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P2061 In vitro antibacterial and bactericidal activity of dalbavancin against different multidrug resistant (MDR) Staphylococcus aureus strains

Floriana Campanile*[1], Dafne Bongiorno[1], Martina Rizzo[1], Stefania Stefani[1]

[1]*University of Catania, Department of Biomedical and Biotecnological Sciences, Catania, Italy*

Background: Dalbavancin, a novel second-generation semi-synthetic lipoglycopeptide, has recently been approved for the treatment of severe skin infections sustained by Gram-positive multi-drug resistant (MDR) pathogens. Emerging vancomycin-intermediate resistance among methicillin-resistant *Staphylococcus aureus* (MRSA) posed a great threat to antimicrobial chemotherapy worldwide. In this context, significant controversy exists regarding the current and future role of glycopeptides in the treatment of serious MRSA infections.

We evaluated the *in vitro* antibacterial and bactericidal activity of dalbavancin against clinically relevant *S. aureus* isolates, including heterogeneous vancomycin-intermediate (hVISA), daptomycin non-susceptible (DNS) and rifampicin resistant (RIF-R), as part of a multicenter Italian study.

Materials/methods: A total of 124 *S. aureus* strains isolated from patients with severe infections (BSIs, LRTIs and SSTI/ABSSSIs) were tested for dalbavancin susceptibility, by broth microdilution method (EUCAST). 2 VISA strains (Mu50; NRS402), two hVISA (Mu3; NRS22), a vancomycin-resistant (VRS1) and an MSSA (ATCC 29213) were included as control strains. Time-kill curves were performed against three isolates belonging to the most resistant and virulent epidemic clones showing different dalbavancin *in vitro* activity.

Results: Except for the RIF-R isolates, dalbavancin showed a potent *in vitro* activity against all *S. aureus* (MIC range ≤0.007-0.125 mg/L), with $MIC_{50/90}$ values within the susceptibility breakpoint. We found non-susceptible values in a HA-MRSA/VSSA strain belonging to the USA500 clone (MIC 0.25mg/L) and in a DNS/VISA strain (MIC 2mg/L). The RIF-R strains showed the highest percentage of isolates with reduced susceptibility (no. 11, 22%). The same increase in MICs was also observed in the VISA (Mu50 and NRS402) control strains.

Dalbavancin exerted potent and rapid bactericidal activity against all MRSA including the dalbavancin non-susceptible RIF-R (3 log10 reduction, at 8 and 24h) and DNS (5 log10 reduction, at 24h) isolates.

Conclusions: Dalbavancin has excellent *in vitro* antibacterial and bactericidal activity against *S. aureus*, including hVISA and DNS isolates. The interpretation of the higher rate of dalbavancin non-susceptibility among RIF-R isolates need further investigations, taking into account that some *rpo*B mutations have been already associated with the emergence of vancomycin intermediate-resistance. Our observations suggest that dalbavancin will be considered an effective therapeutic alternative for the management of severe MRSA infections.