

# Infections ostéo-articulaires sur matériel à *Pseudomonas aeruginosa* : expérience d'un centre de référence français

Implant-associated *P. aeruginosa* bone and joint infections:  
experience in a regional reference center in france

M. Cerioli, C. Batailler, A. Conrad, S. Lustig, M. Fessy, F. Laurent, F.  
Valour, C. Chidiac, T. Ferry on behalf of the **Lyon BJI Study group**

## Déclaration d'intérêts de 2014 à 2018

- **Intérêts financiers : Aucun**
- **Liens durables ou permanents : Aucun**
- **Interventions ponctuelles : DebioPharm, MSD, Gilead, MaaT Pharma, Pfizer, Sanofi-Aventis, Bonesupport**
- **Intérêts indirects : Aucun**

# IMPLANT-ASSOCIATED BONE AND JOINT INFECTIONS

## Background & Key Concepts

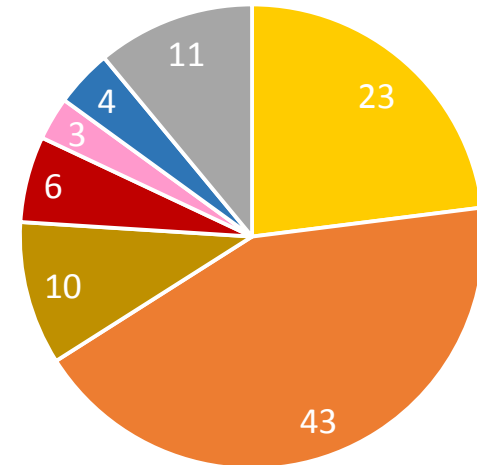
### Incidence

PJI	Fracture-fixation devices
Hip: 1%	Overall: 5-10%
Shoulder: 2%	Closed fractures: 1-2%
Elbow: 9%	Open fractures: 30%

### Pathogenesis

- Internal device
- Biofilm
- Different gradients of growth and metabolic activity
- Resistance to antibiotics and immune system

### Etiology



- *Staphylococcus aureus*
- Coagulase-negative staphylococci
- Streptococci
- GN bacilli
- Enterococci
- Anaerobes
- Mixed flora

Adapted from: Zimmerli, W., A. Trampuz, and P.E. Ochsner, *Prosthetic-joint infections*. N Engl J Med, 2004. **351**(16): p. 1645-54.

# IMPLANT-ASSOCIATED BONE AND JOINT INFECTIONS

## Research Question: subpopulation infected with *P. aeruginosa*

### Literature Review

*P. aeruginosa* causes 5 to 20% of the GNB implant-associated BJIs, yet it is particularly feared due to:

- ❖ Multidrug-resistant strains
- ❖ **Biofilm formation**
- ❖ **Small colony variants**
- ❖ Prolonged hospitalizations



Guidelines recommend:



$\beta$ -lactams



ciprofloxacin

BUT:



- ⚠ Scarcely published experience
- ⚠ Inconsistency between data from different studies
- ⚠ Only retrospective studies
- ⚠ No data exclusively on *P. aeruginosa*

### Research Question

The aims of the present study are to analyse the impact of:

Optimal surgical treatment

Effective initial IV treatment

Ciprofloxacin use

on *P.aeruginosa*  
implant-associated  
BJI

# METHOD

## Sample Selection and statistical analysis

- ❖ Retrospective cohort study in the French reference center for osteoarticular infections CRIOAc Lyon; <http://www.crioac-lyon.fr>
- ❖ Inclusion of all patients with *P. aeruginosa* implant-associated infection managed in our institution between 2011 and 2018
- ❖ At least one positive sample with *P. aeruginosa* in culture from deep perioperative samples was required
- ❖ Risk factors for treatment failures using Kaplan-Meier curves and univariate and multivariate cox analysis



