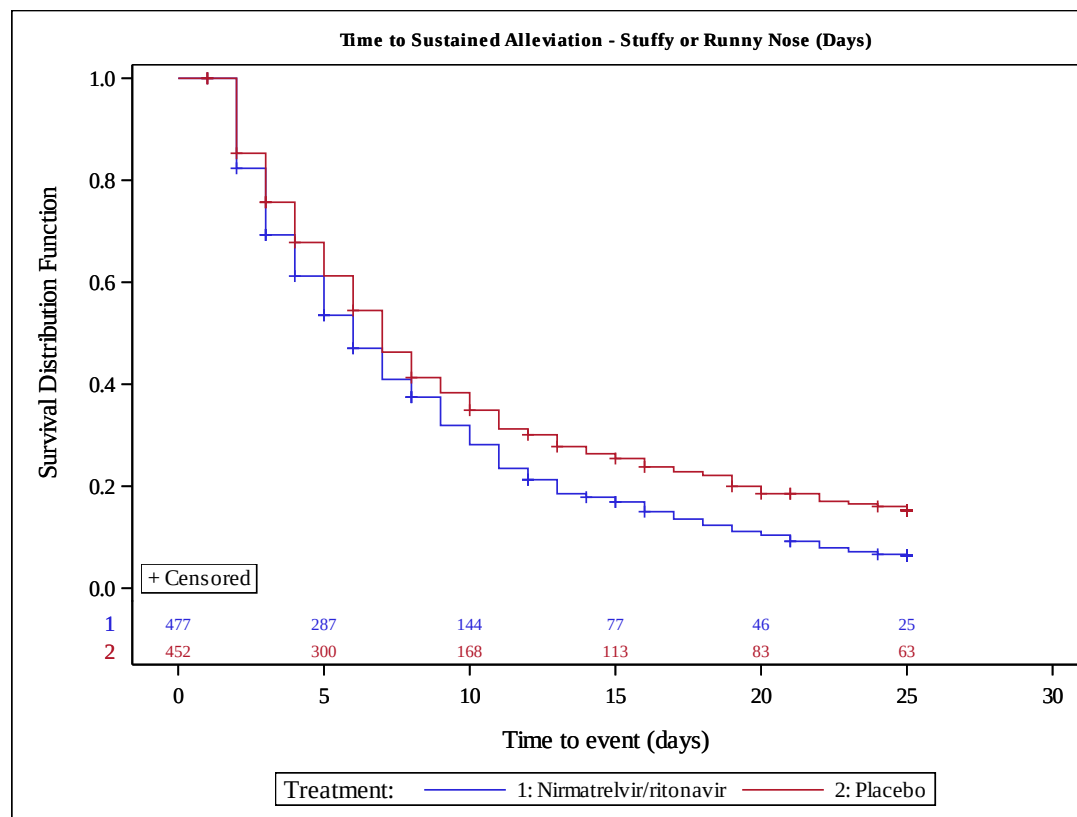
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Stuffy or Runny Nose

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Stuffy or Runny Nose

Final

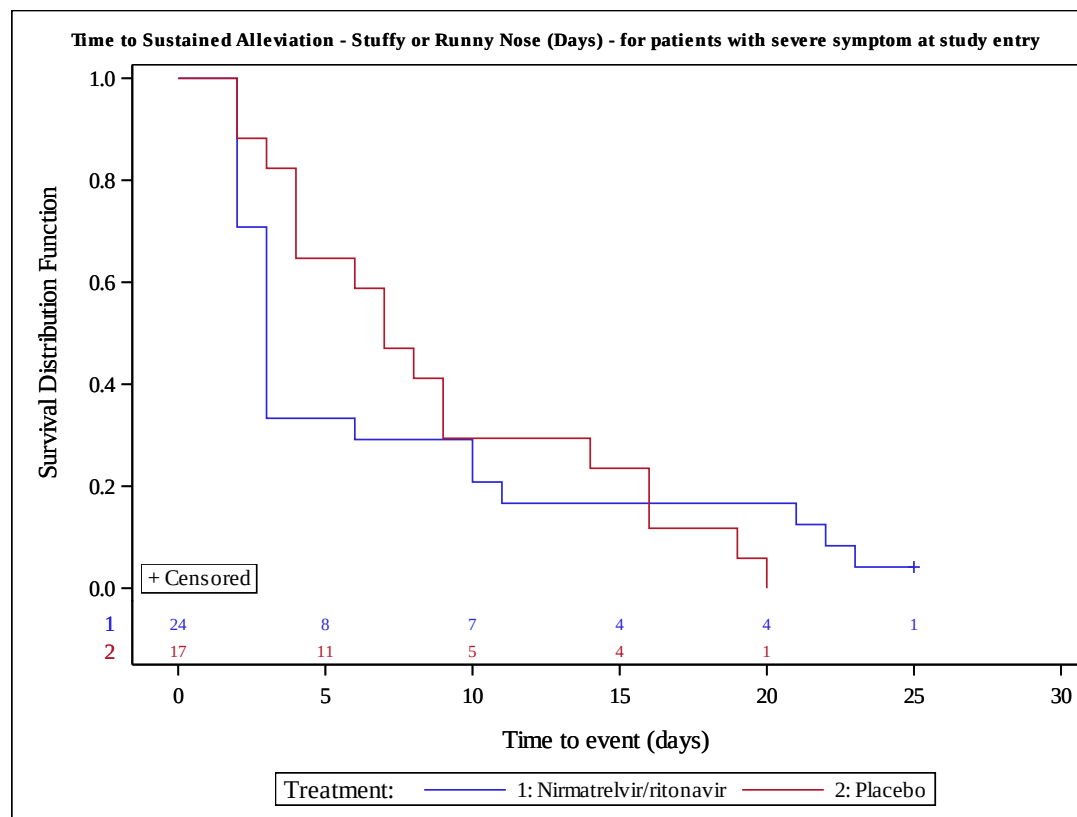
	Nirmatrelvir/ritonavir (N=24)	Placebo (N=17)
Number of subjects with events, n (%)	23 (95.8)	17 (100.0)
Number of censored subjects, n (%)	1 (4.2)	0 (0.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (2.0, 6.0)	7.0 (4.0, 14.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.182 (0.591, 2.364)	
p-value [3]	0.637	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.071 (0.556, 2.065)	
p-value [3]	0.837	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 [1] Based on the Brookmeyer and Crowley Method.
 [2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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 Overall Study population
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Stuffy or Runny Nose

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Stuffy or Runny Nose

Final

	Nirmatrelvir/ritonavir (N=477)	Placebo (N=452)
Number of subjects with events, n (%)	393 (82.4)	336 (74.3)
Number of censored subjects, n (%)	84 (17.6)	116 (25.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	9.0 (9.0, 10.0)	10.0 (9.0, 11.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.293 (1.114, 1.501)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.279 (1.105, 1.480)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

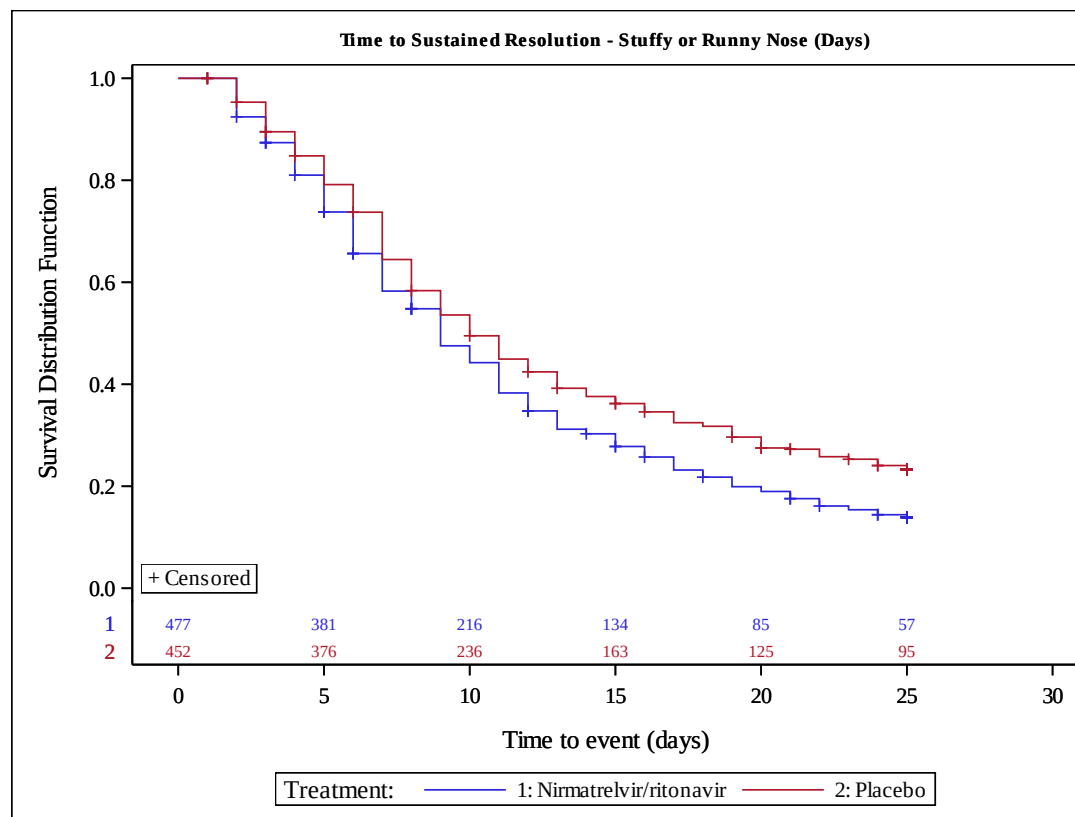
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Stuffy or Runny Nose

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Stuffy or Runny Nose

Final

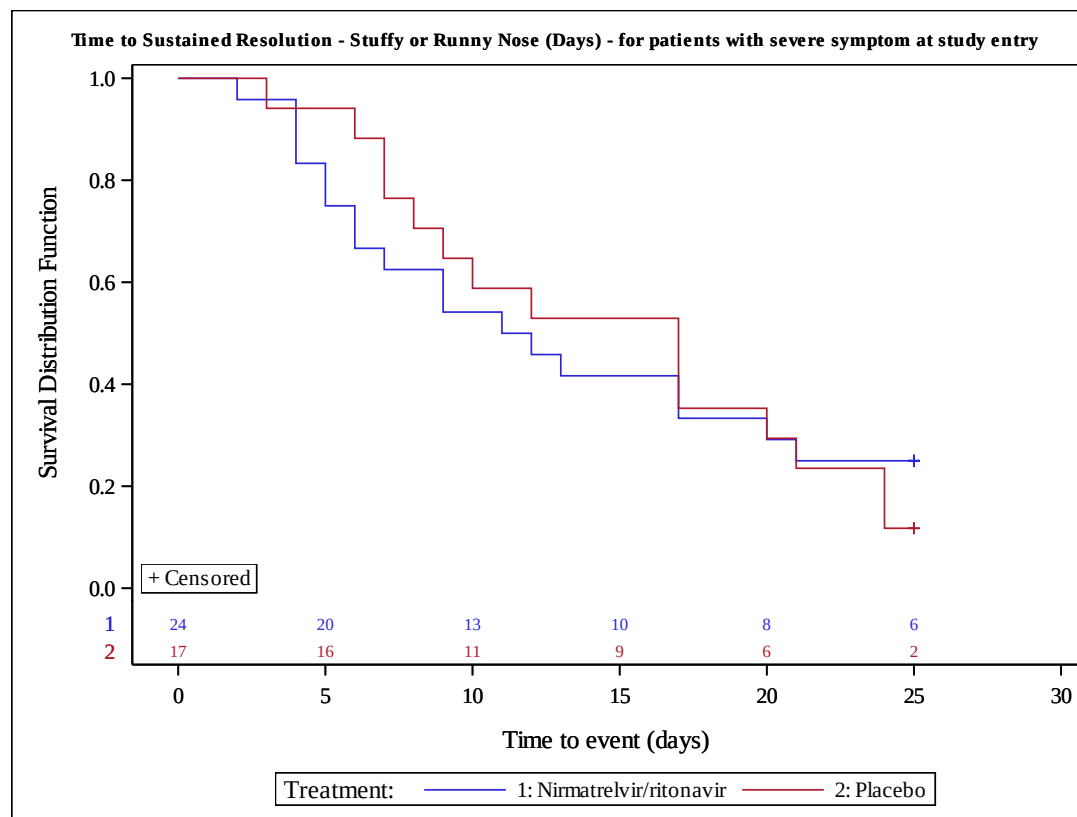
	Nirmatrelvir/ritonavir (N=24)	Placebo (N=17)
Number of subjects with events, n (%)	18 (75.0)	15 (88.2)
Number of censored subjects, n (%)	6 (25.0)	2 (11.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	11.5 (6.0, 20.0)	17.0 (7.0, 21.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.127 (0.530, 2.396)	
p-value [3]	0.757	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	0.968 (0.487, 1.922)	
p-value [3]	0.925	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
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 [1] Based on the Brookmeyer and Crowley Method.
 [2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Stuffy or Runny Nose

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Sore Throat

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	143 (20.8)	160 (23.7)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.825 (0.634, 1.074) 0.153	
Relative Risk (95% CI)	0.864 (0.707, 1.058) 0.157	
Risk Difference (95% CI)	-0.035 (-0.078, 0.008) 0.107	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.846 (0.655, 1.093) 0.200	
Relative Risk (95% CI)	0.878 (0.720, 1.071) 0.200	
Risk Difference (95% CI)	-0.029 (-0.073, 0.015) 0.200	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Sore Throat

Final

	Nirmatrelvir/ritonavir (N=383)	Placebo (N=358)
Number of subjects with events, n (%)	348 (90.9)	299 (83.5)
Number of censored subjects, n (%)	35 (9.1)	59 (16.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 5.0)	5.0 (5.0, 7.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.374 (1.171, 1.612)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.341 (1.147, 1.568)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

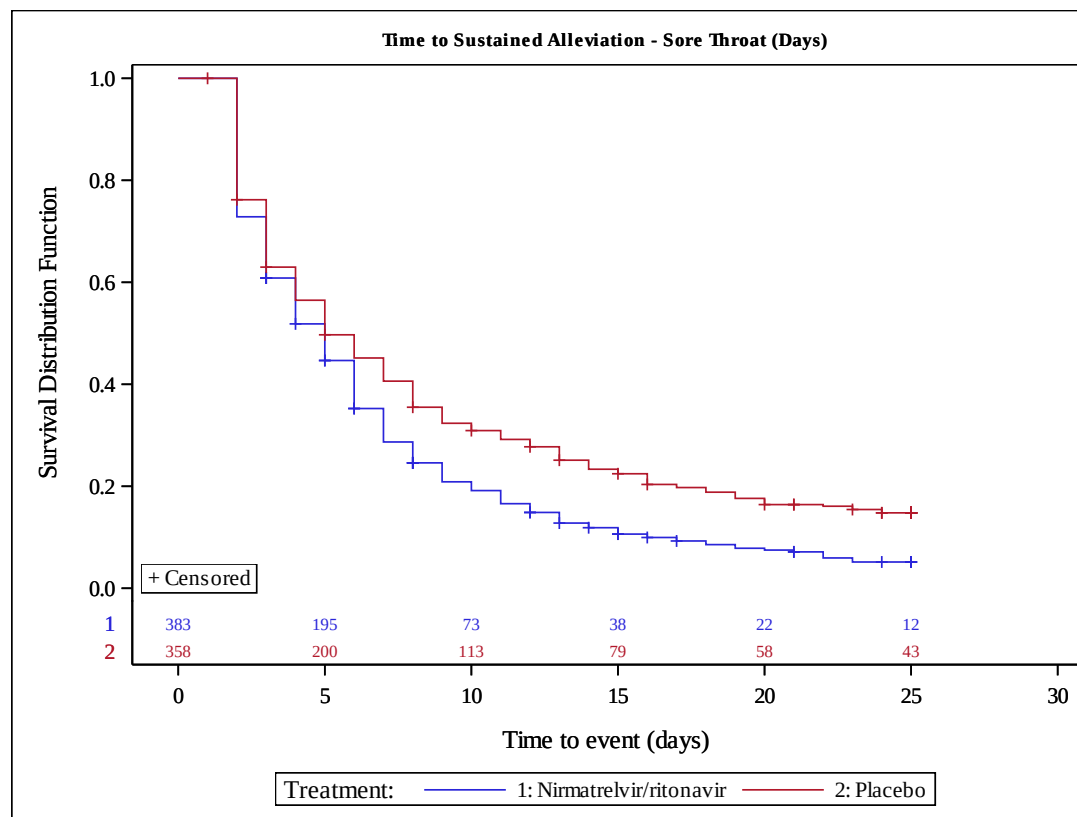
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Overall Study population
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Sore Throat

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Sore Throat

Final

	Nirmatrelvir/ritonavir (N=20)	Placebo (N=17)
Number of subjects with events, n (%)	19 (95.0)	16 (94.1)
Number of censored subjects, n (%)	1 (5.0)	1 (5.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (2.0, 6.0)	6.0 (3.0, 12.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.924 (0.850, 4.357)	
p-value [3]	0.117	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.458 (0.743, 2.860)	
p-value [3]	0.273	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

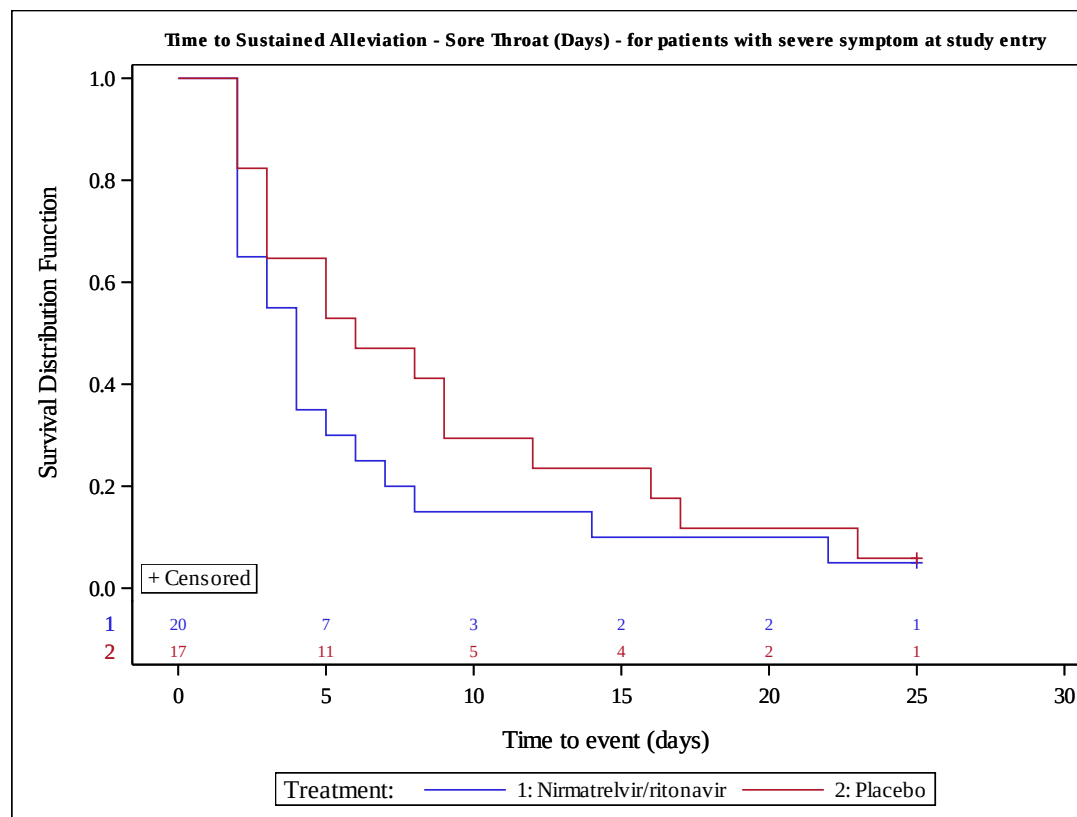
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Sore Throat

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Sore Throat

Final

	Nirmatrelvir/ritonavir (N=383)	Placebo (N=358)
Number of subjects with events, n (%)	325 (84.9)	277 (77.4)
Number of censored subjects, n (%)	58 (15.1)	81 (22.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	7.0 (6.0, 7.0)	9.0 (8.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.338 (1.135, 1.577)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.344 (1.144, 1.579)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

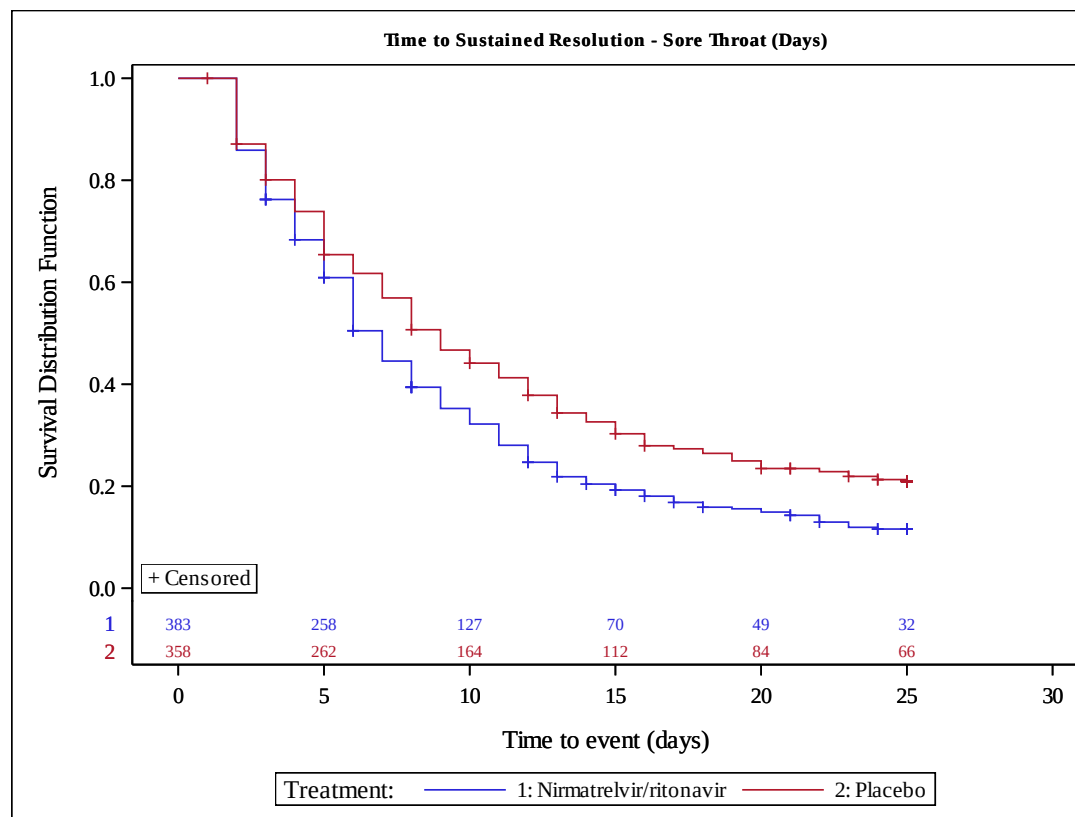
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Sore Throat

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Overall Study population
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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Sore Throat

Final

	Nirmatrelvir/ritonavir (N=20)	Placebo (N=17)
Number of subjects with events, n (%)	15 (75.0)	12 (70.6)
Number of censored subjects, n (%)	5 (25.0)	5 (29.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	13.5 (6.0, 23.0)	13.0 (6.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.499 (0.614, 3.655)	
p-value [3]	0.374	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.129 (0.528, 2.417)	
p-value [3]	0.755	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

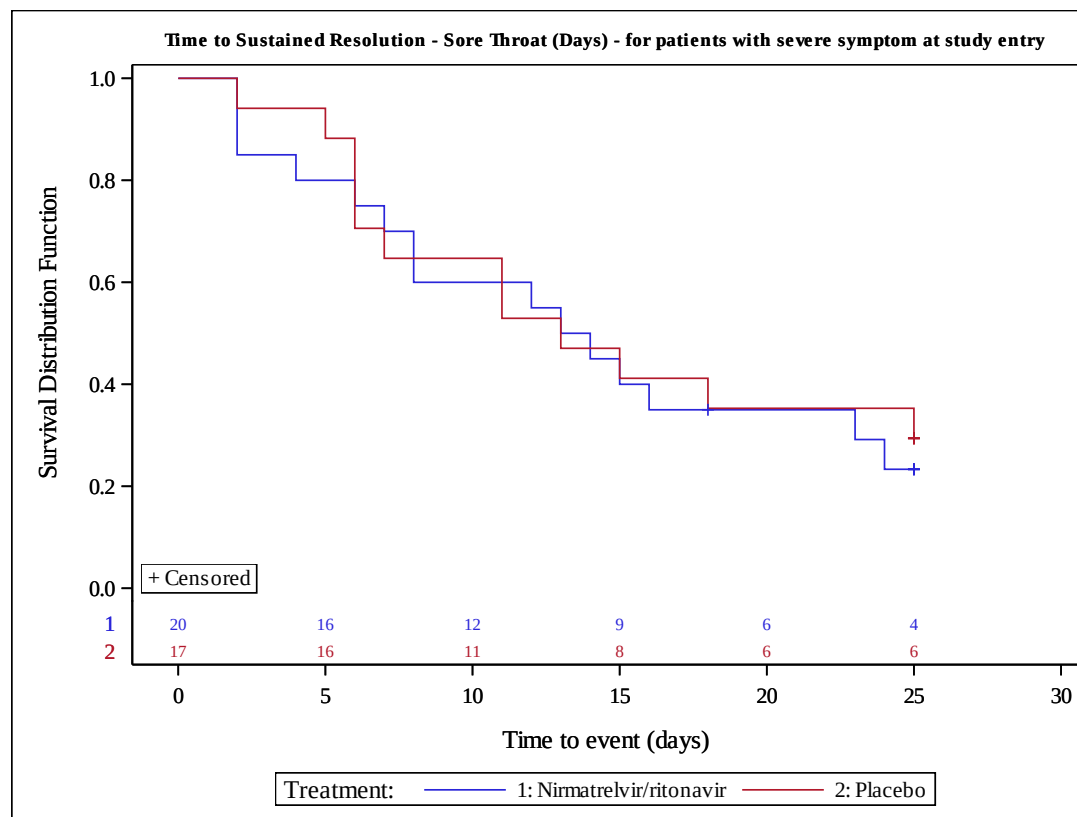
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Sore Throat

Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Shortness of Breath or Difficulty Breathing

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	154 (22.4)	210 (31.2)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.617 (0.480, 0.794) <.001	
Relative Risk (95% CI)	0.707 (0.590, 0.848) <.001	
Risk Difference (95% CI)	NE (NE, NE)	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.640 (0.502, 0.815) <.001	
Relative Risk (95% CI)	0.721 (0.603, 0.861) <.001	
Risk Difference (95% CI)	-0.087 (-0.134, -0.040) <.001	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Shortness of Breath or Difficulty Breathing

Final

	Nirmatrelvir/ritonavir (N=287)	Placebo (N=298)
Number of subjects with events, n (%)	239 (83.3)	235 (78.9)
Number of censored subjects, n (%)	48 (16.7)	63 (21.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	6.0 (5.0, 7.0)	7.0 (6.0, 9.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.296 (1.077, 1.561)	
p-value [3]	0.006	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.279 (1.068, 1.533)	
p-value [3]	0.008	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

