Pre-Clinical Proof of Concept and Characterization of AEZS-120: A Therapeutic Oral Prostate Cancer Vaccine Candidate Based on Live Recombinant Attenuated Salmonella

Introduction and Objective: AEZS-120 is a live, oral recombinant bacterial prostate cancer vaccine candidate secreting a fusion protein of prostate specific antigen (PSA) and choleratoxin subunit B. AEZS-120 is based on *S. typhi* Ty21a, an approved typhoid vaccine, which has been safely applied in more than 250 million doses. In this work, the preclinical efficacy and safety profile of AEZS-120 was evaluated.
Materials and Methods: Animal experiments were performed using *S. typhi* Ty21a (St) or *S. typhimurium* aroA (Sl) strains recombinant for the secretion plasmid pMohly PSA-CtxB-HlyA (MoPC) in immunocompetent DBA/2 or C57Bl/6 mice. Infection aliquots were produced in shaking culture, formulated in 20% sucrose and stored at -80°C. To assess efficacy after one or two immunization cycles, DBA mice were immunized orally with Sl MoPC or the carrier and challenged 14 days after the last immunization with a recombinant PSA expressing syngenic tumor cell line. Single dose, repeated dose toxicity as well as biodistribution and shedding were performed under GLP in C57BL/6 mice applying doses up to $1x10^{10}$ live bacteria.
Results: Both single and repeated oral application of the vaccine resulted in a substantial and significant protection. Protection levels were comparable for both groups and were similar to protection levels obtained with intramuscular DNA immunization using a PSA encoding plasmid. GLP safety and toxicology studies in mice revealed no relevant findings up to the maximal doses and did not exhibit differences between the recombinant strain and the carrier strain. Biodistribution studies mirror the expected infection biology of the carrier strain and did not reveal signs of prolonged infection or DNA delivery in any organ. Shedding studies did not reveal differences between the carrier strain and the recombinant strain. In animals infected with St MoPC (AEZS-120), no shedding was observed at any timepoint up to the highest dose.
Conclusions: The experiments prove the feasibility of an oral therapeutic vaccination approach against prostate cancer. The safety pharmacology and toxicology experiments suggest, that the profile of AEZS-120 is similar to the approved carrier strain and therefore paves the way for phase I clinical testing.