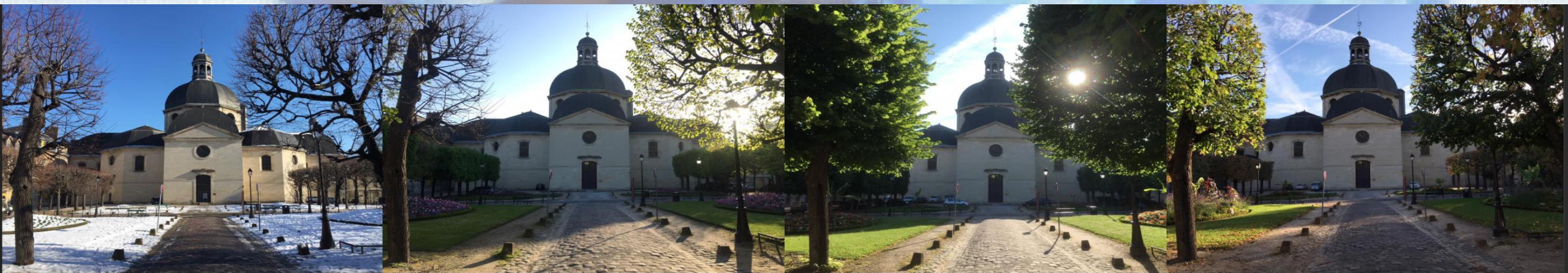
4eme colloque MeS MAYOTTE EN SANTÉ

Escalader pour mieux désescalader

Dr Alexandre Bleibtreu

Médecin Infectiologue - Hôpital Pitié Salpêtrière, APHP Sorbonne Université



Déclaration des liens d'intérêts

J'ai actuellement, ou j'ai eu au cours des trois dernières années, une affiliation ou des intérêts financiers ou intérêts de tout ordre avec les sociétés commerciales suivantes en lien avec la santé.

Liens d'intérêt :

- APHP, INSERM, HAS, ANR, DGOS, ANSM, SpF
- SPILF, ESCMID, Phages.fr, GFTF
- NeuTiger
- Apple, Microsoft

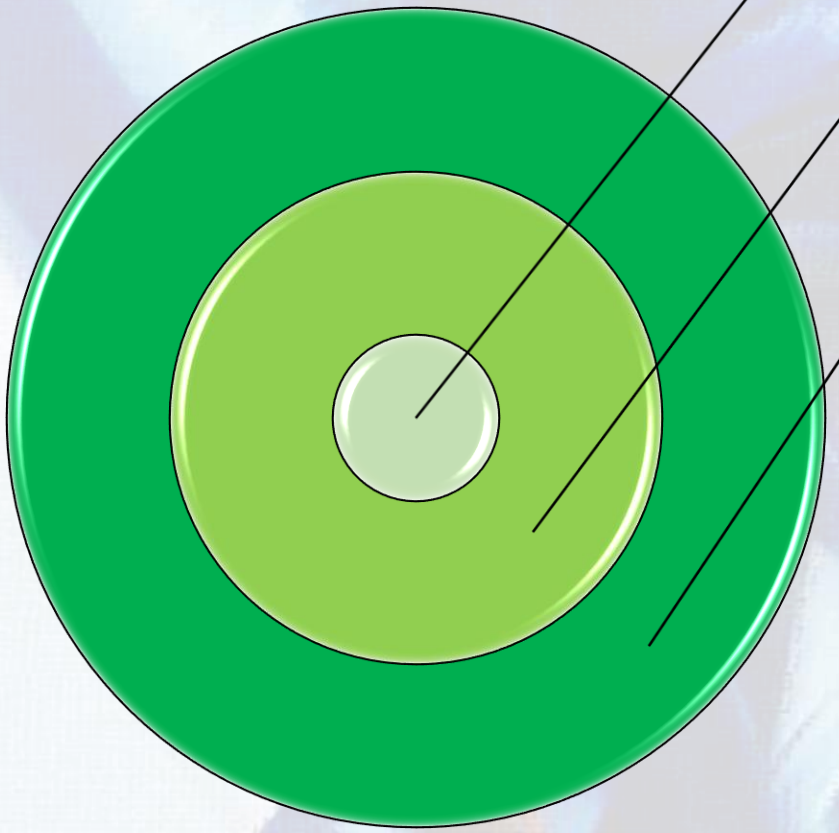
- **Liens d'intérêt en relation avec la présentation :**

Les sociétés suivantes sont partenaires 2023 de la SPILF.

Elles n'interviennent à aucun moment sur le contenu éditorial, la présentation, ou les priorités présentées par infectiologie.com

ADVANZ PHARMA
AstraZeneca
BIOMÉRIEUX
EUMEDICA Pharmaceuticals
eXperf Professionnels de Santé à Domicile
GILEAD Creating Possible
GSK
MENARINI France
moderna
PANPHARMA
Pfizer
sanofi
SHIONOGI
ZERIA GROUP TILLOTTS PHARMA
valneva
ViiV Healthcare

BUA : Bien utilisé ou Bon usage ?



Bien choisir
la molécule

Bien utilisé
l'antibiotique

Bon usage
des
antinfectieux

Antibiothérapie en France

Total ATB

ATB Humaine

ATB en ville

ATB ES

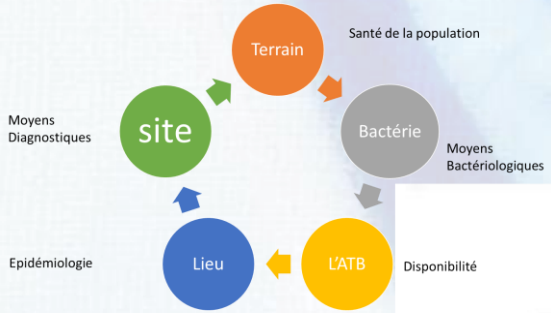
ATB H

ATB H appropriée

ATB H avec AS

- Initiation
- Désescalade
- Adpatation
  - Spectre
  - Diffusion
  - Durée
- Nouvelles molécules
- Politiques locales

Circonstances aggravantes



Hôpitaux précaires, mauvaises conditions d'hygiène

Mauvais usage des antibiotiques

Pas d'accès aux outils diagnostics microbiologiques

Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance

MDR

R à au moins 1 ATB

≥ 3 famille d'ATB ≠

Normalement actives (NA)