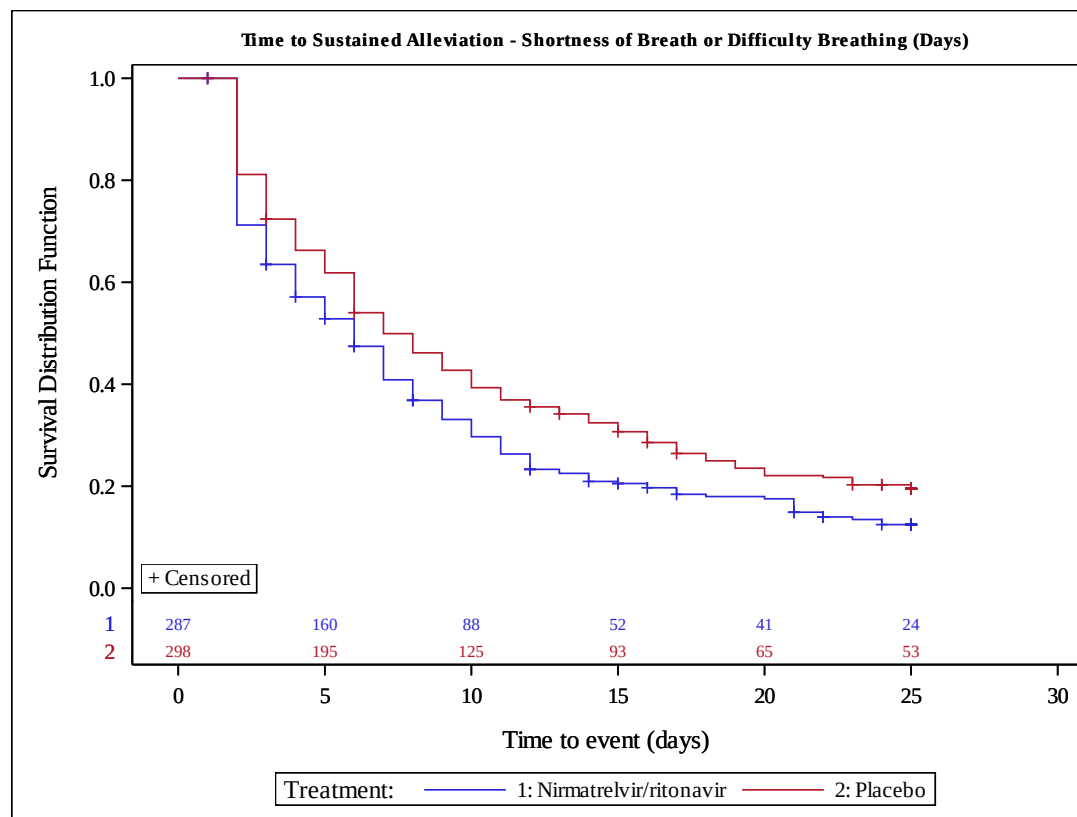
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Overall Study population
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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Pfizer Inc
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Final

	Nirmatrelvir/ritonavir (N=5)	Placebo (N=5)
Number of subjects with events, n (%)	4 (80.0)	3 (60.0)
Number of censored subjects, n (%)	1 (20.0)	2 (40.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	9.0 (2.0, 22.0)	19.0 (3.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.378 (0.071, 26.911)	
p-value [3]	0.833	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.777 (0.384, 8.224)	
p-value [3]	0.462	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

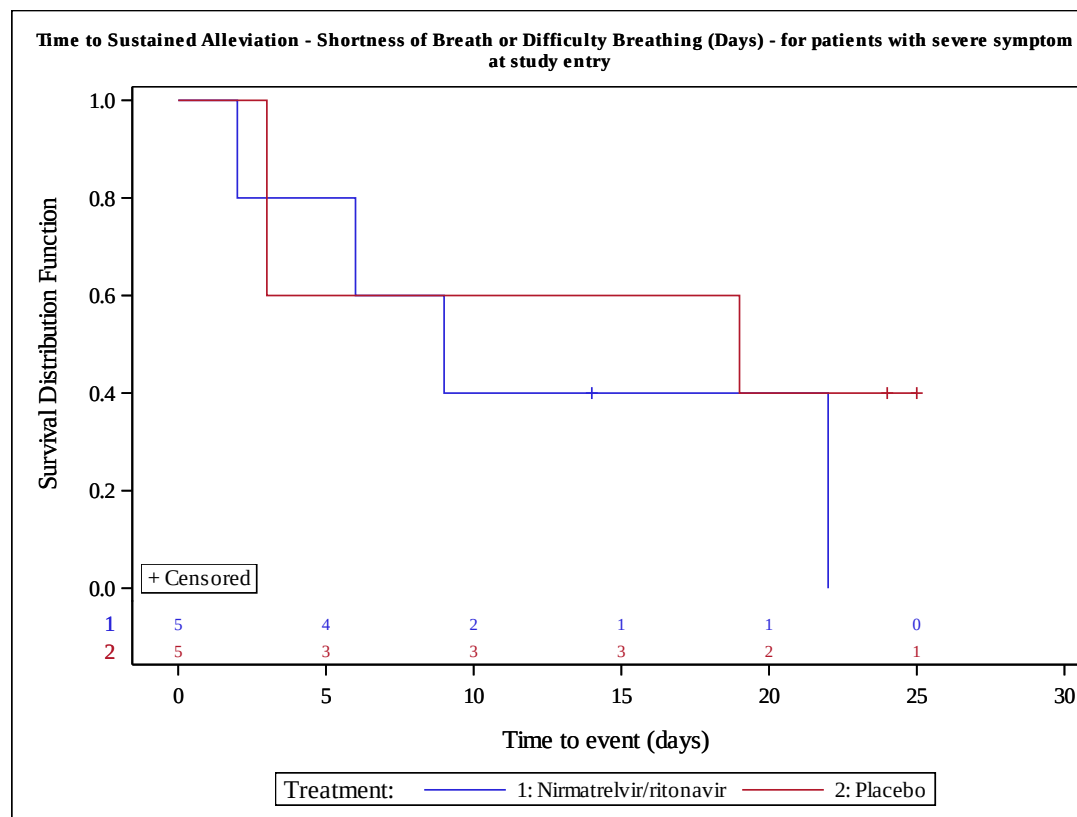
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Shortness of Breath or Difficulty Breathing

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Shortness of Breath or Difficulty Breathing

Final

	Nirmatrelvir/ritonavir (N=287)	Placebo (N=298)
Number of subjects with events, n (%)	224 (78.0)	206 (69.1)
Number of censored subjects, n (%)	63 (22.0)	92 (30.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	8.0 (7.0, 9.0)	11.0 (10.0, 14.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.441 (1.185, 1.751)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.421 (1.175, 1.718)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

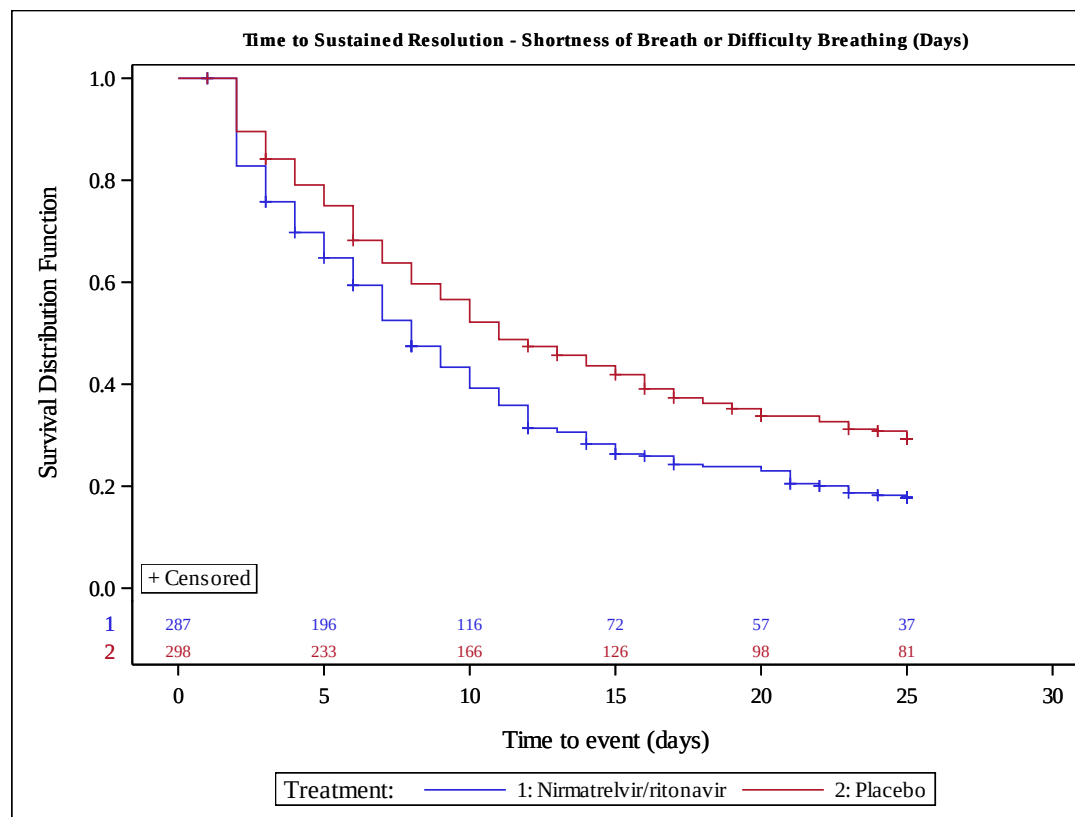
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Pfizer Inc
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Overall Study population
Modified Intent-To-Treat (mITT) set
Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Shortness of Breath or Difficulty Breathing

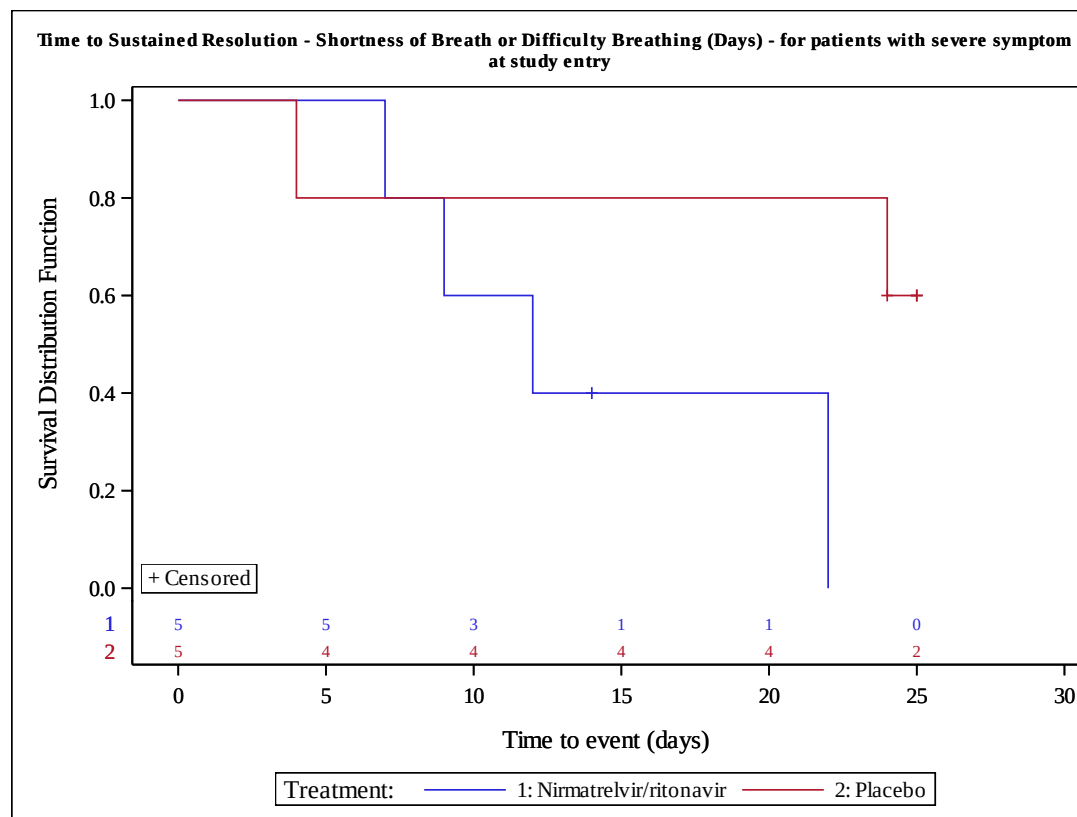
	Nirmatrelvir/ritonavir (N=5)	Placebo (N=5)
Number of subjects with events, n (%)	4 (80.0)	2 (40.0)
Number of censored subjects, n (%)	1 (20.0)	3 (60.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	12.0 (7.0, 22.0)	NE (4.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.869 (0.084, 41.706)	
p-value [3]	0.693	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	5.881 (0.608, 56.933)	
p-value [3]	0.126	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
[1] Based on the Brookmeyer and Crowley Method.
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.
[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Cough

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	156 (22.7)	181 (26.9)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.790 (0.613, 1.019) 0.069	
Relative Risk (95% CI)	0.836 (0.691, 1.010) 0.063	
Risk Difference (95% CI)	-0.038 (-0.084, 0.008) 0.107	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.802 (0.626, 1.026) 0.079	
Relative Risk (95% CI)	0.847 (0.703, 1.020) 0.080	
Risk Difference (95% CI)	-0.041 (-0.087, 0.005) 0.079	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Cough

Final

	Nirmatrelvir/ritonavir (N=556)	Placebo (N=548)
Number of subjects with events, n (%)	475 (85.4)	431 (78.6)
Number of censored subjects, n (%)	81 (14.6)	117 (21.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	8.0 (8.0, 9.0)	10.0 (8.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.214 (1.062, 1.387)	
p-value [3]	0.004	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.235 (1.084, 1.408)	
p-value [3]	0.002	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

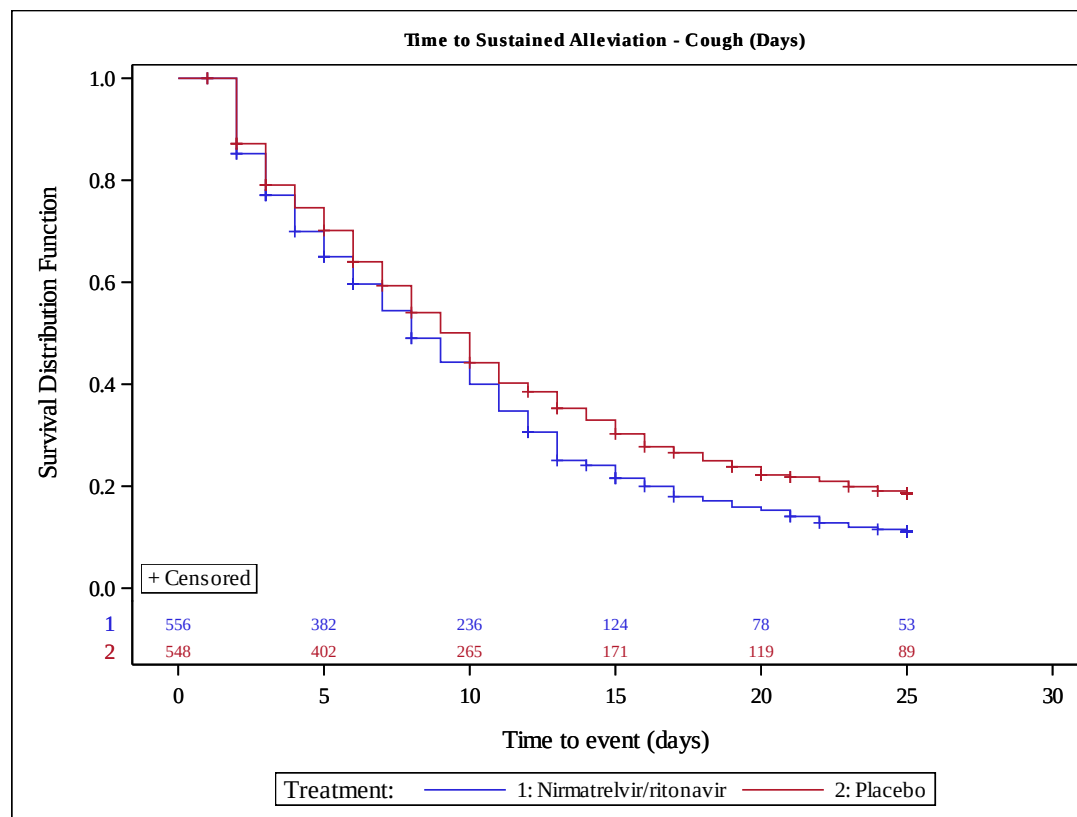
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Cough

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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 Overall Study population
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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough

Final

	Nirmatrelvir/ritonavir (N=34)	Placebo (N=24)
Number of subjects with events, n (%)	29 (85.3)	20 (83.3)
Number of censored subjects, n (%)	5 (14.7)	4 (16.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (3.0, 6.0)	10.0 (5.0, 18.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.338 (0.728, 2.460)	
p-value [3]	0.348	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.478 (0.831, 2.629)	
p-value [3]	0.183	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

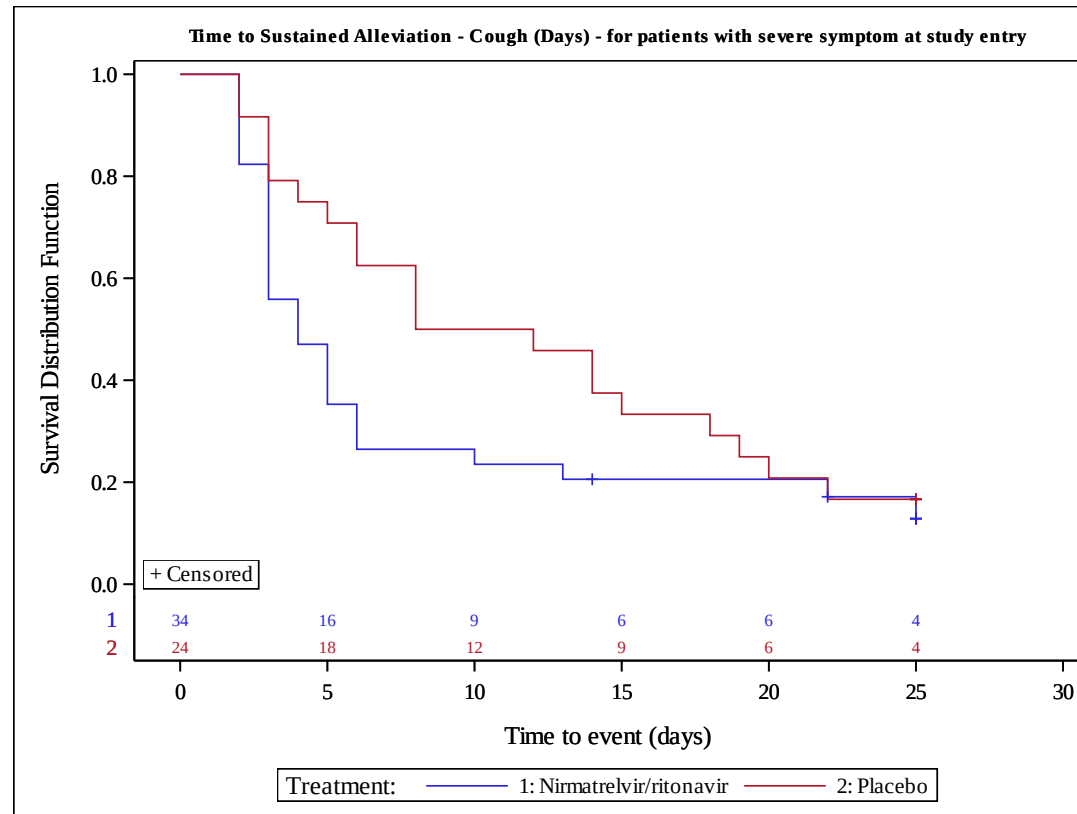
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Pfizer Inc
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Overall Study population
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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Cough

Final

	Nirmatrelvir/ritonavir (N=556)	Placebo (N=548)
Number of subjects with events, n (%)	431 (77.5)	370 (67.5)
Number of censored subjects, n (%)	125 (22.5)	178 (32.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	13.0 (12.0, 13.0)	14.0 (13.0, 16.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.271 (1.103, 1.465)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.318 (1.147, 1.515)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

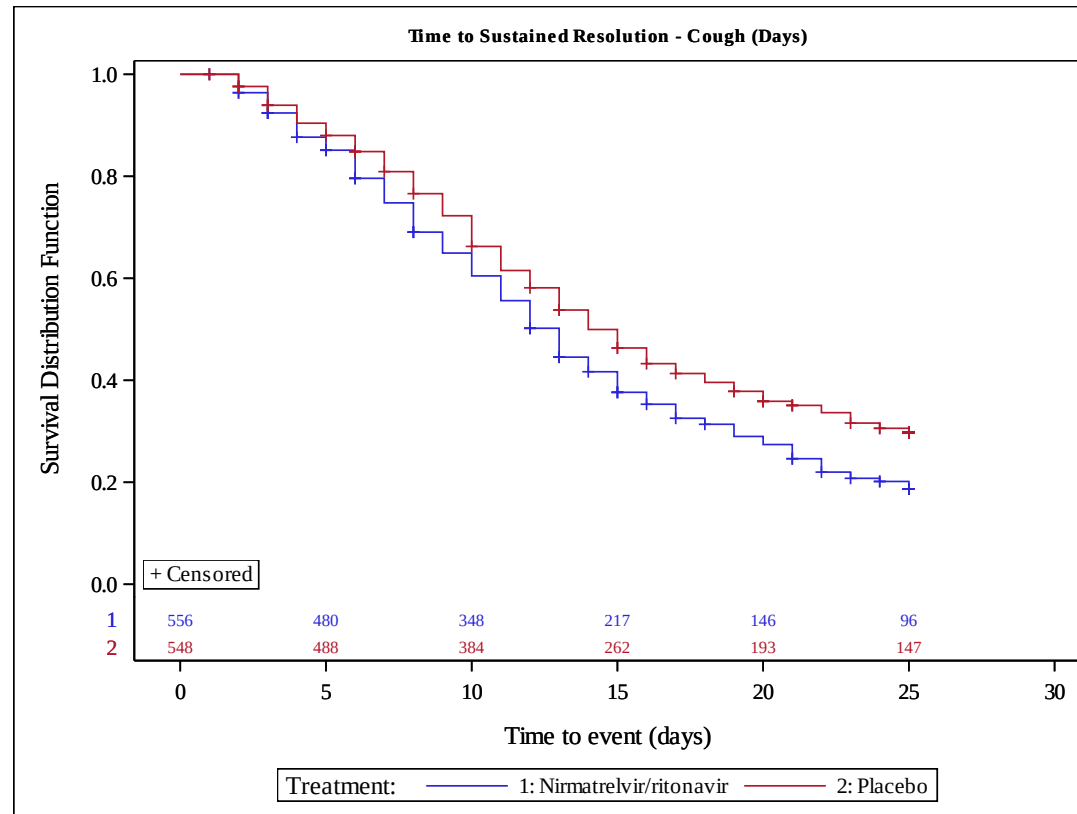
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough

Final

	Nirmatrelvir/ritonavir (N=34)	Placebo (N=24)
Number of subjects with events, n (%)	25 (73.5)	14 (58.3)
Number of censored subjects, n (%)	9 (26.5)	10 (41.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	13.5 (7.0, 20.0)	21.5 (15.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.703 (0.856, 3.391)	
p-value [3]	0.129	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.849 (0.957, 3.570)	
p-value [3]	0.067	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

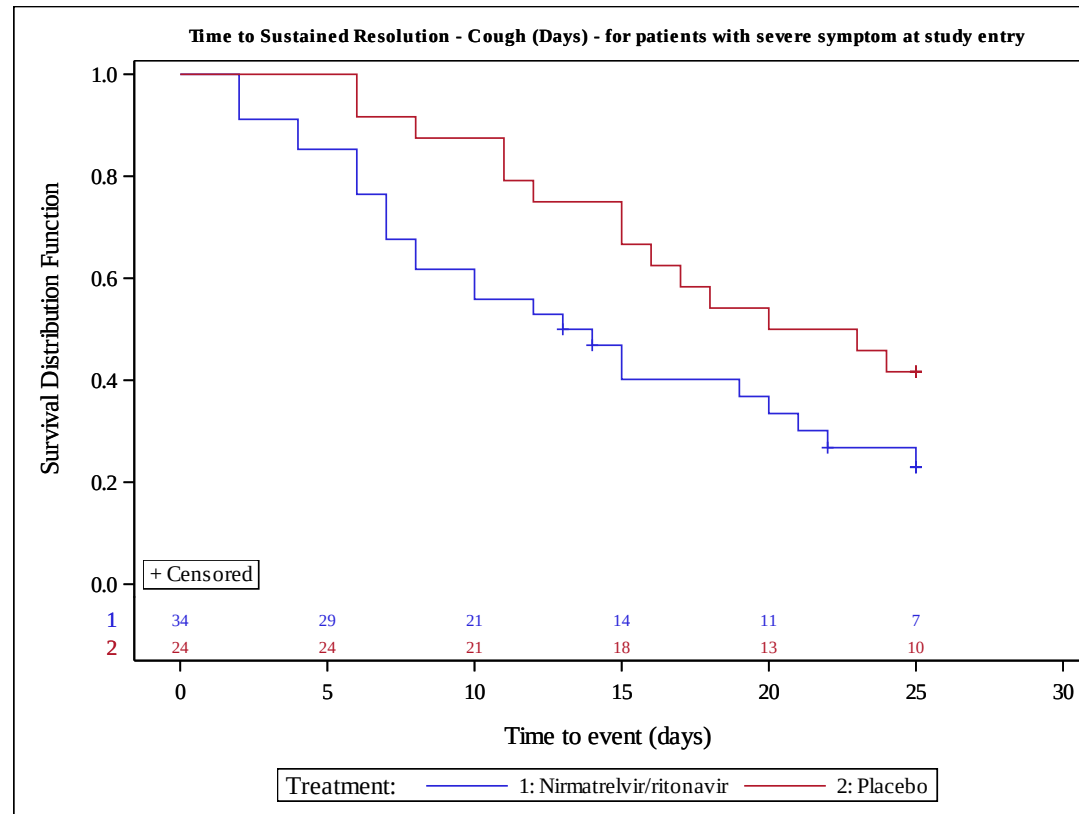
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Cough

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Pfizer Inc
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 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Worsening of Signs and Symptoms - Fatigue (low energy or tiredness)

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	159 (23.2)	183 (27.2)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.801 (0.622, 1.032) 0.086	
Relative Risk (95% CI)	0.850 (0.704, 1.026) 0.091	
Risk Difference (95% CI)	-0.042 (-0.088, 0.004) 0.077	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.810 (0.633, 1.035) 0.092	
Relative Risk (95% CI)	0.854 (0.710, 1.026) 0.092	
Risk Difference (95% CI)	-0.040 (-0.086, 0.006) 0.091	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Fatigue (low energy or tiredness)

Final

	Nirmatrelvir/ritonavir (N=605)	Placebo (N=593)
Number of subjects with events, n (%)	510 (84.3)	463 (78.1)
Number of censored subjects, n (%)	95 (15.7)	130 (21.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	8.0 (7.0, 9.0)	9.0 (8.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.277 (1.123, 1.453)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.269 (1.118, 1.439)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

