Sir, Tumbarello et al. have described the largest retrospective study about invasive infections caused by KPC-producing Klebsiella pneumoniae (KPC-Kp).

The study outlined the importance of combination therapy using two or more drugs in reducing 14 day mortality, in particular in patients with bloodstream infection, lung infection, higher APACHE III score and/or septic shock at infection onset. Furthermore, combinations containing meropenem were significantly associated with reduced mortality, especially when the meropenem MIC was \( \leq 8 \text{ mg/L} \).

This study, although impressive for the amount of data analysed, is based upon Vitek 2 system susceptibility (bioMérieux, Marcy-l’Etoile, France) and therefore classification of patients might not be correct.

In fact, monotherapy patients were classified depending on the number of active drugs that were included in the post-antibiogram regimen used.2

Arena et al.2 have recently demonstrated how Vitek 2 overestimates resistance to gentamicin. The authors tested 57 KPC-Kp bloodstream isolates and demonstrated that, compared with the reference method, broth microdilution, Vitek 2 had an essential agreement of only 31.6%.2 Furthermore, Sbrana et al.3 have demonstrated higher MIC distributions for tigecycline and colistin when KPC-Kp strains were measured with Vitek 2 compared with Etest.

Daikos et al.4 first selected KPC-Kp strains with Vitek 2, but then re-evaluated the susceptibility to imipenem, meropenem, doripenem, colistin and tigecycline using Etest.

The second point is the use of a carbapenem in combination therapy. In many Italian hospitals, a meropenem MIC \( \leq 8 \text{ mg/L} \) for KPC-Kp is extremely rare. Nevertheless, clinicians in Italy start empirical antibiotic therapy, when severe infections due to KPC-Kp are suspected, with a three-drug regimen containing meropenem. Therefore in Pisa Hospital, a 1000 bed teaching hospital, where an outbreak of KPC-Kp has been ongoing since 2010, the amount of meropenem used in 2014 was around 30 kg, an increase of 5 kg compared with 2013 (25 kg). In our opinion, the use of this large amount of meropenem may be one of the leading factors in the persistence of the KPC-Kp outbreak. On the other hand, the use of a carbapenem-sparing regimen might be effective in reducing the selective pressure of meropenem. Furthermore, Tumbarello et al. did not report whether the infections, caused by KPC-Kp, were monomicrobial or polymicrobial. This would be very relevant, since for the patients included in the study, who were at high risk for severe infections, to have only one pathogen would have been very rare. In addition, the length of treatment was not reported and a longer carbapenem treatment may have reduced mortality because of the action against other susceptible Gram-negative pathogens.

In conclusion, we need studies, using reliable microbiological methods, that target the superiority of combination therapy with and without carbapenems, which are obviously difficult to perform and therefore a national effort in Italy is necessary to solve this urgent problem.

Transparency declarations
In the past 2 years, C. T. has been paid for lectures on behalf of Pfizer, Novartis, Merck, AstraZeneca, Gilead, Angelini and Astellas. B. V. and F. M.: none to declare.

References