

Actualització en el maneig i tractament de la Endocarditis Infecciosa



“A pesar de los avances en las técnicas diagnósticas y en el tratamiento la Endocarditis Infecciosa sigue siendo una entidad con una alta mortalidad”



Original article

International experts' practice in the antibiotic therapy of infective endocarditis is not following the guidelines

H. Tissot-Dupont^{1,†}, J.P. Casalta^{1,†}, F. Gouriet¹, S. Hubert², E. Salaun², G. Habib², M.P. Fernandez-Gerlinger³, J.L. Mainardi³, P. Tattevin⁴, M. Revest⁴, F. Lucht⁵, E. Botelho-Nevers⁵, A. Gagneux-Brunon⁵, U. Snygg-Martin⁶, K.L. Chan⁷, J. Bishara⁸, I. Vilacosta⁹, C. Olmos⁹, J.A. San Román¹⁰, J. López¹⁰, P. Tornos¹¹, N. Fernández-Hidalgo¹¹, E. Durante-Mangoni¹², R. Utili¹², M. Paul¹³, L.M. Baddour¹⁴, D.C. DeSimone¹⁴, M.R. Sohail¹⁴, J.M. Steckelberg¹⁴, W.R. Wilson¹⁴, D. Raoult^{1,*}

¹ IIRMITF Aix Marseille Université UMR 7278 IRD 198 INSERM 1095 IHU—Méditerranée Infection Marseille France

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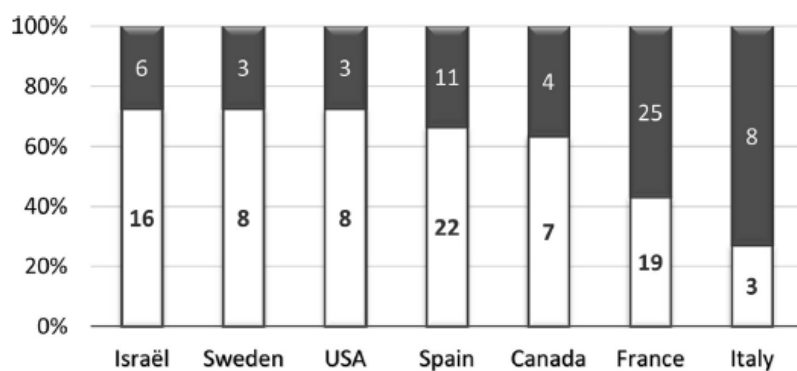


Fig. 2. Adherence to recommendations by country (figures in the bars indicate the number of microorganisms / conditions with or without adherence by the centres of each country).

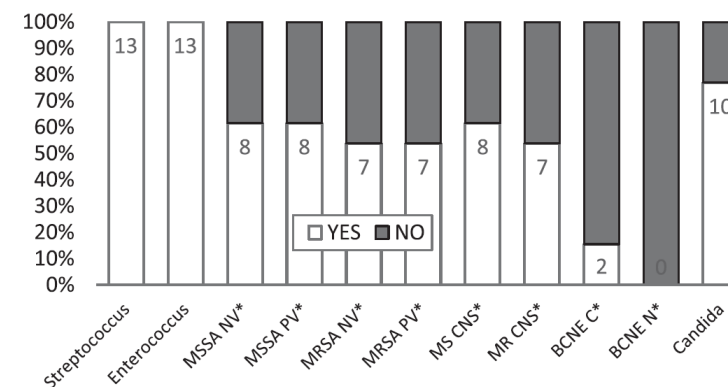


Fig. 1. Adherence to recommendations by microorganism/ conditions (figures in the bars indicate the number of centres adhering to the guidelines). Abbreviations: MSSA NV, methicillin susceptible *Staphylococcus aureus*—native valve; MSSA PV, MSSA—prosthetic valve; MRSA NV, methicillin-resistant *S. aureus*—native valve; MRSA PV, MRSA—prosthetic valve; MS CNS, methicillin-susceptible, coagulase-negative *Staphylococcus*; MR CNS, methicillin-resistant, coagulase-negative *Staphylococcus*; BCNE C, blood-culture-negative endocarditis—community-acquired; BCNE N, blood-culture-negative endocarditis—nosocomial.



Cochrane Database of Systematic Reviews

A comparison of different antibiotic regimens for the treatment of infective endocarditis (Review)

Martí-Carvajal AJ, Dayer M, Conterno LO, Gonzalez Garay AG, Martí-Amarista CE

Introducció: evidència



Estudis inclosos:

- 6 assaigs clínics aleatoritzats petits.
- 1143 participants assignats / 632 analitzats.

Resultats principals:

- **Mortalitat per qualsevol causa:**

No es van observar diferències significatives entre règims.

Conclusió dels autors:

L'evidència actual és **limitada i de qualitat baixa o molt baixa**.

No es pot recomanar ni rebutjar cap règim antibiòtic específic per al tractament de la EI

Es necessiten més estudis ben dissenyats per establir recomanacions sòlides.

