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Abstract (oral session)

Efficacy and safety of V710, a Staphylococcus aureus vaccine, in preventing bacteraemia and/or deep sternal wound infections in patients undergoing cardiac surgery

V.G. Fowler*, K.B. Allen, B.W. Turnbull, E.D. Moreira, M. Moustafa, F. Isgro, H.W. Boucher, R. Corey, Y. Carmeli, J.S. Hartzel, N.A. Kartsonis, D. Guris, S.S. Smugar, M.T. Onorato, A. Sobanjo-ter Meulen (Durham, Kansas City, Ithaca, US; Bahia, BR; Orangeburg, US; Ludwigshafen, DE; Boston, Whitehouse Station, US)

Objectives: Deep sternal wound infection (DSWI) following cardiac surgery occurs in 0.5-3% of patients, is frequently attributable to Staphylococcus aureus, and is associated with increased morbidity/mortality. A novel vaccine candidate (V710) containing the highly conserved S. aureus surface protein iron surface determinant B (IsdB) was shown to be immunogenic and generally well-tolerated in both healthy and immunocompromised subjects. The purpose of this study was to evaluate the efficacy and safety of V710 in preventing S. aureus bactaeremia and/or DSWI in patients undergoing cardiac surgery. Methods: This group-sequential, randomised, multicentre, double-blind, placebo-controlled study evaluated the immunogenicity, safety and efficacy of a single intramuscular 60 µ g dose of V710 in patients >=18 years old scheduled to undergo full median sternotomy within 14 to 60 days of vaccination. The primary efficacy endpoint was prevention of S. aureus bactaeremia and/or DSWI, including mediastinitis, through postoperative Day 90. Secondary endpoints were all invasive infections and surgical-site infections caused by S. aureus through postoperative Day 90. This was an event-driven study, with the estimated total enrolment (N ~15,000) based on the number of subjects required to accrue 107 primary efficacy endpoints. Three interim analyses, including futility assessments, and one final analysis of vaccine efficacy were planned. Results: At the recommendation of the independent Data Monitoring Committee the Sponsor terminated the study after the 2nd interim analysis (N=7983 subjects randomised and vaccinated) based on efficacy and safety results. V710 was not significantly more efficacious than placebo for preventing either the primary or secondary endpoints. V710 was associated with a significantly higher incidence of vaccine-related injection-site adverse events (AEs) (19% vs. 9%) and systemic AEs (17% vs. 15%), but with no significant difference in systemic vaccine-related AEs or serious AEs. There was a marginally significant increase in multi-organ failure in the vaccine recipients compared with the placebo group (rate per 100-person-years: 0.9 vs. 0.5; p=0.042), but there was no significant difference in all-cause mortality (Table). Conclusions: The efficacy and safety data from this trial do not support the use of V710 in preventing S. aureus bactaeremia and/or DSWI in patients undergoing cardiac surgery utilising a median sternotomy.

Table. Efficacy and Safety Summary

EFFICACY[a]			
	V710 60 µg n	**Placebo n**	**Observed Efficacy % (95% CI)**
Efficacy analysis population	**3528**	**3517**	
Primary endpoints *S. aureus* bacteremia/DSWI	22	27	18.5 (-48.6, 55.8)
Secondary endpoints			
Invasive *S. aureus* infections	27	31	12.9 (-50.8, 50.0)
S. aureus surgical- site infections	53	75	29.3 (-1.8, 51.2)
SAFETY (Day 1-14 postvaccination [pre-surgery]), n (%)			
	V710 60 µg n (%)	**Placebo n (%)**	**V710 - Placebo % (95% CI)**
Patients included in AE summary	**3958**	**3967**	
			Risk Difference
Any AE	1219 (30.8)	866 (21.8)	9.0 (7.0, 10.9)
Systemic AE	673 (17.0)	602 (15.2)	1.8 (0.2, 3.4)
Vaccine-related systemic AE	122 (3.1)	11 (2.8)	0.3 (-0.5, 1.0)
Vaccine-related injection-site AE	760 (19.2)	360 (9.1)	10.1 (8.6, 11.7)
Serious AE	66 (1.7)	51 (1.3)	0.4 (-0.2, 0.9)
Discontinued due to AE	0 (0.0)	0 (0.0)	0.0 (-0.1, 0.1)
All-cause deaths (pre-surgery)	11 (0.3)	6 (0.2)	0.1 (-0.1, 0.4)
SAFETY (Duration of the Study), n (rate per 100-person-years)			
	n (rate)	**n (rate)**	**Rate Difference**
Multi-organ failure	31 (0.9)	17 (0.5)	0.4 (0.0, 0.8)
All-cause deaths	201 (5.7)	177 (5.0)	0.7 (-0.4, 1.8)

[a]Adjudicated cases

AE: adverse experience; DSWI: deep sternal wound infection