26. TÜRK KLİNİK MİKROBİYOLOJİ VE İNFEKSİYON HASTALIKLARI KONGRESİ

KLİMİK 2026

29 NİSAN–3 MAYIS 2026

Gelenekselin Ötesinde Endokardit: Yeni Kanıtlar, Zor Sorular

Tedavi Süresini Azaltmak Mümkün mü? Ardışık Ayaktan Tedavi Hangi Hastada Güvenli?

Dr. Ezgi Yılmaz

İstanbul Medipol Üniversitesi

2026

İEÇG

KLİMİK DERNEĞİ İNFEKTİF ENDOKARDİT VE DİĞER KARDİYOVASKÜLER İNFEKSİYONLAR ÇALIŞMA GRUBU

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Sunum Planı

A. İnfektif Endokardit Tedavi Süresi

i. Tarihsel kanıtlar- 1949, 1950 yıllarından literatürden örnekler

ii. *ESC2015, ESC2023* ve *Klimik Uzlaşı Raporu 2019*

iii. Streptokok, Stafilokok, Enterokok İE'lerinde tedavi süreleriyle ilgili literatürden örnekler

B. Oral Ardışık Tedavi

i. POET-1, POET-2, RODEO-1, RODEO-2 ve literatürden örnekler

ii. *Wikiguidelines consensus statement 2023*

İE Tedavi Süresi: KANITLAR, 1949-50

› Med J Aust. 1949 Mar 19;1(12):377-9. doi: 10.5694/j.1326-5377.1949.tb67702.x.

The present status of penicillin therapy in the treatment of subacute bacterial endocarditis

D J THOMAS

MARCH 19, 1949. THE MEDICAL JOURNAL OF AUSTRALIA. 377

3. Reduction of streptococcal concentration in dust and blankets. This is mainly a matter which concerns hospital wards, dormitories, and special convalescent homes for cardiac cripples. Oiling of floors and bedding is very successful in reducing the bacterial count of dust, but germicidal aerosols are expensive and need special heating and cumbersome dispersal equipment.

4. Climate. The value of sending rheumatic children to warmer or tropical climates is now seriously in question. It is a frequent experience that, while they are free from relapse during such a visit, a fresh recrudescence occurs shortly after their return. Such dislocation is expensive and impractical as a general policy and may lead to a loss of acquired streptococcal immunity.

5. Prevention of fatigue. I think many will agree that fatigue, whether of physical or of psychological origin, is a frequent precursor of childhood infection. We are all familiar with the frequency of chorea in the midst of school examinations, and some consideration on detail in the planning of the rheumatic life is worth while. The necessity for the avoidance of long journeys to school, late hours, football, swimming, many messages et cetera is more important in the first year after a relapse. Judgement is required to avoid the development of any inferiority complex in the mind of a child, and once we can be sure that, as judged by the criteria available, rheumatic activity is at an end, physical activity can be steadily increased. I believe that in established mitral disease any exercise short of that producing distress is allowable.

6. The role of the special hospital and of the almoner. To keep a rheumatic child in a general hospital ward is to ask for trouble, as they are hotbeds of respiratory infection. Special convalescent homes have proved their value in both England and America in the case of children coming from an unsuitable economic environment. These institutions are always in charge of physicians of great experience in cardiac rheumatism, with laboratory facilities to assist them in assessing the duration of convalescence and gradual restoration to activity. Much of our more recent knowledge of the fluctuations in the rheumatic state have come from such workers. Wards can be kept free from streptococci and carriers isolated and treated; visitors can be controlled, diet supervised, and school continued. Apparently very few untoward psychological disturbances have been generated among the inmates. The institution must form part of a coordinated pattern whereby contact is continually maintained with the child's parents, his usual medical attendant, school doctor and school mistress, and a supervisory centre where he is constantly observed throughout the remaining years of his susceptibility. This centre is often an out-patient department of the Home, and the bond is maintained by a specially trained band of social service workers who know how to appraise and better the home conditions and psychological environment, visit children and arrange for their instruction or entertainment if in bed in an approved home or foster-home of their own, arrange for school or vocational tuition, arrange transport to the centre or to school, and assist parents to carry out their doctor's advice.

We see then that such care may cost too much for individual or private agencies, or even individual hospitals. We must accept rheumatic fever and rheumatic heart disease as a public and community health problem, requiring broad planning and determined organization. Under the more favourable living standards of this country, and with its relatively small population, we should be able to be just as successful in an all-out attack on the rheumatic heart disease problem as no doubt we shall be against tuberculosis. However slow our authorities may be to commence such a campaign, we as practitioners can play our part at once in the close follow-up of individual streptococcal infections of all types, from sore throats to scarlet fever, in the recognition of atypical types of rheumatic fever, and in the continued unremitting observation and guidance of those affected with cardiac rheumatism.

THE PRESENT STATUS OF PENICILLIN THERAPY IN THE TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS.[1]

By DOUGLAS J. THOMAS,
Melbourne.

I SHOULD like, without further ado, to thank you for the honour done me by asking me to present this paper. Previous speakers have again shown that rheumatic fever remains as one of the major scourges of childhood. Subacute bacterial endocarditis only too frequently intrudes as the final complication which closes the life story of the patient who contracted this disease.

In 1931 my attention was forcibly directed to this malady by the death of a close relation from this cause. The circumstances were of clinical interest. An elder brother contracted erythema nodosum and rapidly made a complete recovery. Then a sister of this patient within a few days developed a sore throat followed also by erythema nodosum. She too made a good recovery. Very shortly a younger sister contracted a sore throat and quinsy. This third patient was a schoolgirl known to have an aortic murmur. There was some doubt as to whether this represented a congenital or an acquired lesion. She too developed erythema nodosum. This was followed by subacute bacterial endocarditis, which ended fatally. At that time (1931) neither penicillin nor "sulpha" drug was known. From that date until June, 1945, I did not personally encounter one case of subacute bacterial endocarditis successfully treated.

The author is aware that from time to time cases of apparent cure were reported in the literature, and with the introduction of "sulpha" drugs such cures did occasionally result.

