VEQ Ciclo 2017 – RISULTATI2

Batteriologia,
Parassitologia,
Micobatteriologia

Consensus Meeting

19 Settembre 2018

Ore 14.30-18.30

Sede: Pad 3 - piano terreno - Aula Magna

I nuovi farmaci antibiotici: caratteristiche, spettro di azione e saggi di sensibilità

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Recenti Farmaci approvati FDA

Infections and Infectious Diseases

Dalvance (dalbavancin); Durata Therapeutics; For the treatment of acute bacterial skin and skin structure infections, Approved May 2014

Sivextro (tedizolid phosphate) ; Cubist Pharmaceuticals; For the treatment of acute bacterial skin and skin structure infections, Approved June 2014

Orbactiv (oritavancin); The Medicines Company; For the treatment of acute bacterial skin and skin structure infections, Approved August 2014

Zerbaxa (ceftolozane + tazobactam) ; Cubist Pharmaceuticals; For the treatment of complicated intra-abdominal and urinary tract infections, Approved December 2014

Avycaz (ceftazidime-avibactam); Actavis; For the treatment of complicated intra-abdominal and urinary tract infections, Approved February 2015

Baxdela (delafloxacin) tablets and injection; Melinta Therapeutics; For the treatment of acute bacterial skin and skin structure infections, Approved June 2017

Vabomere (meropenem and vaborbactam); The Medicines Company; For the treatment of complicated urinary tract infections , Approved August 2017

Nuovi farmaci per Gram-negativi multiresistenti

- **Nuovi antibiotici**
  - **Ceftolozano/tazobactam**
  - **Ceftazidime/avibactam**
  - *Meropenem-Vaborbactam*
  - *Imipenem-Relebactam*
  - *Aztreonam-avibactam*
  - *Cefiderocol*

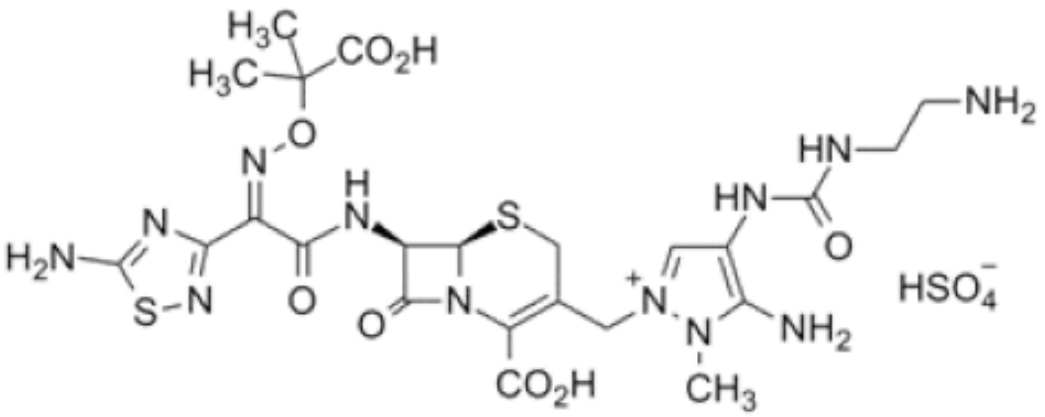
Enterobacteriaceae (new taxonomy: Enterobacterales*)

EUCAST Clinical Breakpoint Tables v. 8.1, valid from 2018-05-15

Cephalosporins[1]	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)	
	S ≤	R >		S ≥	R <
Cefaclor	-	-		-	-
Cefadroxil (uncomplicated UTI only)	16	16	30	12	12
Cefalexin (uncomplicated UTI only)	16	16	30	14	14
Cefazolin	-	-		-	-
Cefepime	1	4	30	27	24
Cefixime (uncomplicated UTI only)	1	1	5	17	17
Cefotaxime	1	2	5	20	17
Cefoxitin (screen)[2]	NA	NA	30	19	19
Cefpodoxime (uncomplicated UTI only)	1	1	10	21	21
Ceftaroline	0.5	0.5	5	23	23
Ceftazidime	1	4	10	22	19
Ceftazidime-avibactam	8[3]	8[3]	10-4	13	13
Ceftibuten (UTI only)	1	1	30	23	23
Ceftobiprole	0.25	0.25	5	23	23
Ceftolozane-tazobactam	1[4]	1[4]	30-10	23	23
Ceftriaxone	1	2	30	25	22
Cefuroxime iv[5], *E. coli, Klebsiella* spp. and *P. mirabilis*	8	8	30	19	19
Cefuroxime oral (uncomplicated UTI only)	8	8	30	19	19

Cephalosporins	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)	
	S ≤	R >		S ≥	R <
Cefaclor	-	-		-	-
Cefadroxil	-	-		-	-
Cefalexin	-	-		-	-
Cefazolin	-	-		-	-
Cefepime[1]	8	8	30	21	21
Cefixime	-	-		-	-
Cefotaxime	-	-		-	-
Cefoxitin	NA	NA		NA	NA
Cefpodoxime	-	-		-	-
Ceftaroline	-	-		-	-
Ceftazidime[2]	8	8	10	17	17
Ceftazidime-avibactam, *P. aeruginosa*	8[3]	8[3]	10-4	17	17
Ceftibuten	-	-		-	-
Ceftobiprole	IE	IE		IE	IE
Ceftolozane-tazobactam, *P. aeruginosa*	4[4]	4[4]	30-10	24	24
Ceftriaxone	-	-		-	-
Cefuroxime iv	-	-		-	-
Cefuroxime oral	-	-		-	-

Ceftolozane



- 3rd generation cefalosporin for injection, endowed with high anti-*Pseudomonas* activity
- Higher affinity and a broader inhibition profile toward the essential PBPs compared to ceftazidime

Zhanel *et al* – Drugs 2014
Moya *et al* – AAC 2010

Ceftolozane: attività anti-*Pseudomonas*

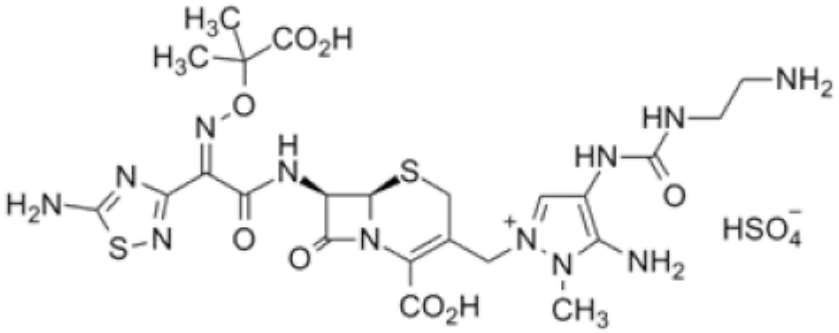
- Stable *vs*. *Psedomonas* AmpC beta-lactamase
- Entry independent of OprD porin
- Not affacted by efflux systems (MexAB, MexXY)

