Phase 2 study of Secutrelvir, a Second-generation 3C-like Protease Inhibitor as Oral Treatment for COVID-19

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COI Declaration

- This work was supported by Shionogi & Co., Ltd.
- All authors are employees of SHIONOGI group.

Background



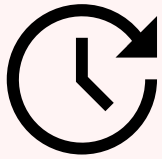
The Evolving COVID-19 Landscape

Despite increased population immunity following vaccination and exposure, SARS-CoV-2 continues to mutate and is highly transmissible. COVID-19 can still progress to severe/critical; it can trigger disease onset (diabetes, long COVID, CKD) and can exacerbate or worsen underlying conditions.



Limitations of Current Antivirals

Although several COVID-19 antivirals are available, concerns around tolerability, drug-drug interactions (DDIs), symptomatic and viral rebound, and high pills count burden have limited their use.



The Unmet Need

New antivirals that favor patient adherence, are well tolerated and reduce the risk of DDIs would be of public health value, particularly during new waves of infection.

 (Ref: Centers for Disease Control and Prevention (CDC). Respiratory Virus Season Outlook: 2024–2025. COVID Data Tracker. Updated October 2025)

Secutrelvir

❖ A second-generation 3C-like protease inhibitor designed for:

Improved tolerability

Reduced drug–drug interactions (DDI)

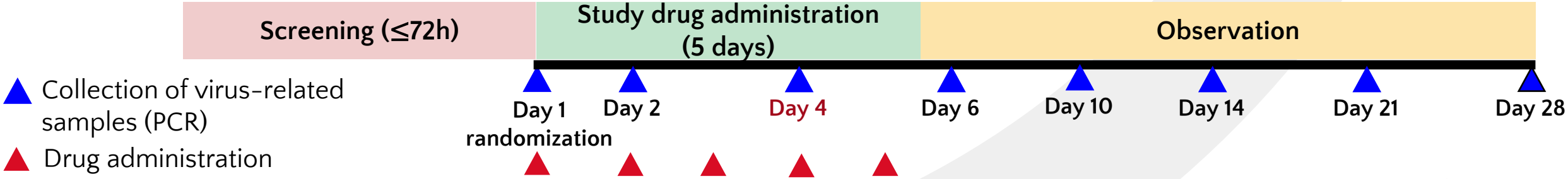
More convenient dosing schedule

Oral treatment and long-acting injectable prevention

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Study Design

Study design	Phase 2, multicenter, randomized, double-blind, placebo-controlled trial
Population	Age 18–64, ≥40 kg, diagnosed with COVID-19 within 72h of symptom onset, no risk factors, nonhospitalized
Primary Endpoint	Change from baseline in SARS-CoV-2 viral RNA level by qRT-PCR (NP swabs) on Day 4
Key Secondary Endpoint	Time to sustained resolution of 14 COVID-19 symptoms (sustained resolution=elimination of any of 14 targeted symptoms for 2 consecutive days)
Treatment arm	• Secutrelvir 120 mg single dose (120mg on day1, placebo on day2-5, QD) • Secutrelvir 80/40 mg (80mg on day1, 40mg on day2-5, QD) • Secutrelvir 40/20 mg (40mg on day1, 20mg on day2-5, QD) • Placebo (day1-5, QD)
Target number of enrollment	280 pts (70 pts/arm)
Country	Japan, United States



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Key Eligibility Criteria

Key inclusion criteria

- ≥18 and <65 years of age, ≥40 kg body weight
- Presence of ≥2 COVID-19 symptoms* of mild or higher severity, or ≥1 symptoms of moderate or higher severity, within 72h prior to randomization
- Confirmed SARS-CoV-2 infection within 72h of symptom onset

