Malaria vaccines

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Malaria vaccines

What can we target?
What do we want?
Where have we got to?
Why haven’t we done better?
Who are they for?
Potential vaccine targets

- Antibody to sporozoites
- T cell response To liver stage
- Antibody to asexual stage
- Antibody to gametocytes
Vaccines in development/trials

- **Sporozoites**: prevent liver entry: attenuated whole sporozoites; RTS,S
- **Liver stage**: facilitate T cell killing of hepatocytes: human challenge
- **Blood stage**: prevent merozoite invasion of RBC, slow replication: merozoite surface proteins (e.g. MSP1/2; AMA1, EBAs and PfRhs)
- **Attenuated parasites**: low dose blood stage infection
- **Pregnancy**: prevent placental infection: VAR2CSA
- **Gametocytes**: reduce transmission- altruistic: Pfs25, Pfs230, Pfs 48/45, Pvs25, Pvs230, Pvs48/45
Malaria vaccine technology roadmap

• Vision: safe and effective vaccines against P falciparum and P vivax that prevent disease and death and prevent transmission to enable malaria eradication.

• Aim: by 2030, vaccines for both species with >75% efficacy against clinical malaria, and with ability to reduce malaria transmission through use in mass campaigns
Who would a malaria vaccine be for?

• Young children, as part of EPI
• Pregnant women?
• The military and other travelers
RTS,S malaria vaccine

• RTS,S vaccine currently under consideration at EMA and review by WHO Joint Technical Expert Group
• Considerations: Timing of immunisation; booster doses
• Phase 3 trial: best efficacy in children 5-17 m, given additional booster after 20 m: 36% for UM, 32% for SM.
• Children <3 m: 26% for UM, no effect against SM
• Booster required for ongoing protection & for SM
Unlikely to get data on whether RTS,S protects travellers, and by how much
Attenuated sporozoites: protection but not practical

- Purified sporozoites
- Intravenous injection
- Five doses required for protection
- Transport in liquid nitrogen
- Duration of protection?

Seder et al Science 2013
A specific vaccine for pregnancy malaria?
Burden of malaria in pregnancy

- >100 million women at risk
- Worst in first pregnancies
- 10,000 maternal anaemia deaths
- 1-200,000 infant deaths from LBW due to malaria
- Leading preventable cause of LBW in Africa
Preventing placental malaria: a pregnancy-specific malaria vaccine

- Parasite protein VAR2CSA binds CSA
- Parity-specific immunity develops
- VAR2CSA antibody blocks binding
- Vaccine candidate
VAR2CSA vaccine: challenges

- Sequence variation
- Large protein >350 kD
- Binding domains?
- Blocking antibodies
- Optimising expression
- GMP production
- Phase I/II trials in Germany & Benin
- Demonstrating efficacy
- (No role in travellers)
Changing malaria burdens: implications for travellers
Malaria reductions in Africa

O’Meara et al, 2010
Malaria-free, Eliminating and Controlling Countries, 2012
178,546 cases, 41 deaths

43,139 cases, 4 deaths

7,342 cases, 0 deaths

400 cases, 0 deaths

Total deaths <100
More than half have decreased Cases by >75% since 2000

*MNote: In this map, countries with areas endemic for malaria are shaded completely even if transmission occurs only in a small part of the country. For more specific within-country malaria transmission information, please see the Travel Vaccines & Malaria Information, by Country section in Chapter 3 and the CDC Malaria Map Application (www.cdc.gov/malaria/map).*
Brazil

Region of the Americas

I. Epidemiological profile

Population: 2013

- High transmission (> 1 case per 1000 population)
  - Argentina: 46 (31000)
  - Brazil: 35 (60000)
- Low transmission (0-1 cases per 1000 population)
  - Colombia: 15 (1000)
- Malaria-free (0 cases)
  - Argentina: 13 (70000)
  - Brazil: 10 (60000)

Total: 131 (200000)

