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Hospital Medicine

Evidence-Based Information for Hospitalists Intensivists, and Acute Care Physicians [ALERT]

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ABSTRACT & COMMENTARY

Can We Safely Discharge Patients on the Weekend?

By Kenneth P. Steinberg, MD, FACP, Editor

Professor of Medicine, University of Washington School of Medicine Seattle, WA

Dr. Steinberg reports no financial relationships in this field of study.

SOURCE: Cloyd JM, e al. Is weekend discharge associated with hospital readmission? *J Hosp Med* 2015; 10:731-737.

This study was designed to investigate whether or not there was an association between weekend discharge and 30- and 90-day readmission rates. The population of interest was patients hospitalized for medical diagnoses included in the Centers for Medicare and Medicaid Services' Hospital Readmission Reduction Program (HRRP): acute myocardial infarction (AMI), congestive heart failure (CHF), or pneumonia (PNA). The authors hypothesized that patients with these primary diagnoses discharged on a weekend would have higher hospital readmission rates compared to patients discharged on a weekday. After obtaining IRB approval, the authors used a large database for this study: the California Office of State Health Planning and Development (OSHPD) Patient Discharge Data (PDD) from 2012. This inclusive database contained records for all patients admitted and discharged from every general, acute, nonfederal hospital in the state of California. In this database, patients could be tracked even if they were discharged from one hospital and readmitted to another facility. Demographic and clinical data were captured including discharge disposition (home, acute rehabilitation, skilled nursing facility, residential facility, or other). Demographic data, hospital variables, and readmission rates were directly compared for patients discharged on a weekend compared to a weekday after an admission for AMI, CHF, or PNA. Hospital readmission for any reason was tracked for 30 and 90 days after the index admission. Univariate and multivariate logistic regression models were built to study the effect on readmission of age, gender, race, Charlson

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Comorbidity Index, discharge disposition, and admission type.

There were 266,519 patients admitted with a principle diagnosis of AMI, CHF, or PNA in California during 2012 who met the criteria for inclusion (patients were excluded if they died during the index hospitalization, were transferred to another acute care facility, and if they had invalid tracking numbers). The majority of patients were discharged on a weekday instead of a weekend (77.5% versus 22.5%). Patients discharged on the weekend had a shorter length of stay for all 3 diagnosis groups, and a higher proportion was discharged to home and a smaller proportion was discharged to a SNF.

Among all patients, there were no significant differences between unadjusted readmission rates for patients discharged on the weekend versus weekday at either 30 days (16.7% vs. 17.0%) or 90 days (26.9% vs. 27.5%). In the subsets, unadjusted readmission rates were the same for patients with AMI and PNA at both 30 and 90 days; the unadjusted readmission rates were higher for weekday discharges in CHF at 30 days (15.4% vs. 16.0%, P= 0.04). The same difference was seen at 90 days.

In multivariate logistic regression, weekend discharge was not associated with increased rate of readmission for any diagnosis. Increasing age, male gender, black race, greater Charlson Comorbidity Index, occurrence of a complication, and increased LOS were all associated with readmission. Interestingly, lack of insurance was associated with decreased odds of readmission for all diagnoses.

■ COMMENTARY

Studies have shown an association between weekend admission and increased mortality but very few studies have focused on the effect of weekend discharge on hospital readmission rate. Hospital readmission is associated with increased short-term morbidity, mortality, and medical costs. Hospitals are now incentivized to reduce readmissions for AMI, CHF, and PNA as part of the Patient Protection and Affordable Care Act of 2013 as penalties are being assessed against hospitals that have high rates of readmission for these diagnoses. Hospitalists are at the forefront of working to reduce readmissions through coordination of safe discharges. Discharge from the hospital is a complex task involving good coordination and communication among team members, and patients and their families. There are many reasons why weekend discharges might be higher risk including decreased staffing, lack of continuity of care, inability to make follow-up appointments, less robust medication reconciliation, and less access to outpatient pharmacies on the weekend.

