SUPPLEMENTAL TABLE 1

Drug efficacy trials including ACT regimens from the ICEMR countries/regions

ICEMR	Specific location	Dates of trial	Trial comparison	Participants (*N*)	Risk failure 28 days, uncorrected	Risk failure 28 days, corrected	Ref.
West Africa	Thies	2011–2013	AL	147	2/147 (1%)	(1%)	–
	Dioro	2011–2013	AL	37	12/37 (32%)	(0%)	–
	Gambissara	2011–2013	AL	25	1/25 (4%)	(0%)	–
Uganda	Kampala	2002–2003	CQ/SP vs. AQ/SP vs. AS/AQ	384	CQ/SP 56%; AQ/SP 17%; AS/AQ 17%	CQ/SP 41%; AQ/SP 10%; AS/AQ 4%	1
	Apac, Arua, Jinja, Tororo	2002–2004	CQ/SP vs. AQ/SP vs. AS/AQ	2,160	CQ/SP 63–88%; AQ/SP 28–59%; AS/AQ 19–74%	CQ/SP 22–46%; AQ/SP 7–18%; AS/AQ 4–12%	2
	Tororo	2004–2005	AS/AQ vs. AL	403	AS/AQ 66%; AL 51%	AS/AQ 0%; AL 1.0%	3
	Kampala	2004–2006	AQ/SP vs. AS/AQ vs. AL	~200/arm	AQ/SP 26.1%; AS/AQ 17.4%; AL 6.7%	AQ/SP 14.1%; AS/AQ 4.6%; AL 1.0%	4
	Apac	2006	AL vs. DP	417	AL 29%; DP 11%	AL 8.9%; DP 1.9%	5
	Kanungu	2006	AL vs. DP	408	AL 17.3%; DP 3.8%	AL 3.2%; DP 0.9%	6
	Tororo	2007–2008	AL vs. DP	671	AL 35%; DP 11%	AL 1.0%; AS/AQ 0.3%	7
	Kampala	2007–2008	QN vs. AL	178	QN 35.3%; AL 4.1%	QN 23.1%; AL 4.1%	8
	Kampala	2004–2008	AQ/SP vs. AS/AQ vs. AL	1,464	AQ/SP 26.7%; AS/AQ 16.1%; AL 6.1%	AQ/SP 16.0%; AS/AQ 3.5%; AL 0.8%	9
	Tororo	2007–2012	AL vs. DP	5,564	AL 51.0%; DP 8.9%	AL 3.7%; DP 4.4% (63 days)	10
	Apac	2013	AL vs. AS/AQ	100/arm	AL 32.0%; AS/AQ 15.0%	AL 2.1%; AS/AQ 0%	–
	Mubende	2013	AL vs. AS/AQ	100/arm	AL 54.9%; AS/AQ 35.0%	AL 4.3%; AS/AQ 0%	–
	Kanungu	2014	AL vs. AS/AQ	100/arm	AL 50.0%; AS/AQ 38.0%	AL 41.1%; AS/AQ 0%	–
South Asia	Jharkhand, Odiisha	2007–2008	AS/AQ vs. AQ	300	AS/AQ 22%; AQ 13%	AS/AQ 5–10%; AQ 5%	11
	Assam, Goa, Karnataka	2006–2007	DP vs. AS/MQ	150	DP 10% vs. AS/MQ 18%	DP 1% vs. AS/MQ 0%	12
	Goa, Karnataka	2007–2008	AS/MQ	77	AS/MQ 1%	AS/MQ 0%	13
	Arunachal Pradesh, Tripura, Mizoram	2012	AS/SP	169	AS/SP 33%	AS/SP 20%	14
	Nine sites	2009–2010	AS/SP vs. AS/SP//PQ	1,335	–	–	15
	Seven countries	2007–2008	AS/PY vs. AS/MQ	1,271	AS/PY 4%; AS/MQ 5%	–	16
PNG	Alexishaven, Kunjinini	2006–2008	AL vs. DP vs. CQ/SP vs. ART/SP	Pf: 110–127/arm; Pv: 39–61	Pf: AL 7%, DP 14%, CQ/SP 32%, ART/SP 13%; Pv: AL 51%, DP 16%, CQ/SP 49%, ART/SP 49%	Pf: AL 3%, DP 10%, CQ/SP 15%, ART/SP 10%	17
	Mugil	2011–2013	AL vs. ART/NQ	Pf:100/arm; Pv: 20 and 27	Pf: AL 2%, ART/NQ 0%; Pv: AL 35%, ART/NQ 0%	Pf: AL 1%, ARCO 0%; Pv: AL 20%, ARCO 0%	–

