

APPENDIX 4

Study 2: Pharmacokinetics of mefloquine given at 6 h and 24 h after the oral dose of dihydroartemisinin

PATIENT CHARACTERISTICS											SUMMARY RESULTS			
Pt. No.	Pt. initials	Gender	Age (yrs)	Weight (kg)	Height (cm)	Province	Occup.	Adm. date	Disch. Date	Last FU date	No. of FU days	UCFM	Parasite density (μ l)	Body T ($^{\circ}$ C)
2	PHV	m	21	53	161	Ldong	Farmer	26-Nov-02	3-Dec-02	7-Jan-03	42	Yes	48996	40
3	TDT	EXCLUDED DUE TO MQ 0h = 452 ng/ml			161									
5	NVD	m	35	52	161	Ldong	Farmer	2-Dec-02	9-Dec-02	13-Jan-03	42	Yes	48984	40
8	KB	m	19	45	160	Ldong	Farmer	17-Jan-03	24-Jan-03	28-Feb-03	42	Yes	23460	40.2
9	DNH	m	21	50	166	Ldong	Farmer	17-Jan-03	24-Jan-03	28-Feb-03	42	Yes	3668	39.5
12	LVT	m	26	54	164	Ldong	Farmer	14-Aug-03	21-Aug-03	25-Sep-03	42	Yes	1365	39
	Count No.	5	5	5	5	5	5	5-Jan-00	5-Jan-00	5-Jan-00	5	5	5	5
	Median		21	52	161						42		23460	40
	Mean		24.4	50.8	162.4						42.0		25294.6	39.7
	Min		19.0	45.0	160.0						42.0		1365.0	39.0
	Max		35.0	54.0	166.0						42.0		48996.0	40.2
	SD		6.5	3.6	2.5						0.0		23273.6	0.5
	CV		26.5	7.0	1.5						0.0		92.0	1.2
1	TQT	m	20	53	160	Ldong	Farmer	20-Nov-02	27-Nov-02	1-Jan-03	42	Yes	47328	39
4	NDH	m	32	53	161	Ldong	Farmer	30-Nov-02	7-Dec-02	11-Jan-03	42	Yes	36423	39.7
6	TVT	m	19	53	165	Ldong	Farmer	30-Dec-02	6-Jan-03	10-Feb-03	42	Yes	76960	39.5
7	TVH	m	36	59	169	Ldong	Farmer	13-Jan-03	20-Jan-03	24-Feb-03	42	Yes	18492	39.3
10	DVH	m	28	58	166	Ldong	Farmer	19-Jan-03	25-Jan-03	2-Mar-03	42	Yes	31824	38.5
11	NLT	m	22	57	167	Ldong	Farmer	11-Feb-03	18-Feb-03	25-Mar-03	42	Yes	20648	40
	Count No.	6	6	6	6	6	6	6-Jan-00	6-Jan-00	6-Jan-00	6-Jan-00	6	6	6
	Median		25	55	165.5						42.0		34123.5	39.4
	Mean		26.2	55.5	164.7						42.0		38612.5	39.3
	Min		19.0	53.0	160.0						42.0		18492.0	38.5
	Max		36.0	59.0	169.0						42.0		76960.0	40.0
	SD		6.9	2.8	3.5						0.0		21563.5	0.5
	CV		26.5	5.1	2.1						0.0		55.8	1.4

