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Pneumonie associée à la ventilation mécanique & pneumonie acquise à l'hôpital à BGN multirésistants : « une bouffée d'air ?»

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Déclaration de liens d'intérêt

- Orateur: Shionogi, MSD, Pfizer, bioMérieux
- Consultant: MSD, Roche Diagnostics
- Congrès: Shionogi, MSD, Pfizer, bioMérieux

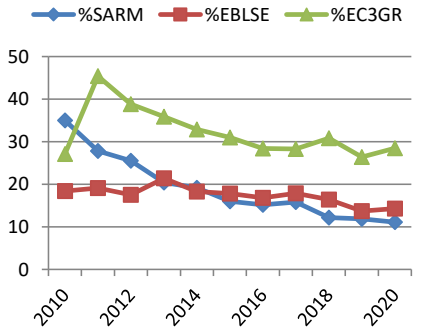
Rea-RAISIN 2013-2018 puis REA-REZO 2019-2021

Pneumonie associée aux soins : généralités

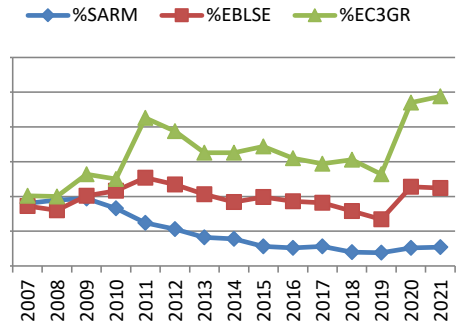
- Pneumonie acquise à l'hôpital
- Pneumonie associée à la ventilation mécanique (PAVM)
- Infection la plus fréquente en réanimation
- 70 % BGN (*Pseudomonas* > Entérobactéries > *Acinetobacter*), 20 % *S. aureus*
- Mortalité associée 20% mais mortalité attribuable 5 à 13%

Variables			2013	2014	2015	2016	2017	2018	2019	2020 tous patients	2020 non covid	2020 covid	2021 tous patients	2021 non covid	2021 covid
Participation	(% lits SAE)	%	47,2	50,4	43,7	45,6	47,2	40,1	26,2	**21,5**			**18,0**		
Etablissements		n	186	186	167	174	174	155	99	**82**	82	82	**76**	76	76
Services		n	213	212	188	200	199	174	110	**90**	90	90	**84**	84	84
Lits		n	2 579	2 548	2 216	2 392	2 474	2 146	1 383	**1 123**	1 123	1 123	**1 103**	1 103	1 103
Patients		n	34 278	34226	63240	67899	68581	61510	39635	**30 105**	23 798	4 465	**29 758**	20 419	9 087
Indicateurs niveau patient															
Taux / 100 patients exposés															
Pneumopathie liée à l'intubation			10,80	11,46	11,67	11,67	11,27	10,70	10,40	**16,51**	12,87	37,02	**20,86**	11,75	45,00
Bactériémie liée au séjour			3,56	3,73	3,64	3,50	3,54	3,29	3,21	**4,43**	3,73	8,69	**5,20**	3,27	9,59
Culture CC+ (COL, ILC, BLC)*			5,93	6,36	6,30	5,84	5,21	4,73	4,67	**4,67**	4,01	8,11	**5,19**	3,67	9,15
ILC *			0,84	0,71	0,71	0,81	0,63	0,60	0,62	**0,70**	0,60	1,29	**0,73**	0,51	1,33
BLC*			0,68	0,56	0,62	0,59	0,51	0,56	0,61	**0,69**	0,64	1,16	**0,76**	0,45	1,56
Incidence / 1000 j d'exposition															
Pneumopathie liée à l'intubation			13,00	14,26	15,05	15,22	15,46	15,01	15,37	**21,99**	18,43	35,62	**27,24**	18,05	42,06
Bactériémie liée au séjour			3,22	3,53	3,52	3,39	3,62	3,36	3,39	**4,31**	3,86	6,40	**4,79**	3,59	6,52

