Pharmacokinetic/pharmacodynamic modelling of the antimalarial effect of Actelion-451840 in an induced blood stage malaria study in healthy subjects

Andreas Krause[1], Jasper Dingemanse[1], Alexandre Mathis[1], Louise Marquart[2], Jörg J. Möhrle[3], James S. McCarthy[2]

Figure S1. PD regression: observed data and individual regression fits

ID = R001

PRR (95% CI): 63 (38 - 104)
Adjusted R-squared = 0.95
Pr = 2e-10

ID = R002

PRR (95% CI): 615 (85 - 4454)
Adjusted R-squared = 0.81
Pr = 2e-04

ID = R003

PRR (95% CI): 49 (25 - 96)
Adjusted R-squared = 0.9
Pr = 4e-08

ID = R004

PRR (95% CI): 776 (116 - 5181)
Adjusted R-squared = 0.85
Pr = 2e-04

ID = R005

PRR (95% CI): 4087 (221 - 75609)
Adjusted R-squared = 0.77
Pr = 5e-04

ID = R006

PRR (95% CI): 319 (92 - 1102)
Adjusted R-squared = 0.9
Pr = 2e-05

ID = R007

PRR (95% CI): 68 (44 - 106)
Adjusted R-squared = 0.96
Pr = 9e-11

ID = R008

PRR (95% CI): 36 (13 - 98)
Adjusted R-squared = 0.79
Pr = 1e-05

Axis labels: log10(parasitemia) on the y-axis; Time (hrs) on the x-axis.

