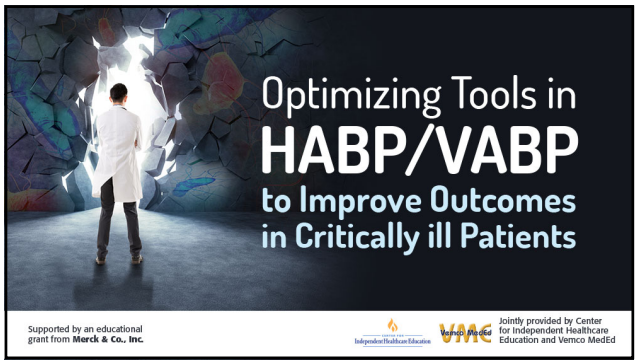
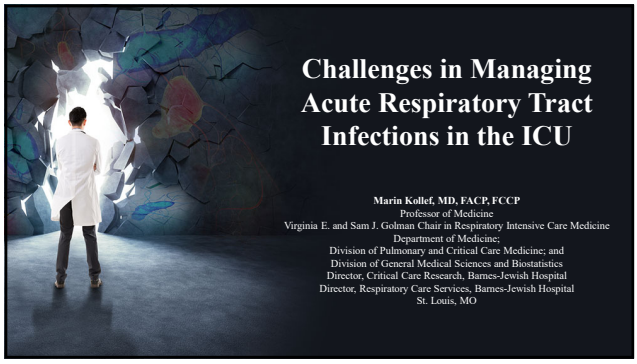
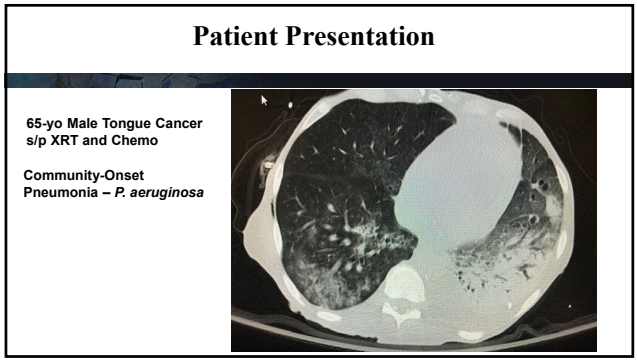

Optimizing Tools in
HABP/VABP
to Improve Outcomes
in Critically ill Patients
Supported by an educational grant from Merck & Co., Inc.
Jointly provided by Center for Independent Healthcare Education and Vemco MedEd

1


Challenges in Managing Acute Respiratory Tract Infections in the ICU
Marin Kollef, MD, FACP, FCCP
Professor of Medicine
Virginia E. and Sam J. Golman Chair in Respiratory Intensive Care Medicine
Department of Medicine;
Division of Pulmonary and Critical Care Medicine; and
Division of General Medical Sciences and Biostatistics
Director, Critical Care Research, Barnes-Jewish Hospital
Director, Respiratory Care Services, Barnes-Jewish Hospital
St. Louis, MO

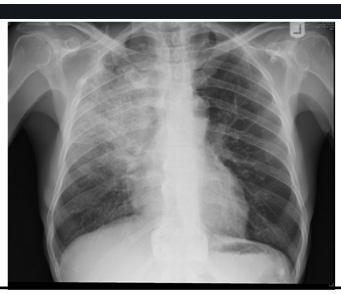
2


Patient Presentation
65-yo Male Tongue Cancer s/p XRT and Chemo
Community-Onset Pneumonia – P. aeruginosa

3

XDR *Pseudomonas aeruginosa*

- 57-yo man with past history of COPD & CVA from SNF, subsequently intubated.
- BAL >10^4 cfu/mL *P. aeruginosa* susceptible only to colistin and C/T.
- Responded to C/T and subsequently extubated and transferred back to SNF.