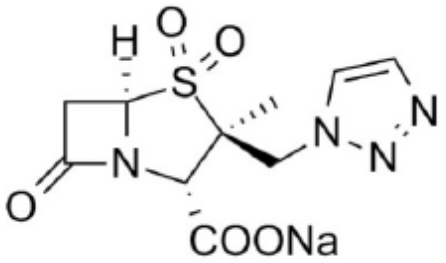
Resistance Mechanisms	Outer Membrane Porin Loss	β-lactamase Enzyme	Efflux Pump	Efflux Pump
	OprD	AmpC	MexXY	MexAB
Ceftolozane	●	●	●	●
Ceftazidime	●	○	●	○
Cefepime	●	◐	○	○
Piperacillin/tazobactam	●	○	●	○
Imipenem	○	●	●	●
Meropenem	◐	●	○	◐

● Not affected ◐ Partially affected ○ Affected

Castanheira *et al* – AAC 2014

Ceftolozane



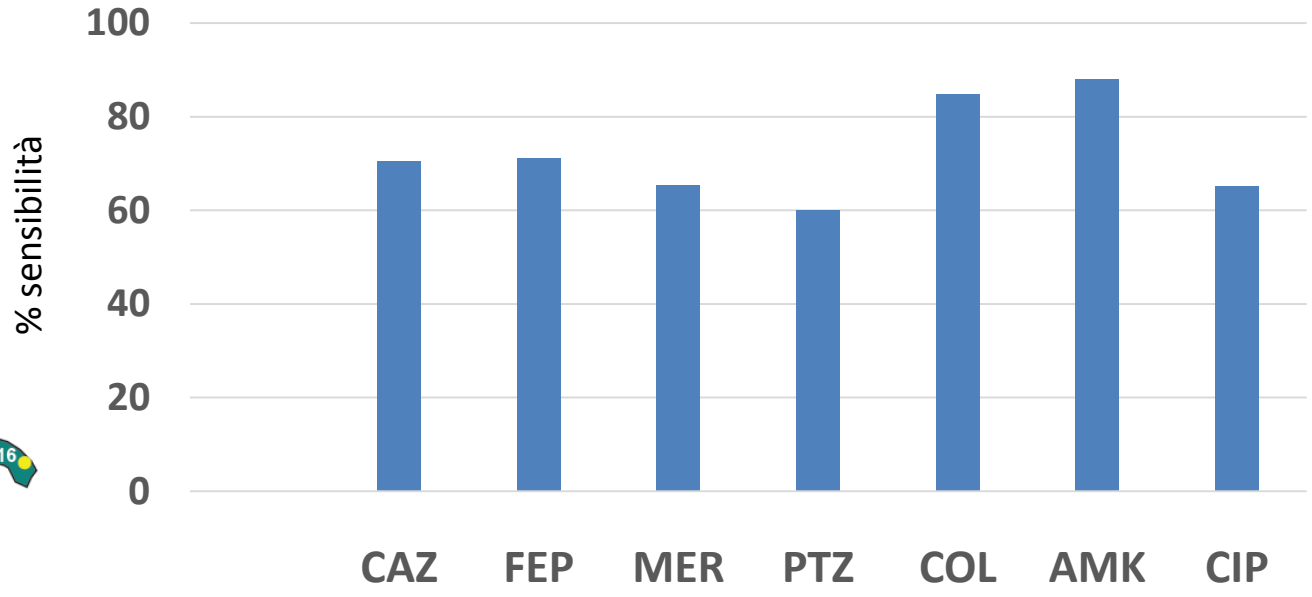


- Cefalosporin for injection, endowed with high anti-*Pseudomonas* activity
- Hydrolyzed by ESBLs
- Used in combination with tazobactam to cover ESBL+ enterics

Zhanel *et al* – Drugs 2014

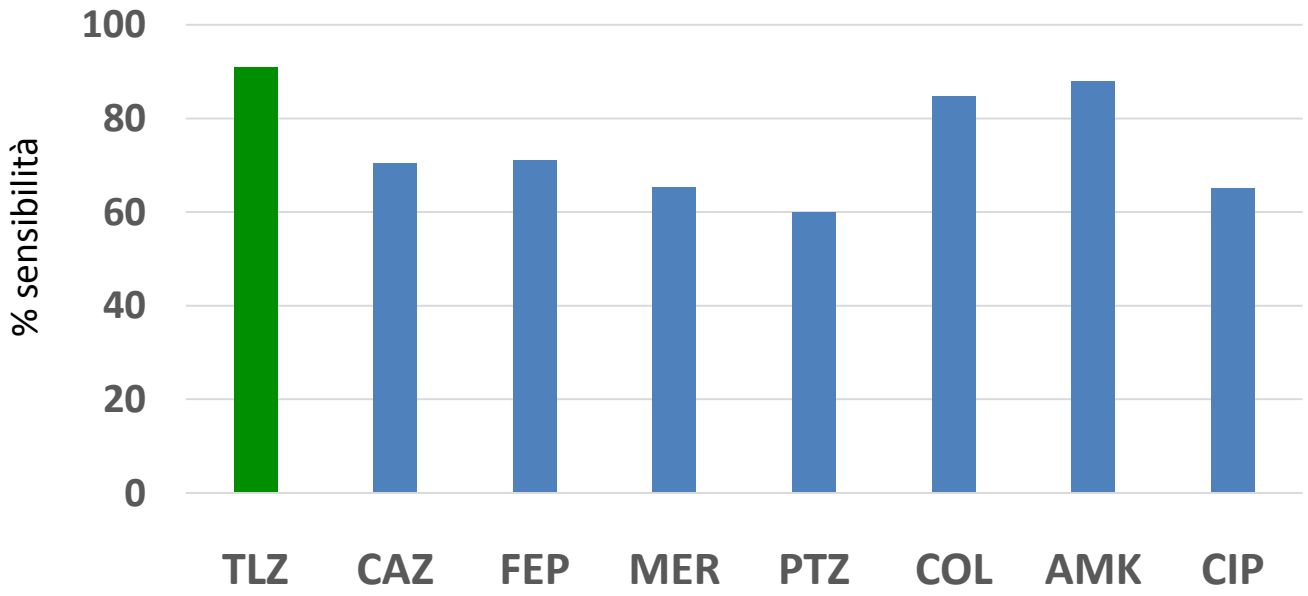
Studio italiano di sorveglianza su *P. aeruginosa* (20 centri, 2013-2014)

