Moderate efficacy malaria vaccines as part of comprehensive malaria control and elimination
Progress and Limitation of Existing Vector Control Tools

Fig. 1. Numbers of *A. gambiense* and *A. funestus* in spray catches in huts.

PARASITE RATES OF INFANTS UP TO ONE YEAR OLD

Draper & Smith 1960 TRSTMH 54: 342
Malaria resurgence: a systematic review and assessment of its causes

Justin M Cohen1, David L Smith2,3, Chris Connor, Abigail Ward, Gavin Yamey, Oliver J Sabot and Bruno Moonen
Global malaria vaccine pipeline

**TRANSLATIONAL PROJECTS**

<table>
<thead>
<tr>
<th>Phase 1a</th>
<th>Phase 2a</th>
<th>Phase 1b</th>
<th>Phase 2b</th>
<th>Phase 3</th>
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</thead>
<tbody>
<tr>
<td>ChAd63/MVA ME-TRAP + Matrix M™</td>
<td>Ad35.CS/RTS,S-AS01</td>
<td>M3V.Ad.PFCA</td>
<td>Ad35.CS</td>
<td>ChAd63/MVA ME-TRAP</td>
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<tr>
<td>Polyepitope DNA EP 1300</td>
<td>Ad35.CS/Ad26.CS</td>
<td>M3V.D/Ad.PFCA</td>
<td>EBA 175.R2</td>
<td>GMZ2</td>
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<tr>
<td>PfCelTOS FMP012</td>
<td>ChAd63/MVA (CS, TRAP, AMA)</td>
<td>ChAd63/MVA MSP 1</td>
<td>SE36</td>
<td>MSP3 [181-276]</td>
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<tr>
<td>CSVAC</td>
<td>ChAd63.AMA1/MVA.AMA1</td>
<td>FMP2.1-AS01B (AMA1 3D7)</td>
<td>P/SPZ</td>
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<tr>
<td>ChAd63.AMA/ MVA.AMA1 +AI/CPG7909</td>
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<tr>
<td>SR11.1</td>
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<tr>
<td>ChAd63/MVA PvDBP</td>
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<td>Pfs25-EPA</td>
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<td>Pfs25-VLP</td>
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**P. falciparum vaccines:**
- Pre-erythrocytic
- Blood-stage
- Transmission-blocking

**P. vivax vaccines:**
- Pre-erythrocytic
- Blood-stage

**VACCINE CANDIDATES**

RTSS Phase 3 Trial in Africa

Randomized, controlled, double-blind trial designed to evaluate vaccine efficacy, safety, reactogenicity, and immunogenicity in children up to 32 months after the administration of the first dose of vaccine.

Two age categories:
- Children 6-12 weeks of age: 7100
- Children 5-17 months of age: 8900

11 centers in 7 African countries

Trial implemented with optimized vector control and malaria treatment

The co-primary endpoints of the trial are: vaccine efficacy against clinical malaria after 12 months of follow-up in each age category.
Efficacy over 18 months follow-up [ATP] and Malaria incidence in Controls

OVERALL
Kilifi
Korogwe
Bagamoyo
Manhiça
Lambarene
Lilongwe
Agogo
Kombewa
Kintampo
Nanoro
Siaya

VE1% 1.8 episodes/yr

VE1% 1.4 episodes/yr
Effect of RTS,S/AS01 on clinical malaria over 18 months of follow-up:

Number of cases averted (per 1000 children vaccinated)

- **OVERALL**
  - Kilifi
  - Korogwe
  - Bagamoyo
  - Manhiça
  - Lambarene
  - Lilongwe
  - Agogo
  - Kombewa
  - Kintampo
  - Nanoro
  - Siaya

- **941 cases averted** (47 to 2356)
- **444 cases averted** (-12 to 1429)
against severe malaria, malaria hospitalization all-cause hospitalization over 18 Months

<table>
<thead>
<tr>
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<th>VE* in children [95%CI]</th>
<th>VE* in infants [95%CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe malaria</td>
<td>36% [15 – 51]</td>
<td>15% [0 – 39]</td>
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<tr>
<td>Malaria hospitalization</td>
<td>42% [29 – 52]</td>
<td>17% [-7 – 36]</td>
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<tr>
<td>All-cause hospitalization</td>
<td>19% [9 – 28]</td>
<td>6% [-7 – 17]</td>
</tr>
</tbody>
</table>

VE calculated as 1-Risk Ratio (Unadjusted)

Over 18 months per 1000 vaccinees; RTS,S/AS01 inserted 21 [range:-4-44] cases and 8 [range:-14-33] cases of severe malaria in children and infants respectively.

Severe fatality rate for malaria and all-cause mortality was low and VE was not demonstrated
incidence of clinical and severe malaria (primary cases) by 6-month periods (per-protocol population)

A. Infants 6-12 weeks of age at enrollment - clinical malaria

B. Infants 6-12 weeks of age at enrollment - clinical malaria

C. In 5-17 months of age at enrollment - clinical malaria

D. Infants 6-12 weeks of age at enrollment - severe malaria

E. In 5-17 months of age at enrollment - severe malaria

F. Infants 6-12 weeks of age at enrollment - severe malaria
O recommends Large scale Pilot Implementation of RTSS in Africa

O recommends the pilot implementations of the 4-dose schedule of the RTS,S/AS01 vaccine in 3–5 distinct epidemiological settings in sub-Saharan Africa, at national level, covering moderate-to-high transmission settings,” with three doses administered to children between 5 and 9 months of age, followed by a fourth dose 18 months later.

This is to involve sufficiently large populations also to assess, feasibly of providing all four doses of RTS,S to the target age group through existing health services; impact of RTS,S on child mortality; evidence of any causal relationship between RTS,S and either meningitis or cerebral malaria, in the context of surveillance of adverse events; as well as the compilation of evidence on the
Applications for Tackling Challenges in Control and Elimination
Occurrence of Artemisinin Resistance

<table>
<thead>
<tr>
<th>Year of Emergence</th>
<th>Suspected Year Detected</th>
<th>Containment Activities Started</th>
<th>AL D3+</th>
<th>TF</th>
<th>AS-MQ D3+</th>
<th>TF</th>
<th>DHA-PPQ D3+</th>
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<td>2006</td>
<td>2009</td>
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</tbody>
</table>

- Parasite clearance half-life ≤5 hr
- Parasite clearance half-life >5 hr, *kelch13* polymorphisms at or beyond amino acid position 441
- Parasite clearance half-life >5 hr, no *kelch13* polymorphisms at or beyond amino acid position 441
Model predictions of Pre-Erythrocytic Vaccine effects over time

Interruption of transmission for initially low EIR settings with very high efficacy vaccines

Initial EIR 5.25

Initial EIR 21

EPI

Mass vaccination

\[ C_f \cdot VE(t) = 0.76 \]
cations in Surveillance Response systems: screening and treatment (FSAT) in areas passively-detected foci

Eliminate all malaria cases in area

Malaria cases presenting at health centres over a few months

Surrounding houses with very sensitive test (e.g. LAMP) to detect asymptomatic cases
ome take home messages

current malaria control and elimination tools do not provide complete protection.
Partially efficacious malaria vaccines are of benefits public health setting especially in high burden areas.

ot implementation of first generation malaria vaccine will provide insights in the best approach for ge scale deployments
ploration of use of vaccines also to address emerging challenges (drug and insecticide resistance and responses to hot spots) to control d elimination need to be implemented.

alaria Vaccines are an essential part of integrated