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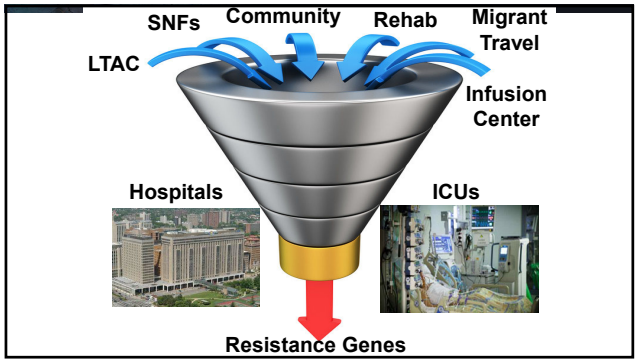
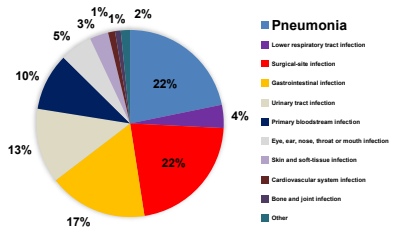


5

Nosocomial Pneumonia is a Leading Healthcare-Associated Infection in the United States

- Prevalence survey conducted at 183 acute care hospitals in 10 states (n=11,282)
  - Highest prevalence of all healthcare-associated infections was pneumonia (21.8%)



SS Magill, et al. *N Engl J Med.* 2018;379:1732-1744.

6

Percentages of All Surveyed Patients with Specific Types of HCAIs, 2011 vs. 2015 Survey

Table 4. Percentages of All Surveyed Patients with Specific Types of Health Care–Associated Infection, 2011 vs. 2015 Survey.*

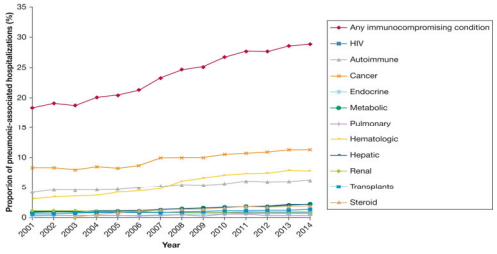
Type of Infection	2011 Survey			2015 Survey			P Value†
	No. of Patients with Infection	No. of Infections	Percentage of Patients with Infection (95% CI)	No. of Patients with Infection	No. of Infections	Percentage of Patients with Infection (95% CI)	
Pneumonia	110	110	0.98 (0.81–1.20)	110	110	0.89 (0.74 – 1.10)	0.52
Ventilator-associated pneumonia	43	43	0.38 (0.28 – 0.51)	39	39	0.32 (0.23 – 0.43)	0.41
Other pneumonia	67	67	0.59 (0.47 – 0.75)	71	71	0.58 0.46 – 0.73)	0.87
Deep incisional or organ-space infection	77	77	0.68 (0.55–0.85)	54	54	0.44 (0.34–0.57)	0.01
Superficial incisional infection	33	33	0.29 (0.21–0.41)	15	15	0.12 (0.07–0.20)	0.004
Bloodstream infection	50	50	0.44 (0.34–0.58)	51	52	0.41 (0.31–0.55)	0.74
Central catheter–associated bloodstream infection	42	42	0.37 (0.27–0.50)	37	38	0.30 (0.22–0.42)	0.35
Other primary bloodstream infection	8	8	0.07 (0.03–0.14)	14	14	0.11 (0.07–0.19)	0.29
Urinary tract infection	65	65	0.58 (0.45–0.73)	39	39	0.32 (0.23–0.43)	0.003
Catheter-associated urinary tract infection	44	44	0.39 (0.29–0.52)	24	24	0.20 (0.13–0.29)	0.005
Other urinary tract infection	21	21	0.19 (0.12–0.29)	15	15	0.12 (0.07–0.20)	0.21
Other infection‖	78	83	0.69 (0.55–0.86)	61	66	0.50 (0.39–0.64)	0.05
Any infection	452	504	4.0 (3.7–4.4)	394	427	3.2 (2.9–3.5)	<0.001

* A total of 12,282 patients were included in the 2011 survey, and 12,299 in the 2015 survey; these values are the denominators for the percentages of patients with infection. Patients could have more than one health care–associated infection.
† P values were calculated by a mid-P exact test.
‡ *Clostridium difficile* is now known as *Clostridioides difficile*.
§ Other infections in the 2011 survey included the following: ear, eye, nose, and throat infections (28 infections); lower respiratory tract infection (20); skin and soft-tissue infections (16); cardiovascular infection (6); bone and joint infections (5); central nervous system infection (4); reproductive tract infection (3); and systemic infection (1). Other infections in the 2015 survey included the following: skin and soft-tissue infections (22 infections); ear, eye, nose, and throat infections (21); lower respiratory tract infection (18); bone and joint infections (2); central nervous system infection (1); cardiovascular infection (1); and reproductive tract infection (1).