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Treatment	Clinic. Result	Pt. No.	Pt. initials	FCT (h)	PCT 100% (h)	PCT 95% (h)	PCT 50% (h)	PCT 5% (h)	FU results	AE	Living endemic area (y)	PAST HISTORY			
												Malaria/ 2 years	Severe malaria/ 2 years	MQ/2 months	Fist date of episode
DHA-MQ-6h	Good	2	PHV	72	60	25.3	8.5	3.8	Cure	None	21	0	None	None	22-Nov-02
		3	TDT												
DHA-MQ-6h	Good	5	NVD	60	36	9.6	1.6	0.1	Cure	None	8	0	None	None	28-Nov-02
DHA-MQ-6h	Good	8	KB	42	36	18.3	5.8	2.3	Cure	None	19	0	None	None	10-Jan-03
DHA-MQ-6h	Good	9	DNH	42	18	10.2	2.9	0.9	Cure	None	6	0	None	None	20-Dec-02
DHA-MQ-6h	Good	12	LVT	48	18	24.2	7.1	2.3	Cure	None	12	0	None	None	11-Aug-03
	5	Count No.		5	5	5	5	5	5	5	5	5	5	5	5
		Median		48	36	18.3	5.8	2.3			12	0			
		Mean		52.8	33.6	17.5	5.2	1.9			13.2	0.0			
		Min		42.0	18.0	9.6	1.6	0.1			6.0	0.0			
		Max		72.0	60.0	25.3	8.5	3.8			21.0	0.0			
		SD		13.0	17.3	7.5	2.9	1.4			6.6	0.0			
		CV		24.6	51.4	42.5	55.5	76.0			50.1				
DHA-MQ-24h	Good	1	TQT	54	42	15.23	0.03	0	Cure	None	3	0	None	None	10-Nov-02
DHA-MQ-24h	Good	4	NDH	42	84	57.1	11.7	0	Cure	None	20	0	None	None	27-Nov-02
DHA-MQ-24h	Good	6	TVT	72	66	31.6	11.9	6.5	Cure	None	3	1	None	None	28-Dec-02
DHA-MQ-24h	Good	7	TVH	54	54	28.1	9.5	4.3	Cure	None	6	0	None	None	04-Jan-03
DHA-MQ-24h	Good	10	DVH	42	36	12.9	4.4	1.9	Cure	None	0	0	None	None	15-Jan-03
DHA-MQ-24h	Good	11	NLT	54	24	12.6	2.4	0	Cure	None	0.8	0	None	None	10-Feb-03
	6	Count No.		6	6	6	6	6	6	6	6	6	6	6	6
		Mean		54	48	21.665	6.95	0.95			3	0			
		Min		53.0	51.0	26.3	6.7	2.1			5.5	0.2			
		Max		42.0	24.0	12.6	0.0	0.0			0.0	0.0			
		SD		72.0	84.0	57.1	11.9	6.5			20.0	1.0			
		CV		11.0	21.7	17.1	5.1	2.7			7.4	0.4			
				20.8	42.6	65.3	76.1	129.3			135.7	244.9			

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PRESENT ILLNESS HISTORY				TREATMENT REGIMEN					CLINICAL OBSERVATIONS				
No. of day before adm	Number of episodes	Pt. No.	Pt. initials	Treat-0h	Treat-6h	Treat-24h	Total dose DHA	Total dose MQ	Fever d0	Chill d0	Sweat d0	Liver d0	Spleen d0
4	4	2	PHV	DHA	MQ	DHA	600	750	3	3	3	0	1
4	5	3	TDT										
7	10	5	NVD	DHA	MQ	DHA	600	750	3	3	3	0	0
28	20	8	KB	DHA	MQ	DHA	600	750	3	3	3	0	0
3	5	9	DNH	DHA	MQ	DHA	600	750	3	3	3	0	0
5	5	12	LVT	DHA	MQ	DHA	600	750	3	3	3	0	0
4	5	5	Count No.	5	5	5	5	5	5	5	5	5	5
9.2	8.8		Median				600	750	3	3	3	0	0
3.0	4.0		Mean				600.0	750.0	3.0	3.0	3.0	0.0	0.2
28.0	20.0		Min				600.0	750.0	3.0	3.0	3.0	0.0	0.0
10.6	6.7		Max				600.0	750.0	3.0	3.0	3.0	0.0	1.0
115.4	76.0		SD				0.0	0.0	0.0	0.0	0.0	0.0	0.4
10	14		CV				0.0	0.0	0.0	0.0	0.0	0.0	223.6
3	4	1	TQT	DHA	None	DHA-MQ	600	750	3	3	3	0	0
2	3	4	NDH	DHA	None	DHA-MQ	600	750	3	3	2	0	0
9	12	6	TVT	DHA	None	DHA-MQ	600	750	3	3	3	0	1
4	8	7	TVH	DHA	None	DHA-MQ	600	750	3	3	3	0	0
1	2	10	DVH	DHA	None	DHA-MQ	600	750	3	2	2	0	0
6	6	11	NLT	DHA	None	DHA-MQ	600	750	3	3	3	0	0
3.5	6	6	Count No.	6	6	6	6	6	6	6	6	6	6
4.8	7.2		Median				600	750	3	3	3	0	0
1.0	2.0		Mean				600.0	750.0	3.0	2.8	2.7	0.0	0.2
10.0	14.0		Min				600.0	750.0	3.0	2.0	2.0	0.0	0.0
3.8	5.0		Max				600.0	750.0	3.0	3.0	3.0	0.0	1.0
77.9	69.7		SD				0.0	0.0	0.0	0.4	0.5	0.0	0.4
			CV				0.0	0.0	0.0	14.4	19.4	#DIV/0!	244.9

