Update on Zika vaccines and related WHO activities

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PDVAC
June 2017
WHO technical consultations on Zika vaccines

- **March 2016**: WHO global consultation on research related to Zika virus infection; 7-9 March 2016, Geneva, Switzerland; call for an emergency use vaccine TPP
- **WHO Zika Virus (ZIKV) Vaccine Target Product Profile (TPP)**
  - First iteration for emergency/outbreak scenarios published July 2016
  - Revised TPP published February 2017
- **June 2016**: WHO consultation on considerations for regulatory expectations of Zika virus vaccines for use during an emergency, 6-7 June 2016;
- **October 2016**: Mosquito-borne viruses: can we build on commonalities to pre-empt the future? 5-7 October 2016; London.
- **January 2017**: Scientific Consultation on ZIKV vaccine development; hosted jointly with US NIH/NIAID, 10-11 January 2017 in Rockville, MD, USA
- **June 2017**: Efficacy trials of ZIKV Vaccines: endpoints, trial design, site selection
WHO/UNICEF TPP for Emergency/Outbreak Use: Public Health Objective

The public health objective in the emergency/ outbreak context is the prevention of **congenital ZIKV syndrome** through the **protection of pregnant women** throughout the **duration of their pregnancy**.

Priority:
Vaccination of **women of reproductive age**, and/or vaccination of **women during pregnancy**, **males of reproductive age**

WHO Vaccine Pipeline Tracker

45 candidates in “development”

Distribution of Candidates in WHO Tracker

- **Subunit**
  - N=18
  - Protein
  - DNA
  - RNA

- **Whole Virus**
  - N=27
  - Inactivated
  - Non-replicating
  - Replicating

Slide adapted courtesy of D. Kaslow

http://www.who.int/immunization/research/vaccine_pipeline_tracker_spreadsheet/en/
https://docs.google.com/spreadsheets/d/19otvINcayJURCMg76xWO4kvuyedYbMZDcXqbyJGdcZM/pubhtml#
Clinical ZIKV Vaccine Development Pipeline – June 2017

- **Phase I**
  - GLS-5700
    - GeneOne / Inovio
  - ZIKV PIV
    - WRAIR / BIDMC / NIAID / Sanofi Pasteur

- **Phase II**
  - VRC ZIKV DNA
    - VRC / NIAID
  - mRNA-1325
    - Valera Moderna

- **Phase IIb**
  - MV-Zika
    - Themis Bioscience

- **Phase III**
  - AGS-v
    - SEEK / NIH
  - BBV121
    - Bharat Biotech

- **Registration**

- **Vaccine Types**
  - Nucleic Acid
  - Inactivated
  - Peptide
  - Live attenuated (recombinant)
## Overview of Clinical Candidates

<table>
<thead>
<tr>
<th></th>
<th>GLS-5700</th>
<th>VRC DNA</th>
<th>PIV</th>
<th>mRNA-1325</th>
<th>MV-Zika</th>
<th>AGS-v</th>
<th>BBV121</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Platform</strong></td>
<td>DNA</td>
<td>DNA</td>
<td>Inactivated</td>
<td>mRNA</td>
<td>Viral Vector</td>
<td>Synthetic Peptide</td>
<td>Inactivated</td>
</tr>
<tr>
<td><strong>Published Preclinical Data</strong></td>
<td>Immunogenic in NHP, protection post-challenge against death, reduced viral load in mice</td>
<td>Immunogenic and protection post-challenge against virema in NHP</td>
<td>Immunogenic and protection post-challenge against virema in NHP</td>
<td>Immunogenic and protection post-challenge against death and viremia in mice</td>
<td>None found</td>
<td>None found</td>
<td>None found</td>
</tr>
<tr>
<td><strong>Most Advanced Phase</strong></td>
<td>Phase 1</td>
<td>Phase 2</td>
<td>Phase 1</td>
<td>Phase 1/2</td>
<td>Phase 1</td>
<td>Phase 1</td>
<td>Phase 1</td>
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<tr>
<td><strong>Study Locations</strong></td>
<td>US, Puerto Rico</td>
<td>US, Puerto Rico</td>
<td>US, Puerto Rico</td>
<td>US</td>
<td>Austria</td>
<td>US</td>
<td>India</td>
</tr>
</tbody>
</table>

Biggest challenge: uncertainty

• **Clinical outcomes**
  – How do viremia, clinical illness, and severe outcomes correlate?
  – What is the full spectrum of clinical illness? Are there other priority risk groups?
  – What is the potential to develop surrogates/correlates?

• **Zika epidemiology**
  – How will the epidemiology evolve? Is there endemic transmission or sporadic outbreaks?
  – What influences Zika epidemiology, spread, clinical picture?
  – What is the burden of / risk of Zika in Africa? In Asia?

• **What will be the future need for a Zika vaccine?**
  – What will be the global demand of a Zika vaccine?
Some conclusions from consultation on Efficacy trials of ZIKV Vaccines (1-2 June 2017)

• Essential to understand epidemiology of disease – key role for seroprevalence studies
• Clinical endpoint efficacy trials might still be feasible
• Multicentric prospective or reactive vaccine cohorts discussed, individually randomized
• Virol. confirmed Disease as primary endpoint, infection as secondary endpoint proposed
• Baseline flavivirus (dengue) immunity assessment, and stratified analysis
• Key next steps:
  a) Develop an annotated interactive generic protocol for ZIKV vaccine efficacy trials, based on preliminary design consensusinventory of seroprevalence studies,
  b) Promote epidemiological data collection, standardization and incentivize data sharing through the WHO R&D observatory
  c) Develop transparent criteria to recommend vaccines for advanced clinical evaluation in endemic settings with highest likelihood of success
Zika landscape analysis and technology roadmap: planned work

**Landscape analysis drawing on:**
- Vaccines: pipeline tracker and technical consultation WHO/NIAID, literature
- Diagnostics: GDAC workshop on arboviral diagnostics
- Therapeutics: commissioned review (U Melbourne)

Peer reviewed publication 3Q17

**Vaccine technology roadmap:**
- Develop strategic goal and vision statement with PDVAC ad hoc WG*
- Develop roadmap for review by PDVAC
- Online public consultation
- Finalization by PD VAC

Publication 4Q17

*Based on TPP working group: A Barrett, K Cichutek, A Durbin, D Kaslow, S Thomas,
Thank you!

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