Supplementary Material

Smit MR, Ochomo EO, Waterhouse D, et al. **Pharmacokinetics-Pharmacodynamics of High-Dose Ivermectin with Dihydroartemisinin-Piperaquine on Mosquitocidal Activity and QT-prolongation (IVERMAL).** *Clinical Pharmacology & Therapeutics 2018.* http://doi.org/10.1002/cpt.1219

Contents

Supplementary Texts

Text S1: Methods for drug analytical quantification of ivermectin and piperaquine

Ivermectin Assay (LC-MS/MS):

Plasma samples were taken out of the -80°C freezer and allowed to come to room temperature. A 60 µL aliquot of each sample was assayed alongside plasma calibration curve standards (5-320 ng/mL) and quality control samples (low 15 ng/mL, medium 150 ng/mL and high 250 ng/mL). A 60 µL aliquot of each plasma sample was taken and placed into 1.5 ml Eppendorf tubes. 940 µL of acetonitrile containing doramectin 100 ng/ml was added as internal standard (IS). Samples were then mixed on a vortexer for 10 seconds and subsequently left to settle for 5 minutes. Following, the samples were centrifuged for 10 minutes at 14,000 rpm. The resulting supernatants were then taken and placed into clean and dry 10 mL glass test-tubes containing 1 ml of water. 3 mL of a 1/1/1 mix of dichloromethane/hexane/methyl-tert-butyl ether mix was added, which was subsequently vortexed for 10 seconds, followed by a 10-minute centrifugation at 4,000 rpm. The resultant supernatants were then removed and placed into clean and dry 7 mL glass test-tubes before being evaporated until dry using a gentle stream of nitrogen free air at 30°C. The dried down supernatants were then reconstituted in 60 µL of mobile phase and then vortexed for 10 seconds. The reconstitute samples were then transferred to clean glass insert vials and then centrifuged at 4,700 rpm for 5 minutes. Samples were then injected (20 µL) onto 100 x 2.1 mm, 1.9 (µm) particle size, Hypersil GOLD (Thermo Scientific) column using an isocratic gradient method of acetonitrile/0.1% formic acid (90/10) at a flowrate of 400 µL/min with a column oven set at 30^{o}C. For the analysis and quantification of ivermectin from capillary plasma samples the above procedure was revalidated using a 30 µL aliquot of capillary plasma. The extraction procedure, calibration curve standards, quality control levels were kept the same except for the lower limit of quantification (LLOQ) which was changed from 5 ng/mL to 10 ng/mL. The method was then revalidated for the reduced aliquot of capillary plasma.

Piperaquine Assay (LC-MS/MS):

Plasma samples were taken out of the -80°C freezer and allowed to come to room temperature. A 10 µL aliquot of each sample was assayed alongside plasma calibration curve standards (1.5-600 ng/mL) and quality control samples (low 4.5 ng/mL, medium 250 ng/mL and high 500 ng/mL). Using a 96-well filter plate, 300 µL of a perception solution (80/20 acetonitrile/methanol) was added to each well, containing 10 ng/ml piperaquine-d6 as internal standard (IS). A 10 µL aliquot of each plasma sample was then added to a corresponding well. The filter plate containing the IS and plasma samples was then transferred to a 96-well vacuum manifold. A corresponding 96-well plate was then placed inside the vacuum manifold to catch the subsequent filtrate after the vacuum had been applied. The resultant filtrate was then evaporated until dry using a gentle stream of nitrogen free air at 30°C. The dried down supernatants were then reconstituted in 60 µL of mobile phase and then vortexed for 10 seconds. The reconstitute samples were then transferred to clean glass insert vials, followed by centrifuging at 4,700 rpm for 5 minutes. Samples were subsequently injected (20 µL) onto 50 x 2 mm, 3 (µm) particle size, Gemini (Phenomenex) column using an isocratic gradient of acetonitrile/2.5 mM ammonium bicarbonate (pH 7) (85/15) at a flowrate of 500 µL/min with a column oven set at 30^{o}C. The capillary plasma samples were analysed and quantified using the exact same method as the venous samples.

Text S2: Supplementary equations

$$\frac{dX_1}{dt} = -k_a \cdot X_1 \quad \text{..... (Eq. S1)}$$

$$\frac{dX_2}{dt} = k_a \cdot X_1 - (k_e + k_{23} + k_{24}) \cdot X_2 + k_{32} \cdot X_3 + k_{42} \cdot X_4 \quad \text{..... (Eq. S2)}$$

$$\frac{dX_3}{dt} = k_{23} \cdot X_2 - k_{32} \cdot X_3 \quad \text{..... (Eq. S3)}$$

$$\frac{dX_4}{dt} = k_{24} \cdot X_2 - k_{42} \cdot X_2 \quad \text{..... (Eq. S4)}$$

$$C_{venous} = \frac{X_2}{V_c/F} \quad \text{..... (Eq. S5)}$$

$$C_{capillary} = \left(\frac{X_2}{V_c/F}\right) \cdot CapVen\ ratio \quad \text{..... (Eq. S6)}$$

$$k_e = \frac{CL}{V_c} \quad \text{..... (Eq. S7)}$$

$$Q_1 = k_{23} \cdot V_c \quad \text{..... (Eq. S8)}$$

$$V_{P1} = \frac{Q_1}{k_{32}} \quad \text{..... (Eq. S9)}$$

$$Q_2 = k_{24} \cdot V_c \quad \text{..... (Eq. S10)}$$

$$V_{P2} = \frac{Q_2}{k_{42}} \quad \text{..... (Eq. S11)}$$

$$CL = CLi \cdot \left[\frac{patient\ weight}{60}\right]^{0.75} \quad \text{..... (Eq. S12)}$$

$$V_c = V_c i \cdot \left[\frac{patient\ weight}{60}\right] \quad \text{..... (Eq. S13)}$$

Where $\boldsymbol{k_a}$ is the absorption rate in hours. $\boldsymbol{X_1}$, $\boldsymbol{X_2}$, $\boldsymbol{X_3}$ and $\boldsymbol{X_4}$ respectively, represent the drug mass (in grams) in the gut (dose compartment), the blood (central compartment), peripheral compartment 1, and for piperaquine only peripheral compartment 2. $\boldsymbol{F}$ is the bioavailable fraction of the drug. $\boldsymbol{CL}$ represents the drug clearance rate from the central compartment. $\boldsymbol{Q_1}$ and $\boldsymbol{Q_2}$ represent the intercompartmental clearance rates between the central and peripheral compartments 1 and 2, respectively. $\boldsymbol{V_c}$, $\boldsymbol{V_{P1}}$ and $\boldsymbol{V_{P2}}$ represent the apparent volumes of distribution of the drug in the central compartment and peripheral compartments 1 and 2, respectively. $\boldsymbol{t}$ represents time in hours, $\boldsymbol{C}$ the concentration in grams per liter, and $\boldsymbol{CL}$ and $\boldsymbol{V_c}$ are the weight adjusted individual clearance ($\boldsymbol{CLi}$) and individual volume of distribution ($\boldsymbol{V_c i}$), respectively. $\boldsymbol{Q_1}$, $\boldsymbol{V_{P1}}$, $\boldsymbol{Q_2}$ and $\boldsymbol{V_{P2}}$ values were assumed to be weight independent as weight scaling for these parameters resulted in similar or poorer PK predictions.

Capillary concentrations were modelled simultaneously with venous ones using ***Equation S6***, where ***CapVen*** ratio represents the parameter that quantifies the ratio between capillary and venous concentration.

Absorption model

The absorption model used was a standard absorption model with an absorption rate k_a estimated for ivermectin and fixed for piperaquine. No other absorption models (e.g. including transit compartments and lag times) were attempted due to the limited number of concentrations at <2 hours post dosing.

Error model

For ivermectin and piperaquine we used a lambda error model (fixed-effect process noise multiplier of assay error), with a fixed L value set to 0.1 for all observations. The values (C0, C1, C2, C3) were used to estimate the error (standard deviation) of each observation for appropriate weighting in the fitting process, using the equation: $SD = C0 + C1*[obs] + C2*[obs]^2 + C3*[obs]^3$ where [obs] is the observation (Neely 2012). For ivermectin, C0 was set to 5 or 10 (equal to LLOQ, for venous and capillary samples respectively) and C1 to 0.15 or 0.20 (assuming 15% or 20% intra-assay variability, the latter for concentrations within 10% of LLOQ). For piperaquine, C0 was set to 1.5 (equal to LLOQ, for both venous and capillary samples) and C1 to 0.15 or 0.20 (as per ivermectin C1). C2 and C3 were set to zero for both drugs.

Text S3: IVERMAL dose-response calculator

The IVERMAL dose-response calculator is available as an Excel file:

1) Attached: in Adobe click "Document" (top ribbon), and then "Attachments" (left sidebar).
2) On the publication's webpage: http://doi.org/10.1002/cpt.1219

Screenshot:

IVERMAL dose-response calculator

Drug properties:

EC50:	15.9	ng/mL
Emin:	3.9	deaths/100 days
Emax:	49.5	deaths/100 days
Emin+Emax:	53.4	deaths/100 days

Calculator 1: What is the mosquitocidal activity of a specified drug concentration?