N = 939 isolati non-replicati da BSI o HAP/VAP



Giani *et al* – JAC 2017

Sensibilità ai farmaci *Pseudomonas aeruginosa* (N= 935 isolates from BSI and HAP/VAP)



Giani *et al* – JAC 2017

Sorveglianza Italiana su *P. aeruginosa* (2014)

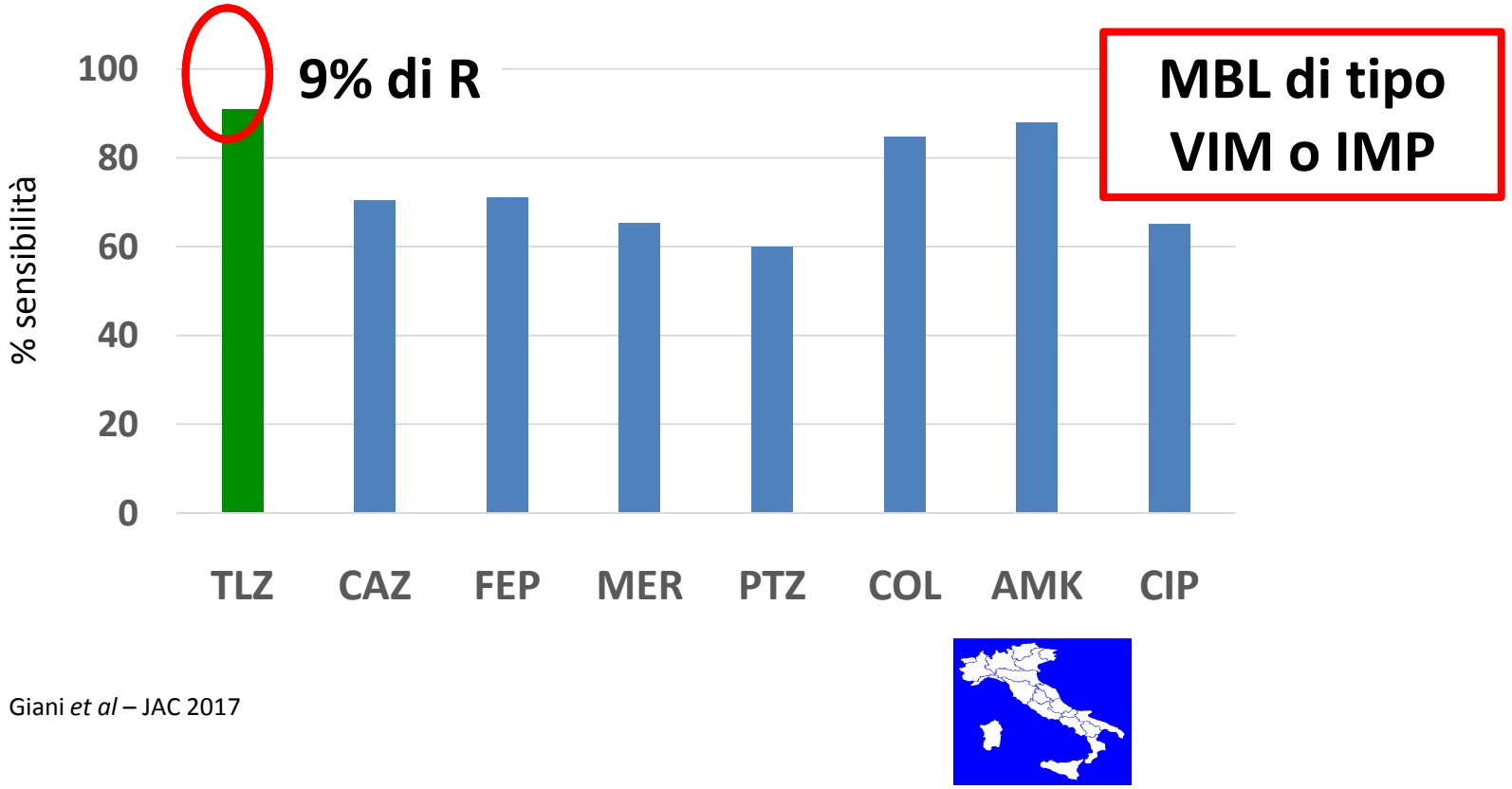
Antibiotic	MIC mg/L (S/I/R)
Pip/Tazo	>16 R
Ceftazidime	>8 R
Cefepime	>8 R
Aztreonam	>16 R
Imipenem	>8 R
Meropenem	>8 R
Amikacin	4 S
Gentamicin	>4 R
Ciprofloxacin	≤0.5 S
Colistin	1 S

CTZ attivo su 60% R a tutti i beta-lattamici

Antibiotic	MIC mg/L (S/I/R)
Pip/Tazo	>16 R
Ceftazidime	>8 R
Cefepime	>8 R
Aztreonam	>16 R
Imipenem	>8 R
Meropenem	>8 R
Amikacin	>16 R
Gentamicin	>4 R
Ciprofloxacin	>1 R
Colistin	2 S