# DEFINITIONS

## Criteria (1/2)

	Type of BJI	Characteristics
Operational Classification	<b>Acute hematogenous</b>	Infection with a duration of symptoms of 3 weeks or less after an uneventful postoperative period
	<b>Early postinterventional</b>	Infection that manifests within 1 month after an invasive procedure such as surgery or arthrocentesis
	<b>Chronic</b>	Infection with symptoms that persist for more than 3 weeks, beyond the early postinterventional period
Treatment Failure	<b>Any type of relapse of implant-associated infection including:</b>	
	<ul style="list-style-type: none"><li>❖ <b>persistence</b> (new surgery with a second finding of the same <i>P. aeruginosa</i>),</li><li>❖ <b>superinfection</b> (either new surgery or joint tap with isolation of another organism(s)), or</li><li>❖ any other cause of relapse such as the need for a <b>subsequent surgery</b></li></ul>	




# DEFINITIONS

## Criteria (2/2)

	Stage		Procedure	
"OPTIMAL" Surgical Management	❖ < 1 month from implantation	➔	<b>Debridement and retention</b>	
	❖ Stable implant			
	❖ No sinus tract or damaged soft tissue			
	❖ > 1 month	➔	<b>One-stage exchange</b>	
	❖ Intact or slightly damaged soft tissue			
	❖ Good condition of the host			
	❖ > 1 month	➔	<b>Two-stage exchange</b>	
	❖ Damaged soft tissue / sinus tract / microorganism difficult to treat			
	❖ Bad condition of the host			

### Effective Initial Antibiotics

Effective **initial** antibiotic treatment against *P. aeruginosa* was defined as the use of an **active IV beta-lactam drug by checking drug-susceptibility on the antibiogram**



# RESULTS

## Demographics & Clinical Features

- ❖ Whole population: **n=90**
- ❖ Median follow up of: **20 months [IQR 9 - 36,5]**
- ❖ Number of patients with a treatment failure: **n=23 (25.6%)**
  - *P. aeruginosa* persistence: **n=7 (7.8%)**
  - Superinfection: **n=16 (17.8%)**



