VIII Jornada grupo GEIO

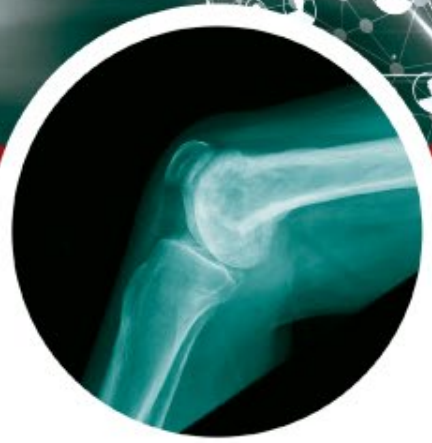
GRUPO DE ESTUDIO DE INFECCIONES OSTEOARTICULARES

2023

# NUEVOS RETOS EN INFECCIÓN OSTEOARTICULAR (IOA)

## INFECCION POR G+ MULTIRRESISTENTE

### O DE UN CASO QUE RESISTE A INFECCIONES POR G+



Madrid

GEIO · SEIMC


**LAURA GUÍO CARRIÓN**

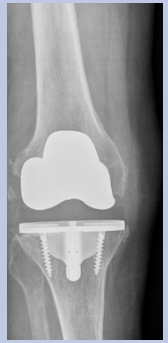
*SERVICIO ENFERMEDADES INFECCIOSAS*

*HOSPITAL UNIVERSITARIO CRUCES-VIZCAYA*

Varon 84 años
DM2
HTA
EPOC SEVERO GOLD 3C +SAOS.
CARDIOPATIA : FA ANTICOAGULADA, HTP SEVERA, IT MASIVA, ICC DCHA
HEPATOPATIA OH + CONGESTIVA CRONICA
BICITOPENIA CRONICA (anemia 11, trombopenia 80000)
ERC estadio 2 con reagudizaciones

PTR BILATERAL (DCHA 2010, IZDA 2008)

# Una sorprendente historia de IHAs por G+



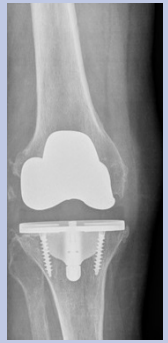
2017

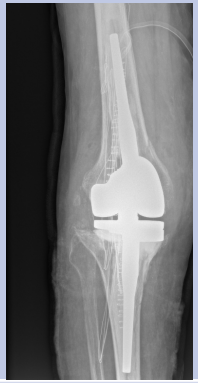
IHA PTR DCHA

**STREPTO ORALIS**

DAIR

# Una sorprendente historia de IHAs por G+





2017

IHA PTR DCHA

**STREPTO ORALIS**

DAIR

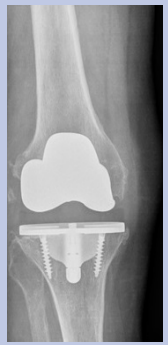
2021

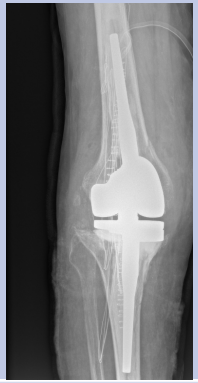
IHA PTR DCHA

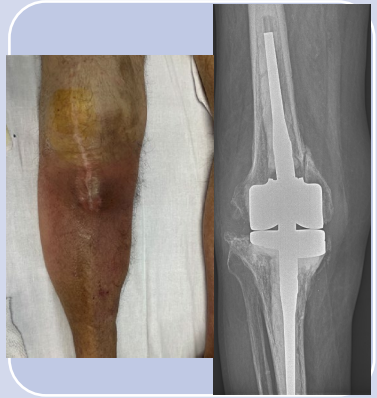
**PARVIMONAS MICRA**

RECAMBIO 1 T

# Una sorprendente historia de IHAs por G+

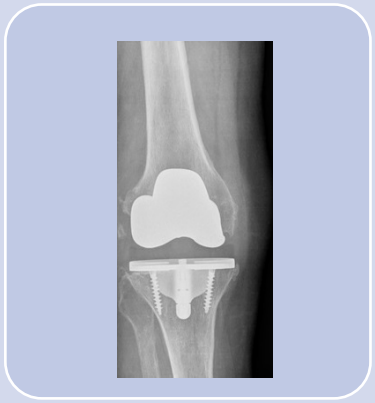


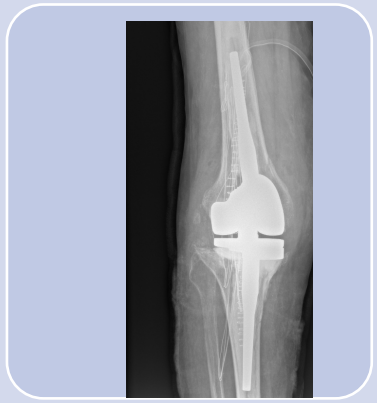


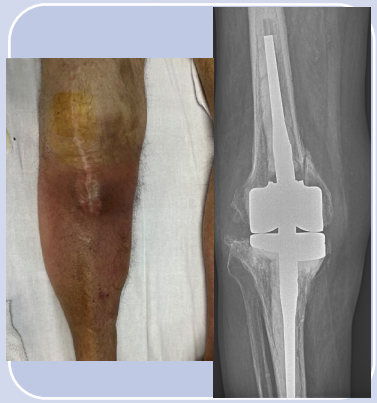


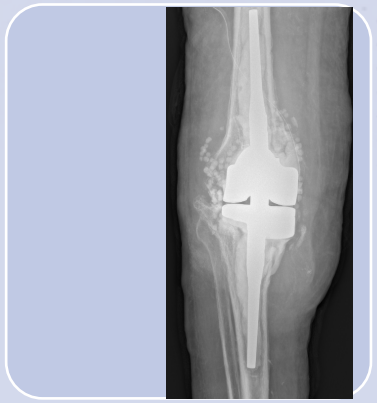
| 2017 | 2021 | ABRIL 2022 | |
|---|---|---|---|
| IHA PTR DCHA | IHA PTR DCHA | IHA PTR BILATERAL | |
| **STREPTO ORALIS** | **PARVIMONAS MICRA** | **LISTERIA MONOCYTOGENES** | |
| DAIR | RECAMBIO 1 T | REC 1 T BILAT | |
| | | COLGAJO GEMELAR DCHO | |

# Una sorprendente historia de IHAs por G+









| 2017 | 2021 | ABRIL 2022 | OCTUBRE 2022 |
|---|---|---|---|
| IHA PTR DCHA | IHA PTR DCHA | IHA PTR BILATERAL | IHA PTR DCHA |
| **STREPTO ORALIS** | **PARVIMONAS MICRA** | **LISTERIA MONOCYTOGENES** | **ENTEROCOCO FAECALIS** |
| DAIR | RECAMBIO 1 T | REC 1 T BILAT | DAIR |
| | | COLGAJO GEMELAR DCHO | |

*MANIPULACION DENTAL*

*MANIPULACION DENTAL*

?

?

SIEMPRE HC NEGATIVOS

ETT SIN EI

TAC BODY SIN FOCOS

COLONO: POLIPECTOMIA

# Una sorprendente historia de IPAs por G+

**2017**

IHA PTR DCHA

**STREPTO ORALIS**

DAIR

| Microorganismo | Streptococcus oralis |
|---|---|
| Antibiótico | Estado |
| Penicilina | Sensible |
| Ampicilina | Sensible |
| Amoxicilina | Sensible |
| Ceftriaxona | Sensible |
| Eritromicina | Sensible |
| Clindamicina | Sensible |
| Vancomicina | Sensible |
| Tetraciclina | Sensible |
| Cloranfenicol | Sensible |
| Cotrimoxazol (sulfametoxazol y trimetoprim) | Sensible |
| Levofloxacino | Sensible |
| Norfloxacino | Resistente |
| Rifampicina | Sensible |

Ceftriaxona
Levo/rifa 8 semanas

**2021**

IHA PTR DCHA

**PARVIMONAS MICRA**

RECAMBIO 1 T

| Microorganismo | Parvimonas micra |
|---|---|
| Antibiótico | Estado |
| Penicilina | Sensible |
| Amoxicilina + clavulanico | Sensible |
| Clindamicina | Sensible |
| Metronidazol | Sensible |

Dapto→ceftriaxona
Levo/rifa 6 semanas

**ABRIL 2022**

IHA PTR BILATERAL

**LISTERIA MONOCYTOGENES**

REC 1 T BILAT

| Microorganismo | Listeria monocytogenes |
|---|---|
| Antibiótico | Estado |
| Penicilina | Sensible |
| Ampicilina | Sensible |
| Gentamicina | Sensible |
| Eritromicina | Sensible |
| Clindamicina | Resistente |
| Vancomicina | Sensible |
| Tetraciclina | Sensible |
| Levofloxacino | Sensible |
| Rifampicina | Sensible |

Ampi/ceftri 6 sem
Septrin 3 meses

**OCTUBRE 2022**

IHA PTR DCHA

**ENTEROCOCO FAECALIS**

DAIR

| Microorganismo | Enterococcus faecalis |
|---|---|
| Antibiótico | Estado |
| Ampicilina | Sensible |
| Amoxicilina + clavulanico | Sensible |
| Linezolid | Sensible |
| Vancomicina | Sensible |
| Teicoplanina | Sensible |
| Tetraciclina | Resistente |
| Levofloxacino | Sensible |
| Rifampicina | Resistente |
| Cotrimoxazol (sulfametoxazol y trimetoprim) | Resistente |