Concentration:	0.16	ng/mL
Effect:	4.4	deaths/100 days
Percentile:	1%	of maximum effect
Incidence rate ratio:	1.13	fold increased mortality rate

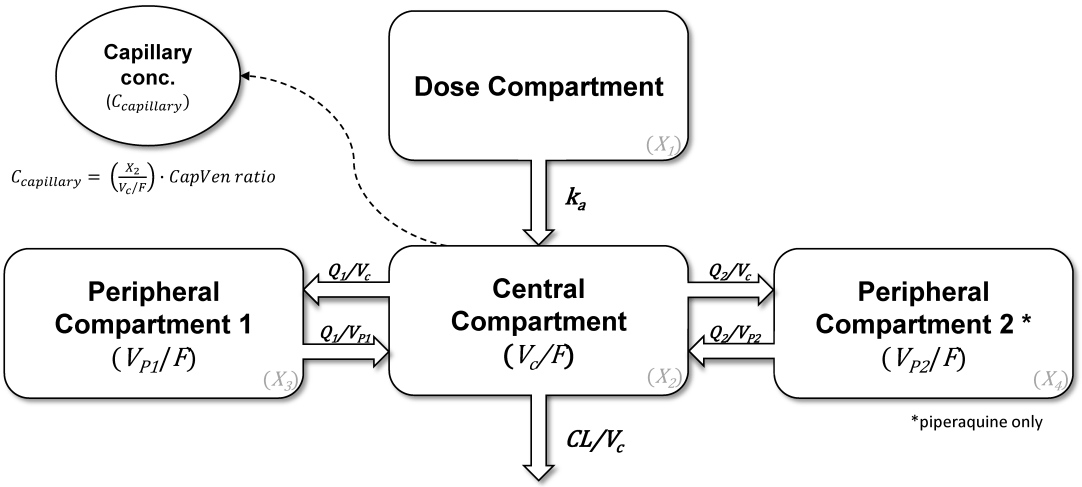
Calculator 2: Which drug concentration is required to achieve a desired mosquitocidal effect?

Incidence rate ratio:	1.33	fold increased mortality rate
Effect:	5.2	deaths/100 days
Percentile:	3%	of maximum effect
Concentration:	0.42	ng/mL

1. Instructions: insert values into the bold boxes
2. Ref: Smit MR (2018) IVERMAL PK-PD Model

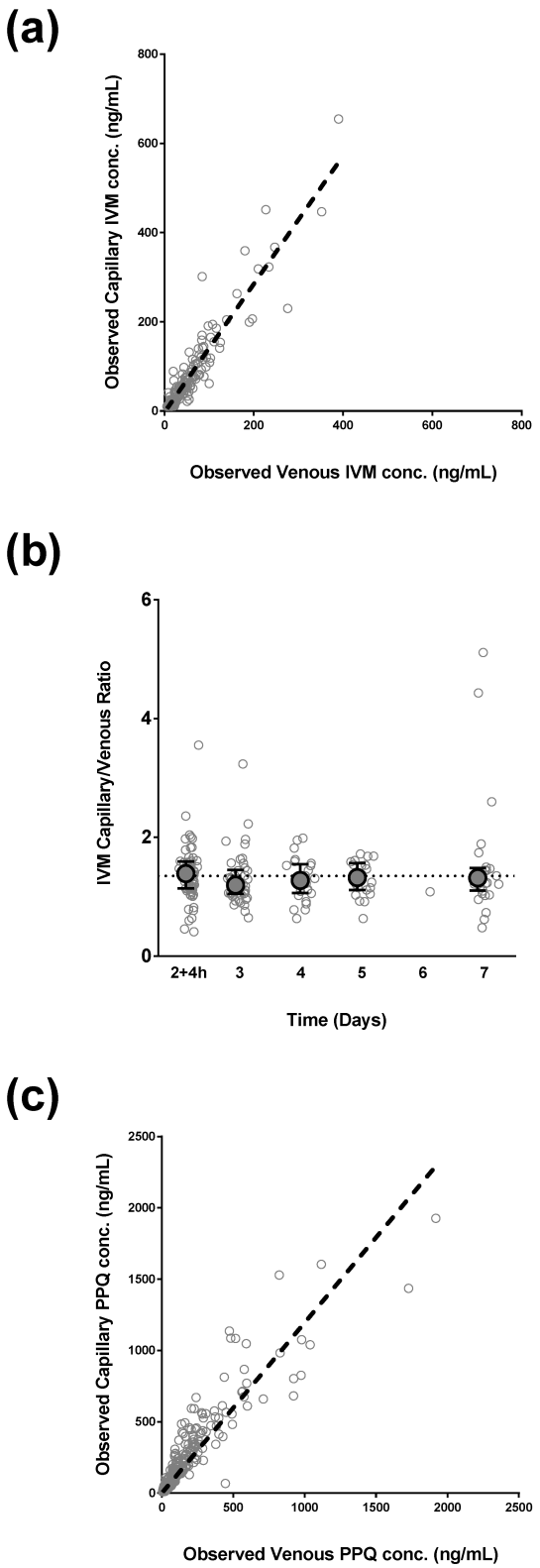
Supplementary Figures

Figure S1: Flowchart of pharmacokinetic model applied separately to both ivermectin and piperaquine



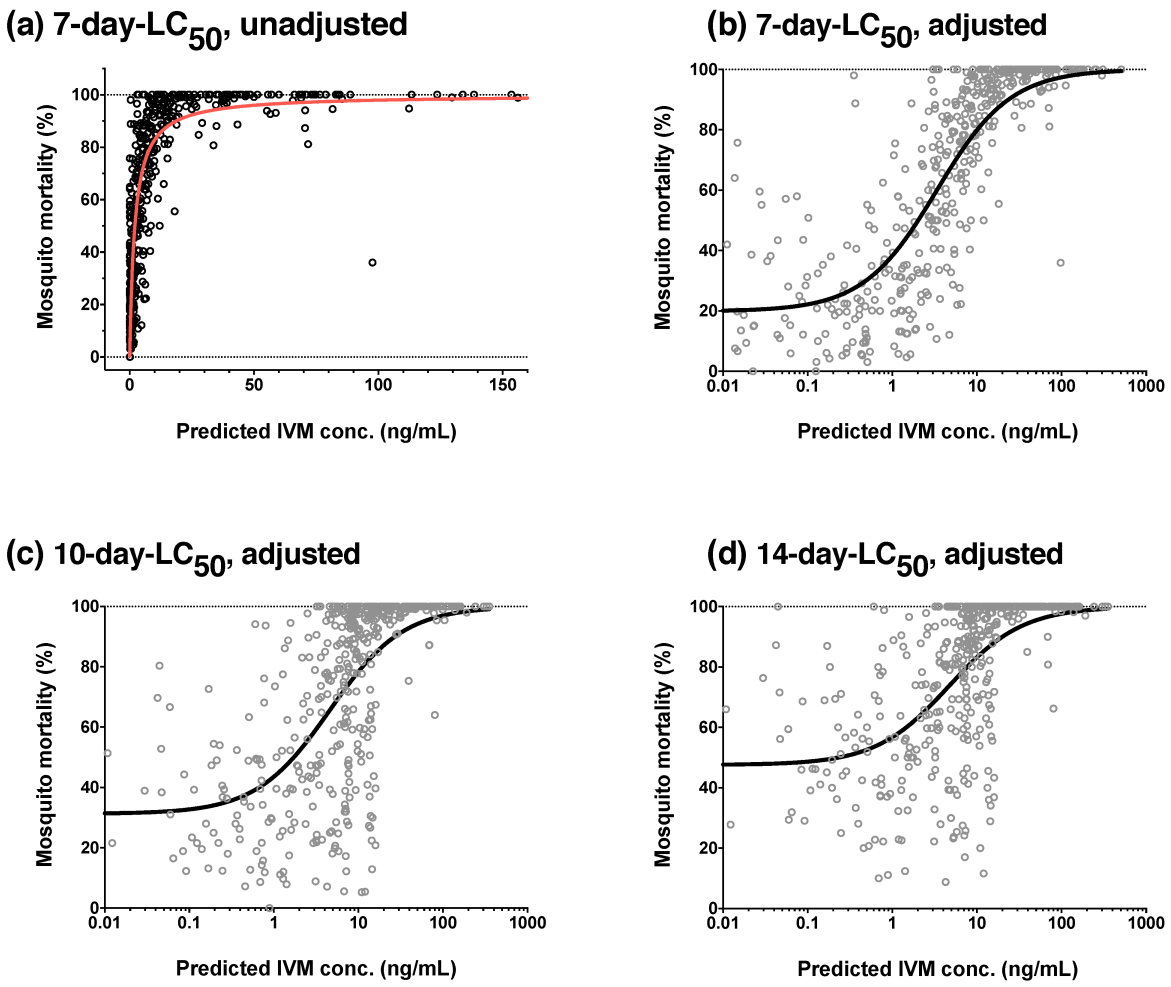
Where k_a is the absorption rate in hours. X_1, X_2, X_3, and X_4, respectively, represent the drug mass (in grams) in the gut (dose compartment), the blood (central compartment), and the two extra peripheral compartments (one for ivermectin). F is the bioavailable fraction of the drug. ***CL*** represents the drug clearance rate from the central compartment. Q_1 and Q_2 represent the intercompartmental clearance rates between the central and peripheral compartments 1 and 2, respectively. V_c, V_{P1} and V_{P2} represent the apparent volumes of distribution of the drug in the central compartment and peripheral compartments 1 and 2, respectively. ***CapVen ratio*** represents the parameter that quantifies the ratio between capillary and venous concentration.

