

FEASIBILITY TRIALS FOR TB VACCINES

AN INDUSTRY PERSPECTIVE

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Emerging Diseases Vaccines

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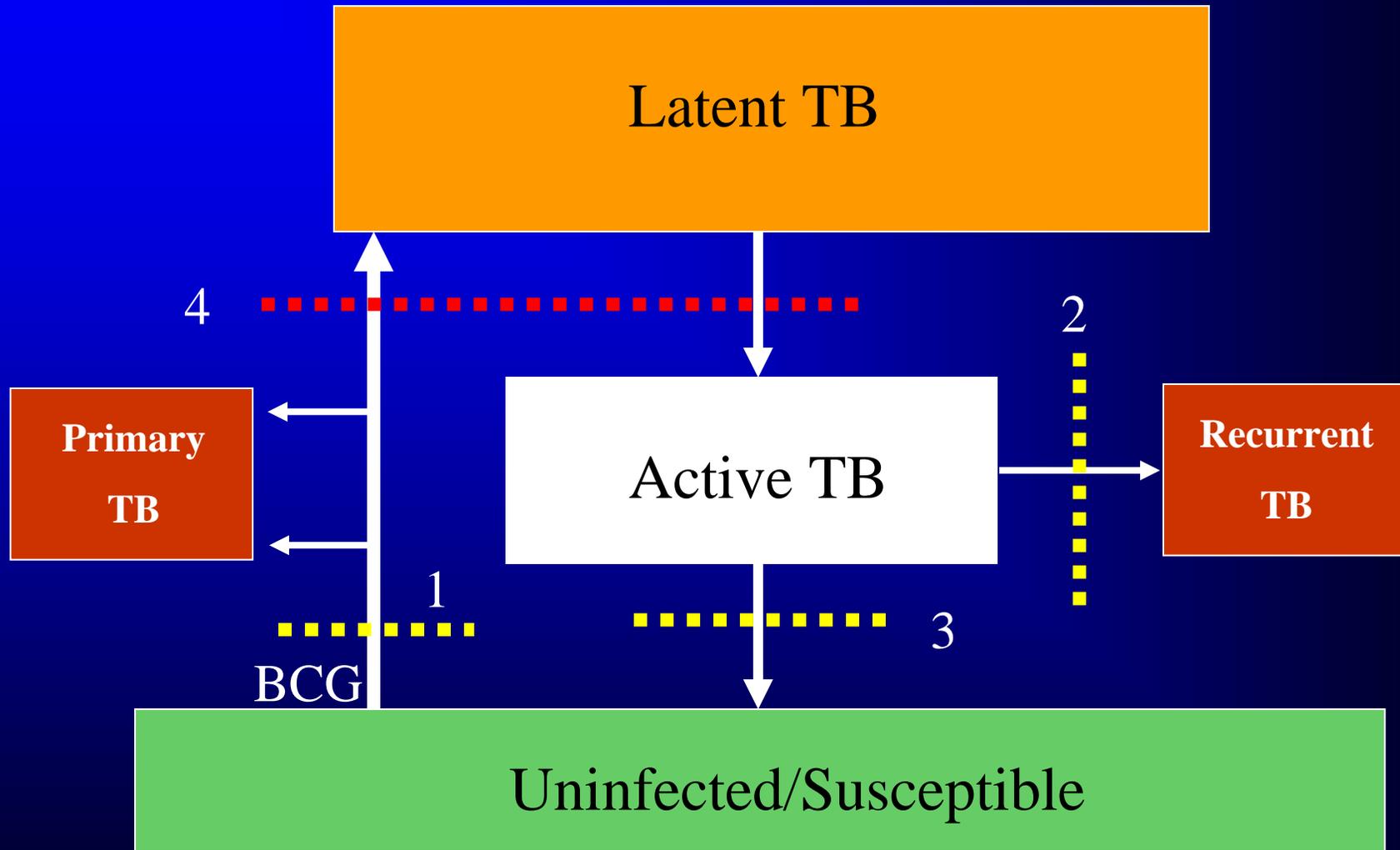
Feasibility Trial Issues

- Target populations
 - Access, ethics, consent issues
 - High incidence disease settings
- Case definition considerations
- Proof of concept
 - Achieve as rapidly as possible
 - Should provide clear Go/NoGo
 - May not need precision of Ph III

Prior to Feasibility Studies...

- Assess vaccine safety in particular settings
 - Prior exposure to BCG
 - LTBI and successfully treated TB
 - HIV coinfection, use of ART
- Optimize dose & schedule (age specific)
- Select optimal formulation (if necessary)
- Conduct appropriate epidemiology studies

Possible Feasibility Trial Strategies



Possible Feasibility Trial Scenarios

- Prevention of pediatric TB

- Pros

- Medical & epidemiological importance
- High incidence populations exist
- Makes optimal use of BCG priming

- Cons

- Specificity of case definition
- Limited ability to assess CMI readouts

Issue: Case definition in pediatric TB

- Largely neglected target population
 - Pose difficult Dx challenges
 - TST unhelpful, diverse clinical picture
 - Unwell child c/w TB, culture negative
 - Well child, household contact, IS/GA+
 - Will clinical scoring systems used for Dx be acceptable for vaccine trials?

Possible Feasibility Trial Scenarios

- Prevention of reinfection with TB

- Pros

- High risk populations exist
- Clearly defined endpoints
- Access through Rx programs

- Cons

- Selection of inherently poor candidates for vaccination?
- Relatively large studies

Possible Feasibility Trial Scenarios

- Prevention of recurrent infection (relapse)

- Pros

- Target population identifiable
- Builds on DOTS infrastructure
- Predictable clinical failure rates

- Cons

- Limited preclinical feasibility data
- Relevance to reactivation of LTBI?

Post-POC Efficacy Studies

- Prevent primary infection in children/adults
- Prevent reactivation of LTBI
 - Pros
 - High public health impact
 - Clearly defined endpoints
 - Cons
 - Very large studies, long F/U required
 - Age-specific regimens may be required

Other Issues

Regulatory strategies

- Development under IND?
- Registration in countries with weak NRA?

Market preparedness

- Understand public health impact
- Inform demand forecasts