VPM1002

A new TB vaccine on the horizon
Vakzine Projekt Management GmbH

- Founded in 2002 as a private company
- Currently 10 employees
- VPM team members represent core competences along the entire value chain – from bench to market authorization and product launches in global market
Every 2\textsuperscript{nd} child receives a vaccine manufactured by SIIPL

SIIPL is the license holder and manufacturer of **VPM1002**
Fast Translational Product Development
VPM1002 and VPM1002BC

< 4 years to bridge the gap from lab to clinics

VPM1002
TB Vaccine (pre- & post-exposure)

VPM1002BC
Immunotherapeutic
(non-muscle invasive bladder cancer)
Regulatory Aspects

- 3 Scientific Advises at Paul Ehrlich Institute/ German authority
- May 2014: Scientific Advise at Swissmedic on bladder cancer study
- In India the project was introduced to DCGI and RCGM
- Meetings with EMA, FDA
- International meetings at WHO:
  - 2012: Potency testing of new TB vaccines
  - 2011: Consensus statement on diagnostic endpoints for infant TB vaccine trials
  - 2009: 2nd Geneva consensus: Recommendations for novel life TB vaccines
  - 2009: Standardization and evaluation of BCG vaccines
  - 2004: Geneva consensus: Essential steps towards clinical development
Pre-clinical development of VPM1002
Mode of action

S.H.E. Kaufmann et. al
The Recombinant BCG ΔureC::hly Vaccine Targets the AIM2 Inflammasome to Induce Autophagy and Inflammation

Hiroyuki Saiga, Natalie Nieuwenhuizen, Martin Gengenbacher, Anne-Britta Koehler, Stefanie Schuerer, Pedro Moura-Alves, Ina Wagner, Hans-Joachim Mollenkopf, Anca Dorhoi and Stefan H. E. Kaufmann

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Pre-clinical development of VPM1002
New Scientific findings

Recombinant BCG ΔureC hly+ Induces Superior Protection Over Parental BCG by Stimulating a Balanced Combination of Type 1 and Type 17 Cytokine Responses

Central Memory CD4+ T Cells Are Responsible for the Recombinant Bacillus Calmette-Guérin ΔureC::hly Vaccine’s Superior Protection Against Tuberculosis

Alexis Vogelzang,1 Carolina Perdomo,1 Ulrike Zedler,1 Stefanie Kuhlmann,1 Robert Hurwitz,2 Martin Gengenbacher,1,4 and Stefan H. E. Kaufmann1

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GMP Manufaecture

Fully scalable state of the art fermentation process.

Prospect for overcoming BCG shortage.
VPM1002-ZA-2.13TB

Phase II double-blind, randomized, controlled study to evaluate safety and immunogenicity of VPM1002 compared with BCG in HIV-exposed and HIV-unexposed, BCG-naive newborn infants.
Project Team

Sponsor: Serum Institute of India Ltd. (SIIL)

Principle Investigator: Mark Cotton, KidCRU, Stellenbosch University

Clinical Sites: 3x Cape Town
(KidCRU, DTTC, SATVI)
1x Johannesburg
(RMPRU)

Immunology lab: Prof. G. Walzl, Stellenbosch University (SUN-IRG)

CRO: Triclinium Limited

Project Management: Vakzine Projekt Management GmbH (VPM)

Manufacturer of IMP: SIIL
Study cohort (n=416)

Randomization
New born babies (0-12 days old)

Allocated to BCG (n=100)
- HIV-unexposed (n=52)
- HIV-exposed (n=52)

Allocated to VPM1002 (n=300)
- HIV-unexposed HmR (n=52)
- HIV-unexposed HmS (n=104)
- HIV-exposed HmS (n=156)

12 months follow-up

Primary objective
Safety & tolerability: VPM1002 (total) vs. BCG (total)

Secondary objective
1. Safety & tolerability: VPM1002 (HIV-exposed) vs. VPM1002 (HIV-unexposed)
2. Immunogenicity

24 months structured medical surveillance period
VPM1002-ZA-3.21TB

A Multicenter phase III study to evaluate the efficacy and safety of VPM1002 in comparison with BCG in HIV-exposed and HIV-unexposed newborn infants
Study cohort (n=7000)
3500 HIV-exposed infants,
3500 HIV-unexposed infants

Randomization

Allocated to BCG (n=3500)  
Allocated to VPM1002 (n=3500)

12 months

Primary objective: superiority in terms of a reduction in the combined incidence of efficacy-related (TB disease/disease due to infection with other virulent mycobacteria of the tuberculosis family) and safety-related events (grade 3 and/or 4 adverse reactions, vaccine related lymphadenitis of 10 mm or greater (diameter) severe BCG disease) in infants vaccinated with VPM1002 compared to those vaccinated with BCG after a follow-up period of 12 months.
A Phase I/II Open Label Clinical Trial Assessing Safety and Efficacy of Intravesical Instillation of the Recombinant BCG VPM1002BC in Patients with Recurrent Non-Muscle Invasive Bladder Cancer after Standard BCG Therapy
RESULTS

➔ No test item related mortality

➔ No test item related toxicity

➔ No systemic spread of mycobacteria with either VPM1002BC or BCG-medac after single intravesical instillation

➔ Immunohistochemistry:

➔ Focal and multifocal infiltration of CD-4 and CD-8 cells with VPM1002BC, only diffuse single cell infiltrates with BCG-medac

➔ Few neutrophils with both VPM1002BC and BCG medac
Fist patient-in

September 21st 2015
VPM1002-IN-3.01TBR

A multicenter phase III study to evaluate the efficacy and safety of VPM1002 in the prevention of Tuberculosis (TB) Recurrence after successful TB treatment in India
Pre-clinical development of VPM1002 Potential as a therapeutic vaccine

H37Rv
200 CFU

\[ \downarrow \]

Vacc.
\[ 10^6 \text{ CFU} \]
s.c.

\[ \downarrow \]

d0 d45 d90

RBT/INH treatment

\[ \downarrow \]

d250

CFU counting lung and spleen

Performed by Martin Gengenbacher / Stefan H.E. Kaufmann at Max Planck Institute for Infection Biology, Berlin (publication submitted)
VPM1002-IN-3.01TBR
Planned study design

VPM1002 / placebo vaccination

In-study phase

anti-tuberculosis treatment (ATT)

Active TB

"cured"

Screening

Sputum smear/culture negative

TB recurrence?

TB recurrence?

TB recurrence?

TB recurrence?

Bacteriologically confirmed TB and/or Clinically confirmed TB

0m

-4w to -2w

3m

6m

9m

12m
Study cohort (n=2000)

Randomization
Successfully treated TB patients

Allocated to placebo (n=1000)  Allocated to VPM1002 (n=1000)

12 months follow-up (every 3 month sputum collection)

Primary objective
Efficacy in prevention of recurrence

Secondary objective
1. Safety & tolerability: VPM1002 after successful ATT
2. Immunogenicity in 200 patients
Meetings with NIRT, National Institute of Biologicals, and RePORT consortium held in QIII 2015

Regular phone calls with RePORT Consortium and SIIL on the planning of the phase III study

Trial Synopsis finalized

- Clinical trial protocol is in preparation
- Site capacity assessment currently ongoing with RePORT sites as well as non-RePORT sites
- Invitation to join RePORT Meetings in India:
  - 9th February 2016: TB vaccine meeting organized with Soumya Swaminathan in New Delhi. (S.H.E.Kaufmann also to join, if possible)
  - 11th-13th February 2016: RePORT Meeting chaired by Dr. Christoph at CMC Vellore
Thank you very much for your attention
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