EV0398
ePoster Viewing
Susceptibility testing methods

Clinical effectiveness and in-vitro activity of meropenem+ertapenem and colistin+meropenem+ertapenem combinations against carbapenemase-producing Klebsiella pneumoniae infections

Alessandra Oliva*[1], Domenico Castaldi[2], Laura Scorzolini[3], Alessia Cipolla[2], Francesca Gizzi[4], Massimiliano De Angelis[1], Francesca Cancelli[2], Alessandra D'abramo[2], Marco Iannetta[4], Maria Teresa Mascellino[2], Claudio M. Mastroianni[2], Vincenzo Vullo[2]

[1]*Sapienza University of Rome, Public Health and Infectious Diseases, Roma, Italy*

[2]*Sapienza University of Rome, Public Health and Infectious Diseases, Rome, Italy*

[3]*Sapienza University of Roma, Pubblic Health and Infectious Disease, Infectious Disease, Rome, Italy*

[4]*Sapienza University of Rome, Rome, Italy*

Background: Therapeutic options against carbapenem-resistant *K. pneumoniae* (CR-Kp) are worringly limited and innovative approaches have been recently investigated. The aim of the study was to evaluate the clinical effectiveness of the double carbapenem regimen [meropenem (MEM) + ertapenem (ERT)] with or without colistin (COL) against CR-Kp infections. Furthermore, synergistic and bactericidal activity of the combinations MEM+ERT and COL+MEM+ERT were investigated.

Material/methods: Over a 3-years period (2012-2015), 32 subjects with CR-Kp infections were included in the study: 18 were treated with MEM+ERT (Group A), 14 with COL+MEM+ERT (Group B). The double carbapenem regimen consisted of ERT 1g (1-h infusion) followed by high-doses of MEM (2g every 8h, 3-h infusion) whereas COL was administered as 9.000.000 IU (loading dose) followed by 4.500.000 IU every 12h. Synergistic and bactericidal analyses were performed on 22 strains throughout checkerboard method and killing curves.

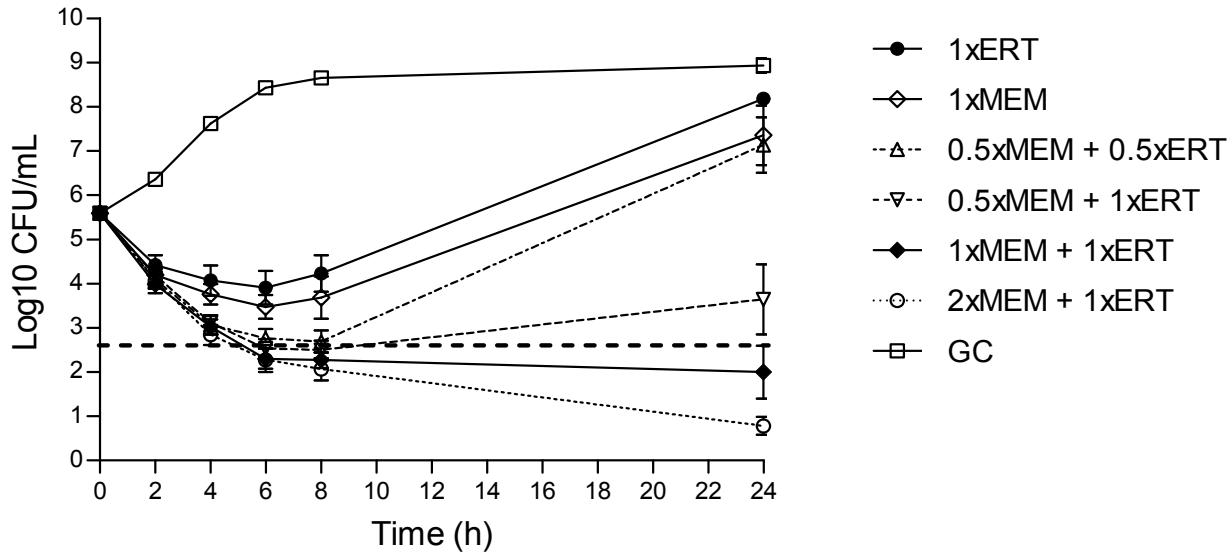
Results: Mean age was 55.1±15.2 years (23 M, 9 F) with a mean APACHE III score of 64.9±29.6 [50.7 ± 28.1 Group A *versus* 83.2 ± 20.3 Group B, p=0.001]. Clinical presentation was sepsis, severe sepsis and septic schock in 5/32 (15.6%), 13/32 (40.6%) and 8/32 (25%), respectively [3/18 (16.6%), 7/18 (38.8%), 2/18 (11.1%) in Group A *versus* 2/14 (14.2%), 6/14 (42.9%), 6/14 (42.9%) in Group B, p=0.99, 0.99, 0.09 respectively]. Six subjects (Group A) did not have sepsis. Bacteremia was observed in 8/18 (44.4%) and 10/14 (71.4%) of Group A and B, respectively (p=0.16). Colistin resistance was 44.4% (8/18) and 21.4% (3/14) in Group A and B, respectively (p=0.26). Early (5th day) clinical response to therapy and mortality at 60-days were similar in Group A and B [11/18 (61.1%) *versus* 12/14 (85.7%) and 3/18 (16.6%) *versus* 3/13 (21.4%), p=0.23 and 0.99 respectively]. Twenty-one out of 22 strains were KPC producers whereas 1 strains was OXA producer. Overall, MEM+ERT was synergic (complete *plus* partial) in 18/22 (81.8%) whereas COL+MEM+ERT showed an absence of growth at COL 0.125xMIC + ERT 0.5xMIC + MEM 0.5xMIC concentration, including COL-resistant strains. Killing results are summarized in Figure 1.

Conclusions: MEM+ERT and COL+MEM+ERT combinations showed clinical efficacy and high bactericidal activity. MEM+ERT might be a valid therapeutic option when COL use is discouraged

whereas COL+MEM+ERT might be considered in subjects presenting with more severe conditions (i.e. septic shock).

Figure 1. Killing curves of MEM+ERT and COL+MEM+ERT in Group A (1A) and Group B (1B). Dashed line represents bactericidal activity.

A)



B)