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Patrocinio científico

AGIDEI
ASOCIACION GALLEGA PARA LA INVESTIGACION Y DOCENCIA EN ENFERMEDADES INFECCIOSAS

Patrocinador

GILEAD

Solicitado:
Interés sanitario
Acreditación de actividad de Formación Continuada

Las opiniones expresadas por los ponentes no reflejan necesariamente la posición oficial de los patrocinadores científico

I REUNIÓN INTERAUTONÓMICA EN ENFERMEDADES INFECCIOSAS 2023

Vigo, 27 y 28 de Octubre 2023

Coordinadores Científicos:

Luis E. Morano Amado Unidad de Patología Infecciosa (UPI). Hospital Universitario Álvaro Cunqueiro. Vigo.

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Update en infección ósea

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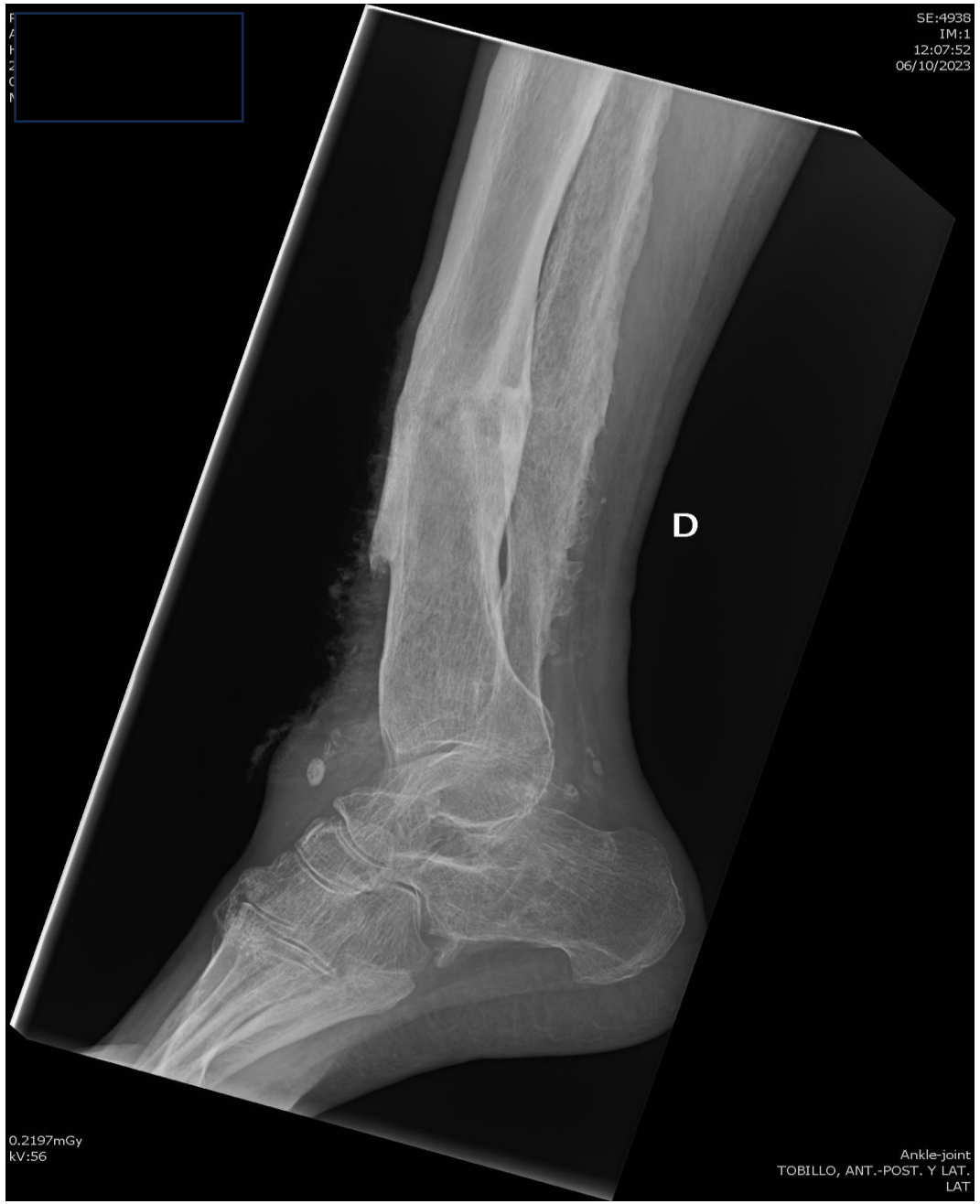
Vigo, Octubre 2023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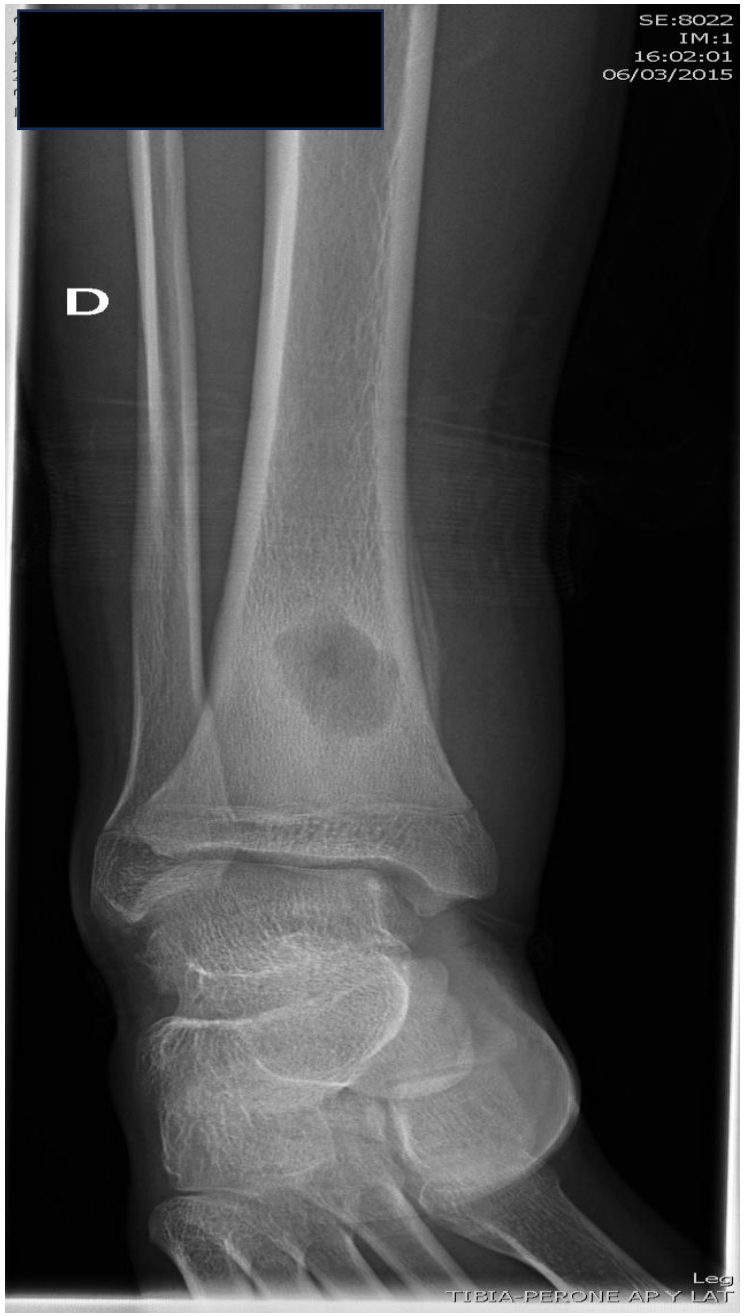
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INFECCIÓN ÓSEA