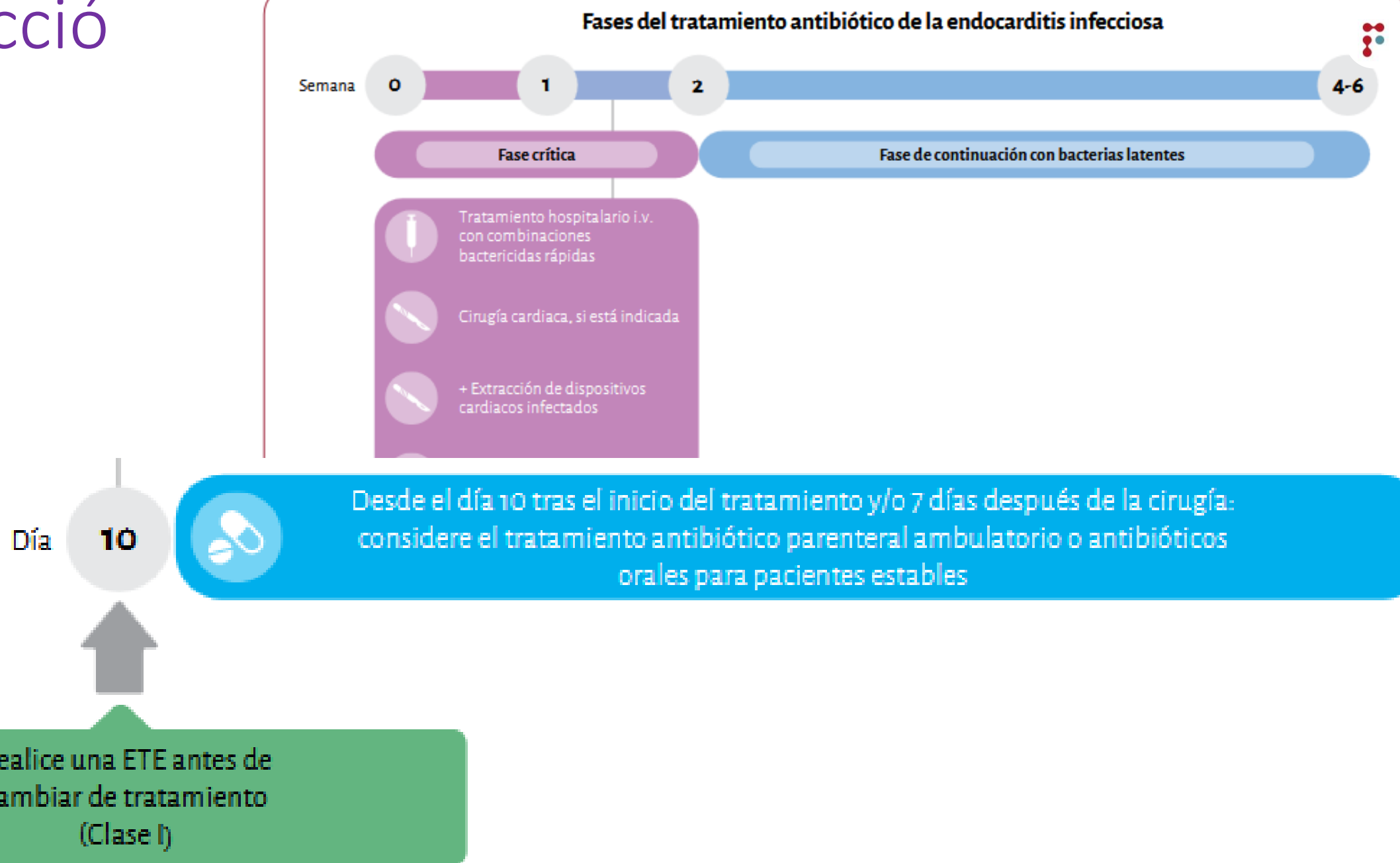
infecció no controlada, insuficiència cardíaca, febre, embòlies sèptiques.

Cap estudi va avaluar la qualitat de vida.



	Study Title	NCT Number	Status	Intervention	Sponsor
1	Short-course Antibiotic Treatment in Gram-positive Cocci Infective Endocarditis	NCT04222257	Terminated	•Drug: Antibiotics •Drug: Antibiotics	Carmen Olmos Blanco
2	Partial Oral Antimicrobials to Treat Infective Endocarditis in People Who Inject Drugs	NCT04544306	Recruiting	•Other: Partial oral antimicrobial therapy	London Health Sciences Centre Research Institute OR Lawson Research Institute of St. Joseph's
3	Oral Antimicrobial Treatment vs. Outpatient Parenteral for Infective Endocarditis	NCT05398679	Recruiting	•Drug: Cefaclor •Drug: Ciprofloxacin Tablets •Drug: Ciprofloxacin Injection •21 more	Fundacion Clinic per a la Recerca Biomédica
4	Ampicillin and Ceftriaxone for the Treatment of Enterococcus Faecalis Infective Endocarditis.	NCT06423898	Recruiting	•Drug: Ampicillin plus ceftriaxone in continuous infusion •Drug: Ampicillin plus ceftriaxone in intermittent infusion of 14 days, after which the treatment may be changed	Fundación Pública Andaluza para la gestión de la Investigación en Sevilla
5	Bacteriophages in Addition to Antibiotics for the Treatment of Patients With Infective Endocarditis	NCT06870409	Recruiting	•Drug: Bacteriophage	University Clinical Hospital na V.V.Vinogradov (branch of RUDN university na Patrice Lumumba)
6	Evaluation of an Antibiotic Regimen Pharmacokinetic Applicable to Enterococcus Faecalis Infective Endocarditis	NCT03681431	Completed	•Drug: Ceftriaxone 4g/ 24h •Drug: Ceftriaxone 2g/ 12h	Fundación Pública Andaluza para la gestión de la Investigación en Sevilla
7	Efficacy and Safety of Dalbavancin Compared to Standard of Care Antibiotic Therapy for the Completion of Treatment of Patients With Complicated Bacteremia or Infective Endocarditis	NCT03148756	Terminated WITH RESULTS	•Drug: Dalbavancin •Drug: Standard of Care	AbbVie
8	Oritavancin for CIED Infections With MDR Gram-positive Cocci New	NCT07013552	Not yet recruiting	•Cardiac Implantable Electronic Devices •Infective Endocarditis •Multidrug-resistant Bacteria Screening •4 more	•Drug: Administration of a single or repeated dose of a long half-life antibiotic - oritavancin •Drug: Administration of a repeated dose of a short half-life antibiotic - vancomycin

