JNI 21es Journées Nationales d'Infectiologie
Poitiers
et la région Nouvelle Aquitaine
Palais des Congrès du Futuroscope
du mercredi 9 septembre 2020
au vendredi 11 septembre 2020

Prise en charge des IOA complexes à l'ère des Bacilles à Gram négatif MDR

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Centre de Référence des IOA complexes de Lyon (CRIOAc Lyon)

Déclaration d'intérêts de 2014 à 2019

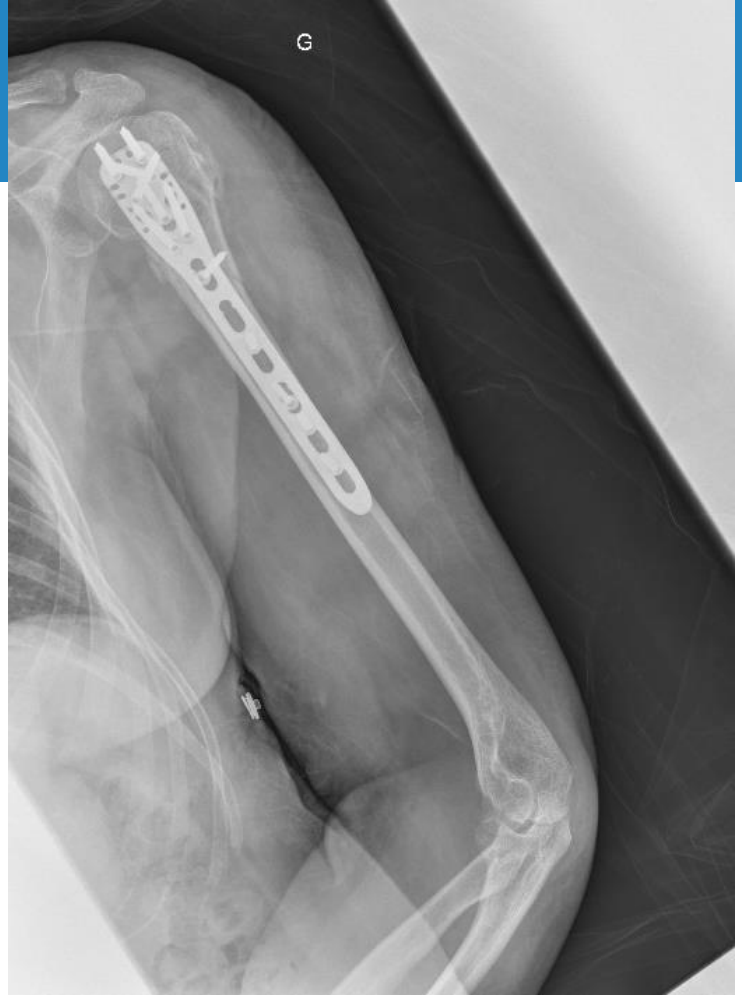
- Intérêts financiers : Aucun
- Liens durables ou permanents : Aucun
- Interventions ponctuelles : Pfizer, Sanofi, Debiopharm, Contrafect, MaaT Pharma, Heraeus, Atlangram
- Intérêts indirects : Astellas, Pfizer, MSD

Cas clinique n° 1

- Patiente de 70 ans, 45 kg
- Cancer du sein en 2011, HTA
- Fracture humérale gauche lors d'un voyage en Ouzbékistan (AVP)
- Ostéosynthèse en Turquie
- Séjour en réanimation avec pneumonie nosocomiale (traitement par colistine-tigécycline)

