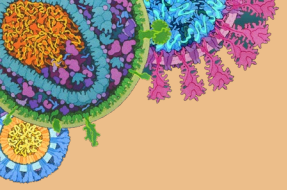

Abstract: #200

Ensitrelvir to Prevent COVID-19 in Households: SCORPIO-PEP Phase III Placebo-Controlled Trial Results

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Introduction

- Households are major sites for SARS-CoV-2 transmission, with secondary attack rates ranging from 18.9% to 42.7%[1,2]
- There is an unmet need for an antiviral for postexposure prophylaxis, particularly in high-risk household members[3,4]
- Ensitrelvir, an oral SARS-CoV-2 3C-like protease inhibitor, is approved in Japan for the treatment of mild-to-moderate COVID-19[5-7]
- The SCORPIO-PEP Phase III trial evaluated the post exposure prophylaxis efficacy of ensitrelvir in household contacts of index patients with confirmed COVID-19

1. Madewell ZJ, et al. *JAMA Netw Open* 2021;4:e2122240; 2. Madewell ZJ, et al. *JAMA Netw Open* 2022;5:e229317; 3. Alpizar SA, et al. *J Infect* 2023;87:392-402; 4. Cox RM, et al. *Nat Commun* 2023;14:4731; 5. Kawashima S, et al. *Biochem Biophys Res Comms* 2023;645:132-136; 6. Kuroda T, et al. *J Antimicrobial Chemother* 2023;78:946-952; 7. Nobori H, et al. *Antiviral Res* 2024;224:105852.
COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Study Design

Index patients
(SARS-CoV-2 infection)

Local test (+)
Symptom (+)

Household contacts (HHCs)

Local test (-)
Symptom (-)

≤72 hours of IP symptom onset

Phase 3 RCT

Enrolled: 2,389 HHCs

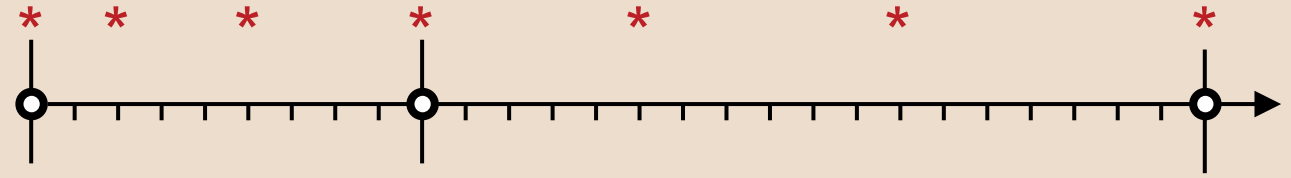
Trial dates: June 2023 - September 2024

Ensitrelvir (Day 1: 375 mg, Days 2–5: 125 mg)

Placebo

1:1

Days 1–5 Day 10 Day 28



Proportion of HHCs who developed COVID-19 by Day 10

*NP swab collection days: 1, 3, 6, 10, 15, 21, 28

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HHC, household contact; US, United States; FU, follow-up; IP, index patient; NP, nasopharyngeal.

Study Populations and Endpoint

mITT population

All randomized HHCs with central laboratory–confirmed SARS-CoV-2 negativity by RT-PCR at baseline*

ITT population

All randomized HHCs including those with central laboratory RT-PCR positivity at baseline

Primary endpoint

Proportion of HHCs with COVID-19 development (central laboratory–confirmed RT-PCR positivity of SARS-CoV-2 and ≥1 of the 14 COVID-19 symptoms lasting ≥48 hours)** through Day 10 (mITT)

*Participants with local (-) and central (+) were excluded from mITT population.
**Or worsening (increase in symptom score from baseline) in the case of preexisting COVID-19–like symptoms for ≥48 hours;
ITT, intention-to-treat; mITT, modified ITT; RT-PCR, reverse transcriptase polymerase chain reaction.

Household Contact Characteristics (mITT)

Characteristic	Ensitrelvir (N=1,030)	Placebo (N=1,011)
Age—yr, mean (SD)	41.8 (17.0)	43.0 (16.1)
≥65, n (%)	99 (9.6)	90 (8.9)
Female, n (%)	584 (56.7)	627 (62.0)
BMI—kg/m^2, mean (SD)	26.4 (5.7)	26.6 (5.3)
Hispanic or Latino, n (%)	620 (60.2)	623 (61.6)
Race, n (%)		
White	632 (61.4)	615 (60.8)
Black or African American	51 (5.0)	56 (5.5)
Asian	325 (31.6)	321 (31.8)
American Indian or Alaska Native	2 (0.2)	4 (0.4)
Other	20 (1.9)	15 (1.5)

BMI, body mass index; SD, standard deviation.

