Clinical trial results:
A Phase 3 randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of S-217622 in the prevention of symptomatic SARS-CoV-2 infection in household contacts of an individual with symptomatic COVID-19

Summary

EudraCT number	2025-000303-24
Trial protocol	Outside EU/EEA
Global end of trial date	18 September 2024

Results information

Result version number	v1 (current)
This version publication date	19 July 2025
First version publication date	19 July 2025

Trial information

Trial identification

Sponsor protocol code	2206T1331

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05897541
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shionogi B.V.
Sponsor organisation address	Herengracht 464, Amsterdam, Netherlands, 1017 CA
Public contact	shionogiclintrials-admin@shionogi.co.jp, Shionogi B.V., 0044 2030534200, shionogiclintrials-admin@shionogi.co.jp
Scientific contact	shionogiclintrials-admin@shionogi.co.jp, Shionogi B.V., 0044 2030534200, shionogiclintrials-admin@shionogi.co.jp

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-003192-PIP03-23
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 September 2024
Global end of trial reached?	Yes
Global end of trial date	18 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare ensitrelvir with placebo in the prevention of symptomatic SARS-CoV-2 infection in participants with a negative screening SARS-CoV-2 infection who are household members (hereinafter referred to as "participants") of SARS-CoV-2-infected patients (hereinafter referred to as "index patients") through Day 10 (using the mITT analysis set)

Protection of trial subjects:

This study will be conducted by all involved parties in accordance with the protocol and with the following:
– Consensus ethical principles derived from international guidelines, including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines
– Applicable ICH GCP Guidelines
– Applicable laws and regulations (including European regulation 536/2014 Annex I Section D No. 17 lit. a)

Background therapy:

Prior/Concomitant Therapy - Any medication or vaccine (including over-the-counter or prescription medicines, recreational drugs, vitamins, and/or herbal supplements) or other specific categories of interest that the participant is receiving at the time of enrollment or receives during the study must be recorded in the eCRF. Any medications specific for COVID-19 (other than symptom alleviation treatment) used by the index patient must also be recorded in the eCRF.
Other concomitant medications may be considered on a case-by-case basis by the investigator in consultation with the medical monitor.

Evidence for comparator:

Not Applicable

Actual start date of recruitment	09 June 2023
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 1601
Country: Number of subjects enrolled	Japan: 614
Country: Number of subjects enrolled	Viet Nam: 140
Country: Number of subjects enrolled	Argentina: 18
Country: Number of subjects enrolled	South Africa: 14

Worldwide total number of subjects	2387
EEA total number of subjects	0

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	175
Adults (18-64 years)	1978
From 65 to 84 years	234
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Dates of recruitment was from 9 June 2023 to 21 August 2024.

This study was a multicenter study conducted at 178 contracted sites, including 95 sites in the US, 67 sites in Japan, 2 sites in Vietnam, 11 Sites in Argentina, and 3 sites in South Africa.

Pre-assignment

Screening details:

Visit 1, Day 1 for the index patient will not necessarily be the same day as Visit 1, Day 1 for the participant. However, the participant must provide informed consent ≤ 72 hours from onset of COVID-19 symptoms in the index patient and ≤ 1 calendar day from the time that the index patient provides consent.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Active

Arm description:

S-217622 at a dose of 375 mg for Day 1 and 125 mg once daily for Days 2 to 5

Arm type	Experimental
Investigational medicinal product name	Ensitrelvir
Investigational medicinal product code	
Other name	S-217622
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

S-217622 at a dose of 375 mg for Day 1 and 125 mg once daily for Days 2 to 5

Arm title	Placebo

Arm description:

Placebo at a dose of 375 mg for Day 1 and 125 mg once daily for Days 2 to 5

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

Dosage and administration details:

Placebo at a dose of 375 mg for Day 1 and 125 mg once daily for Days 2 to 5

Number of subjects in period 1	Active	Placebo
Started	1194	1193
Completed	1172	1158
Not completed	22	35
Consent withdrawn by subject	12	25
Adverse event, non-fatal	-	1
Other	3	1
Lost to follow-up	6	7
Failure to meet eligibility	1	-
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	2387	2387	
Age categorical			
Adolescents = 175 Adults < 65 years of age = 1980 Adults > 65 years of age = 234			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	175	175	
Adults (18-64 years)	1978	1978	
From 65-84 years	234	234	
85 years and over	0	0	
Gender categorical			
Ensitrelvir - Male = 505 and Female = 689 Placebo - Male = 458 and Female = 735			
Units: Subjects			
Female	1424	1424	
Male	963	963	

End points

End points reporting groups

Reporting group title	Active
Reporting group description:	
S-217622 at a dose of 375 mg for Day 1 and 125 mg once daily for Days 2 to 5	
Reporting group title	Placebo
Reporting group description:	
Placebo at a dose of 375 mg for Day 1 and 125 mg once daily for Days 2 to 5	

Primary: Proportion of participants in the mITT analysis set with a negative screening SARS-CoV-2 infection (CLC-negative RT-PCR test) who are infected with SARS-CoV-2 (CLC-positive RT-PCR test) and have COVID-19 symptoms onset through Day 10

End point title	Proportion of participants in the mITT analysis set with a negative screening SARS-CoV-2 infection (CLC-negative RT-PCR test) who are infected with SARS-CoV-2 (CLC-positive RT-PCR test) and have COVID-19 symptoms onset through Day 10
End point description:	
Proportion of participants in the mITT analysis set with a negative screening SARS-CoV-2 infection (CLC-negative RT-PCR test) who are infected with SARS-CoV-2 (CLC-positive RT-PCR test) and have COVID-19 symptoms onset through Day 10	
End point type	Primary
End point timeframe:	
Ten Days	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1194[1]	1193[2]		
Units: COVID-19 symptoms	0	0		

Notes:

[1] - S-217622

[2] - Placebo

Statistical analyses

Statistical analysis title	Risk for Symptomatic COVID-19 Through Day 10
Statistical analysis description:	
The null hypothesis to be tested was that the risk for incident symptomatic COVID-19 over 10 days in participants assigned to treatment with ensitrelvir is the same compared to the risk for incident symptomatic COVID-19 over 10 days in participants assigned to treatment with a matching placebo.	
Comparison groups	Active v Placebo

Number of subjects included in analysis	2387
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.0001 [4]
Method	GEE Poisson Regression Model
Parameter estimate	Risk ratio (RR)
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	0.49
Variability estimate	Standard error of the mean

Notes:

[3] - GEE Poisson Regression Model

[4] - Statistically significant

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 7 days for fatal or life threatening SAE reports 15 days all other SAE reports	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Non-serious adverse events in 300 study participants on ensitrelvir and 305 study on placebo.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 October 2022	The primary purpose of this protocol amendment is to add clarifications to improve study implementation. For example, the requirement for the amount of time from informed consent to randomization was changed from ≤ 96 hours to ≤ 72 hours.
19 April 2023	The primary purpose of this protocol amendment is to incorporate recommendations from the regulatory agency
30 October 2023	The primary purpose of this protocol amendment is to add a data safety monitoring board (DSMB) and to incorporate changes in response to health authority requests
03 November 2023	The primary purpose of this protocol amendment is to add a data safety monitoring board (DSMB), include changes consistent with the country-specific amendment (2.1 – EU), and to make study clarifications.
08 July 2024	The primary purpose of this protocol amendment is to clarify that the sample size may vary from the original estimate. As per the original protocol, the sample size was to be determined based on the targeted number of events (92 events) and was permitted to be adjusted to ensure the targeted number of events was achieved.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported