antibiotic use [Schembri S et al. *BMJ*. 2013; Ray WA et al. *N Engl J Med*. 2012]. The purpose of this post hoc analysis was to determine if cardiac complications were associated with macrolide use in hospitalized patients with CAP.

In the multicenter, crossover CAP-START trial, >2200 hospitalized patients with CAP randomly received β-lactam monotherapy, β-lactam plus macrolide therapy, or fluoroquinolone monotherapy. Each treatment was rotated through participating centers every 4 months. This post hoc analysis examined data from medical charts of new or worsening episodes of heart failure, myocardial ischemia, or arrhythmia according to prespecified criteria using a competing-risk approach. The cause-specific hazard ratio was determined using a Cox proportional hazards model, with the adjusted model accounting for 17 confounders.

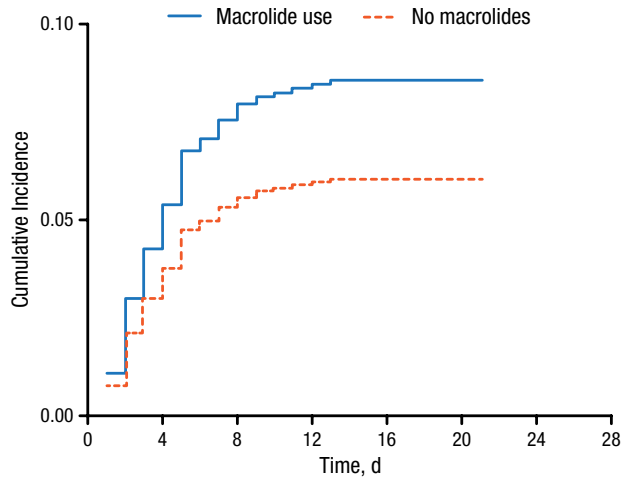
Among the >2000 evaluable patients from the CAP-START study, 15% had CAP due to *Streptococcus pneumoniae* infection, 33% had a history of cardiac disease, 9% had heart failure, and 15% had diabetes mellitus at baseline. In addition, upon hospitalization, the median blood urea nitrogen level was 6.4 mmol/L. The median age was 69.5 years, and 58% of patients were men. Macrolide treatment was administered to 30.8% for a minimum of 1 day.

In patients who receive macrolide therapy, the cumulative incidence of cardiac events was higher than in patients who did not receive macrolides (Figure 1).

Macrolide use was associated with an increased rate (66%) and net risk (81%) of cardiac events in patients with CAP during hospitalization. Furthermore, macrolide use resulted in an increased risk for cardiac events according to cause-specific (adjusted HR, 1.66; 95% CI, 1.18 to 2.34) and subdistribution (adjusted HR, 1.81; 95% CI, 1.29 to 2.55) analyses. Specifically, macrolide use resulted in greater rates of arrhythmia (3.0% vs 2.3%) and heart failure (7.0% vs 3.7%), but not myocardial ischemia (0.3% vs 0.8%). In addition, macrolide use was associated with a greater proportion of patients experiencing in-hospital death (4.2%) compared with patients who did not receive macrolides (2.6%).

In conclusion, Dr Postma indicated that the data from this post hoc analysis of the CAP-START study suggest that macrolide use is associated with an increased risk of cardiac events, as well as in-hospital death, compared with other antibiotic therapies.

Figure 1. Cumulative Incidence of Cardiac Events According to Macrolide Use in Community-Acquired Pneumonia



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Single-Hospital Comparison of Automated MRSA Detection Systems

Written by Brian Hoyle

A head-to-head comparison of 2 automated, polymerase chain reaction–based systems for the detection of methicillin-resistant *Staphylococcus aureus* (MRSA) in nasal swabs and culture samples from 119 high-risk patients has demonstrated the superiority in terms of detection accuracy and speed of the Xpert MRSA Gen 3 system over the BD-MAX MRSA system.

Martin Rottman, MD, PhD, Hôpital Raymond Poincaré AP-HP, Garches, France, and colleagues presented findings that the ongoing evaluation of the diagnostic performance of MRSA molecular assays is necessary, given the emergence of new strains with *mec* gene variations or altered staphylococcal cassette chromosomal junctions. This study focused on the performance of Xpert and BD-MAX automated molecular assays in comparison to 2 culture-based methods on nasal swab samples acquired from patients in the intensive care unit, orthopedic surgery unit, and rehabilitation medicine unit of Hôpital Raymond Poincaré. A hospital policy had designated these units as being at high risk for MRSA outbreaks in the tertiary-care center.

