

Diplôme d'Université d'Antibiothérapie et Chimiothérapie Anti-Infectieuse

Infections Intra-abdominales (IIA) liées aux soins

Pr. Eric Kipnis

Réanimation Chirurgicale | Anesthésie-Réanimation et Médecine Péri-Opératoire | CHU Lille

Opportunistic Infection, Immunity, Environment & Lung Diseases (OpInFIELD) | Univ. Lille - CNRS - Inserm - IPL - CIIL

Déclaration d'intérêts

- Expertise : MSD, Shionogi, Astra-Zeneca
- Interventions : Pfizer, MSD, Shionogi, LFB, Getinge
- Congrès : LFB, Pfizer, MSD, Shionogi, Octapharma
- <https://www.transparence.sante.gouv.fr>



Foyers – étiologies

Perforation de viscère creux

(ulcère, cancer, occlusion, traumatisme, infl)

- Estomac
- Voies biliaires
- Côlon
- Grêle
- Diverticule
- Utérus ou trompes
- Vessie

Ischémies/nécroses

(translocation puis perforation)

- Cholécystite alithiasique
- Infarctus intestinal
- Occlusion
- Cancer du pancréas

Extension de foyers infectieux intra-abdominaux

(abcès, perforations)

- Appendicite compliquée
- Cholécystite compliquée
- Diverticulite compliquée
- Abcès hépatique compliqué
- Pancréatites aiguës/coulées/abcès
- Abcès renal/perirenal post PNA
- Fonte splénique purulente
- Salpingite compliquée

Post-opératoires

- Lâchage de (sutures, anastomoses, moignons)
- Contamination per-opératoire
- Translocation bactérienne

Classifications et terminologies...d'utilité variable et limitée

Mécanisme (classification d'Hambourg)

Primitives

- Infection du liquide d'ascite
- Infection de dialyse péritonéale

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Secondaires (à une cause)

- c.f étiologies

Tertiaires

- *secondaire compliquée*

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- **post-opératoires**

Tertiaires

- *secondaire compliquée*
- **post-opératoires**

Communautaires

Associées aux soins
(nosocomiales)

Classifications et terminologies...d'utilité variable et limitée

Mécanisme (classification d'Hambourg)

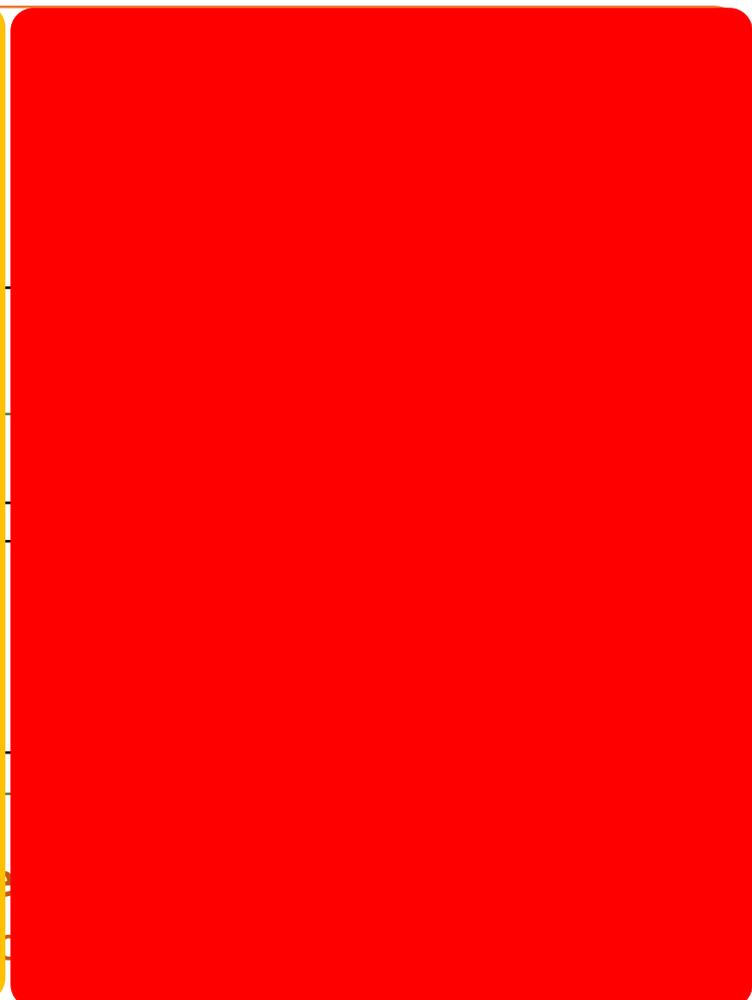
Primitives

- Infection du
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Secondaires (à

- c.f étiologies

Communautaires



AbSeS study (ESICM)

Intensive Care Med (2019) 45:1703–1717
<https://doi.org/10.1007/s00134-019-05819-3>

ORIGINAL

Epidemiology of intra-abdominal infection and sepsis in critically ill patients: “AbSeS”, a multinational observational cohort study and ESICM Trials Group Project



Stijn Blot^{1*} , Massimo Antonelli^{2,3}, Kostoula Arvaniti⁴, Koen Blot¹, Ben Creagh-Brown^{5,6}, Dylan de Lange⁷, Jan De Waele⁸, Mieke Deschepper⁹, Yalim Dikmen¹⁰, George Dimopoulos¹¹, Christian Eckmann¹², Guy Francois¹³, Massimo Girardis¹⁴, Despoina Koulenti^{15,16}, Sonia Labeau^{1,17}, Jeffrey Lipman^{18,19}, Fernando Lipovestky²⁰, Emilio Maseda²¹, Philippe Montravers^{22,23}, Adam Mikstacki^{24,25}, José-Artur Paiva²⁶, Cecilia Pereyra²⁷, Jordi Rello²⁸, Jean-Francois Timsit^{29,30}, Dirk Vogelaers³¹ and the Abdominal Sepsis Study (AbSeS) group on behalf of the Trials Group of the European Society of Intensive Care Medicine

AbSeS study (ESICM) et études ancillaires

Drugs (2021) 81:1065–1078
<https://doi.org/10.1007/s40265-021-01534-w>

REVIEW ARTICLE



Antimicrobial Lessons From a Large Observational Cohort on Intra-abdominal Infections in Intensive Care Units

Dirk Vogelaers^{1,2} · Stijn Blot¹ · Andries Van den Berge¹ · Philippe Montravers³ · for the Abdominal Sepsis Study ('AbSeS') Group on behalf of the Trials Group of the European Society of Intensive Care Medicine

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

International Journal of Antimicrobial Agents 60 (2022) 106591

ORIGINAL

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



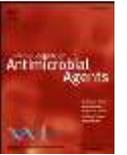
Gennaro De Pascale^{1,2}, Massimo Antonelli^{1,2}, Mieke Deschepper³, Kostoula Arvaniti⁴, Koen Blot^{5,6}, Ben Creagh Brown^{7,8}, Dylan de Lange⁹, Jan De Waele^{5,10}, Yalim Dikmen¹¹, George Dimopoulos¹², Christian Eckmann¹³, Guy Francois¹⁴, Massimo Girardis¹⁵, Despoina Koulenti^{16,17}, Sonia Labeau^{5,18}, Jeffrey Lipman^{19,20}, Fernando Lipovestky²¹, Emilio Maseda²², Philippe Montravers^{23,24}, Adam Mikstacki^{25,26}, José-Artur Paiva²⁷, Cecilia Pereyra²⁸, Jordi Rello^{20,29}, Jean-Francois Timsit^{30,31}, Dirk Vogelaers^{5,32} and Stijn Blot^{5,16*} on behalf of the Abdominal Sepsis Study (AbSeS) group and the Trials Group of the European Society of Intensive Care Medicine

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)



International Journal of Antimicrobial Agents

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



Epidemiology and age-related mortality in critically ill patients with intra-abdominal infection or sepsis: an international cohort study



Kostoula Arvaniti^{a,†}, George Dimopoulos^{b,†}, Massimo Antonelli^{c,d}, Koen Blot^e, Ben Creagh-Brown^{f,g}, Mieke Deschepper^h, Dylan de Langeⁱ, Jan De Waele^j, Yalim Dikmen^k, Christian Eckmann^l, Sharon Einav^{m,n}, Guy Francois^o, Hans Fjeldsoe-Nielsen^p, Massimo Girardis^q, Bojan Jovanovic^r, Matthias Lindner^s, Despoina Koulenti^{t,u}, Sonia Labeau^{v,w}, Jeffrey Lipman^{x,y}, Fernando Lipovestky^z, Luis Daniel Umezawa Makikado^{aa}, Emilio Maseda^{bb}, Adam Mikstacki^{cc,dd}, Philippe Montravers^{ee,ff}, José Artur Paiva^{gg}, Cecilia Pereyra^{hh}, Jordi Relloⁱⁱ, Jean-Francois Timsit^{jj,kk}, Dana Tomescu^{ll,mm}, Dirk Vogelaers^{nn,oo}, Stijn Blot^{oo,*}, The Abdominal Sepsis Study (AbSeS) Group on behalf of the Trials Group of the European Society of Intensive Care Medicine[†]

Epidémio - étude AbSeS

Epidémio **prospective mondiale**

Multicentrique **309 réanimations**

2621 patients admis pour ou se compliquant d’IIA

Type of abdominal sepsis	Total <i>n</i> (%)*	Community-acquired <i>n</i> (%)**	Early onset hospital-acquired <i>n</i> (%)**	Late-onset hospital-acquired <i>n</i> (%)**
Primary peritonitis	103 (3.9)	33 (32)	28 (27.2)	42 (40.8)
Secondary and tertiary peritonitis	1794 (68.4)	588 (32.8)	431 (24)	775 (43.2)
PD-related peritonitis	9 (0.3)	0	2 (20)	7 (70)
Intra-abdominal abscess	180 (6.9)	36 (20)	49 (27.2)	95 (52.8)
Biliary tract infection	319 (12.2)	117 (36.7)	95 (29.8)	107 (33.5)
Pancreatic infection	165 (6.3)	45 (27.3)	33 (20)	87 (52.7)
Typhlitis	9 (0.3)	0	3 (33.3)	6 (66.6)
Toxic megacolon	42 (1.6)	9 (21.4)	15 (35.7)	18 (42.9)

IIA "secondaires" (puis tertiaires) >> biliaires > abcès ou complications infectieuses de PA

associées aux soins (précoces + tardives) > communautaires

Epidémio - étude AbSeS

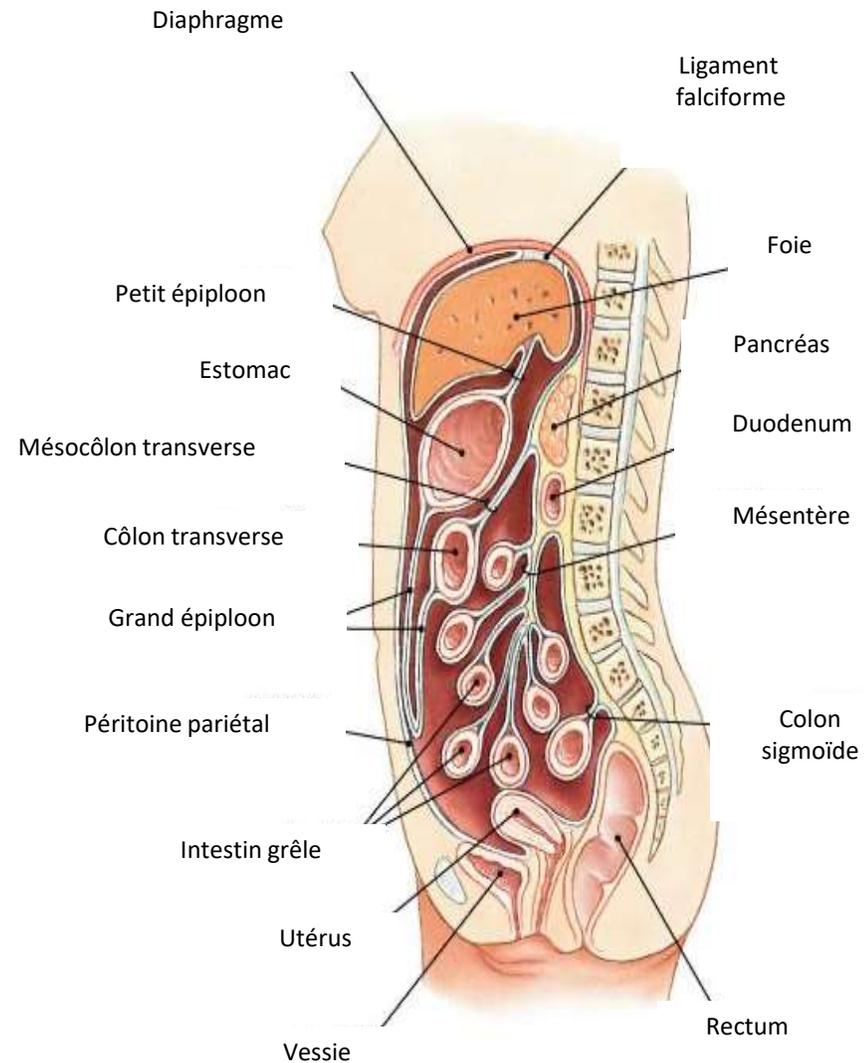
Epidémio prospective mondiale
Multicentrique 309 réanimations
2621 patients admis pour ou se compliquant d'IIA

Characteristic	Total cohort (n = 2621)	Community-acquired (n = 828)	Early onset hospital-acquired (n = 656)	Late-onset hospital-acquired (n = 1137)	p*
Severity of disease expression					
Infection without sepsis	164 (6.3)	51 (6.2)	42 (6.4)	71 (6.2)	0.981
Sepsis	1590 (60.7)	528 (63.8)	399 (60.8)	663 (58.3)	0.050
Septic shock	867 (33.1)	249 (30.1)	215 (32.8)	403 (35.4)	0.043
Anatomical disruption					
Not present	615 (23.5)	186 (22.5)	166 (25.3)	263 (23.1)	0.413
Yes, with localized peritonitis	981 (37.4)	342 (41.3)	256 (39.0)	383 (33.7)	0.002
Yes, with diffuse peritonitis	1025 (39.1)	300 (36.2)	234 (35.7)	491 (43.2)	0.001

93% graves (sepsis ou choc septique) et associées aux soins (un peu) plus graves

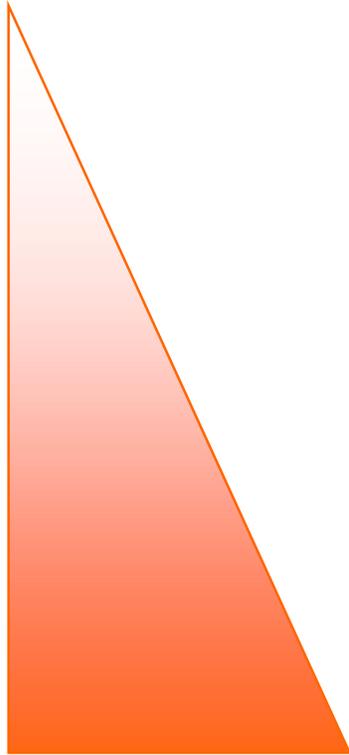
76% avec effraction et pértionite / plus d'effractions et de pértionites diffuses lorsqu'associées aux soins