XDR

R à tous les ATB

Sauf 1 molécule

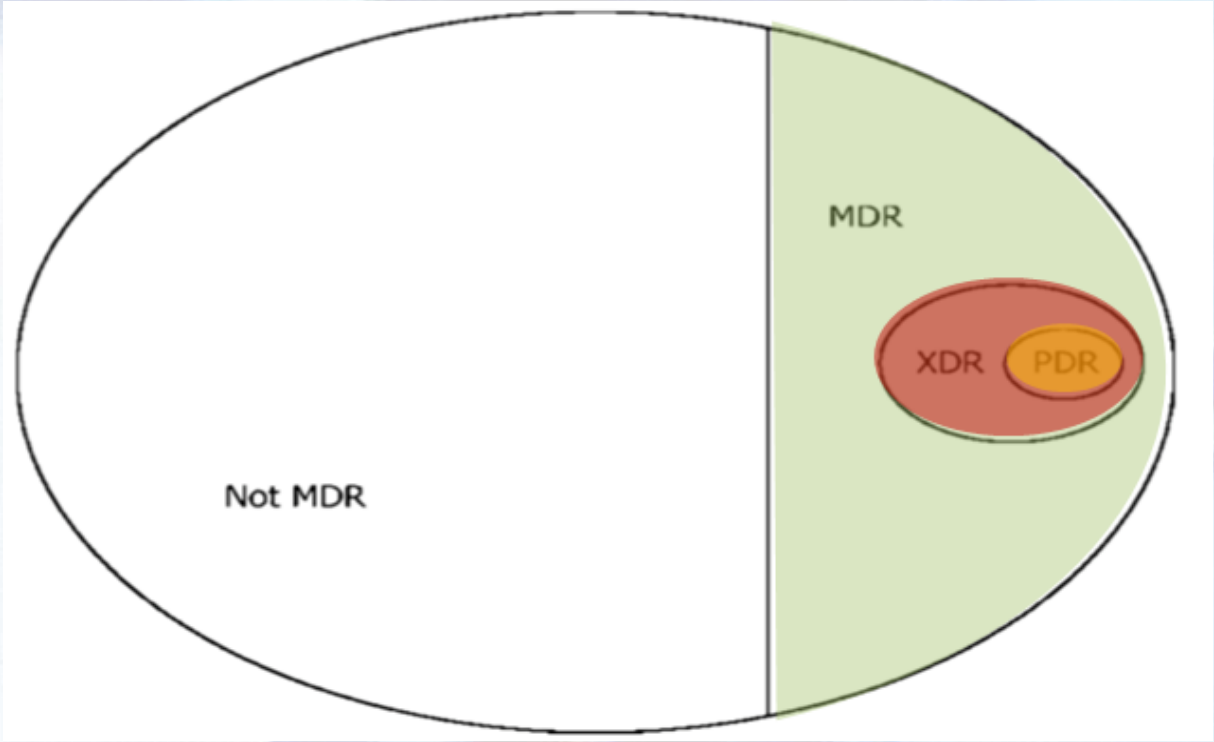
Dans 2 catégories NA

PDR

R à tous les ATB

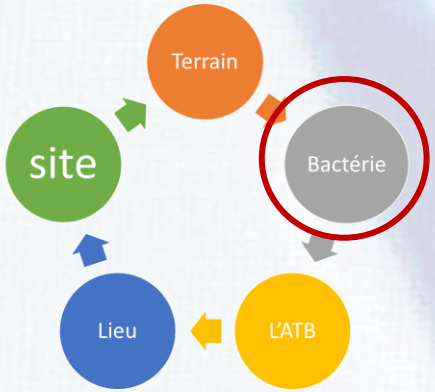
ou

R aux ATB de 1ère ligne



Magiorakos AP CMI 2012; 18 : 268
Gauzit R MMDLE

Acceptez que l'on ne sait pas !



Résistance dans les LMIC

Mapping Antimicrobial Resistance and Antimicrobial Use Partnership

MAAP
Mapping AMR & AMU Partnership

The MAAP project, led by, and for Africans, represents the first time that large quantities of AMR and AMC data are being systematically collected, processed, and evaluated in Africa.

MAAP REVIEWED

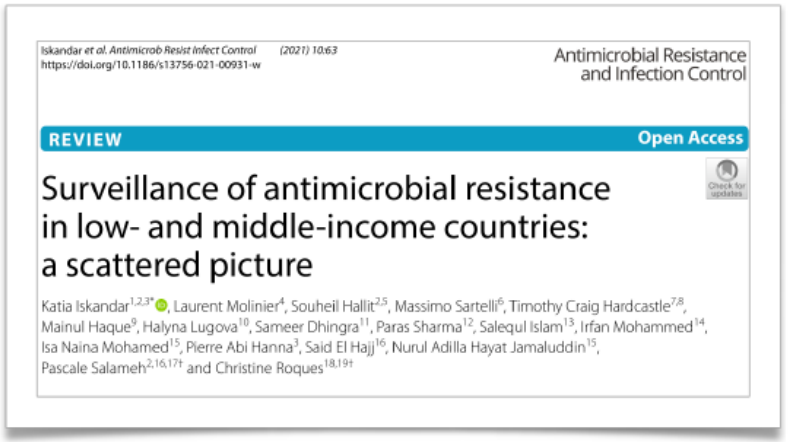
819,584

AMR records spanning from 2016 to 2019, from 205 LABORATORIES across 14 COUNTRIES.

326 hospital and community pharmacies and 16 national level datasets on antimicrobial consumption.

ONLY 1.3% of the biology laboratories across the 14 countries perform bacteriological testing

Out of the **187,000 samples tested** for **antimicrobial resistance, 88%** did not include records of patients' clinical profile—the diagnosis, the origin of infection, comorbidities and previous antimicrobial usage—while the remaining **12%** had incomplete information.



