ECCMID 2021 | Poster #01048

Activity of Meropenem-Vaborbactam and Comparators against *Pseudomonas aeruginosa* Isolates from Patients with Pneumonia in European Hospitals

Dee Shortridge, Jennifer M. Streit, Cecilia Carvalhaes, Mariana Castanheira
JMI Laboratories, North Liberty, IA, USA

Introduction

- Meropenem-vaborbactam (MVB) is a combination of a carbapenem and a carbapenemase inhibitor developed to inhibit serine carbapenemases, such as KPC.
- MVB is approved in Europe for the treatment of complicated urinary tract infection (cUTI), including acute pyelonephritis, complicated intra-abdominal infection (cIAI), hospital-acquired bacterial pneumonia (HAP), ventilator-associated pneumonia (VAP), and bacteremia (BSI) associated with any of the infections listed above.
- This study examined the activity of MVB and comparators against *P. aeruginosa* collected from patients hospitalized with pneumonia in Europe during 2016–2020.
- Isolates from patients in the intensive care unit (ICU) and those with VAP were analysed as subsets, as were Eastern vs. Western European isolates.

Materials and Methods

- A total of 2,926 *P. aeruginosa* isolates were consecutively collected from patients hospitalized with pneumonia in 36 European hospitals from 19 countries during 2016–2020.
  - Isolates were identified by the submitting sites.
  - Isolates were confirmed at JMI Laboratories using MALDI-TOF.
- Susceptibility testing was performed using the broth microdilution method.
  - EUCAST (2021) interpretive criteria were used.
  - An arbitrary susceptible breakpoint of ≤0.001 mg/L has been published by EUCAST for several agents—including cefepime, ceftazidime, levofloxacin, and piperacillin-tazobactam—when applied to *Pseudomonas* spp.
  - In these cases, "susceptible" should not be reported for this organism-agent combination and intermediate should be interpreted as "susceptible, increased exposure."
- Isolates were analyzed for ICU patients and patients with VAP.
  - There were 1,083 ICU isolates and 679 VAP isolates.
  - The designations of ICU and VAP were made by the submitting site.
- Isolate susceptibilities were also analyzed by Eastern (n=986) and Western (n=1,940) Europe.
  - Eastern Europe included the following 10 countries: Belarus, Czech Republic, Greece, Israel, Hungary, Poland, Romania, Russia, Slovenia, and Turkey.
  - Western Europe included the following 11 countries: Belgium, Denmark, France, Germany, Ireland, Italy, Portugal, Spain, Sweden, Switzerland, and the United Kingdom.

Results

- *Pseudomonas aeruginosa* was the most common Gram-negative pathogen isolated from patients hospitalized with pneumonia for all patients, ICU patients, and patients with VAP (Figure 1).
- The susceptibilities of meropenem-vaborbactam and its comparators tested against *P. aeruginosa* isolates and isolate groups are shown in Table 1.
- MIC distributions for meropenem-vaborbactam and meropenem are shown in Table 2.
  - Meropenem-vaborbactam EUCAST breakpoints (≤8/–/>8 mg/L) are higher than meropenem alone (≤2/-/>8 mg/L).
  - The higher meropenem-vaborbactam breakpoints are a result of the higher standard dosing for meropenem-vaborbactam than meropenem alone.
- Meropenem-vaborbactam was the most active beta-lactam tested, with a susceptibility of 82.4% for all isolates (Table 1).
  - Isolates from patients in ICU had lower susceptibilities than non-ICU patients for all drugs tested, including meropenem-vaborbactam (72.1%).
  - Isolates from patients with VAP had the lowest susceptibilities (67.2%).
- Meropenem susceptibility was 67.9% for all isolates, 55.9% for ICU isolates, and 51.1% for VAP isolates.
- The comparison of meropenem-vaborbactam and meropenem susceptibilities between Eastern and Western Europe demonstrated that Eastern Europe had higher levels of resistance to both drugs (Figure 2).
  - Western European susceptibility was 89.0% for all isolates, 83.0% for ICU isolates, and 84.5% for VAP isolates.
  - Eastern European susceptibility was 69.6% for all isolates, 58.5% for ICU isolates, and 56.1% for VAP isolates.
- Amikacin susceptibility was slightly higher than meropenem-vaborbactam for all (86.2%), ICU (82.6%), and VAP (78.3%) isolates.
- Colistin had the highest susceptibility for all 3 groups.
- Other comparator agents inhibited <80% of isolates at the susceptible, increased exposure breakpoint established by EUCAST (Table 1).