Legend: O Points for regression   X Points omitted   — Optimal Regression line   - - 95% Confidence interval
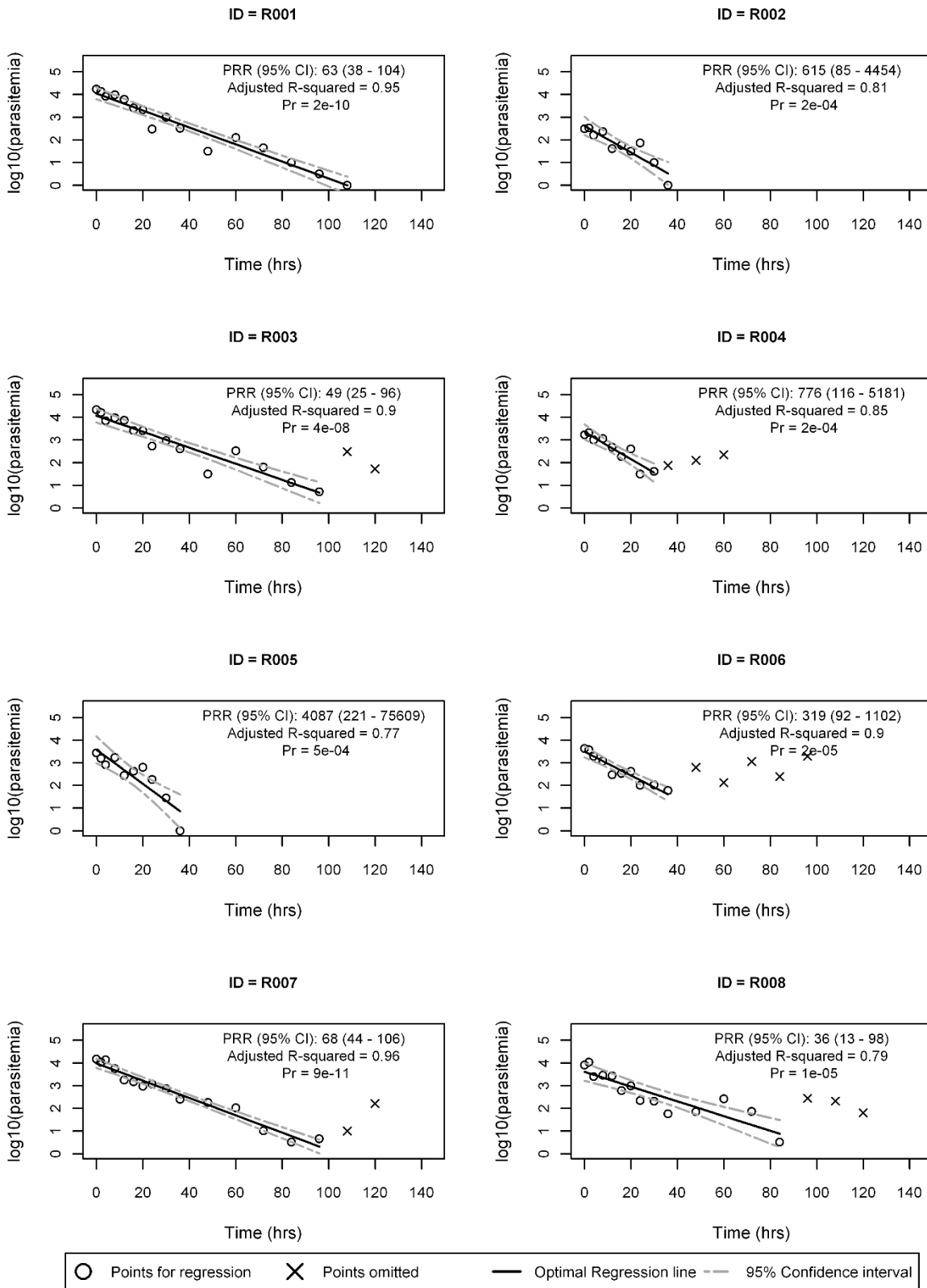