Advancing the Development of an Effective Staphylococcus aureus Vaccine by Targeting Multiple Bacterial Virulence Factors

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INTRODUCTION

S. aureus

Capsular polysaccharide (CP) expression (two prevalent types being CP5 and CP8) enhances virulence by increasing bacterial resistance to phagocytosis.8

Clumping factor A (CIFA) is a member of the MSCRAMM family of proteins—it aids the bacterium binding to extracellular matrix (e.g. fibrinogen)10 and plays an important role in establishing wound and foreign body infections.11

Manganese Transport Protein C (MntC, P305A) is a manganese transport protein whose expression has been associated with virulence and biofilm generation.16

S. aureus Virulence Factors

S. aureus Vaccine Formulations

SA3Ag Immunization Significantly Reduces Bacteremia in S. aureus USA300 Murine Infection Models

S. aureus Vaccine Clinical Trials

SA3Ag Study B2251002: Safety and Immunogenicity

Clinical Study Design

Phase 1/2 Safety and Immunogenicity in Healthy Adults

Safety Summary

A single dose of SA3Ag was well tolerated.

Local reactions mostly mild or moderate in severity increased frequency with higher dose levels.

Frequency of systemic events was comparable between placebo and SA3Ag recipients.

Safety profile of SA3Ag was acceptable.

Frequency of AEs reported in comparable across groups after vaccination.

No related SAEs, no deaths.

Oponophagocytic Activity (OPA) Assay

Principle: Measures the ability of anti-CP5/8 serum antibodies to functionally kill S. aureus

Competitive Luminex ImmunoAssay (cLIA) Assay

Principle: Measures the ability of serum antibodies to block the binding of functional mAbs to antigen-coated (CP5, CP8, CIFA) microspheres

Exploratory Fibrinogen Binding Inhibition (FBI) Assay

Principle: Measures the ability of anti-CIFA serum antibodies to functionally inhibit the binding of S. aureus to fibrinogen (Fg)

REFERENCES


100% Background

N Engl J Med

75% Binding

Titer

SA3Ag & SA4Ag Vaccine Design and Clinical Development Plan

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S. aureus Vaccine Formulations

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CONCLUSIONS

The SA3Ag and SA4Ag vaccines are composed of antigens that target key S. aureus virulence factors (CP5, CP8, CIFA & MntC) as identified in preclinical models. Antigen-specific serological assays have been developed and qualified to detect functional antibody response in humans. In clinical study B2251002, SA3Ag was well tolerated and elicited rapid and robust functional immune responses to all three antigens. Results from SA4Ag clinical trial B3451001 will be presented at ECCMID ePoster 134 on 10 May 2014.

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