# RESULTS

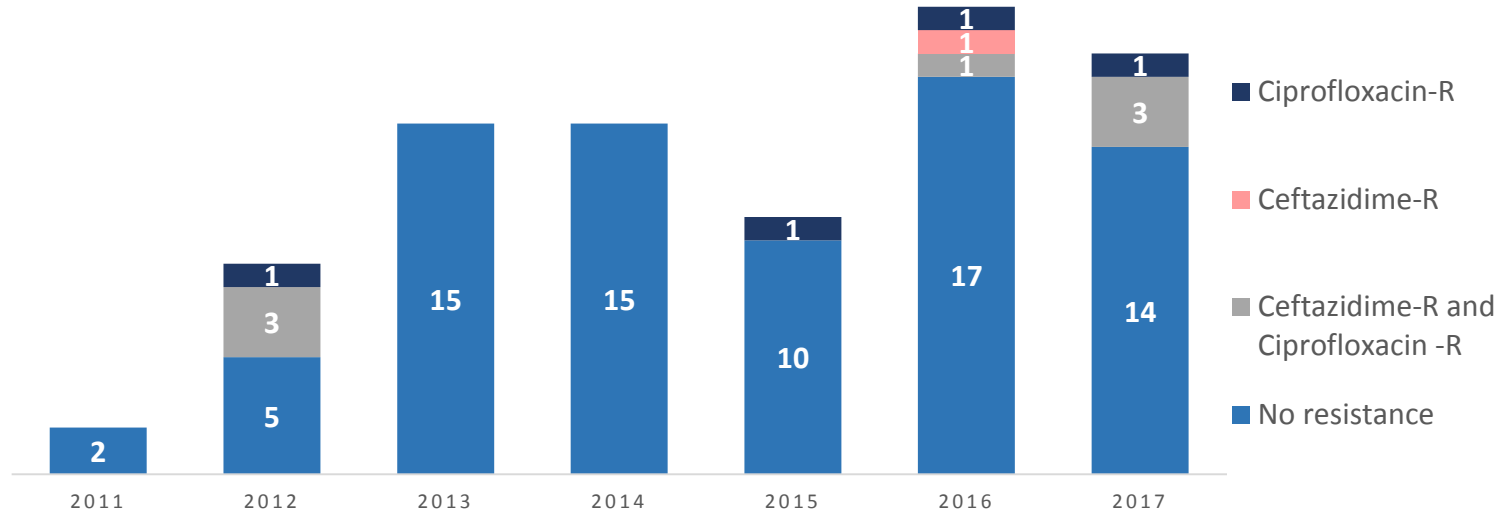
## Demographics & Clinical Features

Characteristics	Whole population (n=90)	Failure (n=23)	Remission (n=67)	<i>p</i> <sup>a</sup>
Age in years (median, IQR)	60 (47-72)	61 (43-74)	59 (47-72)	0.9
Male sex (n, %)	56 (62)	17 (74)	39 (58)	0.18
BMI ≥30 (n, %)	24 (28)	6 (29)	18 (29)	1
Active smoking (n, %)	29 (35)	10 (44)	19 (32)	0.34
Score ASA > 2 (n, %)	30 (34)	8 (35)	22 (33)	0.9
Score Charlson > 4 (n, %)	24 (27)	7 (30)	17 (25)	0.64
Previous infection at the same site (n, %)	19 (21)	6 (26)	13 (19)	0.5
Prosthesis (n, %)	30 (33)	7 (30)	23 (34)	0.73
Age of implant in days (median, IQR)	47 (21.7-247.5)	40 (21-222)	63 (26-798)	0.29
Type of infection (n, %)				
acute	56 (62)	14 (61)	42 (63)	
sub-acute	8 (9)	2 (9)	6 (9)	0.98
chronic	26 (29)	7 (30)	19 (28)	
Polymicrobial infection (n, %)	66 (73)	18 (78)	48 (71)	0.54

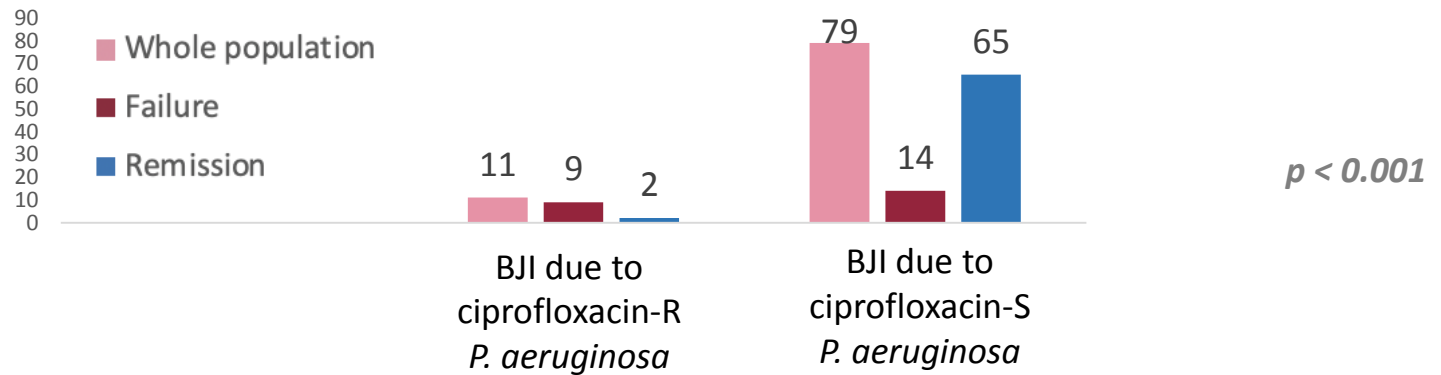
# RESULTS

## Antimicrobial resistance

Epidemiology per year



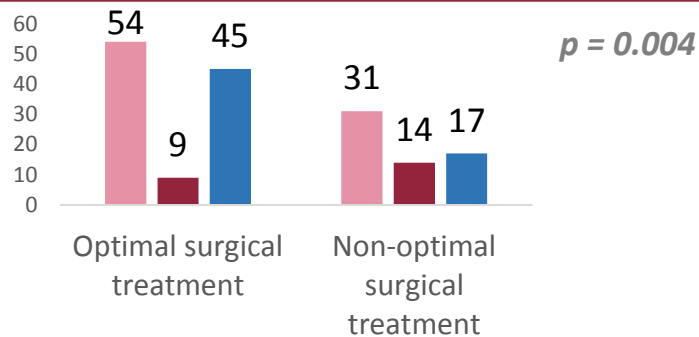
BJI due to *P. aeruginosa* ciprofloxacin-resistant