Conclusions

- These results demonstrate meropenem-vaborbactam had a higher rate of susceptibility than either the comparators or meropenem alone, except for amikacin and colistin.
  - Amikacin and colistin are not considered first-line therapies for systemic use due to toxicity.
- These *in vitro* results suggest that meropenem-vaborbactam may be an effective therapy for patients hospitalized with pneumonia caused by *P. aeruginosa*, including patients in ICU and those with VAP.

Table 1. Activity of meropenem-vaborbactam and comparators stratified against all European *P. aeruginosa* isolates from patients hospitalized with pneumonia (PHP), isolates from PHP in the ICU, and ICU patients with VAP

	All isolates n= 2,926			ICU isolates n=1,083			VAP isolates n=679		
Antimicrobial agent	%S [a]	%I	%R	%S	%I	%R	%S	%I	%R
Meropenem-vaborbactam	82.4		17.6	72.1		27.9	67.2		32.8
Meropenem	67.9	14.6	17.5	55.9	16.9	27.2	51.1	16.8	32.1
Amikacin	86.2 [b]		13.8	82.6 [b]		17.4	78.3 [b]		21.7
Colistin	99.5		0.5	99.6		0.4	99.6		0.4
Cefepime	[c]	77.3	22.7	[c]	70.3	29.7	[c]	68.2	31.8
Ceftazidime	[c]	74.4	25.6	[c]	67.2	32.8	[c]	64.2	35.8
Levofloxacin	[c]	60.1	39.9	[c]	56.9	43.1	[c]	49.9	50.1
Piperacillin-tazobactam	[c]	69.9	30.1	[c]	62.5	37.5	[c]	59.1	40.9

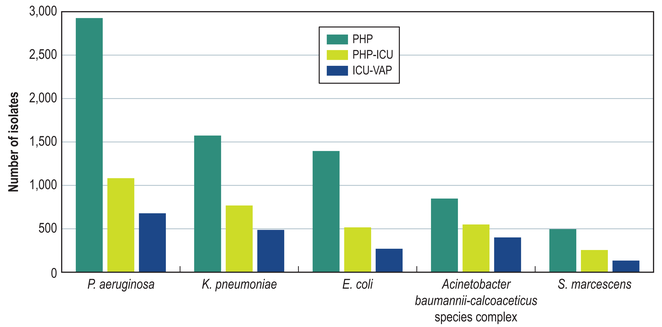
[a] Criteria as published by EUCAST (2021).
[b] For infections originating from the urinary tract. For systemic infections, aminoglycosides must be used in combination with another active therapy.
[c] An arbitrary susceptible breakpoint of ≤0.001 mg/L has been published by EUCAST indicating that susceptible should not be reported for this organism-agent combination and intermediate should be interpreted as susceptible increased exposure.

