

JTEG's RTS,S/AS01 Candidate Policy Recommendations

Peter Smith

On behalf of the Joint Technical Expert Group

JTEG Candidate Policy Recommendations

Introductory remark:

There is a need to evaluate pilot introductions before wider scale-up is considered.

JTEG recommends a precautionary approach.

JTEG Candidate Policy Recommendations:

Key questions

The primary questions are:

1. The extent to which the protection demonstrated in the Phase 3 trial could be replicated in the post-licensure phase because of the challenge of implementing four doses at the population level, including the need for new immunization contacts

JTEG Candidate Policy Recommendations:

Key questions

2. The impact on mortality could not be assessed in the Phase 3 trial and as this is the main driver of the public health impact and cost-effectiveness of the vaccine, it is important to assess the mortality reduction following large-scale vaccination.

JTEG Candidate Policy Recommendations

Key questions

3. The safety signals of most concern (i.e. imbalances in meningitis and cerebral malaria) in the trial may be chance findings, but further evaluation is necessary when the vaccine is given to larger numbers of children

JTEG Candidate Policy Recommendations:

6-12 week age group

Based on the data from the Phase 3 trial, JTEG does not recommend the use of the malaria vaccine in the younger (6-12 weeks) age group.

JTEG Candidate Policy Recommendations:

5-17 months age group

With respect to the older age group (5-17 months), JTEG recommends the initial introduction of 4 doses of the malaria vaccine in 3-5 distinct epidemiological settings in sub-Saharan Africa, likely at subnational level, to generate critical information on the issues described above (large demonstration projects).

JTEG Candidate Policy Recommendations:

Pilot introductions

These settings should be selected such that

- they cover a range of moderate-to-high transmission settings, with at least one setting with strongly seasonal malaria transmission.
- it is possible to ascertain and diagnose cases of meningitis and severe malaria and record deaths.
- there should be high existing use of other proven malaria control measures including LLIN (or IRS), access to RDTs and ACT, and SMC in highly seasonal areas.

JTEG Candidate Policy Recommendations:

Pilot introductions

The population vaccinated should be of sufficient size to allow evaluation of the impact on mortality, probably through a phased introduction of the vaccine within the selected settings. It is likely that **several hundred thousand vaccinated children** will be included in **each setting** and that **phased introduction** would need to be randomized to ensure comparability of vaccinated and unvaccinated groups. **Each initial introduction will be a large demonstration project.**

JTEG Candidate Policy Recommendations:

Pilot introductions

JTEG strongly recommends that WHO oversees the design and evaluation of these phased introductions and monitors the emerging findings. If appropriate, SAGE and MPAC may broaden recommendations on the basis of these emerging findings.

JTEG Candidate Policy Recommendations:

Pilot introductions

JTEG notes that it would be appropriate for WHO to recommend countrywide introduction if concerns about safety have been resolved, and if favourable implementation data become available, including high coverage of the fourth dose.

JTEG Candidate Policy Recommendations:

Age and schedule

As JTEG recommends introduction in 3-5 moderate-to-high transmission settings, where there is a significant burden of malaria in the first year of life, it is important to vaccinate **at a young age within the 5-17 month age range.**



JTEG Candidate Policy Recommendations:

Age and schedule

There is no evidence that vaccine efficacy varied according to the month of age at which vaccination was started within this age group. In the phased introduction of the vaccine, JTEG recommends a **three dose initial series** of the malaria vaccine with a **minimum interval between doses of four weeks**, followed by a **fourth dose at 15-18 months** following the third dose.

JTEG Candidate Policy Recommendations:

Age and schedule

It is encouraged that the **first dose** be initiated as **close as possible to age five months** and the **third dose be completed by nine months of age**, if possible.

Co-administration has been evaluated with measles and DTP-containing vaccines and is considered acceptable.

JTEG Candidate Policy Recommendations:

Communication

Prior to any phased introduction **appropriate communication materials should be developed** and disseminated with particular emphasis on the partial efficacy of the vaccine and the importance of the fourth dose.

Messages should include the importance of **maintaining usage of non-vaccine malaria preventive measures** and the likelihood that **febrile episodes in vaccinated children may still be due to malaria**.

End of JTEG Candidate Policy Recommendations



JTEG Candidate **Research** Recommendations



JTEG Candidate **Research** Recommendations

- There are currently no data to support a fifth dose. Therefore, evaluation of safety and effectiveness of a fifth dose could be included in the proposed phased introductions.
- JTEG recommends monitoring of the emergence of vaccine-resistant strains following widespread use of the vaccine.

JTEG Candidate **Research** Recommendations

- JTEG recommends that there is further exploration of alternative schedules and other strategies to improve the efficacy of the vaccine.
- JTEG recommends an exploration of how to capitalize upon the new immunization contacts for general improvements in child health, including increasing coverage with other vaccines.

JTEG Candidate **Research** Recommendations

- JTEG recommends that there is an evaluation of the malaria vaccine in the context of elimination, including studies evaluating administration and effectiveness against infection over a wide age range. A high priority geographic area for such an evaluation is South-East Asia in areas of artemisinin resistance.