Continuous infusion versus intermittent administration of meropenem in critically ill patients. A multicenter randomized double blind trial.

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Background Hospital-acquired infections are a major challenge: in intensive care units, gram-negative (GN) bacteria account for about 70% of these infections. The emergence of multi- drug resistant GN organisms coupled with an alarming scarcity of new antibiotic classes has forced the healthcare community to optimize the therapeutic potential of available antibiotics. Meropenem is a β-lactam agent with antimicrobial activity against GN whose patent has recently expired. Meta-analytic data show that prolonged infusion β-lactam antibiotics may have value in patients with highly-resistant GN infections and in patients with a higher degree of severity of illness.

Objectives We have designed a large, multicenter, RCT to confirm the beneficial effect of continuous infusion of meropenem against bolus administration as indicated by a composite outcome of reducing death, and emergence of extensive or pan drug resistant pathogens in a population of severely ill patients. Secondary endpoints will be reducing long-term mortality, days under mechanical ventilation, ICU length of stay, fastening reduction of severity of disease.

Methods We've enrolled the first 15 patients, 29 hospitals are willing to participate and we'll still looking for new centers. Enrolled patients receive 1 g of meropenem bolus. After that, subjects are randomized to receive study drug 3 g/day by continuous infusion or bolus administration. Correction for renal function are applied. Principal outcome is a composite of mortality and emergence of new multidrug pathogens at 28 days from first bolus. Secondary outcomes are: mortality at day 90, ICU-, antibiotics- and SOFA-free days.

Expected results We expect a primary outcome reduction from 52 to 40% in the continuous infusion group. Applying an 80% power and a 5% alpha errors, a total of 287 subjects for group will be necessary (rounded to 300), with a total of 600 patients. This study received a grant from AIFA, Ricerca Indipendente 2012, n. FARM12MAEF.