Table 2. MIC distribution of meropenem-vaborbactam and meropenem tested against *P. aeruginosa* pneumonia isolates

Antimicrobial Agent	Dilution (mg/L) 0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	>	Total	MIC_{50}	MIC_{90}
All isolates																
Meropenem-vaborbactam	38	61	168	281	465	515	293	184	206	201	212	140	162	2926	0.5	32
	1.3%	3.4%	9.1%	18.7%	34.6%	52.2%	62.2%	68.5%	75.6%	82.4%	89.7%	94.5%	100.0%			
Meropenem	22	42	137	279	521	496	307	184	204	222	208	139	165	2926	0.5	32
	0.8%	2.2%	6.9%	16.4%	34.2%	51.2%	61.7%	67.9%	74.9%	82.5%	89.6%	94.4%	100.0%			
ICU isolates																
Meropenem-vaborbactam	3	7	28	69	153	187	110	51	82	91	125	73	104	1083	1	32
	0.3%	0.9%	3.5%	9.9%	24.0%	41.3%	51.4%	56.1%	63.7%	72.1%	83.7%	90.4%	100.0%			
Meropenem	2	4	23	73	166	171	115	51	84	99	121	69	105	1083	1	32
	0.2%	0.6%	2.7%	9.4%	24.7%	40.5%	51.2%	55.9%	63.6%	72.8%	83.9%	90.3%	100.0%			
VAP isolates																
Meropenem-vaborbactam	2	4	14	41	86	103	69	31	54	52	86	59	78	679	2	>32
	0.3%	0.9%	2.9%	9.0%	21.6%	36.8%	47.0%	51.5%	59.5%	67.2%	79.8%	88.5%	100.0%			
Meropenem	2	3	10	43	93	87	74	35	58	56	85	55	78	679	2	>32
	0.3%	0.7%	2.2%	8.5%	22.2%	35.1%	45.9%	51.1%	59.6%	67.9%	80.4%	88.5%	100.0%			

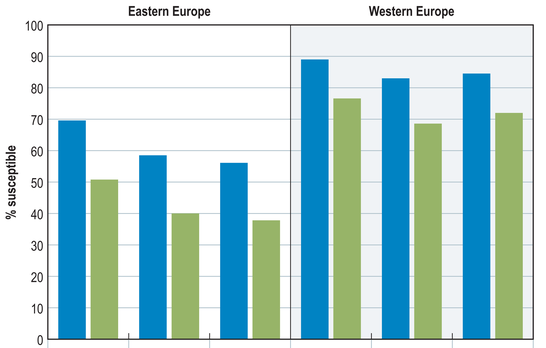
EUCAST (2021) breakpoints are shaded green for susceptible, yellow for intermediate, and red for resistant.
Non-meningitis breakpoints are shown for meropenem.

Figure 1. Most common Gram-negative organisms isolated from patients hospitalized with pneumonia (PHP) in Europe, PHP in the ICU, and ICU-VAP



Patients hospitalized with pneumonia (PHP), PHP in the intensive care unit (PHP-ICU), and ICU patients with ventilator associated pneumonia (ICU-VAP).

Figure 2. Comparison of the susceptibilities of Eastern and Western European *P. aeruginosa* isolates from patients hospitalized with pneumonia (PHP) in Europe, PHP in the ICU, and ICU-VAP, all tested against meropenem-vaborbactam and meropenem



	All East	ICU East	VAP East	All West	ICU West	VAP West
Meropenem-vaborbactam	69.6	58.5	56.1	89.0	83.0	84.5
Meropenem	50.8	40.0	37.8	76.6	68.6	72.0

Acknowledgements

This poster has been funded by A. Menarini Industrie Farmaceutiche Riunite SRL.

References

CLSI. *M07 Eleventh edition. Methods for Dilution Antimicrobial Susceptibility Testing for Bacteria That Grow Aerobically.* Clinical and Laboratory Standards Institute, Wayne, PA, 2018.

EUCAST. The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters, v 11.0, January 1, 2021. http://www.eucast.org (Access Date Jan 31, 2021).

Contact

Dee Shortridge
JMI Laboratories
345 Beaver Kreek Centre, Suite A
North Liberty, Iowa 52317
Phone: 319-665-3370
Email: dee-shortridge@jmilabs.com

To obtain a PDF of this poster:
Scan the QR code or visit https://www.jmilabs.com/data/posters/ECCMID2021_MeroVaborVEuroPneumonia.pdf

Charges may apply. No personal information is stored.