Particularités de l'antibiothérapie (curative) en réanimation

M. Wolff

Réanimation Neurochirurgicale, Hôpital St Anne Paris

Liens d’intérêt

Type de lien	Compagnies
Orateur réunion scientifique	MSD, Advanz
Invitations congrès	Advanz
« Boards scientifiques »	MSD
« Chairman » DMC	MedImmune (AstraZeneca) INOTREM

Sepsis
Choc septique

+/-

Comorbidités
Immunodépression

Germes sensibles ou résistants

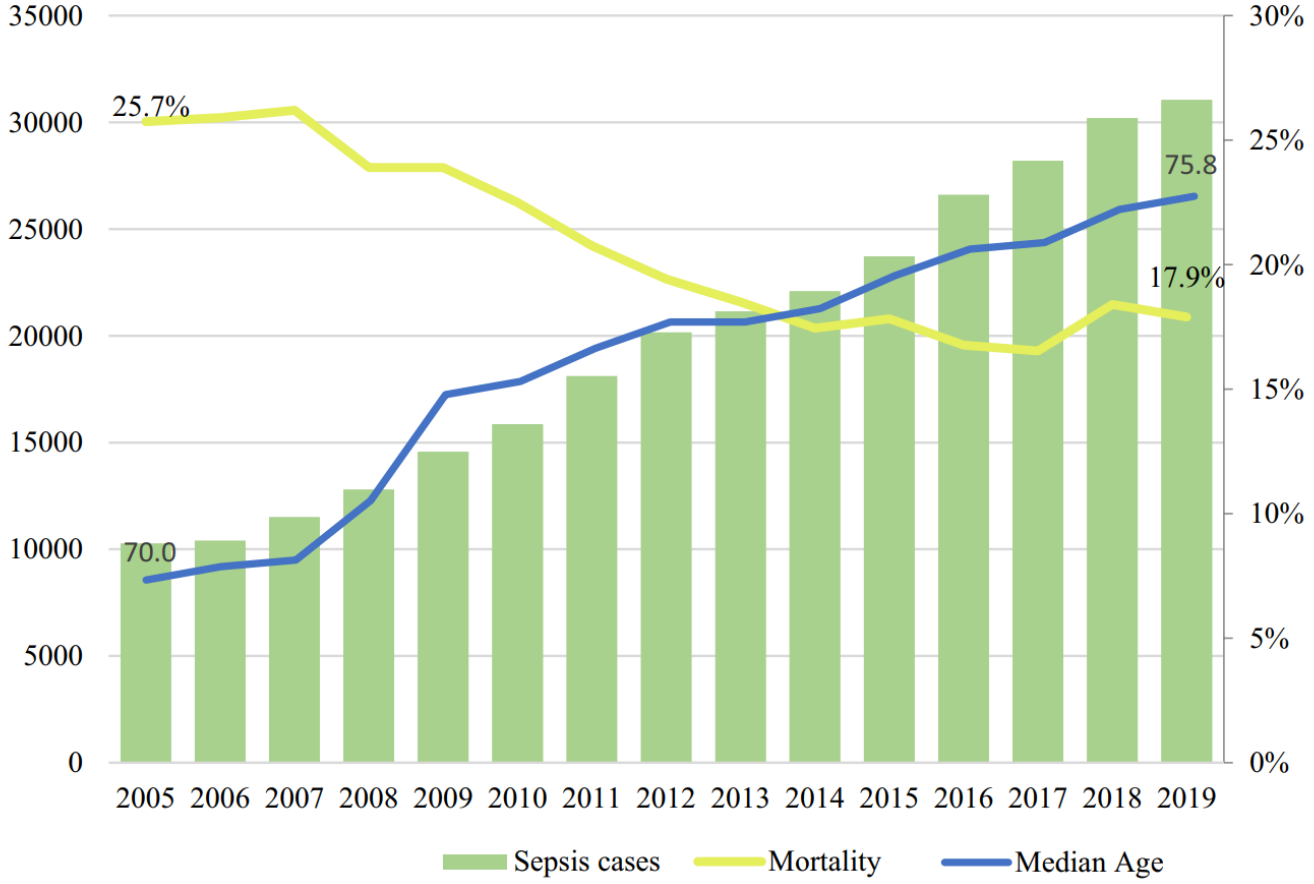
Particularités des sites: poumon, péritoine, SNC

PK modifié

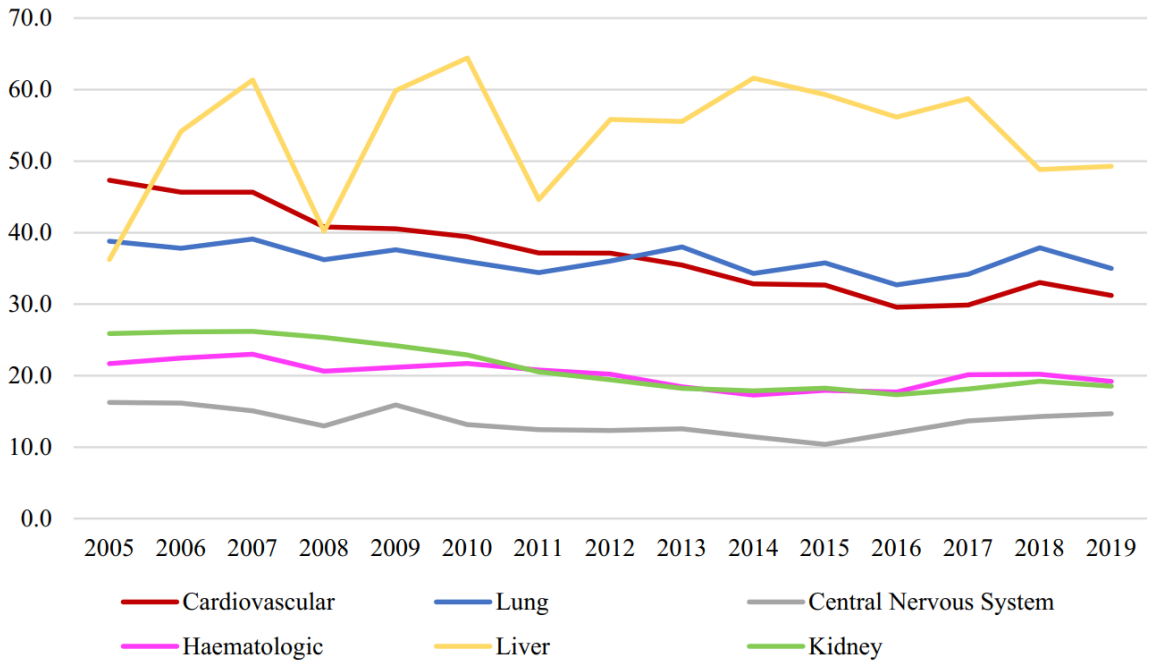
Autres médicaments

RESEARCH

Trends in mortality in septic patients according to the different organ failure during 15 years



Evolution of mortality (%) in sepsis according to organic dysfunction



Lorencio Cárdenas et al. Critical Care (2022)

Santé publique France

MARS 2022

Consommation d'antibiotiques en nombre de DDJ/1 000 JH par secteur d'activité clinique

Secteur d'activité	N	Nb DDJ/1 000 JH
Médecine	839	452
Hématologie	60	856
Maladies infectieuses	51	1 119
Chirurgie	659	535
Réanimation	249	1 145
Gynéco-obstétrique	381	196
Pédiatrie	266	248
SSR	1 148	151
SLD	390	64
Psychiatrie	314	38

2020 JAMA American Medical Association

Prevalence and Outcomes of Infection Among Patients in Intensive Care Units in 2017

Jean-Louis Vincent, MD, PhD, Yasser Sakr, MD, PhD, [...], and Derek C. Angus, MD, MPH

1144 réanimations dans le monde

15165 patients

↓

7723 (51%) : antibiothérapie curative

Antibiothérapie en réanimation : Trois grandes spécificités

1. L'antibiothérapie probabiliste: une situation très fréquente
2. Recherche du meilleur mode d'administration
3. La désescalade (dont raccourcissement de la durée de traitement) est possible aussi en réanimation

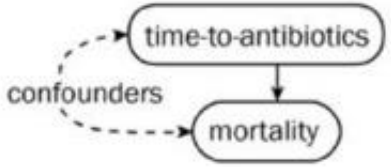
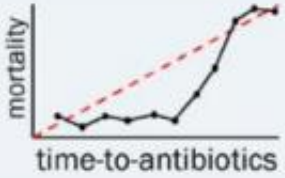
Antibiothérapie en réanimation : Trois grandes spécificités

1. **L'antibiothérapie probabiliste: une situation très fréquente**
   - Immédiatement ? Un peu plus tard ? Abstention?
   - Donner le ou les « bon (s) antibiotiques
2. **Recherche du meilleur mode d'administration, adapté**
   - aux caractéristiques du patient
   - au site de l'infection
   - au (x) germe(s) si infection documentée
   - Administrations in situ
3. **La désescalade (dont raccourcissement de la durée de traitement) est possible aussi en réanimation**

Clinical Infectious Diseases
MAJOR ARTICLE
2023
IDSA Infectious Diseases Society of America
hivma hiv medicine association
OXFORD

Risk of Misleading Conclusions in Observational Studies of Time-to-Antibiotics and Mortality in Suspected Sepsis

Theodore R. Pak,[1,2] Jessica Young,[1] Caroline S. McKenna,[1] Anna Agan,[1] Laura DelloStritto,[1] Michael R. Filbin,[3] Sayon Dutta,[3] Sameer S. Kadri,[4] Edward J. Septimus,[1] Chanu Rhee,[1,5,a] and Michael Klompas[1,5,a]

ANALYTICAL CONCERN	TEST	RESULTS
Insufficient confounding adjustment 	Add progressively more detailed covariates: basics → + comorbidities → + labs → + vitals	Changed
Including time-to-antibiotics outliers 	Pts treated >6h are rare & different. Lower max time-to-antibiotics: 24h → 12h → 6h	Changed
Equating sepsis & septic shock 	Separate analyses for: • suspected infection • suspected sepsis • suspected septic shock	Changed
Linearizing non-linearity 	Remove the assumption of a linear relationship between time-to-antibiotics ↔ log odds of mortality	Changed

CONCLUSIONS

Each of these analytical choices can easily bias estimates of the time-to-antibiotics ↔ mortality association.

In our most defensible model (max adjustment, only time-to-antibiotics <6h) each additional hour until antibiotics was associated with the following changes in mortality:

COHORT		HOURLY aOR
Septic Shock	↑	1.07 (1.04–1.11)
Sepsis	NS	1.03 (0.98–1.09)
Infection	NS	0.99 (0.94–1.05)

Délai > 6 h associé à la mortalité

Rüddel et al. Critical Care (2022) 26:51
https://doi.org/10.1186/s13054-022-03901-9

Critical Care

RESEARCH Open Access

Adverse effects of delayed antimicrobial treatment and surgical source control in adults with sepsis: results of a planned secondary analysis of a cluster-randomized controlled trial

4792 patients

Predictor	No. of patients	Observed mortality	Risk-adjusted mortality	OR (95% CI)	Decreasing mortality / Increasing mortality	P-value
Timing of antimicrobial therapy	4659/4792					0.008*
0–1 hr		364/1270 (28.7)	25.3 (22, 28.9)	1		
1–3 hrs		418/1352 (30.9)	27.8 (24.4, 31.6)	1.14 (0.95, 1.36)		0.149
3–6 hrs		255/836 (30.5)	26 (22.3, 30.2)	1.04 (0.85, 1.27)		0.715
>6 hrs		437/1201 (36.4)	31.5 (27.5, 35.7)	1.36 (1.12, 1.63)		0.001

b Effect of timing of surgical source control

Subgroups	No. of patients	OR per hour (95% CI)	Decreasing mortality / Increasing mortality	P-value in subgroup	P-value effect moderation
All patients	1563/1595	1.008 (0.997, 1.02)		0.143	
Vasopressor use (first 12 hrs)					0.778
No	237/244	1.009 (0.984, 1.035)		0.481	
Yes	1323/1346	1.013 (1.001, 1.026)		0.04	

Intensive Care Med (2022) 48:1593–1606
https://doi.org/10.1007/s00134-022-06883-y

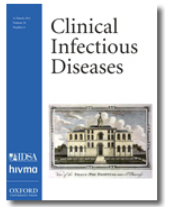
De Pascale G *et al*.

ORIGINAL

Poor timing and failure of source control are risk factors for mortality in critically ill patients with secondary peritonitis

Table 4 Adjusted relationships with mortality in critically ill patients with secondary peritonitis

Variable	Odds ratio (95% confidence interval)
Time-to-source control intervention	
'Emergency' (< 2 h)	Reference
'Urgent' (2 to 6 h)	0.50 (0.34–0.73)
'Delayed' (> 6 h)	0.90 (0.58–1.41)



2015

Adult Bacterial Meningitis: Earlier Treatment and Improved Outcome Following Guideline Revision Promoting Prompt Lumbar Puncture

Martin Glimåker,[1] Bibi Johansson,[1] Örjan Grindborg,[1] Matteo Bottai,[2] Lars Lindquist,[1] and Jan Sjölin[3]

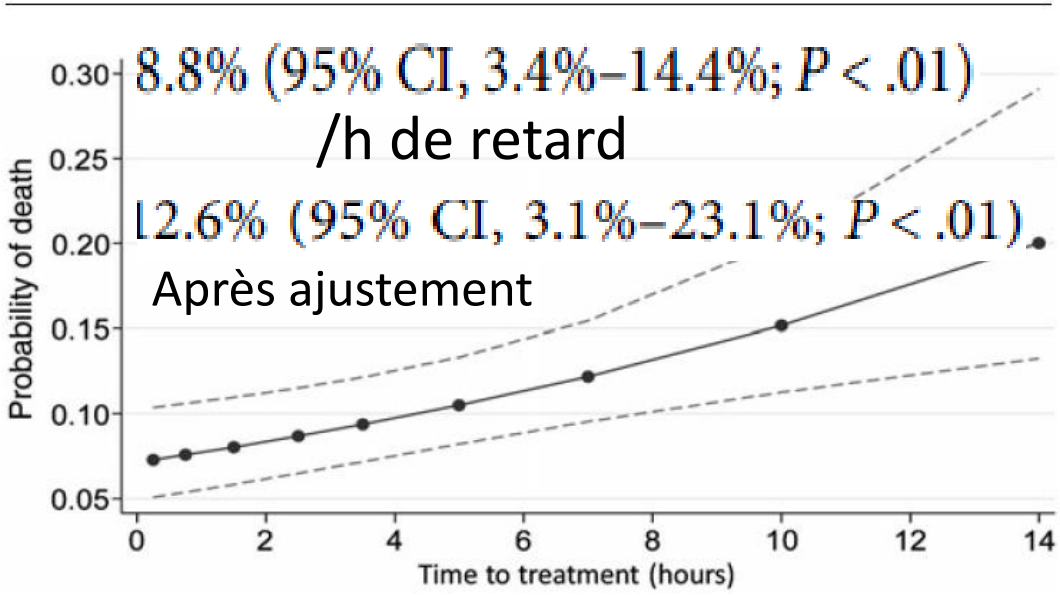


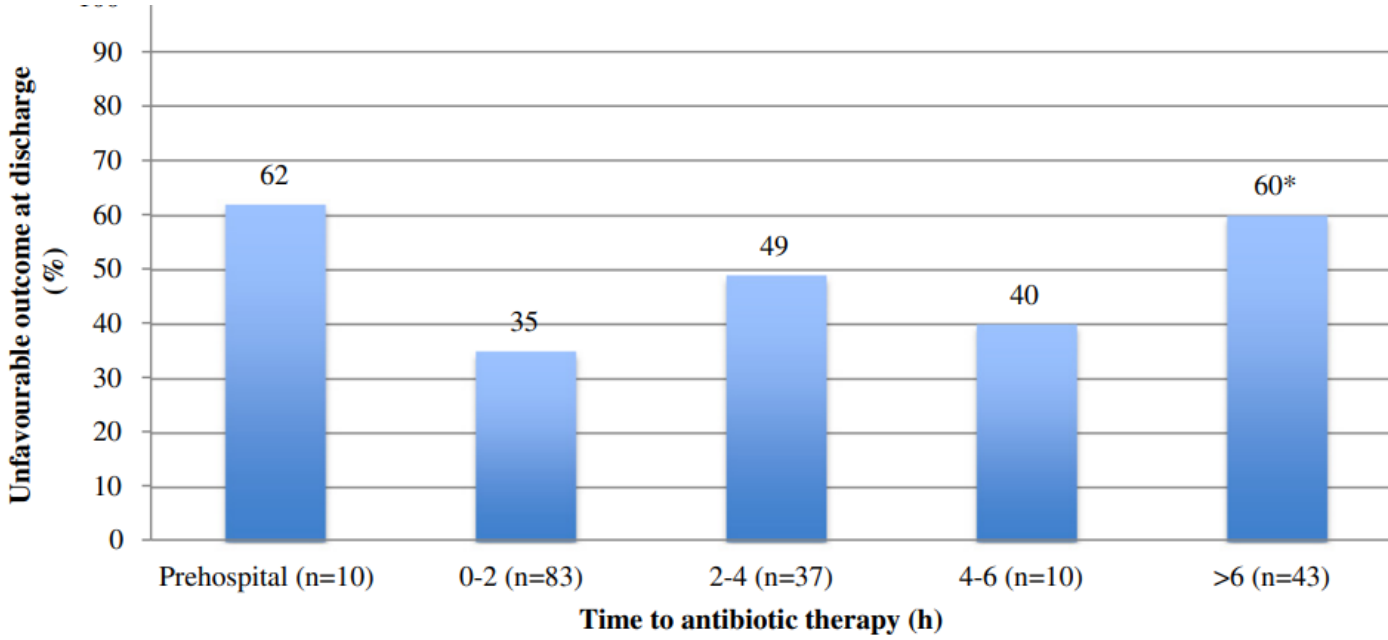
Figure 3. Probability of death related to time from admission to start of antibiotic treatment with 95% confidence intervals.

Bodilsen *et al. BMC Infectious Diseases* (2016) 16:392
DOI 10.1186/s12879-016-1711-z

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Time to antibiotic therapy and outcome in bacterial meningitis: a Danish population-based cohort study

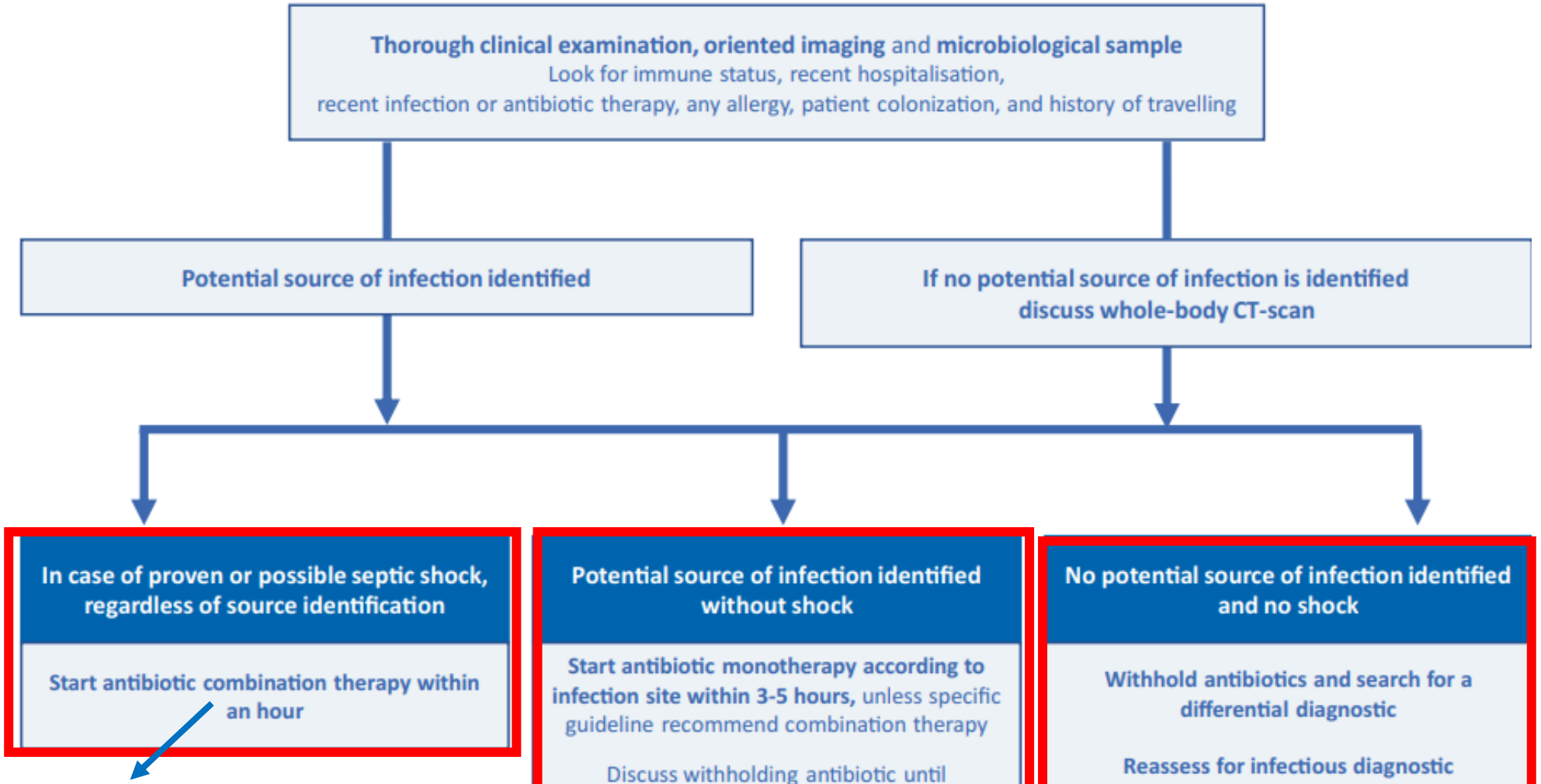


REVIEW Op

Antibiotic stewardship in the ICU: time to shift into overdrive

David Mokrani[1], Juliette Chommeloux[1], Marc Pineton de Chambrun[1], Guillaume Hékimian[1] and Charles-Edouard Luyt[1,2*]

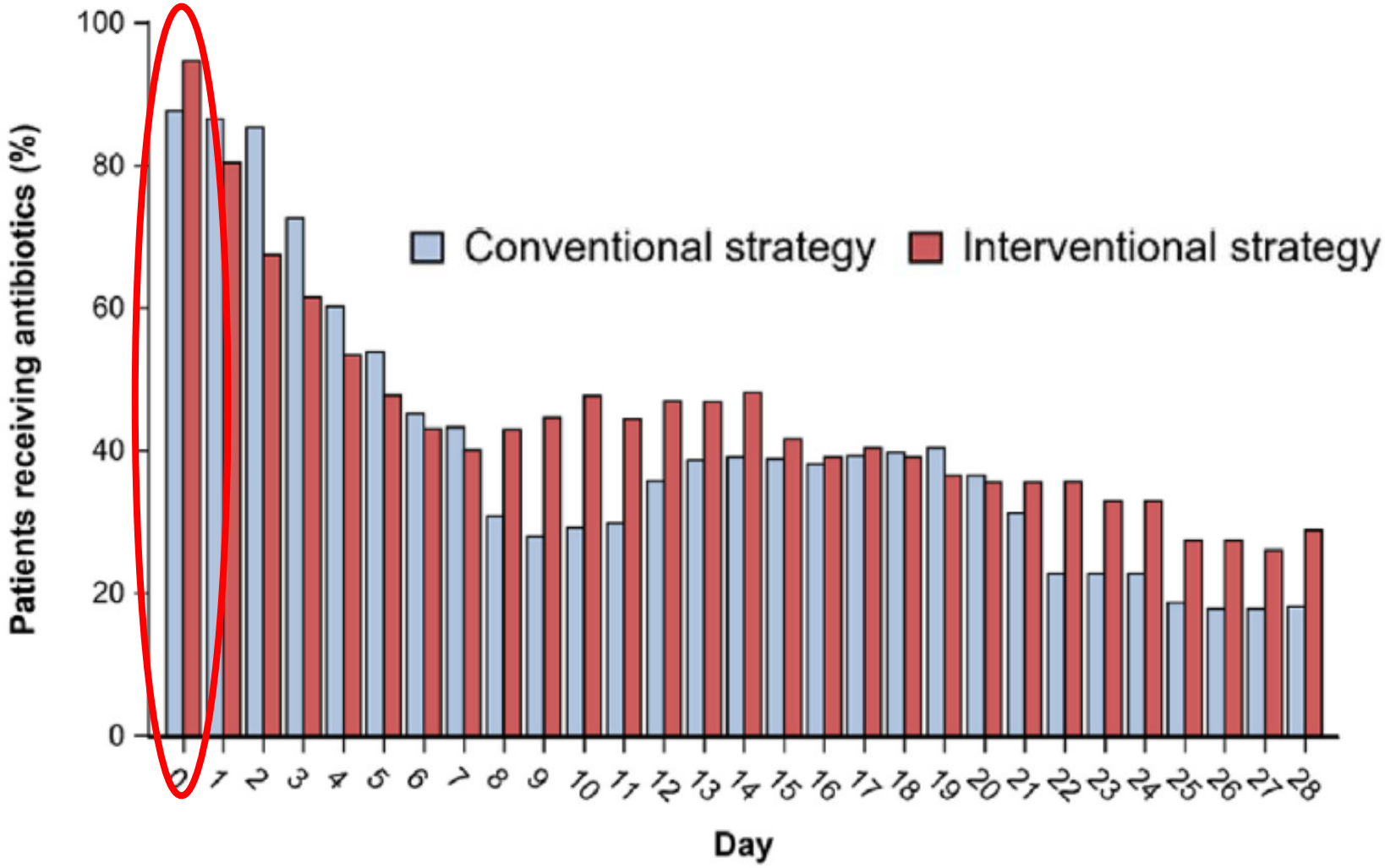
Mokrani *et al. Annals of Intensive Care* (2023) 13:39



Elargissement du spectre : ex aminoside si BL non carbapénème

Respiratory multiplex PCR and procalcitonin to reduce antibiotic exposure in severe SARS-CoV-2 pneumonia: a multicentre randomized controlled trial

Clinical Microbiology and Infection 29 (2023) 734–743



Fartoukh M et al.