Figure S2: Capillary vs. venous concentration ratios for ivermectin and piperaquine



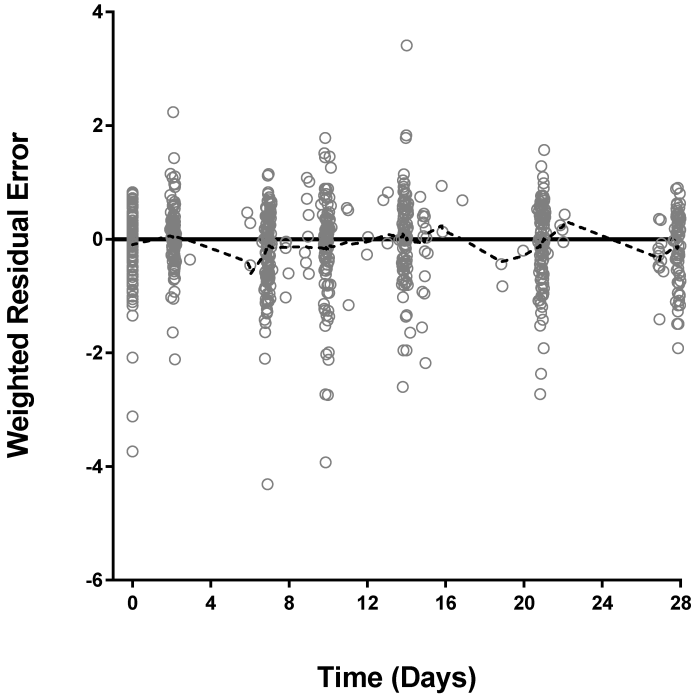
Open circles represent observed individual ratios for each patient at each time point. (a) Ivermectin capillary-venous ratio based on simultaneous PK-PD population model, median [IQR]: 1.33 [0.98-1.63]. (b) Ivermectin capillary-venous ratio over sampling time (ball-whiskers indicate median±IQR per sampling day) (c) Piperaquine capillary-venous ratio based on PK population model, median [IQR]: 1.54 [1.1-2.8].

Figure S3: Ivermectin vs. mosquito mortality (%) dose-response curves (LC_{50} method)



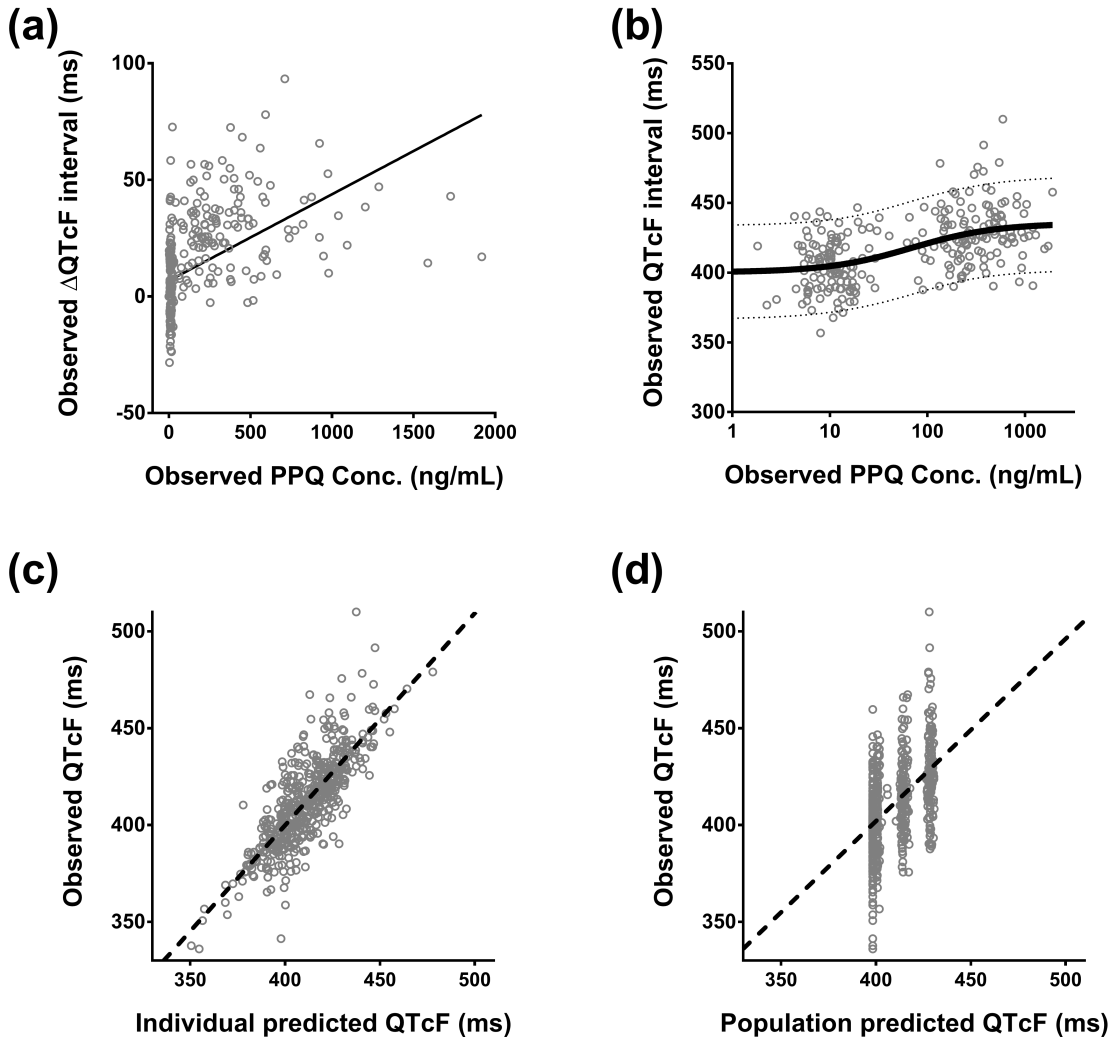
Using data from all study visits, mosquito mortality (expressed as a percentage) was assessed at the specified number of days (7, 10, or 14) post-feeding. In unadjusted models, baseline mortality is disregarded by forcing the model to pass through the origin. In adjusted models, baseline mortality is considered, where the Lethal Concentration 50% (LC_{50}) is the concentration required to kill 50% of mosquitoes that would have otherwise survived the assay without ivermectin exposure. LC_{50} values are shown in Table S3.

Figure S4: Residual analysis of mosquito mortality rates (i.e., ivermectin's pharmacodynamic effect) over time, as predicted by the simultaneous PK/PD model vs. observed data



The lack of a time bias between study visits (Kruskal-Wallis: $p<0.05$; n=109-141) indicates a consistent concentration-effect relationship ($\boldsymbol{EC_{50}}$ and $\boldsymbol{E_{max}}$) through-out the study duration.

Figure S5: Piperaquine vs. QTcF dose-response curves



(a) Linear relationship between pooled (all arms) observed venous piperaquine concentration (ng/mL) and observed change in QTcF (ΔQTcF) from baseline in ms (n=251). **(b)** Sigmoidal relationship between pooled observed venous piperaquine concentrations and observed QTcF (n=251) using a dynamic 3-parameter E_{max} model. The solid line represents the median fit and dashed lines represent the 5-95 percentile limits of the fit. **(c)** Individual predicted QTcF versus observed QTcF (n=524) according to the piperaquine simultaneous PK-PD E_{max} model. **(d)** Population predicted QTcF versus observed QTcF (n=524) according to the piperaquine simultaneous PK-PD E_{max} model.

Supplementary Tables

Table S1: Compartmental model fits for ivermectin and piperaquine				
	Ivermectin		**Piperaquine**	
	One compartment	**Two compartment**	**Two compartment**	**Three compartment**
-2 log likelihood	6528.440	6202.912	17608.90	16375.37
AIC	6538.519	6217.061	17620.95	16391.45
BIC	6561.626	6249.373	17653.27	16434.52

Table S2: Number of observed concentrations and outcomes (ivermectin and piperaquine)

Time (days)	plasma samples venous	plasma samples capillary	ivermectin venous	ivermectin capillary	mortality rate	ivermectin venous + mortality rate	ivermectin: venous + capillary	piperaquine venous	piperaquine capillary	QTcF	piperaquine venous + QTcF	piperaquine: venous + capillary
0	141	-	0	-	141	-	-	1	-	141	1	-
2	-	-	-	-	-	-	-	-	-	132	-	-
2+4h	133	86	88	58	128	86	58	133	87	133	133	87
7	128	85	70	30	128	70	29	128	85	-	-	85
10	118	-	52	-	112	52	-	118	-	-	-	-
14	122	-	29	-	119	28	-	122	-	-	-	-
21	117	-	8	-	111	7	-	115	-	-	-	-
28	118	-	3	-	111	3	-	117	-	118	117	-
Pop PK	516	162	284	93	-	-	90	512	161	-	-	160
Total	1,393	335	534	181	850	246	177	1,246	333	524	251	332

Pop PK= population pharmacokinetic samples which were drawn between days 0 to 28 and did not coincide with other outcomes.
Ivermectin observations for days 21 and 28 are mostly absent as they are below the limit of quantitation.

