Supplemental Table 1: Molecular markers of resistance and association with treatment outcome, artemether-lumefantrine arms, DRC therapeutic efficacy study, 2017

	All samples	Reinfection Day 0	Recrudescence + Reinfection Day of failure	P
Pfk13				
Successfully sequenced	191/209 (91%)	110/118 (93%)	81/91 (89%)	
Wild type	185 (95.9%)	107 (97.3%)	78 (96.3)	Ref
Synonymous[a]	6 (3%)	3 (3%)	3 (4%)	1
Non-synonymous	0 (0%)	0 (0%)	0 (0%)	NA
Pfmdr1[b]				
Successfully sequenced	158/158 (100%)	67/67 (100%)	91/91 (100%)	-
N86	121 (77%)	43 (64%)	78 (86%)	Ref
86N/Y	6 (4%)	4 (6%)	2 (2%)	0.270
86Y	31 (20%)	20 (30%)	11 (12%)	**0.007**
Y184	106 (67%)	39 (58%)	67 (74%)	Ref
184Y/F	28 (18%)	17 (25%)	11 (12%)	**0.040**
184F	24 (15%)	11 (16%)	13 (14%)	0.551
D1246	140 (89%)	60 (90%)	80 (88%)	Ref
1246D/Y	16 (10%)	6 (9%)	10 (11%)	0.895
1246Y	2 (1%)	1 (1%)	1 (1%)	1
NYD	105 (66%)	39 (58%)	66 (73%)	Ref
NFD	43 (27%)	20 (30%)	23 (25%)	0.383
NFY	2 (1%)	0 (0%)	2 (2%)	0.289
NYY	13 (8%)	3 (4%)	10 (11%)	0.499
YFD	10 (6%)	9 (13%)	1 (1%)	**0.003**
YFY	0 (0%)	0 (0%)	0 (0%)	NA
YYD	33 (21%)	20 (30%)	13 (14%)	0.972
YYY	4 (3%)	4 (6%)	0 (0%)	0.715

[a]Synonymous mutations include P417P, C469C, R471R, S477S, T478T, G496G, Y511Y, R539R, S576S,
[b]*pfmdr1* haplotype constructed according to amino acids at positions 86, 184, and 1246; mixed infections included in numerator for each haplotype

Supplemental Table 2: Molecular markers of resistance and association with treatment outcome, artesunate-amodiaquine arms, Democratic Republic of the Congo therapeutic efficacy study, 2017

	All samples	Reinfection Day 0	Recrudescence + Reinfection Day of failure	p-value
Pfk13				
Successfully sequenced	87/90 (97%)	42/43 (98%)	45/47 (96%)	-
Wild type	85 (98%)	41 (98%)	43 (96%)	Ref
Synonymous[a]	3 (3%)	1 (2%)	2 (4%)	1
Non-synonymous	0 (0%)	0 (0%)	0 (0%)	NA
Pfmdr1[b]				
Successfully sequenced	81/85 (95%)	36/38 (95%)	45/47 (96%)	-
N86	15 (19%)	9 (25%)	6 (13%)	Ref
86N/Y	13 (16%)	6 (17%)	7 (16%)	0.725
86Y	53 (65%)	21 (58%)	32 (71%)	0.268
Y184	49 (60%)	22 (61%)	27 (60%)	Ref
184Y/F	14 (17%)	6 (17%)	8 (18%)	1
184F	18 (22%)	8 (22%)	10 (22%)	1
D1246	51 (63%)	22 (61%)	29 (64%)	Ref
1246D/Y	12 (15%)	5 (14%)	7 (16%)	1
1246Y	18 (22%)	9 (25%)	9 (20%)	0.817
NYD	17 (21%)	9 (25%)	8 (18%)	Ref
NFD	18 (22%)	8 (22%)	10 (22%)	0.870
NFY	4 (5%)	1 (3%)	3 (7%)	0.662
NYY	5 (6%)	3 (8%)	2 (4%)	1
YFD	69 (85%)	27 (75%)	42 (93%)	0.446
YFY	5 (6%)	1 (3%)	4 (9%)	0.436
YYD	40 (49%)	17 (47%)	23 (51%)	0.663
YYY	26 (32%)	13 (36%)	13 (29%)	1
Pfcrt[c, d]				
Successfully sequenced	85/85 (100%)	38/38 (100%)	47/47 (100%)	-
M74	8 (9%)	6 (16%)	2 (4%)	Ref
74M/I	2 (2%)	2 (5%)	0 (0%)	1
74I	75 (88%)	30 (79%)	45 (96%)	0.128
N75	10 (12%)	8 (21%)	2 (4%)	Ref

