Update on the Malaria Vaccine Implementation Programme

MPAC 2 Oct 2019
Outline

1. Background

2. Key data availability and framework for policy decision

3. Vaccine launch in three countries

4. Long term access and stakeholders’ meeting

5. Feedback from the Immunization and Vaccines Implementation Research Advisory Committee (IVRAC)
**Partially effective vaccine with potential for high impact**

5-17 months at first vaccination, 4 doses, 4 years:

- 39% reduction clinical malaria; 29% reduction severe malaria
- 62% reduction in severe malaria anemia; 29% reduction in blood transfusions
- 37% reduction in malaria hospitalization; 18% reduction all cause hospitalizations

Measured benefit on top of that provided by ITNs, provided to study children

Safety: Well tolerated, febrile convulsions, safety signals without established causality: Meningitis (RR 10:1), Cerebral Malaria; in *post hoc* analysis, greater number of female deaths

Thousands of clinical malaria cases averted over 4 years with 3 or 4 doses

Clinical malaria cases averted, 3 or 4 doses, by study site and transmission, Mal 055

MVIP briefing for PMI/USAID - 4 September 2019
Malaria vaccine could avert between ~254-516K future deaths and ~49-142M future cases through 2035

On top of that provided by current malaria control tools, including ITNs
RTS,S/AS01 vaccine is cost effective

At a hypothetical vaccine price of $5 a dose

- Median incremental vaccine cost effectiveness ratio is **$87** (range **$48-$244**) per DALY averted and **$25** ($16-$222) per clinical case averted*
- RTS,S considered to provide value for money in comparison with other vaccines (Gavi 2018 VIS)

RTS,S compared with other malaria control tools**

**Figures should be considered indicative**
Caution required due to different assumptions in the different models & lack of consideration of equity

Recognizing potential for high impact, outstanding questions, recommended pilot phased introduction, in 3-5 countries

- Feasibility of reaching children with 4 doses
- Safety, emphasis on safety signals in Phase III trial
- Impact in routine use

Data will inform policy on wider use of RTS,S/AS01

Call for expressions of interest
- 10 countries
- 3 selected using standardized criteria
The four components of the MVIP

1. RTS,S/AS01 Implementation through EPI Programme
   - In selected areas

2. Pilot evaluation commissioned by WHO
   - Incl. sentinel hospitals surveillance; community-based mortality surveillance; 3 household surveys

3. Qualitative assessment (HUS) & economic analyses
   - commissioned by PATH

4. GSK Phase IV study
   - Safety, effectiveness and impact
   - Part of GSK’s EMA Risk Management Plan

Vaccination

Evaluation
Communication is a key priority

Extracts from countries’ information, education and communication materials

Extract from Ghana fact sheet

Extract from Kenya fact sheet

Extract from Ghana Flip chart for health workers

Extract from Kenya Flyer for health workers and caregivers

Extract from Malawi Flyer and Key Facts Booklet
Recognizing that any rebound seen with the 3-dose regimen was time limited, and children benefit from 3 or 4 doses:

**SAFETY**

Reassuring safety data are considered of primary importance and precondition for a positive policy recommendation.

**IMPACT**

Data trends assessed as consistent with a beneficial impact of the vaccine for:
- **Impact on severe malaria**: an acceptable surrogate indicator for impact on mortality or
- **Impact on all-cause mortality**

**FEASIBILITY**

Recommendation for broader use of RTS,S/AS01 need not be predicated on attaining high coverage including coverage of the 4th dose.
Step-wise approach to policy recommendation

Malaria Vaccine Implementation Programme

- Vaccination start (first country)
- 24 months after start* (46 months in last country)
- Evaluation complete