Ampi/ceftri 4 sem
Amoxicilina 4 sem

# ENTEROCOCO FAECALIS… ¿FÁCIL O DIFÍCIL?

The NEW ENGLAND JOURNAL of MEDICINE

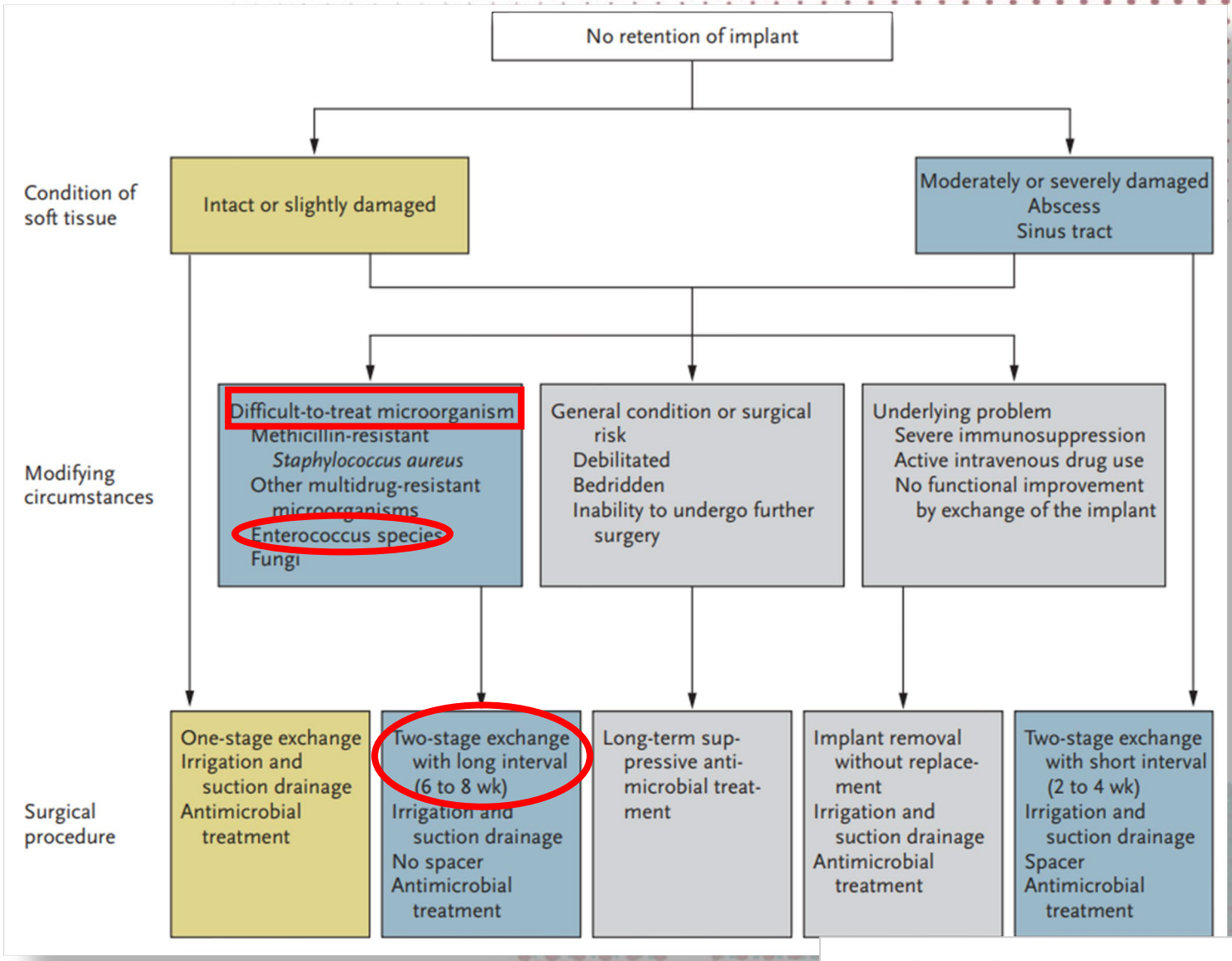
REVIEW ARTICLE

CURRENT CONCEPTS

## Prosthetic-Joint Infections

Werner Zimmerli, M.D., Andrej Trampuz, M.D., and Peter E. Ochsner, M.D.

*"In the presence of a foreign body, enterococcal infections present an additional challenge, since most antibiotics lack antibiofilm activity against enterococci "*




N Engl J Med 2004;351:1645-54.

# ENTEROCOCO FAECALIS… ¿FÁCIL O DIFÍCIL?

| | AÑO | n pacientes | TASA CURACION GLOBAL | CIRUGIA MAS EXITOSA | ENTONCES..? |
|---|---|---|---|---|---|
| EL HELOU | 2008 | 50 | 88% | REC 2 T |  |
| TORNERO | 2014 | 203 | 66% | REC 2 T |  |
| DUIJF | 2015 | 44 | 48% | EXPLANTE |  |
| KHEIR | 2017 | 87 | 62,8% | REC 2 T |  |
| THOMPSON | 2019 | 55 | 67%<br>80% | EXPLANTE |  |
| RENZ | 2019 | 75 | 84% | DAIR |  |

2023

# ENTEROCOCO FAECALIS… ¿FÁCIL O DIFÍCIL?

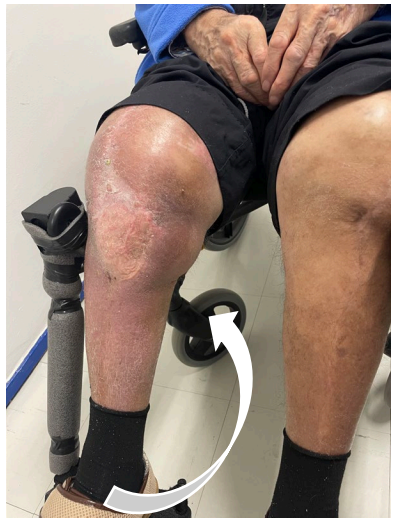
## Enterococcal periprosthetic joint infection: clinical and microbiological findings from an 8-year retrospective cohort study

Nora Renz[1], Rihard Trebse[2], Doruk Akgün[1], Carsten Perka[1] and Andrej Trampuz[1*]

| | All episodes ($n = 75$) | Mono-microbial ($n = 37$) |
|---|---|---|
| Intravenous antibiotic agent | | |
| Penicillin derivative | 61/74 (82) | 30/37 (81) |
| Vancomycin or daptomycin | 12/74 (16) | 6/37 (16) |
| Other | 1/74 (3) | 1/37 (3) |
| Additive agent for combination treatment | | |
| Fosfomycin | 17/74 (23) | 9/37 (24) |
| Gentamicin | 16/74 (22) | 11/37 (30) |
| Fosfomycin and gentamicin | 8/74 (11) | 5/37 (14) |
| Vancomycin or daptomycin | 18/74 (24) | 4/37 (11) |
| None | 15/74 (20) | 8/37 (22) |

Renz *et al. BMC Infectious Diseases* (2019) 19:1083

# A las 2 semanas de suspender el tratamiento....



| | |
|---|---|
| -Aspecto | Hemorragico |
| -Hematies | 73.000 /µL |
| -Otras células | 58.065 /µL |
| -Linfocitos | 2 % |
| -Neutrofilos | 98 % |
| -Glucosa | 62 mg/dL |

| Microorganismo | Enterococcus faecalis |
|---|---|
| Antibiótico | Estado |
| Ampicilina | Sensible |
| Amoxicilina + clavulanico | Sensible |
| Linezolid | Sensible |
| Vancomicina | Sensible |
| Teicoplanina | Sensible |
| Tetraciclina | Resistente |
| Levofloxacino | Sensible |
| Rifampicina | Resistente |
| Cotrimoxazol (sulfametoxazol y trimetoprim) | Resistente |

Reinicio de amoxicilina 1 gr/8 h…
y nuevo planteamiento medico quirúrgico en sesión GEMIO

IPP REFRACTARIA REAGUDIZADA/INFECCION CRONICA SOBRE PROTESIS EN 2º REVISION POR E. FAECALIS

NUEVO DAIR

Posible fracaso

RETIRADA PROTÉSICA

SUPRESION ANTIBIOTICA INDEFINIDA

RECAMBIO 1 TIEMPO

Limitacion stock oseo
Problemas de cobertura
VIDA CAMA-SILLA RUEDAS
¿Riesgo/beneficio?

RECAMBIO 2 TIEMPOS

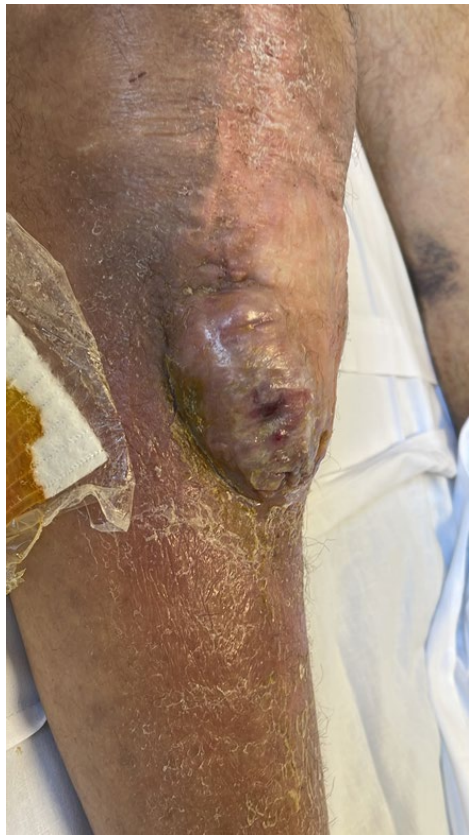
Limitacion stock oseo
Problemas de cobertura
VIDA CAMA-SILLA RUEDAS

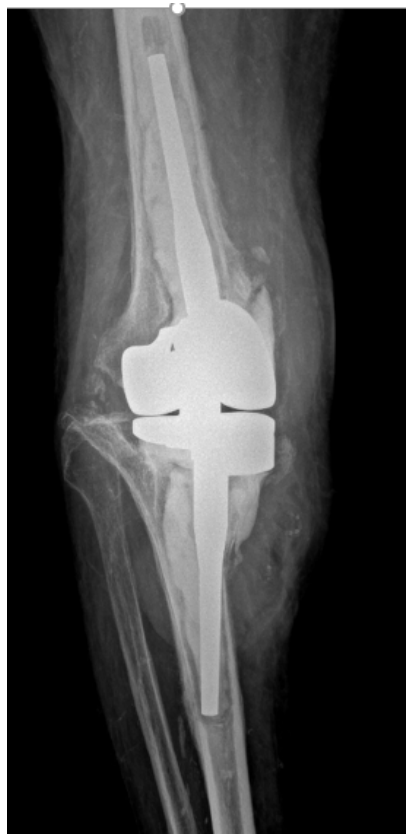
ARTRODESIS

VIDA CAMA-SILLA RUEDAS
¿DISFUNCIONAL???

AMPUTACION

# A los pocos días .. Ingreso por HDB





RECTORRAGIA

Insuficiencia respiratoria-oxigenoterapia
HB 7
Plaquetas 50000
Deterioro fx hepática
Creat 2,8 FG 30

IPP REFRACTARIA REAGUDIZADA/INFECCION CRONICA SOBRE PROTESIS EN 2º REVISION POR E. FAECALIS

NUEVO DAIR

Posible fracaso

RETIRADA PROTÉSICA (DIFERIDA)

SUPRESION ANTIBIOTICA (INDEFINIDA )

Inestabilidad hemodinámica

RECAMBIO 1 TIEMPO

Limitacion stock oseo
Problemas de cobertura
VIDA CAMA-SILLA RUEDAS
¿Riesgo/beneficio?