Iskandar et al. Antimicrob Resist Infect Control (2021) 10:63
https://doi.org/10.1186/s13756-021-00931-w

Antimicrobial Resistance and Infection Control

REVIEW Open Access

Surveillance of antimicrobial resistance in low- and middle-income countries: a scattered picture

Katia Iskandar[1,2,3*], Laurent Molinier[4], Souheil Hallit[2,5], Massimo Sartelli[6], Timothy Craig Hardcastle[7,8], Mainul Haque[9], Halyna Lugova[10], Sameer Dhingra[11], Paras Sharma[12], Salequl Islam[13], Irfan Mohammed[14], Isa Naina Mohamed[15], Pierre Abi Hanna[3], Said El Hajj[16], Nurul Adilla Hayat Jamaluddin[15], Pascale Salameh[2,16,17†] and Christine Roques[18,19†]

Obstacles à une surveillance efficace

- Accès limité ou non-disponibilité des réactifs
- Infrastructures du laboratoire insuffisantes
- Personnel labo et clinique limité, en termes de nombre et de formation
- Problèmes de communications labo <-> cliniciens
- Assurance qualité insuffisante - pas de règles
- Dépendance à des financements extérieurs
- Pas de standardisation des AST
- Fragmentation des sources de données

Credit Martin Vandeputte MD, PhD student

4eme colloque MeS MAYOTTE EN SANTÉ

ONHETO-PREV

Contents lists available at ScienceDirect

Infectious Diseases Now

journal homepage: www.sciencedirect.com/journal/infectious-diseases-now

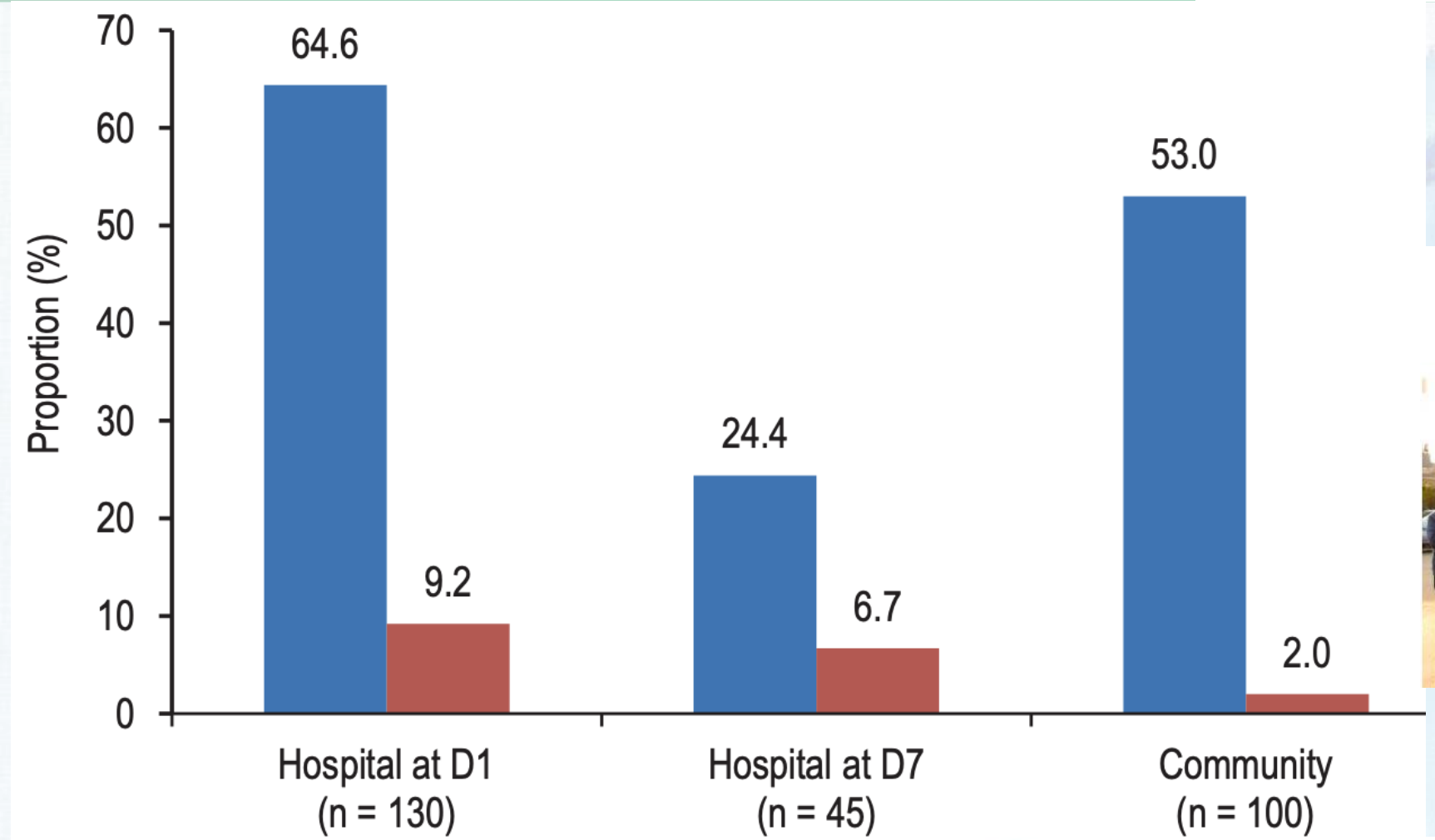
ELSEVIER

Short communication

Prevalence of digestive carriage of multi-drug resistant enterobacterales in hospitalized and community-based patients in Togo: a prospective study

Rogatien Comlan Atoun [a,b,*], Iman Frédéric Youa [a,b], Lidaw Déassoua Bawe [c], Isidore Tchaou [d], Bodombossou Madera [e], Awereou Kotosso [d], Alexandre Bleibtreu [f], Taïssiri Adedjouma [a,b], André Pouwedeou Bedekelabou [g], Jules Tchédié [h], Yvette Siliadin [i], Eric Cardinale [e], Laurence Armand Lefevre [j,k], Brücker Gilles [l], Salou Mounerou [m], Claver Anoumou Dagnra [n], Didier Koumavi Ekouevi [a,b,o], Dominique Salmon [j,p]

SOCIETE DE PATHOLOGIE INFECTIEUSE DE LANGUE FRANÇAISE Spilf



RÉPUBLIQUE TOGOLAISE · RÉPUBLIQUE FRANÇAISE · EXPERTISE FRANCE · ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS · cirad · H

ONHETO-PREV Carbapénémases

Familles	Antibiotiques		1980	2000	2010
Pénicillines	Amoxicilline	S	R	R	R
Péni + inhibiteurs	Augmentin	S	S/I	R	R
Céphalo 1ère gen.	Céfalotine	S	S/I	R	R
Céphalo 2ème gen.	Cefuroxime	S	S	R	R
Céphalo 3ème gen.	Cefotaxime	S	S	R	R
Carbapénèmes	Imipénème	S	S	S	R
Aminosides	Genta/Amikacine	S	S	S/I	R
Fluoroquinolones	Ofloxacine	S	S	R	R
Sulfamide/tmp	Bactrim	S	S	R	R