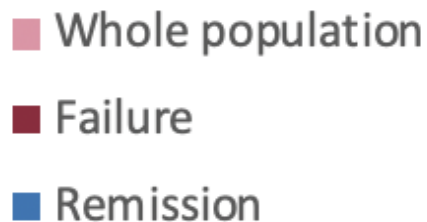
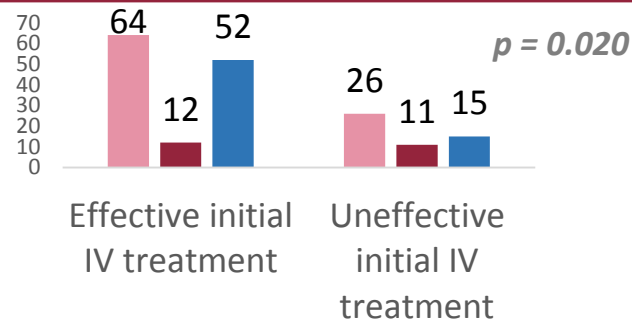
# RESULTS

## Clinical management

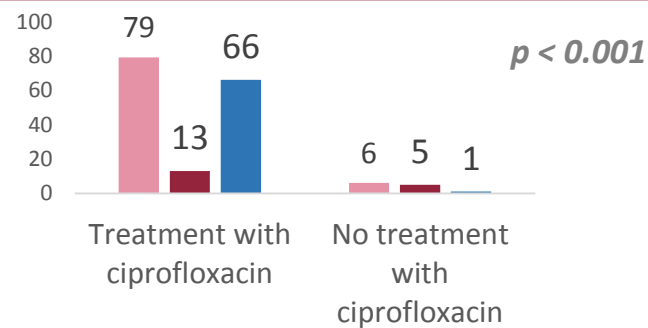
### Optimal surgical treatment



### Effective initial IV treatment



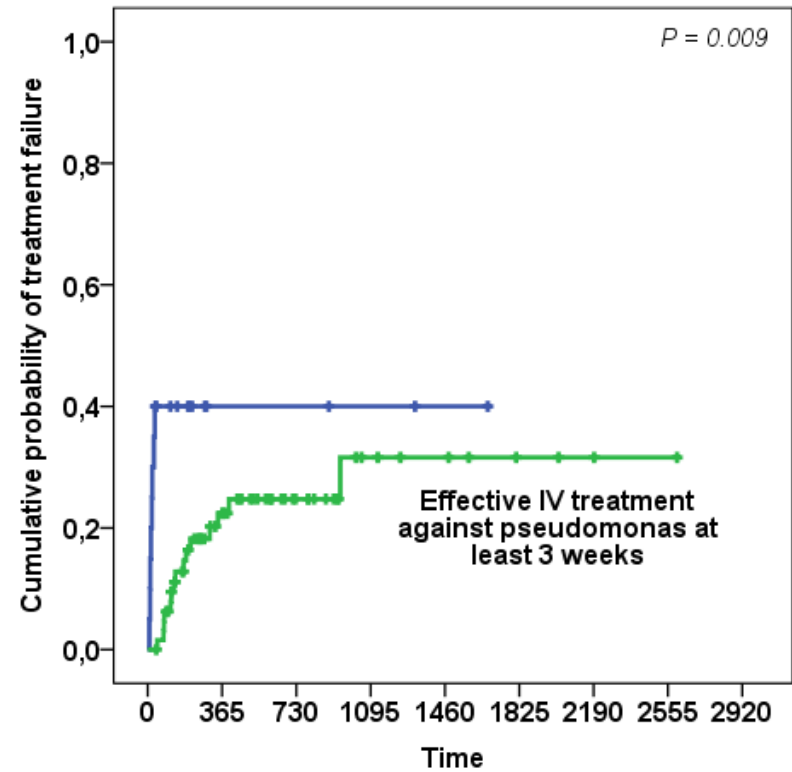
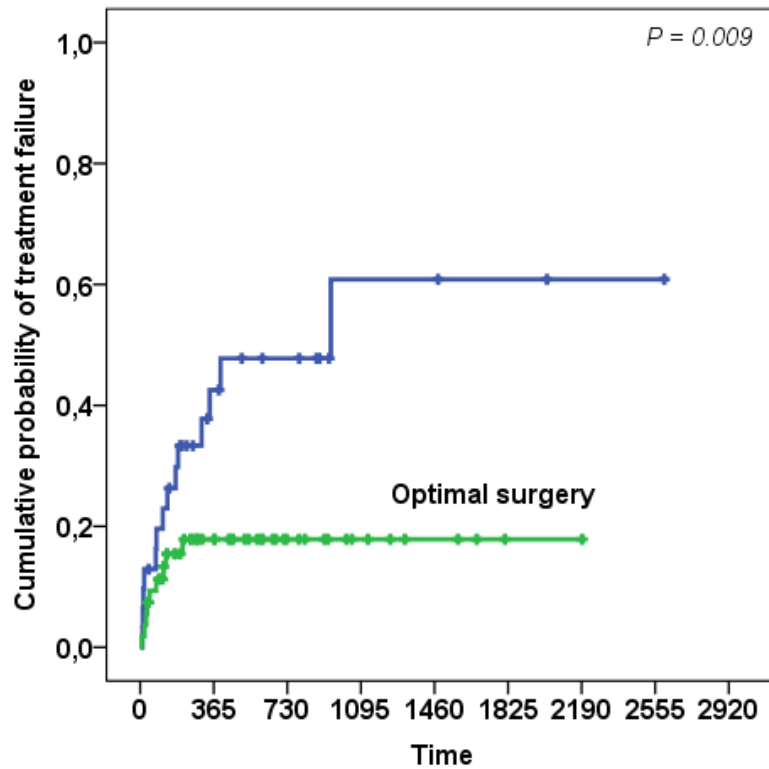
### Treatment with ciprofloxacin