Rappatriement à Lyon 1 mois plus tard

- Ecoulement de la cicatrice humérale
- Reprise chirurgicale, ablation du matériel
- Abcès, pus franc, fracture encore non consolidée
- Antibiothérapie post-opératoire par céfépime-vancomycine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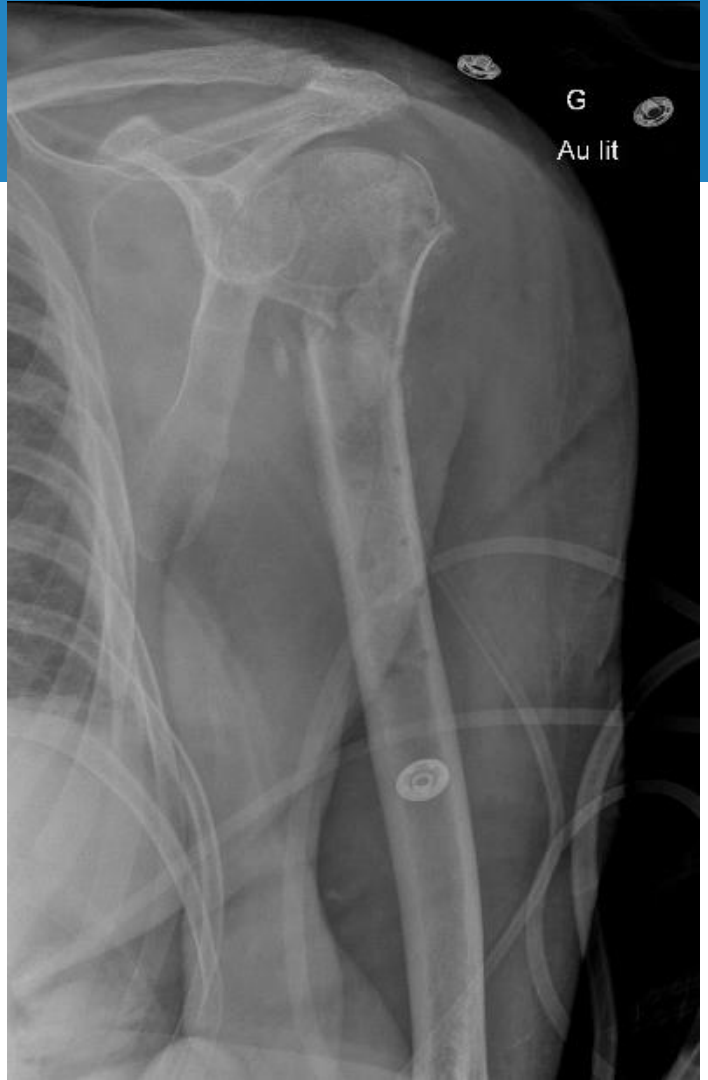
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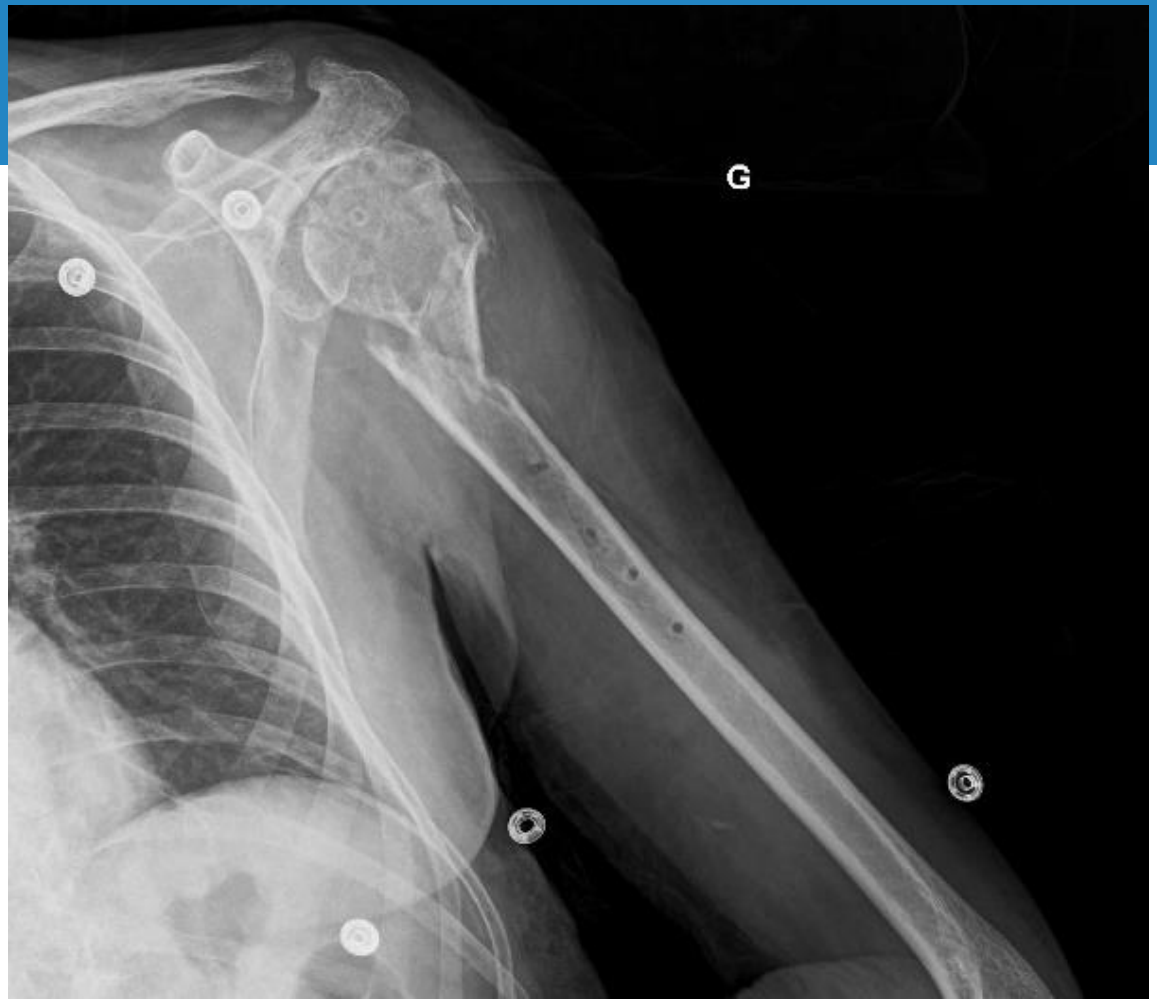
Au lit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	Klebsiella pneumoniae CMI (mg/l)
Ampicilline	R
Amoxicilline	R
Amoxicilline + Ac.Clavulanique	R
Ticarcilline	R
Ticarcilline + Ac. Clav	R
Temocilline	R
Pipéracilline	
Pipéracilline + Tazobactam	
Céfoxitine	R
Céfotaxime	R
Ceftazidime	R
Céfépime	
Aztréonam	
Ertapénème	R
Imipénème	S
Meropeneme	R
Gentamicine	R
Tobramycine	R
Amikacine	R
Tigécycline	S
Norfloxacine	R
Ciprofloxacine	R
Moxifloxacine	R
Acide Nalidixique	R
Cotrimoxazole	R

R

Fosfomycine (Etest)	S CMI : 64
Aztreonam (Etest)	R CMI : > 256
Cefepime (Etest)	R CMI : 64
Imipeneme (Etest)	S CMI : 0.380
Meropeneme (Etest)	R CMI : > 32
Tobramycine (Etest)	S CMI : 0.250
Tigecycline (Etest)	S CMI : 0.250
Ceftolozane-tazobactam (Etest)	R CMI : > 256
Ceftazidime-Avibactam (Etest)	R CMI : > 256
Colistine (UMIC)	R CMI : 64

CMI par E-test Aztréonam + Ceftazidime/Avibactam : 0.19 mg/L.

Adaptation thérapeutique

- Aztréonam 2g/8h – Ceftazidime/avibactam 2g/8h – Daptomycine
- Aztréonam 2g/8h – Ceftazidime/avibactam 2g/8h – Fosfomycine 3g en 3h/8h

Adaptation thérapeutique

- Aztréonam 2g/8h – Ceftazidime/avibactam 2g/8h – Daptomycine

- Aztréonam 2g/8h – Ceftazidime/avibactam 2g/8h – Fosfomycine 3g en 3h/8h

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- Aztréonam 3g dans un diffuseur sur 12h – Ceftazidime/avibactam 3g dans un diffuseur sur 12h

Aztréonam + Ceftazidime/avibactam ?

Can Ceftazidime-Avibactam and Aztreonam Overcome β-Lactam Resistance Conferred by Metallo-β-Lactamases in *Enterobacteriaceae*?