Inoculum et écologie selon l'anatomie

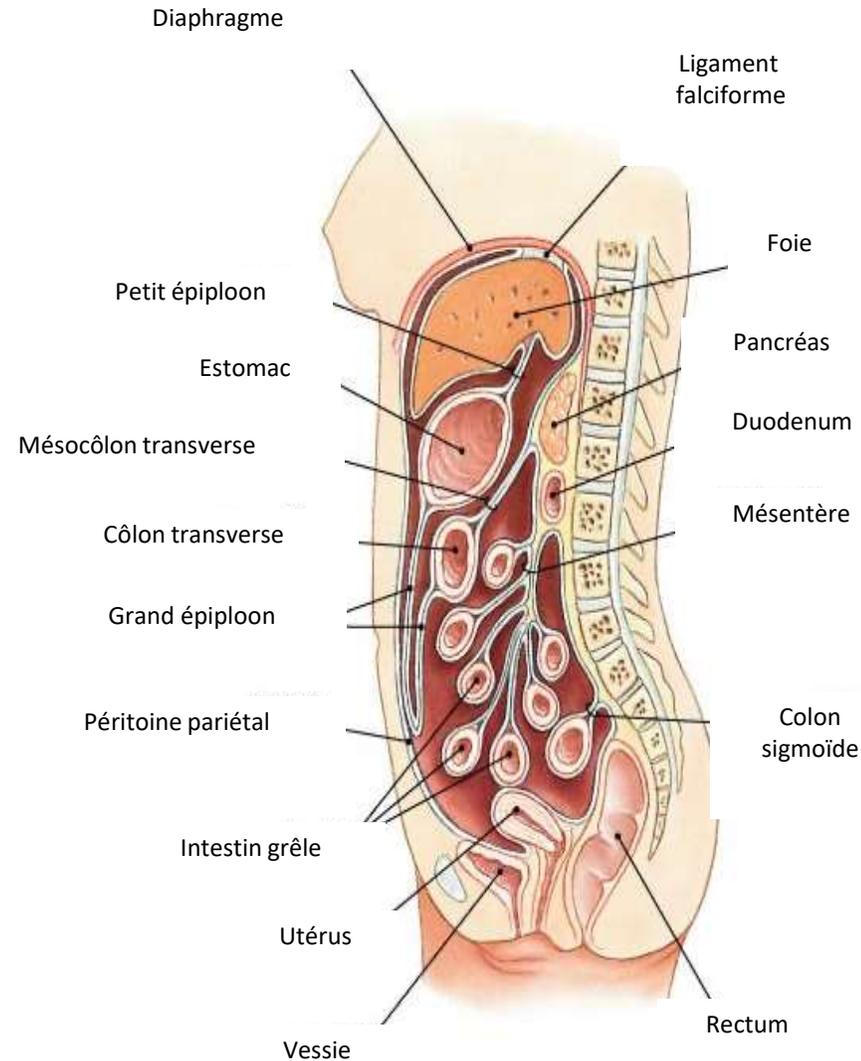


Inoculum et écologie selon l'anatomie

10^2 bactéries/g matières
(anaerobies=10 x aerobies)

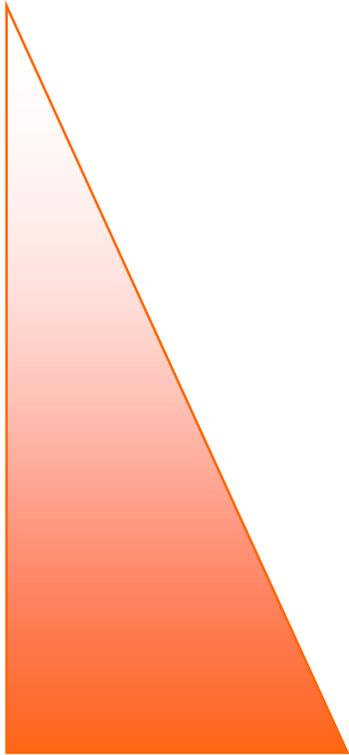


10^{14} bactéries/g matières
(anaerobies=1000 x aerobies)

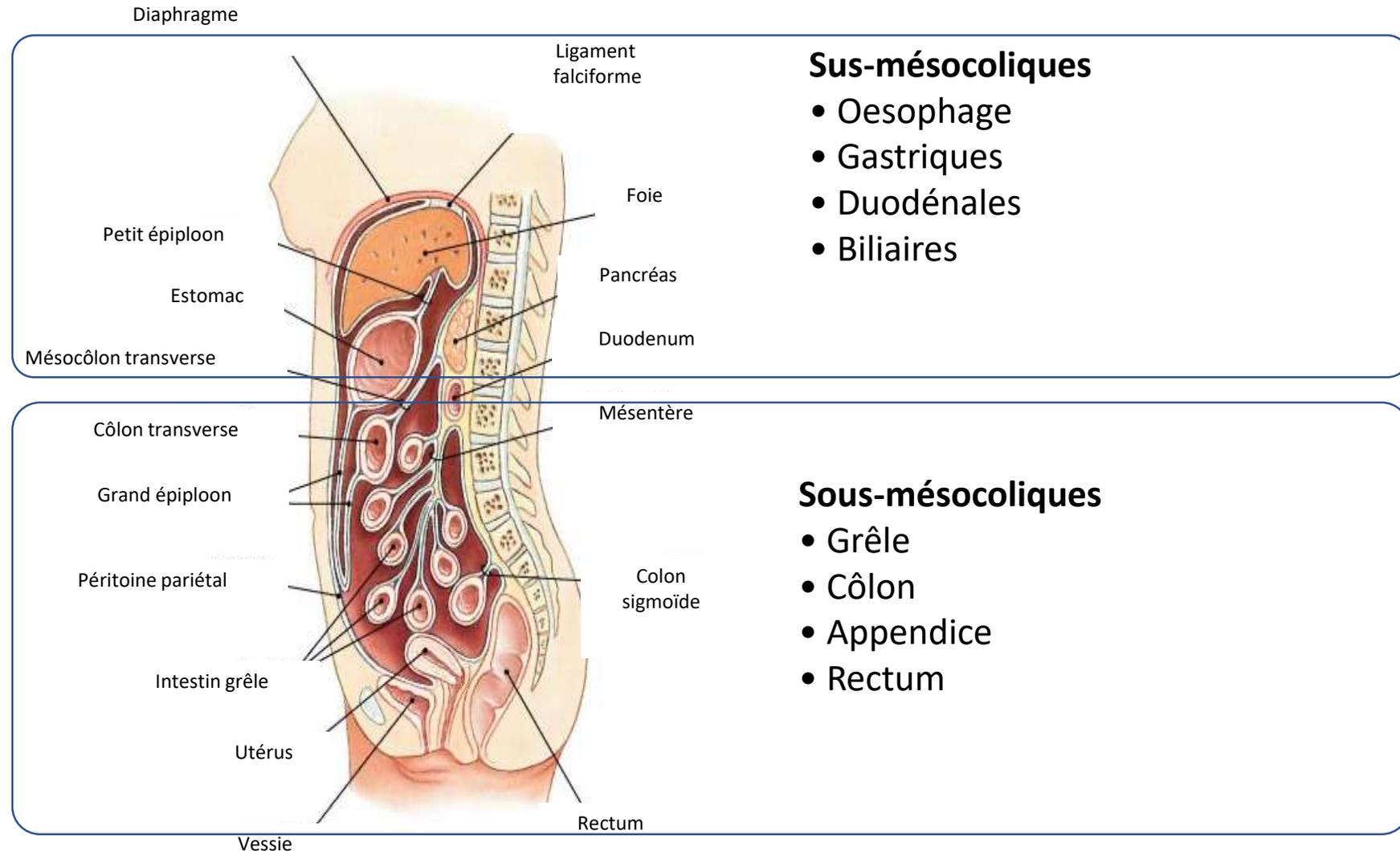


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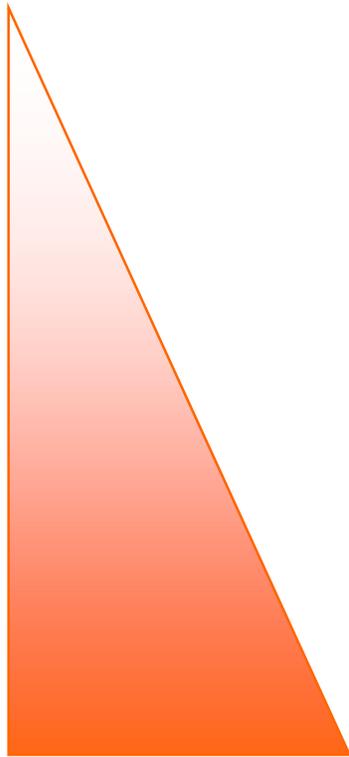


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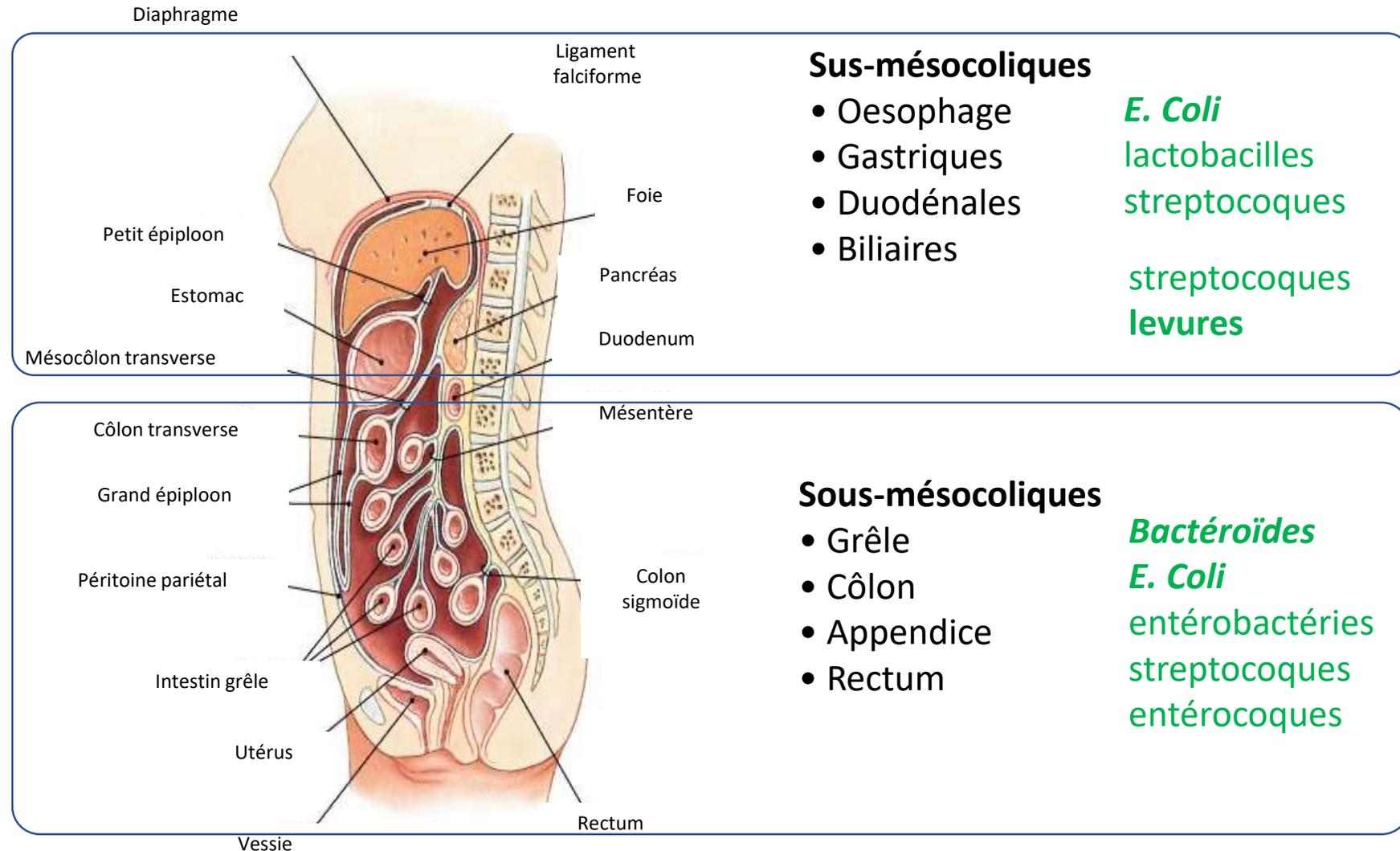


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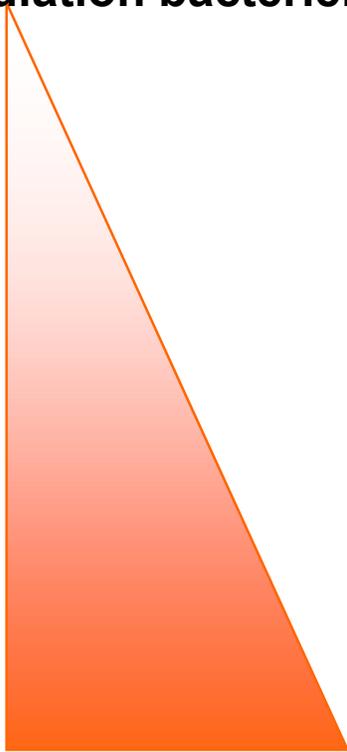


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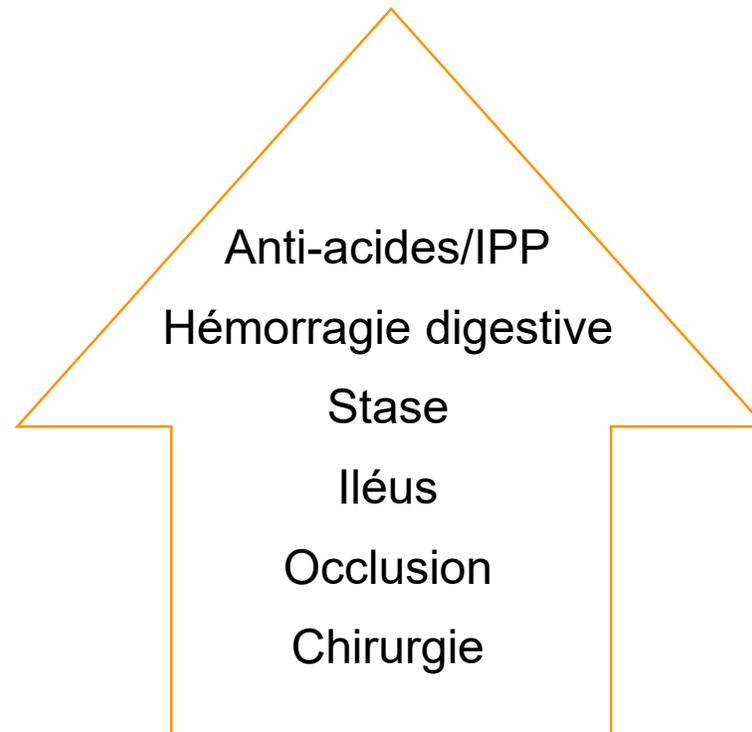
Inoculum et écologie selon facteurs modificateurs de flore

↗ inoculum
pullulation bactérienne



10¹⁴ bactéries/g matières
(anaerobies=1000 x aerobies)

Modifications



Flore "colique"

Bactéroïdes

E. Coli

entérobactéries

streptocoques

entérocoques

streptocoques

levures

Messages préalables

1. Anaerobies de culture (très) difficile MAIS TOUJOURS présents

→ anaerobies *obligatoirement dans le spectre ATB probabiliste même si plvts négatifs*

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→ anaerobies *obligatoirement dans le spectre ATB probabiliste même si plvts négatifs*

2. Ecologie (hors anaérobie) ± selon site MAIS déviation fréquente vers flore sous-mésocolique

→ entérobactéries *obligatoirement dans le spectre ATB probabiliste*

Messages préalables

1. Anaerobies de culture (très) difficile MAIS TOUJOURS présents

→ **anaerobies obligatoirement dans le spectre ATB probabiliste même si plvts négatifs**