E-BLSE EPC

Bactéries multi-résistantes

Espèces :

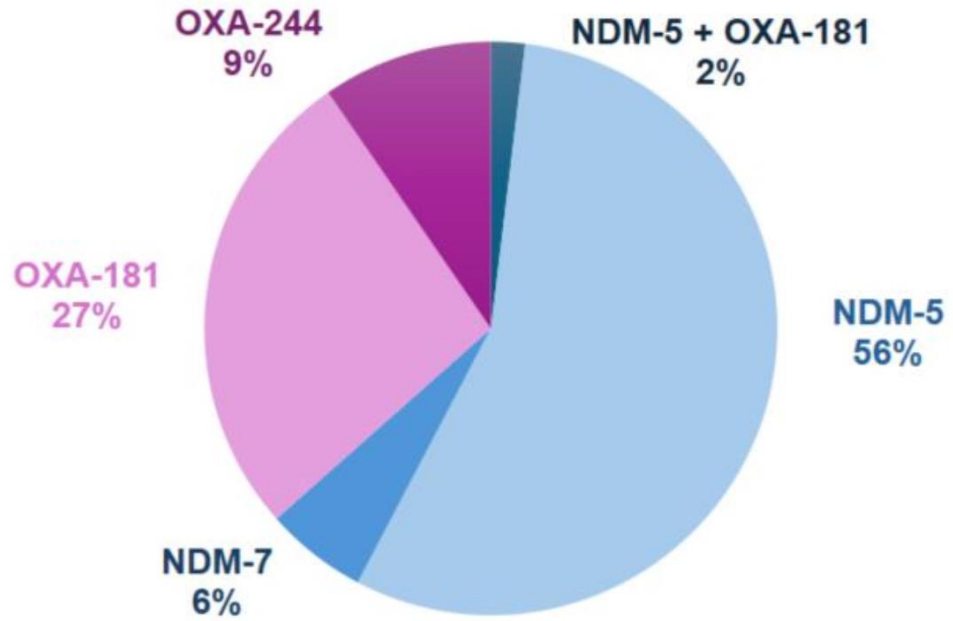
E. coli (n=46)

K. pneumoniae (n=5)

E. cloacae (n=1)

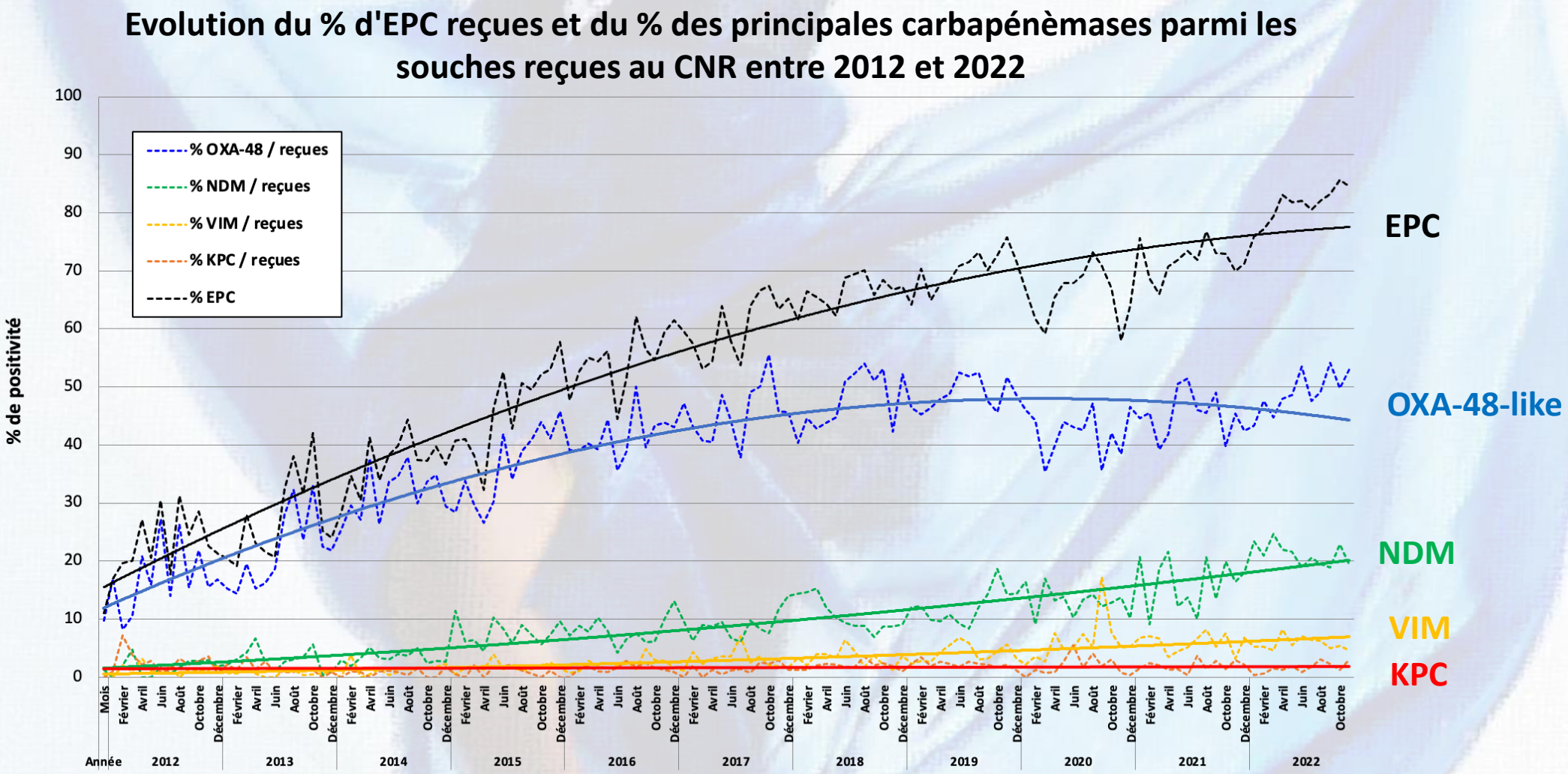
Le nombre moyen de gène de résistance est de 11,7 gènes par souches d'EPC