RECAMBIO 2 TIEMPOS

Limitacion stock oseo
Problemas de cobertura
VIDA CAMA-SILLA RUEDAS

ARTRODESIS

VIDA CAMA-SILLA RUEDAS
¿DISFUNCIONAL???

AMPUTACION

2023

# IPP REFRACTARIA REAGUDIZADA/INFECCION CRONICA SOBRE PROTESIS EN 2º REVISION POR E. FAECALIS

- AMOXICILINA — FAIL
- LINEZOLID
- DOXICICLINA
- VANCOMICINA/TEICOPLANINA
- DAPTOMICINA
- DALBAVANCINA/ORITAVANCINA
- TEDIZOLID
- FOSFOMICINA
- LEVOFLOXACINO

SUPRESION ANTIBIOTICA (INDEFINIDA)

| 27/12/2022 | LIQUIDO SINOVIAL |
|---|---|
| Microorganismo | Enterococcus faecalis |
| Antibiótico | Estado |
| Ampicilina | Sensible |
| Amoxicilina + clavulanico | Sensible |
| Linezolid | Sensible |
| Vancomicina | Sensible |
| Teicoplanina | Sensible |
| Tetraciclina | Resistente |
| Levofloxacino | Sensible |
| Rifampicina | Resistente |
| Cotrimoxazol (sulfametoxazol y trimetoprim) | Resistente |

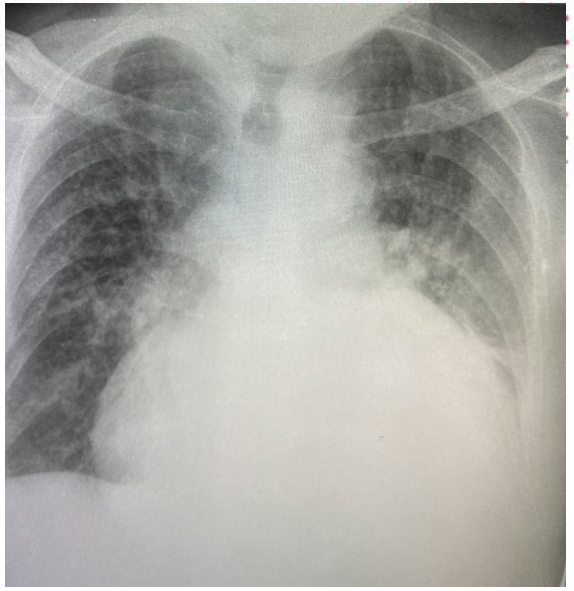
2023

# DAPTOMICINA

MEJORIA CLINICA DE LA RODILLA → MEJORIA ANALITICA → 5º dia

Empeoramiento respiratorio, radiológico, gasométrico, tos → ¿¿ NEUMONITIS POR DAPTO??

o su ICC….



- FIEBRE
- DISNEA
- INFILTRADOS EN RX
- >25% EOSINOFILOS EN LBA
- 4 SEM DE TTO DAPTOMICINA
- RAPIDA MEJORIA TRAS LA SUSPENSION

Kim Pwet al. Eosinophilic pneumonia in patients treated with daptomycin: review of the literature and US FDA adverse event reporting system reports. Drug Saf 2012; 35:447–57

# DAPTOMICINA

# NEUMONITIS POR DAPTOMICINA

## Eosinophilic Syndromes Associated With Daptomycin Use: Re-exposure Hypersensitivity Pneumonitis and Prior Peripheral Eosinophilia

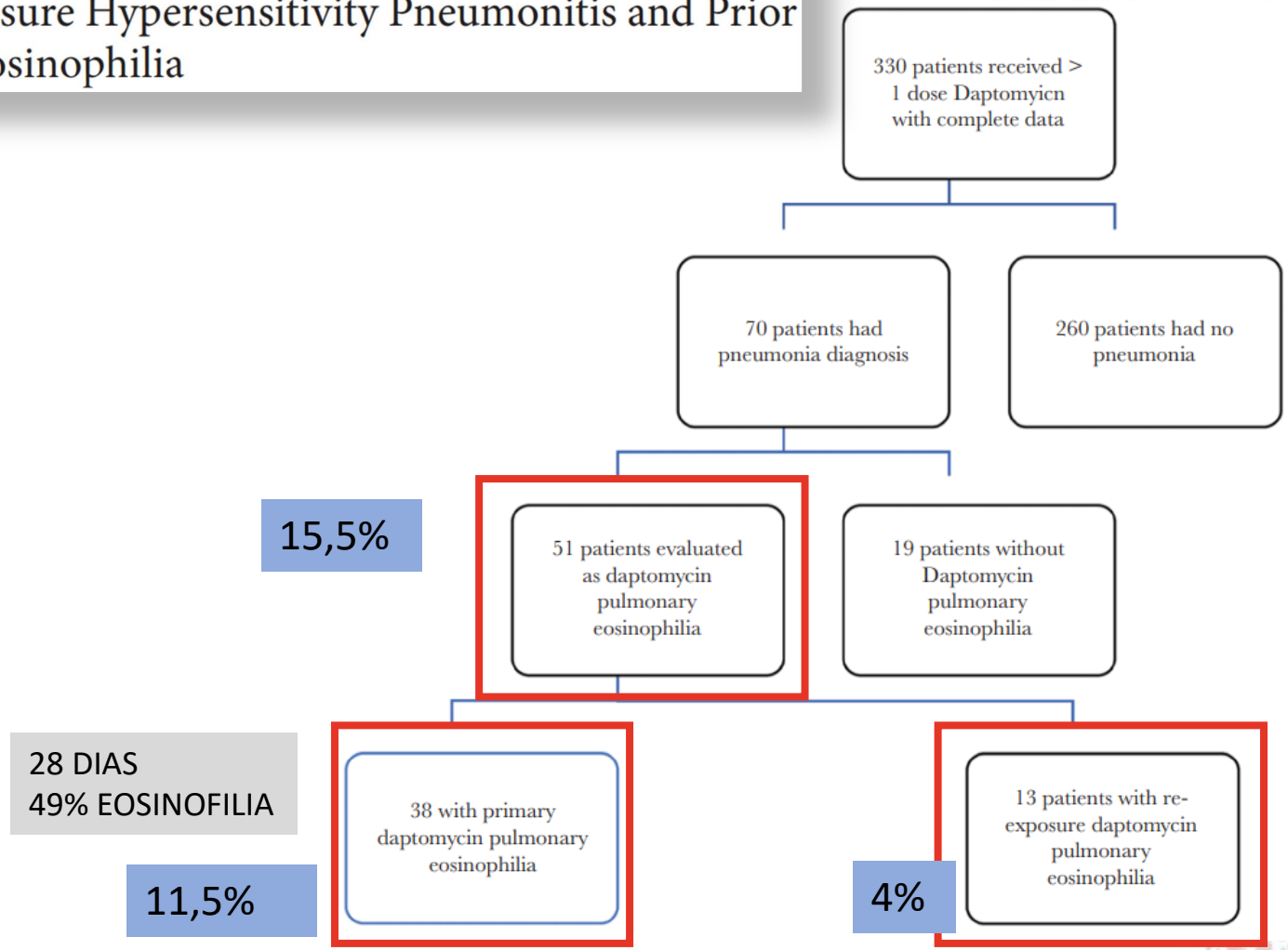



**Table 3. Clinical Presentation of Hyperacute Pneumonitis After Daptomycin Re-exposure**

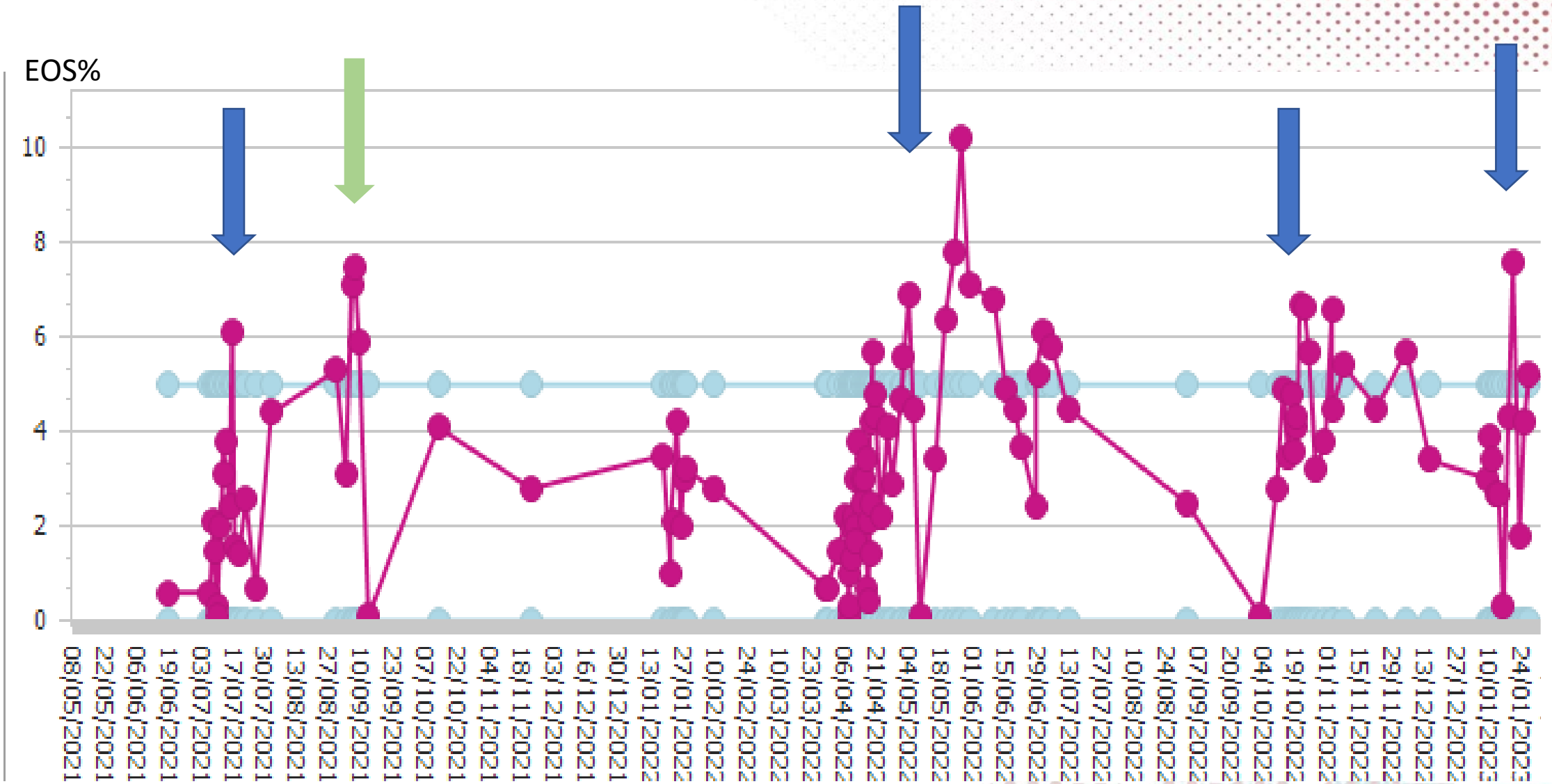
| Clinical Factors | No. (%) |
|---|---|
| Cough | 13 (100) |
| Shortness of breath | 13 (100) |
| Fevers >38°C | 11 (78) |
| Rash | 1 (7) |
| Abnormal chest x-ray—diffuse infiltrates | 13 (100) |
| Peripheral eosinophilia >5% | 12 (92.5) |
| Corticosteroid therapy | 7 (54) |
| ICU admission | 7 (54) |
| Renal insufficiency | 1 (7) |
| Prior eosinophilia >5% of previous treatment | 13 (100) |
| Median time to onset of symptoms, d | 3 |