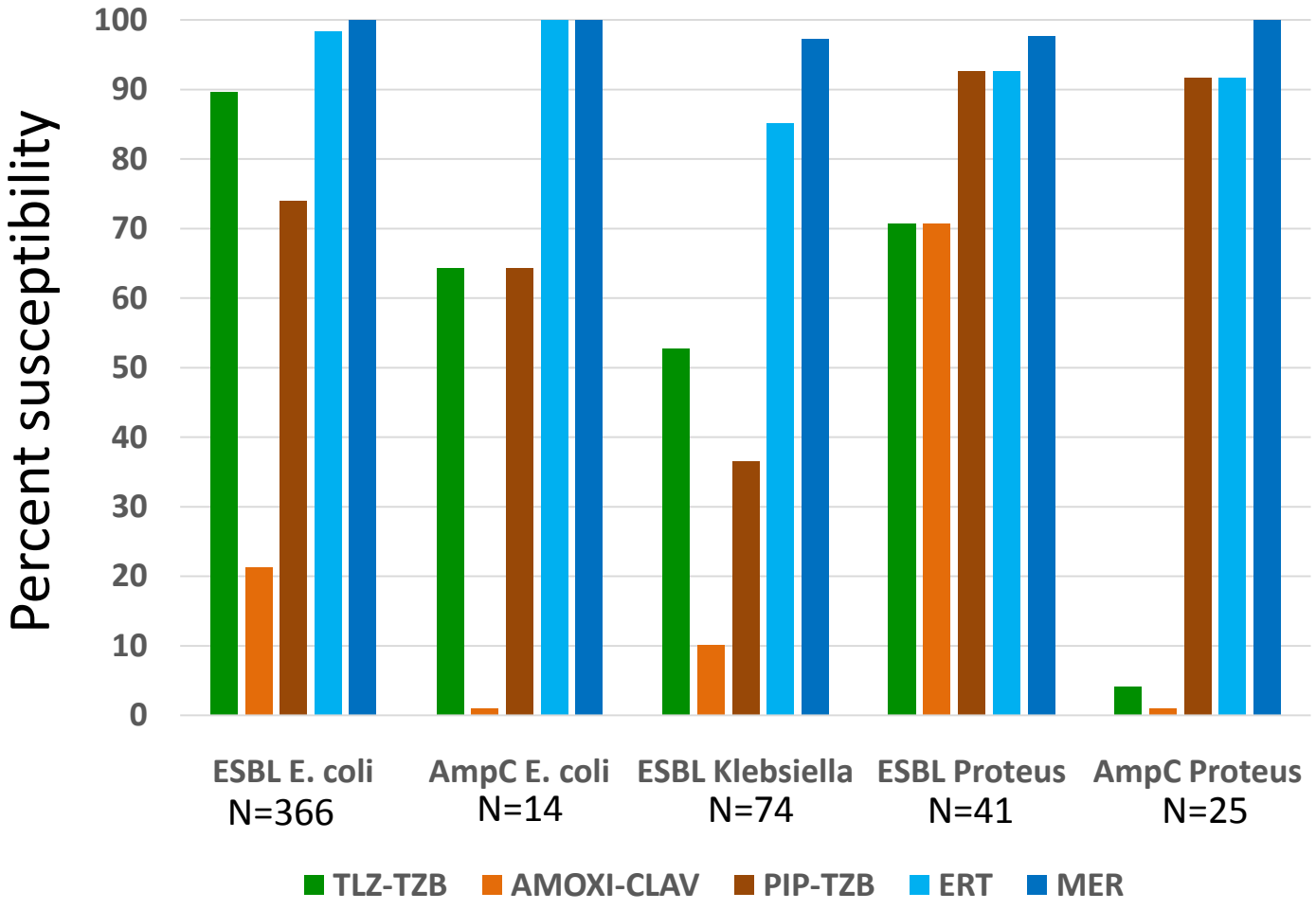
CTZ attivo su 50% ceppi COS

Sensibilità ai farmaci *Pseudomonas aeruginosa* (N= 935 isolates from BSI and HAP/VAP)



Giani *et al* – JAC 2017

CTZ activity vs. ESBL/AmpC-positive Enterobacterales from Italy



Studio AMCLI_CoSA, Rossolini et al, unpublished results

The Continued Value of Disk Diffusion for Assessing Antimicrobial Susceptibility in Clinical Laboratories: Report from the Clinical and Laboratory Standards Institute Methods Development and Standardization Working Group

Romney M. Humphries,[a] Susan Kircher,[b] Andrea Ferrell,[b] Kevin M. Krause,[c] Rianna Malherbe,[d] Andre Hsiung,[d] Carey-Ann D. Burnham[e]

TABLE 1 Summary of antimicrobial drugs approved since 2010 and times to AST devices

Antimicrobial agent	Month/year approved by FDA	Time (mo)[a] to: First disk clearance[b]	First gradient diffusion strip clearance	Manual MIC test (Sensititre) clearance	Rapid automated AST device clearance
Delafloxacin	6/2017	2	2	2	NA
Meropenem-vaborbactam	8/2017	2	4	4	6
Ceftazidime-avibactam	2/2015	8	7	10	25
Ceftolozane-tazobactam	12/2014	11	19	8	36
Dalbavancin	5/2014	ND	25	14	NA
Oritavancin	8/2014	ND	NA	7	NA
Tedizolid	6/2014	NA	36	15	NA
Ceftaroline	5/2010	7	29	14	34

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Test di ceftolozane/tazobactam

Shields et al. JCM, vol. 56, issue 2, February 2018

TABLE 2 Essential and categorical agreement between BMD and Etest or disk diffusion for testing susceptibility to ceftazidime-avibactam and ceftolozane-tazobactam[a]

Drug, pathogen (no. of isolates)	BMD			Etest			Disk diffusion	
	Median MIC (μg/ml)[b]	Range of MIC (μg/ml)[b]	No. (%) of resistant isolates	No. (%) of isolates with EA	No. (%) of isolates with CA	No. of errors	No. (%) of isolate with CA	No. of errors
Ceftazidime-avibactam, CRE (n = 74)	2	0.25–512	13 (18)	66 (89)	72 (97)	2 (VME)	56 (76)	18 (ME)
Ceftolozane-tazobactam, CRP (n = 72)	1	0.5–256	6 (8)	57 (79)	69 (96)	3 (minor)	68 (94)	4 (minor)

