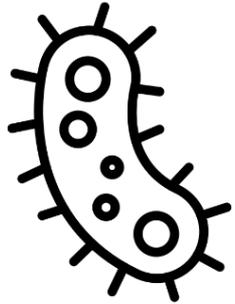


Céfoxitine versus carbapénèmes comme antibiothérapie définitive dans les bactériémies à *Klebsiella pneumoniae* productrices de bêta-lactamases à spectre élargi en réanimation médicale

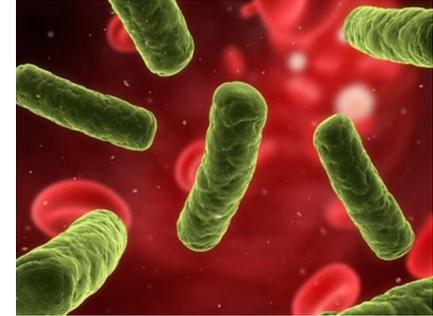
## Déclaration d'intérêt de 2014 à 2023

- Intérêts financiers : Aucun
- Liens durables ou permanents : Aucun
- Interventions ponctuelles : Aucun
- Intérêts indirects : Aucun



ATB probabiliste

*Klebsiella pneumoniae* BLSE



ATB  
définitive



Carbapénèmes



Céfoxitine



ATB définitive

Céfoxitine

VS

Carbapénèmes





❖ Rétrospective, monocentrique, RNIPH



❖ Janvier 2013 - Janvier 2023



❖ Bactériémie à KP BLSE sensible à la céfoxitine



❖ Critères d'exclusion



- ✓ Hémocultures polymicrobiennes
- ✓ Décès  $\leq$  24h
- ✓ Traitement par un autre antibiotique
- ✓ Antibiothérapie définitive  $\leq$  50% durée totale de l'ATB
- ✓ Absence d'accès au dossier clinique
- ✓ Refus du patient



1

- ❖ **Succès clinique à J30** : Survie à J30 + absence de récurrence + absence de changement d'ATB



2

- ❖ **Efficacité** : Mortalité à J30, récurrence, changement d'ATB, mortalité à J7, échec microbiologique
- ❖ **Résistance** : ID bactérie CEFOX-R et CARBA-R dans n'importe quel prélèvement après 24h d'ATB – J30



Characteristics	Baseline population		SMD	p value
	Cefoxitin n = 63 (57%)	Carbapenem n = 47 (43%)		
Age, years	57 ± 17	57 ± 13	<0.001	.585
≥ 65	27 (42)	18 (40)	.093	.630
Male	42 (67)	31 (66)	.015	.938
Year of inclusion				
2018 - 2022	32 (51)	25 (53)	.048	.803
Body-mass index	27 ± 5	27 ± 8	.123	.582
Charlson comorbidity index	4 (2-6)	3 (1-4)	.328	.141
Surgery, previous 30 days	21 (34)	13 (28)	.121	.535
Immunosuppressive therapy	4 (6)	6 (13)	.224	.319
Sickle cell disease	2 (3)	2 (4)	.059	1.00
Radio or chemotherapy within the last 3 months	1 (2)	1 (2)	.041	1.00
Unknown disease	0 (0)	1 (2)	.211	.426
Origin:			.021	.913
Community-acquired (ref)	5 (8)	4 (9)		
Nosocomial infection	58 (92)	43 (91)		
Source of bacteremia:				
Central line associated	24 (38)	12 (26)	.272	.165
With thrombophlebitis	9 (15)	3 (7)	.262	.188
Pneumonia	7 (11)	14 (30)	.476	<b>.014</b>
Urinary tract	13 (21)	3 (6)	.426	.054
Intra abdominal	8 (13)	4 (9)	.136	.489
Liver abscess	1 (1)	1 (2)	.040	1.00
Skin and soft tissue	2 (3)	0 (0)	.256	.506
Neuromeningeal	0 (0)	4 (8)	.431	<b>.031</b>
Unknown	8 (13)	9 (19)	.177	.428



