Severe Malaria
Definition of Severe Malaria

- World Health Organisation (WHO)
- Severe Malaria in African Children (SMAC)
SMAC Studies

- Prospective studies of more than 26,000 children with severe malaria
- LODS
- Site heterogeneity in disease manifestation
- Mortality 4%
SMAC LODS Studies (JID 2009)
SEAQUAMAT Study (Lancet 2005)
AQUAMAT Study (Lancet 2010)

Log-rank p = 0.0022
Simplified Artesunate (JID 2012)

- 2 study arms (5 doses vs. 3 doses of iv Artesunate)
- 197 patients at 3 African study sites
### Table 2. Secondary Efficacy Analyses: Time in Hours to Parasite Clearance

<table>
<thead>
<tr>
<th>Degree of Clearance</th>
<th>5-Dose Group</th>
<th>3-Dose Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCT100</td>
<td>36 (30–48)</td>
<td>36 (30–48)</td>
</tr>
<tr>
<td>PC99</td>
<td>24 (18–24)</td>
<td>18 (18–30)</td>
</tr>
<tr>
<td>PCT90</td>
<td>18 (12–18)</td>
<td>12 (12–18)</td>
</tr>
<tr>
<td>PCT50</td>
<td>12 (6–12)</td>
<td>12 (6–12)</td>
</tr>
</tbody>
</table>

Abbreviations: IQR, interquartile range, PCT100, 100% parasite clearance; PC99, 99% parasite clearance; PCT90, 90% parasite clearance; PCT50, 50% parasite clearance.
Artesunate Dose Optimization Study

- 3 study arms (3 doses iv vs. 3 doses im vs. 5 doses im of Artesunate)
- 1054 patients at 7 African study sites
Artesunate Dose Optimization Study

Analysis of preliminary data shows comparable safety and efficacy profiles in all 3 cohorts. Study results, e.g. regarding clearance rates can be revealed upon database lock and completion of data analysis in early 2014.
Co-Infections: Background

- Disease manifestation
- Therapeutic relevance
Co-Infections: Future Studies

- Use of antibiotics in combination with antimalarial treatment
Malaria Diagnosis: Background

- Thick blood smear
- Rapid tests
Malaria Diagnosis: Future Studies

- Rapid tests for detecting parasites and their antimalarial resistance patterns plus other microbes
Malaria Prevention: Background

- Malaria control measures
- Malaria vaccine
Malaria Prevention: Future studies

Investigation of severe malaria in interventional preventive trials (e.g. vaccine studies)
Malaria Adjunct Therapy: Background

- Multifactorial cause of complications
- Many published studies with many different interventions over the last 30 years – no success

- Mortality: AQUAMAT: 10%
  SMAC1:     4%
  SMAC2:     2%
  RTSS:      0%
Malaria Adjunct Therapy: Future studies

- Investigation of pathophysiology of severe malaria
Malaria Chemotherapy: Background

- AQUAMAT: Artesunate reduced mortality from 11% to 9% compared to quinine

- SMAC studies: Artesunate three dose regimen vs. five dose regimen

- SMAC studies: Artesunate intramuscular vs. intravenous
Malaria Chemotherapy: Background

- **Resistance**: first reports from South East Asia

- **Haemolytic anaemia**: first described in travellers; in SMAC studies 9%
Malaria Chemotherapy: Future Studies

- Immediate studies: haemolytic anaemia

- Long-term studies: development of artemisinin alternatives (e.g. artemisone, OZ439, spiroindolones)