

**Electronic supplementary material**

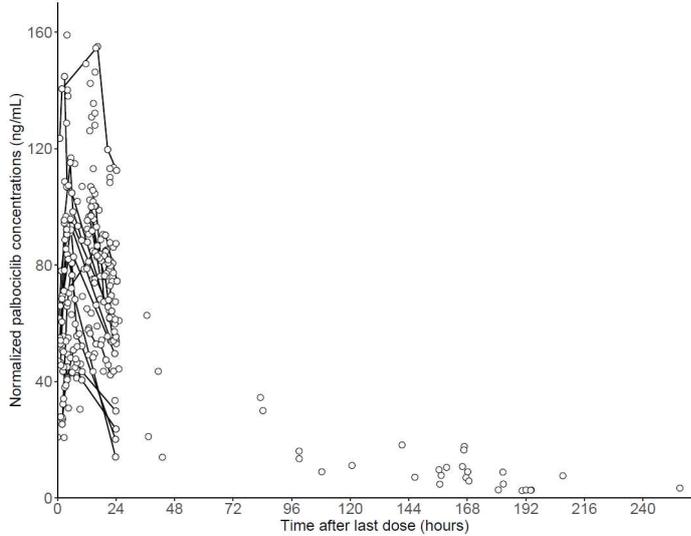
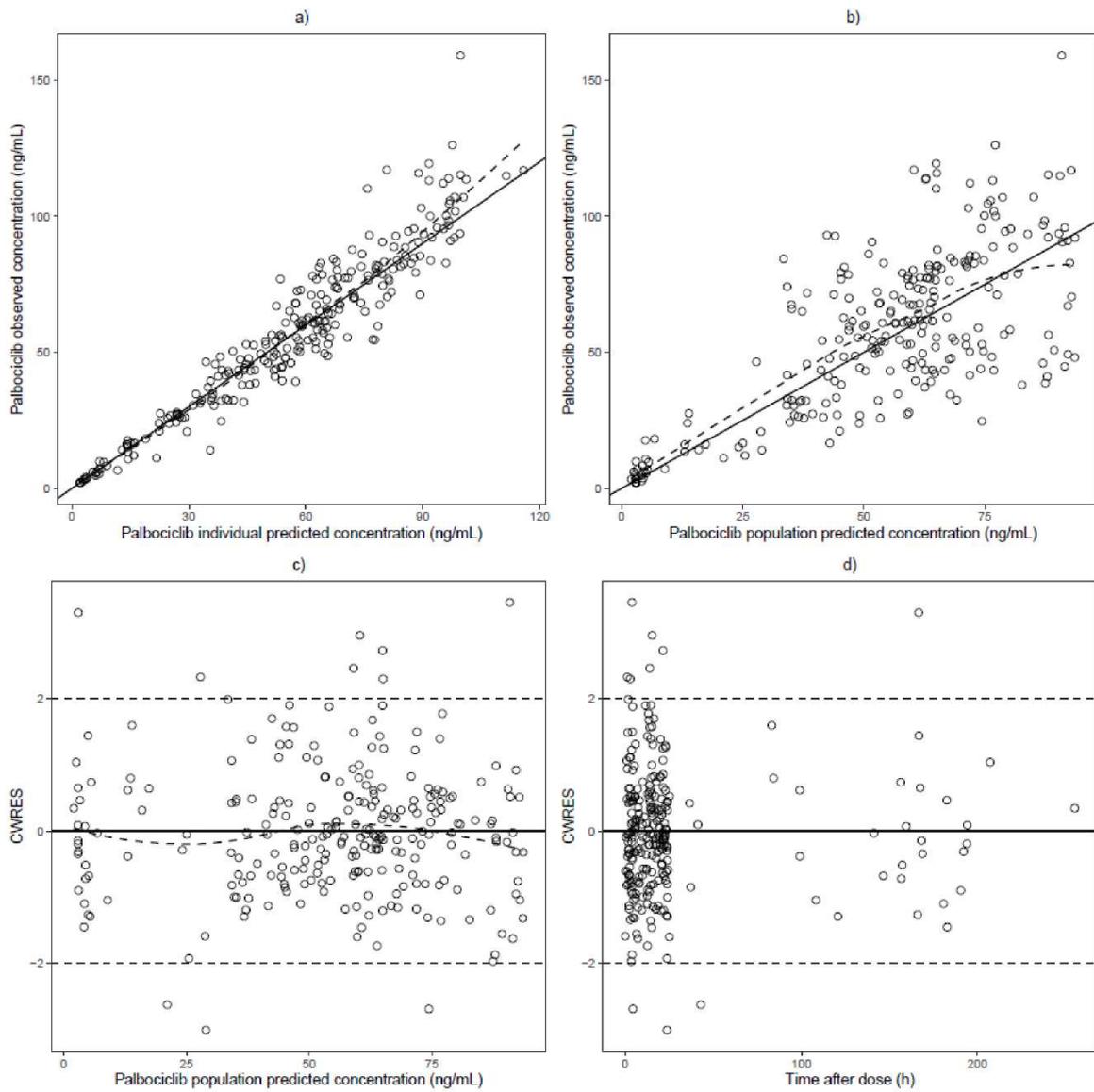