# RESULTS

## Clinical management

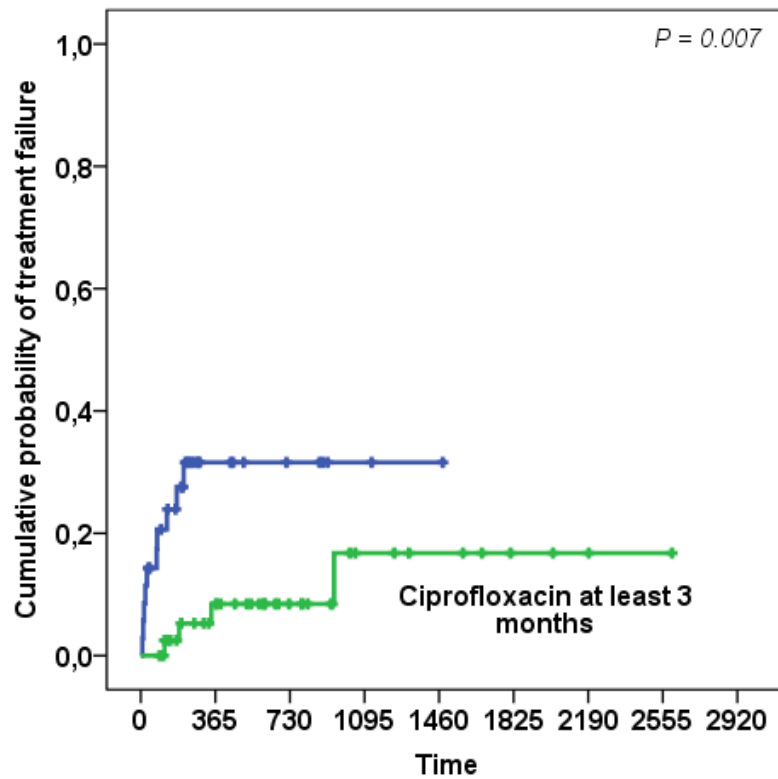
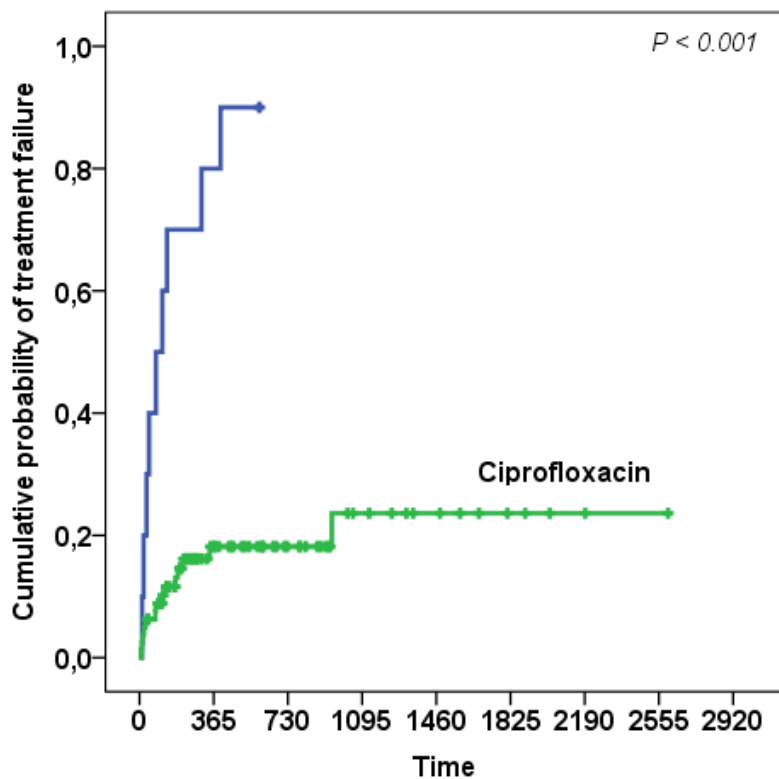
Kaplan-Meier curves showing the probability of treatment failure depending on surgical and medical management