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CLINICAL OBSERVATIONS				SYSTOLIC PRESSURE (mmHg)										PULSE (beats/min)			
No. of days with fever (d)	No. of days with chill (d)	No. of days with sweat (d)	No. of days with spleen (d)	Pt. No.	Pt. initials	Sys P 0h	Sys P 24h	Sys P 48h	Sys P 96h	Pulse 0h	Pulse 24h	Pulse 48h	Pulse 96h	0h	6h		
2	2	1	7	2	PHV	110	110	110	110	105	96	98	92	40	39.9		
2.5	2	1.5		3	TDT												
3	2.5	2.5		5	NVD	110	100	100	100	24	20	20	18	40	38.8		
3	2.5	2		8	KB	120	100	100	110	115	92	82	82	40.2	39		
3	2.5	2		9	DNH	100	90	90	100	120	86	80	82	39.5	38.5		
3	3	2		12	LVT	90	100	100	100	100	98	100	110	39	39.2		
5	5	5	5		Count No.	5	5	5	5	5	5	5	5	5	5		
3	2.5	2			Median	110	100	100	100	105	92	82	82	40	39		
2.7	2.4	1.8			Mean	106.0	100.0	100.0	104.0	92.8	78.4	76.0	76.8	39.7	39.1		
2.0	2.0	1.0			Min	90.0	90.0	90.0	100.0	24.0	20.0	20.0	18.0	39.0	38.5		
3.0	3.0	2.5			Max	120.0	110.0	110.0	110.0	120.0	98.0	100.0	110.0	40.2	39.9		
0.4	0.4	0.6			SD	11.4	7.1	7.1	5.5	39.3	33.0	32.6	34.8	0.5	0.5		
16.6	17.4	31.7			CV	10.8	7.1	7.1	5.3	42.3	42.0	42.9	45.3	1.2	1.3		
2	1	1		1	TQT	100	100	100	100	100	86	90	88	39	40		
2	1.5	1		4	NDH	120	120	120	110	100	94	90	86	39.7	38.8		
2.5	2	2	3	6	TVT	110	100	110	100	100	96	92	88	39.5	40		
2	2	1.5		7	TVH	130	100	110	110	110	84	78	72	39.3	39.3		
3	2	2		10	DVH	100	100	100	100	96	94	88	86	38.5	38.5		
3	2.5	2.5		11	NLT	100	110	110	100	120	96	90	80	40	40		
6	6	6	6		Count No.	6	6	6	6	6	6	6	6	6	6		
2.25	2	1.75			Median	105	100	110	100	100	94	90	86	39.4	39.65		
2.4	1.8	1.7			Mean	110.0	105.0	108.3	103.3	104.3	91.7	88.0	83.3	39.3	39.4		
2.0	1.0	1.0			Min	100.0	100.0	100.0	100.0	96.0	84.0	78.0	72.0	38.5	38.5		
3.0	2.5	2.5			Max	130.0	120.0	120.0	110.0	120.0	96.0	92.0	88.0	40.0	40.0		
0.5	0.5	0.6			SD	12.6	8.4	7.5	5.2	9.0	5.3	5.1	6.3	0.5	0.7		
20.3	28.2	36.3			CV	11.5	8.0	6.9	5.0	8.6	5.8	5.7	7.5	1.4	1.7		

