O409
1-hour Oral Session
Vaccines in the pipeline: far and close

A phase Ia clinical trial of the blood-stage Plasmodium falciparum vaccine ChAd63-MVA RH5

Ruth Payne*[1], Sarah Silk[1], Sean Elias[1], Kazutoyo Miura[2], Ababacar Diouf[2], Daniel Alanine[1], Jing Jin[1], Genevieve Labbe[1], Kathryn Milne[1], Nick Edwards[1], Ian Poulton[1], Eleanor Berrie[3], James Mccarthy[4], Loredana Siani[5], Alexander Douglas[1], Johan Vekemans[6], Adrian Hill[1], Carole Long[2], Alison Lawrie[1], Simon Draper[1]

[1]*The Jenner Institute, University of Oxford, Oxford, United Kingdom*

[2]*Laboratory of Malaria and Vector Research, Niaid/Nih, Maryland, United States*

[3]*Clinical Biomanufacturing Facility, University of Oxford, Oxford, United Kingdom*

[4]*Qimr Berghofer Medical Research Institute, Brisbane, Australia*

[5]*Reithera, Rome, Italy*

[6]*Glaxosmithkline Vaccines, Rixensart, Belgium*

Background: *Plasmodium falciparum* malaria remains a significant public health problem, particularly in sub-Saharan Africa where the vast majority of the nearly 600,000 deaths/year occur. Successful eradication of this parasite is widely thought to require an effective malaria vaccine. The most promising blood-stage *P. falciparum* candidate antigen to date is the reticulocyte-binding protein homologue 5 (RH5), which is essential for parasite survival and erythrocyte invasion. Unlike other blood-stage *P. falciparum* antigens (e.g. AMA1 and MSP1) RH5 does not appear to come under significant immune pressure in endemic settings, and there is limited polymorphism. Antibodies against RH5 induced by vaccination have been shown to protect against malaria in non-human primates and are able to cross-inhibit *in vitro* all *P. falciparum* lines and field isolates tested to date. We report here on the first Phase Ia clinical trial of an RH5-based vaccine delivered using the viral vectors chimpanzee adenovirus serotype 63 (ChAd63) and modified vaccinia virus Ankara (MVA) in a prime-boost strategy.

Methods: Twenty-four healthy, malaria-naïve volunteers aged 18-50 were enrolled in the clinical trial. The first four volunteers received a lead-in dose (5 x 10^9 vp) of the ChAd63 RH5 vaccine alone (Group 1) before dose escalation to the full dose (5 x 10^{10} vp) in Group 2. The first four volunteers in Group 2 received ChAd63 alone, and the final sixteen were boosted with MVA RH5 8 weeks after ChAd63 RH5 at doses of 1 – 2 x 10^8 pfu. Data on adverse events were collected via an electronic diary for 28 days after each vaccination, as well as at clinic visits. Blood samples were taken to assess vaccine immunogenicity and safety. T cell and serum antibody responses were assessed by *ex vivo* interferon-γ ELISpot, ELISA and *in vitro* growth inhibition activity (GIA) assays.

Results: The vaccines were well tolerated, with no safety concerns throughout the study. As expected, the volunteers receiving higher doses of both vaccines experienced more adverse events than those receiving the lower doses, in keeping with previous trials using the same viral vectors. Immunogenicity data will be presented.

Conclusions: This first-in-human Phase Ia study demonstrated no safety concerns relating to either the ChAd63 RH5 or MVA RH5 vaccines. Work is ongoing to assess the immunological responses to the vaccines.