

Appendix A. Supplementary Material

1. Statistical methods and analyses

1.1. Evaluation of the Cox PHZ assumption:

The proportional hazards (PH) assumption was checked using statistical tests (Cox PHZ) based on the *scaled Schoenfeld residuals* ($\rho=0.11$; $\text{chisq}=1.19$; $p=0.28$). The test output was not statistically significant for the covariate. Therefore, we can assume the proportional hazards model is the proper test for this data set.

1.2. Power calculations:

The power calculation was done for all models based on the available sample size in each model ($n=13-31$). Power for GLM models were estimated using the (pwr) package in R. The models had a range of power from 65% to 85% that were very close to the target value of 95%. Stimulation based analysis for GLMM models pinpoints the inadequacy of classical analytical power analysis. Freely available (simr) functions was used for estimating the power of GLMM models and (powersurvEpi) package was applied for estimating the 90% power of the Cox PHZ model (Hsieh et al., 2000).

Supplementary Table 1: Patient characteristics

	Total population (N=36)
Age, years	
Median (range)	39.5 (21-70)
Sex	
Male, n (%)	31 (86.1)
Patient origin (country of birth), n (%)	
Non-endemic	10 (27.8)
Endemic	26 (72.2)
Years out of endemic area ^a	
Median (range)	15 (2-46)
Area of infection ^b , n (%)	
Eastern Africa	11 (30.6)
Central Africa	10 (27.8)
Western Africa	13 (36.1)
Asia (Indonesia)	1 (2.7)
Missing data	1 (2.7)
Parasitemia, % infected erythrocytes	
Median (range)	0.95 (0.09-17)
Hyperparasitemia >2%, n (%)	8 (22.2)
Severe malaria ^c , n (%)	3 (8.3)
Treatment, n (%)	
iv artesunate+AL	8 (22.2)
AL monotherapy	26 (77.8)
AL administration ^d	
6 doses	17 (47.2)
2-5 doses	17 (41.7)
All doses home	2 (5.6)
Late treatment failure ^e , n (%)	4 (11.1)
Possible slow treatment response, n (%)	1 (2.7)

^aIn individuals with origin in Sub-Saharan Africa

^bCountries are classified into regions according to United Nations geoscheme.

^cAccording to WHO criteria 2015. All three patients presented with circulatory shock.

^dThe intake of the medicine was observed by a nurse and signed in the patient's medical record.

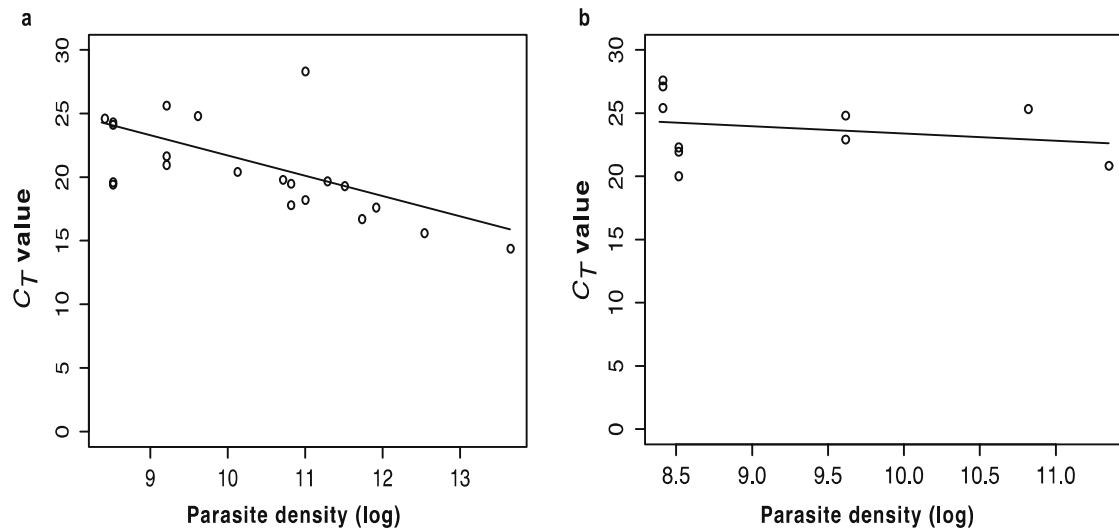
^eLate treatment failure was defined as parasites re-appearing 7-42 days after a microscopy negative slide.

Supplementary Table 2: Samples available at different time-points for each study participant

Patient nr	D 0-9			Day 10			1 M			3 M			6M			12 M		
#	Mic	DNA	RNA	Mic	DNA	RNA	Mic	DNA	RNA	Mic	DNA	RNA	Mic	DNA	RNA	Mic	DNA	RNA
1	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
2	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
3	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
4	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
5	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
6	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
7	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
8	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
9	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
10	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
11	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
12	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
13	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
14	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
15	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
16	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
17	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
18	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
19	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
20	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
21	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
22	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
23	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
24	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
25	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
26	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
27	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
28	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
29	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
30	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
31	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■

Available and missing time-points for microscopy (thin and thick films), DNA (PCR: species typing and *msp2*-genotyping), and RNA (gametocyte-PCR) for 31 patients with successful treatment, included in statistical analysis. Available samples (data) are presented as filled block (■), missing samples (data) as white blocks (□), and samples not included in the sampling scheme as hachure blocks (▨). RNA-tube was introduced to the sampling later during the study, therefore only available for a subset of patients (from # 23 onward). In addition, the last two patients were in the process of 12-month follow-up when the analysis were finalized for the present study.

Supplementary Figure 1: Correlations between microscopy-defined parasite densities and C_T values



a) Correlation between microscopy-defined parasite densities and C_T values before and/or on the day treatment started [linear regression, lm, $F=6.28$; ($df=20$); $R^2=0.24$; $p=0.02$]. b) The correlation was lost in microscopy positive samples collected one day after treatment and onwards [$F=1.80$; ($df=10$); $R^2=0.15$; $p=0.20$]. In performed regression models, values of parasite/ μl were transformed to \log_e .