

# Effect of Renal Impairment on Pharmacokinetics and Safety of Ensitrelvir, a SARS-CoV-2 3CL Protease Inhibitor

Takayuki Katsube, PhD<sup>1</sup>, Kezbor Safwan, MD<sup>2</sup>, Ryosuke Shimizu<sup>1</sup>, and Ryuji Kubota, PhD<sup>1</sup>

<sup>1</sup>Clinical Pharmacology & Pharmacokinetics, Shionogi & Co., Ltd., 3-13, Imabashi 3-chome, Chuo-ku, Osaka 541-0042, Japan

<sup>2</sup>Shionogi Inc. 400 Campus Drive, 4th Fl. Florham Park, NJ 07932, US

E-mail address

Takayuki Katsube: [takayuki.katsube@shionogi.co.jp](mailto:takayuki.katsube@shionogi.co.jp)

Kezbor Safwan: [safwan.kezbor@shionogi.com](mailto:safwan.kezbor@shionogi.com)

Ryosuke Shimizu: [ryosuke.shimizu@shionogi.co.jp](mailto:ryosuke.shimizu@shionogi.co.jp)

Ryuji Kubota: [ryuji.kubota@shionogi.co.jp](mailto:ryuji.kubota@shionogi.co.jp)

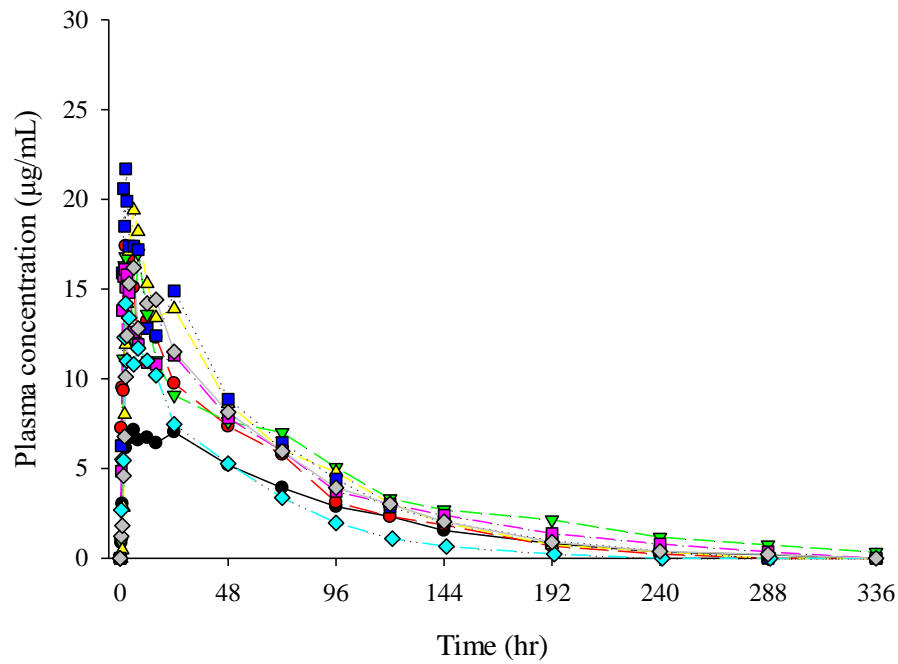
Corresponding author: Takayuki Katsube, [takayuki.katsube@shionogi.co.jp](mailto:takayuki.katsube@shionogi.co.jp)

Clinical Pharmacology & Pharmacokinetics, Shionogi & Co., Ltd., 3-13, Imabashi 3-chome, Chuo-ku, Osaka 541-0042, Japan