## Baseline population



LE  
andie  
2024



Characteristics	Baseline population		SMD	p value
	Cefoxitin n = 63 (57%)	Carbapenem n = 47 (43%)		
Time between admission to ICU and bacteremia, <i>days</i>	12 ± 13	15 ± 13	.252	.053
SAPS II admission score	47 ± 17	49 ± 22]	.111	.557
SOFA score at inclusion	9 ± 4]	11 ± 5	.415	<b>.046</b>
Pitt bacteremia score at inclusion	6 ± 3	7 ± 3	.273	.062
Septic shock	25 (40)	19 (40)	.015	.937
Mechanical ventilation	40 (63)	41 (87)	.573	<b>.005</b>
Appropriate empirical therapy	31 (56)	28 (65)	.180	.380
Duration of empirical therapy, <i>days</i>	1 ± 1	1 ± 2	.113	.788
Time to effective antibiotic therapy, <i>hours</i>	26 ± 25	12 ± 35	.460	.075
Co-infection at inclusion	11 (18)	4 (9)	.234	.208
Other antibiotic therapy at inclusion	12 (19)	5 (11)	.208	.298

Data are presented as mean ± SD or count (%). p values in bold are statistically significant. SMD=standardized mean difference. ICU=intensive care unit. SAPS II=Simplified Acute Physiology score II. SOFA=Sequential Organ Failure Assessment score.

→ Groupe « carbapénèmes » :  grave

Characteristics	Baseline population				PS-matched patients			
	Cefoxitin n = 63 (57%)	Carbapenem n = 47 (43%)	SMD	p value	Cefoxitin n = 42 (50%)	Carbapenem n = 42 (50%)	SMD	p value
Age, years	57 ± 17	57 ± 13	<0.001	.585	55 ± 17	57 ± 12	.121	.864
≥ 65	27 (42)	18 (40)	.093	.630	17 (40)	15 (36)	.098	.653
Male	42 (67)	31 (66)	.015	.938	29 (69)	26 (62)	.151	.491
Year of inclusion								
2018 - 2022	32 (51)	25 (53)	.048	.803	23 (55)	22 (52)	.048	.827
Body-mass index	27 ± 5	27 ± 8	.123	.582	27 ± 5	28 ± 8	.140	.567
Charlson comorbidity index	4 (2-6)	3 (1-4)	.328	.141	3 ± 3	3 ± 2	.161	.664
Surgery, previous 30 days	21 (34)	13 (28)	.121	.535	14 (33)	11 (26)	.142	.518
Immunosuppressive therapy	4 (6)	6 (13)	.224	.319	4 (9)	6 (14)	.157	.520
Sickle cell disease	2 (3)	2 (4)	.059	1.00	1 (2)	2 (5)	.134	.616
Radio or chemotherapy within the last 3 months	1 (2)	1 (2)	.041	1.00	1 (2)	1 (2)	.004	1.00
Unknown disease	0 (0)	1 (2)	.211	.426	0 (0)	1 (2)	.224	.494
Origin:			.021	.913			.101	.645
Community-acquired (ref)	5 (8)	4 (9)			2 (5)	3 (7)		
Nosocomial infection	58 (92)	43 (91)			40 (95)	39 (93)		
Source of bacteremia:								
Central line associated	24 (38)	12 (26)	.272	.165	17 (41)	11 (26)	.306	.165
With thrombophlebitis	9 (15)	3 (7)	.262	.188	5 (12)	3 (7)	.163	.713
Pneumonia	7 (11)	14 (30)	.476	<b>.014</b>	7 (17)	12 (29)	.287	.192
Urinary tract	13 (21)	3 (6)	.426	.054	4 (10)	3 (7)	.086	1.00
Intra abdominal	8 (13)	4 (9)	.136	.489	6 (14)	4 (10)	.147	.738
Liver abscess	1 (1)	1 (2)	.040	1.00	1 (2)	1 (2)	<0.001	1.00
Skin and soft tissue	2 (3)	0 (0)	.256	.506	1 (2)	0 (0)	.221	1.00
Neuromeningeal	0 (0)	4 (8)	.431	<b>.031</b>	0 (0)	3 (7)	.392	.241
Unknown	8 (13)	9 (19)	.177	.428	6 (14)	8 (19)	.128	.558

