Future Prospects for TB Vaccine and Biomarker Development

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Berlin
Agenda

• The problem
• The future
• The promise of new TB vaccines
• Potential complications & solutions
• The global perspective: Global TB Vaccine Partnership – GTBVP
• Concluding remarks
TB: the biggest killer ever
No. of deaths in the past 200 years (source: Nature)
Projected acceleration of TB incidence decline to target levels

Optimize current tools, pursue universal health coverage and social protection

Current global trend: -2%/year

Average -10%/year

Introduce new vaccine

Average -17%/year

-5%/year
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• The global perspective: Global TB Vaccine Partnership – GTBVP
• The way forward
Agenda

• The problem
• The future ... Money
• The new ... Time
• Potential ... Innovation solutions
• The global ... Strategy
  Global TB Vaccine Partnership - GTBVP
• The way forward
Agenda

- The problem
- The future … *Money*
- The new … *Time*
- Potential … *Innovation Solutions*
- The global … *Strategy* Global TB Vaccine Partnership - GTBVP
- The way forward
New TB vaccines
Financial constraints

Cost and time for TB vaccine trials:

- Phase I for safety and efficacy: 500,000 US$, >2 year
- Phase IIa in target population: 1 million US$, >2 years
- Phase IIb for first proof of efficacy: 20 million US$, >5 years
- Phase III for ultimate safety & efficacy: 100 million US$, > 6 years

Global funding for TB vaccine R&D: 250 million US$

Conclusion: We need to be selective.

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- The problem
- The future... *Money*
- The new... *Time*
- Potential... *Innovation Solutions*
- The global... *Strategy*
- The global TB Vaccine Partnership - GTBVP
- The way forward
Rational selection of TB vaccine candidates

- Establish **global criteria** for selecting vaccine candidates for clinical studies
- Obtain **consensus** on criteria to advance new candidates
GTBVP well placed to shift the risk curve

Shifting the gate to the left of the pipeline

Phase III

assessment of efficacy in Phase IIB clinical trial

Phase II

discovery

prediction in preclinical plus early human

Phase I

MONEY

RISK
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New TB vaccines
Global portfolio management

- Tuberculosis Vaccine Initiative (TBVI)
- Aeras
- Bill & Melinda Gates Foundation (BMGF)
- European and Developing Countries Trials Partnership (EDCTP)
- European Commission (EC)
- European Investment Bank (EIB)

Formation of Global TB Vaccine Partnership (GTBVP)
Strong EU-US axis, also include South/BRICS

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Accelerate clinical trials
Adaptive trial design

Shared biorepositories
Develop biosignatures

Do not ignore research
Be cooperative/iterative
New TB vaccines
Accelerating vaccine trials

• “Plausibility of efficacy trials” with individuals at high TB risk
• Newborns (even BCG vaccinated) incidence rate (2x > adolescents/adults)
• Household contacts of newly diagnosed TB cases
• Health careworkers entering into TB settings
• Miners
• Patients with recurrent TB disease after chemotherapy (4%)
• Prevention of infection rather than disease (individuals with negative IGRA/TST)

New TB vaccines
Adaptive trial design

- Modification of ongoing trial in response to interim results

- Change in participant numbers in response to:
  - New TB incidence data
  - New prognostic clinical surrogate endpoints
  - New prognostic correlates of vaccine protection

- Complementation by revised regulatory and licensure processes for expedited approval

New TB vaccines


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Shared biorepositories
New TB vaccines
Bio-repositories

More than assessment of a single vaccine
Also guidance for future vaccine by iterations between clinical trial and basic research

- Collection and storage of samples from trials
- Free availability to research community
- State-of-the-art assays and analyses
- Data sharing early and transparently

New TB vaccines
Biosignatures

Natural infection:
- Prognostic signature of TB disease
- Adolescent cohort study
- Grand Challenge 6

Vaccine studies:
- Placebo-controlled efficacy trial
- Precedent: Thai RV144 HIV vaccine trial with 31% protection

Biomarkers of Protective Immunity against TB in the context of HIV/AIDS in Africa (GC6-74)

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Index: 850 HIV - newly diagnosed pulmonary TB patients
Household contacts: 4500
Recruitment completed 2010
Follow-up completed 2012
Analysis started 2014

Expected household contacts with TB after 2 years follow-up:
112 (0% loss) TB cases
91 (20% loss) TB cases
Current status: > 80 TB cases
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