Répartition des types de carbapénémase



Prédominance +++ des EPC porteuses de NDM-5 particulièrement résistantes

Connaitre son ennemi



La résistance est associée à un sur risque de mortalité

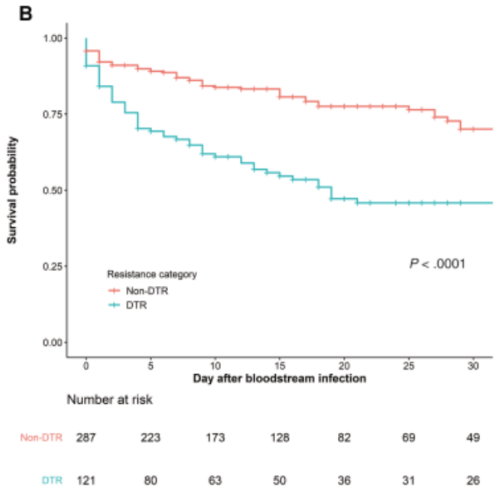
MAJOR ARTICLE

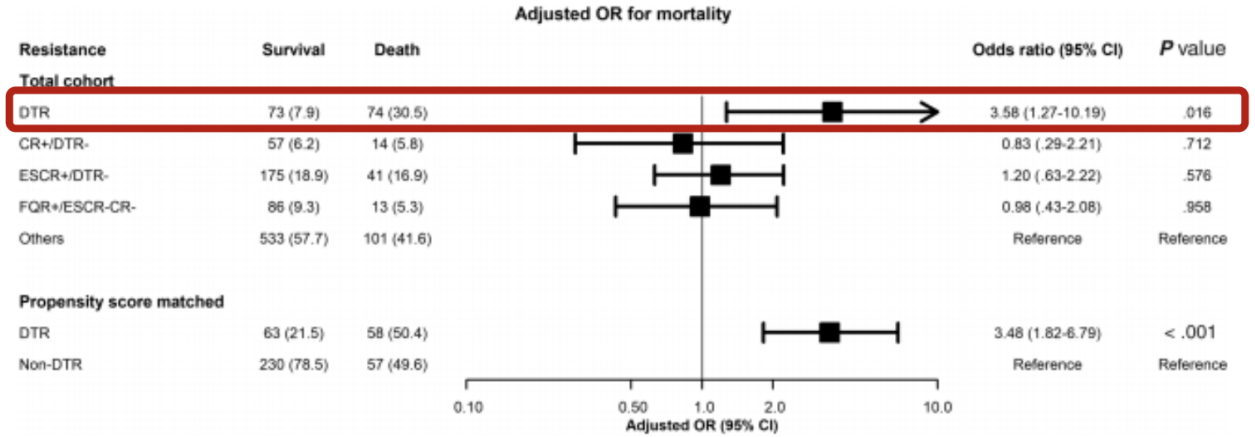
2020

Infectious Diseases Society of America | hiv medicine association | OXFORD

Impact of Difficult-to-Treat Resistance in Gram-negative Bacteremia on Mortality: Retrospective Analysis of Nationwide Surveillance Data

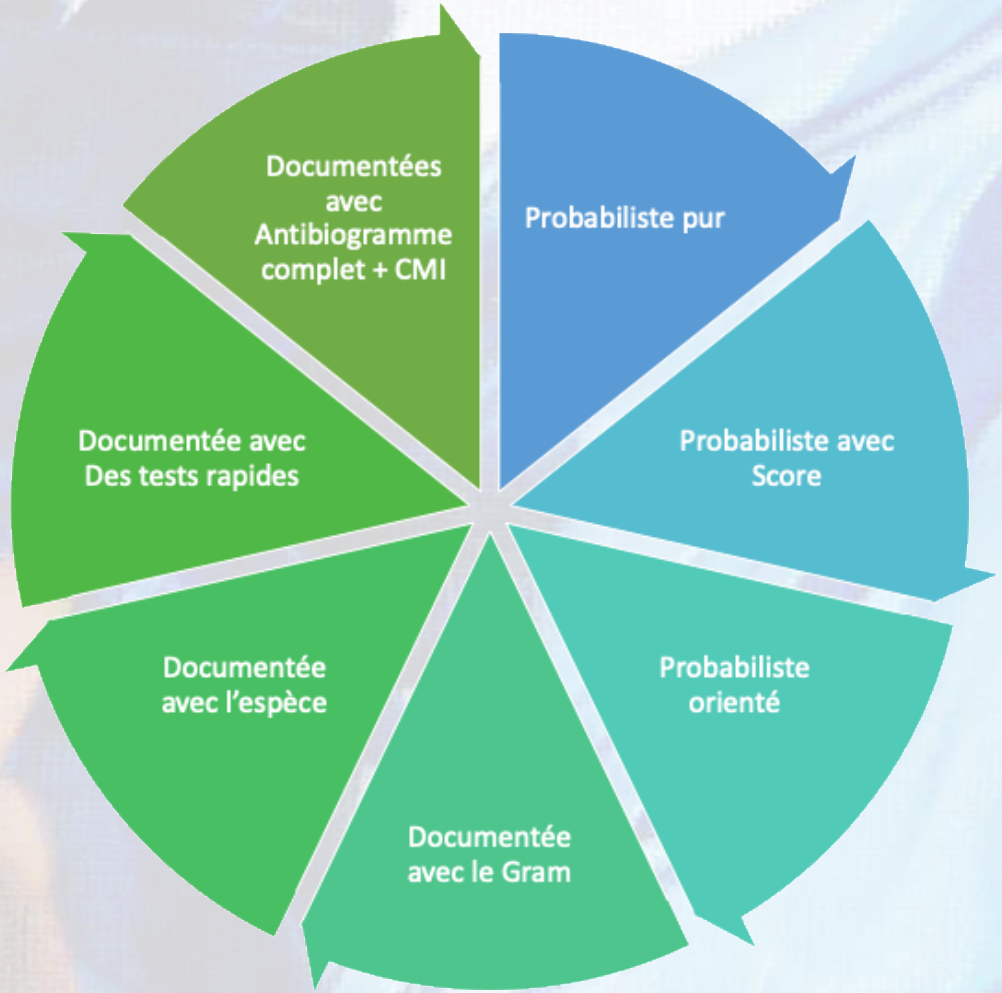
Kyungmin Huh,[1,2] Doo Ryeon Chung,[1,2] Young Eun Ha,[3] Jae-Hoon Ko,[1] Si-Ho Kim,[1] Min-Ji Kim,[4] Hee Jae Huh,[5] Nam Yong Lee,[5] Sun Young Cho,[1] Cheol-In Kang,[1] Kyong Ran Peck,[1] and Jae-Hoon Song[1,2]; for the Korean Antimicrobial Resistance Surveillance Network (KARS-Net) Investigators[a]





Difficult To Treat = résistance aux antibiotiques de première ligne (β-lactamines, carbapénèmes, fluoroquinolones)

Quels sont les situations de prescriptions ?