Steven Marshall,[a] Andrea M. Hujer,[a,b] Laura J. Rojas,[a,b,c] Krisztina M. Papp-Wallace,[a] Romney M. Humphries,[d] Brad Spellberg,[e] Kristine M. Hujer,[a,b] Emma K. Marshall,[a] Susan D. Rudin,[a,b] Federico Perez,[a] Brigid M. Wilson,[a] Ronald B. Wasserman,[f] Linda Chikowski,[g] David L. Paters Alejandro J. Vila,[i] David van Duin,[j] Barry N. Kreiswirth,[k] Henry F. Chambers Vance G. Fowler, Jr.,[m] Michael R. Jacobs,[n] Mark E. Pulse,[o] William J. Weiss,[c] Robert A. Bonomo[a,b,c,p]

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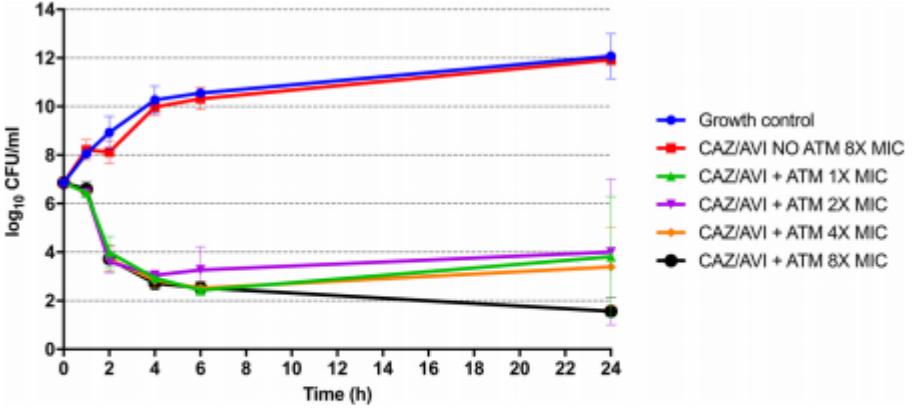

FIG 2 Time-kill curve for *K. pneumoniae* isolate 1.41. ATM concentrations were held constant at 8 μg/ml for all combinations, with two exceptions: (i) the growth control (no antibiotics added) and (ii) CAZ-AVI with no ATM at 8× the MIC. Various ceftazidime-avibactam (CAZ-AVI) concentrations were added corresponding to 1× (1 μg/ml CAZ plus 0.25 μg/ml AVI), 2× (2 μg/ml CAZ plus 0.5 μg/ml AVI), 4× (4 μg/ml CAZ plus 1 μg/ml AVI), and 8× (8 μg/ml CAZ plus 2 μg/ml AVI) the MIC of the combination CAZ-AVI plus ATM obtained by agar dilution (1 μg/ml). Three replicates were conducted for each of the conditions reported in the time-kill assay.

K. Pneumoniae NDM-1, CTX-M-15, DHA, SHV, TEM

Aztréonam + Ceft

Aztreonam plus Clavulanate, Tazob Treatment of Infections Caused by Producing Gram-Negative Bacteria

Cécile Emeraud,[a,b,c,d] Lelia Escaut,[e] Athénaïs Boucly,[d,f,g] Nicolas Fortin
Laurent Dortet[a,b,c,d]

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TABLE 2 MICs and categorization according to CLSI breakpoints for antimicrobials on MBL-producing *Enterobacteriaceae*, MBL-producing *P. aeruginosa*, and *S. maltophilia*

		MICs (mg/liter) by treatment[a]						
Enterobacteriaceae sp.	β-Lactamases	ATM	CZA	C/T	AMC	ATM+ CZA	ATM+ C/T	ATM+ AMC
E. coli	NDM-1 + OXA-1 + OXA-10 + CMY-16 + TEM-1	32	>256	>256	16	0.125	24	8
E. coli	NDM-1 + CTX-M-15 + TEM-1	>256	>256	>256	12	1	>256	2
E. coli	NDM-1 + OXA-1 + OXA-2 + CTX-M-15 + TEM-1	>256	>256	>256	24	2	>256	8
E. coli	NDM-1 + CTX-M-15 + TEM-1	>256	>256	>256	32	6	>256	8
E. coli	NDM-4 + CTX-M-15 + OXA-1	>256	>256	>256	96	6	>256	4
E. coli	NDM-4 + CTX-M-15 + CMY-6	>256	>256	>256	>256	6	>256	24
E. coli	NDM-5 + TEM-1 + CTX-M-15	>256	>256	>256	96	8	>256	64
E. coli	NDM-6 + CTX-M-15 + OXA-1	>256	>256	>256	16	1	>256	2
E. coli	NDM-7 + ESBL	>256	>256	>256	96	4	>256	32
K. pneumoniae	NDM-1 + CTX-M-15 + SHV-11 + OXA-1	>256	>256	>256	12	0.125	24	0.38
K. pneumoniae	NDM-1 + CTX-M-15 + CMY-4 + OXA-1	>256	>256	>256	32	0.75	>256	16
K. pneumoniae	NDM-1 + CTX-M-15 + OXA-1 + OXA-9 + TEM-1 + SHV-28 + SHV-11	>256	>256	>256	32	0.25	>256	3
K. pneumoniae	NDM-1 + OXA-1 + SHV-11	>256	>256	>256	12	0.047	0.094	0.094
K. pneumoniae	NDM-1 + OXA-1 + CTX-M-15 + TEM-1 + SHV-28 + OXA-9 + CMY-6	>256	>256	>256	16	0.047	3	0.25
K. pneumoniae	NDM-1 + TEM-1 + CTX-M-15 + SHV-12 + OXA-9	>256	>256	>256	12	0.125	96	1
K. pneumoniae	NDM-1 + TEM-1 + CTX-M-15 + SHV-12 + OXA-9	>256	>256	>256	12	0.125	96	0.5
K. pneumoniae	NDM-1 + TEM-1 + CTX-M-15 + SHV-11 + OXA-1	>256	>256	>256	12	0.064	8	0.38
Salmonella enterica	NDM-1 + CTX-M-15 + TEM-1 + OXA-1 + OXA-9 + OXA-10	>256	>256	>256	16	0.125	16	0.5
E. coli	VIM-1 + CTX-M-3	>256	>256	>256	16	0.125	24	0.5
E. coli	VIM-4 + ESBL	16	>256	>256	24	1.5	24	16
K. pneumoniae	VIM-1 + SHV-5	>256	>256	>256	>256	0.25	192	1.5
K. pneumoniae	VIM-1 + SHV-12	>256	>256	>256	16	0.125	4	0.25
K. pneumoniae	VIM-1 + ESBL	>256	>256	>256	>256	12	16	12
K. pneumoniae	VIM-1 + SHV-5	16	>256	>256	>256	6	12	32
K. pneumoniae	VIM-1 + TEM-1 + SHV-5	96	>256	>256	>256	96	64	48
K. pneumoniae	VIM-1 + SHV-5	>256	>256	>256	24	0.25	8	0.75
K. pneumoniae	VIM-1 + SHV-5	>256	>256	>256	12	0.125	2	0.38
K. pneumoniae	VIM-19 + CTX-M-3 + TEM-1 + SHV-1	6	32	>256	16	0.047	2	1.5
Enterobacter cloacae	VIM-1 + SHV-70	256	128	>256	48	0.094	0.25	0.19
E. cloacae	VIM-4 + CTX-M-15 + TEM-1 + SHV-31	64	>256	>256	64	1	64	32
Citrobacter freundii	VIM-2 + TEM-1 + ESBL	16	16	>256	32	0.25	2	24
C. freundii	VIM-2 + TEM-1 + OXA-9 + OXA-10	32	24	>256	32	1.5	16	24
E. coli	IMP-8 + SHV-12	128	>256	>256	24	0.19	2	0.38
K. pneumoniae	IMP-8 + SHV-12	>256	48	>256	12	0.094	32	0.25
E. cloacae	IMP-8 + SHV-12	12	>256	>256	24	0.032	0.064	0.094
E. cloacae	GIM-1 + ESBL	12	>256	48	24	0.5	8	16
Enterobacter hormaechei	TMB-1 + overexpressed Case[b]	64	64	32	32	0.5	12	12
C. freundii	TMB-1 + overexpressed Case	64	96	32	12	0.125	12	12
K. pneumoniae	NDM-1 + OXA-181 + SHV-11 + TEM-1 + CTX-M-15 + OXA-1	64	>256	>256	48	0.094	8	2
K. pneumoniae	NDM-1 + OXA-181 + SHV-27 + CTX-M-15 + TEM-1 + OXA-1	128	>256	>256	96	0.25	16	3
K. pneumoniae	NDM-1 + OXA-181 + SHV-11 + CTX-M-15 + OXA-1	256	>256	>256	>256	0.19	32	3
K. pneumoniae	NDM-1 + OXA-181 + SHV-11 + TEM-1 + CTX-M-15 + OXA-9	>256	>256	>256	>256	0.19	>256	12
K. pneumoniae	NDM-1 + OXA-181 + SHV-2 + CTX-M-15 + OXA-1	>256	>256	>256	32	0.125	32	1.5
C. freundii	NDM-1 + OXA-181 + OXA-1 + OXA-9 + OXA-10 + CTX-M-15 + TEM-1	>256	>256	>256	64	0.75	>256	12
E. coli	NDM-1 + OXA-48 + ESBL	32	>256	>256	48	0.094	12	8
E. coli	NDM-1 + OXA-48 + ESBL	>256	>256	>256	>256	0.75	>256	4
E. coli	NDM-1 + OXA-48 + ESBL	>256	>256	>256	>256	1	>256	4
K. pneumoniae	NDM-1 + OXA-232 + ESBL	64	>256	>256	>256	0.094	24	3
E. coli	NDM-1 + OXA-232 + ESBL	>256	>256	>256	>256	1	>256	8
E. coli	NDM-5 + OXA-232 + ESBL	>256	>256	>256	96	1	>256	64
S. maltophilia		>256	>256	>256	32	2	128	2
S. maltophilia		>256	>256	6	96	1.5	6	2
S. maltophilia		>256	>256	>256	>256	4	>256	4
S. maltophilia		>256	16	72	16	1	8	2
S. maltophilia		>256	>256	>256	>256	0.75	24	0.75
P. aeruginosa	VIM-2 + overexpressed cephalosporinase	16	24	>256	>256	8	12	16
P. aeruginosa	IMP-2 + overexpressed cephalosporinase	12	>256	>256	>256	6	12	24
P. aeruginosa	IMP-1 + overexpressed cephalosporinase	128	>256	>256	>256	96	48	64