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BODY TEMPERATURES (°C)											PARASITE DENSITY (/ μ l)										
12h	18h	24h	30h	36h	42h	48h	54h	60h	66h	Pt. No.	Pt. initials	PD 0h	PD 6h	PD 12h	PD 18h	PD 24h	PD 30h	PD 36h	PD 42h		
39.5	40	37.9	37.8	38	37.6	37.8	37.5	37.6	37.5	2	PHV	48995	35328	28416	6012	2736	2004	444	198		
39	38.6	38.5	38	37.9	38	37.5	37.6	37.1	37	3	TDT										
39.2	37.8	38.4	38	37.8	37	36.8	37	37.2	36.8	5	NVD	48984	4344	1536	216	95	0	0	0		
37.5	37.5	38	37.8	37.6	37	37	36.8	37	37	8	KB	23460	16800	2760	1320	1110	60	0	0		
38.4	38.2	39.5	38.6	38.2	37.5	37.2	37	36.6	37	9	DNH	3668	1092	84	0	0	0	0	0		
5	5	5	5	5	5	5	5	5	5	12	LVT	1365	1326	273	0	0	0	0	0		
											Count No.	5	5	5	5	5	5	5	5		
39	38.2	38.4	38	37.9	37.5	37.2	37	37.1	37		Median	23460	4344	1536	216	95	0	0	0		
38.7	38.4	38.5	38.0	37.9	37.4	37.3	37.2	37.1	37.1		Mean	25294.4	11778.0	6613.8	1509.6	788.2	412.8	88.8	39.6		
37.5	37.5	37.9	37.8	37.6	37.0	36.8	36.6	36.6	36.8		Min	1365.0	1092.0	84.0	0.0	0.0	0.0	0.0	0.0		
39.5	40.0	39.5	38.6	38.2	38.0	37.8	37.6	37.6	37.5		Max	48995.0	35328.0	28416.0	6012.0	2736.0	2004.0	444.0	198.0		
0.8	1.0	0.6	0.3	0.2	0.4	0.4	0.3	0.4	0.3		SD	23273.4	14650.3	12235.4	2575.8	1185.4	889.9	198.6	88.5		
2.0	2.5	1.7	0.9	0.6	1.1	1.1	0.9	1.0	0.7		CV	92.0	124.4	185.0	170.6	150.4	215.6	223.6	223.6		
40	38	37.8	38	37.7	38	37.7	37	37.2	37	1	TQT	47328	6048	4080	672	576	480	72	0		
38.1	38.4	37.8	37.8	37.5	37	37	37	37	36.8	4	NDH	36423	27113	19684	13718	12255	5168	4256	2679		
40.1	39.6	37.8	40	38	38.2	37.8	38	37.9	37.5	6	TVT	76960	51072	40160	24023	15232	11328	2464	2016		
37.8	37	38.5	37	38.5	37	37.5	37.3	37	37.3	7	TVH	18492	9279	9263	4656	3082	1105	368	268		
39	38.6	37.8	38	37.9	37.4	37.2	36.8	37	37.1	10	DVH	31824	23325	2371	255	51	24	0	0		
39.5	39	38.6	38	39	38.4	37.5	37.4	37.2	37	11	NLT	20648	3446	1372	305	0	0	0	0		
6	6	6	6	6	6	6	6	6	6		Count No.	6	6	6	6	6	6	6	6		
39.25	38.5	37.8	38	37.95	37.7	37.5	37.15	37.1	37.05		Median	34123.5	16302	6671.5	2664	1829	792.5	220	134		
39.1	38.4	38.1	38.1	38.1	37.7	37.5	37.3	37.2	37.1		Mean	38612.5	20047.2	12821.7	7271.5	5199.3	3017.5	1193.3	827.2		
37.8	37.0	37.8	37.0	37.5	37.0	37.0	36.8	37.0	36.8		Min	18492.0	3446.0	1372.0	255.0	0.0	0.0	0.0	0.0		
40.1	39.6	38.6	40.0	39.0	38.4	37.8	38.0	37.9	37.5		Max	76960.0	51072.0	40160.0	24023.0	15232.0	11328.0	4256.0	2679.0		
1.0	0.9	0.4	1.0	0.6	0.6	0.3	0.4	0.3	0.2		SD	21563.5	17948.5	14992.5	9698.7	6779.9	4513.4	1776.6	1200.7		
2.5	2.3	1.0	2.6	1.5	1.6	0.8	1.1	0.9	0.7		CV	55.8	89.5	116.9	133.4	130.4	149.6	148.9	145.2		