There have been many milestones in the history of medicine. Some will remember the thrill they experienced when they first used insulin in the treatment of acidotic coma, or when as a result of liver therapy a patient with pernicious anaemia was restored to an active and happy life.

The story I have to tell today concerning the control of subacute bacterial endocarditis by penicillin is equally dramatic.

Before proceeding to the discussion of treatment of the established infection I should like to say something about preventing its occurrence after extraction of teeth. It is essential that proper penicillin cover be given whenever teeth are extracted from a patient with a past history of rheumatic infection. This will require further education of both the medical and the dental profession. I sometimes feel that the young sufferer from rheumatic carditis should be given an identity card and that this should be shown to each and every medical man and dentist who attends the patient, and that on this card should be the inscription: "I once suffered from rheumatic carditis." In too many public hospitals the dental services are taken for granted, and we as a profession exhibit gross discourtesy in not admitting our dental colleagues to full status and in denying them full cooperation. In my opinion every in-patient of a hospital should, on admission, be seen by a dental officer, who could thereupon attach his dental report to the case history. In this manner full reciprocity would be fostered.

Turning now to the question of treatment of subacute bacterial endocarditis by penicillin, I should like, briefly, to state the principles involved. We hope to establish rapidly and maintain in the blood-stream such a concentration of the drug as will be adequately bacteriostatic. Furthermore, we will continue with treatment, not merely until the blood-stream is sterile, but until every single colony within the vegetations on the valves has perished. Moreover, because of the possibility of relapse, we will

[1] Read at a meeting of the Section of Medicine, Australasian Medical Congress (British Medical Association), Sixth Session, Perth, August, 1949.

› Circulation. 1950 Dec;2(6):801-10. doi: 10.1161/01.cir.2.6.801.

The present status of treatment of subacute bacterial endocarditis

A L BLOOMFIELD

Circulation
The Journal of the American Heart Association
DECEMBER 1950
VOL. II NO. 6

The Lewis A. Conner Lecture of the American Heart Association

The Present Status of Treament of Subacute Bacterial Endocarditis

By ARTHUR L. BLOOMFIELD, M. D.

Some considerations concerning the fundamental pathology of bacterial endocarditis which have a bearing on treatment are discussed. In using antibiotics the importance of time-dose relationships is emphasized. It is pointed out that tests for strain sensitivity give a useful clue to the total daily dosage but that regardless of this, treatment must be carried out over a period of at least a month in order to achieve permanent bacteriologic cures. The difficulties and complications of treatment are discussed. Special methods for the treatment of highly resistant strains and the results with some of the newer antibiotics are outlined.

I WANT to say first of all how very much I appreciate the honor of being invited to give the Lewis A. Conner Lecture before the members of the American Heart Association. As an internist whose practice is in no sense confined to cardiology I hesitated to accept, but then I took courage from the realization that Dr. Conner himself was, after all, primarily a general doctor who, only after years of practice, claimed a special interest in problems of the circulation. Furthermore, the title suggested by your Chairman was too tempting to resist when one realizes that the new treatment of bacterial endocarditis is, barring insulin, probably the greatest therapeutic triumph of the century in internal medicine.

We were fortunate, as long ago as 1943, in being asked to participate in the bacterial endocarditis program of the Committee on Medical Research.[1] Six years of experience have modified some of our original views, but more or less definite policies as to procedure have now become crystallized, and these we wish to bring before you today. We shall touch especially on the use of newer preparations, singly and in combination, on routes of administration of antibiotics, and on the importance of sensitivity tests in determining time-dose relationships. It is perhaps only natural that emphasis be placed on the work of our own group.

It would be superfluous to review to this audience the background, clinical features, and bacteriologic findings of infectious endocarditis; they are familiar to all.[2-5] It may be recalled, however, that prior to the introduction of penicillin most clinicians, even those of wide experience, could not recall instances of actual recovery from proved bacterial endocarditis.[4] At best, the measures then in vogue, such as sulfonamides and anticoagulants, were a feeble crutch to lean on and the hazards of therapy almost outweighed the occasional cure which was claimed.[5] One felt that another such vic-

Presented at the Twenty-Third Annual Scientific Session of the American Heart Association, San Francisco, Calif., June 22, 1950.

From the Department of Medicine, Stanford University Medical School.

İE Tedavi Süresi: KANITLAR, 1949

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In the *British Medical Jou*
Professor R. V. Christie reporte
Council the results of trials car
patients suffering from this dis
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4. For
be given daily for eight weeks.

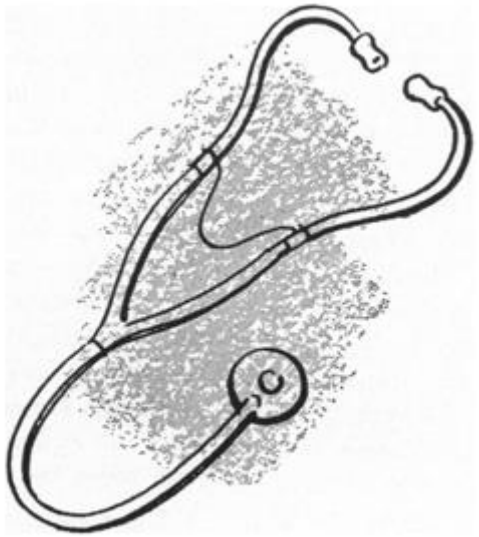
5. In cases of resistant infection, if adequately bacteriostatic serum levels of penicillin are maintained for long periods, therapy failure may be converted to therapy

İE Tedavi süresi: KANITLAR, 1950

HİÇBİR AJAN, BAKTERİSİDAL ETKİSİ NE KADAR BÜYÜK OLURSA OLSUN BİRKAÇ GÜN İÇİNDE VEJETASYONUN DERİNLİKLERİNDEKİ KOKLARI TEMİZLEYEMEZ.