Table S3: Ivermectin LC_{50} values by assay duration, and vs. previous studies

Duration of mosquito follow-up post-feeding (days):	A. LC_{50} unadjusted to baseline mortality (CI95%) (ng/mL):	B. LC_{50} adjusted to baseline mortality (CI95%) (ng/mL):	C. Comparator in vivo study[15] LC_{50} adjusted to baseline mortality (CI95%) (ng/mL):	D. Comparator in vitro studies LC_{50} adjusted to baseline mortality (CI95%) (ng/mL):	Relative Difference:
1	1656 (1281-2287)	3883 (2378-9552)	1172 (499-N/A)		
2	19.71(17.5-22.3)	26.79 (22.64-31.93)	43.95 (36.30-54.87)		
3	7.89 (7.13-8.73)	10.29 (8.96-11.86)	20.94 (17.73-25.15)	6.1 (3.4-11.0)[15]	D vs B: 0.6
4	5.07 (4.57-5.61)	6.92 (6.02-7.98)	15.40 (13.04-18.44)		
5	3.61 (3.24-4.01)	5.26 (4.56-6.09)	13.39 (11.24-16.18)	22.4 (18.0-26.9)[16]	D vs B: 4.3
6	2.68 (2.39-32.99)	4.13 (3.57-4.79)	8.59 (7.09-10.52)		
7	2.08 (1.85-2.33)	3.35 (2.89-3.89)	7.92 (6.49-9.77)	15.9 (14.6-17.3)[17]	D vs B: 4.7
8	1.74 (1.55-1.96)	2.97 (2.56-3.46)	7.43 (6.03-9.25)		
9	1.50 (1.32-1.70)	2.78 (2.38-3.25)	7.06 (5.69-8.86)	19.8 (14.3-25.3)[18]	D vs B: 7.1
10	1.24 (1.08-1.41)	2.55 (2.17-3.01)	6.52 (5.22-8.23)		C vs B: 2.6
11	1.15 (0.99-1.32)	2.62 (2.22-3.11)			
12	0.97 (0.83-1.13)	2.60 (2.18-3.10)			
13	0.80 (0.67-0.95)	2.56 (2.13-3.08)			
14	0.62 (0.51-0.74)	2.53 (2.09-3.07)			
15	0.45 (0.36-0.56)	2.50 (2.04-3.07)			
16	0.31 (0.23-0.40)	2.45 (1.98-3.06)			
17	0.17 (0.11-0.25)	2.43 (1.95-3.06)			
18	0.012 (0.0054-0.027)	2.34 (1.85-2.98)			
19	<0.01	2.44 (1.90-3.16)			
20	<0.01	2.42 (1.85-3.18)			
21	<0.01	2.32 (1.74-3.12)			
22	<0.01	2.31 (1.69-3.18)			
23	<0.01	2.21 (1.58-3.13)			
24	<0.01	2.19 (1.52-3.20)			
25	<0.01	2.08 (1.40-3.14)			
26	<0.01	1.92 (1.23-3.06)			
27	<0.01	1.87 (1.14-3.12)			
28	<0.01	1.97 (1.15-3.44)			

LC_{50}'s using predicted concentrations and 3-parameter method; Hill's coefficient was fixed to 1. LC_{50}'s adjusted to baseline mortality are the concentrations required to kill 50% of mosquitoes that would have otherwise survived the assay without ivermectin exposure. Adjusted LC_{50}'s are more consistent during follow-up than unadjusted LC_{50}'s. Additionally, unadjusted LC_{50}'s cannot be determined over longer follow-up periods due to high baseline mortality. Comparator *in vivo* values were calculated using author's dataset.[15] Comparator *in vitro* values as reported,[16, 17] except for one study that was converted from mol/L to ng/mL,[15] and another study for which the SE was converted to CI95%.[18] One study did not report whether it was adjusted to baseline, however probit analysis with control population was used, so baseline adjustment is assumed.[18]

Table S4: Piperaquine concentration and QTcF interval (observed data)						
Outcome	**IVM-3x600 (N=47)**	**IVM-3x300 (N=48)**	**Placebo (N=46)**	**Mean†Δ or Risk‡ difference (95% CI), p-value**		
				IVM-3x600 vs Placebo	**IVM-3x300 vs Placebo**	**IVM-3x600 vs IVM-3x300**
QTcF interval (Day 2+4h), change from baseline (ms)	27 (17) (n=42)	33 (17) (n=45)	29 (18) (n=44)	-0.8 (-8.0, 6.5), 0.84†	4.7 (-2.6, 11.9), 0.21†	-5.4 (-12.3, 1.5), 0.13†
QTcF interval (Day 2+4h), ≥500 ms	0/42 (0%)	1/45 (2.2%)	0/44 (0%)	0.0% (-0.4%, 3.7%), 1.00‡	2.2% (-1.4%, 5.8%), 0.23‡	-2.2% (-5.9%, 1.5%), 0.24‡
Piperaquine plasma concentration (Day 2+4h) (ng/mL)	313 (208-586) (n=43)	327 (179-545) (n=45)	269 (169-399) (n=45)	35.8 (-107.2, 178.7), 0.62Δ	28.9 (-108.1, 165.9), 0.68Δ	6.9 (-126.3, 140.0), 0.92Δ

Data are mean (SD), median (IQR), or n/N (%), unless otherwise specified. IVM-3x600=ivermectin 600 mcg/kg/day for 3 days. IVM-3x300=ivermectin 300 mcg/kg/day for 3 days.
QTcF=electrocardiogram QT interval, corrected for heart rate using Fredericia's formula.
Δ Mean difference (95% CI), p-value: obtained from GLM models.
† Mean difference (95% CI), p-value: obtained from GEE models adjusted for baseline measurement and repeated measures.
‡ Risk Difference (95% CI), p-value: obtained from GLM models.

Table S5: Piperaquine concentration and QTcF interval (population fitted data)				
Parameter	**All Patients (N=141) [p5-p95]**	**IVM-3x600 (N=47) [p5-p95]**	**IVM-3x300 (N=48) [p5-p95]**	**Placebo (N=46) [p5-p95]**
QTcF, baseline (E_{min}) (ms)	399.3 [377.5-416.3]	398.7 [371.9-413.2]	399.1 [379.5-415]	399.5 [379.8-416.5]
ΔQTcF, maximum possible change from baseline (E_{max}) (ms)	53.5 [31.1-122.9]	51.2 [32.2-119.6]	49.7 [31.2-123.3]	66.3 [27.2-118.3]
QTcF, maximum possible effect (E_{max}+E_{min}) (ms)	449.8 [415.1-520.0]*	445.2 [421.3-520.0]	447.8 [417.2-520.0]	464.1 [415.4-520.0]
Piperaquine concentration achieving half-maximal effect on QTcF (EC_{50}) (ng/mL)	181.7 [16.0-1200.0]	169.2 [16.0-1200.0]	199.0 [16.1-1200.0]	218.2 [15.9-1200.0]

Data are median [p5-p95]. IVM-3x600=ivermectin 600 mcg/kg/day for 3 days. IVM-3x300=ivermectin 300 mcg/kg/day for 3 days. QTcF=electrocardiogram QT interval, corrected for heart rate using Fredericia's formula.
* 18 subjects did not display a concentration-effect relationship for piperaquine and QT interval and their EC_{50} was estimated at the upper limit of the prediction, 1200 ng/mL. Upper limit for maximum possible effect (E_{max}+E_{min}) was set to be 520 ms which is 10 ms higher than the highest QT interval observed amongst all the patients.