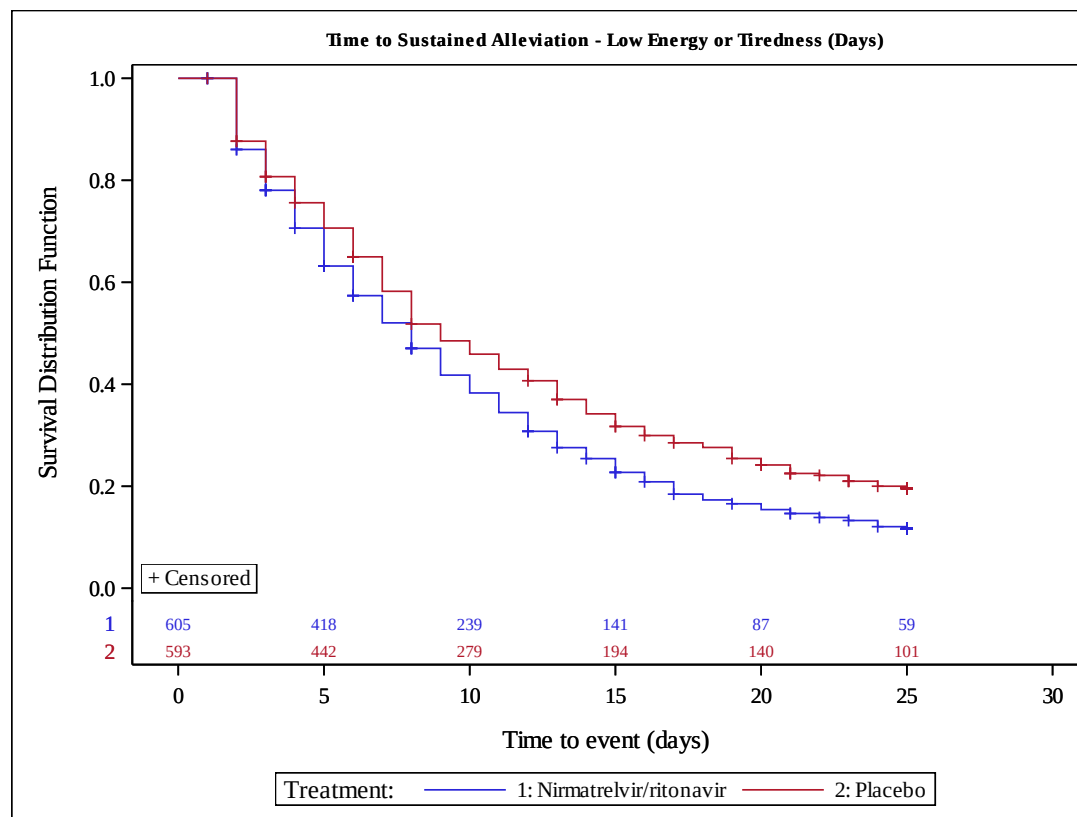
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Fatigue (low energy or tiredness)

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Fatigue (low energy or tiredness)

Final

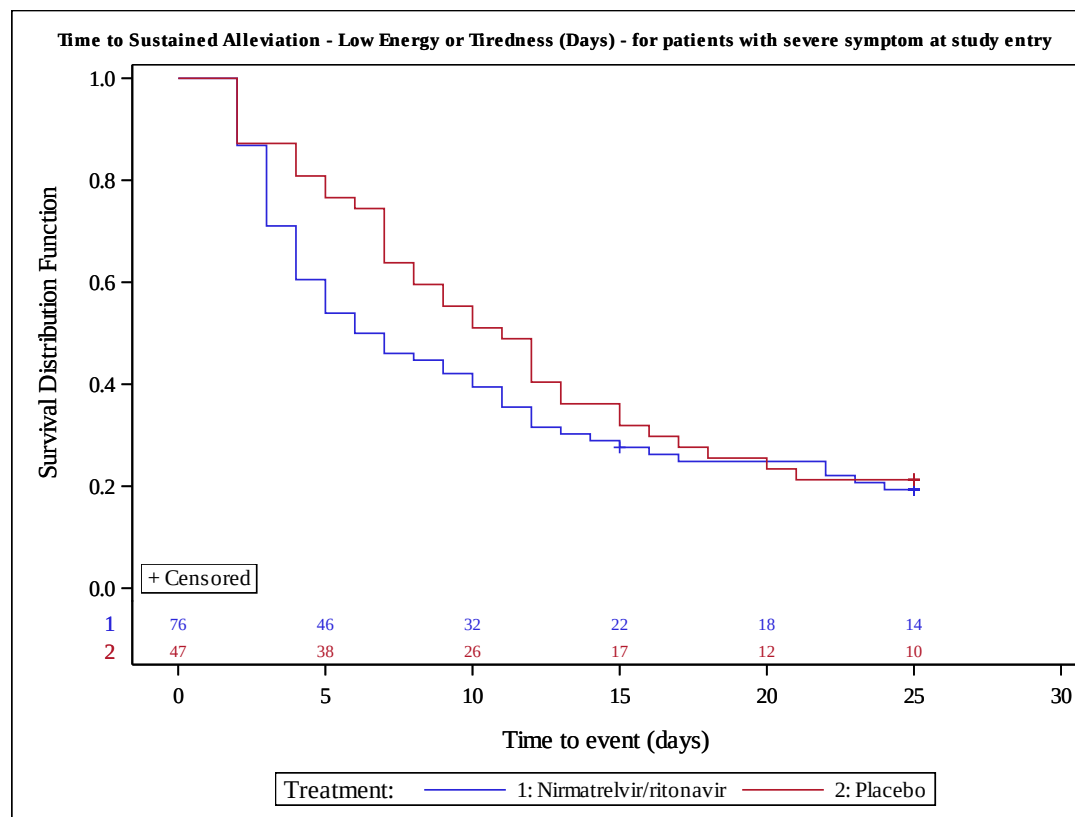
	Nirmatrelvir/ritonavir (N=76)	Placebo (N=47)
Number of subjects with events, n (%)	61 (80.3)	37 (78.7)
Number of censored subjects, n (%)	15 (19.7)	10 (21.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	6.5 (4.0, 11.0)	11.0 (7.0, 13.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.373 (0.886, 2.127)	
p-value [3]	0.157	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.226 (0.814, 1.847)	
p-value [3]	0.329	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 [1] Based on the Brookmeyer and Crowley Method.
 [2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Fatigue (low energy or tiredness)

Final

	Nirmatrelvir/ritonavir (N=605)	Placebo (N=593)
Number of subjects with events, n (%)	431 (71.2)	385 (64.9)
Number of censored subjects, n (%)	174 (28.8)	208 (35.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	14.0 (13.0, 15.0)	18.0 (16.0, 19.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.288 (1.119, 1.482)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.286 (1.121, 1.476)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

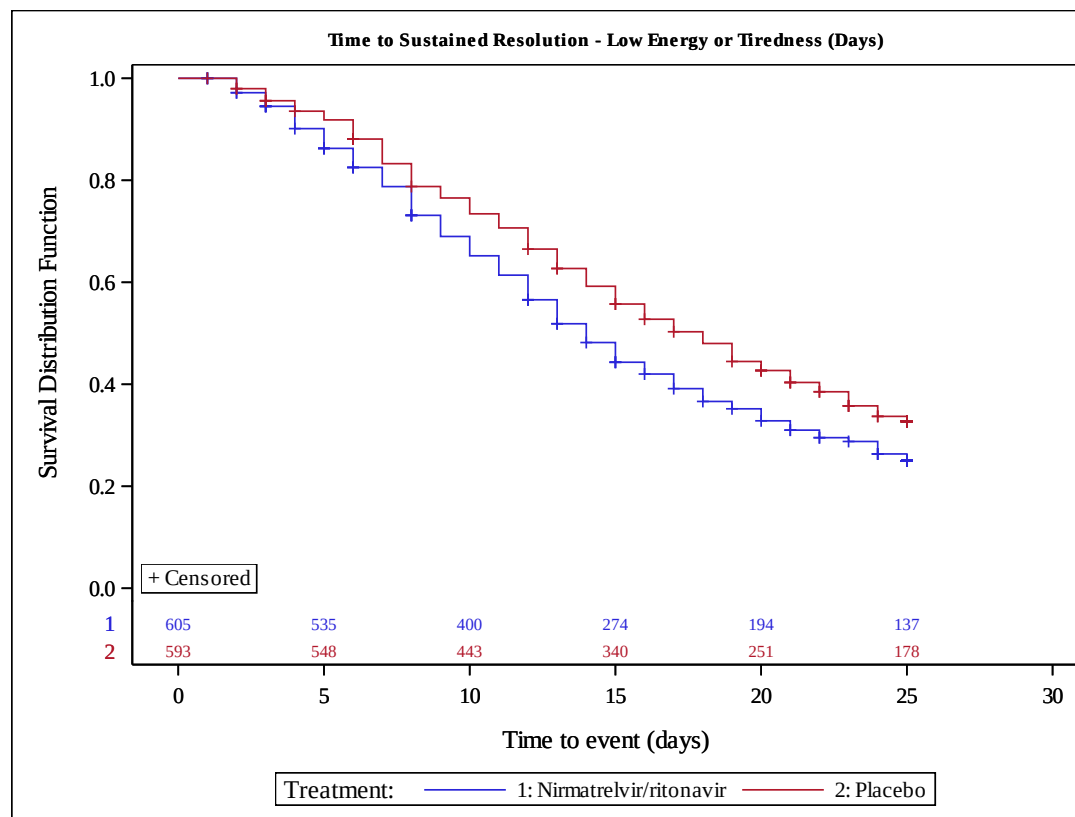
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Kaplan-Meier Plot of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Fatigue (low energy or tiredness)

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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Fatigue (low energy or tiredness)

Final

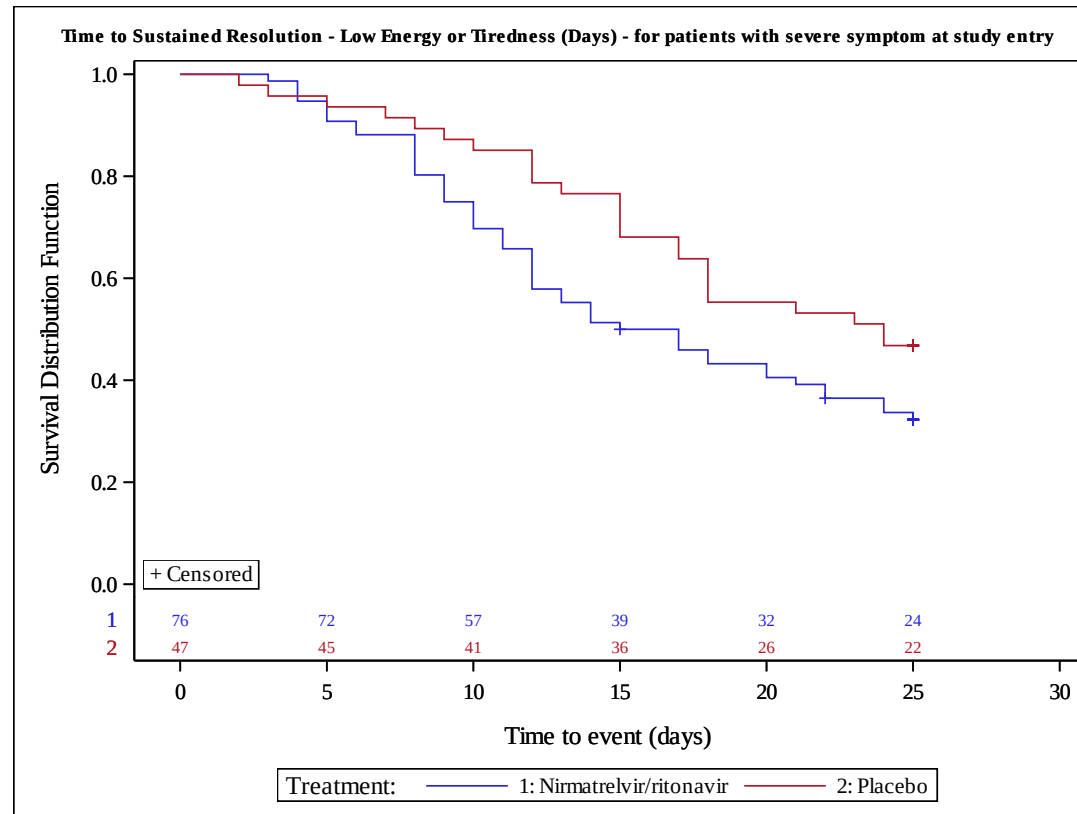
	Nirmatrelvir/ritonavir (N=76)	Placebo (N=47)
Number of subjects with events, n (%)	51 (67.1)	25 (53.2)
Number of censored subjects, n (%)	25 (32.9)	22 (46.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	16.0 (12.0, 21.0)	24.0 (17.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.914 (1.153, 3.176)	
p-value [3]	0.012	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.574 (0.974, 2.543)	
p-value [3]	0.064	

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 [1] Based on the Brookmeyer and Crowley Method.
 [2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Muscle or Body Aches

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	152 (22.2)	156 (23.1)
Adjusted analysis [1] Odds Ratio (95% CI)	0.975 (0.750, 1.267) 0.849	
Relative Risk (95% CI)	0.976 (0.798, 1.193) 0.811	
Risk Difference (95% CI)	0.001 (-0.043, 0.045) 0.967	
Unadjusted analysis [2] Odds Ratio (95% CI)	0.945 (0.733, 1.218) 0.663	
Relative Risk (95% CI)	0.957 (0.787, 1.165) 0.663	
Risk Difference (95% CI)	-0.010 (-0.054, 0.035) 0.663	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Muscle or Body Aches

Final

	Nirmatrelvir/ritonavir (N=548)	Placebo (N=532)
Number of subjects with events, n (%)	480 (87.6)	434 (81.6)
Number of censored subjects, n (%)	68 (12.4)	98 (18.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	6.0 (5.0, 7.0)	7.0 (6.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.290 (1.129, 1.474)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.275 (1.119, 1.452)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

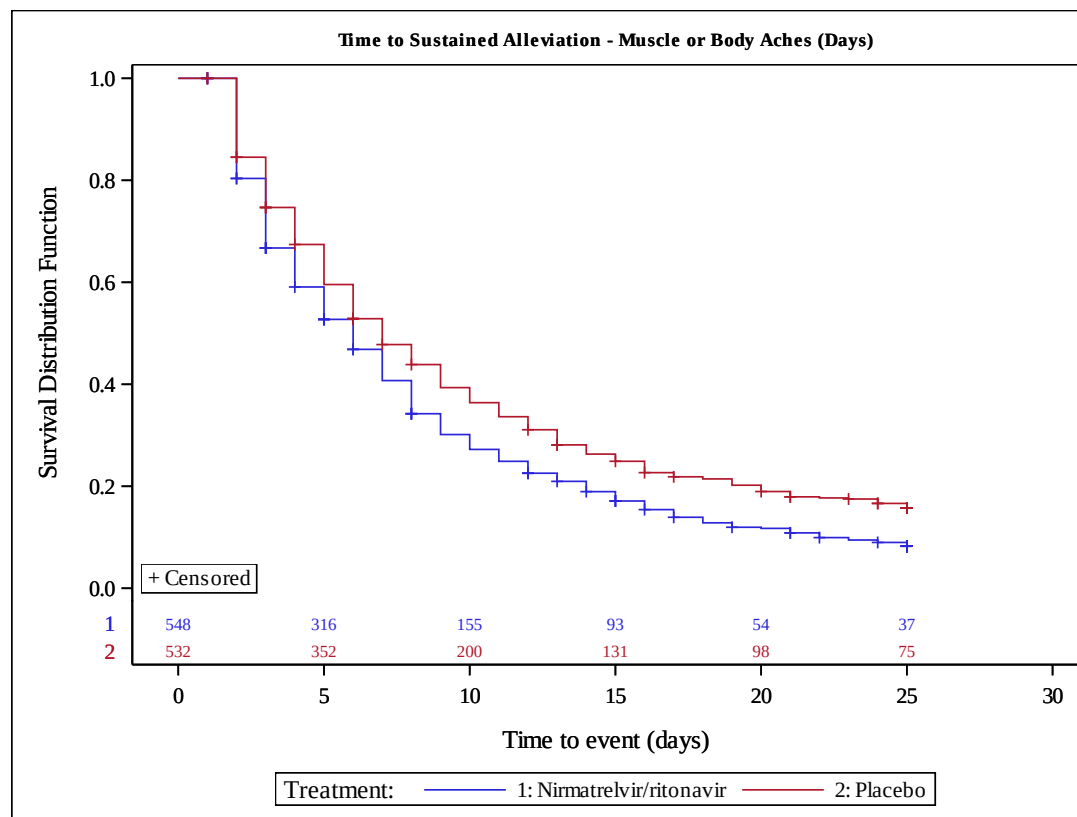
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Muscle or Body Aches

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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

	Nirmatrelvir/ritonavir (N=58)	Placebo (N=47)
Number of subjects with events, n (%)	51 (87.9)	42 (89.4)
Number of censored subjects, n (%)	7 (12.1)	5 (10.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (3.0, 5.0)	5.0 (4.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.233 (0.800, 1.899)	
p-value [3]	0.343	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.264 (0.838, 1.905)	
p-value [3]	0.264	

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[1] Based on the Brookmeyer and Crowley Method.

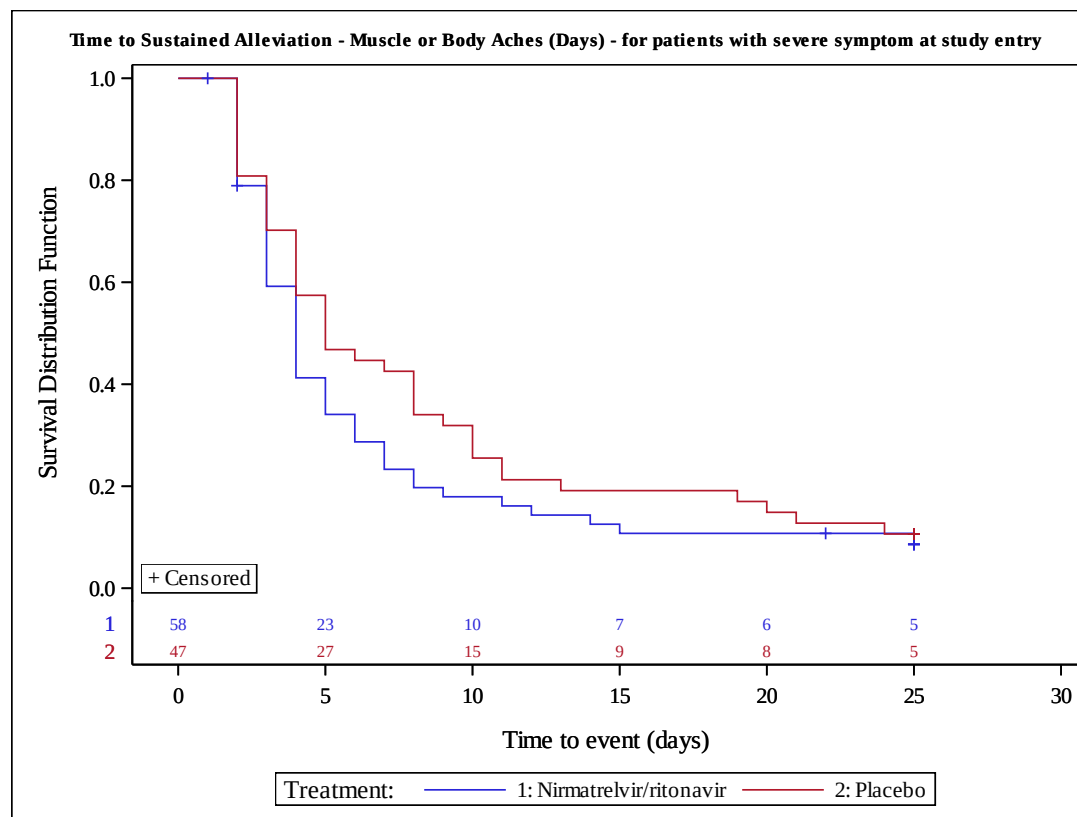
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Muscle or Body Aches

Final

	Nirmatrelvir/ritonavir (N=548)	Placebo (N=532)
Number of subjects with events, n (%)	429 (78.3)	387 (72.7)
Number of censored subjects, n (%)	119 (21.7)	145 (27.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	9.0 (8.0, 11.0)	12.0 (11.0, 13.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.282 (1.114, 1.476)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.258 (1.097, 1.444)	
p-value [3]	0.001	

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[1] Based on the Brookmeyer and Crowley Method.

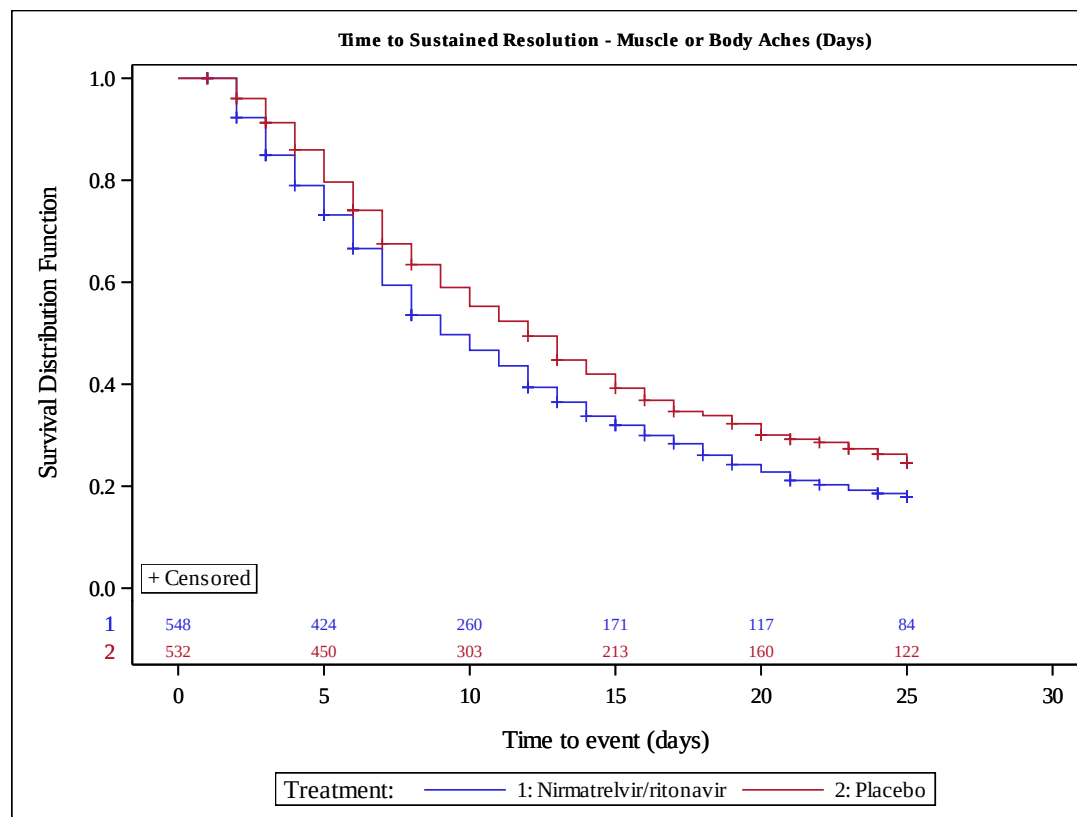
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Muscle or Body Aches

Final

	Nirmatrelvir/ritonavir (N=58)	Placebo (N=47)
Number of subjects with events, n (%)	42 (72.4)	36 (76.6)
Number of censored subjects, n (%)	16 (27.6)	11 (23.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	10.0 (7.0, 12.0)	13.0 (8.0, 16.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.140 (0.715, 1.819)	
p-value [3]	0.582	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.121 (0.718, 1.750)	
p-value [3]	0.616	

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[1] Based on the Brookmeyer and Crowley Method.

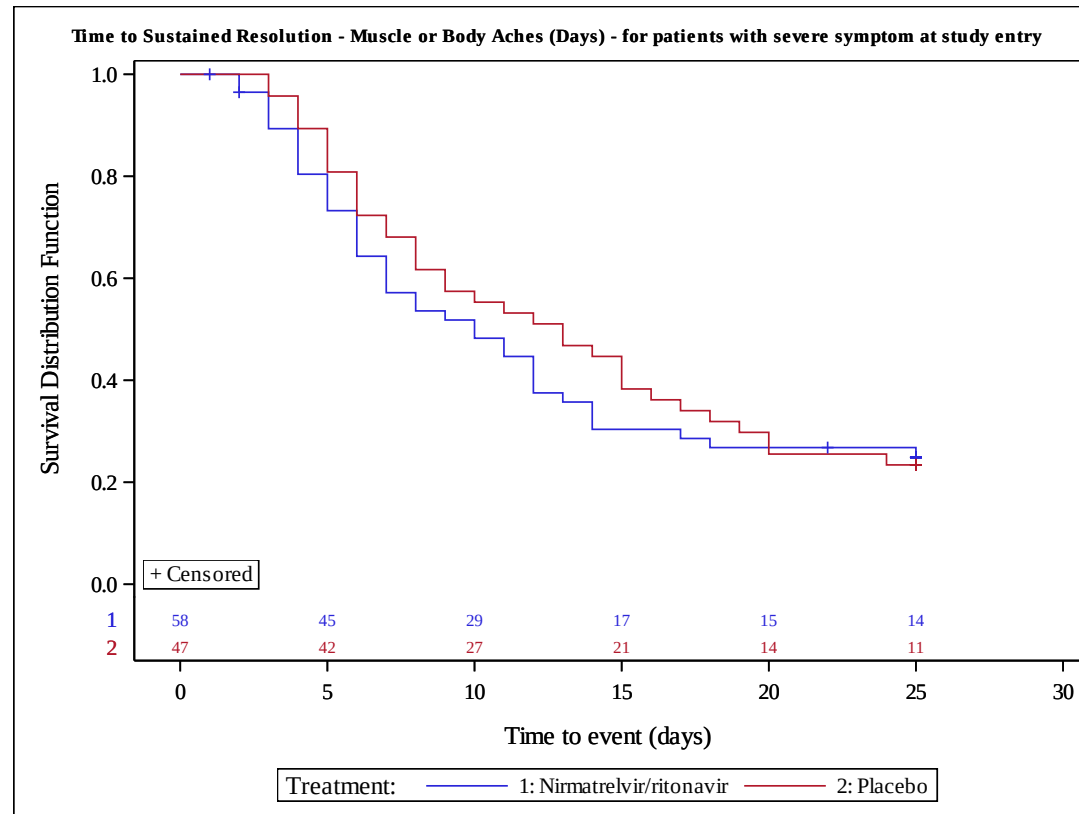
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

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Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	169 (24.6)	196 (29.1)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.802 (0.626, 1.028) 0.081	
Relative Risk (95% CI)	0.849 (0.709, 1.015) 0.073	
Risk Difference (95% CI)	-0.037 (-0.084, 0.010) 0.127	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.797 (0.627, 1.014) 0.065	
Relative Risk (95% CI)	0.847 (0.710, 1.010) 0.065	
Risk Difference (95% CI)	-0.044 (-0.092, 0.003) 0.064	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

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[2] Computed using normal approximation (Wald).

