Comment on: Best in class: a good principle for antibiotic usage to limit resistance development?

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Sir,

We wish to comment on the article by Ames et al.,1 in which we are referenced2 as stating that ‘the concept that ertapenem is unlikely to increase resistance in non-fermenters is flawed’. We in fact did not state this and, on the contrary, we agree with the conclusions of Livermore et al.,3 that selection (of carbapenem-resistant Pseudomonas aeruginosa in particular) is unlikely under physiologically relevant ertapenem concentrations.

In this regard, the following points are critical. First, the BSAC/EUCAST ertapenem breakpoint for susceptibility is ≤0.5 mg/L and for resistance is >2 mg/L. The former value is far below the MICs for most P. aeruginosa strains, which range between 2 and 32 mg/L with MIC50 and MIC90 values of 4–8 and ≥16 mg/L, respectively.4 Secondly, the free ertapenem plasma concentration is less than the MIC50 by 4 h post-dose.5 In critically ill patients, the protein-unbound plasma concentration after a single intravenous administration of 1 g has been documented to be 0.87 ± 0.76 mg/L 12 h after infusion and 0.24 ± 0.43 mg/L 24 h after infusion.5 In other words, relevant ertapenem concentrations are below those likely to be active against P. aeruginosa.6 Thirdly, the OASIS (Optimizing Abdominal Surgery with Invanz Study) studies indicated no significant colonization by P. aeruginosa, either with imipenem-resistant or imipenem-susceptible strains, during ertapenem therapy.6

We acknowledge that under laboratory conditions with high drug concentrations, it is possible to select for imipenem-resistant P. aeruginosa with ertapenem, but the clinical relevance seems doubtful, because in the clinical scenario adequate concentrations are not maintained for a sufficiently long duration.

It seems relevant to ask whether, using similar logic, the authors of this article would restrict the use of cefotaxime and ceftriaxone in that they might undermine ceftazidime against P. aeruginosa, or similarly levofloxacin with regard to ciprofloxacin?

We would still recommend that ertapenem be used as the preferred therapy for infections due to extended-spectrum β-lactamase producers and, in certain specific settings as outlined in our article, for intra-abdominal sepsis, pneumonia and skin and soft tissue (including diabetic foot) infections.

Transparency declarations

A. J. B. is on the advisory board for Merck. C. F. and G. A. R. are on the advisory board for Merck and speakers bureau for Astra Zeneca.

References