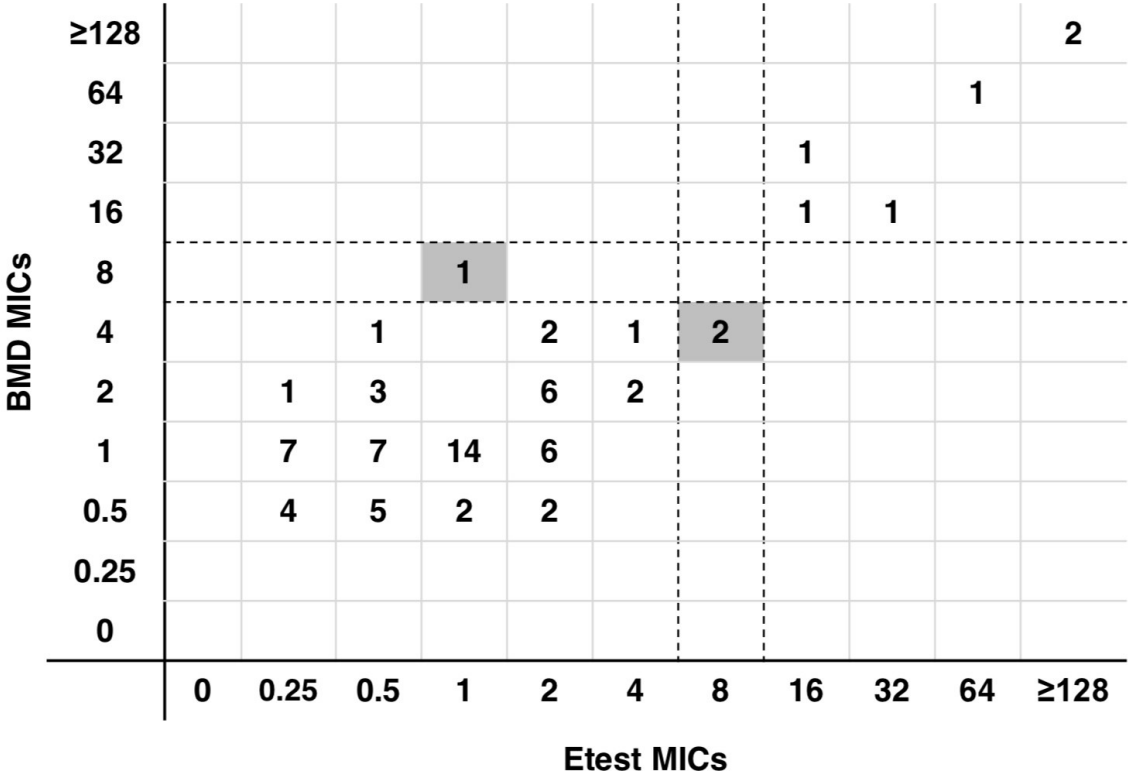
[a]BMD, broth microdilution; CA, categorical agreement; CRE, carbapenem-resistant *Enterobacteriaceae*; CRP, carbapenem-resistant *Pseudomonas aeruginosa*; EA, essential agreement; ME, major error; VME, very major error. Minor errors were identified as BMD results that were categorized as resistant or susceptible and Etest/disk diffusion results that were categorized as intermediate. Major errors were identified as BMD results that were categorized as susceptible and Etest/disk diffusion results that were categorized as resistant. Very major errors were identified as BMD results that were categorized as resistant and Etest/disk diffusion results that were categorized as susceptible.

CTZ Etest correla con i risultati ottenuti con la microdiluizione in brodo (anche se con EA basso)

Test di ceftolozane/tazobactam

Shields et al. JCM, vol. 56, issue 2, February 2018

Figure 2A. Distribution of ceftolozane-tazobactam MICs by BMD and Etest against CRP.



Test di ceftolozane/tazobactam

Humphries et al. JCM, vol. 56, issue 3 March 2018

TABLE 2 Performance of disk diffusion, Etest, and MTS compared to rBMD for 308 *P. aeruginosa* isolates[a]

Assay	EA (%)	CA (%)	No. (%) of isolates with:		
			VME	ME	mE
Hardy disk	NA	92.9	0 (0)	0 (0)	22 (7.1)
Etest	96.8	96.8	0 (0)	0 (0)	10 (3.2)
MTS	89.0	87.0	0 (0)	2 (0.9)	38 (12.3)

CTZ **Etest** correla con i risultati ottenuti con la microdiluizione in brodo, **MTS** ha invece bassi livelli di concordanza

Test di ceftolozane/tazobactam

Bailey et al. JCM, vol. 56, issue 9 September 2018

TABLE 2 Challenge study of C/T Etest[a]

Organism(s)	Site	No. of isolates	No. with indicated result by BMD			Performance, no. (%)				
			S	I	R	EA	CA	VMEs	MEs	mEs
Enterobacteriaceae	A	51	27	1	23	47 (92.2)	51 (100)	0 (0)	0 (0)	0 (0)
	B	51	27	1	23	49 (96.1)	49 (96.1)	0 (0)	1 (3.7)	1 (2.0)
	C	51	27	1	23	48 (94.1)	49 (96.1)	1 (4.3)	0 (0)	1 (2.0)
P. aeruginosa	A	39	21	0	18	39 (100)	39 (100)	0 (0)	0 (0)	0 (0)
	B	39	21	0	18	39 (100)	39 (100)	0 (0)	0 (0)	0 (0)
	C	39	21	0	18	39 (100)	39 (100)	0 (0)	0 (0)	0 (0)

CTZ (challenge study) Etest correlazione con la microdiluizione in brodo, soprattutto per *Pseudomonas aeruginosa*

Test di ceftolozane/tazobactam

Bailey et al. JCM, vol. 56, issue 9 September 2018

TABLE 3 Clinical performance of C/T Etest

Organism(s)	No. of isolates	No. (%) matching CLSI breakpoint criteria							
		Result by BMD			Performance				
		S	I	R	EA	CA	VMEs	MEs	mEs
Enterobacteriaceae (total)	793	728 (91.8)	9 (1.1)	56 (7.1)	768 (96.8)	781 (98.5)	0 (0)	2 (0.3)	10 (1.3)
Citrobacter koseri	48	48 (100)	0 (0)	0 (0)	48 (100)	48 (100)	0 (ND[a])	0 (0)	0 (0)
Enterobacter cloacae	53	44 (83.0)	1 (1.9)	8 (15.1)	51 (96.2)	51 (96.2)	0 (0)	0 (0)	2 (3.8)
Escherichia coli	159	146 (91.8)	1 (0.6)	12 (7.5)	153 (96.2)	159 (100)	0 (0)	0 (0)	2 (1.3)
Klebsiella oxytoca	58	52 (89.7)	1 (1.7)	7 (12.1)	56 (96.6)	58 (100)	0 (0)	0 (0)	0 (0)
Klebsiella pneumoniae	167	153 (91.6)	1 (0.6)	13 (7.8)	156 (93.4)	164 (98.2)	0 (0)	1 (0.7)	2 (1.2)
Morganella morganii	50	45 (90.0)	0 (0)	5 (10.0)	50 (100)	50 (100)	0 (0)	0 (0)	0 (0)
Proteus mirabilis	65	62 (95.4)	1 (1.5)	2 (3.1)	64 (98.5)	64 (98.5)	0 (0)	0 (0)	1 (1.5)
Proteus vulgaris	49	48 (98.0)	1 (2.0)	0 (0)	48 (98.0)	48 (98.0)	0 (ND)	0 (0)	1 (2.0)
Providencia rettgeri	40	39 (97.5)	0 (0)	1 (2.5)	39 (97.5)	39 (97.5)	0 (0)	1 (2.6)	0 (0)
Providencia stuartii	42	34 (81.0)	3 (7.1)	5 (11.9)	40 (95.2)	41 (97.6)	0 (0)	0 (0)	1 (2.4)
Serratia liquefaciens	10	10 (100)	0 (0)	0 (0)	10 (100)	10 (100)	0 (ND)	0 (0)	0 (0)
Serratia marcescens	52	47 (90.4)	0 (0)	5 (9.6)	52 (100)	51 (98.1)	0 (0)	0 (0)	1 (1.9)
Pseudomonas aeruginosa	173	152 (87.9)	4 (2.3)	17 (9.8)	171 (98.8)	172 (99.4)	0 (0)	0 (0)	1 (0.6)

