Supplementary Information (SI)

Clinical Pharmacology of Asciminib: A Review

Clinical Pharmacokinetics

Matthias Hoch[1], Felix Huth[1], Paul W. Manley[1], Ioannis Loisios Konstantinidis[1], Francois Pierre Combes[2], Ying Fei Li[2], Yunlin Fu[2], Sherwin K. B. Sy[2], Vanessa Obourn[3], Abhijit Chakraborty[2], Florence Hourcade-Potelleret[1]

[1]Novartis Biomedical Research, Basel, Switzerland

[2]Novartis Pharmaceuticals, East Hanover, NJ, USA

[3]Novartis Development, Cambridge, MA, USA

Corresponding author:

Matthias Hoch, PhD

Novartis Biomedical Research, Fabrikstrasse 2, CH-4056 Basel, Switzerland

Email: Matthias.hoch@novartis.com

Supplementary Table 1: Population pharmacokinetic parameters of asciminib and covariate relationships.

Definition of parameters	Parameter (unit)	Variability† SD
Lag time	$T_{lag}(h) = 0.38$	-
Absorption rate constant	$k_a(1/h) = 1.96 \cdot \exp[-1.02, if\ formulation\ is\ capsule]$	0.79
Apparent Clearance (CL/F)	$CL\ (L/h) = 6.31 \cdot \exp\left[-0.34 \cdot \log\left(\frac{NTDD}{80\ mg}\right) + 0.31 \cdot \log\left(\frac{aGFR}{90.4\ mL/min}\right) + 0.75 \cdot \log\left(\frac{BW}{70\ kg}\right)\right]$	0.42
Apparent Central compartment volume (V/F)	$V_c(L) = 46.5 \cdot \exp\left[1 \cdot \log\left(\frac{BW}{70\ kg}\right)\right]$	0.42
Apparent Intercompartment clearance (Q/F)	$Q\ (L/h) = 6.51$	-
Apparent Peripheral compartment volume (Vp/F)	$V_p(L) = 64.5$	1.57
Relative bioavailability	$F = 1$	-
Correlations	$Corr(V_c, CL)$	0.57

NTDD, nominal total daily dose in mg; aGFR, actual glomerular filtration rate in mL/min; BW, body weight in kg; SD, standard deviation

† Variability incorporated as exponential model

Reference:

Li YF, Combes FP, Hoch M, Lorenzo S, Sy SKB, Ho YY. Population Pharmacokinetics of Asciminib in Tyrosine Kinase Inhibitor-Treated Patients with Philadelphia Chromosome-Positive Chronic Myeloid Leukemia in Chronic and Acute Phases. Clin Pharmacokinet. 2022 Oct;61(10):1393-403.