Tipos y etiología

- TIPOS.- Osteomielitis (OM), artritis séptica (AS), infección protésica (IP)
- 30-60% de los casos son debidos a *Staphylococus aureus*
- CARACTERÍSTICAS de *S. aureus* favorecedoras de la infección ósea:
  - Proteínas de superficie que facilitan su adherencia a matriz ósea y colágeno → adhesinas o MSCRAMM
  - Formación de biopelículas sobre material extraño → santuario
  - Formación de variantes de pequeñas colonias (SCVs) → hibernación

El “mantra” del tratamiento prolongado IV de la OM y otras infecciones osteo-articulares

En Psicología, el término «mantra» se utiliza como figura retórica que se repite para reforzar un pensamiento, reafirmando su significado con las repeticiones

Selection of antimicrobial therapy and routes of administration

Antimicrobial therapy is adequate for the treatment of most cases of acute osteomyelitis of any type. A conventional choice of antimicrobial agents for the most commonly encountered microorganisms is given in table 2.[7,74,75] Single-agent antimicrobial therapy is generally adequate for the treatment of osteomyelitis except for infections of prosthetic joints (for which an antimicrobial combination including rifampicin is commonly used) and chronic osteomyelitis. As a general principle, these antibiotics should be given for 4—6 weeks, if possible by the intravenous route. Where quinolones are used, an early switch to oral administration is appropriate.

Lew D, Waldvogel FA. Lancet 2004; 364: 369-79

The Ten Commandments of the Medical Management of Osteomyelitis

1.	A good surgical specimen (sequestrum) must always be procured before starting the antimicrobial therapy
2.	If the antimicrobial therapy has already been started and the infection is under control, stop antibiotics for 2 weeks and then take the surgical specimen.
3.	Do not be fooled by sinus tract culture results, except for *S. aureus*
4.	Chronic osteomyelitis is never a medical emergency. Empirical antimicrobial therapy is reserved for acute, mostly hematogenous, osteomyelitis
5.	If empirical antimicrobial therapy is needed, antimicrobials active against *S. aureus* must be always selected (antistaphylococcal penicillins, cephalosporins, clindamycin, quinolones)
6.	If MRSA, coagulase negative Staphylococcus, Enterococus spp, or Gram negative bacterias are cultured, switch the empirical to the appropriate antimicrobial
7.	Antimicrobial therapy of chronic osteomyelitis must be extended. Normally, 2-6 weeks of IV antibiotics after bone debridement and additional 6-8 weeks of oral antibiotics. Shorter antimicrobial courses are always doomed to fail
8.	Antimicrobials must be appropriate for the microorganism cultured from the surgical specimen, must have good bone and (for staphylococci) biofilm penetration, and, if applied, good oral bioavailability
9.	To cure a chronic osteomyelitis patient without bone debridement is not a question of faith, is a miracle
10.	Chronic osteomyelitis management is a burden too heavy for the clinician or the infectious diseases doctor to carry alone. Cooperation with the orthopedic surgeon, and, in many cases, with the plastic surgeon is not only convenient, it is necessary

Asensi, V; et al.: «A new aproach to osteomyelitis, a forgotten old friend». Osteomyelitis: Risk Factors, Diagnosis and Treatment Options. Mario E. López Covas and Elí Arroyo Ramírez, ed. Nova Publishers, NY, USA, 2011.

Antibiotic treatment for 6 weeks versus 12 weeks in patients with pyogenic vertebral osteomyelitis: an open-label, non-inferiority, randomised, controlled trial

*Louis Bernard, Aurélien Dinh, Idir Ghout, David Simo, Valerie Zeller, Bertrand Issartel, Vincent Le Moing, Nadia Belmatoug, Philippe Lesprit, Jean-Pierre Bru, Audrey Therby, Damien Bouhour, Eric Dénes, Alexa Debard, Catherine Chirouze, Karine Fèvre, Michel Dupon, Philippe Aegerter, Denis Mulleman, on behalf of the Duration of Treatment for Spondylodiscitis (DTS) study group**

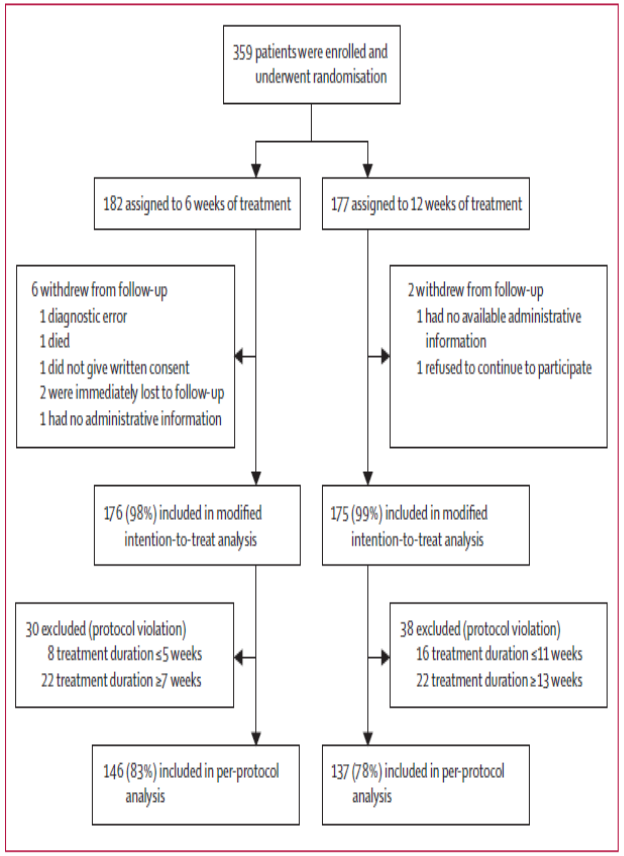


Figure: **Trial profile**

All randomly assigned patients were included in the intention-to-treat analysis except eight patients who were excluded by the independent validation committee. 68 patients whose treatment duration violated the protocol (24 shortening and 44 extensions of 1 week or more than 1 week of treatment) were excluded from the per-protocol analysis.

	6-week regimen (n=176)	12-week regimen (n=175)	Total (n=351)
Age, years	62 (16)	60 (17)	61 (17)
Female	61 (35%)	48 (27%)	109 (31%)
Comorbidity			
Immunodepression	5 (3%)	11 (6%)	16 (5%)
Diabetes	36 (20%)	18 (10%)	54 (15%)
Clinical characteristics			
Fever	87 (49%)	95 (54%)	182 (52%)
Back pain	172 (98%)	165 (94%)	337 (96%)
Duration of infection, days	34 (19–58)	34 (18–57)	34 (18–58)
Number of sites of vertebral osteomyelitis			
1	159 (90%)	154 (88%)	313 (89%)
≥2	17 (10%)	21 (12%)	38 (11%)
Type of site of vertebral osteomyelitis			
Cervical level	28 (16%)	24 (14%)	52 (15%)
Thoracic level	46 (26%)	50 (29%)	96 (27%)
Lumbar level	125 (71%)	121 (69%)	246 (70%)
Sacral level	19 (11%)	26 (15%)	45 (13%)
Associated endocarditis*			
Duke definite	23/127 (18%)	28/130 (22%)	51/257 (20%)
Probable	4/127 (3%)	1/130 (1%)	5/257 (2%)
Neurological signs	25 (14%)	32 (18%)	57 (16%)
Radiological biological characteristics			
MRI	157 (89%)	159 (91%)	316 (90%)
CT scan	88 (50%)	80 (46%)	168 (48%)
C-reactive protein concentration			
Absolute concentration, mg/L	118 (103)	126 (108)	122 (105)
Concentration >10 mg/L	157 (89%)	161 (92%)	318 (91%)
Microbiological diagnosis			
Blood culture	119 (68%)	121 (69%)	240 (68%)
CT-vertebral biopsy	67 (38%)	71 (41%)	138 (39%)
Perioperative surgical biopsy	9 (5%)	10 (6%)	19 (5%)
Microbiological identification			
Staphylococcus aureus†	69 (39%)	76 (43%)	145 (41%)
Coagulase-negative *Staphyloccocus*‡	29 (16%)	32 (18%)	61 (17%)
Streptococcus spp	32 (18%)	31 (18%)	63 (18%)
Enterococcus spp	11 (6%)	15 (9%)	26 (7%)
Enterobacterial spp	22 (13%)	16 (9%)	38 (11%)
Anaerobia	7 (4%)	6 (3%)	13 (4%)
Other Gram-negative bacteria	6 (3%)	4 (2%)	10 (3%)
Other *Streptococcus*	4 (2%)	4 (2%)	8 (2%)