Household Contact Characteristics (mITT) (Contd.)

Characteristic	Ensitrelvir (N=1,030)	Placebo (N=1,011)
Hours from symptom onset in the IP to enrollment of HHC, n (%)		
<48	732 (71.1)	720 (71.2)
Geographic region, n (%)		
US	692 (67.2)	683 (67.6)
Japan	266 (25.8)	270 (26.7)
Vietnam	59 (5.7)	49 (4.8)
Argentina	7 (0.7)	4 (0.4)
South Africa	6 (0.6)	5 (0.5)
Risk status, n (%)		
High risk*	382 (37.1)	374 (37.0)
Positive baseline serology, n (%)[a]**		
S-antibody	1018 (99.4)	1004 (99.7)

[a]Number of participants with non-missing each serology data was used as denominator (Ensitrelvir: n=1024; Placebo: 1007).
*Key representative high-risk factors: BMI ≥30 kg/m^2, smoking (current or former), age (≥65 years), heart disease, diabetes (type 1 or type 2); high risk is ≥1 risk factor listed.
**Number of participants with non-missing serology data was used as denominator.

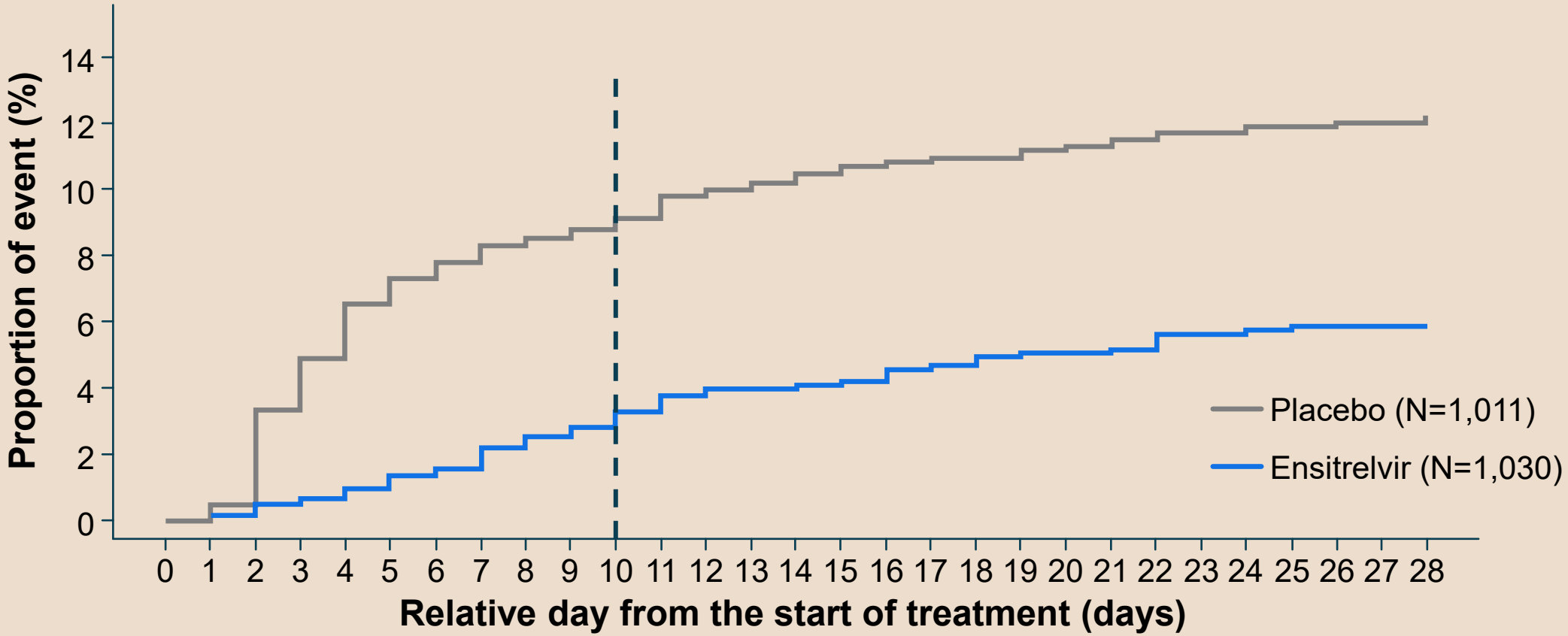
Primary Analysis: Proportion of HHCs with COVID-19 Development Through Day 10 (mITT)

	Ensitrelvir (N=1,030)	Placebo (N=1,011)
COVID-19 development, n (%)	30 (2.9)	91 (9.0)
[95% CI]*	[1.97, 4.13]	[7.31, 10.94]
Risk ratio**	0.33	
[95% CI]***	[0.22, 0.49]	
P-value****	<0.0001	