SS Magill, et al. *N Engl J Med*. 2018;379:1732-1744.

7

Burden of Pneumonia-associated Hospitalizations: National Inpatient Sample (NIS) Data



Hayes BH, et al. *Chest*. 2018;153:427-437.

8

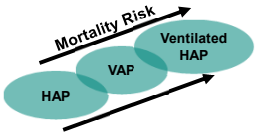
Forms of Nosocomial Pneumonia and Relative Mortality Risk

Hospital-Acquired Pneumonia (HAP)
- Occurs ≥48 hours after admission
- Not intubated at the time of admission
- Not associated with mechanical ventilation

Ventilator-Associated Pneumonia (VAP)
- Arises ≥48 hours after mechanical ventilation

Ventilated HAP
- Patients with severe HAP who require mechanical ventilation
- Occurs ≥48 hours after admission
- Not intubated at the time of admission
- Not associated with mechanical ventilation

ICU HAP
- Occurs ≥48 hours after ICU admission



Ibn Saied W, et al. *Crit Care Med*. 2019;47:345-52.
Torres A, et al. *Eur Respir J*. 2017;50: pii: 1700582.
Kalil AC, et al. *Clin Infect Dis*. 2016;63:e61-111.

9

Different Types of Pneumonia have Different Outcomes!

Outcomes	CAP	HCAP	HAP	VAP
Death during hospitalization				
Death	12,181 (7.9)	13,403 (15.6)	8,209 (20.7)	952 (21.6)
No death	141,977 (92.1)	72,253 (84.4)	31,503 (79.3)	3,449 (78.4)
LOS, days				
≤ 2	27,678 (18.0)	9,129 (10.7)	587 (1.5)	60 (1.4)
3-7	74,537 (48.4)	34,508 (40.3)	6,094 (15.3)	527 (12.0)
8-13	32,181 (20.9)	24,662 (28.8)	10,946 (27.6)	914 (20.8)
≥ 14	19,762 (12.8)	17,357 (20.3)	22,085 (55.6)	2,900 (65.9)
Readmission within 30 days				
Readmission	8,061 (5.2)	9,458 (11.0)	2,627 (6.6)	622 (14.1)
No readmit	146,097 (94.8)	76,198 (89.0)	37,085 (93.4)	3,779 (85.9)

Corrado RE, et al. *Chest*. 2017;152:930-942.

10

Pneumonia & Respiratory Failure, 2016 Barnes-Jewish Hospital MICU (34 beds)*

	Antibiotic Susceptible (N = 63)	Antibiotic Resistant (N = 104)	Viral (N = 79)	*P* Value
HAP	13 (20.6)	25 (24.0)	25 (31.6)	0.384
VAP#	3 (4.8)	22 (21.2)	2 (2.5)	<0.001
CAP	47 (74.6)	57 (54.8)	52 (65.8)	0.052

*364 patients with pneumonia during mechanical ventilation (118 [32.4%] were pathogen negative)
#VAP = 27/364 = 7.4%

Fisher K, et al. *Surg Infect (Larchmt)*. 2017;18:827-33.

11

Pathogen Distribution for Antibiotic Susceptible, Antibiotic Resistant, and Viral Pneumonia*

Antibiotic Susceptible (n=63)		Antibiotic Resistant (n=104)		Viral (n=79)	
S. aureus	32 (50.8)	*S. aureus*	28 (26.9)	Rhinovirus/ Enterovirus	20 (25.3)
S. pneumoniae	9 (14.3)	*P. aeruginosa*	23 (22.1)	Influenza A	12 (15.2)
K. pneumoniae	8 (12.7)	*S. maltophilia*	10 (9.6)	RSV	11 (13.9)
H. influenzae	4 (6.3)	*Enterobacter* spp.	10 (9.6)	Coronavirus	11(13.9)
E. coli	3 (4.8)	*A. fumigatus*	7 (6.7)	Metapneumovirus	8 (10.1)
M. catarrhalis	3 (4.8)	*E. coli*	5 (4.8)	Parainfluenza	7 (8.9)
Proteus spp.	3 (4.8)	*K. pneumoniae*	3 (2.9)	Adenovirus	6 (7.6)
M. morganii	2 (3.2)	*A. baumannii*	3 (2.9)	Cytomegalovirus	5 (6.3)
C. koseri	1 (1.6)	*Achromobacter* spp.	3 (2.9)	Influenza B	1 (1.3)
P. stuartii	1 (1.6)	*Providencia* spp.	3 (2.9)		
		L. pneumophila	3 (2.9)		
		Other	11 (10.6)		

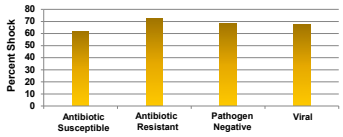
*During 2016, 364 patients with pneumonia during mechanical ventilation (118 [32.4%] were pathogen negative)

Fisher K, et al. *Surg Infect (Larchmt)*. 2017;18:827-33.