Table S6: Spearman's correlations (ivermectin and piperaquine)

(see following pages)

[Table S6]

Correlations

			sex	age	weight
Spearman's rho	sex	Correlation Coefficient	1.000	-.014	-.070
		Sig. (2-tailed)	.	.869	.411
		N	141	141	141
	age	Correlation Coefficient	-.014	1.000	.178*
		Sig. (2-tailed)	.869	.	.035
		N	141	141	141
	weight	Correlation Coefficient	-.070	.178*	1.000
		Sig. (2-tailed)	.411	.035	.
		N	141	141	141
	height	Correlation Coefficient	-.661**	.058	.467**
		Sig. (2-tailed)	.000	.493	.000
		N	141	141	141
	KalVM	Correlation Coefficient	.027	.072	-.197*
		Sig. (2-tailed)	.749	.399	.019
		N	141	141	141
	VilVM	Correlation Coefficient	-.094	-.120	-.014
		Sig. (2-tailed)	.267	.157	.871
		N	141	141	141
	CLilVM	Correlation Coefficient	-.062	.112	-.020
		Sig. (2-tailed)	.463	.186	.818
		N	141	141	141
	KCP_IVM	Correlation Coefficient	.226**	.233**	.030
		Sig. (2-tailed)	.007	.005	.724
		N	141	141	141
	KPC_IVM	Correlation Coefficient	-.005	.121	-.151
		Sig. (2-tailed)	.949	.151	.073
		N	141	141	141
	Va_IVM	Correlation Coefficient	-.146	.031	.019
		Sig. (2-tailed)	.084	.716	.827
		N	141	141	141
	AUC_IVM	Correlation Coefficient	.002	.010	.224*
		Sig. (2-tailed)	.982	.923	.029
		N	95	95	95
	Cmax_IVM	Correlation Coefficient	.095	.032	-.011
		Sig. (2-tailed)	.359	.760	.917
		N	95	95	95
	QTcF_0	Correlation Coefficient	.415**	.108	.000
		Sig. (2-tailed)	.000	.204	1.000
		N	141	141	141

Correlations

			height	KalVM	VilVM
Spearman's rho	sex	Correlation Coefficient	-.661**	.027	-.094
		Sig. (2-tailed)	.000	.749	.267
		N	141	141	141
	age	Correlation Coefficient	.058	.072	-.120
		Sig. (2-tailed)	.493	.399	.157
		N	141	141	141
	weight	Correlation Coefficient	.467**	-.197*	-.014
		Sig. (2-tailed)	.000	.019	.871
		N	141	141	141
	height	Correlation Coefficient	1.000	-.054	.014
		Sig. (2-tailed)	.	.526	.872
		N	141	141	141
	KalVM	Correlation Coefficient	-.054	1.000	-.116
		Sig. (2-tailed)	.526	.	.171
		N	141	141	141
	VilVM	Correlation Coefficient	.014	-.116	1.000
		Sig. (2-tailed)	.872	.171	.
		N	141	141	141
	CLilVM	Correlation Coefficient	-.042	.230**	.360**
		Sig. (2-tailed)	.624	.006	.000
		N	141	141	141
	KCP_IVM	Correlation Coefficient	-.173*	.595**	-.305**
		Sig. (2-tailed)	.041	.000	.000
		N	141	141	141
	KPC_IVM	Correlation Coefficient	-.089	.639**	-.238**
		Sig. (2-tailed)	.291	.000	.004
		N	141	141	141
	Va_IVM	Correlation Coefficient	.080	-.311**	.344**
		Sig. (2-tailed)	.347	.000	.000
		N	141	141	141
	AUC_IVM	Correlation Coefficient	.159	.069	-.363**
		Sig. (2-tailed)	.124	.507	.000
		N	95	95	95
	Cmax_IVM	Correlation Coefficient	.028	.399**	-.753**
		Sig. (2-tailed)	.784	.000	.000
		N	95	95	95
	QTcF_0	Correlation Coefficient	-.168*	-.144	.018
		Sig. (2-tailed)	.046	.088	.831
		N	141	141	141

Correlations

			CLilVM	KCP_IVM	KPC_IVM
Spearman's rho	sex	Correlation Coefficient	-.062	.226**	-.005
		Sig. (2-tailed)	.463	.007	.949
		N	141	141	141
	age	Correlation Coefficient	.112	.233**	.121
		Sig. (2-tailed)	.186	.005	.151
		N	141	141	141
	weight	Correlation Coefficient	-.020	.030	-.151
		Sig. (2-tailed)	.818	.724	.073
		N	141	141	141
	height	Correlation Coefficient	-.042	-.173*	-.089
		Sig. (2-tailed)	.624	.041	.291
		N	141	141	141
	KalVM	Correlation Coefficient	.230**	.595**	.639**
		Sig. (2-tailed)	.006	.000	.000
		N	141	141	141
	ViIVM	Correlation Coefficient	.360**	-.305**	-.238**
		Sig. (2-tailed)	.000	.000	.004
		N	141	141	141
	CLilVM	Correlation Coefficient	1.000	.431**	.084
		Sig. (2-tailed)	.	.000	.321
		N	141	141	141
	KCP_IVM	Correlation Coefficient	.431**	1.000	.531**
		Sig. (2-tailed)	.000	.	.000
		N	141	141	141
	KPC_IVM	Correlation Coefficient	.084	.531**	1.000
		Sig. (2-tailed)	.321	.000	.
		N	141	141	141
	Va_IVM	Correlation Coefficient	.077	-.310**	-.283**
		Sig. (2-tailed)	.362	.000	.001
		N	141	141	141
	AUC_IVM	Correlation Coefficient	-.455**	-.015	.089
		Sig. (2-tailed)	.000	.887	.392
		N	95	95	95
	Cmax_IVM	Correlation Coefficient	-.284**	.351**	.252*
		Sig. (2-tailed)	.005	.000	.014
		N	95	95	95
	QTcF_0	Correlation Coefficient	-.163	-.077	-.152
		Sig. (2-tailed)	.053	.361	.072
		N	141	141	141

Correlations

			Va_IVM	AUC_IVM	Cmax_IVM
Spearman's rho	sex	Correlation Coefficient	-.146	.002	.095
		Sig. (2-tailed)	.084	.982	.359
		N	141	95	95
	age	Correlation Coefficient	.031	.010	.032
		Sig. (2-tailed)	.716	.923	.760
		N	141	95	95
	weight	Correlation Coefficient	.019	.224*	-.011
		Sig. (2-tailed)	.827	.029	.917
		N	141	95	95
	height	Correlation Coefficient	.080	.159	.028
		Sig. (2-tailed)	.347	.124	.784
		N	141	95	95
	KaIVM	Correlation Coefficient	-.311**	.069	.399**
		Sig. (2-tailed)	.000	.507	.000
		N	141	95	95
	ViIVM	Correlation Coefficient	.344**	-.363**	-.753**
		Sig. (2-tailed)	.000	.000	.000
		N	141	95	95
	CLiIVM	Correlation Coefficient	.077	-.455**	-.284**
		Sig. (2-tailed)	.362	.000	.005
		N	141	95	95
	KCP_IVM	Correlation Coefficient	-.310**	-.015	.351**
		Sig. (2-tailed)	.000	.887	.000
		N	141	95	95
	KPC_IVM	Correlation Coefficient	-.283**	.089	.252*
		Sig. (2-tailed)	.001	.392	.014
		N	141	95	95
	Va_IVM	Correlation Coefficient	1.000	-.224*	-.517**
		Sig. (2-tailed)	.	.029	.000
		N	141	95	95
	AUC_IVM	Correlation Coefficient	-.224*	1.000	.663**
		Sig. (2-tailed)	.029	.	.000
		N	95	95	95
	Cmax_IVM	Correlation Coefficient	-.517**	.663**	1.000
		Sig. (2-tailed)	.000	.000	.
		N	95	95	95
	QTcF_0	Correlation Coefficient	.103	-.005	-.066
		Sig. (2-tailed)	.226	.963	.528
		N	141	95	95

Correlations

			QTcF_0	QTcF_48	QTcF_52
Spearman's rho	sex	Correlation Coefficient	.415**	.391**	.420**
		Sig. (2-tailed)	.000	.000	.000
		N	141	134	131
	age	Correlation Coefficient	.108	.181*	.061
		Sig. (2-tailed)	.204	.037	.489
		N	141	134	131
	weight	Correlation Coefficient	.000	.050	-.059
		Sig. (2-tailed)	1.000	.562	.501
		N	141	134	131
	height	Correlation Coefficient	-.168*	-.216*	-.251**
		Sig. (2-tailed)	.046	.012	.004
		N	141	134	131
	KalVM	Correlation Coefficient	-.144	-.187*	-.206*
		Sig. (2-tailed)	.088	.030	.018
		N	141	134	131
	VilVM	Correlation Coefficient	.018	.004	-.051
		Sig. (2-tailed)	.831	.965	.563
		N	141	134	131
	CLilVM	Correlation Coefficient	-.163	-.221*	-.257**
		Sig. (2-tailed)	.053	.010	.003
		N	141	134	131
	KCP_IVM	Correlation Coefficient	-.077	-.112	-.181*
		Sig. (2-tailed)	.361	.197	.038
		N	141	134	131
	KPC_IVM	Correlation Coefficient	-.152	-.098	-.047
		Sig. (2-tailed)	.072	.258	.595
		N	141	134	131
	Va_IVM	Correlation Coefficient	.103	.125	.126
		Sig. (2-tailed)	.226	.150	.151
		N	141	134	131
	AUC_IVM	Correlation Coefficient	-.005	.002	-.044
		Sig. (2-tailed)	.963	.985	.689
		N	95	89	87
	Cmax_IVM	Correlation Coefficient	-.066	-.119	-.090
		Sig. (2-tailed)	.528	.266	.409
		N	95	89	87
	QTcF_0	Correlation Coefficient	1.000	.617**	.669**
		Sig. (2-tailed)	.	.000	.000
		N	141	134	131