Inappropriate empirical antibiotic therapy for bloodstream infections based on discordant in-vitro susceptibilities: a retrospective cohort analysis of prevalence, predictors, and mortality risk in US hospitals

Sameer S Kadri, Yi Ling Lai, Sarah Warner, Jeffrey R Strich, Ahmed Babiker, Emily E Ricotta, Cumhur Y Demirkale, John P Dekker, Tara N Palmore, Chanu Rhee, Michael Klompas, David C Hooper, John H Powers 3rd, Arjun Srinivasan, Robert L Danner, Jennifer Adjemian, forming the National Insititutes of Health Antimicrobial Resistance Outcomes Research Initiative (NIH-ARORI)

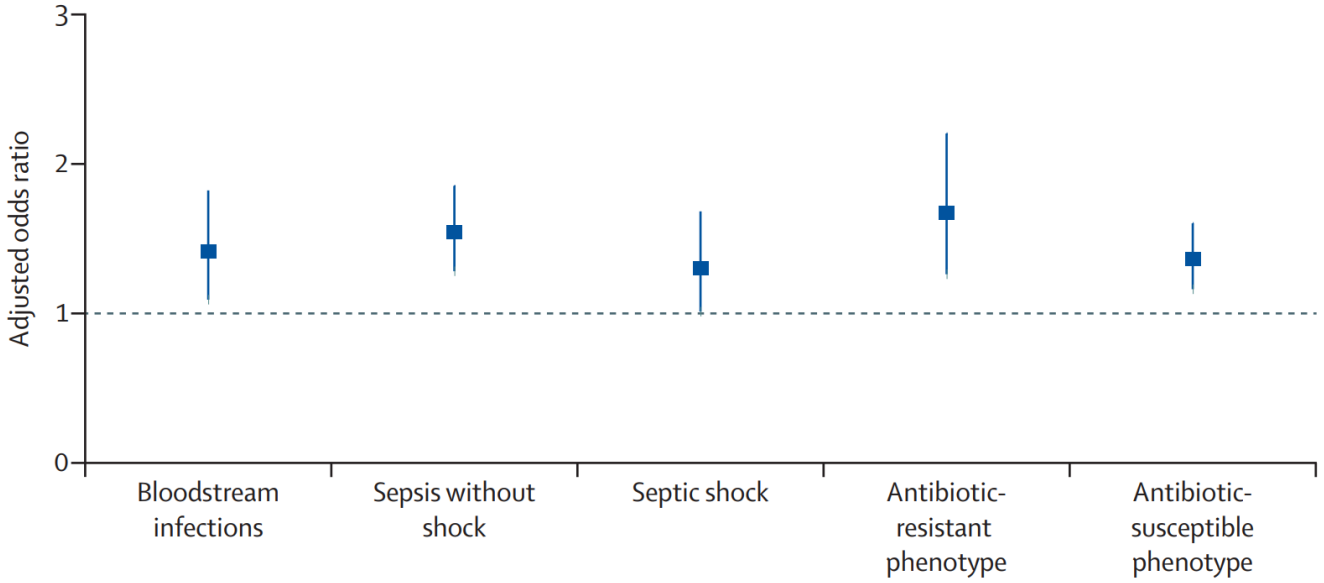
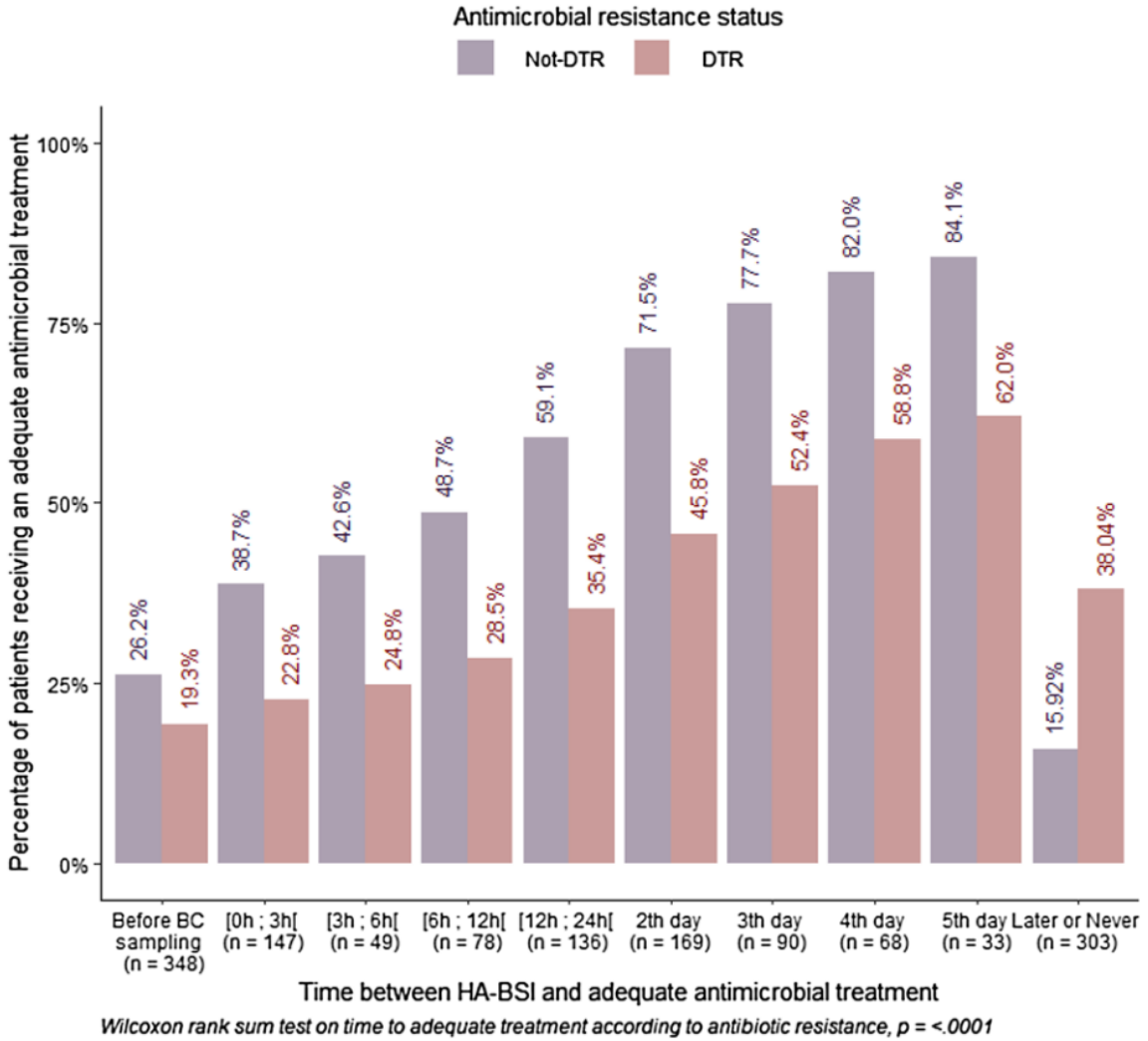


Figure 4: Adjusted odds of mortality associated with discordant empirical antibiotic therapy by causative organism (A), sepsis and antibiotic resistance status (B), and in sensitivity analyses (C, D)

Lancet Infect Dis 2021

ORIGINAL

Epidemiology and outcomes of hospital-acquired bloodstream infections in intensive care unit patients: the EUROBACT-2 international cohort study



A Tabah *et al.* Intensive Care Med (2023)

Choix probabiliste de la ou des molécules en réanimation

Délai de survenue si IAS

Données épidémiologiques
- Colonisation
- Voyages étranger
- Ecologie du service
- Epidémie/endémie BMR

Gravité : choc ou pas

Antibiothérapie probabiliste en réanimation

Antibiothérapie préalable : molécules, n de lignes..

Tests microbiologiques rapides, phénotypiques ou génotypiques

Valeur prédictive négative d'une absence de colonisation digestive à BLSE pour exclure une BLSE en cas de PAVM

Prevel *et al. Antimicrobial Resistance and Infection Control* (2019) 8:112
https://doi.org/10.1186/s13756-019-0572-9

Antimicrobial Resistance and Infection Control

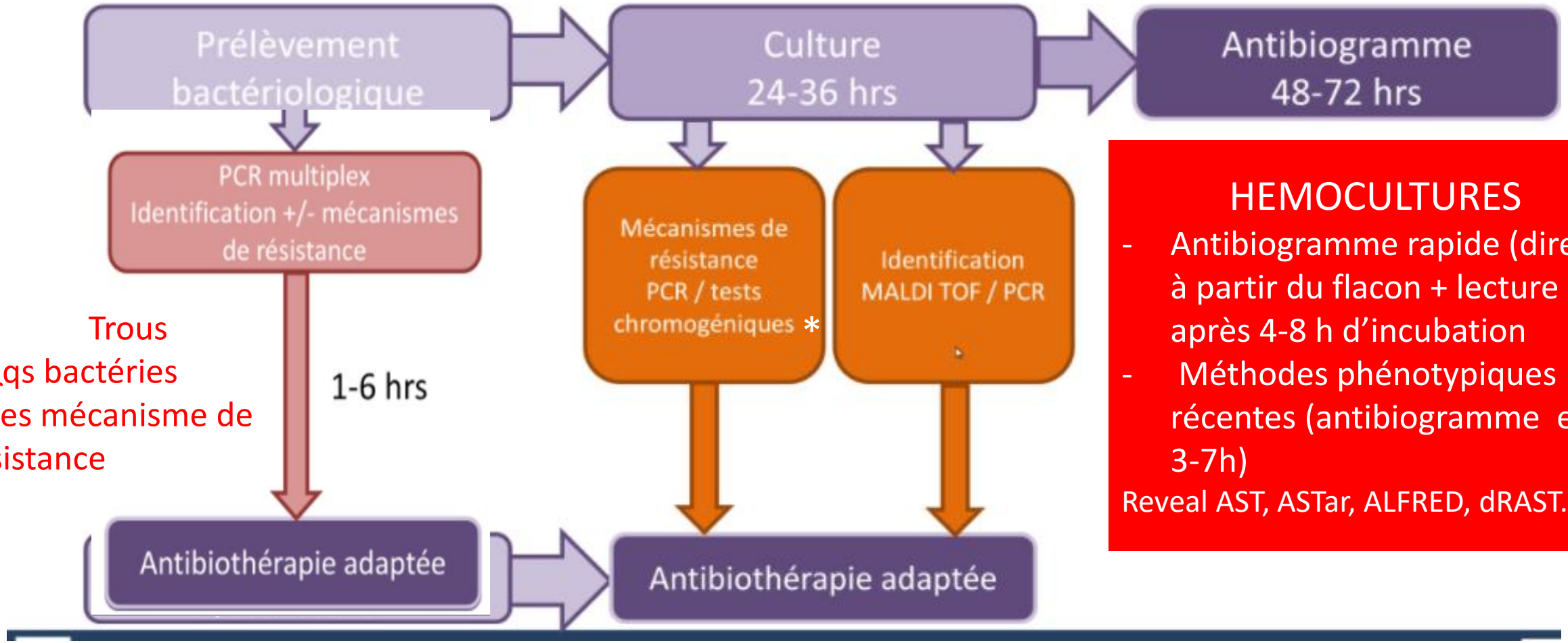
RESEARCH Open Access

Extended spectrum beta-lactamase producing *Enterobacterales* faecal carriage in a medical intensive care unit: low rates of cross-transmission and infection

Renaud Prevel[1,2*], Alexandre Boyer[1], Fatima M'Zali[2], Thibaut Cockenpot[3], Agnes Lasheras[4], Véronique Dubois[2,3] and Didier Gruson[1]

ESBL-E faecal carriage had thus a positive predictive value (PPV) of 40%, a negative predictive value (NPV) of 100%, a sensitivity of 100% and a specificity of 10% for ESBL-E causing the VAP.

Tests rapides: Infections respiratoires/hémocultures



Trous
- Qqs bactéries
- Des mécanisme de résistance

HEMOCULTURES
- Antibiogramme rapide (direct à partir du flacon + lecture après 4-8 h d'incubation
- Méthodes phénotypiques récentes (antibiogramme en 3-7h)

Reveal AST, ASTar, ALFRED, dRAST..

* PLP2a, betalactatest, Carba NP ..

D'après CE Luyt 2023

Un exemple de l'impact positif d'un test rapide

Etude observationnelle: 137 patients avec bactériémie à EPC dont 89 à KPC

51 avec PCR KPC *versus* 38 sans PCR KPC

	PCR +	PCR-	p
Délai ATB appropriée (h)	24	50	0,009
Mortalité J14 (%)	16	37	0,007
Mortalité J30 (%)	24	47	0,007

PCR testing was associated with decreased 30-day mortality (adjusted odds ratio: .37; 95% CI: .16–.84) in an adjusted model

Satlin MJ *et al* Clin Infect Dis 2022

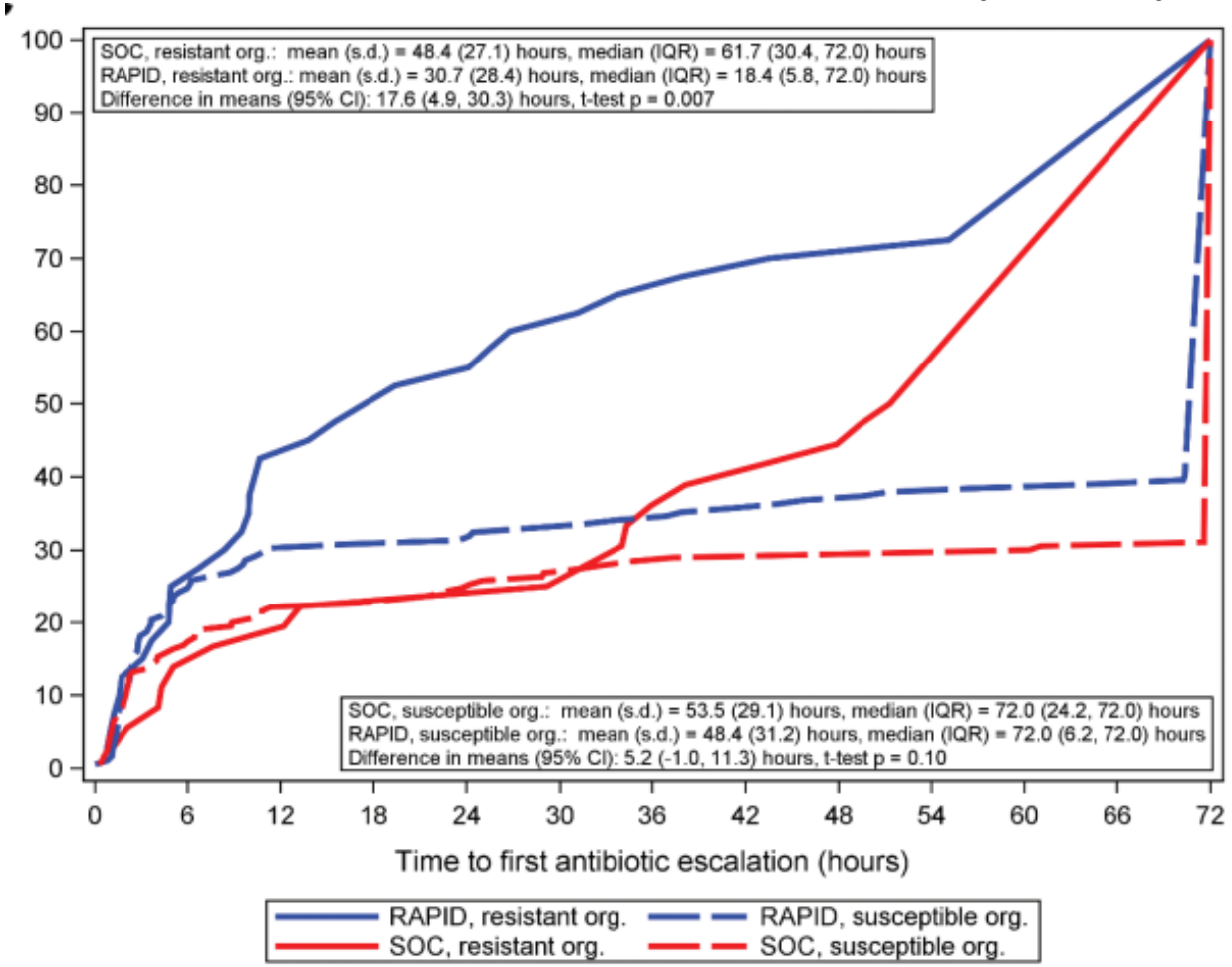
Clinical Infectious Diseases

MAJOR ARTICLE

2021

Randomized Trial Evaluating Clinical Impact of RAPid IDentification and Susceptibility Testing for Gram-negative Bacteremia: RAPIDS-GN

Ritu Banerjee,[1] Lauren Komarow,[2] Abinash Virk,[3] Nipunie Rajapakse,[3] Audrey N. Schuetz,[3] Brenda Dylla,[3] Michelle Earley,[2] Judith Lok,[4] Peggy Kohner,[3] Sherry Ihde,[3] Nicolynn Cole,[3] Lisa Hines,[3] Katelyn Reed,[3] Omai B. Garner,[5] Sukantha Chandrasekaran,[5] Annabelle de St. Maurice,[5] Meganne Kanatani,[5] Jennifer Curello,[5] Rubi Arias,[5] William Swearingen,[5] Sarah B. Doernberg,[6] and Robin Patel[3]; for the Antibacterial Resistance Leadership Group



Pas de différences sur les « outcomes » cliniques: mortalité à J30, durée de séjour, réadmissions

European Journal of Clinical Microbiology & Infectious Diseases (2018) 37:2107–2115
https://doi.org/10.1007/s10096-018-3345-0

ORIGINAL ARTICLE

Multicenter performance evaluation of the Unyvero IAI cartridge for detection of intra-abdominal infections

H. Ciesielczuk[1] · M. Wilks[1,2] · S. Castelain[3,4] · M. Choquet[3,4] · M. Morotti[5] · E. Pluquet[3,4] · V. Sambri[5,6] · M. Tassinari[5] · S. Zannoli[5] · L. Cavalié[7] · H. Dupont[8] · H. Guet-Revillet[7]

Délai avant identification de l'agent pathogène

calculé prospectivement sur 50 échantillons.
en prenant en compte le moment où le laboratoire était ouvert pour faire l'analyse

- **Microbiologie conventionnelle : 39 ± 16 heures**
- **Unyvero IAI: 22 ± 4 heures**

Délai avant obtention du profil de sensibilité de l'agent pathogène

calculé prospectivement sur 15 échantillons:
avec l'identification de l'agent pathogène et son profil de sensibilité

- **Microbiologie conventionnelle : 64 ± 12 heures**
- **Unyvero IAI: 23 ± 3 heures**

P. Montravers 2023

Antibiothérapie en réanimation : Trois grandes spécificités

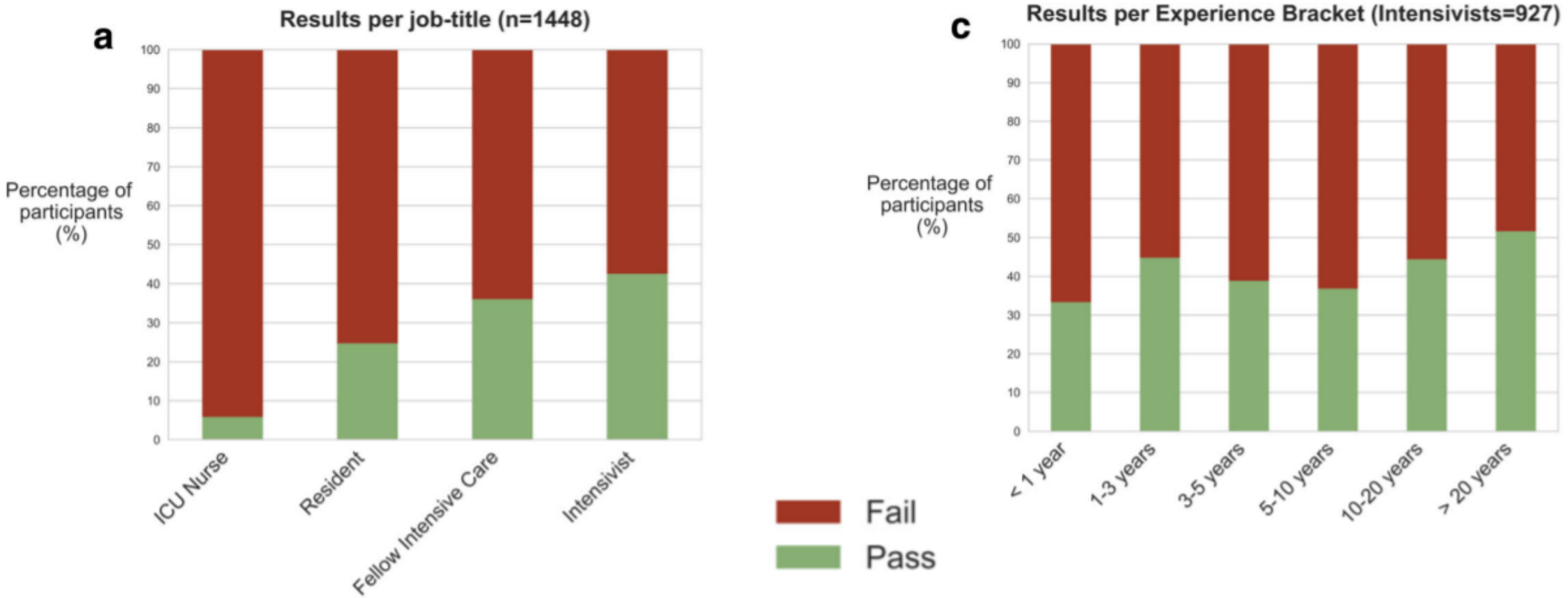
1. **L'antibiothérapie probabiliste: une situation très fréquente**
   - Immédiatement ? Un peu plus tard ? Abstention?
   - Donner le ou les « bon (s) antibiotiques
2. **Recherche du meilleur mode d'administration, adapté**
   - aux caractéristiques du patient
   - au site de l'infection
   - au (x) germe(s) si infection documentée
   - Administrations *in situ*
3. **La désescalade (dont raccourcissement de la durée de traitement) est possible aussi en réanimation**

Fleuren *et al. Critical Care* (2019) 23:185
https://doi.org/10.1186/s13054-019-2438-1

Critical Care

Clinically relevant pharmacokinetic knowledge on antibiotic dosing among intensive care professionals is insufficient: a cross-sectional study

Lucas M. Fleuren[1*], Luca F. Roggeveen[1], Tingjie Guo[1], Petr Waldauf[2], Peter H. J. van der Voort[3], Rob J. Bosman[3], Eleonora L. Swart[4], Armand R. J. Girbes[1] and Paul W. G. Elbers[1]



Infection grave en réanimation: beaucoup de paramètres

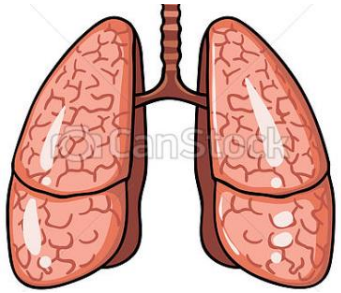
Etat hémodynamique
Ventilation mécanique
EER
ECMO
…

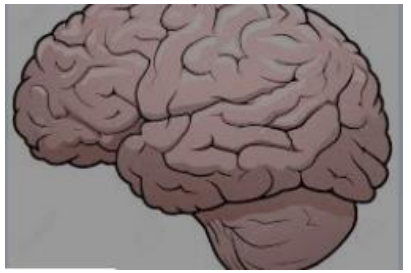
Volume de distribution
Demi-vie élimination
Mode élimination

Sensibilité aux antibiotiques (CMI, ECOFF)

Fonction rénale
Fonction hépatique
Albuminémie
….

Paramètre
PK/PD prédictif
activité





- Augmented renal clairance
- High distribution volume

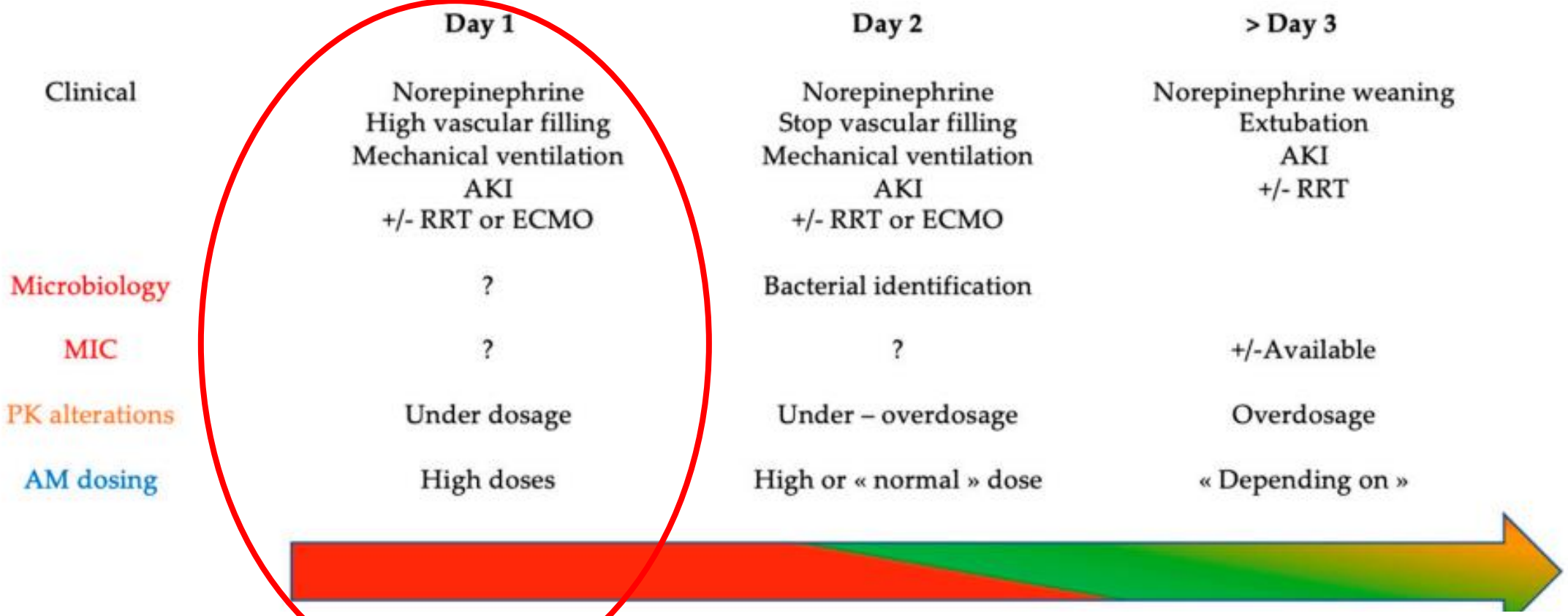


Figure 1. Timeline of PK/PD alterations in critically ill patients with septic shock. AKI: acute kidney injury, RRT: renal replacement therapy, ECMO: extracorporeal membrane oxygenation, VF: vascular filling, MIC: minimal inhibitory concentration, PK: pharmacokinetics, AM: antimicrobial; Arrow with color: level of inadequate BL concentration risk: red = very high, green = low, orange = variable.