12

Predictors of Mortality – Multivariable Logistic Regression

Variables	aOR	95% CI	*P* Value
Age (1-point increments)	1.05	1.03 – 1.07	0.032
Male gender	3.67	2.02 – 6.67	0.030
APACHE II Score (1-point)	1.14	1.09 – 1.19	0.003
Shock	10.69	5.21 – 21.93	0.001
Inappropriate initial antibiotic	5.28	2.72 – 10.22	0.012



Fisher K, et al. *Surg Infect (Larchmt).* 2017;18:827-33.

13

Case-Control Study Non-Ventilated HAP

Outcome	Cases - NVHAP n = 174	Controls w/o NVHAP n = 696	*P* Value
ICU admit, No. (%)	98 (56.3)	159 (22.8)	< .01
MV, No. (%)	33 (19)	27 (3.9)	< .01
Mortality, No. (%)	27 (15.5)	11 (1.6)	< .01
Hospital LOS, d, range	15.9 (9.8–26.3)	4.4 (2.9–7.3)	< .01
Readmit 30 d, No. (%)	37 (25.2)	145 (21.2)	.29

Mortality Predictors

Variable	Adjusted OR	95% CI	*P* Value
HAP	8.4	5.6–12.5	< .01
MV*	8.0	5.3–11.9	< .01
Charlson Score (1-point increments)	1.2	1.1–1.2	.01

*Ventilated HAP

Micek ST, et al. *Chest.* 2016;150:991-992.

14

15

TABLE 4. INITIAL EMPIRIC THERAPY FOR HOSPITAL-ACQUIRED PNEUMONIA, VENTILATOR-ASSOCIATED PNEUMONIA, AND HEALTHCARE-ASSOCIATED PNEUMONIA IN PATIENTS WITH LATE-ONSET DISEASE OR RISK FACTORS FOR MULTIDRUG-RESISTANT PATHOGENS AND ALL DISEASE SEVERITY

Potential Pathogens	Combination Antibiotic Therapy*
Pathogens listed in Table 3 and MDR pathogens *Pseudomonas aeruginosa* *Klebsiella pneumoniae* (ESBL+)† *Acinetobacter* species†	Antipseudomonal cephalosporin (cefepime, ceftazidime) or Antipseudomonal carbepenem (imipenem or meropenem) or β-Lactam/β-lactamase inhibitor (piperacillin–tazobactam) *plus* Antipseudomonal fluoroquinolone‡ (ciprofloxacin or levofloxacin) or Aminoglycoside (amikacin, gentamicin, or tobramycin) *plus*
Methicillin-resistant *Staphylococcus aureus* (MRSA) *Legionella pneumophila*§	Linezolid or vancomycin‖

HCAP Requires Broad-spectrum Empiric Therapy (2005 ATS/IDSA)

Agent 1 + Agent 2 + Agent 3

ATS/IDSA. *Am J Resp Crit Care Med.* 2005;171:388-416.

16

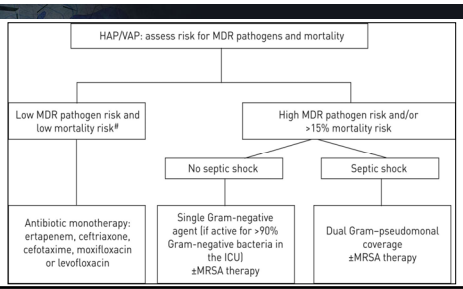
2016 ATS/IDSA: Empiric Antibiotic Therapy for HAP/VAP

