Malaria Vaccine Advisory Committee
MALVAC – An Update

Chetan Chitnis
Chair, MALVAC

Malaria Policy Advisory Committee Meeting
Geneva
2nd October 2019
WHO and Malaria Vaccine Research

- IMMAL Committee – research and capacity building in immunology of tropical infectious diseases 80s-90s
- VDR Committee – research and capacity building in vaccine development for tropical infectious diseases
WHO and Malaria Vaccine Research

• IMMAL Committee – research and capacity building in immunology of tropical infectious diseases 80s-90s
• VDR Committee – research and capacity building in vaccine development for tropical infectious diseases

• MALVAC: Malaria Vaccine Advisory Committee 2008-2013
  – Advise WHO on strategic priorities, technical issues related to malaria vaccine development
  – Meetings/working groups to develop consensus views on priorities and best practices for vaccine R & D strategies
    • Adjuvants
    • Controlled human malaria infection (CHMI) – challenge trials
    • Assays and trial designs for transmission blocking vaccines
    • Whole organism vaccines (eg. attenuated sporozoites)
    • R & D for P. vivax vaccines
The evolving landscape of malaria

• Major changes in malaria epidemiology
  – Intensive malaria control efforts have greatly reduced malaria incidence and mortality 2000 – 2015
  – IRS, ITN, RDT, ACT
  – 219 million malaria cases, 435,000 deaths in 2017
  – No further reduction in malaria incidence or mortality since 2015

• Are further reductions possible with currently available tools especially in high transmission settings?
The evolving landscape of malaria

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  – Intensive malaria control efforts have greatly reduced malaria incidence and mortality 2000 – 2015
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• Are further reductions possible with currently available tools especially in high transmission settings?

• 1st malaria vaccine in pilot implementation studies - RTS,S/AS01
  – 39% protection over 4 years in 5-17 month children with 4 dose regimen
  – Pilot implementation initiated in 3 African countries mid-2018

• Other vaccines under development – R21, PfSPZ, PfRH5, PvDBPII

• Role for vaccines/other tools in malaria control and elimination?
Reconvening MALVAC

- Assist WHO in the prioritisation of specific malaria vaccine R&D avenues
- Review the state-of-the-art in malaria vaccine development
- Define priority targets and preferred clinical development pathways, mindful of emerging data and changing public health priorities
- Update the vision for the role of vaccines in future malaria control and elimination efforts
- Jointly convened by WHO’s Initiative for Vaccine Research (IVR) & Global Malaria Program (GMP)
The Committee

• Members:
  – Edwin Asturias, University of Colorado, Denver
  – Philip Bejon, KEMRI-Wellcome Trust Research Programme
  – Chetan Chitnis, Institut Pasteur, Paris (Chair)
  – Katharine Collins, Radboud University
  – Brendan Crabb, Burnet Institute
  – Socrates Herrera, Consorcio para la Investigacion Cientifica, Cali
  – Miriam Laufer, University of Maryland
  – Regina Rabinovich, IS Global
  – Meta Roestenberg, Leiden University Medical Centre
  – Adelaide Shearley, John Snow Inc
  – Halidou Tinto, Institut de Recherche en Sciences de la Santé
  – Marian Wentworth, Management Sciences for Health (WHO Product Development for Vaccines Advisory Committee)

• Committee may be supplemented by other experts, including those from other WHO advisory groups
Highlights of Consultation on Malaria Vaccines and Biologicals R &D: July 15/16, 2019

• RTS,S/AS01:
  – Pilot implementation initiated in 3 African countries mid-2018
  – Study to assess potential in highly seasonal transmission areas
  – Evaluation of potential to help interrupt transmission
  – Fractional dose of RTS,S regimen
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• R21 – an RTS,S-like particle – showing promise
  – PfCSP-HBsAg fusion produced in *P. pastoris*
  – Formulated with Matrix M
  – Protection in Phase IIa challenge model
  – Currently being tested in Phase IIb field trials
  – R21 manufactured by Serum Institute of India, commitment for commercial supplies
Highlights of Consultation on Malaria Vaccines and Biologicals R &D: July 15/16, 2019

