



This study improves our understanding of teicoplanin PD against MRSA and defines an in vivo AUC/MIC target for efficacy and suppression of resistance” Ramos-Martín et al (2017).

Abstract:

Objectives: The overall study aim was to identify the relevant preclinical teicoplanin pharmacokinetic (PK)/pharmacodynamic (PD) indices to predict efficacy and suppression of resistance in MRSA infection.

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Methods: A hollow-fibre infection model and a neutropenic murine thigh infection model were developed. The PK/PD data generated were modelled using a non-parametric population modelling approach with Pmetrics. The posterior Bayesian estimates derived were used to study the exposure–effect relationships. Monte Carlo simulations from previously developed population PK models in adults and children were conducted to explore the probability of target attainment (PTA) for teicoplanin dosage regimens against the current EUCAST WT susceptibility range.

Results: There was a concentration-dependent activity of teicoplanin in both the in vitro and in

vivo models. A total in vivo AUC/MIC of 610.4 (total AUC of 305.2 mg·h/L) for an MRSA strain with an MIC of 0.5 mg/L was needed for efficacy (2 log₁₀ cell kill) against a total bacterial population. A total AUC/MIC ratio of ~1500 (total AUC of ~750 mg·h/L) was needed to suppress the emergence of resistance. The PTA analyses showed that adult and paediatric patients receiving a standard regimen were only successfully treated for the in vivo bactericidal target if the MIC was ≤0.125 mg/L in adults and ≤0.064 mg/L in children.

Conclusions: This study improves our understanding of teicoplanin PD against MRSA and defines an in vivo AUC/MIC target for efficacy and suppression of resistance. Additional studies are needed to further corroborate the PK/PD index in a variety of infection models and in patients.

Full Text

Reference:

Ramos-Martín, V., Johnson, A., McEntee, L., Farrington, N., Padmore, K., Cojutti, P., Pea, F., Neely, M.N. and Hope, W.W. (2017) Pharmacodynamics of teicoplanin against MRSA. *Journal of Antimicrobial Chemotherapy*. 72(12), p.3382–3389.

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