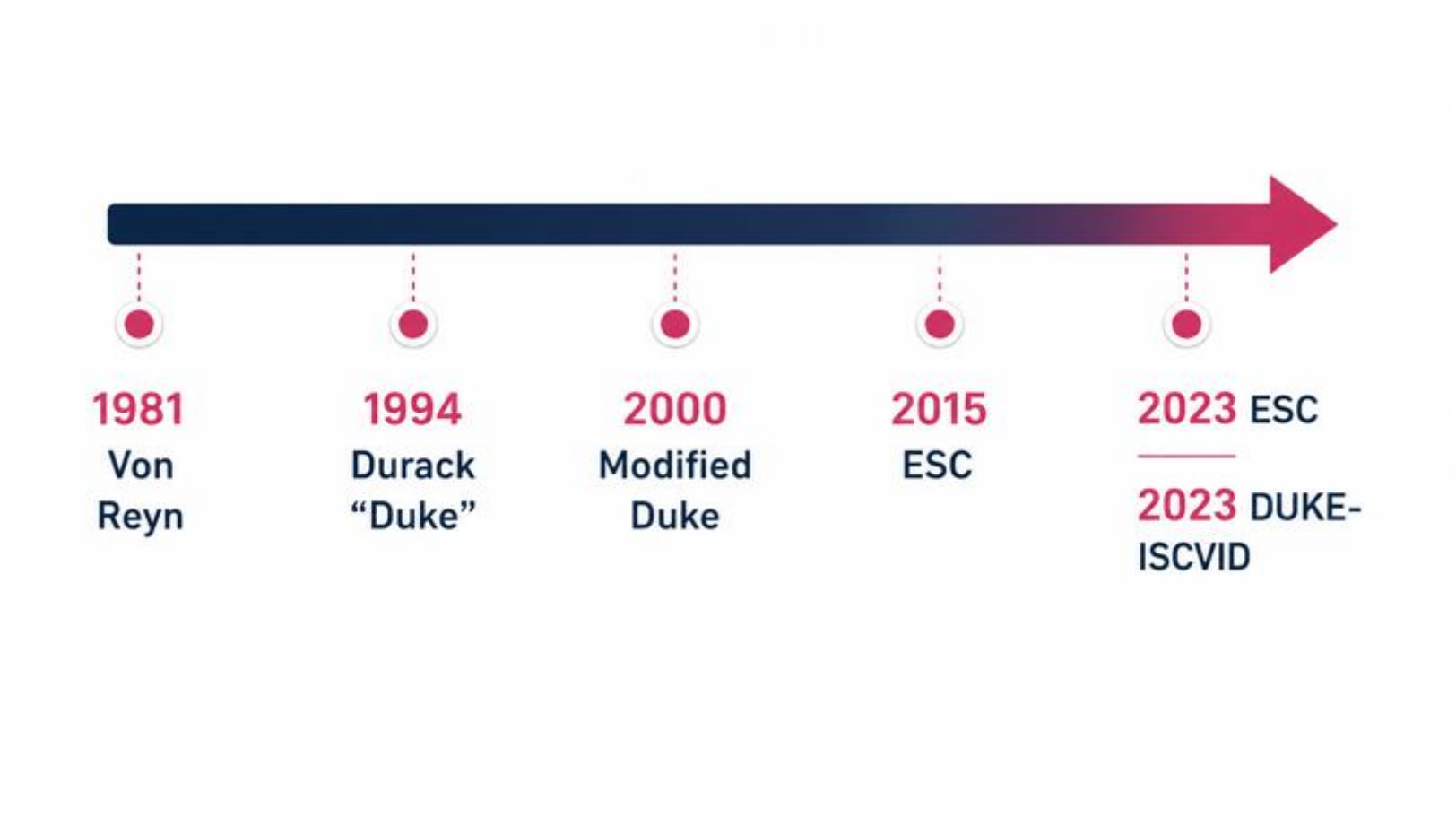
Yüksek doz penisilin kısa süre; hızlı nüks

30 günlük kesintisiz ama günlük uygun doz; ***YETERLİ***



Bloomfield 1950

Tedavi Süresinde Yıllar İçerisindeki Değişimler



Doğal ve Protez Kapak İE'de ESC 2015 ve ESC 2023 Rehberlerine Göre Tedavi Süreleri

Clinical scenario / pathogen group	ESC 2015	ESC 2023
General principle	NVE usually 2–6 weeks; PVE usually ≥6 weeks.	NVE usually 2–6 weeks; PVE usually >6 weeks (longer than NVE in most scenarios).
Viridans streptococci / Streptococcus gallolyticus (penicillin-susceptible)	NVE: 4 weeks standard; 2 weeks possible in selected uncomplicated NVE. PVE: 6 weeks.	NVE: 4 weeks standard; 2 weeks possible in selected uncomplicated NVE. PVE: 6 weeks.
Staphylococcus aureus or coagulase-negative staphylococci (MSSA-focused, duration only)	NVE: 4–6 weeks. PVE: ≥6 weeks.	NVE: 4–6 weeks. PVE: >6 weeks.
MRSA endocarditis (duration only)	NVE: generally 6 weeks. PVE: ≥6 weeks.	NVE: generally 6 weeks. PVE: >6 weeks.
Enterococcus faecalis / enterococcal IE	NVE: 4–6 weeks depending on regimen and symptom duration; 6 weeks in many cases. PVE: 6 weeks.	NVE: 4–6 weeks depending on regimen and complexity; 6 weeks in many cases. PVE: 6 weeks (or longer in complex disease).
HACEK organisms	NVE: 4 weeks. PVE: 6 weeks.	NVE: 4 weeks. PVE: 6 weeks.
Culture-negative IE	Duration depends on clinical setting, valve type, and suspected pathogen; PVE generally treated longer than NVE.	Duration depends on timing, prior antibiotics, and suspected pathogen; PVE generally treated longer than NVE.

