Effectiveness of three days of beta-lactam antibiotics for hospitalized community-acquired pneumonia: a randomized non-inferiority double-blind trial

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Background: Community acquired pneumonia (CAP) is a major cause of antibiotic prescriptions. Although most guidelines recommend 7 days of antibiotic treatment, duration of treatment (TT) is not evidence-based. The objective of this study was to compare 3 days versus 8 days of beta-lactams treatment (BLT) for moderately severe hospitalized CAP with early response after three days of TT.

Materials/methods: We performed a multicenter (20 centers) randomized double blind (versus placebo) controlled trial with 2 parallel groups, with a non-inferiority design using 10% as non-inferiority margin, comparing 3 versus 8 days of BLT.

Patients hospitalized on day 0 with fever (>38°C), and clinical signs of CAP (cough, dyspnea, sputum, pulmonary crackles) with new infiltrate on X-ray, and thereafter meeting stability criteria of IDSA (Infectious Disease Society of America), i.e. temperature <37.9°C, heart rate≤100/min, respiratory rate≤24/min, systolic blood pressure ≥90mmHg, oxygen saturation≥90%, ability to have oral intake and normal mental status, after 3 days of BLT (day 3) were included.

Non-inclusion criteria were: combination antibiotic TT, suspected or documented intracellular pathogens, immunosuppression, aspiration pneumonia, allergy to BL, pregnancy.

Randomization was stratified on pneumonia severity index (PSI).

Follow-up period was 30 days. The primary endpoint was cure at day 15, and secondary endpoints were cure at day 30, CAP score evolution and adverse events.

Results: A first safety analysis at 131 inclusions performed by a DSMB (data safety monitoring board) concluded to the safety of the trial and authorized to continue inclusions.

The trial has now completed its targeted inclusion figure: 310 were included between 22nd December 2013 and 2nd February 2018.

The data are currently completing the process of data quality monitoring before statistical analysis.

Final results of Intention-to-treat and per protocol analyses will be available for the ECCMID meeting.
Conclusions: The non-inferiority of three days versus 8 days of BLT for CAP is evaluated in our trial. If non-inferiority is demonstrated, our results would help fight the ever-increasing bacterial resistance by reducing antibiotic consumption in one of our most common infectious diseases and pave the way for similar reductions of antibiotic duration in other diseases.