Malaria vaccine deployment in Africa: focus on Ghana

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The announcement by the Ghana Health Service /Ministry of Health at the beginning of May to begin the pilot implementation of the malaria vaccine – RTS,S/AS01 (Mosquirix®) – manufactured by GSK Biologicals was greeted with rumours about conspiracy theories of secret agenda to depopulate Africa through the use of vaccines and all the other stories that are often propagated by the anti vaxxers. This was not unlike the fear and panic spread throughout the country that prevented investigators from conducting clinical trials on new vaccines against the Ebola virus disease a few years ago.[1]

The malaria vaccine, Mosquirix®, received market authorization from the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) for markets outside of the European Union where *Plasmodium falciparum* malaria is most prevalent in 2015.[2] The "positive regulatory assessment" followed the review of data from more than 3 decades of product development, going through all the phases of clinical trials to determine its safety and efficacy. Ghana has been part of this process from as far back as 2006 when Phase II studies were conducted at the Kintampo Health Research Centre after review and approval by the GHS Ethics Review Committee and the regulatory body, Ghana Food and Drugs Authority (FDA). The definitive Phase III trial was subsequently conducted among children at 11 different sites in 7 African countries with varying transmission intensities, including two in Ghana (Kintampo and Agogo) between 2009 and 2013. The vaccine was effective at reducing the cases of clinical malaria by 28% in children aged 6 to 12 weeks at time of first dose and 44% in children who received the first dose between 5 to 17 months of age.[3]

The overall efficacy results were not as high as we have come to expect of vaccines. However, it can be said to be impressive if one considers that this is the first anti parasitic vaccine and against a wily parasite. It should also be appreciated that the efficacy results were those seen over and above the use of available control methods (use of insecticide treated nets (ITNs) provided to all children in the trial, and very good and high-quality clinical care).

Issues have been raised about the data leading to the decision made by Ghana to introduce the vaccine among her population. The main ones are; there was no effect of the vaccine on mortality, there was an excess mortality among girls and there was an imbalance of meningitis cases between children who received RTS,S/AS01 and control vaccines.

It is important to note that the Phase III trial was not designed with mortality as an endpoint. Indeed, fewer number of deaths were observed among all study children because of the higher than expected clinical care provided under the trial settings. While there was also an imbalance of meningitis between vaccinated children and control children, the total number of all meningitis cases were less than 40 among more than 16000 children in the study (27 out of 11439 who received Mosquirix® and 6 out of 6096 that received control vaccines). There was no temporal association between receipt of the vaccine and the occurrence of meningitis, and no mechanism has so far been found to explain a possible causal link.

The introduction of Mosquirix® in the routine health systems of Ghana, Kenya and Malawi by the respective country health ministries and World Health Organisation (WHO) is in line with further development of the vaccine. The introduction of the vaccine provides the opportunity to evaluate the impact of the vaccine on mortality, meningitis and cerebral malaria in a larger population than that of the Phase 3 trials and the Ghanaian authorities must be commended for accepting to be part of the pilot implementation of Mosquirix®, a product with the potential to prevent many cases of malaria. It is also heartening to note that Ghanaian scientists have been and continue to be actively involved in the development of the product.

The question of mosquito control and reduction in transmission cannot be wished away on the use of a vaccine. In the Phase 3 clinical trials, the efficacy was upon the use of other malaria control interventions, so the vaccine is implemented as an additional tool in the fight against malaria. We should be reminded about the impact of BCG vaccine, that has contributed to a significant reduction in childhood tuberculosis, was recommended for use at a time when its proven efficacy was less than 50%. Ultimately, improvement in socio-economic conditions including improved housing and environmental conditions, leading to the avoidance of mosquito bites, will be the measures that provide long lasting control and elimination of malaria. Until then, all safe and effective tools should be brought on board.

Dr Kwaku Poku Asante MB ChB, MPH, PhD
Kintampo Health Research Centre, Kintampo, Ghana
E-mail: kwakupoku.asante@kintampo-hrc.org
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Professor Fred N. Binka MB ChB, MPH, PhD
School of Public Health, University of Health and Allied Sciences, Hohoe, Ghana
E-mail: fred.binka@gmail.com
Conflict of interest: None declared

Professor Kwadwo A. Koram MB ChB, MPH, PhD
Noguchi Memorial Institute for Medical Research, University of Ghana, Legon, Ghana
E-mail: kkoram@noguchi.ug.edu.gh
Conflict of interest: None declared

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