Novy E *et al.* Antibiotics 2023

Table 1. Summary of Populations Exhibiting Augmented Renal Clearance

Population	Prevalence (%)	Mean Cl_{cr} values
Burn[5]	65	172.1 ml/min/1.73 m^2
Febrile neutropenia[19]	16.4	157.4 ml/min/1.73 m^2
Sepsis[14, 18]	39.5–56	154–210 ml/min/1.73 m^2
Subarachnoid hemorrhage[11]	100	326 ml/min
Trauma[10]	85.7	166 ml/min/1.73 m^2
Traumatic brain injury[9]	85	179 ml/min/1.73 m^2 150 ml/min/1.73 m^2 (while not receiving CPP treatment)

Cl_{cr} = creatinine clearance; CPP = cerebral perfusion pressure.

Cook AM et coll Pharmacotherapy 2019

antibiotics

MDPI

Article

Empirical Antibiotic Therapy for Gram-Negative Bacilli Ventilator-Associated Pneumonia: Observational Study and Pharmacodynamic Assessment

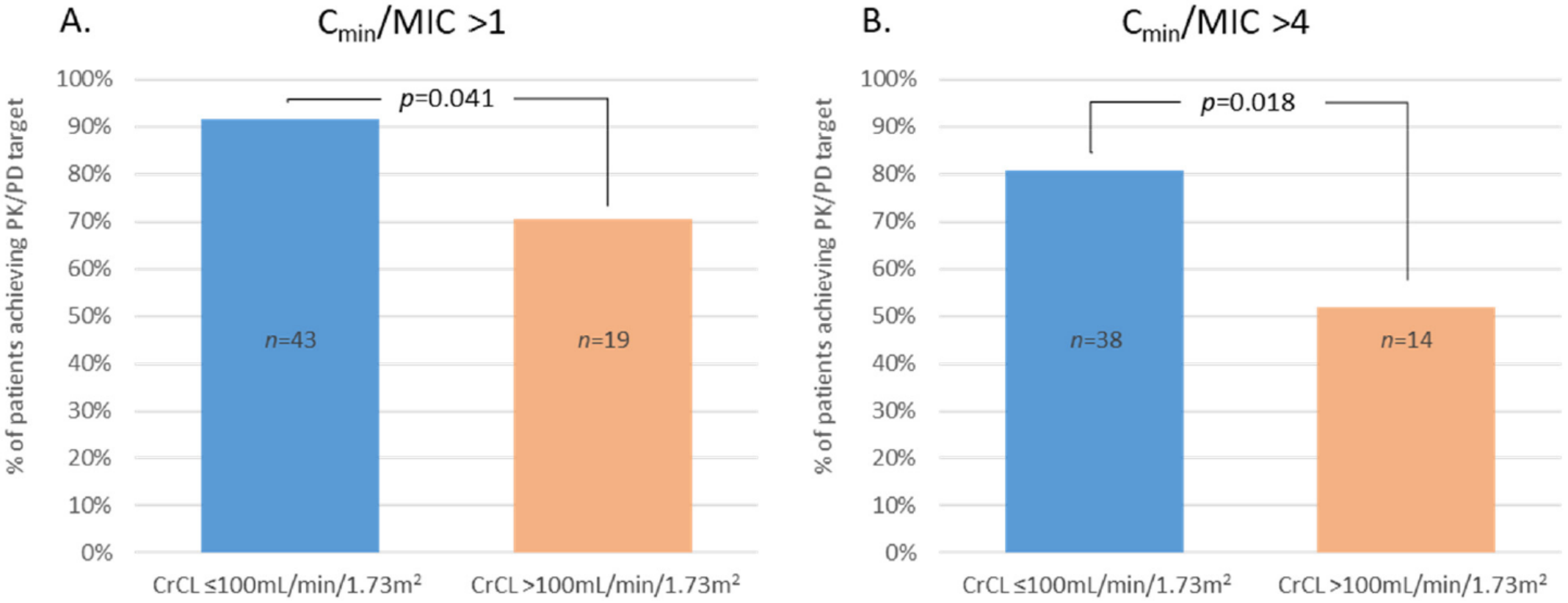


Figure 2. Proportion of patients achieving PK/PD targets for β-lactams, i.e., C_{min}/MIC > 1 (**A**) or C_{min}/MIC > 4 (**B**), according to CrCL.

O. Pajot *et al* 2022

Hyperclairance: une nouvelle catégorie dans les AMM

CEFIDEROCOL

Renal function	Dose regimen
Augmented (CG-CL_{CR}, ≥120 ml/min)	2 g q6h, 3-h infusion
Normal (MDRD-eGFR, ≥90 ml/min/1.73 m^2)	2 g q8h, 3-h infusion
Mild impairment (MDRD-eGFR, 60 to <90 ml/min/1.73 m^2)	2 g q8h, 3-h infusion
Moderate impairment (MDRD-eGFR, 30 to <60 ml/min/1.73 m^2)	1.5 g q8h, 3-h infusion
Severe impairment (MDRD-eGFR, 15 to <30 ml/min/1.73 m^2)	1 g q8h, 3-h infusion
ESRD (MDRD-eGFR, <15 ml/min/1.73 m^2)	0.75 g q12h, 3-h infusion
Requiring intermittent HD	0.75 g q12h, 3-h infusion[a]

Diapositive Claire Roger 1er décembre 2022

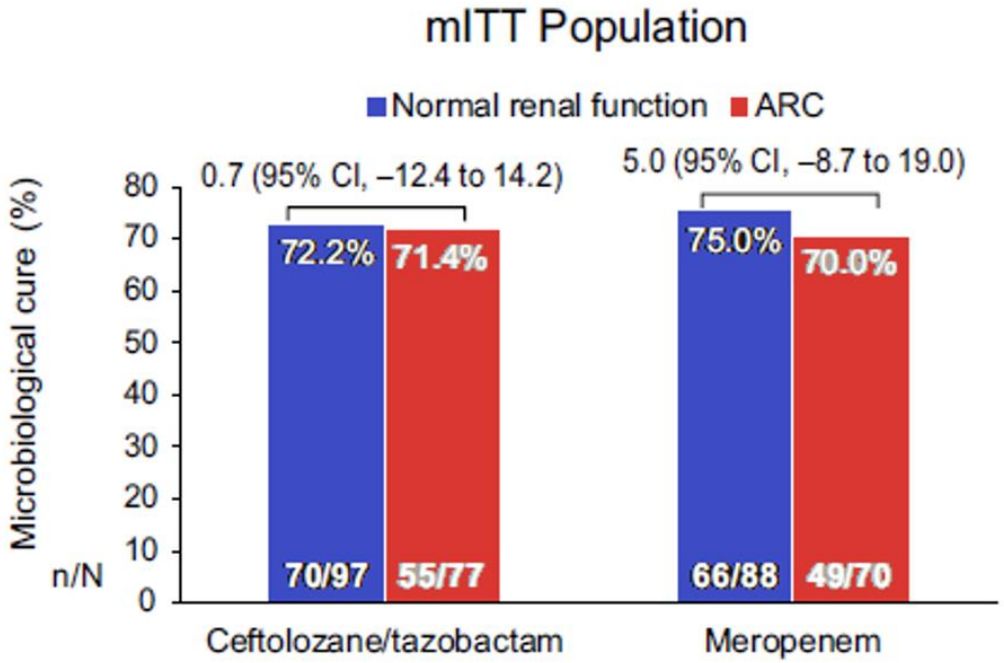
Katsube et al. AAC 2017; 61: e01381-16.

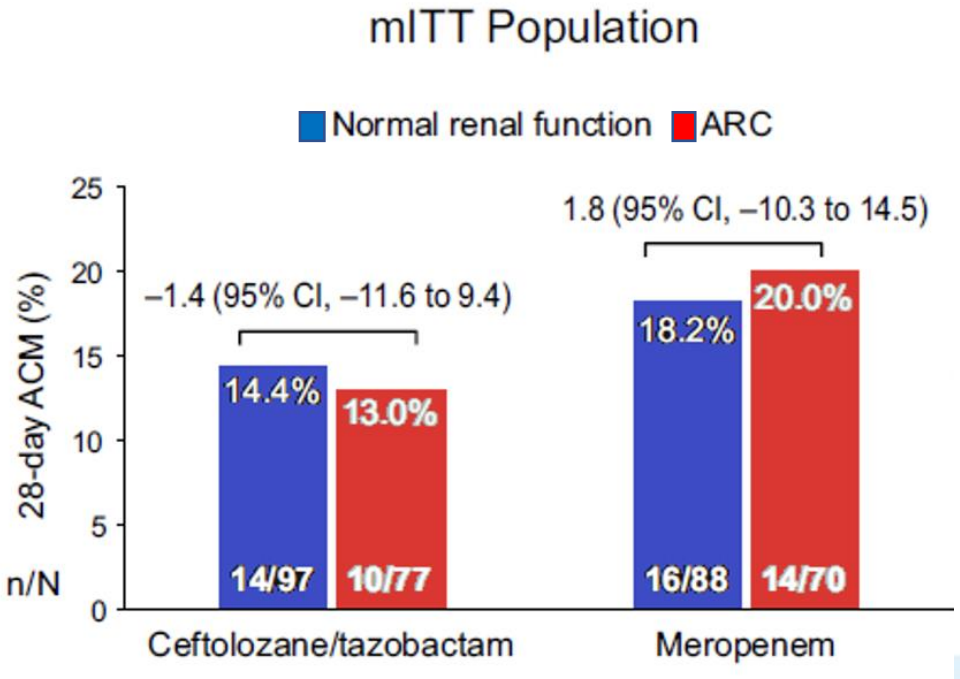
Baseline CrCl, mL/min, median			
Normal		ARC	
C/T	MERO	C/T	MERO
99.0	100.5	172.3	164.0

RESEARCH Open Access

Ceftolozane/tazobactam probability of target attainment and outcomes in participants with augmented renal clearance from the randomized phase 3 ASPECT-NP trial

Andrew F. Shorr[1], Christopher J. Bruno[2*], Zufei Zhang[2], Erin Jensen[2], Wei Gao[2], Hwa-Ping Feng[2], Jennifer A. Huntington[2], Brian Yu[2], Elizabeth G. Rhee[2], Carisa De Anda[2], Sumit Basu[2] and Marin H. Kollef[3]





Diapositive Claire Roger 1er décembre 2022

Shorr et al. Crit Care (2021) 25:354

High-Dose Ceftriaxone for Bacterial Meningitis and Optimization of Administration Scheme Based on Nomogram

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®
2019

Matthieu Grégoire,[a,b] Eric Dailly,[a,c] Paul Le Turnier,[d] Denis Garot,[e] Thomas Guimard,[f] Louis Bernard,[g] Pierre Tattevin,[h] Yves-Marie Vandamme,[i] Jérôme Hoff,[j] Florian Lemaitre,[k,l] Marie-Clémence Verdier,[k,l] Guillaume Deslandes,[a] Ronan Bellouard,[a] Véronique Sébille,[m] Anne Chiffoleau,[n] David Boutoille,[d,o] Dominique Navas,[o,p] Nathalie Asseray[d]

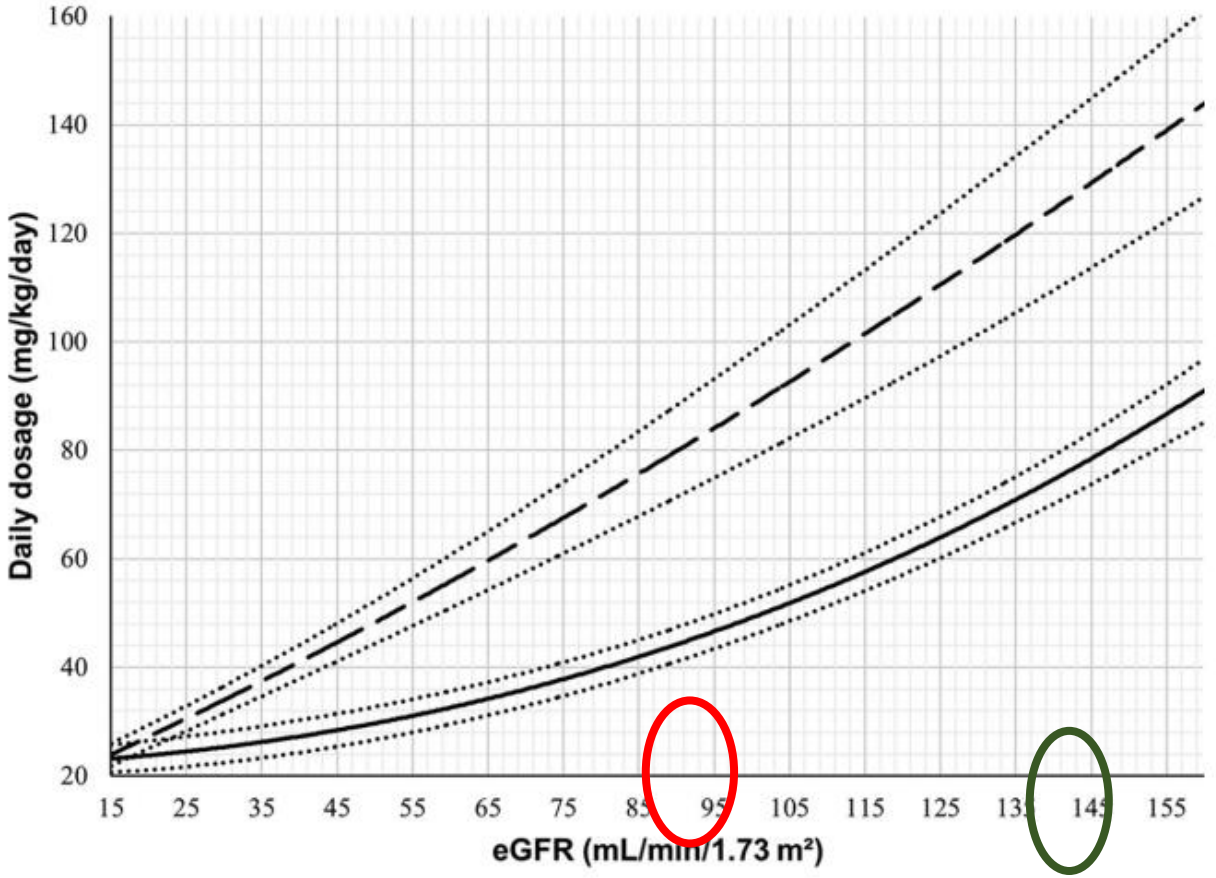


FIG 3 Nomogram of the daily dose of ceftriaxone per kilogram of total weight to be administered to achieve a trough concentration target of 20 mg/liter (full line) and to not exceed 100 mg/liter (broken line) with a probability of 0.9, accounting for renal function estimated by the CKD-EPI formula (eGFR) using a twice-daily regimen. Dotted lines represent the 95% confidence interval.

Exemple : patient de 75 kg

- e.GFR 90 mL/min/1.73 m²
  ↓
  3,5 -,5,3 g/24

- e.GFR 140 mL/min/1.73 m²
  ↓
  5,8 -8 g/24/24h

- Augmented renal clairance
- High distribution volume

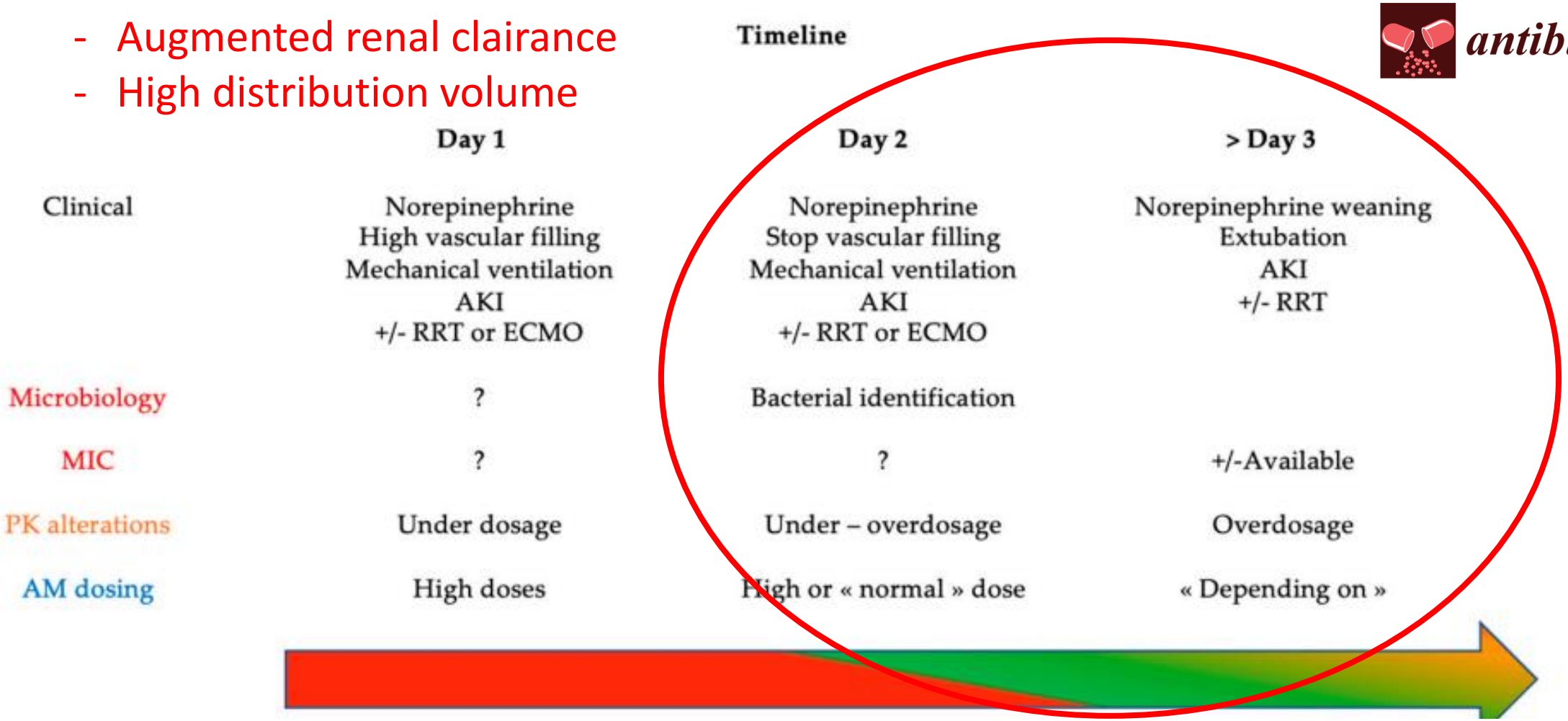
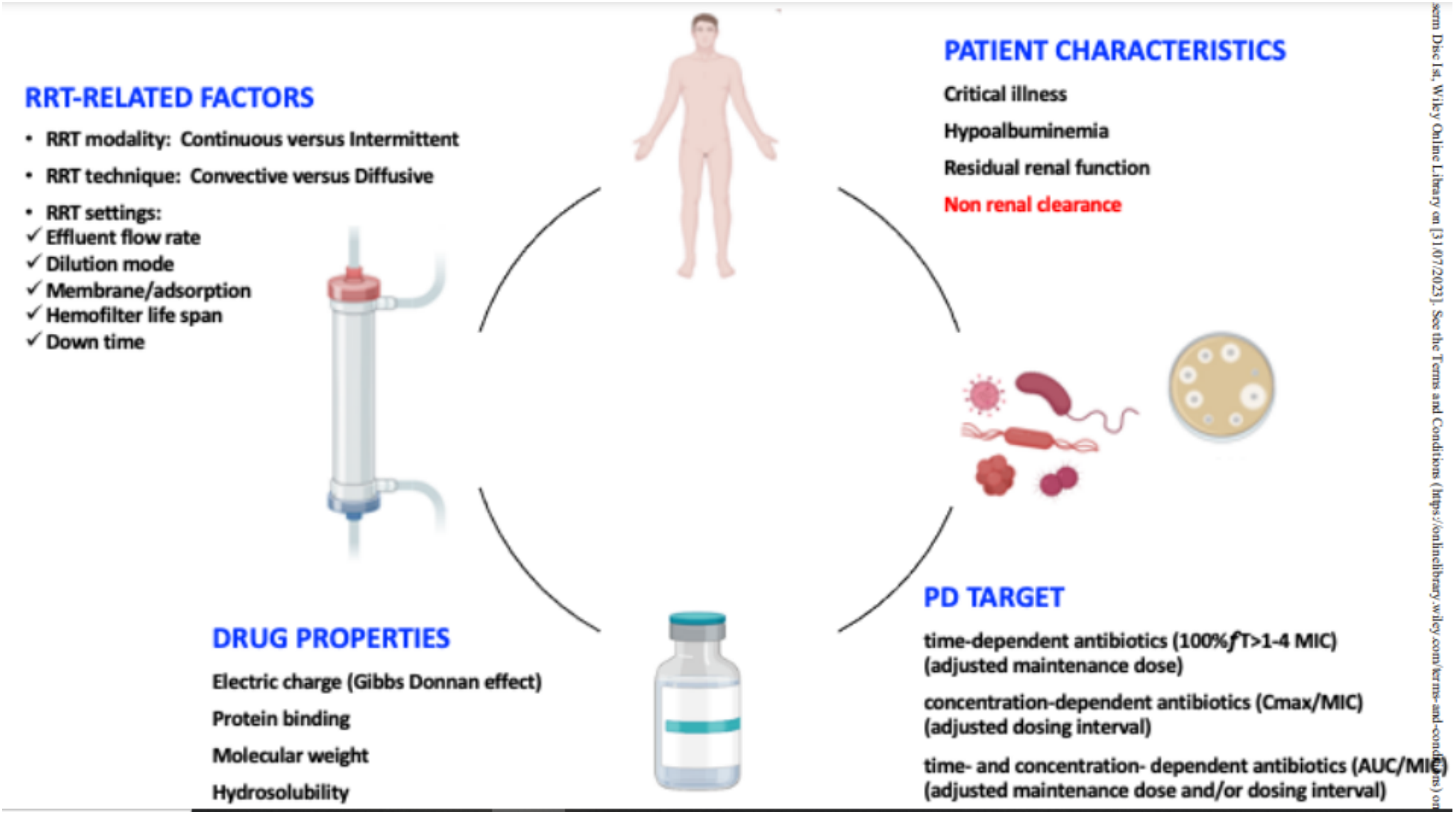


Figure 1. Timeline of PK/PD alterations in critically ill patients with septic shock. AKI: acute kidney injury, RRT: renal replacement therapy, ECMO: extracorporeal membrane oxygenation, VF: vascular filling, MIC: minimal inhibitory concentration, PK: pharmacokinetics, AM: antimicrobial; Arrow with color: level of inadequate BL concentration risk: red = very high, green = low, orange = variable.

Novy E *et al.* Antibiotics 2023

Anti-infectieux et épuration extra-rénale en réanimation



Kanji S *et al*. Pharmacotherapy 2023

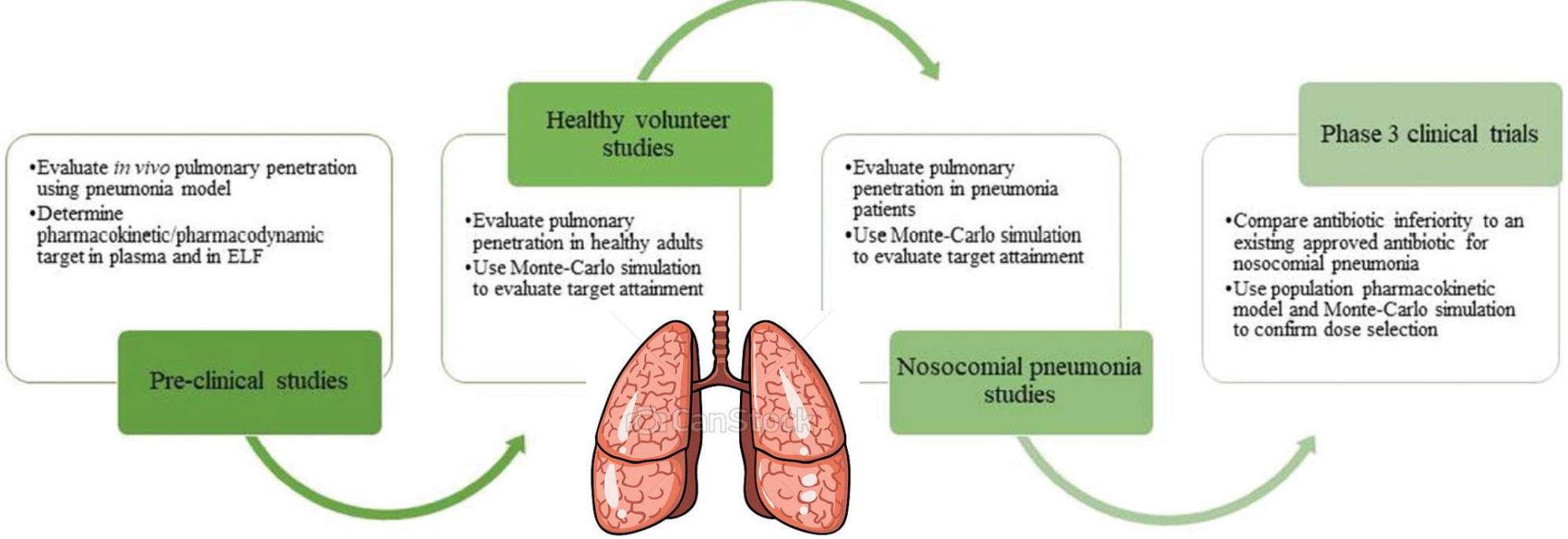
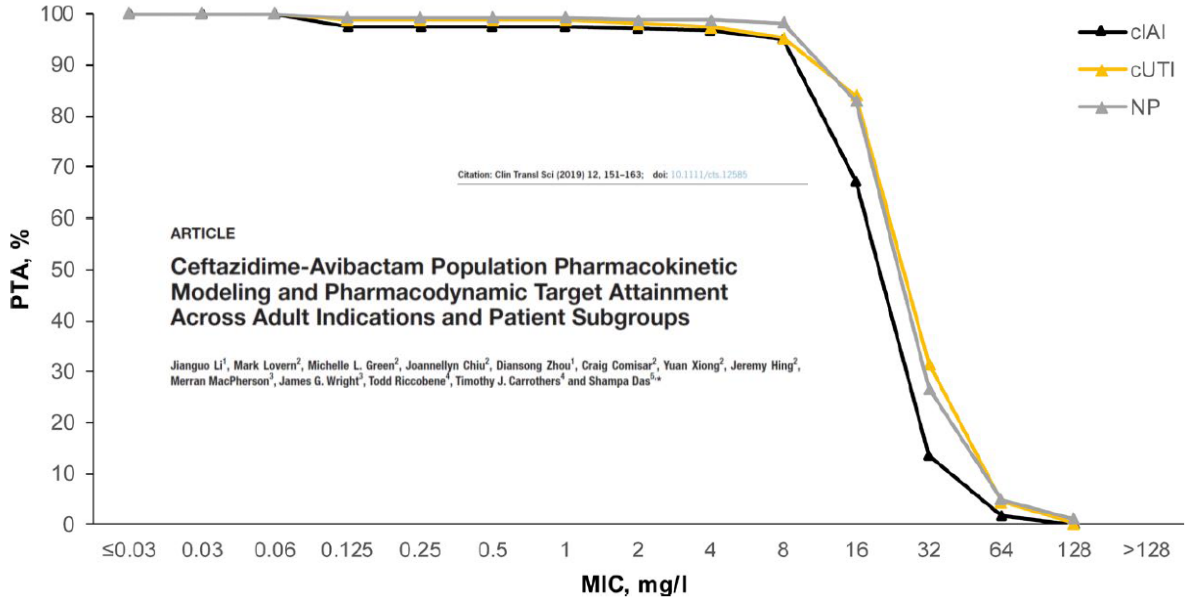


Figure 3. Suggested pathway for hospital acquired bacterial pneumonia/ventilator-associated bacterial pneumonia (HABP/VABP) drug development and dosage optimization.



