



Université Claude Bernard Lyon 1



UNIVERSITÀ DEGLI STUDI DI MILANO
FACOLTÀ DI MEDICINA E CHIRURGIA

IMPLANT-ASSOCIATED P. AERUGINOSA BONE AND JOINT INFECTIONS: EXPERIENCE IN A REGIONAL REFERENCE CENTER IN FRANCE

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Background & Key Concepts

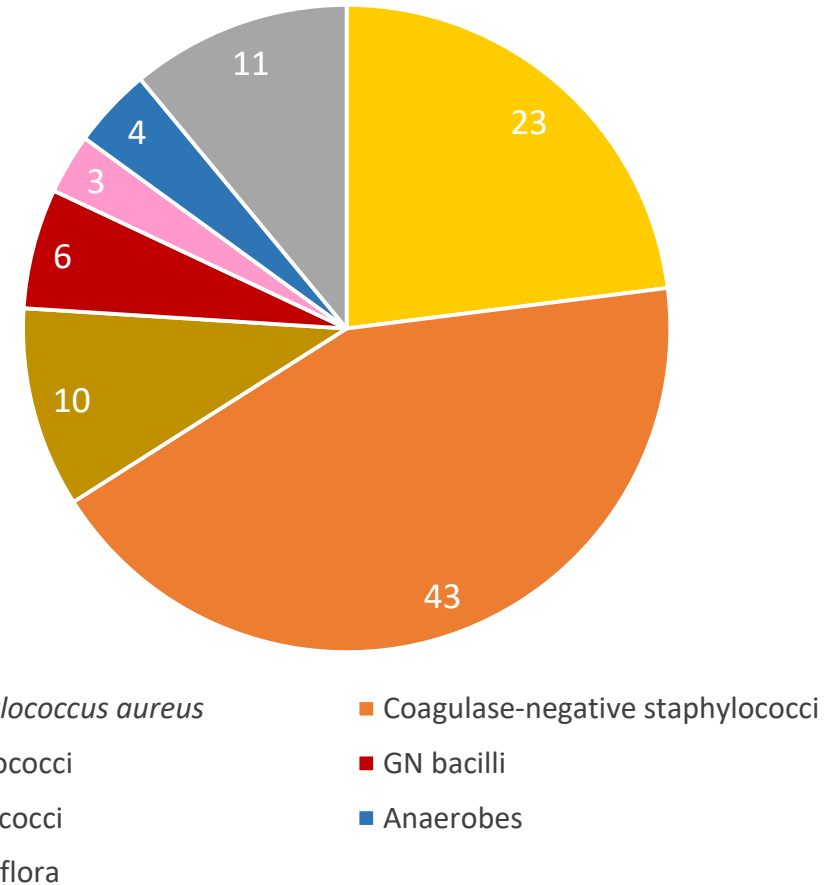
Incidence

PJI	Fracture-fixation devices
Hip: 1%	Overall: 5-10%
Shoulder: 2%	Closed fractures: 0.5-2%
Elbow: 9%	Grade 3 open fractures: 30%

Pathogenesis

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

Etiology



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

How To Diagnose

Criteria

IDSA (For the diagnosis of PJI at least one of the five criteria is required):

- ❖ Presence of a sinus tract communicating with the prosthetic joint
- ❖ Presence of purulence without another known aetiology surrounding the prosthetic device
- ❖ Acute inflammation consistent with infection at histopathological examination of periprosthetic tissue
- ❖ Elevated leucocyte count in the synovial fluid and/or predominance of neutrophils
- ❖ Growth of identical microorganism in at least two intraoperative cultures or combination of preoperative aspiration and intraoperative cultures in case of a low-virulence microorganism (coagulase-negative staphylococci, *Propionibacterium acnes*, etc.).

