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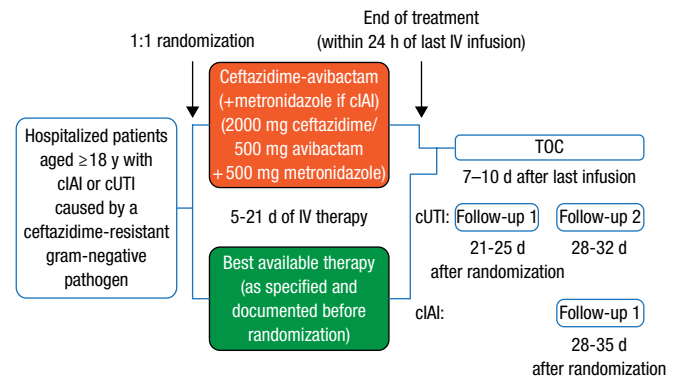
cIAI, complicated intra-abdominal infection; cUTI, complicated urinary tract infection; IV, intravenous; TOC, test of cure.

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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).

Table 1. Baseline Characteristics of the Study Groups

	cUTI		cIAI	
	CAZ-AVI (n = 144)	**BAT (n = 137)**	**CAZ-AVI + MET (n = 10)**	**BAT (n = 11)**
Age, y	64.3 ± 14.6	61.3 ± 15.3	49.9 ± 16.1	68.4 ± 11.1
Female	64 (44.4)	63 (46.0)	6 (60.0)	4 (36.4)
Race				
White	136 (94.4)	131 (95.6)	9 (90.0)	11 (100)
Other[a]	8 (5.6)	6 (4.4)	1 (10.0)	0
BMI, kg/m^2	28.1 ± 5.5	28.0 ± 5.8	25.2 ± 6.3	28.6 ± 4.6
Renal status[b]				
> 50	118 (81.9)	113 (82.5)	10 (100)	6 (54.5)
31-50	19 (13.2)	18 (13.1)	0	3 (27.3)
16-30	4 (2.8)	5 (3.6)	0	2 (18.2)
6-15	3 (2.1)	1 (0.7)	0	0

Data presented in mean ± SD or No. (%).

BAT, best available therapy; BMI, body mass index; CAZ-AVI, ceftazidime-avibactam; cIAI, complicated intra-abdominal infection; cUTI, complicated urinary tract infection; MET, metronidazole.

[a]Black or African American, Asian, or other.

[b]Creatinine clearance, mL/min.

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The majority of patients were infected with Enterobacteriaceae, most commonly *Escherichia coli* and *Klebsiella pneumoniae*. The overall clinical cure rate (cUTI and cIAI) at TOC in the mMITT population was 140 of 154 (90.9%; 95% CI, 85.6% to 94.7%) for CAZ-AVI and 135 of 148 (91.2%; 95% CI, 85.9% to 95.0%) for BAT. For patients with cUTI, the clinical cure rate at TOC in the mMITT population was 132 of 144 (91.7%; 95% CI, 86.3% to 95.4%) for CAZ-AVI and 129 of 137 (94.2%; 95% CI, 89.3% to 97.2%) for BAT. The per-patient favorable microbiological response rate in patients with cUTI treated with CAZ-AVI (n = 118 of 144, 81.9%; 95% CI, 75.1% to 87.6%) was higher than that with BAT (n = 88 of 137, 64.2%; 95% CI, 56.0% to 71.9%). Rates of clinical cure declined with time but remained ≥85% for the CAZ-AVI arm.

AEs occurred in 51 of 164 (31.1%) and 66 of 168 (39.3%) patients in the CAZ-AVI and BAT arms, respectively, with serious AEs in 5.5% and 6.0% of patients, respectively. The most frequent AEs were gastrointestinal disorders (12.8% and 17.9%, respectively). Seven deaths (3 in the CAZ-AVI arm and 4 in the BAT arm) were not considered related to the therapy.

The results indicate the potential value of CAZ-AVI in the treatment of cUTI caused by ceftazidime-resistant gram-negative bacteria. The small numbers of cIAI patients preclude any definitive conclusion about the efficacy of CAZ-AVI in treating this sort of infection.

New Antibiotic Combination for Treating Complicated Intra-abdominal Infections

Written by Jill Shuman

The growing prevalence of third-generation cephalosporin-resistant Enterobacteriaceae and *Escherichia coli* isolates throughout the world has caused an increase in the utilization of carbapenems. This has led to a resultant surge in carbapenem resistance and has presented an unmet need for antibiotics that will decrease the reliance on carbapenems for treating these infections.

John E. Mazuski, MD, Washington University School of Medicine, St Louis, Missouri, USA, presented pooled data on 2 identical phase 3 studies: RECLAIM 1 [NCT01499290] and RECLAIM 2 [NCT01500239]. The 2 studies investigated the safety and efficacy of ceftazidime-avibactam (CAZ-AVI) plus metronidazole (MTZ) compared with meropenem (MER) in treating complicated intra-abdominal infections.

RECLAIM 1 and 2 originally enrolled 1149 adults with a diagnosis of complicated intra-abdominal infection from 30 countries between March 2012 and April 2014. Patients (n = 1066) were then randomized on a 1:1 basis to receive either CAZ-AVI plus MTZ (n = 532) or MER (n = 534) for 5 to 14 days (Figure 1). With agreement from both the European Medicines Agency and the FDA, the 2 studies were subsequently combined to form 1 global phase 3 study and analyzed using a single pooled data set. The primary end point of the trial was the clinical cure rate at the test-of-cure visit 28 to 35 days following randomization.

Noninferiority was assessed in the modified intention-to-treat (MITT; n = 1043) and clinically evaluable (n = 826) populations for the European Medicines Agency and the microbiologically modified intention-to-treat (mMITT) (n = 823) population for the FDA. The level of noninferiority was determined to be met if the lower limit of the 95% confidence interval for the between-group difference was > –12.50%. Adverse events (AEs) and serious AEs, including significant laboratory findings, were compared between groups in the safety population (n = 1058).

Clinical cure rates at test-of-cure visit in the MITT, clinically evaluable, and mMITT populations are summarized in Figure 2. Based on the preset definitions of inferiority,