Ensitrelvir in hospitalized patients with SARS-CoV-2 during the Omicron epidemic: a single-center observational study

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Supplementary Table 1: Patient information collected

Information Type	**Data collected**
Basic Information	Age, gender, date of hospital admission, length of hospital stay, underlying conditions/comorbidities, concurrent medications, status of SARS-CoV-2 vaccination, CoV-NP-IgG, CoV-SP-IgM, CoV-SP-IgG, duration of isolation.
COVID-19 Treatment Information	Start and end dates of administration of SARS-CoV-2 medication.
Clinical Information	Date of COVID-19 onset, severity at the start of treatment, presence of pneumonia, oxygen requirement, need for dialysis, presence of chemotherapy, immunosuppression status, presence of EICU management, occurrence of transfer to EICU, Day 28 survival/all-cause mortality, final outcome.
Virological Information	Results of SARS-CoV-2 viral tests (antigen testing, RT-PCR)

Supplementary Table 2: COVID-19 disease severity criteria.

Severity	SpO2	Clinical condition
Mild	≥ 96%	No respiratory symptoms or, Cough only (no dyspnea, no evidence of pneumonia)
Moderate I	93% < SpO2 < 96%	Dyspnea, pneumonia
Moderate II	SpO2 ≤ 93%	Requires oxygen
Severe		ICU admission or, Requires mechanical ventilator

SpO2, oxygen saturation.

Translated from the Japanese guidelines on COVID-19 treatment [1].

1, Ministry of Health LaW, Japan. New Coronavirus Infectious Disease (COVID-19) Medical Treatment Guide Version 10.1. Ministry of Health LaW. Ministry of Health, Labor and Welfare Treatment guideline of COVID-19. April 2024. https://www.mhlw.go.jp/content/001248424.pdf.

Supplementary Table 3

Demographics and baseline characteristics of analysis population (IPTW-adjusted)

Baseline Characteristics	Ensitrelvir (N=246)	Remdesivir (N=246)	SMD
Sex			
Male	151 (61.3%)	151 (61.3%)	0.00
Female	95 (38.7%)	96 (38.7%)	
Age			0.02
Average (SD)	75.7 (11.6)	76.0 (14.0)	
10-59	19 (7.9%)	33 (12.9%)	
60-69	52 (21.1%)	29 (11.6%)	
70-79	61 (24.8%)	57 (23.3%)	
80-89	87 (35.2%)	105 (42.6%)	
90+	27 (11.1%)	24 (9.6%)	
COVID-19 Disease Severity			
Mild	140 (56.8%)	142 (57.6%)	
Moderate I	13 (5.3%)	14 (5.7%)	0.02
Moderate II	59 (23.9%)	58 (23.5%)	0.01
Severe	35 (14.0%)	33 (13.2%)	0.02
Oxygen Supplementation	102 (41.5%)	104 (42.0%)	0.01
Hemodialysis	9 (3.8%)	10 (3.9%)	0.01
Chemotherapy	24 (9.6%)	25 (10.1%)	0.02
Immunosuppressive Conditions	40 (16.1%)	44 (18.0%)	0.05
Presence of Pneumonia	93 (37.7%)	91 (36.9%)	0.02
Vaccination History			
Yes	208 (84.2%)	210 (85.1%)	0.03
No	38 (15.6%)	36 (14.7%)	0.03
Unknown	1 (0.3%)	1 (0.3%)	0.00
Underlying Risk Factor			
Diabetes Mellitus	65 (26.2%)	72 (29.0%)	0.06
Hyper Lipidemia	50 (20.2%)	54 (21.8%)	0.04
Hypertension	115 (46.7%)	118 (47.7%)	0.02
Malignancy	76 (30.8%)	78 (31.7%)	0.02
Cardiovascular	153 (61.9%)	161 (65.5%)	0.07
Respiratory	34 (13.7%)	32 (13.1%)	0.02
Hepatic	12 (5.0%)	13 (5.2%)	0.01
Renal	35 (14.4%)	43 (17.5%)	0.09

SD, standard deviation

Data are presented as n (%), or mean ± SD.