Introducción



The NEW ENGLAND JOURNAL *of* MEDICINE

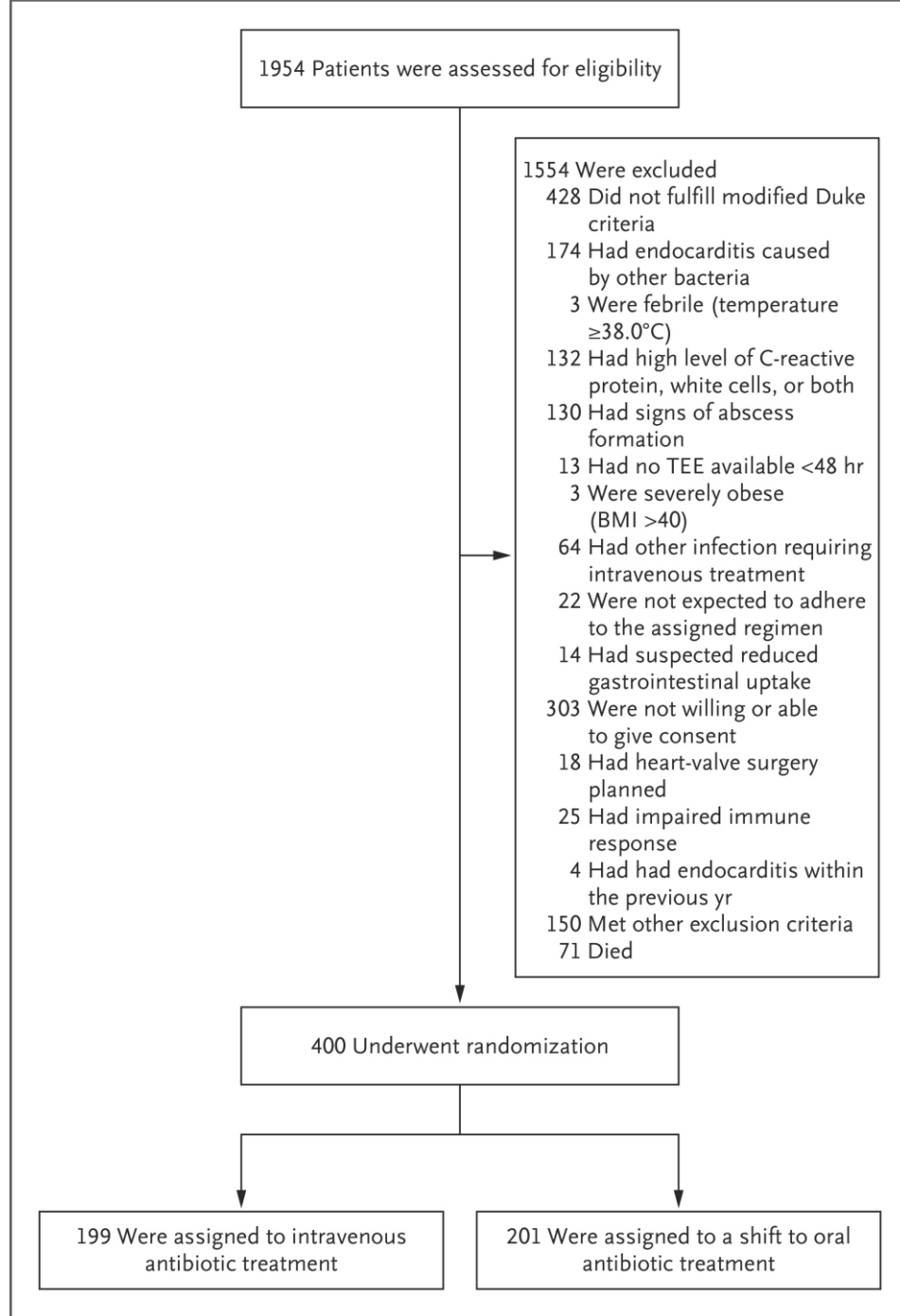
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Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen, M.D., D.M.Sc., Nikolaj Ihlemann, M.D., Ph.D., Sabine U. Gill, M.D., Ph.D.,
Trine Madsen, M.D., Ph.D., Hanne Elming, M.D., Ph.D., Kaare T. Jensen, M.D., Ph.D.,
Niels E. Bruun, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Kurt Fursted, M.D., D.M.Sc.,
Jens J. Christensen, M.D., D.M.Sc., Martin Schultz, M.D., Christine F. Klein, M.D., Emil L. Fosbøll, M.D., Ph.D.,
Flemming Rosenvinge, M.D., Henrik C. Schönheyder, M.D., D.M.Sc., Lars Køber, M.D., D.M.Sc.,
Christian Torp-Pedersen, M.D., D.M.Sc., Jannik Helweg-Larsen, M.D., D.M.Sc., Niels Tønder, M.D., D.M.Sc.,
Claus Moser, M.D., Ph.D., and Henning Bundgaard, M.D., D.M.Sc.



CRITERIS D'INCLUSIÓ

- Endocarditis bacteriana esquerra confirmada (criteris Duke).
- Microorganismes implicats: *Streptococcus*, *Enterococcus*, *Staphylococcus aureus*, *Staphylococcus coagulasa-negativus*.
- Edat ≥ 18 anys.
- **≥ 10 dies de tractament antibiòtic parenteral adequat.**
- **≥ 1 setmana de tractament postquirúrgic (si escau).**
- **Queden ≥ 10 dies de tractament planificat.**
- Temperatura $< 37,5^{\circ}\text{C}$ durant > 2 dies.
- **Descens significatiu de CRP i leucòcits.**
- **Sense empitjorament ecocardiogràfic (TTE/TEE < 48 h).**

CRITERIS D'EXCLUSIÓ

- Endocarditis prèvia en l'últim any amb la mateixa bactèria.
- **IMC > 40 kg/m².**
- Cirurgia cardíaca planificada dins de 6 setmanes.
- Infecció concomitant que requereixi antibiòtic intravenós.
- Problemes abdominals que dificultin l'absorció oral.
- **Immunosupressió coneguda o sospitada** (VIH, quimioteràpia, prednisona > 20 mg/dia).
- Compliment reduït (inclòs ús de drogues intravenoses).