ACT = artemisinin-based combination therapy; AL = artemether/lumefantrine; AQ = amodiaquine; ARCO = ART/NQ; ART = artemisinin; AS = artesunate; CQ = chloroquine; DP = dihydroartemisinin/piperaquine; ICEMR = the International Centers of Excellence for Malaria Research; MQ = mefloquine; NQ = naphthoquine, PNG = Papua New Guinea; PQ = piperaquine; PY = pyronaridine; QN = quinine; Ref. = references include both published data (shown below) and unpublished data; SP = sulfadoxine/pyrimethamine.

SUPPLEMENTAL TABLE 2

Ex vivo/in vitro drug efficacy results from the ICEMR countries/regions

ICEMR	Specific location	Date of collection	Source of samples	*N*	Assay	Mean (or median) IC_{50} (nM)								Ref.
						CQ	DEAQ	QN	LM	MQ	PQ	DHA	Other	
West Africa	Thies	2008	Adult, child	~400	Ex vivo; DAPI assay	30.7	9.6	NT	NT	34.5	NT	NT	–	[18]
		2009												
		2010				15.0	6.5	176.9	NT	44.6	NT	NT		
		2011				22.4	11.2	45.65	NT	32.6	NT	4.3		
		2012				76.1	14.5	239.9	119	42.1	101	2.1		
						36.5	14,3	178.2	168.1	36.6	173	1.9		
						23.8	6.65	182.4	316.9	38.5	20.3	2.0		
Uganda	Kampala	2006–2008	Child cohort	241	Ex vivo; HRP ELISA	101.1	66.4	94.4	0.51	–	6.1	0.55	–	[19]
	Tororo	2010–2012		286	Ex vivo; HRP ELISA	486.2	83.3	126.4	2.7	–	20.3	1.7	–	[20]
South Asia	Assam	2007	Child cohort	115	Ex vivo; microscopy	"221 uM/L"	–	–	–	–	–	–	–	[21]
	West Bengal	2008–2009	All ages	126	In vitro; hypoxanthine	54	–	–	–	–	–	–	–	[22]
Southeast Asia	China–Myanmar border	2006–2009	PCD samples	60	In vitro, SYBR Green	–	–	> 500	–	–	–	–	–	[23]
		2007–2009	PCD samples	51	In vitro, SYBR Green	–	–	–	5.9	50.4	–	23.0	AS 5.8	[24]
		2007–2010	PCD samples	63	In vitro, SYBR Green	252.7	–	–	–	–	28.4	–	–	[25]
PNG	Madang	2006–2007	Community survey	64	Ex vivo; pLDH ELISA	167	19.3	–	5.4	11.7	11.7	2.1	NQ 7.0	[26]

AS = artesunate; CQ = chloroquine; DAPI = 4′,6-diamidino-2-phenylindole; DEAQ = desethylamodiaquine; DHA = dihydroartemisinin; ELISA = enzyme-linked immunosorbent assay; HRP = horseradish peroxidase; ICEMR = the International Centers of Excellence for Malaria Research; LM = lumefantrine; MQ = mefloquine; NQ = naphthoquinone; NT = not tested; PCD = passive case detection; pLDH = *Plasmodium* lactate dehydrogenase; PNG = Papua New Guinea; PQ = piperaquine; QN = quinine; Ref. = references include both published data (shown below) and unpublished data.