Etest mostrava una buona correlazione con la microdiluizione in brodo, sia per gli enterobatteri che per *Pseudomonas aeruginosa*

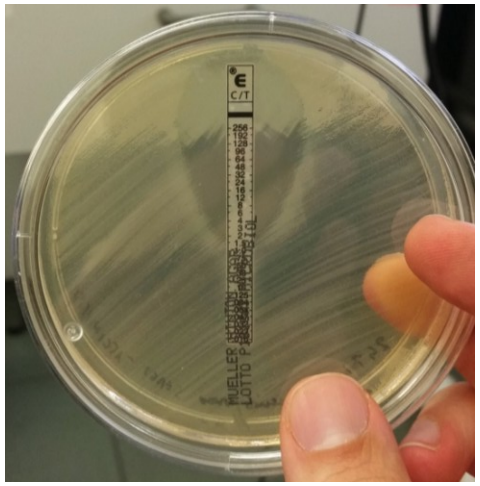
CASO MICROBIOLOGICO

- Paziente maschio 65 anni
- Infezione urinaria complicata da *P. aeruginosa*
- Trattato empiricamente con CEFTOLOZANE/Tazobactam

Antibiotico	MIC mg/L (S/I/R)
Piperacillin/Tazo	32 R
Ceftazidime	64 R
Cefepime	32 R
Imipenem	>64 R
Meropenem	>64 R
Amikacina	>64 R
Gentamicina	>32 R
Ciprofloxacina	>16 R
Colistina	1 S

MIC Etest 2 µg/mL S

MIC brodo diluizione: >128 R

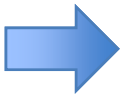


Collaborazione Unità Malattie Infettive, Azienda Ospedaliera Universitaria Pisana

CASO MICROBIOLOGICO

Antibiogramma molecolare (home brew real-time PCR):

-KPC: Negativo
-NDM: Negativo
-VIM: Positivo
-IMP: Negativo
-OXA: Negativo



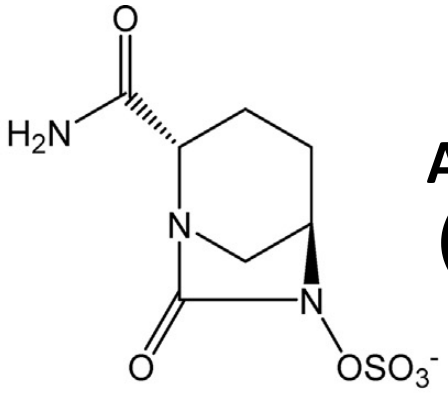
Fallimento terapeutico e cambio terapia

Collaborazione Unità Malattie Infettive, Azienda Ospedaliera Universitaria Pisana

Nuovi farmaci per Gram-negativi multiresistenti

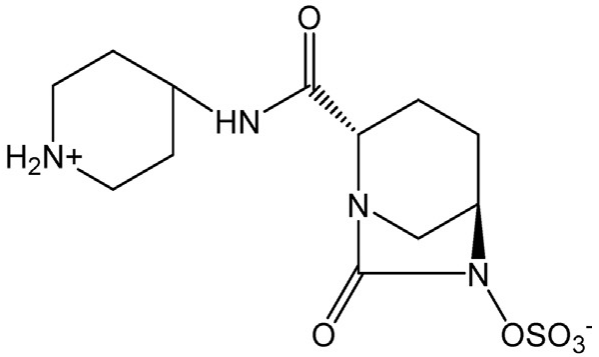
- **Nuovi antibiotici**
  - **Ceftolozano/tazobactam**
  - **Ceftazidime/avibactam**
  - *Meropenem-Vaborbactam*
  - *Imipenem-Relebactam*
  - *Aztreonam-avibactam*
  - *Cefiderocol*

The new generation of β-lactamase inhibitors (non β-lactam-based)



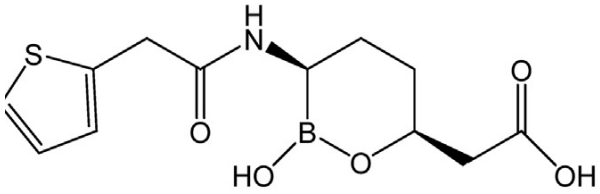
Avibactam (NXL-104)

Diaza-bicyclo-octanes (DBO)



Relebactam (MK-7655)

Boronates



Vaborbactam (RPX7009)

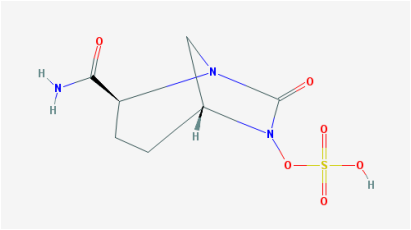
Bush K. *Int J Antimicrob Agents* 2015

Spettro di azione di avibactam vs. vecchi inibitori

		Clavulanic acid	Tazobactam	Avibactam
Class A	TEM, SHV	✓	✓	✓
	CTX-M	✗	✓	✓
	PER, VEB, GES	✗	✓	✓
	KPC	✗	✗	✓
Class B	**e. g. IMP, VIM, NDM1**	✗	✗	✗
Class C	**Enterics chromos. AmpC**	✗	✗	✓
	***Pseudomonas* chromos. AmpC**	✗	✗	✓
	Plasmid-encoded ACC, DHA, CMY, FOX, LAT, MOX, MIR, ACT	✗	✗	✓
Class D	**Non carbapenemase e. g. OXA-1, -31, -10, -13**	**Variable**	**Variable**	**Variable**
	Carbapenemase e. g. OXA-23, -40, -48, -58	**Variable**	**Variable**	**Variable** **OXA-48**

Lagacé-Wiens P et al. *Core Evid.* 2014;9:13.