Oral regimens recommended in the POET trial	
Penicillin and Methicillin sensitive <i>S. aureus</i> and coagulase-negative staphylococci	
Amoxicillin 1 g x 4	Fusidic acid 0.75 g x 2
Amoxicillin 1 g x 4	Rifampicin 0.6 g x 2
Linezolid 0.6 g x 2	Fusidic acid 0.75 g x 2
Linezolid 0.6 g x 2	Rifampicin 0.6 g x 2
Methicillin sensitive <i>S. aureus</i> and coagulase-negative staphylococci	
Dicloxacillin 1 g x 4	Fusidic acid 0.75 g x 2
Dicloxacillin 1 g x 4	Rifampicin 0.6 g x 2
Linezolid 0.6 g x 2	Fusidic acid 0.75 g x 2
Linezolid 0.6 g x 2	Rifampicin 0.6 g x 2
Methicillin resistant coagulase-negative staphylococci	
Linezolid 0.6 g x 2	Fusidic acid
Linezolid 0.6 g x 2	Rifampicin 0.6 g x 2
Enterococcus faecalis	
Amoxicillin 1 g x 4	Rifampicin 0.6 g x 2
Amoxicillin 1 g x 4	Moxifloxacin 0.4 g x 1
Linezolid 0.6 g x 2	Rifampicin 0.6 g x 2
Linezolid 0.6 g x 2	Moxifloxacin 0.4 g x 1
Streptococci (MIC < 1 mg/L)	
Amoxicillin 1 g x 4	Rifampicin 0.6 g x 2
Linezolid 0.6 g x 2	Rifampicin 0.6 g x 2
Linezolid 0.6 g x 2	Moxifloxacin 0.4 g x 1
Streptococci (MIC ≥ 1 mg/L)	
Linezolid 0.6 g x 2	Rifampicin 0.6 g x 2
Moxifloxacin 0.4 g x 1	Rifampicin 0.6 g x 2
Moxifloxacin 0.4 g x 1	Clindamycin 0.6 g x 3



Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Intravenous Treatment (N=199)	Oral Treatment (N=201)
Mean age — yr	67.3±12.0	67.6±12.6
Female sex — no. (%)	50 (25.1)	42 (20.9)
Body temperature — °C	36.9±0.45	37.0±0.44
Coexisting condition or risk factor — no. (%)		
Diabetes	36 (18.1)	31 (15.4)
Renal failure	25 (12.6)	21 (10.4)
Dialysis	13 (6.5)	15 (7.5)

Pathogen — no. (%)†

Streptococcus	104 (52.3)	92 (45.8)
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<i>Enterococcus faecalis</i>	46 (23.1)	51 (25.4)
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<i>Staphylococcus aureus</i> ‡	40 (20.1)	47 (23.4)
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Coagulase-negative staphylococci	10 (5.0)	13 (6.5)
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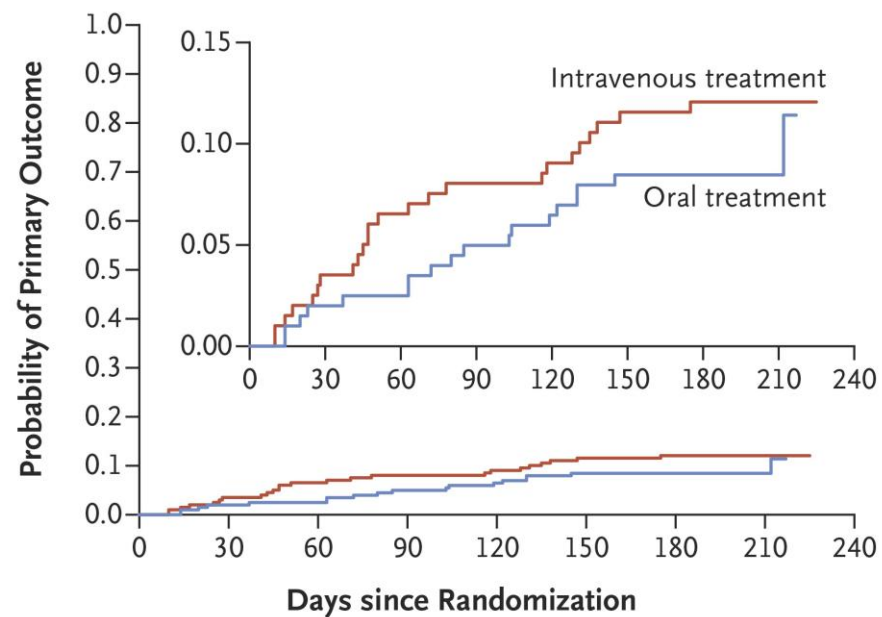
Prosthetic heart valve	53 (26.6)	54 (26.9)
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Pacemaker endocarditis	6 (3.0)	8 (4.0)
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Vegetation size >9 mm	7 (3.5)	11 (5.5)
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Moderate or severe valve regurgitation	19 (9.5)	23 (11.4)
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Valve surgery during current disease course	75 (37.7)	77 (38.3)
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No. at Risk

Intravenous treatment	199	192	186	183	181	176	174	28	0
Oral treatment	201	197	196	191	188	184	183	36	0

Table 2. Distribution of the Four Components of the Primary Composite Outcome.*

Component	Intravenous Treatment (N = 199)	Oral Treatment (N = 201)	Difference	Hazard Ratio (95% CI)
	number (percent)		percentage points (95% CI)	
All-cause mortality	13 (6.5)	7 (3.5)	3.0 (−1.4 to 7.7)	0.53 (0.21 to 1.32)
Unplanned cardiac surgery	6 (3.0)	6 (3.0)	0 (−3.3 to 3.4)	0.99 (0.32 to 3.07)
Embolic event	3 (1.5)	3 (1.5)	0 (−2.4 to 2.4)	0.97 (0.20 to 4.82)
Relapse of the positive blood culture†	5 (2.5)	5 (2.5)	0 (−3.1 to 3.1)	0.97 (0.28 to 3.33)

Real-World Application of Oral Therapy for Infective Endocarditis: A Multicenter, Retrospective, Cohort Study

Sarah Freling,^{1,2} Noah Wald-Dickler,^{1,2} Josh Banerjee,¹ Catherine P. Canamar,¹ Soodtida Tangpraphaphorn,¹ Dara Bruce,³ Kusha Davar,¹ Fernando Dominguez,¹ Daniel Norwitz,³ Ganesh Krishnamurthi,^{1,2} Lilian Fung,^{1,2} Ashley Guanzon,^{1,4} Emi Minejima,^{1,4} Michael Spellberg,¹ Catherine Spellberg,¹ Rachel Baden,¹ Paul Holtom,^{1,2} and Brad Spellberg¹

