| IC (nM) | Drug | $D10^{wt}$ | $D10^{mut}$ | p |
|---|---|---|---|---|
| **$IC_{20}$** | CQ | 15.5 (14.4 – 16.7) | 14.5 (13.5 – 15.6) | 0.33 |
| | AQ | 5.7 (4.6 – 7.5) | 12.5 (12.2 – 12.9) | $1.47 \times 10^{-3}$ |
| | DEAQ | 8.3 (7.9 – 8.8) | 8.6 (7.9 – 9.5) | 0.61 |
| **$IC_{50}$** | CQ | 28.0 (26.3 – 29.7) | 26.6 (25.4 – 27.9) | 0.21 |
| | AQ | 15.1 (13.1 – 17.1) | 28.7 (26.8 – 30.6) | $7.97 \times 10^{-12}$ |
| | DEAQ | 15.3 (13.5 – 17.0) | 20.5 (19.4 -21.5) | $1.32 \times 10^{-5}$ |
| **$IC_{90}$** | CQ | 54.1 (52.4 – 55.7) | 52.9 (50.9 – 55.0) | 0.66 |
| | AQ | 34.6 (33.3 – 35.8) | 49.9 (49.3 – 50.5) | $1.15 \times 10^{-4}$ |
| | DEAQ | 33.5 (32.2 – 34.8) | 42.2 (40.8 – 43.6) | $7.22 \times 10^{-4}$ |

**Table S1.** D10 susceptibilities to CQ, AQ and DEAQ (nM; $CI_{95\%}$). P-values (p) for the difference in between the clones were controlled according to the Bonferroni method.

| | Start | Drug removal | End | *g* |
|---|---|---|---|---|
| **Control** | 48.0 (46.4 – 49.6) | 42.1 (36.9 – 47.2) | 30.9 (29.9 – 31.9) | 0.89 |
| **$IC_{20}$ CQ** | 47.3 (45.0 – 49.7) | 31.7 (31.2 – 32.2) | 39.3 (36.8 – 41.9) | 0.95 |
| **$IC_{20}$ AQ** | 47.3 (45.0 – 49.7) | 29.7 (29.1 – 30.3) | 39.5 (38.6 – 40.4) | 0.95 |
| **$IC_{20}$ DEAQ** | 47.3 (45.0 – 49.7) | 34.2 (26.3 – 42.2) | 39.2 (36.2 – 42.3) | 0.94 |
| **$IC_{50}$ CQ** | 48.8 (46.6 – 51.0) | 58.1 (56.1 – 60.2) | 64.2 (56.1 – 72.4) | 1.11 |
| **$IC_{50}$ AQ** | 48.8 (46.6 – 51.0) | 57.8 (56.7 – 58.9) | 65.0 (59.2 – 70.7) | 1.12 |
| **$IC_{50}$ DEAQ** | 48.8 (46.6 – 51.0) | 46.0 (44.2 – 47.8) | 56.3 (50.6 – 62.0) | 1.05 |

**Table S2.** Proportion (%; $CI_{95\%}$) of the *pfmdr1* 1246Y allele in mixed cultures under drug free conditions (control) or after exposure to an $IC_{20}$ or $IC_{50}$ concentration of CQ, AQ or DEAQ. The relative growth (*g*) for the mutated clone as compare with the wild-type clone.

| Recurrent infections | pfmdr1 1246 | Day 0 | Day 1-7 | Day 8-14 | Day 15-21 | Day 22-28 | Day 29-35 | Day 36-42 | Day 1-42 |
|---|---|---|---|---|---|---|---|---|---|
| AQ | D | 17 | 1 | 2 | 3 | | | | 6 |
| | Y | 11 | 1 | 10 | 4 | | | | 15 |
| | Total | 28 | 2 | 12 | 7 | | | | 21 |
| ASAQ 2002-3 | D | 126 | 0 | 0 | 13 | 13 | 9 | 5 | 40 |
| | Y | 13 | 0 | 2 | 4 | 0 | 3 | 2 | 11 |
| | Total | 139 | 0 | 2 | 17 | 13 | 12 | 7 | 51 |
| ASAQ 2005 | D | 132 | 0 | 2 | 7 | 7 | 2 | 7 | 25 |
| | Y | 23 | 0 | 3 | 5 | 2 | 1 | 3 | 14 |
| | Total | 155 | 0 | 5 | 12 | 9 | 3 | 10 | 39 |

| Recrudescent infections | pfmdr1 1246 | Day 0 | Day 1-7 | Day 8-14 | Day 15-21 | Day 22-28 | Day 29-35 | Day 36-42 | Day 1-42 |
|---|---|---|---|---|---|---|---|---|---|
| AQ | D | 17 | 0 | 0 | 0 | | | | 0 |
| | Y | 11 | 1 | 6 | 4 | | | | 11 |
| | Total | 28 | 1 | 6 | 4 | | | | 11 |
| ASAQ 2002-3 | D | 126 | 0 | 0 | 4 | 0 | 2 | 0 | 6 |
| | Y | 13 | 0 | 0 | 1 | 0 | 0 | 0 | 1 |
| | Total | 139 | 0 | 0 | 5 | 0 | 2 | 0 | 7 |
| ASAQ 2005 | D | 132 | 0 | 0 | 3 | 2 | 0 | 1 | 6 |
| | Y | 23 | 0 | 1 | 4 | 0 | 1 | 0 | 6 |
| | Total | 155 | 0 | 1 | 7 | 2 | 1 | 1 | 12 |

**Table S3.** *Pfmdr1* D1246Y allele distribution (n) in all recurrent infections and in recrudescent infections specifically during follow-up after AQ monotherapy in Kenya 2003

(n=53) or ASAQ combination therapy in Zanzibar 2002 – 2003 (n=198) and 2005 (n=174). Mixed and unknown genotype results excluded.