DATA

1. Safety data
2. Impact data
3. Feasibility data

24 months after start*

Policy recommendation for broader use if and when:

i. Concerns regarding safety signals satisfactorily resolved; and

ii. Severe malaria data trends assessed as consistent with a beneficial impact of the vaccine; or

iii. Mortality data trends assessed as consistent with beneficial impact of the vaccine

urence complete

POLICY

1. Adjustments or refinements to policy recommendation if needed based on the final MVIP data set

2. *Timing dependent on acquisition of and rate of events (among other factors)
Timeline of MVIP evidence generation and review

**Policy review**
- 2019: Regular updates to SAGE/MPAC
- 2020:
- 2021: Potential policy recommendation and policy refinement
- 2022:
- 2023:

**Vaccine implementation**
- 2019: Start of vaccinations (Q1/Q2 2019)
- 2020: First 4th dose (Sep 2020 – Jan 2021)
- 2021: 30 months of routine vaccination (Sep 2021 – Jan 2022)
- 2022: Continued vaccination

**Safety data**
- Sentinel hospital surveillance
- Routine pharmacovigilance
- GSK Phase 4 study
- GSK baseline study

**Impact data**
- Community-based mortality surveillance
- Sentinel hospital surveillance
- Impact on severe malaria
- Impact on mortality

**Feasibility data**
- Household surveys
- New vaccine post-introduction evaluation
- Health care utilization study
- Health economic assessments

**Administrative coverage data monitoring**
- Baseline
- Coverage of dose 1-3
- Coverage of dose 4
- PIE
- Qualitative longitudinal study
- Costing of vaccine delivery
- Budget impact analysis

*Indicates 3rd country*
Vaccine Launch: World’s first malaria vaccinations

World Health Organization (WHO)

WHO's first #Malaria vaccine pilot is launched in #Malawi, the first country in Africa to roll out this landmark vaccine, known as RTS.S. The vaccine will be available to children from 5 months old to 2 years. bit.ly/ZZpASGN

23 April 2019 in Malawi

30 April 2019 in Ghana

13 Sept 2019 in Kenya
Building into a functional delivery system
Ghana

As of 04 September 2019

- Launch of vaccination: 30th April 2019
- RTS,S/AS01 introduced into the routine immunization schedule in selected districts of seven regions with combined annual birth cohort of ~168k children\(^1\)
- Monthly reports based on routine administrative data in DHIMS2

Cumulative May – June 2019*

<table>
<thead>
<tr>
<th>Description</th>
<th>Quantity</th>
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<tr>
<td>No. Vaccine doses</td>
<td>51,960</td>
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<tr>
<td>No. of children vaccinated (1st dose)</td>
<td>28,477</td>
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<td>No. of reported Adverse Events Following Immunization (AEFI)</td>
<td>40(^2)</td>
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1. Pilot regions: Volta, Oti, Bono, Bono East, Ahafo, Central, Upper East
2. Data for May-June 2019

*Data source: GHS/EPI
Ghana
Children vaccinated with RTS,S from May – July 2019

Cumulatively **28,497** children have received the first dose of the RTS,S vaccine (May-July) representing **68% of the target population**

Source: GHS/EPI DHIMS2 – reported as of Aug 2019
Malawi

As of 4 September 2019

- Launch of vaccination: 23rd April 2019
- RTS,S/AS01 introduced into the routine immunization schedule in selected areas of 11 districts with combined annual birth cohort of ~148k children

Cumulative – April - June 2019

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<tr>
<td>No. Vaccine doses</td>
<td>31,721</td>
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<tr>
<td>No. vaccinated (1st dose)</td>
<td>18,348</td>
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<td>No. of reported AEFI</td>
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1. Pilot districts: Karonga, Nkhabay, Ntchisi, Mchinji, Lilongwe rural, Balaka, Mangochi, Machinga, Phalombe, Chikwawa, Nsanje
2. Data for May-June 2019

Data source: WHO Malawi based on information received from Malawi MOH, including from DHIS2
Malawi
Children vaccinated with RTS,S from April – July 2019

Cumulatively 18,348 children have received the first dose of the RTS,S vaccine (23 April-July) representing 46% of the target population.