75N/E	1 (1%)	0 (0%)	1 (2%)	0.546
75E	74 (87%)	30 (79%)	44 (94%)	**0.042**
K76	9 (11%)	8 (21%)	1 (2%)	Ref
76K/T	1 (1%)	0 (0%)	1 (2%)	0.4
76T	75 (88%)	30 (79%)	45 (96%)	**0.013**
CVMNK	9 (11%)	8 (21%)	1 (2%)	Ref
CVIET	75 (88%)	30 (79%)	45 (96%)	**0.013**
CVMNT	1 (1%)	0 (0%)	1 (2%)	0.400
CVINK	3 (6%)	2 (6%)	1 (2%)	0.909

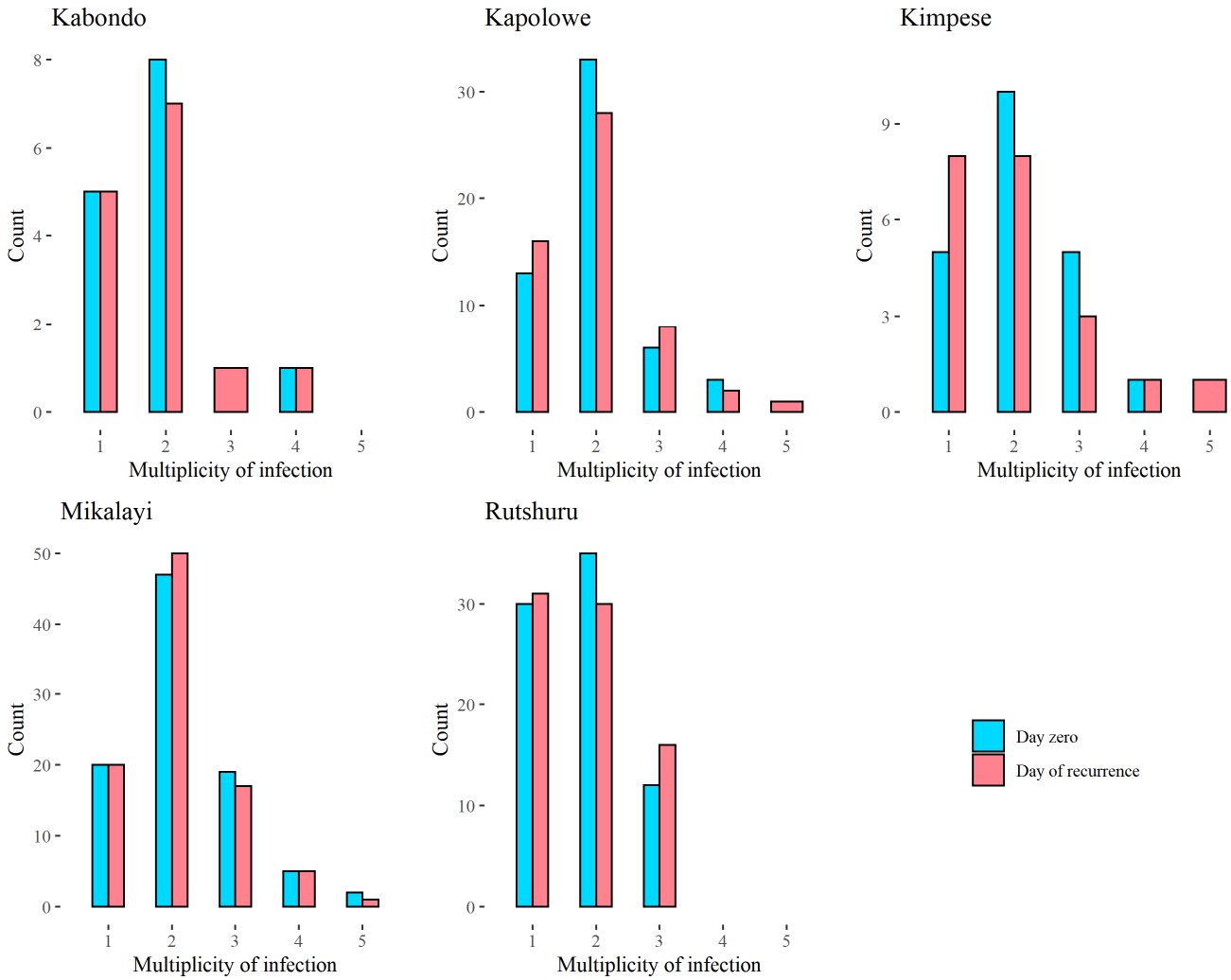
[a]Synonymous mutations include P417P, C469C, R471R, S477S, T478T, G496G, Y511Y, R539R, S576S,
[b]*pfmdr1* haplotype constructed according to amino acids at positions 86, 184, and 1246; mixed infections included in numerator for each haplotype
[c]*pfcrt* haplotype constructed according to amino acids at positions 72, 73, 74, 75, and 76; mixed infections included in numerator for each haplotype
[d]all samples were wildtype for positions 72 (C) and 73 (D)

