2240. Can Antibiotic Duration Be Reduced By the Sequential Use of Procalcitonin and Endotoxin in Patients with Sepsis? A Prospective Double-Blind Clinical Trial

**Background.** Patients hospitalized with sepsis are commonly treated with antibiotics for 10–21 days. Evidence is lacking to support this duration. We hypothesize that antibiotic treatment can be reduced when using procalcitonin (PCT) and endotoxin assays to guide antibiotic use.

**Methods.** We enrolled 215 patients. Median age: 60 years old; Female 45%; source: 33% abdominal, 22% line, 19% urinary, 12% cutaneous; 8% pulmonary; 6% miscellaneous. Patients also demonstrated clinical response. The median duration of antibiotics was 16 days [7 inpatient plus 9 outpatient-days]. Compared with both total and in-hospital antibiotic use, time to clearance was significantly shorter: PCT (P < 0.0001), EAA (P < 0.0001), PCT/EAA (P < 0.0001). After multivariate adjustment for disease severity, time to clearance for each or both biomarkers remained significantly shorter by 12 and 3 days compared with total and in-hospital antibiotic use, respectively. Additionally, a faster time to PCT/EAA clearance was associated with a 75% mortality reduction at 28 days (OR 0.25 (0.09–0.68); p = 0.007).

**Conclusion.** The median time-to-clearance of procalcitonin and endotoxin was 4 days, and faster clearance was associated with significant mortality reduction. However, patients received additional 12 days of antibiotics. Our new findings support the use of shorter antibiotic courses for patients with bacteremic sepsis.

**Disclosures.** All authors: No reported disclosures.
Results. We reviewed 299 charts, with 198 (66.2%) included for analysis. The mean age was 76.4 ± 15.0 years, 53% female and 49.5% black. PCT testing was done in 72 (36%) patients; 117 (59%) had antimicrobials given in the emergency department (ED). If the PCT was performed, patients were more likely to receive antibiotics in the ED (79.2% vs. 47.6%; P < 0.0001). Patients who had a PCT drawn were less likely to have a blood culture drawn after admission to the ED (27.6% vs. 73.3%, P < 0.0001). The median duration of antimicrobials was shorter in patients who had a PCT level drawn than those who did not, 1 day (range 0.5–14) vs. 3 days (0.5–61), P < 0.0001. The duration of antimicrobials also tended to be shorter in patients with PCT levels ≤ 0.25 compared with those with levels >0.25; 0.5 days (0.5–12) vs. 1.0 day (0.5–14), P = 0.06.

Conclusion. Among patients with a discharge diagnosis of CHF, there was an association between the use of the PCT assay and both discontinuation of antibiotics given in the ED as well as decreased duration of antimicrobials in patients. These results support the ongoing use of this test to promote antimicrobial stewardship.

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2243. Using Host Biomarkers and Time to Blood Culture Positivity to Predict Necessity for Echocardiogram in Patients with Staphylococcus aureus Endocarditis

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Background. Patients with complicated S. aureus bacteremia (SaB) require a transesophageal echocardiogram (TEE) to rule out endocarditis. Risks of TEE may exceed benefits in patients with a low pretest probability of endocarditis. Given our prior findings that endovascular bacterial burden drives elevated serum IL-10 concentrations, we hypothesize that time to positive blood culture and IL-10 serum concentrations may be used to risk stratify patients for selection of TEE. We compared time to positive blood culture and serum IL-10 in patients with negative and positive TEE.

Methods. Patients with SaB were included if they had a diagnosis of primary, endovascular infection source of bacteria identified by an infectious diseases consult team and a TEE performed. A retrospective chart review was done to identify the time to positivity (hours) of patient blood cultures grown aerobically or anaerobically and TEE results. Sera collected at clinical presentation of these patients were tested for biomarkers IL-10 and IL-1β. Mann–Whitney U test compared the data between positive and negative TEE.

Results. This study included 66 patients with SaB: 17 with negative TEE and 49 with positive TEE. Patients with a positive TEE confirming endocarditis had a faster time to positive blood cultures compared with patients with negative TEE (P = 0.031; figure). IL-10 serum concentrations were significantly higher in patients with positive TEE (26.2 ± 29.9 pg/mL) vs. negative TEE (14.3 ± 11.7 pg/mL). Time-to-positivity in blood culture was linearly associated with IL-10 serum concentrations (P = 0.004; figure). Serum IL-10 concentrations were also higher in TEE positive vs. negative patients (32.1 ± 41.7 vs. 14.7 ± 17.9 pg/mL, P = 0.067).

Conclusion. These data lend further evidence to link high endovascular bacterial burden (measured by shorter time to positive blood culture) and serum IL-10 concentrations. Patients with positive TEE had significantly shorter time to blood culture positivity and higher IL-10 serum concentrations than those with negative TEE. With further study on a larger number of patients, time to positive blood cultures and serum biomarkers like IL-10 may be used to risk stratify patients for performance of TEE, as well as to select antimicrobial therapy and to adjust treatment duration.

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2244. Clinical Outcomes with Extended Infusion (EI) vs. Intermittent Infusion (II) of Ceftolozane/Tazobactam (TZP), and Meropenem (MEM) in Patients with Gram-Negative (GN) Bacteremia

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Background. The increase in drug-resistant pathogens has prompted interest in extending antibiotic durations. Site-of-care decisions (e.g., admission vs. outpatient) in CABP management can be challenging for healthcare providers. Here we describe a post hoc analysis of adults with CABP managed as outpatients in the LEAP 2 double-blind, non-inferiority, Phase 3 trial.

Methods. LEAP 2 compared the efficacy and safety of oral lefamulin (LEF) 600 mg every 12 hours for 5 days vs. oral moxifloxacin (MOX) 400 mg every 24 hours for 7 days in adults with PORT Risk Class II-IV. Descriptive statistics were generated to characterize demographics, baseline characteristics, efficacy, and safety outcomes in the subpopulation of outpatients in LEAP 2.

Results. Overall, 42% (310/736) of patients started treatment as outpatients (41% [151/368] LEF and 43% [159/368] MOX). Age, gender, and BMI were generally similar in both treatment groups. 46% (66/151) LEF and 40% (64/159) MOX outpatients had PORT Risk Class III or IV, and 21% in both groups (31/151 LEF and 34/159 MOX) had CURB-65 score 2 or 3. Comorbidities included smoking history (43% LEF vs. 34% MOX), hypertension (26% vs. 30%), COPD (14% vs. 11%), and diabetes mellitus (7% vs. 11%). Early clinical response (ECR) responder rates and investigator’s assessment of clinical response (IACR) success rates at the test of cure (TOC) visit were high and similar in both groups among all PORT Risk Class III/IV, and CURB-65 score 2 or 3 outpatients (Table 1). In the PORT Risk Class II/III group, 86% LEF vs. 80% MOX patients were both an ECR responder and IACR success at TOC. In the CURB-65 score 2 or 3 subset, 87% LEF vs. 74% MOX patients were both an ECR responder and IACR success at TOC. Treatment-emergent adverse event (TEAE) rates were similar in both groups (Table 1). Overall adverse event rates were similar between groups in related TEAEs driven by gastrointestinal disorders (20% LEF vs. 5% MOX), specifically diarrhea (15% vs. 1%). Rates of TEAEs leading to discontinuation were low and similar in both groups. No LEF outpatient had an SAE or was admitted during the study, compared with 5% (35/678) SAEs, including 2 deaths, in the MOX group.