Pourcentage de résistance dans l'espèce ou la famille

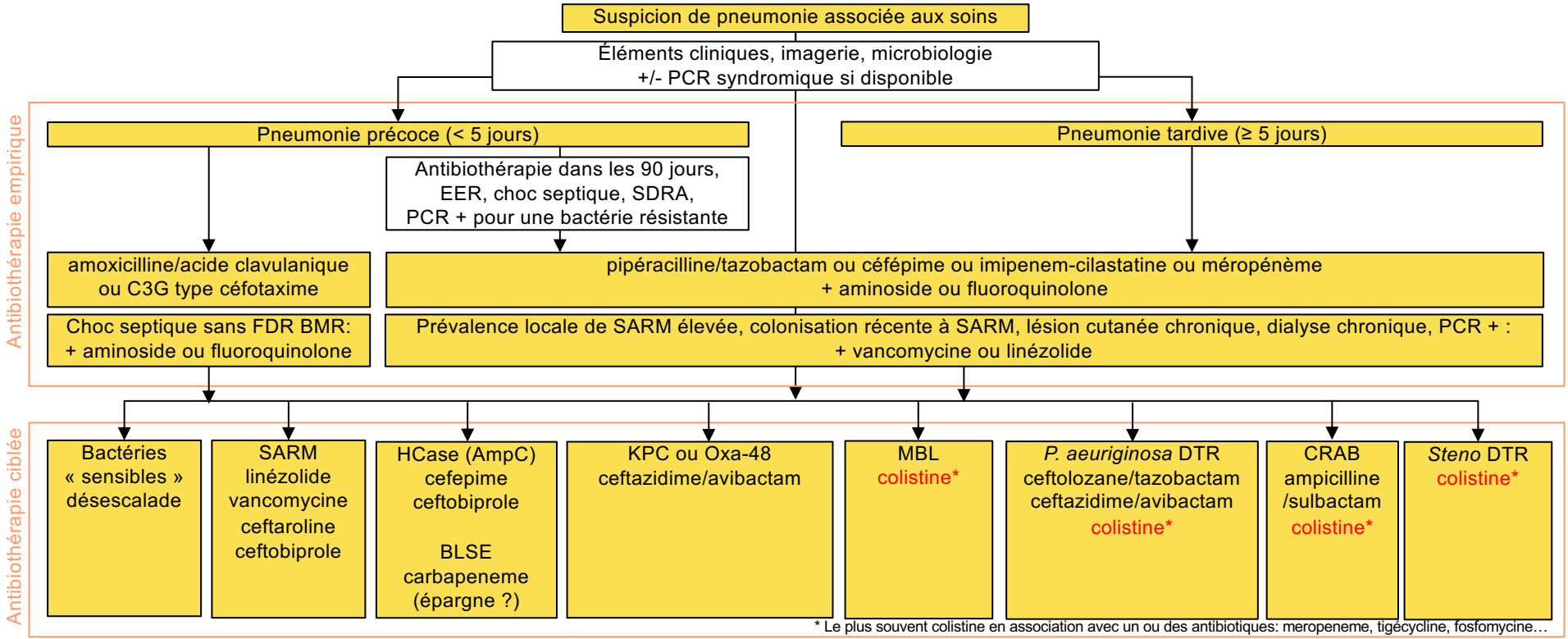


Taux d'incidence cumulée des IAS à SARM, EBLSE et EC3GR / 100 patients



Rea-RAISIN 2013-2018 puis REA-REZO 2019-2021
Bekaert et al AJRCCM 2011 & Melsen et al. Lancet ID 2013

Pneumonie associée aux soins : prise en charge



* Le plus souvent colistine en association avec un ou des antibiotiques: meropeneme, tigécycline, fosfomycine…

Inspiré de Zaragoza et al. Critical Care 2020 & RFE SFAR SRLF 2017

Pneumonie associée aux soins : prise en charge, apport des nouvelles molécules

Potential *in vitro* activity of antibiotics against target carbapenem-resistant Gram-negative bacteria and approved indications

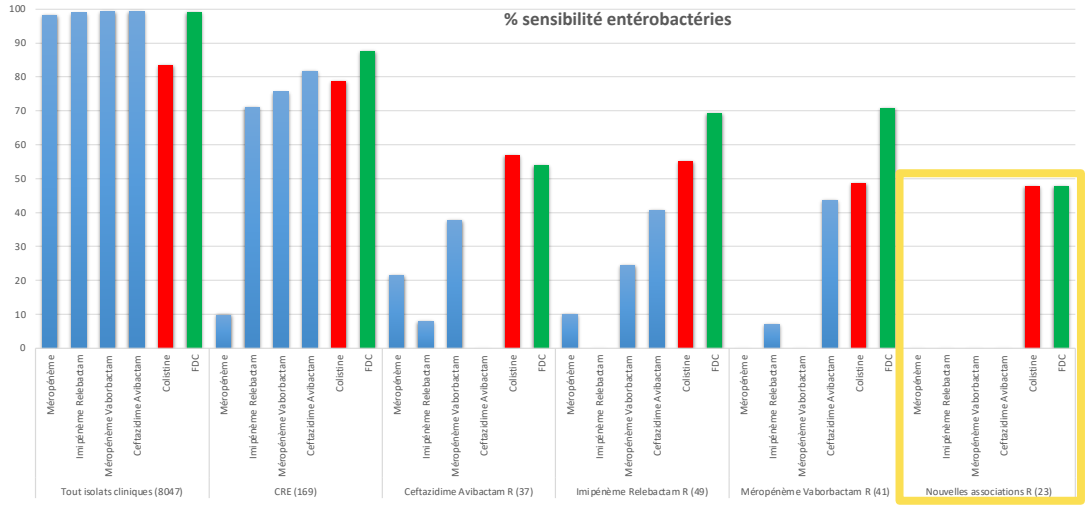
	CRAB	ESBLs	CRPA non-MBL	CRE non-CP	CRE-KPC	CRE-OXA-48	CRE-MBL	Current clinical indications/approval
New antibiotics								
Meropenem-vaborbactam	No	Yes	No	+/−	Yes	No	No	FDA approved for cUTI, EMA approved for cUTI, HAP and VAP, and for the treatment Gram-negative infections in patients with limited treatment options
Imipenem-cilastatin/ relebactam	No	Yes	Yes	+/−	Yes	No	No	FDA approved for cUTI and cIAI; EMA approved for HAP and VAP and for BSI with a suspected respiratory source, and for the treatment Gram-negative infections in patients with limited treatment options
Cefiderocol	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA cUTI, HAP and VAP; EMA for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options
Ceftazidime-avibactam + Aztreonam	No	Yes	Yes	Yes	Yes	Yes	Yes	-