Gram-Positive Antibiotics with MRSA Activity	Gram-Negative Antibiotics with Antipseudomonal Activity: β-Lactam-Based Agents	Gram-Negative Antibiotics with Antipseudomonal Activity: Non β-Lactam-Based Agents
Glycopeptides • Vancomycin 15mg/kg IV q8-12h (consider a loading dose of 25-30 mg/kg x 1 for severe illness)	**Antipseudomonal pencillins** • Piperacillin-tazobactam 4.5 g IV q6h	**Fluoroquinolones** • Ciprofloxacin 400 mg IV q8h • Levofloxacin 750 mg IV q24h
OR	**OR**	**OR**
Oxazolidinones • Linezolid 600 mg IV q12h	**Cephalosporins** • Cefepime 2 g IV q8h • Ceftazidime 2 g IV q8h	**Aminoglycosides** • Amikacin 15-20 mg/kg IV q24h • Gentamicin 5-7 mg/kg IV q24h • Tobramysin 5-7 mg/kg IV q24h
	OR	**OR**
	Carbapenems • Imipenem 500 mg IV q6h • Meropenem 1 g IV q8h	**Polymyxins** • Colistin 5 mg/kg IV x 1 (loading dose) followed by 2.5 mg x (1.5 x CrCl +30) IV q12h (maintenance dose) • Polymyxin B 2.5-3.0 mg/kg/d divided in 2 daily IV doses
	OR	
	Monobactams • Aztreonam 2 g IV q8h	

Kalil AC, et al. *Clin Infect Dis.* 2016;63:e61-111.

17

ERS/ESICM/ESCMID/ALAT 2017: Empiric Antibiotic Algorithm for HAP/VAP

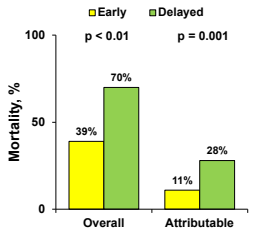


Torres A, et al. *Eur Respir J.* 2017;50: pii: 1700582.

18

Early Appropriate Therapy is Critical in ICU NP/VAP

- 107 patients with VAP
- Mean time from diagnosis of VAP to initiation of appropriate therapy was:
  - 28.6 hr in delayed group
  - 12.5 hr in early group



Iregui M, et al. *Chest.* 2002;122:262-268.

19

[Editorial]

CHEST

CAP, HCAP, HAP, VAP
The Diachronic Linguistics of Pneumonia

Jason P. Burnham, MD
Marin H. Kollef, MD, FCCP
St. Louis, MO

In this issue of *CHEST*, Corrado et al[1] report their experience with 283,927 cases of pneumonia in New York City hospitals from 2010 to 2014. They characterize the epidemiology of pneumonia by categorizing cases into community-acquired pneumonia (CAP), health care-

Recent guidelines have recommended elimination of the term *HCAP* from the medical lexicon,[1] thereby leaving providers with little guidance on how best to characterize patients admitted from the community who are at risk for drug-resistant pneumonia and, as evidenced by this study, at risk for mortality.

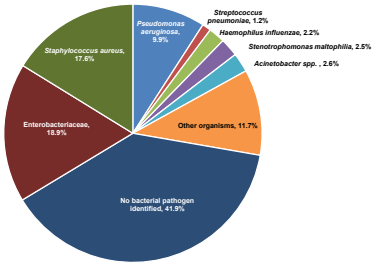
The term *HCAP* was initially developed to identify patients with risk factors for drug-resistant infections, in an effort to prevent inappropriate empiric antimicrobial therapy, a known risk factor for mortality in sepsis.[4,5] Unfortunately, adherence to HCAP treatment guidelines has resulted in increased usage of broad-spectrum antimicrobials without an increase in the isolation of drug-resistant organisms over time.[3] In addition, HCAP criteria were shown to be poorly predictive of mortality.[2] Use of empiric broad-spectrum antimicrobials based on

"In summary, rapid diagnostic tests are needed to identify drug-resistant pathogens and reduce time to appropriate antimicrobial therapy. In addition, national and/or international repositories of drug-resistant pathogens are needed to be able to correlate pathogen characteristics, drug resistance profiles, and treatment choices with clinical outcomes on a large scale."

Burnham JP, Kollef MH. *Chest.* 2017;152:909-910.

20

Pathogens Associated with HABP/VABP



Clinical Trials Transformation Initiative (CTTI) HABP/VABP Risk Factors. Available at: https://www.ctti-clinicaltrials.org/projects/habpvabp-studies.

