Chikungunya Vaccines in the Pipeline

Countries and territories where chikungunya cases have been reported*
(as of April 22, 2016)

[Map showing countries with reported chikungunya cases as of April 22, 2016]

- Current or previous local transmission of chikungunya virus
Health impact

**Symptoms**

- Fever, usually lasts about 1 week (90% of patients)
- Myalgia, usually lasts 7–10 days (90% of patients)
- Polyarthralgia, polyarthritis, or both, can last weeks to months (95% of patients)
- Rash, lasts about 1 week (40–50% of patients)

**Infection**

- 2–6 days Incubation period
- Approximately 1 week
- Weeks to months
- Viremia, usually lasts 5–7 days
- Years
Public health burden: 1.3 billion people live in areas endemic for Chikungunya. Prevalent in ~60 countries over the world.

Has high attack rates and the virus has been able to adapt to different mosquito vectors.

No treatment/cure

Not fatal but very debilitating, has been apparently fatal in recent epidemics, potential for mother to child transmission.
Workshop on Chikungunya vaccines, Delhi, Feb 5-6, 2018
Create opportunities for cross-sectoral and cross-geographical R&D collaborations, innovation and data sharing

### Public health need
- Global outbreaks
- One of 11 WHO priority EIDs
- Ranked fourth based on CEPI SAC’s assessment
  - after Lassa, MERS, and Nipah

### Promising pipeline
- Third most mature vaccine R&D pipeline amongst 11 WHO priority EIDs
- CEPI pipeline data demonstrate
  - >35 vaccines in development;
  - 9 in clinical phase trials

### Funding gaps
- A US$ 0.7 – 1.5 bn investment across current pipeline could generate 2 – 5 vaccine candidates ready for efficacy testing in 5 to 9 years*

### Coordination potential
- Bringing stakeholders together to explore:
  - R&D opportunities
  - Actor competencies and limitations
  - Gap-filling roles to play in moving the pipeline forward

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*CEPI own, unpublished estimates*)
Chikungunya vaccines

• Efforts to develop Chikungunya vaccines initiated in 1960s
• Interest resurfaced from 2000 onwards with the re-emergence of the disease
• Over 80 organizations are engaged in efforts to develop a Chikungunya vaccine
• As of 2018, 39 candidates
Vaccine candidates in pre-clinical development

- There are multiple candidates in pre-clinical stages of development (>20)
- Different technologies-DNA, m-RNA, viral vectored vaccines etc.
# Candidates in Phase I

<table>
<thead>
<tr>
<th>Name of Candidate</th>
<th>Validated (Trial registries; publications)</th>
<th>Platform</th>
<th>Developers</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAL 181388</td>
<td>![check]</td>
<td>m-RNA</td>
<td>Moderna Therapeutics</td>
</tr>
<tr>
<td>VLA 1533</td>
<td>![check]</td>
<td>Replicating</td>
<td>Valneva SE</td>
</tr>
<tr>
<td>BBV87</td>
<td>![check]</td>
<td>Inactivated</td>
<td>Bharath Biotech</td>
</tr>
<tr>
<td>CHIKV 181/25</td>
<td>![check]</td>
<td>Inactivated</td>
<td>Tested previously by US Army Medical Research and Material Command (USAMRMC). Has now been transferred to Indian Immunologicals Ltd</td>
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</tbody>
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Surveys and publications have indicated that there are 4 other candidates that are likely to be in Phase I/enter phase I soon and one which has been terminated.
# Candidates in Phase II

<table>
<thead>
<tr>
<th>Name of Candidate</th>
<th>Validated (Trial registries; publications)</th>
<th>Platform</th>
<th>Developers</th>
</tr>
</thead>
<tbody>
<tr>
<td>MV-CHIK</td>
<td>![Checkmark]</td>
<td>Replicating</td>
<td>Themis</td>
</tr>
<tr>
<td>VRC-CHKVLP059-00-VP (37997)</td>
<td>![Checkmark]</td>
<td>Virus like particle (VLP)</td>
<td>National Institute of Allergy and Infectious Diseases (NIAID); The EMMES Corporation; Leidos; FHI 360; PaxVax</td>
</tr>
</tbody>
</table>
Challenges

• Pre-clinical studies
  • Animal Models Best suited model for challenge studies are non-human primates, requires a BSL-3 facility
  • Assays used and availability of reference material. Assay variability, no international reference reagents
• Neutralizing antibody levels for protection not clearly defined
Clinical studies

Clinical Trial Designs
• Vaccine efficacy study/ Phase III study is hard and expensive to conduct as epidemics/outbreaks are sporadic, hard to predict and likely to be over in 6-8 months.

Identification of Trial Sites
• Difficult to identify Phase III trial sites as timing, size and duration of epidemics is unpredictable

Trial Participant Enrolment
• In endemic countries, screening of a large number of people is required because of high pre-existing CHIKV antibodies

 Diagnosis and Assays
• Absence of a GMT of neutralizing antibodies which can be associated with protection in humans based on a standard international reference assay
• Clinical diagnosis and case definitions are not clear and it is easy to confuse Chikungunya with other febrile diseases such as Zika and Dengue
Regulatory challenges

• Requirement of a classical Phase III trial for proof of vaccine efficacy and licensure- Very long timelines, costs and very expensive to do

• Regulatory timelines in endemic countries are long and these are lengthened even further for candidates requiring additional permissions for example separate committees for candidates that are genetically modified (GMOs)

• Some candidates based on newer technologies (for e.g. mRNA vaccines) may have small safety databases and may have additional requirements for examples insect cell substrates
Other challenges

Many endemic countries for CHIKV have **poor surveillance** systems with no active surveillance.

Chikungunya can be confused with other febrile illnesses; **exact incidence rates are hard to predict/interpret**.

**Low funding** - not considered a serious disease.

Size and duration of epidemics is uncertain.

**Low awareness of the disease** and other competing priorities such as Zika, Dengue.
Possible solutions/support strategies

- International reference reagents, validated virological and serological assays and standard neutralizing antibody assay/reference serum to normalize results from assays used by different developers.
- Laboratory diagnostic methods need to be standardized
- Standard and uniform case definitions for acute and chronic disease including that for arthralgia. Case definition for Chikungunya should be based on both clinical and laboratory assessment
- GMP master seed of CHIKV challenge virus strain
- To aid studies, collaborations with endemic countries would be useful
- Master protocols to initiate trials rapidly
- Alternate pathways need to be explored for approval and licensure of the vaccine and regulatory agencies should be involved from early stages. This could involve use of human challenge models, the demonstration of correlates of protection.
- In case alternate pathways are explored there is a need to define early the post-licensure studies that would be needed to demonstrate clinical benefit.
Next steps

• One inactivated vaccine being supported in India

• Call for Chikungunya vaccines expected in 2018