Importantly, this study demonstrated that it might be safe to discharge patients on the weekend as there was not an increased readmission rate for that group of patients compared to patients discharged on a weekday. This is a robust study with a very large number of patients across many institutions in a large state with a very complete database. Although there are always inherent limitations to studies using administrative databases, the observation that weekend discharge is not a predictor of readmission in patients with AMI, CHF, or PNA in California is likely valid. However, one important caveat for the lack of correlation between weekend discharge and readmission could be that sicker and higher risk patients were selected for discharge on a weekday, a possibility that could make it difficult to see an increased risk of readmission for weekend discharges. The authors correctly point out, though, that the despite fears that access to staffing and supplies are reduced during the weekend, it might be that weekend discharge resources are in fact not the limiting factor in efforts to reduce readmissions.

In summary, this study challenges the preconceptions that weekend discharges are less safe and are a predictor for readmission. Routinely delaying a discharge until Monday likely only increases costs and may not reduce the risk for readmission. Efforts to reduce readmission rates should focus on reducing risk factors other than day of discharge. Hospitalists need to be aware of these observations to reduce healthcare costs and help their hospitals reduce readmission rates. ■

ABSTRACT & COMMENTARY

Optimal Beta-blocker Dose Post-MI

By Michael Crawford, MD, Editor

SOURCES: Goldberger JJ, el al. Effect of beta-blocker dose on survival after acute myocardial infarction. *J Am Coll Cardiol* 2015;66: 1431-1441.

Taqueti VR, O'Gara PT. Beta-blocker therapy after myocardial infarction: More questions than answers. *J Am Coll Cardiol* 2015;66: 1442-1444.

Beta-blocker therapy after acute myocardial infarction (MI) was retired as a hospital performance measure because its almost universal acceptance removed its discriminating value. However, it is well known that clinically used doses are significantly lower than those achieved in the randomized trials, establishing their mortality-reducing benefits. Thus, the investigators from the Outcome of Beta-blocker Therapy After Myocardial Infarction (OBTAIN) study hypothesized that the higher the dose of beta-blocker the lower the mortality. The OBTAIN study was a multicenter registry that recorded beta-blocker dosing information and tracked survival. The beta-blocker and the dose were determined by the treating physician. More than 90% of the subjects were on either metoprolol or carvedilol and 91.5% of the subjects were prescribed a beta-blocker. Almost 86% were on doses < 50% of the trial target doses. After a median follow-up of 2 years, there was a 12% all-cause mortality, which was the primary endpoint. The unadjusted data showed that survival was significantly higher for any dose of beta-blockers vs no beta-blockers. The multivariate adjustment of the data showed that higher doses were not associated with better survival. In fact, the lowest mortality was observed at 25% of the target dose. The authors concluded that they had failed to demonstrate that higher doses of beta-blockers approximating those used in randomized trials improved survival compared to lower doses.

■ COMMENTARY

This retrospective, observational study tends to support what most clinicians are doing with post-MI beta-blockade: Titrate the dose to reduce the heart rate to < 70 bpm and avoid adverse effects. This practice exhibits reduced mortality compared to no beta-blocker use, but fails to identify an optimal dose. Most patients end up on 25% or less of the target doses achieved in the randomized trials or ≤ 50mg/day of metoprolol or ≤ 12.5 mg/day of carvedilol. Interestingly, perhaps realizing the wisdom of this approach, the various society guidelines do not recommend a particular dose. It is always nice to have a study validate what we are practicing rather than vilifying it.

Why the disconnect between the randomized trials and today's practice? The authors advanced several possibilities. First, perhaps the hypothesis is correct, but they couldn't demonstrate it in this study due to unmeasured confounders. Second, there may be a beta-blocker dose threshold and once you exceed it, you cannot show increased benefits with higher doses. Third, perhaps there is no optimal dose and it varies by patient depending on their adrenergic tone, left ventricular performance, and sensitivity to adverse effects.