Figure S1. Normalized observed palbociclib plasma concentrations-time profiles. Concentrations are normalized for a daily dose of 125 mg. Concentrations from patients with rich sampling are joined with black lines.

(A)



**(B)**

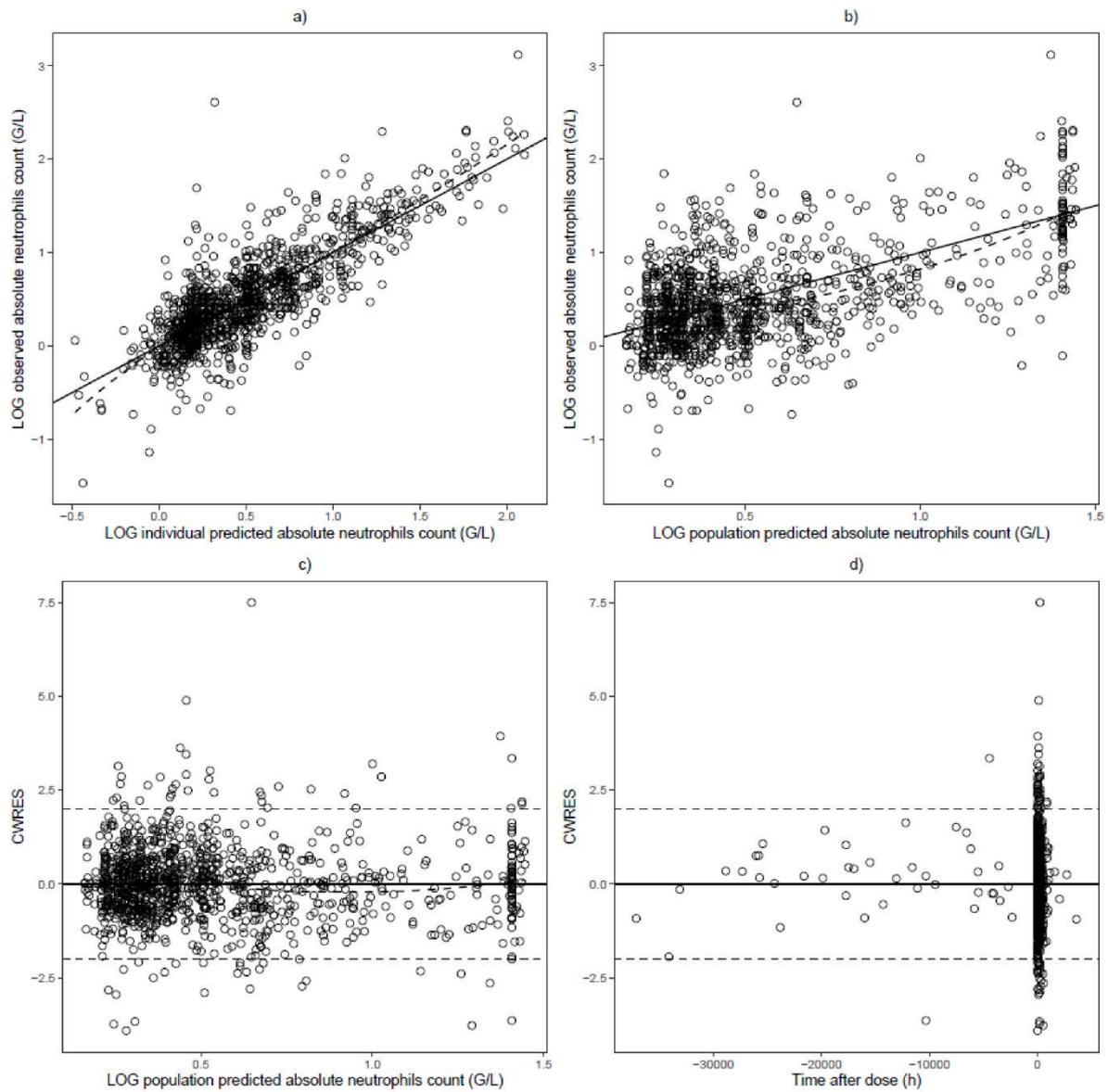


Figure S2: Goodness-of-fit plots of the final model for palbociclib concentrations (A) and ANC time course (B). Loess smooth curves are printed in grey. a) Observed concentrations vs. individual predictions; line of identity is printed in black. b) Observed concentrations vs. population predictions; identity line is printed in black. c) Conditional weighted residuals (CWRES) vs. population predictions; ordinate value zero line is printed in black. d) CWRES vs. time post-dose; ordinate value zero line is printed in black

Table S1: Parameter estimates of the final palbociclib PK-only model with bootstrap results.

Parameter	Final model		Bootstrap (n=2000 samples)	
	Estimate	RSE (%)	Median	CI <sub>95%</sub>
$k_a$ ( $h^{-1}$ )	0.73	34	0.78	0.39-3.27
$\omega_{k_a}$ (CV%)	126	25	121	33-458