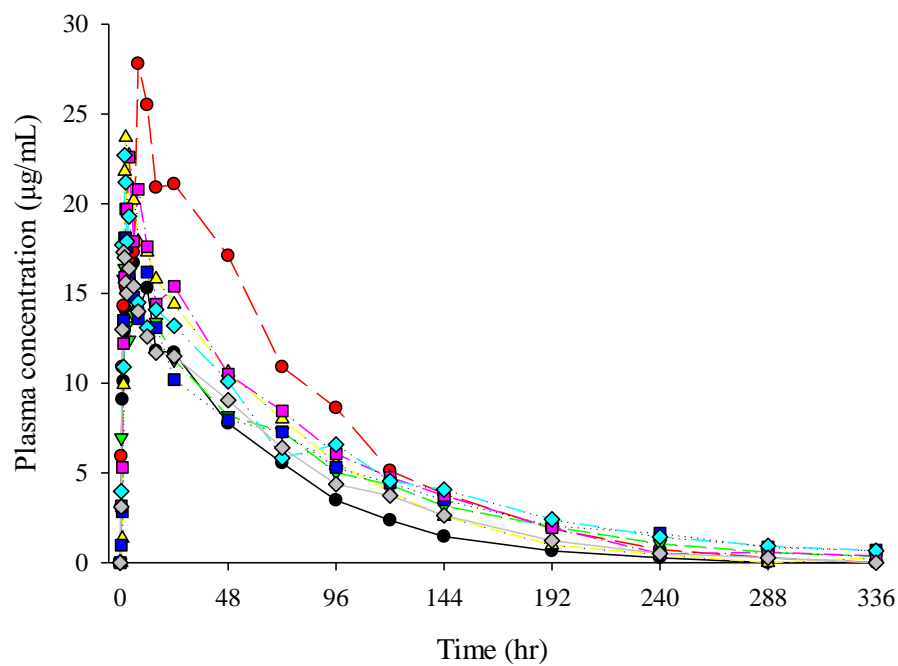
## Supplemental Material

### Supplemental Figure S1 Spaghetti plot of plasma concentration profiles of ensitrelvir

(a) Participants with normal renal function

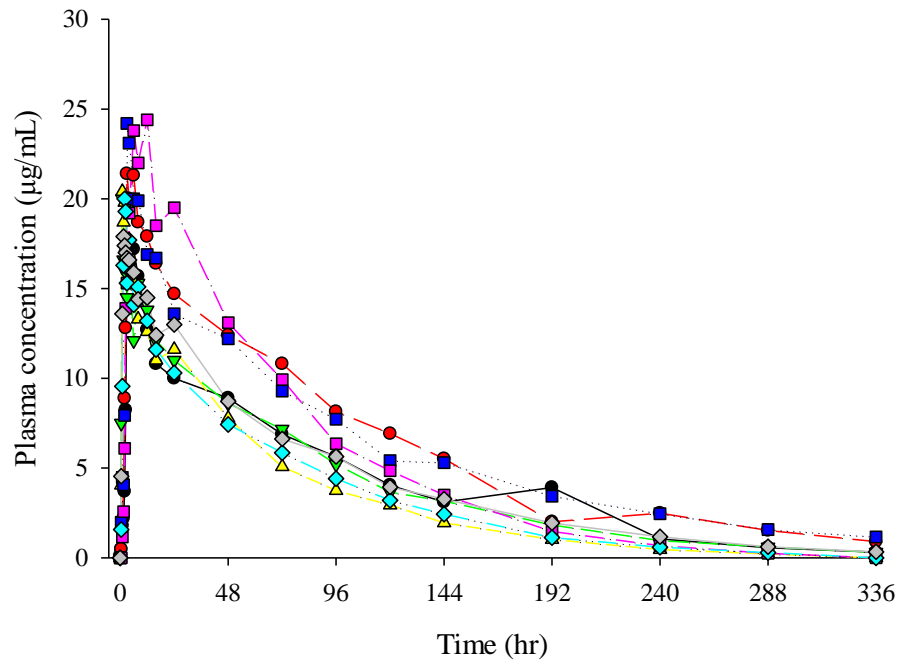


(b) Participants with mild renal impairment

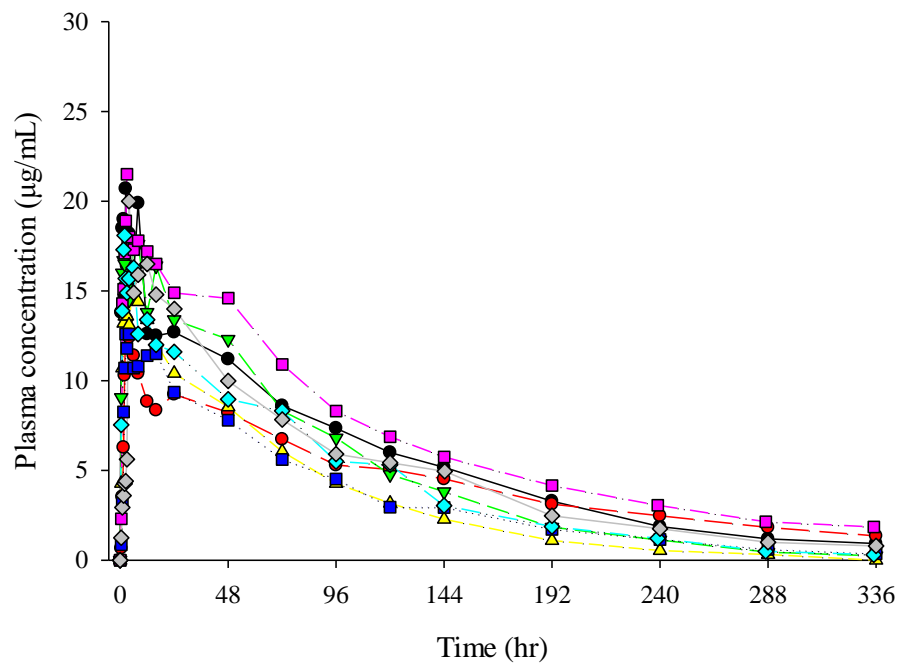


Supplemental Figure S1 (continued)

(c) Participants with moderate renal impairment



(d) Participants with severe renal impairment



Supplemental Table S1

## Incidence of treatment-emergent adverse events by severity

System organ class Preferred term	Normal renal function (N = 8)	Mild renal impairment (N = 8)	Moderate renal impairment (N = 8)	Severe renal impairment (N = 8)	Overall (N = 32)
Any TEAE; n (%)					
Mild	0	2 (25.0)	1 (12.5)	0	3 (9.4)
Moderate	0	1 (12.5)	1 (12.5)	0	2 (6.3)
Severe	0	0	0	0	0
Blood and lymphatic system disorders					
Anaemia					
Mild	0	1 (12.5)	0	0	1 (3.1)
Moderate	0	0	0	0	0
Severe	0	0	0	0	0
Gastrointestinal disorders					
Dry mouth					
Mild	0	1 (12.5)	0	0	1 (3.1)
Moderate	0	0	0	0	0
Severe	0	0	0	0	0
General disorders and administration site conditions					
Vessel puncture site haemorrhage					
