Malaria

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Despite 42% reduction since 2000, a child dies every minute in Africa from malaria

207 million malaria cases in 2012, 79% in Africa
627,000 deaths in 2012, 90% in Africa

Three biggest risks:
- Financing fragility
- Artemisinin resistance
- Insecticide resistance

WHO World Malaria Report 2013
Global Malaria Financing

Key existing malaria control measures

- Long-lasting insecticidal nets (LLIN)
  - Supported by multiple RCTs for reduction in all-cause mortality
- Indoor Residual Spraying with insecticide
- Various modalities for use of drugs as prevention (SMC (children), iPTi (infants), iPTp (pregnant women))
- Rapid Diagnostic Tests to allow targeting of drugs
- Artemisinin Combination Treatments

All preventive and treatment measures suffer from the risk of drug and insecticide resistance
NATURALLY ACQUIRED IMMUNITY: SLOW TO DEVELOP, INCOMPLETE, AND OF LIMITED DURATION

Vaccine must do better

Parasite Immunology, 2006, 28, 51–60 Marsh & Kinyanjui

Malaria Vaccines design: Points of intervention

<table>
<thead>
<tr>
<th>Target stage</th>
<th>Clinical effect</th>
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<tbody>
<tr>
<td>Prevent infection and disease</td>
<td></td>
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<tr>
<td>Reduce clinical disease severity</td>
<td></td>
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<tr>
<td>Interrupt transmission</td>
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Translational Research

Vaccine construct

Evaluation

Refine based on outcome

Product Development

Pre-clinical

Go/No Go

Clinical

Go/No Go

Pivotal

Regulatory & Policy Outcomes

Stage-gated investments

Global malaria vaccine pipeline

**TRANSLATIONAL PROJECTS**

**Phase 1a**

- ChAd63/MVA ME-TRAP + Matrix M™
- Polyepitope DNA EP 1300
- PGatO5/MP012
- CSVAC
- ChAd63-AMA1/MVA-AMA1 + AUCPG7909
- SR11.1

**Phase 2a**

- Ad35-CS/RTS,5-AS01
- Mlv Ad.PCA
- ChAd63/MVA ME-TRAP
- MP02

**Phase 1b**

- Ad35-CS
- ChAd63/MVA ME-TRAP
- EBA 175.K2
- GS02

**Phase 2b**

- GMZ
- MSP3 [181-276]

**Phase 3**

- RTS.S-AS01

**VACCINE CANDIDATES**

- P. falciparum vaccines:
  - Pre-erythrocytic
  - Blood-stage
  - Transmission-blocking

- P. vivax vaccines:
  - Pre-erythrocytic
  - Blood-stage
  - Transmission-blocking

Testing of RTSS show good results

In children 5–17 months of age during 12 months of follow-up
- Vaccine efficacy against clinical disease: 55.8% (97.5% CI: 50.6-60.4)
- Vaccine efficacy against severe disease: 47.3% (95% CI: 22.4-64.2)

46% for over 18 months of follow-up and which is about 941 cases for every 1000 children vaccinated

In children 6–12 weeks of age during 12 months of follow-up
- Vaccine efficacy against clinical disease: 31.3% (97.5% CI: 23.6-38.3)
- Vaccine efficacy against severe disease: 36.6% (95% CI: 4.6-57.7)

27% for over 18 months of follow-up and which is about 444 cases for every 1000 children vaccinated

Pathways for WHO Policy Recommendations on Malaria Vaccines

**RTS,S/AS01: implications for 2nd generation**

- Earliest policy recommendation and PQ from WHO late 2015
- Earliest licensure in-country? End 2016
- Efficacy and duration of protection “modest”
- Therefore there will remain a major role for additional malaria vaccines

**Assessment**

- In malaria 2-4 approaches are evaluated per year for clinical proof-of-concept in CHMI model (controlled human malaria infection/challenge trials)
- Lead approaches at least 5-10 years away from licensure (other than RTS,S)
Malaria Vaccine Technology Roadmap