	Study Title	NCT Number	Status	Intervention	Sponsor
3	Oral Antimicrobial Treatment vs. Outpatient Parenteral for Infective Endocarditis	NCT05398679	Recruiting	•Drug: Cefaclor •Drug: Ciprofloxacin Tablets •Drug: Ciprofloxacin Injection •21 more	Fundacion Clinic per a la Recerca Biomédica



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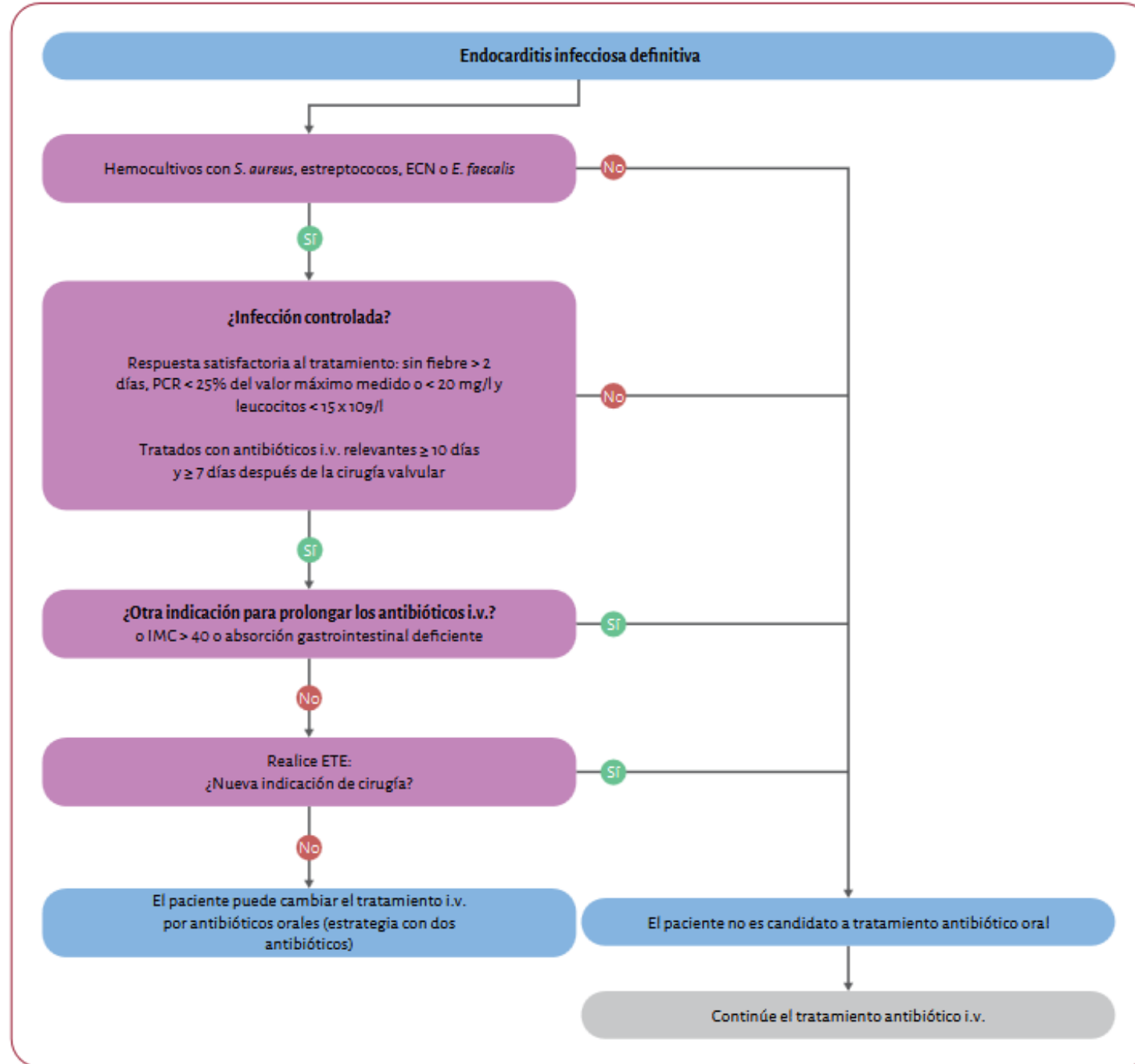


Table S9 Combinations of antibiotics for oral step-down treatment

Penicillin-and methicillin-susceptible <i>S. aureus</i> & CoNS	Methicillin-susceptible <i>S. aureus</i> & CoNS	Methicillin-resistant CoNS	<i>E. faecalis</i>	Penicillin-susceptible streptococci	Penicillin-resistant streptococci
Amoxicillin 1 g × 4 Rifampin 600 mg × 2	Dicloxacillin 1 g × 4 Rifampin 600 mg × 2	Linezolid 600 mg × 2 Fusidic acid 750 mg × 2	Amoxicillin 1 g × 4 Moxifloxacin 400 mg × 1	Amoxicillin 1 g × 4 Rifampin 600 mg × 2	Linezolid 600 mg × 2 Rifampin 600 mg × 2
Amoxicillin 1 g × 4 Fusidic acid 750 mg × 2	Dicloxacillin 1 g × 4 Fusidic acid 750 mg × 2	Linezolid 600 mg × 2 Rifampin 600 mg × 2	Amoxicillin 1 g × 4 Linezolid 600 mg × 2	Amoxicillin 1 g × 4 Moxifloxacin 400 mg × 1	Moxifloxacin 400 mg × 1 Rifampin 600 mg × 2
Moxifloxacin 400 mg × 1 Rifampin 600 mg × 2	Moxifloxacin 400 mg × 1 Rifampin 600 mg × 2		Amoxicillin 1 g × 4 Rifampin 600 mg × 2	Amoxicillin 1 g × 4 Linezolid 600 mg × 2	Linezolid 600 mg × 2 Moxifloxacin 400 mg × 1
Linezolid 600 mg × 2 Rifampin 600 mg × 2	Linezolid 600 mg × 2 Rifampin 600 mg × 2		Linezolid 600 mg × 2 Moxifloxacin 400 mg × 1	Linezolid 600 mg × 2 Rifampin 600 mg × 2	
Linezolid 600 mg × 2 Fusidic acid 750 mg × 2	Linezolid 600 mg × 2 Fusidic acid 750 mg × 2		Linezolid 600 mg × 2 Rifampin 600 mg × 2	Linezolid 600 mg × 2 Moxifloxacin 400 mg × 1	

CoNS, coagulase-negative staphylococci.