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PARASITE DENSITY (μl)													PARASITE DURING FOLLOW-UP										HEMATOLOGY				
PD 48h	PD 54h	PD 60h	PD 66h	PD 72h	PD 78h	PD 84h	PD 90h	d7	d14	d21	d28	d35	d42	Treat. No.	Pt. initials	HCTd0 (%)	HCTd2 (%)	HCTd4 (%)	HB d0 (g/dl)	HB d2 (g/dl)	HB d4 (g/dl)						
36	18	0	0	0	0	0	0	0	0	0	0	0	0	2	PHV	40.9	39.4	36.6	13.8	12.8	11.9						
0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	TDT												
0	0	0	0	0	0	0	0	0	0	0	0	0	0	5	NVD	37	31.5	31.6	11	10.6	10.6						
0	0	0	0	0	0	0	0	0	0	0	0	0	0	8	KB	36	33.3	35.8	11.9	11.5	12.2						
0	0	0	0	0	0	0	0	0	0	0	0	0	0	9	DNH	28.5	27.4	29	9.5	9.3	9.9						
0	0	0	0	0	0	0	0	0	0	0	0	0	0	12	LVT	35	31.1	32.8	10.9	10.1	10.6						
5	5	5	5	5	5	5	5	5	5	5	5	5	5		Count No.	5	5	5	5	5	5						
0	0	0	0	0	0	0	0	0	0	0	0	0	0			36	31.5	32.8	11	10.6	10.6						
7.2	3.6	0.0	0	0	0	0	0	0	0	0	0	0	0		Mean	35.5	32.5	33.2	11.4	10.9	11.0						
0.0	0.0	0.0	0	0	0	0	0	0	0	0	0	0	0		Min	28.5	27.4	29.0	9.5	9.3	9.9						
36.0	18.0	0.0	0	0	0	0	0	0	0	0	0	0	0		Max	40.9	39.4	36.6	13.8	12.8	12.2						
16.1	8.0	0.0	0	0	0	0	0	0	0	0	0	0	0		SD	4.5	4.4	3.1	1.6	1.3	1.0						
223.6	223.6														CV	12.7	13.5	9.4	13.9	12.4	8.8						
0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	TQT	32	33	28.3	10.9	11.3	9.6						
2470	2299	1995	988	931	38	0	0	0	0	0	0	0	0	4	NDH	40.6	39.2	34.4	13.7	13.1	11.6						
480	224	64	0	0	0	0	0	0	0	0	0	0	0	6	TVT	39.1	31.1	31.6	13	10.3	10.6						
67	0	0	0	0	0	0	0	0	0	0	0	0	0	7	TVH	42.8	31.8	26.9	14.7	10.9	9.7						
0	0	0	0	0	0	0	0	0	0	0	0	0	0	10	DVH	41.8	40	40.1	14.4	13.8	13.2						
0	0	0	0	0	0	0	0	0	0	0	0	0	0	11	NLT	46.1	46	40	15.9	15.2	23.9						
6	6	6	6	6	6	6	6	6	6	6	6	6	6		Count No.	6	6	6	6	6	6						
33.5	0	0	0	0	0	0	0	0	0	0	0	0	0		Median	41.2	36.1	33	14.05	12.2	11.1						
502.8	420.5	343.2	164.7	155.2	6.3	0.0	0	0	0	0	0	0	0		Mean	40.4	36.9	33.6	13.8	12.4	13.1						
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0	0	0	0	0	0	0		Min	32.0	31.1	26.9	10.9	10.3	9.6						
2470.0	2299.0	1995.0	988.0	931.0	38.0	0.0	0	0	0	0	0	0	0		Max	46.1	46.0	40.1	15.9	15.2	23.9						
981.7	924.6	809.6	403.3	380.1	15.5	0.0	0	0	0	0	0	0	0		SD	4.7	5.9	5.7	1.7	1.9	5.5						
195.2	219.9	235.9	244.9	244.9											CV	11.7	15.9	16.9	12.4	15.3	41.7						

APPENDIX 4

Study 2: Pharmacokinetics of mefloquine given at 6 h and 24 h after the oral dose of dihydroartemisinin

HEMATOLOGY

RBC d0 (10 ⁶ /µl)	RBC d2 (10 ⁶ /µl)	RBC d4 (10 ⁶ /µl)	WBC d0 (10 ³ /µl)	WBC d2 (10 ³ /µl)	WBC d4 (10 ³ /µl)	Neu d0 (%)	Neu d2 (%)	Neu d4 (%)	Lym d0 (%)	Lym d2 (%)	Lym d4 (%)	Pt. No.	Pt. initials	PLT d0 (10 ³ /µl)	PLT d2 (10 ³ /µl)	PLT d4 (10 ³ /µl)
4.59	4.56	4.26	2.4	3.6	3.9	70	66	59	30	34	41	2	PHV	24	49	110
4.1	3.5	3.45	4.8	4.6	4.9	82	58	43	18	42	57	3	TDT	200	350	97
5.29	4.97	5.27	6	6.1	5	83	57	40	17	43	60	5	NVD	59	52	178
3.2	3.15	3.33	5.6	5.5	4.5	72	62	52	28	38	48	8	KB	101	122	152
3.99	3.83	3.8	7.8	4.2	4.5	82	55	45	18	45	55	9	DNH	40	125	193
5	5	5	5	5	5	5	5	5	5	5	5	12	LVT	5	5	5
4.1	3.83	3.8	5.6	4.6	4.5	82	58	45	18	42	55	Count No.				
4.23	4.00	4.02	5.3	4.8	4.6	77.8	59.6	47.8	22.2	40.4	52.2	Mean				
3.20	3.15	3.33	2.4	3.6	3.9	70.0	55.0	40.0	17.0	34.0	41.0	Min				
5.29	4.97	5.27	7.8	6.1	5.0	83.0	66.0	59.0	30.0	45.0	60.0	Max				
0.77	0.75	0.79	2.0	1.0	0.4	6.3	4.4	7.7	6.3	4.4	7.7	SD				
18.25	18.77	19.54	37.0	20.9	9.5	8.0	7.4	16.0	28.2	10.9	14.7	CV				
5.3	5.66	4.8	4.8	5.1	3.7	59	60	42	41	40	58	1	TQT	61	213	200
4.78	4.7	4.05	3.8	4.3	3.8	78	63	40	22	37	60	4	NDH	64	75	123
4.2	3.27	3.43	6.4	3.6	3.3	81	70	51	19	30	49	6	TVT	74	66.4	90
4.81	3.57	3.09	6.7	4.8	4.6	65	43	48	35	57	52	7	TVH	25	57	94
4.59	4.21	4.04	5.1	5.7	5.4	77	65	60	23	35	40	10	DVH	95	125	147
5.18	5.17	4.4	6.1	4.9	3.9	77	75	52	23	25	48	11	NLT	118	67	84
6	6	6	6	6	6	6	6	6	6	6	6	Count No.				
4.795	4.455	4.045	5.6	4.85	3.85	77	64	49.5	23	36	50.5	Median				
4.81	4.43	3.97	5.5	4.7	4.1	72.8	62.7	48.8	27.2	37.3	51.2	Mean				
4.20	3.27	3.09	3.8	3.6	3.3	59.0	43.0	40.0	19.0	25.0	40.0	Min				
5.30	5.66	4.80	6.7	5.7	5.4	81.0	75.0	60.0	41.0	57.0	60.0	Max				
0.40	0.92	0.62	1.1	0.7	0.8	8.7	11.0	7.3	8.7	11.0	7.3	SD				
8.31	20.85	15.74	20.2	15.2	18.4	12.0	17.6	14.9	32.1	29.5	14.2	CV				

