Musings on malaria morbidity and mortality after the new Mosquirix® vaccine

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There are some facts relating to the new malaria vaccine (Mosquirix® or RTS,S/AS01) recently introduced in Ghana, which need to be more widely known.

Contrary to expectations based on mathematical modelling and on the vaccine's effect on clinical malaria and severe malaria, mortality was not reduced in children receiving the Mosquirix® vaccine in the phase 3 trial.[1] This (surprising) result has been attributed to the fact that mortality was reduced in both the vaccinated and unvaccinated children due to better implementation of malaria control measures such as use of bed nets and prompt treatment of malaria.[2] The startling implication of this finding is that when the existing malaria control measures are implemented more effectively, the vaccine in its current form does not offer any measurable mortality advantages. This means that if there were a willingness to implement malaria control measures intensively, there would be no need to expose our children to the unknown effects of a new vaccine.

The European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) issued "a positive regulatory assessment," for the vaccine but as a medicinal product intended exclusively for markets outside of the European Union.[3] They also emphasised several potential concerns regarding the vaccine:

- The unknown duration of protection against Malaria under trial conditions.
- Whether the known limited effectiveness of the vaccine will translate into field settings.
- Whether the vaccine will reduce deaths when it is given as part of routine medical care as opposed to the higher quality care during the phase 3 trial.
- Whether the increased occurrence of meningitis noted during the trial is causally related to the Mosquirix®.
- Whether vaccinated children may be at higher risk of disease when the protection from the vaccine decreases over time.
- Whether there will be decreased use of other malaria prevention measures (e.g. bed nets, indoor spraying) resulting in decreased overall impact of malaria control programmes.
- Whether there will be an increase of non-vaccine type disease, i.e. disease caused by *P. falciparum* strains or other species of parasite other than *P. falciparum*.
- Whether when Mosquirix® is given with other vaccines, the risk of fever and seizures might increase.
- Whether protective antibody responses will be mounted when Mosquirix® is co- administered with measles and yellow fever vaccines.
- Whether there will be an antibody response to the catalase component of the vaccine, and if this will have any clinical implications.

So, it is regrettable that we should expose Ghanaian children to these unknown risks when proven effective measures are not being maximally applied.[4]

At the launch of the pilot Mosquirix program on 30th April 2019, several parties expressed concern about the insufficient local resources allocated to the malaria control program.[5] It is salutary to learn the large number of external partners funding Ghana's malaria control program and vaccine trials.[4-6]

In response to concerns expressed about the lack of an evident mortality benefit of Mosquirix, the vaccine researches responded that "no conclusions on the impact of RTS,S/AS01 on mortality can, nor should, be drawn from this phase 3 trial". Therefore, any claims for potential lives to be saved by the vaccine are unfounded and should be disregarded. We should put more effort and resource in avoiding contact with mosquitoes.

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