00393 *In vitro* activity of dalbavancin against glycopeptide-resistant *Enterococcus faecium* and coagulase-negative staphylococci recovered from patients in Germany

03. Bacterial susceptibility & resistance

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Background

Dalbavancin (DAL) is a lipoglycopeptide antibiotic which is more potent than vancomycin or teicoplanin against Gram-positive pathogens. Plasmid-encoded resistance to DAL in *Staphylococcus aureus* and *Enterococcus* spp. is mediated by the VanA genotype but not the VanB genotype. Isolates harbouring *vanA* are resistant to vancomycin, teicoplanin and dalbavancin, while resistance is limited to vancomycin in isolates harbouring *vanB*. About 80% of the vancomycin-resistant *Enterococcus faecium* (VR*Efm*) in Germany harbour *vanB*. Teicoplanin-resistant coagulase-negative staphylococci (TRCoNS) have been isolated from patients subjected to prolonged glycopeptide treatment. The purpose of this study was to evaluate the *in vitro* activity of DAL against VR*Ef*m and TRCoNS.

Methods

76 VR*Efm* and 76 TRCoNS collected at 25 laboratories in Germany (22), Switzerland (2) and Austria (1) during a resistance surveillance study conducted by the Paul Ehrlich Society from January 2016 to April 2017 were tested. Susceptibility testing was performed with the microdilution method according to ISO 20776-1. EUCAST breakpoints (v.11.0) were applied to interpret DAL MICs of TRCoNS (≤0.125 mg/L [S] and >0.125 mg/L [R]), and CLSI breakpoints (M100-S30) were applied to interpret DAL MICs of both VR*Efm* and TRCoNS (≤0.25 mg/L [S]; see footnote of **Table**). EUCAST breakpoints of DAL for *Enterococcus* spp. have not been defined. Genetic testing of VR*Efm* was performed at the Robert Koch-Institute.

Results

VR*Efm* isolates harboured *vanA* (n=20), *vanB* (n=55) or both (n=1). The collection of TRCoNS comprised *Staphylococcus epidermidis* (n=54), *Staphylococcus haemolyticus* (n=15), and *Staphylococcus hominis* (n=7). 29/76 (38.2%) VR*Efm* and 26/76 (34.2%) TRCoNS were obtained from intensive care patients. $MIC_{50/90}$s of DAL were 8/≥16 mg/L for VanA type isolates and 0.06/0.125 mg/L for VanB type isolates. DAL inhibited all VanB type isolates at 0.25 mg/L, whereas DAL MICs of VanA type isolates were 4-≥16 mg/L (**Table**). MICs of DAL for TRCoNS ranged from 0.03 mg/L to 4 mg/L. Susceptibility and resistance rates are presented in the **Table**.

Conclusions

DAL showed excellent activity against VanB type VR*Efm*, all of which were DAL-susceptible. Further, DAL inhibited about 70% of the TRCoNS (even 87% of *S. epidermidis*) at the EUCAST breakpoint of 0.125 mg/L, and >96% at the CLSI breakpoint of 0.25 mg/L.

Table: Distribution of dalbavancin MICs and percent susceptible (S) and resistant (R) isolates

Species / group	n	MIC (mg/l)										EUCAST		CLSI	
		≤0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	≥16	S	R	S	R[$]
VR*E. faecium*	76		12	32	9	2				7	10	4			72.4	-
vanA	20									7	10	3	No breakpoint defined		0	-
vanB	55		12	32	9	2									100	-
vanA+vanB	1											1			0	-
TRCoNS	76		1	29	24	19	2			1			71.1	28.9	96.1	-
S. epidermidis	54		1	28	18	6	1						87.0	13.0	98.1	-
S. haemolyticus	15				4	10				1			26.7	73.3	93.3	-
S. hominis	7			1	2	3	1						42.9	57.1	85.7	-

The underlined numbers indicate the median MIC. The solid vertical line indicates the EUCAST breakpoint for *Staphylococcus* spp. and the dashed vertical lines indicate the CLSI breakpoints, that were actually defined for *S. aureus* and *Enterococcus* spp.

[$] No resistance breakpoint defined