Data are mean (SD), number (%), or median (IQR). No significant between-group differences were noted, except that the proportion of patients with diabetes was slightly higher in the 6-week group than in the 12-week group (p=0·024). *227 patients were assessed for endocarditis by echocardiography. †Of the 145 patients with *Staphylococcus aureus*, eight had meticillin-resistant *S aureus* (three in the 6-week group and five in the 12-week group). ‡Of the 61 patients with coagulase-negative staphylococci, 28 had positive CT-vertebral endocarditis biopsies, 15 had positive blood cultures, and 17 had positive CT-vertebral biopsies and positive blood cultures. No significant association between endocarditis and coagulase-negative staphylococci infections was noted (p=0·346); however, post-surgical vertebral spondylodiscitis without implant (PSVS) was a risk factor for osteomyelitis caused by coagulase-negative staphylococci (18 [53%] of 34 PSVS infections were caused by coagulase-negative staphylococci whereas only 43 [14%] of 317 other infections were caused by coagulase-negative staphylococci, p<0·0001).

Table 1: **Baseline characteristics of the study population**

	6-week regimen	12-week regimen	Difference in proportion of patients*	95% CI
Intention-to-treat analysis, n	176	175		
Cured	160 (90·9%)	159 (90·9%)	+0·1	−6·2 to 6·3
Cured and alive†	156 (88·6%)	150 (85·7%)	+2·9	−4·2 to 10·1
Cured without further antibiotic treatment‡	142 (80·7%)	141 (80·6%)	+0·1	−8·3 to 8·5
Per-protocol analysis, n	146	137		
Cured	137 (93·8%)	132 (96·4%)	−2·5	−8·2 to 2·9
Cured and alive†	133 (91·1%)	126 (92·0%)	−0·9	−7·7 to 6·0
Cured without further antibiotic treatment‡	NA	NA	NA	NA

Data are number, or number (%) unless otherwise specified. 32 patients (16 in the 6-week group and 16 in the 12-week group) were classified as cases of probable failure of treatment by the independent validation committee. Of 68 protocol violations excluded from the per-protocol population, 18 cases were classified as failure and 50 as cure in the intention-to-treat population. *6-week group minus 12-week group. †Death in cases classified as probable cure by the independent validation committee were classified as failure. ‡Further antibiotic treatment was regarded as a treatment failure. NA=not applicable.

Table 2: **Primary outcome analyses of patients with vertebral osteomyelitis according to duration of antibiotic treatment**

	6-week regimen (n=176)	12-week regimen (n=175)	Total (n=351)	p value
Treatment duration, weeks	6 (6–6·6)	12·1 (12–13)	9·3 (6–12·1)	--
Oral fluoroquinolone and rifampicin	76 (43%)	79 (45%)	155 (44%)	0·793
Other combinations				--
Rifampicin and aminoglycoside	22 (13%)	25 (14%)	47 (13%)	--
Rifampicin and amoxicillin	3 (2%)	4 (2%)	7 (2%)	--
Fluoroquinolone and aminoglycoside	14 (8%)	11 (6%)	25 (7%)	--
Fluoroquinolone and meticillin	4 (2%)	3 (2%)	7 (2%)	--
Fluoroquinolone and cephalosporin	6 (3%)	6 (3%)	12 (3%)	--
Amoxicillin and aminoglycoside	15 (9%)	17 (10%)	32 (9%)	--
Cephalosporin and aminoglycoside	4 (2%)	3 (2%)	7 (2%)	--
Meticillin and aminoglycoside	2 (1%)	0	2 (1%)	--
Other	30 (17%)	27 (15%)	57 (16%)	--
Intravenous treatment duration, weeks	15 (7·0–28·0)	14 (6·5–26·5)	14 (7·0–27)	0·579

Data are median (IQR) or number (%) unless otherwise specified.

Table 4: **Duration and type of antibiotics used in the study**

Interpretation 6 weeks of antibiotic treatment is not inferior to 12 weeks of antibiotic treatment with respect to the proportion of patients with pyogenic vertebral osteomyelitis cured at 1 year, which suggests that the standard antibiotic treatment duration for patients with this disease could be reduced to 6 weeks.

Bernard L et al . Lancet 2014; 385: 785-82

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Antibiotic Therapy for 6 or 12 Weeks for Prosthetic Joint Infection

L. Bernard, C. Arvieux, B. Brunschweiler, S. Touchais, S. Ansart, J.-P. Bru, E. Oziol, C. Boeri, G. Gras, J. Druon, P. Rosset, E. Senneville, H. Bentayeb, D. Bouhour, G. Le Moal, J. Michon, H. Aumaître, E. Forestier, J.-M. Laffosse, T. Begué, C. Chirouze, F.-A. Dauchy, E. Devaud, B. Martha, D. Burgot, D. Boutoille, E. Stindel, A. Dinh, P. Bemer, B. Giraudeau, B. Issartel, and A. Caille

ANTIBIOTIC THERAPY FOR PROSTHETIC JOINT INFECTION

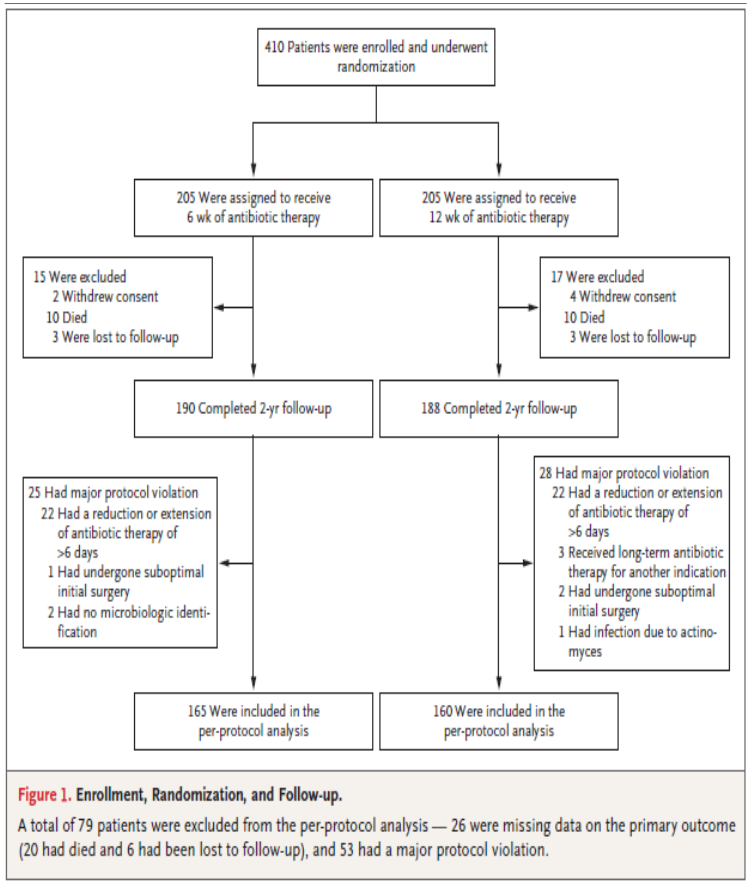


Figure 1. Enrollment, Randomization, and Follow-up.