Tablo 19. Streptokoksik İnfektif Endokarditin Antimikrobik Tedavisi (3,65,207)

Mikroorganizma	Antimikrobik	Süre (Hafta)
Penisilin G MIC ≤0.125 µg/ml olan viridans streptokoklar ve SGG	Penisilin G veya Seftriakson* + Gentamisin†	
	Penisilin G veya Seftriakson*	
Penisilin G MIC >0.125 ve <0.5 µg/ml arasında olan viridans streptokoklar ve SGG	Penisilin G veya Seftriakson* + Gentamisin†	
Penisilin G MIC ≥0.5 ve ≤2 µg/ml arasında olan viridans streptokoklar, SGG, *Abiotrophia* spp., *Granulicatella* spp. ve *Gemella* spp.	Penisilin G veya Ampisilin veya Seftriakson* + Gentamisin†	
Penisilin G MIC >2 µg/ml olan dirençli streptokoklar veya β-laktam alerjisi	Vankomisin‡ veya Teikoplanin§	

Tablo 20. Enterokoksik İnfektif Endokarditin Antimikrobik Tedavisi (3,65,207)

Mikroorganizma	Antimikrobik	Günlük Uygular	Süre (Hafta)
Penisilin ve gentamisine dirençli olmayan enterokoklar	Ampisilin veya Penisilin G + Gentamisin	12 gr, 4- 24 MU, 3 mg/kg	
	Ampisilin + Seftriakson*	6 gr, 6 d 4 gr, 2 d	
Penisiline dirençli ve gentamisine yüksek düzeyde dirençli olmayan enterokoklar veya β-laktam alerjisi	Vankomisin veya Teikoplanin + Gentamisin	30 mg/k 10 mg/k 3 mg/kg	
Penisiline duyarlı ve gentamisine yüksek düzeyde dirençli olan enterokoklar (gentamisin MIC >500 µg/ml, streptomisin MIC <2000 µg/ml)	Ampisilin + Streptomisin	200 mg 15 mg/k	
Penisiline duyarlı ve gentamisin ve streptomisine yüksek düzeyde dirençli olan enterokoklar (gentamisin MIC >500 µg/ml, streptomisin MIC >2000 µg/ml)	Ampisilin + Seftriakson*	6 gr, 6 d 4 gr, 2 d	
Penisiline, aminoglikozidlere ve vankomisine dirençli enterokoklar	Linezolid veya Daptomisin + Ampisilin	1200 mg 10-12 m 12 gr, 6	

MIC: Minimum inhibitör konsantrasyon

Tablo 23. Stafilokoksik İnfektif Endokarditlerin Antimikrobik Tedavisi (3,65,207)

Mikroorganizma	Antimikrobik	Günlük Doz, Doz Aralığı, Uygulama Yolu	Süre (Hafta) Doğal Kapak	Süre (Hafta) Yapay Kapak	Yorum
Metisiline duyarlı stafilokoklar*	Nafsilin veya	12 gr, 6 dozda, İV	4-6	≥6	Ülkemizde nafsilin ve flukloksasilin bulunamamaktadır.
	Flukloksasilin veya	12 gr, 6 dozda, İV	4-6	≥6	
	Sefazolin‡	6 gr, 3 dozda, İV	4-6	≥6	
	+				
	Gentamisin	3 mg/kg, tek dozda, İV	Verilmez	2	
	+				
	Rifampisin‡	900 mg, tek dozda, oral/İV	Verilmez	≥6	
	Daptomisin¶ veya	8-12 mg/kg, tek dozda, İV	4-6	≥6	Sadece β-laktamları tolere edemeyen veya β-laktam alerjisi olan hastalarda kullanılmalıdır.
	Vankomisin	30 mg/kg, 2 dozda, İV	4-6	≥6	
Metisiline dirençli vankomisine duyarlı (MIC ≤2 µg/ml) stafilokoklar	Vankomisin‡	30 mg/kg, 2 dozda, İV	4-6	≥6	Kardiyak veya ekstrakardiyak tüm apse odakları uygun cerrahi girişimlerle kontrol altına alınmalıdır.
	+				
	Gentamisin¶ (duyarlıysa)	3 mg/kg, tek dozda, İV	Verilmez	2	
	+				
	Rifampisin (duyarlıysa)	900 mg, 3 dozda, oral/İV	Verilmez	≥6	
	Daptomisin¶	8-12 mg/kg, tek dozda, İV	4-6		
Metisiline duyarlı stafilokoklar (İVDU'da sağ kalp endokarditi)**	Nafsilin veya	12 gr, 6 dozda, İV	2		Ülkemizde nafsilin ve flukloksasilin bulunamamaktadır.
	Flukloksasilin	12 gr, 6 dozda, İV	2		
	Siprofloksasin	1500 mg, 2 dozda, oral	2		Hastanede yatırılamayan komplike olmamış olgularda suşun her iki ajana da duyarlı olduğu gösterilmeli ve hasta uyumu yakından izlenmelidir.
	+				
	Rifampisin	600 mg, 2 dozda, oral	2		

Şimşek-Yavuz S. [Diagnosis, treatment and prevention of infective endocarditis: Turkish consensus report]. Klimik Derg. 2019; 32(Suppl. 1): 2-116. Turkish.

İE Tedavi Süresi

Kanıtlar

RKÇ ?

Standard süre vs. kısaltılmış tedavi süresi


BMC Infectious Diseases

STUDY PROTOCOL Open Access

Short-course antibiotic regimen compared to conventional antibiotic treatment for gram-positive cocci infective endocarditis: randomized clinical trial (SATIE)


European Journal of Clinical Microbiology & Infectious Diseases (2024) 43:95–104
https://doi.org/10.1007/s10096-023-04705-7

ORIGINAL ARTICLE

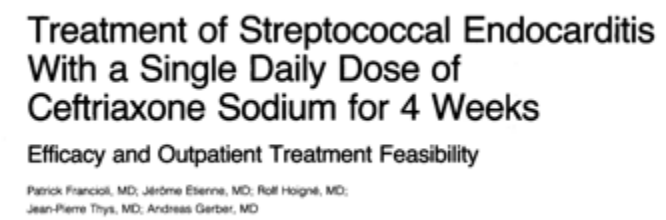
Prognosis of prosthetic valve infective endocarditis due to *Streptococcus* spp., a retrospective multi-site study to assess the impact of antibiotic treatment duration