Aztréonam + Ceftazidime/avibactam ?

TABLE 2 MICs and categorization according to CLSI breakpoints for antimicrobials on MBL-producing *Enterobacteriaceae*, MBL-producing *P. aeruginosa*, and *S. maltophilia*

Enterobacteriaceae sp.	β-Lactamases	MICs (mg/liter) by treatment[a]						
		ATM	CZA	C/T	AMC	ATM+ CZA	ATM+ C/T	ATM+ AMC
K. pneumoniae	NDM-1 + CTX-M-15 + SHV-11 + OXA-1	>256	>256	>256	12	0.125	24	0.38
K. pneumoniae	NDM-1 + CTX-M-15 + CMY-4 + OXA-1	>256	>256	>256	32	0.75	>256	16
K. pneumoniae	NDM-1 + CTX-M-15 + OXA-1 + OXA-9 + TEM-1 + SHV-28 + SHV-11	>256	>256	>256	32	0.25	>256	3
K. pneumoniae	NDM-1 + OXA-1 + SHV-11	>256	>256	>256	12	0.047	0.094	0.094
K. pneumoniae	NDM-1 + OXA-1 + CTX-M-15 + TEM-1 + SHV-28 + OXA-9 + CMY-6	>256	>256	>256	16	0.047	3	0.25
K. pneumoniae	NDM-1 + TEM-1 + CTX-M-15 + SHV-12 + OXA-9	>256	>256	>256	12	0.125	96	1
K. pneumoniae	NDM-1 + TEM-1 + CTX-M-15 + SHV-12 + OXA-9	>256	>256	>256	12	0.125	96	0.5
K. pneumoniae	NDM-1 + TEM-1 + CTX-M-15 + SHV-11 + OXA-1	>256	>256	>256	12	0.064	8	0.38
Salmonella enterica	NDM-1 + CTX-M-15 + TEM-1 + OXA-1 + OXA-9 + OXA-10	>256	>256	>256	16	0.125	16	0.5
E. coli	VIM-1 + CTX-M-3	>256	>256	>256	16	0.125	24	0.5
E. coli	VIM-4 + ESBL	16	>256	>256	24	1.5	24	16
K. pneumoniae	VIM-1 + SHV-5	>256	>256	>256	>256	0.25	192	1.5
K. pneumoniae	VIM-1 + SHV-12	>256	>256	>256	16	0.125	4	0.25
K. pneumoniae	VIM-1 + ESBL	>256	>256	>256	>256	12	16	12
K. pneumoniae	VIM-1 + SHV-5	16	>256	>256	>256	6	12	32
K. pneumoniae	VIM-1 + TEM-1 + SHV-5	96	>256	>256	>256	96	64	48
K. pneumoniae	VIM-1 + SHV-5	>256	>256	>256	24	0.25	8	0.75
K. pneumoniae	VIM-1 + SHV-5	>256	>256	>256	12	0.125	2	0.38
K. pneumoniae	VIM-19 + CTX-M-3 + TEM-1 + SHV-1	6	32	>256	16	0.047	2	1.5

ATM, aztreonam; CZA, ceftazidime-avibactam; C/T, ceftolozane-tazobactam; AMC, amoxicillin-clavulanate

Aztréonam + Ceftazidime/avibactam ?