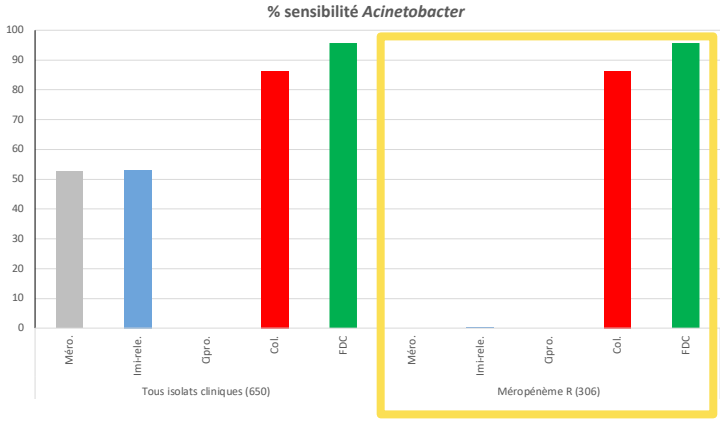
Antibiothérapie ciblée

Bactéries « sensibles » désescalade	SARM	HCase (AmpC)	KPC ou Oxa-48	MBL	*P. aeuriginosa* DTR	CRAB	*Steno* DTR
	linézolide vancomycine ceftaroline ceftobiprole	cefepime ceftobiprole BLSE carbapeneme (épargne ?)	ceftazidime/avibactam KPC meropenem/vaborbactam imipenem/relebactam KPC ou Oxa-48 cefiderocol	colistine* aztreonam+ ceftazidime/ avibactam cefiderocol	ceftolozane/tazobactam ceftazidime/avibactam colistine* imipenem/relebactam cefiderocol	ampicilline /sulbactam colistine* cefiderocol	colistine* cefiderocol aztreonam +ceftazidime /avibactam

* Le plus souvent colistine en association avec un ou des antibiotiques: meropeneme, tigécycline, fosfomycine…

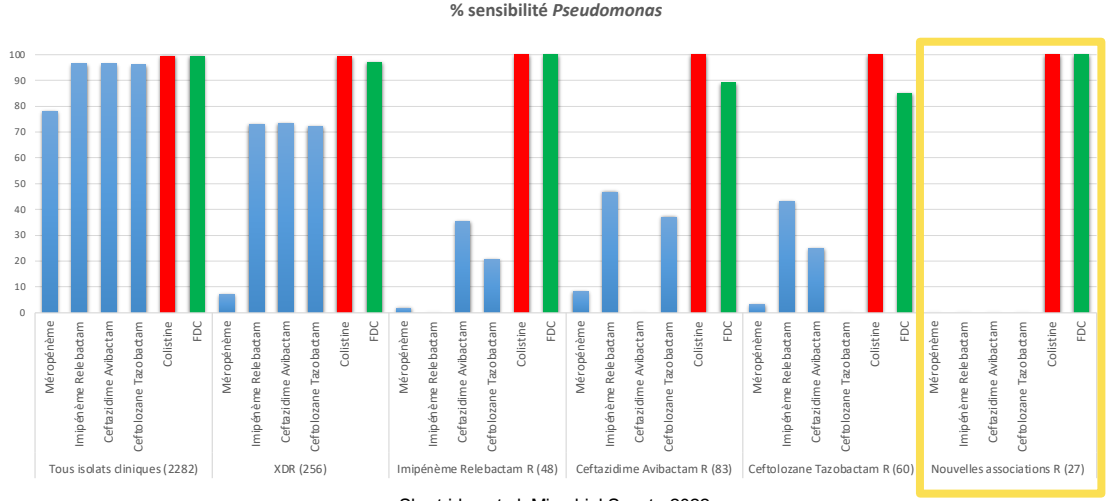
Inspiré de Zaragoza et al. Critical Care 2020, RFE SFAR SRLF 2017 & ESCMID Guidelines 2022





Spectre des nouveaux antibiotiques :

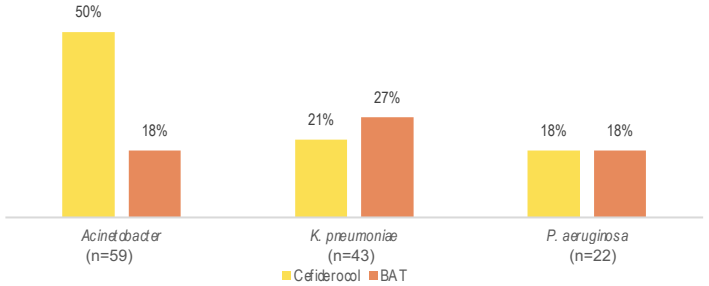
résistances croisées

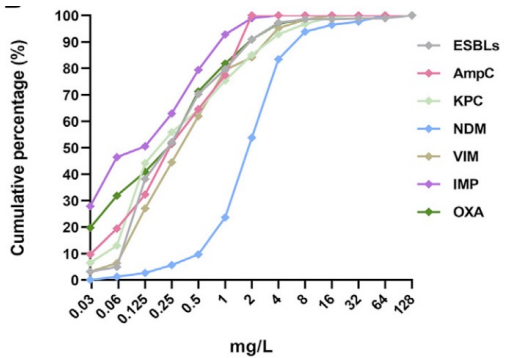


Shortridge et al, Microbiol Spectr. 2022

Limites des essais cliniques sur les nouveaux antibiotiques anti-BGN-DTR

- Peu de patients présentant une PAVM causée par des BGN-DTR sont inclus
- Peu de patients dans les essais ciblés sur les BGN-DTR :
  - incluent de nombreux mécanismes de résistance
  - comparent monothérapie vs bithérapie (BAT colistine en association)
- Surmortalité chez les patients traités par cefiderocol pour CRAB (CREDIBLE-CR)
- Cefiderocol moins actif sur les carbapénémases de type NDM





	Clinical Cure at TOC		Eradication at EOT		ACM Day 28	
CREDIBLE-CR + APEKS-NP[e]	Cefiderocol (N = 24)	All Comparators[f] (N = 10)[a]	Cefiderocol (N = 24)	All Comparators[f] (N = 10)[a]	Cefiderocol (N = 24)	All Comparators[f] (N = 10)[a]
Overall	70.8 (17/24)	40.0 (4/10)	58.3 (14/24)	30.0 (3/10)	12.5 (3/24)	50.0 (5/10)
Type of infection						
Pneumonia	71.4 (10/14)	50.0 (3/6)	42.9 (6/14)	33.3 (2/6)	21.4 (3/14)	33.3 (2/6)
Other diagnoses[b]	70.0 (7/10)	25.0 (1/4)	80.0 (8/10)	25.0 (1/4)	0 (0/10)	75.0 (3/4)
MBL type						
NDM	56.3 (9/16)	33.3 (2/6[a])	62.5 (10/16)	16.7 (1/6[a])	18.8 (3/16)	50.0 (3/6[a])
Non-NDM	100 (8/8)	40.0 (2/5[a])	50.0 (4/8)	40.0 (2/5[a])	0 (0/8)	40.0 (2/5[a])
Pathogen type						
Enterobacterales	73.3 (11/15)	20.0 (1/5)	66.7 (10/15)	20.0 (1/5)	13.3 (2/15)	60.0 (3/5)
Non-fermenters	66.7 (6/9)	60.0 (3/5)	44.4 (4/9)	40.0 (2/5)	11.1 (1/9)	40.0 (2/5)

