Safety, immunogenicity and durability of a novel malaria vaccine candidate, R21 adjuvanted with Matrix-M™

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Burden and Progress

Mapping *Plasmodium falciparum* Mortality in Africa between 1990 and 2015
Why do we still need a vaccine??

Artemisinin resistance


Insecticide resistance


Spread of chloroquine resistance
Approaches to a malaria vaccine
Circumsporozoite protein (CSP)

• Discovered in the 1960s
• Expressed on sporozoite surface and to a lesser degree on hepatic schizonts
• Pivotal role in alignment and invasion of hepatocytes

• RTS,S, which has completed Phase III testing and is due to enter pilot deployment in Africa in 2018, confers partial short-lived efficacy by inducing antibodies against the CSP (Agnandji et al *NEJM* 2012;367(24):2284-95.)
Phase III efficacy of RTS,S/AS01: 12 months

12 month efficacy in infants aged 6-12 weeks

12 month efficacy in children aged 5-17 months


RTS,S Vaccine Efficacy Wanes Rapidly

Greenwood et al. Lancet 2015
Antibodies to CS Wane Rapidly
- but can be increased with a 20 month booster dose

Greenwood et al. Lancet 2015
RTS,S/AS01: Pilot Deployment

WHO says funds secured for Africa pilots of world's first malaria vaccine
R21 vaccine production

- Produced by expressing a CSP-HBsAg fusion protein in the yeast *Pichia pastoris*
- R21 particles spontaneously formed from the **single fusion protein** without additional unfused HBsAg.
  - Potential benefit over RTS,S as greater proportion of particle is malaria antigen
  - 50% vs 10%

Matrix-M\textsuperscript{TM}

• Saponin based (purified fractions of Quillaja saponin)

• Nano-particulate formulation (approx 40 nm particles)

• Synergistic mixture of Matrix-A and Matrix-C
  • 85% Matrix-A mixed with 15% Matrix-C
VAC053 - Overview

- Phase Ia study
- Open-labelled; Non-randomised
- Healthy adults aged 18 to 50 years
  - Oxford
  - London (Imperial)
- 31 volunteers in total
Preliminary Data

1. Immunogenicity dependent on MM co-administration

2. 10µg R21/MM comparable with 50µg RTS,S/AS01

### Median NAP IgG - comparison with RTS,S

- **10µg R21/MM**
- **50µg R21/MM**
- **50µg RTS,S/AS01B**

### VAC53: Median NAP IgG

- 10µg R21/MM
- 50µg R21/MM
- 50µg R21 alone
Durability of antibody response

10µg R21/MM significantly higher than 50µg R21/MM at 6 months
In addition to comparable D84 immunogenicity, reactogenicity was found to be minimal and clearly reduced compared to both 10µg and 50µg
Safety profile of low dose 2µg R21/MM

10µg R21/MM: 1st Vaccination

2µg R21/MM: 1st Vaccination
Safety profile of low dose 2µg R21/MM

10µg R21/MM: 2nd Vaccination

2µg R21/MM: 2nd Vaccination
Safety profile of low dose 2µg R21/MM

10µg R21/MM: 3rd Vaccination

2µg R21/MM: 3rd Vaccination
SAEs and SUSARs

• No SUSARs reported to date
• 1 SAE – ‘not related’ to vaccination

• Unsolicited AEs – predominantly mild in nature
• Laboratory AEs (FBC, UE, LFT) – predominantly grade 1
DISCUSSION

• R21/MM has been well tolerated at all tested doses

• R21/MM induced comparable NANP-specific IgG responses to 50µg RTS,S/AS01 28d after 3rd vaccination at much lower doses

• Use of 2µg R21/MM would have dose-sparing and cost saving benefit with no apparent loss to immunogenicity and associated with improved tolerability

• Durable responses are observed at 6 months - 10 µg R21/MM inducing significantly higher titres than 50 µg R21/MM

• Safety and immunogenicity currently being assessed in African adults

• Phase II a study ongoing in UK to assess efficacy against malaria infection in CHMI
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