ALAG (h)	1.9	4	1.9	1.7-2.6
CL ( $L \cdot h^{-1}$ )	68	5	68.0	61-75
$\omega_{CL}$ (CV%)	30	12	29	22-36
CL <sub>IPP,no food</sub> ( $L \cdot h^{-1}$ )	106	9	106	88-144
$V_c$ (L)	2730	10	2700	2136-3229
$\omega_{V_c}$ (CV%)	36	24	34	14-56
Q ( $L \cdot h^{-1}$ )	5.1	43	5.2	3.2-23.7
$V_p$ (L)	717	10	807	655-2931
Proportional residual error (%)	18	19	17	14-20

ALAG: absorption lag-time, CI: confidence interval, CL: clearance, CL<sub>IPP,nofood</sub>: clearance with concomitant coadministration of IPP under fasting conditions, CV: coefficient of variation,  $k_a$ : absorption rate constant, RSE: relative standard error, Q: inter-compartmental clearance,  $V_c$ : central volume of distribution,  $V_p$ : peripheral volume of distribution,  $\omega$ : between subject variability.

Table S2: Results from the Cox analysis.

Parameter	Coefficient	Hazard ratio	p-value
AUC <sub>cum90</sub>	0.030	1.030	0.682
Older age (>65 years)	-0.872	0.418	0.048
Interaction AUC <sub>cum90</sub> *older age	-0.125	0.883	0.266

Results are presented for an increase in 100 AUC units.