Supplemental Table 3: Molecular markers of resistance and association with treatment outcome, dihydroartemisinin-piperaquine arms, Democratic Republic of the Congo therapeutic efficacy study, 2017

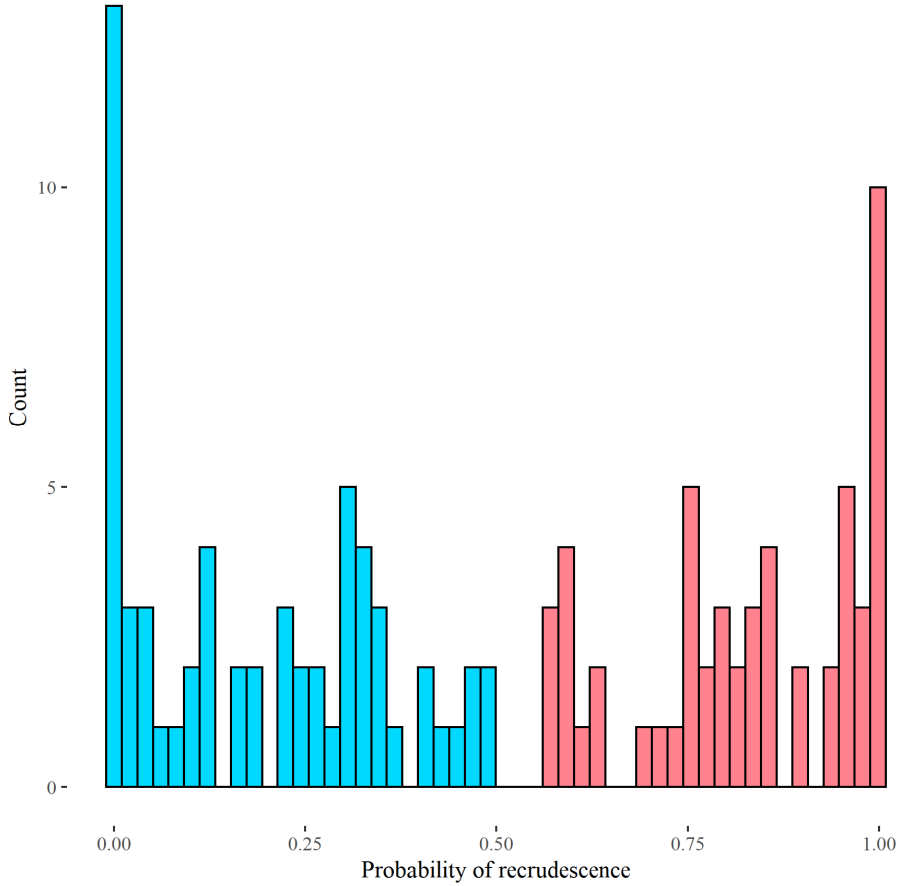
	All samples	Reinfection Day 0	Recrudescence + Reinfection Day of failure	*P*
Pfk13				
Successfully sequenced	208/224 (93%)	99/102 (97%)	109/122 (89%)	-
Wild type	199 (96%)	96 (97%)	103 (95%)	Ref
Synonymous[a]	8 (4%)	0 (0%)	5 (5%)	0.796
Non-synonymous[b]	1 (0.5%)	0 (0%)	1 (0.9%)	1
Pfmdr1[c]				
Successfully sequenced	223/223 (100%)	101/101 (100%)	122/122(100%)	-
N86	127 (57%)	57 (56%)	70 (57%)	Ref
86N/Y	33 (15%)	16 (16%)	17 (14%)	0.859
86Y	63 (28%)	28 (28%)	35 (29%)	1
Y184	113 (51%)	58 (57%)	55 (45%)	Ref
184Y/F	60 (27%)	22 (22%)	38 (31%)	0.092
184F	50 (22%)	21 (21%)	29 (24%)	0.353
D1246	188 (84%)	84 (83%)	104 (85%)	Ref
1246D/Y	7 (3%)	2 (2%)	5 (4%)	0.662
1246Y	28 (13%)	15 (15%)	13 (11%)	0.497
NYD	118 (53%)	53 (52%)	65 (53%)	Ref
NFD	81 (36%)	35 (35%)	46 (38%)	0.927
NFY	11 (5%)	4 (4%)	7 (6%)	0.828
NYY	11 (5%)	5 (5%)	6 (5%)	1
YFD	71 (32%)	34 (34%)	37 (30%)	0.805
YFY	9 (4%)	3 (3%)	6 (5%)	0.755
YYD	59 (26%)	25 (25%)	34 (28%)	0.874
YYY	28 (13%)	15 (15%)	13 (11%)	0.538