Ceftazidime-Avibactam and Aztreonam, an Interesting Strategy To Overcome β-Lactam Resistance Conferred by Metallo-β-Lactamases in *Enterobacteriaceae* and *Pseudomonas aeruginosa*

Benjamin Davido,[a] Lesly Fellous,[b] Christine Lawrence,[c,d] Virginie Maxime,[e] Martin Rottman,[d,f] Aurélien Dinh[a]

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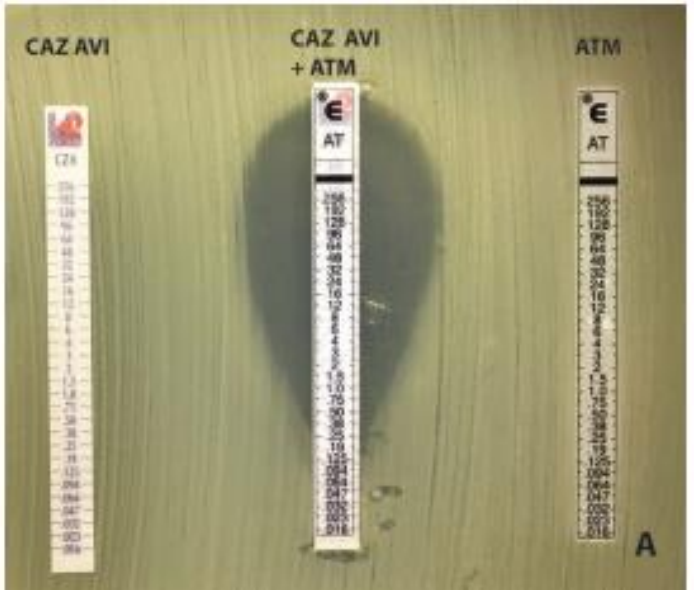
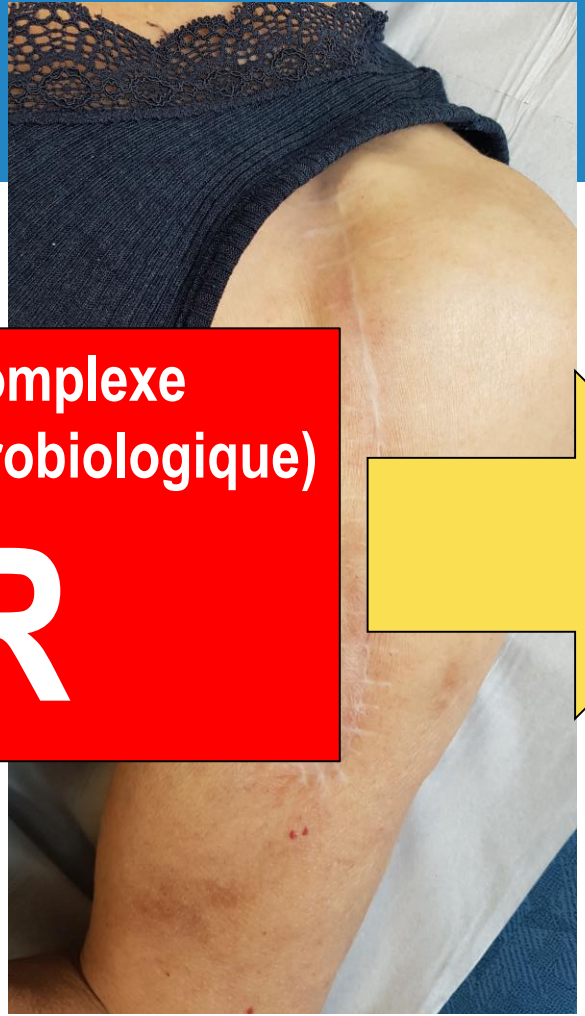


Susceptibility testing showing with ellipsometry the effect of the synergistic combination of CAZ-AVI and ATM. The combination (middle strip) was tested by first applying an ATM strip to the Mueller-Hinton (MH) agar, removing it after 5 min, and then applying a CAZ-AVI strip on the exact same location and placing back the ATM strip to read the susceptibility to ATM in the presence of AVI (and CAZ). K. pneumoniae NDM-1/OXA-48 from patient 1.



IOA Complexe
(critère microbiologique)

R

Solutions « simples »

Ablation du matériel

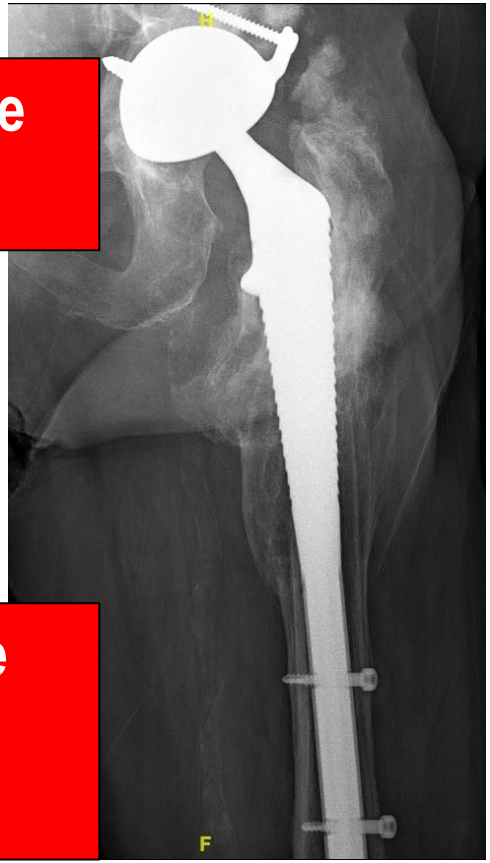
Antibiothérapie « originale »

Sur diffuseur

Cas clinique n° 2

- Patiente de 85 ans
- Troubles cognitifs
- Prothèse de hanche gauche de révision
- Infection post-opératoire à *K. pneumoniae BLSE* uniquement sensible aux carbapénèmes

Evolution défavorable
Lavages itératifs

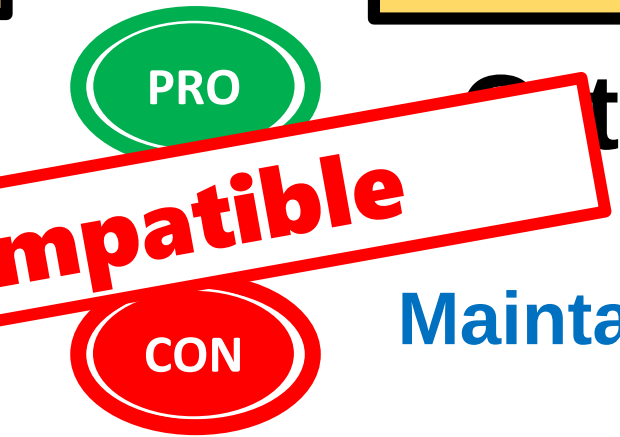


Infection persistante
CMI Ertapénème
0.064 mg/L

Discussion en RCP au CRIOAc

Infectious challenge
Eradication of the pathogen

Functional challenge
Limit bone loss



Infect. Dis.