Mild	0	1 (12.5)	1 (12.5)	0	2 (6.3)
Moderate	0	0	0	0	0
Severe	0	0	0	0	0
Investigations					
Glomerular filtration rate decreased					
Mild	0	0	0	0	0
Moderate	0	0	1 (12.5)	0	1 (3.1)
Severe	0	0	0	0	0
Metabolism and nutrition disorders					
Hypertriglyceridaemia					
Mild	0	0	0	0	0
Moderate	0	1 (12.5)	0	0	1 (3.1)
Severe	0	0	0	0	0

TEAE = treatment emergent adverse event.

Supplemental Table S2

## Incidence of treatment-related adverse events by severity

System organ class Preferred term	Normal renal function (N = 8)	Mild renal impairment (N = 8)	Moderate renal impairment (N = 8)	Severe renal impairment (N = 8)	Overall (N = 32)
Any treatment-related TEAE; n (%)					
Mild	0	1 (12.5)	0	0	1 (3.1)
Moderate	0	0	1 (12.5)	0	1 (3.1)
Severe	0	0	0	0	0
Gastrointestinal disorders					
Dry mouth					
Mild	0	1 (12.5)	0	0	1 (3.1)
Moderate	0	0	0	0	0
Severe	0	0	0	0	0
Investigations					
Glomerular filtration rate decreased					
Mild	0	0	0	0	0
Moderate	0	0	1 (12.5)	0	1 (3.1)
Severe	0	0	0	0	0

TEAE = treatment emergent adverse event.

A treatment-related AE was defined as an AE that could be reasonably explained as having been caused by the study intervention.