[a]Synonymous mutations include P417P, C469C, R471R, S477S, T478T, G496G, Y511Y, R539R, S576S,
[b]Non-synonymous mutation, S477Y
[c]*pfmdr1* haplotype constructed according to amino acids at positions 86, 184, and 1246; mixed infections included in numerator for each haplotype

Supplemental figure 1: Multiplicity of infection of day 0 and day of recurrence samples from treatment failures as determined by the maximum number of alleles detected among seven neutral microsatellite markers, Democratic Republic of the Congo therapeutic efficacy study, 2017

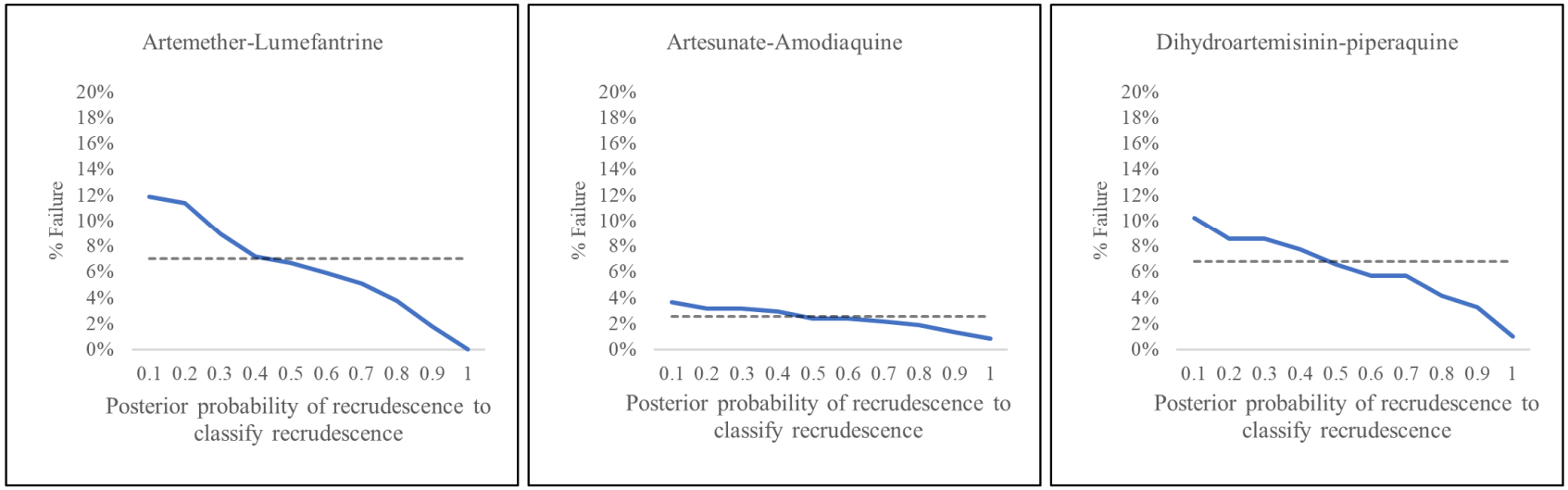


Supplemental figure 2: Histogram of posterior probability of recrudescence of all late treatment failures for which the probability of recrudescence is over 0% (n=114).



The sum posterior probability of recrudescence was 57. There were 54 samples with a posterior probability of recrudescence of .5 or higher (and labeled as a recrudescence). The mean posterior probability of recrudescence was 0.04 (standard deviation= 0.17). Among late failures for which the posterior probability of recrudescence was >0 (n=114, 42.5%), the mean posterior probability of recrudescence was 0.49 (standard deviation= 0.37)

Supplemental figure 3: Assessment of the use of different cutoffs of posterior probability of recrudescence derived using a Bayesian algorithm for interpreting microsatellite data for molecular correction, Democratic Republic of the Congo therapeutic efficacy study, 2017



Failure rate estimates obtained using the Bayesian analysis algorithm for artemether-lumefantrine, artesunate-amodiaquine, and dihydroartemisinin-piperaquine. The failure rate derived by summing the posterior probability of recrudescence for each arm is denoted in each plot by a horizontal gray line. The cutoff for posterior probability at which a recurrence was classified as a recrudescence varied between ≥0.1 and 1.

Supplemental File: Microsatellite data