2. Ecologie (hors anaérobie) ± selon site MAIS déviation fréquente vers flore sous-mésocolique

→ **entérobactéries obligatoirement dans le spectre ATB probabiliste**

3. Inoculum énorme ne sera pas “décapité” par 1^è dose d’ATB

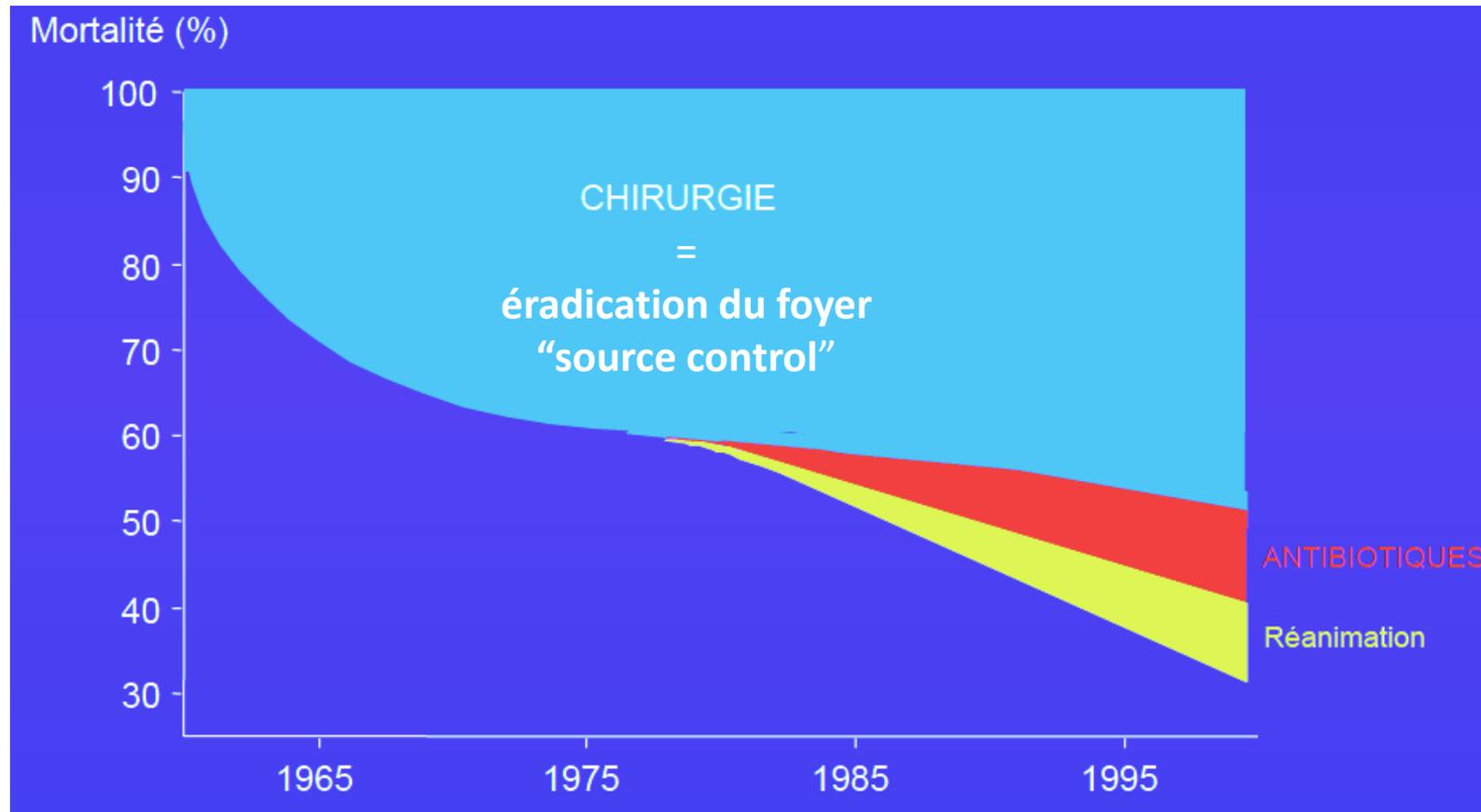
→ **ATB urgente pré-op avant prélèvements intra-abdo**

Messages préalables

1. Anaerobies de culture (très) difficile MAIS TOUJOURS présents
→ **anaerobies obligatoirement dans le spectre ATB probabiliste même si plvts négatifs**
2. Ecologie (hors anaérobie) ± selon site MAIS déviation fréquente vers flore sous-mésocolique
→ **entérobactéries obligatoirement dans le spectre ATB probabiliste**
3. Inoculum énorme ne sera pas “décapité” par 1^è dose d’ATB
→ **ATB urgente pré-op avant prélèvements intra-abdo**
4. Inoculum énorme...donc éradication microbiologique par ATB seuls IMPOSSIBLE
→ **éradication du foyer impérative**

Eradication du foyer

Eradication du foyer (“source control”) = chirurgie (ou drainage)



La plus grande part du pronostic = éradication du foyer

Eradication

Etapes	But (s)	Moyen (s)
Evaluation pré-op	Gravité	Critères réa
Réanimation pré-op	Limitation du sepsis	ATB probabiliste
	Stabilisation pour chirurgie	Hémodynamique
Eradication du foyer		
1	Prévention ISO	Champs, ATB probabiliste
	Diagnostic microbiologique	Plvts péritonéaux per-op
	Diminution de l'inoculum	Lavage péritonéal
	Identification foyer	Identification cause chirurgicale
2	Eradication du foyer	Fermeture perforation
		Résections/anastomose (s)
		Stomie (s)
		Re-lavage péritonéal
3	Fermeture paroi	en 1 temps ou différée
4	Inoculum résiduel	ATB probabiliste puis adaptée
	Nombreuses étapes de l'éradication du foyer; toutes critiques	
Réanimation post-op	amélioration pronostic	principes de la SSC

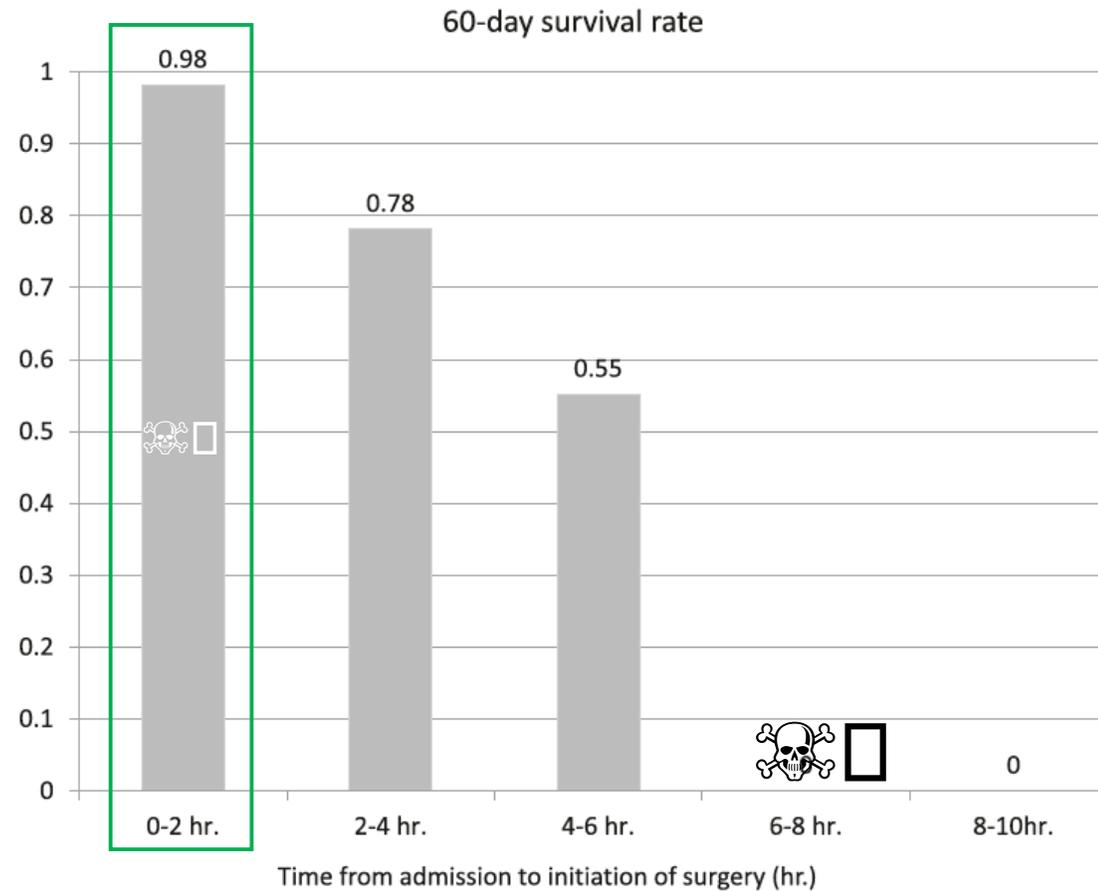
Eradication // antibiothérapie

Foyers	ODDS RATIOS de sur-mortalité		reference
	Eradication foyer (réalisation et/ou délai)	Antibiothérapie (adéquation et/ou délai)	
Eradicables (85% IIA)	2,37	NS	<i>Bloos Crit Care 2014</i>
Angiocholites	3,4	1,12	<i>Karvellas Alim Pharm Ther 2016</i>
IIA bactériémiques	7,46	NS	<i>Tellor Surg Infect 2015</i>

La plus grande part du pronostic, voire LE pronostic = éradication du foyer

Délai d'éradication du foyer

156 péritonites
par perforation
en **choc septique**
dans le cadre d'un protocole d'EGDT



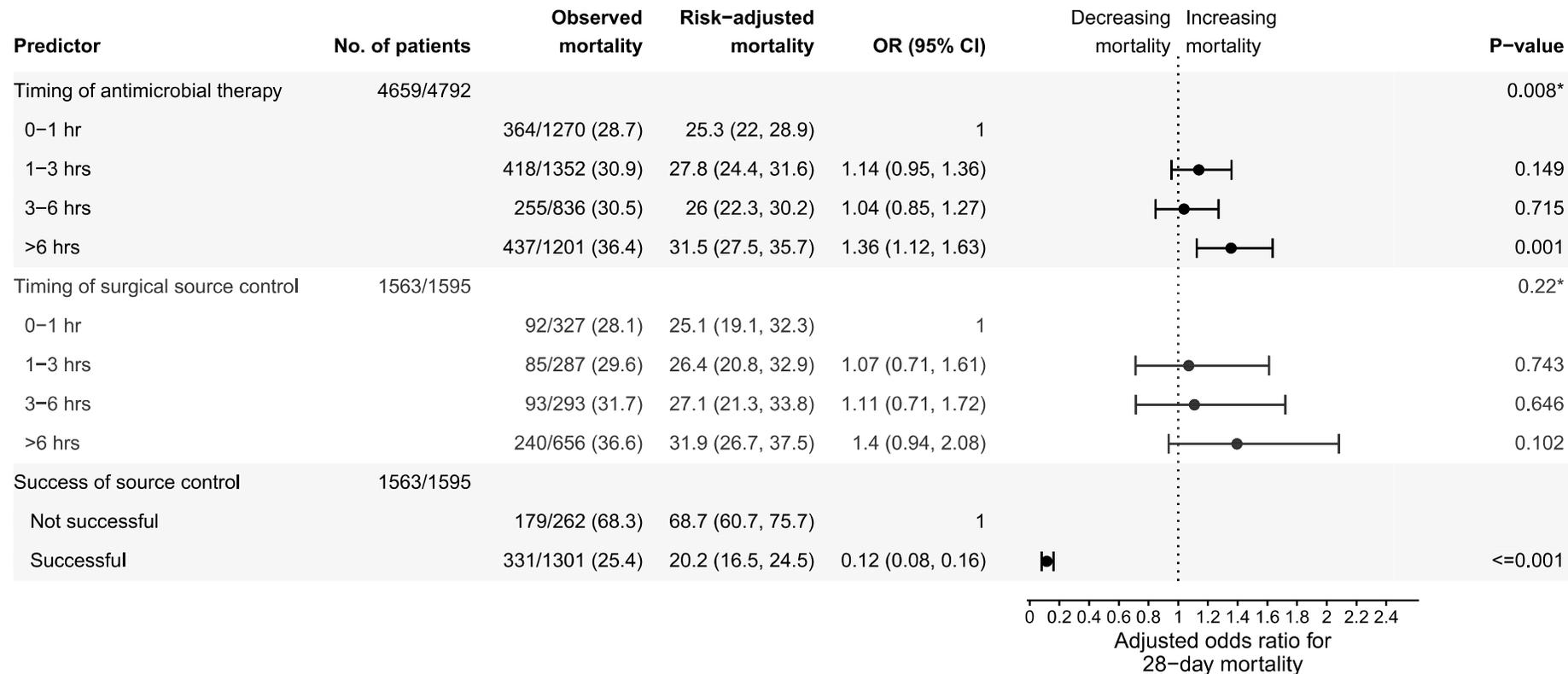
pronostic = délai rapide (OR = 0.29; 95% CI, 0.16-0.47; P <0.0001)

Succès de l'éradication du foyer

Analyse post-hoc RCT multicentrique sepsis en réa Allemagne

délais ttt :

4792 patients sepsis ATB dont 1595 patients avec eradication foyer chir



succès de l'éradication ...plus que le délai

Succès de l'éradication du foyer - étude AbSeS

Echec = inflammation persistante j7 et/ou réintervention dans les 7j

Succès = absence d'échec

	Community-acquired infection		Early-onset hospital-acquired		Late-onset hospital-acquired	
	Localized peritonitis (%)	Diffuse peritonitis (%)	Localized peritonitis (%)	Diffuse peritonitis (%)	Localized peritonitis (%)	Diffuse peritonitis (%)
Septic shock						
Successful source control	5/28 (17.9)	10/26 (38.5) ^b	3/22 (13.6) ^b	7/22 (31.8) ^b	10/28 (35.7)	13/52 (25.0)
Failure of source control ^a	10/18 (55.6)	11/28 (39.3) ^b	4/13 (30.8) ^b	11/18 (61.1) ^b	12/16 (75.0)	32/45 (71.1)
Sepsis						
Successful source control	12/98 (12.2)	9/58 (15.5) ^b	3/57 (5.3)	4/38 (10.5)	10/72 (13.9)	25/94 (26.6)
Failure of source control ^a	16/44 (36.4)	14/45 (31.1) ^b	14/39 (35.9)	17/35 (48.6)	26/51 (51.0)	30/55 (54.5)

gradients de surmortalité significatifs surtout si échec d'éradication

selon gravité

selon péritonite diffuse

selon nosocomial et tardif

Succès de l'éradication du foyer - étude AbSeS

95% d'interventions d'éradication

Succès

Echecs

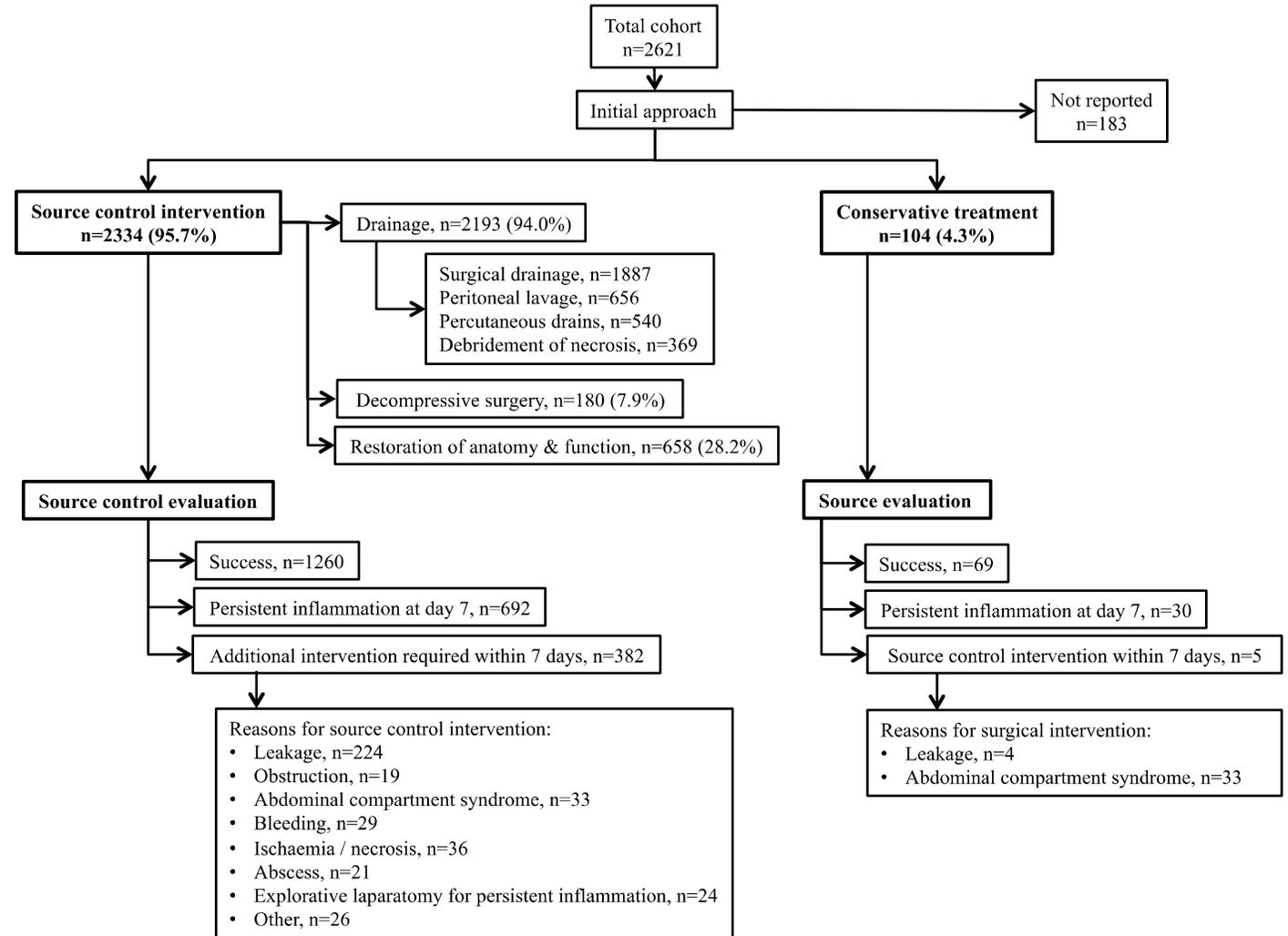
persistance inflammation j7

réintervention dans les 7j

54%

29%

16%



Succès de l'éradication du foyer - étude AbSeS

Multivariée FdR décès

Source control achievement at day 7

Success

Reference

Failure, persistent signs of inflammation

4.85 (3.79–6.22)

