eP146
ePoster Viewing
Vaccine development

ADVANCING THE DEVELOPMENT OF AN EFFECTIVE STAPHYLOCOCCUS AUREUS VACCINE BY TARGETING MULTIPLE BACTERIAL VIRULENCE FACTORS.

A.S. Anderson[1], I.L. Scully[1], P.A. Liberator[1], **D. Cooper**[1], J. Baber[2], D.Q. Girgenti[1], E. Zito[3], J. Eiden[1], W. Gruber[1], E. Emini[3], K.U. Jansen[1]

[1]Vaccine Research and Development, Pfizer, Pearl river, USA ; [2]Vaccine Research and Development, Pfizer, Sydney, Australia ; [3]Vaccine Research and Development, Pfizer, Collegeville, USA

Objectives

The Gram-positive organism *Staphylococcus aureus* is responsible for a wide range of serious healthcare- and community-associated infections, including postoperative deep tissue infections and bacteremia. There is currently no licenced vaccine to prevent *S. aureus* infections despite several attempts. Investigational vaccines that have reached Phase 3 have not been efficacious, potentially due to insufficient immunologic activity and/or failure to target multiple *S. aureus* virulence factors. A key aspect of *S. aureus* pathogenesis is its ability to rapidly adapt to the host environment during the course of infection by altering expression of a number of specific virulence factors that facilitate the acquisition of essential nutrients, adhesion to host tissues, and evasion of host defenses by production of a polysaccharide capsule. We present a strategy for developing an effective vaccine against *S. aureus* disease focused on the elicitation of immune responses targeting these multiple virulence factor targets.

Methods

Each vaccine candidate component was assessed pre-clinically in various *in vivo* models designed to mimic human disease and by the development of *in vitro* immunoassays that measure relevant functional vaccine responses.

Results

To target multiple *S. aureus* virulence factors, a 4-antigen (SA4Ag) vaccine was developed, consisting of capsular polysaccharides type 5 and type 8 conjugated to CRM_{197}, and recombinant forms of two *S. aureus* surface proteins, Clumping factor A (ClfA) and Manganese transporter C (MntC). MntC and ClfA were also demonstrated to be required for virulence in preclinical animal models. In initial clinical trials, a single administration of different formulations of the investigational vaccine exhibited a satisfactory safety profile and elicited a functional bactericidal antibody response in a high proportion of study subjects, including the elderly.

Conclusions

The results support the planned testing of the vaccine in human efficacy studies, and represent an important step forward in preventing severe *S. aureus* disease.