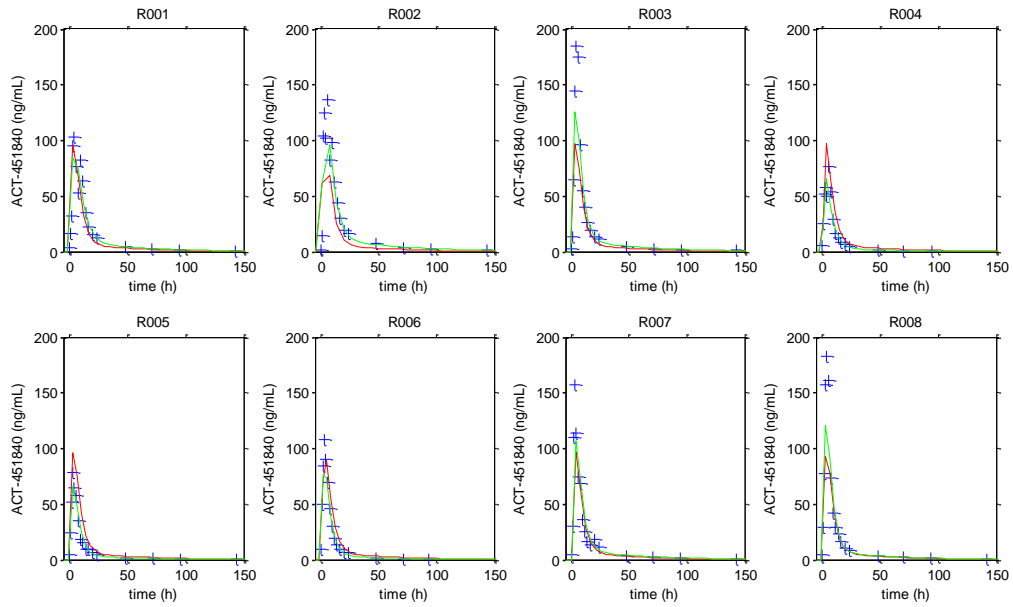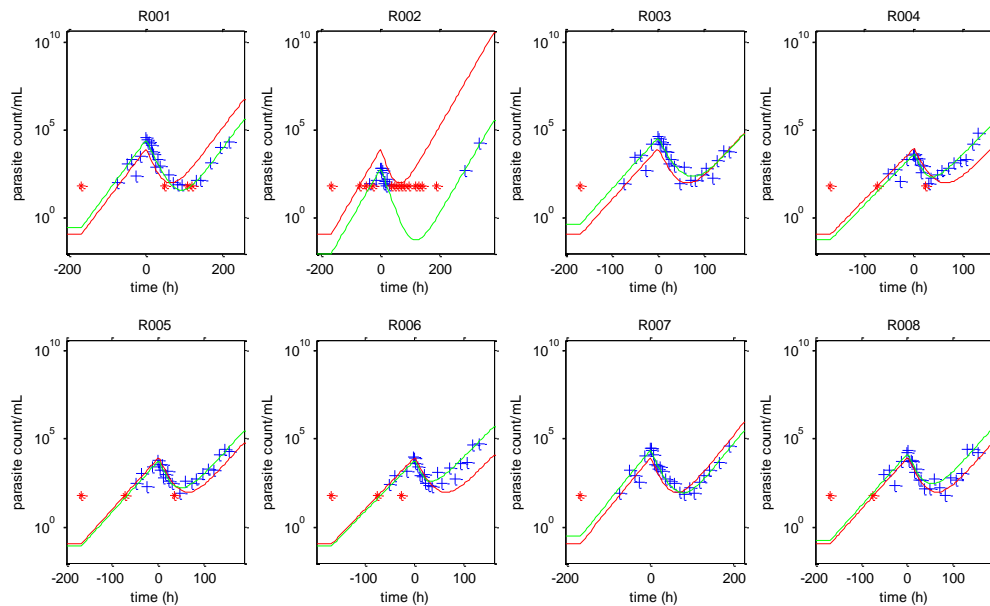
Figure S2. Model diagnostics PK: observed concentration and model fits by subject