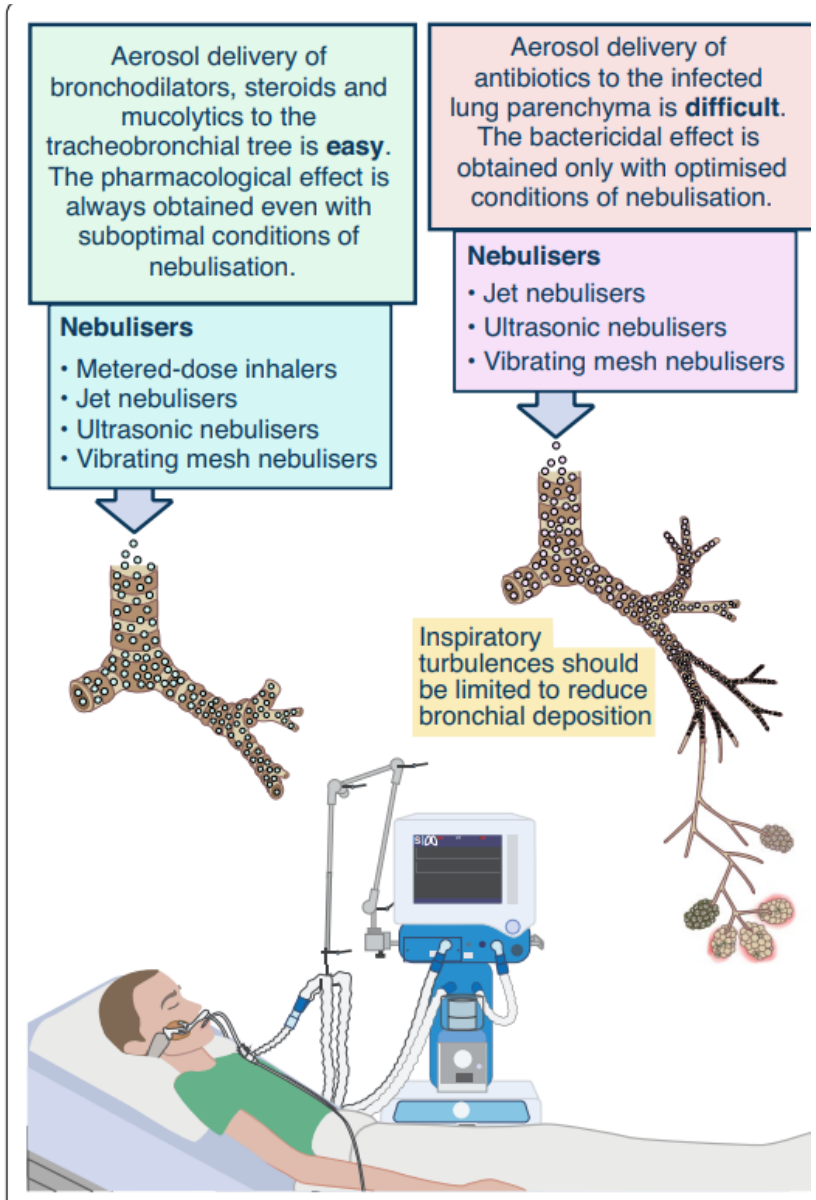
Optimizing antibiotic dosing regimens for nosocomial pneumonia: a window of opportunity for pharmacokinetic and pharmacodynamic modeling

Yuwei Shen & Joseph L. Kuti

EXPERT OPINION ON DRUG METABOLISM & TOXICOLOGY 2023

Aerosolised antibiotics in critical care

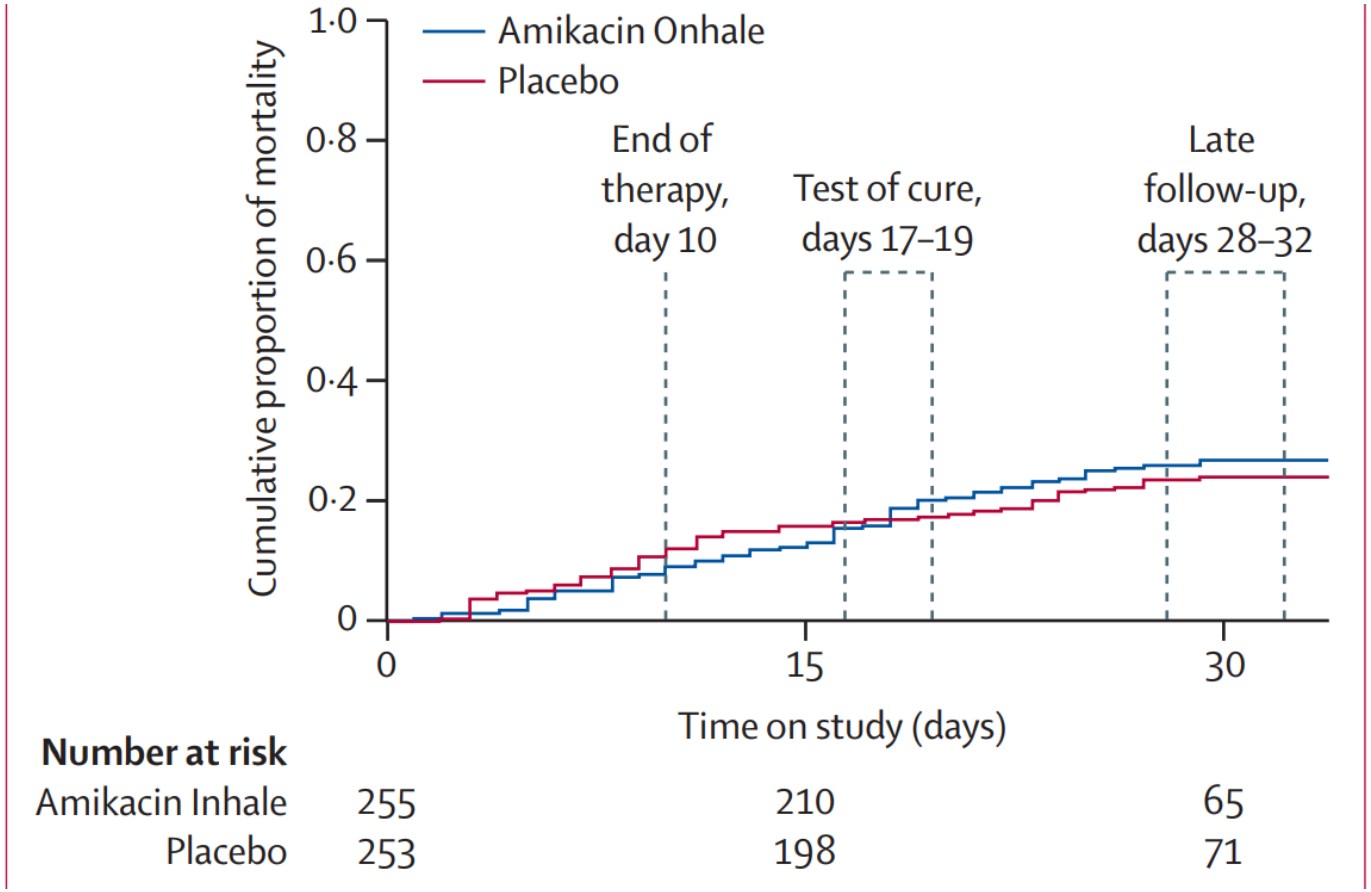
Jordi Rello[1,2,3*], Adrien Bouglé[4] and Jean-Jacques Rouby[5]



Inhaled amikacin adjunctive to intravenous standard-of-care antibiotics in mechanically ventilated patients with Gram-negative pneumonia (INHALE): a double-blind, randomised, placebo-controlled, phase 3, superiority trial

Michael S Niederman, Jeff Alder, Matteo Bassetti, Francis Boateng, Bin Cao, Kevin Corkery, Rajiv Dhand, Keith S Kaye, Robert Lawatscheck, Patrick McLeroth, David P Nicolau, Chen Wang, G Christopher Wood, Richard G Wunderink, Jean Chastre

***Lancet Infect Dis* 2020; 20: 330–40**



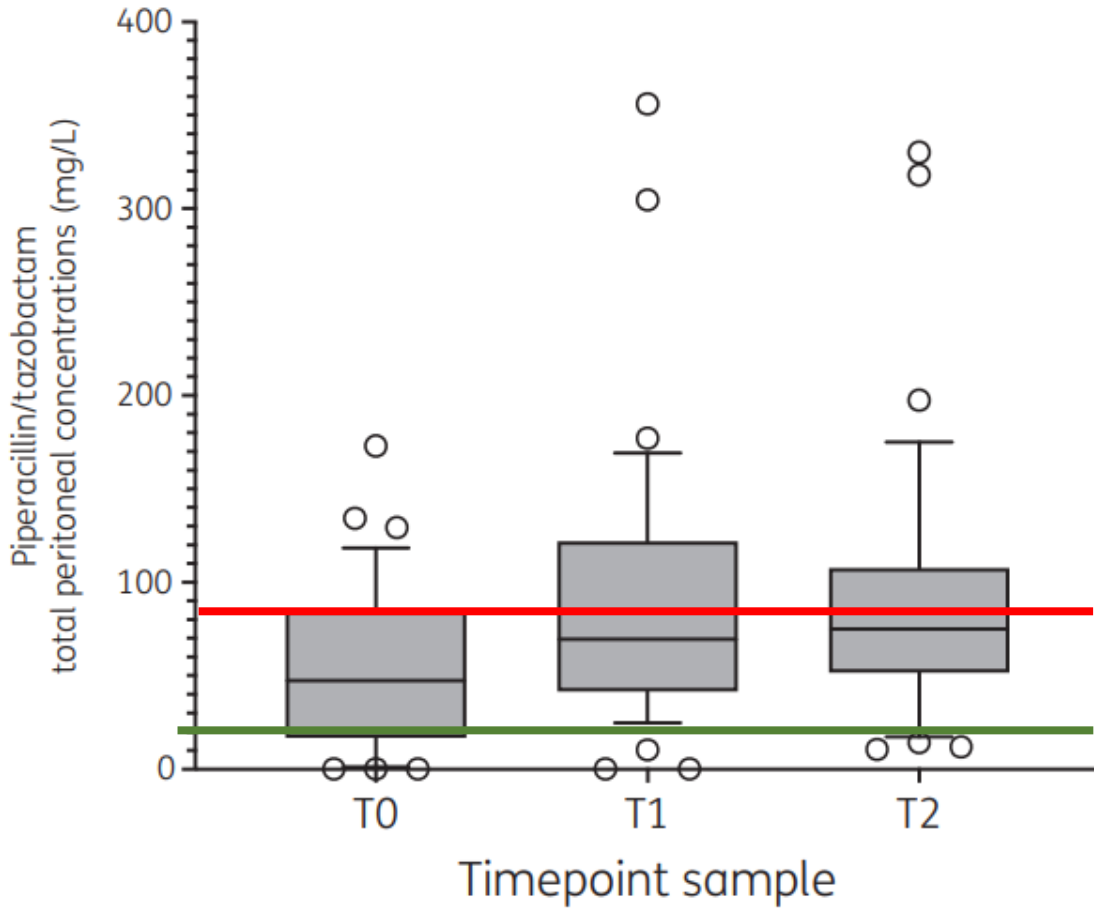
J Antimicrob Chemother 2020; **75**: 156–161
doi:10.1093/jac/dkz407 Advance Access publication 10 October 2019

Journal of Antimicrobial Chemotherapy

Serum and peritoneal exudate concentrations after high doses of β-lactams in critically ill patients with severe intra-abdominal infections: an observational prospective study

Lisa Leon[1,2], Philippe Guerci[1,2], Elise Pape[2,3], Nathalie Thilly[2,4], Amandine Luc[2,4], Adeline Germain[2,5], Anne-Lise Butin-Druoton[1,2], Marie-Reine Losser[1,2], Julien Birckener[1,2], Julien Scala-Bertola[2,3] and Emmanuel Novy[1,2]*

Objective: > 4 the MIC (free fraction 80%)



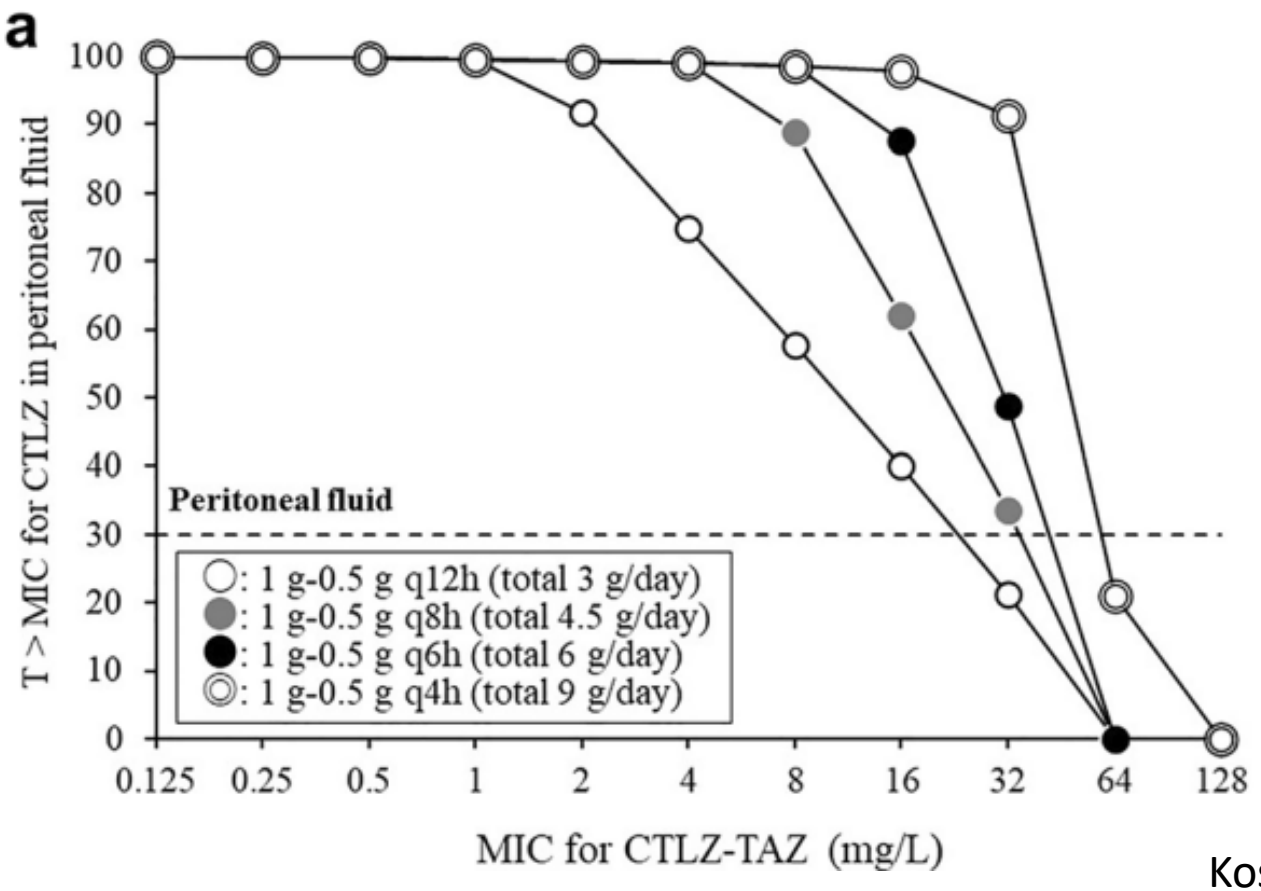
ECOFF-based (*a priori*)

MIC-based (*a posteriori*)

Infect Dis Ther (2023) 12:193–207
https://doi.org/10.1007/s40121-022-00720-x

ORIGINAL RESEARCH

Ceftolozane–Tazobactam Pharmacokinetics in the Abdominal Tissue of Patients Undergoing Lower Gastrointestinal Surgery: Dosing Considerations Based on Site-Specific Pharmacodynamic Target Attainment



Kosuke Yoshimura *et al.*

Concentrations de céfotaxime dans le LCS

Méningites à pneumocoques chez l'adulte : 87% sous DXM

Table 2. CSF concentrations of cefotaxime according to weight-based daily dosage ($n = 40$ dosages, four missing data)

	Daily dosage (mg/kg/day)			
	<150	150–199	200–280	>280
Number of patients	6	6	11	6
Number of dosages	9	8	13	10
Time since CTX initiation (h), median	120	144	96	193
Creatinine clearance (mL/min), median	51	77.5	86.0	96.5
Creatinine clearance <30 mL/min, *n*	4 (1 md)	0	1 (2 md)	0
CSF concentration (mg/L), median (range)	7.5 (1.2–29.3)	10.3 (2.2–15.4)	5.4 (1.6–23.8)	18.3 (3.0–43.4)

CMI médiane 0,25mg/L (0.008–1)

Le Turnier P *et al* J Antimicrob Chemother 2021

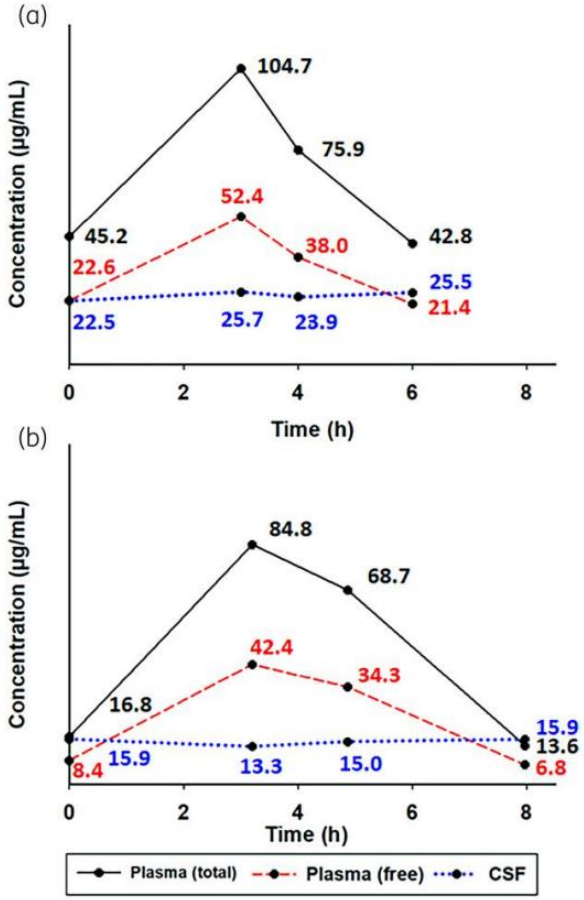
Céfiderocol *vs* ventriculites à BGN « DTR »

J Antimicrob Chemother 2022; **77**: 2737–2741
https://doi.org/10.1093/jac/dkac248 Advance Access publication 23 July 2022

Journal of Antimicrobial Chemotherapy

Plasma and cerebrospinal fluid concentrations of cefiderocol during successful treatment of carbapenem-resistant *Acinetobacter baumannii* meningitis

Wesley D. Kufel[1,2,3]*, Yasmeen Abouelhassan[4], Jeffrey M. Steele[2,3], Ramiro L. Gutierrez[2], Talha Perwez[2], George Bourdages[5] and David P. Nicolau[4,6]

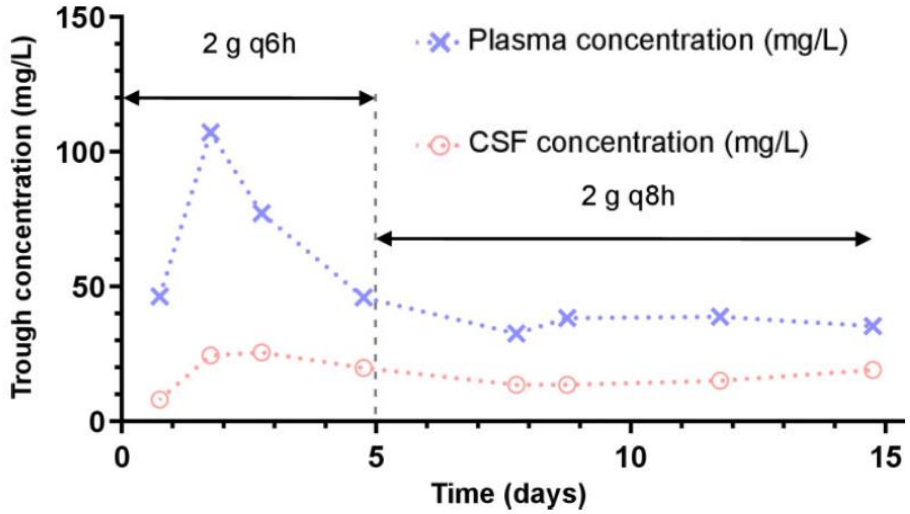


CMI: 0,25 mg/L

J Antimicrob Chemother 2022; **77**: 1787–1789
https://doi.org/10.1093/jac/dkac066
Advance Access publication 4 March 2022

Cerebrospinal fluid concentrations of cefiderocol during the treatment of extensively drug-resistant *Pseudomonas aeruginosa* ventriculitis

David Luque-Paz[1,2]*, Youssef Bennis[3], Paul Jaubert[1], Vincent Dubée[4], Michel Wolff[5] and Satar Mortaza[1]



CMI: 0,20 mg/L

Open Forum Infectious Diseases
NOVEL ID CASES

Clinical Cure of a Difficult-to-Treat Resistant *Pseudomonas aeruginosa* Ventriculitis Using Cefiderocol: A Case Report and Literature Review

Cristina Marcelo,[1,©] Alejandro de Gea Grela,[2,©] Maria Martinez Palazuelos,[3] Javier Veganzones,[3] David Grandioso,[4,©] and Beatriz Díaz-Pollán[1,5,©]

Table 3. Cefiderocol Levels Achieved in Cerebrospinal Fluid (CSF) (Samples 1 and 2) and CSF Simultaneously With Plasma (Samples 3 and 4)

Days of Cefiderocol	Sample No.	Matrix	Cefiderocol Concentration, μg/mL
10	1 (peak)	CSF	3.628
11	2 (peak)	CSF	No peak
12	3 (peak)	CSF	No peak
		Serum	219.2
13	4 (trough)	CSF	1.586
		Serum	40.18

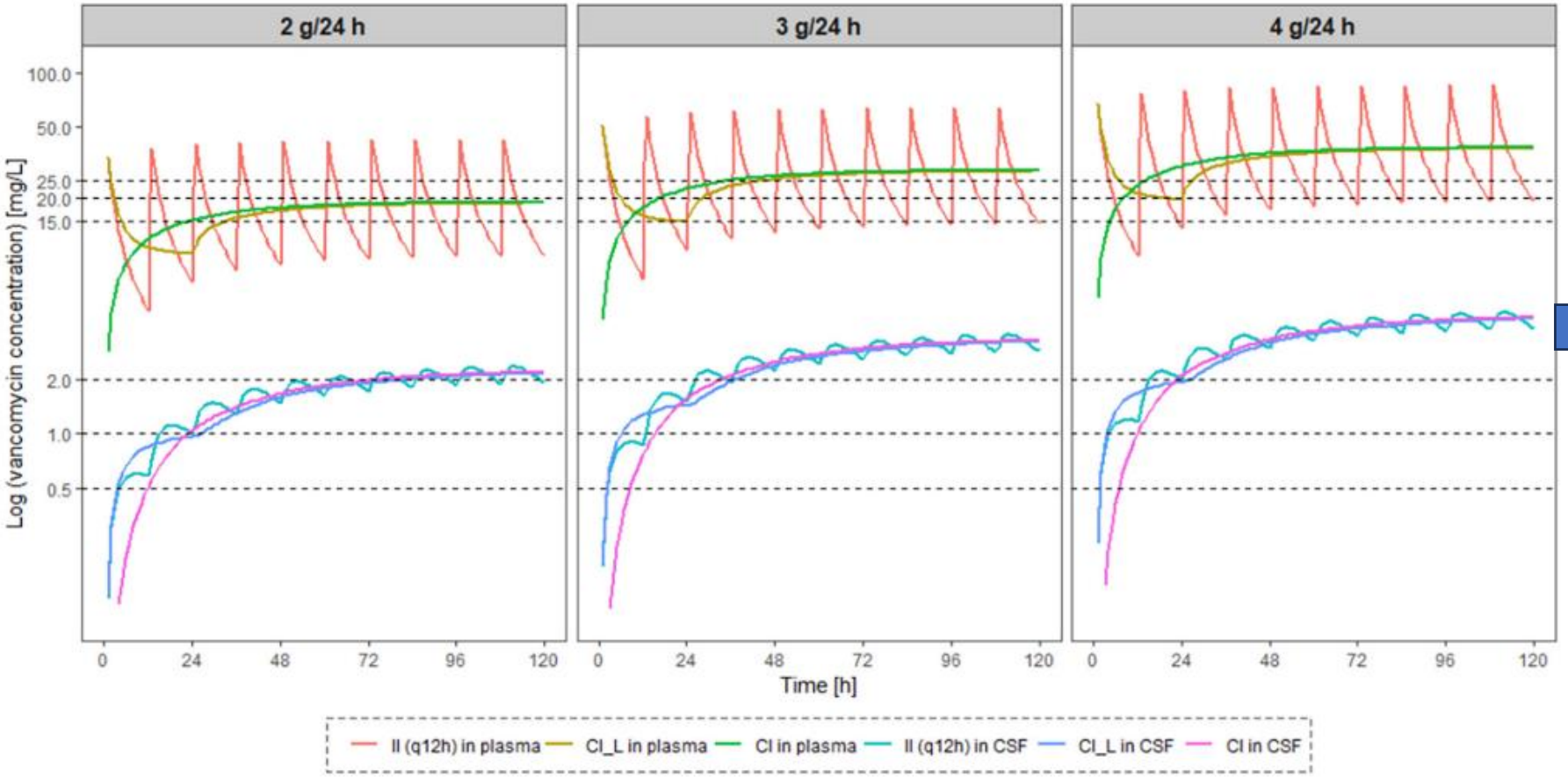
CMI: 0,5 mg/L

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

2023

Plasma and Cerebrospinal Fluid Population Pharmacokinetics of Vancomycin in Patients with External Ventricular Drain

Forme libre : 50%



- Vancomycine intraventriculaire
- Linezolide

Chen Z *et al*.