Failure, additional intervention required following initial approach

1.93 (1.41–2.65)

LE principal déterminant de la mortalité est l'échec d'éradication du foyer (j7)

Facteurs de mortalité (*si foyer éradiqué !*) – étude AbSeS

Variable	Model with source control achievement* OR (95% CI)

Donnés chez les patients ayant eu une éradication du foyer avec succès

Facteurs de mortalité (*si foyer éradiqué !*) – étude AbSeS

	Variable	Model with source control achievement* OR (95% CI)
	Setting of infection acquisition	
	Community-acquired infection	Reference
<i>nosocomial précoce</i>	Early onset hospital-acquired infection (≤ 7 days)	1.15 (0.84–1.58)
<i>nosocomial tardif</i>	Late-onset hospital-acquired infection (> 7 days)	1.76 (1.34–2.32)
	Anatomical disruption	
	No anatomical barrier disruption	Reference
<i>effraction</i>	Anatomical disruption with localized peritonitis	1.28 (0.95–1.75)
<i>péritonite diffuse</i>	Anatomical disruption with diffuse peritonitis	1.99 (1.49–2.67)
	Severity of disease expression	
	Infection	Reference
<i>gravité</i>	Sepsis	2.44 (1.37–4.66)
	Septic shock	5.22 (2.91–10)

Facteurs de mortalité chez patients immunodéprimés (AbSes)

Etude Post-hoc de l'étude AbSes

n = 239 (9.2%)

Variable	Odds ratio (95 % confidence interval)	p-value
Severity of disease expression at time of diagnosis		
Infection	Reference category	–
Sepsis	4.15 (0.80 – 34.67)	0.127
Septic shock	6.64 (1.27 – 55.72)	0.043
Length of ICU stay per 7 days increase		
1–7 days	Reference category	–
8–14 days	0.75 (0.29 – 1.91)	0.548
15–21 days	3.61 (1.16 – 11.53)	0.026
22–28 days	2.17 (0.43 – 10.62)	0.336
>28 days	1.03 (0.35 – 2.95)	0.960
Source control achievement at day 7		
Successful	Reference category	–
Failure, persistent signs of inflammation	5.48 (2.29 – 12.57)	<0.001
Failure, need for additional intervention	1.66 (0.52 – 4.93)	0.367

Source control interventions in the immunocompromised population.

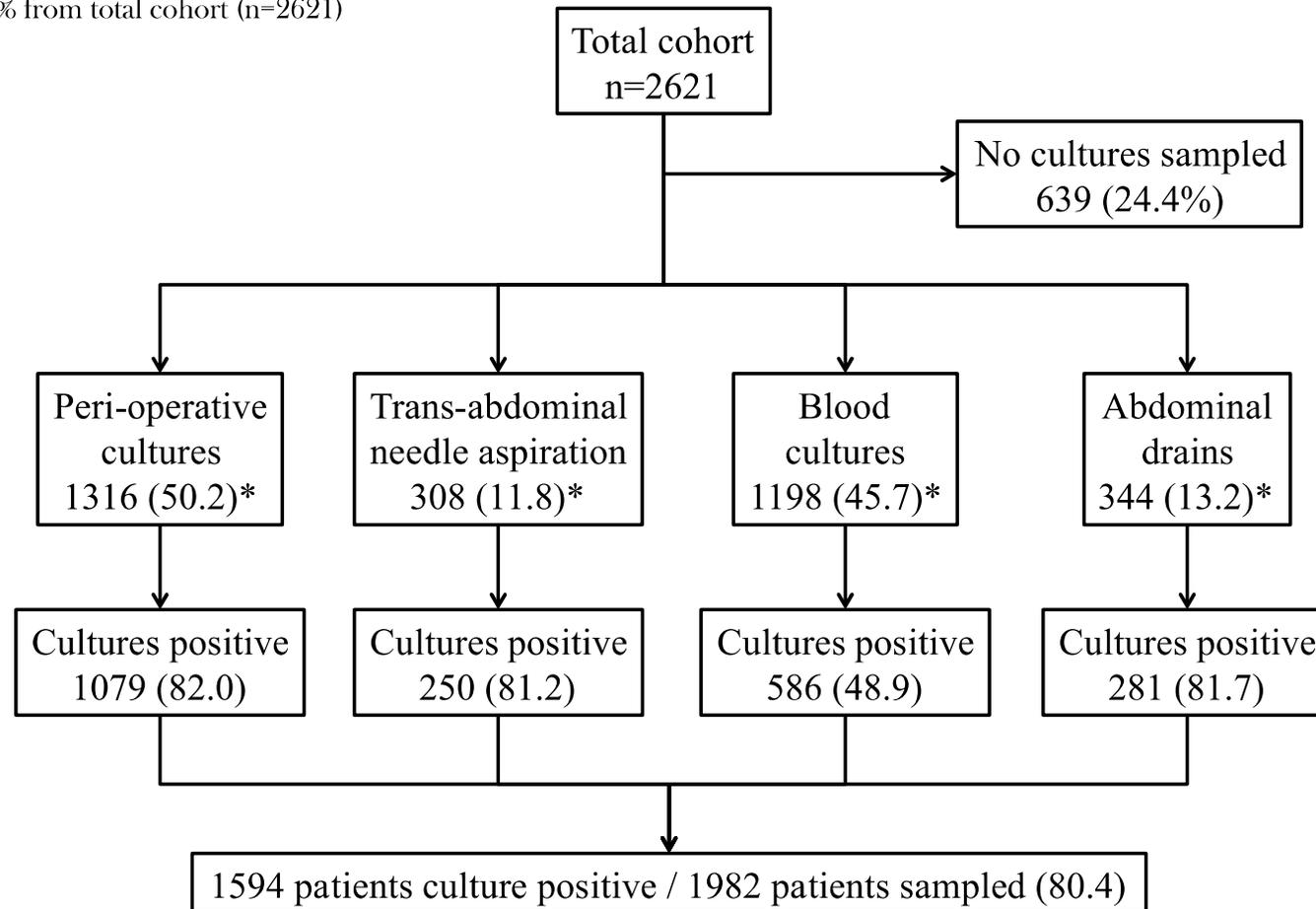
Type of intervention	N (%)
Any type of source control	214*/228** (93.9)
Drainage	201/228 (88.2)
Surgical drainage	175/201 (87.1)
Laparoscopic drainage	7/201 (3.5)
Peritoneal lavage	57/201 (28.4)
Percutaneous drains	49/201 (24.4)
Debridement of necrosis	28/201 (13.9)
Decompressive surgery	17/228 (7.5)
Restoration of anatomy	49/228 (21.5)

FdR mortalité : choc septique et l'échec d'éradication du foyer (j7) sur le mode persistance de l'inflammation

Microbiologie

Rentabilité des prélèvements – étude AbSeS

*% from total cohort (n=2621)



80 % information microbiologique

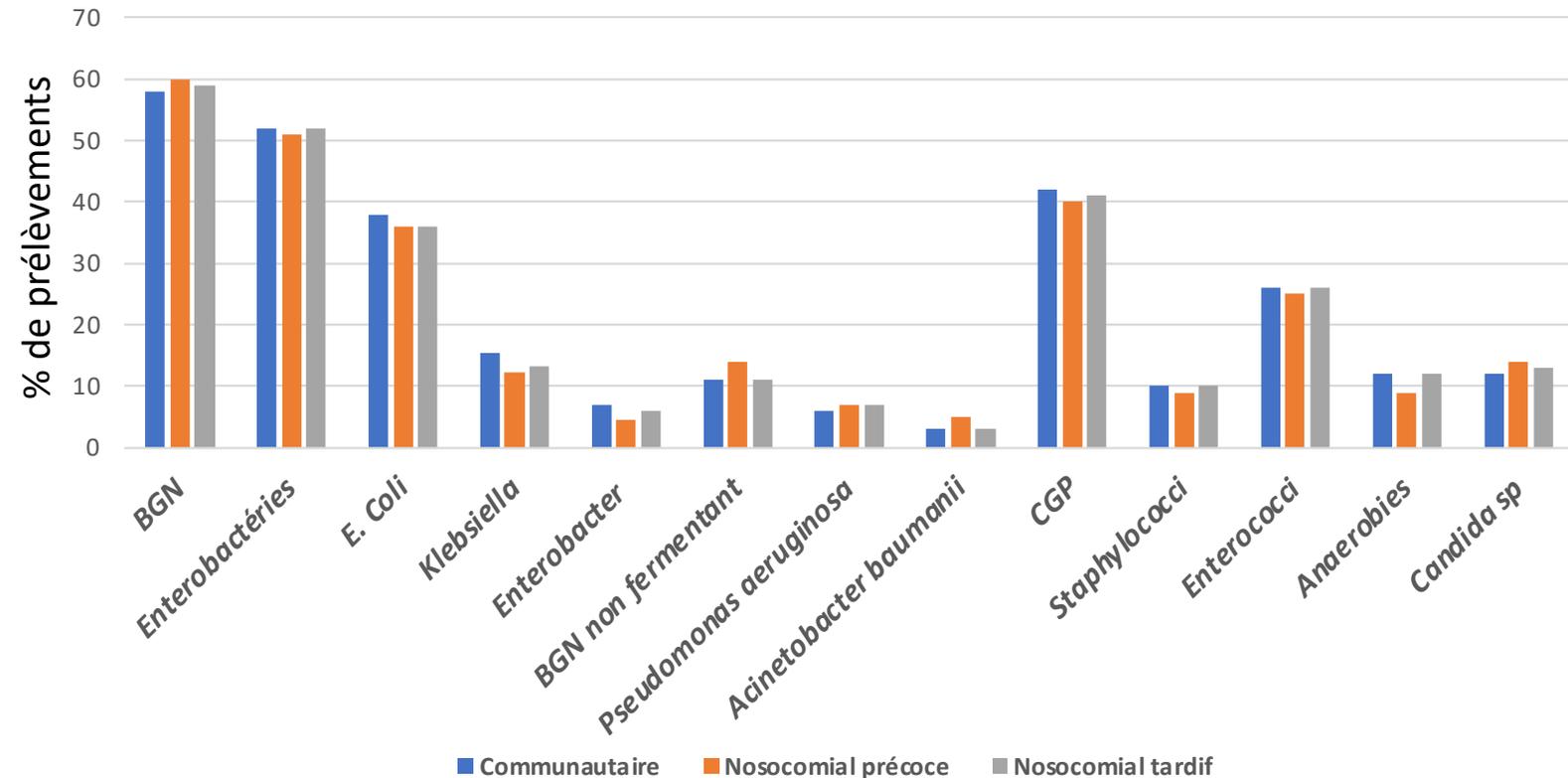
Ecologie – étude AbSeS

		Micro-organism	Total cohort (n = 1982)	Setting of infection acquisition		
				Community-acquired (n = 664)	Early onset hospital- acquired (n = 482)	Late-onset hospital-acquired (n = 836)
BGN	(60%)					
	<i>E. coli</i>					
	Klebielles					
		Gram-negative bacteria	1161 (58.6)	385 (58)	287 (59.5)	498 (58.5)
		<i>Enterobacterales</i>	1024 (51.7)	344 (51.8)	247 (51.2)	433 (51.8)
Non-fermentants	(12%)					
	<i>P. aeruginosa</i>					
	<i>A. baumannii</i>					
		<i>Escherichia coli</i>	729 (36.8)	252 (38)	172 (35.7)	304 (36.4)
		<i>Klebsiella sp.</i>	51 (2.6)	22 (3.3)	12 (2.5)	17 (2)
		<i>Klebsiella oxytoca*</i>	44 (2.2)	23 (3.5)	11 (2.3)	10 (1.2)
		<i>Klebsiella pneumoniae</i>	170 (8.6)	57 (8.6)	37 (7.7)	76 (9.1)
		Non-fermenting bacteria	233 (11.8)	72 (10.8)	66 (13.7)	95 (11.4)
Entérocoques	(25%)					
	<i>E. faecalis</i>					
	<i>E. faecium</i>					
		<i>Pseudomonas aeruginosa</i>	131 (6.6)	41 (6.2)	34 (7.1)	56 (6.7)
		<i>Acinetobacter baumannii</i>	61 (6.2)	18 (2.7)	22 (4.6)	21 (2.5)
		Enterococci	513 (25.9)	173 (26.1)	121 (25.1)	219 (26.2)
		<i>Enterococcus faecalis</i>	257 (13)	83 (12.5)	59 (12.2)	115 (13.8)
		<i>Enterococcus faecium</i>	216 (10.9)	70 (10.5)	46 (9.5)	100 (12)
Anaerobies	(12%)					
	<i>Bacteroides</i>					
		Anaerobe bacteria	231 (11.7)	83 (12.5)	45 (9.3)	103 (12.3)
		<i>Bacteroides sp.*</i>	103 (5.2)	46 (6.9)	17 (3.5)	40 (4.8)
		Fungi	258 (13)	80 (12)	71 (14.7)	107 (12.8)
		<i>Aspergillus sp.</i>	3 (0.2)	0	2 (0.4)	1 (0.1)
Fongique	(13%)					
	<i>Candida</i>					
		<i>Candida sp.</i>	257 (13)	81 (12.2)	69 (14.3)	107 (12.8)
		<i>Candida albicans</i>	173 (8.7)	56 (8.4)	50 (10.4)	67 (8)

Ecologie – étude AbSeS

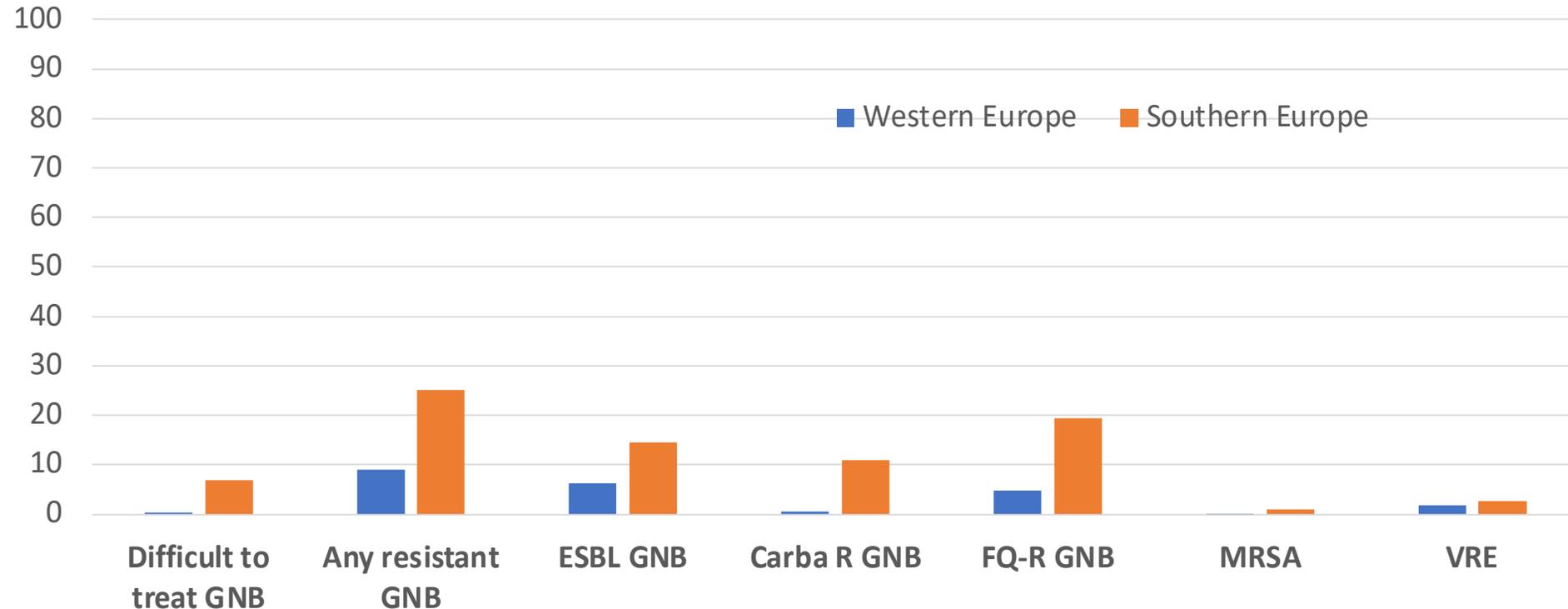
Microorganismes isolés dans les prélèvements intra-abdominaux

BGN	(60%)
<i>E. coli</i>	(35%)
Klebsielles	(15%)
Non-fermentants	(12%)
<i>P. aeruginosa</i>	(6%)
<i>A. baumannii</i>	(6%)
Entérocoques	(25%)
<i>E. faecalis</i>	(13%)
<i>E. faecium</i>	(12%)
Anaérobies	(12%)
<i>Bacteroides</i>	(5%)
Fongique	(13%)
<i>Candida</i>	(9%)



PAS de différences marquées d'espèces entre communautaire et nosocomial précoce ou tardif !