Physician

Cure the infe

thopaedic

Surgeon

Maintain the function

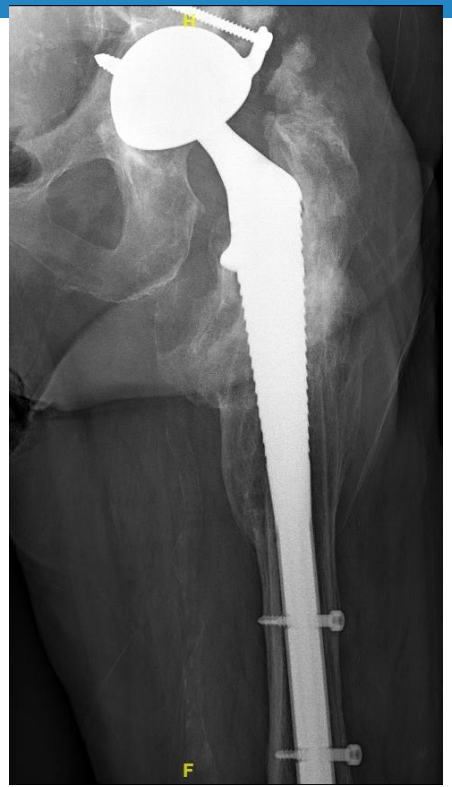
RCP au lit du malade

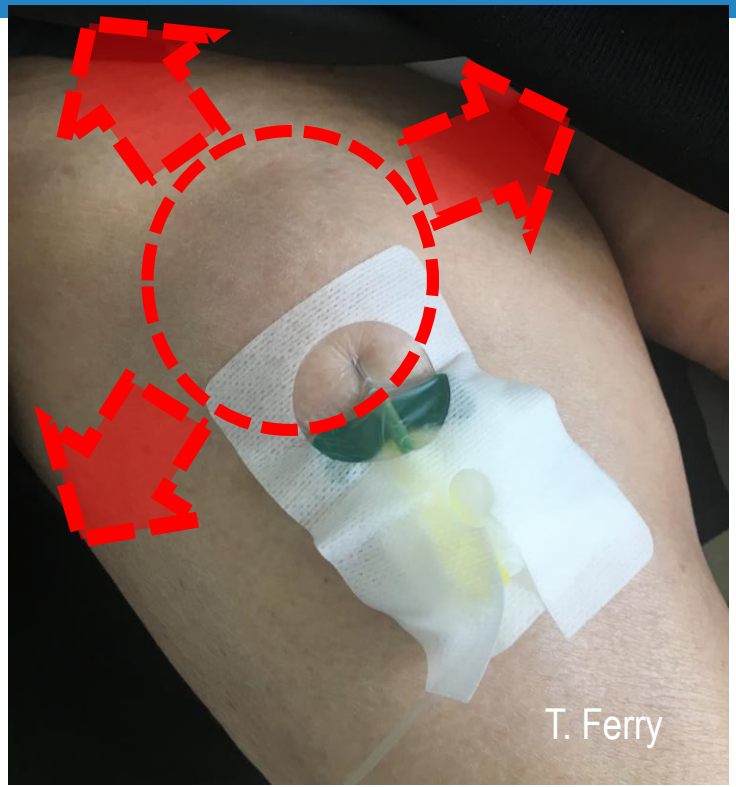
HCL
HOSPICES CIVILS DE LYON

CRIOAc LYON

Centre de Référence des Infections Ostéo-Articulaires complexes

Une solution simple : *OSCAT* !



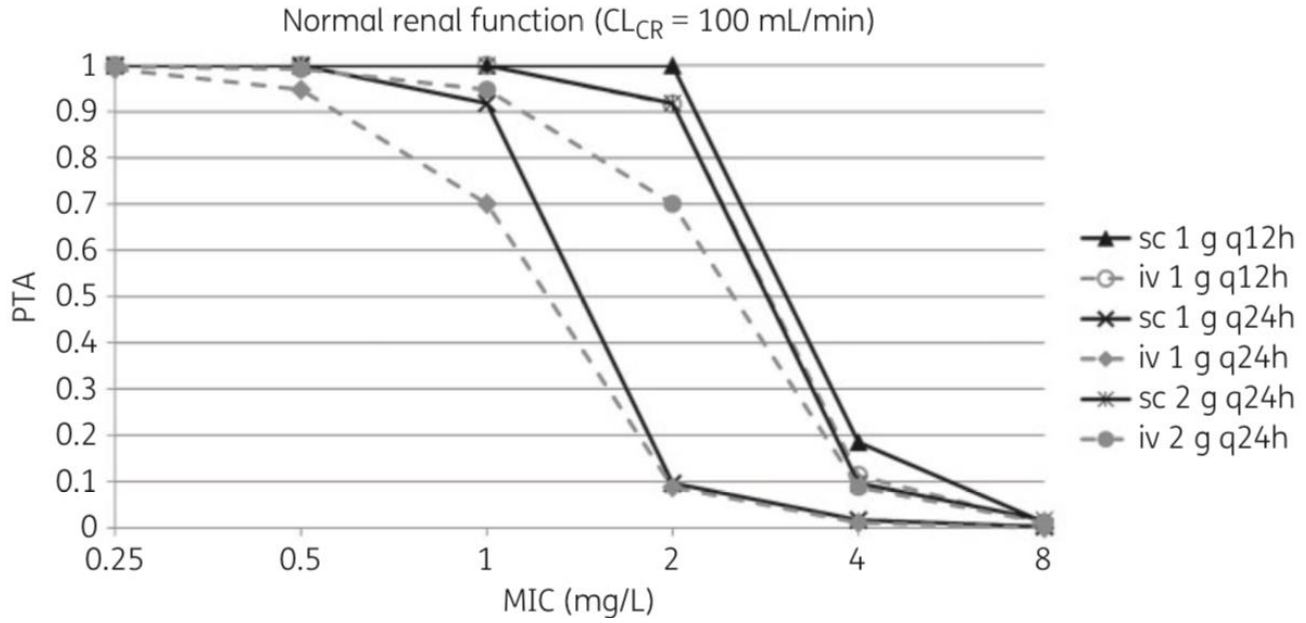


Outpatient SubCutaneous Antimicrobial Therapy

T. Ferry et al. *Front med* Submitted

Population pharmacokinetics and probability of target attainment of ertapenem administered by subcutaneous or intravenous route in patients with bone and joint infection

Sylvain Goutelle[1–3]*, Florent Valour[2,4,5], Marie-Claude Gagnieu[6], Frédéric Laurent[2,5], Christian Chidiac[2,4,5] and Tristan Ferry[2,4,5] on behalf of the Lyon Bone and Joint Infection Study Group†



Journal of Antimicrobial Therapy 2017

Une solution simple : *OSCAT* !