• Originally launched in 2006 with Vision, Strategic Goal and 11 Priority Areas
• Major progress since 2006 in the Priority Areas
• Increased collaboration within malaria vaccine community since 2006
• Funders liaising closely to identify gaps
Process for updating of roadmap

- First public consultation in September 2012 – 45 written submissions from agencies and vaccine development groups
- Second public consultation in November 2012 – few comments.
- WHO Meeting on 5 February 2013 with 40 participants
- Vision and Strategic Goals finalized in April 2013 at meeting of funding agencies and WHO

New Vision

“Safe and effective vaccines against *Plasmodium falciparum* and *Plasmodium vivax* that prevent disease and death, and prevent transmission to enable malaria eradication.”

- Expands to include *P. vivax* in addition to *P. falciparum*
- Expands to all geographical regions rather than sub-Saharan Africa alone
- Expands to include target groups beyond children alone depending on goal and risk groups
Two new Strategic goals
By 2030, license vaccines targeting *Plasmodium falciparum* and *Plasmodium vivax* that encompass the following two objectives, for use by the international public health community:

1. Development of malaria vaccines with protective efficacy of at least 75 percent against clinical malaria suitable for administration to appropriate at-risk groups in malaria-endemic areas.

2. Development of malaria vaccines that reduce transmission of the parasite and thereby substantially reduce the incidence of human malaria infection. This will enable elimination in multiple settings. Vaccines to reduce transmission should be suitable for administration in mass campaigns.

Clinical Development Pathways

<table>
<thead>
<tr>
<th>GOAL</th>
<th>Preventing Clinical Malaria</th>
<th>Preventing Transmission</th>
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<tbody>
<tr>
<td>TARGET GROUP</td>
<td>Those at risk of disease &amp; death</td>
<td>Children and adults (transmitters)</td>
</tr>
<tr>
<td>REGULATORY</td>
<td>First/all episodes of clinical malaria</td>
<td>?</td>
</tr>
<tr>
<td>POLICY</td>
<td>All episodes of clinical malaria</td>
<td>All incident human malaria infections</td>
</tr>
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Prioritity Area for Further Work
Priority Areas – Research

• One reworded to focus more attention on confirming new vaccine targets, including potential use of CHMI to accelerate timelines
• New area on reporting clinical trial and non-human primate results promptly

Priority Areas – Vaccine Development

• PRIORITIZATION of vaccine candidates including use of Preferred Product Characteristics, back validation, immune correlates and/or head-to-head comparisons
• New Area: DEVELOP immunological correlates of vaccine-induced protection and surrogate efficacy endpoints to advance vaccine development and licensure timelines.
Priority Areas – Key Capacities

• 3 areas (one new)
• New area on ensuring post-approval pharmacovigilance and effectiveness structures are in place to support introductions

Priority Areas – Policy & Commercialization

• 3 areas (one new)
• New area: DEVELOP and encourage responsible stewardship and support for malaria vaccine development and implementation through appropriate project management and investment strategies (e.g., through developing a business case).
Summary on roadmap

- New Roadmap is a reflection of the shared vision and goals of the malaria vaccine development community
- Extended Vision to include *P. vivax*, in addition to *P. falciparum*. Geographical focus extended. Age groups extended.
- Retains the original roadmap’s 2015 goal for a first-generation *P. falciparum* vaccine
- Retains the need to develop next generation vaccines to prevent disease and death
- Adds the concept of vaccines to prevent transmission as a global priority for vaccine development
- WHO will work within the framework of the updated Roadmap for next generation vaccines

Ongoing roles for WHO

- Facilitating interactions between group of major R&D funders “malaria vaccine funders group”
  - Aim to identify gaps and reduce unhelpful overlaps in global funding (if any)
- Finalising preferred product characteristics to provide details on desired profile of vaccines to meet 2 Strategic Goals of the roadmap
Ongoing roles for WHO

• Engaging in development of trial designs/assays to advance second generation malaria vaccines
  – Eg related to transmission-blocking vaccines
  – Eg related to strengthened controlled human malaria infection studies

• Maintaining 2x year updates for global portfolio (known as rainbow table)

Asante Sana