Blue symbols indicate observed data, red lines population fits, and green lines individual fits.

Figure S3. Model diagnostics PD: observed parasite count and model fits

Blue symbols indicate observed data, red symbols data below the limit of quantification, red lines population fits, and green lines individual fits.

Figure S4. Model diagnostics PK: prediction-corrected VPC (linear and logarithmic scale)

Figure S5. Model diagnostics PD: prediction-corrected VPC (linear and logarithmic scale)
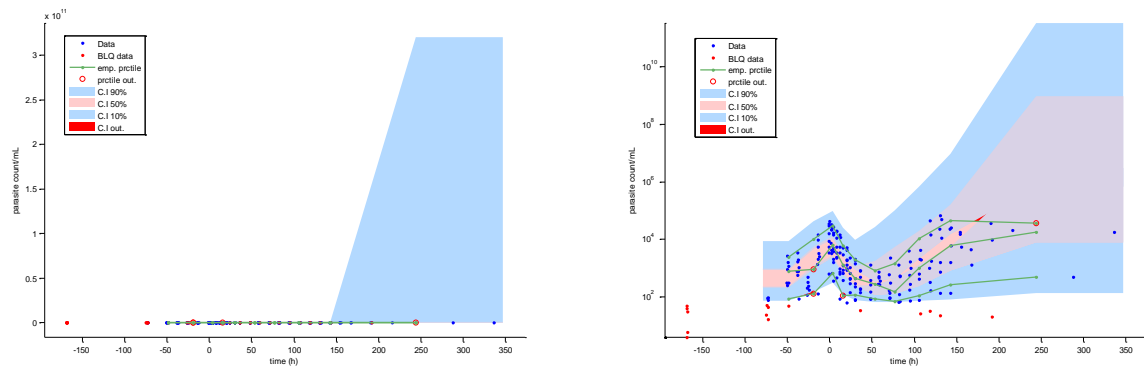
