ORAL ABSTRACTS

599. Rapid rises in antibody titers observed following single dose administration of a novel 4-antigen *Staphylococcus aureus* vaccine (SA4Ag) to healthy adults

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Background. *Staphylococcus aureus* is a leading cause of serious healthcare-associated infections, resulting in substantial healthcare system burden. To date, there is no licensed vaccine to prevent invasive *S. aureus* disease. In this first-in-human study, we evaluated the safety, tolerability and immunogenicity of a single-dose of a 4-antigen *S. aureus* vaccine (SA4Ag) containing capsular polysaccharide serotypes 5 and 8 (CP5 and CP8) individually conjugated to CRM_{197}, a recombinant surface protein clumping factor A (r*m*ClfA), and a recombinant manganese transporter protein C (rP305A).

Methods. 456 healthy adults in 2 age strata (18 to 49 years; 50 to 64 years) were randomized to receive a single intramuscular injection with one of 3 SA4Ag formulations (fixed doses of 30 μg CP5-CRM_{197}, 30 μg CP8-CRM_{197}, and 60 μg r*m*ClfA and either low- [20 μg], mid- [60 μg], or high- [200 μg] dose rP305A) or placebo. Reactogenicity and adverse event data were collected. Functional opsonophagocytic activity (OPA) killing was assayed at multiple time points using CP5- and CP8-expressing clinical *S. aureus* strains. Antigen-specific immunogenicity was assessed using a fibrinogen binding inhibition (FBI) assay and a 4-plex competitive Luminex® immunoassay (cLIA). Predefined immunogenicity thresholds were applied to assess the response to each antigen.

Results. SA4Ag was well tolerated with an acceptable safety profile at all rP305A dose levels evaluated. At Day 29, all SA4Ag recipients achieved the CP5 OPA threshold and 96.2-99.0% of vaccine recipients achieved the OPA threshold for CP8. A dose-response was noted for rP305A with 46.7%, 63.2%, and 82.9% of the low-, mid-, and high-dose rP305A recipients achieving the cLIA threshold, respectively. For both age strata, substantial increases in cLIA geometric mean titers (GMTs) for all antigens were evident by Day 8 with peak responses between Day 11 and 15. Rapid rises in OPA and FBI GMTs demonstrated robust functional responses. Immune responses were maintained through Month 12.

Conclusion. SA4Ag was safe and well tolerated and induced rapid and functional antibody responses in healthy adults aged 18 to 49 years and 50 to 64 years. These results support ongoing development of SA4Ag for the prevention of invasive *S. aureus* disease.

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