Key exclusion criteria

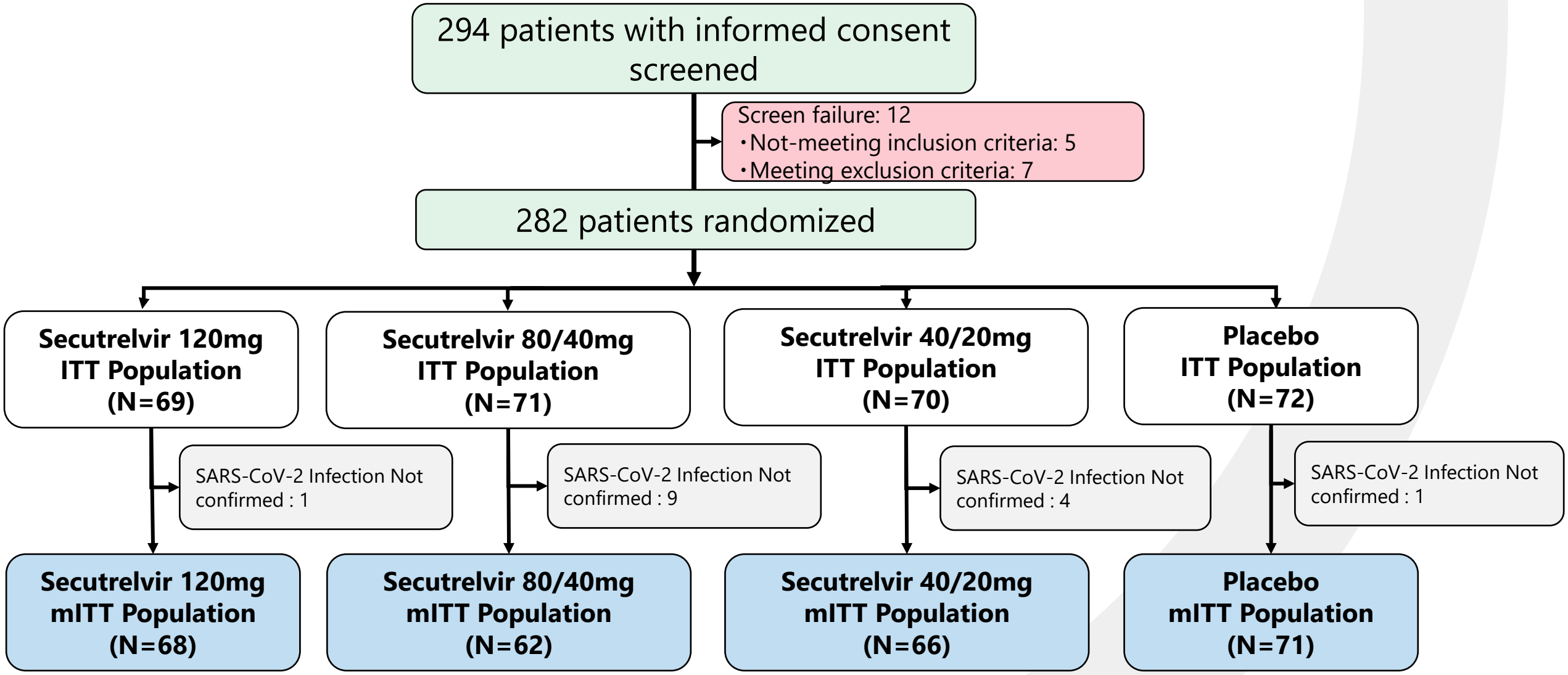
- At high-risk** for severe COVID-19
- History of hospitalization for the current SARS-CoV-2 infection or anticipated need for hospitalization within 24 h of randomization

*fever, shortness of breath or difficulty breathing, cough, sore throat, stuffy or runny nose, chills, fatigue, body pain or muscle pain or aches, headache, nausea, vomiting, diarrhea

**Based on “Underlying Conditions and the Higher Risk for Severe COVID-19” (Feb 6, 2025, US CDC)

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Patient Disposition (Efficacy analysis)



ITT (intent-to-treat) : All participants randomly assigned to investigational intervention
mITT (modified intent-to-treat) : Participants in the ITT population who took ≥1 dose of secutrelvir or placebo and had SARS-CoV-2 infection confirmed by RT-PCR at baseline

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Participant Demographics, mITT