# RESULTS

## Clinical management

Kaplan-Meier curves showing the probability of treatment failure depending on surgical and medical management



# RESULTS

## Clinical management

Multivariate Cox analysis that includes significant determinants for failure identified in the univariate analysis.

Determinant	HR	95%CI	<i>p</i>
Optimal surgical treatment*	0.32	0.11-0.98	0.045
IV effective treatment of at least 3 weeks*	0.15	0.004-0.054	0.003
ciprofloxacin for at least 3 months*	0.23	0.07-0.75	0.015

**Note.** HR, Hazard ratio; 95%CI, 95% confidence interval.

\* after exclusion of the 5 patients who eventually received suppressive antimicrobial therapy

# *P. AERUGINOSA* IMPLANT-ASSOCIATED BJI

## Conclusions

- ❖ *P. aeruginosa* implant-associated BJI is one of the most difficult-to-treat implant-associated BJI, with the surgical strategy having a strong impact on the prognosis
- ❖ Conclusions obtained with others Enterobacteriaceae are not completely transposable
- ❖ **An effective initial IV antibiotic treatment for at least 3 weeks seems to be required, followed by oral ciprofloxacin for a total duration of 3 months**
- ❖ Crucial need to take into account the microorganism (and its drug susceptibility) responsible for implant-associated BJI, and adapt the type of antibiotic treatment and its duration

# Lyon BJI Study group

**Coordinator:** Tristan Ferry

**Infectious Diseases Specialists** – Tristan Ferry, Florent Valour, Thomas Perpoint, Florence Ader, Sandrine Roux, Patrick Miaillhes, Claire Triffault-Philit, Agathe Becker, Anne Conrad, Marielle Perry, Cécile Pouderoux, Marie-Elodie Langlois, Johanna Lippman, Evelyne Braun, Christian Chidiac

**Surgeons** – Sébastien Lustig, Elvire Servien, Cécile Batailler, Romain Gaillard, Stanislas Gunst, Julien Roger, Charles Fiquet, Michel Henri Fessy, Anthony Viste, Philippe Chaudier, Jean Luc Besse, Lucie Louboutin , Gaël Gaudin , Tanguy Ledru, Adrien Van Haecke, Quentin Ode , Marcelle Mercier, Florie Alech-tournier, Sébastien Martres, Franck Trouillet, Philippe Céruse, Carine Fuchsmann, Cédric Barrey, Emmanuel Jouanneau, Brice Gérenton, Ana Velicanu, Ali Mojallal, Fabien Boucher

**Anesthesiologists** – Frédéric Aubrun, Mikhail Dziadzko, Caroline Macabéo

**Microbiologists** – Frederic Laurent, Céline Dupieux, Laetitia Berraud, Camille Kolenda, Jérôme Josse

**Nuclear Medicine** – Isabelle Morelec, Marc Janier, Francesco Giammarile

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

**Clinical Research Assistant** – Eugénie Mabrut





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