Figure S6. Model diagnostics PK: Observed vs. predicted drug concentration (linear and logarithmic scale)
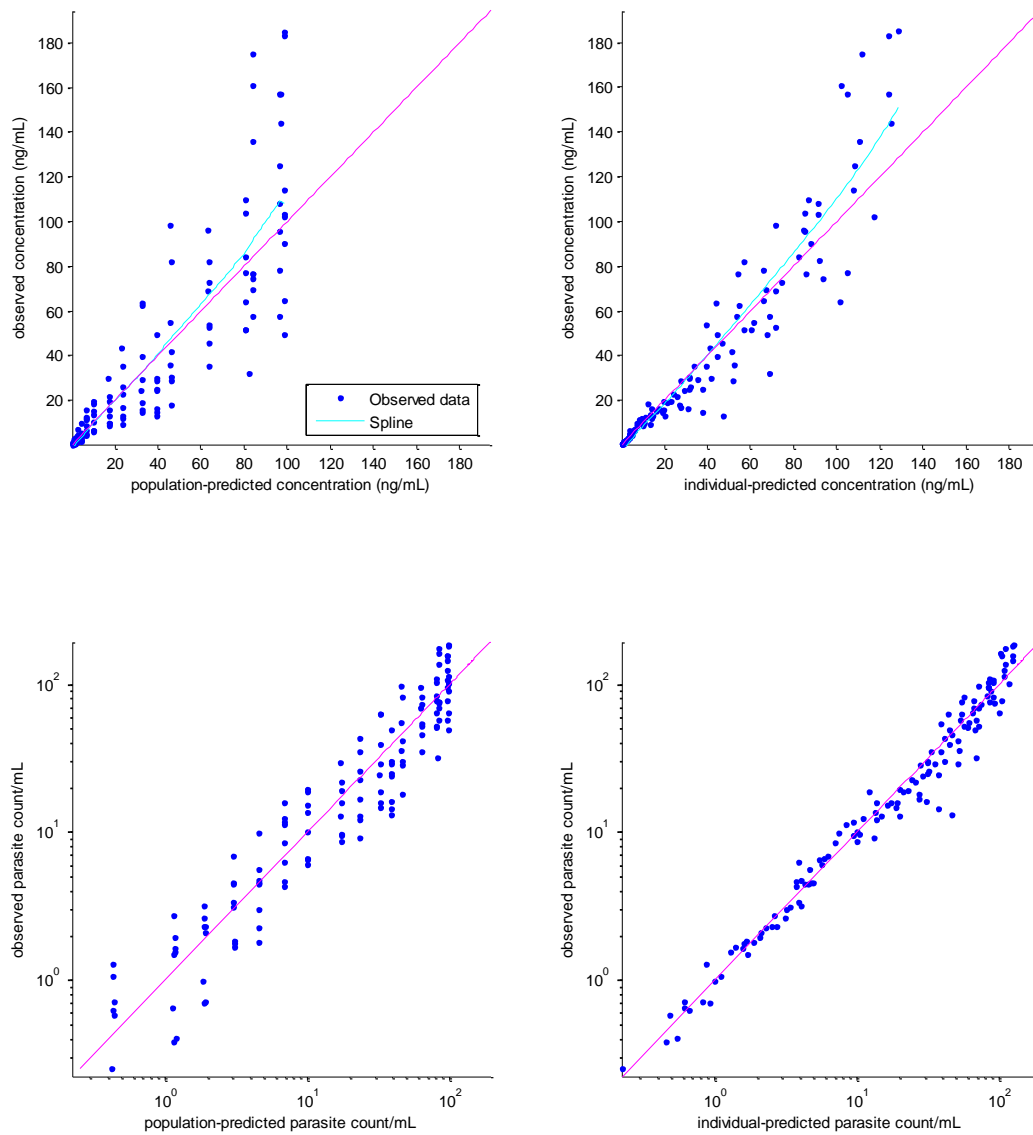
Figure S7. Model diagnostics PD: Observed vs. predicted parasite count (linear and logarithmic scale)
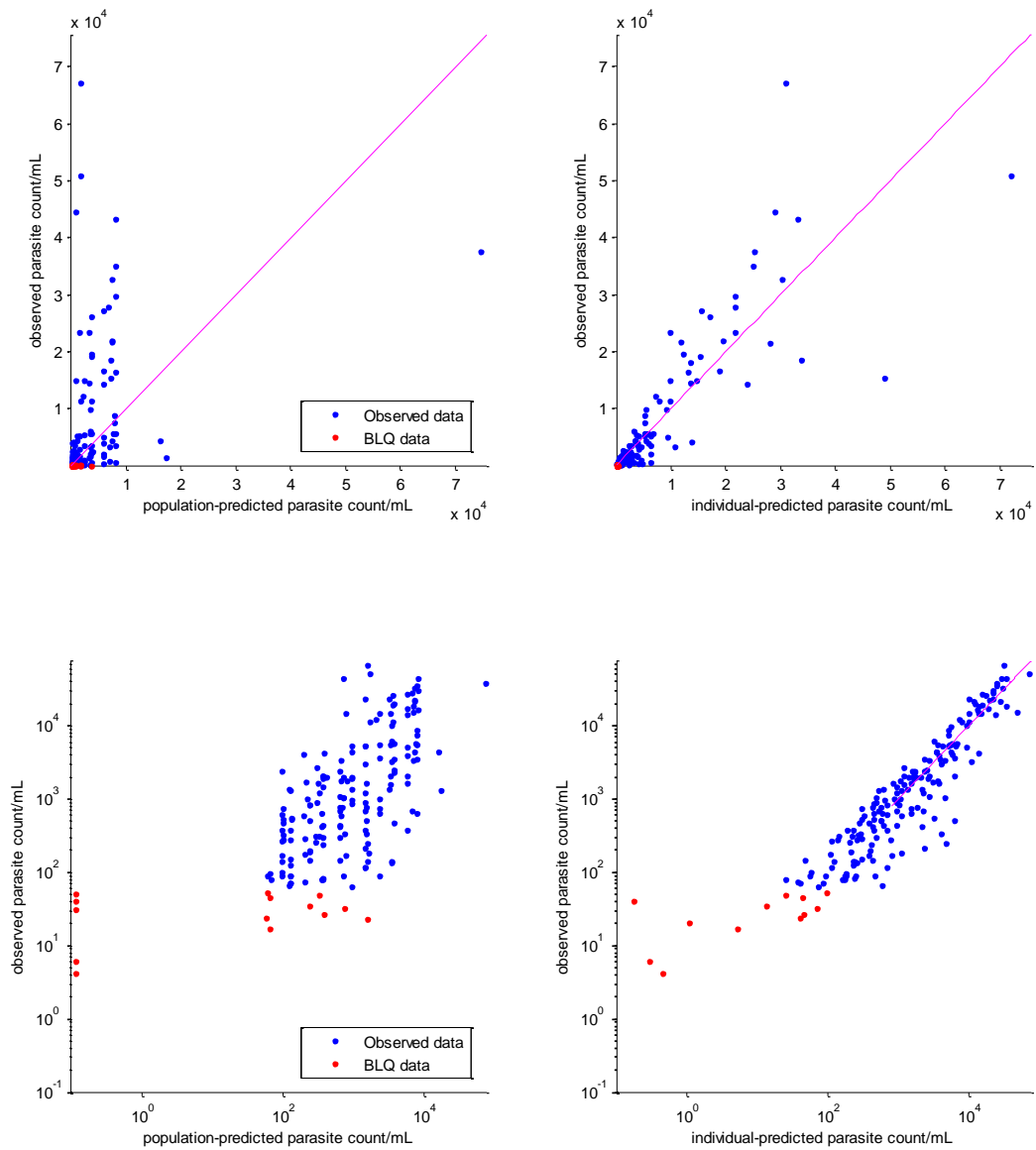
Figure S8. Model diagnostics PK: Residual diagnostics. Individual-weighted residuals (IWRES) and normalised prediction distribution errors (NPDE) vs. time and predicted concentration, residual distribution (theoretical