Table S8 General recommendations, treatment phases, and clinical scenarios to consider outpatient parenteral or outpatient oral antibiotic therapy for infective endocarditis

General recommendations		
Outpatient parenteral or oral antibiotic therapy can be considered if: • Patient is clinically stable. • Home environment is stable, preferably with a cohabitant caregiver. • Patient is self-reliant or home healthcare can be provided. Contraindications: • Heart failure. • Severe valvular regurgitation, vegetations >10 mm, progression, or local complications. • Neurological involvement. • Renal impairment. • Malabsorption. • PVID.		
Timing and indications in various clinical scenarios		
Critical phase (rapid shift to OPAT or oral step-down treatment, 0–2 weeks): • Consider OPAT in NVE caused by oral streptococci or <i>S. gallolyticus</i>. • Oral step-down treatment may be considered after a minimum of 10 days of i.v. antibiotic treatment.		
NVE	PVE	CIED
• >10 days of i.v. antibiotic treatment after admission or performed surgery. • IE by any causative agent except highly difficult-to-treat microorganisms*. • Negative blood cultures at 72 h. • TOE ruling out severe aortic regurgitation and prosthetic valve dysfunction. • No anticoagulation issues.	• >10 days of i.v. antibiotic treatment after admission. • IE caused by oral streptococci, <i>S. gallolyticus</i>, or <i>E. faecalis</i>. • Cardiac surgery not indicated • Negative blood cultures at 72 h. • TOE ruling out severe aortic regurgitation and prosthetic valve dysfunction. • No anticoagulation issues.	• >7 days of i.v. antibiotic treatment after non-complicated early lead extraction (<1 week from admission). • IE by any causative agent except highly difficult-to-treat microorganismsa. • No signs of pocket infection. • Negative blood cultures at 72 h after reimplantation of CIED. • Normal echocardiography.
Continuation phase (postponed shift to OPAT or oral step-down treatment, beyond week 2): • Consider oral step-down treatment if i.v. minimum 10 days, and <i>Streptococcus</i> spp., <i>E. faecalis</i>, <i>S. aureus</i>, or CoNS.		
NVE	PVE	CIED
• >3 weeks of i.v. antibiotic treatment after admission or surgery performed. • IE by any causative agent except highly difficult-to-treat microorganisms*. • Negative blood cultures at 72 h. • TOE ruling out severe aortic regurgitation and prosthetic valve dysfunction. • No anticoagulation issues. • No severe sequelae or clinical complications. • No need for daily and/or complex cures.	• >3 weeks of i.v. antibiotic treatment after admission or surgery performed. • Patients undergoing cardiac surgery and not infected with highly difficult-to-treat microorganism* and without severe complications. • Negative blood cultures at 72 h. • TOE ruling out severe aortic regurgitation and prosthetic valve dysfunction. • No anticoagulation issues. • No severe sequelae or clinical complications. • No need for daily and/or complex cures.	• >2 weeks of i.v. antibiotic treatment after device removal/reimplantation. • Associated right-sided IE with vegetations >2 cm. • Associated with left-sided IE (apply then criteria for NVE/PVE) • Late or complicated lead extraction • IE by any causative agent except highly difficult-to-treat microorganisms. • No signs of pocket infection. • Negative blood cultures at 72 h after reimplantation of CIED. • Normal echocardiography. • No severe sequelae or clinical complications. • No need for daily and/or complex cures.

Tractament endovenós



UHAD

Long-Acting

UHAD

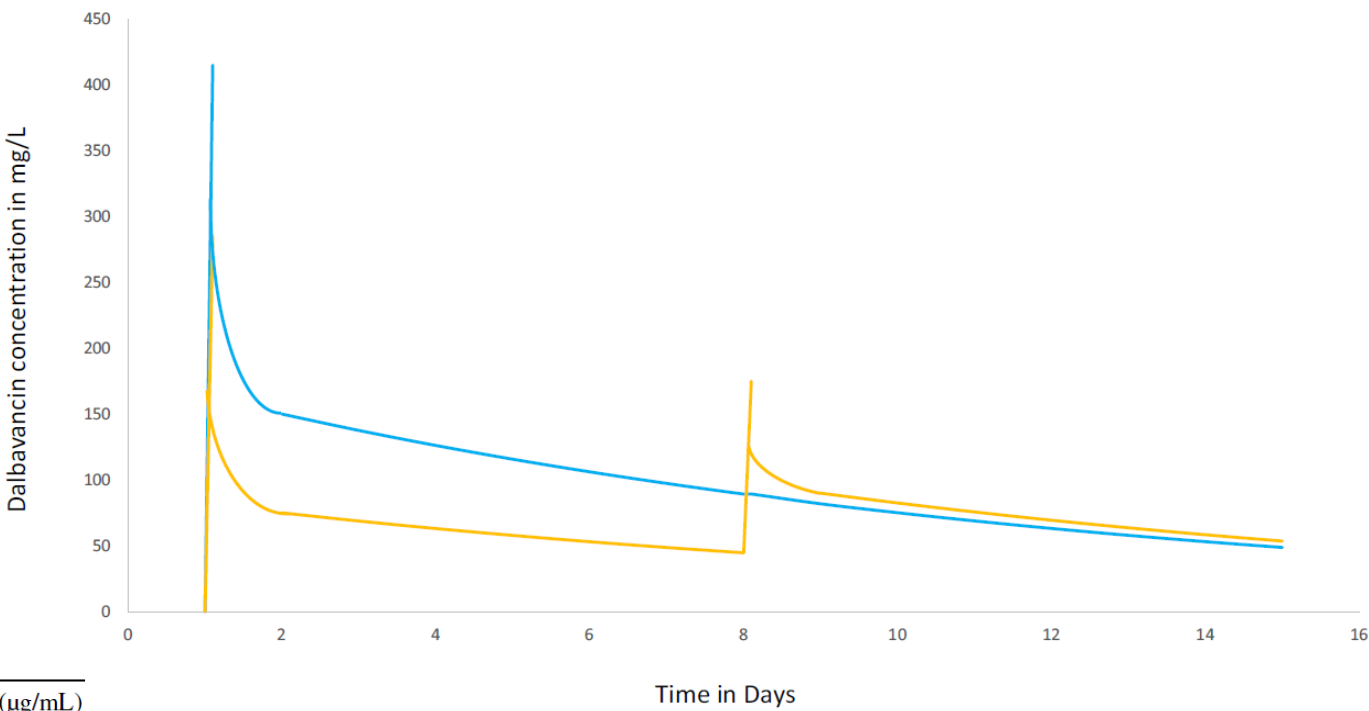
- ✓ Via
- ✓ Posologia antibiòtic
- ✓ Àrea geogràfica
- ✓ Cuidador
- ✓ Disponibilitat