Bassetti et al. Lancet ID 2021, Timsit CID 2022, Kanj et al. IJAA 2022 & Lodise et al. Expert Review Of Anti-infective Therapy 2022, Wang et al. Frontiers in Pharmacology 2022

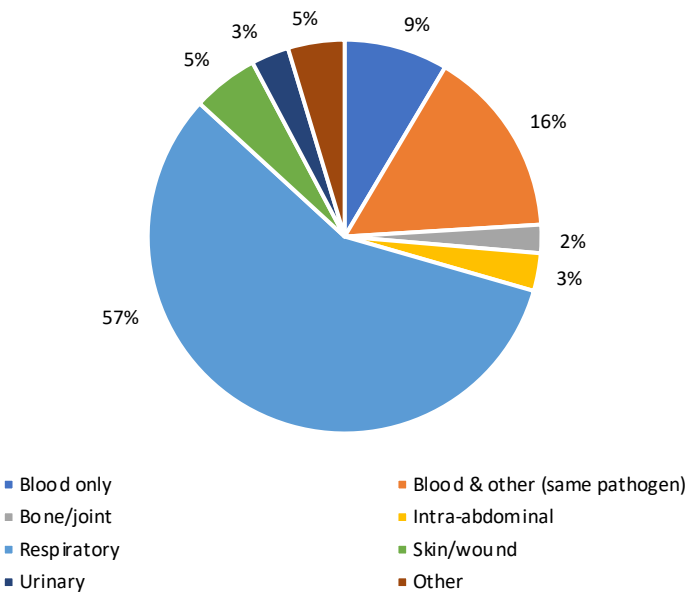
Quelles sont les données de l'utilisation en vie réelle des nouvelles molécules anti-BGN pour traiter la PAVM ?

Cefiderocol : *Pseudomonas aeruginosa*

Real-world use of cefiderocol in the EU and US for *Pseudomonas aeruginosa*: interim data from the PROVE study

191 patients with PA infections

63% from the US and the rest from EU, mostly France (22%)



	Overall		Clinical cure		30- day mortality	
	N	%	N	Row%	N	Row%
Number of patients	191	100%	124	64.9%	37	19.4%
Patient in ICU	143	74.9%	87	60.8%	34	23.8%
Mechanical ventilation	92	48.2%	53	57.6%	26	28.3%
Vasopressor support	70	36.6%	36	51.4%	24	34.3%
Reason for starting CFD						
Documented infection	147	77.0%	100	68.0%	29	19.7%
Salvage treatment	26	13.6%	11	42.3%	7	26.9%
Empirical	15	7.9%	11	73.3%	1	6.7%
CFD as monotherapy	109	57.1%	81	74.3%	14	12.8%
Monomicrobial	129	67.5%	86	66.7%	28	21.7%
Respiratory only	74	38.7%	45	60.8%	20	27.0%
Polymicrobial	62	32.5%	38	61.3%	9	14.5%
Respiratory only	31	16.2%	22	71.0%	3	9.7%
Other pathogens						
Klebsiella pneumoniae	15	7.9%	13	86.7%	0	-
S. maltophilia	16	8.4%	10	62.5%	1	6.3%
A. baumannii	15	7.9%	6	40.0%	5	33.3%

Larcher et al., ECCMID 2023, Abs #02010

Quelles sont les données de l'utilisation en vie réelle des nouvelles molécules anti-BGN pour traiter la PAVM ?

Cefiderocol : *Acinetobacter baumannii*

Real-world use of cefiderocol in the EU and US for *Acinetobacter baumannii*: interim data from the PROVE study

98 patients with AB were treated with cefiderocol

71 from the USA, 27 from Europe

Table 2. Cefiderocol patterns of utilization (n=98)

Characteristic		
Duration of CFDC in days, median (IQR)	11.5 (8–17)	
Reason for starting CFDC	**n**	**%**
Documented infection	77	78.6%
Salvage treatment, prior antibiotics failed	12	12.2%
Empiric for suspected CR GNBI	8	8.2%
Other	1	1.0%
Reason for stopping CFDC		
Clinical signs/symptoms resolved	50	52.1%
Patient death or clinical failure	17	17.7%
Palliative care commenced	8	8.3%
Switched to alternative susceptible drug	5	5.2%
AST showed resistance to CFDC	2	2.1%
Adverse drug reaction	2	2.1%
Other	12	12.5%
CFDC as monotherapy		
Yes	40	40.8%
Any GNA used with CFDC[a] (n=58)		
Aminoglycosides	2	2.0%
Carbapenems	4	4.1%
Polymyxins	17	17.3%
Tetracyclines and tigecycline	26	26.5%
Others	29	29.6%

[a]GNA used for at least 2 days with start date on or after CFDC initiation date but not after last CFDC dose. AST, antibiotic susceptibility testing; CFDC, cefiderocol; GNA, Gram-negative antibiotic; IQR, interquartile range.

