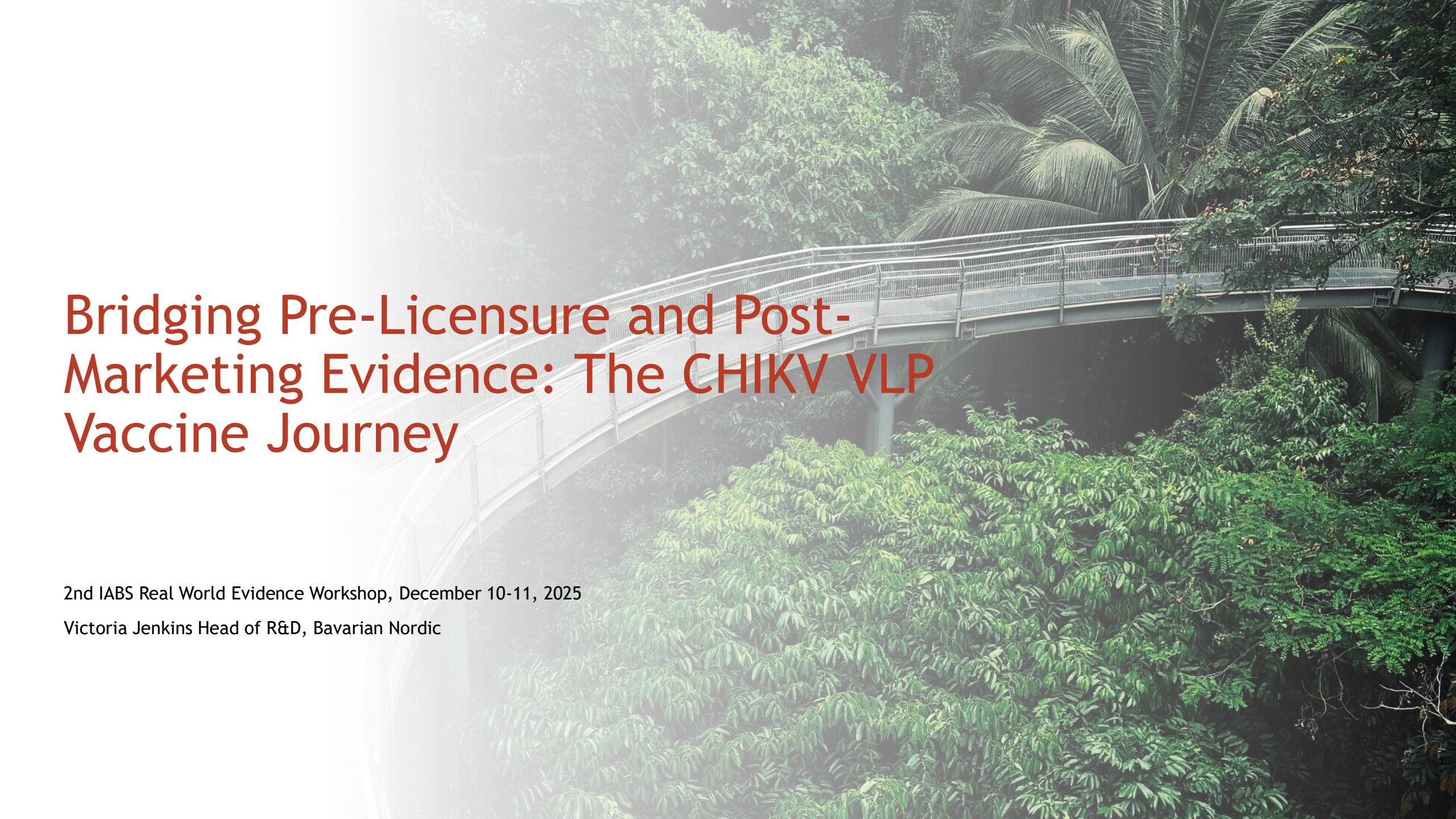

Bridging Pre-Licensure and Post-Marketing Evidence: The CHIKV VLP Vaccine Journey

2nd IABS Real World Evidence Workshop, December 10-11, 2025

Victoria Jenkins Head of R&D, Bavarian Nordic

Chikungunya virus

Chikungunya virus is an arthropod-borne alphavirus transmitted by the *Aedes aegypti* and *Aedes albopictus* mosquitoes [1,2]

Infection can lead to debilitating disease in individuals of all age groups[1,3,4]

- Patients present with an acute febrile illness characterized by fever, fatigue, myalgia and incapacitating joint pain
- More than 40% may experience chronic disease, with arthralgia as the predominant symptom. This may last from months to years.

https://iris.paho.org/handle/10665.2/4009

1. Burt FJ, et al. Lancet Infect Dis. 2017;17:e107–117; 2. Liumbruno GM, et al. Blood Transfus. 2008;6(4):199–210; 3. Bartholomeeusen K, et al. Nat Rev Dis Primers. 2023;9(1):17; 4. Pan American Health Organization and World Health Organization. Chikungunya fever; 5. Centers for Disease Control and Prevention. Chikungunya. 5. Rama K et al. PLoS Negl Trop Dis. 2024;18(6):e0012254.17

VIMKUNYA®

Chikungunya vaccine (recombinant, absorbed)

- Virus-like particle (VLP) technology
- Pre-filled syringe
- 3-year shelf life
- Single dose

- 0.8 ml dose: 40 µg VLPs, adjuvanted with aluminium hydroxide (300 µg Al^{3+})

- **Indication:** prevention of disease caused by CHIKV in ≥12-year-olds
- **Contraindications:** hypersensitivity to the vaccine components

FDA: U.S. Food and Drug Administration; EC: European Commission: MAA: Marketing Authorisation Application

VIMKUNYA, US Prescribing Information. Available at: Link. Accessed November 2025

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14 February
FDA Approval, United States

28 February
EC Approval, European Union

01 May
MHRA Approval, United Kingdom

FDA: U.S. Food and Drug Administration; EC: European Commission: MAA: Marketing Authorisation Application
VIMKUNYA, US Prescribing Information. Available at: Link. Accessed November 2025

Challenges to a pre-authorisation efficacy study

Nov 2019 ➔ VRBPAC meeting on CHIKV:

- CHIKV recognised as a global threat
- Epidemiology of CHIKV acknowledged as unpredictable and sporadic
- Due to challenge of conducting efficacy study, agreement to use surrogate marker of protection for initial licensure
- Passive transfer and challenge study in NHPs to establish a NAB threshold reasonably likely to predict protection in humans (surrogate marker)

Key considerations

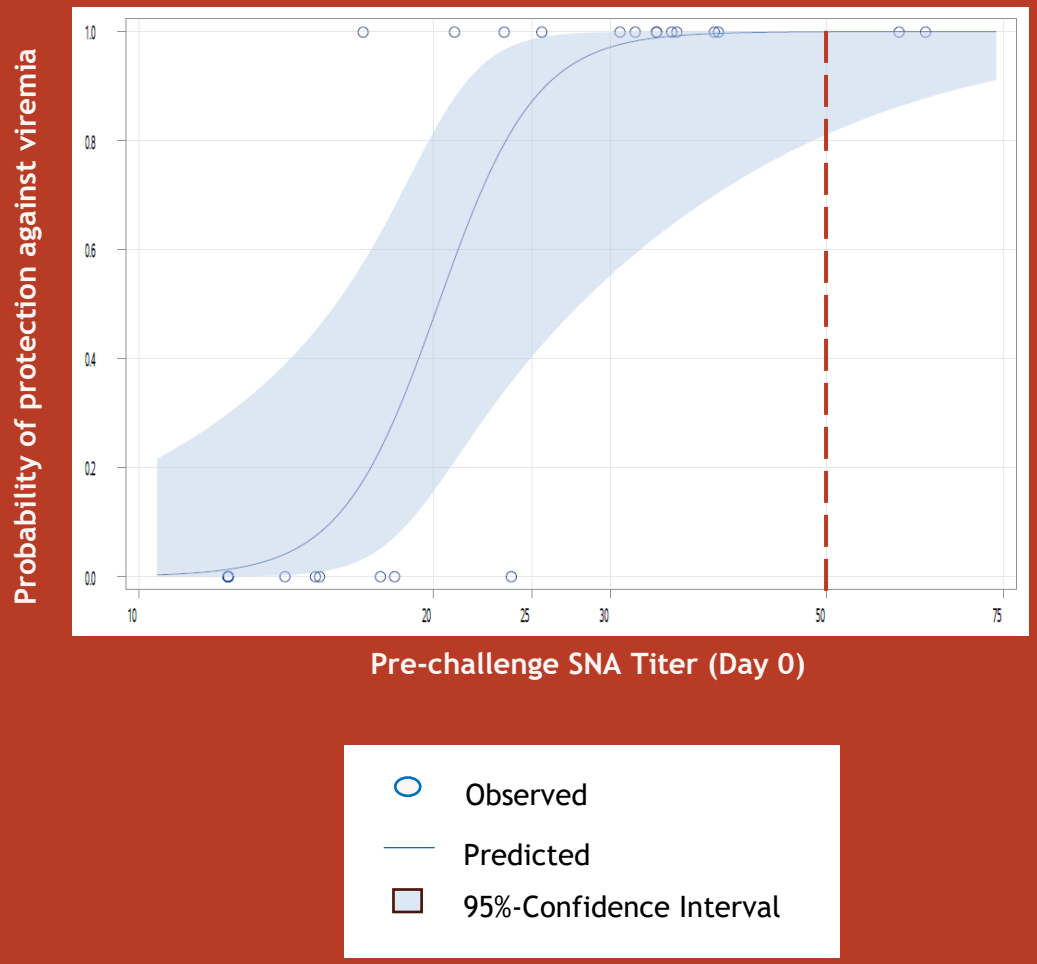
- Definition of anti-CHIKV serum neutralising antibodies threshold
- Post-authorisation commitments including a confirmatory efficacy study

VRBPAC, Vaccines and Related Biological Products Advisory Committee
158th VRBPAC Meeting: Chikungunya Vaccine Development, 8 November 2019. Available at: Link. Accessed November 2025.

Serum Neutralising Antibody threshold for Phase 3 endpoints

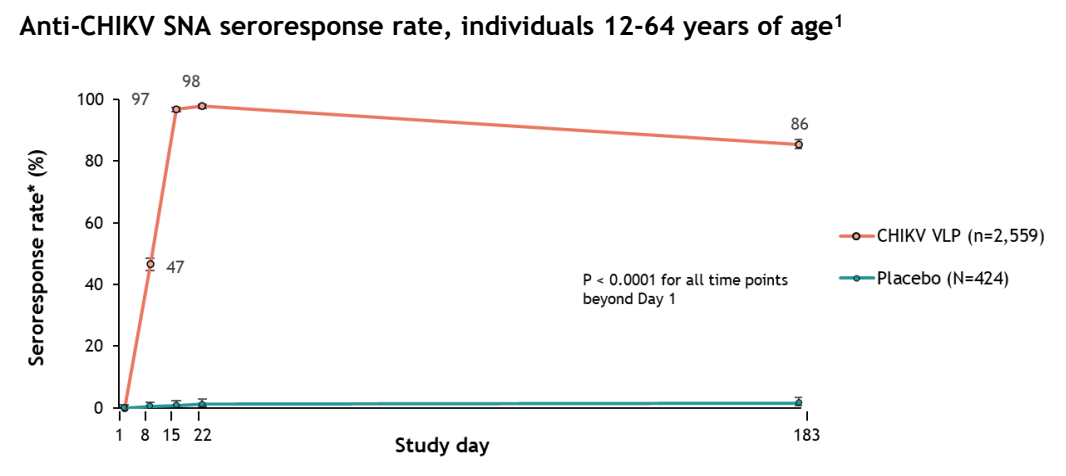
Serum passive transfer and challenge study in NHP

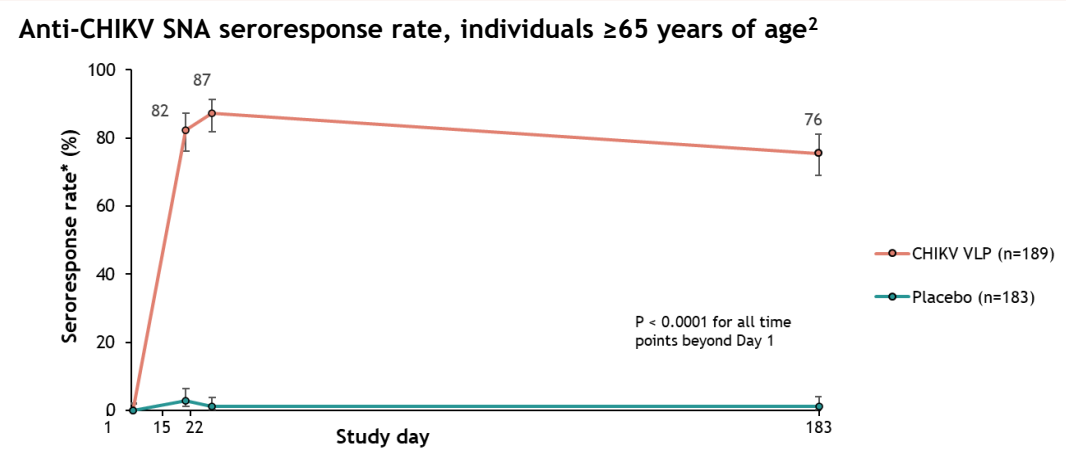
- NHPs received pooled sera from human participants vaccinated with CHIKV VLP at various dilutions intravenously and were challenged with CHIKV 24 hours later
- SNA titers were measured by the validated NHP SNA assay and viraemia by the validated RT-qPCR assay, demonstrating that all NHPs that had a pre-challenge SNA titer ≥25.7 were protected from CHIKV challenge
- Logistic regression model: SNA titre of 50 results in 99.97% [81-100] probability of protection **against viraemia**
- Agreement with regulatory agencies on a more conservative SNA titre threshold of 100 to be an acceptable surrogate endpoint



NHPs, nonhuman primate; SNA, serum neutralizing antibodies; CI, confidence interval
Data presented at ESCMID Global 2024 (publication in development)

Rapid induction of robust seroresponse

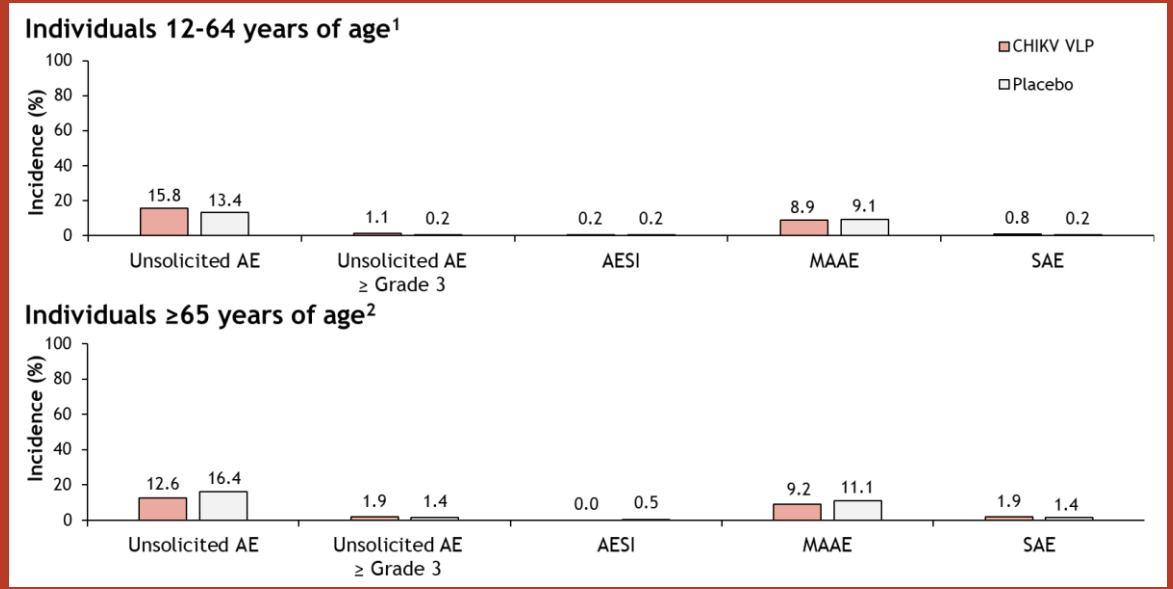




BAVARIAN NORDIC

1. Richardson *et al*. doi: https://doi.org/10.1101/2024.10.11.24315179. 2. Tindale et al. doi: https://doi.org/10.1101/2024.10.10.24315205

Mostly mild/moderate Adverse Events



- Incidence of Adverse Events of Special Interest (AESI) and Medically-Attended Adverse Events (MAAEs) did not differ between the vaccine group and the placebo group
- No treatment-related Serious Adverse Events, including medically-attended arthralgia

AESI = adverse event of special interest: defined as new onset or worsening arthralgia that was medically attended; AE = adverse event; MAAE = medically attended adverse event; SAE = serious adverse event. Seroresponse= % of participants with an SNA titre ≥100

Post-authorisation activities

Pregnancy Registry

Efficacy Study

Paediatric Trials

Long-term Follow Up

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Post Approval Efficacy Study

A Phase 3b Randomised, Double-blind, Placebo-controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of an Adjuvanted Chikungunya Virus Virus-like Particle (CHIKV VLP) Vaccine for the Prevention of Chikungunya Disease in Adolescents (12 to <18 Years) and Adults (≥18 Years)

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Objectives

Efficacy: To evaluate the vaccine efficacy of VIMKUNYA compared to placebo in the prevention of laboratory confirmed acute CHIKV disease in adolescents and adults (12 years of age and older)

Safety: To evaluate the safety of VIMKUNYA in adolescents and adults (12 years of age and older)

Efficacy Study

Up to 6000 participants, randomised 1:1 to VIMKUNYA or placebo

6-month to 3-year follow up

Event-driven study enrolment

Initiation planned from 2026 dependent on the declaration of a CHIKV outbreak

Final study report tentatively planned for submission by August 2030

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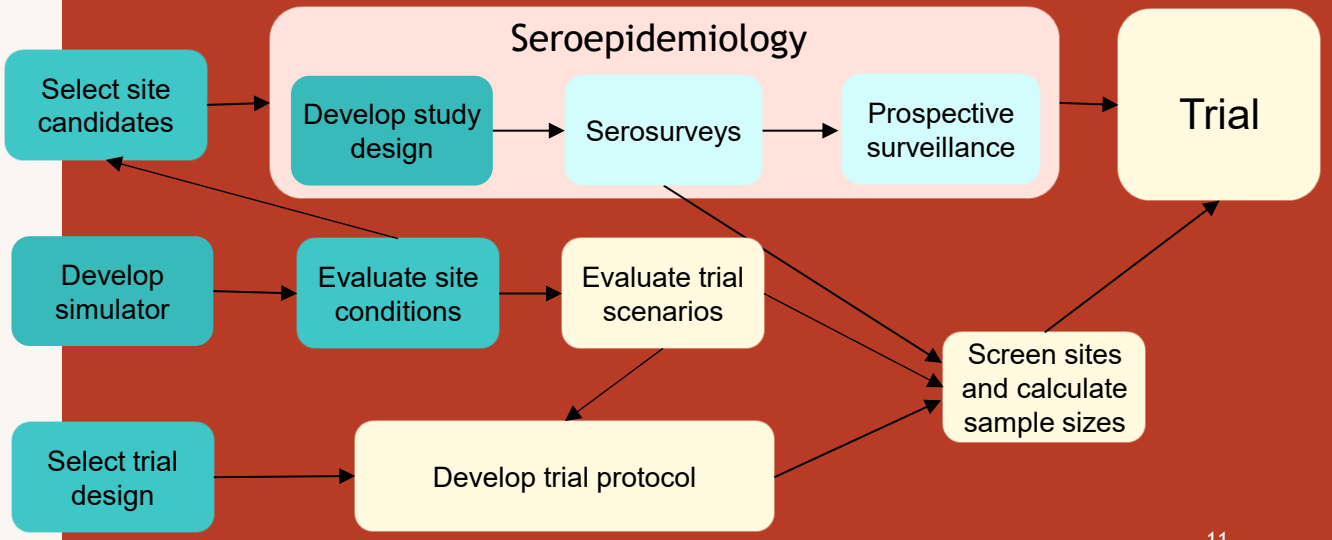
Multiple sites engagement across several countries

Sero-epidemiological studies, sites assessment and simulation modelling

Adoption of a design responsive to CHIKV surveillance and focus on communities with the highest transmission potential

Elucidate epidemiology
- Transmission criteria:
  - Identify ideal/likely scenarios
  - Assess historical data
  - Develop simulation model

Assess feasibility
- Feasibility criteria
  - Identify constraints
  - Profile eligible sites
  - Rank sites



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The CHIKV Challenge

Pivotal study based on neutralising Ab titres, not an established correlate of protection → effectiveness data needed & deemed feasible; however, there are feasibility constraints

PAES requirement = "randomised, placebo-controlled, double-blind efficacy study in CHIKV-endemic area"

- *Benefit is placebo control*
- *Risk is unknown timing of outbreak (and, therefore, study results) and outbreak characteristics, timing of vaccination, etc.*
- *Also note: 3 years from start of study discussions with regulators to local authority approvals*

Also considering options for reactive study design optimised for rapid set-up

- *External consultants brought in to establish minimum methodological & operational criteria for reactive study "green light"*

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Reactive Outbreak Control Effectiveness
Reflections on criteria for reactive effectiveness study in case of an outbreak

Test-negative design mimics RCT but utilises passive controls

- *No active recruitment may help truncate study set up time*

What quantitative outbreak parameters provide sufficient power to measure VE?

- *CHIKV (and control infection) attack rate*
- *Population size under surveillance*
- *Vaccine coverage, etc.*

Initial analyses indicate study population must be very large (>>>10,000)

