primary studies - published RCT

Pharmacokinetics of intravenous and oral linezolid in adults with cystic fibrosis.

Code: PM21518837 **Year:** 2011 **Date:** 2011 **Author:** Keel RA

Study design (if review, criteria of inclusion for studies)

RCT, crossover design with a 9-day washout.

Participants

8 adults with CF

Interventions

patients were randomized to receive intravenous (i.v.) and oral linezolid at 600 mg twice daily for 9 doses in a crossover design with a 9-day washout.

Outcome measures

Plasma samples were collected after the first and ninth doses of each phase. Population pharmacokinetic analyses were performed by nonlinear mixed-effects modeling using a previously described 2-compartment model with time-dependent clearance inhibition. Monte Carlo simulation was performed to assess the activities of the linezolid dosing regimens against 42 contemporary MRSA isolates recovered from CF patients.

Main results

d nonlinear clearance after 9 doses, which was reduced by a mean of 38.9% (range, 28.8 to 59.9%). Mean bioavailability was 85% (range, 47 to 131%). At steady state, 600 mg given twice daily produced 93.0% and 87.2% probabilities of obtaining the target pharmacodynamic exposure against the MRSA isolates for the i.v. and oral formulations, respectively. Thrice-daily dosing increased the probabilities to 97.0% and 95.6%, respectively. Linezolid pharmacokinetics in these adults with CF were well described by a 2-compartment model with time-dependent clearance inhibition. Standard i.v. and oral dosing regimens should be sufficient to reliably attain pharmacodynamic targets against most MRSA isolates; however, more frequent dosing may be required for isolates with MICs of â‰¥ 2 Î¼g/ml.

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See also

Antimicrobial agents and chemotherapy

Keywords

Bacterial Infections; Infection; pharmacological_intervention; Respiratory Tract Diseases; Respiratory Tract Infections; Anti-Bacterial Agents; Adult; Linezolid; Staphylococcus aureus; Intravenous; Oral; other anti-bacterial agents;