Supplementary Tables

Supplementary table S1. Subgroup analysis of ECG measurements after each course of DHA/PQP by sex and age.

| Time        | Measurement |            | Sex        |         | Age        |             |         |  |  |
|-------------|-------------|------------|------------|---------|------------|-------------|---------|--|--|
|             |             | Male       | Female     | p-value | <15 years  | Adult       | p-value |  |  |
| 52h course1 | QTcF (ms)   | 406.9±19.4 | 427.1±23.1 | <0.001  | 416.4±21.1 | 416.9± 23.9 | 0.961   |  |  |
|             | ΔQTcF (ms)  | 13.5±12.2  | 25.8±20.5  | 0.003   | 21.4±22.1  | 19.4±17.4   | 0.772   |  |  |
| 52h course2 | QTcF (ms)   | 416.2±21.1 | 425.8±17.7 | 0.047   | 414.3±15.4 | 421.8±20.3  | 0.351   |  |  |
|             | ΔQTcF (ms)  | 22.7±15.9  | 24.5±14.9  | 0.627   | 19.3±17.8  | 24.1±15.1   | 0.433   |  |  |
| 52h course3 | QTcF (ms)   | 407.5±22.9 | 421.3±22.5 | 0.014   | 408.3±18.3 | 415.0±24.2  | 0.481   |  |  |
|             | ΔQTcF (ms)  | 14.3±15.5  | 20.1±18.4  | 0.158   | 13.3±21.3  | 17.6±16.7   | 0.534   |  |  |

Legend: Results of paired t-test between different subgroups of sex and age per each point of time. Results are mean ± Standard Deviation (SD).

P-value corresponds to the results of the paired T-test. Abbreviations: ms= milliseconds; bpm= beats per minute. Statistically significant results are reflected in bold.

## Supplementary table S2. Comparison of QTcF segment and ΔQTCF 7-days after treatment completion

| ECG parameter | 7d course1  | 7d cours         | e2      | 7d course3  |         |  |
|---------------|-------------|------------------|---------|-------------|---------|--|
| (units)       | measurement | Measurement      | p-value | Measurement | p-value |  |
| QTcF (ms)     | 405.7±20.9  | $407.7 \pm 22.7$ | 0.09    | 407.7±22.4  | 0.37    |  |
| ΔQTcF (ms)    | 8.0±15.7    | 11.1±16.2        | 0.09    | 11.2±17.0   | 0.37    |  |

Legend: Results of measurements and p-values for the paired t-test for comparison with course 1 measurements.

Measurements are described in mean  $\pm$  Standard Deviation (SD). Abbreviations: ms= milliseconds.

Supplementary table S3. Electrocardiographic measurements (QTcF and  $\Delta$ QTCF not included) at 52 hours post dose during the second and third monthly course with dihydroartemisinin-piperaquine compared with the first month.

| ECG               |            |             |                |         |                            |                |         |                            |
|-------------------|------------|-------------|----------------|---------|----------------------------|----------------|---------|----------------------------|
| parameter (units) | Oh course1 | 52h course1 | 52h course2    | p-value | Risk difference<br>(95%CI) | 52h course3    | p-value | Risk difference<br>(95%CI) |
| HR (bpm)          | 68.4±12.4  | 66.1±12.8   | 65.6±11.8      | 0.685   | -0.5 (-3.0 to 2.0)         | 68.2±12.5      | 0.060   | 2.1 (-0.1 to 4.4)          |
| ΔHR (bpm)         | -          | -2.0±9.8    | $-2.6\pm9.5$   | 0.689   | -0.5 (-2.9 to 1.9)         | $0.2 \pm 10.2$ | 0.047   | 2.2 (0.0 to 4.4)           |
| PR (ms)           | 166.9±18.7 | 171.8±17.8  | 171.8±18.2     | 0.986   | 0.0 (-1.7 to 1.6)          | 172.3±20.2     | 0.714   | 0.5 (-2.1 to 3.1)          |
| ΔPR (ms)          | -          | 4.8±7.8     | $4.8 \pm 8.4$  | 0.987   | 0.0 (-1.7 to 1.7)          | 5.6±11.5       | 0.536   | 0.8 (-1.8 to 3.4)          |
| QRS (ms)          | 90.9±9.5   | 89.3±9.0    | $90.0 \pm 8.8$ | 0.176   | 0.7 (-0.3 to 1.8)          | $88.9 \pm 8.8$ | 0.534   | -0.4 (-1.6 to 0.9)         |
| ΔQRS (ms)         | -          | -1.2±4.9    | -0.5±4.6       | 0.158   | 0.7 (-0.3 to 1.7)          | -1.8±5.0       | 0.323   | -0.6 (-1.8 to 0.6)         |

Legend: 52h readings were conducted 4h after administration of the third dose. The parameter measurements are the arithmetic mean of measurements from the triplicate reading. Results of measurements, p-values and 95%CI for the paired t-test for comparison with measurement of 52h course1. Measurements are described in mean ± Standard Deviation (SD). Abbreviations: bpm= beats per minute; ms= milliseconds. Statistically significant results are reflected in bold.

Supplementary Table S4. Electrocardiographic measurements (QTcF and QTCF not included) at 7 days after the start of each course of DHA/PQP and before the start (at 0 hours) of the following monthly course compared with 0h measurements on day0 first course.

| ECG parameter | 0h course1     | 7d course1   |         | Oh course2     |         | 7d course2  |         | Oh course3  |         | 7d course3  |         |
|---------------|----------------|--------------|---------|----------------|---------|-------------|---------|-------------|---------|-------------|---------|
| (units)       | UII course1    | measurement  | p-value | measurement    | p-value | measurement | p-value | measurement | p-value | measurement | p-value |
| HR (bpm)      | 68.4±12.4      | 76.7±14.0    | <0.001  | 70.6±11.4      | 0.091   | 74.4±13.6   | <0.001  | 67.5±11.1   | 0.539   | 72.1±11.4   | 0.020   |
| ΔHR (bpm)     | -              | 8.2±13.4     | -       | 2.3±10.8       | -       | 5.6±12.2    | -       | -0.9±12.3   | -       | 3.2±10.4    | -       |
| PR (ms)       | 166.9±18.7     | 166.0±17.4   | 0.309   | 175.4±19.5     | <0.001  | 167.5±16.8  | 0.982   | 173.7±20.7  | <0.001  | 165.1±17.4  | 0.010   |
| ΔPR (ms)      | -              | -1.6±10.3    | -       | 8.2±11.7       | -       | -0.1±10.6   | -       | 6.8±13.6    | -       | -3.3±9.5    | -       |
| QRS (ms)      | $90.9 \pm 9.5$ | 86.5±8.3     | <0.001  | $88.5 \pm 8.8$ | 0.003   | 87.2±8.4    | <0.001  | 87.3±8.7    | <0.001  | 86.3±8.4    | < 0.001 |
| ΔQRS (ms)     | -              | $-4.8\pm6.6$ | -       | -2.6±6.6       | -       | -3.9±6.1    | -       | -3.65±6.0   | -       | -3.8±6.3    | -       |

Legend: Results of measurements and p-values for the paired t-test for comparison with baseline 0h course1 measurements. Measurements are described in mean ± Standard Deviation (SD). Abbreviations: bpm= beats per minute, ms= milliseconds. Statistically significant results are reflected in bold.