Correlations

			QTcF_672	dQTcF_52	Cli_PPQ
Spearman's rho	sex	Correlation Coefficient	.561**	.000	-.119
		Sig. (2-tailed)	.000	.996	.159
		N	118	131	141
	age	Correlation Coefficient	.200*	-.069	.225**
		Sig. (2-tailed)	.030	.436	.007
		N	118	131	141
	weight	Correlation Coefficient	.120	.034	.114
		Sig. (2-tailed)	.195	.702	.180
		N	118	131	141
	height	Correlation Coefficient	-.307**	-.079	.053
		Sig. (2-tailed)	.001	.368	.536
		N	118	131	141
	KalVM	Correlation Coefficient	-.077	-.087	.029
		Sig. (2-tailed)	.406	.323	.735
		N	118	131	141
	VilVM	Correlation Coefficient	-.090	-.079	.094
		Sig. (2-tailed)	.334	.372	.269
		N	118	131	141
	CLilVM	Correlation Coefficient	-.197*	-.121	.239**
		Sig. (2-tailed)	.032	.169	.004
		N	118	131	141
	KCP_IVM	Correlation Coefficient	.068	-.100	.087
		Sig. (2-tailed)	.465	.256	.307
		N	118	131	141
	KPC_IVM	Correlation Coefficient	.055	.060	.015
		Sig. (2-tailed)	.552	.498	.864
		N	118	131	141
	Va_IVM	Correlation Coefficient	.145	.067	-.011
		Sig. (2-tailed)	.118	.448	.901
		N	118	131	141
	AUC_IVM	Correlation Coefficient	-.029	.031	-.145
		Sig. (2-tailed)	.803	.774	.160
		N	78	87	95
	Cmax_IVM	Correlation Coefficient	-.066	-.043	-.072
		Sig. (2-tailed)	.567	.689	.490
		N	78	87	95
	QTcF_0	Correlation Coefficient	.686**	-.362**	.002
		Sig. (2-tailed)	.000	.000	.986
		N	118	131	141

Correlations

			Vi_PPQ	k23_PPQ	k32_PPQ
Spearman's rho	sex	Correlation Coefficient	-.160	-.067	-.128
		Sig. (2-tailed)	.057	.433	.129
		N	141	141	141
	age	Correlation Coefficient	.156	.101	.013
		Sig. (2-tailed)	.065	.234	.881
		N	141	141	141
	weight	Correlation Coefficient	.167*	.071	-.002
		Sig. (2-tailed)	.048	.405	.977
		N	141	141	141
	height	Correlation Coefficient	.092	.030	.131
		Sig. (2-tailed)	.277	.727	.121
		N	141	141	141
	KalVM	Correlation Coefficient	-.025	-.091	-.060
		Sig. (2-tailed)	.770	.283	.477
		N	141	141	141
	ViIVM	Correlation Coefficient	.226**	.045	-.135
		Sig. (2-tailed)	.007	.596	.110
		N	141	141	141
	CLiIVM	Correlation Coefficient	.260**	.030	-.137
		Sig. (2-tailed)	.002	.724	.106
		N	141	141	141
	KCP_IVM	Correlation Coefficient	.022	-.016	-.079
		Sig. (2-tailed)	.798	.853	.354
		N	141	141	141
	KPC_IVM	Correlation Coefficient	-.015	-.159	.079
		Sig. (2-tailed)	.856	.060	.351
		N	141	141	141
	Va_IVM	Correlation Coefficient	-.028	.180*	.074
		Sig. (2-tailed)	.743	.033	.385
		N	141	141	141
	AUC_IVM	Correlation Coefficient	-.186	-.114	.041
		Sig. (2-tailed)	.071	.273	.690
		N	95	95	95
	Cmax_IVM	Correlation Coefficient	-.194	-.170	.019
		Sig. (2-tailed)	.060	.100	.852
		N	95	95	95
	QTcF_0	Correlation Coefficient	-.138	-.019	-.029
		Sig. (2-tailed)	.102	.822	.732
		N	141	141	141

Correlations

			k24_PPQ	k42_PPQ	CAP_PPQ
Spearman's rho	sex	Correlation Coefficient	.046	-.124	-.018
		Sig. (2-tailed)	.586	.142	.832
		N	141	141	141
	age	Correlation Coefficient	.103	.034	.131
		Sig. (2-tailed)	.223	.690	.121
		N	141	141	141
	weight	Correlation Coefficient	.011	-.012	-.026
		Sig. (2-tailed)	.895	.888	.760
		N	141	141	141
	height	Correlation Coefficient	-.078	.083	-.082
		Sig. (2-tailed)	.359	.326	.336
		N	141	141	141
	KalVM	Correlation Coefficient	.057	-.051	-.078
		Sig. (2-tailed)	.503	.546	.358
		N	141	141	141
	ViIVM	Correlation Coefficient	-.072	-.031	.210*
		Sig. (2-tailed)	.396	.717	.012
		N	141	141	141
	CLiIVM	Correlation Coefficient	.023	.004	.109
		Sig. (2-tailed)	.789	.965	.200
		N	141	141	141
	KCP_IVM	Correlation Coefficient	.172*	-.037	-.029
		Sig. (2-tailed)	.041	.662	.734
		N	141	141	141
	KPC_IVM	Correlation Coefficient	.105	.040	-.004
		Sig. (2-tailed)	.215	.637	.963
		N	141	141	141
	Va_IVM	Correlation Coefficient	.027	.057	.043
		Sig. (2-tailed)	.748	.505	.615
		N	141	141	141
	AUC_IVM	Correlation Coefficient	-.029	-.012	-.050
		Sig. (2-tailed)	.777	.906	.632
		N	95	95	95
	Cmax_IVM	Correlation Coefficient	.019	-.032	-.129
		Sig. (2-tailed)	.853	.760	.212
		N	95	95	95
	QTcF_0	Correlation Coefficient	.216*	.095	.164
		Sig. (2-tailed)	.010	.265	.052
		N	141	141	141

Correlations

			PPQAUC	PPQCmax	ARM
Spearman's rho	sex	Correlation Coefficient	.113	.171*	.011
		Sig. (2-tailed)	.182	.043	.901
		N	141	141	141
	age	Correlation Coefficient	-.187*	-.058	-.014
		Sig. (2-tailed)	.026	.492	.869
		N	141	141	141
	weight	Correlation Coefficient	-.069	-.115	.009
		Sig. (2-tailed)	.417	.173	.917
		N	141	141	141
	height	Correlation Coefficient	-.028	-.100	.030
		Sig. (2-tailed)	.744	.237	.720
		N	141	141	141
	KaIVM	Correlation Coefficient	-.078	-.040	.008
		Sig. (2-tailed)	.360	.638	.928
		N	141	141	141
	ViIVM	Correlation Coefficient	-.201*	-.259**	-.104
		Sig. (2-tailed)	.017	.002	.219
		N	141	141	141
	CLiIVM	Correlation Coefficient	-.349**	-.280**	-.078
		Sig. (2-tailed)	.000	.001	.359
		N	141	141	141
	KCP_IVM	Correlation Coefficient	-.133	-.019	.135
		Sig. (2-tailed)	.115	.819	.112
		N	141	141	141
	KPC_IVM	Correlation Coefficient	-.037	.064	-.074
		Sig. (2-tailed)	.666	.448	.383
		N	141	141	141
	Va_IVM	Correlation Coefficient	-.001	.005	-.007
		Sig. (2-tailed)	.988	.949	.937
		N	141	141	141
	AUC_IVM	Correlation Coefficient	.424**	.248*	.577**
		Sig. (2-tailed)	.000	.015	.000
		N	95	95	95
	Cmax_IVM	Correlation Coefficient	.186	.207*	.591**
		Sig. (2-tailed)	.071	.044	.000
		N	95	95	95
	QTcF_0	Correlation Coefficient	.058	.167*	-.008
		Sig. (2-tailed)	.491	.047	.923
		N	141	141	141

Correlations

			sex	age	weight
	QTcF_48	Correlation Coefficient	.391**	.181*	.050
		Sig. (2-tailed)	.000	.037	.562
		N	134	134	134
	QTcF_52	Correlation Coefficient	.420**	.061	-.059
		Sig. (2-tailed)	.000	.489	.501
		N	131	131	131
	QTcF_672	Correlation Coefficient	.561**	.200*	.120
		Sig. (2-tailed)	.000	.030	.195
		N	118	118	118
	dQTcF_52	Correlation Coefficient	.000	-.069	.034
		Sig. (2-tailed)	.996	.436	.702
		N	131	131	131
	Cli_PPQ	Correlation Coefficient	-.119	.225**	.114
		Sig. (2-tailed)	.159	.007	.180
		N	141	141	141
	Vi_PPQ	Correlation Coefficient	-.160	.156	.167*
		Sig. (2-tailed)	.057	.065	.048
		N	141	141	141
	k23_PPQ	Correlation Coefficient	-.067	.101	.071
		Sig. (2-tailed)	.433	.234	.405
		N	141	141	141
	k32_PPQ	Correlation Coefficient	-.128	.013	-.002
		Sig. (2-tailed)	.129	.881	.977
		N	141	141	141
	k24_PPQ	Correlation Coefficient	.046	.103	.011
		Sig. (2-tailed)	.586	.223	.895
		N	141	141	141
	k42_PPQ	Correlation Coefficient	-.124	.034	-.012
		Sig. (2-tailed)	.142	.690	.888
		N	141	141	141
	CAP_PPQ	Correlation Coefficient	-.018	.131	-.026
		Sig. (2-tailed)	.832	.121	.760
		N	141	141	141
	PPQAUC	Correlation Coefficient	.113	-.187*	-.069
		Sig. (2-tailed)	.182	.026	.417
		N	141	141	141
	PPQCmax	Correlation Coefficient	.171*	-.058	-.115
		Sig. (2-tailed)	.043	.492	.173
		N	141	141	141