Résistances – étude AbSeS

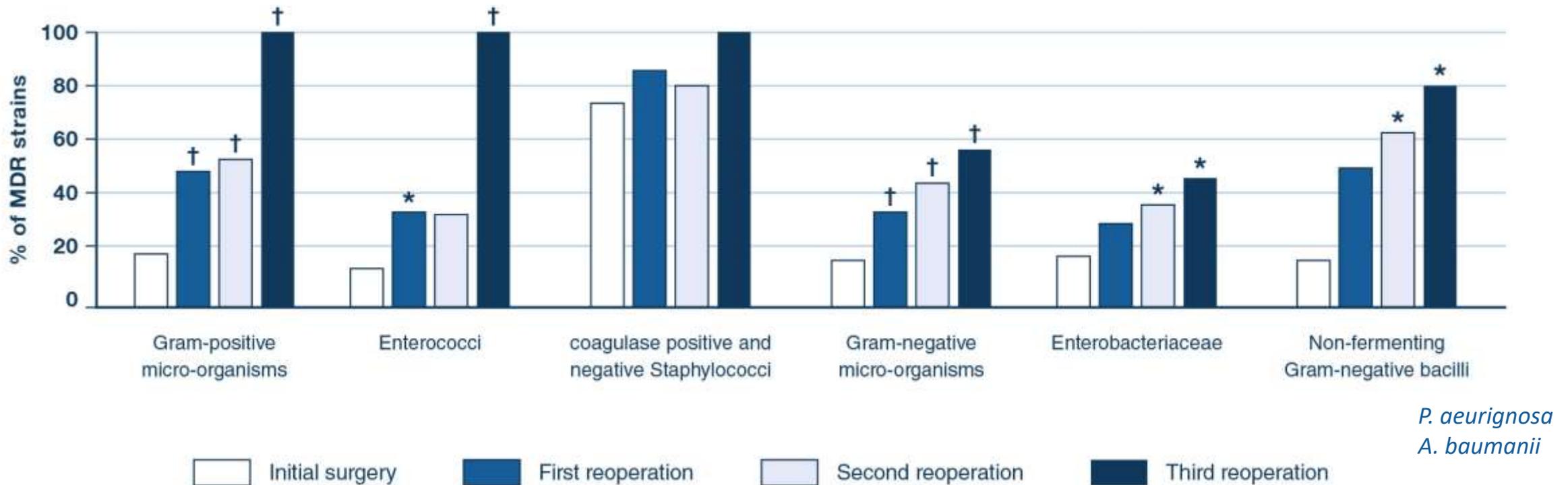


Faibles incidences de résistances problématiques (“difficult to treat”, BLSE, EPC...)

Différences surtout géographiques Europe ouest / sud (et est et centrale) – PAS entre communautaire/noso (NS)

Remarque sur la multirésistance = IIA tertiaires

monocentrique, n = 122



non-éradication du foyer favorise péritonites tertiaires et sélection de résistances

Résistances et pronostic – étude AbSeS

Multivarié avec succès d'éradication du foyer

Variable	Model with source control achievement* OR (95% CI)
Empiric antimicrobial coverage	
Anti-MRSA agent	0.77 (0.59–1)
Double anaerobe coverage	–
Antibiotic resistance involvement *	1.49 (1.07 – 2.05)
<i>*BGN BLSE ou BGN productrice de carbapénémase(s) ou ERV ou SARM</i>	

Traitement antibiotique approprié – étude AbSeS

	Community-acquired infection		Early-onset hospital-acquired		Late-onset hospital-acquired	
	Localized peritonitis (%)	Diffuse peritonitis (%)	Localized peritonitis (%)	Diffuse peritonitis (%)	Localized peritonitis (%)	Diffuse peritonitis (%)
Septic shock						
Appropriate empiric antimicrobial therapy	8/30 (26.7)	9/31 (29.0)	4/24 (16.7)	12/30 (40.0)	15/31 (48.4)	32/65 (49.2)
Inappropriate empiric antimicrobial therapy	7/16 (43.8)	12/23 (52.2)	3/11 (27.3)	6/10 (60.0)	7/13 (53.8)	13/32 (40.6)
Sepsis						
Appropriate empiric antimicrobial therapy	20/93 (21.5)	12/66 (18.2)	8/55 (14.5)	11/45 (24.4)	22/80 (27.5)	35/99 (35.4)
Inappropriate empiric antimicrobial therapy	8/49 (16.3)	11/37 (29.7)	9/41 (22.0)	10/28 (35.7)	14/43 (32.6)	20/50 (40.0)

globalement 64.8% de traitement approprié
gain global de survie de 6% MAIS NS (manque de puissance)

gain de survie si approprié plus marqué si choc septique et s'atténuant pour les nosocomiales tardives

Couvrir les entérocoques ? – etude AbSeS

Multivarié avec succès d'éradication du foyer

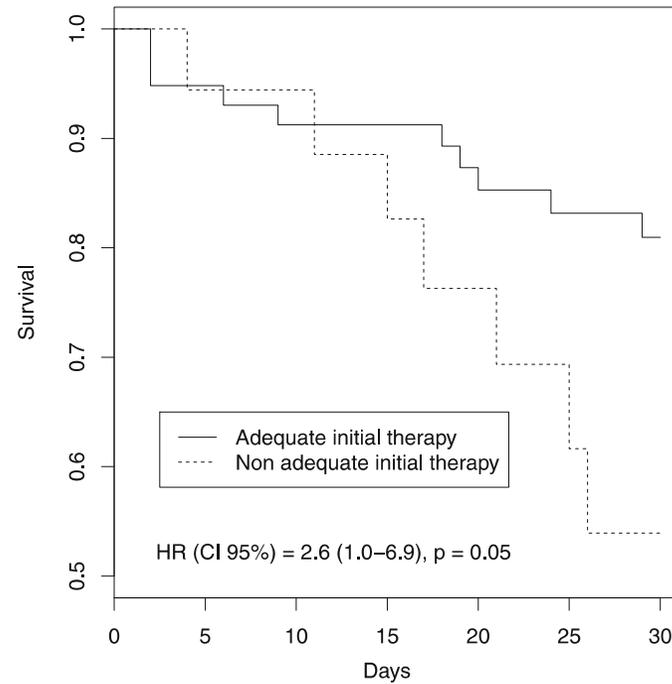
Variable	Model with source control achievement* OR (95% CI)
Empiric antimicrobial coverage	
Anti-MRSA agent	0.77 (0.59–1)
Double anaerobe coverage	–
Antibiotic resistance involvement	1.49 (1.07 – 2.05)

l'isolement d'entérocoques ne sortant pas / anti-SARM = vancomycine ou linézolid = anti- E. faecium

Couvrir les entérocoques ?

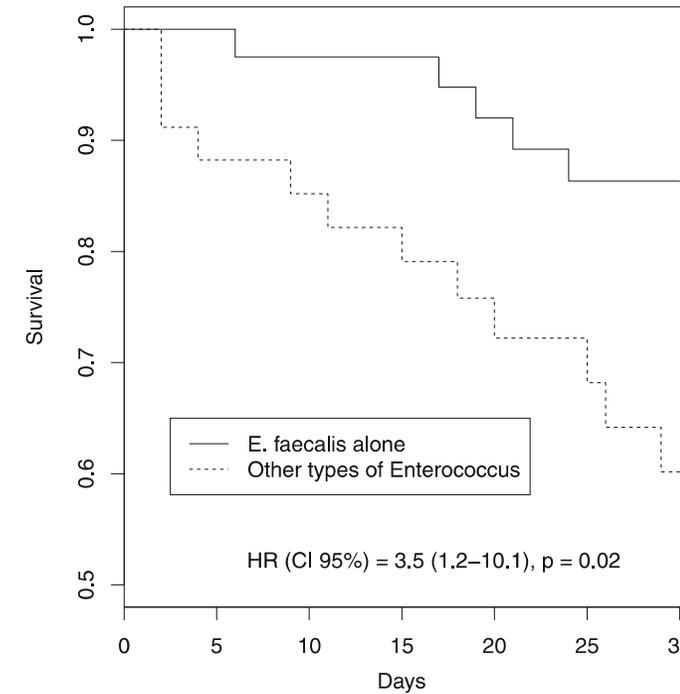
Rétro OutcomeRea 1997-2016

1017 patients IIA, 76 (8%) à *Enterococcus*



No. of patients at risk

	0	5	10	15	20	25	30
Adequate	58	53	51	50	43	39	37
Non adequate	18	16	16	15	11	9	7



No. of patients at risk

	0	5	10	15	20	25	30
E. faecalis	42	40	39	38	33	30	29
Other	34	29	28	27	21	18	15

adéquation anti-Entérocooccus et/ou E. faecalis (sensible)

Couvrir les entérocoques ?

Méta-analyse n = 36 dont 23 essais randomisés contrôlés

<i>Suspected Factors</i>	<i>Included studies</i>	<i>OR (95% CI)</i>	<i>I² for heterogeneity</i>
<u>1 Community Acquired</u>			
1.1 Female	11	0.92 [0.78, 1.09]	0%
1.2 Malignancy	6	1.53 [1.16, 2.03]	49%
1.3 Diabetes Mellitus	6	1.21 [0.96, 1.53]	0%
1.4 Cardiovascular Disease	5	1.27 [0.98, 1.63]	38%
1.5 Liver Disease	4	1.09 [0.49, 2.44]	73%
1.6 Chronic Lung Disease	4	1.24 [0.87, 1.78]	24%
1.7 Renal Diseases	3	1.42 [0.80, 2.52]	0%
1.8 Immunosuppression	3	1.27 [0.83, 1.93]	22%
1.9 Chronic Vascular Disease	2	1.12 [0.79, 1.59]	0%
1.10 GI Hemorrhage	2	3.23 [0.92, 11.37]	65%
1.11 Corticosteroid Use	2	2.46 [1.71, 3.54]	0%
1.12 Myocardial infarction	1	2.033 [0.9548, 4.244]	NA
<u>2 Hospital Acquired</u>			
2.1 Operation	7	2.88 [2.21, 3.75]	0%
2.2 Nosocomial Infection	7	2.81 [2.34, 3.39]	33%
2.3 Any Antibiotic Treatment	5	2.40 [1.74, 3.31]	42%
2.4 Admission to ICU	3	2.54 [1.75, 3.68]	0%
2.5 Indwelling Urinary Catheter	2	1.78 [1.02, 3.11]	0%
2.6 CVC	2	7.80 [0.63, 96.20]	89%
2.7 Inadequate Empirical ATB	1	2.088 [1.006, 4.253]	NA
2.8 Generalized Peritonitis	1	1.449 [0.7129, 2.948]	NA
2.9 Peritonitis Duration more than 24h	1	2.679 [1.157, 6.012]	NA
2.10 MOF	1	2.017 [0.8483, 5.147]	NA

Nosocomial et post-op = FdR significatifs

Antifongiques ? – étude AbSeS

Multivarié avec succès d'éradication du foyer

Variable

**Model with source control achievement*
OR (95% CI)**

Empiric antimicrobial coverage

ne sort pas : PAS de différence de mortalité avec ou sans traitement antifongique

Antifongiques ? FdR candidose invasive intra-abdo

2015-2016

cas controle dans 26 réanimations Europe

101 patients réa **candidose invasive intra-abdominale** vs. 101 patients sans

Risk factors^a	OR (95% CI)	<i>p</i>
Recurrent gastrointestinal perforation	13.90 (2.65–72.82)	0.002
Anastomotic leakage	6.61 (1.98–21.99)	0.002
Abdominal drain	6.58 (1.73–25.06)	0.006
Receipt of antifungal drugs (7 or more days)	4.26 (1.04–17.46)	0.04
Receipt of antibiotics (7 or more days)	3.78 (1.32–10.52)	0.01

Antifongiques ? - RFE IIA 2015

R16 :

Communautaire **grave**

± si FdR/Scores

échinocandine

R41 :

Dans les IIA associées aux soins,

si une levure est observée à l'examen direct

culture du liquide péritonéal est positive à levures

(échinocandine si grave)

Prospective multicenter randomized double-blind study comparing caspofungin to placebo for the treatment of ICU yeast intra-abdominal infection

CASPER study

Sponsor code : PI2018_843_0007

INTERVENTIONAL RESEARCH PROTOCOL

(Research involving the human person)

Version No. 1.4 of 04/12/2018

EudraCT number: 2018-000407-16

This interventional research study has received funding from a PHRC-N 2017

Sponsor:

Amiens-Picardie University Hospital (CHU d'Amiens-Picardie)

Direction de la Recherche Clinique et de l'Innovation,

CHU d'Amiens-Picardie

F-80054 Amiens Cedex 1, France

Phone: +33 322 088 371; Fax: +33 322 089 645

Coordinating investigator:

Professor DUPONT Hervé

Antifongiques ? - RFE IIA 2015

R16 :

Communautaire **grave**

± si FdR/Scores

échinocandine

R41 :

Dans les **IIA associées aux soins**,

si une levure est observée à l'examen direct

culture du liquide péritonéal est positive à levures

(échinocandine si grave)

Spectres conventionnels d'intérêt

Antibiotic	Anaerobic coverage	<i>Pseudomonas</i> coverage	Non-resistant enterococci coverage	Enterobacteriaceae coverage	ESBL coverage
Amikacin	-	+	-	+	+/-
Amoxicillin/ clavulanate	+	-	+	+/- ^a	-
Ceftazidime/ avibactam	-	+ ^b	-	+ ^c	+
Ceftolozane/ tazobactam	-	+ ^b	-	+	+
Cefotaxime	-	-	-	+	-
Ceftazidime	-	+	-	+	-
Ceftriaxone	-	-	-	+	-
Ciprofloxacin	-	+	-	+/- ^a	-
Eravacycline	+	-	+	+ ^e	+
Ertapenem	+	-	+/-	+	+
Imipenem-cilastatin	+	+	+ ^d	+	+
Meropenem	+	+	+/-	+	+
Metronidazole	+	-	-	-	+/-
Piperacillin/ tazobactam	+	+	+	+	+/-
Tigecycline	+	-	+	+ ^e	+

^aIncreasing rates of antimicrobial resistance among Enterobacteriaceae worldwide