Beta-blockers in the randomized trials were thought to reduce post-MI mortality by reducing ischemia, recurrent MI, and sudden death. However, these trials were conducted before widespread use of reperfusion therapy. Early reperfusion probably abrogates ischemia and re-infarction, leaving sudden arrhythmic death as the only effect left for beta-blockers. Recent studies of post-MI sudden death note that compared to the pre-reperfusion era, patients today are more likely to present with pulseless electrical activity rather than ventricular tachycardia. So widespread beta-blocker use post-MI may be affecting ventricular arrhythmias. Recent analyses suggest that unlike the 25% reduction in death or post-MI observed during the trials, beta-blocker use today reduces these endpoints by 15%, which would be at the margin of statistical significance.

The randomized trials also showed that beta-blockers were most beneficial in large ST elevation MIs or patients with reduced left ventricular performance. We know beta-blockers are good for heart failure, so with less post-MI heart failure in the current era, their effectiveness may be less. This is in line with other trends in beta-blocker use, as is pointed out by Drs. Taqueti and O'Gara. Their value in hypertension, perioperative care, and chronic stable ischemic heart disease has been questioned by recent studies. It may be that modern therapy is reducing the value of beta-blockers in cardiovascular disease. Until researchers conduct a randomized, dose-ranging trial of beta-blockers in post-MI patients in the current therapeutic milieu, we should continue doing what we are doing and not worry that we are underdosing beta-blockers in post-MI patients. ■

PHARMACOLOGY UPDATE

Idarucizumab Injection (Praxbind)

By William Elliott, MD, FACP, and James Chan, PharmD, PhD

Dr. Elliott is Medical Director, Pharmacy, Northern California Kaiser Permanente, Assistant Clinical Professor of Medicine, University of California, San Francisco. Dr. Chan is Pharmacy Quality and Outcomes Manager, Kaiser Permanente, Oakland, CA.

Drs. Elliott and Chan report no financial relationships relevant to this field of study.

The FDA has approved the first reversal agent for a direct oral anticoagulant (DOAC). Idarucizumab is a humanized monoclonal antibody fragment derived from an IgG1 isotype molecule. The monoclonal antibody directly binds to dabigatran (Pradaxa), rapidly neutralizing its pharmacologic effect. The drug was approved under the FDA's accelerated approval process. It is marketed as Praxbind by Boehringer Ingelheim.

INDICATIONS

Idarucizumab is indicated in patients treated with dabigatran when reversal of the anticoagulant effect is needed.[1]

DOSAGE

The recommended dose is 5 g given as two consecutive intravenous infusions or as two consecutive bolus injections.[1] Idarucizumab is available as 2.5 g vials.

POTENTIAL ADVANTAGES

Idarucizumab effectively reverses the anticoagulant effect of dabigatran[1,2] and has minimal side effects.

POTENTIAL DISADVANTAGES

Reversing the effect of dabigatran exposes patients to thromboembolic risk of their underlying disease.[1] Elevated coagulation parameters have been observed between 12 and 24 hours after administration.[1] Treatment-emergent, possibly persistent anti-idarucizumab antibodies were observed in 4% of subjects. The formulation contains sorbitol; thus, there is a risk of serious reaction in patients with hereditary fructose intolerance.[1]

COMMENTS

The safety and efficacy of idarucizumab was evaluated in three trials in healthy volunteers (n = 283) and in one study in subjects taking dabigatran who received idarucizumab due to uncontrolled bleeding or requiring emergency surgery (n = 123, with n = 90 evaluable). Compared to placebo, the infusion of idarucizumab significantly reduced coagulation parameters (dTT, aPTT, ECT, TT, and ACT) at the end of the infusion. Reductions ranged from 51%-90% compared to no change for placebo. In the second study, subjects were divided into two groups. Fifty-one had serious bleeding (Group A) and 39 required an urgent procedure (Group B). The primary endpoint was the maximum percentage reversal of anticoagulation effect at any point from the end of the first infusion to 4 hours after the second administration. The median maximum percent reversal was 100%. The effect was evident within minutes. The secondary endpoints included the proportion of subjects who had complete normalization of the dilute thrombin time or ecarin clotting time in the first 4 hours and reduction in the concentration of unbound dabigatran. Dilute thrombin time was normalized in 98% of Group A and 93% in Group B and 89% and 88%, respectively, for ecarin clotting time.[2] At 4 hours, 97% had dabigatran levels near the lower limit of quantification. Of the subjects in group B who underwent a procedure, 33 reported normal intraoperative hemostasis restored, with two mildly and one moderately abnormal. Thrombotic events occurred in five subjects ranging from 2 to 26 days after treatments. There were 18 deaths overall, with 10 due to vascular causes and five due to fatal bleeding events.[2] Ten fatalities occurred within 96 hours of idarucizumab and the remaining ranged from 4 to 101 days. Early deaths appear to be related to the index event and later deaths to coexisting conditions.[2] There is redistribution of dabigatran 12 hours after idarucizumab administration from extravascular compartment into the intravascular compartment.