In participants with central negative tests at baseline, ensitrelvir demonstrated a statistically significant reduction in the risk of COVID-19 vs placebo (2.9% vs 9.0%)

COVID-19 development was defined as a central laboratory–confirmed positive RT-PCR test and the occurrence (or worsening [increase in symptom score from baseline] in the case of preexisting COVID-19–like symptoms) of ≥1 of the 14 specified COVID-19 symptoms for ≥48 hours.
*CI for the proportion of participants with symptomatic COVID-19 using the Clopper-Pearson method.
**Risk ratio based on the GEE Poisson regression model with covariates of time from symptom onset in the index patient to the enrollment (<48 hours / ≥48 hours) and the pooled geographic regions (North America/Japan/RoW.
***CI calculated from the GEE Poisson regression model.
****P-value for the log coefficient of treatment effect equal to 0 in the GEE Poisson regression model.
CI, confidence interval; GEE, generalized estimating equation.

Primary Endpoint: HHCs with COVID-19 Development Through Day 28 (mITT)



Participants who were randomized but did not receive treatment were excluded from this analysis

Key Secondary Analysis: Proportion of HHCs with COVID-19 Development Through Day 10 (ITT)

	Ensitrelvir (N=1,194)	Placebo (N=1,193)
COVID-19 development, n (%)	52 (4.4)	122 (10.2)
[95% CI]*	[3.27, 5.67]	[8.56, 12.09]
Risk ratio**	0.43	
[95% CI]***	[0.32, 0.59]	
P-value****	<0.0001	

The overall proportion of HHCs developing COVID-19 was significantly lower with ensitrelvir vs placebo (4.4% vs 10.2%)

COVID-19 development was defined as a central laboratory–confirmed positive RT-PCR test and the occurrence (or worsening [increase in symptom score from baseline] in the case of preexisting COVID-19–like symptoms) of ≥1 of the 14 specified COVID-19 symptoms for ≥48 hours.
*CI for the proportion of participants with symptomatic COVID-19 using the Clopper-Pearson method.
**Risk ratio based on the GEE Poisson regression model with covariates of time from symptom onset in the index patient to the enrollment (<48 hours / ≥48 hours) and the pooled geographic regions (North America/Japan/RoW).
***CI calculated from the GEE Poisson regression model.
****P-value for the log coefficient of the treatment effect equal to 0 in the GEE Poisson regression model.

Subgroup Analysis: HHCs With or Without High Risk for Severe COVID-19 (mITT)

	Ensitrelvir (N=1,030)	Placebo (N=1,011)
High risk present, n (%)	382	374
COVID-19 development	9 (2.4)	37 (9.9)
Risk ratio*	0.24	
P-value**	<0.0001	
High risk absent, n (%)	648	637
COVID-19 development	21 (3.2)	54 (8.5)
Risk ratio*	0.39	
P-value**	0.0001	

COVID-19 development was defined as a CLC positive RT-PCR test and the occurrence (or worsening [increase in symptom score from baseline] in the case of preexisting COVID-19–like symptoms) of ≥1 of the 14 specified COVID-19 symptoms for ≥48 hours.
*Risk ratio was calculated by generalized estimating equation (GEE) Poisson regression model.
**P-value for the log coefficient of the treatment effect equal to 0 in the GEE Poisson regression model.

Safety

TEAEs, n (%)	Ensitrelvir (N=1,190)*	Placebo (N=1,187)*
Any TEAEs	180 (15.1)	184 (15.5)
Any serious TEAEs	2 (0.2)	2 (0.2)
Any study drug-related TEAEs	19 (1.6)	21 (1.8)
Any study drug-related serious TEAEs	0	0
Any TEAEs leading to treatment discontinuation	1 (<0.1)	1 (<0.1)
Any TEAEs leading to study discontinuation	0	1 (<0.1)

Both treatments had similar rates of TEAEs and serious TEAEs, with no deaths and hospitalization

*N represents the number of participating HHCs with each type of adverse event. Percentages are based on the number of participating HHCs in the safety analysis set within each treatment group.
TEAE, treatment-emergent adverse event.

Summary

- Oral ensitrelvir post exposure prophylaxis ≤72 hours after symptom onset in index patients was effective in significantly protecting HHCs from COVID-19, including those at high risk.
- Ensitrelvir demonstrated a significant 67% reduction in the risk of COVID-19 development through Day 10 in HHCs uninfected at baseline.
- Ensitrelvir was well tolerated, with no new safety concerns.
- Ensitrelvir PEP reductions in SARS-CoV-2 transmission within households suggest a potential for protection in other settings (eg, outbreaks in acute and long-term care facilities).

Thank you!

We also thank the study participants, who generously gave their time, and the site investigative staff.

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