Doripenem (S-4661), A Novel Carbapenem: Comparative Activity Against Contemporary Pathogens Including Anaerobes, Bactericidal Activity and Method Evaluations

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ABSTRACT

Doripenem (S-4661) is a novel carbapenem with activity extending beyond the spectrum of other marketed carbapenem antibiotics. This new agent was evaluated against contemporary clinical isolates of Enterobacteriaceae, Pseudomonas aeruginosa and non-fermentative Gram-negative bacillus isolates and some Gram-positive cocci. The agents included: imipenem (IMP), meropenem (MER), ertapenem (ERT), and doripenem (DOR). The organisms included: Enterobacteriaceae (22 strains), non-fermentative Gram-negative bacilli (22 strains), and Gram-positive cocci (4 strains).

RESULTS

- Doripenem was very active against strains of Enterobacteriaceae with MIC₉₀ ≤ 0.06 g/ml. doripenem was more active than imipenem (IMP) against Enterobacteriaceae and P. aeruginosa. doripenem was ≥2-fold more active against multi-drug resistant Enterobacteriaceae strains.
- doripenem showed excellent activity against non-fermentative Gram-negative bacilli strains (MIC ≤ 0.12 g/ml). doripenem was ≥2-fold more active than imipenem against multi-drug resistant non-fermentative Gram-negative bacilli strains.
- doripenem was in the range of 0.06-0.25 g/ml against anaerobic isolates (Clostridium, Peptostreptococcus spp. and Bacteroides thetaiotaomicron).
- doripenem was bacteraemic versus Gram-negative and positive cocci (S. pneumoniae and S. aureus) with MIC values near the MBC results (data not shown).
- doripenem was ≥4-fold more active than meropenem against Enterobacteriaceae, P. aeruginosa and non-fermentative Gram-negative bacilli strains.
- doripenem was acceptable for use as a diagnostic agent, a concentration also used for susceptibility testing of other carbapenems.

MATERIALS & METHODS

The broth microdilution method was performed using both aerobic and anaerobic broth and Anaplastometric broth method using anaerobic and anaerobic broth methods. doripenem was evaluated against Enterobacteriaceae, P. aeruginosa and non-fermentative Gram-negative bacilli isolates and some Gram-positive cocci. MIC₉₀ and MBC results were compared to those of imipenem (IMP), meropenem (MER), ertapenem (ERT), and doripenem (DOR). The organisms included: Enterobacteriaceae (22 strains), non-fermentative Gram-negative bacilli (22 strains), and Gram-positive cocci (4 strains).

CONCLUSIONS

- Doripenem was identified as a potent carbapenem with a spectrum of activity extending beyond currently marketed carbapenem antibiotics to some Gram-negative bacilli and anaerobic pathogens.
- doripenem’s potency was superior overall to other carbapenems primarily against multi-drug resistant Gram-negative bacilli isolates and some Gram-positive cocci (e.g. Methicillin-resistant Staphylococcus aureus).
- doripenem, with anti-anaerobic activity and the above noted features with cidal action, can be considered a potent agent to treat infections caused by resistant organisms. Further development in human clinical trials appears warranted.

SELECTED REFERENCES

- The JONES Group/JMI Laboratories North Liberty, IA, USA.
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