CLINICAL IMPLICATIONS

Idarucizumab is the first agent to effectively reverse the anticoagulant effect of a DOAC. Lack of a reversal agent has been seen as a major drawback for administration of these drugs, especially in individuals who may be at higher risk of bleeding or falls. A reversal agent for the Xa inhibitors (rivaroxaban, apixaban, edoxaban) is in Phase 2 trials. Meanwhile, approval of idarucizumab gives Boehringer Ingelheim a marketing advantage for dabigatran over other DOACs. The wholesale cost is $3500 for a single administration (5 g). ■

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Ceftazidime-avibactam — Formulary Considerations

By Jamie Kuo, PharmD, Stanford Health Care, CA

Dr. Kuo reports no financial relationships relevant to this field of study.

Ceftazidime-avibactam is a new beta-lactam/beta-lactamase inhibitor combination approved for the treatment of complicated intra-abdominal infections in combination with metronidazole, and complicated urinary tract infections, including pyelonephritis in patients with limited alternative treatment options. The addition of avibactam to ceftazidime extends its spectrum of activity to include organisms that produce Ambler class A and C beta-lactamases, including AmpC, extended spectrum beta-lactamases (ESBLs), and most notably, *Klebsiella pneumoniae* carbapenemases (KPCs).

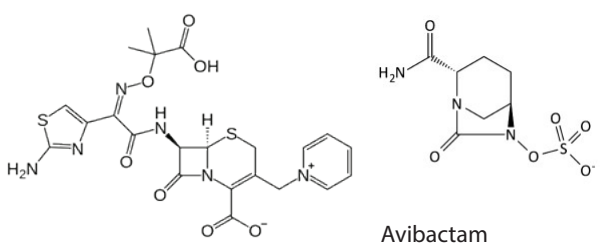
GENERIC NAME: Ceftazidime-avibactam
TRADE NAME: Avycaz™
U.S. FDA APPROVAL DATE: February 25, 2015

SIMILAR DRUGS
Meropenem, imipenem-cilastatin, doripenem, ceftolozane-tazobactam

INDICATIONS[1]
Treatment of adult patients 18 years or older with the following infections:
- Complicated intra-abdominal infections (cIAI), in combination with metronidazole, caused by *Enterobacter cloacae, Escherichia coli, Klebsiella oxytoca, K. pneumoniae, Proteus mirabilis, Providencia stuartii, and Pseudomonas aeruginosa*.
- Complicated urinary tract infections (cUTI) including pyelonephritis caused by *Citrobacter freundii, C. koseri, Enterobacter aerogenes, E. cloacae, Escherichia coli, Klebsiella pneumoniae, Proteus spp, and Pseudomonas aeruginosa*.