Correlations

			height	KalVM	VilVM
	QTcF_48	Correlation Coefficient	-.216*	-.187*	.004
		Sig. (2-tailed)	.012	.030	.965
		N	134	134	134
	QTcF_52	Correlation Coefficient	-.251**	-.206*	-.051
		Sig. (2-tailed)	.004	.018	.563
		N	131	131	131
	QTcF_672	Correlation Coefficient	-.307**	-.077	-.090
		Sig. (2-tailed)	.001	.406	.334
		N	118	118	118
	dQTcF_52	Correlation Coefficient	-.079	-.087	-.079
		Sig. (2-tailed)	.368	.323	.372
		N	131	131	131
	Cli_PPQ	Correlation Coefficient	.053	.029	.094
		Sig. (2-tailed)	.536	.735	.269
		N	141	141	141
	Vi_PPQ	Correlation Coefficient	.092	-.025	.226**
		Sig. (2-tailed)	.277	.770	.007
		N	141	141	141
	k23_PPQ	Correlation Coefficient	.030	-.091	.045
		Sig. (2-tailed)	.727	.283	.596
		N	141	141	141
	k32_PPQ	Correlation Coefficient	.131	-.060	-.135
		Sig. (2-tailed)	.121	.477	.110
		N	141	141	141
	k24_PPQ	Correlation Coefficient	-.078	.057	-.072
		Sig. (2-tailed)	.359	.503	.396
		N	141	141	141
	k42_PPQ	Correlation Coefficient	.083	-.051	-.031
		Sig. (2-tailed)	.326	.546	.717
		N	141	141	141
	CAP_PPQ	Correlation Coefficient	-.082	-.078	.210*
		Sig. (2-tailed)	.336	.358	.012
		N	141	141	141
	PPQAUC	Correlation Coefficient	-.028	-.078	-.201*
		Sig. (2-tailed)	.744	.360	.017
		N	141	141	141
	PPQCmax	Correlation Coefficient	-.100	-.040	-.259**
		Sig. (2-tailed)	.237	.638	.002
		N	141	141	141

Correlations

		CLiIVM	KCP_IVM	KPC_IVM
QTcF_48	Correlation Coefficient	-.221*	-.112	-.098
	Sig. (2-tailed)	.010	.197	.258
	N	134	134	134
QTcF_52	Correlation Coefficient	-.257**	-.181*	-.047
	Sig. (2-tailed)	.003	.038	.595
	N	131	131	131
QTcF_672	Correlation Coefficient	-.197*	.068	.055
	Sig. (2-tailed)	.032	.465	.552
	N	118	118	118
dQTcF_52	Correlation Coefficient	-.121	-.100	.060
	Sig. (2-tailed)	.169	.256	.498
	N	131	131	131
Cli_PPQ	Correlation Coefficient	.239**	.087	.015
	Sig. (2-tailed)	.004	.307	.864
	N	141	141	141
Vi_PPQ	Correlation Coefficient	.260**	.022	-.015
	Sig. (2-tailed)	.002	.798	.856
	N	141	141	141
k23_PPQ	Correlation Coefficient	.030	-.016	-.159
	Sig. (2-tailed)	.724	.853	.060
	N	141	141	141
k32_PPQ	Correlation Coefficient	-.137	-.079	.079
	Sig. (2-tailed)	.106	.354	.351
	N	141	141	141
k24_PPQ	Correlation Coefficient	.023	.172*	.105
	Sig. (2-tailed)	.789	.041	.215
	N	141	141	141
k42_PPQ	Correlation Coefficient	.004	-.037	.040
	Sig. (2-tailed)	.965	.662	.637
	N	141	141	141
CAP_PPQ	Correlation Coefficient	.109	-.029	-.004
	Sig. (2-tailed)	.200	.734	.963
	N	141	141	141
PPQAUC	Correlation Coefficient	-.349**	-.133	-.037
	Sig. (2-tailed)	.000	.115	.666
	N	141	141	141
PPQCmax	Correlation Coefficient	-.280**	-.019	.064
	Sig. (2-tailed)	.001	.819	.448
	N	141	141	141

Correlations

			Va_IVM	AUC_IVM	Cmax_IVM
	QTcF_48	Correlation Coefficient	.125	.002	-.119
		Sig. (2-tailed)	.150	.985	.266
		N	134	89	89
	QTcF_52	Correlation Coefficient	.126	-.044	-.090
		Sig. (2-tailed)	.151	.689	.409
		N	131	87	87
	QTcF_672	Correlation Coefficient	.145	-.029	-.066
		Sig. (2-tailed)	.118	.803	.567
		N	118	78	78
	dQTcF_52	Correlation Coefficient	.067	.031	-.043
		Sig. (2-tailed)	.448	.774	.689
		N	131	87	87
	Cli_PPQ	Correlation Coefficient	-.011	-.145	-.072
		Sig. (2-tailed)	.901	.160	.490
		N	141	95	95
	Vi_PPQ	Correlation Coefficient	-.028	-.186	-.194
		Sig. (2-tailed)	.743	.071	.060
		N	141	95	95
	k23_PPQ	Correlation Coefficient	.180*	-.114	-.170
		Sig. (2-tailed)	.033	.273	.100
		N	141	95	95
	k32_PPQ	Correlation Coefficient	.074	.041	.019
		Sig. (2-tailed)	.385	.690	.852
		N	141	95	95
	k24_PPQ	Correlation Coefficient	.027	-.029	.019
		Sig. (2-tailed)	.748	.777	.853
		N	141	95	95
	k42_PPQ	Correlation Coefficient	.057	-.012	-.032
		Sig. (2-tailed)	.505	.906	.760
		N	141	95	95
	CAP_PPQ	Correlation Coefficient	.043	-.050	-.129
		Sig. (2-tailed)	.615	.632	.212
		N	141	95	95
	PPQAUC	Correlation Coefficient	-.001	.424**	.186
		Sig. (2-tailed)	.988	.000	.071
		N	141	95	95
	PPQCmax	Correlation Coefficient	.005	.248*	.207*
		Sig. (2-tailed)	.949	.015	.044
		N	141	95	95

Correlations

		QTcF_0	QTcF_48	QTcF_52
QTcF_48	Correlation Coefficient	.617**	1.000	.790**
	Sig. (2-tailed)	.000	.	.000
	N	134	134	131
QTcF_52	Correlation Coefficient	.669**	.790**	1.000
	Sig. (2-tailed)	.000	.000	.
	N	131	131	131
QTcF_672	Correlation Coefficient	.686**	.746**	.724**
	Sig. (2-tailed)	.000	.000	.000
	N	118	114	112
dQTcF_52	Correlation Coefficient	-.362**	.247**	.357**
	Sig. (2-tailed)	.000	.004	.000
	N	131	131	131
Cli_PPQ	Correlation Coefficient	.002	-.037	-.107
	Sig. (2-tailed)	.986	.673	.224
	N	141	134	131
Vi_PPQ	Correlation Coefficient	-.138	-.095	-.220*
	Sig. (2-tailed)	.102	.277	.012
	N	141	134	131
k23_PPQ	Correlation Coefficient	-.019	.060	-.072
	Sig. (2-tailed)	.822	.495	.412
	N	141	134	131
k32_PPQ	Correlation Coefficient	-.029	-.157	-.018
	Sig. (2-tailed)	.732	.070	.843
	N	141	134	131
k24_PPQ	Correlation Coefficient	.216*	.102	.103
	Sig. (2-tailed)	.010	.241	.241
	N	141	134	131
k42_PPQ	Correlation Coefficient	.095	-.092	.010
	Sig. (2-tailed)	.265	.292	.911
	N	141	134	131
CAP_PPQ	Correlation Coefficient	.164	.035	.039
	Sig. (2-tailed)	.052	.691	.654
	N	141	134	131
PPQAUC	Correlation Coefficient	.058	.010	.145
	Sig. (2-tailed)	.491	.910	.099
	N	141	134	131
PPQCmax	Correlation Coefficient	.167*	.040	.243**
	Sig. (2-tailed)	.047	.644	.005
	N	141	134	131