Long-Acting

Dalbavancina



Licoglicopèptid



Organism	No. of isolates	MIC ₅₀ (µg/mL)	MIC ₉₀ (µg/mL)
<i>S. aureus</i>	14,319	0.03	0.03
Methicillin-susceptible	9111	0.03	0.03
Methicillin-resistant	5208	0.03	0.03
Vancomycin MIC ≥ 2 µg/mL	44	0.06	0.12
Coagulase-negative staphylococci	1992	0.03	0.06
<i>S. pneumoniae</i>	3487	0.015	0.015
<i>β-hemolytic streptococci</i>	3269	0.015	0.03
<i>Viridans group Streptococci</i>	1063	0.008	0.03
<i>Enterococcus faecalis</i>	2071	0.03	0.06
Van A—vancomycin-resistant	43	> 2	> 2
Van B—vancomycin-resistant	6	0.06	–
<i>Enterococcus faecium</i>	936	0.12	> 2
Van A—vancomycin-resistant	386	> 2	> 2
Van B—vancomycin-resistant	19	0.06	> 2

Data adapted from Pfaller et al. [14]
MIC minimum inhibitory concentration



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<https://doi.org/10.1007/s15010-024-02393-9>

REVIEW



A systematic review of dalbavancin efficacy as a sequential therapy for infective endocarditis

Gabriele Maria Leanza¹ · Emanuele Rando¹ · Federico Frondizi¹ · Eleonora Taddei² · Francesca Giovannenze² · Juan P. Horcajada³ · Giancarlo Scoppettuolo² · Carlo Torti^{1,2}

Table 1 Cohort studies included in the review

Author, year	Study period	Number of endocarditis	Endocarditis type	Pathogens	Time to first dalbavancin infusion (median)	Dalbavancin therapy duration/ number of dalbavancin doses	Study outcome	Quality assessment
Tobudic, 2018 [21]	2015–2016	31 (4 lost at FU)	NVE 16, PVE 6, CIED 5	MSSA 9, CoNS 6, <i>Enterococcus</i> spp. 4, <i>Streptococcus</i> spp. 8	1 week	6 weeks of dalbavancin administration (median)	6-months clinical/ microbiological failure: 7.4%	6/9
Dinh, 2019 [19]	2017–2018	19 (1 lost at FU)	NVE 8, PVE 10	CoNS 8, MSSA 3, MRSA 2, PId 3, <i>E. faecalis</i> 3, <i>S. gallolyticus</i> 1, <i>L. monocytogenes</i> 1	13 d	2 injections (median). One patient was under chronic suppressive therapy	Clinical failure at last visit (mean of 97.9 ± 99.7 d since first dose): 27.8%	5/9
Wunsch, 2019 [20]	2016–2019	25 (2 lost at FU)	NVE 15, PVE 6, CIED 4	NBCe 8, CoNS 5, PI 5, MSSA 2, MRSA 2, <i>Streptococcus</i> spp. 2, <i>Enterococcus</i> spp. 1	Not specified	2 doses (median)	90 d-clinical failure: 8.7% (2/23 patients with a complete FU)	6/9
Morata, 2022 [22]	2018–2019	38	Left-sided endocarditis 26 Right-sided endocarditis 12	MSSA 7, MRSA 3, CoNS 14, <i>Enterococcus</i> spp. 5	28 d	Mean: right heart IE 2.5 weeks, left heart IE 2 weeks 1 chronic therapy	Clinical failure: 2.6% (timing not specified)	6/9
Hidalgo-Tenorio, 2023 [14]	2016–2021	124 (1 lost at FU)	NVE 58, PVE 54, CIED 18	MSSA 28, MRSA 3, CoNS 48, <i>Enterococcus</i> spp. 27, <i>Streptococcus</i> spp. 18	Not specified	14 d of dalbavancin coverage (median)	12-months clinical failure: 4.8%	6/9
Courjon, 2023 [15]	2018–2020	21	PVE 17, NVE 4	Not specified for IE	Not specified for IE	Not specified for IE	30 d-clinical failure: 0% (for patients who completed the FU)	5/9



REVIEW



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- ✓ Potencial terapèutic en EI, especialment en vàlvula nativa (NVE) i infeccions per CoNS.
- ⚠ Evidència limitada: estudis observacionals amb biaixos i sense grups de control.
- ! Precaució en la pràctica clínica: manca de dades en EI relacionada amb dispositius cardíacs i patògens no-CoNS.
- 🔬 Calen estudis amb grups de control, seguiment post-teràpia IV i distinció entre consolidació i teràpia supressiva.
- 💉 El monitoratge terapèutic pot ajudar a mantenir nivells plasmàtics adequats durant el tractament.