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Final

	Nirmatrelvir/ritonavir (N=511)	Placebo (N=476)
Number of subjects with events, n (%)	455 (89.0)	396 (83.2)
Number of censored subjects, n (%)	56 (11.0)	80 (16.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 6.0)	7.0 (6.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.337 (1.164, 1.535)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.325 (1.157, 1.516)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

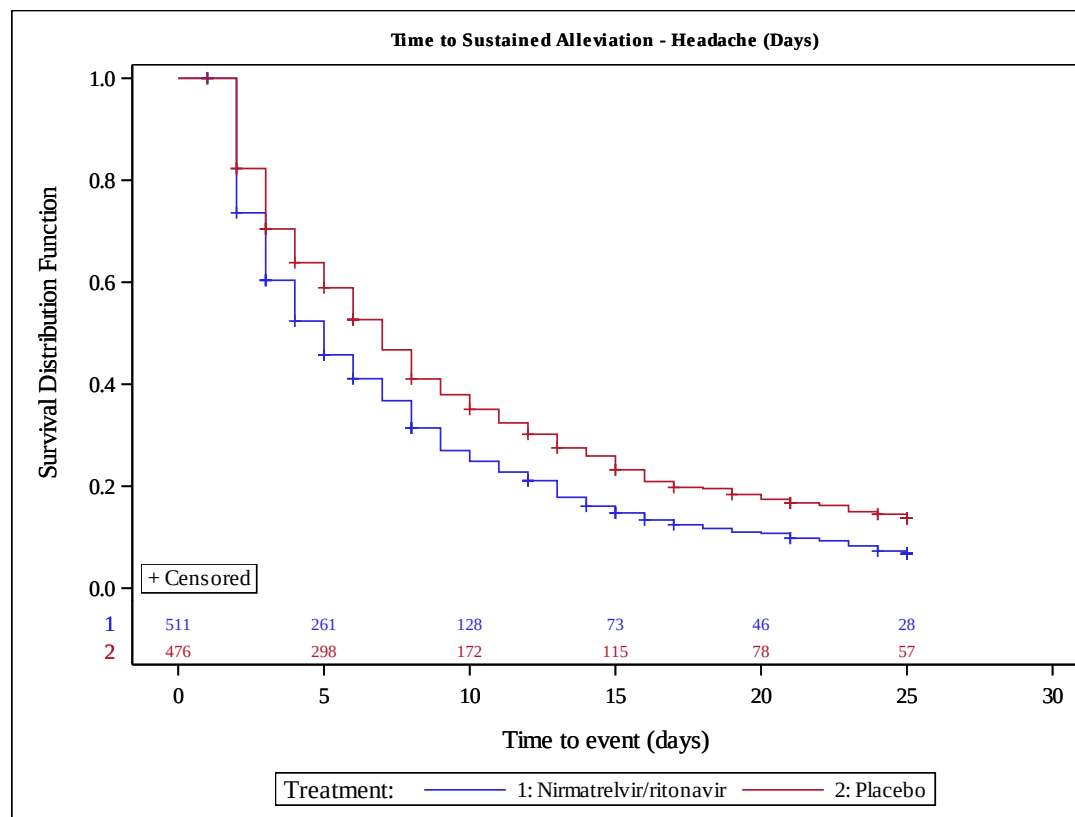
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Final



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Final

	Nirmatrelvir/ritonavir (N=65)	Placebo (N=46)
Number of subjects with events, n (%)	58 (89.2)	42 (91.3)
Number of censored subjects, n (%)	7 (10.8)	4 (8.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (3.0, 5.0)	7.0 (4.0, 9.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.246 (0.817, 1.901)	
p-value [3]	0.307	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.287 (0.863, 1.918)	
p-value [3]	0.216	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

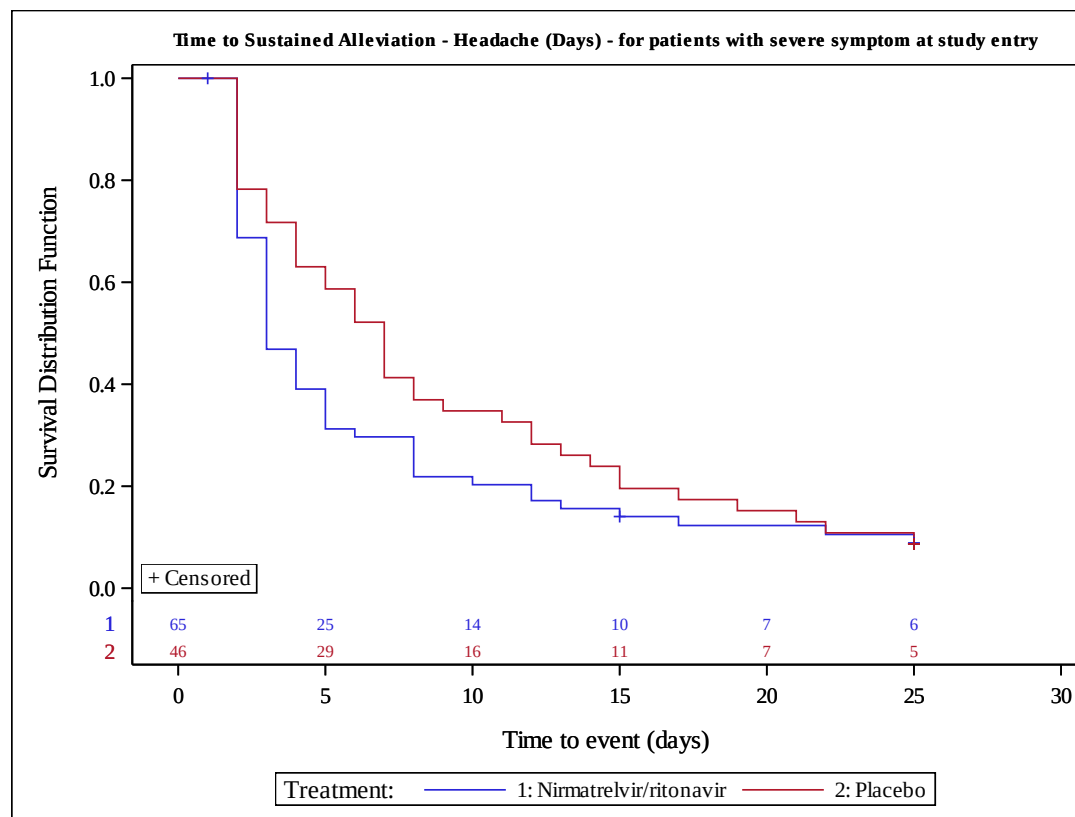
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Headache

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Headache

Final

	Nirmatrelvir/ritonavir (N=511)	Placebo (N=476)
Number of subjects with events, n (%)	422 (82.6)	357 (75.0)
Number of censored subjects, n (%)	89 (17.4)	119 (25.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	8.0 (8.0, 9.0)	11.0 (9.0, 13.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.304 (1.129, 1.505)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.328 (1.153, 1.530)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

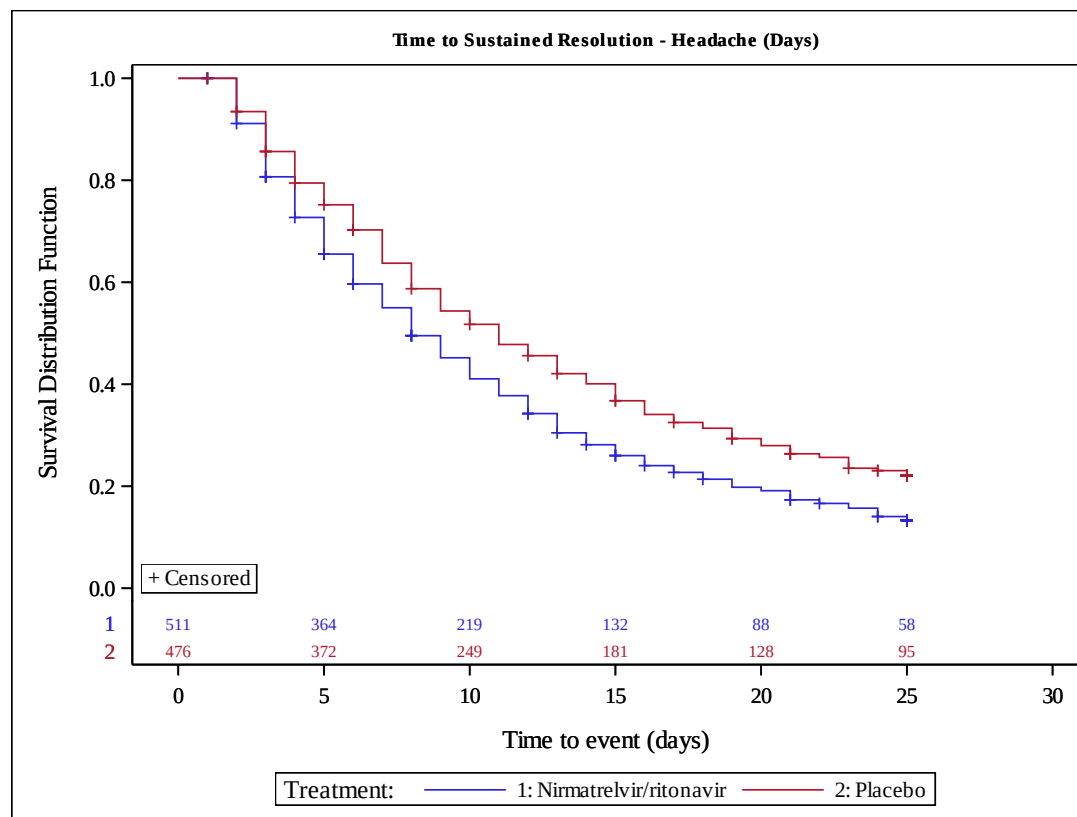
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Headache

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Headache

Final

	Nirmatrelvir/ritonavir (N=65)	Placebo (N=46)
Number of subjects with events, n (%)	54 (83.1)	33 (71.7)
Number of censored subjects, n (%)	11 (16.9)	13 (28.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	10.0 (7.0, 12.0)	17.0 (11.0, 21.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.586 (1.009, 2.491)	
p-value [3]	0.046	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.606 (1.039, 2.482)	
p-value [3]	0.033	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

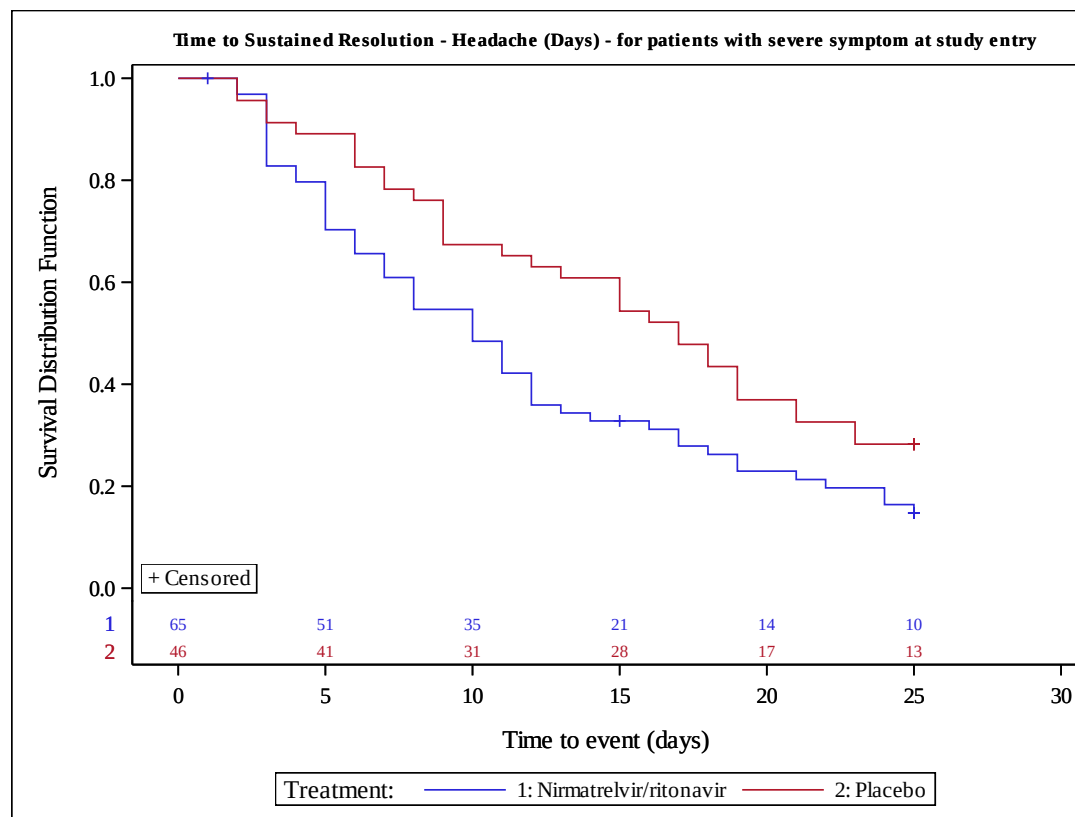
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Headache

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Chills or Shivering

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	102 (14.9)	125 (18.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.818 (0.609, 1.099) 0.182	
Relative Risk (95% CI)	0.849 (0.665, 1.083) 0.188	
Risk Difference (95% CI)	-0.032 (-0.070, 0.006) 0.101	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.767 (0.576, 1.021) 0.070	
Relative Risk (95% CI)	0.802 (0.631, 1.018) 0.070	
Risk Difference (95% CI)	-0.037 (-0.076, 0.003) 0.069	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Chills or Shivering

Final

	Nirmatrelvir/ritonavir (N=428)	Placebo (N=400)
Number of subjects with events, n (%)	386 (90.2)	333 (83.3)
Number of censored subjects, n (%)	42 (9.8)	67 (16.8)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (3.0, 4.0)	4.0 (4.0, 5.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.306 (1.123, 1.518)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.297 (1.120, 1.504)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

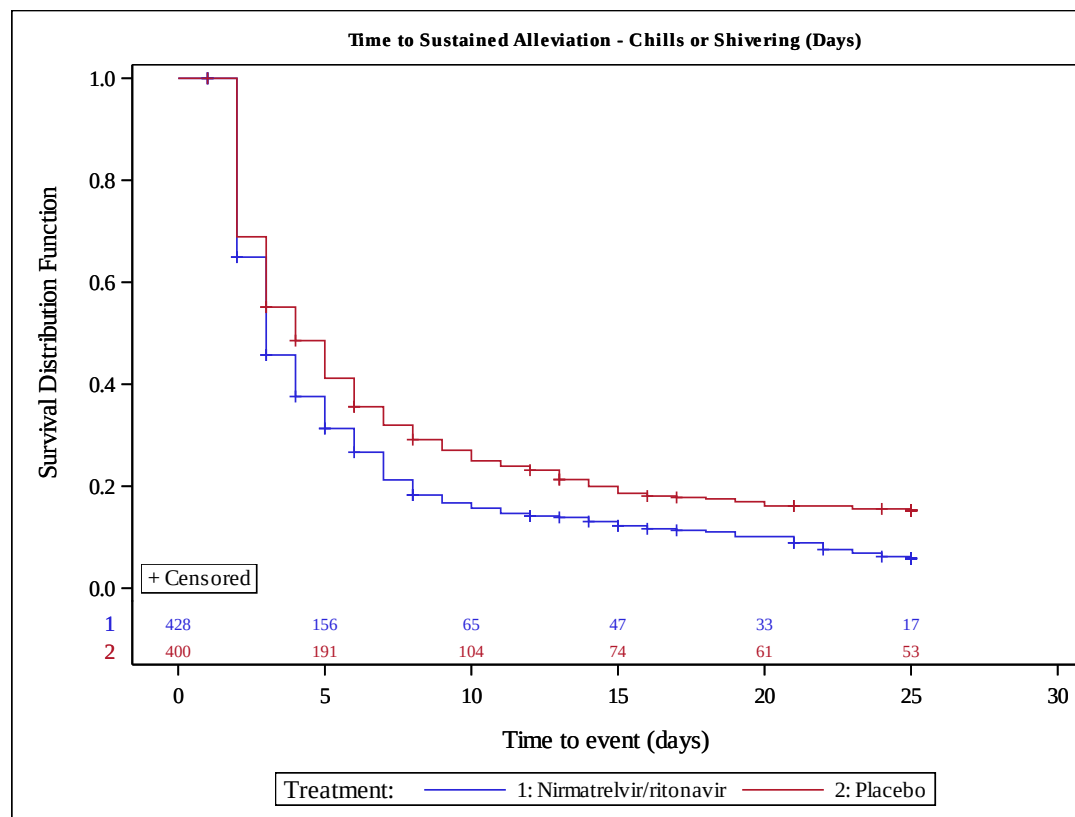
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Chills or Shivering

Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Chills or Shivering

Final

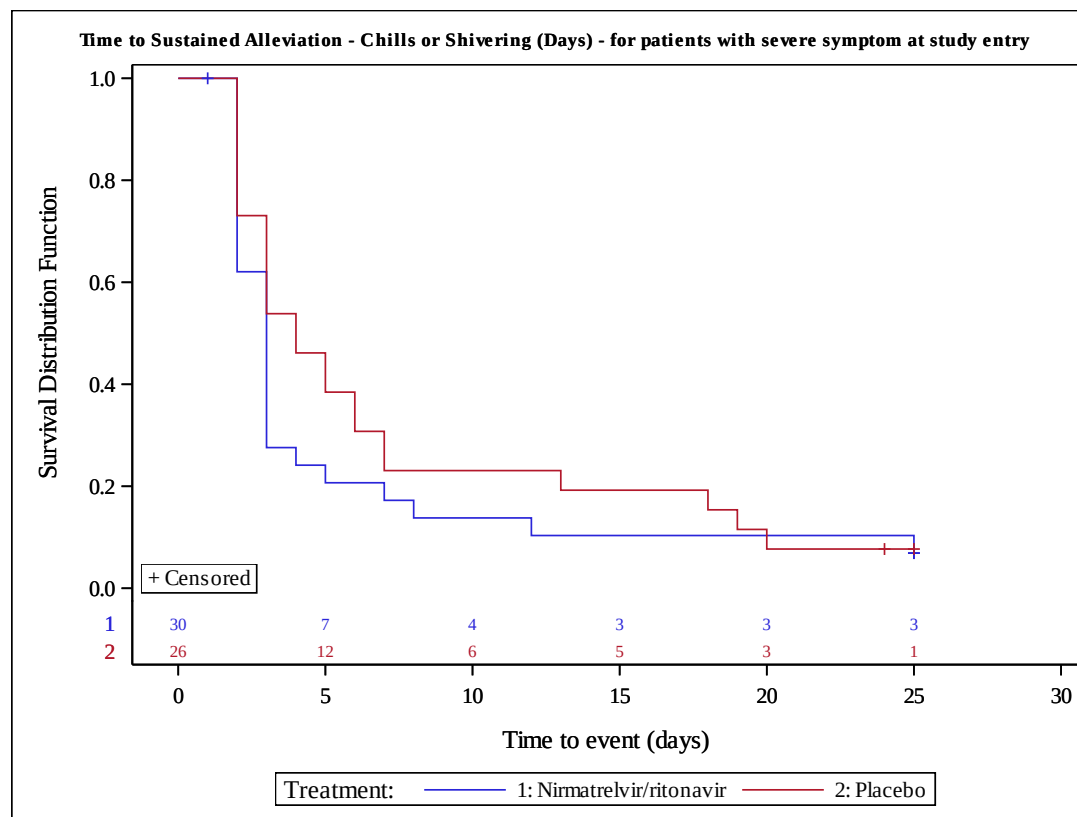
	Nirmatrelvir/ritonavir (N=30)	Placebo (N=26)
Number of subjects with events, n (%)	27 (90.0)	24 (92.3)
Number of censored subjects, n (%)	3 (10.0)	2 (7.7)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (2.0, 3.0)	4.0 (3.0, 6.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.319 (0.734, 2.373)	
p-value [3]	0.355	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.246 (0.715, 2.171)	
p-value [3]	0.438	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
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 [1] Based on the Brookmeyer and Crowley Method.
 [2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Chills or Shivering

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Chills or Shivering

Final

	Nirmatrelvir/ritonavir (N=428)	Placebo (N=400)
Number of subjects with events, n (%)	376 (87.9)	314 (78.5)
Number of censored subjects, n (%)	52 (12.1)	86 (21.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 5.0)	6.0 (5.0, 7.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.365 (1.170, 1.593)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.374 (1.182, 1.598)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

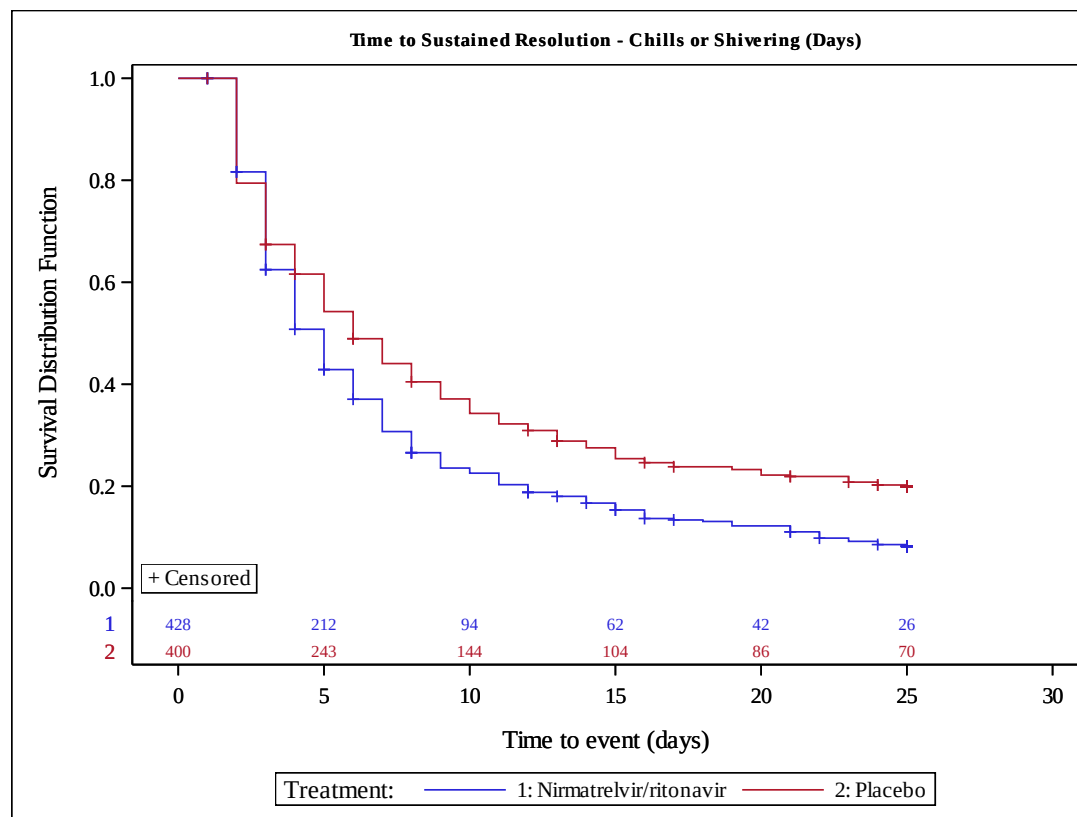
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Chills or Shivering

Final

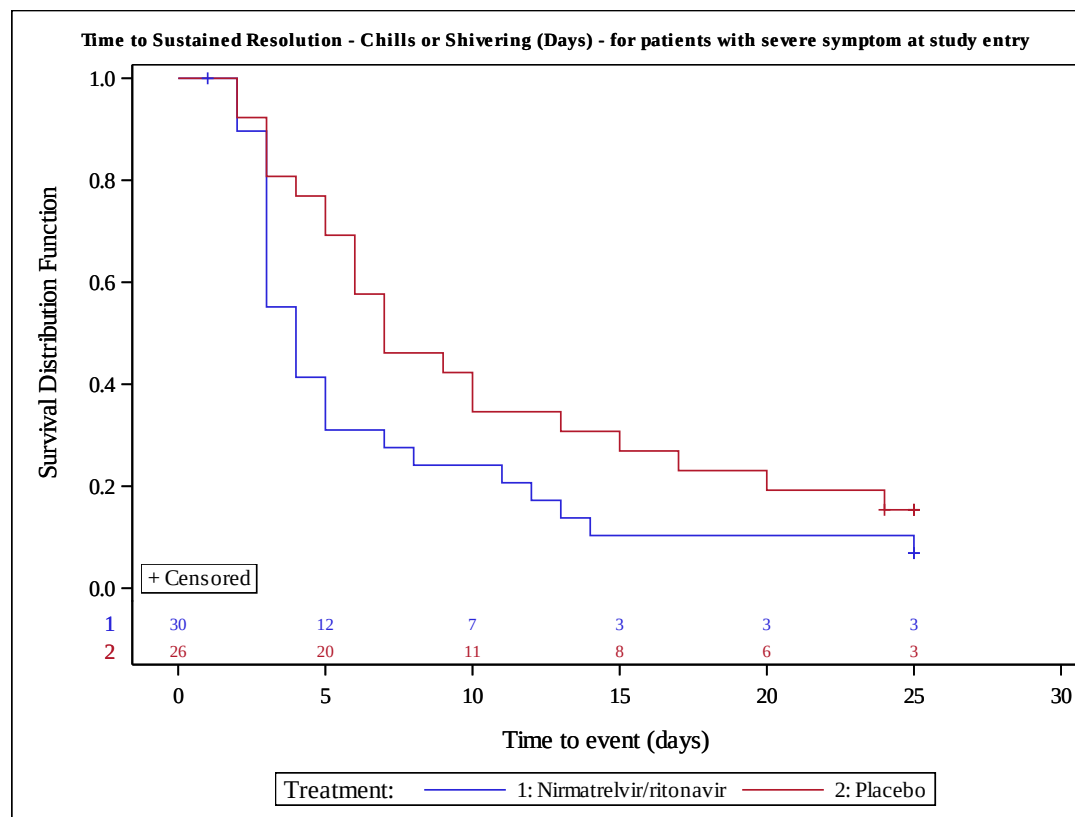
	Nirmatrelvir/ritonavir (N=30)	Placebo (N=26)
Number of subjects with events, n (%)	27 (90.0)	22 (84.6)
Number of censored subjects, n (%)	3 (10.0)	4 (15.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (3.0, 5.0)	7.0 (5.0, 13.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.737 (0.958, 3.151)	
p-value [3]	0.069	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.637 (0.925, 2.894)	
p-value [3]	0.090	

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 [1] Based on the Brookmeyer and Crowley Method.
 [2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Feeling Hot or Feverish

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	116 (16.9)	136 (20.2)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.795 (0.599, 1.054) 0.111	
Relative Risk (95% CI)	0.830 (0.662, 1.041) 0.107	
Risk Difference (95% CI)	-0.028 (-0.068, 0.013) 0.184	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.805 (0.612, 1.059) 0.121	
Relative Risk (95% CI)	0.838 (0.670, 1.048) 0.122	
Risk Difference (95% CI)	-0.033 (-0.074, 0.009) 0.121	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Feeling Hot or Feverish

Final

	Nirmatrelvir/ritonavir (N=432)	Placebo (N=416)
Number of subjects with events, n (%)	396 (91.7)	345 (82.9)
Number of censored subjects, n (%)	36 (8.3)	71 (17.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (NE, NE)	4.0 (4.0, 5.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.368 (1.178, 1.589)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.370 (1.184, 1.585)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

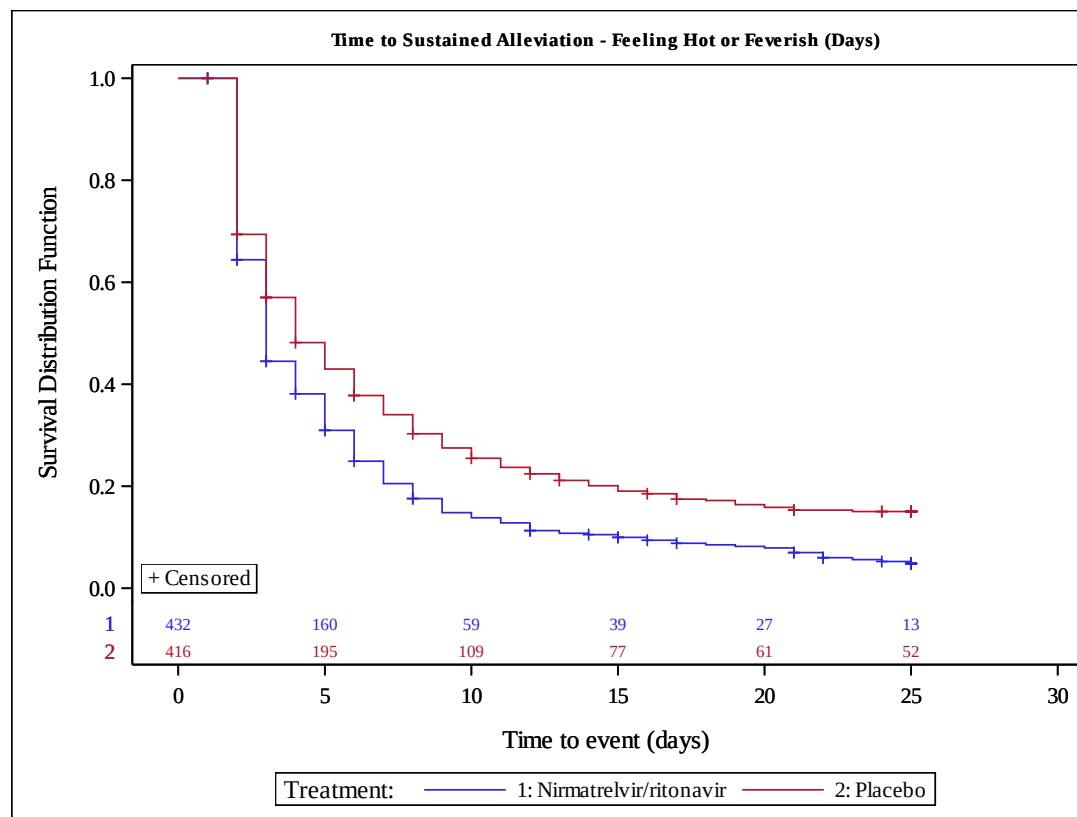
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Feeling Hot or Feverish

Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish

Final

	Nirmatrelvir/ritonavir (N=34)	Placebo (N=32)
Number of subjects with events, n (%)	34 (100.0)	24 (75.0)
Number of censored subjects, n (%)	0 (0.0)	8 (25.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (2.0, 3.0)	4.5 (3.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	2.372 (1.306, 4.307)	
p-value [3]	0.005	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	2.310 (1.328, 4.019)	
p-value [3]	0.003	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

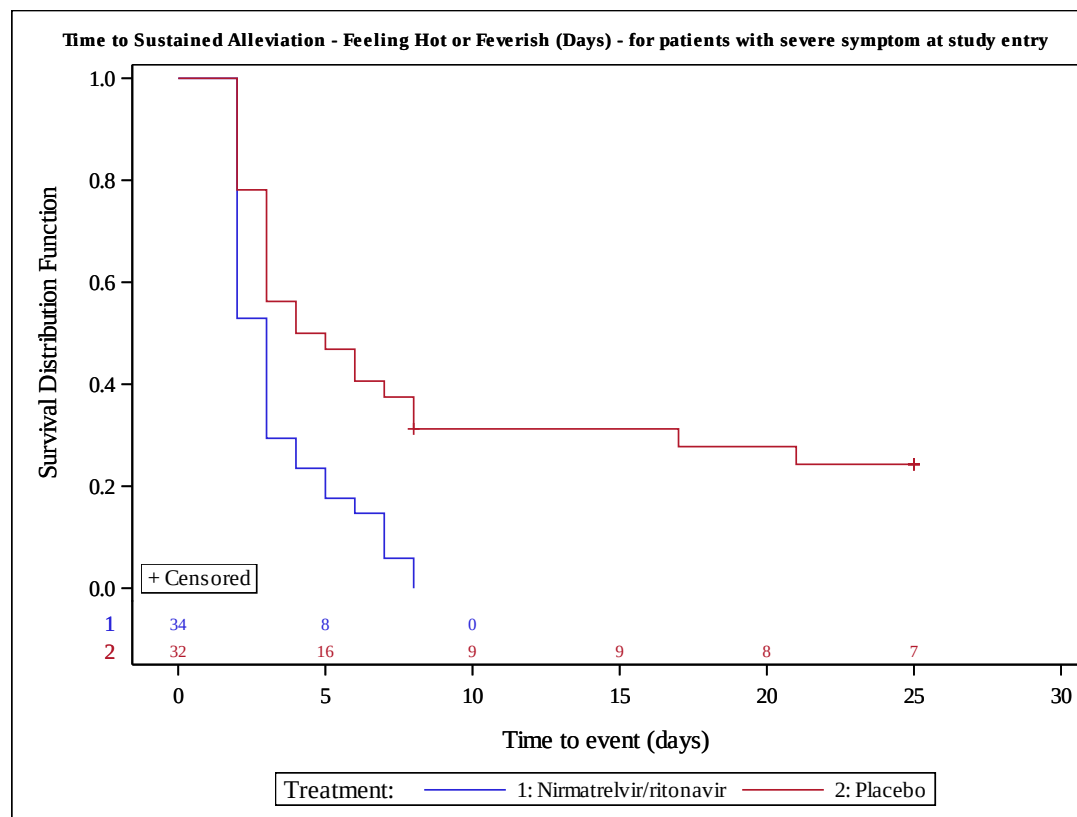
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Feeling Hot or Feverish

Final

	Nirmatrelvir/ritonavir (N=432)	Placebo (N=416)
Number of subjects with events, n (%)	386 (89.4)	326 (78.4)
Number of censored subjects, n (%)	46 (10.6)	90 (21.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 5.0)	7.0 (6.0, 7.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.425 (1.224, 1.660)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.423 (1.227, 1.651)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

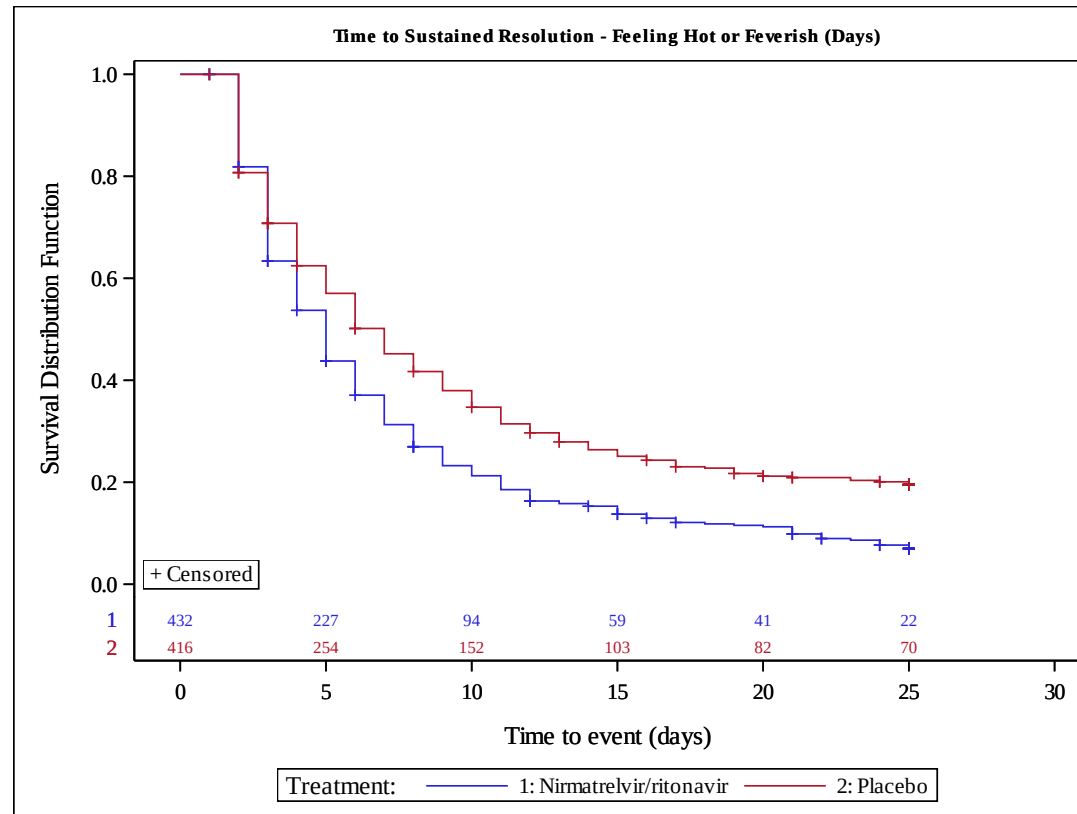
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Feeling Hot or Feverish

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish

Final

	Nirmatrelvir/ritonavir (N=34)	Placebo (N=32)
Number of subjects with events, n (%)	34 (100.0)	23 (71.9)
Number of censored subjects, n (%)	0 (0.0)	9 (28.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.5 (3.0, 8.0)	10.0 (7.0, 17.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	2.817 (1.543, 5.143)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	2.829 (1.580, 5.065)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

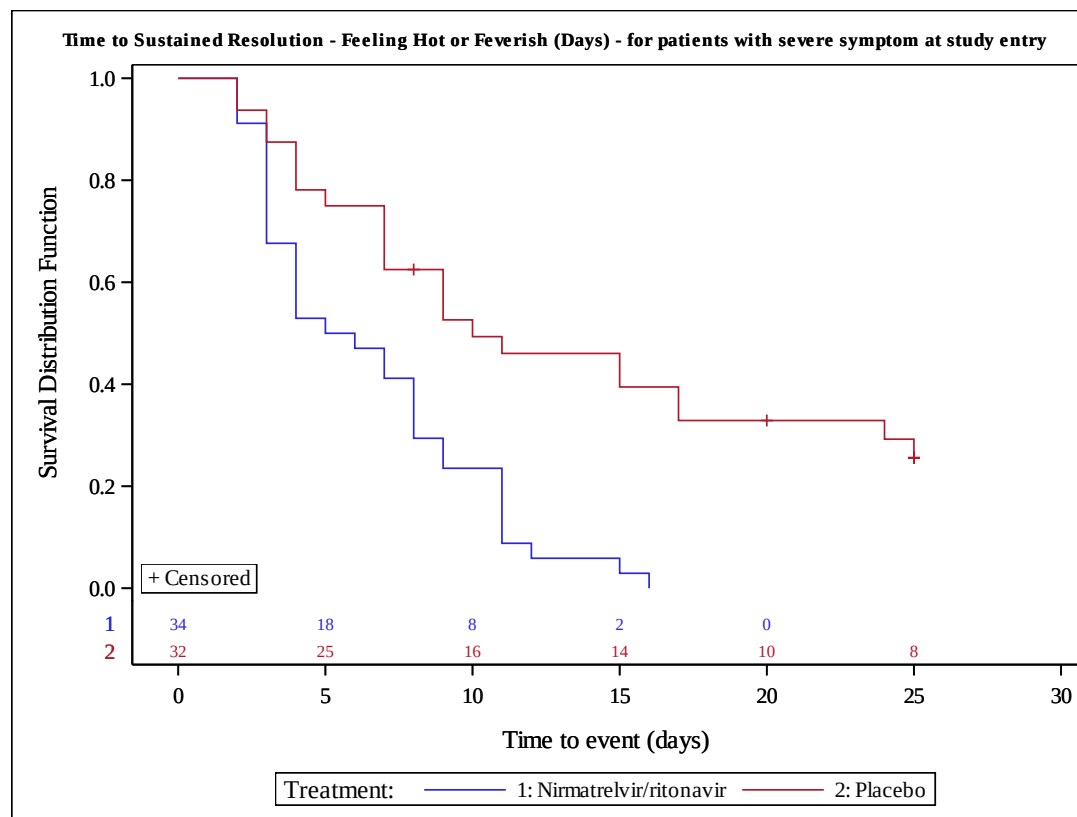
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Feeling Hot or Feverish

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Nausea

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	155 (22.6)	169 (25.1)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.893 (0.691, 1.154) 0.388	
Relative Risk (95% CI)	0.926 (0.765, 1.121) 0.431	
Risk Difference (95% CI)	-0.029 (-0.073, 0.015) 0.201	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.872 (0.680, 1.120) 0.283	
Relative Risk (95% CI)	0.901 (0.745, 1.090) 0.284	
Risk Difference (95% CI)	-0.025 (-0.070, 0.020) 0.283	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Nausea

Final

	Nirmatrelvir/ritonavir (N=230)	Placebo (N=226)
Number of subjects with events, n (%)	200 (87.0)	184 (81.4)
Number of censored subjects, n (%)	30 (13.0)	42 (18.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (3.0, 5.0)	5.0 (4.0, 6.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.253 (1.018, 1.541)	
p-value [3]	0.033	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.230 (1.006, 1.504)	
p-value [3]	0.044	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

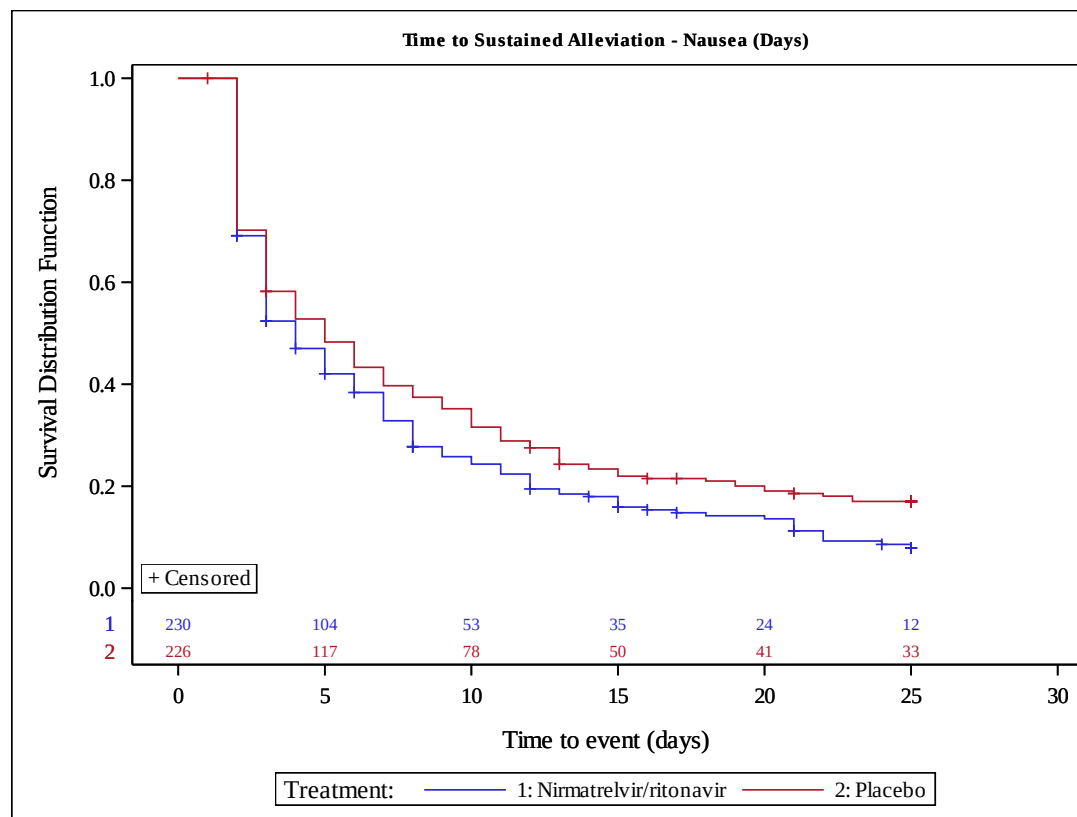
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Nausea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Nausea

Final

	Nirmatrelvir/ritonavir (N=9)	Placebo (N=10)
Number of subjects with events, n (%)	8 (88.9)	8 (80.0)
Number of censored subjects, n (%)	1 (11.1)	2 (20.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	11.0 (2.0, 25.0)	6.5 (2.0, 11.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.203 (0.359, 4.030)	
p-value [3]	0.764	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	0.818 (0.303, 2.208)	
p-value [3]	0.692	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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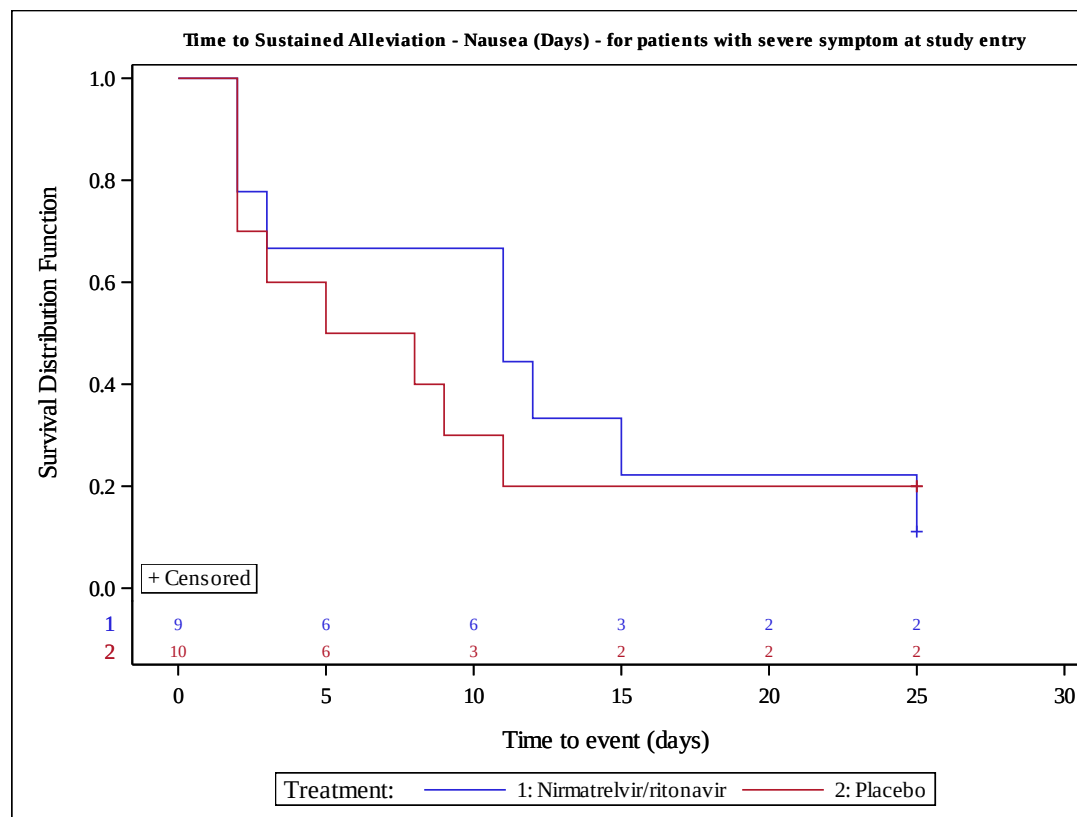
[1] Based on the Brookmeyer and Crowley Method.

[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Nausea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Nausea

Final

	Nirmatrelvir/ritonavir (N=230)	Placebo (N=226)
Number of subjects with events, n (%)	193 (83.9)	169 (74.8)
Number of censored subjects, n (%)	37 (16.1)	57 (25.2)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	5.0 (4.0, 7.0)	7.0 (6.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.370 (1.108, 1.695)	
p-value [3]	0.004	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.360 (1.105, 1.674)	
p-value [3]	0.004	

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[1] Based on the Brookmeyer and Crowley Method.

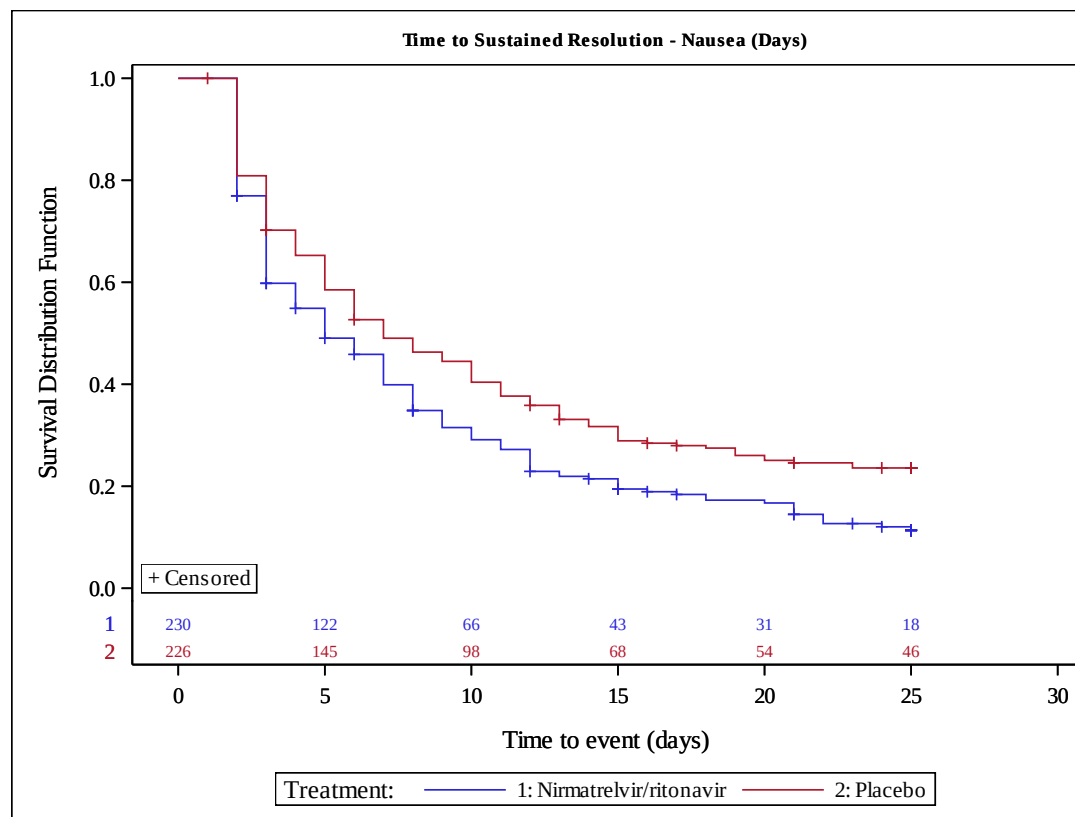
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Nausea

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final

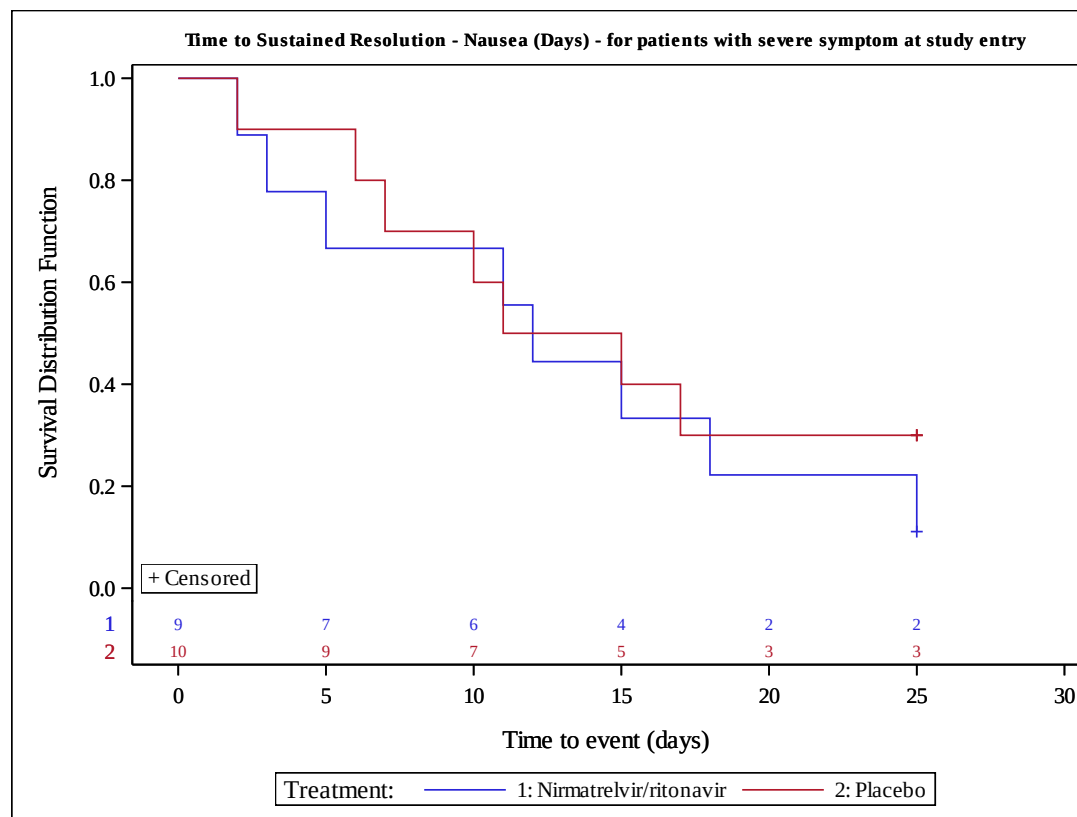
	Nirmatrelvir/ritonavir (N=9)	Placebo (N=10)
Number of subjects with events, n (%)	8 (88.9)	7 (70.0)
Number of censored subjects, n (%)	1 (11.1)	3 (30.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	12.0 (2.0, 25.0)	13.0 (2.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	2.159 (0.640, 7.279)	
p-value [3]	0.214	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.357 (0.491, 3.751)	
p-value [3]	0.556	

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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Overall Study population
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 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Vomit

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	54 (7.9)	65 (9.6)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.773 (0.526, 1.138) 0.192	
Relative Risk (95% CI)	0.793 (0.560, 1.121) 0.189	
Risk Difference (95% CI)	NE (NE, NE) NE	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.801 (0.549, 1.168) 0.248	
Relative Risk (95% CI)	0.816 (0.578, 1.152) 0.249	
Risk Difference (95% CI)	-0.018 (-0.048, 0.012) 0.248	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

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[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Vomit

Final

	Nirmatrelvir/ritonavir (N=73)	Placebo (N=71)
Number of subjects with events, n (%)	63 (86.3)	60 (84.5)
Number of censored subjects, n (%)	10 (13.7)	11 (15.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (2.0, 4.0)	3.0 (2.0, 5.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.155 (0.793, 1.682)	
p-value [3]	0.452	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.135 (0.796, 1.619)	
p-value [3]	0.484	

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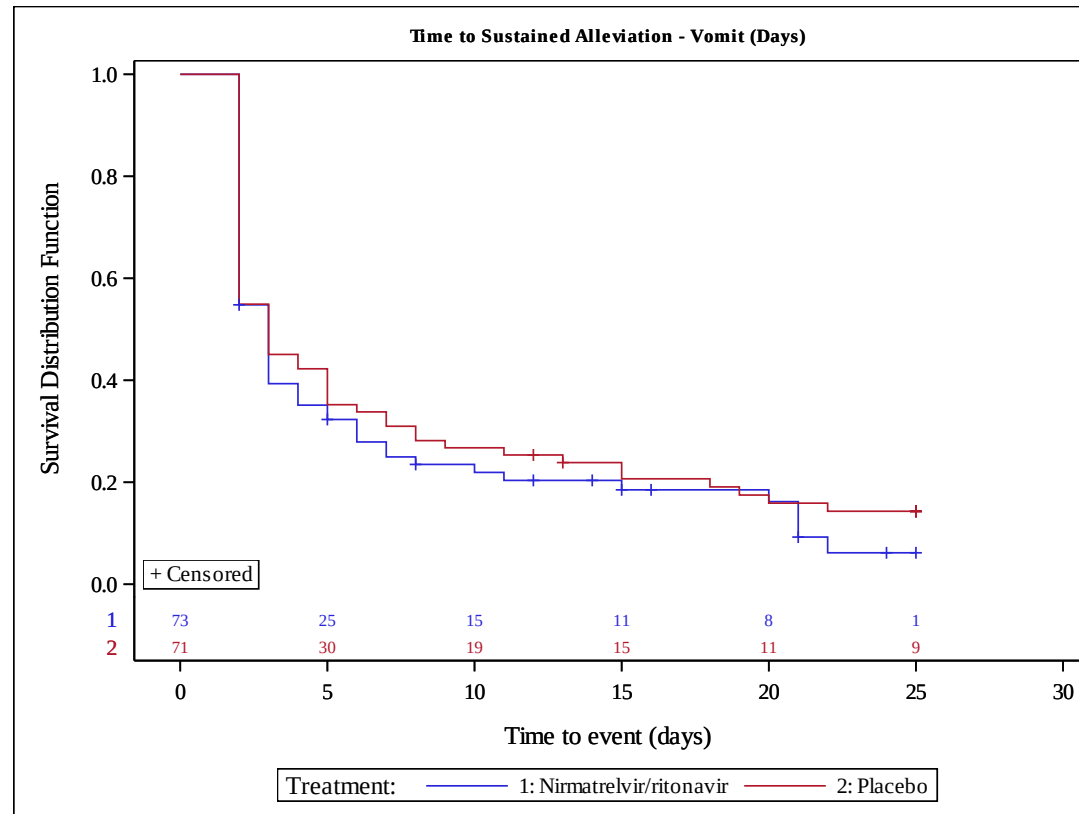
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[3] Estimated by cox regression model assuming proportional hazards.