A total of 79 patients were excluded from the per-protocol analysis — 26 were missing data on the primary outcome (20 had died and 6 had been lost to follow-up), and 53 had a major protocol violation.

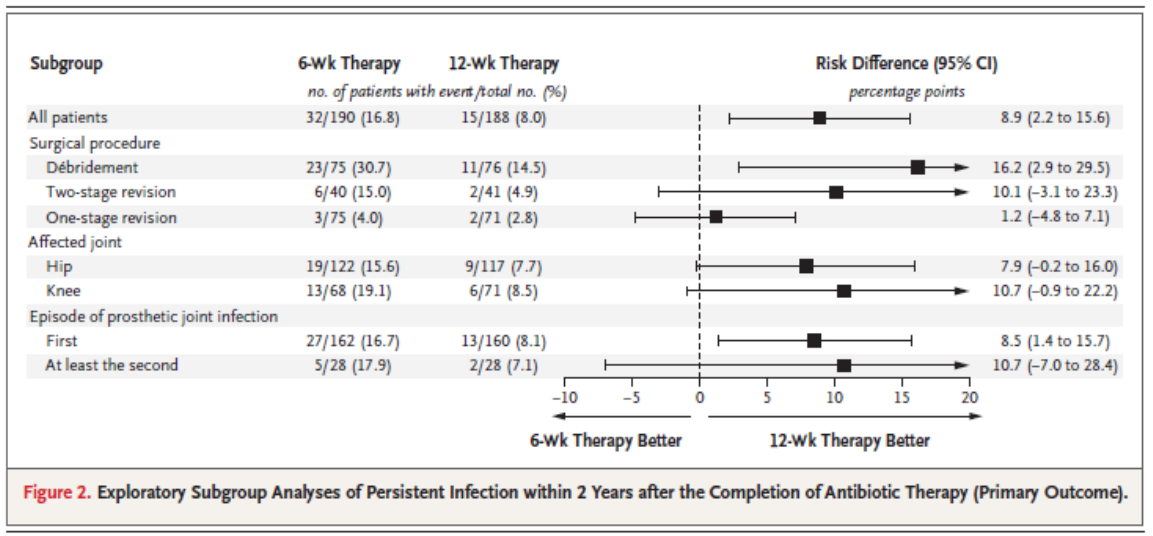


Figure 2. Exploratory Subgroup Analyses of Persistent Infection within 2 Years after the Completion of Antibiotic Therapy (Primary Outcome).

CONCLUSIONS

Among patients with microbiologically confirmed prosthetic joint infections that were managed with standard surgical procedures, antibiotic therapy for 6 weeks was not shown to be noninferior to antibiotic therapy for 12 weeks and resulted in a higher percentage of patients with unfavorable outcomes. (Funded by Programme Hospitalier de Recherche Clinique, French Ministry of Health; DATIPO ClinicalTrials.gov number, NCT01816009.)

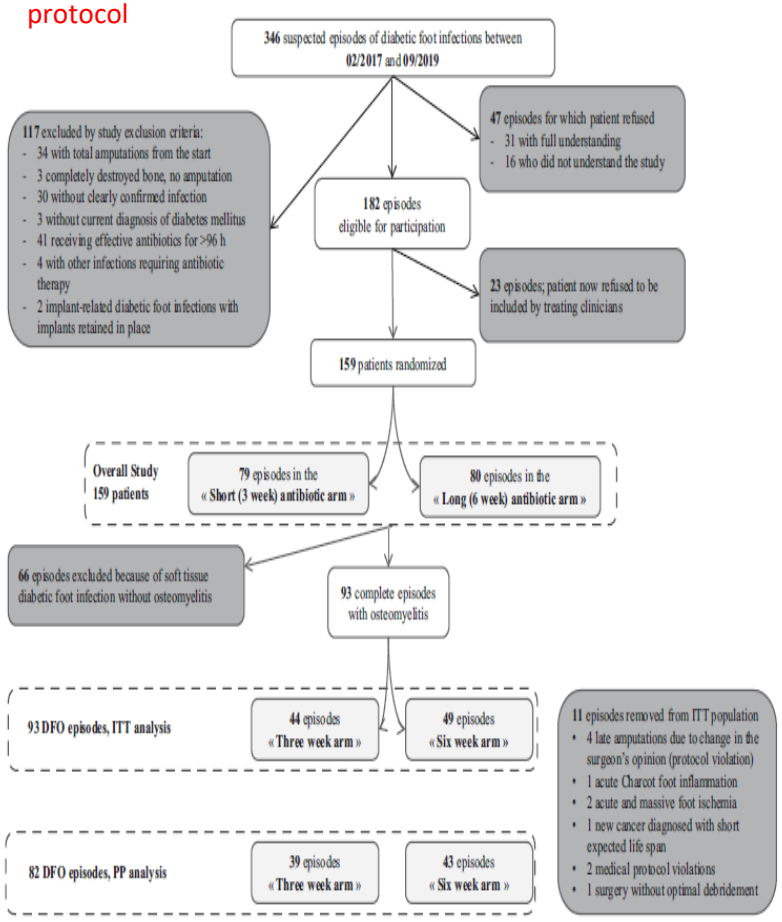
Bernard L et al . New Engl J Med 2021; 384: 1991-2001

Clinical Infectious Diseases
MAJOR ARTICLE

Three Weeks Versus Six Weeks of Antibiotic Therapy for Diabetic Foot Osteomyelitis: A Prospective, Randomized, Noninferiority Pilot Trial

Karim Gariani,[1,a] Truong-Thanh Pham,[2,3,a] Benjamin Kressmann,[2,3] François R. Jornayvaz,[1] Giacomo Gastaldi,[1] Dimitrios Stafylakis,[3] Jacques Philippe,[1] Benjamin A. Lipsky,[2,4] and Ilker Uçkay[2,3,5,6]

STUDY FLOWCHART. Abreviations: DFO, diabetic foot osteomyelitis; ITT, intention to treat; PP, per protocol



Characteristics of Cases in Which There Was a Clinical Remission Versus a Clinical Failure Iintention-to-Treat Population) (n=93)

Characteristic	Clinical Failure (n = 20)	Clinical Remission (n = 73)	*P* Value[a]
Female sex	2 (10)	15 (21)	.28
Median age	62 years	68 years	.02[b]
Osteomyelitis involving toe (vs another anatomic site)	12 (60)	41 (56)	.76
Lower extremity angioplasty performed	0 (0)	8 (11)	.12
Osteomyelitis due to *Staphylococcus aureus*	12 (60)	32 (44)	.10
No. of surgical debridements, median	1 intervention	1 intervention	.83
Partial amputations	9 (45)	25 (34)	.38
3-week course of antibiotic therapy	7 (35)	37 (51)	.21
Estimated episodes with adequate adherence by nurses/clinicians	18 (90)	59 (81)	.34
Length of hospital stay, median	13 days	10 days	.87

Data are presented as No. (%) unless otherwise indicated.
[a]Pearson χ^2 test or Wilcoxon rank-sum test.
[b]Statistically significant ($P < .05$).