Antibiothérapie cet ersatz de l'amour

- **Choix :**
  - Action de choisir quelque chose, quelqu'un, de le prendre de préférence aux autres.
  - Résultat de cette action.
- **Ne pas avoir le choix :**
  - Être obligé, contraint d'agir d'une certaine manière.

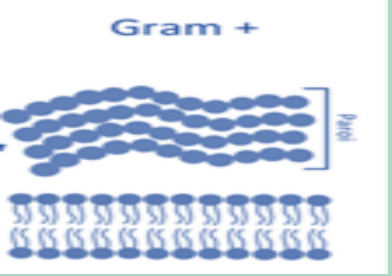
Marcel Proust (1871-1922)
On a tort de parler en amour de mauvais choix, puisque dès qu'il y a choix il ne peut être que mauvais.
À la recherche du temps perdu

Classification d'Ambler

	β- lactamase KPC	Metallo-β-lactamase NDM, VIM, IMP	Céphalosporinase AmpC	Oxacillinase OXA-48
Ambler	A	B	C	D
Substrates of hydrolysis	All β-lactams	All β-lactams except for aztreonam	Penicillins, Cephalosporin	Penicillins and carbapenems
Clavulanate Tazobactam* Sulbactam	Minimally	No	No Intermediate	No
Enmetazobactam	Partially (BLSE)	No	Yes	Yes
Avibactam*	Yes	No	Yes	Yes
Vaborbactam*	Yes	No	Yes	No
Relebactam	Yes	No	Yes	No
Zidebactam	Yes		Yes	Yes
Durlobactam	Yes		Yes	Yes
Nacubactam	Yes		Yes	Yes

Place des nouveaux inhibiteurs de β-lactamases

Inhibiteur	BLSE	AmpC	KPC	MBL	OXA-48-like	Activité ATB intrinsèque
Ac. clavulanique	++	-	+	-	-	-
Sulbactam	++	-	+	-	-	PBP2
Tazobactam	++	-	+	-	-	-
Enmetazobactam	+++	++	++	-	-	-
Avibactam	+++	++	+++	-	+	-
Relebactam	+++	++	+++	-	+/-	-
Vaborbactam	+++	++	+++	-	+/-	-
Zidebactam	+++	++	+++	-	?	PBP2
Taniborbactam	+++	++	+++	++ (sauf IMP)	?	?



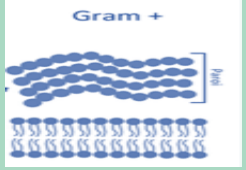
Avant 2015

SARM/SCN MR	SAMS/SCN MS	STREPTO	ENTEROCOQUE	ENTEROBACTERIE	PSEUDOMONAS	ANAEROBIE
		AMOX				
		PIPERACILLINE				
		C1G		C1G		
		C2G		C2G		
		C3G		C3G		
				CEFTAZIDIME		
				AZTREONAM		
		C4G		C4G		
		IMIPENEM				
		MEROPENEM		MEROPENEM		
		ERTAPENEM		ERTAP		

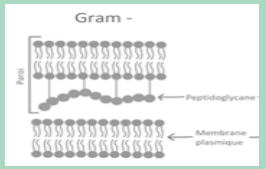
IBL

BLase

Ac clavulanique
Sulbactam
Tazobactam



EN 2022

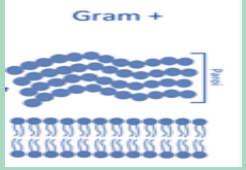


SARM/SCN MR	SAMS/SCN MS	STREPTO	ENTEROCOQUE	ENTEROBACTERIE	PSEUDOMONAS	ANAEROBIE
		AMOX				
		PIPERACILLINE				
		C1G		C1G		
		C2G		C2G		
		C3G		C3G		
				CEFTAZI CEFTOLO		
				AZTREONAM		
		C4G		C4G		
	C5G CEFTAROLINE			CEFTARO		
	C5G CEFTOBIPROLE				C5G	
				CEFIDEROCOL		
		IMIPENEM				
		MEROPENEM		MEROPENEM		
		ERTAPENEM		ERTAP		

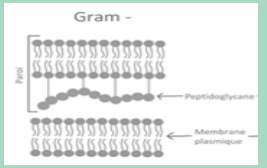
BLase

IBL

Ac clavulanique
Sulbactam
Tazobactam
Avibactam
Relebactam
Vaborbactam



EN 2026



SARM/SCN MR	SAMS/SCN MS	STREPTO	ENTEROCOQUE	ENTEROBACTERIE	PSEUDOMONAS	ANAEROBIE

AMOX

PIPERACILLINE

C1G

C1G

C2G

C2G

C3G

C3G

CEFTAZI CEFTOLO

IBL

BLase

AZTREONAM

C4G

C4G

C5G CEFTAROLINE

CEFTARO

C5G CEFTOBIPROLE

C5G

CEFIDEROCOL

Cyclines (Tigé-Erava-omada)

Cyclines

IMIPENEM

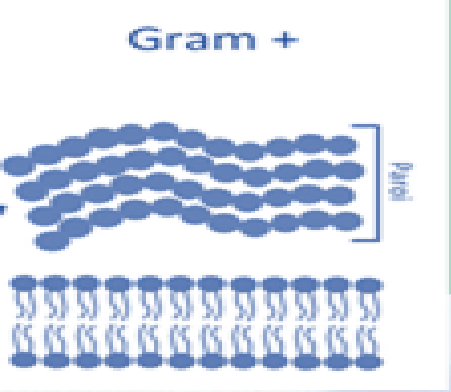
MEROPENEM

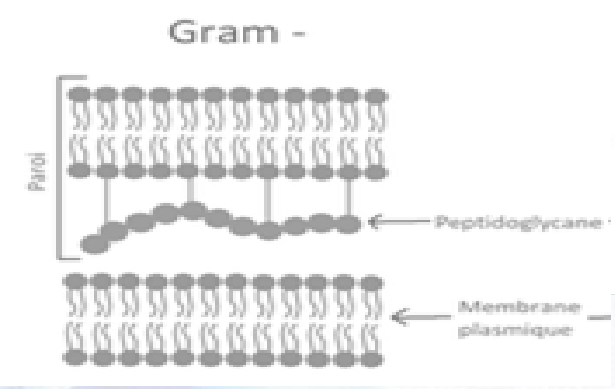
MEROPENEM

ERTAPENEM

ERTAP

Ac clavulanique
Sulbactam
Tazobactam
Avibactam
Relebactam
Vaborbactam
Taniborbactam
Durlobactam
Enmetazobactam
Nacubactam
Zidebactam
zvevtera