APPENDIX 4

Study 2: Pharmacokinetics of mefloquine given at 6 h and 24 h after the oral dose of dihydroartemisinin

BIOCHEMISTRY

Protein d0 (g/dl)	Protein d2 (g/dl)	Protein d4 (g/dl)	Alb d0 (g/dl)	Alb d2 (g/dl)	Alb d4 (g/dl)	SGOT d0 (U/l)	SGOT d2 (U/l)	SGOT d4 (U/l)	SGPT d0 (U/l)	SGPT d2 (U/l)	SGPT d4 (U/l)	Pt. No.	Pt. initials	Billi-d0 (mg/dl)
6.8	6.4	5.8	4.3	4.3	3.6	34	39	54	36	43	45	2	PHV	1.23
6.8	5.3	6	3.6	3.5	3.9	46	59	47	29	37	41	3	TDT	1.14
7.5	6.5	6.7	4.1	3.6	3.7	27	30	27	19	29	24	8	NVD	2.18
7	7	6.3	3.6	3.7	3.8	30	37	38	28	31	38	9	KB	1
7.2	6.7	7.6	3.9	3.6	4	27	27	33	15	14	28	12	DNH	2.06
5	5	5	5	5	5	5	5	5	5	5	5	Count No.	LVT	5
7	6.5	6.3	3.9	3.6	3.8	30	37	38	28	31	38	Count No.	PHV	1.23
7.1	6.4	6.5	3.9	3.7	3.8	32.8	38.4	39.8	25.4	30.8	35.2	Mean	TDT	1.5
6.8	5.3	5.8	3.6	3.5	3.6	27.0	27.0	27.0	15.0	14.0	24.0	Min	NVD	1.0
7.5	7.0	7.6	4.3	4.3	4.0	46.0	59.0	54.0	36.0	43.0	45.0	Max	KB	2.2
0.3	0.6	0.7	0.3	0.3	0.2	7.9	12.5	10.8	8.4	10.9	8.9	SD	DNH	0.6
4.2	10.1	11.0	7.9	8.6	4.2	24.1	32.6	27.1	33.0	35.3	25.2	CV	LVT	36.4
5.9	6.2	6.7	3.8	3.9	3.9	39	66	52	37	45	50	1	TQT	1.43
7.1	7.2	6	4	4	4.3	39	43	38	41	40	30	4	NDH	1.22
7.7	6.25	6.4	4.8	3.88	4.3	27	47	61	16	18	30	6	TVT	1.84
6.5	5.8	6.8	3.7	2.8	3.2	123	89	55	81	73	53	7	TVH	1.47
7.1	6.9	6.7	4.2	3.9	4	36	42	51	49	52	56	10	DVH	2.67
7.8	7.6	7.6	5.3	4.7	4	40	974	251	25	307	294	11	NLT	1.8
6	6	6	6	6	6	6	6	6	6	6	6	Count No.	NLT	6
7.1	6.575	6.7	4.1	3.9	4	39	56.5	53.5	39	48.5	51.5	Median	PHV	1.635
7.0	6.7	6.7	4.3	3.9	4.0	50.7	210.2	84.7	41.5	89.2	85.5	Mean	TDT	1.7
5.9	5.8	6.0	3.7	2.8	3.2	27.0	42.0	38.0	16.0	18.0	30.0	Min	NVD	1.2
7.8	7.6	7.6	5.3	4.7	4.3	123.0	974.0	251.0	81.0	307.0	294.0	Max	KB	2.7
0.7	0.7	0.5	0.6	0.6	0.4	35.8	374.6	81.8	22.6	108.2	102.8	SD	DNH	0.5
10.3	10.3	7.9	14.6	15.8	10.2	70.6	178.3	96.7	54.5	121.3	120.2	CV	LVT	29.5