S. B. Gressens · B. Souhail · B. Pilmis · J. Lourtet-Hascoët · I. Podglajen · A. Fiore · V. Fihman · J. L. Mainardi · R. Lepeule · D. Lebeaux · M. Dubert


PLOS ONE

RESEARCH ARTICLE

Four weeks *versus* six weeks of ampicillin plus ceftriaxone in *Enterococcus faecalis* native valve endocarditis: A prospective cohort study


Treatment of Streptococcal Endocarditis With a Single Daily Dose of Ceftriaxone Sodium for 4 Weeks

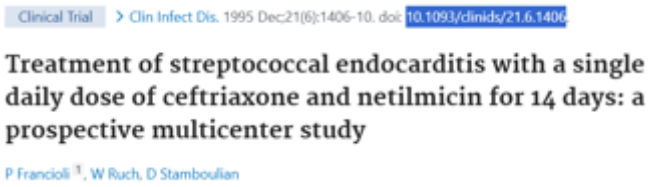
Efficacy and Outpatient Treatment Feasibility

Patrick Francioli, MD; Jérôme Etienne, MD; Rolf Hoigné, MD; Jean-Pierre Thys, MD; Andreas Gerber, MD


Am Heart J. 2007 Dec;154(6):1086-94. doi: 10.1016/j.ahj.2007.07.023. Epub 2007 Sep 12.

The relationship between the initiation of antimicrobial therapy and the incidence of stroke in infective endocarditis: an analysis from the ICE Prospective Cohort Study (ICE-PCS)

Stuart A Dickerman, Elias Abrutyn, Bruno Barsic, Emilio Bouza, Enrico Cecchi, Asuncion Moreno, Thanh Doco-Lecompte, Damon P Eisen, Claudio Q Fortes, Vance G Fowler Jr, Stamatios Lerakis, Jose M Miro, Paul Pappas, Gail E Peterson, Ethan Rubinstein, Daniel J Sexton, Fredy Suter, Pilar Tornos, Dominique W Verhagen, Christopher H Cabell; ICE Investigators


Clinical Trial · Clin Infect Dis. 1995 Dec;21(6):1406-10. doi: 10.1093/clinids/21.6.1406

Treatment of streptococcal endocarditis with a single daily dose of ceftriaxone and netilmicin for 14 days: a prospective multicenter study

P Francioli, W Ruch, D Stamboulian

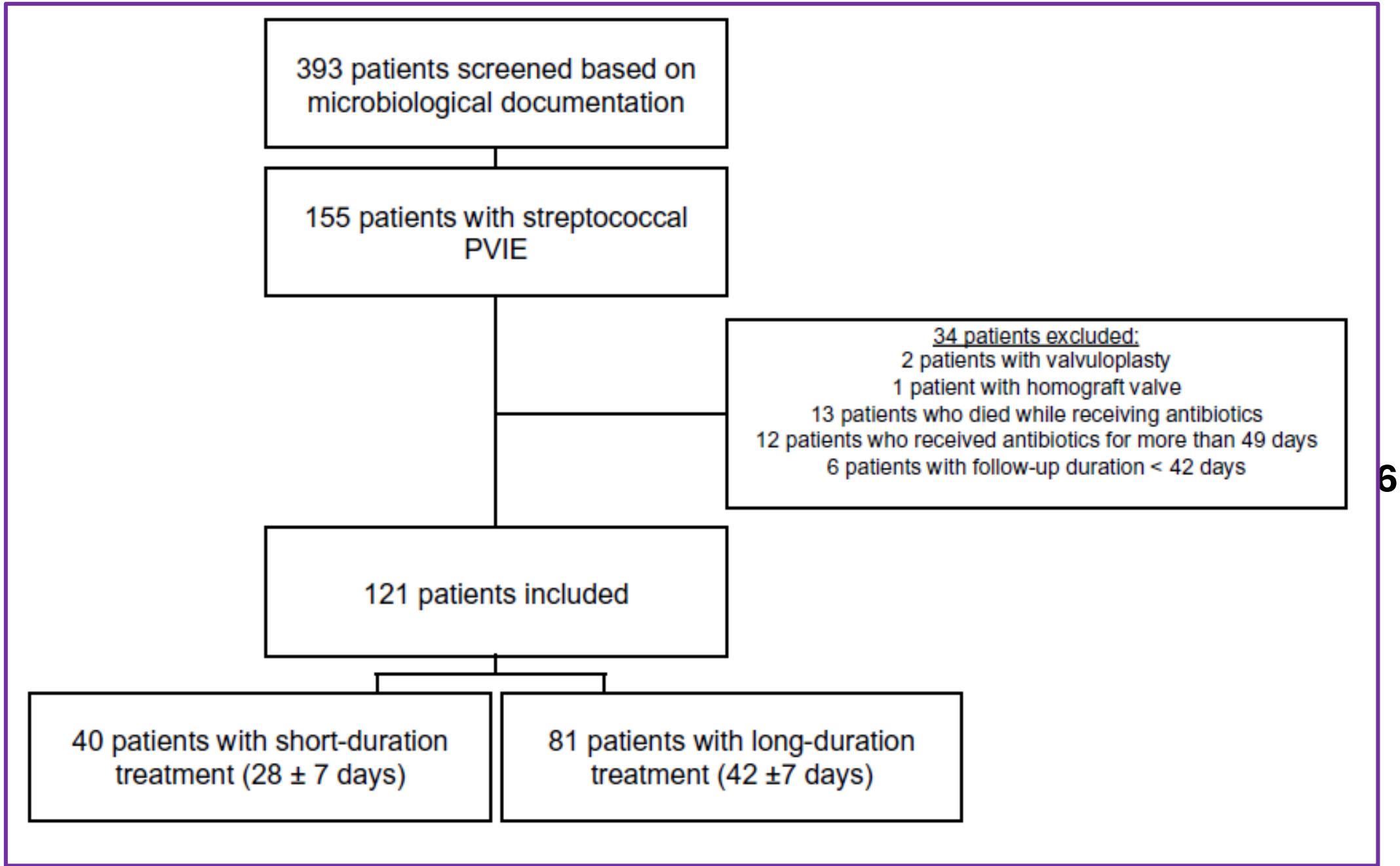

Effectiveness of Cloxacillin with and without Gentamicin in Short-Term Therapy for Right-Sided *Staphylococcus aureus* Endocarditis