SARM/SCN MR	SAMS/SCN MS	STREPTO	ENTERO	ENTEROBACTERIE	PSEUDOMONAS
DAPTOMYCiNE					
VANCOMYCINE / TEICOPLANINE					
LINEZOLIDE / TELIDOZOLIDE					
TIGECYCLINE					
DALBAVANCINE / ORITAVANCINE					
OMADACYCLINE					
ERAVACYCLINE					

Recommandations concernent les traitements d'infections microbiologiquement documentées causées par des bacilles à Gram négatif multi-résistants

Tamma et al. Clinical Infectious Diseases **2021**;72(7):e169–83

Paul M et al. Clinical Microbiology and Infection **2022**; 28:521e547

Jeu de diapositives réalisé par le groupe recommandation de la SPILF le **11.10.2023** (https://www.infectiologie.com/fr/recommandations.html)

Nouveaux antibiotiques et BGN résistantes aux carbapénèmes

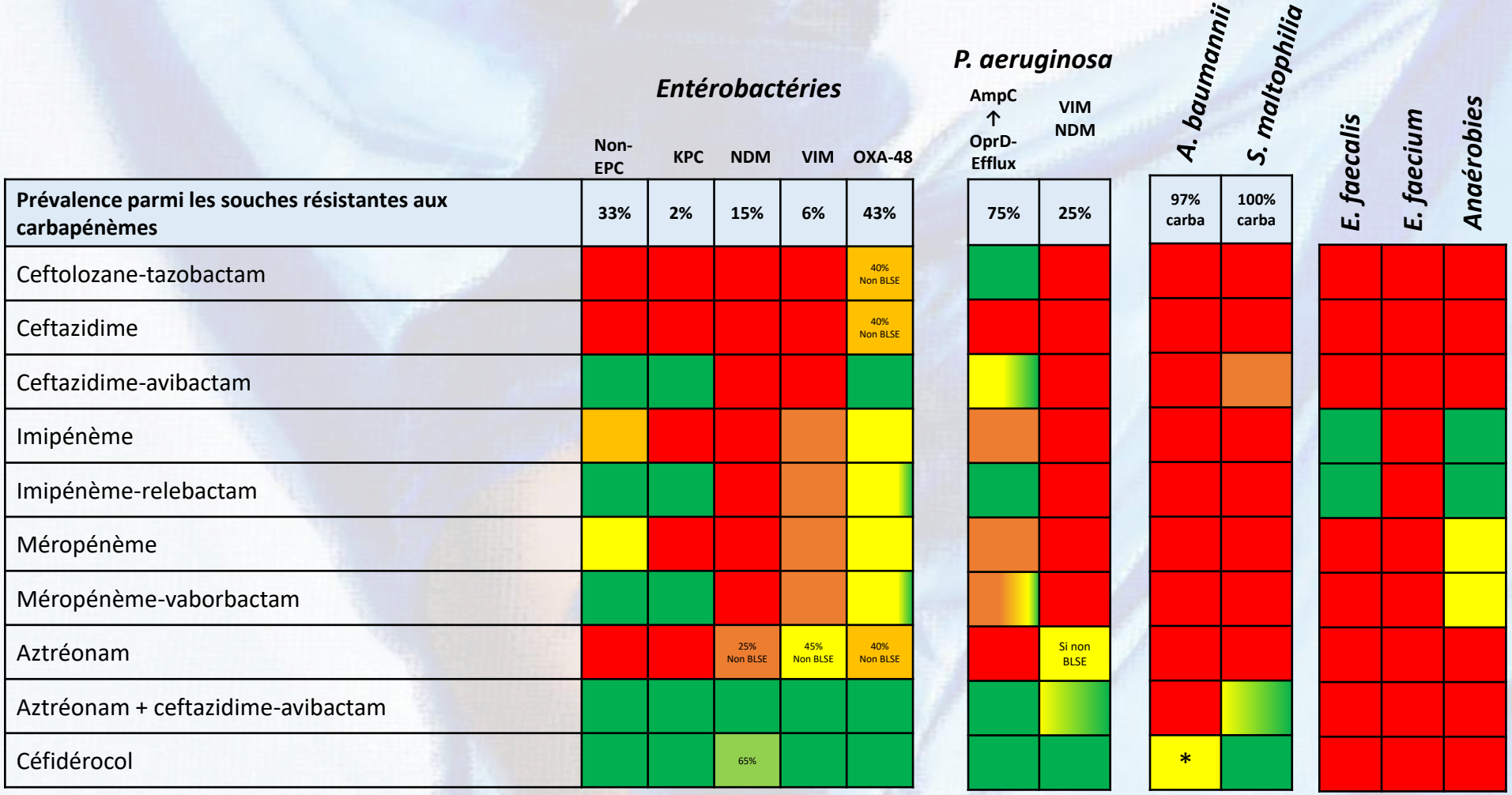
Entérobactéries

	Non-EPC	KPC	NDM	VIM	OXA-48
Prévalence parmi les souches résistantes aux carbapénèmes	**33%**	**2%**	**15%**	**6%**	**43%**
Ceftolozane-tazobactam					40% Non BLSE
Ceftazidime					40% Non BLSE
Ceftazidime-avibactam					
Imipénème					
Imipénème-relebactam					
Méropénème					
Méropénème-vaborbactam					
Aztréonam			25% Non BLSE	45% Non BLSE	40% Non BLSE
Aztréonam + ceftazidime-avibactam					
Céfidérocol			65%		

← 1er choix

* HAS avis de CT (20 jan 2021) : Les incertitudes liées au surcroît de mortalité observé avec le céfidérocol dans l'étude CREDIBLE-CR,inexpliqué à ce jour, en particulier en cas pneumopathie ou de bactériémie/sepsis dues à *Acinetobacter baumannii*, ne permet pas de conclure sur l'intérêt de cet antibiotique en cas d'infection due à ce germe