Clinical monitoring of peripheral eosinophilia while on daptomycin therapy could be a future predictor for a re-exposure fulminant DPE

**<7 DIAS**
**92% EOSINOFILIA**
**EOSINOFILIA PREVIA 100%**
**SI EOS PREVIOS>5%: VPP 100%**

West et al. Open Forum Infect Dis . 2022 Mar 16;9(4)

# DAPTOS PREVIAS….



# IPP REFRACTARIA  REAGUDIZADA/INFECCION CRONICA SOBRE PROTESIS EN 2º REVISION POR E. FAECALIS

- AMOXICILINA 

- LINEZOLID 
- DOXICICLINA 
- VANCOMICINA/TEICOPLANINA 
- DAPTOMICINA 
- DALBAVANCINA/ORITAVANCINA
- TEDIZOLID
- FOSFOMICINA
- LEVOFLOXACINO

SUPRESION ANTIBIOTICA INDEFINIDA

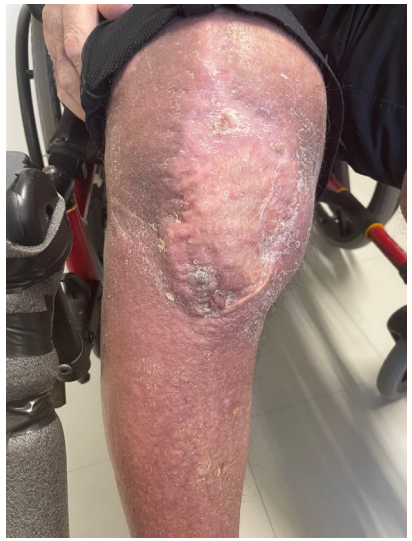
| 27/12/2022 | LIQUIDO SINOVIAL |
|---|---|
| Microorganismo | Enterococcus faecalis |
| Antibiótico | Estado |
| Ampicilina | Sensible |
| Amoxicilina + clavulanico | Sensible |
| Linezolid | Sensible |
| Vancomicina | Sensible |
| Teicoplanina | Sensible |
| Tetraciclina | Resistente |
| Levofloxacino | Sensible |
| Rifampicina | Resistente |
| Cotrimoxazol (sulfametoxazol y trimetoprim) | Resistente |

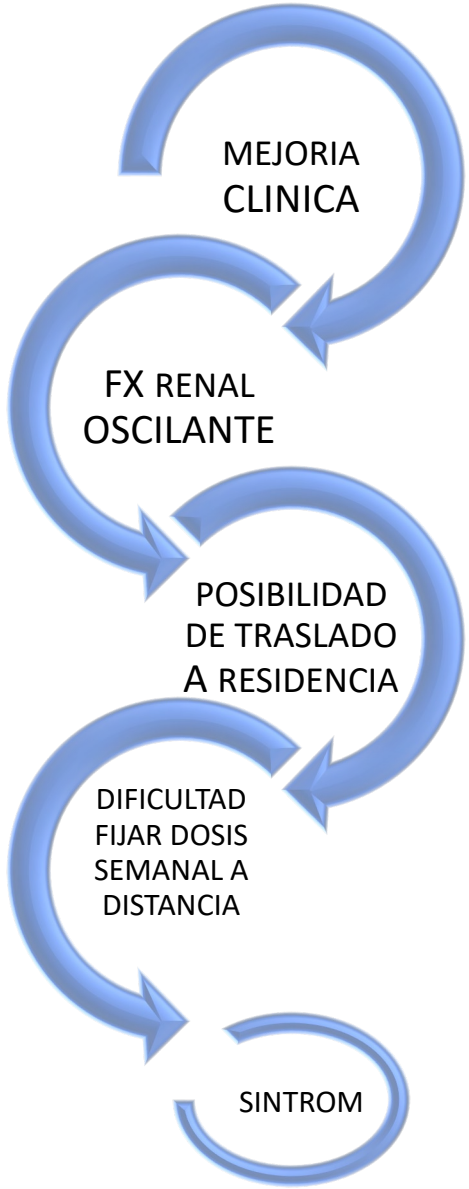
2023

# DALBAVANCINA

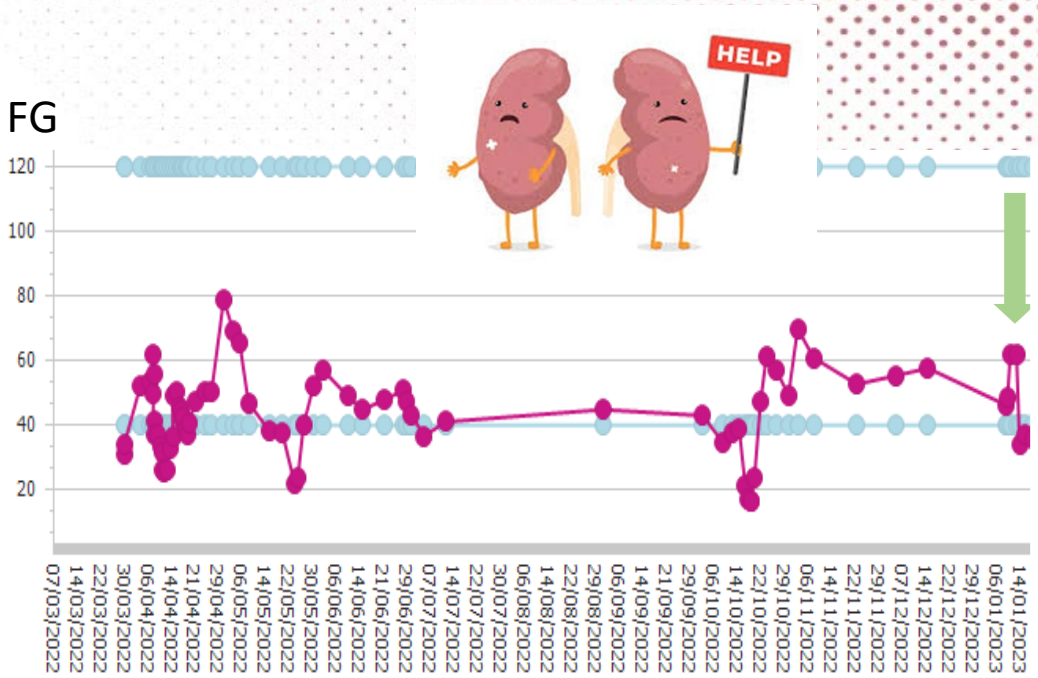
1ª DOSIS 1000 mg
2º DOSIS 500 mg

3ª dosis….?






FG




¿NEFROTOXICIDAD?

¿¿DATOS DE DALBA EN PACIENTES CON ERC ESTADIO AVANZADO???

¿¿DATOS DE DALBA COMO TOS EN ESTOS PACIENTES??

# DALBAVANCINA


*Aunque en los estudios reportados no se encontró ningún efecto adverso grave en lo referente a ototoxicidad y nefrotoxicidad, éstos son comunes en la familia de antibióticos glicopeptídicos, como la vancomicina y teicoplanina. Por su similitud estructural, no se puede excluir el hallazgo de estos efectos adversos después de tratamientos prolongados o repetidos con dalbavancina*

# DALBAVANCINA

## Dalbavancin in the treatment of different gram-positive infections: a real-life experience

Emilio Bouza [a,b,c,d], Maricela Valerio [a,*], Alex Soriano [e], Laura Morata [e], Enrique García Carus [e], Carmen Rodríguez-González [b,f], Ma Carmen Hidalgo-Tenorio [g], Antonio Plata [h], Patricia Muñoz [a,b,c,d,*], Antonio Vena [a,b,d] on behalf of the DALBUSE Study Group (Dalbavancina: Estudio de su uso clinico en España)

**Table 1**
Baseline patient characteristics ($n = 69$).

| Characteristic | n (%) [a] |
|---|---|
| Age (years) [median (IQR)] | 63.5 (49.3–72.0) |
| Male sex | 40 (58.0) |
| Department | |
| Medical | 36 (52.2) |
| Surgical | 29 (42.0) |
| Outpatient setting | 4 (5.8) |
| Underlying diseases | |
| Diabetes mellitus | 23 (33.3) |
| Cardiovascular disease | 22 (31.9) |
| Respiratory tract disease | 15 (21.7) |
| Neurological disorder | 14 (20.3) |
| Immunosuppressive therapy | 9 (13.0) |
| Solid-organ malignancy | 8 (11.6) |
| Gastrointestinal disease | 7 (10.1) |
| Haematological malignancy | 3 (4.3) |
| HIV infection | 2 (2.9) |
| Bone marrow transplant | 1 (1.4) |
| Solid-organ transplant | 1 (1.4) |
| Renal function | |
| Chronic renal failure | 15 (21.7) |
| Haemodialysis | 4 (5.8) |
| Liver disease [b] | 7 (10.1) |
| A | 3 (4.3) |
| B | 3 (4.3) |
| C | 1 (1.4) |
| Charlson comorbidity index [median (IQR)] | 3 (1–5) |
| McCabe score | |
| Non-fatal | 52 (75.4) |
| Ultimately fatal | 14 (20.3) |
| Rapidly fatal | 3 (4.3) |

1 day in 23 patient
14 days in 12 patients;
21 days in 5 patients
28 days in 9 patients
35 days in 6 patients
42 days in 8 patients

Only one patient, treated for 56 days, received a dosage reduction for chronic renal disease with CLCr ≤ 30 mL/min.