Characteristics	Baseline population				PS-matched patients			
	Cefoxitin n = 63 (57%)	Carbapenem n = 47 (43%)	SMD	p value	Cefoxitin n = 42 (50%)	Carbapenem n = 42 (50%)	SMD	p value
Time between admission to ICU and bacteremia, <i>days</i>	12 ± 13	15 ± 13	.252	.053	12 ± 11	14 ± 12	.166	.485
SAPS II admission score	47 ± 17	49 ± 22]	.111	.557	48 ± 17	51 ± 21	.168	.443
SOFA score at inclusion	9 ± 4]	11 ± 5	.415	<b>.046</b>	10 ± 4	11 ± 5	.297	.193
Pitt bacteremia score at inclusion	6 ± 3	7 ± 3	.273	.062	7 ± 3	7 ± 3 (6-9)	.129	.303
Septic shock	25 (40)	19 (40)	.015	.937	17 (40)	18 (43)	.048	.825
Mechanical ventilation	40 (63)	41 (87)	.573	<b>.005</b>	33 (78)	37 (88)	.258	.380
Appropriate empirical therapy	31 (56)	28 (65)	.180	.380	22 (52)	27 (64)	.251	.260
Duration of empirical therapy, <i>days</i>	1 ± 1	1 ± 2	.113	.788	1 ± 1	1 ± 2	.110	.765
Time to effective antibiotic therapy, <i>hours</i>	26 ± 25	12 ± 35	.460	.075	26 ± 24	11 ± 36	.493	.065
Co-infection at inclusion	11 (18)	4 (9)	.234	.208	8 (19)	6 (14)	.251	.591
Other antibiotic therapy at inclusion	12 (19)	5 (11)	.208	.298	8 (19)	7 (17)	.120	.816

Data are presented as mean ± SD or count (%). p values in bold are statistically significant. SMD=standardized mean difference.

ICU=intensive care unit. SAPS II=Simplified Acute Physiology score II. SOFA=Sequential Organ Failure Assessment score.

→ Groupes comparables



Outcomes	Cefoxitin (n = 63)	Carbapenem (n = 47)	Univariate analysis		PS-matched analysis	
			HR (95%CI)	<i>p</i> value	aHR (95%CI)	<i>p</i> value
30-day clinical success	36 (57)	25 (53)	0.9 (0.5-1.6)	.823	1.0 (0.5-1.8)	.919
30-day all-cause mortality	18 (29)	20 (42)	0.6 (0.3-1.2)	.131	0.7 (0.3-1.3)	.277
Relapse	6 (11)	4 (11)	1.1 (0.3-3.9)	.887	0.7 (0.2-3.2)	.670
Change of antibiotic	11 (17)	0 (0)	N/A	<b>.002</b>	N/A	<b>.002</b>
7-day all-cause mortality	9 (14)	7 (15)	0.9 (0.3-2.5)	.889	1.1 (0.4-3.1)	.827
Microbiological failure	10 (16)	7 (15)	1.1 (0.4-2.8)	.897	0.9 (0.3-2.5)	.414

Data are presented as median [IQR] or count (%). *p* values in bold are statistically significant. aHR= adjusted hazard ratio. N/A=not applicable.

\*Fisher's exact test used for this variable for which one of the counts is 0.

## ❖ Causes de changement d'ATB :

- Echec clinique et/ou microbiologique (n=7, 64%)
- Co-infection par une bactérie CEFOX-R (n=4, 36%)



30-day clinical success	Cefoxitin n = 63 (57%)	Carbapenem n = 47 (43%)	OR (95% CI)	p value
<b>Source of bacteremia:</b>				
Central line associated	20/24 (83%)	10/12 (83%)	1.0 (0.1-8.5)	1.00
Pneumonia	1/7 (14%)	3/14 (21%)	0.6 (0.1-10.0)	1.00
Urinary tract	8/13 (61%)	2/3 (67%)	0.8 (0.1-19.7)	1.00
Intra abdominal	2/8 (25%)	1/4 (25%)	1.0 (0.1-78.4)	1.00
Unknow	4/8 (50%)	7/9 (78%)	0.3 (0.2-3.4)	.335