SUPPLEMENTAL TABLE 3

Assessment of drug resistance polymorphisms in samples from the ICEMR countries/regions, transporters

ICEMR	Specific location	Date of collection	Source of samples	*N*	Single nucleotide polymorphism prevalence (%; WT/mixed/mutant)						Ref.
					Pfcrt K76T	*Pfmdr1* N86Y	*Pfmdr1* Y184F	*Pfmdr1* S1034C	*Pfmdr1* N1042D	*Pfmdr1* D1246Y	
West Africa	Pikine, Thies	2008	–	~700	44/3/53	88/2/10	64/4/32	100/0/0	75/1/24	100/0/0	18,27
		2009			49/5/46	81/5/14	42/7/51	100/0/0	82/0/8	100/0/0	
		2010			53/6/41	84/0/16	30/9/61	100/0/0	90/0/10	90/0/10	
		2011			54/3/43	89/11/0	41/9/50	Not done	89/0/11	Not done	
Zambia	Choma	2006	All ages, DBS	59	3.4/10.2/86.4	–	–	–	–	–	–
		2008	–	42	23.7/5.3/71.1	–	–	–	–	–	
		2009	–	30	37.9/0/62.1	–	–	–	–	–	
		2010	–	70	80.0/1.4/18.6	–	–	–	–	–	
Zimbabwe	Mutasa	2003	All ages, DBS	49	33.0/3.0/63.6	–	–	–	–	–	
		2013	–	54	97.0/0.0/3.0	–	–	–	–	–	
Uganda	Six sites	2002–2004	–	2,049	2.4/15.0/82.6	–	–	–	–	–	28
	Tororo	2004–2005	DBS	201	–	8/30/62	90/8/2	–	–	14/48/38	29
		2003–2004	–	79	0/1/99	10/71/19	75/23/2	–	–	2/48/50	30
		2005		201	0/0/100	9/38/53	85/14/1			17/40/43	
		2007		39	0/0/100	32/19/49	68/19/13			23/31/46	
		2008		147	0/2/98	23/61/16	71/15/14			24/34/42	
		2009		96	4/2/94	23/27/44	83/7/10			17/23/60	
		2010		111	0/4/96	44/37/19	37/41/22			19/50/31	
		2011		111	0/8/92	47/37/16	59/7/34			20/48/32	
		2012		79	17/16/67	51/41/8	68/6/26			53/34/13	
South Asia	Assam	2006–2008	All ages, PHC	200	0/1/99	30/-/68	–	–	–	–	31
				65	15/-/50	15/-/50	–	–	–	–	21
	Arunachal Pradesh	2006–2008		50	0/-/50	0/-/50	–	–	–	–	21
	West Bengal	2008–2009	All ages	126	45/-/55	39/-/61	100/-/0	34/-/66	100/-/0	54/0/46	22
	Madhya Pradesh	2004–2006	All ages, PHC	104	5/-/95	19/-/81	35/0/65	–	–	–	32
	Car Nicobar Islands	2008	Community	48	0/3/97	–	–	–	–	–	33
				204							
Southeast Asia	China–Myanmar border	2007–2009	PHC	51	–	2	27.5	–	7.8	–	24
		2007–2010	PHC	63	100	1.6	25.4	–	6.3	–	25

DBS = dry blood spots; ICEMR = the International Centers of Excellence for Malaria Research; PHC = public health center; Ref. = references include both published data (shown below) and unpublished data; WT = wild type.

SUPPLEMENTAL TABLE 4

Assessment of drug resistance polymorphisms in samples from the ICEMR countries/regions, antifolates