Consecutive nasal swab samples were collected from both anterior nares of 119 patients over a 45-day period. These and 36 nasal swab samples collected from patients who were culture-positive for MRSA were used for the 2 automated molecular assays as well as 2 culture-based methods. The culture-based methods were the Tryptic Soy Broth enriched culture method (gold standard) followed by MRSA select agar (culture time, 24 to 72 hours),

and direct culture on MRSA select agar (culture time, 18 hours). A bank of 12 control strains was also tested, including a bovine strain that contained *mecC*. Each sample was dispensed in 500 µL distilled deionized water, with aliquots of 100 µL used for each of these four methods. A total of 119 consecutive samples were tested, followed by testing of 36 direct positive samples. In the subsequent statistical analyses, the agreement of each method was compared with the Tryptic Soy Broth enriched culture (gold standard).

Based on the results of the gold standard method, 12 of 119 patients (10%) harbored MRSA in their nasal passages. Both automated assays detected the *mecC* strain. The Xpert system correctly identified MRSA in 45 of 47 samples (95.7%) known to be MRSA-positive, with 98.7% agreement with the gold standard method. The BD-MAX assay correctly identified 42 of 48 samples (87.5%), with a 94.0% agreement with the gold standard method. The difference in accuracies significantly favored the Xpert system ($P = .023$, McNemar nonparametric test). When MRSA culture-negative samples were tested, the Xpert assay correctly identified all 107 samples tested. The BD-MAX assay correctly identified 100 of 103 samples. The 3 false-positive results in the BD-MAX assay were traced to problems with the interpretive software of the instrument. Positive predictive values were 100% and 93.3% with Xpert and BD-MAX, respectively, whereas negative predictive values were 99.0% and 96.1%, respectively.

The hands-on time needed to run 4 samples in the Xpert system was 12 minutes, with a turn-around time of 91 minutes. The comparable times for the BD-MAX system were 15 and 117 minutes.

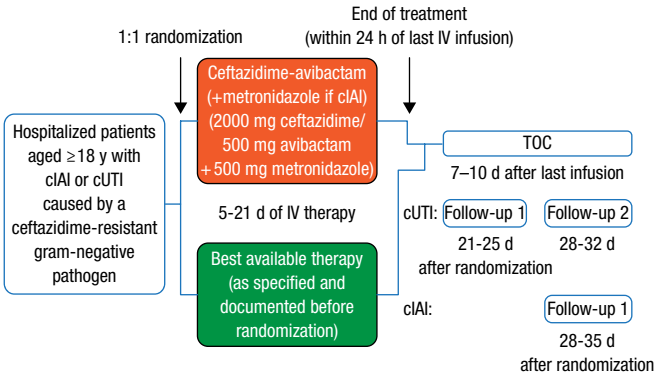
The data demonstrate the detection superiority and lower hands-on time of the Xpert automated assay compared to the BD-MAX automated assay in detecting MRSA in nasal samples obtained from patients in units regarded to be at high risk for MRSA.

Ceftazidime-Avibactam Can Treat UTIs Caused by Multidrug-Resistant Enterobacteriaceae

Written by Brian Hoyle

Urinary tract infections (UTIs) due to multidrug-resistant gram-negative bacteria (including ceftazidime resistant) respond to treatment via a combination of ceftazidime and avibactam. The results of REPRISE [NCT01644643], a prospective open-label phase 3 trial, were presented by Yehuda Carmeli, MD, MPH, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel.

Figure 1. Study Design



cIAI, complicated intra-abdominal infection; cUTI, complicated urinary tract infection; IV, intravenous; TOC, test of cure.

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The burgeoning prevalence of multidrug-resistant gram-negative pathogens spurred the use of carbapenems, but resistance to carbapenems is also spreading. Ceftazidime-avibactam (CAZ-AVI) may have merit as an alternative, and it was the focus of the REPRISE trial.

Patients aged ≥18 years who were hospitalized with complicated intra-abdominal infection (cIAI) or complicated urinary tract infection (cUTI) due to ceftazidime-resistant gram-negative bacteria were randomized 1:1 for 5 to 21 days of intravenous therapy involving either best available therapy (BAT; carbapenem antibiotic monotherapy in 97% of cases) or CAZ-AVI (followed by metronidazole in the case of cIAI that could involve anaerobes), with dose reduction for patients with renal impairment. Treatment outcome (test of cure [TOC]) was ascertained 7 to 10 days after the last treatment in the microbiologically modified intention-to-treat (mMITT) population (Figure 1).

Ceftazidime-resistant Enterobacteriaceae and *Pseudomonas aeruginosa* were defined as having a ceftazidime minimal inhibitory concentration of ≥8 and ≥16 mg/L, respectively. The primary end point was the clinical response to treatment. Secondary end points included favorable microbiological response in the mMITT population and safety, as determined by emergent adverse events (AEs) and laboratory testing.

The 53-center, 16-country trial involved 333 patients randomized to CAZ-AVI (n = 165; cUTI, n = 153) or BAT (n = 168; cUTI, n = 153). The mMITT population comprised 302 patients (CAZ-AVI, n = 154; BAT, n = 148). At baseline, the characteristics were generally similar in the cUTI patients in both groups. Patients with cIAI were broadly similar, considering the small number of patients (Table 1).