Supplementary Table 4: Ensitrelvir Clinical Trials

Phase	Study Population	Study Arm (number of patients)	Proportion of patients with risk factors	Variants in study	Primary endpoints	Number of patients with severe outcomes
Phase 2b [1]	mild to moderate COVID-19	[ITT Population] Ensitrelvir 125 mg (114) Ensitrelvir 250 mg (116) Placebo (111)	n/a	Delta, Omicron	[Co-primary endpoints] ● Change from baseline in the SARS-CoV-2 viral titer. ● Time weighted average change from baseline in the total score of 12 COVID-19 symptom.	n/a
Phase 3 [2]	mild to moderate COVID-19	[ITT Population] Ensitrelvir 125 mg (347) Ensitrelvir 250 mg (340) Placebo (343)	27.8%	Omicron	Time to resolution of the 5 COVID-19 symptoms	2 COVID-19-related hospitalization or equivalent recuperation

Phase 3 [3]	mild to moderate COVID-19	[mITT Population] Ensitrelvir 125 mg (945) Placebo (943)	33%	Omicron	Time to sustained resolution of 15 COVID-19 symptoms	4 COVID-19 -related hospitalization

n/a: data was not presented in the manuscript.

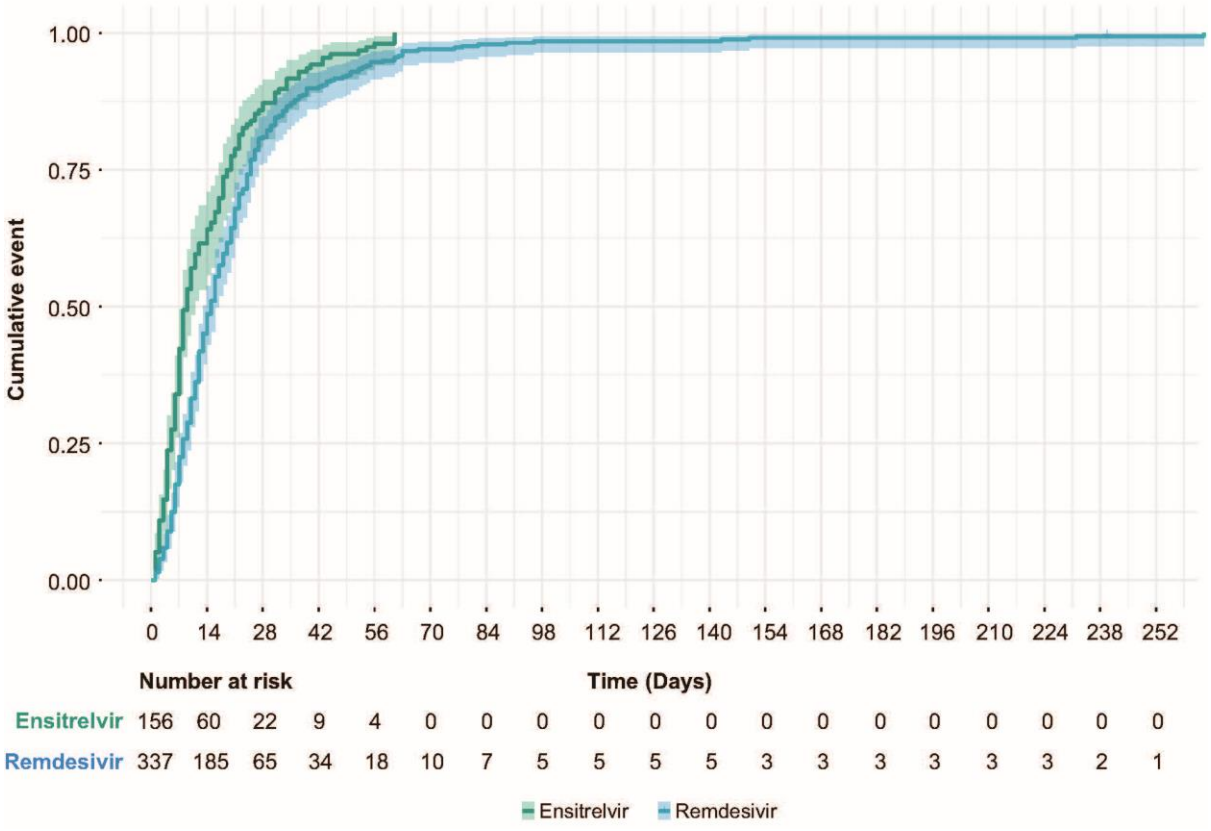
Reference:

1: Mukae H, Yotsuyanagi H, Ohmagari N, *et al*. Efficacy and Safety of Ensitrelvir in Patients With Mild-to-Moderate Coronavirus Disease 2019: The Phase 2b Part of a Randomized, Placebo-Controlled, Phase 2/3 Study. Clin Infect Dis. 2023 Apr 17;76(8):1403-1411.