A Randomized, Controlled Trial

Esteban Ribera, MD; Jose Gómez-Jimenez, MD; Emilia Cortes, MD; Oscar del Valle, MD; Ana Planes, MD; M. Teresa Gonzalez-Alujas, MD; Benito Almirante, MD; Imma Ocaña, MD; and Albert Pahissa, MD

Background: It is often difficult to administer extended antibiotic therapy in the hospital for right-sided *Staphylococcus aureus* endocarditis. Although the effectiveness of single-drug therapy given for 4 to 6 weeks and that of two-drug therapy given for 2 weeks have been shown, no short-course therapy with penicillinase-resistant penicillin alone and therapy with combined regimens are warranted.

Ann Intern Med. 1996;125:969-974.


393 patients screened based on microbiological documentation
155 patients with streptococcal PVIE
34 patients excluded:
2 patients with valvuloplasty
1 patient with homograft valve
13 patients who died while receiving antibiotics
12 patients who received antibiotics for more than 49 days
6 patients with follow-up duration < 42 days
121 patients included
40 patients with short-duration treatment (28 ± 7 days)
81 patients with long-duration treatment (42 ±7 days)

Characteristics of the current episode of infective endocarditis	Total (*N*=115)	Antibiotic duration		*p*-value
		Short (28±7d) (*N*=40)	Long (42±7d) (*N*=75)	
Intensive care unit stay > 3 days	20 (17%)	3 (8%)	17 (21%)	0.105
Initial left ventricular flow ejection (*n*=116)				0.072
>50%	92 (79%)	26 (61%)	66 (85%)	
30–50%	23 (20%)	12 (39%)	11 (14%)	
<30%	1 (1%)	0 (0%)	1 (1%)	
Endocarditis side (*n*=121)				**0.02**
Right	21 (17%)	12 (30%)	9 (11%)	
Left	100 (83%)	28 (70%)	72 (89%)	
Main valve involved (*n*=121)				**0.023**
Aortic	85 (70%)	21 (52%)	64 (79%)	
Mitral	15 (12%)	7 (18%)	8 (10%)	
Pulmonary	19 (17%)	11 (28%)	8 (10%)	
Tricuspid	2 (2%)	1 (2%)	1 (1%)	
Type of the involved valve (*n*=121)				0.226
Surgically inserted bioprosthesis	64 (53%)	17 (42%)	47 (58%)	
Surgically inserted mechanical prosthesis	27 (22%)	12 (30%)	15 (19%)	
Percutaneous inserted bioprosthesis	30 (25%)	11 (28%)	19 (23%)	
Detectable blood stream infection (*n*=121)	118 (98%)	39 (98%)	79 (98%)	1
Duration (days)	3.0 [1.0; 4.0]	3.0 [1.0; 6.0]	2.0 [2.0; 4.0]	0.669
Species involved (*n*=121)				0.244
S. mitis/oralis group	28 (23%)	12 (30%)	16 (20%)	
S. gallolyticus group	28 (23%)	11 (28%)	17 (21%)	
S. sanguinis	18 (15%)	2 (5%)	16 (20%)	
S. gordonii	8 (7%)	2 (5%)	6 (8%)	
S. mutans	7 (6%)	4 (10%)	3 (4%)	
S. anginosus	6 (5%)	2 (5%)	3 (4%)	
S. agalactiae	5 (4%)	3 (8%)	2 (3%)	
Point of entry (*n*=121)				0.849
Non-oral GI	32 (26%)	11 (28%)	21 (26%)	
Oral	45 (37%)	16 (40%)	29 (36%)	
Other	1 (1%)	0 (0%)	1 (1%)	
Unknown	43 (36%)	13 (32%)	30 (37%)	
ß-lactam MIC (mg/L) (*n*=85)				0.597
≤ 0.125	68 (75%)	22 (76%)	46 (74%)	
[0.125 ; 0.25]	4 (4%)	2 (7%)	2 (3%)	
[0.25; 0.50]	10 (11%)	4 (14%)	6 (10%)	

Gressens, S. *European journal of clinical microbiology & infectious diseases. 2024*

Streptokoksik PVE İE: 4w vs. 6w

Table 3 Treatment modalities among a retrospective cohort of 121 streptococcal PVE

Treatment modalities	Total (*N*=121)	Antibiotic duration		*p*-value
		Short (28±7d) (*N*=40)	Long (42±7d) (*N*=81)	
Use of aminoglycoside	89 (74%)	28 (70%)	61 (75%)	0.686
Associated with amoxicillin	74 (83%)	27 (100%)	47 (58%)	
Associated with third generation cephalosporin	10 (11%)	0	10 (12%)	
Duration of aminoglycoside (days)	5.0 [1.0; 14]	3.0 [0; 14]	7.0 [1.8; 14]	0.185
Use of aminoglycoside > 5 days	53 (44%)	15 (38%)	38 (47%)	0.347
Surgical Indication (following ESC guidelines)	37 (23%)	7 (18%)	30 (37%)	0.047
Indication type				0.240
Hemodynamic instability	1 (1%)	0 (0%)	1 (1%)	
Infection control	20 (17%)	2 (5%)	18 (22%)	
Mechanical valvular failure	16 (13%)	5 (12%)	11 (14%)	
Surgery effectively done	28 (23%)	7 (18%)	21 (26%)	0.421

Categorical variables are expressed as number of events (%)

Table 4 Outcome based on antibiotics duration among a retrospective cohort of 115 streptococcal PVE