Avibactam partners:



❖ Ceftazidime/Avibactam

- **EUCAST bp: ≤8 S, >8 R**
- Enterics, including ESBL, AmpC, CRE **(no MBL)**
- *Pseudomonas* **(no MBL)**
- No advantage with *Acinetobacter*

Activity on MBL producers

❖ *Aztreonam/Avibactam*

- Aztreonam not a substrate of MBLs
- Avibactam inhibits relevant enzymes active on Aztreonam

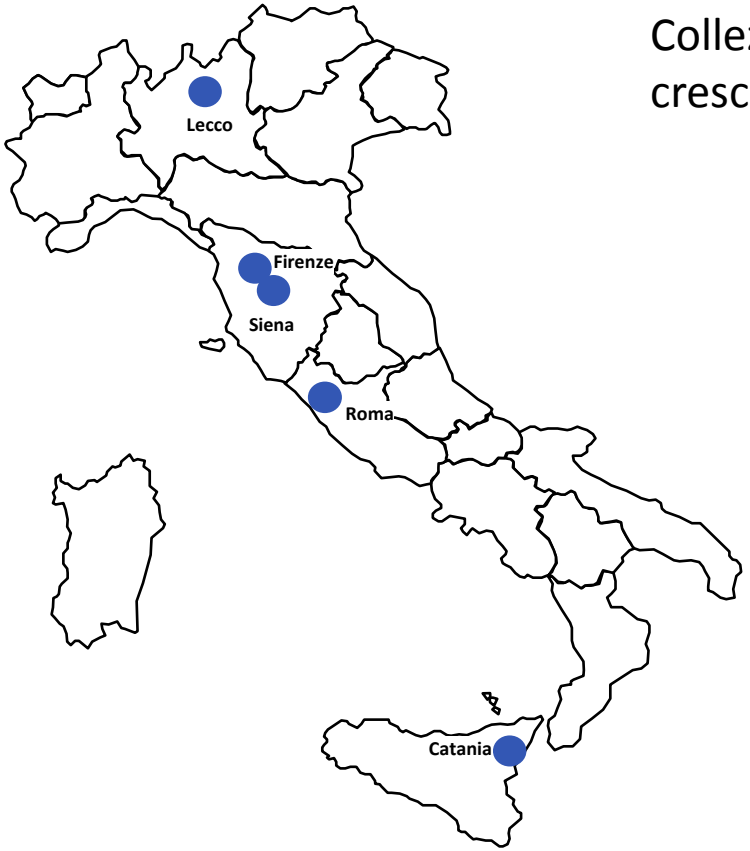
Spettro attività CAZ-AVI su Enterobatteri (studi Europei)

Year	Isolates n.	Species	R-mechanism	% of susceptibility	REFs
2015-16	**238**	Enterics	KPC, 85%, other class A carbapenemase , 15%	**99.2%**	Livermore *et al*., JAC 2017
	333		OXA-48	**98.5%**	
	302		MBL (VIM, NDM, IMP)	**1.3%**	
	655		ESBL	**99.7%**	
	897		AmpC	**98.3%**	
2012	**290**	Enterics	unknown	100%	Testa *et al*., IJAA 2015
2012-13	**139**	Enterics-NS to carbapenems	Mostly Porin loss (1 OXA-48)	100%	Dupont *et al*., AAC 2015

Spettro attività CAZ-AVI *P. aeruginosa*

Year	Isolates n.	R-mechanism	% of susceptibility CAZ-AVI	% of susceptibility CTZ	REFs
2015-16	**147**	ampC derepressed	**94.6%**	**96.6%**	Livermore *et al.*, JAC 2017
	388	Moderate efflux	**86.1%**	**99.7%**	
	302	High efflux	**41.6%**	**95.3%**	
2012	**5328**	unknown	**96.8%**	Not tested	Sader *et al.*, DMID 2015
2012	**7868**	unknown	**97.1%**	Not tested	Sader *et al.*, AAC 2017
2013-14	**290**	Unknown (meropenem R)	**81%**	**91%**	Grupper et al., AAC 2017

Sorveglianza CPE da urine (studio i-CREST)-2016



Collezione di enterobatteri da urine cresciuti su terreno CARBA-SMART

Rossolini, unpublished results

Sorveglianza CPE da urine (studio i-CREST)-2016

9405 Gram-negatives were analysed

318 were CRE

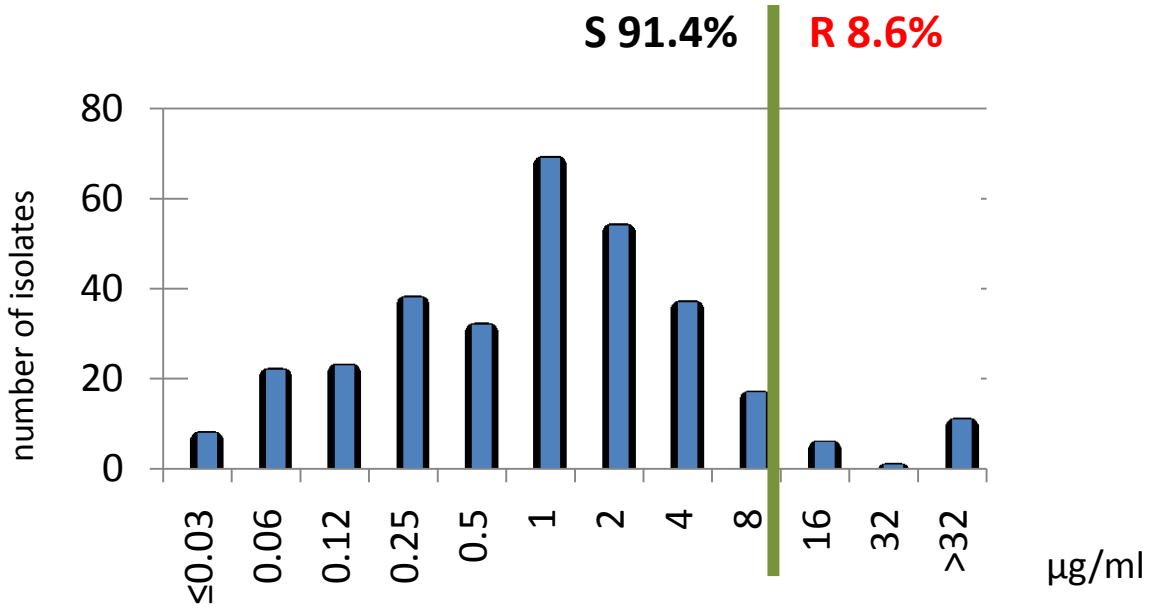
209 CPE

Center	City	Total Gram-negatives	number of positive isolates	proportion of positive isolates	N. of carbapenemase genes
1	Lecco	2259	39	1.7%	38
2	Florence	2000	70	3.5%	55
3	Siena	846	9	1.0%	7
4	Rome	2500	100	4%	95
5	Catania	1800	100	5.5%	12

Rossolini, unpublished results

Sorveglianza CPE da urine (studio i-CREST)-2016

distribuzione delle MIC a CAZ-AVI (BMD, n=209)