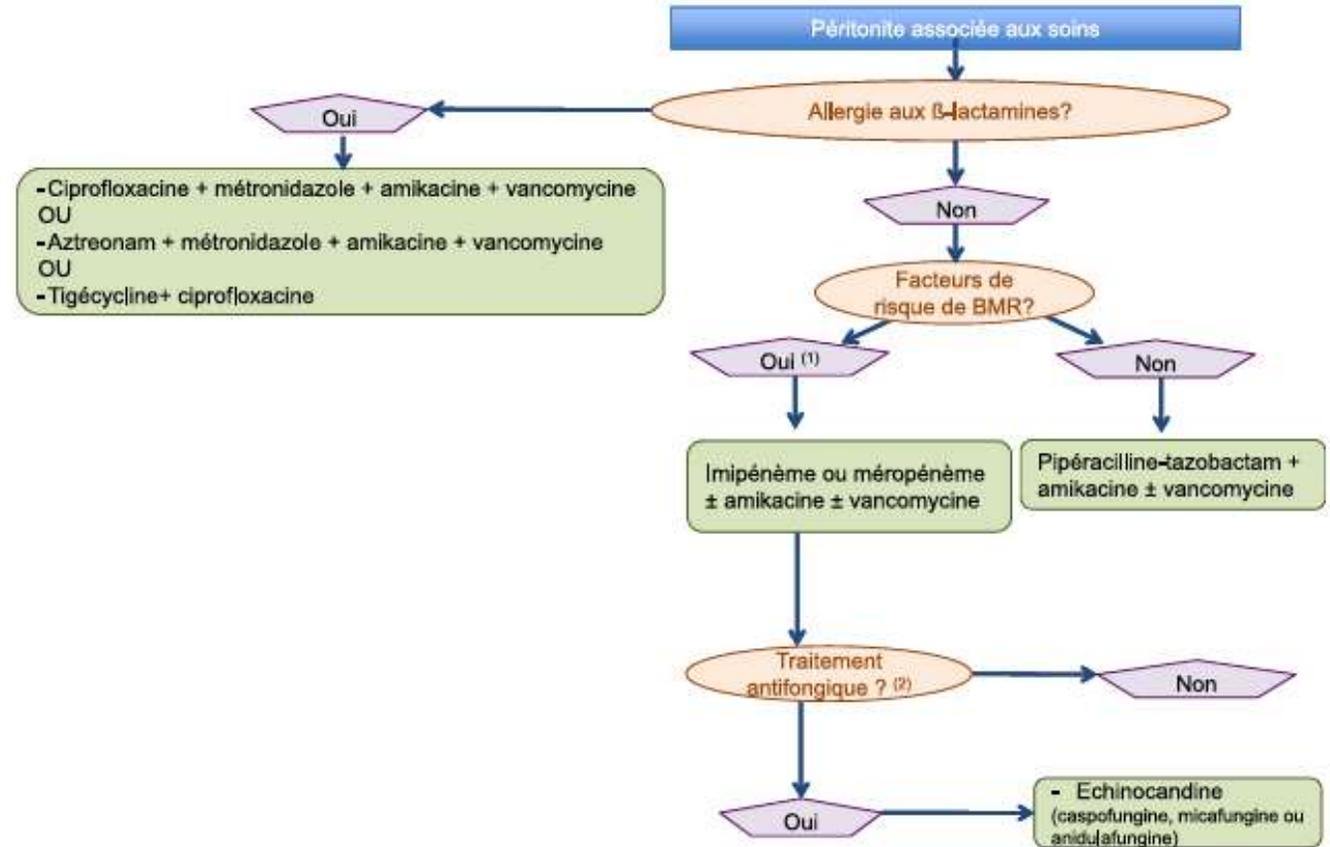
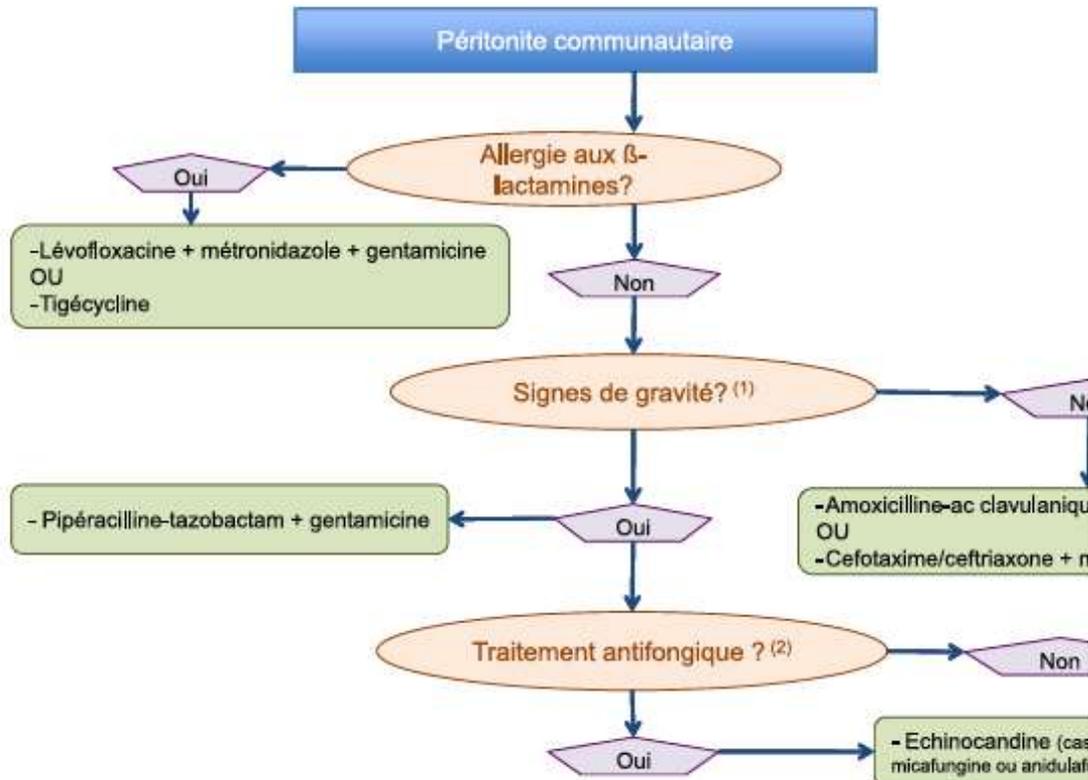
^bActive against MDR *Pseudomonas aeruginosa* except metallo-beta-lactamases (MBL)-producing *Pseudomonas aeruginosa*

^cActive against carbapenemase-producing *Klebsiella pneumoniae* except MBL-producing Enterobacteriaceae

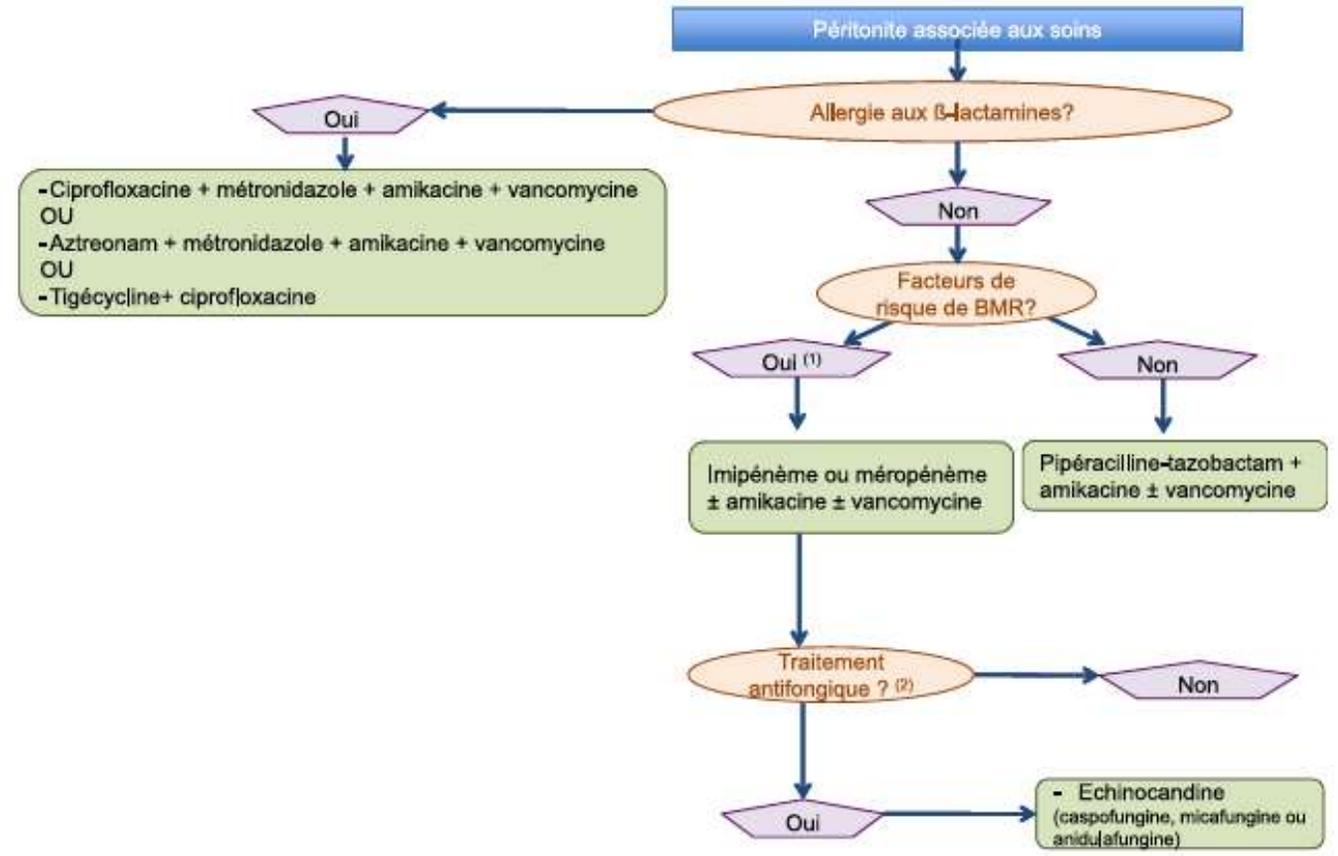
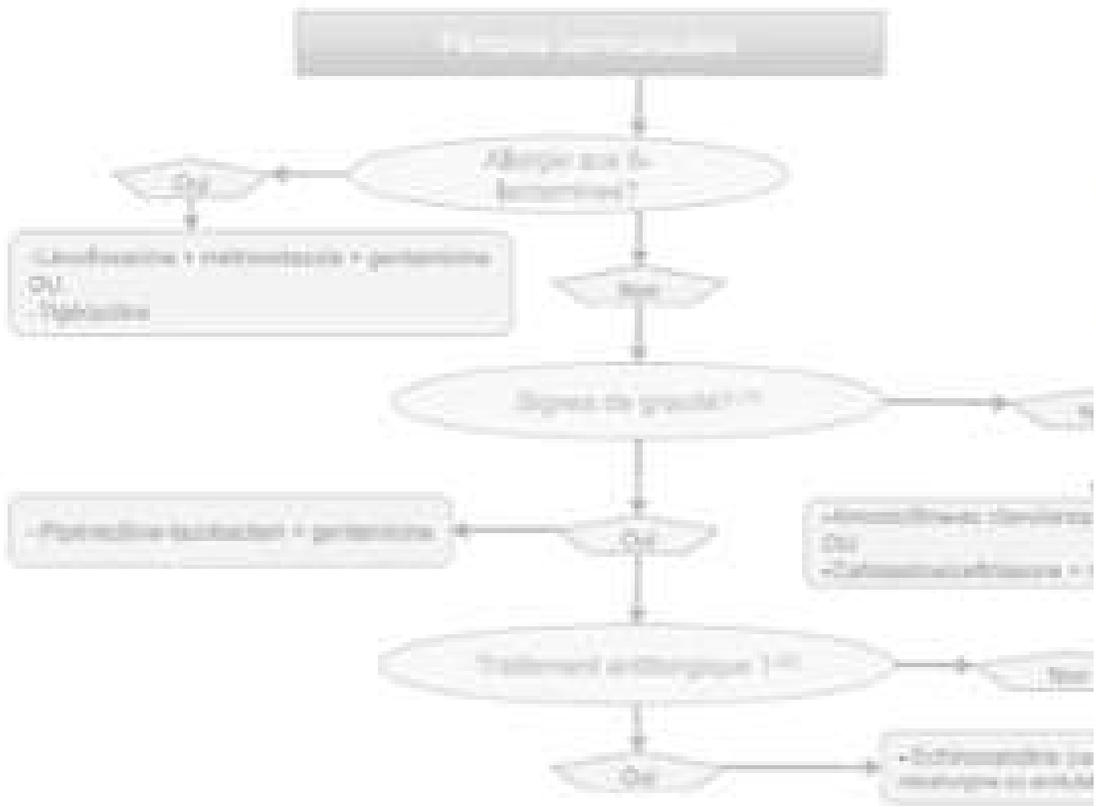
^dImipenem/cilastatin is more active against ampicillin-susceptible enterococci than ertapenem, meropenem, and doripenem

^eNot active against *Proteus*, *Morganella*, and *Providencia*

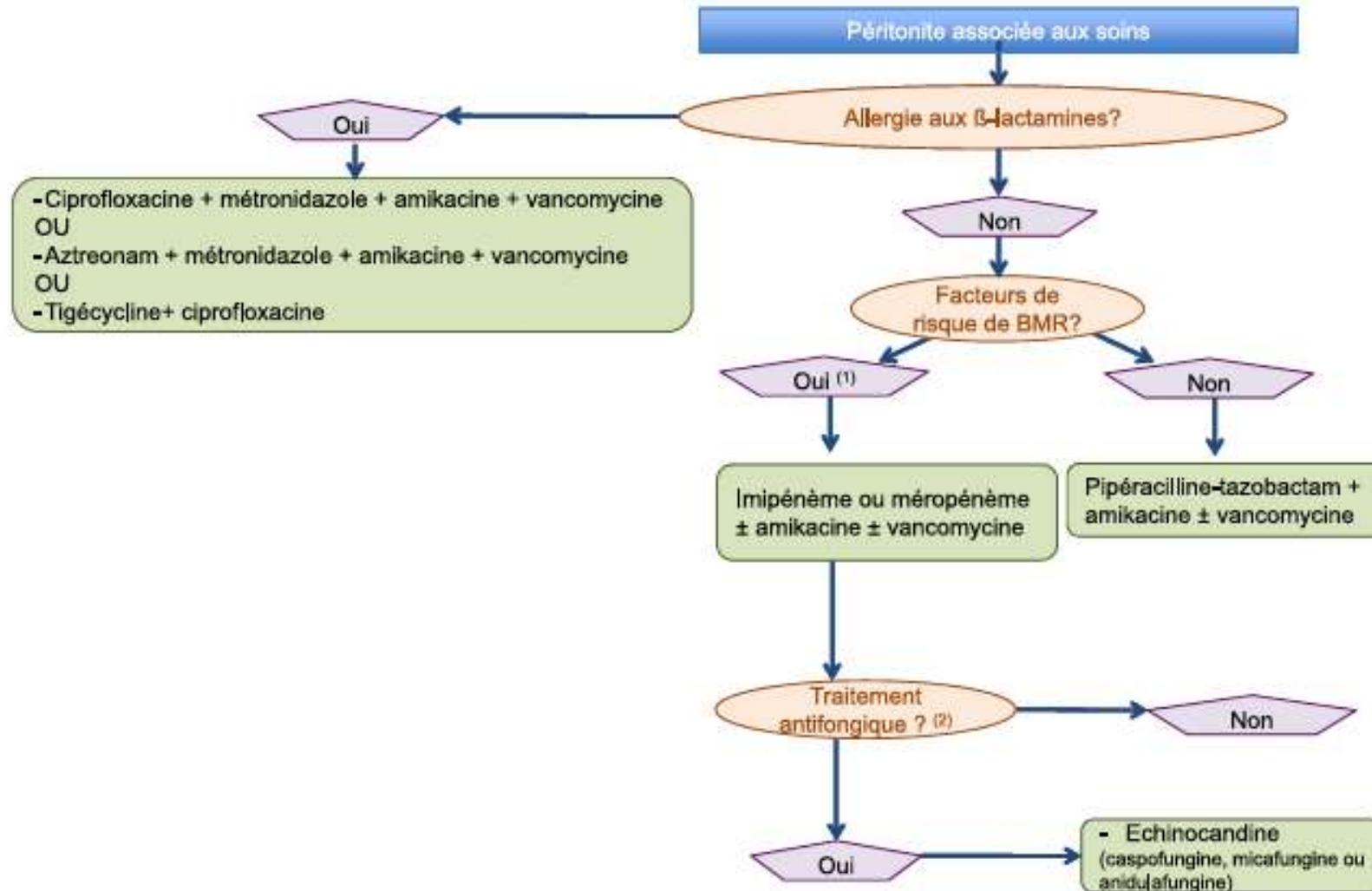
Comment se positionner en antibiothérapie des IIA de réa ?