CONCLUSIONS.- In the randomized controlled pilot trial, a postdebridement systemic antibiotic therapy course for DFO of 3 weeks gave similar (and statistically noninferior) incidences of remission and AE to a course of 6 weeks

Univariate and Multivariate Associations with the Outcome "Clinical Remission" in the intention-to-Treat and Per-Protocol Populations (Cox Regressions Analysis)

Characteristic	Univariate Analysis	Multivariate Analysis
ITT population (n = 93)		
Demographics		
Female sex	0.9 (.5–1.6)	—
Age	1.0 (1.0–1.0)	—
Body mass index	1.0 (.9–1.0)	—
Toe osteomyelitis	1.0 (.6–1.7)	—
Peripheral arterial disease	0.9 (.5–1.5)	—
Ankle-brachial index	0.7 (.2–1.9)	—
Angioplasty	1.4 (.6–3.2)	1.6 (.8–3.2)
Wound score (size) at admission	1.0 (1.0–1.0)	—
Pathogen		
Staphylococcus aureus	1.1 (.7–1.9)	1.4 (.8–2.4)
Gram-negative bacilli	0.9 (.5–1.5)	—
Polymicrobial infection	1.4 (.8–2.3)	—
Therapy		
3-week antibiotic therapy arm	1.0 (.6–1.6)	1.1 (.6–1.7)
Intravenous antibiotic duration	1.0 (1.0–1.0)	1.0 (1.0–1.0)
No. of surgical debridements	1.0 (.8–1.2)	—
Partial amputations	0.7 (.4–1.2)	0.5 (.2–.9)[a]
Adequate patient adherence	0.9 (.5–1.7)	—
PP population (n = 82)		
Demographics		
Female sex	1.0 (.5–1.9)	—
Age	1.0 (1.0–1.0)	—
Body mass index	1.0 (.9–1.0)	—
Toe osteomyelitis	1.2 (.7–2.1)	—
Peripheral arterial disease	0.9 (.5–1.6)	—
Ankle-brachial index	0.8 (.3–2.2)	—
Angioplasty	1.9 (.8–4.6)	1.9 (.9–3.8)
Wound score (size) at admission	1.0 (.9–1.0)	—
Pathogens		
Staphylococcus aureus	1.1 (.6–1.8)	1.3 (.8–2.1)
Gram-negative bacilli	1.0 (.5–1.7)	—
Polymicrobial infection	1.3 (.7–2.2)	—
Therapy		
Short (3-week) antibiotic therapy	0.8 (.4–1.3)	0.8 (.5–1.4)
Intravenous antibiotic duration	1.0 (1.0–1.0)	1.0 (1.0–1.0)
No. of surgical debridements	1.1 (.8–1.5)	—
Partial amputations	0.6 (.3–1.1)	0.5 (.3–1.0)
Adequate patient adherence	0.6 (.3–1.2)	—

Results are expressed as hazard ratios with 95% confidence intervals. Dashes indicate not included in the multivariate model.
[a]Statistically significant.

Gariani K et al. Clin Infect Dis 2021; 73: e1539-45

Clinical Infectious Diseases
MAJOR ARTICLE

Successful 6-Week Antibiotic Treatment for Early Surgical-site Infections in Spinal Surgery

Marie-Paule Fernandez-Gerlinger,[1,2] Robin Arvieu,[3] David Lebeaux,[1,2] Karama Rouis,[1] Pierre Guigui,[2,3] Jean-Luc Mainardi,[1,2] and Benjamin Bouyer[2,3]

PATIENTS CHARACTERISTICS

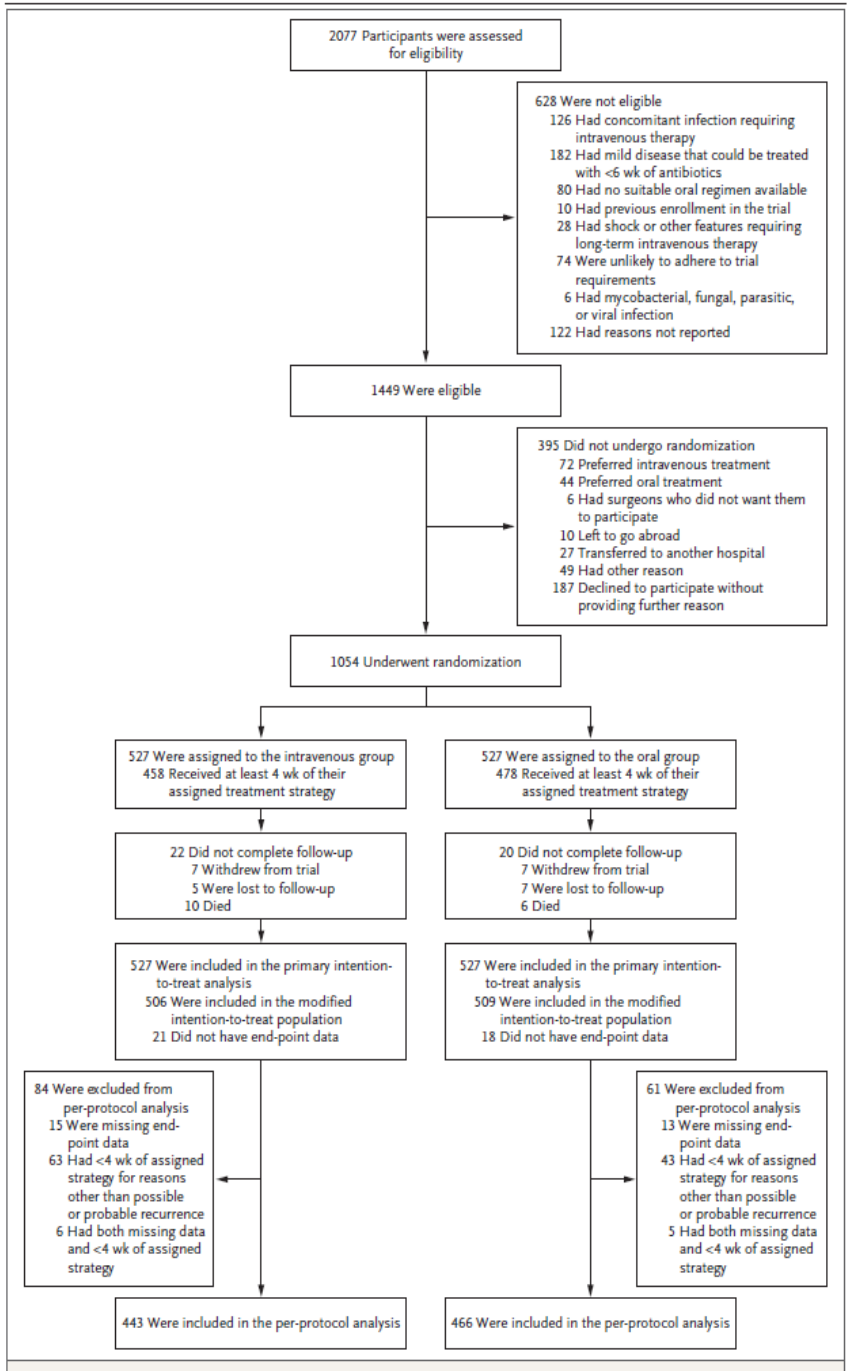
Patient Cohort	Success	Failure	Odds Ratio	*P* Value
Men	44 (56.4%)	2 (28.6%)	0.31 (0.06–1.7)	.18
Age (y)[a]	62.3 (52.5–72.1)	60.1 (20.2–75.5)	0.97 (0.9–1.1)	.24
Risk factors for surgical site infection				
Diabetes	5 (6.41%)	2 (28.6%)	5.84 (0.9–38.0)	.07
History of smoking	1 (1.28%)	2 (28.6%)	30.8 (2.4–400.6)	.009
Immunosuppression[b]	21 (27%)	2 (28.6%)	1.09 (0.2–6.0)	.9
Cardiovascular disease	23 (29.5%)	4 (57.1%)	3.2 (0.7–15.4)	.15
Morbid obesity	1 (1.28%)	1 (14.3%)	12.8 (0.7–231.7)	.08
Surgical indication			0.41 (0.15–1.1)	.08
Degenerative spine disease	37 (47.4%)	2 (28.6%)	…	…
Spinal deformity	11 (14.1%)	4 (57.2%)	…	…
Vertebral metastasis	9 (11.5%)	0	…	…
Vertebral fracture	19 (24.3%)	1 (14.3)	…	…
Spondylodiscitis	2 (2.6%)	0	…	…
Extent of surgery (number of operated vertebra)[a]	4 (3–6)	8 (7–16)	1.26 (1.1–1.5)	.003
Surgical implants[a,c]	67 (85.9%)	7 (100%)	1.14	.29
Spinopelvic arthrodesis	22 (28.2%)	6 (85.7%)	15.3 (1.7–134.3)	.014
Pathogen				
Staphylococcus aureus	32 (41.1%)	1 (14.3%)	0.24 (0.03–2.1)	.2
Coagulase-negative *staphylococci*[c]	15 (19.2%)	0	1.63	.22
Enterobacteriaceae and *enterococci*	21(26.9%)	6 (85.7%)	16.3 (1.85–143.4)	.012
Pseudomonas aeruginosa	8 (10.3%)	1 (14.3%)	1.46 (0.16–13.7)	.74
Cutibacterium acnes	8 (10.3%)	0	0.79	.38
Streptococci	5 (6.41%)	0	0.48	.49
Anaerobes	4 (5.13%)	1 (14.3%)	3.1 (0.29–32.1)	.34