• Attenuated sporozoite vaccine: PfSPZ
  – 1046 volunteers, 12 countries including 3 countries in Africa
  – 11 trials (9 in Africa), 5 m – 65 y, PfSPZ/saline similar AE profiles
  – No breakthrough infections - safe
  – Efficacy in CHMI (heterologous): 83% at 10 wks, 55% at 8 m
  – Efficacy in field: 55% at 6 m (time to event); 39% at 6 m (prop. analysis)
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• PfSPZCVAC: sporozoites under chemoprophylaxis cover
  – 100% VE at 13 wks (heterologous)
  – 1/5th dose needed for PfSPZ

• Next generation - genetically attenuated SPZ
  – PfSPZ-GA1
  – PfSPZ-GAP3KO
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• PfRH5 – *P. falciparum* blood stage vaccine
  – PfRH5-Basigin interaction is essential for RBC invasion
  – PfRH5.1/AS01 Phase I/IIa blood stage challenge trial
  – 33% reduction in parasite multiplication rate (PMR) *in vivo*
  – 50% reduction in GIA *in vitro* at IgG conc. of 2.5 mg/ml
  – Next gen PfRH5 construct: PfRH5-VLP conjugation
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• Transmission blocking vaccines
  – Lead candidate: Pfs230-EPA/AS01
  – Blocking of transmission in membrane feeding assays
  – Direct skin feeding assays following CHMI with Pf
  – Pvs230-EPA/AS01: CHMI with Pv
  – Field trials – cluster randomized trials to measure efficacy in the field
  – Clinical development path – dialog with regulatory authorities
• **P. vivax** vaccines
  – Standard malaria control measures are less effective against *P. vivax*
  – Hypnozoite stage: contributes >50% of *P. vivax* cases in PNG
  – Partially effective PEV can have significant impact on Pv transmission
  – Combination of PEV + BSV + TBV can significantly drive down transmission – modeling
  – Vaccine candidates under development
    • PvCSP/AS01; PvR21/Matrix M
    • PvDBPII/GLA-SE safe and immunogenic in Phase I
    • PvDBPII to be tested against blood stage challenge in CHMI
    • Pvs230D1-EPA/AS01 – transmission blocking vaccine
Monoclonal antibodies for malaria?

- Human mAbs to PE and BS antigens
- Target 80% efficacy for 3-6 months (cover a transmission season)
- Prevent infection and reduce transmission
- Combine with an anti-malarial to clear parasites and provide prophylaxis over a transmission season
- Evaluate efficacy in CHMI to validate mAbs
- Likely to be safe, cost-effective, ease of administration and delivery
Developments in CHMI

• Controlled Human Malaria Infection (CHMI) increasingly used to evaluate vaccines
  – Sporozoite and blood stage challenge – evaluate both PEV and BSV
  – Dose & formulation optimization, duration of protection
  – Define and evaluate immune correlates
  – Development of CHMI platforms in malaria endemic countries

• Use of CHMI to evaluate transmission-blocking vaccines

• CHMI for *P. vivax*
  – Blood stage and sporozoite challenge
  – Measure transmission blocking activity
Next Tasks for MALVAC

• Recognise importance of development and use of 1\textsuperscript{st} generation vaccines in malaria control
  – \textasciitilde50\% efficacy for 1 y (transmission season)
  – Can have important public health benefits in terms of reducing morbidity and mortality
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- Assist development of 2\textsuperscript{nd} generation vaccines
  - Retain ambitious target: >75% efficacy for at least 2 y
  - *P. falciparum* and *P. vivax*
  - Will require discovery & translational research
  - Develop target product profiles & preferred product characteristics for specific use cases - provide guidance to researchers
  - Increase cross-talk between malaria vaccine researcher and malaria program communities
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  – mAbs to prevent & protect against malaria & reduce transmission
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