Overcoming Cefiderocol AST Challenges in MDR-GN Infections: A Stepwise Approach

Infographic 1 of 2 in the 'Accelerating time to effective therapy' series

The publication of this infographic was supported by **Shionogi**. This educational infographic is intended for healthcare professionals only.

In the UK, Fetcroja® (Cefiderocol) is indicated for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options. Consideration should be given to official guidance on the appropriate use of antibacterial agents. The label may differ in other countries; please check local prescribing information. Please access the full Fetcroja® Summary of Product Characteristics here. Adverse Events Reporting information can be found at the bottom of this infographic.

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Inappropriate and delayed appropriate antibiotic therapy has a major impact on survival.[1,2]

Antimicrobial susceptibility results obtained as early as possible may reduce time to effective therapy.[3-6]

To reduce delays, susceptibility to cefiderocol should be determined alongside that of other therapies for CR pathogens wherever possible.[1,7]

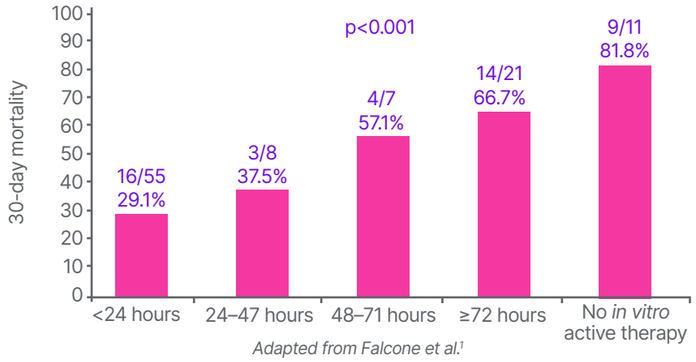
Overcoming the challenges of cefiderocol AST is crucial for its clinical application and patient safety.[7]

A new comprehensive review and expert opinion paper offers a standardised, reproducible way forward.[7]

Stefani et al. designed two practical decision trees, based on:[7]

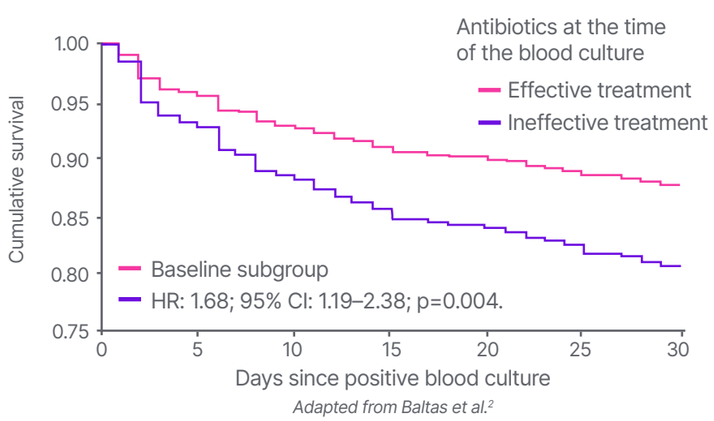
- Thirteen published papers on AST methods.
- The expert opinion of six microbiology experts.

Time from blood culture to appropriate therapy in KPC *K. pneumoniae* infection[1]



Adapted from Falcone et al.[1]

Time to appropriate antibiotic therapy is a predictor of outcome.[1]

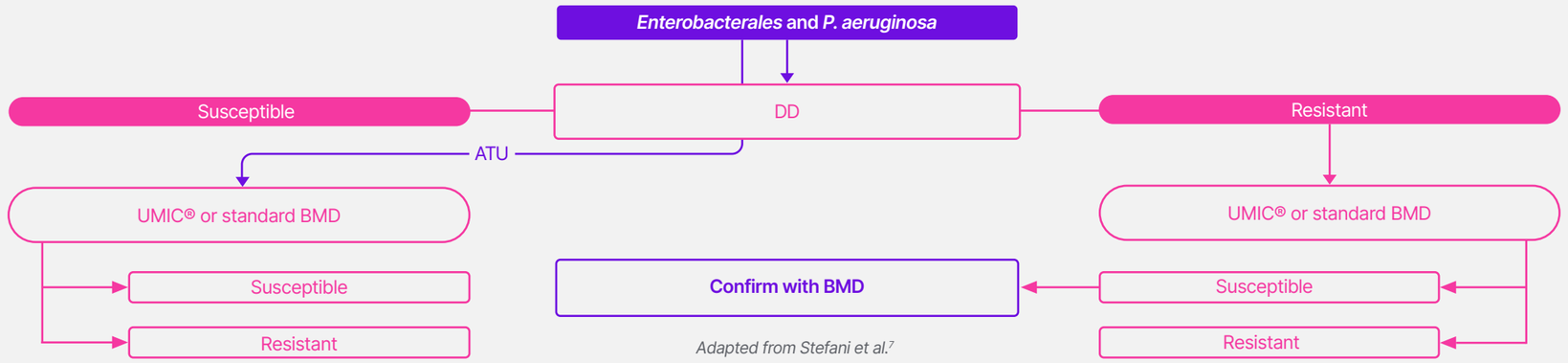


Adapted from Baltas et al.[2]