[a]Median (interquartile range).
[b]Human immunodeficiency virus, cancer, transplantation, or immunosuppressive drug.
[c]Odds ratio irrelevant, replaced by χ^2.

CONCLUSIONS.- Surgical management of SSI followed by a 6-week antibiotic treatment is associated with favorable outcome. Anaerobic bacteria seem to play a role in the occurrence of relapses. A 6-week reduction in antibiotic treatment leads to reduction in cost and, likely, also to reduction in the emergence and spread of resistant microorganisms.

Fernandez-Garlinger MP et al. Clin Infect Dis 2019; 68: 1856-61

Enrollement, Randomization, and Follow-up



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Oral versus Intravenous Antibiotics for Bone and Joint Infection

H.-K. Li, I. Rombach, R. Zambellas, A.S. Walker, M.A. McNally, B.L. Atkins, B.A. Lipsky, H.C. Hughes, D. Bose, M. Kümin, C. Scarborough, P.C. Matthews, A.J. Brent, J. Lomas, R. Gundle, M. Rogers, A. Taylor, B. Angus, I. Byren, A.R. Berendt, S. Warren, F.E. Fitzgerald, D.J.F. Mack, S. Hopkins, J. Folb, H.E. Reynolds, E. Moore, J. Marshall, N. Jenkins, C.E. Moran, A.F. Woodhouse, S. Stafford, R.A. Seaton, C. Vallance, C.J. Hemsley, K. Bisnauthsing, J.A.T. Sandoe, I. Aggarwal, S.C. Ellis, D.J. Bunn, R.K. Sutherland, G. Barlow, C. Cooper, C. Geue, N. McMeekin, A.H. Briggs, P. Sendi, E. Khatamzas, T. Wangrangsimakul, T.H.N. Wong, L.K. Barrett, A. Alvand, C.F. Old, J. Bostock, J. Paul, G. Cooke, G.E. Thwaites, P. Bejon, and M. Scarborough, for the OVIVA Trial Collaborators*

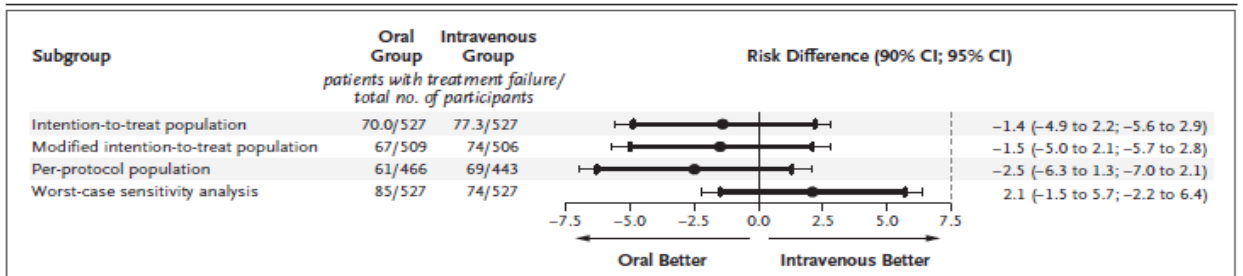


Figure 3. Differences in Risk According to the Analysis Performed.
The point estimates for the differences in failure rates are shown with 90% (thick lines) and 95% (thin lines) two-sided confidence intervals. The noninferiority margin is indicated by the vertical dashed line. The use of two-sided 90% confidence intervals was prespecified in the trial protocol in accordance with the sample-size calculation. Because two-sided 95% confidence intervals are also now commonly included in noninferiority trials, they are shown here to assess the sensitivity of the results to a change in significance level. In the intention-to-treat population, missing data were imputed with the use of multiple imputation by chained equations. The modified intention-to-treat population included only the participants with complete end-point data. The worst-case sensitivity analysis shows the results based on the worst-case assumption that, for participants with missing data, all participants who were randomly assigned to receive oral therapy and no participants who were randomly assigned to receive intravenous therapy had definitive treatment failures, thus introducing the worst possible bias against the oral strategy.

CONCLUSIONS

Oral antibiotic therapy was noninferior to intravenous antibiotic therapy when used during the first 6 weeks for complex orthopedic infection, as assessed by treatment failure at 1 year. (Funded by the National Institute for Health Research; OVIVA Current Controlled Trials number, ISRCTN91566927.)