21

Diagnostic Options

Technology	ID/AST	Examples	Pathogen/Resistance Detection	Turnaround Time	Clinical Considerations
Real time PCR	+ / -	Xpert® MRSA/SA BC	MRSA, MSSA, mec A/C	≤ 2 hr	• Prompt differentiation between MRSA and MSSA
	+ / -	BD Max™ MRSA Staph SR/XT	MRSA, MSSA, mec A/C	≤ 2 hr	
Multiplex PCR	+ / -	Biofire Filmarray® BC	GBP, GNB, *Candida* spp., mecA, vanA/B, KPC	≤ 2 hr	• Comprehensive number of targets • Not Gram-stain dependent
	+ / -	Verigene® BC-GP	GPB, mecA, vanA/B	2.5 hr	
	+ / -	Verigene® BC-GN	GNB, CTX-M, IMP, KPC, NDM, OXA, VIM	2 hr	
	+ / -	Curetis Unyuero™ BCU	GPB, GNB, fungal panel, mycobacteria, 16 resistance genes	4 hr	
	+ / -	Icubate IC GPC	GPC, mec A, vanA, vanB	4-5hr	• Many false neg for *S. pneumoniae*
MALDI-TOF MS	+ / -	bioMérieux VITEK® MS	Database for bacteria, fungi, mycobacteria, molds	<2 hr	• Detect many potential pathogens • Able to detect limited resistance mechanisms
	+ / -	Bruker Sepsityper®		<2 hr	
PNA-FISH	+ / -	AdvanDx QuickFISH®	GPB, GNB, *Candida* spp.	<2 hr	• Limited target detection • Rapid phenotypic AST

Vazquez Guillamet CA, et al. *Semin Respir Crit Care Med.* 2019 Aug;40(4):454-464.

22

Curetis

Group	Pathogen
Gram-positive bacteria	*Staphylococcus aureus*
	Streptococcus pneumoniae
Enterobacteriaceae	*Citrobacter freundii*
	Escherichia coli
	Enterobacter cloacae complex
	Enterobacter aerogenes
	Proteus spp.
	Klebsiella pneumoniae
	Klebsiella oxytoca
	Klebsiella varicola
	Serratia marcescens
	Morganella morganii
Non-fermenting bacteria	*Moraxella catarrhalis*
	Pseudomonas aeruginosa
	Acinetobacter baumanni complex
	Stenotrophomonas maltophilia
	Legionella pneumophila
Others / Fungi	*Pneumocystis jirovecii*
	Heamophilus influenzae
	Mycoplasma pneumoniae
	Chlamydophila pneumoniae

Gene	Resistance Against
ermB	Macrolide/Lincosamide
mecA	Oxacillin
mecC (LGA251)	Oxacillin
tem	Penicillin
shv	Penicillin
ctx-M	3rd generation cephalosporins
kpc	Carbapenem
imp	Carbapenem
ndm	Carbapenem
oxa-23	Carbapenem
oxa-24/40	Carbapenem
oxa-48	Carbapenem
oxa-58	Carbapenem
vim	Carbapenem
sulf	Sulfonamide
gyrA83	Fluoroquinolone
gyrA87	Fluoroquinolone

Biofire

Organism	Organism
Acinetobacter	Adenovirus
E. coli	Coronavirus
Enterobacter	FluA
H. influenzae	FluB
K. oxytoca	hMPV
K. pneumoniae	HRV
M. catarrhallis	PIV
P. aeruginosa	RSV
Proteus spp.	MERS-CoV
S. agalactiae	*C. pneumoniae*
S. aureus	*M. pneumoniae*
MREJ-mecA/C	*Cryptococcus*
S. marcescens	*P. jiroveci*
S. pneumoniae	CTX-M
S. pyogenes	IMP
	KPC
	NDM
	VIM
	OXA-48

23

New Antibiotics

	MRSA	ESBL	CRE-KPC	CRE-OXA48	CRE-MBL	MDR pseudomonas	MDR acinteobater
Tedizolid	Yes	No	No	No	No	No	No
Cefiderocol	No	Yes	Yes	Yes	Yes	Yes	Yes
Ceftaroline/avibactam	Yes	Yes	Yes	Yes	Yes	Yes	No
Ceftolozane/tazobactam	No	Yes	No	No	No	Yes	No
Ceftazidime–avibactam	No	Yes	Yes	Yes	No	Yes	No[a]
Meropenem–vaborbactam	No	Yes	Yes	No	No	No[a]	No[a]
Imipenem–relebactam	No	Yes	Yes	No	No	No[a]	No[a]
Aztreonam–avibactam	No	Yes	Yes	Yes	Yes	Yes	No
Plazomicin	Yes	Yes	Yes	Yes	Yes[b]	Yes	No
Eravacyclin	Yes	Yes	Yes	Yes	Yes	No	Yes
Murepavadin	No	No	No	No	No	Yes	No