2: Yotsuyanagi H, Ohmagari N, Doi Y, et al. Efficacy and Safety of 5-Day Oral Ensitrelvir for Patients With Mild to Moderate COVID-19: The SCORPIO-SR Randomized Clinical Trial. JAMA Netw Open. 2024 Feb 9;7(2) :e2354991.

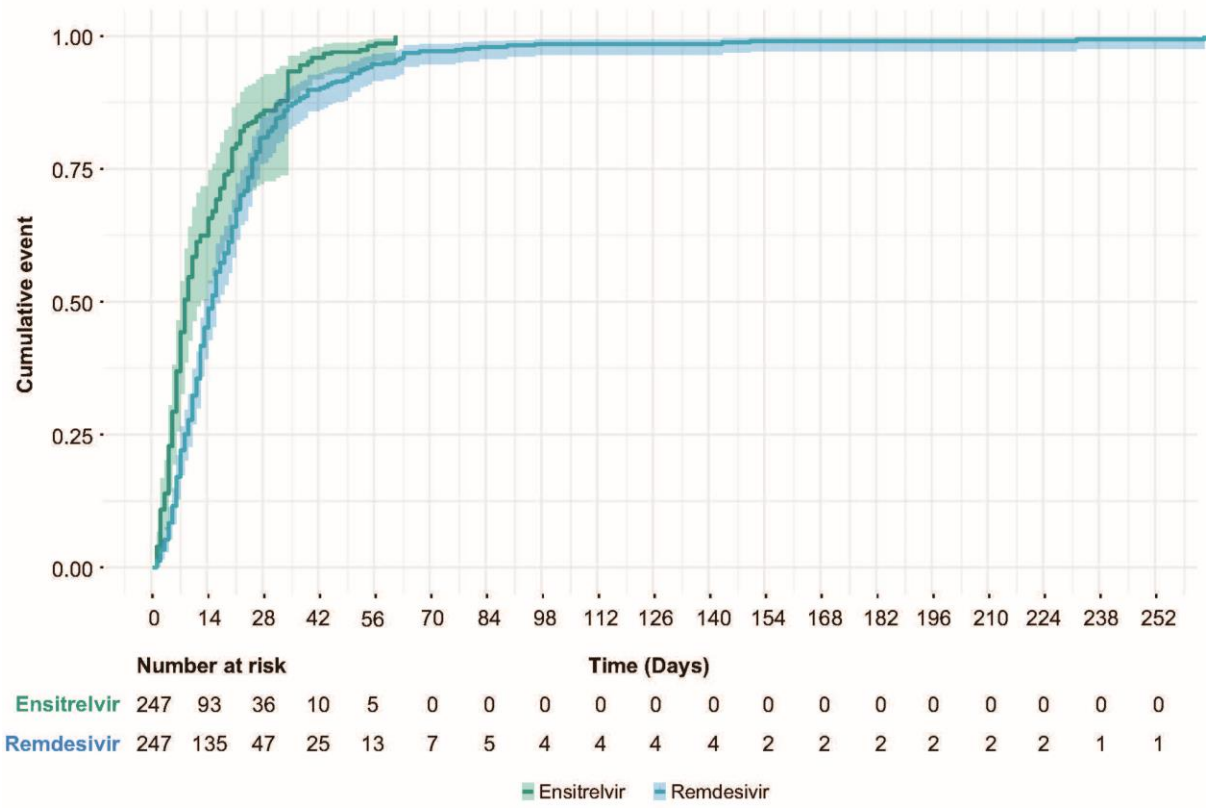
3: Luetkemeyer AF, Chew KW, Lacey S, et al. Ensitrelvir for the Treatment of Nonhospitalized Adults with COVID-19: Results from the SCORPIO-HR, Phase 3, Randomized, Double-blind, Placebo-Controlled Trial. Clin Infect Dis. 2025 Feb 17:ciaf029. doi: 10.1093/cid/ciaf029.

Supplementary Figure 1A Time to discharge (non-adjusted)



Note: 95% confidence bands were shown. Unit of Time: Days

Supplementary Figure 1B Time to discharge (IPTW-adjusted)



Note: 95% confidence bands were shown. Unit of Time: Days