**Table 4**
Safety of dalbavancin therapy in study population ($n = 69$).

| Safety parameter | n (%) |
|---|---|
| Mild adverse events | 7 (10.1) |
| Severe adverse events | 2 (2.9) [a] |
| Overall adverse events | 9 (13.0) |
| Potential type of adverse event | |
| Rash | 2 (2.9) |
| Tachycardia | 2 (2.9) |
| Impaired renal function | 2 (2.9) |
| Nausea | 1 (1.4) |
| Rectal bleeding | 1 (1.4) |
| Candidiasis | 1 (1.4) |
| Liver failure | 0 |
| Haematological disorder | 0 |

[a] Rectal bleeding ($n = 1$) and tachycardia ($n = 1$).

International Journal of Antimicrobial Agents 51 (2018) 571–577

# DALBAVANCINA

## Safety and Efficacy of Prolonged Use of Dalbavancin in Bone and Joint Infections

L. Morata,[a] J. Cobo,[b] M. Fernández-Sampedro,[c] P. Guisado Vasco,[d] E. Ruano,[e] J. Lora-Tamayo,[f] M. Sánchez Somolinos,[g] P. González Ruano,[h] A. Rico Nieto,[i] A. Arnaiz,[j] M. Estébanez Muñoz,[k] M. E. Jiménez-Mejías,[l] A. B. Lozano Serrano,[m] E. Múñez,[n] D. Rodriguez-Pardo,[o] R. Argelich,[p] A. Arroyo,[q] J. M. Barbero,[r] F. Cuadra,[s] A. Del Arco,[t] M. D. del Toro,[u,v] L. Guio,[w] D. Jimenez-Beatty,[x] N. Lois,[y] O. Martin,[z] R. M. Martínez Alvarez,[aa] F. J. Martinez-Marcos,[bb] L. Porras,[cc] M. Ramírez,[dd] J. Vergas García,[ee] A. Soriano[a]

Éxito: 80% en secuenciación
50% en fracaso

**TABLE 2** Characteristics and outcomes of patients with implant-associated infections ($n = 45$)

| Variable[f] | Value |
|---|---|
| Age (yrs), mean (SD) | 64 (15) |
| Male sex, no. (%) | 24 (53.3) |
| Comorbidity, no. (%) | |
| Diabetes mellitus | 7 (15.5) |
| Rheumatoid arthritis | 3 (6.6) |
| Chronic renal failure | 5 (11.1) |
| Median (IQR) SCr (mg/dl) before dalbavancin treatment[a] | 1 (0.6–1) |
| Median (IQR) highest SCr (mg/dl) during dalbavancin[a] | 1 (0.6–1) |
| Median (IQR) no. of dalbavancin doses | 5 (3–8) |

1 case with a documented increase of 0.5 mg/dl of serum creatinine

The first conclusion of our study is that dalbavancin is well tolerated, with minor adverse events without any treatment interruption or evidence of nephrotoxicity. Indeed, dalbavancin is a derivative of teicoplanin, and it is significantly less toxic than vancomycin

Antimicrob Agents Chemother. 2019

# DALBAVANCINA

## Dalbavancin in clinical practice in Spain: a 2 year retrospective study

Laura Morata[1], José María Aguado[2], Miguel Salavert[3], Juan Pasquau[4], Enrique Míguez[5], Patricia Muñoz[6], Irantzu Rosselló[7] and Benito Almirante[8*9]

187 patients were finally analysed

The median number of doses was 1
The median number of weeks was 2.
One patient on suppressive treatment (34 weeks)

| | Patients (*N*=187) |
|---|---|
| Age (years), mean (SD) | 63.9 (18.6) |
| Gender, *n* (%) | |
| Male | 122 (65.2) |
| Female | 65 (34.8) |
| Comorbidities, *n* (%) | |
| None | 27 (14.4) |
| Cardiovascular | 51 (27.3) |
| Diabetes mellitus | 44 (23.5) |
| Chronic kidney disease | 22 (11.8) |
| Solid tumour | 28 (15.0) |
| Respiratory disease | 8 (4.3) |
| Leukaemia | 7 (3.7) |
| Lymphoma | 7 (3.7) |
| Metastatic solid tumour | 4 (2.1) |
| Charlson comorbidity index, mean (SD) | 4.0 (3.0) |
| Estimated 10 year survival, mean (SD) | 46.4 (39.2) |

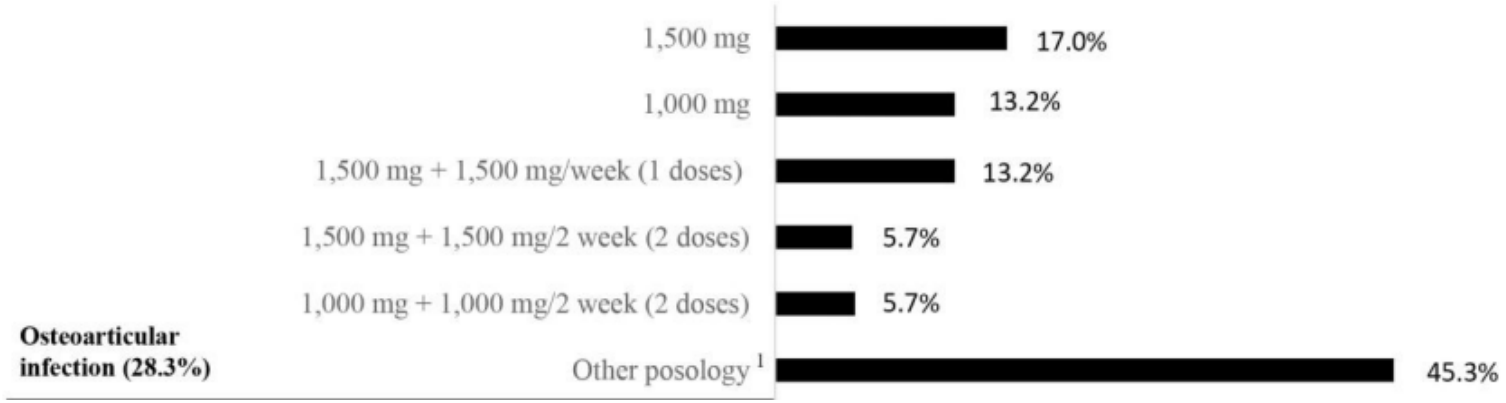



**Table 3.** Safety of dalbavancin treatment

| | Patients (*N*=187) |
|---|---|
| Adverse events[a], *n* (%) | 6 (3.2) |
| Intensity, *n* (%) | |
| Mild | 4 (66.7) |
| Moderate | 1 (16.6) |
| Severe | 1 (16.6) |
| Related to dalbavancin, *n* (%) | |
| Possible | 4 (66.7) |
| Probable | 2 (33.3) |
| Treatment discontinuation due to adverse events[b], *n* (%) | 2 (1.1) |

[a]Mild testicular oedema (*n*=1), mild dizziness (*n*=1), mild pruritus (*n*=1), mild asthenia (*n*=1), moderate balanitis (*n*=1), severe thrombopenia (*n*=1).
[b]Reasons: testicular oedema, severe thrombopenia.

JAC Antimicrob Resist. 2022

## DALBAVANCINA

# Safety of Dalbavancin in the Treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSI): Nephrotoxicity Rates Compared with Vancomycin: A Post Hoc Analysis of Three Clinical Trials

The rate of nephrotoxicity was lower in patients receiving **dalbavancin** (49/1325, **3.7%**) than in those receiving **vancomycin** (5/54, **9.3%**; P = 0.039, Table 3). Rates of nephrotoxicity were similar for patients receiving dalbavancin as a single dose and those receiving two-dose therapy

| | | | | | |
|---|---|---|---|---|---|
| Nephrotoxicity on therapy[c] | | | | | |
| All dalbavancin patients vs patients intravenously administered vancomycin only | 15/345 (4.3) | 34/980 (3.5) | 49/1325 (3.7) | 5/54 (9.3) | 0.039 |

Infect Dis Ther (2021) 10:471–481

# DALBAVANCINA



GFR did not result associated with drug CL, probably as a consequence of the lack of patients with impaired renal function in our cohort

Assessing drug exposure by means of therapeutic drug monitoring (TDM) after 3–5 weeks from starting treatment, depending on the degree of the patient's renal function, and expert Interpretation of TDM results by skilled clinical pharmacologists, may be the way forward for properly managing the duration of optimal treatment

Antimicrob Agents Chemother. 2023 May

Antibiotics 2022, 11,

# Y LA ORITAVANCINA?

**Table 1. Comparative In Vitro Minimum Inhibitory Morbidity Concentrations of Oritavancin for Gram-Positive Organisms**

| Organism | Oritavancin | Vancomycin | Daptomycin | Telavancin [14] | Dalbavancin [13] |
|---|---|---|---|---|---|
| MSSA | 0.06 | 1 | 0.5 | 0.06 | 0.06 |
| MRSA | 0.06 | 1 | 0.5 | 0.06 | 0.06 |
| VISA | 2 | 8 | 4 | 0.75 | . . . |
| VRSA | 1 | >64 | 1 | 6 | . . . |
| CoNS | 0.06 | 2 | 0.5 | 0.06 | 0.06–0.12 |
| Vancomycin susceptible | | | | | |
| *Enterococcus faecalis* | 0.03 | 2 | 2 | 0.16 | 0.06 |
| *Enterococcus faecium* | <0.008 | 1 | 4 | 0.06 | 0.12 |
| Vancomycin resistant (VanA) | | | | | 32–>128 |
| *E. faecalis* | 0.5 | >16 | 1 | . . . | . . . |
| *E. faecium* | 0.12 | >16 | 2 | 2 | . . . |
| Vancomycin resistant (VanB) | | | | | 0.12–1 |
| *E. faecalis* | 0.03 | >16 | 2 | . . . | . . . |
| *E. faecium* | ≤0.008 | >16 | 2 | 8 | . . . |
| *Streptococcus pneumoniae* | ≤0.008 | ≤1 | . . . | ≤0.015 | ≤0.03–0.06 |
| Viridans group streptococci | 0.03 | 1 | 1 | 0.03 | 0.016–0.03 |
| β-hemolytic streptococci | 0.12 | 0.5 | 0.25 | 0.06 | 0.015–0.06 |

Clin Infect Dis. 2015 Aug 15;61(4):627-32.