Spectre pour les infections mixtes (infections digestives principalement)



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Comment je raisonne
Espèce, Mécanisme de résistance
+ site de l'infection

	EB BLSE	EB Oxa-48	EB KPC	EB NDM	EB autre carba	PA AMP c	PA Mex-AB	PA VIM	PA NDM
Carbapénème									
Cefto-tazo									
Cefta-avi									
ATM-avi									
FEP-enmetazo									
Imi-rele									
Mero-vabor									
Cefiderocol									
FEP-zide									

Clinical Infectious Diseases

IDSA GUIDELINE

2022

Infectious Diseases Society of America Guidance on the Treatment of AmpC β-Lactamase–Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections

Pranita D. Tamma,[1] Samuel L. Aitken,[2] Robert A. Bonomo,[3] Amy J. Mathers,[4] David van Duin,[5] and Cornelius J. Clancy[6]

Question 1: What Is a General Approach for the Treatment of Infections Caused by *S. maltophilia*?

Suggested Approach

For mild infections, TMP-SMX, minocycline, tigecycline, levofloxacin, or cefiderocol monotherapy are suggested

Question 2: What Is the Role of Trimethoprim-Sulfamethoxazole for the Treatment of Infections Caused by *S. maltophilia*?

Suggested Approach

TMP-SMX monotherapy is a preferred treatment agent for mild *S. maltophilia* infections. TMP-SMX either as monotherapy or, preferably, in combination with another active agent is suggested for moderate to severe *S. maltophilia* infections.

Question 3: What Is the Role of Tetracycline Derivatives for the Treatment of Infections Caused by *S. maltophilia*?

Suggested Approach

High-dose minocycline monotherapy is a treatment consideration for mild *S. maltophilia* infections. High-dose minocycline

Question 4: What Is the Role of Fluoroquinolones for the Treatment of Infections Caused by *S. maltophilia*?

Suggested Approach

Levofloxacin monotherapy is a treatment option for mild *S. maltophilia* infections. The emergence of resistance during levofloxacin therapy is a concern. If administered for the treatment of moderate to severe *S. maltophilia* infections, levofloxacin should only be considered in combination with a second active agent (TMP-SMX, minocycline, tigecycline, cefiderocol).

Question 5: What Is the Role of Cefiderocol for the Treatment of Infections Caused by *S. maltophilia*?

Suggested Approach

Cefiderocol monotherapy is a treatment option for mild *S. maltophilia* infections, acknowledging the limited clinical data available with this agent. Cefiderocol in combination with a second active agent, at least until clinical improvement is observed, is suggested for the treatment of moderate to severe *S. maltophilia* infections.

Question 6: What Is the Role of Ceftazidime-Avibactam and Aztreonam for the Treatment of Infections Caused by *S. maltophilia*?

Suggested Approach

The combination of ceftazidime-avibactam and aztreonam is suggested for moderate to severe *S. maltophilia* infections when neither TMP-SMX nor minocycline are considered viable treatment options.

Question 7: What Is the Role of Ceftazidime for the Treatment of Infections Caused by *S. maltophilia*?

Suggested Approach

Ceftazidime is not a suggested treatment option for *S. maltophilia* infections due to the presence of β-lactamase genes intrinsic to *S. maltophilia* that are expected to render ceftazidime inactive.

Clinical Infectious Diseases

IDSA GUIDELINE

2022

Infectious Diseases Society of America Guidance on the Treatment of AmpC β-Lactamase–Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections

Pranita D. Tamma,[1] Samuel L. Aitken,[2] Robert A. Bonomo,[3] Amy J. Mathers,[4] David van Duin,[5] and Cornelius J. Clancy[6]

Question 1: What Is a General Approach for the Treatment of Infections Caused by *S. maltophilia*?

Suggested Approach

For mild infections, TMP-SMX, minocycline, tigecycline, levofloxacin, or cefiderocol monotherapy are suggested

Question 2: What Is the Role of Trimethoprim-Sulfamethoxazole for the Treatment of Infections Caused by *S. maltophilia*?

Suggested Approach

TMP-SMX monotherapy is a preferred treatment agent for mild *S. maltophilia* infections. TMP-SMX either as monotherapy or, preferably, in combination with another active agent is suggested for moderate to severe *S. maltophilia* infections.

Question 3: What Is the Role of Tetracycline Derivatives for the Treatment of Infections Caused by *S. maltophilia*?

Suggested Approach

High-dose minocycline monotherapy is a treatment consideration for mild *S. maltophilia* infections. High-dose minocycline

Question 4: What Is the Role of Fluoroquinolones for the Treatment of Infections Caused by *S. maltophilia*?

Suggested Approach

Levofloxacin monotherapy is a treatment option for mild *S. maltophilia* infections. The emergence of resistance during levofloxacin therapy is a concern. If administered for the treatment of moderate to severe *S. maltophilia* infections, levofloxacin should only be considered in combination with a second active agent (TMP-SMX, minocycline, tigecycline, cefiderocol).

Question 5: What Is the Role of Cefiderocol for the Treatment of Infections Caused by *S. maltophilia*?

Suggested Approach

Cefiderocol monotherapy is a treatment option for mild *S. maltophilia* infections, acknowledging the limited clinical data available with this agent. Cefiderocol in combination with a second active agent, at least until clinical improvement is observed, is suggested for the treatment of moderate to severe *S. maltophilia* infections.

Question 6: What Is the Role of Ceftazidime-Avibactam and Aztreonam for the Treatment of Infections Caused by *S. maltophilia*?

Suggested Approach

The combination of ceftazidime-avibactam and aztreonam is suggested for moderate to severe *S. maltophilia* infections when neither TMP-SMX nor minocycline are considered viable treatment options.

Question 7: What Is the Role of Ceftazidime for the Treatment of Infections Caused by *S. maltophilia*?

Suggested Approach

Ceftazidime is not a suggested treatment option for *S. maltophilia* infections due to the presence of β-lactamase genes intrinsic to *S. maltophilia* that are expected to render ceftazidime inactive.

- A retenir

- Connaitre le couple bactérie et mécanisme de résistance
- Frapper fort mais ciblé
- à réception de l'antibiogramme
  - Molécule la plus ciblée possible
  - Couvrir le moins de domaines possibles (G+ G-, Anaérobies)
  - IV=> PO
  - Pas de raison de faire plus long car BMR
  - Ce qui compte c'est avoir une molécule active

Escalader pour mieux désescalader

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