Li HK et al. New Engl J Med 2019; 308: 425-36

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

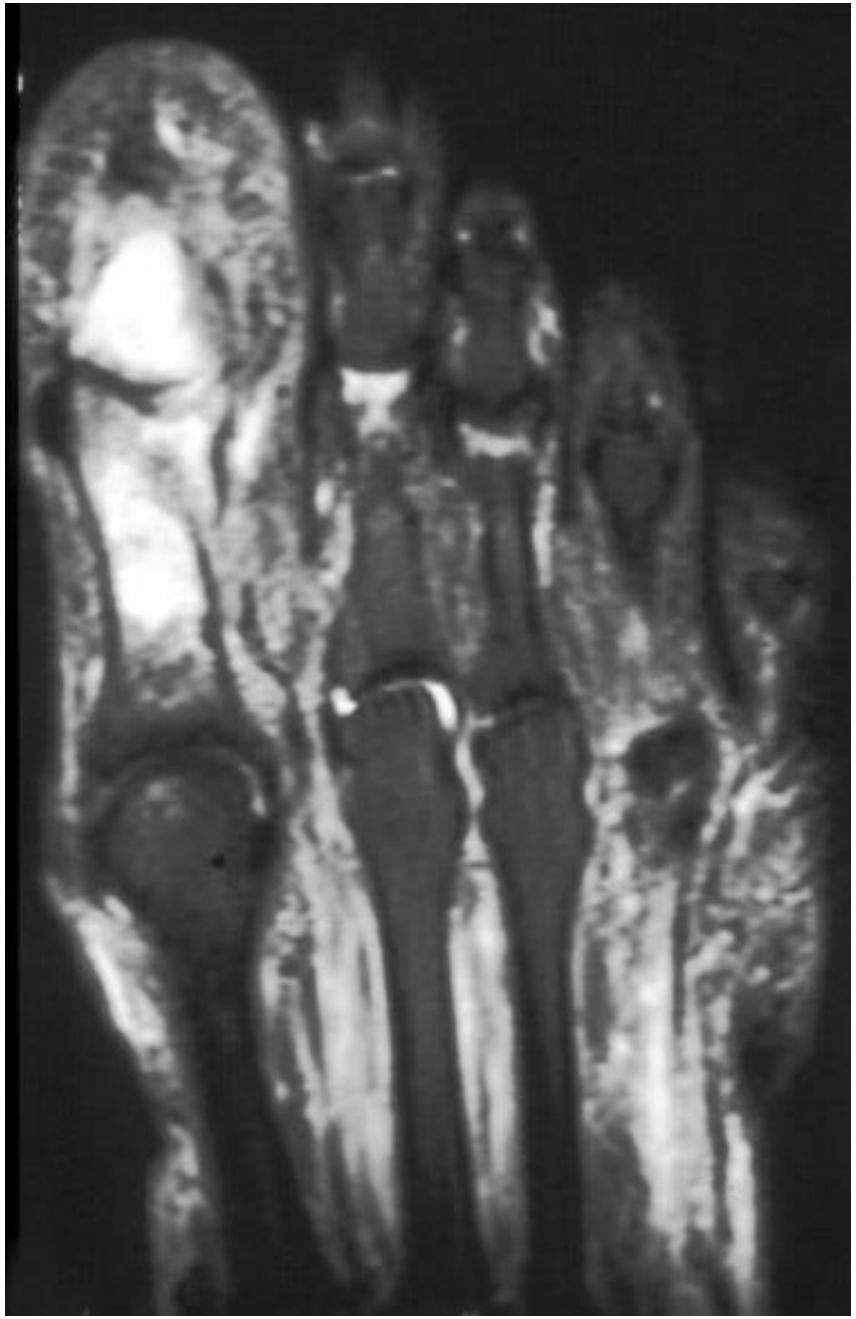
C. Corey Hardin, M.D., Ph.D., *Editor*

Periprosthetic Joint Infection

Robin Patel, M.D.

Prolonged antimicrobial therapy, guided by the results of antimicrobial susceptibility testing, is used to treat PJI. The preferred antibiotics, routes of administration, and durations of therapy are incompletely defined. In a randomized, controlled trial comparing 6 weeks with 12 weeks of antibiotic therapy in patients with PJI that is managed with either DAIR or one- or two-stage revisions, persistent infection within 2 years occurred in 18% of patients in the 6-week group and 9% in the 12-week group, with noninferiority not shown.[87] However, as the authors noted, "Most of the treatment failures in the 6-week group occurred among the patients who had undergone débridement with implant retention." These results differ from the findings of other investigators.[88,89] Intravenous antibiotics were given for just 9 days (median).[87] Although an early transition to oral antibiotics is not common in the United States, the OVIVA (Oral versus Intravenous Antibiotics for Bone and Joint Infection) trial showed that oral antibiotic therapy was noninferior to intravenous therapy for complex orthopedic infections.[90] Many orthopedic surgeons and infectious disease physicians, at least in the United States, recommend that patients undergoing treatment with DAIR receive

Patel R. New Engl J Med 2023; 388: 251-62



Nuevos antimicrobianos para tratamiento de infecciones por Gram positivos

General features of nine Food and Drug Administration (FDA) – or European Medicines Agency (EMA) – approved antibiotic drugs with Gram-positive activity discussed in this paper

	Cephalosporins	Lipopeptides		Lipoglycopeptides		Oxazolidinones		Fluoroquinolones	Tetracyclines
	Ceftaroline	**Daptomycin**	**Telavancin**	**Dalbavancin**	**Oritavancin**	**Linezolid**	**Tedizolid**	**Delafloxacin**	**Omadacycline**
In vitro activity	MSSA, MRSA, CoNS, streptococci, some *Enterococcus faecalis* isolates	MSSA, MRSA, CoNS, streptococci, enterococci including VRE *vanA, vanB*	MSSA, MRSA, CoNS, streptococci, enterococci including VRE *vanB*	MSSA, MRSA, CoNS, streptococci, enterococci including VRE *vanB*	MSSA, MRSA, CoNS, streptococci, enterococci including VRE *vanA, vanB*	MSSA, MRSA, CoNS, streptococci, enterococci including VRE *vanA, vanB*	MSSA, MRSA, CoNS, streptococci, enterococci including VRE *vanA, vanB*	MSSA, MRSA, CoNS, streptococci, *E. faecalis*	MSSA, MRSA, CoNS, streptococci, enterococci including VRE *vanA, vanB*
No activity	*Enterococcus faecium*, VRE *vanA, vanB*		VRE *vanA*	VRE *vanA*				*E. faecium*, VRE *vanA, vanB*	
Drug target	Cell wall synthesis	Cell wall synthesis	Cell wall synthesis	Cell wall synthesis	Cell wall synthesis	Protein synthesis	Protein synthesis	DNA replication	Protein synthesis
FDA/EMA approved dosing regimen (for ABSSSI, unless otherwise mentioned)	600 mg b.i.d. IV	ABSSSI 4 mg/kg/day IVBSI/IE 6 mg/kg/day IV	10 mg/kg/day IV	1500 mg IV single doseAlternative: 1000 mg IV single dose at day 1, followed by 500 mg IV single dose at day 8	1200 mg IV single dose	600 mg b.i.d. IV / PO	200 mg q.d. IV / PO	300 mg b.i.d. IV OR450 mg b.i.d. PO	Loading dose: - IV: 200 mg q.d. on day 1 OR 100 mg b.i.d on day 1- PO (for ABSSSI only): 450 mg q.d. on day 1 and 2. Maintenance: - IV: 100 mg q.d. OR- PO: 300 mg q.d.
Recommended dosing regimen for IE and OSM/PJI	600 mg b.i.d. - t.i.d. IV (15-18)	6-12 mg/kg/day IV (34, 37, 46)	No data	No data	No data	No data	No data	No data	No data

Bloem A et al . J Clin Med 2021; 10: 1743

LIPOGLICOPEPTIDOS

Características

- Elevada vida media que mantiene niveles plasma > 7 días → Ideal para TAPA
- Buena penetración en hueso y líquido sinovial
- Activo frente a biopelícula
- Activo frente a Gram positivos resistentes
- Dalbavancina precisa ajuste por insuficinecia renal, oritavancina no
- Muy escasos efectos 2os. Pero riesgo de exposición prolongada si se presentan
- Alto coste comparado con otros glicopéptidos

Thomas G et al. Intern J Antimicrob Agents 2020; 56: 106069

pharmaceuticals

MDPI

Systematic Review

Dalbavancin in Bone and Joint Infections: A Systematic Review

Sofia Lovatti [1], Giorgio Tiecco [1], Alice Mulé [1], Luca Rossi [1], Anita Sforza [1], Martina Salvi [1], Liana Signorini [2], Francesco Castelli [1] and Eugenia Quiros-Roldan [1,*]

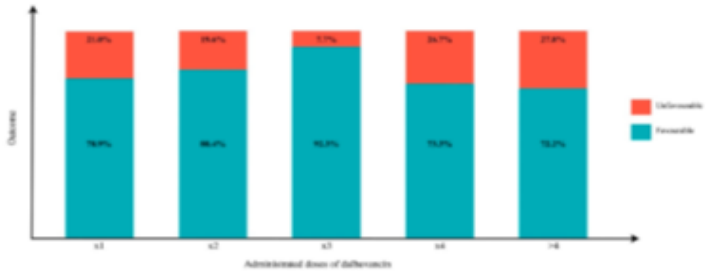
Outcome and Follow-up

Outcome at last visit		
N. of patients included		401 (89.1%)
Success (n,%)		318 (79.3%)
Failure for persistent infection (n,%)		44 (11.0%)
Failure for relapse (n,%)		21 (5.2%)
Failure for need to switch therapy (n,%)		10 (2.5%)
Lost-to-follow-up (n,%)		5 (1.2%)
Infection-related death (n,%)		1 (0.2%)
Unrelated death (n,%)		2 (0.5%)
Outcome within and after 4 weeks since the end of treatment		
N. of patients included		12; 274 (60.9%)
	Outcome within 4 weeks	**Outcome after 4 weeks**
Success (n,%)	231 (84.3%)	212 (77.4%)
Failure-persistent infection (n,%)	37 (13.5%)	25 (9.1%)
Failure-relapse (n,%)	2 (0.7%)	20 (7.3%)
Failure-switch therapy (n,%)	0 (0.0%)	10 (3.6%)
Lost-to-follow-up (n,%)	4 (1.5%)	5 (1.8%)
Infection-related death (n,%)	0 (0.0%)	0 (0.0%)
Unrelated death (n,%)	0 (0.0%)	2 (0.7%)

