Figures and figure supplements

A randomized feasibility trial comparing four antimalarial drug regimens to induce Plasmodium falciparum gametocytemia in the controlled human malaria infection model

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Figure 1. Trial profile. ECG = electrocardiography, BMI = body mass index, AST = aspartate aminotransferase, ALP = alkaline phosphatase

DOI: https://doi.org/10.7554/eLife.31549.003
Figure 2. Asexual parasitemia and gametocytemia. Black line represents 18S qPCR asexual parasitemia. Black dotted-line represents 18S qPCR after treatment 1. Red line represents Pfs25 qRT-PCR gametocytemia. DOI: https://doi.org/10.7554/eLife.31549.004
Figure 2—figure supplement 1. Asexual parasitemia and gametocytemia per study participant. Black line represents 18S qPCR asexual parasitemia. Black dotted-line represents 18S qPCR after treatment 1. Red line represents Pfs25 qRT-PCR gametocytemia. Grey lines represent individual PCR curves of other participants of the same group.
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Figure 3. Gametocyte kinetics between study arms. (A) Percentage gametocyte carriers between study arms (B) Estimated mean area under the curve for concentration of gametocytes per arm (Bayesian framework). The shaded area of each density curve represents the middle 95% percentiles (i.e. 2.5th to 97.5th percentiles) of the estimated mean AUC for a study arm; the density curve itself spans the middle 99% percentiles of the posterior; the posterior mean is indicated by the vertical solid line within each density plot. (C) Association of area under the curves of asexual parasitemia and gametocytemia. The different plotting shapes are the individual participants per group. (D) Thin- and thick- blood smears of concentrated gametocytes after magnetic cell sorting of blood samples from two individuals from LD-PIP/SP arm.

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Figure 4. Total female and male gametocyte density of all participants. Dots represent individual gametocyte data. Circles and squares represent mean and error (SEM) of gametocytes per timepoint.
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Figure 4—figure supplement 1. Female and male gametocytes per study arm.
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Figure 4—figure supplement 2. Female and male gametocyte clearance dynamics per participant included in analysis. Curves are log gametocytes/mL. Recoded days are the days of gametocyte observations from 12 days after the last detection of asexual parasites until the end of study.

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Figure 5. Standard curves of qRT-PCR and qPCR. Standard curves (Mean, SD) obtained using 10-fold dilutions of cultured gametocytes. The highest concentration was enumerated by two independent expert microscopists. The mean and standard deviation of 54, 28, 72 replicates of the standard curve during the study was determined for the Pfs 25-, PfMGET, and 18S target genes, respectively. For PfMGET, six points starting from $10^6$ pure male gametocytes/mL were measured. $10^1$ was positive in 6/28 replicates (black dot).

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Figure 5—figure supplement 1. Standard curves of Pfs25 qRT-PCR – low-density trendlines. Standard curves (Mean, SD) obtained using serial dilutions of cultured gametocytes including low-density trendlines to determine the limit of detection (LOD) and limit of quantification (LOQ) of the Pfs25 qRT-PCR.

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Figure 5—figure supplement 2. Correlation of duplo Pfs25 qRT-PCR measurements in all study samples. All duplo-estimation data points of the study participants as measured by Pfs25 qRT PCR. All samples with $\geq 5$ parasites/mL were duplo positive (190/190, 100%), and showed a correlation coefficient $R^2$ of 0.94. Variation of samples $< 5$ parasites/mL was considerably larger and positivity could not be reliably estimated with 35/75 (47%) of samples that were positive in at least one qRT-PCR being single positives ($R^2$ of 0.46).

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Figure 6. Adverse events. (A) Adverse events per study arm (B) Total no. of adverse events and time course.
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Figure 6—figure supplement 1. Liver function test derangements. ALT = alanine aminotransferase, AST = aspartate aminotransferase, γGT = gamma glutamyl transferase, ALP = alkaline phosphatase, T1 = Treatment 1, T2 = Treatment 2.
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