Table 3. Outcomes by key characteristics of AB primary infections

	Overall		Clinical cure[b]		30-day post-CFDC mortality	
	n	%	n	Row%	n	Row%
Number of patients[a]	**96**		**58**	**60.4%**	**23**	**24.0%**
Index infection type						
Monomicrobial - primary infection site	**61**	**63.5%**	**36**	**59.0%**	**14**	**23.0%**
Blood only	7	7.3%	3	42.9%	3	42.9%
Blood & other (same pathogen)[c]	2	2.1%	2	100.0%	–	–
Respiratory only	22	22.9%	14	63.6%	3	13.6%
Other sites[d]	25	26.0%	16	64.0%	4	16.0%
Polymicrobial - primary infection site	**35**	**36.5%**	**22**	**62.9%**	**9**	**26.0%**
Blood only	1	1.0%	1	100.0%	–	–
Blood & other (same pathogen)[c]	2	2.1%	1	50.0%	1	50.0%
Respiratory only	20	20.8%	12	60.0%	5	25.0%
Other sites[d]	12	12.5%	8	67.0%	3	25.0%
Other primary infection site pathogens (≥10%)						
Klebsiella pneumoniae	11	11.5%	7	63.6%	4	36.4%
Pseudomonas aeruginosa	15	15.6%	6	40.0%	5	33.3%
Severity upon starting CFDC						
Patient in ICU while receiving CFDC						
Yes	55	57.3%	23	41.8%	20	36.4%
No	41	42.7%	35	85.4%	3	7.3%
Mechanical ventilation						
Yes	43	44.8%	18	41.9%	14	32.6%
No	53	55.2%	40	75.5%	9	17.0%
Vasopressor support						
Yes	29	30.2%	11	37.9%	13	44.8%
No	67	69.8%	47	70.1%	10	14.9%
CFDC utilization						
Reason for starting CFDC						
Documented infection	77	80.2%	45	58.4%	21	27.3%
Salvage treatment (failure of prior GNA)	12	12.5%	7	58.3%	2	16.7%
Empiric for suspected CR GNBI	6	6.3%	5	83.3%	–	–
Other	1	1.0%	1	100.0%	–	–
CFDC as monotherapy[e]						
Yes	39	40.6%	27	69.2%	6	15.4%
No	57	59.4%	31	54.4%	17	29.8%
Local S,I,R classification						
Susceptible	38	39.6%	24	63.2%	11	28.9%
Intermediate	1	1.0%	1	100.0%	–	–
Resistant	8	8.3%	2	25.0%	3	37.5%
Not tested or not available	49	51.0%	31	63.3%	9	18.4%
Carbapenem resistant (n=90)						
Yes	83	92.2%	50	60.2%	23	27.7%
No	7	7.3%	5	71.4%	–	–

[a]Number of patients includes only those with a primary site culture of AB; 2 coinfections unrelated to the primary infection that prompted CFDC use were excluded. [b]Clinical cure based on answer to the Clinical Assessment question: resolved, improved = cured; resolved then relapse, failure, or unknown = Not cured. [c]Same AB pathogen at both sites. [d]Other sites include bone/joint, skin/wound, urine, intra-abdominal, other. [e]Monotherapy defined as CFDC only without overlap of other GNAs. CFDC, cefiderocol; CR, carbapenem resistant; GNA, Gram-negative antibiotic; ICU, intensive care unit.

Timsit et al., ECCMID 2023, Abs #P2272

Antibiotic regimens including vs not including cefiderocol for the treatment of carbapenem-resistant *A. baumannii* ventilator-associated pneumonia in intensive care unit: a propensity-weighted retrospective observational cohort study

- **119 patients with CRAB-VAP**
  - Cefiderocol was used as monotherapy in 19% (11/58), in combination with colistin in 67% (39/58), and in combination with other agents in 14% (8/58).
  - Propensity score (PS) of receiving cefiderocol (FDC) and PS multiple logistic regression for risk factors for 28-day mortality using IPTW

Characteristic	Non-FDC, N = 61	FDC, N = 58	*p*-value
Age	67 (67,74)	62 (54,70)	0.016
Female sex	12 (20)	16 (28)	0.31
BMI ≥ 30 kg/m²	27 (44)	18 (31)	0.14
COVID-19	61 (100)	54 (93)	0.053
SARS-CoV-2 vaccination	**2 (3.3)**	**16 (28)**	**<0.001**
Charlson index	4.00 (3.00, 6.00)	4.00 (2.25, 6.00)	0.79
Tracheo. before VAP	**9 (15)**	**20 (34)**	**0.012**
SOFA score	7.0 (5.0, 10.0)	7.0 (5.0, 10.0)	0.50
Septic shock	18 (30)	15 (26)	0.66
CRRT	9 (15)	9 (16)	0.91
ECMO	1 (1.6)	2 (3.4)	0.61
28-day mortality	**39 (64)**	**25 (43)**	**0.023**

Characteristic	OR	95% CI
Cefiderocol	**0.46**	**0.24 - 0.88**
Age	**1.05**	**1.00 - 1.09**
Tracheostomy before VAP	0.72	0.31 - 1.65
SARS-CoV-2 vaccine	0.86	0.29 - 2.49
SOFA score	**1.16**	**1.02 - 1.34**
Aspergillus spp co-infection	2.26	0.63 - 9.18
Charlson index	1.12	0.91 - 1.37
CRRT	1.60	0.52 - 5.12
Septic shock	**3.98**	**1.65 - 10.3**
CRAB-BSI	0.46	0.15 - 1.28
BMI ≥ 30 kg/m²	0.96	0.48 - 1.93