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Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Vomit

Final

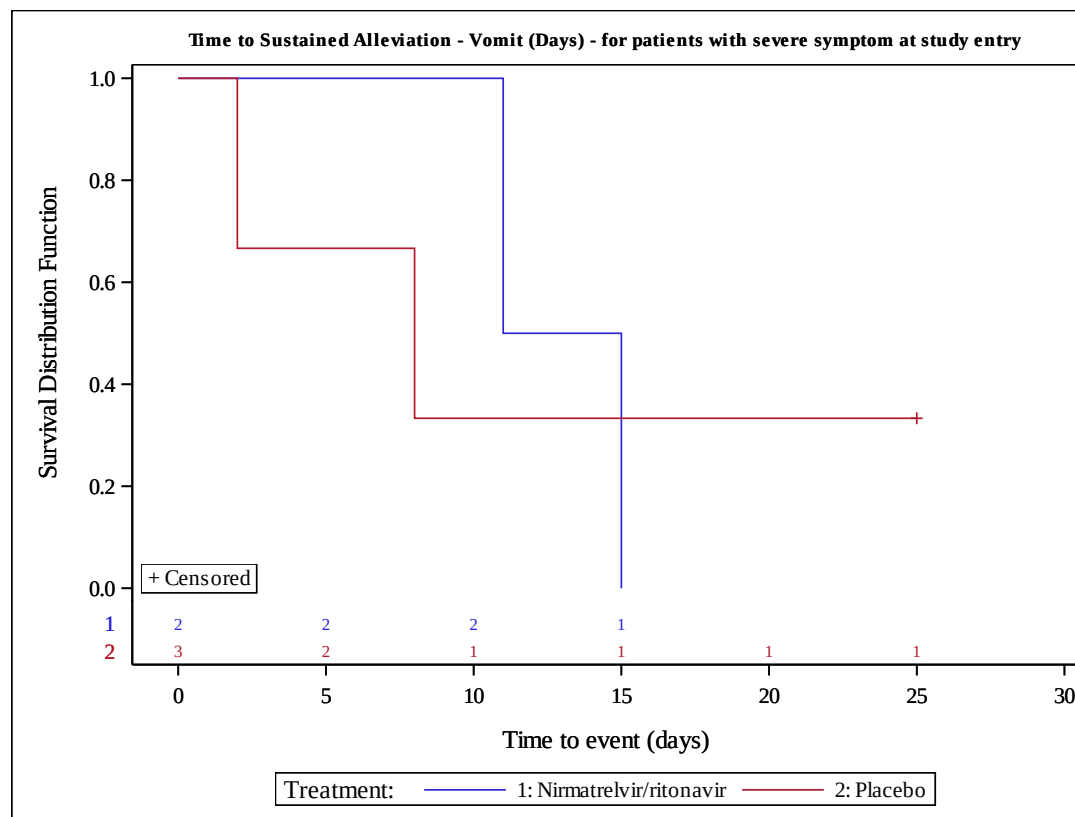
	Nirmatrelvir/ritonavir (N=2)	Placebo (N=3)
Number of subjects with events, n (%)	2 (100.0)	2 (66.7)
Number of censored subjects, n (%)	0 (0.0)	1 (33.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	13.0 (11.0, 15.0)	8.0 (2.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.206 (0.074, 19.709)	
p-value [3]	0.896	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	0.933 (0.127, 6.876)	
p-value [3]	0.946	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
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 [2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Vomit

Final



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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Vomit

Final

	Nirmatrelvir/ritonavir (N=73)	Placebo (N=71)
Number of subjects with events, n (%)	63 (86.3)	60 (84.5)
Number of censored subjects, n (%)	10 (13.7)	11 (15.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.0 (2.0, 5.0)	3.0 (2.0, 5.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.155 (0.793, 1.681)	
p-value [3]	0.453	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.124 (0.788, 1.603)	
p-value [3]	0.519	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

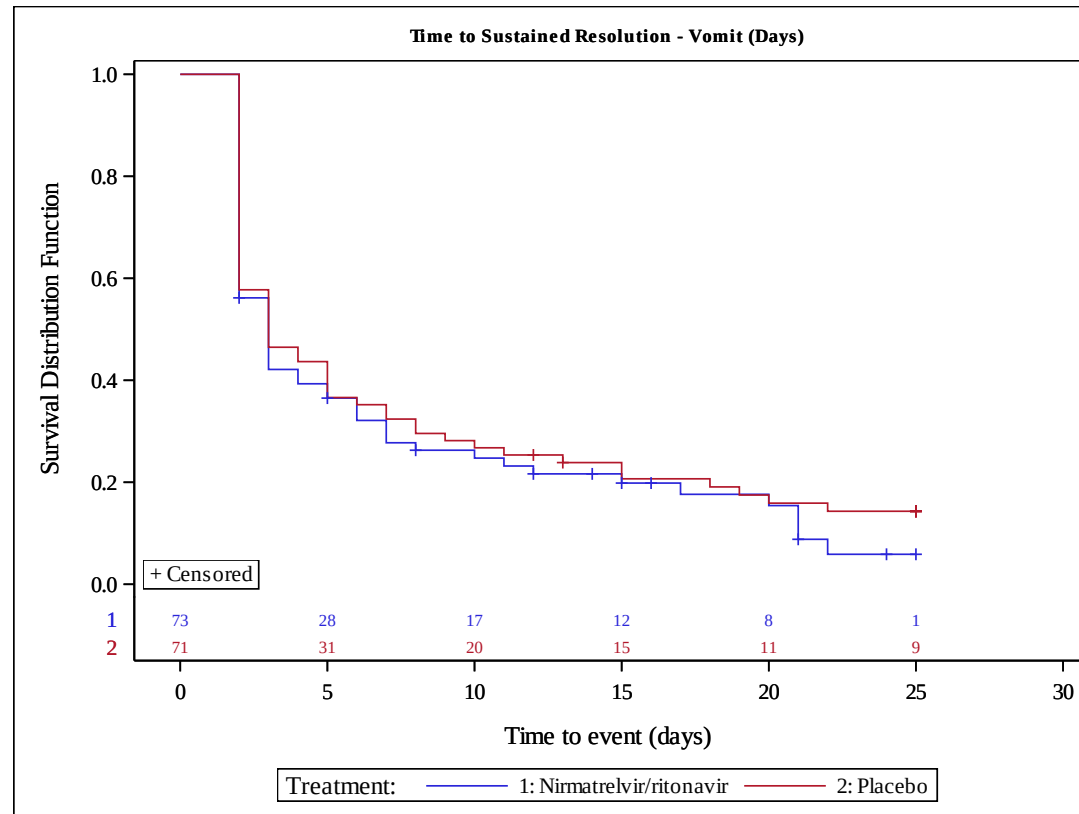
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Vomit

Final

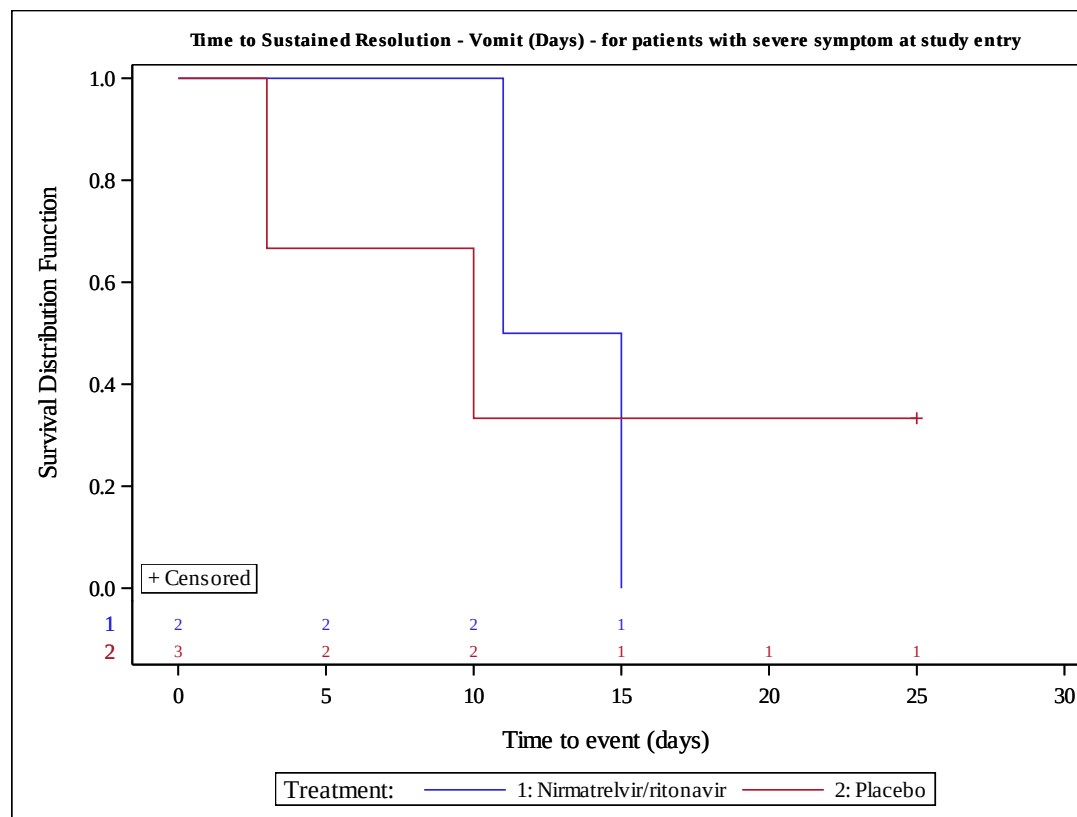
	Nirmatrelvir/ritonavir (N=2)	Placebo (N=3)
Number of subjects with events, n (%)	2 (100.0)	2 (66.7)
Number of censored subjects, n (%)	0 (0.0)	1 (33.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	13.0 (11.0, 15.0)	10.0 (3.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.206 (0.074, 19.709)	
p-value [3]	0.896	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	0.933 (0.127, 6.876)	
p-value [3]	0.946	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Vomit

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Worsening of Each Targeted Signs and Symptoms - Diarrhea

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	173 (25.2)	151 (22.4)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.182 (0.909, 1.535) 0.212	
Relative Risk (95% CI)	1.147 (0.950, 1.385) 0.153	
Risk Difference (95% CI)	0.013 (-0.025, 0.050) 0.510	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.168 (0.910, 1.500) 0.223	
Relative Risk (95% CI)	1.126 (0.930, 1.362) 0.224	
Risk Difference (95% CI)	0.028 (-0.017, 0.073) 0.223	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Diarrhea

Final

	Nirmatrelvir/ritonavir (N=170)	Placebo (N=148)
Number of subjects with events, n (%)	147 (86.5)	125 (84.5)
Number of censored subjects, n (%)	23 (13.5)	23 (15.5)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (3.0, 6.0)	4.0 (3.0, 6.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	0.997 (0.777, 1.279)	
p-value [3]	0.981	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.024 (0.807, 1.300)	
p-value [3]	0.844	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

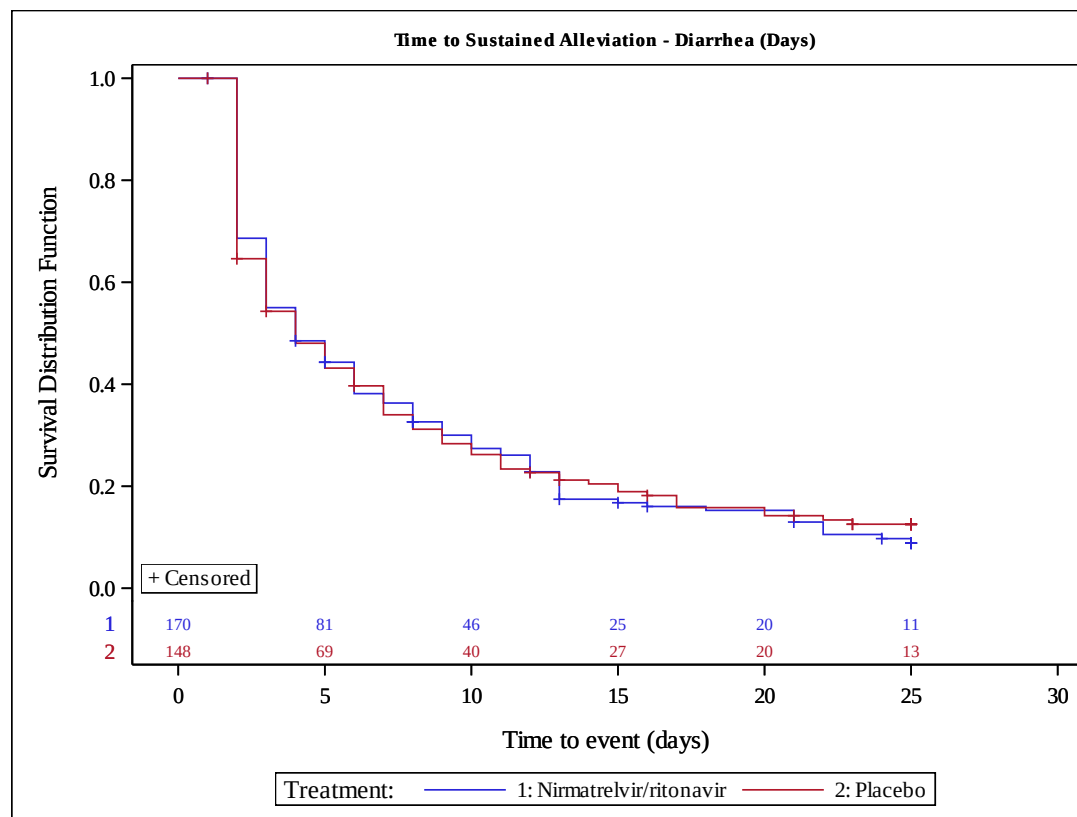
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 - Diarrhea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea

Final

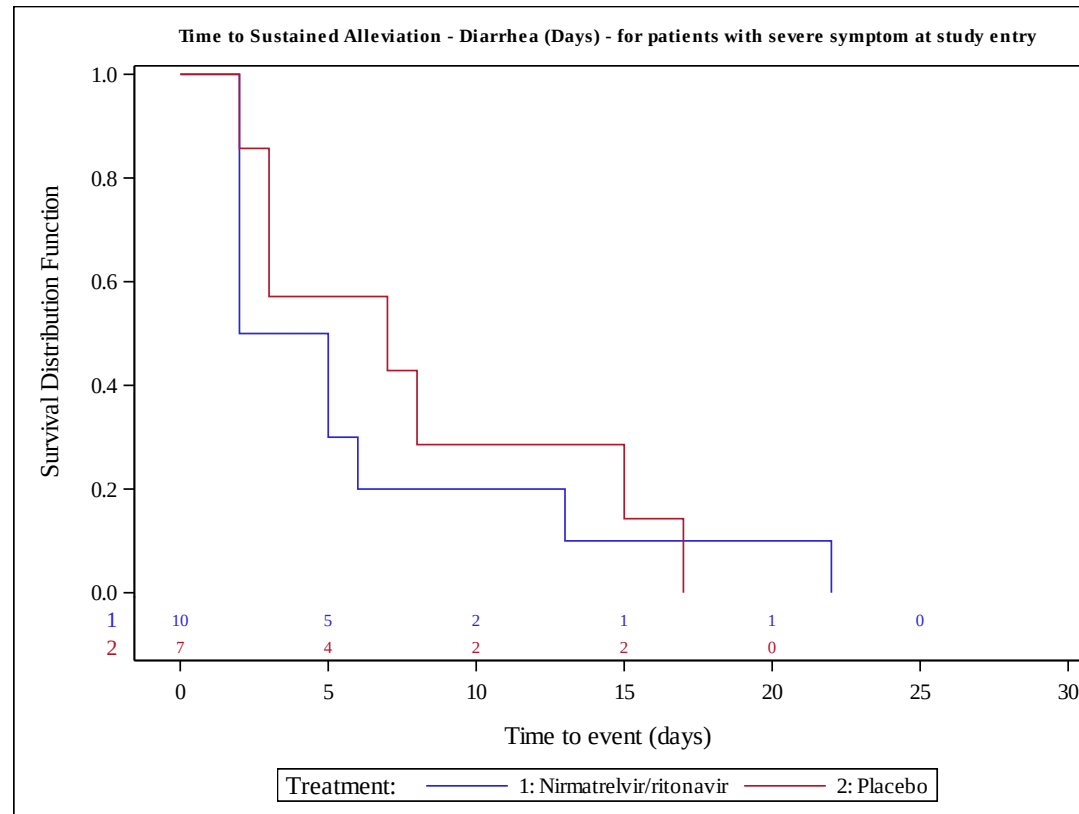
	Nirmatrelvir/ritonavir (N=10)	Placebo (N=7)
Number of subjects with events, n (%)	10 (100.0)	7 (100.0)
Number of censored subjects, n (%)	0 (0.0)	0 (0.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	3.5 (2.0, 6.0)	7.0 (2.0, 15.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.485 (0.443, 4.970)	
p-value [3]	0.522	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.282 (0.470, 3.498)	
p-value [3]	0.628	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 [1] Based on the Brookmeyer and Crowley Method.
 [2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Diarrhea

Final

	Nirmatrelvir/ritonavir (N=170)	Placebo (N=148)
Number of subjects with events, n (%)	143 (84.1)	116 (78.4)
Number of censored subjects, n (%)	27 (15.9)	32 (21.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	6.0 (5.0, 8.0)	6.0 (4.0, 9.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.118 (0.864, 1.447)	
p-value [3]	0.395	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.154 (0.902, 1.475)	
p-value [3]	0.255	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

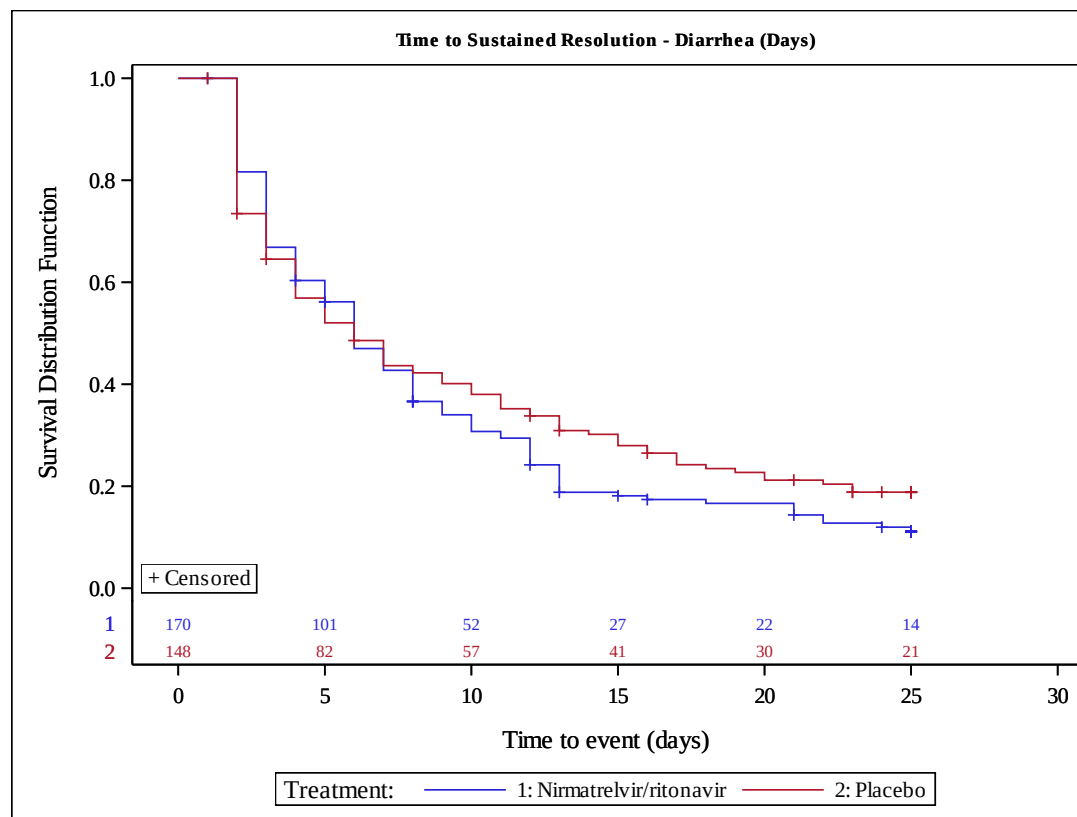
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 - Diarrhea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea

Final

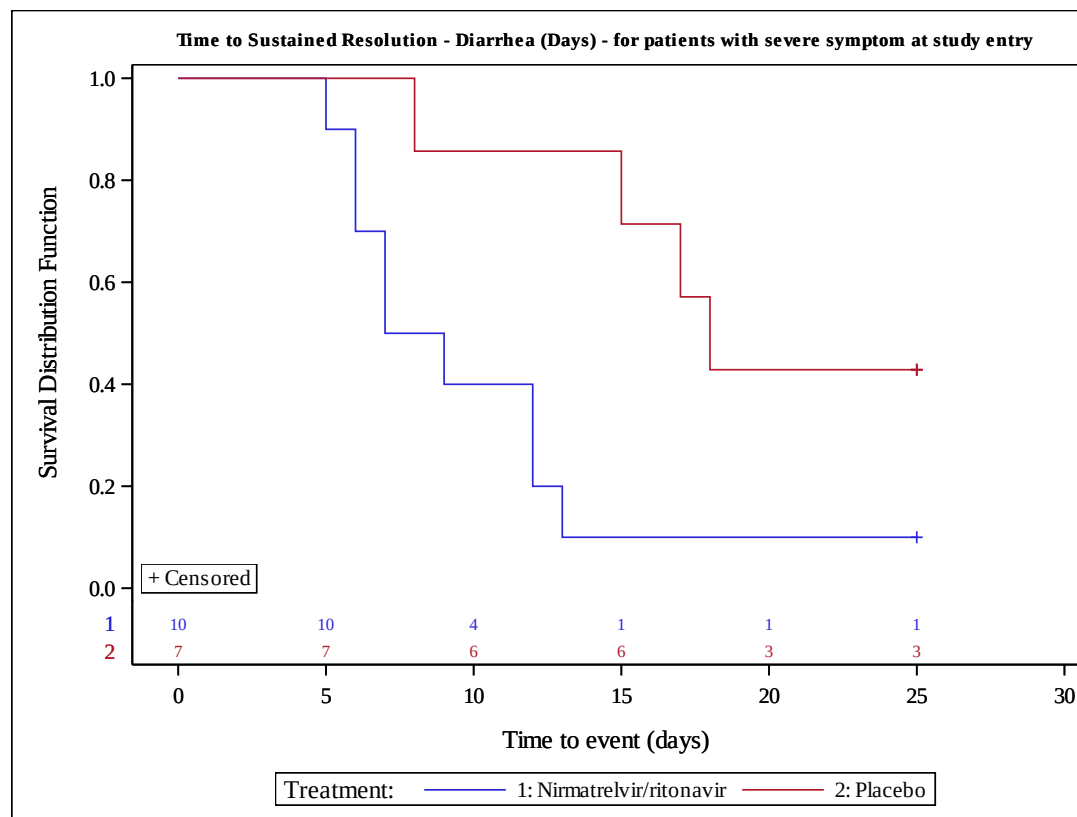
	Nirmatrelvir/ritonavir (N=10)	Placebo (N=7)
Number of subjects with events, n (%)	9 (90.0)	4 (57.1)
Number of censored subjects, n (%)	1 (10.0)	3 (42.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	8.0 (5.0, 12.0)	18.0 (8.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	4.892 (0.957, 24.998)	
p-value [3]	0.056	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	3.990 (1.146, 13.890)	
p-value [3]	0.030	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 [1] Based on the Brookmeyer and Crowley Method.
 [2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
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 Kaplan-Meier Plot of Time to Sustained Resolution of Each Targeted Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Diarrhea

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Worsening of Signs and Symptoms - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	179 (26.1)	198 (29.4)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.843 (0.657, 1.082) 0.180	
Relative Risk (95% CI)	0.894 (0.752, 1.063) 0.205	
Risk Difference (95% CI)	-0.038 (-0.083, 0.008) 0.104	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.849 (0.669, 1.077) 0.176	
Relative Risk (95% CI)	0.888 (0.748, 1.055) 0.177	
Risk Difference (95% CI)	-0.033 (-0.080, 0.015) 0.176	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=351)	Placebo (N=342)
Number of subjects with events, n (%)	254 (72.4)	218 (63.7)
Number of censored subjects, n (%)	97 (27.6)	124 (36.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	11.0 (10.0, 13.0)	14.0 (12.0, 16.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.292 (1.073, 1.555)	
p-value [3]	0.007	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.278 (1.066, 1.532)	
p-value [3]	0.008	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

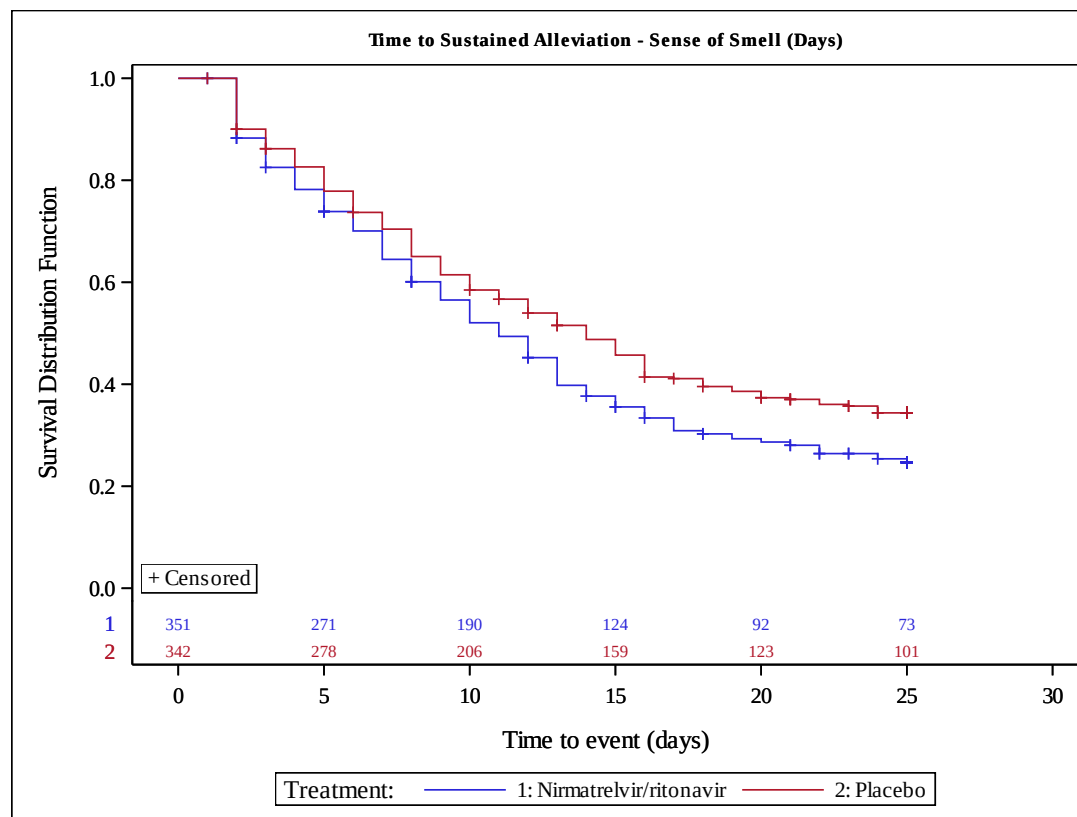
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Loss of smell

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=158)	Placebo (N=152)
Number of subjects with events, n (%)	125 (79.1)	108 (71.1)
Number of censored subjects, n (%)	33 (20.9)	44 (28.9)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	8.0 (7.0, 10.0)	9.0 (7.0, 11.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.240 (0.950, 1.619)	
p-value [3]	0.113	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.198 (0.926, 1.551)	
p-value [3]	0.170	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

