TB Vaccine Development Pathway

DCVMN - Webinar
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Introduction to tuberculosis, BCG, portfolio vaccine candidates

The TB Vaccine Development Pathway
  • History
  • Objectives
  • Going through stages, functions, guidance

Examples of use

Conclusions
Mycobacterium tuberculosis

In 2018,

- 10.0 million people ill from tuberculosis (TB)
  - 1.1 million children

- 1.5 million people died
  - 205,000 children
  - 251,000 HIV+

- 484,000 new cases of rifampicin-resistant TB, of which 78% were multidrug-resistant

- Geographically, cases were for 44% in South East Asia, 24% in Africa and 18% in Western Pacific

*WHO Global Tuberculosis Report 2019*
Tuberculosis, incidence rate, 2018

WHO Global Tuberculosis Report 2019
BCG, Bacillus Calmette-Guérin:

- Attenuated *M. bovis*; only TB vaccine licensed (1921), widely used
- Efficacious against severe TB disease in children, though variable protection in adolescents and adults, and safety considerations in HIV-infected infants / children

New vaccines are needed to end TB

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From Voss et al, 2018, Progress and challenges in TB vaccine development. F1000 Research
Promising data...

- Nemes et al, 2018
- Van Der Meeren et al, 2019
The Stage-Gate Pathway

- Initiated in 2010 by TBVI and AERAS (now IAVI) with the aims:
  - to provide TB vaccine developers a body of knowledge and a data-driven methodology that standardizes the development of any TB vaccine
  - to provide the TB scientific community, funders and decision-makers rational criteria for assessment of candidates and accelerate progression of the most promising
  - to manage and sustain the pipeline with balanced investment

- First published in 2012*


What is a ‘Stage-Gate’?

Stage-Gate * is a project management methodology that divides large projects into:

• segments of activities performed in parallel, the Stages,
• separated by check points, the Gates
• where continuation is decided based on Criteria.

* Cooper, 2008, The Stage-Gate: idea-to-launch process
Structure of the Pathway

The Pathway is a matrix:

• Lines: Stages and Gates, from discovery to implementation

• Columns: expertise, as Functions

• Each box: activities, criteria, guidance with indications
TB VACCINE DEVELOPMENT PATHWAY

Stage A: Discovery
Stage B: POC Studies
Stage C: Pre-Clinical Evaluations
Stage D: Prepare FIH/Ph1
Stage E: FIH/Ph1
Stage F: Ph2
Stage G: Ph 2B
Stage H: Ph3
Stage I: Registration
Stage J: Launch

STAGE: Period during which one conducts the activities described in the relevant stage

GATE: Point at which one applies gating criteria to decide whether to move to the next stage

CRITICAL INVESTMENT GATE
Introduction and Guidance
Stage Gates
Functions
Feedback
Examples of use

• Education: overview of development from concept to commercialization, progression of activities within each function

• By developers, as a guide for planning their research and development, monitor progress, refer to criteria for decision

• By organisations, to structure the portfolio of vaccine candidates per stages, indications and technologies and to document progression of candidates

• By committees, to use criteria for selection of projects
Example: structure of portfolio

TBVAC2020 stage gating
Example: selection

Applications reviewed by Portfolio Management Committee
Selection based on stage-gate and prioritisation on criteria – up to Stage C

64 Applications

42 Selected

22 Not selected

44 Different vaccine concepts/formulations = Potential candidates

Stage A: Discovery
Preliminary in vivo safety, immunogenicity and efficacy

Stage B: Proof of Concept
- Independent verification of safety
  immuno or efficacy
- Data from second model/species
- Head to head comparisons for prioritisation

Stage C: Pre-clinical
- Advanced, human-relevant model e.g. NHP
- Efficacy and Immune correlates
- Go/No-Go decisions and to refine/feedback

Data to support entry to PoC development

Iterative improvement

Down-selection

TBVAC 2020
Moreover...

The Pathway …

• Is generic and could be a baseline for the development of any vaccine, or a ‘check list’ of activities, deliverables

• Activities are sequential, no ‘shortcuts’

• Refers to guidelines, publications, public information

• Continuously updated from feedback, surveys, with a revision in 2021
Conclusions

The Pathway is a body of knowledge and a data-driven methodology,

• that offers developers structure and guidance for their product development plan, from concept to commercialization,

• a structure to the TB vaccine pipeline, with objective criteria for assessment, selection and progression of candidates, critical for balanced investments and a healthy pipeline.

It is available on internet and free, with dissemination ongoing and a revision planned. Use it, share it, criticize it, contribute to it...
Acknowledgements

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Working Group

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