Source: MOH/EPI DHIMS2 – reported as of 03 Sept 2019
Evaluation: Start of safety and mortality data collection

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<td>Community-Based Mortality Surveillance</td>
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DSMB met 26 Sept, first opportunity to review data from MVIP
Recommended continue programme
Timelines and long-term access considerations *(illustrative)*

Source: World Health Organization (modified)
Timelines and long-term access considerations *(illustrative)*

Source: World Health Organization (modified)

Stakeholders meeting on access
Oct 18, 2019
Immunization and Vaccine Related Implementation Research Advisory Committee (IVIR-AC): Considered CE modeling for malaria vaccines

- Reviewed selected papers on CE related to RTS,S (Penny, 2016; Wilkins 2017; Sauboin 2019)

- Considered how CE models should be used to inform policy (final report pending):
  1. Models should look at packages of interventions, in a realistic scenario, rather than assessing sequential introduction, which is not practical.
  2. Equity, including poverty/financial risk protection should be incorporated. Consider heterogeneity across SES in malaria burden, vaccine/intervention coverage, delivery costs, and malaria transmission.
  3. Indirect effects of reducing malaria infection should be considered
  4. CE is one of many inputs that inform policy decisions; broader societal and economic benefits should be considered, including equity, poverty protection, protection from catastrophic health care costs, improved performance in school, etc
Globally, 219 million cases of malaria were reported in 2018, and an estimated 435,000 people, including 260,000 African children, died from malaria in 2017. Scale up of WHO-recommended preventive measures resulted in a substantial decline in malaria morbidity and mortality between 2000 and 2015. However, in 2015 and 2016, progress with malaria control stalled and started to reverse, with an upswing in malaria cases, particularly in sub-Saharan Africa. A malaria vaccine such as RTS,S has the potential to help get malaria control back on track, and may prove to be an important addition to current control tools. The RTS,S vaccine, with its reported level of efficacy, has been shown to provide substantial and significant added protection on top of that provided by optimal case management and high coverage of insecticide-treated mosquito nets (ITNs), reducing clinical malaria by 55% during the 12 months following primary vaccination, and by 39% over 4 years. Recent data from long term follow-up are reassuring regarding its long term efficacy and safety. The well-established Expanded Programme on Immunization can reach even the poorest children, who are generally at highest risk of malaria, and suffer the highest mortality rates.

The opportunity to evaluate the feasibility of delivery, safety and effectiveness of the RTS,S vaccine, through pilot implementation in three countries, comes at a critical time in malaria control: no other malaria vaccine has entered phase 3 clinical trials. Additional preventive tools are in the development pipeline, and MPAC looks forward to reviewing their potential to reduce the malaria burden. However the development, evaluation and deployment of these new tools is expected to take several years. Moreover, it is likely that they will also offer only partial protection.

At a time when the downward trend in malaria cases and deaths has stalled, when our current control efforts are threatened by resistance, and when no new intervention approaching the efficacy of RTS,S is available, MPAC looks forward to reviewing the results of the pilot implementations, in accordance with the Framework for Policy Decision on RTS,S/AS01 approved at the April 2019 MPAC and SAGE meetings. If these results are promising, the RTS,S vaccine, in combination with ITNs and other control measures, is likely to be an important additional tool to change the course of malaria incidence and reduce malaria deaths in African children.

August 26, 2019
The Cabinet Secretary for Health Sicily Kariuki spoke at the ongoing 74th regular Session of the General Assembly, GAVI Alliance and Global Fund side event on putting the U in UHC where she highlighted how Kenya is reaching the previously un reached populations in a bid to leave no one behind.

The CS highlighted initiatives like the recently launched malaria vaccine in Kenya among three African countries and took the opportunity to invite participants to the ICPD 25+ conference which will be held in Nairobi in November, 25 years after it was held last in Cairo.
Thank you