				Single nucleotide polymorphism prevalence (%; WT/mixed/mutant)										
				Pfdhfr					*Pfdhps*					
ICEMR/region	Specific location	Date of collection	*N*	A16V	N51I	C59R	S108N (*T)	I164L	S436A	A437G	K540E	A581G	A613T/S	Ref.
West Africa	Pikine, Thies	2003	700	–	47/13/40	46/13/41	26/7/67	100/0/0	77/14/9	26/6/67	100/0/0	100/0/0	100/0/0	18,27,34
		2008	–	–	8/4/88	7.8/3.2/89	3/2/95	100/0/0	74/3/23	79/1/20	100/0/0	100/0/0	100/0/0	
		2009	–	–	7/6/87	7/6/87	23/1/76	100/0/0	74/3/23	70/1/29	100/0/0	100/0/0	100/0/0	
		2010	–	–	6/6/88	6/6/88	9/3/88	100/0/0	86/1/13	36/1/63	100/0/0	100/0/0	100/0/0	
		2011	–	–	0/7/93	0/3/97	0/4/96	100/0/0	97/1/2	36/7/57	100/0/0	100/0/0	100/0/0	
		2012	–	–	2/15/83	2/16/82	1/95.8/3.2	100/0/0	90/1/9	36/5/54	100/0/0	100/0/0	100/0/0	
Zambia	–	2000	49	100//0	–	44.9/0.0/55.1	49.0/0.0/51.2	100/0/0	93.9/0/6.1	60.6/0.0/39.4	93.5/0.0/6.5	100/0/0	100/0/0	35,36
		2003	25	100/0/0	32.0/0.0/68.0	44.0/0.0/56.0	16.0/0.0/84.0	100/0/0	92/0/8	64.7/0.0/35.3	88.0/0.0/12.0	100/0/0	100/0/0	
		2006	136	1.5/0/98.5	20.8/4.8/74.4	40.3/8.5/51.2	5.9/8.1(1.5)/ 80.9(3.8)	100/0/0	92.9/0/7.1	78.6/0.0/21.4	83.9/0.0/16.1	100/0/0	100/0/0	
Malawi	Southern region	2012	3,000	–	0.77/0.64/98.6	1.19/3.14/95.0	0.28/2.02/97.7	99.66/0.34/0	99.4/0.4/0.2	1.09/1.66/97.24	2.38/1.19/96.44	95.7/2.16/2.08	91.3/8.7/0	–
Uganda	Kampala	1998–2003	812	–	8/4/88	34/20/56	2/12/88	–	–	24/22/64	20/20/60	–	–	37
	Six sites	2002–2004	2,049	–	0.4/3.1/96.5	19.8/24.3/55.8	0/0.4/99.6	99.8/0.2/0	–	9.2/14.2/76.6	10.8/19.0/70.2	–	–	28
	Tororo	2003–2004	79	–	0/6/94	7/37/56	0/0/100	80/0/0	–	2/14/84	2/26/72	100/0/0	–	30
		2005	201		1/2/97	7/31/62	1/2/97	99/1/0		2/12/86	1/13/86	98/1/1		
		2007	39		0/0/100	8/3/89	0/59/41	100/0/0		0/0/100	0/0/100	100/0/0		
		2008	147		1/0/99	3/6/91	0/23/77	99/1/0		1/1/98	0/4/96	88/11/1		
		2009	96		1/0/99	7/3/90	0/11/89	91/8/1		1/1/98	0/4/96	89/10/1		
		2010	111		0/1/99	9/11/80	1/16/83	88/11/1		1/2/97	1/4/95	87/4/9		
		2011	111		0/0/100	4/13/83	0/9/91	100/0/0		1/1/98	1/13/86	88/8/4		
		2012	79		0/0/100	8/6/86	0/2/98	100/0/0		0/5/95	0/4/96	98/2/0		
South Asia	Uttar Pradesh	2003–2004	35	100/0/0	97/0/3	24/0/66	3/0/97	97/0/3	100/0/0	91/0/9	100/0/0	100/0/0	100/0/0	38
	Assam	2003–2004	37	100/0/0	86/0/14	8/0/92	8/0/92	92/0/08	78/0/22	68/0/32	78/0/22	95/0/5	100/0/0	38
	Assam	2006–2008	200	99/0/1	80/0/20	3/0/97	0/0/100	86/0/14	75/025	40/0/60	61/0/39	79/0/21	76/0/22	31
	Madhya Pradesh	2004–2006	104	–	–	22/-/78	12/0/88	–	–	−88/-/12	96/-/4	97/0/3	–	32
	Goa	2012–2013	50	29/-/71	–	–	19/-/81	–	100/-/0	78/0/22	100/-/0	100/-/0	100/-/0	–
	Car Nicobar Island	2003–2004	33	100/0/0	10/0/90	0/0/100	0/0/100	12/0/88	54/0/46	20/0/80	80/0/20	80/0/20	100/0/00	39
Southeast Asia	China–Myanmar border	2010	117	0	63.2	99.1	99.1	78.6	62.3	98.3	87.2	37.6	0	40

ICEMR = the International Centers of Excellence for Malaria Research; PHC = public health center; Ref. = references include both published data (shown below) and unpublished data; WT = wild type.

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