Comparation of different features in patiens with favourables or unfavourables outcomes. Acronym used – MRSA: methicillin – resistant Staphylococcus aureus; CoNS: Coagulase Negative Staphylococcus app

	Favourable Outcome	**Unfavourable Outcome**
N. of patients included	318	76
Surgery before DBV		
Patients with available data	112	16
Subjected to surgery before DBV (n,%)	90 (80.4%)	4 (25%)
Did not undergo surgery before DBV (n,%)	22 (19.6%)	12 (75%)
Isolated pathogens		
Patients with available data	68	10
MRSA (n,%)	39 (57.4%)	8 (80%)
MSSA (n,%)	14 (20.6%)	2 (20%)
Other Gram-positive (n,%)	6 (8.8%)	0 (0.0%)
CoNS (n,%)	6 (8.8%)	0 (0.0%)
Enterococcus spp. (n,%)	2 (2.9%)	0 (0.0%)
Streptococcus spp. (n,%)	1 (1.5%)	0 (0.0%)
Type of osteoarticular infections		
Patients with available data	242	59
Osteomyelitis	180 (74.4%)	41 (70.7%)
Spondylodiscitis	45 (18.6%)	14 (23.7%)
Septic arthritis	17 (7%)	4 (6.8%)

Favourable versus unfavourable outcomes in different administration schedules of DBV



Lovatti S et al . Pharmaceutical 2023; 16: 1005

Baseline demographics in 134 osteomyelitis cases

Male	66 (49.3)
Female	68 (50.7)
Age, years, mean (range)	60 (19–97)
Age group, years	
< 30	7 (5.2)
31–49	28 (20.9)
50–65	54 (40.3)
≥ 66	45 (33.6)
Weight, kg, mean (range), SD	78 (38–164), 23.8
BMI (kg/m^2), mean, (range), SD	27 (15.8–48.4), 6.7
Baseline MRI	134 (100)
Infection confirmed on MRI	128 (95.5)
Baseline CRP	134 (100)
Baseline ESR	132 (98.5)
Previous antibiotic therapy	18 (13.4)
Baseline bacteremia (MRSA)	9 (6.7)
Debridement of bone or joint	121 (90.3)
Positive wound, bone, joint culture	119 (88.8)
Culture positive (wound, joint, deep wound) MRSA	92/128 with cultures obtained (71.9)
Prosthetic source	24 (17.9)
Anatomic location of infection	
Lower extremity source	74 (55.2)
Upper extremity source	25 (18.7)
Pelvic source	18 (13.4)
Head and shoulder source	9 (6.7)
Vertebral source	8 (6)
Renal function at baseline	
CrCl > 61 mL/min	89 (66.4)
CrCl 31–60 mL/min	12 (9)
CrCl 15– 30 mL/min	8 (6)
ESRD	7 (5.2)
Co-morbidities	
≥ 3 co-morbidities	57 (42.5)
Hyperlipidemia	59 (44)
Diabetes	51 (38.1)
Peripheral vascular disease	36 (26.9)
COPD	33 (24.6)
History of MI	25 (18.7)
Congestive heart failure	25 (18.7)
Malignancy	20 (14.9)
Peptic ulcer disease	13 (9.7)
Current chemotherapy/immunotherapy	13 (9.7)
Miscellaneous	
IVDU (past or present)	6 (4.5)
HIV positive	5 (3.7)
Liver disease	3 (2.2)
Chronic steroids (≥ 20 mg/day prednisone)	1 (0.75)
Chronic kidney insufficiency	33 (24.6)
Patient preference or transportation issues as reason for use of oritavancin	120 (89.6)

BMI body mass index, *CrCl* creatinine clearance, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *ESRD* end-stage renal disease, *COPD* chronic obstructive pulmonary disease, *IVDU* intra-

Drugs - Real World Outcomes (2020) 7 (Suppl 1):S41–S45
https://doi.org/10.1007/s40801-020-00195-7

ORIGINAL RESEARCH ARTICLE

Treatment of Acute Osteomyelitis with Once-Weekly Oritavancin: A Two-Year, Multicenter, Retrospective Study

Nicholas W. Van Hise[1] · Vishnu Chundi[1] · Vishal Didwania[1] · Michael Anderson[1] · David McKinsey[2] · Ingrid Roig[3] · Akhilesh Sharma[4] · Russell M. Petrak[1]

Baseline microbiology

Culture and pathogen by unique patient	*n/N* (%)
Positive cultures with ≥ 1 GP result	119/134 (88.8)
Staphylococcus aureus, monomicrobial	
MRSA	92
MSSA	25
S. aureus, mixed	
MRSA + ≥ 1 other GP pathogen[a]	16
MSSA + ≥ 1 other GP pathogen[a]	10
Vancomycin-resistant enterococci[b]	7
Vancomycin-intermediate *S. aureus*[b]	2
VRE with daptomycin MIC ≥ 4 mg/L	2

MRSA methicillin-resistant *Staphylococcus aureus*, *MSSA* methicillin-sensitive *Staphylococcus aureus*, *GP* Gram-positive

[a]Includes *Streptococcus pyogenes*, group B streptococci, coagulase-negative staphylococci, and *Enterococcus* spp

[b]Identified in polymicrobial Gram-positive infections, usually with MRSA or MSSA

Clinical outcomes

	No. of patients, *n* (%)	Clinical cure, *n* (%)
Clinical success ETE	134	118 (88.1)
Clinical success PTE	130	104 (80.0)
Subgroups evaluated at ETE		
Four-dose regimen	118 (88.1)	107 (90.7)
Five-dose regimen	16 (11.9)	11 (68.8)
MRI-proven infection	128 (95.5)	113 (90.4)
Diabetes	51 (38.1)	43 (84.3)
Prosthetic device	24 (17.9)	20 (88.3)
Heart failure	25 (18.7)	21 (84)
Previous antibiotic therapy	18 (13.4)	14 (77.8)
Malignancy on immunosuppression	12 (9)	11 (91.7)

ETE end of the last dose, *MRI* magnetic resonance imaging, *PTE* post-treatment

Conclusion This is the largest real-world clinical study of adult patients treated with oritavancin for acute osteomyelitis. Use of oritavancin for acute osteomyelitis infection resulted in a high rate of positive clinical outcomes and a low incidence of adverse events, thereby providing potential for a convenient, effective, and safe therapeutic option. Future prospective and comparative studies are needed to validate these findings.

Van Hisse NW et al. Drugs-Real World Outcomes 2020; 7 (supp1): S412-S45

Take -home message …

- El tratamiento antimicrobiano de las infecciones osteo-articulares durante 6-8 semanas es no inferior a tratamientos más prolongados tanto en el pie diabético como en infecciones de prótesis ortopédicas si se acompaña del tratamiento quirúrgico adecuado
- El tratamiento antimicrobiano oral de las infecciones osteo-articulares es no inferior al IV si va combinado con agentes anti-biopelícula (rifampicina, quinolonas)
- Los nuevos lipoglicopéptidos (dalbavancina, oritavancina) son útiles en las infecciones osteo-articulares frente a Gram positivos incluyendo los más resistentes
- Su larga vida media, buena penetración ósea y en bio-película los convierte en una excelente opción para tratamiento IV de las infecciones osteo-articulares como TAPA cada 7-14 días
- Su elevado coste actual se compensa por la reducción de la estancia media hospitalaria

PETER BRUEGUEL EL VIEJO
Los mendigos. 1568
Museo del Louvre, París