Pharmacokinetics-Pharmacodynamics of CEM-102 Against Methicillin-Resistant Staphylococcus aureus

Using an in vitro Pharmacodynamic Model and Mechanism-Based Modeling


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Abstract

Background: The pharmacodynamics-pharmacokinetics (PK-PD) profile of CEM-102, an oral antibiotic in development for the treatment of complicated skin and skin-structure infections, has been well characterized. However, the mechanism of action (PK-PD) targets have not been elucidated and the bacterial killing profile of CEM-102 has not been fully characterized.

Objectives:

- To characterize the bacterial reduction profiles of CEM-102 in an in vitro PK-PD model.
- To identify optimal PK-PD targets of CEM-102 against S. aureus.
- To develop a MB PK-PD model that can describe and predict the killing of CEM-102 and aid in development of optimal dosage regimens.

Results

- Reduction of S. aureus colonies in the presence of CEM-102 was evaluated using microdilution and plaquing assays. CEM-102 was highly active against MRSA and MSSA strains, with MICs ranging from 0.25 to 1 mg/L.
- The PK-PD model was developed using NONMEM VI, fitting all regimens simultaneously.
- The model was used to predict the effect of different dosing regimens on MRSA and MSSA populations.

Conclusions

- The PK-PD model developed for CEM-102 was able to accurately predict the killing of MRSA and MSSA populations.
- The model provided insights into the optimal dosing regimens for maximal killing of MRSA and MSSA.

References


Figure 1. PK-PD of CEM-102 against MRSA USA300 at Varying Dosage Regimens

Figure 2. MB PK-PD Model (A) and Model Fitted Parameter Estimates (B)

Figure 3. Predicted vs. Observed Plot

Figure 4. Model Fits for MB PK-PD Model

Figure 5. Sensitivity Analysis

Tables

- Table 1: MIC and AUC values for CEM-102 against MRSA and MSSA strains.
- Table 2: Summary of fitted parameters for the PK-PD model.

Graphs

- Figure 1: PK-PD of CEM-102 against MRSA USA300 at Varying Dosage Regimens
- Figure 2: MB PK-PD Model (A) and Model Fitted Parameter Estimates (B)
- Figure 3: Predicted vs. Observed Plot
- Figure 4: Model Fits for MB PK-PD Model
- Figure 5: Sensitivity Analysis