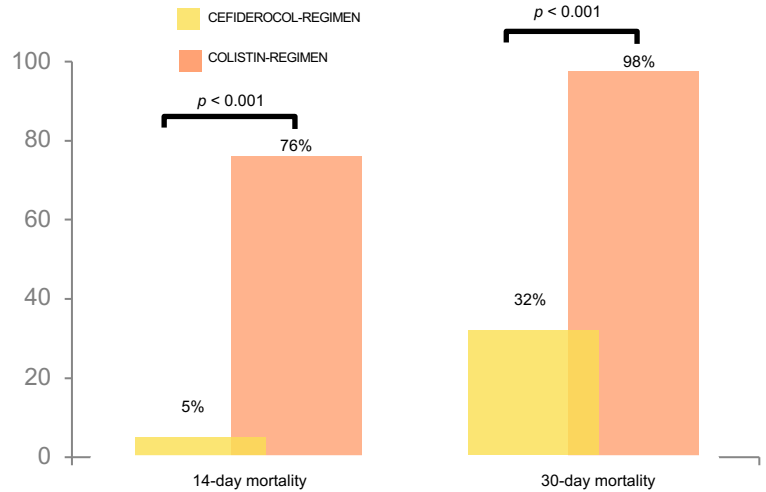
E. Rando et al., ECCMID 2023, Abs #E0166

Efficacy of cefiderocol- versus colistin-containing regimen for treatment of bacteremic ventilator-associated pneumonia caused by carbapenemresistant *Acinetobacter baumannii* in COVID-19 patients

- **73 patients COVID avec une PAVM bactériémiante à CRAB**
  - 54 patients (74%) ont reçu une antibiothérapie à base de colistine
    - Colistine (n = 12)
    - Colistine + meropenem + tigécycline (n = 12)
    - Colistine + meropenem (n = 9)
  - 19 patients (26%) ont reçu une antibiothérapie à base de cefiderocol
    - Cefiderocol + fosfomycine (n = 6)
    - Cefiderocol + fosfomycine + tigécycline (n = 3)
    - Cefiderocol + fosfomycine + tigécycline + meropenem (n = 3)

COX regression analysis: risk factors associated with death at 30 days and propensity-score analysis

Variables	Adjusted-HR (95% CI)	*p*-value
COPD	1.4 (1.3-12.2)	0.022
Age	1.12 (1.01-1.1)	0.001
Cefiderocol-containing regimens (colistin-containing regimens as reference variable)	0.34 (0.18-0.56)	< 0.001
Cefiderocol-Fosfomycin	0.22 (0.1-0.55)	< 0.001
Propensity score analysis		
Cefiderocol-containing regimens (IPTW-adjusted)	0.44 (0.22-0.66)	< 0.001
Cefiderocol-Fosfomycin (IPTW-adjusted)	0.33 (0.12-0.54)	< 0.001

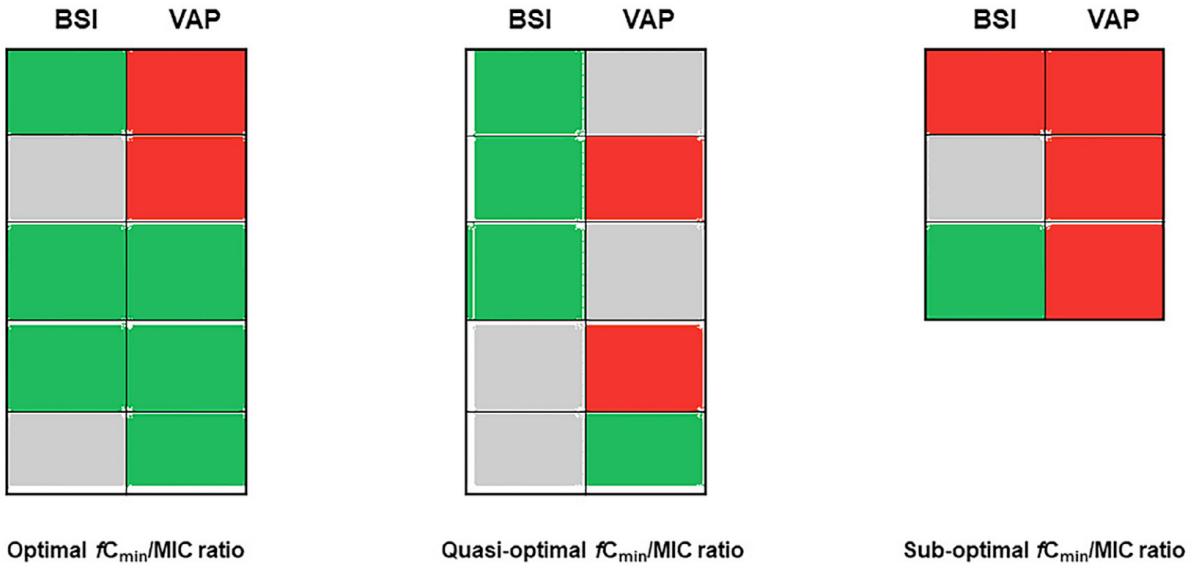


Russo et al IJAA 2023

Place de l'optimisation PK/PD et du suivi thérapeutique

PK/PD target attainment and microbiological outcome in ICU patients with CRAB infection (MIC < 1 mg/L)

Median (IQR) cefiderocol fCmin = 2.39 mg/L (0.68–6.47 mg/L).



MIC, minimum inhibitory concentration; BSI, bloodstream infection; VAP, ventilator-associated pneumonia.

Gatti et al. JGAR 2021

Quelles sont les données de l'utilisation en vie réelle des nouvelles molécules anti-BGN pour traiter la PAVM ?