II. Intervention policies and strategies

<table>
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<tr>
<th>Intervention</th>
<th>Policies/strategies</th>
<th>Yes</th>
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<th>Year adopted</th>
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<td>ITN/LLIN</td>
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<td>Yes</td>
<td>No</td>
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<td>IRS</td>
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<tr>
<td>Long-lasting insecticide treated bednets (LITB)</td>
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<td>Larval control</td>
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<td>IPT</td>
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<td>Diagnosis</td>
<td>Reports of all cases should include diagnostic test</td>
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<td>No</td>
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<td>Treatment</td>
<td>ACT is fixed for all ages in public sector</td>
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<td>No</td>
<td>2012</td>
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<tr>
<td>Artemisinin-based monotherapy withdrawn</td>
<td>Yes</td>
<td>No</td>
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<tr>
<td>Single-dose of primaquine is used as prophylaxis for P. falciparum</td>
<td>Yes</td>
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<td>Fluoroquinolones used for treatment of P. vivax</td>
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<tr>
<td>Treatment failure of P. falciparum</td>
<td>Yes</td>
<td>No</td>
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<td>Treatment of severe malaria</td>
<td>Yes</td>
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<td>Treatment of P. vivax</td>
<td>Yes</td>
<td>No</td>
<td>2012</td>
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<td>Diagnosis of P. vivax for radical treatment of P. vivax</td>
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<td>Type of IPT used</td>
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III. Financing

Sources of financing:

- Government
- Global Fund
- Private Sector
- USAID
- UNICEF
- Other

IV. Coverage

ITN and IRS coverage

Cases tested and treated in public sector

Vivax and falciparum in Indonesia

http://www.map.ox.ac.uk/ (not a public travel information source)
Mefloquine at the crossroads? Implications for malaria chemoprophylaxis in Europe

Patricia Schlagenhauf a,*, Christoph Hatz a, b, Ron Behrens c, Leo Visser d, Maia Funk a, Benedikt Holzer e, Bernhard Beck b, Cathérine Bourquin f, Hermann Etter g, Hansjakob Furrer h, Blaise Genton i, Pierre Landry j, Francois Chappuis j, Louis Loutan j, Ulrich Stössel k, Eva Jeschko l, Andrea Rossanese m, Hans Dieter Nothdurft n

- Compulsory checklist for contraindications before using mefloquine
- Becoming demoted to second line treatment?
- Limited options in pregnancy, small children, long term travellers, affordable prevention for VFRs
Malaria Prophylaxis 2015

Recommendations by the expert committee for travel medicine (ECTM / Switzerland).

1.) Protection against mosquito bites is recommended in all endemic regions, including areas where the risk is considered minimal*.
2.) Chemoprophylaxis and/or emergency self-treatment are prescribed based on the travel destination*.

* a detailed list of countries is regularly published in the Bulletin of the Swiss Federal Office of Public Health (SFOPH) in French and German [http://www.bag.admin.ch].

Atovaquone/proguanil (APP), Mefloquine (MP) or doxycycline (DP) for chemoprophylaxis

Chemoprophylaxis (seasonal) recommended: atovaquone/proguanil (APP), Mefloquine (MP) or doxycycline (DP)

Carry standby emergency self-treatment: artemether/Lumefantrin (ALT) or atovaquone/proguanil (APT) in special situations (See Bulletin of the SFOPH)

No chemoprophylaxis is recommended.

Carry artemether/Lumefantrin (ALT) or atovaquone/proguanil (APT) for standby emergency self-treatment

No chemoprophylaxis is recommended.

Carry standby emergency self-treatment: artemether/Lumefantrin (ALT) or atovaquone/proguanil (APT) in special situations (See Bulletin of the SFOPH)

Figure 1 Recommendations for the use of malaria chemoprophylaxis and stand-by emergency treatment according to the Central European Guidelines.
Glass half....?

- A moderately effective vaccine
- An effective but complicated alternative
- A shrinking malaria map
- A shrinking pot of funds
- New tools to assess risk
- A small evidence base for travellers
Malaria vaccines: summary

- What can we target? Sporozoites; sexual stage promising
- What do we want? >75% efficacy against Pf and Pv, suitable for mass administration
- Where have we got to? ~30% protection from RTS,S with booster
- Who are they for? Control disease and facilitate elimination in endemic countries. Travellers an “off label” use?