TuBerculosis Vaccine Initiative

Preclinical candidates – (revised d.d. July 2018)

rBCGΔais1/zmp1

rBCGΔzmp1 is a recombinant BCG developed by the University of Zürich. Its primary target is global boosting. On the basis of its attenuated profile, it also aims to safely replace BCG in the (HIV-exposed) new-borns. Proof of concept studies on immunogenicity, safety and protective efficacy were performed in mice, guinea pigs and cattle. Further studies are ongoing.

H64 + CAF01

H64 is a protein fusion vaccine developed by Statens Serum Institut. H64 consists of six strongly expressed proteins. The fusion protein is highly immunogenic when administered in CAF01, an adjuvant that has recently demonstrated induction of CMI responses in humans. The primary target of the H64 vaccine is to supplement the BCG vaccine. Ongoing experiments within the TBVAC2020 consortium are investigating which epitopes are immunodominant during M.tb infection and if removal of the dominant epitopes will allow for exposure of cryptic/subdominant epitopes and improved protection.

Therapeutic vaccine-MVA platform, Transgene SA

Transgene is developing therapeutic candidate vaccine against Mycobacterium tuberculosis. A range of MVA constructs expressing from 6-10 TB antigens covering all 3 phases of the infection (active, latency/dormancy, resuscitation) was generated. One lead MVA candidate expressing 10 antigens was selected in preclinical studies showing its immunogenicity in different mouse strains and its efficacy in two mouse post-exposure models. Transgene aims to bring the MVA lead candidate to the clinic to improve treatment of TB, in particular linked to DR (drug resistant) strains, and to prevent reactivation and/or re-infection in the adult DS (drug sensitive)/DR population, in particular from endemic countries.

ChAdOxPPE15, UOXF

ChAdOx1.PPE15 is a recombinant, replication deficient chimpanzee adenovirus constructed in Oxford, expressing the mycobacterial PPE15 protein. This candidate is part of the overall UOXF TB vaccine programme to work towards a BCG booster vaccination regimen in adolescents and young adults. Four candidate antigens were identified and cloned into the simian adenoviral vector, ChAdOx1. In mouse experiments, ChAdOx1.PPE15 showed the most interesting results to further evaluate. Currently ChAdOx.PPE15, is being evaluated in guinea pigs to test whether protective efficacy of BCG can be improved in this more stringent model.

CysVac2, UNISYD

CysVac2/Advax is a fusion protein vaccine developed by the The University of Sydney and Vaxine. The vaccine includes proteins designed to target both active and chronic infection with Mycobacterium tuberculosis. Preclinical experiments in mice demonstrate that the fusion protein affords strong protective efficacy against M. tuberculosis infection when combined with the novel polysaccharide adjuvant AdvaxC. AdvaxC has shown a good safety profile and induction of T and B cell responses in previous human vaccine trials. On-going preclinical experiments are examining the ability of the vaccine to protect in additional animal models (e.g guinea pigs) and define efficacy in post-exposure models, in order to strengthen the case for clinical development of the vaccine.