In case of a virulent microorganism (e.g.; *Staphylococcus aureus*, *E. coli*, *P. aeruginosa*):

- ❖ growth in a single specimen from synovial fluid and/or periprosthetic tissue and/or sonication fluid may also represent PJI

Research Question

Literature Review

GN bacteria are a minor cause of all implant-associated BJI and *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:



β -lactams



ciprofloxacin

BUT:



- ⚠ Scarce published experience
- ⚠ Only retrospective studies

- ⚠ Inconsistency between data from different studies
- ⚠ No data exclusively on *P. aeruginosa*

Research Question

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

Optimal surgical treatment

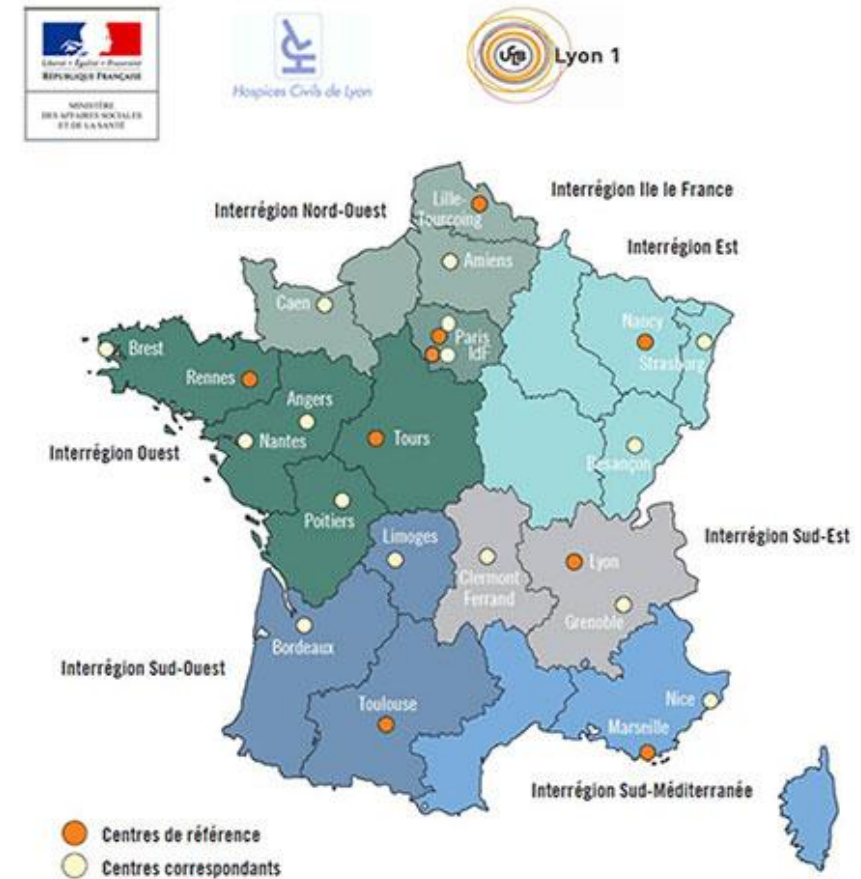
Effective initial IV treatment

Ciprofloxacin use

on *P.aeruginosa* implant-associated B&J infections

Sample Selection

- ❖ Retrospective study in the national French reference center for osteoarticular infections of the South-East region (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 with a median follow up of **20 months** [IQR 9 - 36,5]
- ❖ At least **one** positive sample with *P. aeruginosa* in culture from deep perioperative samples was required
- ❖ All cases present in this cohort were discussed and dealt with thanks to the cooperation of a multidisciplinary group composed of infectious diseases consultants, orthopedic surgeons, plastic surgeons and microbiologists.



Operational Classification

Type of implant-associated BJI

Characteristics

Acute hematogenous

Infection with a duration of symptoms of 3 weeks or less after an uneventful postoperative period

Early postinterventional

Infection that manifests within 1 month after an invasive procedure such as surgery or arthrocentesis

Chronic



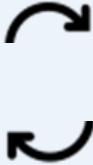

Infection with symptoms that persist for more than 3 weeks, beyond the early postinterventional period

Treatment Failure

Any type of relapse of implant-associated infection including:

- ❖ persistence (new surgery with a second finding of the same *P. aeruginosa*),
- ❖ superinfection (either new surgery or joint tap with isolation of another organism(s)) or
- ❖ any other cause of relapse such as the need for a subsequent surgery.