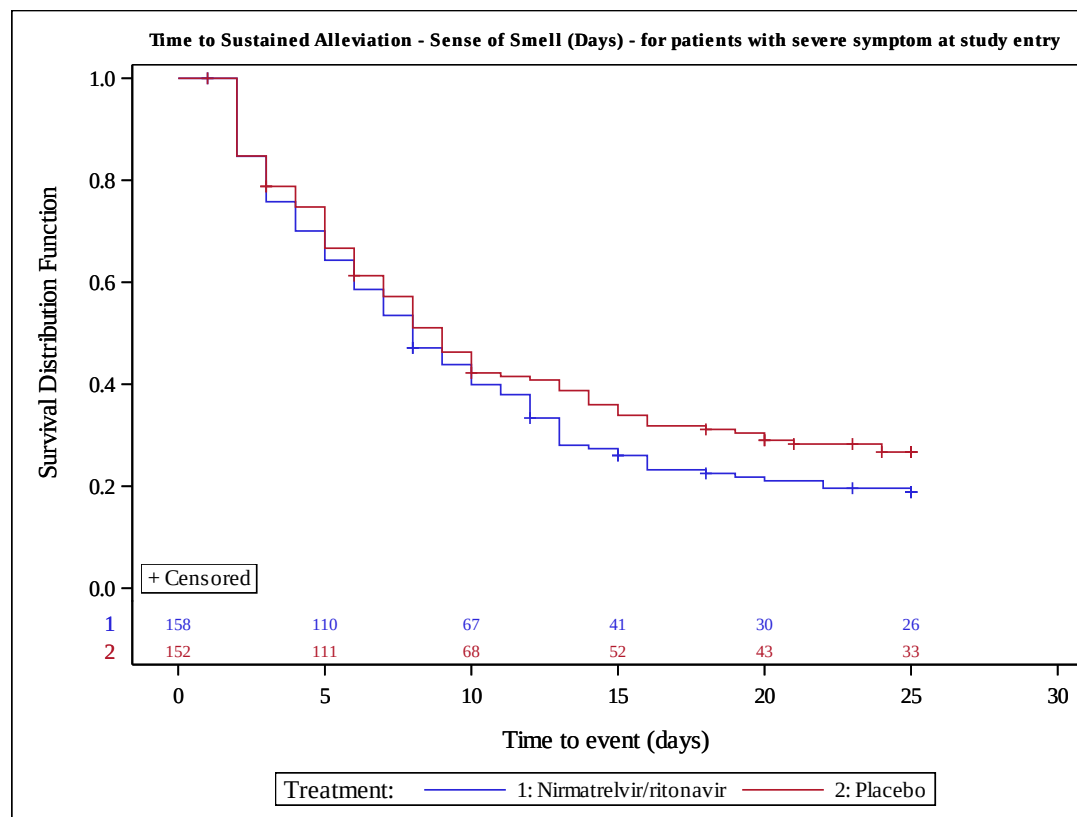
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of smell

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=351)	Placebo (N=342)
Number of subjects with events, n (%)	215 (61.3)	181 (52.9)
Number of censored subjects, n (%)	136 (38.7)	161 (47.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	17.0 (15.0, 19.0)	22.0 (16.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.274 (1.041, 1.558)	
p-value [3]	0.019	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.265 (1.038, 1.542)	
p-value [3]	0.020	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

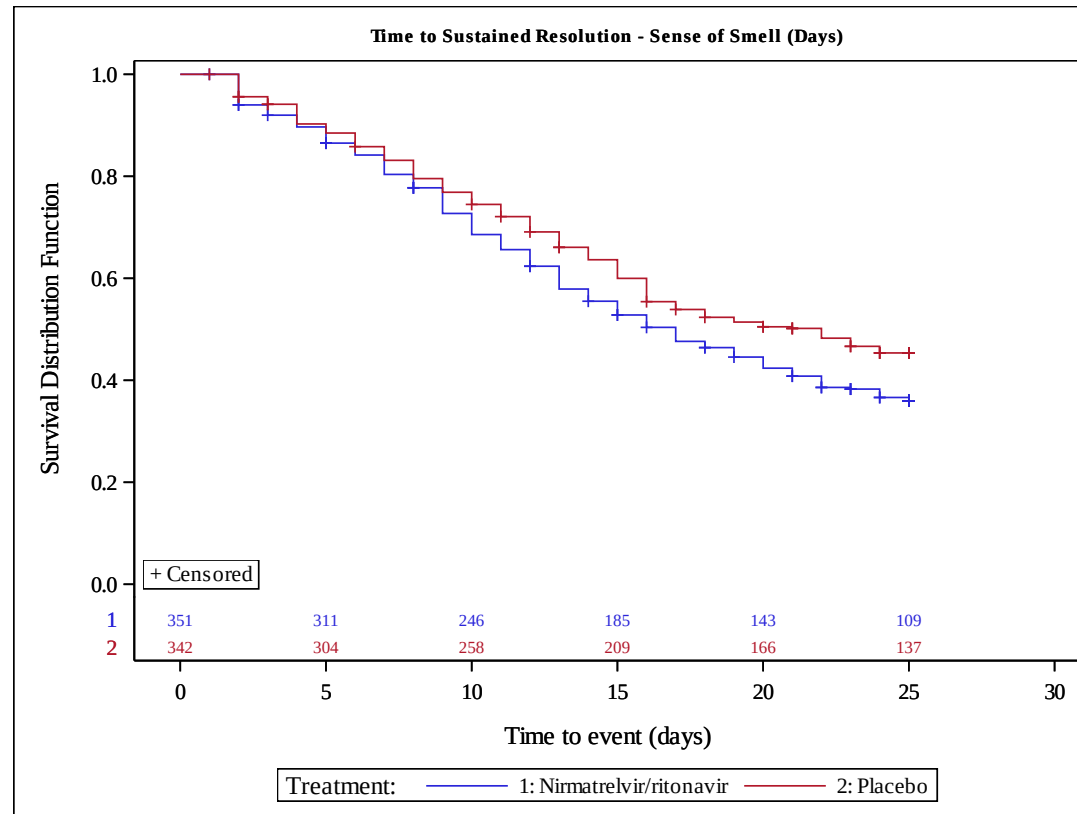
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Signs and Symptoms Through Day 28 - Loss of smell

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Resolution of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of smell

Final

	Nirmatrelvir/ritonavir (N=158)	Placebo (N=152)
Number of subjects with events, n (%)	86 (54.4)	71 (46.7)
Number of censored subjects, n (%)	72 (45.6)	81 (53.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	21.0 (18.0, NE)	NE (21.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.234 (0.894, 1.704)	
p-value [3]	0.201	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.201 (0.877, 1.645)	
p-value [3]	0.253	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

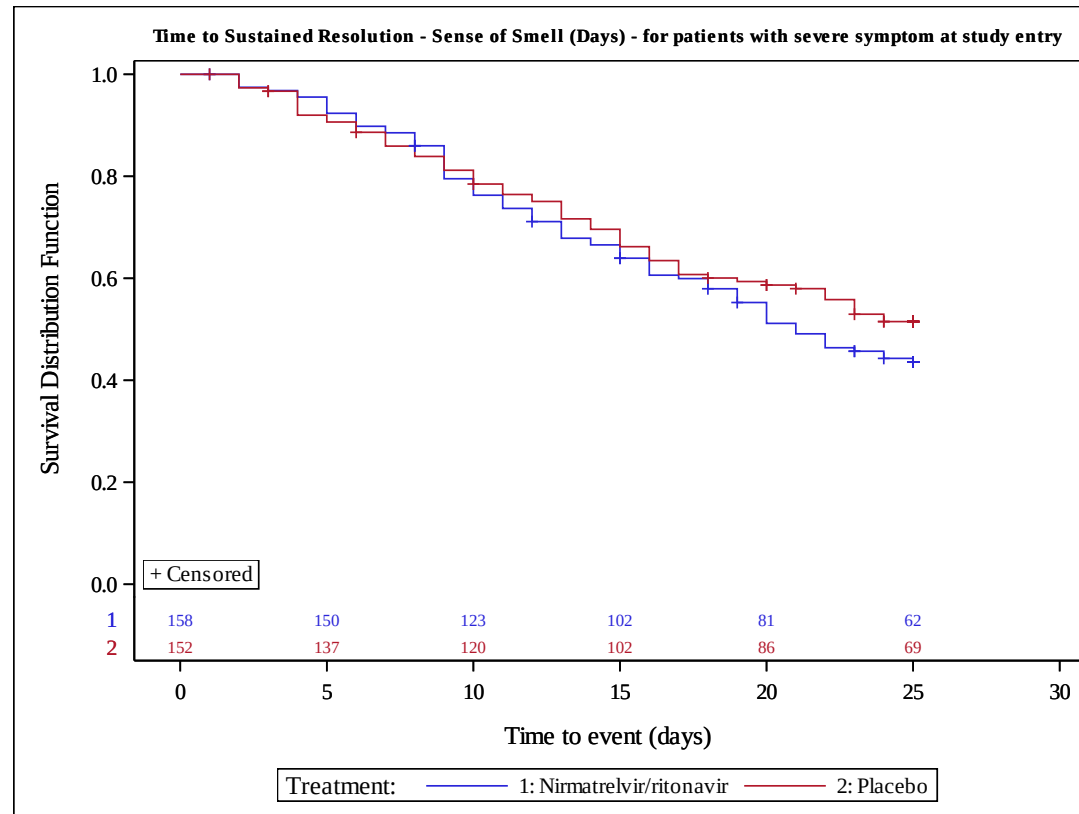
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Kaplan-Meier Plot of Time to Sustained Resolution of Signs and Symptoms Through Day 28 for patients with severe symptom at study entry - Loss of smell

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Worsening of Signs and Symptoms - Loss of taste

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	189 (27.6)	188 (27.9)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.990 (0.772, 1.270) 0.936	
Relative Risk (95% CI)	1.004 (0.845, 1.193) 0.962	
Risk Difference (95% CI)	-0.012 (-0.057, 0.033) 0.606	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.983 (0.775, 1.247) 0.888	
Relative Risk (95% CI)	0.988 (0.832, 1.173) 0.888	
Risk Difference (95% CI)	-0.003 (-0.051, 0.044) 0.888	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Alleviation of Signs and Symptoms Through Day 28 - Loss of taste

Final

	Nirmatrelvir/ritonavir (N=343)	Placebo (N=333)
Number of subjects with events, n (%)	252 (73.5)	216 (64.9)
Number of censored subjects, n (%)	91 (26.5)	117 (35.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	11.0 (9.0, 12.0)	13.0 (12.0, 14.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.292 (1.072, 1.556)	
p-value [3]	0.007	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.284 (1.071, 1.541)	
p-value [3]	0.007	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

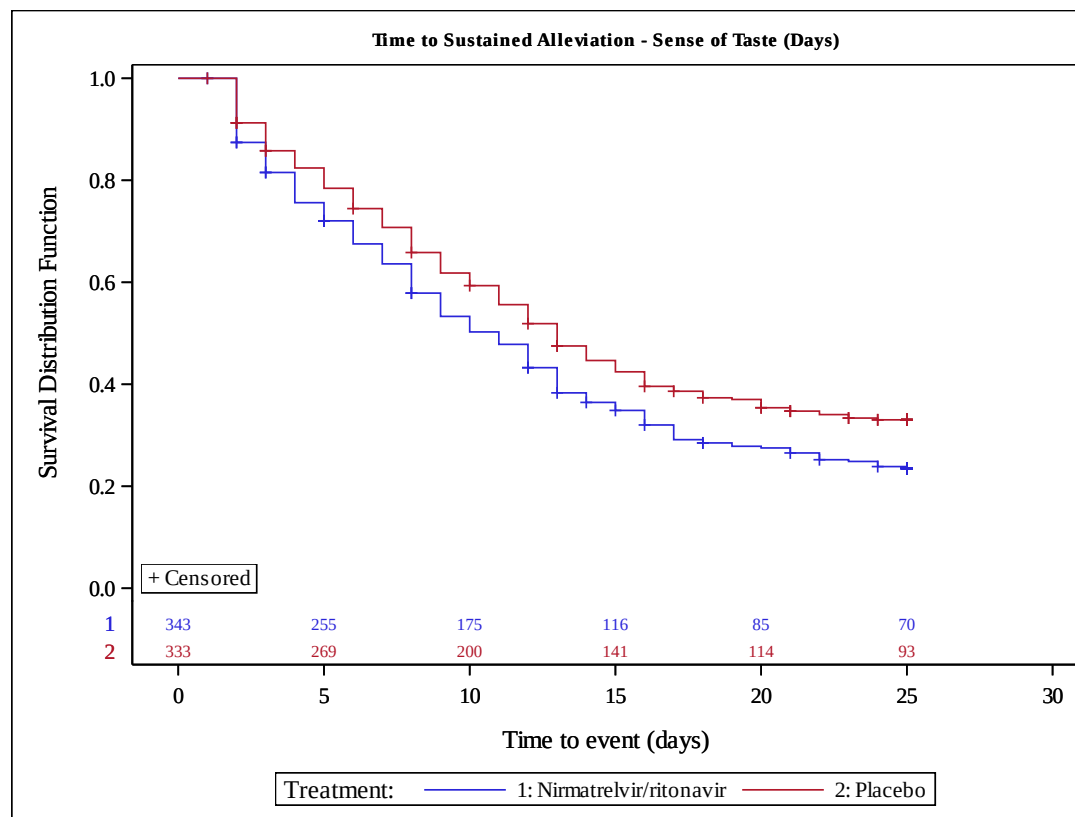
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

	Nirmatrelvir/ritonavir (N=138)	Placebo (N=137)
Number of subjects with events, n (%)	114 (82.6)	101 (73.7)
Number of censored subjects, n (%)	24 (17.4)	36 (26.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	7.0 (5.0, 8.0)	8.0 (7.0, 11.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.302 (0.983, 1.725)	
p-value [3]	0.066	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.279 (0.978, 1.673)	
p-value [3]	0.072	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

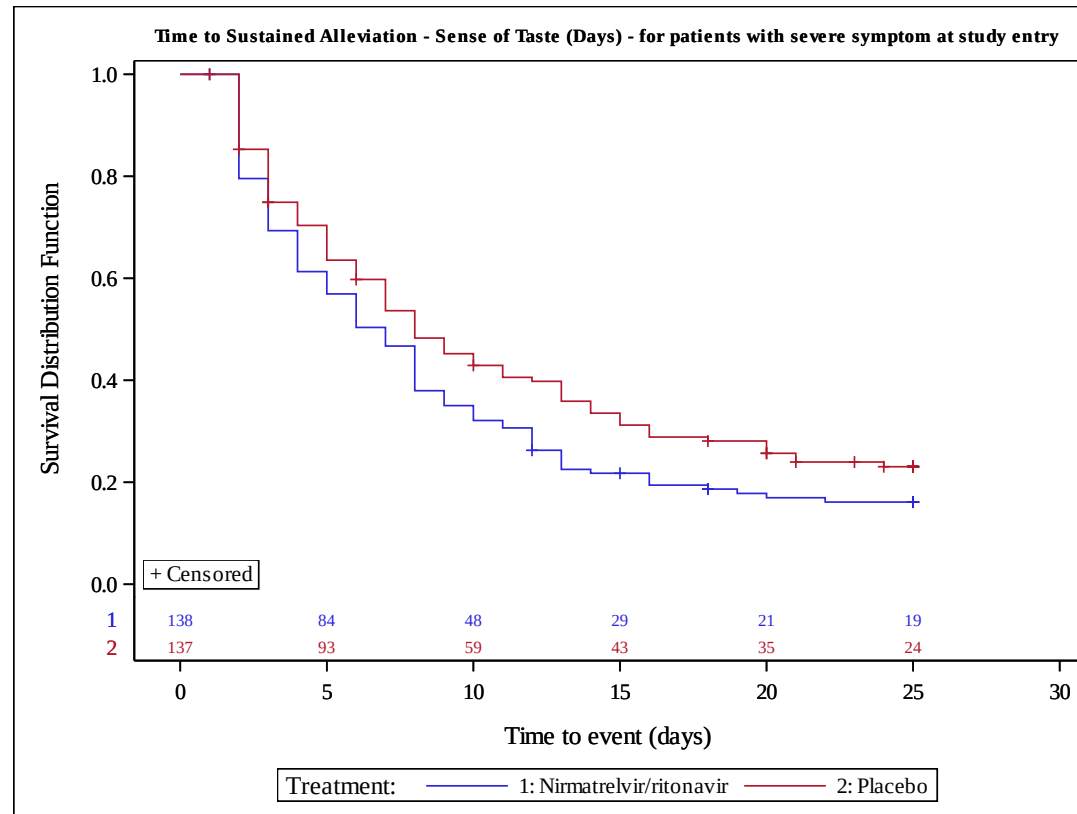
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Final

	Nirmatrelvir/ritonavir (N=343)	Placebo (N=333)
Number of subjects with events, n (%)	216 (63.0)	182 (54.7)
Number of censored subjects, n (%)	127 (37.0)	151 (45.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	16.0 (14.0, 18.0)	18.0 (15.0, 24.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.239 (1.013, 1.517)	
p-value [3]	0.037	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.234 (1.013, 1.504)	
p-value [3]	0.036	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

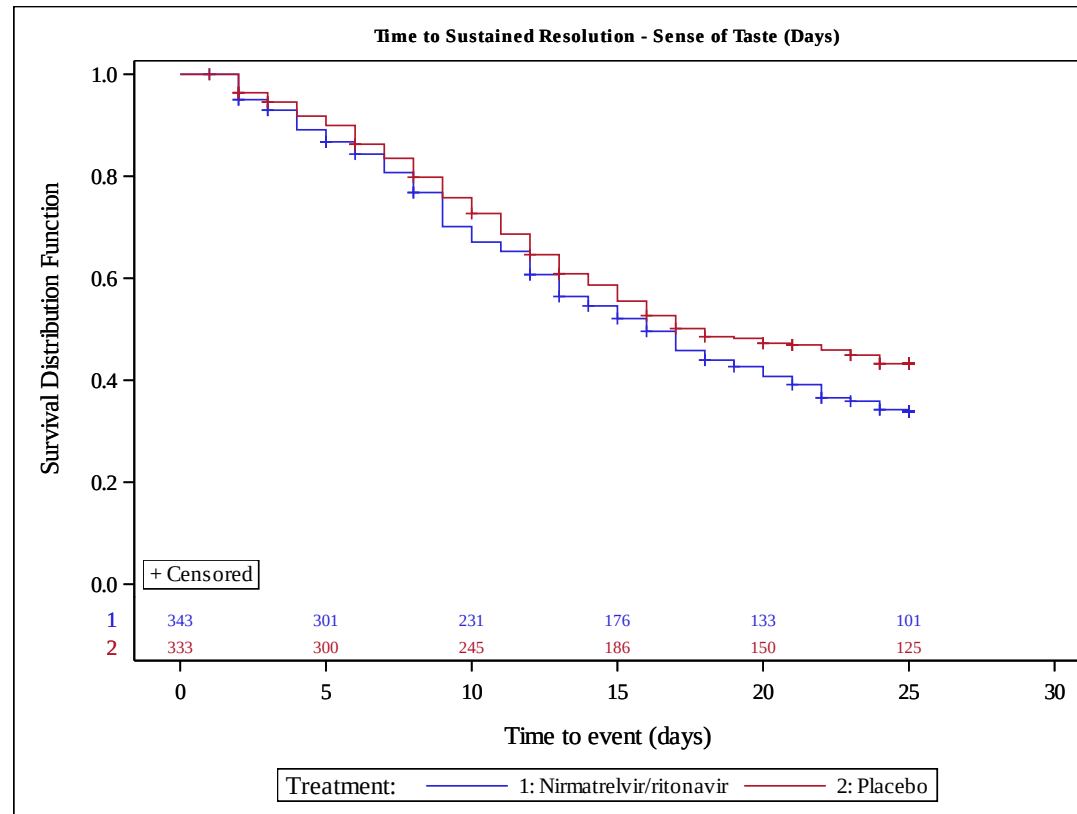
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Final

	Nirmatrelvir/ritonavir (N=138)	Placebo (N=137)
Number of subjects with events, n (%)	78 (56.5)	67 (48.9)
Number of censored subjects, n (%)	60 (43.5)	70 (51.1)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	20.0 (18.0, 24.0)	24.0 (17.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.135 (0.808, 1.595)	
p-value [3]	0.465	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.141 (0.823, 1.582)	
p-value [3]	0.428	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

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[1] Based on the Brookmeyer and Crowley Method.

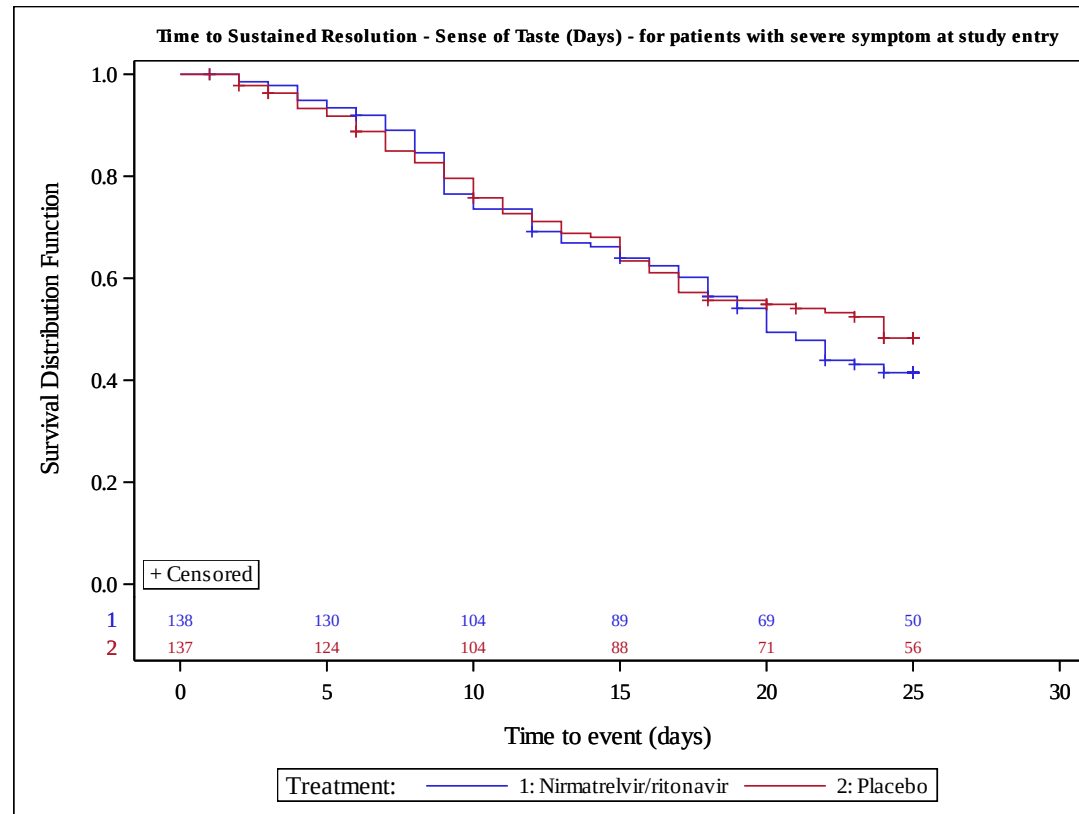
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Analysis of Participants with Any Severe Targeted Signs and Symptoms

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	123 (17.9)	137 (20.3)
Adjusted analysis [1]		
Odds Ratio (95% CI)	0.882 (0.662, 1.173) 0.387	
Relative Risk (95% CI)	0.897 (0.720, 1.117) 0.330	
Risk Difference (95% CI)	NE (NE, NE) NE	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	0.856 (0.653, 1.123) 0.261	
Relative Risk (95% CI)	0.882 (0.709, 1.098) 0.262	
Risk Difference (95% CI)	-0.024 (-0.066, 0.018) 0.261	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	324 (47.2)	318 (47.2)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.006 (0.804, 1.259) 0.958	
Relative Risk (95% CI)	1.009 (0.904, 1.125) 0.877	
Risk Difference (95% CI)	-0.001 (-0.053, 0.050) 0.959	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.002 (0.810, 1.240) 0.985	
Relative Risk (95% CI)	1.001 (0.895, 1.120) 0.985	
Risk Difference (95% CI)	0.000 (-0.053, 0.054) 0.985	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	523 (76.2)	504 (74.8)
Adjusted analysis [1] Odds Ratio (95% CI)	1.108 (0.855, 1.435) 0.437	
Relative Risk (95% CI)	1.021 (0.963, 1.082) 0.495	
Risk Difference (95% CI)	0.017 (-0.028, 0.062) 0.463	
Unadjusted analysis [2] Odds Ratio (95% CI)	1.082 (0.845, 1.386) 0.531	
Relative Risk (95% CI)	1.020 (0.960, 1.083) 0.531	
Risk Difference (95% CI)	0.015 (-0.031, 0.060) 0.531	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with Response, n (%)	570 (83.1)	536 (79.5)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.250 (0.944, 1.655) 0.119	
Relative Risk (95% CI)	1.036 (0.986, 1.090) 0.164	
Risk Difference (95% CI)	0.031 (-0.011, 0.072) 0.146	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.265 (0.962, 1.663) 0.092	
Relative Risk (95% CI)	1.045 (0.993, 1.100) 0.092	
Risk Difference (95% CI)	0.036 (-0.006, 0.077) 0.092	

N: Number of participants with non-missing data, CI: Confidence Interval, NE: Not estimable

For missing data a mixed baseline observation carried forward (BOCF)/ last observation carried forward (LOCF) approach will be used. Missing data at baseline will be treated as mild.