PHARMACOLOGY[1,2]

Ceftazidime is a previously FDA-approved, third-generation cephalosporin with broad activity against Gram-negative organisms, including *Pseudomonas aeruginosa*. It is a bactericidal beta-lactam antibiotic that inhibits cell wall synthesis by binding to penicillin-binding proteins. Avibactam is a novel, non-beta-lactam beta-lactamase inhibitor of Ambler classes A and C beta-lactamases through covalent-binding to the enzyme active site. The addition of avibactam preserves ceftazidime activity by inhibiting its degradation by beta-lactamases and confers enhanced activity against Gram-negative bacteria, including ESBL-producing organisms. More importantly, ceftazidime-avibactam is the only beta-lactam/beta-lactamase inhibitor to date to have activity against KPCs. However, ceftazidime-avibactam has limited activity against Ambler class D beta-lactamases (except OXA-48 carbapenemases) and no activity against Ambler class B metallo-beta-lactamases (MBLs). Additionally, ceftazidime-avibactam has minimal activity against *Acinetobacter*, anaerobes, and Gram-positive organisms.



Ceftazidime

Avibactam

PHARMACOKINETICS & PHARMACODYNAMICS[1-3]
Ceftazidime and avibactam have similar volumes of distribution and half-lives. The volume of distribution of ceftazidime and avibactam is 17 L and 22.2 L, respectively. The half-life of ceftazidime is approximately 3 hours and avibactam is approximately 2.5 hours. Ceftazidime-avibactam dosed at 2.5 g every 8 hours achieves steady-state peak concentrations of ceftazidime and avibactam of 90 and 15 mg/L, respectively. Protein binding is relatively low at less than 10% with ceftazidime and 5.7-8.2% with avibactam. Both are also predominantly excreted renally and removed by hemodialysis. Ceftazidime is minimally metabolized, with 80-90% of the dose being eliminated in urine as unchanged drug. Avibactam is not metabolized, and 97% of the dose is eliminated in urine as unchanged drug.

Similar to the pharmacodynamics of other beta-lactam antibiotics, ceftazidime bactericidal activity is optimized by maximizing the proportion of the time of the dosing interval that the free drug concentration is above the MIC. The suggested pharmacodynamic target of avibactam is the proportion of the time of the dosing interval that the free beta-lactamase inhibitor concentration is above the threshold concentration.

CLINICAL TRIALS/EVIDENCE SUMMARY
- Clinical efficacy and safety of ceftazidime-avibactam is

CLINICAL TRIALS/EVIDENCE SUMMARY

<table>
<tr><th>Trial</th><th>Population</th><th>Intervention</th><th>Efficacy & Safety Results</th></tr>
<tr><td>Vazquez et al.[5]
Phase 2, multi-center, prospective, double-blind, randomized study</td><td>N = 137 adult patients with cUTI, including pyelonephritis, requiring parenteral antimicrobials</td><td>Ceftazidime-avibactam 500 mg/125 mg IV q8h

vs

Imipenem-cilastatin 500 mg IV q6h

Then step down to oral therapy

Duration: 7-14 days total</td><td>
<table>
<tr><th colspan="8">Endpoints at Test of Cure Visit</th></tr>
<tr><th>TREATMENT ARMS</th><th>N</th><th>ME N</th><th>ME MR</th><th>CE N</th><th>CE CR</th><th>MITT N</th><th>MITT MR</th></tr>
<tr><td>Ceftazidime-avibactam</td><td>69</td><td>27</td><td>70.4%</td><td>28</td><td>85.7%</td><td>46</td><td>67.4%</td></tr>
<tr><td>Imipenem-cilastatin</td><td>68</td><td>35</td><td>71.4%</td><td>36</td><td>80.6%</td><td>49</td><td>63.3%</td></tr>
</table>
• This study was not statistically powered for non-inferiority.
• The most common uropathogen isolated was E. coli.
• The dose of ceftazidime-avibactam studied is lower than the currently recommended dose.
• The most commonly reported adverse events were headache, infusion site reactions, constipation, diarrhea, abdominal pain, and anxiety.</td></tr>
<tr><td>Lucasti et al.[6]
Phase 2, multi-center, prospective, double-blind, randomized study</td><td>N = 204 hospitalized, adult patients with cIAI requiring surgical intervention</td><td>Ceftazidime-avibactam 2.5 g IV q8h + Metronidazole 500 mg IV q8h

