Phase IIB efficacy trial of the malaria blood stage vaccine candidate GMZ2

Michael Theisen

on behalf of the GMZ2 consortium
MULTICOMPONENT ASEXUAL BLOOD-STAGE VACCINE CANDIDATE

GMZ2

GLURP-R0

473 aa residues

MSP3-C-term

172 aa residues

651 aa residues

Disrupt parasite development in blood
**SELECTION CRITERIA**

- **Immune epidemiology**
  
  High levels of IgG1 and/or IgG3 to GLURP & MSP3 are associated with protection against clinical disease in children
  
  Meraldi, V., et al. 2004. Parasite Immunology, **26**: 265–72

- **Functional bioassays**

  IgG against GLURP & MSP3 promote ADCI in vitro


Excellent safety and tolerability of 10-100 µg GMZ in alum

No vaccine related Serious Adverse Events

GMZ2 / alum elicit functional antibodies
**GMZ2 / Al(OH)₃ PHASE II B TRIAL**

**SSI, Denmark**
Sponsor/Coordinator from June 2012

**CNFRP**
Burkina Faso

**MRC**
The Gambia

**Navrongo**
Ghana

**CERMEL**
Gabon

**UKT**
Germany

**Makerere University**
Uganda

**AMANET**
Sponsor/Coordinator
January 2009 – May 2012
Tanzania
GMZ2 PHASE IIB: BASICS

- **Title:** Phase II, randomized, controlled, double-blind, multi-centre study to evaluate the efficacy, safety, and immunogenicity of GMZ2 candidate malaria vaccine in Gabonese, Burkinabe, Ghanaian and Ugandan children aged 12 – 60 months

- **Funding:**
  - European & Developing Countries Clinical Trials Partnership
  - German Federal Ministry of Education and Research

- **Registration:** PACTR ATMR2010060002033537

- **Project duration:** Jan 19, 2009 to Jan 18, 2014

- **Statistics:** London School of Hygiene and Tropical Medicine

- **Sponsor:** AMANET then SSI

- **IP:** Alum adjuvanted 100 µg GMZ2

- **Control:** Rabies (Verorab)
EFFICACY ENDPOINTS

ício efficacy endpoint:
• Number of clinical episodes of malaria (tympanic temperature ≥38°C or history of fever and > 5,000 parasites/µl) over 6 months post-vaccination

Secondary efficacy endpoints:
• Number of anemia episodes
• Number of malaria episodes (fever and parasite densities of 500, 2,500 and 20,000 parasites/µl) over 6, 12 and 22 months post vaccination
ENDPOINT MEASUREMENTS

- Passive Case Detection with field workers visits
- Slides collected from unwell children with fever
- Modified WHO method for quantification of *P. falciparum*
- SAE’s reported to Sponsor and DSMB
## GMZ2 PROJECT

### Last vaccination last child  21 Sept, 2011

<table>
<thead>
<tr>
<th></th>
<th>Total enrolled</th>
<th>First vaccination</th>
<th>Last vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabon</td>
<td>512</td>
<td>8/11-2010</td>
<td>21/9-2011</td>
</tr>
<tr>
<td>Burkina Faso</td>
<td>880</td>
<td>29/4-2011</td>
<td>26/8-2011</td>
</tr>
<tr>
<td>Uganda</td>
<td>257</td>
<td>9/5-2011</td>
<td>1/8-2011</td>
</tr>
<tr>
<td>Ghana</td>
<td>200</td>
<td>2/6-2011</td>
<td>1/8-2011</td>
</tr>
<tr>
<td>Overall</td>
<td>1,849</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
STATUS OF THE DATABASE

- Electronic data capture at clinical sites – DB softlock, October 2012.
- GCP audit (PPD) during sponsor transition from AMANET to SSI – critical findings in data management, August 2013.
- Decision to re-enter data at one site (UKT) into a new validated DB (Larix), December 2013.
- Start of data entry, June 2014.
TRIAL PROFILE (PRELIMINARY)

2366 Screened

1849 Randomized

517 Not enrolled

923 Rabies vaccine

926 GMZ2 vaccine

2 received GMZ2 in error

1 received rabies vaccine in error

Dose 1

Dose 2

Dose 3

921 withdrawal lost to followup

925 withdrawal lost to followup

895

873

868

901

796

803

~ 1100 episodes 6 months after last injection
ANTIBODY RESPONSE (PRELIMINARY)

1601 paired samples
<table>
<thead>
<tr>
<th>Date</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>18/1-2009 – 28/5 2012</td>
<td>AMANET sponsor &amp; coordinator</td>
</tr>
<tr>
<td>1/6-2012</td>
<td>Interim Grant Agreement between SSI and EDCTP</td>
</tr>
<tr>
<td>23/6-2013</td>
<td>Final Grant Agreement</td>
</tr>
<tr>
<td>1/9-2013</td>
<td>Corrective Action Plan (CAP)</td>
</tr>
<tr>
<td></td>
<td>i) Trial Master File</td>
</tr>
<tr>
<td></td>
<td>ii) Data Management Plan</td>
</tr>
<tr>
<td></td>
<td>iii) Entry into validated database</td>
</tr>
<tr>
<td>4/12-2013 – 30/3 2014</td>
<td>Study completion visits at the 5 African sites, site-specific corrections are implemented</td>
</tr>
<tr>
<td>18/1-2014</td>
<td>No-Cost extension until 30/9-2014</td>
</tr>
</tbody>
</table>
CONCLUSIONS

- 1,849 children enrolled at 5 sites in Burkina, Ghana, Gabon, and Uganda
- Randomized into two groups receiving either GMZ2 or Rabies and followed up for 24 months
- Site-specific findings have been corrected
- CRF’s are being re-entered in Tübingen
- Statistical analysis before the end of September
Participants of the studies

EDCTP

Bundesministerium für Bildung und Frauen

GMZ2 consortium partners;

AMANET, Tanzania
CNRFP, Burkina Faso
LSHTM, UK
Makerere University, Uganda
MRC, the Gambia
MRU, Gabon
NHRC, Ghana
UKT, Germany
SSI, Denmark