Editorial

2015: The beginning of the end of the war against malaria?

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In May 2015 the 62th World Health Assembly formulated a global malaria strategy for 2016-2030 aiming to "reduce the global disease burden by 40% by 2020, and by at least 90% by 2030. It also aims to eliminate malaria in at least 35 new countries by 2030".[1] As a reminder, it was 60 years ago that the Eighth World Health Assembly decided in 1955 to shift from malaria control to malaria eradication, with the aim to make many areas of free of malaria "within 10 to 15 years".[2] This has yet to be accomplished in many malaria endemic countries such as Indonesia, where the earliest program was the malaria eradication program of 1959, evolving into the malaria control program, the roll-back malaria program, and finally in 2012 into the malaria elimination program.[3]

In view of the ever-present insecticide-resistance in the mosquito vector and antimalarial drug resistance in the malaria parasite, a long-term goal has been the development of malaria vaccines. There is currently no commercially available malaria vaccine, but the best candidate seems to be the RTS,S/AS01 vaccine.[4]

The RTS,S vaccine was developed by GlaxoSmithKline Biologicals (GSK), with additional funding by the Program for Appropriate Technology in Health Malaria Vaccine Initiative (PATH-MVI), which received a grant from the Bill and Melinda Gates Foundation. The vaccine is now manufactured by GSK under the trade name Mosquirix.[4]

The RTS,S/AS01 vaccine has been shown to protect children and infants older than 6 weeks against *Plasmodium falciparum* malaria and has an acceptable side-effect profile. Furthermore, the vaccine can be administered safely with other childhood vaccines, and provides protection against severe malaria. RTS,S/AS01 vaccine efficacy against severe falciparum malaria in young children (5 to 17 months of age at first vaccination) was around 50% in multicenter phase 3 trials.[4,5] According to the final study results, vaccination with the 3-dose primary series reduced clinical malaria cases by 28% in young children and 18% in infants to the end of the study. Administration of a booster dose 18 months after the primary series reduced the number of of clinical malaria cases in young children by 36% and in infants (aged 6-12 weeks at first vaccination) by 26% to the end of the study. However, the vaccine efficacy decreased over time after the booster dose.[4,6] Around 80% of study subjects used insecticide-treated bed nets, therefore these study results were achieved in the presence of existing antimalaria measures.[4]

The goal of the RTS,S vaccine is to prevent the sporozoites that are introduced by a mosquito bite into the blood from entering liver cells for maturation and multiplication.[4,5]

The active substance in the current malaria vaccine is RTS,S, a recombinant antigen expressed in *Saccharomyces cerevisiae*. The

RTS,S antigen consists of the RTS and S proteins, that spontaneously assemble into mixed polymeric particles intracellularly. The RTS polypeptide contains the *P. falciparum* circumsporozoite protein (CS), including the putative universal T cell epitope, fused to the hepatitis B virus surface antigen (S).[7,8] The final vaccine for administration is obtained by reconstituting a lyophilized preparation of RTS,S antigen with the adjuvant AS01 and has to be injected intra-muscularly, within 6 hours of reconstitution.[7]

The RTS,S vaccine has now received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA), which was announced on 24 July 2015. Accordingly, the WHO may reach a policy recommendation for RTS,S by the end of 2015.[4] Since it has only limited efficacy, the RTS,S vaccine is to be regarded as an additional tool for malaria control, to be used with established control measures, such as insecticides, bed nets, and antimalarials.[6]

In view of emerging parasite resistance against artemisine antimalarials, any addition to the armamentarium against malaria should be welcomed, however slight its efficacy, as long as standard antimalaria measures are not neglected and their funds are not diverted. Let us give the RTS,S/AS01 vaccine the opportunity to prove itself in real-life situations and hope that the WHO malaria control goals for 2030 may be achieved.

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