vs

Meropenem 1 g IV q8h

Duration: 5-14 days</td><td>
<table>
<tr><th colspan="8">Endpoints at Test of Cure Visit</th></tr>
<tr><th>TREATMENT ARMS</th><th>N</th><th>ME N</th><th>ME CR</th><th>CE N</th><th>CE CR</th><th>MITT N</th><th>MITT CR</th></tr>
<tr><td>Ceftazidime-avibactam + metronidazole</td><td>102</td><td>68</td><td>91.2%</td><td>87</td><td>92%</td><td>85</td><td>82.4%</td></tr>
<tr><td>Meropenem</td><td>102</td><td>76</td><td>93.4%</td><td>90</td><td>94.4%</td><td>89</td><td>88.8%</td></tr>
</table>
• This study was not statistically powered for non-inferiority.
• The most common Gram-negative isolated in blood cultures was E. coli.
• Approximately 50% of patients had appendix-related cIAI.
• The most commonly reported adverse events were nausea, vomiting, abdominal pain, pyrexia, wound secretion, cough, increased AST, ALT and/or AlkPhos, increased platelet count, leukocytosis, or hematuria.</td></tr>
<tr><td colspan="4">cUTI = complicated urinary tract infection; cIAI = complicated intra-abdominal infection; MITT = modified intent-to-treat; ME = microbiologically evaluable; CE = clinically evaluable; MR = favorable microbiological response; CR = favorable clinical response</td></tr>
</table>

currently limited to Phase 2 studies.

• Results from Phase 3 trials in cUTI and cIAI are completed but have not yet been published. In a Phase 3 cIAI trial, clinical efficacy of ceftazidime-avibactam was decreased in patients with moderate renal impairment (CrCl 30-50 mL/min) compared to patients with normal renal function (CrCl > 50 mL/min).[3]

ADVERSE EFFECTS[3]

• Limited safety data are available at this time, given FDA approval was based on Phase 1 and 2 studies only. Therefore, the manufacturer recommends that ceftazidime-avibactam be reserved for patients who have limited or no alternative treatment options.

• Adverse effects reported at ≥ 10% incidence include nausea, vomiting, constipation, and anxiety.

CONTRAINDICATIONS/WARNINGS/PRECAUTIONS[1,3]

• Serious hypersensitivity to ceftazidime-avibactam, individual components, or other cephalosporins are considered contraindications. Caution is advised in patients with hypersensitivity to penicillins or carbapenems due to potential for cross-reactivity.

• Neurologic toxicity has been reported with ceftazidime, and the risk is increased in patients with impaired renal function. Symptoms include encephalopathy, myoclonus, seizures, or non-convulsive status epilepticus. Dose adjustment is recommended in patients with renal impairment.

•Similar to other antibiotics, prolonged use may result in superinfection, including *Clostridium difficile*-associated diarrhea.

• In a Phase 3 cIAI trial, decreased efficacy was reported in patients with moderate renal impairment (CrCl 30-50 mL/min) compared to patients with normal renal function (CrCl > 50 mL/min). Dose adjustment for renal impairment is recommended (*see dosage and administration section*).

POTENTIAL FOR MEDICATION ERRORS

	CrCl > 50 mL/min		CrCl 30-50 mL/min*	
Phase 3 cIAI	Ceftazidime-avibactam + metronidazole	Meropenem	Ceftazidime-avibactam + metronidazole	Meropenem
Clinical cure	85%	86%	45%	74%
Mortality	1%	1%	25.8%	8.6%
*Note ceftazidime-avibactam dose in subgroup with CrCl 30-50 mL/min was 33% lower than is currently recommended.				

Cost				
	How Supplied	Average Wholesale Price (per vial)	Usual Dose	Cost of Therapy per day
Ceftazidime-avibactam	2.5 g vials	$342	2.5 g q8h	$1026.00
Ceftolozane-tazobactam	1.5 g vials	$99.60	1.5 g q8h	$298.80
Meropenem	1 g vials	$18.48	1 g q8h	$55.44

• Dosing should be stated in total grams rather than grams of individual components to avoid dosing errors.