Données françaises

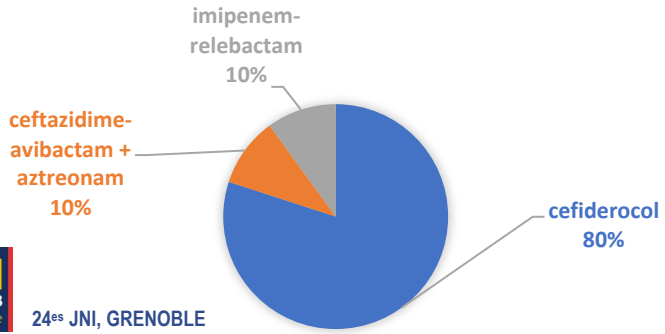
Utilisation des antibiotiques de dernier recours pour traiter les infections à BGN DTR aux CHU de Nîmes

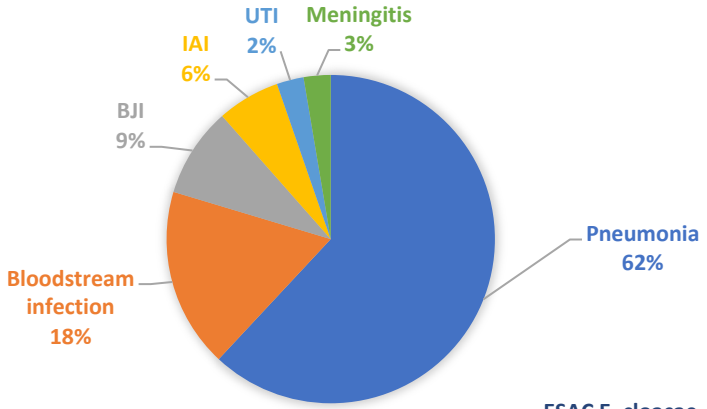
Patients admitted to a French teaching hospital between January 1st, 2020, and May 31st, 2022 (N≈120 000)

Patients treated with last resort antibiotics (N=40):
- Cefiderocol (N=25)
- Imipenem-cilastatin-relebactam (N=4)
- Meropenem-vaborbactam (N=0)
- Ceftazidime-avibactam + aztreonam (N=11)

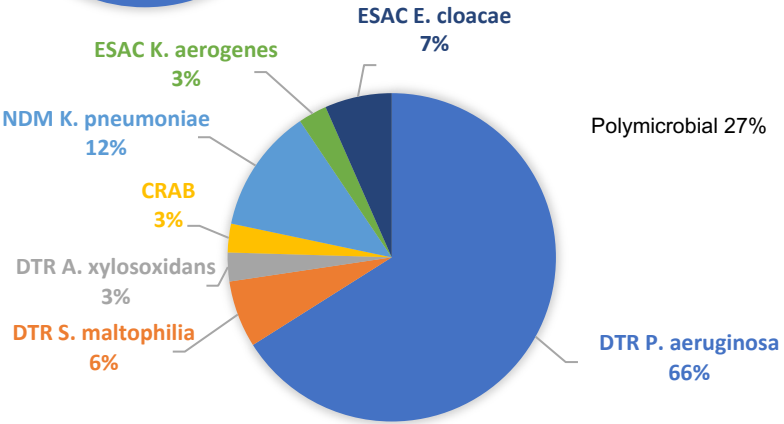
Patients excluded from the study (N=10):
- refusal to participate after information (N=1)
- imipenem alone instead of imipenem-cilastatin-relebactam (N=1)
- ceftazidime-avibactam and aztreonam not at the same time (N=8)

Patients included in the study (N=30):
- Cefiderocol (N=24)
- Imipenem-cilastatin-relebactam (N=3)
- Ceftazidime-avibactam + aztreonam (N=3)





Bitherapy 60%
- Ciprofloxacin
- Colistin
- Aminoglycoside
- Tigecycline
- Fosofomycin



Polymicrobial 27%

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Utilisation des antibiotiques de dernier recours pour traiter les infections à BGN DTR aux CHU de Nîmes

Microorganism	Antimicrobial susceptibility testing					
	CAZ-AVI	TOL-TAZ	MER-VAB	IMI-REL	CAZ-AVI-ATM	CFD
P. aeruginosa	61% (14/23)	73% (16/22)	47% (8/17)	59% (10/17)	100% (2/2)	95% (21/22)
DTR	*57% (12/21)*	*67% (14/21)*	*36% (5/14)*	*50% (7/14)*	-	*95% (18/19)*
S. maltophilia	0% (0/3)	-	-	-	100% (1/1)	100% (4/4)
A. baumannii	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	-	100% (1/1)
A. xylosoxidans	0% (0/1)	0% (0/1)	0% (0/1)	-	-	0% (0/1)
Enterobacterales	73% (8/11)	40% (4/10)	75% (9/12)	73% (8/11)	100% (5/5)	73% (8/11)
ESAC	*100% (0/3)*	*0% (0/1)*	*100% (3/3)*	*100% (2/2)*	*100% (2/2)*	*33% (1/3)*
NDM	*0% (0/3)*	*0% (0/3)*	*0% (0/3)*	*0% (0/3)*	*100% (3/3)*	*33% (1/3)*
Total	56% (22/39)	59% (20/34)	55% (17/31)	62% (18/29)	100% (8/8)	97% (34/39)

Microorganism	Free-infection survival		
	IMI-REL	CAZ-AVI-ATM	CFD
P. aeruginosa			
DTR	67% (2/3)	-	58% (11/19)
S. maltophilia		50% (1/2)	25% (1/4)
A. baumannii	-	-	0% (0/1)
A. xylosoxidans	-	-	100% (1/1)
Enterobacterales			
ESAC	-	0% (0/1)	0% (0/2)
NDM	-	33% (1/3)	0% (0/1)

Clinical cure at EoT: 67%

ACM D30: 20%

ACM D90: 26%

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Treatment of Severe Infections Due to Metallo-Betalactamases Enterobacterales in Critically Ill Patients : ceftazidime-avibactam + aztreonam

Table 1. Cases series of severe NDM infections treated with CZA/ATM in ICU patients—experience of Bichat-Claude Bernard hospital.