Correlations

			QTcF_672	dQTcF_52	Cli_PPQ
	QTcF_48	Correlation Coefficient	.746**	.247**	-.037
		Sig. (2-tailed)	.000	.004	.673
		N	114	131	134
	QTcF_52	Correlation Coefficient	.724**	.357**	-.107
		Sig. (2-tailed)	.000	.000	.224
		N	112	131	131
	QTcF_672	Correlation Coefficient	1.000	.099	-.011
		Sig. (2-tailed)	.	.300	.906
		N	118	112	118
	dQTcF_52	Correlation Coefficient	.099	1.000	-.054
		Sig. (2-tailed)	.300	.	.542
		N	112	131	131
	Cli_PPQ	Correlation Coefficient	-.011	-.054	1.000
		Sig. (2-tailed)	.906	.542	.
		N	118	131	141
	Vi_PPQ	Correlation Coefficient	-.088	-.111	.579**
		Sig. (2-tailed)	.345	.208	.000
		N	118	131	141
	k23_PPQ	Correlation Coefficient	-.035	-.037	-.066
		Sig. (2-tailed)	.703	.672	.436
		N	118	131	141
	k32_PPQ	Correlation Coefficient	.020	.097	.110
		Sig. (2-tailed)	.833	.268	.194
		N	118	131	141
	k24_PPQ	Correlation Coefficient	.168	-.161	.166*
		Sig. (2-tailed)	.069	.066	.048
		N	118	131	141
	k42_PPQ	Correlation Coefficient	-.007	-.028	.549**
		Sig. (2-tailed)	.938	.747	.000
		N	118	131	141
	CAP_PPQ	Correlation Coefficient	.085	-.142	.264**
		Sig. (2-tailed)	.361	.106	.002
		N	118	131	141
	PPQAUC	Correlation Coefficient	.052	.164	-.674**
		Sig. (2-tailed)	.576	.062	.000
		N	118	131	141
	PPQCmax	Correlation Coefficient	.190*	.137	-.426**
		Sig. (2-tailed)	.040	.120	.000
		N	118	131	141

Correlations

			Vi_PPQ	k23_PPQ	k32_PPQ
	QTcF_48	Correlation Coefficient	-.095	.060	-.157
		Sig. (2-tailed)	.277	.495	.070
		N	134	134	134
	QTcF_52	Correlation Coefficient	-.220*	-.072	-.018
		Sig. (2-tailed)	.012	.412	.843
		N	131	131	131
	QTcF_672	Correlation Coefficient	-.088	-.035	.020
		Sig. (2-tailed)	.345	.703	.833
		N	118	118	118
	dQTcF_52	Correlation Coefficient	-.111	-.037	.097
		Sig. (2-tailed)	.208	.672	.268
		N	131	131	131
	Cli_PPQ	Correlation Coefficient	.579**	-.066	.110
		Sig. (2-tailed)	.000	.436	.194
		N	141	141	141
	Vi_PPQ	Correlation Coefficient	1.000	-.226**	-.198*
		Sig. (2-tailed)	.	.007	.019
		N	141	141	141
	k23_PPQ	Correlation Coefficient	-.226**	1.000	.122
		Sig. (2-tailed)	.007	.	.151
		N	141	141	141
	k32_PPQ	Correlation Coefficient	-.198*	.122	1.000
		Sig. (2-tailed)	.019	.151	.
		N	141	141	141
	k24_PPQ	Correlation Coefficient	-.161	.203*	.299**
		Sig. (2-tailed)	.057	.016	.000
		N	141	141	141
	k42_PPQ	Correlation Coefficient	.054	-.016	.621**
		Sig. (2-tailed)	.527	.851	.000
		N	141	141	141
	CAP_PPQ	Correlation Coefficient	.224**	.024	.015
		Sig. (2-tailed)	.008	.780	.856
		N	141	141	141
	PPQAUC	Correlation Coefficient	-.797**	.059	.242**
		Sig. (2-tailed)	.000	.484	.004
		N	141	141	141
	PPQCmax	Correlation Coefficient	-.816**	.034	.424**
		Sig. (2-tailed)	.000	.690	.000
		N	141	141	141

Correlations

			k24_PPQ	k42_PPQ	CAP_PPQ
	QTcF_48	Correlation Coefficient	.102	-.092	.035
		Sig. (2-tailed)	.241	.292	.691
		N	134	134	134
	QTcF_52	Correlation Coefficient	.103	.010	.039
		Sig. (2-tailed)	.241	.911	.654
		N	131	131	131
	QTcF_672	Correlation Coefficient	.168	-.007	.085
		Sig. (2-tailed)	.069	.938	.361
		N	118	118	118
	dQTcF_52	Correlation Coefficient	-.161	-.028	-.142
		Sig. (2-tailed)	.066	.747	.106
		N	131	131	131
	Cli_PPQ	Correlation Coefficient	.166*	.549**	.264**
		Sig. (2-tailed)	.048	.000	.002
		N	141	141	141
	Vi_PPQ	Correlation Coefficient	-.161	.054	.224**
		Sig. (2-tailed)	.057	.527	.008
		N	141	141	141
	k23_PPQ	Correlation Coefficient	.203*	-.016	.024
		Sig. (2-tailed)	.016	.851	.780
		N	141	141	141
	k32_PPQ	Correlation Coefficient	.299**	.621**	.015
		Sig. (2-tailed)	.000	.000	.856
		N	141	141	141
	k24_PPQ	Correlation Coefficient	1.000	.456**	.304**
		Sig. (2-tailed)	.	.000	.000
		N	141	141	141
	k42_PPQ	Correlation Coefficient	.456**	1.000	.110
		Sig. (2-tailed)	.000	.	.192
		N	141	141	141
	CAP_PPQ	Correlation Coefficient	.304**	.110	1.000
		Sig. (2-tailed)	.000	.192	.
		N	141	141	141
	PPQAUC	Correlation Coefficient	-.090	-.062	-.263**
		Sig. (2-tailed)	.286	.467	.002
		N	141	141	141
	PPQCmax	Correlation Coefficient	.156	.123	.056
		Sig. (2-tailed)	.064	.147	.510
		N	141	141	141

Correlations

			PPQAUC	PPQCmax	ARM
	QTcF_48	Correlation Coefficient	.010	.040	.007
		Sig. (2-tailed)	.910	.644	.932
		N	134	134	134
	QTcF_52	Correlation Coefficient	.145	.243**	-.010
		Sig. (2-tailed)	.099	.005	.912
		N	131	131	131
	QTcF_672	Correlation Coefficient	.052	.190*	.028
		Sig. (2-tailed)	.576	.040	.760
		N	118	118	118
	dQTcF_52	Correlation Coefficient	.164	.137	-.034
		Sig. (2-tailed)	.062	.120	.701
		N	131	131	131
	Cli_PPQ	Correlation Coefficient	-.674**	-.426**	.017
		Sig. (2-tailed)	.000	.000	.844
		N	141	141	141
	Vi_PPQ	Correlation Coefficient	-.797**	-.816**	-.057
		Sig. (2-tailed)	.000	.000	.498
		N	141	141	141
	k23_PPQ	Correlation Coefficient	.059	.034	-.072
		Sig. (2-tailed)	.484	.690	.396
		N	141	141	141
	k32_PPQ	Correlation Coefficient	.242**	.424**	-.057
		Sig. (2-tailed)	.004	.000	.504
		N	141	141	141
	k24_PPQ	Correlation Coefficient	-.090	.156	.036
		Sig. (2-tailed)	.286	.064	.673
		N	141	141	141
	k42_PPQ	Correlation Coefficient	-.062	.123	.042
		Sig. (2-tailed)	.467	.147	.622
		N	141	141	141
	CAP_PPQ	Correlation Coefficient	-.263**	.056	.013
		Sig. (2-tailed)	.002	.510	.874
		N	141	141	141
	PPQAUC	Correlation Coefficient	1.000	.780**	.024
		Sig. (2-tailed)	.	.000	.777
		N	141	141	141
	PPQCmax	Correlation Coefficient	.780**	1.000	.029
		Sig. (2-tailed)	.000	.	.732
		N	141	141	141

Correlations

		sex	age	weight
ARM	Correlation Coefficient	.011	-.014	.009
	Sig. (2-tailed)	.901	.869	.917
	N	141	141	141

Correlations

		height	KalVM	VilVM
ARM	Correlation Coefficient	.030	.008	-.104
	Sig. (2-tailed)	.720	.928	.219
	N	141	141	141

Correlations

		CLilVM	KCP_IVM	KPC_IVM
ARM	Correlation Coefficient	-.078	.135	-.074
	Sig. (2-tailed)	.359	.112	.383
	N	141	141	141

Correlations

		Va_IVM	AUC_IVM	Cmax_IVM
ARM	Correlation Coefficient	-.007	.577**	.591**
	Sig. (2-tailed)	.937	.000	.000
	N	141	95	95

Correlations

		QTcF_0	QTcF_48	QTcF_52
ARM	Correlation Coefficient	-.008	.007	-.010
	Sig. (2-tailed)	.923	.932	.912
	N	141	134	131

Correlations

		QTcF_672	dQTcF_52	Cli_PPQ
ARM	Correlation Coefficient	.028	-.034	.017
	Sig. (2-tailed)	.760	.701	.844
	N	118	131	141

Correlations

		Vi_PPQ	k23_PPQ	k32_PPQ
ARM	Correlation Coefficient	-.057	-.072	-.057
	Sig. (2-tailed)	.498	.396	.504
	N	141	141	141

Correlations

		k24_PPQ	k42_PPQ	CAP_PPQ
ARM	Correlation Coefficient	.036	.042	.013
	Sig. (2-tailed)	.673	.622	.874
	N	141	141	141

Correlations

		PPQAUC	PPQCmax	ARM
ARM	Correlation Coefficient	.024	.029	1.000
	Sig. (2-tailed)	.777	.732	.
	N	141	141	141

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).