Medical innovations to maintain the function in patients with chronic PJI for whom explantation is not desirable: a pathophysiology-, multidisciplinary-, and experience-based approach

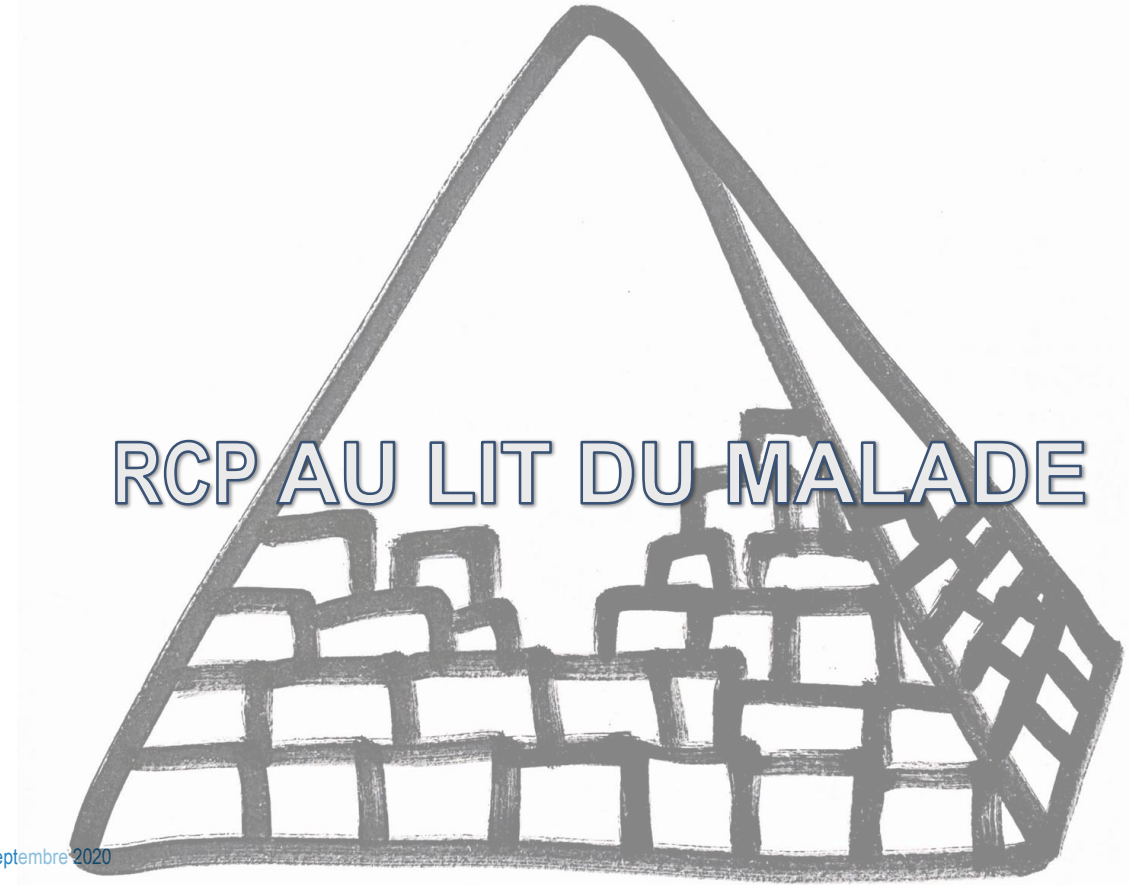
T. Ferry *SICOT-J* 2020, 6, 26

SICOT-J

Outpatient SubCutaneous Antimicrobial Therapy

T. Ferry et al. *Frontiers med* Submited

Traitement personnalisé au cours des IOA



Traitement personnalisé au cours des IOA

RCP AU LIT DU MALADE

Chirurgie adaptée

Antibiothérapie adaptée, optimale et faisable

Traitement personnalisé au cours des IOA

AntibioticS-loaded PMMA cements

Antibiotic-loaded bone substitutes

New antibiotics

PK-PD based antimicrobial therapy

Bacteriophage-derived lysins

Bacteriophages

Traitement adjuvant innovant ou pratique innovante

RCP AU LIT DU MALADE

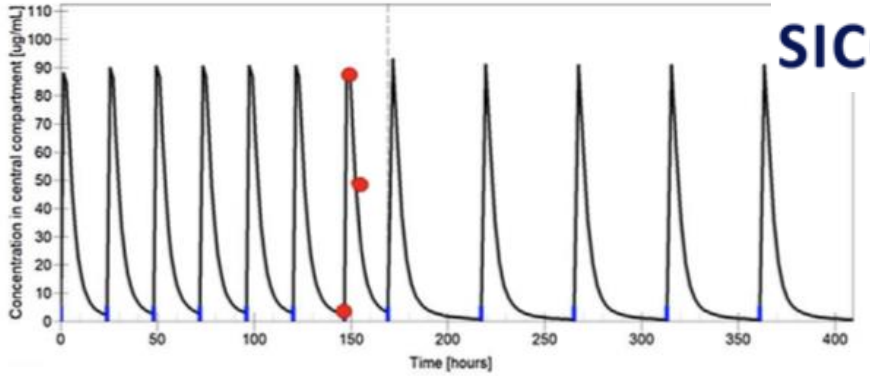
Chirurgie adaptée

Antibiothérapie adaptée, optimale et faisable

Une solution simple : *OSCAT* !