Clinical Infectious Diseases
IDSA GUIDELINE

2017 Infectious Diseases Society of America's Clinical Practice Guidelines for Healthcare-Associated Ventriculitis and Meningitis*

Allan R. Tunkel,[1] Rodrigo Hasbun,[2] Adarsh Bhimraj,[3] Karin Byers,[4] Sheldon L. Kaplan,[5] W. Michael Scheld,[6] Diederik van de Beek,[7]

VII. What is the Role of Intraventricular Antimicrobial Therapy in Patients with Healthcare-Associated Ventriculitis and Meningitis?

Recommendations

55. Intraventricular antimicrobial therapy should be considered for patients with healthcare-associated ventriculitis and meningitis in which the infection responds poorly to systemic antimicrobial therapy alone (strong, low).

Table 3. Recommende ed by the Intraventricular I

Antimicrobial Agent	Daily Intraventricular Dose
Amikacin	5–50 mg[a]
Amphotericin B deoxycholate[b]	0.01–0.5 mg in 2 mL of 5% dextrose in water
Colistin (formulated as colistimethate sodium)	10 mg
Daptomycin	2–5 mg[c]
Gentamicin	1–8 mg[d,e,f]
Polymyxin B	5 mg[g]
Quinupristin/dalfopristin	2–5 mg
Tobramycin	5–20 mg
Vancomycin	5–20 mg[e,f,h]

According to ventricular size

	Vanco (mg)	Genta (mg)
Slit	5	2
Normal	10	3
Enlarged	15-20	4-5

According to EVD output

EVD output (ml/24h)	Vanco	Genta
< 50	Every 3rd day	
50-100	Every 2nd day	
100-150	Every day	
150-200	↑ 5 mg OD	↑ 1mg OD
200-250	↑ 10 mg OD	↑ 2mg OD

Guilhaumou et al. Critical Care (2019) 23:104
https://doi.org/10.1186/s13054-019-2378-9

Critical Care

REVIEW Open Access

Optimization of the treatment with beta-lactam antibiotics in critically ill patients—guidelines from the French Society of Pharmacology and Therapeutics (Société Française de Pharmacologie et Thérapeutique—SFPT) and the French Society of Anaesthesia and Intensive Care Medicine (Société Française d'Anesthésie et Réanimation—SFAR)

Romain Guilhaumou[1], Sihem Benaboud[2], Youssef Bennis[3], Claire Dahyot-Fizelier[4], Eric Dailly[5], Peggy Gandia[6], Sylvain Goutelle[7], Sandrine Lefeuvre[8], Nicolas Mongardon[9], Claire Roger[10], Julien Scala-Bertola[11], Florian Lemaitre[12] and Marc Garnier[13*]

Intensive Care Med (2019) 45:172–189
https://doi.org/10.1007/s00134-019-05520-5

REVIEW

Rationalizing antimicrobial therapy in the ICU: a narrative review

Jean-François Timsit[1,2*], Matteo Bassetti[3], Olaf Cremer[4], George Daikos[5], Jan de Waele[6], Andre Kallil[7], Eric Kipnis[8], Marin Kollef[9], Kevin Laupland[10], Jose-Artur Paiva[11], Jesús Rodríguez-Baño[12], Étienne Ruppé[2,13], Jorge Salluh[14], Fabio Silvio Taccone[15], Emmanuel Weiss[16,17] and François Barbier[18]

Intensive Care Med (2020) 46:1127–1153
https://doi.org/10.1007/s00134-020-06050-1

CONFERENCE REPORT AND EXPERT PANEL

Antimicrobial therapeutic drug monitoring in critically ill adult patients: a Position Paper#

Mohd H. Abdul-Aziz[1], Jan-Willem C. Alffenaar[2,3,4], Matteo Bassetti[5], Hendrik Bracht[6], George Dimopoulos[7], Deborah Marriott[8], Michael N. Neely[9,10], Jose-Artur Paiva[11,12], Federico Pea[13], Fredrik Sjovall[14], Jean F. Timsit[15,16], Andrew A. Udy[17,18], Sebastian G. Wicha[19], Markus Zeitlinger[20], Jan J. De Waele[21], Jason A. Roberts[1,22,23,24*] on behalf of the Infection Section of European Society of Intensive Care Medicine (ESICM), Pharmacokinetic/pharmacodynamic and Critically Ill Patient Study Groups of European Society of Clinical Microbiology and Infectious Diseases (ESCMID), Infectious Diseases Group of International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) and Infections in the ICU and Sepsis Working Group of International Society of Antimicrobial Chemotherapy (ISAC)

J Antimicrob Chemother 2018; **73**: 3087–3094
doi:10.1093/jac/dky314 Advance Access publication 17 August 2018

Journal of Antimicrobial Chemotherapy

Therapeutic drug monitoring of β-lactam antibiotics in the critically ill: direct measurement of unbound drug concentrations to achieve appropriate drug exposures

Gloria Wong[1,2], Scott Briscoe[3], Brett McWhinney[3], Mumtaz Ally[1], Jacobus Ungerer[3], Jeffrey Lipman[1,2] and Jason A. Roberts[1,2,4*]

Intensive Care Med (2018) 44:189–196
https://doi.org/10.1007/s00134-017-5036-1

CONFERENCE REPORTS AND EXPERT PANEL

Antimicrobial resistance and antibiotic stewardship programs in the ICU: insistence and persistence in the fight against resistance. A position statement from ESICM/ESCMID/WAAAR round table on multi-drug resistance

Jan J. De Waele[1*], Murat Akova[2], Massimo Antonelli[3], Rafael Canton[4], Jean Carlet[5], Daniel De Backer[6], George Dimopoulos[7], José Garnacho-Montero[8], Jozef Kesecioglu[9], Jeffrey Lipman[10,11], Mervyn Mer[11,12], José-Artur Paiva[13], Mario Poljak[14], Jason A. Roberts[15], Jesus Rodriguez Bano[16], Jean-François Timsit[17,18], Jean-Ralph Zahar[18,19] and Matteo Bassetti[20]

https://doi.org/10.1007/s00134-019-05522-3

EDITORIAL

Personalized antibiotic dosing for the critically ill

Jason A. Roberts[1,2,3,4*], Claire Roger[5] and Jan J. De Waele[6]

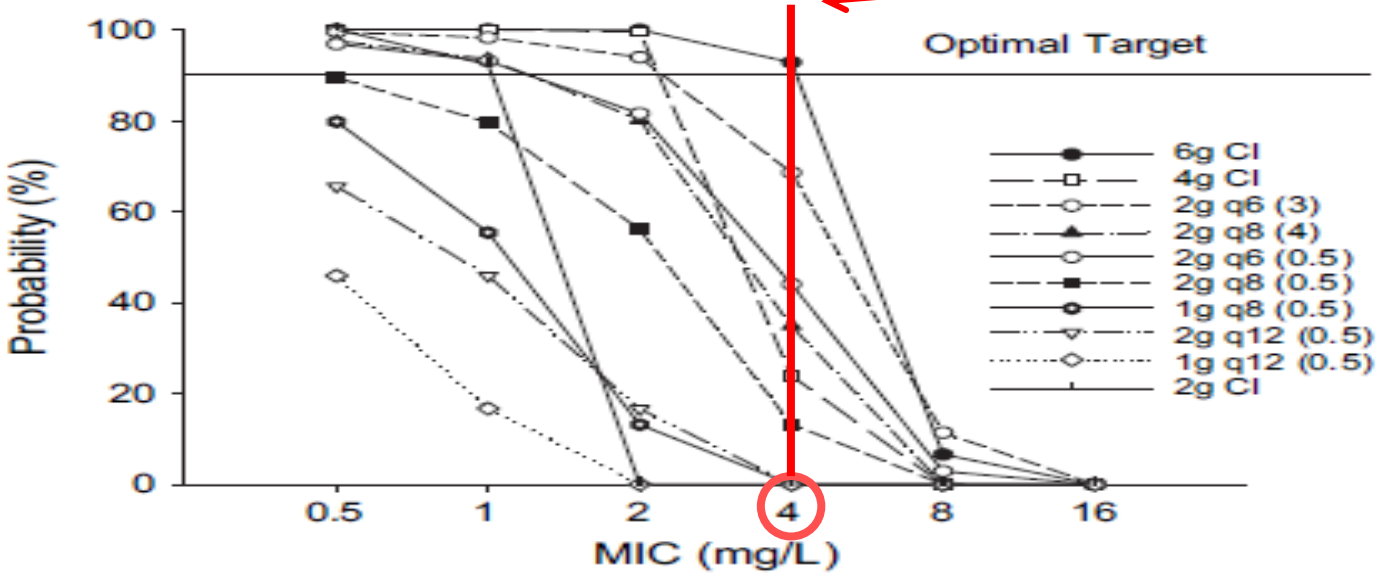
Deux questions majeures concernant les β-lactamines en réanimation

1. Quel bénéfice pour l' administration prolongée ou continue ?
2. Quel bénéfice à mesurer les concentrations plasmatiques ?

Cefepime pharmacodynamics in patients with extended spectrum β-lactamase (ESBL) and non-ESBL infections☆

Su Young Lee, Joseph L. Kuti, David P. Nicolau*

CMI 4 mg/l



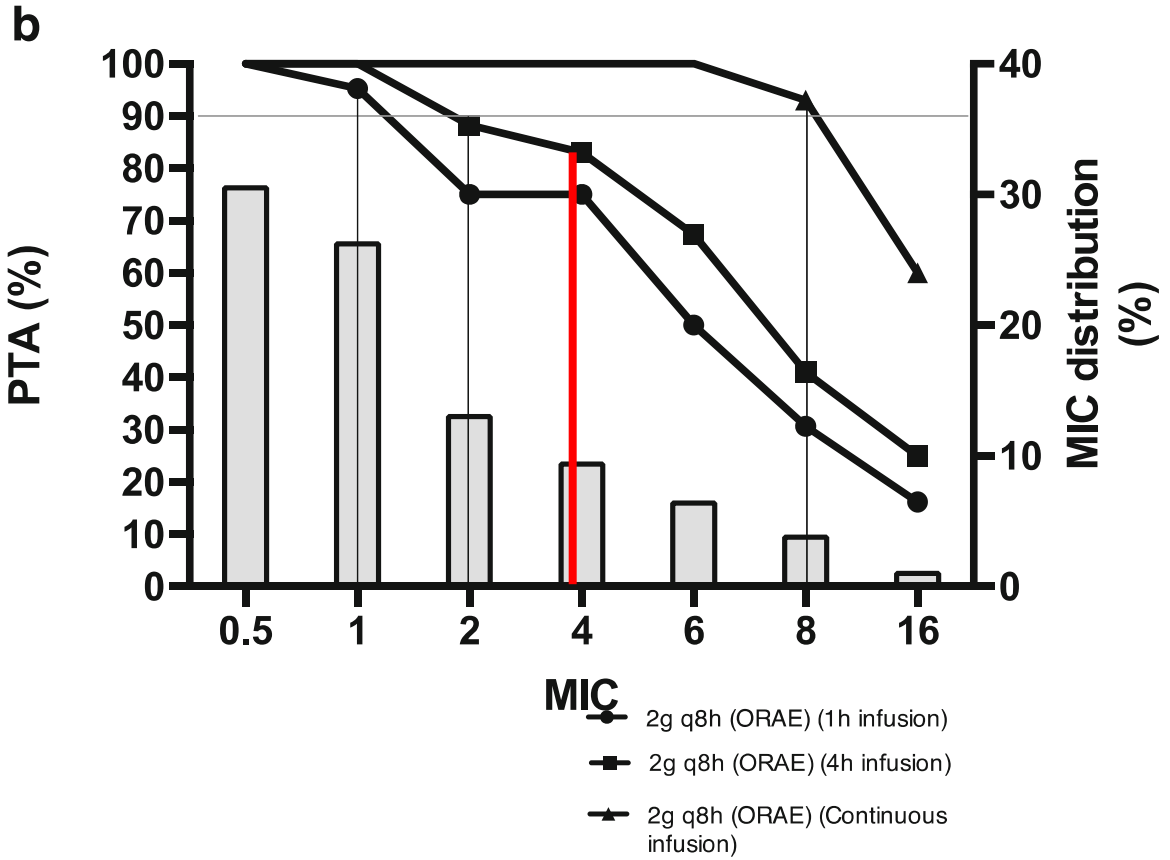
Objectif atteint avec 6g en continu
(après un bolus de 2 g)

Figure 2 Probability of target attainment (PTA) of each drug regimen (infusion time) to obtain $fCmin/MIC > 7.6$ for simulated subjects with CL_{CR} between 60 and 120 ml/min.

Journal of Infection 2007, 54: 463-68

Modèles pharmacocinétiques: ceftolozane-tazobactam

- 72 pts (essentiellement en réanimation) traités par C/T: dosages plasmatiques
- 2/3 de pneumonies
- Modélisation de la probabilité d'atteindre >90% du temps au dessus de 4xCMI
- Distribution des CMI observées
- Comparaison perf discontinue *vs* prolongée vs continue



(CMI=4mg/L, seuil critique pour *P. aeruginosa*)

Pilmis B *et al*, Eur J Clin Microbiol Infect Dis. 2019

International Journal of Antimicrobial Agents 43 (2014) 68–72

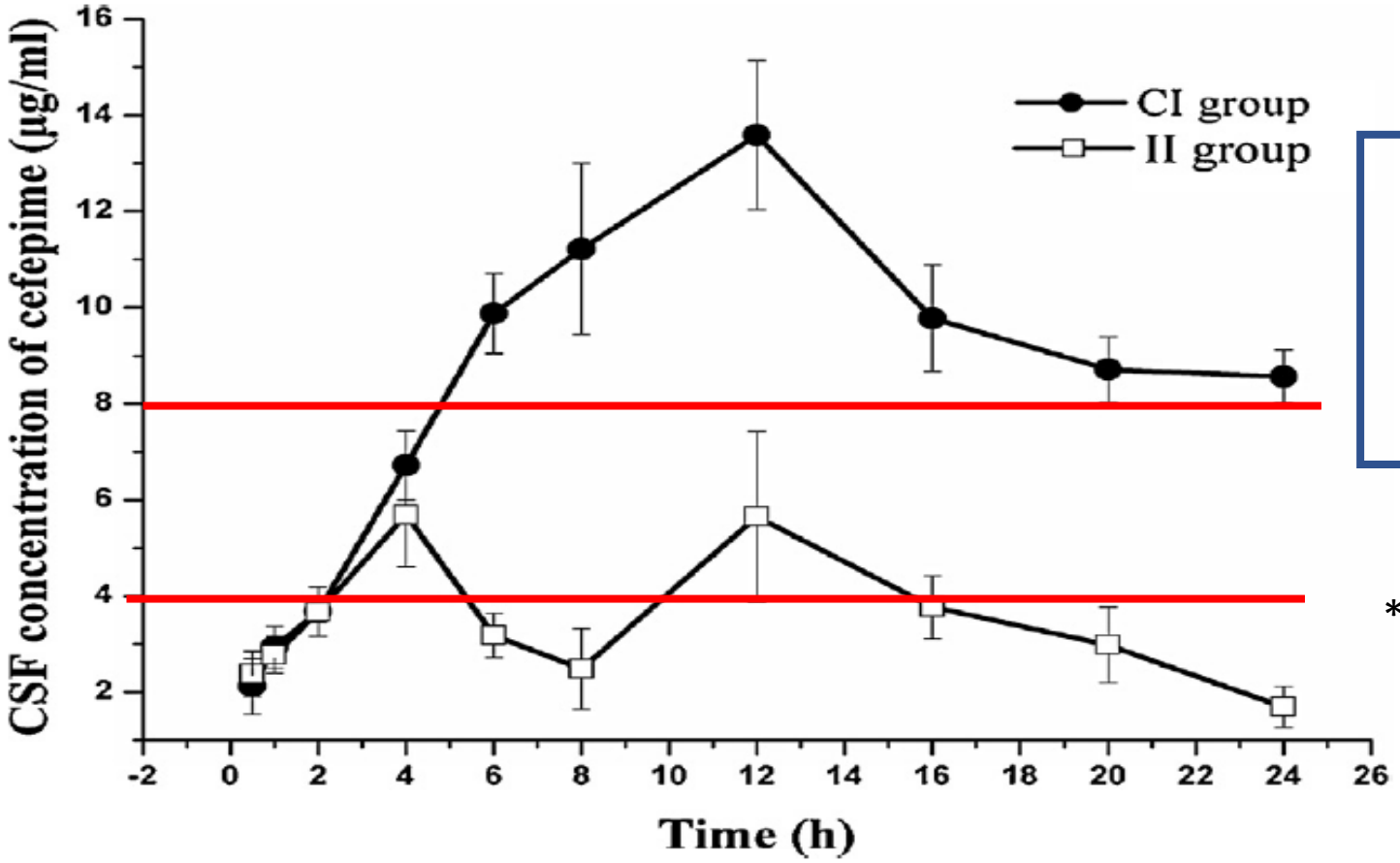
Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: http://www.elsevier.com/locate/ijantimicag

Continuous versus intermittent infusion of cefepime in neurosurgical patients with post-operative intracranial infections

68 patients



	CI	II
%t > MIC*	83	25
AUC (μg/h/ml)	220	86

* MIC: 4 mg/L

Huang H *et coll*.

Intensive Care Med
DOI 10.1007/s00134-015-4188-0

ORIGINAL

Mohd H. Abdul-Aziz
Helmi Sulaiman
Mohd-Basri Mat-Nor
Vineya Rai
Kang K. Wong
Mohd S. Hasan
Azrin N. Abd Rahman
Janattul A. Jamal
Steven C. Wallis
Jeffrey Lipman
Christine E. Staatz
Jason A. Roberts

Beta-Lactam Infusion in Severe Sepsis (BLISS): a prospective, two-centre, open-labelled randomised controlled trial of continuous versus intermittent beta-lactam infusion in critically ill patients with severe sepsis

Perfusion prolongée des beta-lactamines?

Table 2 Primary and secondary endpoints by treatment arm in the intention-to-treat population and the subgroups of interest

Primary endpoint	Intervention (n = 70)	Control (n = 70)	Absolute difference (95 % CI)	Significance (p value)[a,b]
Clinical cure for ITT population, n (%)	39 (56)	24 (34)	22 (−0.4 to −0.1)	**0.011**
Clinical cure by antibiotic, n (%)[c]				
Piperacillin/tazobactam	22 (58)	15 (32)	26 (−0.4 to −0.1)	**0.016**
Meropenem	14 (67)	8 (38)	29 (−0.5 to 0.1)	0.064
Cefepime	3 (27)	1 (50)	23 (−0.3 to 0.7)	1.000
Clinical cure by concomitant antibiotic treatment, n (%)[d]				
Yes	14 (42)	13 (39)	3 (−0.3 to 0.2)	0.802
No	25 (68)	11 (30)	38 (−0.6 to −0.2)	**0.001**
Clinical cure by site of infection, n (%)[e]				
Lung	27 (59)	12 (33)	25 (−0.4 to −0.1)	**0.022**
Clinical cure by *A. baumannii* or *P. aeruginosa* infection, n (%)[f]				
Yes	13 (52)	6 (25)	27 (−0.5 to 0.1)	0.052
No	10 (44)	12 (38)	6 (−0.3 to 0.2)	0.655

Secondary endpoints	Intervention (n = 70)	Control (n = 70)	Absolute difference (95 % CI)	Significance (p value)[a,b]
PK/PD target attainment, n (%)[g]				
50 % $fT_{>MIC}$ on day 1	56 (98)	49 (93)	5 (−0.2 to 0.1)	0.194
100 % $fT_{>MIC}$ on day 1	55 (97)	37 (70)	27 (−0.4 to −0.1)	**<0.001**
50 % $fT_{>MIC}$ on day 3	56 (98)	49 (93)	5 (−0.2 to 0.1)	0.194
100 % $fT_{>MIC}$ on day 3	55 (97)	36 (68)	29 (−0.4 to −0.1)	**<0.001**
ICU-free days	20 (12–23)	17 (0–24)	3 (−3 to 9)	0.378
ICU survivors[h]	21 (19–23)	21 (14–24)	0 (−3 to 3)	0.824
Ventilator-free days	22 (0–24)	14 (0–24)	8 (−2 to 18)	**0.043**
ICU survivors[i]	23 (21–25)	21 (0–25)	2 (−3 to 7)	0.076
14-day survival, n (%)	56 (80)	50 (71)	9 (−0.2 to 0.1)	0.237
30-day survival, n (%)	52 (74)	44 (63)	11 (−0.3 to 0.1)	0.145
WCC normalisation days	3 (2–7)	8 (4–15)	5 (1 to 5)	**<0.001**

Received: 9 July 2020 | Revised: 6 October 2020 | Accepted: 6 October 2020
DOI: 10.1111/jcpt.13301

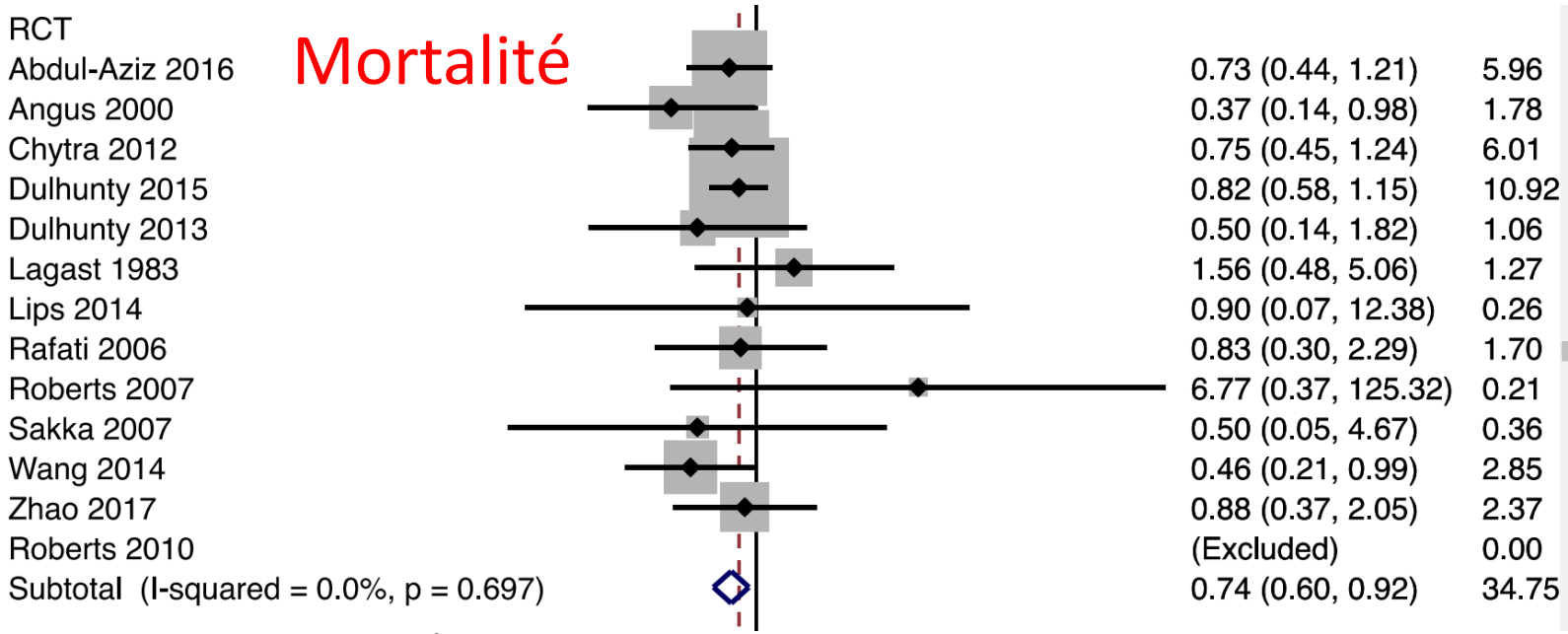
ORIGINAL ARTICLE

Journal of Clinical Pharmacy and Therapeutics WILEY

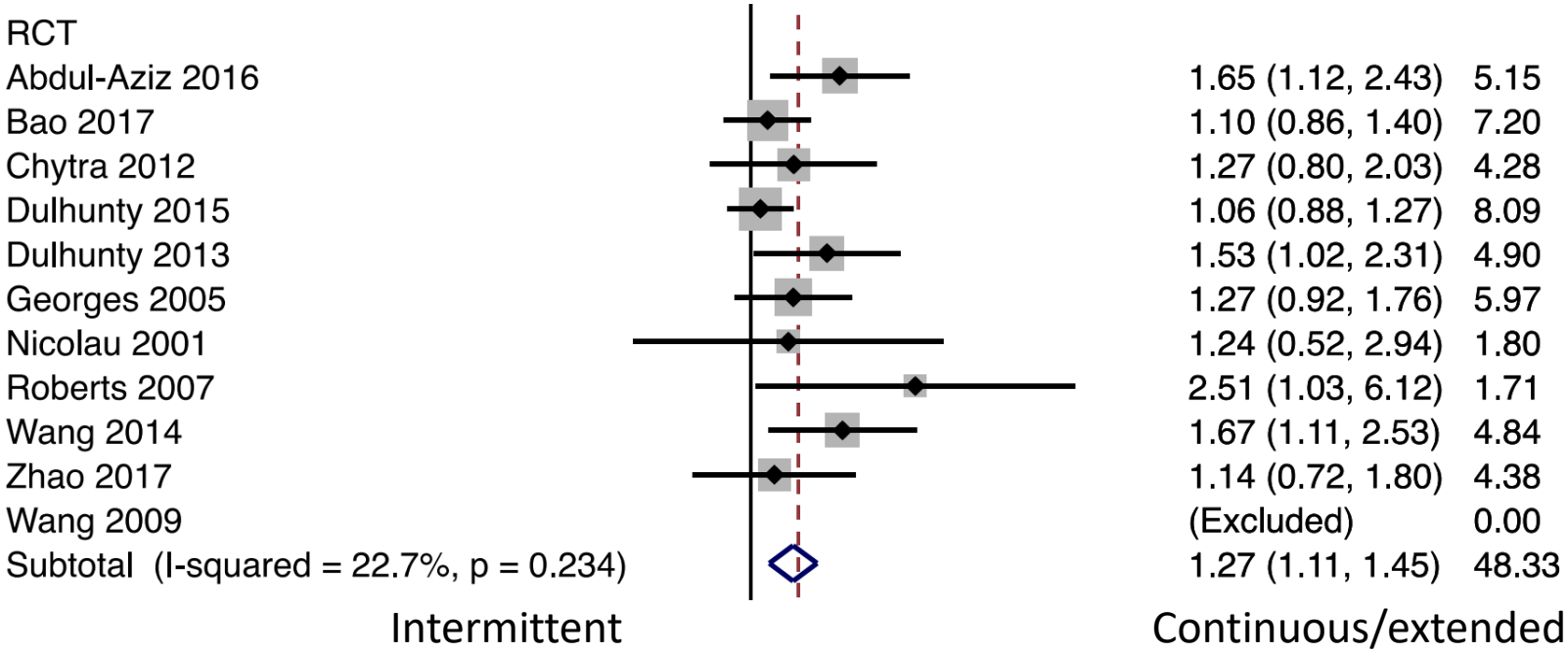
Loading dose and efficacy of continuous or extended infusion of beta-lactams compared with intermittent administration in patients with critical illnesses: A subgroup meta-analysis and meta-regression analysis

