Reply to Woerther et al

Jesús Rodríguez-Baño, Zaira R Palacios-Baena, Alvaro Pascual

To the Editor:

We thank Woerther et al for their interest in our article. Their comments are mostly related to the lack of evidence that carbapenems are associated with a stronger impact on intestinal microbiota and risk of intestinal colonization by resistant bacteria than other alternatives. The objective of our study was not to investigate the impact of the different antibiotic regimens on the intestinal microbiota but to analyze the clinical impact of de-escalation in a well-defined setting (bloodstream infection due to Enterbacterales). We must point out that our study did not evaluate de-escalation from carbapenems but from all antipseudomonal β -lactam drugs or ertapenem; in fact, more than 55% of the patients were de-escalated from drugs other than carbapenems, with piperacillin-tazobactam being the most frequent.

We agree that more information is needed about the ecologic impact of the different antimicrobials and that their spectrum of activity is not the only aspect to consider. However, comparing the impact of antibiotics on the colonization risk by resistant bacteria in individual patients is complex, as it may depend on the epidemiological context (which is continuously evolving and different among wards and hospitals), the base composition of the microbiota of the patients, and other reservoirs of the microorganisms considered.

In terms of antimicrobial stewardship, recommendations must be based on the available evidence. So far, multiple studies have shown that individual exposure to several broad-spectrum drugs (mostly fluoroquinolones, extended-spectrum cephalosporins, and carbapenems) is associated with increased risk of acquisition and infection by multidrug-resistant gram-negative bacteria. In fact, exposure to carbapenems showed a strong association with infection due to carbapenem-resistant Enterobacteriaceae, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* in recent meta-analyses and a multicenter study; in addition, reducing the consumption of carbapenems may contribute to reduce carbapenem resistance in *P. aeruginosa* [6], which makes sense because unless it is due to the production of carbapenemases, carbapenem resistance in this organism may be induced by exposure to these drugs. Therefore, until more information is available, we think that we should continue recommending the use of narrower-spectrum drugs whenever possible, and specifically avoiding the use of carbapenems whenever other options with similar efficacy are available.