Patients' outcome	Total (*N*=121)	Antibiotic duration		*p*-value
		Short (28±7d) (*N*=40)	Long (42±7d) (*N*=81)	
Mortality at 12 months	7 (6%)	4 (10%)	3 (4%)	0.344
Overall mortality	41 (34%)	10 (25%)	31 (38%)	0.151
Reinfection	7 (6%)	2 (5%)	5 (7%)	0.855
Relapse	3 (3%)	1 (2%)	2 (2%)	1

Categorical variables are expressed as number of events (%)

Mortalite analizi 43. günde;
kısa tedavi grubu 4-6 haftaları arasında 4 ex

Gressens, S. *European journal of clinical microbiology & infectious diseases. 2024*

Olmos et al. BMC Infectious Diseases (2020) 20:417
https://doi.org/10.1186/s12879-020-05132-1

BMC Infectious Diseases

STUDY PROTOCOL Open Access

Short-course antibiotic regimen compared to conventional antibiotic treatment for gram-positive cocci infective endocarditis: randomized clinical trial (SATIE)

Carmen Olmos[1*], Isidre Vilacosta[1], Javier López[2], Carmen Sáez[3], Manuel Anguita[4], Pablo Elpidio García-Granja[2], Cristina Sarriá[3], Jacobo Silva[5], Belén Álvarez-Álvarez[6], María Amparo Martínez-Monzonís[6], Juan Carlos Castillo[4], José Seijas[6], Amanda López-Picado[7], Vicente Peral[8], Luis Maroto[1] and J. Alberto San Román[2]

Dizayn: Çok merkezli, randomize, prospektif, açık etiketli, kontrollü, faz 4

Amaç: 2 hafta vs. 4-6 hafta standard tedavi *(ESC)*

Hasta popülasyonu: Persistan infeksiyon ekarte edilenlerde 10 gün IV ve/veya post-op ≥7 gün IV (Streptokok, Enterokok, KNS ve *S. aureus*), 298 hasta dahil edilmesi planlanmış

Komplikasyonlar kritik fazda daha sık

Kritik faz sonrası hospitalizasyon = KOMPLİKASYON

Primer sonlanım: Tüm nedenlere bağlı mortalite + planlanmamış kardiyak cerrahi + semptomatik emboli + dahil edildikten sonra 6 ay içinde relaps

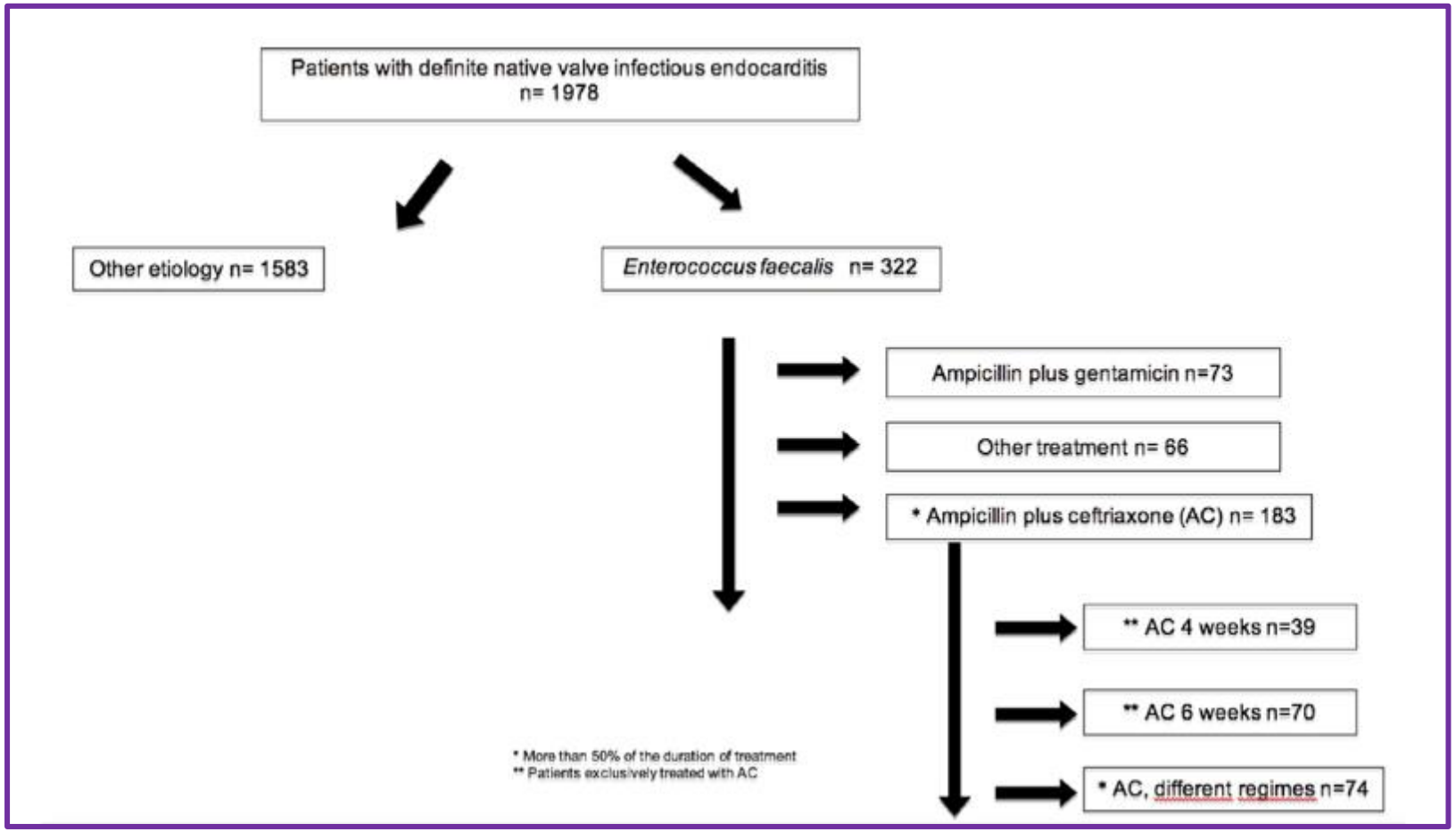
Durum: 2020 Mayıs→ Hasta dahil etme

PLoS One. 2020 Aug 3;15(8):e0237011. doi: 10.1371/journal.pone.0237011. eCollection 2020.