Chih-Chien Wu MD[1,2] | Yi-Chia Su MS[3,4] | Kuan-Sheng Wu MD[2,5] | Tung-Ho Wu MD[6] | Ching-Shiang Yang MS[3]

Mortalité



Guérison clinique



Clinical Infectious Diseases
MAJOR ARTICLE

Ceftazidime-Avibactam Use for Klebsiella pneumoniae Carbapenemase–Producing *K. pneumoniae* Infections: A Retrospective Observational Multicenter Study

577 patients dont
391 bactériémiques

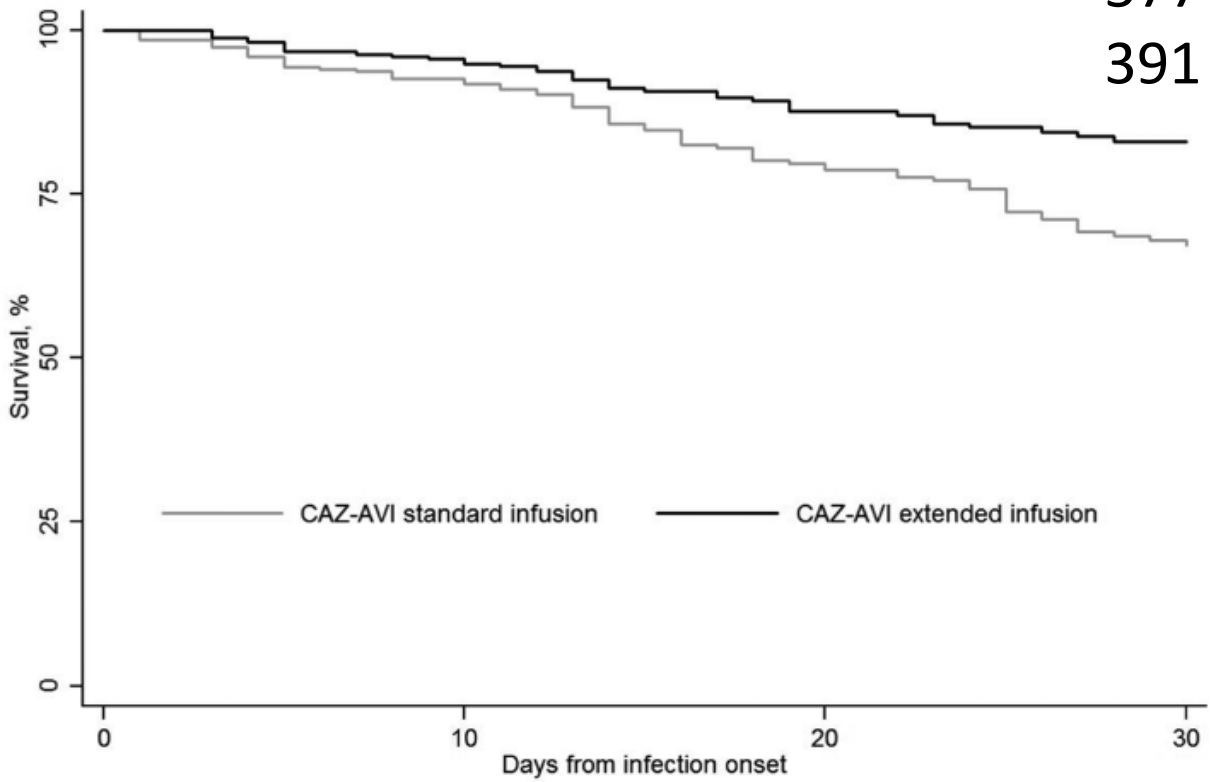


Figure 3. Kaplan-Meyer analysis of the impact of CAZ-AVI infusion times on 30-day survival. Significantly better survival was observed when CAZ-AVI was administered by prolonged infusion (standard dose given over ≥3 hours) versus standard infusion ($P < .001$). Abbreviation: CAZ-AVI, ceftazidime-avibactam.

M Tumbarello *et al*.2021

JAMA

QUESTION Does continuous administration of meropenem reduce a composite of mortality and emergence of drug-resistant bacteria among critically ill patients with sepsis compared with intermittent administration?

CONCLUSION Continuous administration of meropenem, compared with intermittent administration, does not improve clinically relevant outcomes in critically ill patients with sepsis.

POPULATION

404 Men
203 Women

Critically ill adults with sepsis

Mean age: 64 years

LOCATION

31
Intensive care units in Croatia, Italy, Kazakhstan, and Russia

INTERVENTION

607 Patients randomized

303
Continuous administration
3 g of meropenem administered over 24 hours

304
Intermittent administration
1 g of meropenem administered over 30 to 60 minutes every 8 h

PRIMARY OUTCOME

All-cause mortality and emergence of pandrug-resistant or extensively drug-resistant bacteria at day 28

FINDINGS

Incidence of composite primary outcome at day 28

Continuous administration
142 of 303 patients

Intermittent administration
149 of 304 patients

The between-group difference was not significant:

Relative risk, **0.96** (95% CI, 0.81 to 1.13); *P* = .60

Monti G, Bradić N, Marzaroli M, et al; for the MERCY Investigators. Continuous vs intermittent meropenem administration in critically ill patients with sepsis: the MERCY randomized clinical trial. *JAMA*. Published online June 16, 2023. doi:10.1001/jama.2023.10598

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

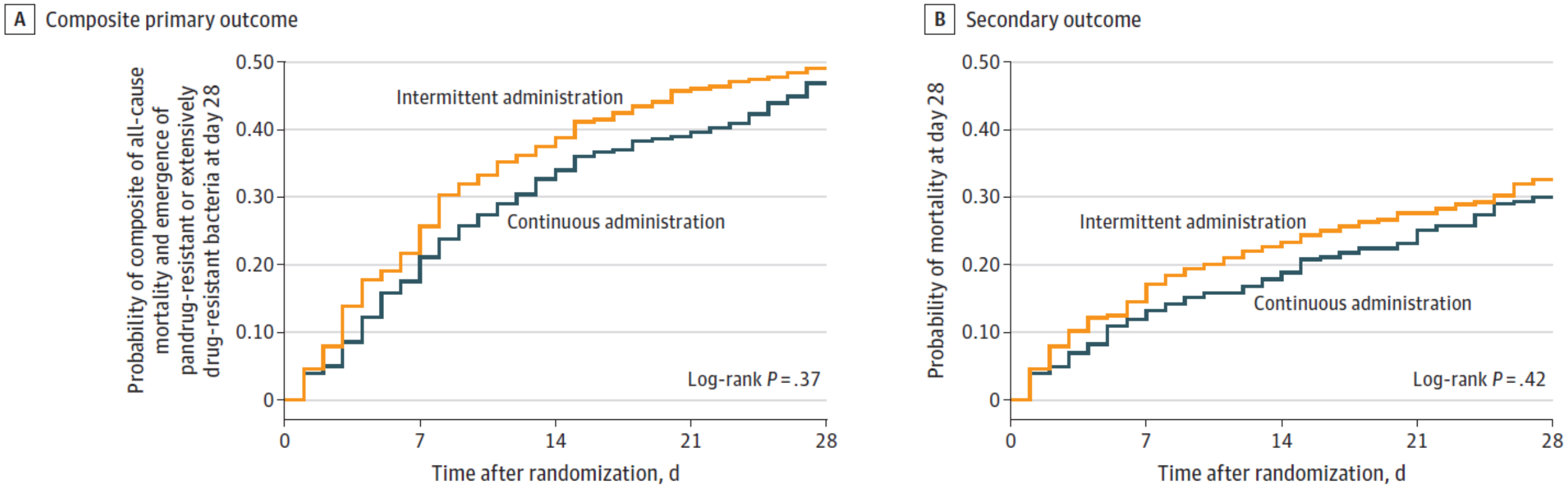
Continuous vs Intermittent Meropenem Administration in Critically Ill Patients With Sepsis

The MERCY Randomized Clinical Trial

31 ICUs 310 patients, septic shock : 6%

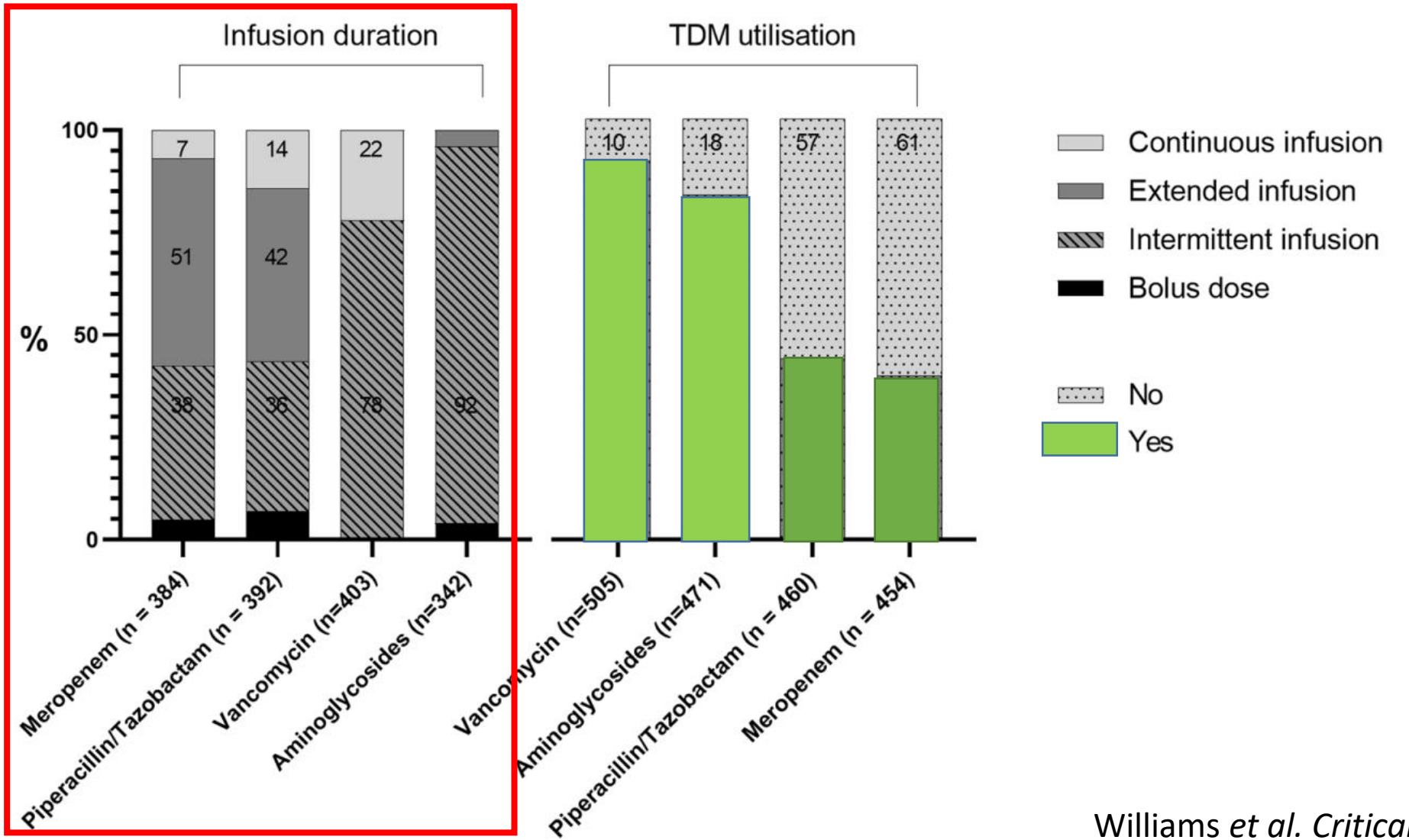
Monti G et al. 2023

Figure 2. Kaplan-Meier Analysis for the Composite Primary Outcome and the Secondary Outcome of Probability of Mortality at Day 28



RESEARCH Open Access

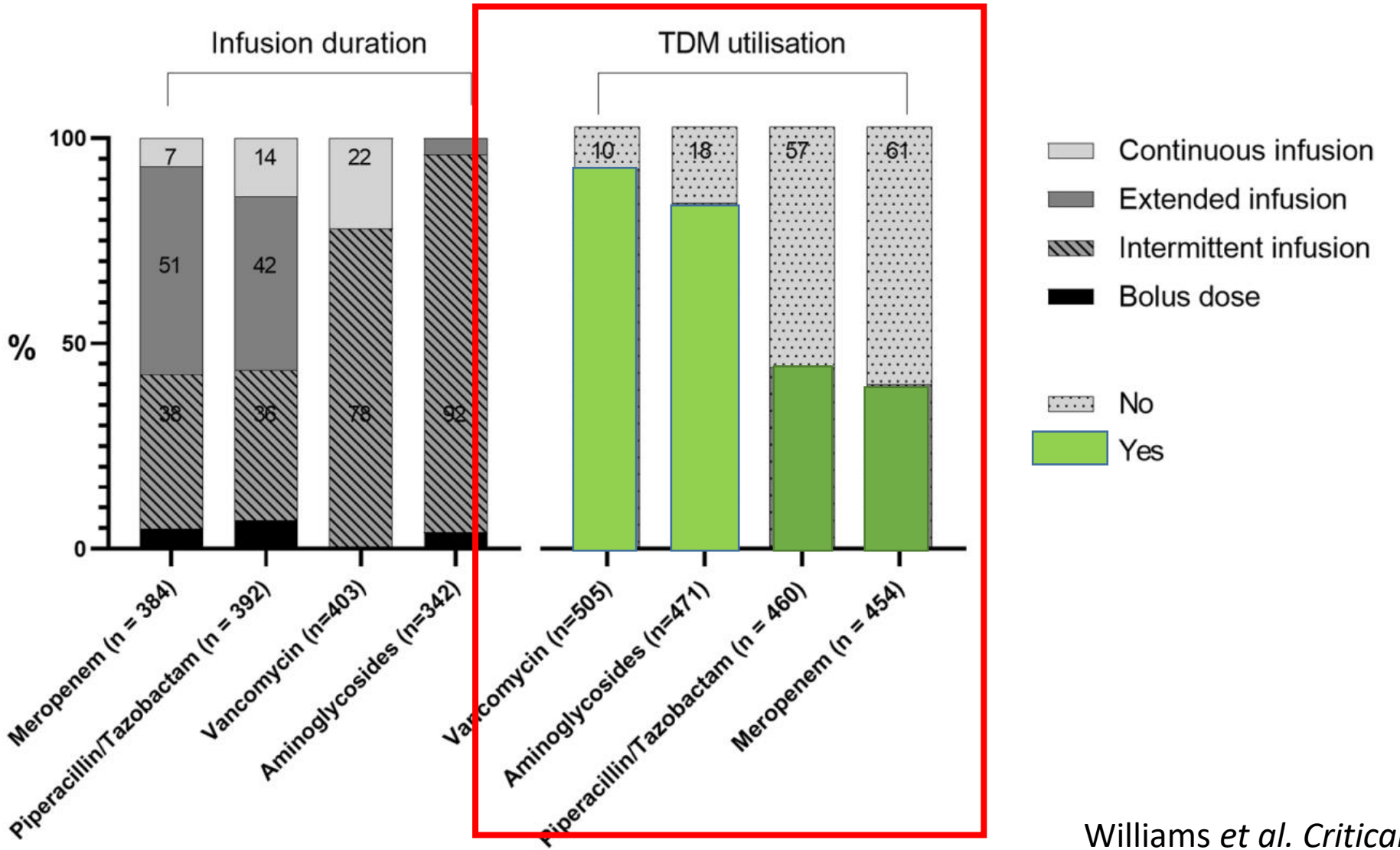
International survey of antibiotic dosing and monitoring in adult intensive care units



Williams *et al. Critical Care (2023)*

RESEARCH Open Access

International survey of antibiotic dosing and monitoring in adult intensive care units



Williams *et al. Critical Care (2023)*

Intensive Care Med (2020) 46:1127–1153
https://doi.org/10.1007/s00134-020-06050-1

CONFERENCE REPORT AND EXPERT PANEL

Antimicrobial therapeutic drug monitoring in critically ill adult patients: a Position Paper#

"The Panel recommends that TDM be routinely performed when beta-lactam antibiotics are used in critically ill patients"

Dosage des β-lactamines en réanimation: objectifs

Objectif	Utilité démontrée
Ne pas être au dessous des cibles PK-PD	Peut-être (germes moins sensibles, Hyper-clairance, ↑VD, EER)

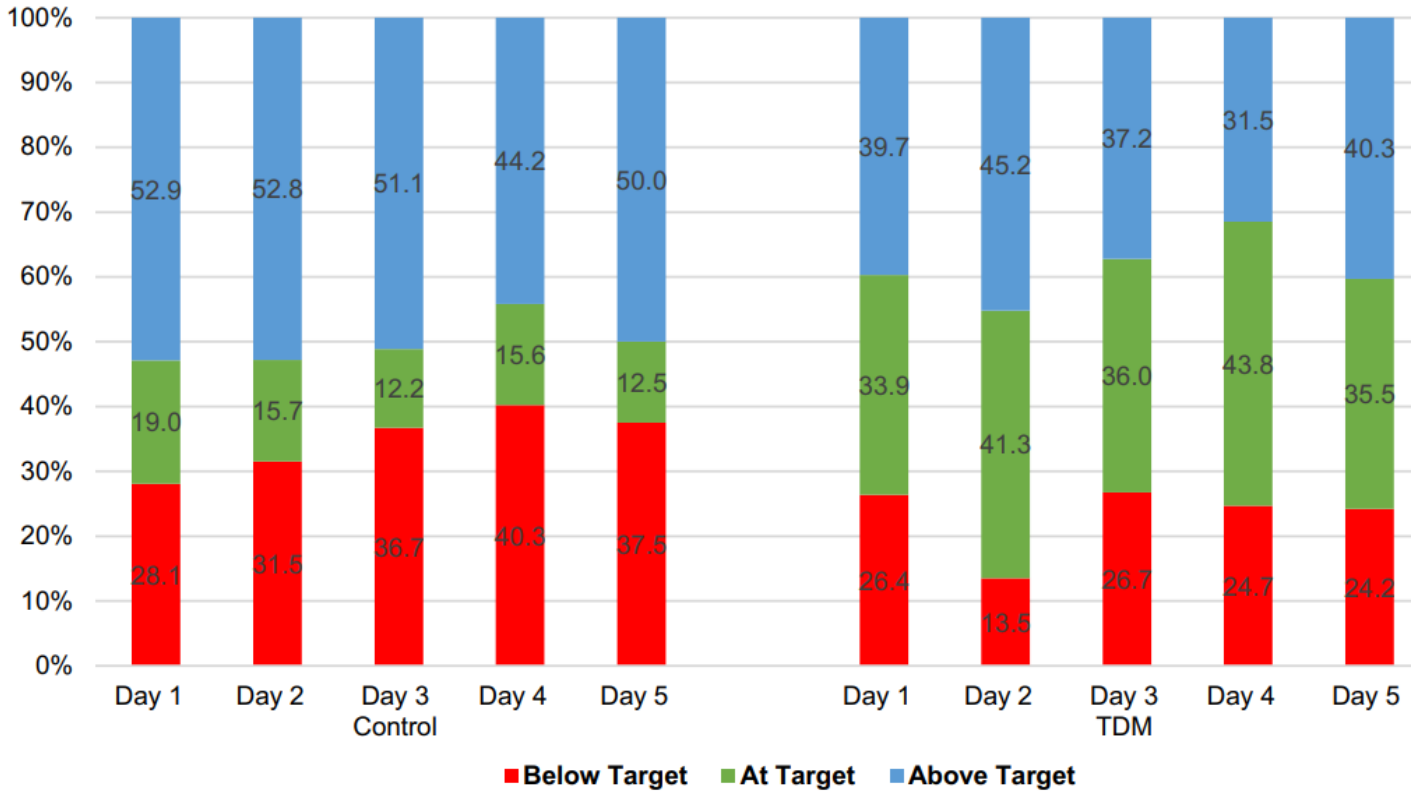
Intensive Care Med (2022) 48:311–321
https://doi.org/10.1007/s00134-021-06609-6

ORIGINAL

Effect of therapeutic drug monitoring-based dose optimization of piperacillin/tazobactam on sepsis-related organ dysfunction in patients with sepsis: a randomized controlled trial

Stefan Hagel[1,2*], Friedhelm Bach[3], Thorsten Brenner[4,5], Hendrik Bracht[6], Alexander Brinkmann[7], Thorsten Annecke[8,9], Andreas Hohn[8,10], Markus Weigand[5], Guido Michels[11], Stefan Kluge[12], Axel Nierhaus[12], Dominik Jarczak[12], Christina König[12], Dirk Weismann[13], Otto Frey[14], Dominic Witzke[3], Carsten Müller[15], Michael Bauer[16], Michael Kiehntopf[17], Sophie Neugebauer[2,17], Thomas Lehmann[18], Jason A. Roberts[19,20,21] and Mathias W. Pletz[1,2] on behalf of the TARGET Trial Investigators

249 patients



Perfusion continue après dose de charge

Dosage des β-lactamines en réanimation: objectifs

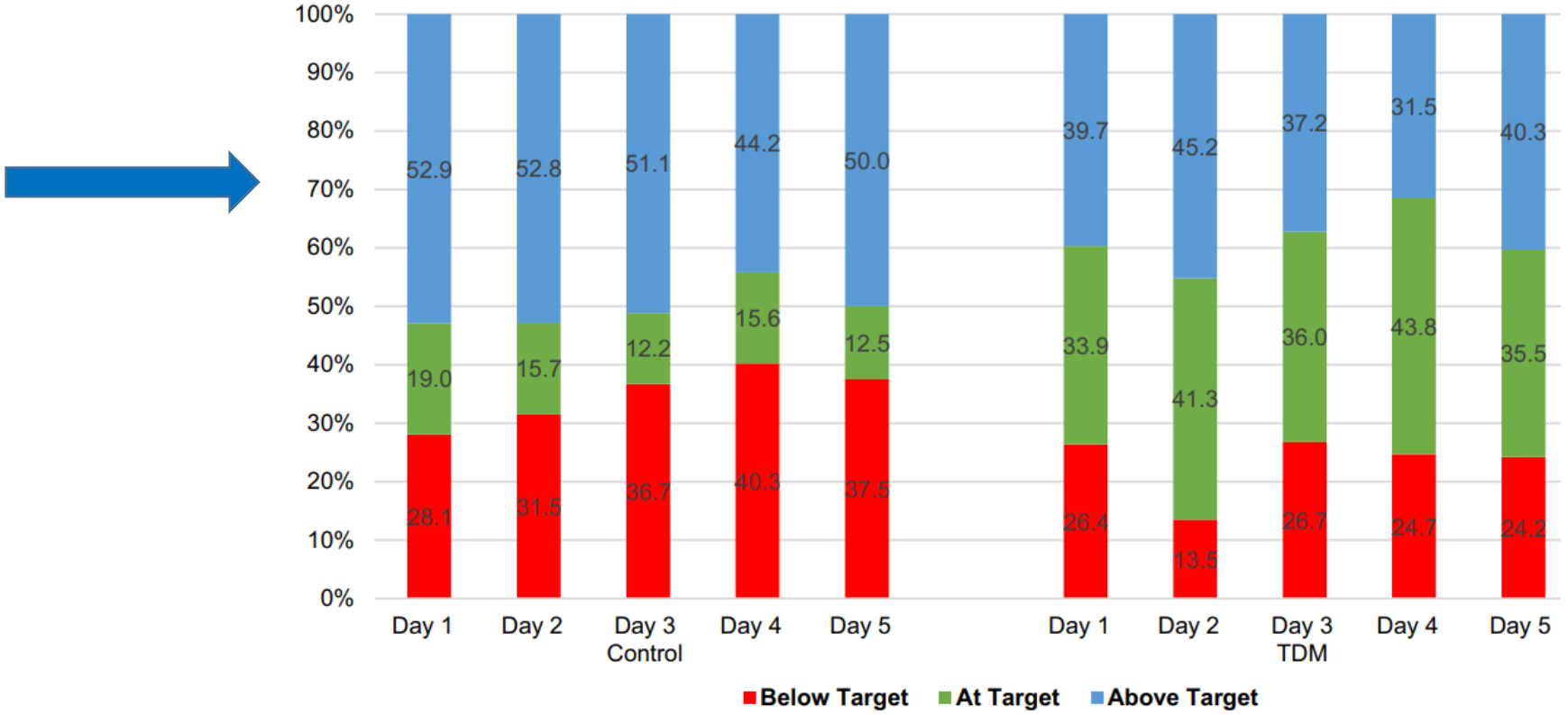
Objectif	Utilité démontrée
Ne pas être au dessous des cibles PK-PD	Peut-être (germes moins sensibles, Hyper-clairance, ↑VD, EER)
Ne pas être au dessus des cibles PK-PD (toxicité)	Oui (en particulier si insuffisance rénale)