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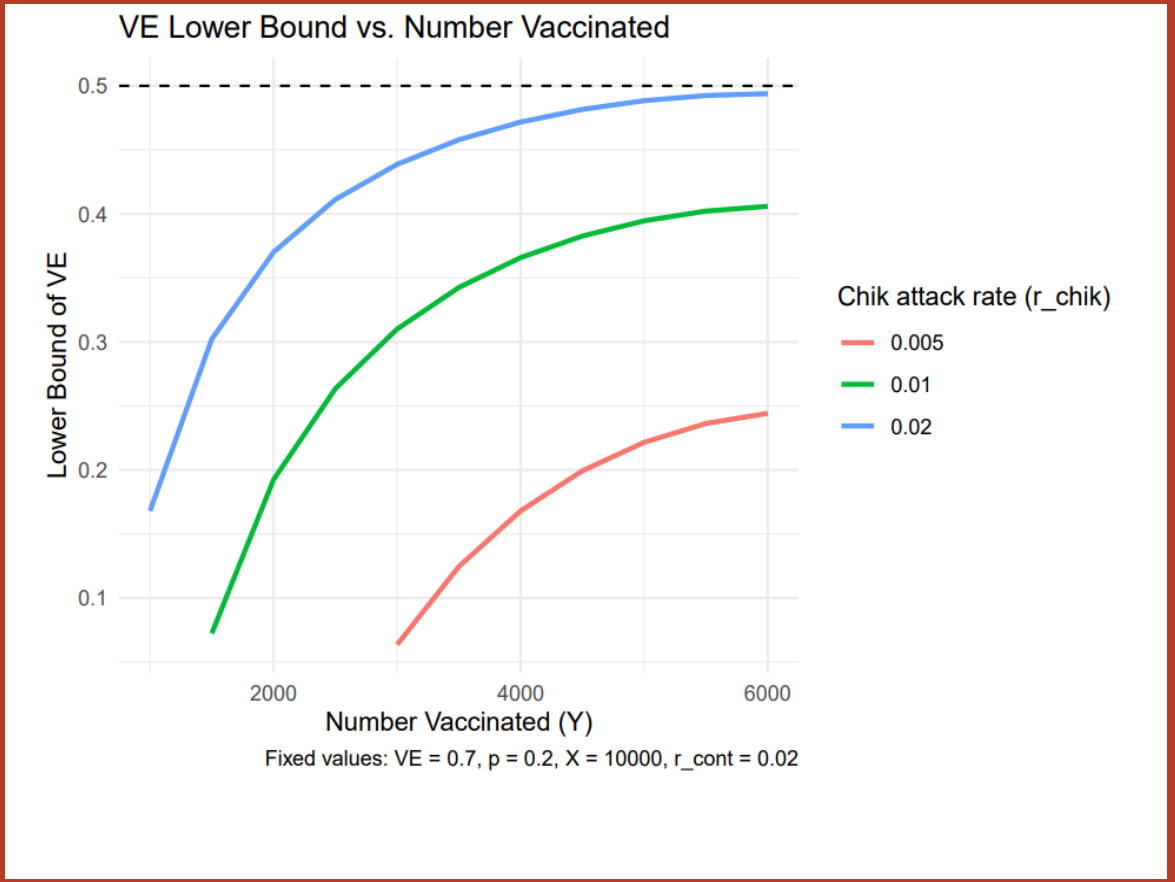
Example: measurable vaccine effectiveness as a function of attack rate and number of vaccinated individuals



Operational Constraints

Identification of critical structural elements to support real-world study feasibility

Interim conclusions re: minimum feasibility requirements:

1. *The "right" outbreak conditions for study power (i.e., n=40,000 study catchment?)*
2. *Pre-existing surveillance infrastructure w/capacity for rapid enhancement*
3. *Health authority willingness to collaborate for very fast set-up*

Highlights the importance of starting discussions with authorities in settings where criteria might be met

Study element		Key criteria
Detection of an outbreak		Need pre-existing (stable) surveillance
Vaccine coverage		Industry needs to be ready to make doses available, but local authorities determine use
Ability to verify outbreak characteristics		Establish standardised outbreak reporting?
Surveillance capacity & access		Industry can support enhanced surveillance, but foundation must already exist
Existing lab capacity		Requires existing local public health system. Industry sponsor may be able to assist in rapid enhancement of surveillance
Local, qualified, PI		Should be identified in key regions before any potential outbreak
Time (collaborative agreements w/local institutions, IRB approvals, etc.)		***May be most critical bottleneck in any reactive observational study set up

Conclusions

The development and approval of the VIMKUNYA exemplifies the importance of strategic engagement with regulatory authorities and a harmonised approach to licensure and post-marketing requirements.

Achieving PRIME, Fast Track, and Breakthrough Therapy designations, alongside accelerated submissions in both the US and EU, highlights the value of early and ongoing dialogue with regulators.

Operational feasibility for real-world evidence or Phase 3b efficacy studies hinges on several critical factors: the right outbreak conditions, robust surveillance infrastructure, rapid collaboration with health authorities, and pre-identified local investigators. These elements are essential to ensure timely and effective study set-up, especially in the unpredictable context of infectious disease outbreaks.

The lessons learnt here—about collaboration, flexibility, and preparedness—will inform future vaccine development efforts and help bridge the gap between pre-licensure evidence and real-world effectiveness.