distribution line and empirical histogram), quantile-quantile plot of empirical residual quantiles vs. normal distribution
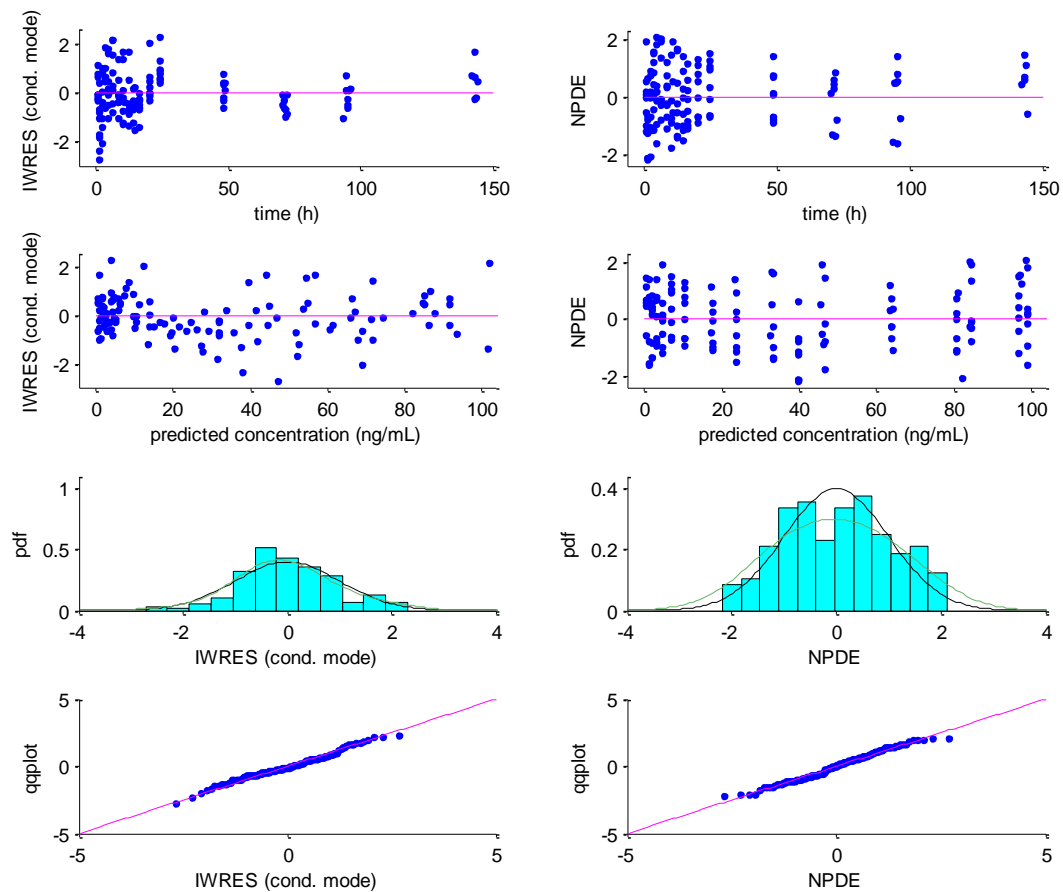
Figure S9. Model diagnostics PD: Residual diagnostics. Residual diagnostics. Individual-weighted residuals (IWRES) and normalised prediction distribution errors (NPDE) vs. time and predicted concentration, residual distribution (theoretical distribution line and empirical histogram), quantile-quantile plot of empirical residual quantiles vs. normal distribution