Intensive Care Med (2022) 48:311–321
https://doi.org/10.1007/s00134-021-06609-6

249 patients

ORIGINAL

Effect of therapeutic drug monitoring-based dose optimization of piperacillin/tazobactam on sepsis-related organ dysfunction in patients with sepsis: a randomized controlled trial



Perfusion continue après dose de charge

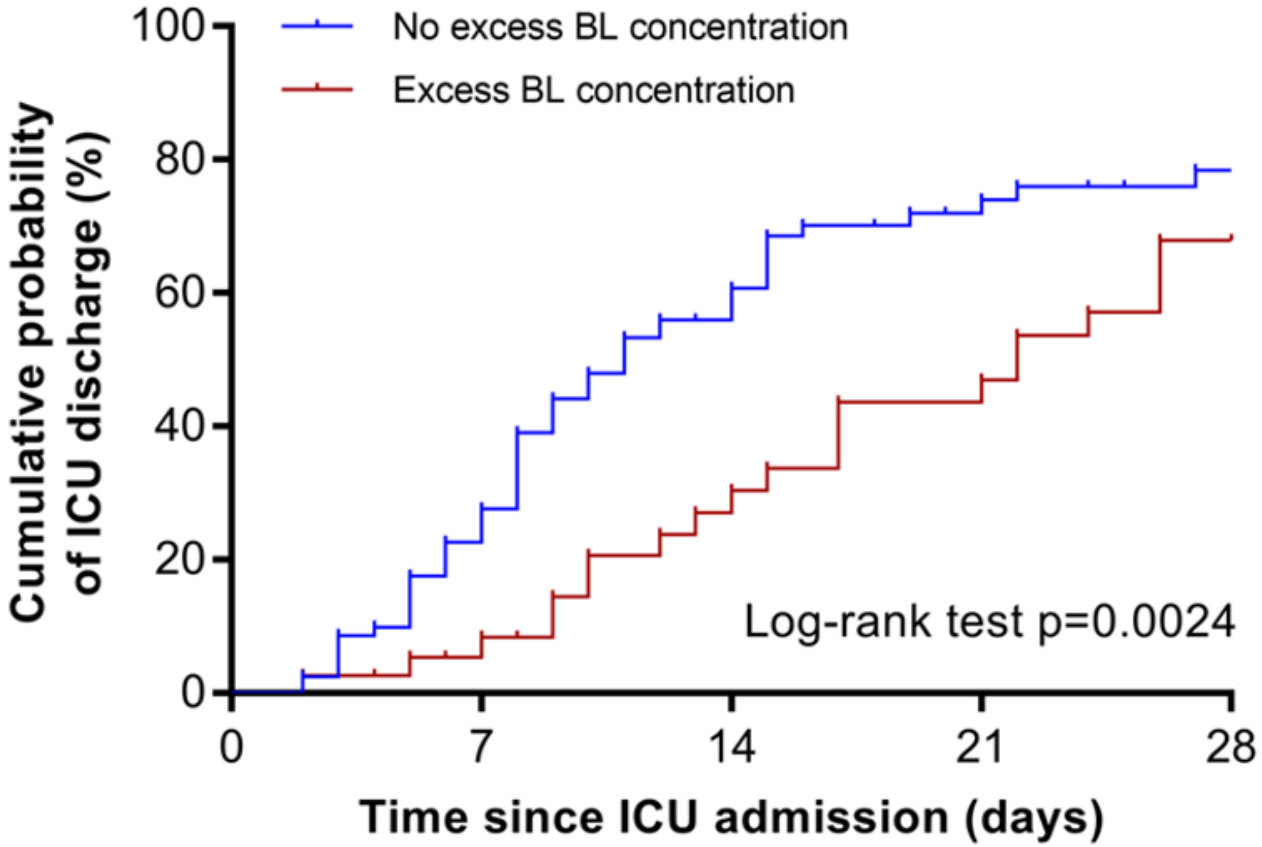
J Antimicrob Chemother 2023; **78**: 2691–2695
https://doi.org/10.1093/jac/dkad284 Advance Access publication 11 September 2023

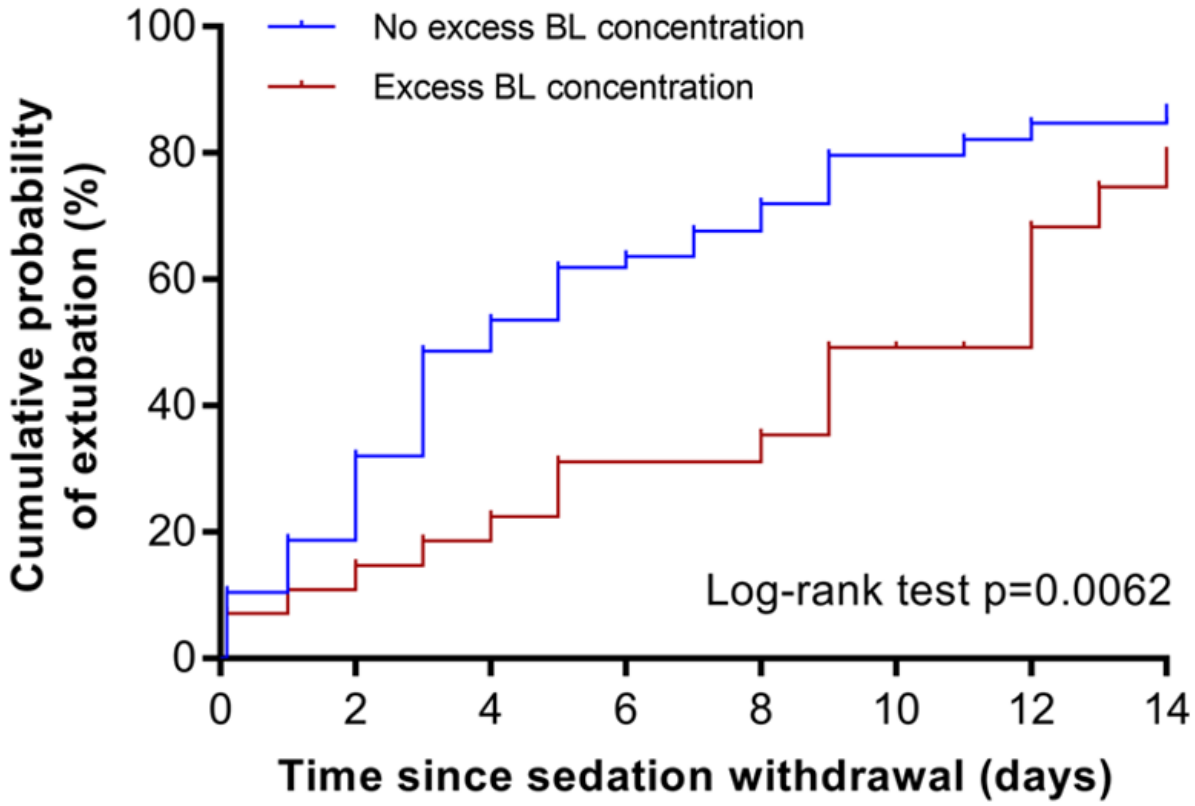
Journal of Antimicrobial Chemotherapy

Neurological burden and outcomes of excessive β-lactam serum concentrations of critically ill septic patients: a prospective cohort study

Yoann Zerbib[1], Clement Gaulin[1], Sandra Bodeau[2,3], Benjamin Batteux[2,3], Anne-Sophie Lemaire-Hurtel[2], Julien Maizel[1,3], Loay Kontar[1] and Youssef Bennis[2,3]*

119 patients



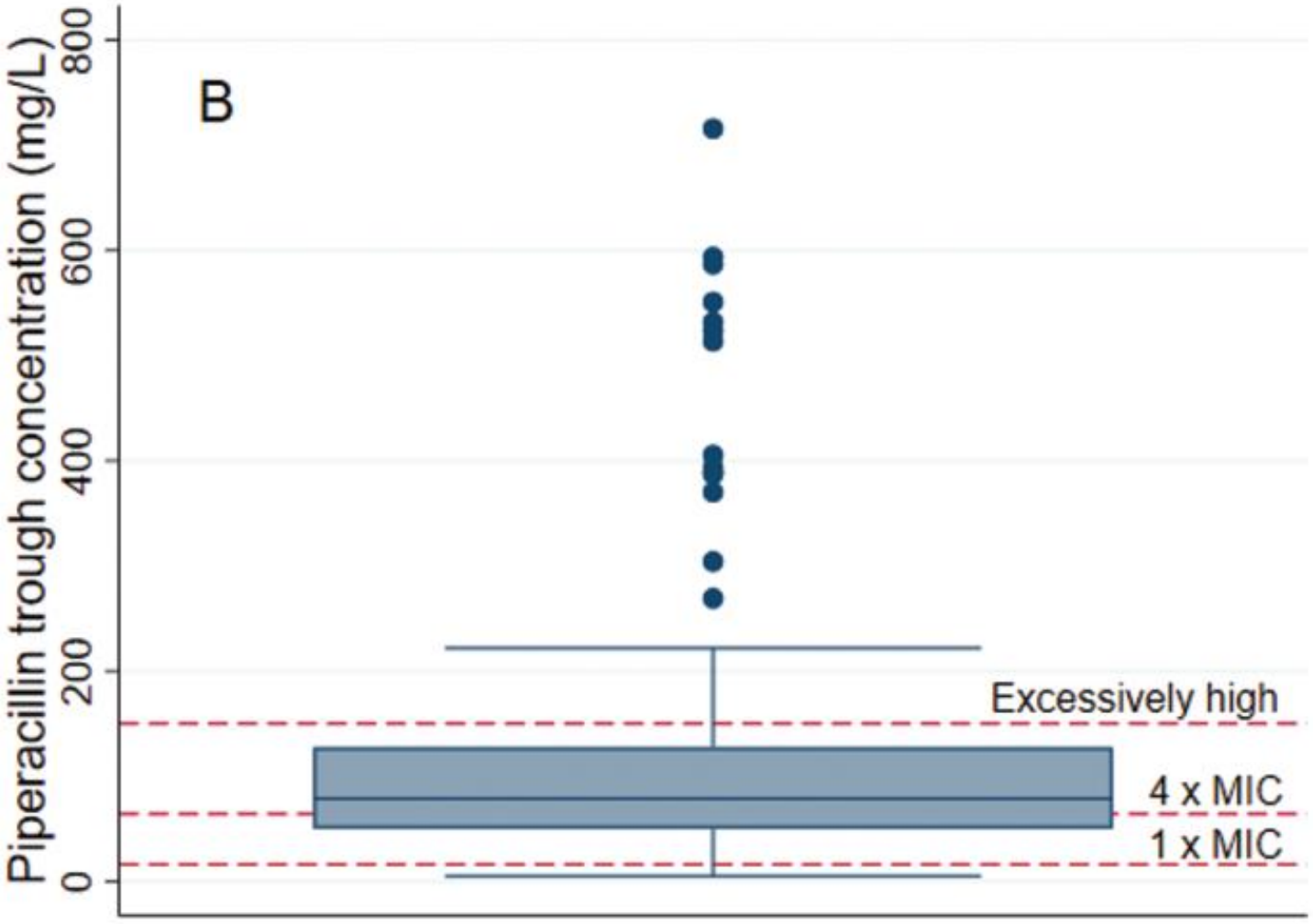


2021;72(8):1369–78

Clinical Infectious Diseases

MAJOR ARTICLE

The Effect of Renal Replacement Therapy and Antibiotic Dose on Antibiotic Concentrations in Critically Ill Patients: Data From the Multinational Sampling Antibiotics in Renal Replacement Therapy Study



"In critically ill patients treated with RRT, antibiotic dosing regimens, RRT prescription, and eTRCL varied markedly and resulted in highly variable antibiotic concentrations that failed to meet therapeutic targets in many patients".

JA Roberts *et coll*.

Dosage des β-lactamines en réanimation: objectifs

Objectif	Utilité démontrée
Ne pas être au dessous des cibles PK-PD	Peut-être (germes moins sensibles, Hyper-clairance, ↑VD, EER)
Ne pas être au dessus des cibles PK-PD (toxicité)	Oui (en particulier si insuffisance rénale)
Améliorer le pronostic	Plutôt Non

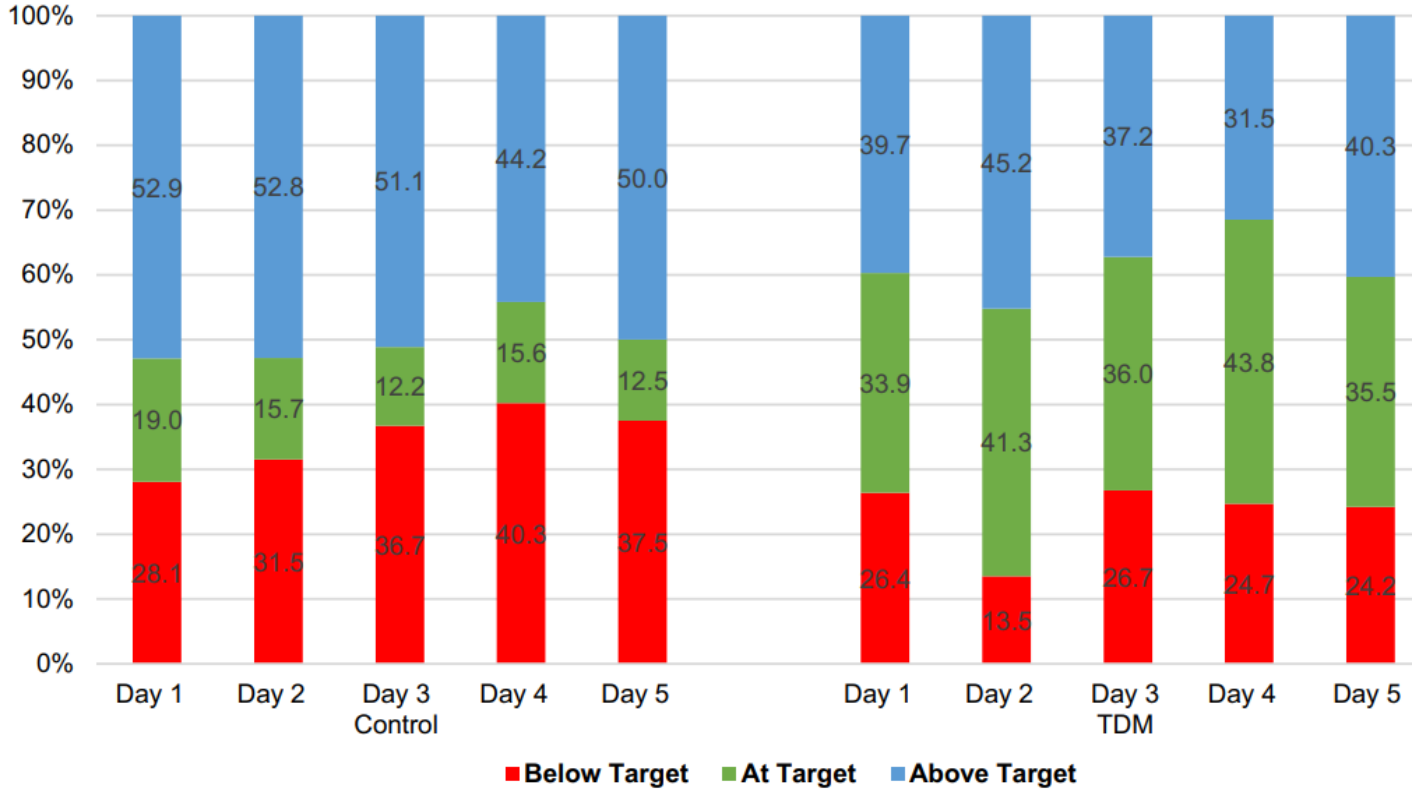
Intensive Care Med (2022) 48:311–321
https://doi.org/10.1007/s00134-021-06609-6

249 patients

ORIGINAL

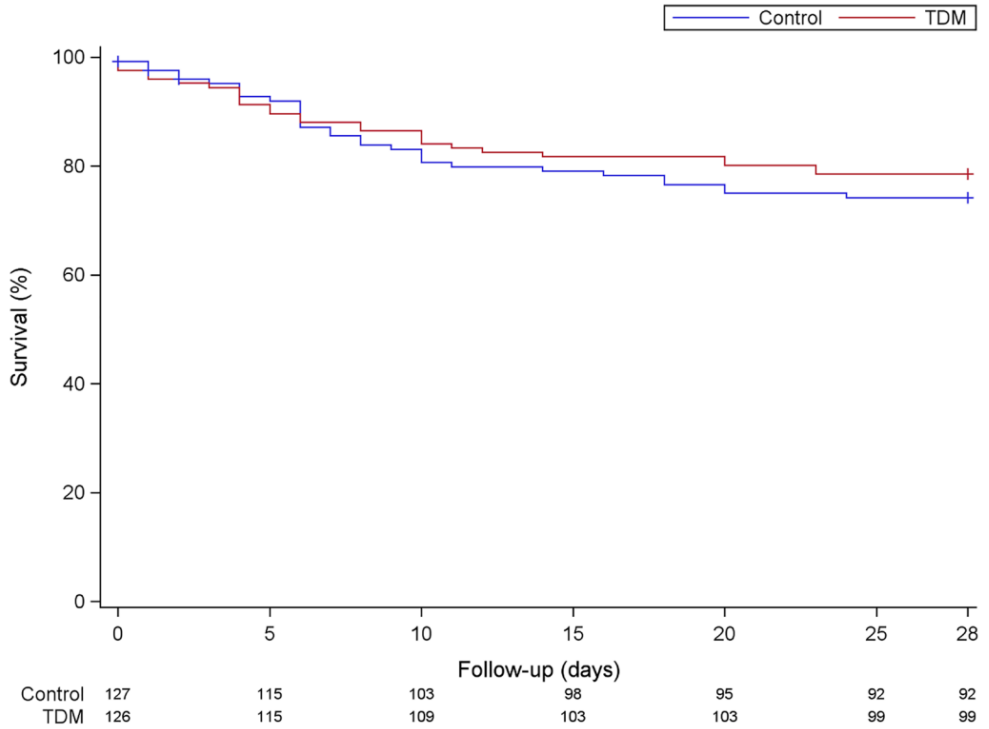
Effect of therapeutic drug monitoring-based dose optimization of piperacillin/tazobactam on sepsis-related organ dysfunction in patients with sepsis: a randomized controlled trial

Hagel S et al



Perfusion continue après dose de charge

Pas de différence sur le delta de SOFA score à J10 (CJP)



	Mortalité
[C] > 96 mg/L	34%
[C]: 32-64 mg/L	8%

OR 2.5, 95% CI 1.1–5.8, p=0.03)

Intensive Care Med (2022) 48:1760–1771
https://doi.org/10.1007/s00134-022-06921-9

ORIGINAL

Model-informed precision dosing of beta-lactam antibiotics and ciprofloxacin in critically ill patients: a multicentre randomised clinical trial

Tim M. J. Ewoldt[1,2,3*], Alan Abdulla[2,3], Wim J. R. Rietdijk[2], Anouk E. Muller[3,4,5], Brenda C. M. de Winter[2,3], Nicole G. M. Hunfeld[1,2], Ilse M. Purmer[6], Peter van Vliet[7], Evert-Jan Wils[1,8], Jasper Haringman[9], Annelies Draisma[10], Tom A. Rijpstra[11], Attila Karakus[12], Diederik Gommers[1], Henrik Endeman[1] and Birgit C. P. Koch[2,3]

Take-home message

There is currently no evidence for a clinical effect of model-informed precision dosing (MIPD) of beta-lactam antibiotics or ciprofloxacin in critically ill patients. Other approaches will need to be explored

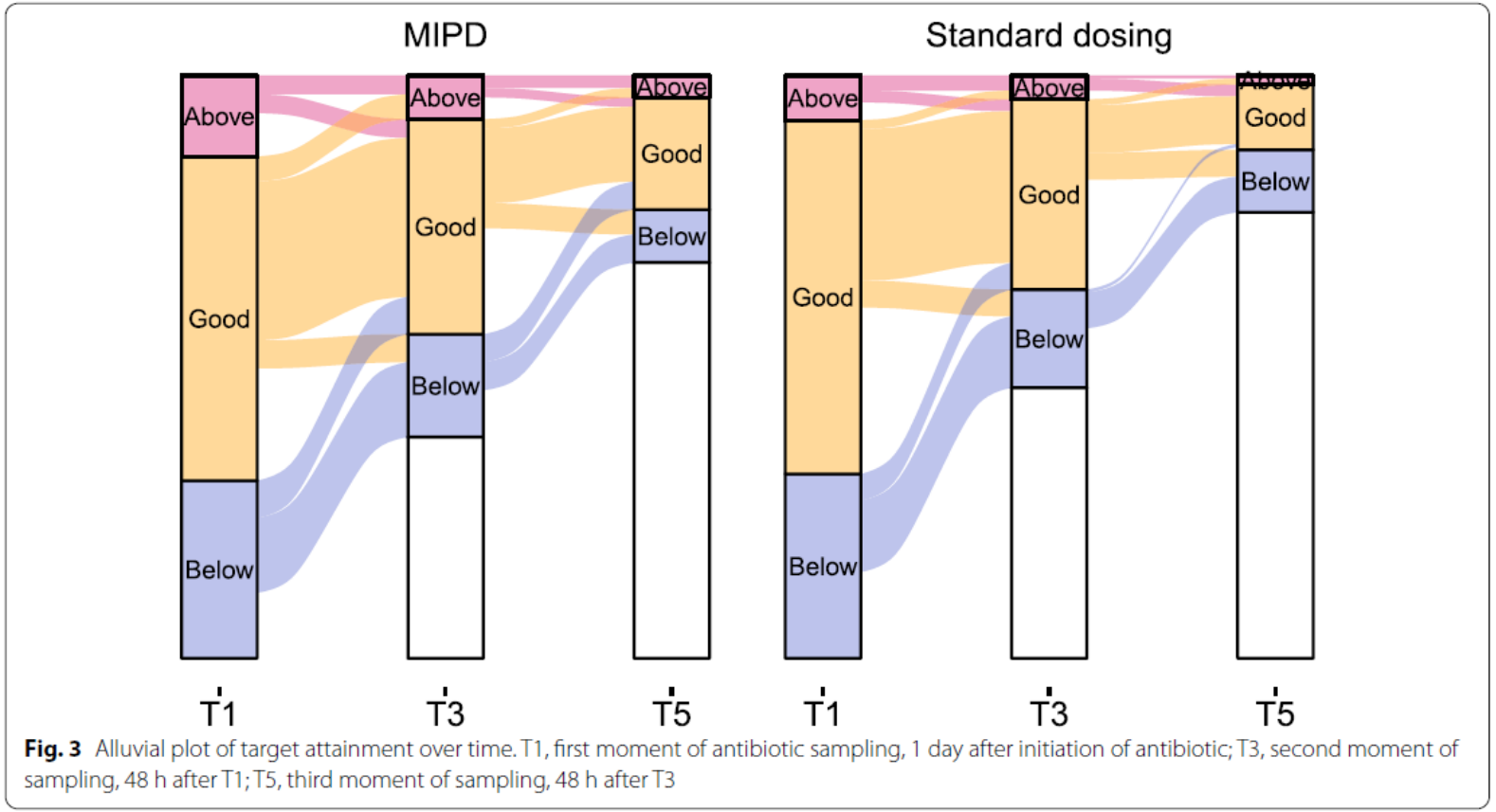


Fig. 3 Alluvial plot of target attainment over time. T1, first moment of antibiotic sampling, 1 day after initiation of antibiotic; T3, second moment of sampling, 48 h after T1; T5, third moment of sampling, 48 h after T3

Pas de différence sur:

1. Le CPJ: durée de séjour en réanimation
2. Les critère secondaires: mortalité, évolution du SOFA, qualité de vie
3. Coût supérieur dans le groupe expérimental