	Secutrelvir 120 mg (N=68)	Secutrelvir 80/40 mg (N=62)	Secutrelvir 40/20 mg (N=66)	Placebo (N=71)
Age (Years)				
Mean (SD)	38.9 (11.9)	39.0 (11.5)	38.3 (13.0)	40.2 (12.9)
Age Group n (%)				
<50 years	52 (76.5)	48 (77.4)	50 (75.8)	51 (71.8)
50 to 64 years	16 (23.5)	14 (22.6)	16 (24.2)	20 (28.2)
Sex n (%)				
Male	27 (39.7)	30 (48.4)	26 (39.4)	28 (39.4)
Female	41 (60.3)	32 (51.6)	40 (60.6)	43 (60.6)
Race n (%)				
White	31 (45.6)	31 (50.0)	32 (48.5)	35 (49.3)
Black or African American	2 (2.9)	1 (1.6)	0	0
Asian	35 (51.5)	29 (46.8)	33 (50.0)	36 (50.7)
Other	0	1 (1.6)	1 (1.5)	0
Weight (kg)				
Mean (SD)	66.41 (14.02)	70.03 (14.76)	67.39 (13.27)	66.49 (11.81)
Body Mass Index (kg/m^2)				
Mean (SD)	24.05 (3.66)	24.41 (3.51)	24.19 (3.80)	24.33 (3.45)
Geographic Region, n (%)				
North America	33 (48.5)	32 (51.6)	33 (50.0)	35 (49.3)
Japan	35 (51.5)	30 (48.4)	33 (50.0)	36 (50.7)
Time from Onset, n (%)				
≤ 48 hours	47 (69.1)	44 (71.0)	47 (71.2)	51 (71.8)
> 48 hours	21 (30.9)	18 (29.0)	19 (28.8)	20 (28.2)

The demographic factors distribution was well balanced across all groups.

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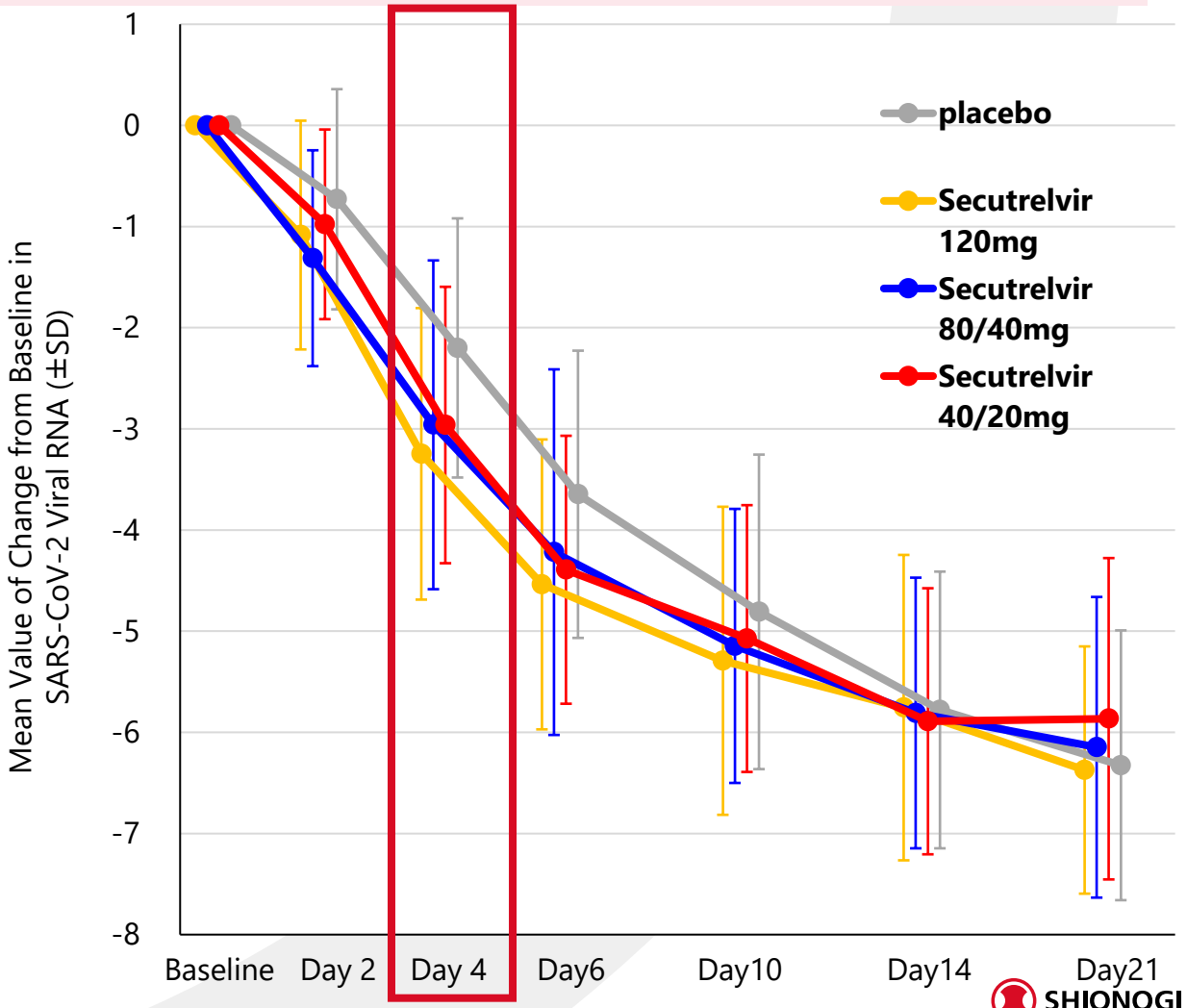
Primary Endpoint:

Change from Baseline in SARS-CoV-2 Viral RNA by qRT-PCR Testing (NP Swabs), mITT

All secutrelvir demonstrated the significant reduction of SARS-CoV-2 viral RNA level at Day4 compared with placebo.

Change in SARS-Cov-2 Viral RNA (log_{10} copies/mL) on Day 4

	N#	LS Mean [95% CI]	LS Mean Difference [95% CI]	P-value
Placebo	69	-2.124 [-2.474, -1.773]	---	---
Secutrelvir 120 mg	66	-3.131 [-3.488, -2.774]	-1.007 [-1.505, -0.510]	<0.0001
Secutrelvir 80/40 mg	60	-3.046 [-3.420, -2.672]	-0.922 [-1.432, -0.412]	0.0004
Secutrelvir 40/20 mg	66	-2.986 [-3.345, -2.627]	-0.862 [-1.362, -0.363]	0.0008



#Number of participants after removal of those without the samples on Day 4 in mITT population

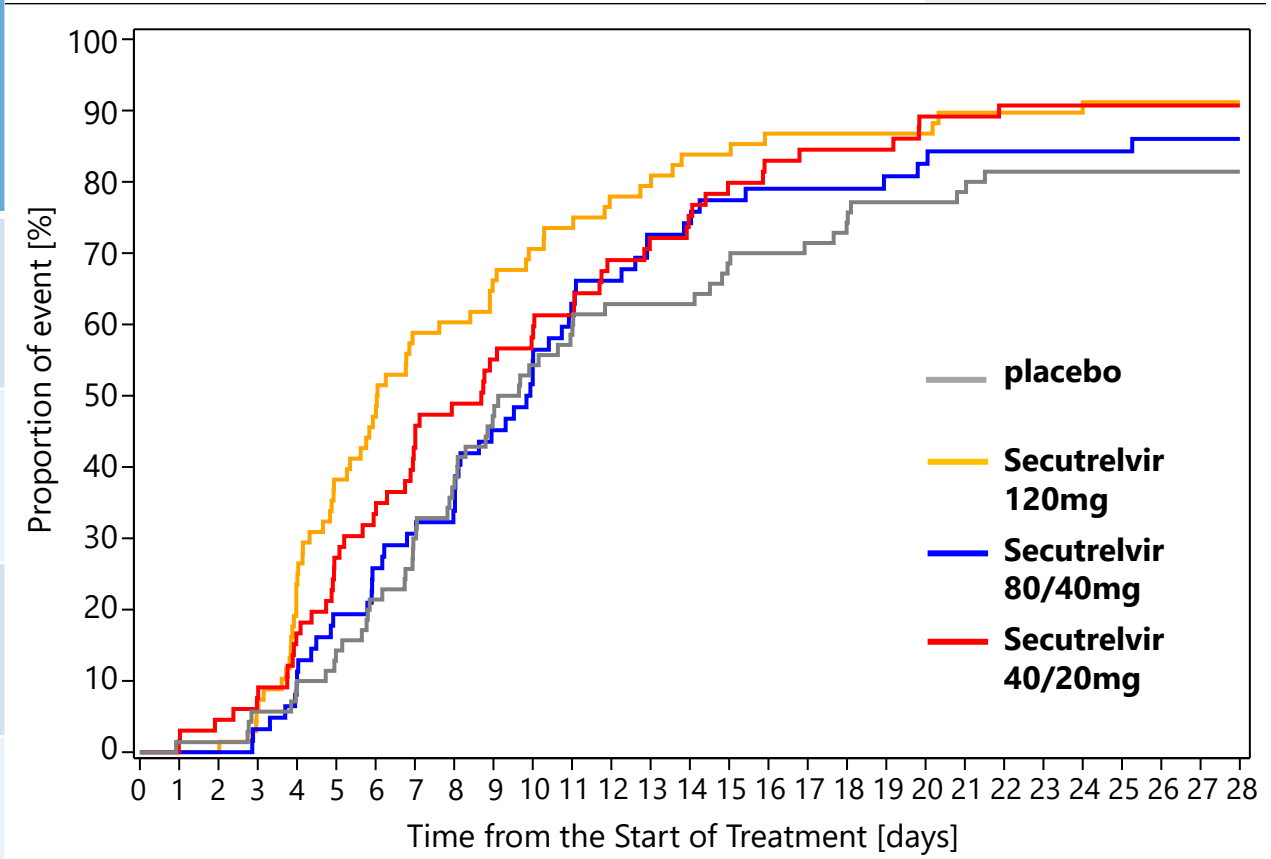
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Secondary Endpoint:

Time to Sustained Resolution of 14 COVID-19 Symptoms*, mITT

Secutrelvir was associated with a numerical reduction in time to sustained resolution of COVID-19 symptoms, with the 120mg dose showing the largest improvement.

	N	Mean time to sustained symptom resolution by Day 28 (days) [95% CI]	Difference [95% CI]
Placebo	71	13.007 [10.980, 15.034]	---
Secutrelvir 120 mg	68	9.301 [7.534, 11.069]	-3.706 [-6.395, -1.016]
Secutrelvir 80/40 mg	62	11.986 [9.989, 13.983]	-1.021 [-3.866, 1.824]
Secutrelvir 40/20 mg	66	10.575 [8.754, 12.396]	-2.432 [-5.157, 0.293]



*fever, shortness of breath or difficulty breathing, cough, sore throat, stuffy or runny nose, chills, fatigue, body pain or muscle pain or aches, headache, nausea, vomiting, diarrhea, change in sense of taste, change in sense of smell

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Overall Treatment-Emergent Adverse Events, Safety

Number of Participants With	Secutrelvir 120 mg (N=70) n (%)	Secutrelvir 80/40 mg (N=70) n (%)	Secutrelvir 40/20 mg (N=70) n (%)	Placebo (N=72) n (%)
Any TEAE	12 (17.1)	20 (28.6)	12 (17.1)	12 (16.7)
(Number of Events)	19	28	18	17
Mild	9 (12.9)	13 (18.6)	9 (12.9)	6 (8.3)
Moderate	2 (2.9)	6 (8.6)	3 (4.3)	6 (8.3)
Severe	1 (1.4)	1 (1.4)	0	0
Any Serious TEAE	0	0	0	1 (1.4)
Any TEAE Leading to Discontinuation	0	0	0	0
Any Treatment-related TEAE	2 (2.9)	1 (1.4)	2 (2.9)	2 (2.8)
(Number of Events)	2	1	3	4

- The incidence of TEAE was similar across the groups.
- No serious TEAEs and TEAEs leading to discontinuation were observed with secutrelvir treatment arms.
- Secutrelvir was well tolerated.

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Conclusions

- Secutrelvir, in all treatment arms, showed a significant reduction of SARS-CoV-2 viral RNA level at Day4 compared with placebo.
- Secutrelvir treatment showed a numerical reduction of the time to sustained resolution of 14 COVID-19 symptoms.
- A single 120 mg dose of secutrelvir has the potential to be highly effective.
- Secutrelvir was well-tolerated with AE profile comparable to placebo.

These results suggest that secutrelvir could be the first oral antiviral with single dose administration for COVID-19 treatment, supporting the further development of this compound.

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Acknowledgement

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