Age, (Year), Gender	Medical History	SAPS II	SOFA Score (Treatment)	Invasive Ventilation	Shock	HD/CVVH	Source	Germ/MIC of CZA/ATM	Ttreatment Duration (Days)	Combo	Clinical Cure	Microbiological Cure	Survival (Hospital)	Cause of Death
76, Female	Obese; DiabetesARDS SARS-Cov2	42	2	Yes	No	No	VAP	Esherichia coli	1	Colistine	Yes	Yes	Alive	
42, Male	Obese, Diabetes, ARDS SARS-Cov2	46	10	Yes	Yes	Yes	VAP	Enterobacter cloacae; 0.064 mg/L	6		Yes	Yes	Death	Coma
58, Male	Endocarditis, mitral valve replacement	53	4	Yes	Yes	No	Septic shock in NDM colonized patient	Citrobacter freundii	2		Yes	Yes	Alive	
67, Female	renal transplant; hemorragic shock	47	10	No	No	No	BSI	Klebsiella pneumonia; 0.032 mg/L	15		No	Yes	Alive	
44, Female	lung transplant; acute respiratory failure	27	5	Yes	Yes	No	VAP	Klebsiella pneumoniae: 0.064 mg/L	52	Tigecycline	Yes	Yes	Alive	
53, Male	intraventricular communica-tion/Endocarditis	40	9	Yes	Yes	Yes	Petitonitis; cellulitis	Echerichia coli; 0.094 mg/L (+ESBLE Klebsiella pneumoniae);	24	Colistine	Yes	Yes	Death	Shock
40, Female	Myocarditis, ECMO	34	8	Yes	Yes	Yes	SSI (ECMO cannulas)	Klebsiella pneumoniae; 0.38 mg/L	10		Yes	Yes	Death	Shock
36, Male	ARDS, SARS Cov2	23	3	Yes	No	No	VAP	Klebsiella pneumoniae; 0.064 mg/L	9		Yes	Yes	Alive	
70, Male	Chronic renal failure; Cardiac surgery (mitral valve replacement, tamponnade)	54	6	Yes	Yes	No	VAP	Enterobacter cloacae; 0.064 mg/L	9		No	Yes	Death	MOF

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Cefiderocol Treatment for Severe Infections due to Difficult-to-Treat-Resistant Non-Fermentative Gram-Negative Bacilli in ICU Patients: A Case Series and Narrative Literature Review

Table 3. Baseline characteristics at ICU admission and at cefiderocol initiation.

	All (*n* = 16)
Age	56.5 [52–66.8]
Gender	
Male	10 (62.5)
Female	6 (37.5)
Body mass index	27 [22–39]
Comorbidities	
Hypertension	11 (69)
Diabetes	7 (43.8)
Chronic kidney disease	4 (25)
COPD	1 (6.3)
Immunocompromised	2 (12.5)
ICU admission	
Cardiac surgery	6 (37.5)
SARS-CoV-2 pneumonia	8 (50)
Sepsis	1 (6.3)
Cardiac arrest	1 (6.3)
SOFA score	8 [3–13]
Albumin (g/L)	20 [18–22]
Treatment initiation	
SOFA score	10 [6–12]
Mechanical ventilation	15 (93.8)
Renal replacement therapy	8 (50)
Glomerular hyperfiltration	2 (12.5)
ECMO	9 (56.3)

Table 3. *Cont.*

	All (*n* = 16)
Previous known colonization with CR pathogens	10 (62.5)
Site of infection	
VAP	14 (87.5)
SSTI	3 (18.8)
c-UTI	1 (6.3)
Pathogens	
CPE	-
CR-Ab	9 (56.3)
XDR-Pa	7 (43.8)
P. putida	1 (6.3)
S. maltophilia	4 (25)

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Cefiderocol Treatment for Severe Infections due to Difficult-to-Treat-Resistant Non-Fermentative Gram-Negative Bacilli in ICU Patients: A Case Series and Narrative Literature Review

Table 4. Main outcomes after treatment with FDC.

	All (*n* = 16)
Duration of antibiotic course (days)	8 [7–13.5]
Antibiotic association ¶	5 (31.3)
Source control ¥	3 (18.8)
Clinical failure	5 (31.3)
Persistent colonization	13 (81.3)
Relapse	9 (56.3)
Adverse events	
C. difficile colitis	1 (6.3)
Hepatitis	3 (18.8)
Eosinophilia	1 (6.3)
Encephalopathy	9 (56.3)
Rash	1 (6.3)
Discharged from ICU	11 (68.8)
ICU length of stay (days)	60.5 [40–90.5]
ICU mortality	5 (31.3)
In-hospital death	6 (37.5)
1-year death	6 (37.5)

¶ at least 2 or 3 antibiotics (administered intravenously or nebulized, see text for details); ¥ surgery or catheter removal. Results are presented as *n* (%) or median [IQR] for qualitative and quantitative variables, respectively. Abbreviations: FDC: Cefiderocol; ICU: intensive care unit.

1/3 de bi/trithérapie :
Colimycine +/- ciprofloxacine
Ou tigécycline

Aucun arrêt de traitement

TDM (12 patients)
Cmin 34 mg/L [21–66]
(target Cmin 20 - 40 mg/L)

Wicky et al. Antibiotics 2023

PAVM & pneumonie acquise à l'hôpital à BGN multirésistants : « une bouffée d'air ?»

- Les PAVM à BGN multirésistants sont rares mais en augmentation (COVID), et difficiles à traiter
- Dans les études de « vraie vie » les nouveaux antibiotiques semblent être des options thérapeutiques valables
- Dans certains cas, il faut probablement envisager une bithérapie
- Dans certains cas, il faut probablement envisager une optimisation PK/PD reposant sur les dosages
- Les antibiogrammes doivent être réalisés dans un laboratoire expérimenté

Opinions personnelles