Criteria (2/2)

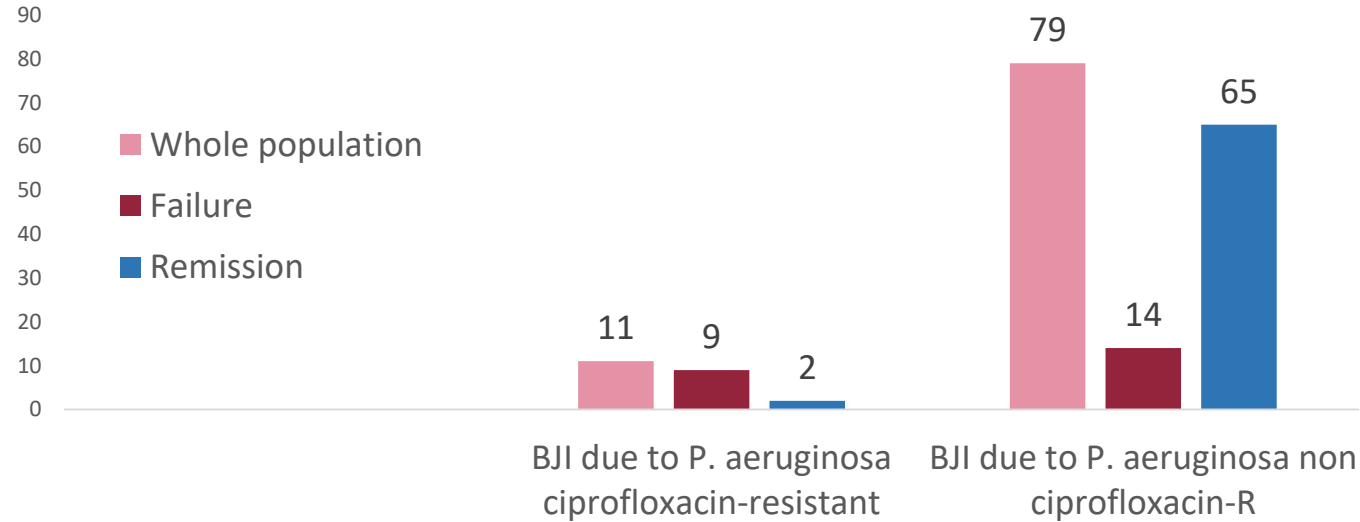
Surgical Management	Stage	Procedure	
	<ul style="list-style-type: none">❖ < 1 month from implantation❖ Stable implant❖ No sinus tract or damaged soft tissue	➡ Debridement and retention	
	<ul style="list-style-type: none">❖ > 1 month❖ intact or slightly damaged soft tissue❖ Good condition of the host	➡ One-stage exchange	
	<ul style="list-style-type: none">❖ > 1 month❖ damaged soft tissue / sinus tract / microorganism difficult to treat❖ Bad condition of the host	➡ Two-stage exchange	
Effective Antibiotics	Effective initial antibiotic treatment against <i>P. aeruginosa</i> was defined as the use of an IV drug such as piperacilline, piperacilline-tazobactam, ceftazidime, cefepime, imipenem-cilastatin, ceftolozane-tazobactam, ceftazidime-avibactam and by checking drug-susceptibility on the antibiogram.		

Demographics & Clinical Features

Characteristics	Whole population (n=90)	Failure (n=23)	Remission (n=67)	<i>p</i> ^a
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

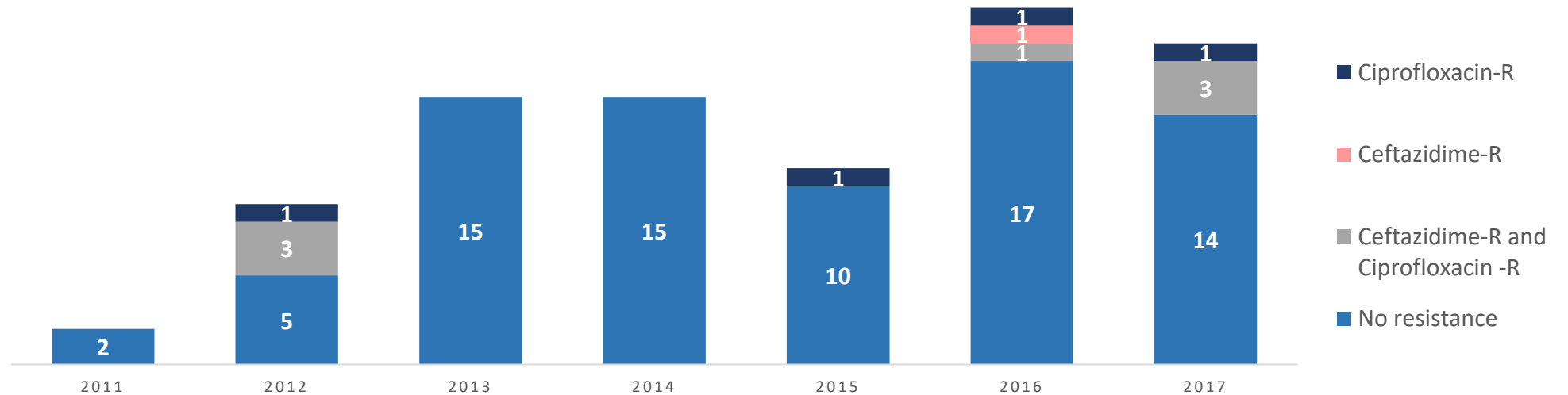
Results (1/4)