CRE, carbapenem-resistant Enterobacteriacae; ESBL extended-spectrum beta-lactamase; MBL, metallo-β-lactamase; KPC, Klebsiella pneumoniae carbapenemase; MDR, multidrug-resistant; MRSA, methicillin-resistant Staphylococcus aureus; NDM, New Delhi metallo-betalactamase; OXA, oxacillinase.
[a]Actives against no MDR-resistant strains.
[b]Not active against many NDMs.

Bassetti M, et al. *Curr Opin Infect Dis.* 2018;31:177-86.

24

Newer Agents for Nosocomial Pneumonia

- **Ceftazidime-avibactam: FDA-approved indication**
- **Ceftolozane-tazobactam: FDA-approved indication – NEW DOSE**
- **Currently none of the other agents with indications for nosocomial pneumonia**

25

Ceftazidime-Avibactam for Nosocomial Pneumonia: REPROVE Trial

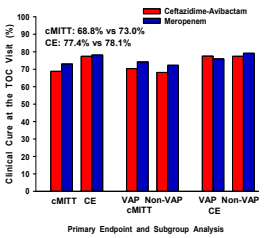
- Compared ceftazidime-avibactam (2000-500 mg q8h) vs meropenem (1000 mg q8h) in adults with nosocomial pneumonia
  - About 1/3 VAP
  - APACHE II score 20–30: ~13.5%
- Predominant pathogens:
  - *K. pneumoniae* (n=130, 36.6%)
  - *P. aeruginosa* (n=105, 29.6%)
  - *S. aureus* (n=58, 16.3%)
  - Polymicrobial: ~20%

Torres A, et al. *Lancet Infect Dis*. 2018;18:285-295.

26

Ceftazidime-avibactam for Nosocomial Pneumonia

Phase 3, Randomized, Multicenter Study (REPROVE Study)



Torres A, et al. *Lancet Infect Dis*. 2018;18:285-295.

Secondary Efficacy Endpoints

Per Pathogen Clinical Cure Rates and Favorable Microbiological Response at TOC	Ceftazidime-Avibactam	Meropenem
Clinical Cure		
K. pneumoniae	83.8% (31/37)	79.6% (39/49)
P. aeruginosa	64.3% (27/42)	77.1% (27/35)
eME		
K. pneumoniae	78.4% (29/37)	79.6% (39/49)
P. aeruginosa	42.9% (18/42)	40.0% (14/35)

TOC, test-of-cure ; cMITT, clinically modified intent-to-treat; CE, clinically evaluable; mMITT, microbiological MITT; eME, extended microbiologically evaluable population

27

ASPECT-NP: a randomised, controlled, double-blind, phase 3, non-inferiority trial of ceftolozane/tazobactam versus meropenem for treatment of nosocomial pneumonia

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Key Points: **1) All patients were ventilated**
2) Used a 3 g dose of ceftolozane/tazobactam

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* Please note that since this live meeting, the study has been published online at *Lancet Infect Dis* 2019.

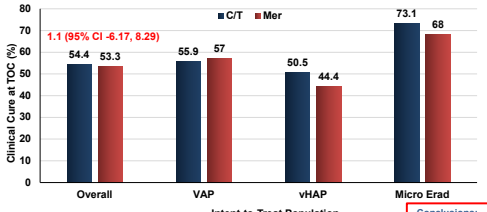
28

Baseline LRT pathogen (mITT population)	N=264	N=247
Gram-negative pathogens, n (%)	259 (98.1%)	240 (97.2%)
Pseudomonas aeruginosa, n (%)	63 (23.9%)	65 (26.3%)
MDR, n (%)	24 (9.1%)	11 (4.5%)
XDR, n (%)	10 (3.8%)	5 (2.0%)
Enterobacteriaceae, n (%)	195 (73.9%)	185 (74.9%)

Kollef MH, et al. *Lancet Infect Dis*. 2019;pii: S1473-3099(19)30403-7 [Epub ahead of print].