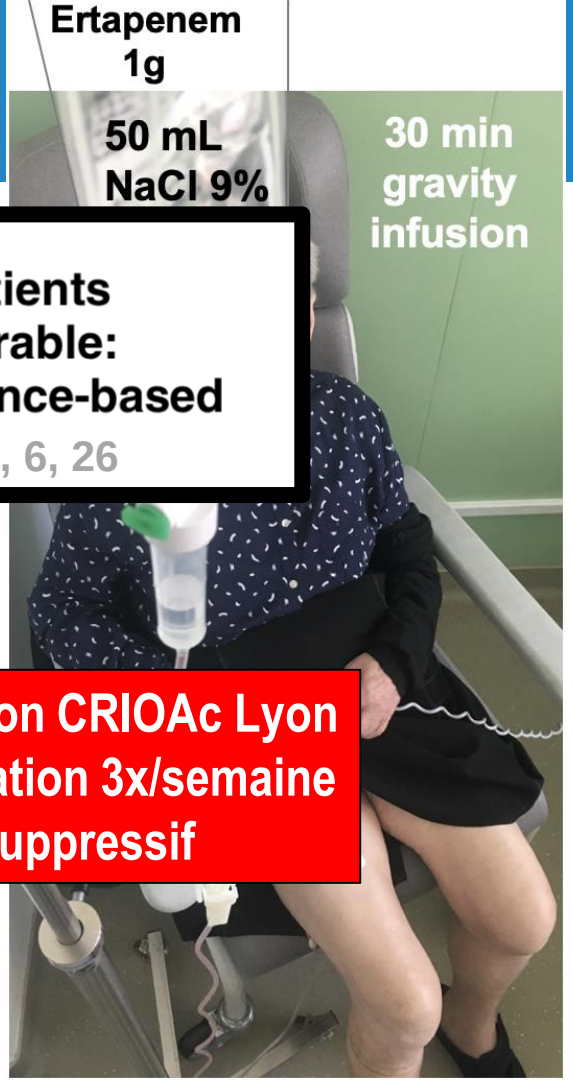
Medical innovations to maintain the function in patients with chronic PJI for whom explantation is not desirable: a pathophysiology-, multidisciplinary-, and experience-based approach

T. Ferry *SICOT-J* 2020, 6, 26



SICOT-J

Modélisation CRIOAc Lyon
Administration 3x/semaine en suppressif



Outpatient SubCutaneous Antimicrobial Therapy

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Une solution simple : *OSCAT* !

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Journal of Antimicrobial Chemotherapy

Subcutaneous suppressive antibiotic therapy for bone and joint infections: safety and outcome in a cohort of 10 patients

Cécile Pouderoux[1–3]*, Agathe Becker[1–3], Sylvain Goutelle [2–4], Sébastien Lustig[2,3,5], Claire Triffault-Fillit[1–3], Fatiha Daoud[1,3], Michel Henry Fessy[2,3,6], Sabine Cohen[2,7], Frédéric Laurent[2,3,8,9], Christian Chidiac[1–3], Florent Valour[1–3,9] and Tristan Ferry[1,3,9] on behalf of the Lyon Bone and Joint Infection Study Group†

Une solution simple : *OSCAT* !

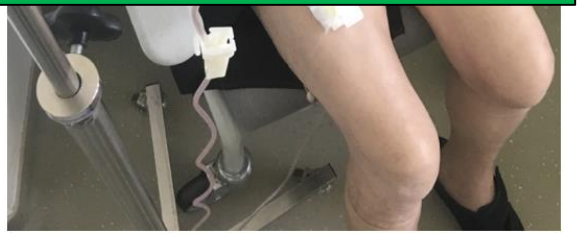
IOA Complexe
critère microbiologique

R

Critère chirurgical

Solutions « simples »

Pas d'explantation
Antibiothérapie suppressive
Modélisation CRIOAc
SC 3x/semaine
Conservation de la fonction !



Conclusion

- **Les Bacilles à Gram négatif MDR sont responsables d'IOA complexes !**
- **Rôle pivot de l'infectiologue dans la gestion de ces patients**
  - Discussion RCP en CRIOAc et orientation de la prise en charge médicochirurgicale
  - Adaptation de l'antibiothérapie
  - Réussir à transformer une situation complexe en une situation finalement simple !

Lyon BJI Study group

Coordinator: Tristan Ferry

Infectious Diseases Specialists – Tristan Ferry, Florent Valour, Thomas Perpoint, Florence Ader, Sandrine Roux, Claire Triffault-Filit, Agathe Becker, Anne Conrad, Marielle Perry, Cécile Pouderoux, Nicolas Benech, Pierre Chauvelot, Johanna Lippman, Evelyne Braun, Christian Chidiac

Surgeons – Sébastien Lustig, Elvire Servien, Cécile Batailler, Stanislas Gunst, Axel Schimdt, Matthieu Malatray, Eliott Sappey-Marinier, Michel-Henry Fessy, Anthony Viste, Jean-Luc Besse, Philippe Chaudier, Lucie Louboutin, Quentin Ode, Adrien Van Haecke, Marcelle Mercier, Vincent Belgaid, Arnaud Walch, Sébastien Martres, Franck Trouillet, Cédric Barrey, Ali Mojallal, Sophie Brosset, Camille Hanriat, Hélène Person

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Nuclear Medicine – Isabelle Morelec, Marc Janier, Francesco Giammarile

PK/PD specialists – Michel Tod, Marie-Claude Gagnieu, Sylvain Goutelle

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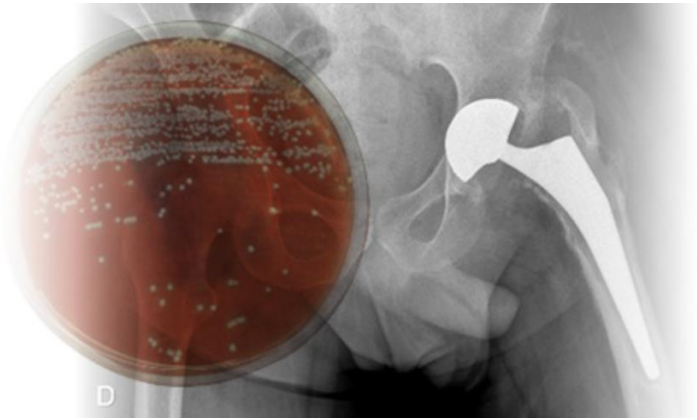
http://www.crioac-lyon.fr



- Published cases
- Open acces studies in pdf
- All thesis in pdf
- All recommendations
- **Newsletter**

Lyon 1

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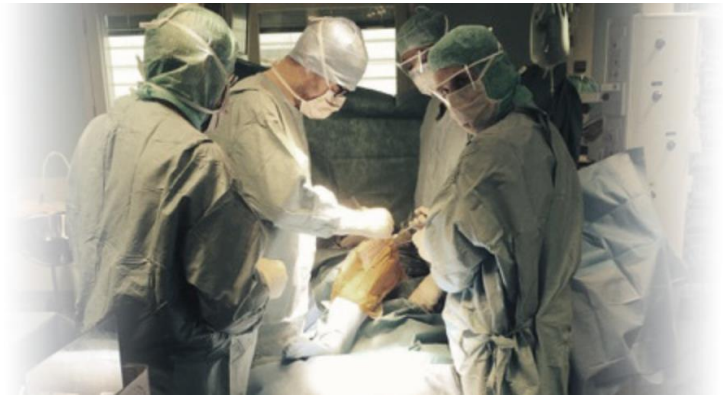
CRIOAC LYON

HCL HOSPICES CIVILS DE LYON



YouTube

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