# Y LA ORITAVANCINA?

The CHROME Study, a Real-world Experience of Single- and Multiple-Dose Oritavancin for Treatment of Gram-Positive Infections

Mark Redell,[1] Miguel Sierra-Hoffman,[2,3] Maha Assi,[4] Markian Bochan,[5] David Chansolme,[6] Anurag Gandhi,[7] Kathleen Sheridan,[8] Ivan Soosaipillai,[9] Thomas Walsh,[10] and Jill Massey[1]

Successful treatment of a prosthetic hip infection due to *Enterococcus faecalis* with sequential dosing of oritavancin and prosthesis preservation without prosthetic joint surgical manipulation

IDCases. 2020 Sep 5;22

**Table 4. Clinical and Microbiologic Outcomes in 438 Evaluable Patients[a]**

| Outcome | Single Dose, no./No. (%) | Multiple Doses (Interrupted by ≤14 d), no./No. (%) | Overall, no./No. (%) |
|---|---|---|---|
| Clinical success[b] | 356/406 (87.7) | 30/32 (93.8) | 386/438 (88.1) |
| Clinical cure | 262/406 (64.5) | 20/32 (62.5) | 282/438 (64.4) |
| Clinical improvement | 94/406 (23.2) | 10/32 (31.3) | 104/438 (23.7) |
| Clinical failure | 50/406 (12.3) | 2/32 (6.2) | 52/438 (11.9) |

7 patients joint infections: 4 septic arthritis and 3 PJI

Open Forum Infect Dis. 2019 Nov 4;6(11)

**FICHA TÉCNICA O RESUMEN DE LAS CARACTERÍSTICAS DEL PRODUCTO**

No es necesario un ajuste de la dosis de oritavancina en pacientes con insuficiencia renal leve o moderada. No se ha evaluado la farmacocinética de oritavancina en pacientes con insuficiencia renal grave.

https://www.ema.europa.eu/en/documents/product-information

2023

# IPP REFRACTARIA REAGUDIZADA/INFECCION CRONICA SOBRE PROTESIS EN 2º REVISION POR E. FAECALIS

- AMOXICILINA 

- LINEZOLID 
- DOXICICLINA 
- VANCOMICINA/TEICOPLANINA 
- DAPTOMICINA 
- DALBAVANCINA/ORITAVANCINA 
- TEDIZOLID
- FOSFOMICINA
- LEVOFLOXACINO

SUPRESION ANTIBIOTICA INDEFINIDA

| 27/12/2022 | LIQUIDO SINOVIAL |
|---|---|
| Microorganismo | Enterococcus faecalis |
| Antibiótico | Estado |
| Ampicilina | Sensible |
| Amoxicilina + clavulanico | Sensible |
| Linezolid | Sensible |
| Vancomicina | Sensible |
| Teicoplanina | Sensible |
| Tetraciclina | Resistente |
| Levofloxacino | Sensible |
| Rifampicina | Resistente |
| Cotrimoxazol (sulfametoxazol y trimetoprim) | Resistente |

2023

# TEDIZOLID… POR CI LINEZOLID?

## Predictive score of haematological toxicity in patients treated with linezolid

J. González-Del Castillo [1,2] & F. J. Candel [2,3] & R. Manzano-Lorenzo [4] & L. Arias [4] & E. J. García-Lamberechts [1,2] & F. J. Martín-Sánchez [1,2] & Representatives of the Emergency Department Investigation Unit (addendum)

**Table 3** Score for developing haematological toxicity

| Variable | Value of each item |
|---|---|
| Basal platelet count ≤90,000/mm$^3$ | 8 |
| Renal failure | 2 |
| Moderate or severe liver disease | 2 |
| Cerebrovascular disease | 2 |

The points assigned to each variable must be added to obtain a total score (0–14 points)

Low risk: 0–4 points; Intermediate risk: 5–10 points; High risk: >10 points

Eur J Clin Microbiol Infect Dis (2017) 36:1511–1517

TEDIZOLID

# TEDIZOLID EN INF PROTESICA?

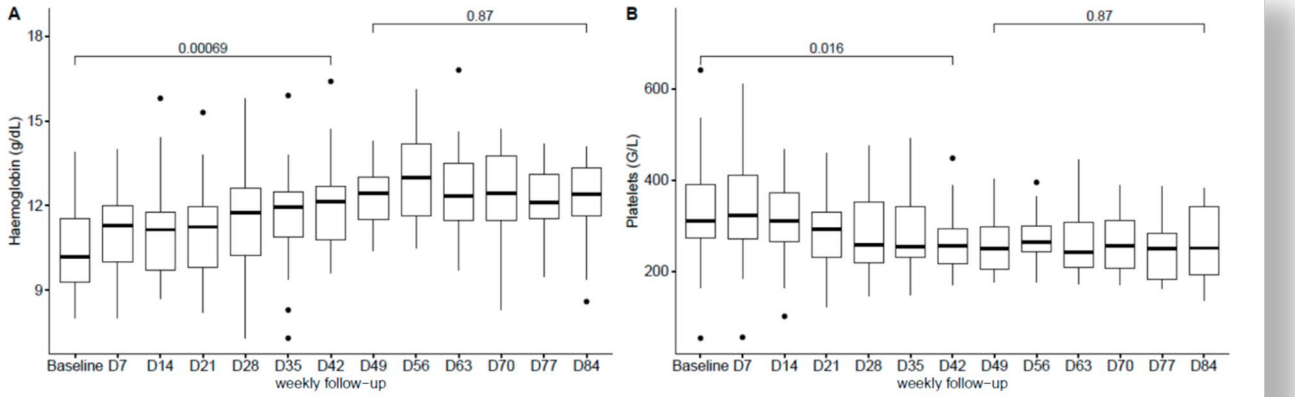
## Tolerance of Prolonged Oral Tedizolid for Prosthetic Joint Infections: Results of a Multicentre Prospective Study

Eric Senneville [1,2,3,*], Aurélien Dinh [4,5], Tristan Ferry [6,7], Eric Beltrand [3,8], Nicolas Blondiaux [3,9] and Olivier Robineau [1,2,3]

Primer studio prospectivo de uso prolongado en infecciones protesicas (6-12 semanas)
33 pacientes ---8 enterococo

60% ef adversos:
Suspension del tto solo en 2 pacientes con sangrado y anemia

**Hb**




**Plaquetas**




**Table 3.** Episodes of adverse effects reported in 33 patients during tedizolid therapy.

| Adverse Event (N° of Discontinuation of Tedizolid Therapy) | N° of Episodes of Adverse Effects * |
|---|---|
| anemia (2) | 4 |
| asthenia | 1 |
| leukopenia | 2 |
| thrombocytopenia | 2 |
| headache | 2 |
| pruritus | 4 |
| abdominal pain | 1 |
| nausea/vomiting (1) | 2 |
| vertigo | 1 |
| xerosis | 1 |
| dysgeusia | 1 |
| epistaxis | 1 |
| arthralgia (1) | 2 |
| thrush | 1 |
| insomnia | 2 |
| intermittent blurred vision | 1 |
| Total | 28 |

Antibiotics (Basel). 2021 Jan

# TEDIZOLID EN INF PROTESICA?

## Long-Term Use of Tedizolid in Osteoarticular Infections: Benefits among Oxazolidinone Drugs

Eva Benavent [1,2], Laura Morata [2,3,4], Francesc Escrihuela-Vidal [1], Esteban Alberto Reynaga [5], Laura Soldevila [1,2], Laia Albiach [3], Maria Luisa Pedro-Botet [5], Ariadna Padullés [6], Alex Soriano [2,3,4] and Oscar Murillo [1,2,4,*]

51 casos
30 casos (59%) infecciones relacionadas con material ortopedico (17 IPAs) ----Enterococcus spp.: 4
Media 29 días de tratamiento
**OVERALL CURE RATE 83%**

| Hematological Parameters | N | At the Beginning of Treatment with Tedizolid (mean, SD) | At the End of Treatment with Tedizolid (mean, SD) | *p* Value | Use of Rifampicin | Days with Tedizolid (Median, IQR) |
|---|---|---|---|---|---|---|
| Hemoglobin (g/L) | 45 | 108.6 ± 20.3 | 116.3 ± 18.4 | 0.079 | - | 29 (15–44) |
| No anemia * | 10 | 137.5 ± 15.5 | 141.5 ± 11.8 | 0.596 | 30% | 29 (17–42) |
| Mild anemia * | 10 | 114.2 ± 4.4 | 116.4 ± 11.9 | 0.586 | 10% | 20.5 (15–29) |
| Moderate and severe anemia * | 25 | 94.7 ± 2 | 105.4 ± 3.2 | 0.004 | 28% | 31 (14–44) |
| Platelet count ($\times 10^9$/L) | 45 | 240.6 ± 114.6 | 238.9 ± 92.3 | 0.942 | - | 29 (15–44) |
| >150 × $10^9$/L | 33 | 290.7 ± 15.6 | 252 ± 20.7 | 0.134 | 30.3% | 29 (17–42) |
| <150 × $10^9$/L | 12 | 102.7 ± 8.3 | 196.5 ± 17.5 | 0.001 | 8.3% | 37 (9–100) |
| Leucocytes($\times 10^9$/L) | 45 | 6.42 | 6.51 | 0.887 | - | 29 (15–44) |