Comment se positionner en antibiothérapie des IIA de réa ?



Comment se positionner en antibiothérapie des IIA de réa ?



Comment se positionner en antibiothérapie des IIA de réa ?

piéracilline/tazobactam
+
gentamicine

**piéracilline/tazobactam
+
amikacine**

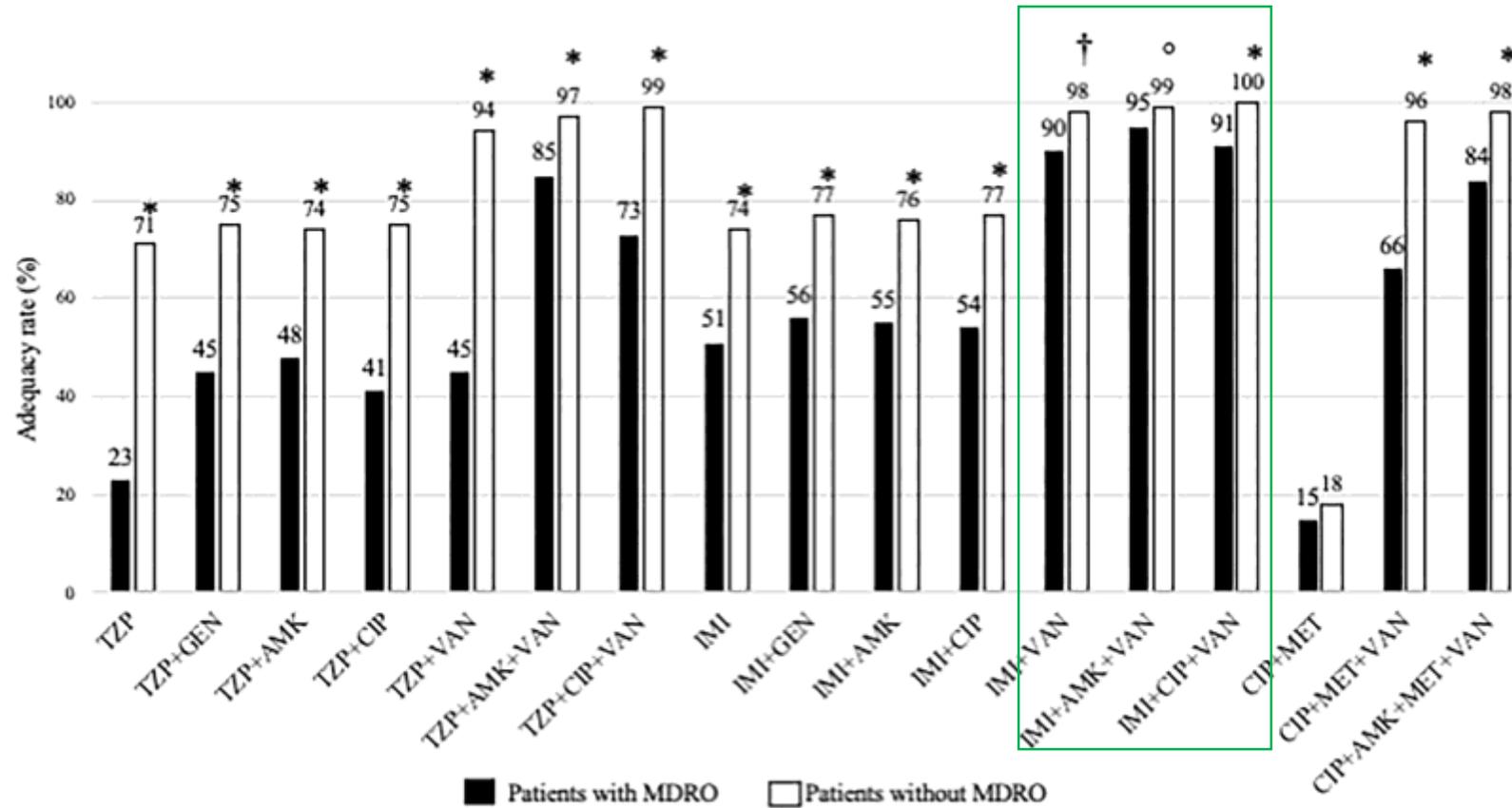
**pénème
+
amikacine**

± échinocandine

± vancomycine

Résistance et IIA post-opératoires

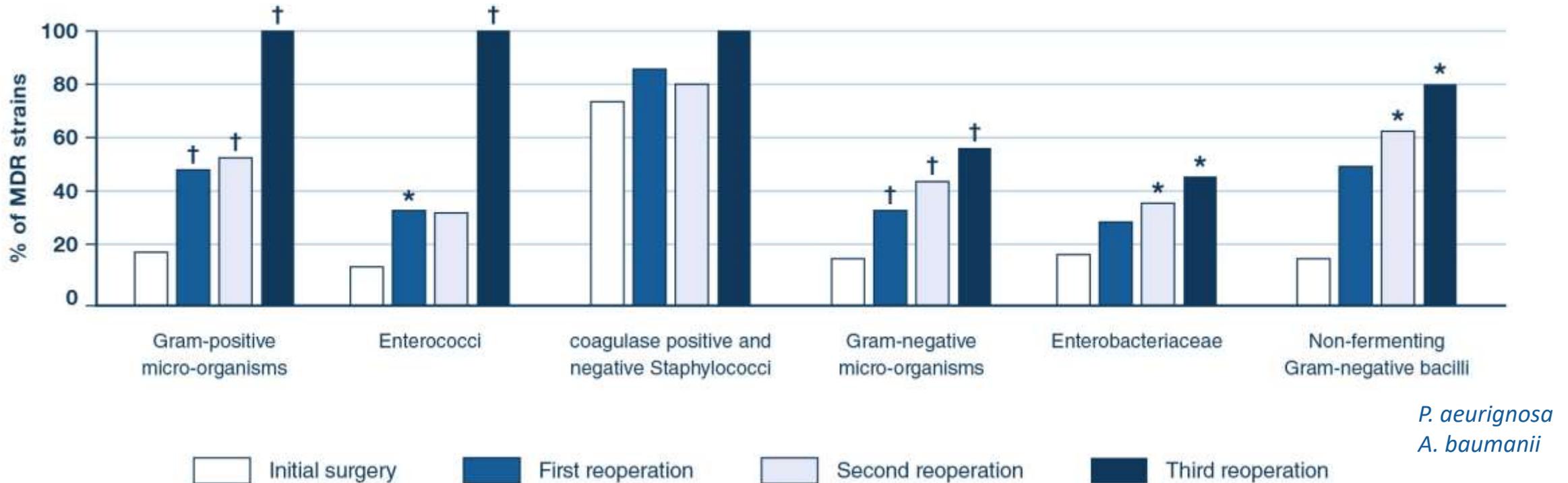
rétrospective monocentrique n =422 1999-2019



avantage des associations avec pénèmes car augmentation de l'incidence des Enterobacterales BLSE

Remarque sur la multirésistance = IIA tertiaires

monocentrique, n = 122



non-éradication du foyer favorise péritonites tertiaires et sélection de multi-résistances

IIA Liées aux soins = FdR classique de BGN multi-R

Box 18.1 Risk factors and clinical scenarios with increased likelihood of multidrug-resistant (MDR) pathogens in intra-abdominal infections [65–70]

Risk factors for recovery of multidrug-resistant bacteria in patients with intra-abdominal infections

Healthcare-associated infection (outpatient intravenous treatment, wound treatment, antineoplastic therapies, hemodialysis, nursing home residents)

Recent exposure to broad-spectrum antibiotics (<3 months)

Length of hospitalization >5 days

Prior or current admission in intensive care unit

Liver disease

Pulmonary disease

Diabetic foot infection with antibiotic use

Organ transplantation

Corticosteroid use

Patient receiving immunosuppressive agents

Patient with recent exposure in areas with MDR prevalence in the community or in environmental sources

Patient hospitalized in areas with MDR prevalence

Postoperative peritonitis

Long time between first and second surgery

Tertiary peritonitis

Recurrent interventions in the biliary tract

Pretreated necrotizing pancreatitis

Péritonite post-opératoire

Péritonite tertiaire

Les multirésistances des BGN...et les nouvelles molécules

	<i>Enterobacteriaceae</i>					<i>Pseudomonas aeruginosa</i>			<i>Acinetobacter spp.</i>	
	ESBL	AmpC	Class-A CBP	mCBP	Class-D CBP	WT	MDR	mCBP	WT	MDR
Ceftolozane-tazobactam	+	IE	-	-	-	+	+	-	-	-
Ceftazidime-avibactam	+	+	+	-	+	+	+	-	-	-
Meropenem-vaborbactam	+	+	+	-	-	+	IE	-	+	-
Imipenem-relebactam	+	+	+	-	IE	+	IE	-	+	-
Plazomycin	+	+	+	+	IE	-	-	-	-	-
Eravacycline	+	+	+	+	+	-	-	-	+	IE
(céfidéocol)	+	+	+	+	+	+	+	+		

Nouveaux ATB : spectres

BL-IBL / AMM	Ambler Blase Enzymes	<i>Enterobacterales</i>					<i>P. aeruginosa</i>	<i>A. baumannii</i>
		Classe A BLSE (TEM, SHV, CTX-M)	Classe C Sérine AmpC	Classe A Sérine KPC	Classe D Sérine OXA-48	Classe B Métallo (MBL) (NDM, VIM, IMP)	CARB-R / DTR (AmpC, OXA, VIM)	ABRI (OXA-23, NDM)
ceftazidime		Red	Red	Red	Green	Red	Red	Red
cefepime		Red	Yellow *	Red	Green	Red	Red	Red
aztreonam		Red	Red	Red	Green	Green	Red	Red
carbapenemes		Green	Green	Red	Yellow *	Red	Red	Red
ceftolozane/tazobactam	2015	Green	Yellow	Red	Red	Red	Green *	Red
meropenem/vaborbactam	2020	Green	Green	Green	Red	Red	Red	Red
imipenem/relebactam	2021	Green	Green	Green	Red	Red	Light Green *	Red
ceftazidime/avibactam	2016	Green	Green	Green	Green	Red	Green *	Red
cefepime/enmetazobactam	2024	Green	Green	Yellow	Green	Red	Red	Red
aztreonam/avibactam	2024	Green	Green	Green	Green	Green	Yellow	Red
(cefiderocol)	2021	Green	Green	Green	Green	Sauf NDM	Sauf NDM	Sauf NDM
sulbactam/durlobactam	(2023 FDA)	Light Green	Light Green	Light Green	Light Green	?	Red	Green
eravacycline	2024	Green	Green	Green	Green	Green	Red	Green

Attention aux anaérobies !

BL-IBL / AMM

ANAEROBIES !

ceftazidime		
cefepime		
aztreonam		
carbapenemes		
ceftolozane/tazobactam	2015	
meropenem/vaborbactam	2020	
imipenem/relebactam	2021	
ceftazidime/avibactam	2016	
cefepime/enmetazobactam	2024	
aztreonam/avibactam	2024	
(cefiderocol)	2021	
sulbactam/durlobactam	(2023 FDA)	
eravacycline	2024	

***+ metronidazole pour
toutes les associations non-carbapénèmes
hors tigecycline/éravacycline***

Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

								CRE-MBL	Current clinical indications/approval
New antibiotics									
Ceftolozane-tazobactam							No	FDA and EMA approved for cUTI, cIAI, HAP and VAP	
Ceftazidime-avibactam							No	FDA and EMA approved for cIAI and cUTI, HAP and VAP, and (in EMA only) for the treatment Gram-negative infections in patients with limited treatment options	
Meropenem-vaborbactam	No	Yes	No	+/-	Yes	No	No	FDA approved for cUTI, EMA approved for cUTI, HAP and VAP, and for the treatment Gram-negative infections in patients with limited treatment options	
Imipenem-cilastatin/relebactam	No	Yes	Yes	+/-	Yes	No	No	FDA approved for cUTI and cIAI; EMA approved for HAP and VAP and for BSI with a suspected respiratory source, and for the treatment Gram-negative infections in patients with limited treatment options	
Plazomicin	No	Yes	+/-	Yes	Yes	Yes	+/-	FDA approval cUTI, EMA application withdrawn	
Eravacycline	Yes	Yes	No	Yes	Yes	Yes	Yes	FDA and EMA approved for cIAI	
Cefiderocol	Yes	FDA cUTI, HAP and VAP; EMA for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options							

Ceftazidime-avibactam et IIA (AMM poolées)

Etudes poolées d'AMM, toutes randomisées contrôlées notamment RECLAIM/RECLAIM 3 (cIAI) vs. meropenem REPRISE (cIAI/cUTI) vs. BAT

Patients, n (%)	cIAI	
	Ceftazidime/ avibactam + metronidazole (n = 103)	Comparator (n = 128)
Clinical response		
Clinical cure	88 (85.4)	110 (85.9)
95% CI ^a	77.7–91.2	79.1–91.1
Clinical failure	7 (6.8)	3 (2.3)
Indeterminate	8 (7.8)	15 (11.7)
Microbiological response		
Favourable	88 (85.4)	110 (85.9)
95% CI ^a	77.7–91.2	79.1–91.1
Unfavourable	7 (6.8)	3 (2.3)
Indeterminate	8 (7.8)	15 (11.7)

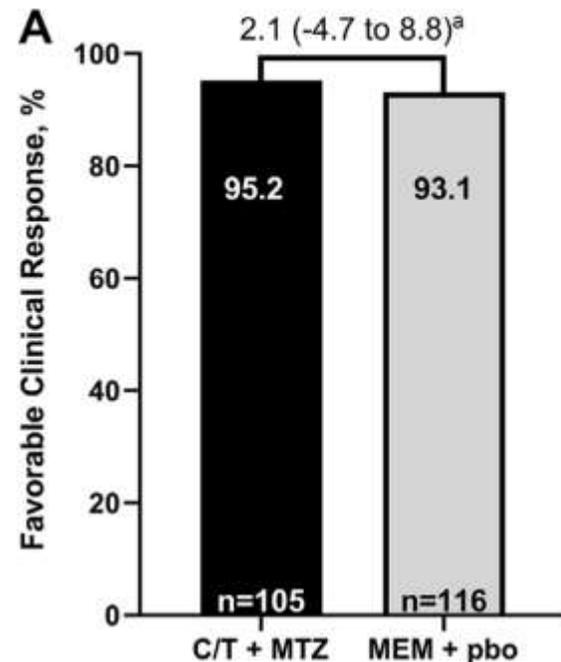
Patients, n/N (%)	cIAI	
	Ceftazidime/ avibactam + metronidazole (n = 103)	Comparator (n = 128)
Enterobacterales (all)	86/101 (85.1)	109/127 (85.8)
<i>C. freundii</i> complex	0/1 (0.0)	2/2 (100)
<i>Enterobacter aerogenes</i>	0/0	1/1 (100)
<i>E. cloacae</i>	6/7 (85.7)	6/8 (75.0)
<i>E. coli</i>	62/75 (82.7)	83/96 (86.5)
<i>K. pneumoniae</i>	23/27 (85.2)	16/21 (76.2)
<i>P. mirabilis</i>	3/3 (100)	3/3 (100)
<i>Serratia marcescens</i>	2/2 (100)	1/1 (100)
Other Gram-negative pathogens (all)	7/11 (63.6)	12/12 (100)
<i>P. aeruginosa</i>	3/7 (42.9)	12/12 (100)

Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

								CRE-MBL	Current clinical indications/approval
New antibiotics									
Ceftolozane-tazobactam								No	FDA and EMA approved for cUTI, cIAI, HAP and VAP
Ceftazidime-avibactam								No	FDA and EMA approved for cIAI and cUTI, HAP and VAP, and (in EMA only) for the treatment Gram-negative infections in patients with limited treatment options
Meropenem-vaborbactam	No	Yes	No	+/-	Yes	No	No	FDA approved for cUTI, EMA approved for cUTI, HAP and VAP, and for the treatment Gram-negative infections in patients with limited treatment options	
Imipenem-cilastatin/relebactam	No	Yes	Yes	+/-	Yes	No	No	FDA approved for cUTI and cIAI; EMA approved for HAP and VAP and for BSI with a suspected respiratory source, and for the treatment Gram-negative infections in patients with limited treatment options	
Plazomicin	No	Yes	+/-	Yes	Yes	Yes	+/-	FDA approval cUTI, EMA application withdrawn	
Eravacycline	Yes	Yes	No	Yes	Yes	Yes	Yes	FDA and EMA approved for cIAI	
Cefiderocol	Yes	FDA cUTI, HAP and VAP; EMA for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options							

Ceftolozane-avibactam et IIA (AMM poolées)

Essai randomisé contrôlé
ceftolozane –tazobactam + MTZ vs. meropenem



Characteristics	C/T + metronidazole (N=134)	Meropenem + placebo (N=134)
Male, n (%)	79 (59.0)	85 (63.4)
Age, n (%)		
≤65 y	108 (80.6)	103 (76.9)
66-75 y	26 (19.4)	31 (23.1)
Median (range), y	48.0 (18-75)	55.0 (18-74)
APACHE II score		
Mean (SD)	4.9 (3.1)	5.1 (2.8)
Category, n (%)		
<10	119 (88.8)	126 (94.0)
≥10	15 (11.2)	8 (6.0)

Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

									Current clinical indications/approval
New antibiotics									
Ceftolozane-tazobactam									FDA and EMA approved for cUTI, cIAI, HAP and VAP
Ceftazidime-avibactam									FDA and EMA approved for cIAI and cUTI, HAP and VAP, and (in EMA only) for the treatment Gram-negative infections in patients with limited treatment options
Meropenem-vaborbactam									FDA approved for cUTI, EMA approved for cUTI, HAP and VAP, and for the treatment Gram-negative infections in patients with limited treatment options
Imipenem-cilastatin/relebactam									FDA approved for cUTI and cIAI; EMA approved for HAP and VAP and for BSI with a suspected respiratory source, and for the treatment Gram-negative infections in patients with limited treatment options
Plazomicin	No	Yes	+/-	Yes	Yes	Yes	+/-	FDA approval cUTI, EMA application withdrawn	
Eravacycline	Yes	Yes	No	Yes	Yes	Yes	Yes	FDA and EMA approved for cIAI	
Cefiderocol	Yes	FDA cUTI, HAP and VAP; EMA for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options							

Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

								Current clinical indications/approval
New antibiotics								
Ceftolozane-tazobactam	No	Yes		No	No	No	No	FDA and EMA approved for cUTI, cIAI, HAP and VAP
Ceftazidime-avibactam	No	Yes		+/-	Yes	Yes	No	FDA and EMA approved for cIAI and cUTI, HAP and VAP, and (in EMA only) for the treatment Gram-negative infections in patients with limited treatment options
Meropenem-vaborbactam	No	Yes		+/-	Yes	No	No	FDA approved for cUTI, EMA approved for cUTI, HAP and VAP, and for the treatment Gram-negative infections in patients with limited treatment options
Imipenem-cilastatin/relebactam	No	Yes		+/-	Yes	No	No	FDA approved for cUTI and cIAI; EMA approved for HAP and VAP and for BSI with a suspected respiratory source, and for the treatment Gram-negative infections in patients with limited treatment options
Plazomicin	No	Yes		Yes	Yes	Yes	+/-	FDA approval cUTI, EMA application withdrawn
Eravacycline								FDA and EMA approved for cIAI
Cefiderocol	Yes	FDA cUTI, HAP and VAP; EMA for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options						

Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

	Green		Red	Green				Current clinical indications/approval
Old antibiotics								
Polymyxins	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA: serious infections caused by susceptible strains, when less potentially toxic drugs are ineffective or contraindicated. EMA: treatment of serious infections due to aerobic Gram-negative pathogens in patients with limited treatment options
Aminoglycosides	+/-	+/-	+/-	+/-	+/-	+/-	+/-	EMA and FDA: for the treatment of a variety of bacterial infections
Fosfomycin iv	No	Yes	+/-	+/-	+/-	+/-	+/-	EMA: to treat serious infections when other antibiotic treatments are not suitable. FDA: under review
Aztreonam	No	No	+/-	No	No	No	+/-	EMA and FDA: for the treatment of infections caused by susceptible Gram-negative microorganisms
Tigecycline	Green		Red	Green				EMA and FDA: complicated SSTI and IAI (FDA also CAP)
Temocillin	No	Yes	No	No	+/-	No	No	EMA and FDA: orphan drug status for the treatment of infections caused by <i>Burkholderia cepacia</i> in patients with cystic fibrosis

Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

								Current clinical indications/approval
New antibiotics								
Ceftolozane-tazobactam	No	Yes	Yes	No	No	No	No	FDA and EMA approved for cUTI, cIAI, HAP and VAP
Ceftazidime-avibactam	No	Yes	Yes	+/-	Yes	Yes	No	FDA and EMA approved for cIAI and cUTI, HAP and VAP, and (in EMA only) for the treatment Gram-negative infections in patients with limited treatment options
Meropenem-vaborbactam	No	Yes	No	+/-	Yes	No	No	FDA approved for cUTI, EMA approved for cUTI, HAP and VAP, and for the treatment Gram-negative infections in patients with limited treatment options
Imipenem-cilastatin/relebactam	No	Yes	Yes	+/-	Yes	No	No	FDA approved for cUTI and cIAI; EMA approved for HAP and VAP and for BSI with a suspected respiratory source, and for the treatment Gram-negative infections in patients with limited treatment options
Plazomicin	No	Yes	+/-	Yes	Yes	Yes	+/-	FDA approval cUTI, EMA application withdrawn
Eravacycline	Yes	Yes	No	Yes	Yes	Yes	Yes	FDA and EMA approved for cIAI
Cefiderocol								FDA cUTI, HAP and VAP; EMA for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options

Aztreonam-avibactam (ATM-AVI) : étude REVISIT

Essai

- Randomisé contrôlé
- Monde, 81 centres, 20 pays
- **n = 422**

Foyers

- **PAVM/PAS** 26%
- **IIAc** appendicites 50%
- cholecystites 16%

Pathogènes/R

- **PAVM/PAS** *Kp/Pa* 54%/20%
- **IIAc** *E. coli* 78%
- **BLSE/KPC/MBL** 9%/2%/1%

Gravité

- **APACHE moy** = 10
 - PAVM/PAS = 17
 - IIAc = 7,6

ABx / comparateurs

aztreonam-avibactam
(+ metronidazole si IIAc)

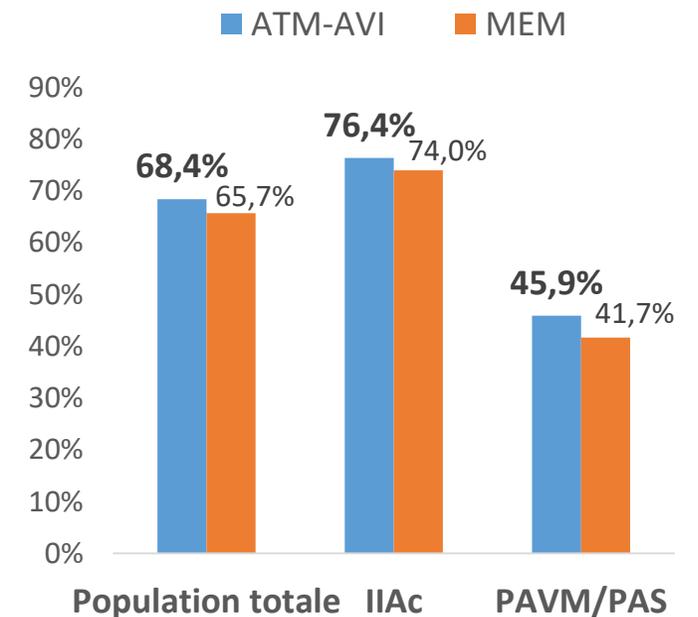
vs.

meropenem
(± colistine)

Objectif principal

- **Guérison clinique j28**

Résultat



Guérison clinique j28

- **PAS d'analyse de non-inf ou sup !**

Aztreonam-avibactam (étude d'AMM - REVISIT)

Essai randomisé contrôlé multicentrique n = 422
 aztreonam-avibactam vs. meropenem ± colistine
 cIAI ou HAP/VAP

	cIAI	
	Aztreonam-avibactam group (n=208)	Meropenem group (n=104)
APACHE II score category*		
≤10	162 (78%)	80 (77%)
>10	46 (22%)	24 (23%)
Primary cIAI diagnosis		
Acute gastric or duodenal perforations	16 (8%)	10 (10%)
Appendiceal perforation or peri-appendiceal abscess	106 (51%)	49 (47%)
Cholecystitis-gangrenous rupture or perforation or progression beyond gallbladder wall	30 (14%)	19 (18%)
Diverticular disease with perforation or abscess	15 (7%)	6 (6%)
Intra-abdominal abscess	26 (13%)	13 (13%)
Other secondary peritonitis	11 (5%)	4 (4%)
Traumatic perforation of the intestines	4 (2%)	3 (3%)

	cIAI		
	Aztreonam-avibactam group	Meropenem group	Difference, % (95% CI)
ITT analysis set	159/208 (76.4%, 70.3 to 81.8)	77/104 (74.0%, 65.0 to 81.7)	2.4% (-7.4 to 13.0)
CE analysis set	143/168 (85.1%, 79.2 to 89.9)	66/83 (79.5%, 69.9 to 87.1)	5.6% (-4.0 to 16.6)

Les limites des études ATB et IIA...et du raisonnement

- Gravité très variable (souvent modérée, péritonites appendiculaires)
- Effet écrasant de l'éradication de la source
- IIA = polymicrobiens (même si non apparent car culture = sélection)

Exemple : eravacycline vs. meropénème (IGNITE 4)

Population	Eravacycline	Meropenem	Difference (95% Confidence Interval)
Modified intent-to-treat	N = 250	N = 249	...
Clinical cure	231 (92.4)	228 (91.6)	0.8 (-4.1, 5.8)
Clinical failure	7 (2.8)	9 (3.6)	...

non-infériorité
92% de succès

Actual primary disease diagnosis		
Complicated appendicitis, n (%)	94 (48.2)	90 (43.9)
Other complicated intra-abdominal infection	101 (51.8)	115 (56.1)
Diagnosed and enrolled preoperatively	7 (3.6)	11 (5.4)
Diagnosed intra-/postoperatively	188 (96.4)	194 (94.6)
Intra-abdominal abscess(es) ^a	119 (63.3)	110 (56.7)
Peritonitis	94 (50.0)	95 (49.0)
Gastric/duodenal perforation	11 (5.9)	12 (6.2)
Complicated cholecystitis	40 (21.3)	45 (23.2)
Perforation of small intestine	7 (3.7)	7 (3.6)
Complicated appendicitis	93 (49.5)	91 (46.9)
Perforation of large intestine	8 (4.3)	12 (6.2)
Diverticulitis with perforation, peritonitis, or abscess	5 (2.7)	7 (3.6)
Other	0	2 (1.0)

50% d'appendicites compliquées

peu graves (SAPS II = 6)

Recommandations ESCMID/ESICM antibiothérapie BGN Multi-R

	ESCMID				ESICM				Current clinical indications/approval
New antibiotics									
Ceftolozane-tazobactam	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA and EMA approved for cUTI, cIAI, HAP and VAP
Ceftazidime-avibactam	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA and EMA approved for cIAI and cUTI, HAP and VAP, and (in EMA only) for the treatment Gram-negative infections in patients with limited treatment options
Meropenem-vaborbactam	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA approved for cUTI, EMA approved for cUTI, HAP and VAP, and for the treatment Gram-negative infections in patients with limited treatment options
Imipenem-cilastatin/ relebactam	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA approved for cUTI and cIAI; EMA approved for HAP and VAP and for BSI with a suspected respiratory source, and for the treatment Gram-negative infections in patients with limited treatment options
Plazomicin	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA approval cUTI, EMA application withdrawn
Eravacycline	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA and EMA approved for cIAI
Cefiderocol	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	FDA cUTI, HAP and VAP; EMA for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options

Exemple : eravacycline vs. meropénème (IGNITE 4)

Table 6. Clinical Cure at the Test-of-cure Visit by Baseline Pathogen: Microbiological Intent-to-treat Population

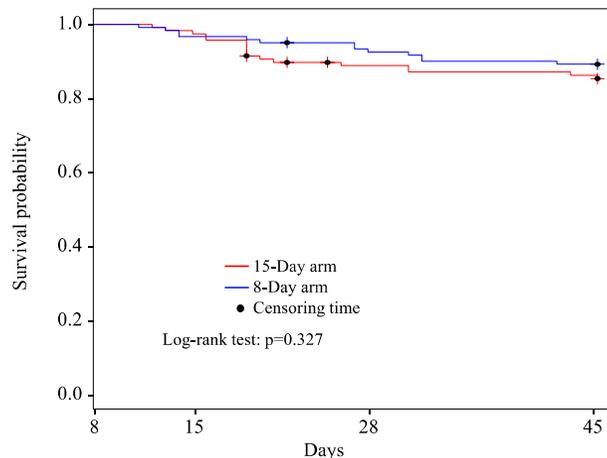
Baseline Pathogen ^a	Eravacycline (N = 195)	Meropenem (N = 205)
Gram-negative aerobes	141/158 (89.2)	153/166 (92.2)
Enterobacteriaceae	129/146 (88.4)	142/154 (92.2)
<i>Escherichia coli</i>	111/126 (88.1)	125/134 (93.3)
<i>Klebsiella pneumoniae</i>	21/21 (100.0)	23/27 (85.2)
Non-enterobacteriaceae	36/38 (94.7)	28/30 (93.3)
<i>Acinetobacter baumannii</i> complex	5/5 (100.0)	2/2 (100.0)
<i>Pseudomonas aeruginosa</i>	18/19 (94.7)	18/20 (90.0)



**eravacycline est inactive sur Pa
et néanmoins...94% de guérison clinique !**

Durée de l'antibiothérapie des IIA en réa

Etude DURAPOP
21 réanimations, France
8j vs. 15j
succès éradication source +



Number at risk (number censored)	8	15	28	45
8-Day arm	120 (0)	118 (0)	111 (1)	107 (100)
15-Day arm	116 (0)	114 (0)	101 (3)	97 (92)

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 x 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 (%) ^g	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 (%) ^h	23/104 (22)	20/107 (19)	0.81 (0.39—1.67)	0.54
Emergence of MDR bacteria in clinical isolates, n (%) ⁱ	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 (%) ^j	52/104 (50)	46/108 (43)	0.74 (0.41—1.32)	0.28
Emergence of fungi, n (%) ^k	27/106 (25)	22/107 (21)	0.75 (0.37—1.51)	0.39

Durée courte 8j

Conclusions...plus de questions que de réponses

- Les classifications ont peu de sens et les études sont à revoir et homogénéiser en fonction de
 - **éradication** du foyer/succès ou non
 - **gravité** choc septique/sepsis
 - **effraction** digestive/péritonite
 - \pm nosocomial tardif/précoce/communautaire
- Impact de l'antibiothérapie très difficile à déterminer,
 - uniquement si éradication avec succès
 - **possible rôle dans les tertiaires/persistantes (et donc R ou multi-R)**

Conclusions...en pratique, IIA en réanimation = grave et/ou noso

- **piperacilline/tazobactam + aminoside (si noso et/ou FdR Pa = amikacine)**

ou

- **pénème + aminoside (surtout si FdR multi-R : post-op, tertiaires...)**
- **± nouvelles molécules**
 - si colonisation MDR connue avec ATB gramme
 - si écologie locale particulièrement MDR
- entérocoques ?
- **levures (échinocandines...& wait for CASPER)**

Conclusion – Antibiothérapie des IIA liées aux soins

ERADICATION DU FOYER



Antibiothérapie