APPENDIX 4

Study 2: Pharmacokinetics of mefloquine given at 6 h and 24 h after the oral dose of dihydroartemisinin

BIOCHEMISTRY

Bili-d2 (mg/dl)	Bili-d4 (mg/dl)	Urea d0 (mg/dl)	Urea d2 (mg/dl)	Urea d4 (mg/dl)	Crea d0 (mg/dl)	Crea d2 (mg/dl)	Crea d4 (mg/dl)	Glu d0 (mg/dl)	Glu d2 (mg/dl)	Glu d4 (mg/dl)	Urine d0	Urine d2	Urine d4	Pt. No.	Pt. initials
1.15	0.84	47.4	41.4	27	0.89	0.96	0.96	119	177	108	normal	normal	normal	2	PHV
0.78	0.83	51.0	42.03	27.6	1	1.02	0.77	103	119	83	normal	normal	normal	3	TDT
0.95	0.9	28.2	40.8	31.8	1.1	1.03	0.94	126	95	81	normal	normal	normal	5	NVD
0.94	0.83	30.6	41.4	19.2	1.12	1.26	1.06	133	96	87	normal	normal	normal	8	KB
0.97	1.02	33.0	32.4	25.2	1.51	1.01	1	92	88	108	normal	normal	normal	9	DNH
5	5	5	5	5	5	5	5	5	5	5	5	5	5	12	LVT
0.95	0.84	33.02083333	41.4	27	1.1	1.02	0.96	119	96	87	normal	normal	normal	5	Count No.
1.0	0.9	38.1	39.6	26.2	1.1	1.1	0.9	114.6	115.0	93.4					Mean
0.8	0.8	28.2	32.4	19.2	0.9	1.0	0.8	92.0	88.0	81.0					Min
1.2	1.0	51.0	42.0	31.8	1.5	1.3	1.1	133.0	177.0	108.0					Max
0.1	0.1	10.4	4.1	4.6	0.2	0.1	0.1	16.8	36.6	13.5					SD
13.7	9.2	27.4	10.2	17.5	20.9	11.1	11.5	14.7	31.8	14.5					CV
1.49	1.6	33	37.2	27	1.36	1.06	1.26	174	124	157	normal	normal	normal	1	TQT
1.11	0.82	42	38.4	30	1.2	1.11	1.1	139	103	153	normal	normal	normal	4	NDH
1.4	1.02	55.7	35.4	42	1.12	0.95	0.88	112	148	180	normal	normal	normal	6	TVT
1.79	0.86	49.8	28.2	20.4	1.18	0.89	1.27	171	121	110	normal	normal	normal	7	TVH
1.44	1.12	19.2	24	24.6	1.24	1.2	1.16	92	123	130	normal	normal	normal	10	DVH
1.63	1.71	48.6	63.6	42	1.08	1.21	1.2	110	115	99	normal	normal	normal	11	NLT
6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	Count No.
1.465	1.07	45.3	36.3	28.5	1.19	1.085	1.18	125.5	122	141.5					Median
1.5	1.2	41.4	37.8	31.0	1.2	1.1	1.1	133.0	122.3	138.2					Mean
1.1	0.8	19.2	24.0	20.4	1.1	0.9	0.9	92.0	103.0	99.0					Min
1.8	1.7	55.7	63.6	42.0	1.4	1.2	1.3	174.0	148.0	180.0					Max
0.2	0.4	13.3	13.8	9.1	0.1	0.1	0.1	34.1	14.8	30.7					SD
15.5	31.9	32.3	36.6	29.3	8.2	12.2	12.6	25.6	12.1	22.2					CV

APPENDIX 4

Study 2: Pharmacokinetics of mefloquine given at 6 h and 24 h after the oral dose of dihydroartemisinin