29

ASPECT-NP Results: Clinical Cure at Test-of-Cure (TOC)

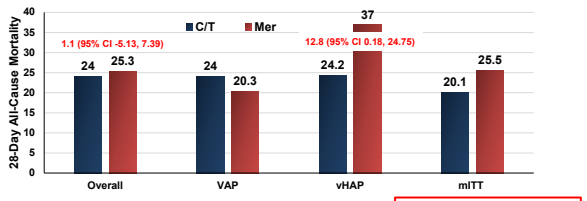


Conclusions:
- Non-inferior in all patient populations

Kollef MH, et al. *Lancet Infect Dis*. 2019;pii: S1473-3099(19)30403-7 [Epub ahead of print].
Kollef M, et al. Poster presented at ECCMID (April 13-16, 2019), Amsterdam, poster Abstract #P1917.

30

ASPECT-NP Results: 28-Day All-Cause Mortality



Conclusions:
- Non-inferior in overall patient population
- Advantage with ceftolozane-tazobactam among ventilated HAP

Kollef MH, et al. *Lancet Infect Dis*. 2019;pii: S1473-3099(19)30403-7 [Epub ahead of print].
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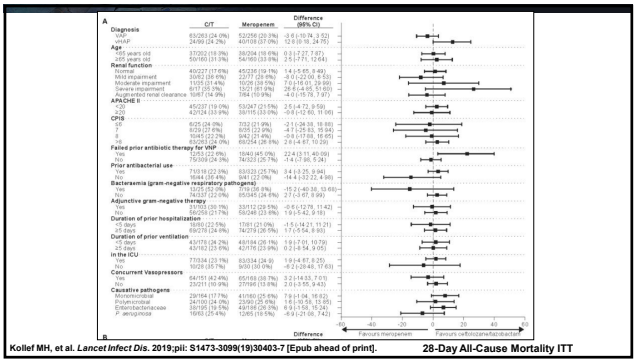
31



Kollef MH, et al. *Lancet Infect Dis*. 2019;pii: S1473-3099(19)30403-7 [Epub ahead of print].

32

ASPECT-NP: Results by Pathogen

Microbiological Eradication in Microbiologically Evaluable Population

Pathogen	C/T n /N (%)	MER n/N (%)	% Treatment Difference (95% CI)
Overall	79/113 (69.9)	73/117 (62.4)	7.5 (-4.69, 19.38)
Enterobacteriaceae	57/83 (68.7)	59/90 (65.6)	3.1 (-10.80, 16.75)
ESBL+	30/45 (66.7)	27/39 (69.2)	-2.6 (-21.59, 17.14)
Enterobacteriaceae	18/23 (78.3)	17/23 (73.9)	4.3 (-19.94, 28.04)
E. coli	10/12 (83.3)	6/7 (85.7)	-2.4 (-32.86, 36.53)
ESBL+ *E. coli*	30/42 (71.4)	32/48 (66.7)	4.8 (-14.23, 22.92)
K. pneumoniae	20/30 (66.7)	18/27 (66.7)	0.0 (-23.15, 23.54)
ESBL+ *K. pneumoniae*			
P. aeruginosa	23/29 (79.3)	21/38 (55.3)	24.0 (1.11, 43.01)
H. influenzae	11/12 (91.7)	4/8 (50.0)	41.7 (2.39, 70.96)

Martin-Loeches I, et al. Poster presented at ECCMID (April 13-16, 2019), Amsterdam, poster Abstract #O0302.

33

ASPECT-NP: Ceftolozane/tazobactam (C/T) vs. Meropenem (MER) for HABP/VABP

- **No significant differences in safety profile in critically ill patients**
- **Benefit in subgroup of patients who had failed prior therapy**
  - **Clinical cure at TOC: C/T: 49.1%**
    MER: 37.5%
- **NOTE: All ventilated patients**
  Dose was 3 grams q8 hours (not lower dose approved for cUTI/cIAI)

Martin-Loeches I, et al. Poster presented at ECCMID (April 13-16, 2019), Amsterdam, poster Abstract #O0302.

34

Conclusions

- HABP/VABP is an important nosocomial infection frequently caused by antibiotic-resistant bacteria including *Pseudomonas aeruginosa*.
- Early antibiotic therapy appropriate for the causative pathogens for HABP/VABP will be associated with improved outcomes including lower mortality.
- Clinicians caring for patients with HABP/VABP should be aware of when to consider the empiric use of newer antimicrobial agents in patients at risk for infection with carbapenem-resistant GNB or based on rapid microbiologic testing.

35