Table 5
Pharmacoeconomic analysis.

	Drug cost	Specialist consultation	Nursing consultation	Total
Treatment with DBV 1500-mg dose	1341.90 €	400.83 €	64.58 €	1807.31 €
	Drug cost	Hospital stay (14 d)		Total
Usual IE treatment 14-d hospital stay	417.62 €	6938.26 €		7355.88 €
	Drug cost	Consultations and stays		Difference per patient
Difference between DBV and usual treatment (Ref. DBV)	924.28 €	–6,472.85 €		–5,548.57 €

DBV, dalbavancin; IE, infective endocarditis.



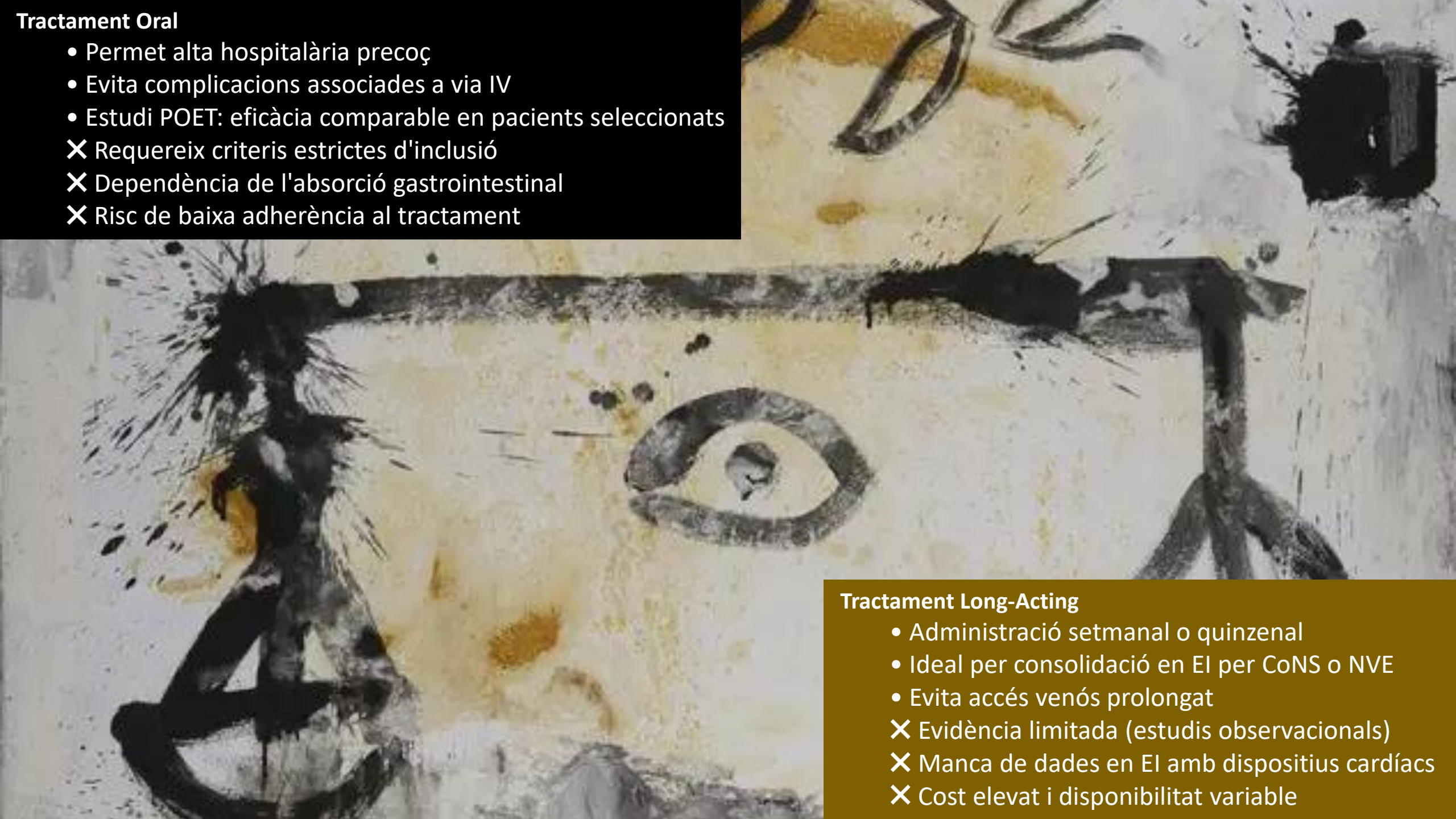
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7.13.2. *Otras consideraciones sobre el tratamiento antimicrobiano oral o parenteral ambulatorio*

En el programa de tratamiento antibiótico parenteral ambulatorio, los pacientes continúan con los mismos antibióticos que se usaron en la fase aguda en regímenes de administración una vez al día o con bomba de infusión si es necesaria la administración intermitente de los antibióticos o con infusión continua. La dalbavancina es un antibiótico glucopéptido que tiene una vida media muy larga y se puede administrar una vez a la semana. La experiencia previa en la endocarditis infecciosa por bacterias Gram positivas sensibles es buena, aunque no está claro cuál es el plan de administración más efectivo^{274,402}. La prescripción recomendada es una dosis de carga de 1,5 g seguida de 0,5-1 g a la semana hasta completar 6 semanas de tratamiento antibiótico.



Tractament Oral

- Permet alta hospitalària precoç
- Evita complicacions associades a via IV
- Estudi POET: eficàcia comparable en pacients seleccionats
- ✗ Requereix criteris estrictes d'inclusió
- ✗ Dependència de l'absorció gastrointestinal
- ✗ Risc de baixa adherència al tractament

Tractament Long-Acting

- Administració setmanal o quinzenal
- Ideal per consolidació en EI per CoNS o NVE
- Evita accés venós prolongat
- ✗ Evidència limitada (estudis observacionals)
- ✗ Manca de dades en EI amb dispositius cardíacs
- ✗ Cost elevat i disponibilitat variable



Cecilie Thoresen Krog

She passed the [examen artium](#) in 1882, as the first Norwegian woman