Data are presented as count (%). OR= odd ratio

→ 100% des bactériémies liées à un cathéter sans thrombophlébite prouvée ont guéri sous céfoxitine

# Sélection de bactéries résistantes



Characteristic	Cefoxitin n = 63	Carbapenem n = 47	p value
Selection of at least one cefoxitin-resistant gram-negative bacteria at 30 days	30 (48)	22 (47)	.933
<i>Klebsiella pneumoniae</i> cefoxitin-resistant	7 (11)	4 (8)	.755
Including colonization	4 (6)	1 (2)	
Including infection	3 (5)	3 (6)	
AmpC $\beta$ -lactamase-producing Enterobacteriaceae	15 (24)	2 (4)	<b>.006</b>
Including colonization	6 (9)	0 (0)	
Including infection	9 (14)	2 (4)	
<i>Pseudomonas aeruginosa</i>	13 (21)	18 (38)	<b>.042</b>
Including colonization	3 (5)	8 (17)	
Including infection	10 (16)	10 (21)	
<i>Pseudomonas aeruginosa</i> carbapenem-resistant	3 (5)	11 (23)	<b>.007</b>
Including colonization	2 (3)	5 (11)	
Including infection	1 (2)	6 (13)	
<i>Stenotrophomonas maltophilia</i>	0 (0)	1 (2)	.427
<i>Acinetobacter baumannii</i>	2 (3)	0 (0)	1.00



1

Etude **comparative** CEFOX vs CARBA  
bactériémie à KP BLSE en réanimation



Contrôle des biais



Bactéries céfoxitine-R et **carba-R**



Rétrospectif



**Biais d'indication**



Administration discontinuée

Guet-Revillet et al, 2014 ; Pilmis et al, 2021

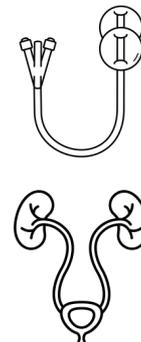
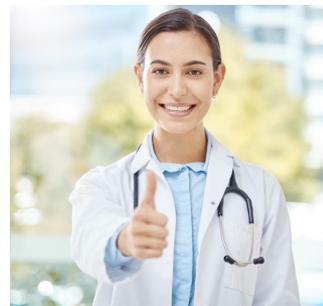


ATB définitive

Céfoxitine

VS

Carbapénèmes



Dequidt et al. *Critical Care* (2023) 27:418  
<https://doi.org/10.1186/s13054-023-04712-2>

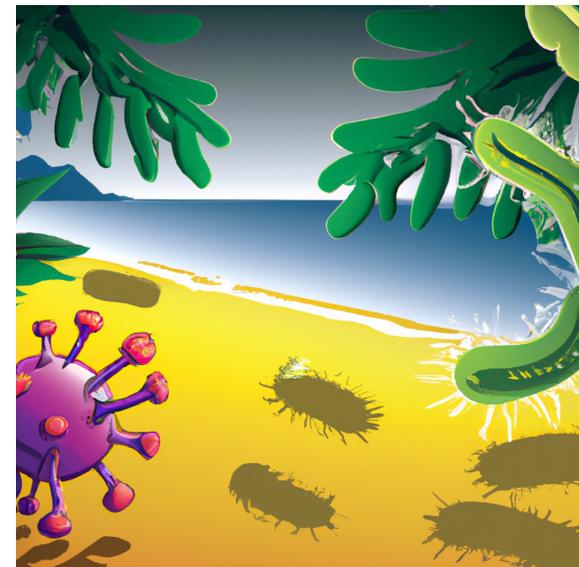


RESEARCH

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## Cefoxitin versus carbapenems as definitive treatment for extended-spectrum $\beta$ -lactamase-producing *Klebsiella pneumoniae* bacteremia in intensive care unit: a propensity-matched retrospective analysis

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Merci de votre attention