SIDE EFFECTS

Pt. No.	Pt. initials	Nausea severity (d0)	Nausea after treatment	Vomit severity (d0)	Vomit after treatment	Abdo. pain severity (d0)	Abdo. pain after treatment	Abdominal pain after treatment	Diarrhea severity (d0)	Diarrhea after treatment	Anorexia severity (d0)	Anorexia after treatment	Weakness severity (d0)	Weakness after treatment	Vertigo severity (d0)
2	PHV	2	0	1	0	0	0	0	0	0	2	0	2	0	0
3	TDT	2	1	0	0	0	0	0	0	0	3	0	3	0	2
5	NVD	3	0	1	0	0	0	0	0	0	2	0	3	0	1
8	KB	1	0	0	0	0	0	0	0	0	2	0	3	0	2
9	DNH	2	0	0	0	0	0	0	0	0	2	0	2	0	0
12	LVT	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	Count No.	2	0	0	0	0	0	0	0	0	2	0	3	0	1
	Mean	2.0	0.2	0.4	0.0	0.0	0.0	0.0	0.0	0.0	2.2	0.0	2.6	0.0	1.0
	Min	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0	0.0	2.0	0.0	0.0
	Max	3.0	1.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	3.0	0.0	3.0	0.0	2.0
	SD	0.7	0.4	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.0	0.5	0.0	1.0
	CV	35.4	223.6	136.9							20.3		21.1		100.0
1	TQT	2	0	1	0	0	0	0	0	0	2	0	2	0	1
4	NDH	2	0	0	0	0	0	0	0	0	2	0	3	0	2
6	TVT	3	0	1	0	0	0	0	0	0	2	0	3	0	2
7	TVH	2	0	1	0	0	0	0	0	0	2	0	3	0	2
10	DVH	2	0	0	0	1	0	0	0	0	3	0	3	0	2
11	NLT	1	0	0	0	0	0	0	0	0	1	0	2	0	1
	Count No.	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	Median	2	0	0.5	0	0	0	0	0	0	2	0	3	0	2
	Mean	2.0	0.0	0.5	0.0	0.2	0.0	0.0	0.0	0.0	2.0	0.0	2.7	0.0	1.7
	Min	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	0.0	2.0	0.0	1.0
	Max	3.0	0.0	1.0	1.0	1.0	0.0	0.0	0.0	0.0	3.0	0.0	3.0	0.0	2.0
	SD	0.6	0.0	0.5	0.4	0.4	0.0	0.0	0.0	0.0	0.6	0.0	0.5	0.0	0.5
	CV	31.6		109.5	244.9						31.6		19.4		31.0

APPENDIX 4

Study 2: Pharmacokinetics of mefloquine given at 6 h and 24 h after the oral dose of dihydroartemisinin

Vertigo after treatment	Pt. No.	Pt. initials	SIDE EFFECT											
			Tinnitus severity (d0)	Tinnitus after treatment	Headache severity (d0)	Headache after treatment	Confusion severity (d0)	Confusion after treatment	Chill severity (d0)	Chill after treatment	Palpitation severity (d0)	Palpitation after treatment		
0	2	PHV	0	0	2	0	0	0	0	2	0	0	0	0
0	3	TDT	0	0	3	0	0	0	0	3	0	0	0	0
0	5	NVD	1	0	3	0	0	0	0	3	0	0	0	0
0	8	KB	0	0	3	0	0	2	0	3	0	0	0	0
0	9	DNH	0	0	2	0	0	0	0	3	0	0	0	0
0	12	LVT	0	5	5	5	5	5	5	5	5	5	5	5
0		Count No.	0	0	3	0	0	0	0	3	0	0	0	0
0.0		Mean	0.2	0.0	2.6	0.0	0.0	0.4	0.0	2.8	0.0	0.0	0.0	0.0
0.0		Min	0.0	0.0	2.0	0.0	0.0	0.0	0.0	2.0	0.0	0.0	0.0	0.0
0.0		Max	1.0	0.0	3.0	0.0	0.0	2.0	0.0	3.0	0.0	0.0	0.0	0.0
0.0		SD	0.4	0.0	0.5	0.0	0.0	0.9	0.0	0.4	0.0	0.0	0.0	0.0
		CV	223.6		21.1			223.6		16.0				
0	1	TQT	0	0	3	0	0	0	0	3	0	0	0	0
0	4	NDH	0	0	0	3	0	0	0	3	0	0	0	0
0	6	TVT	0	0	3	0	0	0	0	3	0	0	0	0
0	7	TVH	0	0	3	0	0	1	0	3	0	0	0	0
0	10	DVH	0	0	3	0	0	0	0	3	0	0	0	0
0	11	NLT	0	0	3	0	0	0	0	3	0	0	0	0
6		Count No.	6	6	6	6	6	6	6	6	6	6	6	6
0		Median	0	0	3	0	0	0	0	3	0	0	0	0
0.0		Mean	0.0	0.0	2.5	0.5	0.2	0.2	0.0	3.0	0.0	0.0	0.0	0.0
0.0		Min	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.0	0.0	0.0	0.0	0.0
0.0		Max	0.0	0.0	3.0	3.0	3.0	1.0	0.0	3.0	0.0	0.0	0.0	0.0
0.0		SD	0.0	0.0	1.2	1.2	0.4	0.4	0.0	0.0	0.0	0.0	0.0	0.0
		CV			49.0	244.9	244.9	244.9		0.0				