If participant discontinues study due to Adverse Event or discontinues study at same time of treatment discontinuation due to lack of efficacy, missing data will use BOCF. Otherwise, missing data will use LOCF.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with events, n (%)	526 (76.7)	464 (68.8)
Number of censored subjects, n (%)	160 (23.3)	210 (31.2)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	12.0 (12.0, 13.0)	15.0 (13.0, 16.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.267 (1.115, 1.439)	
p-value [3]	<.001	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.272 (1.123, 1.441)	
p-value [3]	<.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

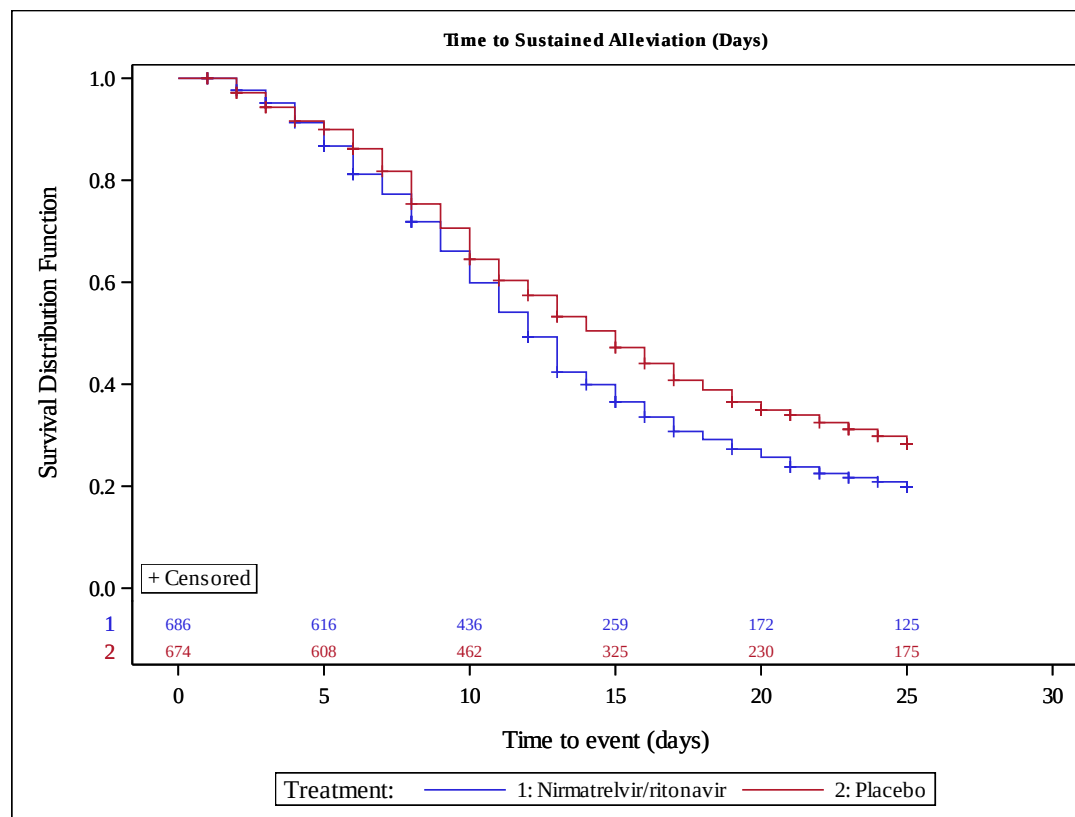
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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Final

	Nirmatrelvir/ritonavir (N=144)	Placebo (N=112)
Number of subjects with events, n (%)	129 (89.6)	97 (86.6)
Number of censored subjects, n (%)	15 (10.4)	15 (13.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	4.0 (3.0, 5.0)	7.0 (5.0, 8.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.383 (1.051, 1.820)	
p-value [3]	0.020	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.360 (1.044, 1.773)	
p-value [3]	0.023	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

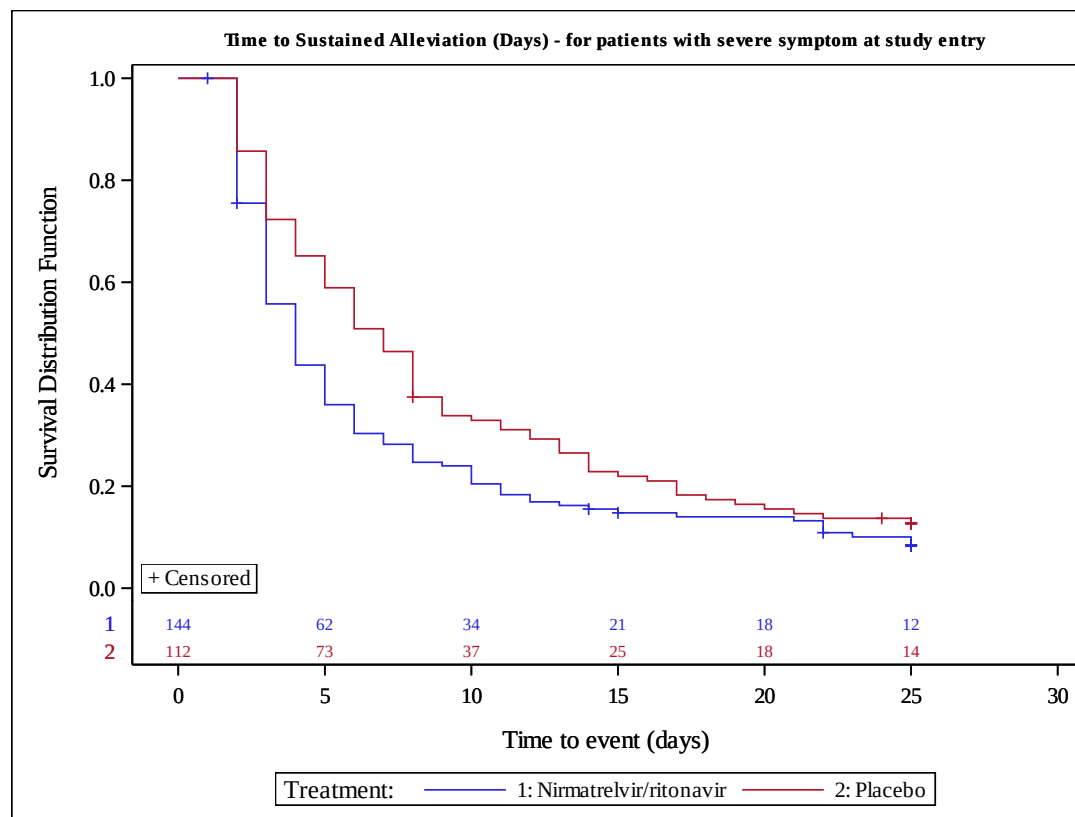
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with events, n (%)	446 (65.0)	395 (58.6)
Number of censored subjects, n (%)	240 (35.0)	279 (41.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	16.0 (15.0, 17.0)	19.0 (18.0, 21.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.239 (1.079, 1.423)	
p-value [3]	0.002	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.232 (1.076, 1.411)	
p-value [3]	0.003	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

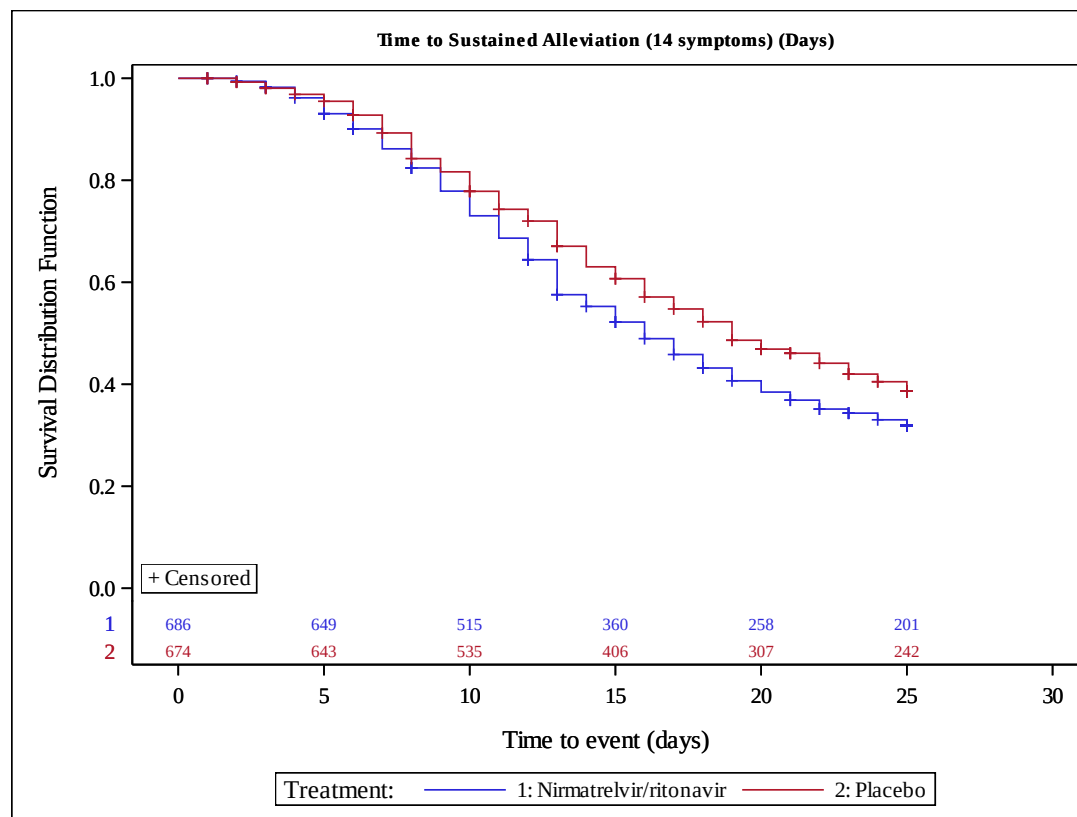
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Final

	Nirmatrelvir/ritonavir (N=283)	Placebo (N=254)
Number of subjects with events, n (%)	226 (79.9)	195 (76.8)
Number of censored subjects, n (%)	57 (20.1)	59 (23.2)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	7.0 (5.0, 8.0)	8.0 (7.0, 10.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.211 (0.994, 1.474)	
p-value [3]	0.057	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.170 (0.966, 1.417)	
p-value [3]	0.109	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

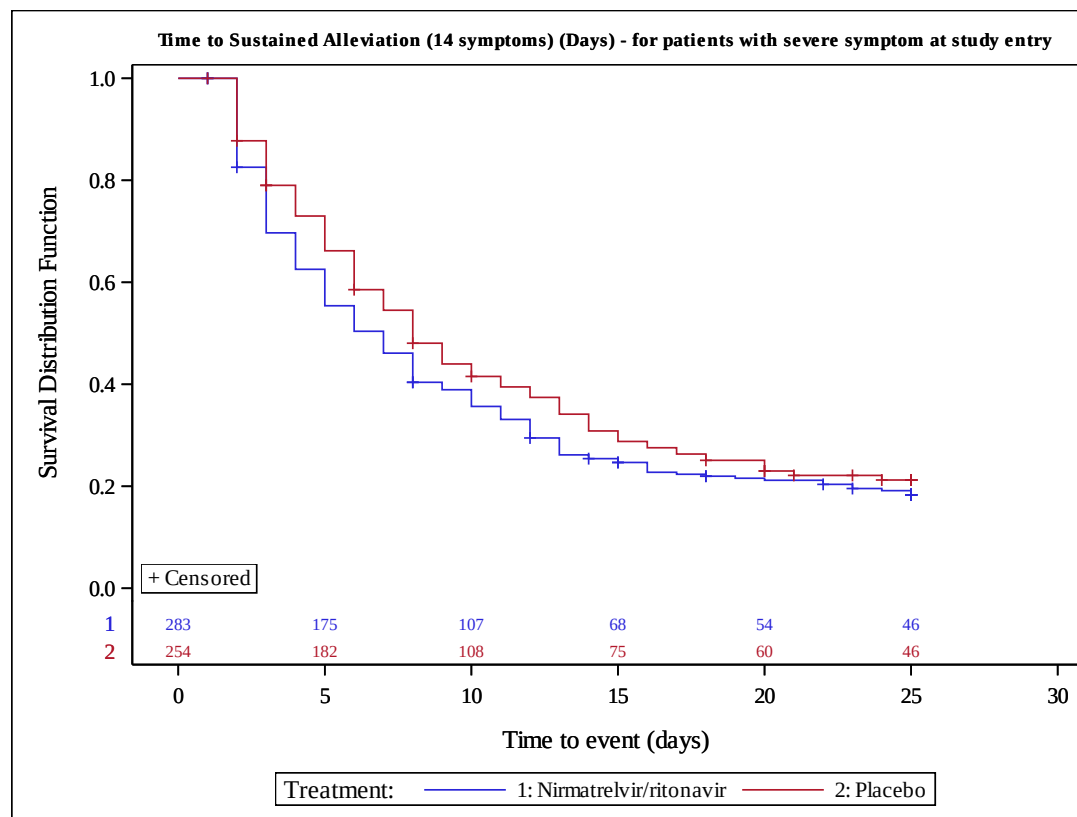
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with events, n (%)	464 (67.6)	415 (61.6)
Number of censored subjects, n (%)	222 (32.4)	259 (38.4)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	16.0 (15.0, 17.0)	18.0 (17.0, 20.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.198 (1.047, 1.371)	
p-value [3]	0.009	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.212 (1.062, 1.384)	
p-value [3]	0.004	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

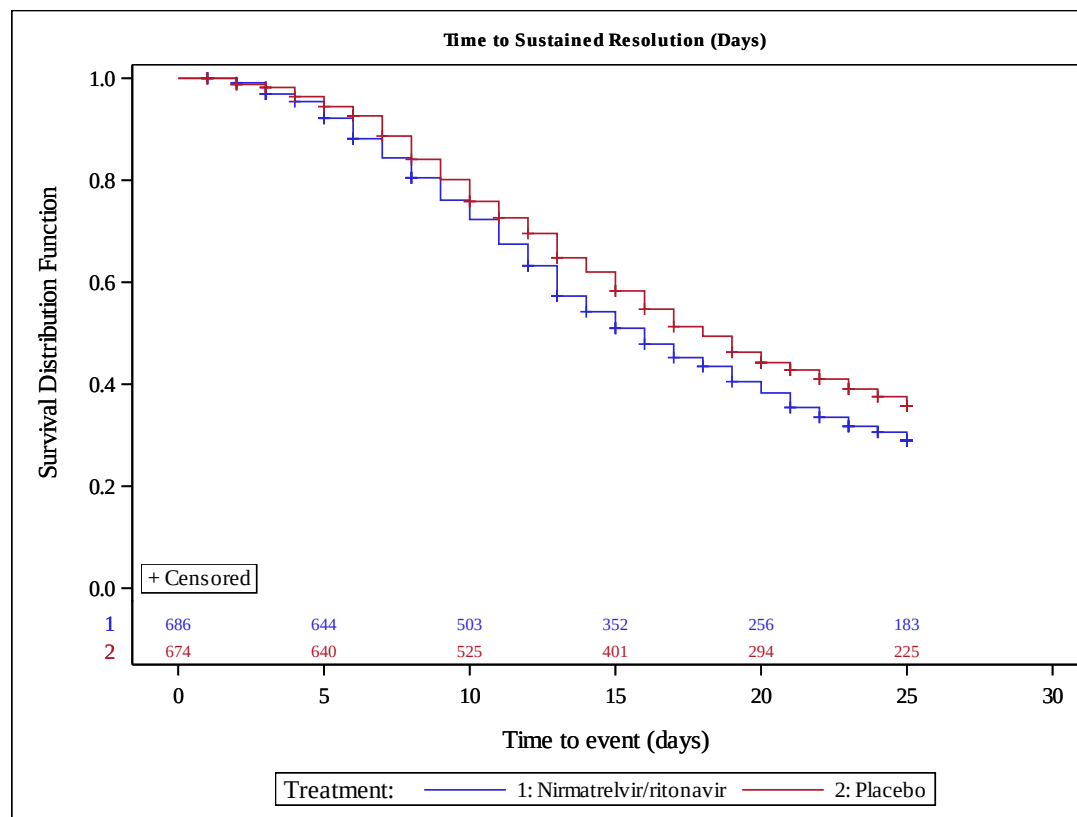
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Pfizer Inc
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 Kaplan-Meier Plot of Time to Sustained Resolution of All Targeted Signs and Symptoms Through Day 28

Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Pfizer Inc
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 Overall Study population
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Final

	Nirmatrelvir/ritonavir (N=144)	Placebo (N=112)
Number of subjects with events, n (%)	108 (75.0)	75 (67.0)
Number of censored subjects, n (%)	36 (25.0)	37 (33.0)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	11.0 (9.0, 12.0)	17.0 (13.0, 18.0)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.490 (1.099, 2.020)	
p-value [3]	0.010	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.437 (1.070, 1.931)	
p-value [3]	0.016	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

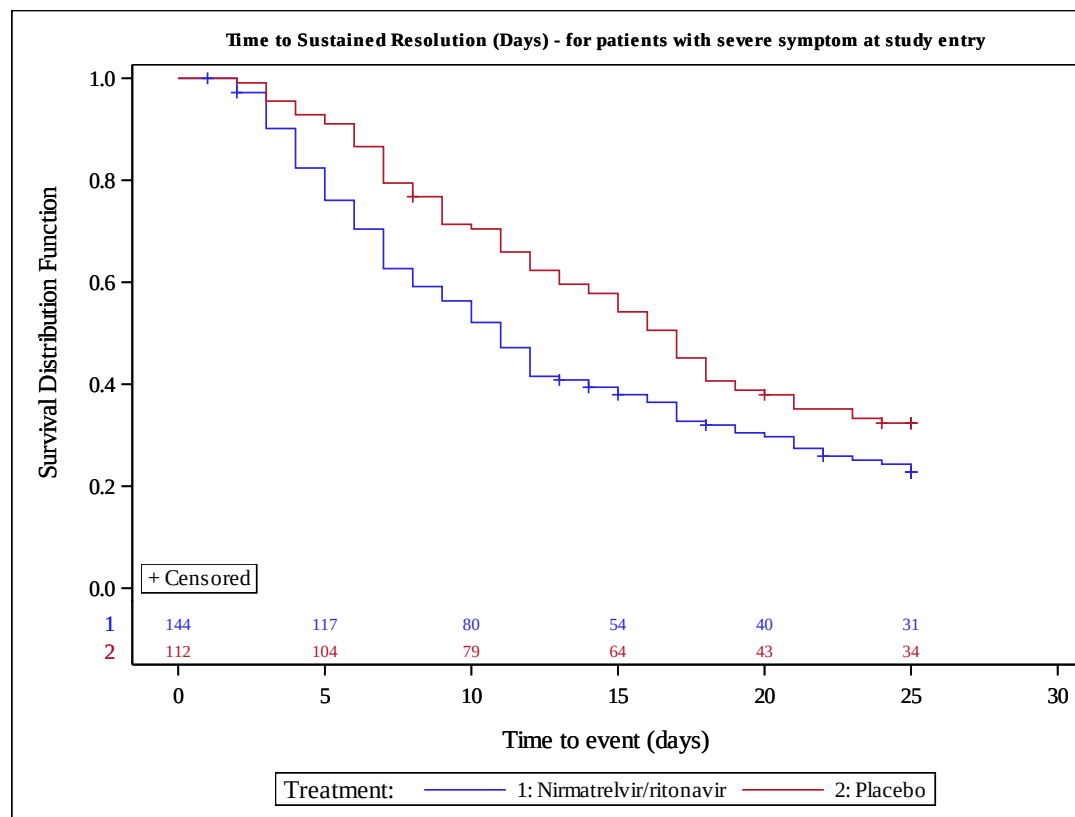
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Time to Sustained Resolution of All Signs and Symptoms Through Day 28

Final

	Nirmatrelvir/ritonavir (N=686)	Placebo (N=674)
Number of subjects with events, n (%)	401 (58.5)	342 (50.7)
Number of censored subjects, n (%)	285 (41.5)	332 (49.3)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	20.0 (18.0, 22.0)	24.0 (22.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.257 (1.085, 1.455)	
p-value [3]	0.002	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.266 (1.096, 1.463)	
p-value [3]	0.001	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.

[1] Based on the Brookmeyer and Crowley Method.

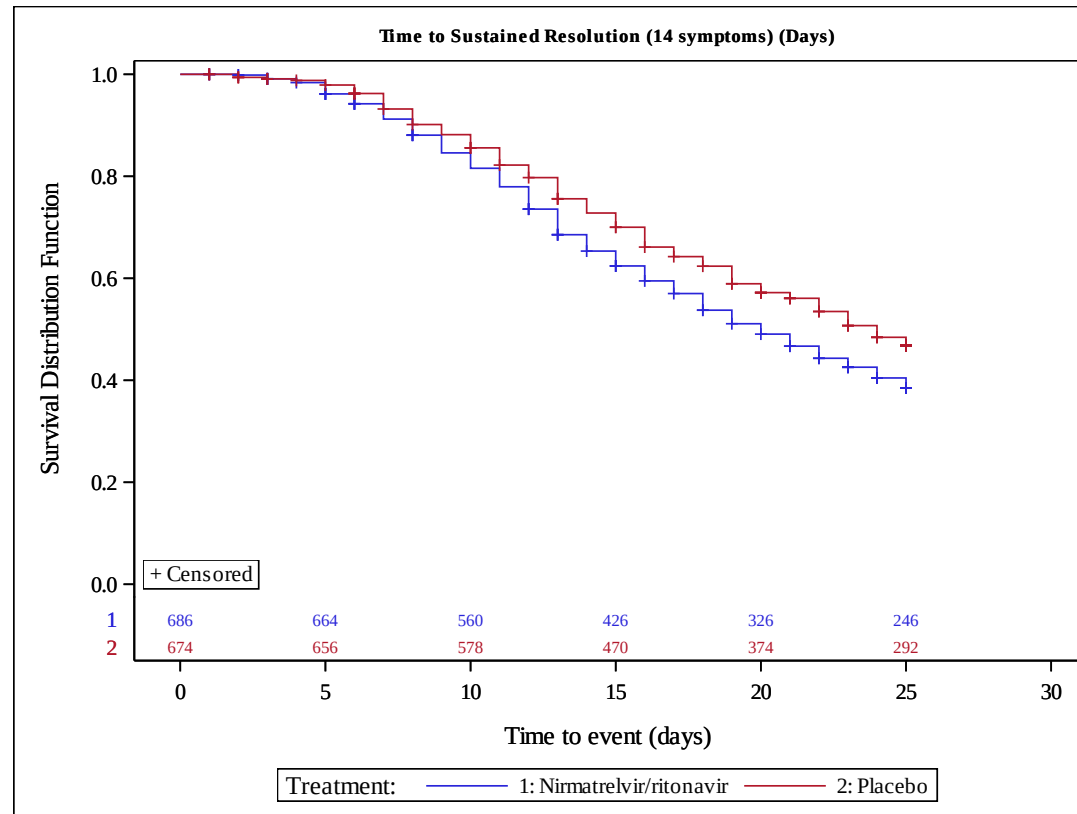
[2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant (alpha<=0.05)

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 Overall Study population
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Final

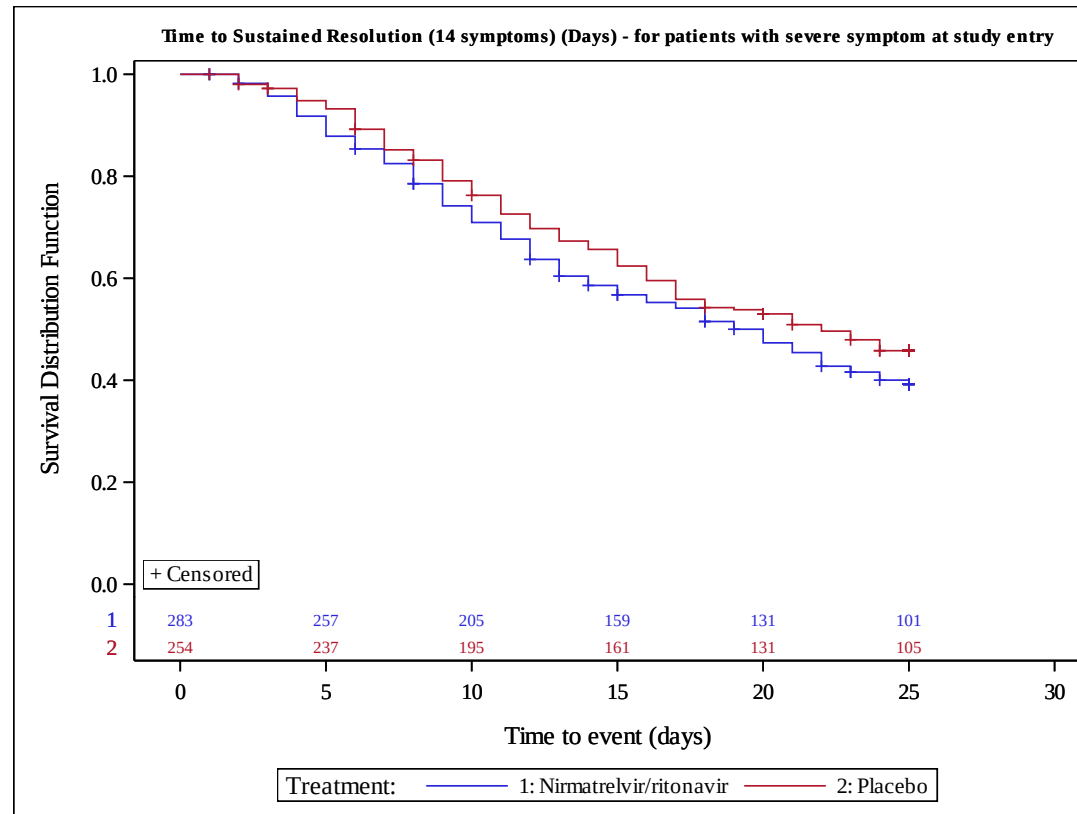
	Nirmatrelvir/ritonavir (N=283)	Placebo (N=254)
Number of subjects with events, n (%)	166 (58.7)	133 (52.4)
Number of censored subjects, n (%)	117 (41.3)	121 (47.6)
Kaplan-Meier estimates of Time to Event (Days) [1]		
25%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Median (95%-CI)	20.0 (16.0, 22.0)	22.0 (17.0, NE)
75%-ile (95%-CI)	NE (NE, NE)	NE (NE, NE)
Adjusted Analysis [2]		
Hazard Ratio (95% CI) [3]	1.250 (0.991, 1.578)	
p-value [3]	0.060	
Unadjusted Analysis		
Hazard Ratio (95% CI) [3]	1.198 (0.954, 1.506)	
p-value [3]	0.120	

N: Number of participants, CI: Confidence Interval, NE: Not estimable
 Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 [1] Based on the Brookmeyer and Crowley Method.
 [2] Adjusted by geographic region, baseline SARS-CoV-2 serology status and baseline viral load.
 [3] Estimated by cox regression model assuming proportional hazards.

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Final



Participants without event are censored at minimum(last assessment date, Day 25). Day 25 is the last possible day symptom alleviation and resolution can be achieved, Day 28 is the last day participants report.
 Kaplan-Meier Plots for subgroups are generated if p-value for interaction is significant ($\alpha \leq 0.05$)

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with EQ 5D-VAS >= 15 points improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=697)	Placebo (N=682)
Number of subjects with Response, n (%)	18 (2.6)	13 (1.9)
Adjusted analysis [1] Odds Ratio (95% CI)	NE (NE, NE)	
Relative Risk (95% CI)	NE (NE, NE)	
Risk Difference (95% CI)	NE (NE, NE)	
Unadjusted analysis [2] Odds Ratio (95% CI)	1.364 (0.663, 2.806) 0.399	
Relative Risk (95% CI)	1.355 (0.669, 2.743) 0.399	
Risk Difference (95% CI)	0.007 (-0.009, 0.022) 0.396	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Global Impression Questionnaire overall COVID-19-related symptoms ≥ 1 point improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=697)	Placebo (N=682)
Number of subjects with Response, n (%)	466 (66.9)	451 (66.1)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.069 (0.845, 1.353) 0.580	
Relative Risk (95% CI)	1.045 (0.975, 1.119) 0.211	
Risk Difference (95% CI)	0.023 (-0.025, 0.071) 0.349	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.033 (0.826, 1.292) 0.774	
Relative Risk (95% CI)	1.011 (0.938, 1.090) 0.774	
Risk Difference (95% CI)	0.007 (-0.043, 0.057) 0.774	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Global Impression Questionnaire return to usual health 1 point improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=697)	Placebo (N=682)
Number of subjects with Response, n (%)	402 (57.7)	370 (54.3)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.161 (0.929, 1.452) 0.189	
Relative Risk (95% CI)	1.089 (0.998, 1.189) 0.057	
Risk Difference (95% CI)	0.039 (-0.012, 0.091) 0.137	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.149 (0.929, 1.422) 0.200	
Relative Risk (95% CI)	1.063 (0.968, 1.168) 0.201	
Risk Difference (95% CI)	0.034 (-0.018, 0.087) 0.200	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with Global Impression Questionnaire return to usual activities 1 point improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=697)	Placebo (N=682)
Number of subjects with Response, n (%)	411 (59.0)	394 (57.8)
Adjusted analysis [1]		
Odds Ratio (95% CI)	1.066 (0.852, 1.333) 0.577	
Relative Risk (95% CI)	1.041 (0.957, 1.133) 0.347	
Risk Difference (95% CI)	0.018 (-0.033, 0.070) 0.489	
Unadjusted analysis [2]		
Odds Ratio (95% CI)	1.050 (0.848, 1.301) 0.652	
Relative Risk (95% CI)	1.021 (0.934, 1.116) 0.653	
Risk Difference (95% CI)	0.012 (-0.040, 0.064) 0.652	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).

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Pfizer Inc
 EPIC-HR (C4671005) / Nirmatrelvir/ritonavir - (Database snapshot date : 29APR2022)
 Overall Study population
 Modified Intent-To-Treat (mITT) set
 Analysis of Participants with WPAI Question 6 >= 15 points improvement from baseline

Final

	Nirmatrelvir/ritonavir (N=697)	Placebo (N=682)
Number of subjects with Response, n (%)	16 (2.3)	22 (3.2)
Adjusted analysis [1] Odds Ratio (95% CI)	0.700 (0.357, 1.372) 0.298	
Relative Risk (95% CI)	NE (NE, NE) NE	
Risk Difference (95% CI)	NE (NE, NE) NE	
Unadjusted analysis [2] Odds Ratio (95% CI)	0.705 (0.367, 1.354) 0.294	
Relative Risk (95% CI)	0.712 (0.377, 1.343) 0.294	
Risk Difference (95% CI)	-0.009 (-0.027, 0.008) 0.292	

N: Number of participants, CI: Confidence Interval, NE: Not estimable

For missing data a non-responder imputation (NRI) approach will be used.

[1] Computed from a logistic regression model including main effects of treatment, geographic region, baseline SARS-CoV-2 serology status and baseline viral load.

[2] Computed using normal approximation (Wald).