BJI due to *P. aeruginosa* ciprofloxacin-resistant



$p < 0.001$

Epidemiology per year



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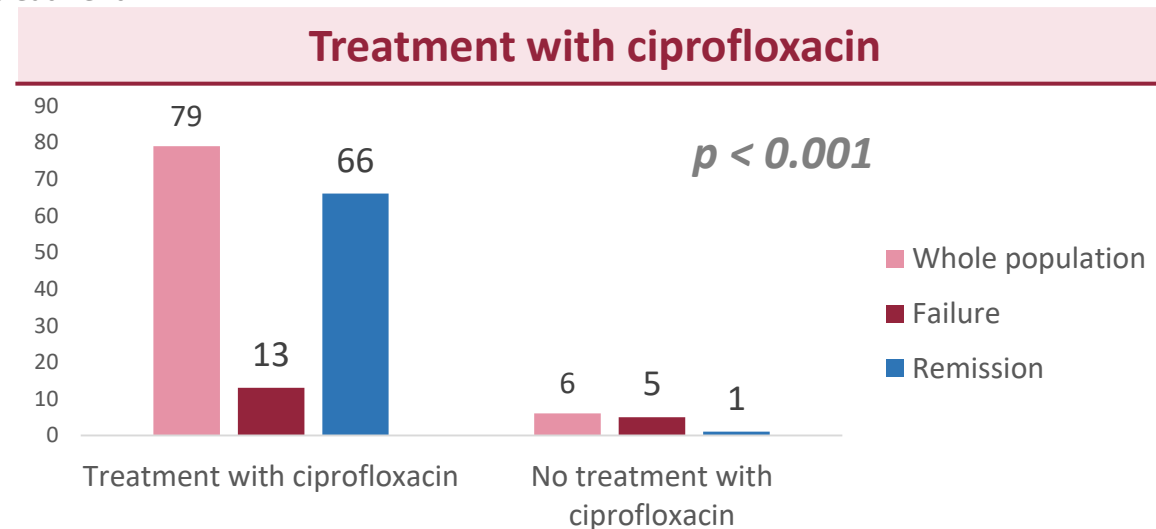
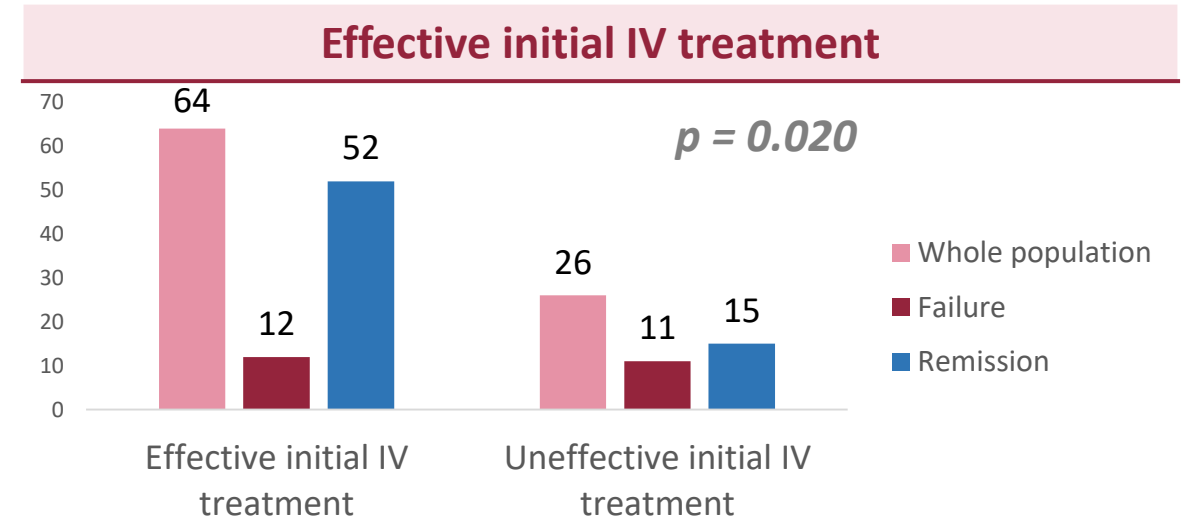
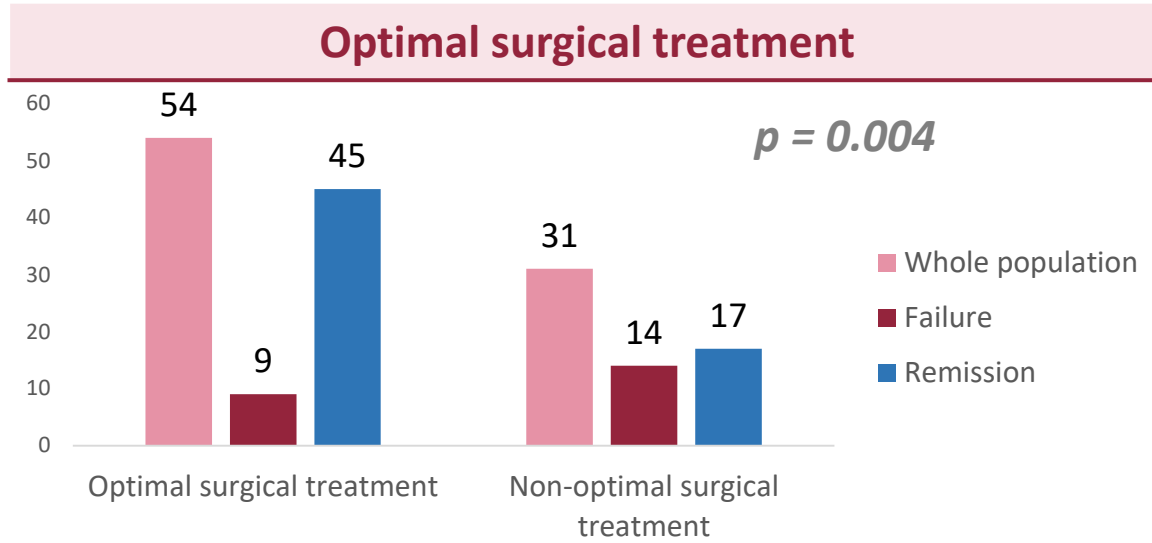
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Results