Rossolini, unpublished results

Sorveglianza CPE da urine (studio i-CREST)-2016

Meccanismi di resistenza e sensibilità a CAZ-AVI (n=209)

CARBAPENEMASE	CAZ-AVI-S (%)	CAZ-AVI-R (%)
KPC	185 (96.3)	7 (3.7)
VIM	-	3 (100)
NDM	-	3 (100)
OXA-48	6 (100)	-
KPC+VIM	-	1 (100)
NDM+OXA-48	-	4 (100)
TOTAL	191 (91.4)	18 (8.6)

Unpublished results

CAZ-AVI: meccanismi di resistenza acquisita

- **Mutazioni KPC**
  - D179Y (perdita di attività su carbapenemi, pip/tazo e aztreonam)
  - T243M (perdita di attività su carbapenemi e pip/tazo)
  - 165EL166 (perdita di attività su carbapenemi, pip/tazo e aztreonam)
  - V240G (ridotta attività su meropenem)
- **Mutazioni in OmpK36**
  - T333N
  - Inattivazione inserzionale (IS*5*)

- **Aumentata espressione di KPC**
  - aumento del numero di copie plasmidiche

Haidar *et al* – AAC 2017
Compain & Arthur – AAC 2017
Shields *et al* – AAC 2017
Humphries & Hamarajata AAC 2017
Shields *et al* – OFID 2017

Test di CAZ/AVI

Jones et al. JCM, vol. 59, issue 8 August 2015

Ceftazidime-avibactam is a broad-spectrum-β-lactamase inhibitor combination in late-stage clinical development for the treatment of serious infections. In preparation for clinical microbiology laboratory use, a validation experiment was initiated to evaluate a commercial broth microdilution product (Sensititre dried MIC susceptibility system) compared to reference panels using 525 recent clinical isolates. Among 11 pathogen groups, all had Sensititre MIC/reference MIC ratios predominantly at 1 (47.5% to 97.5%), and automated and manual endpoint results did not differ. *Enterobacteriaceae* MIC comparisons showed a modest skewing of Sensititre MIC results toward an elevated MIC (33.9%), but the essential agreement was 98.9% with 100.0% reproducibility. In conclusion, Sensititre panels produced accurate ceftazidime-avibactam MIC results, allowing quality MIC guidance for therapy following regulatory approvals.

I pannelli Sensititre hanno risultati accurati per il CAZ/AVI: essential agreement = (98.9%) per gli enterobatteri (n=525) con il 100 % di riproducibilità.

Test di CAZ/AVI

Kresken et al. JCM, vol. 56, issue 9 September 2018

TABLE 3 Evaluation of agreement and errors between results of the Etest and BMD

Organism(s)	No. of strains tested	CA[a]		ME[b]		VME[c]		Overall EA[d]		EA of evaluable results[e]	
		No.[f]	%	No.	%	No.	%	No.	%	No.	%
Enterobacterales	140	140	100.0	0	0.0	0	0.0	139	99.3	130	100.0
P. aeruginosa	60	59	98.3	0	0.0	1	4.5	59	98.3	48	100.0
Total	200	199	99.5	0	0.0	1	0.5	198	99.0	178	100.0

Risultati anche migliori rispetto ai precedenti sono stati pubblicati del tutto recentemente per l'Etest, che appare una opzione utilizzabile per la determinazione della MIC per ceftazidime-avibactam.

Test di CAZ/AVI

Correlazione BMD, Etest e dischetto CAZ-AVI

Verification of ceftazidime-avibactam and ceftolozane-tazobactam susceptibility testing methods against carbapenem-resistant Enterobacteriaceae and *Pseudomonas aeruginosa*

Ryan K. Shields[1,2], *Cornelius J. Clancy[1-3], A. William Pasculle[1,4], Ellen G. Press[1], Ghady Haidar[1], Binghua Hao[2], Liang Chen[5], Barry N. Kreiswirth[5], M. Hong Nguyen[1,2]

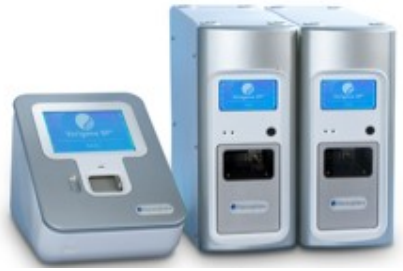
Table 2. Essential and categorical agreement between BMD and Etest or disk diffusion susceptibility testing methods for ceftazidime-avibactam and ceftolozane-tazobactam

Drug – Pathogen	BMD MIC (µg/mL)*			Etest			Disk Diffusion	
	Median	Range	n (%) Resistant	n (%) EA	n (%) CA	Errors	n (%) CA	Errors
Ceftazidime-avibactam CRE (n=74)	2	0.25 – 512	13 (18)	66 (89)	72 (97)	2 VME	56 (76)	18 ME
Ceftolozane-tazobactam CRP (n=72)	1	0.5 – 256	6 (8)	57 (79)	69 (96)	3 Minor	68 (94)	4 Minor

BMD = Broth microdilution, CA = Categorical agreement, CRE = Carbapenem-resistant *Enterobacteriaceae,* CRP = Carbapenem-resistant *Pseudomonas aeruginosa,* EA = Essential agreement, ME = Major error, MIC = Minimum inhibitory concentration, VME = Very major error

Nuove opportunità antibiotiche

	ESBL	KPC	OXA-48	VIM/IMP/NDM
ceftolozane tazobactam	🟢	🔴	🟢	🔴
ceftazidime avibactam	🟢	🟢	🟢	🔴
meropenem vaborbactam	🟢	🟢	🔴	🔴
imipenem relebactam	🟢	🟢	🔴	🔴
aztreonam avibactam	🟢	🟢	🟢	🟢



🟢 ATTIVO 🔴 NON ATTIVO

Utilità della rilevazione rapida del meccanismo di resistenza

Conclusioni

- Disponibilità di nuovi antibiotici soprattutto anti-Gram-negativi XDR (*a major unmet clinical need*)
- Copertura parziale delle esigenze (CRA e MBL largamente scoperti)
- Difficoltà nel test di sensibilità (impossibilità di test nei sistemi automatici, poche esperienze nei metodi alternativi)
- CTZ: Etest dubbia efficacia, No DD, microdiluizione OK
- CAZ/AVI: Etest OK, No DD, microdiluizione OK
- Ruolo della Microbiologia nella *stewardship* antibiotica (diagnostica rapida, test sensibilità, sorveglianza)

GRAZIE

per

l' ATTENZIONE

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