Les limites du dosage des β-lactamines

1. Délais dans l'obtention des résultats
2. Qu'en fait on pour l'évaluation de la cible PK-PD: quelle CMI ?

    - CMI « vraie » : pas toujours mesurée, délais, à une dilution prés…

    - ECOFF ? : risque d'exigence de concentrations trop élevées

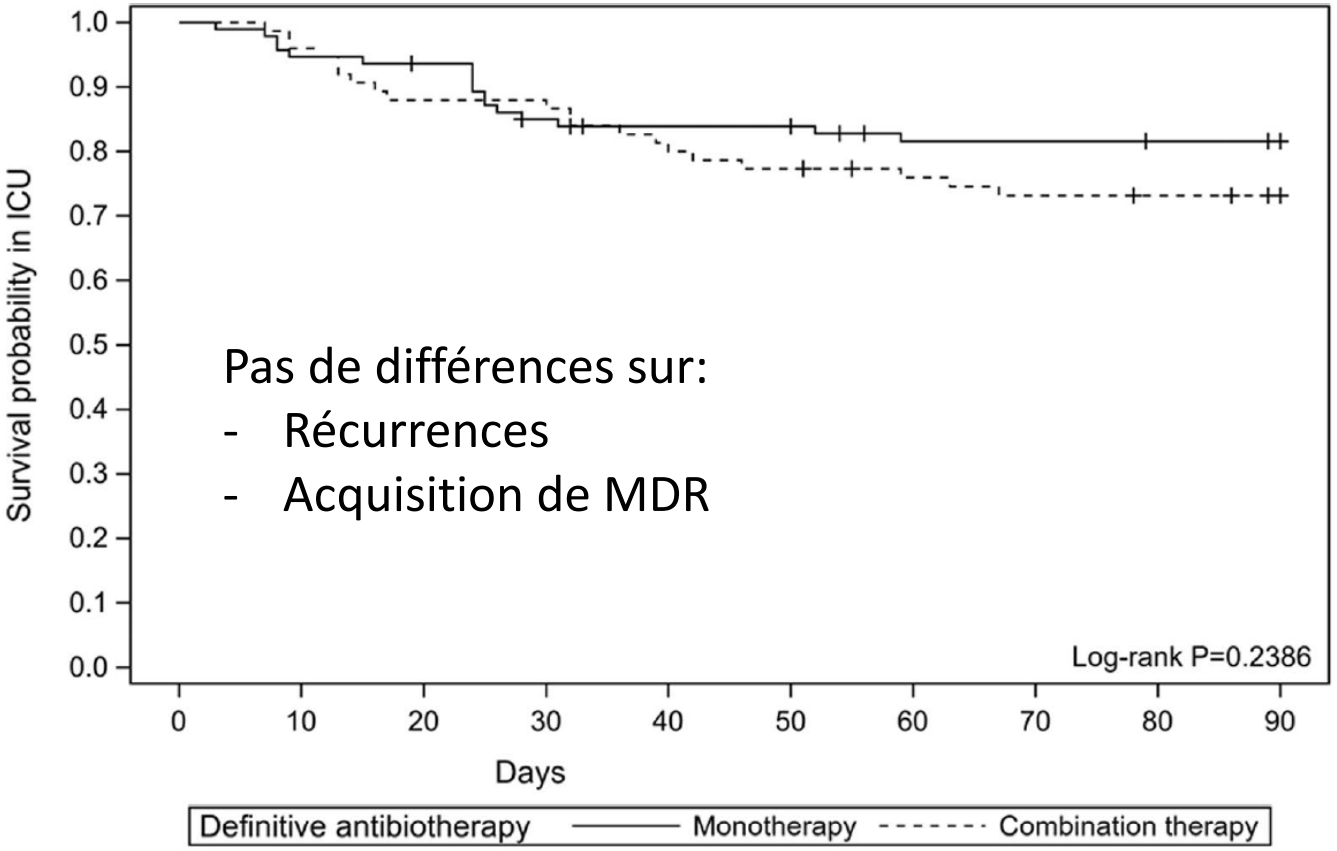
3. Modifications rapides des conditions hémodynamiques, rénales, hépatiques chez certains patients de réanimation

4. Fraction libre *vs* totale

Foucrier *et al. Critical Care* (2023) 27:211
https://doi.org/10.1186/s13054-023-04457-y

RESEARCH Open Access

Association between combination antibiotic therapy as opposed as monotherapy and outcomes of ICU patients with *Pseudomonas aeruginosa* ventilator-associated pneumonia: an ancillary study of the iDIAPASON trial



Pas de différences sur:
- Récurrences
- Acquisition de MDR

Mais quand même, possible association

- Bactéries multi-résistantes
- Risque de mutant en cours de traitement
- Inoculum élevé
- Traitement *in situ*

Antibiothérapie en réanimation : Trois grandes spécificités

1. **L'antibiothérapie probabiliste: une situation très fréquente**
   - Immédiatement ? Un peu plus tard ? Abstention?
   - Donner le ou les « bon (s) antibiotiques
2. **Recherche du meilleur mode d'administration, adapté**
   - aux caractéristiques du patient
   - au site de l'infection
   - au (x) germe(s) si infection documentée

3. La désescalade (dont raccourcissement de la durée de traitement) est possible aussi en réanimation

Intensive Care Med (2020) 46:1404–1417
https://doi.org/10.1007/s00134-020-06111-5

ORIGINAL

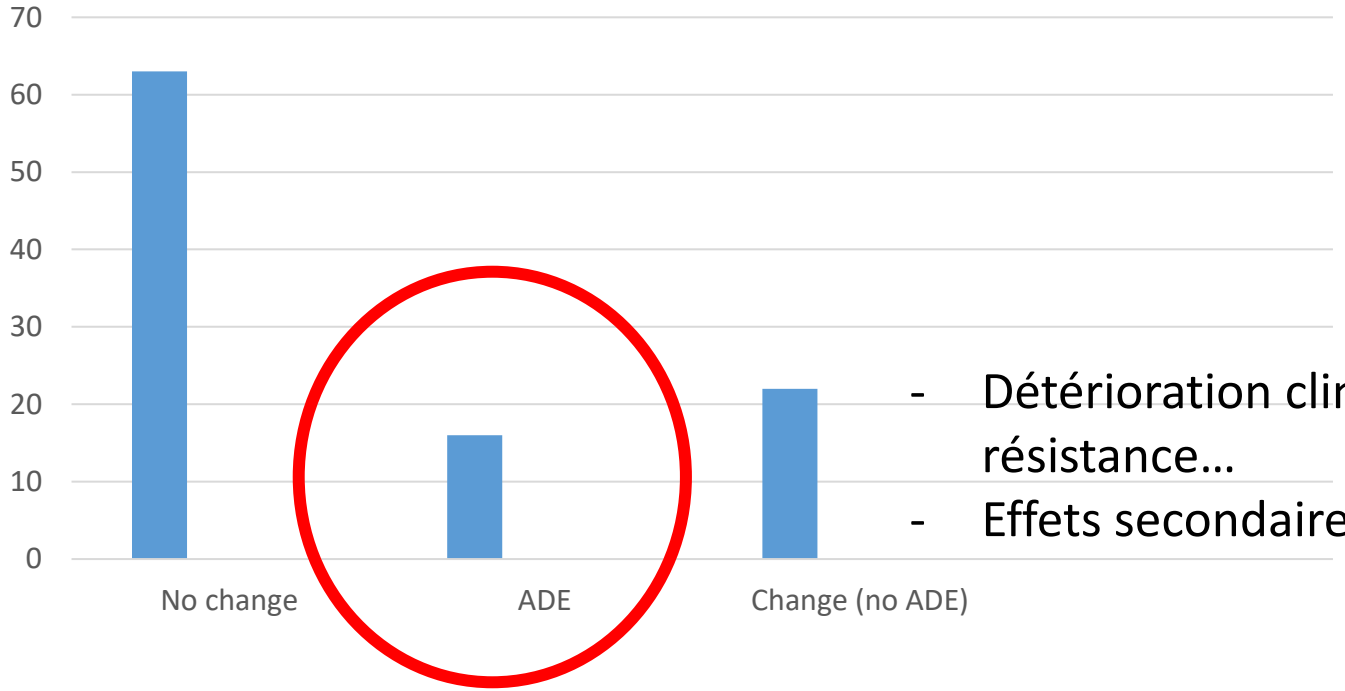
Antimicrobial de-escalation in the critically ill patient and assessment of clinical cure: the DIANA study

Liesbet De Bus[1*], Pieter Depuydt[1,2], Johan Steen[1,3,4], Sofie Dhaese[1], Ken De Smet[1], Alexis Tabah[5,6], Murat Akova[7], Menino Osbert Cotta[8,9], Gennaro De Pascale[10,11], George Dimopoulos[12,13], Shigeki Fujitani[14], Jose Garnacho-Montero[15,16], Marc Leone[17], Jeffrey Lipman[9,18,19], Marlies Ostermann[20], José-Artur Paiva[21,22], Jeroen Schouten[23,24], Fredrik Sjövall[25,26], Jean-François Timsit[27,28], Jason A. Roberts[8,9,18,19,29], Jean-Ralph Zahar[30,31], Farid Zand[32], Kapil Zirpe[33], Jan J. De Waele[1] and DIANA study group

Take-home message

ADE was performed within 3 days following empirical prescription in only 16% of critically ill-infected patients, despite the fact that half of the empirical prescriptions consisted of combination therapy and one-quarter contained a carbapenem. The observational effect estimate on clinical cure suggested no deleterious impact of ADE compared to no-ADE; however, residual confounding is likely to be present.

1495 patients from 152 ICUs in 28 countries were studied.



- Détérioration clinique, résistance…
- Effets secondaires

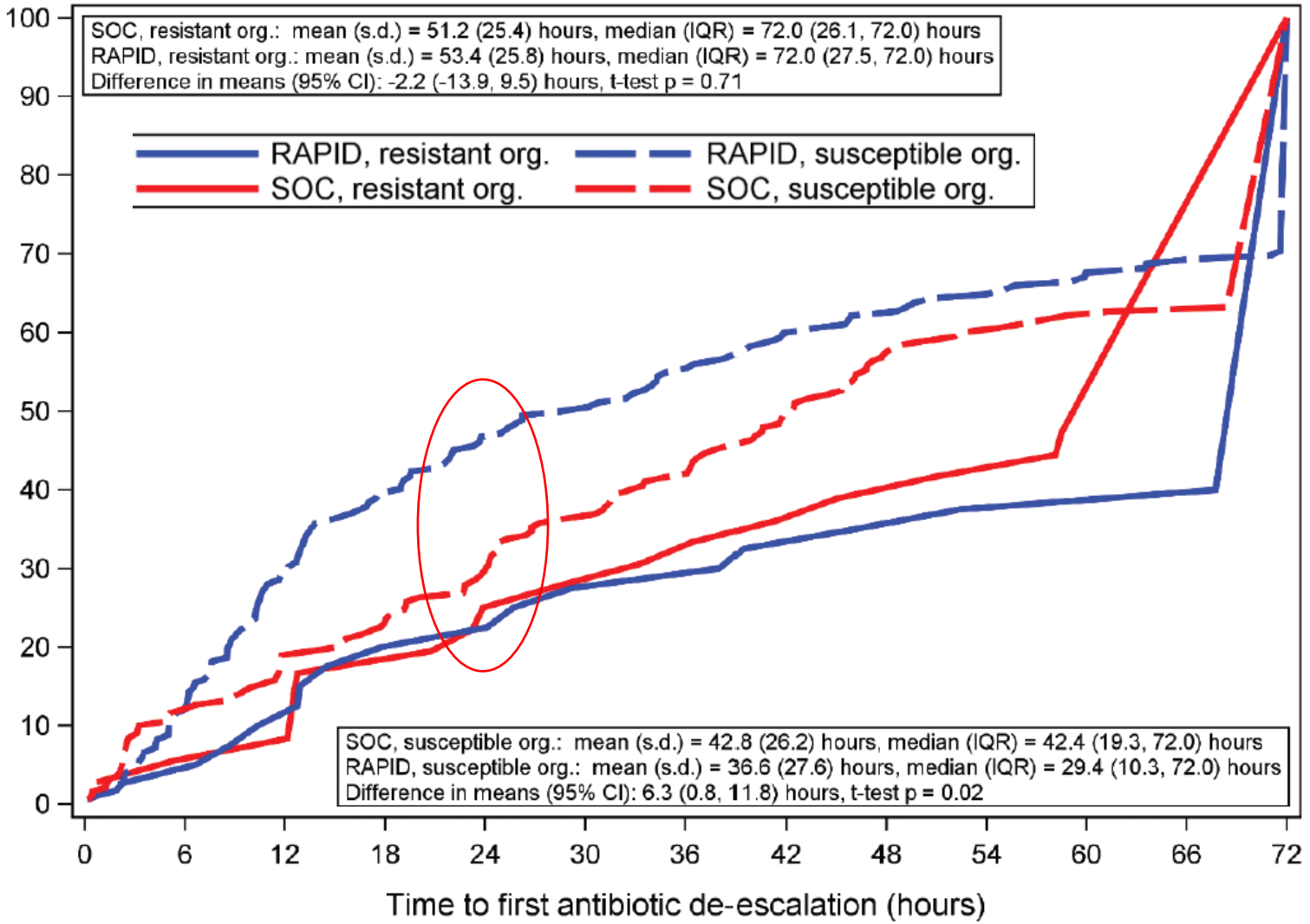
Clinical Infectious Diseases

MAJOR ARTICLE

2021

Randomized Trial Evaluating Clinical Impact of RAPid IDentification and Susceptibility Testing for Gram-negative Bacteremia: RAPIDS-GN

Ritu Banerjee,[1] Lauren Komarow,[2] Abinash Virk,[3] Nipunie Rajapakse,[3] Audrey N. Schuetz,[3] Brenda Dylla,[3] Michelle Earley,[2] Judith Lok,[4] Peggy Kohner,[3] Sherry Ihde,[3] Nicolynn Cole,[3] Lisa Hines,[3] Katelyn Reed,[3] Omai B. Garner,[5] Sukantha Chandrasekaran,[5] Annabelle de St. Maurice,[5] Meganne Kanatani,[5] Jennifer Curello,[5] Rubi Arias,[5] William Swearingen,[5] Sarah B. Doernberg,[6] and Robin Patel[3]; for the Antibacterial Resistance Leadership Group



Comparison of a short versus long-course antibiotic therapy for ventilator-associated pneumonia: a systematic review and meta-analysis of randomized controlled trials

eClinicalMedicine
2023;58: 101880

Mortalité

Rechutes

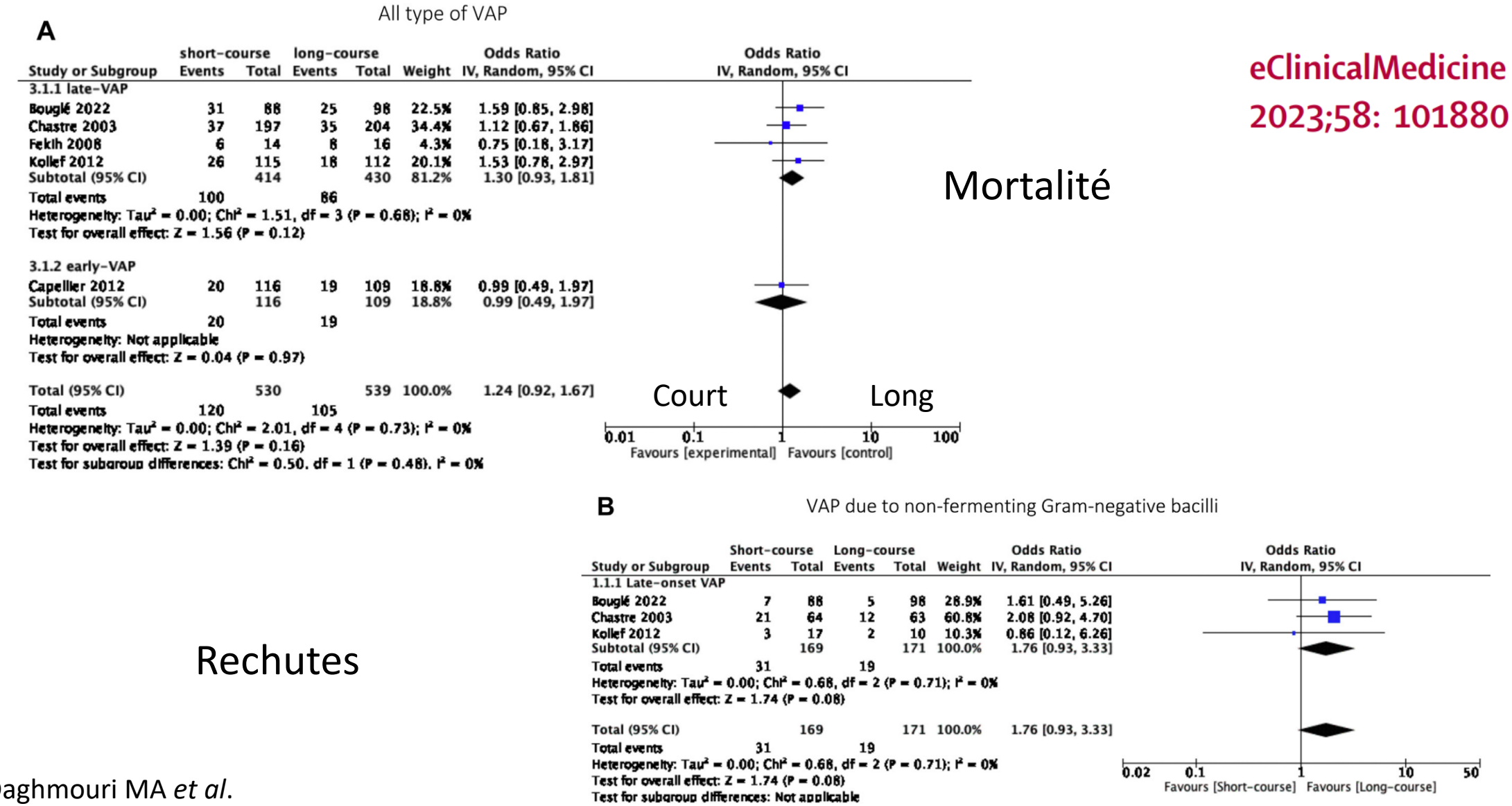
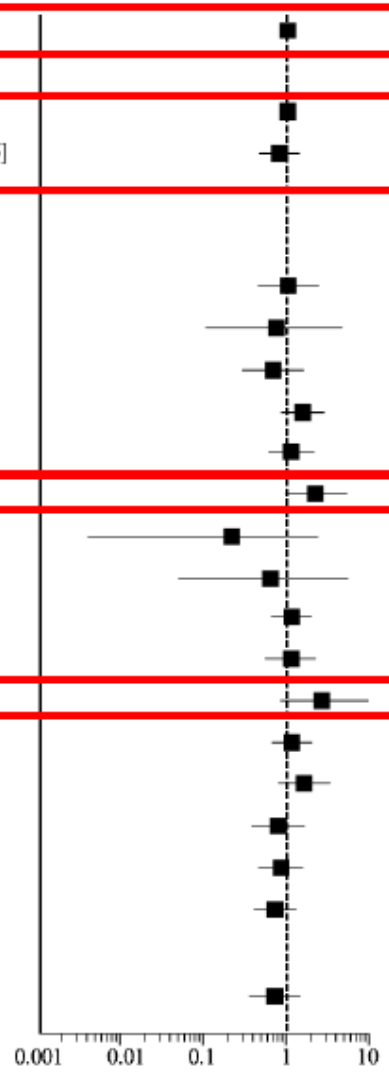


Fig. 3: Forest plot of relapses.

Daghmouri MA *et al*.

Etude DURAPOP: Durée de traitement des péritonites postop

Primary and secondary outcomes	15-day arm (n=116)	8-day arm (n=120)	Odd-ratios (95%CI)	P value
Primary outcome				
Antibiotic-free days on Day28, median [IQR][a]	12 [6—13]	15 [6—20]	1.08 (1.04—1.125)	1.9×10^{-4}
Secondary outcome				
Length of ICU stay between Day0 and Day45, median [IQR][b]	12 [7—20]	13 [7.75—25]	1.02 (0.99—1.04)	0.14
Length of hospital stay between Day0 and Day45, median [IQR][c]	30 [20—45]	30.5 [18.75—45]	0.80 (0.46—1.38)	0.42
Secondary outcomes				
Organ failure on Day15, n (%)[d]	17/96 (18)	15/90 (17)	1.08 (0.47—2.50)	1.00
Organ failure on Day28, n (%)[e]	4/60 (5)	3/63 (6)	0.78 (0.11—4.82)	1.00
45-day mortality, n (%)	17/116 (15)	13/120 (11)	0.71 (0.30—1.64)	0.43
Additional source control between Day8 and Day45, n (%)	34/116 (28)	48/120 (40)	1.61 (0.90—2.87)	0.101
Reoperations between Day8 and Day45, n (%)	27/166 (23)	31/120 (26)	1.15 (0.61—2.17)	0.65
Percutaneous drainages between Day8 and Day45, n (%)	11/116 (9)	23/120 (19)	2.26 (0.99—5.41)	0.041
Recurrent infection, n (%)[f]	13/14 (93)	14/19 (74)	0.22 (0.004—2.40)	0.21
Superinfection, n (%)[c]	11/32 (34)	14/44 (32)	0.65 (0.05—5.52)	1
New antibiotic therapy, n (%)	45/116 (39)	51/120 (42)	1.17 (0.67—2.03)	0.59
New antibiotic therapy between Day16 and Day28, n (%)	25/102 (25)	29/106 (27)	1.16 (0.56—2.27)	0.75
Bacteraemia between Day8 and Day45, n (%)	5/116 (4)	13/120 (11)	2.69 (0.86—9.96)	0.059
Clinical failure between Day8 and Day45, n (%)	16 (14)	28 (24)	1.18 (0.68—2.05)	0.54
Microbiological failure between Day8 and Day45, n (%)	18 (16)	28 (23)	1.65 (0.82—3.40)	0.13
Emergence of MDR bacteria in surveillance samples, n (%)[g]	23/104 (22)	20/107 (19)	0.81 (0.39—1.67)	0.54
Emergence of MDR bacteria in clinical isolates, n (%)[d]	40/104 (38)	38/108 (35)	0.87 (0.47—1.58)	0.72
Emergence of MDR bacteria in both surveillance samples and clinical isolates confounded, n (%)[g]	52/104 (50)	46/108 (43)	0.74 (0.41—1.32)	0.28
Emergence of fungi, n (%)[g]	27/106 (25)	22/107 (21)	0.75 (0.37—1.51)	0.39



Montravers P et al. Intensive Care Med 2018; 44:300-10

Infections neurologiques centrales (1)

Méningites bactériennes

- *Streptococcus pneumoniae* (quelle que soit la CMI de l'amoxicilline) et streptocoque du groupe B : 10 jours
- *Neisseria meningitidis* (quelle que soit la CMI de l'amoxicilline) : 5 jours
- *Listeria monocytogenes :* 21 jours

Synthèse réalisée le 10 Mars 2021 par la SPILF

Procalcitonin-Guided Antibiotic Therapy May Shorten Length of Treatment and May Improve Survival - A Systematic Review and Meta-Analysis

Does procalcitonin (PCT)-guided antibiotic (AB) therapy safely reduce the length of AB treatment in adult critically ill patients compared to standard of care?

26 RCTs
9048 patients

Up to 14 th of Nov, 2022

PRISMA checklist
Revised Risk of Bias tool
GradePro
R software

PCT-guided AB therapy		Standard of care
PCT group	VERSUS	SOC group
Using a predefined PCT protocol		*Not including PCT in the treatment algorithm*

		MD/OR [95% CI]
Length of AB therapy	**1.79 days lower in PCT group**	-1.79 days [-2.65, -0.92]
28-day mortality	**16% lower in PCT group**	0.84 [0.74, 0.95]
Rate of recurrent infection	**36% higher in PCT group**	1.36 [1.10, 1.68]

CONCLUSION: PCT-guided AB therapy may be associated with *reduced AB use*, *lower 28-day mortality* but *higher infection recurrence*, with *similar ICU and hospital length of stay*. Our results render the need for better designed studies investigating the role of PCT-guided AB stewardship in critically ill patients.

Papp *et al. Critical Care* (2023) 27:394
https://doi.org/10.1186/s13054-023-04677-2

Intensive Care Med (2023) 49:1232–1234
https://doi.org/10.1007/s00134-023-07186-6

En guise de conclusion

EDITORIAL

2030: will we still need our microbiologist?

Ines Lakbar[1*], Mervyn Singer[2] and Marc Leone[3,4]

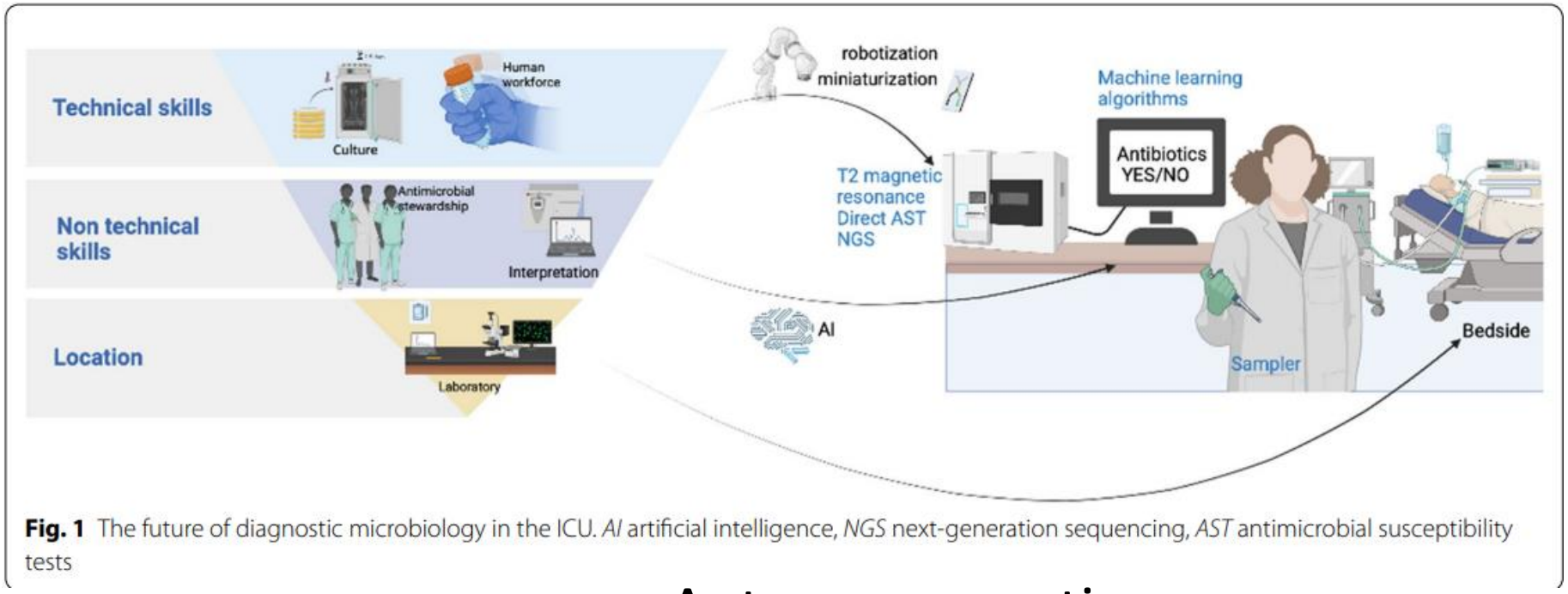


Fig. 1 The future of diagnostic microbiology in the ICU. *AI* artificial intelligence, *NGS* next-generation sequencing, *AST* antimicrobial susceptibility tests

Mais le dialogue clinicien microbiologiste restera toujours une nécessité

Autres perspectives

Mesure de la charge microbienne
Distinction colonisation/infection
Dynamique acquisition résistance

Intégration rapide du PK-PD individualisé en vie réelle

Etc…