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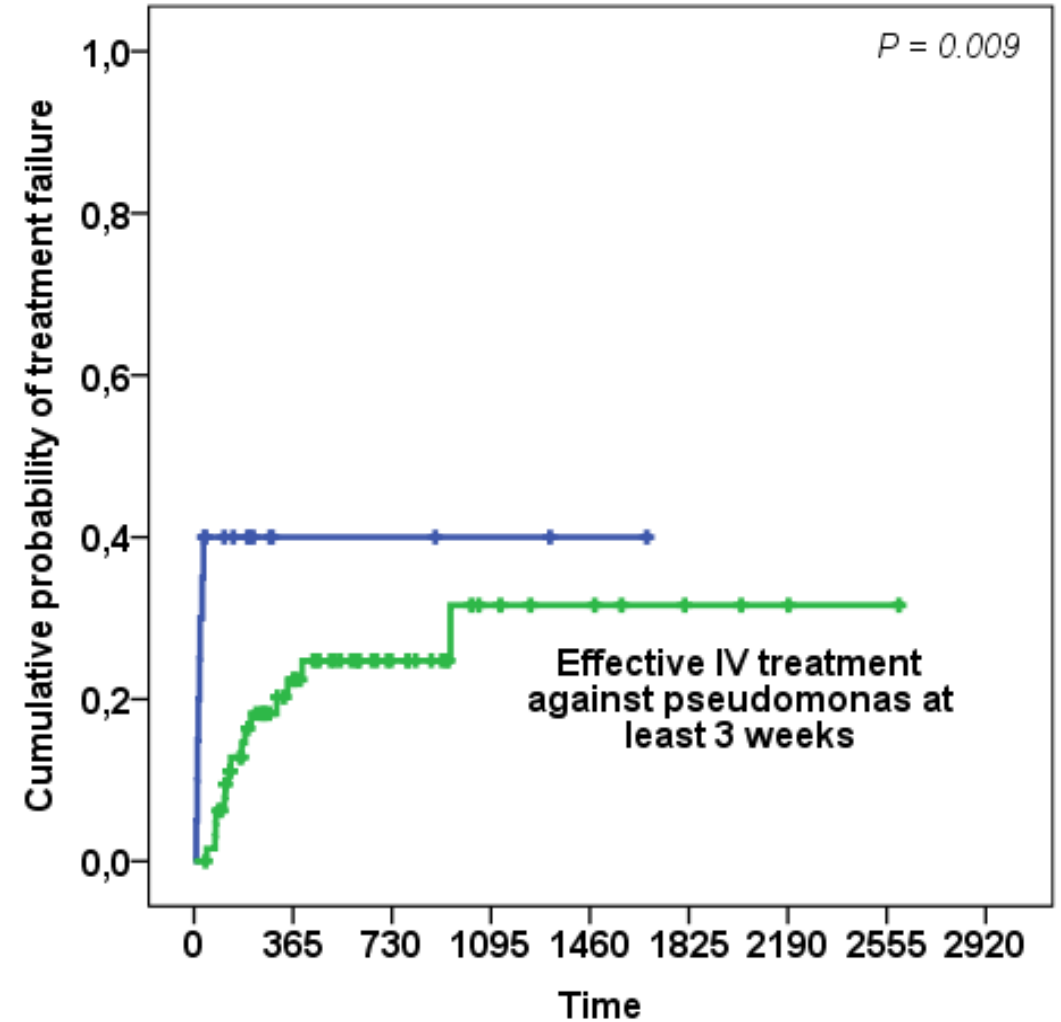