DRUG INTERACTIONS[1,4]

• Organic anion transporters (OAT) inhibitors (e.g., probenecid) can decrease elimination of avibactam, and their concurrent use with ceftazidime-avibactam should be avoided.

Table. Dosing		
Indication	Dose	Duration
cIAI	2.5 g IV every 8 hours in combination with metronidazole	5-14 days
cUTI, including pyelonephritis	2.5 g IV every 8 hours	7-14 days

DOSAGE AND ADMINISTRATION[3,4]

Recommended dose/duration:

• Dosing is expressed as total grams of the ceftazidime-avibactam combination in a ratio of 4:1, i.e., 2.5 g is 2 g ceftazidime and 0.5 g avibactam.

• Patients with renal impairment should have doses adjusted based on creatinine clearance as calculated by the Cockcroft-Gault equation.

• Both ceftazidime and avibactam are removed by dialysis. Following a 4-hour dialysis session, 55% of the dose was recovered in the dialysate.

• Dose adjustment for hepatic function is not necessary.

Administration instructions:

Administer as an intermittent intravenous infusion over 2 hours.

Estimated Creatinine Clearance (mL/min)	Recommended Dose
> 50	2.5 g (2 g/0.5 g) every 8 hours
31-50	1.25 g (1 g/0.25 g) every 8 hours
16-30	0.94 g (0.75 g/0.19 g) every 12 hours
6-15*	0.94 g (0.75 g/0.19 g) every 24 hours
≤ 5*	0.94 g (0.75 g/0.19 g) every 48 hours
*ESRD on HD	Administer after HD on HD days
HD = hemodialysis	

CONCLUSIONS

The addition of avibactam to ceftazidime retains ceftazidime's spectrum of activity and has added activity against some ESBL- and KPC-producing pathogens. Expedited FDA approval of ceftazidime-avibactam was granted based on two small Phase 2 trials and the previously established efficacy and safety of ceftazidime alone. In Phase 2 trials, ceftazidime-avibactam showed similar efficacy to active comparators and appeared to be well-tolerated when used to treat hospitalized adult patients with cUTI and cIAI in combination with metronidazole.

Currently, ceftazidime-avibactam is the only beta-lactam/beta-lactamase inhibitor to have activity against KPCs. In a climate of increasing carbapenem resistance, ceftazidime-avibactam represents an important treatment option in the management of multidrug-resistant Gram-negative infections. With ongoing Phase 3 trials, the precise role of ceftazidime-avibactam remains to be determined and will need to be weighed against the risk of developing drug-resistant bacteria.

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CME QUESTIONS

1. **The study by Cloyd and colleagues demonstrated all of the following were risk factors for readmission after hospitalization for AMI, CHF, or PNA except:**

   a. Age

   b. Weekend discharge

   c. Charlson Comorbidity Index

   d. Increased length of stay

   e. Male gender

2. **According to the OBTAIN study as reported by Goldberger et al., regarding beta-blocker doses after myocardial infarction demonstrated that:**

   a. The majority of patients were on doses of beta-blockers that were ≥ 80% of the doses in the randomized trials of beta-blockers after MI

   b. The minority of patients were on doses of beta-blockers that were ≥ 80% of the doses in the randomized trials of beta-blockers after MI

   c. Higher doses of beta-blockers after MI were associated with higher survival

   d. Higher doses of beta-blockers after MI were not associated with higher survival

   e. B and D

3. **Which of the following statements are true regarding the new antibiotic ceftazidime-avibactam?**

   a. Both components are excreted renally and removed by dialysis and thus need dose adjustments in patients with renal impairment.

   b. The drug combination has minimal activity against Acinetobacter.

   c. The drug combination has minimal activity against anerobes.

   d. The drug combination has enhanced activity against Gram-negative bacteria including ESBL-producing and KPC-producing organisms.

   e. All of the above

CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- discuss pertinent safety, infection control and quality improvement practices;
- explain diagnosis and treatment of acute illness in the hospital setting; and;
- discuss current data on diagnostic and therapeutic modalities for common inpatient problems.

[IN FUTURE ISSUES]

More original, peer-reviewed content by and for hospitalists.