Antibiotics (Basel). 2021 Jan

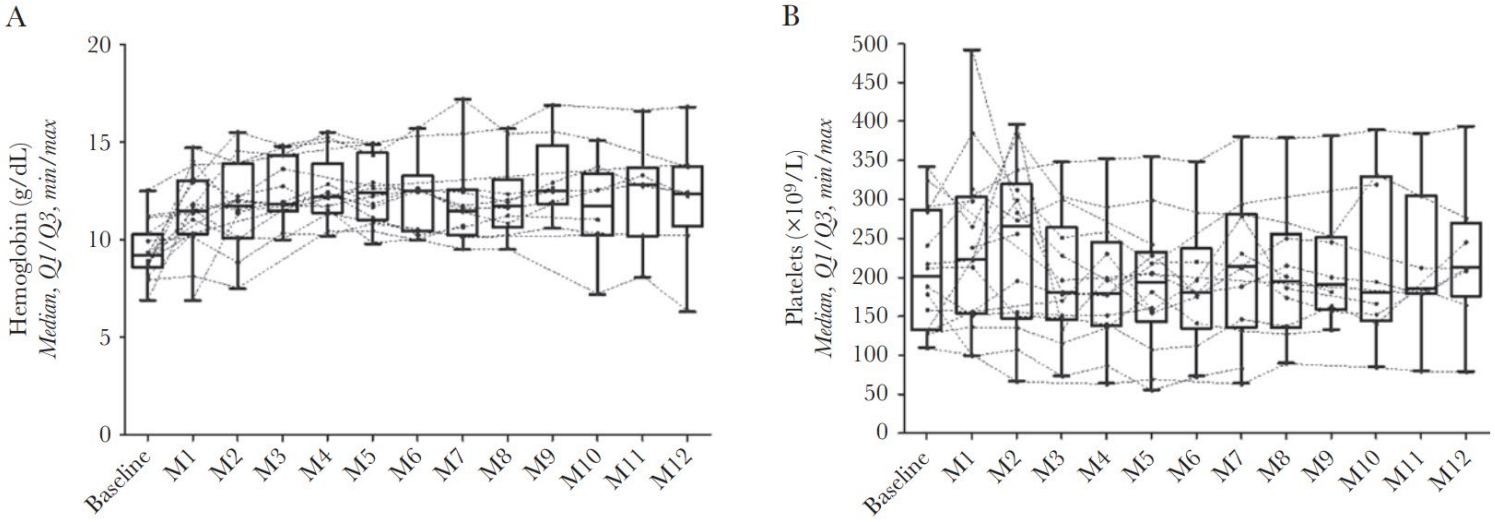
# TEDIZOLID EN INF PROTESICA?

Safety of Tedizolid as Suppressive Antimicrobial Therapy for Patients With Complex Implant-Associated Bone and Joint Infection due to Multidrug-Resistant Gram-Positive Pathogens: Results From the TediSAT Cohort Study

Tristan Ferry,[1,2,3] Anne Conrad,[1,2,3] Eric Senneville,[4,5,6] Sandrine Roux,[1,2] Céline Dupieux-Chabert,[1,2,3] Aurélien Dinh,[7,8] Sébastien Lustig,[2,9] Sylvain Goutelle,[1,2,10] Thomas Briot,[1,2] Truong-Thanh Pham,[1,2,11] Florent Valour[1,2,3]

Serie mas larga de pacientes en tto con TZD como TOS para infecciones asociadas a implantes ortopedicos complejos

17 pacientes------ 1 ENTEROCOCO R VANCO
Duración media de tratamiento **6 meses (rango 1-31 meses)**
8 pacientes previa mielotoxicidad inducida por Linezolid
**OVERALL CURE RATE 76,5%**

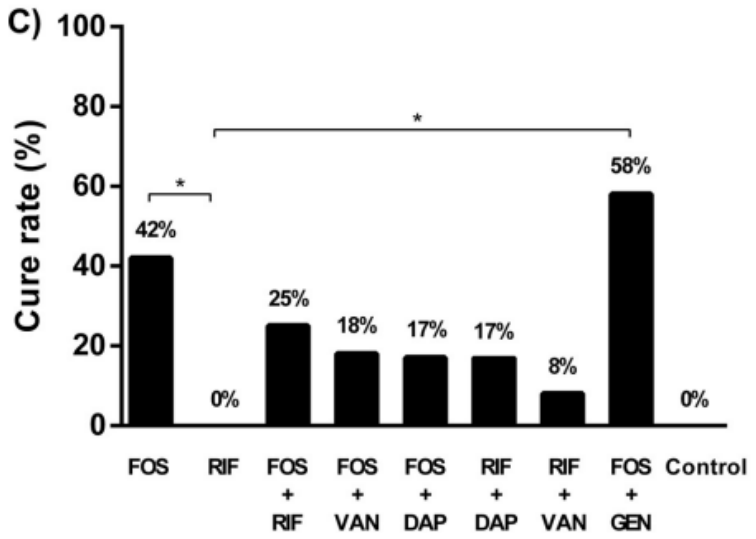



Open Forum Infect Dis. 2021 Jul

# Y LA FOSFO…?

AAC Journals.ASM.org

**Activities of Fosfomycin and Rifampin on Planktonic and Adherent *Enterococcus faecalis* Strains in an Experimental Foreign-Body Infection Model**




**Enterococcal periprosthetic joint infection: clinical and microbiological findings from an 8-year retrospective cohort study**

Nora Renz[1], Rihard Trebse[2], Doruk Akgün[1], Carsten Perka[1] and Andrej Trampuz[1*]

| | All episodes (*n* = 75) | Mono-microbial (*n* = 37) |
|---|---|---|
| Intravenous antibiotic agent | | |
| Penicillin derivative | 61/74 (82) | 30/37 (81) |
| Vancomycin or daptomycin | 12/74 (16) | 6/37 (16) |
| Other | 1/74 (3) | 1/37 (3) |
| Additive agent for combination treatment | | |
| Fosfomycin | 17/74 (23) | 9/37 (24) |
| Gentamicin | 16/74 (22) | 11/37 (30) |
| Fosfomycin and gentamicin | 8/74 (11) | 5/37 (14) |
| Vancomycin or daptomycin | 18/74 (24) | 4/37 (11) |
| None | 15/74 (20) | 8/37 (22) |

EUCAST: No puntos de corte. No recomendado tto monoterapia
No diferencias en éxito en tto con o sin fosfomicina

Oliva et al. Antimicrob Agents Chemother 2014.

Renz et al. BMC Infect Dis. 2019

# LEVOFLOXACINO .. ESCASA EVIDENCIA

**Characteristics of prosthetic joint infections due to *Enterococcus* sp. and predictors of failure: a multi-national study**

| Age of implant at the moment of infection | Type of antibiotic | Remission (%) | Failure (%) | p value |
|---|---|---|---|---|
| ≤30 days | Vancomycin | 9 (36) | 16 (64) | 0.41 |
| | Ampicillin | 6 (40) | 9 (60) | 1 |
| | Rifampin[a,b] | 12 (60) | 8 (40) | 0.04 |
| | Aminoglycoside[a] | 3 (30) | 7 (70) | 0.49 |
| | Linezolid | 4 (80) | 1 (20) | 0.15 |
| | Daptomycin | 0 | 1 | 1 |
| >30 days | Vancomycin | 37 (65) | 20 (35) | 0.60 |
| | Ampicillin | 30 (67) | 15 (33) | 0.49 |
| | Rifampin[a] | 35 (58) | 25 (42) | 0.31 |
| | Aminoglycoside[a] | 20 (54) | 17 (46) | 0.20 |
| | Linezolid | 6 (46) | 7 (54) | 0.22 |
| | Daptomycin | 3 (43) | 4 (57) | 0.42 |

Tornero et al. Clin Microbiol Infect 2014.

**Moxifloxacin-rifampicin combination for the treatment of non-staphylococcal Gram-positive orthopedic implant-related infections**

| Classification of infection[a] | Non-staphylococcal bacteria[d] | Surgical management | Intravenous treatment (days) | Total treatment (weeks) | Outcome |
|---|---|---|---|---|---|
| Early postop. | *E. faecalis* | Debridement | 18 | 10 | Success |
| Early postop. | *E. faecalis* | Debridement | 19 | 1.2 | Death |
| Late chronic | *E. faecalis* | Removal | 12 | 6 | Success |
| Early postop. | *E. faecalis* | Removal | 12 | 8 | Success |
| Late chronic | *E. faecalis* | 2-stage exchange | 7 | 8 | Failure |

Todas las infecciones enterococicas fueron polimicrobianas

Fily et al. Clin Med Mal Infect 2019

# IPP REFRACTARIA REAGUDIZADA/INFECCION CRONICA SOBRE PROTESIS EN 2º REVISION POR E. FAECALIS

SUPRESION ANTIBIOTICA INDEFINIDA

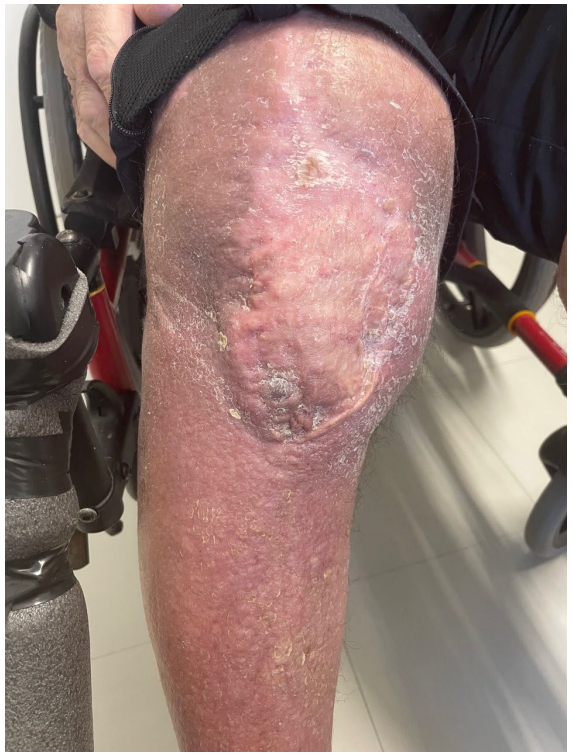
- AMOXICILINA — FAIL
- LINEZOLID
- DOXICICLINA
- VANCOMICINA/TEICOPLANINA
- DAPTOMICINA
- DALBAVANCINA/ORITAVANCINA — ?
- TEDIZOLID
- FOSFOMICINA — ??
- LEVOFLOXACINO — ??