In patients with bacteremia due to *P. aeruginosa*, *Klebsiella spp.*, and *E. coli* (n=789), ineffective empirical antibiotics at time of blood culture was associated with **increased risk of mortality within 30 days**.[2]

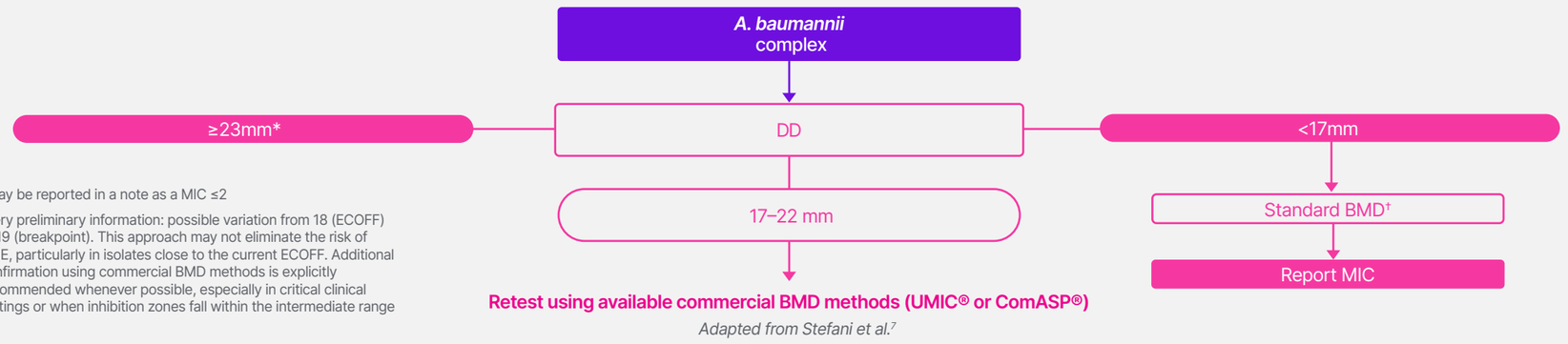
Stefani et al. outlines a stepwise approach to cefiderocol AST in which DD is used for initial screening.[7]

Cefiderocol susceptibility testing for *Enterobacterales* and *P. aeruginosa*[7]



Adapted from Stefani et al.[7]

Cefiderocol susceptibility testing for *A. baumannii*.[7]



*May be reported in a note as a MIC ≤2

†Very preliminary information: possible variation from 18 (ECOFF) to 19 (breakpoint). This approach may not eliminate the risk of VME, particularly in isolates close to the current ECOFF. Additional confirmation using commercial BMD methods is explicitly recommended whenever possible, especially in critical clinical settings or when inhibition zones fall within the intermediate range

Adapted from Stefani et al.[7]

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme, website: https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Shionogi on +44 (0) 203 053 4190 or email contact@shionogi.eu.

References

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4. Bonine NG et al. Am J Med Sci. 2019;357:103-10.
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Abbreviations:

AST: antibiotic susceptibility testing; ATU: areas of technical uncertainty; BMD: broth microdilution; CLSI: Clinical and Laboratory Standards Institute; CR: Carbapenem-resistant; DD: disk diffusion; ECOFF: Epidemiological Cut-off Values; EUCAST: European Committee on Antimicrobial Susceptibility Testing; FDC: fixed-dose combination; HR: hazard ratio; ID-CAMHB: iron-depleted cation-adjusted Mueller-Hinton broth; KPC: klebsiella pneumoniae carbapenemase; MIC: minimum inhibitory concentration; VME: very major error.

Key Learnings

Reliance on DD results alone may overcall cefiderocol resistance when compared with BMD and may lead to patients receiving suboptimal treatment.[8]

Stefani et al. recommend a stepwise approach of screening with DD, and isolates in the ATU range or showing reduced susceptibility being confirmed using commercial BMD methods, preferably UMIC® or ComASP®.[7]