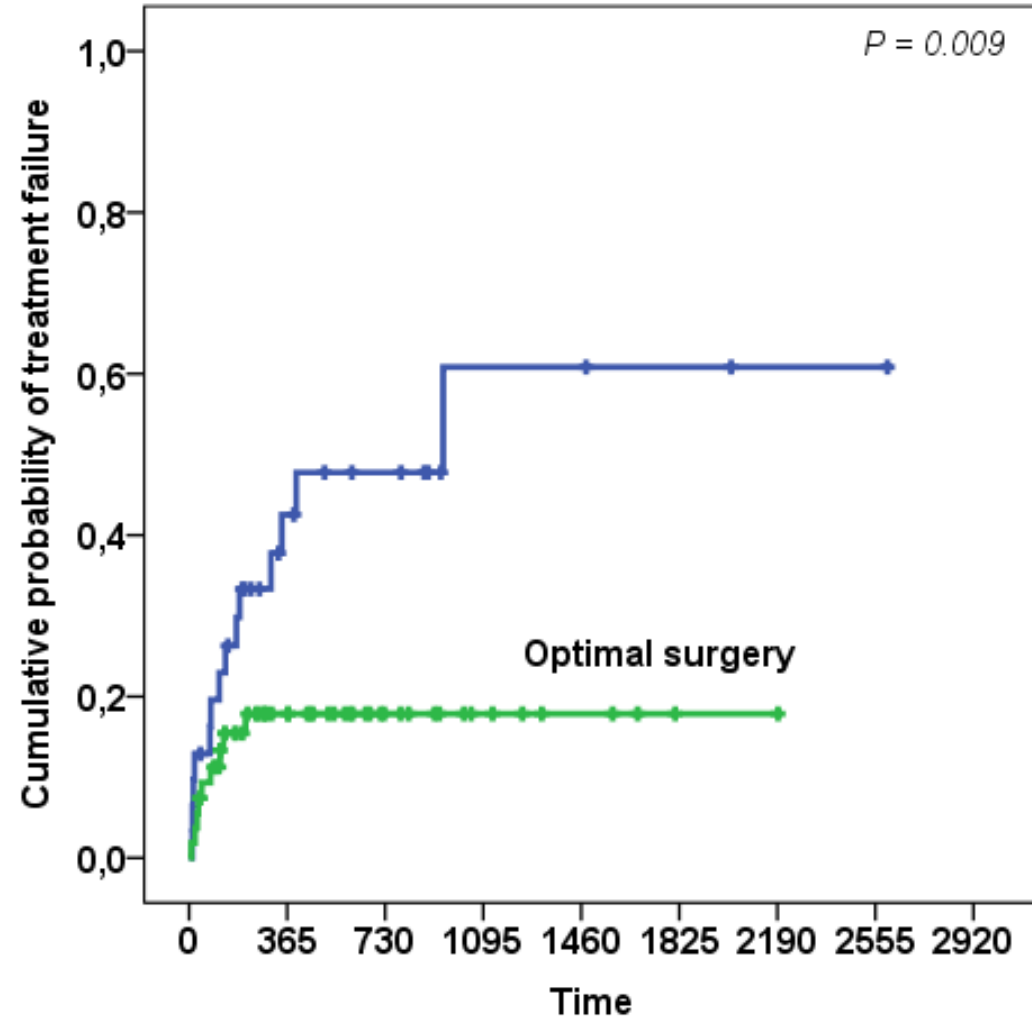
Conclusions

