Last updated: 13 July 2021

CONCEPT NOTE

Malaria monoclonal antibodies for malaria prevention: Preferred Product Characteristics and clinical development

Proposed Dates: 3, 11, and 29 November 2021
Location: Web meeting

1. Background and Aims

Over the last 20 years, significant declines in malaria have been achieved, and the Global Technical Strategy for Malaria adopted by the World Health Assembly in 2015 set goals to reduce incidence and mortality rates by at least 90% by 2030. In recent years, progress with disease control has stalled, with increases in malaria incidence in some areas. While medicines and vector control have been the mainstay of malaria control strategies, the emergence of drug and insecticide resistance, and challenges in achieving high coverage and compliance of existing tools, present significant hurdles for further progress. Future strategies to combat malaria will likely require an expanded and improved set of tools, including interventions for prevention. RTS,S/AS01E is a first generation malaria vaccine, and pilot implementation is currently assessing its suitability for wide-scale introduction. Second generation vaccines, including R21 and PfSPZ, are also approaching phase 3 evaluation. However, vaccine development faces the challenges of limited efficacy, impaired immunogenicity in naturally exposed individuals, the time required to mount an effective vaccine-induced immune response, and the time and cost of vaccine development. Work is ongoing to develop new drugs for malaria chemoprevention, but they are unlikely to be available in the short term.

In parallel to the development of highly efficacious long-lasting malaria vaccines and chemoprevention medicines, recent scientific advances have raised the possibility that single dose monoclonal antibodies (mAbs) could be used for malaria prevention. Passive immunisation with mAbs may overcome some of the limitations of vaccines by providing immediate protection through direct administration of functional antibodies. Malaria mAbs could be used as prophylaxis for several months in many endemic areas, providing short-term prevention to vulnerable populations such as infants and children, pregnant women and high-risk workers, as well as a supplement or alternative to chemoprevention in emergency situations. The simplified dose regimen of mAbs administration may overcome some of the coverage and compliance issues currently faced by seasonal malaria chemoprevention, vector control, and intermittent preventive treatment in pregnant women (IPTp).

Historically, mAbs against malaria antigens have been used as a research tool to guide vaccine development. For example, neutralising mAbs have been used to map critical epitopes in the design of immunogens and potential vaccine antigens. Technical innovations in mAb identification, optimisation and manufacturing have increased the possibility of producing lower cost mAbs and reduced the time required to isolate and characterize candidate antibodies. Additionally, new methods have been developed to extend the half-life of mAbs and to improve their potency and safety profiles via modifications in antibody Fc regions. To date, most mAbs in preclinical development confer protection against infection in the sporozoite stage, but strategies to screen for new mAbs across the entire parasite life cycle are rapidly evolving. The malaria mAb CIS43LS has been shown to prevent malaria infection in mouse models and is currently in Phase 1 in humans, and mAbs against blood-stage and sexual stage epitopes are also in development.

To support this quickly developing R&D area, the Global Malaria Programme (GMP) and the WHO Immunization, Vaccines, and Biologicals (IVB) Department will convene a scientific development group to consider the preferred product characteristics for mAbs used as malaria prevention. The malaria mAbs PPCs will be aligned with other malaria PPCs currently being developed for vaccines and chemoprevention. This meeting will consider:

- An overview of the state of mAbs used as health interventions (for malaria and other diseases)
- Innovations in pre-clinical development (e.g., half-life extension, optimising potency and safety profiles)
- Proof-of-concept study designs (animal and human models), preclinical requisites (safety, efficacy, dosing, duration of protection)
- Clinical development pathways (trial design considerations, regulatory, post-licensure studies)
- Administration efficiencies compared to chemoprevention and vaccines, including special groups such as infants or pregnant women
- Manufacturing and production to ensure access and affordability

Existing PPCs of malaria mAbs for malaria prevention will be considered with a view to creating a WHO malaria mAb PPC that will guide malaria mAb developers and help ensure the programmatic suitability of candidate products. Delivery of a complete data package showing how candidate mAbs meet the PPC criteria should smooth the policy and regulatory reviews of new products, although there is no guarantee a positive recommendation by WHO or licensure will follow. The meeting will lead to the development of a draft WHO malaria mAb PPC which, according to standard procedures, will be made available for public consultation. A final meeting of the Scientific Committee for PPC Development may be needed to consider the feedback and finalise the WHO malaria mAb PPC.

2. Specific Objectives

1. Review the landscape of malaria mAbs and mAbs PPCs for other pathogens
2. Agree on a set of PPC criteria for malaria mAbs
3. Ensure alignment with WHO guidance on mAbs development and PPCs for mAbs for other pathogens (HIV, RSV, COVID) and complementarity with PPCs for malaria vaccines and chemoprevention.