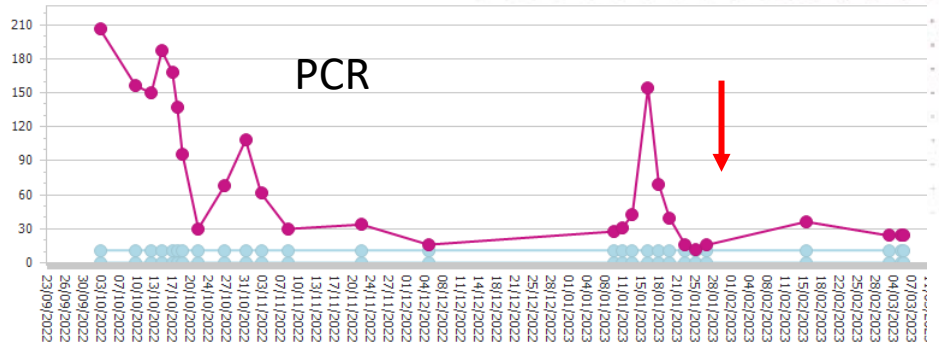
→ AMOXICILINA

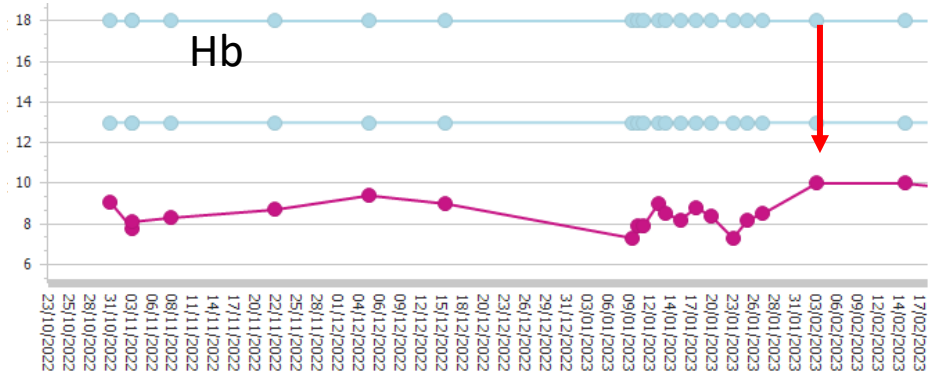
8 SEMANAS

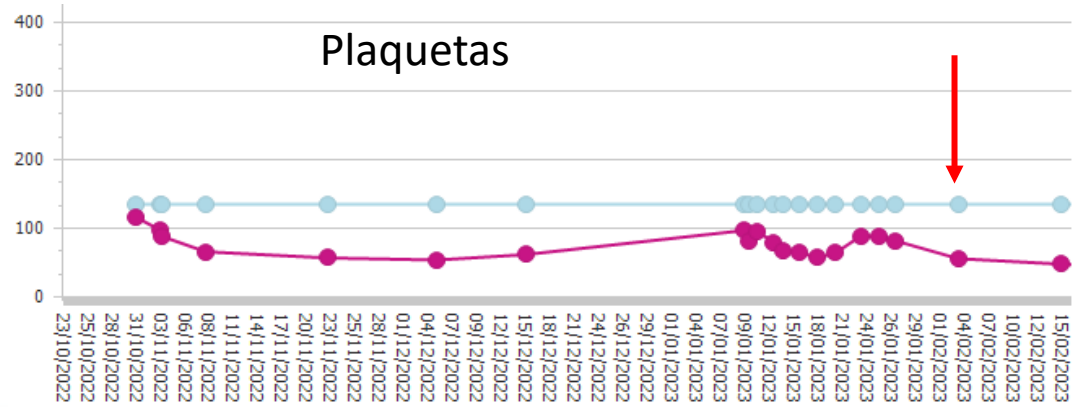
INDEFINIDO.. HASTA CIRUGIA

# Tras 3 semanas de tratamiento con TEDIZOLID

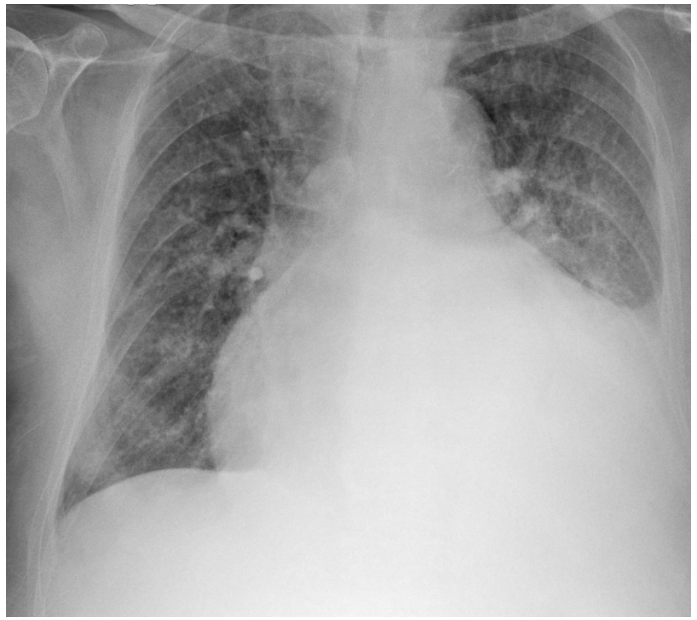




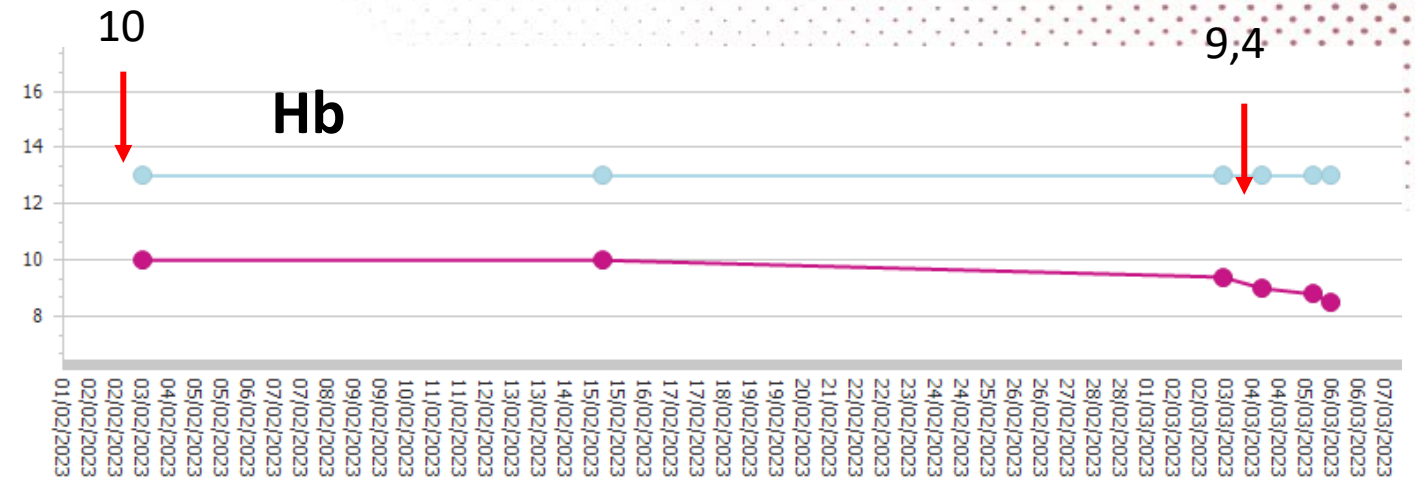



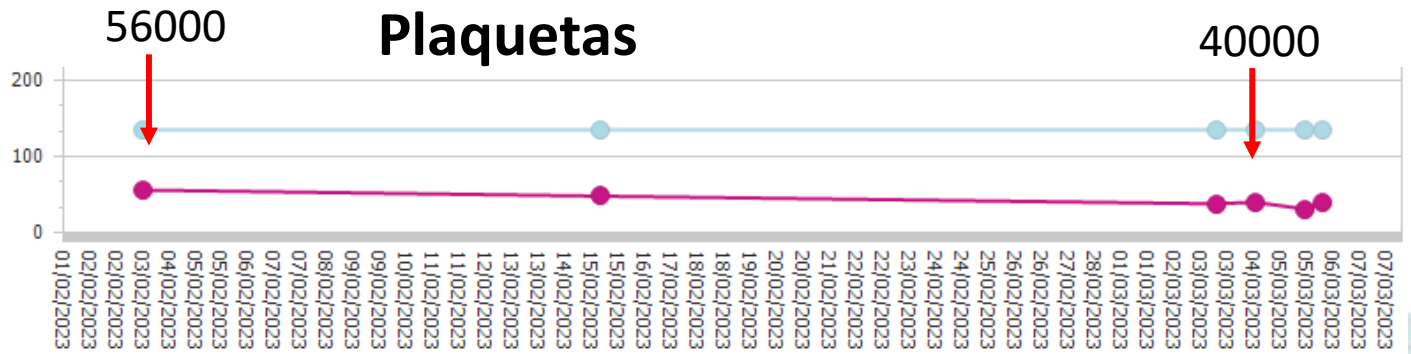



# Reingreso a la 5 º semana de tto ….Marzo 2023…
# EPOC severo reagudizado + ERC OLIGURICA+ICC



| | | |
|---|---|---|
| Tipo de Oxigenoterapia | | Ventimask 28% (FiO2 = 28%) |
| -Gasometria arterial | | |
| aSan-pH | ↓ | 7,33 |
| aSan-Presion parcial de CO2 (pCO2) | ↑ | 76 mm Hg |
| aSan-Presion parcial de Oxigeno (pO2) | ↓ | 33 mm Hg |
| aSan-Bicarbonato | ↑ | 40 mmol/L |
| aSan-Exceso de base | ↑ | 12,1 mmol/L |
| aSan-Saturacion de Oxigeno (calculado) | ↓ | 59 % |

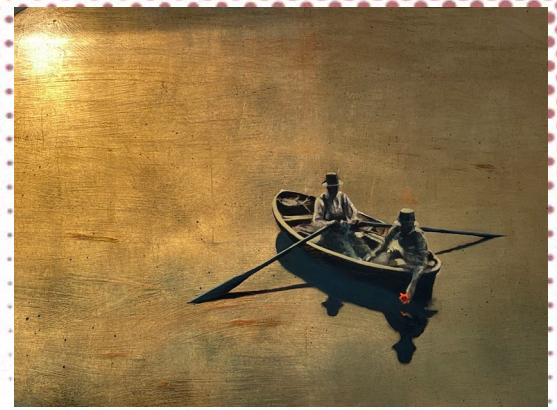



NTproBNP 2.362 pg/mL

A pesar de bipap…… el paciente fallece a las 72 horas

# CONCLUSIONES



Enterococo faecalis:  germen de difícil tratamiento

Escasos tratamientos antibiofilm

Arsenal terapéutico poco potente o tóxico… supresión antibiótica difícil

Nuevos (Tedi, dalba, oritavancina) o viejos (quinolonas, fosfomicina) antibióticos tendrán que demostrar aún su validez, sobre todo en poblaciones especiales (ERC avanzada)

# GRACIAS A TODO EL EQUIPO GEMIO DEL HOSPITAL DE CRUCES

TRAUMATOLOGÍA

CIRUGIA PLÁSTICA

MICROBIOLOGÍA

HOSPITALIZACIÓN A DOMICILIO

INFECCIOSAS

2023