Results (2/4)



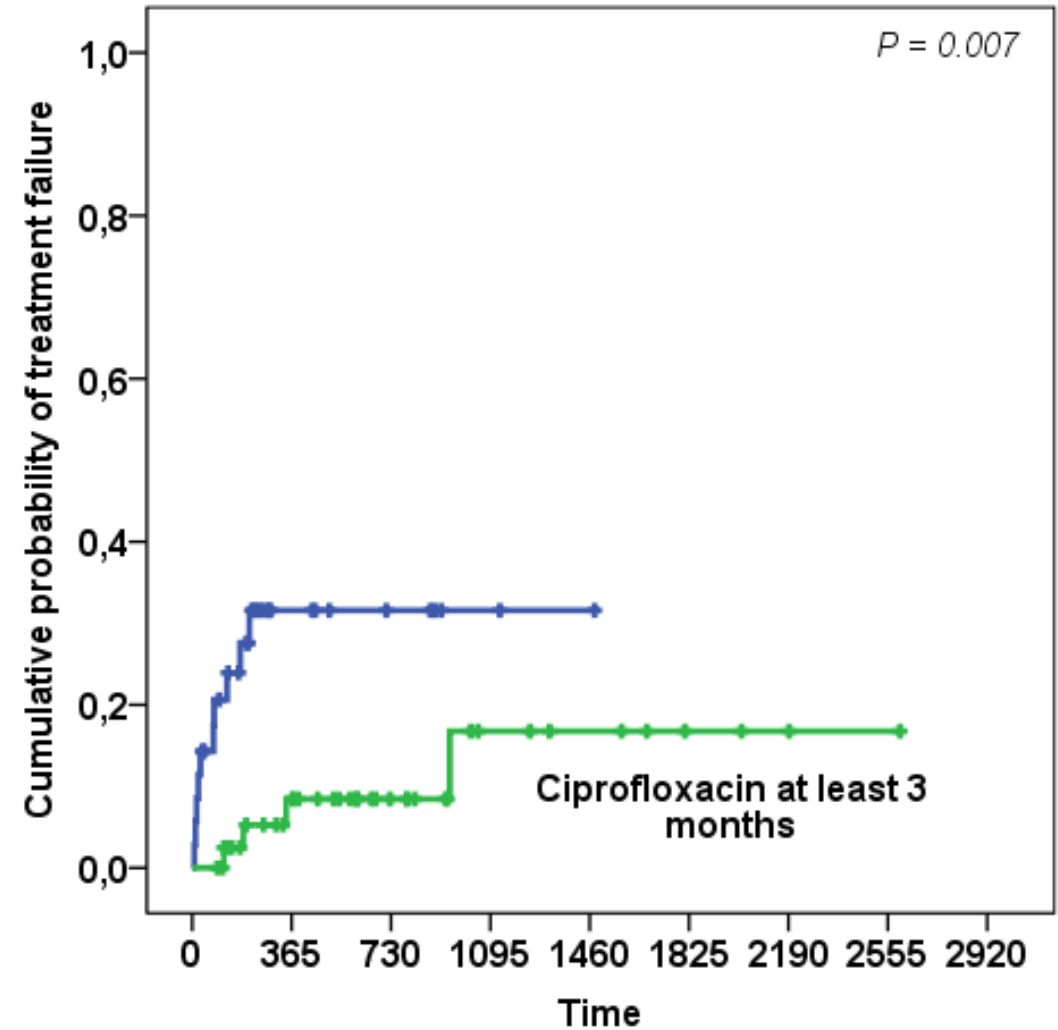
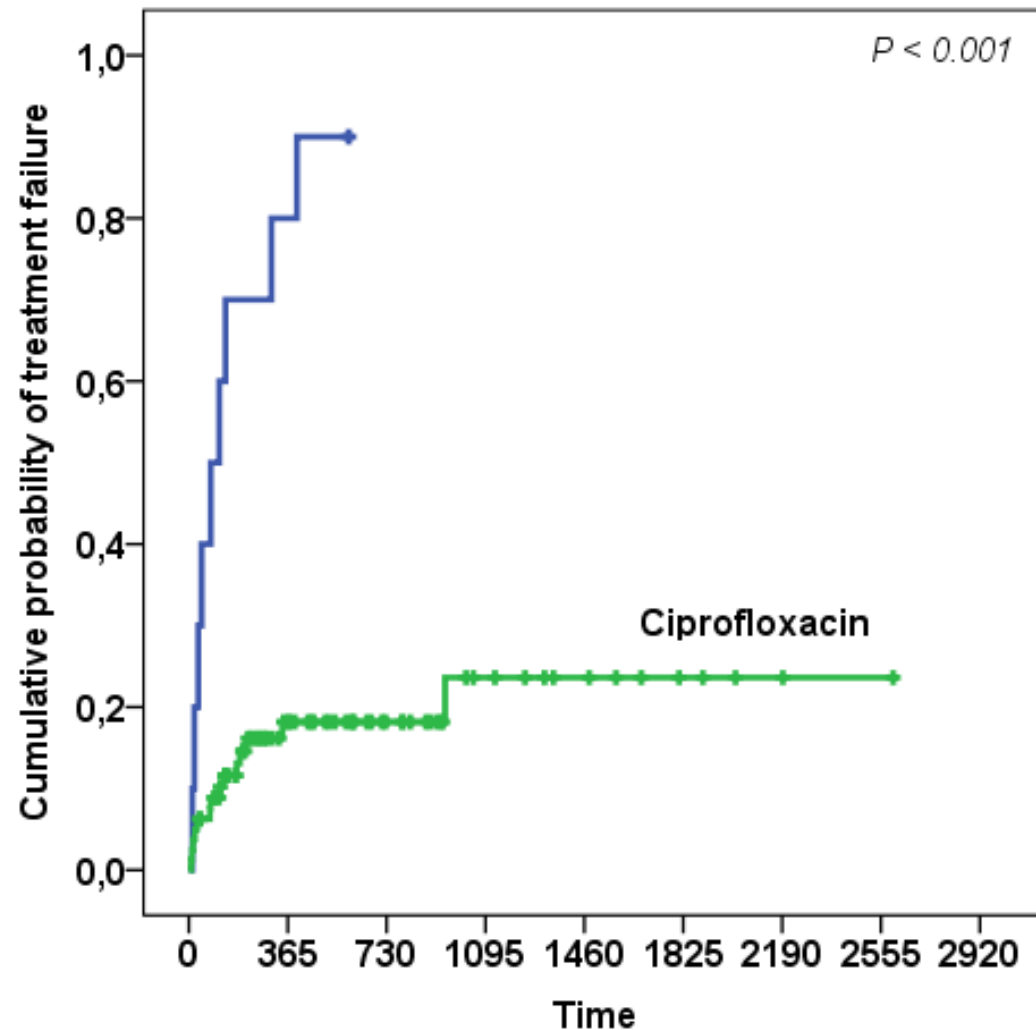
Results (3/4)

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



Results (3/4)

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

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
- ❖ 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

Limitations

- ❖ Our work is an observational retrospective study with all the limits inherently associated to this study design
- ⚠ However, surgical and clinical management of implant-associated BJIs cannot be randomized

Further Research

- ❖ Still not enough studies centered on *P. aeruginosa*
- ❖ Conclusions obtained with others Enterobacteriaceae are not completely transposable
- ❖ Crucial need to focus on this microorganism and collect further information



Thank you