Four weeks versus six weeks of ampicillin plus ceftriaxone in Enterococcus faecalis native valve endocarditis: A prospective cohort study

Antonio Ramos-Martínez [1 2], Juan Manuel Pericàs [3], Ana Fernández-Cruz [1], Patricia Muñoz [4 5], Maricela Valerio [4], Martha Kestler [4], Miguel Montejo [6], M Carmen Fariñas [7], Dolores Sousa [8], Fernando Domínguez [9], Guillermo Ojeda-Burgos [10], Antonio Plata [11], Laura Vidal [12], José María Miró [13]; Grupo de Apoyo al Manejo de la Endocarditis Infecciosa en España (GAMES)

Dizayn: Çok merkezli, prospektif, kohort çalışması
Amaç: 4 hafta vs. 6 hafta AMPİSİLİN+SEFTRİAKSON tedavi kıyaslaması
Hasta popülasyonu: *E. faecalis* NVE
Primer sonlanım: Tüm nedenlere bağlı mortalite



Ramos-Martínez, A, Miró, J. M., & Grupo de Apoyo al Manejo de la Endocarditis Infecciosa en España (GAMES) (2020). PloS one,

to the duration of antibiotic treatment.

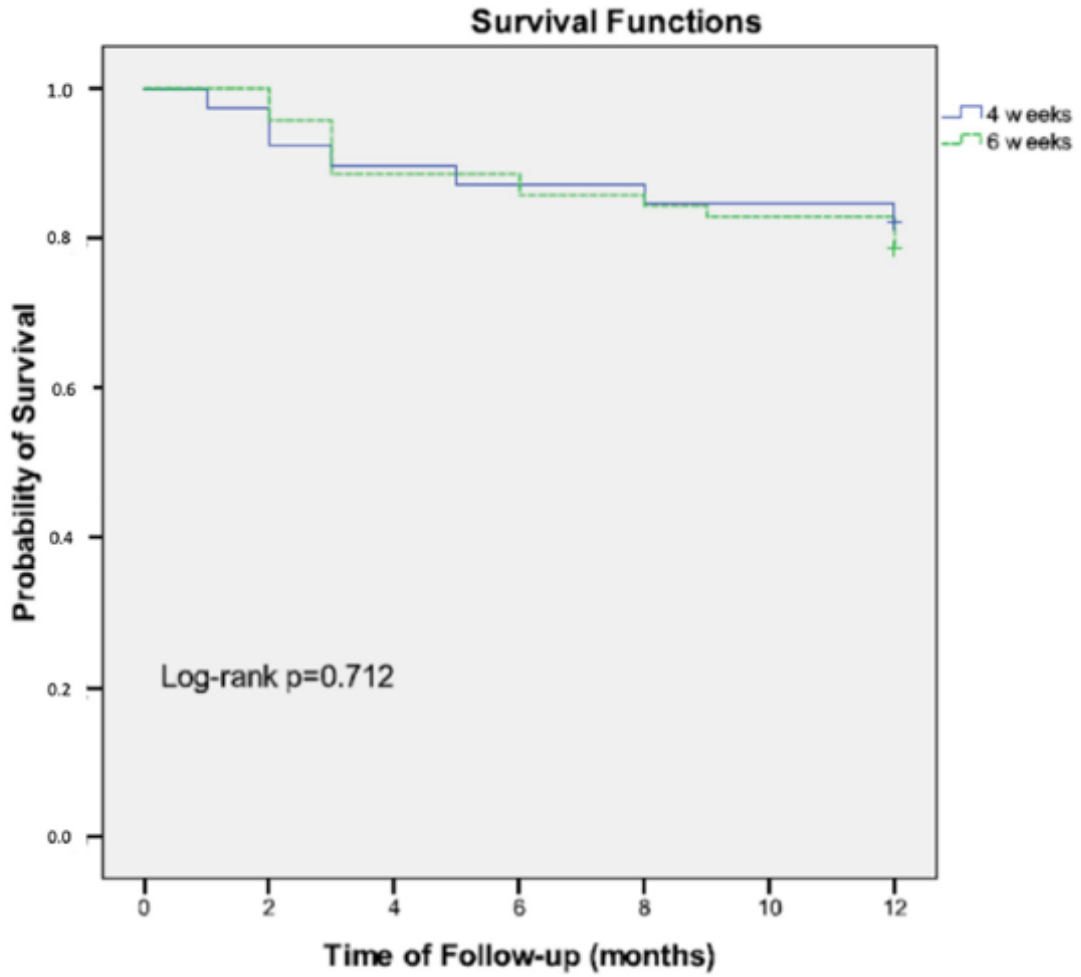
	4 weeks (n = 39)	6 weeks (N = 70)	P
Site of infection			
Mitral	22 (56.4)	48 (68.6)	0.204
Aortic	17 (43.6)	33 (47.1)	0.721
Tricuspid	1 (2.6)	5 (7.1)	0.417
Pulmonary	0	0	-
Duration of symptoms before diagnosis (days)	7 (1–22)	21 (7–60)	0.002
Septic shock	2 (5.1)	4 (5.7)	0.922
Persistent bacteremia	6 (15.4)	10 (14.7)	0.925
CNS vascular events	5 (12.8)	12 (17.1)	0.551
Embolism	8 (20.5)	16 (22.9)	0.717
Heart failure	18 (46.2)	34 (48.6)	0.809
New or worsening renal insufficiency	10 (25.6)	20 (28.6)	0.743
Echocardiographic findings			
Vegetation	34 (87.1)	62 (88.6)	0.925
Median size vegetation (IQR)	12 (8–18)	14 (7–20)	0.471
Perivalvular abscess	0	6 (8.6)	0.060
Valve perforation or rupture	4 (10.3)	17 (24.3)	0.060
Pseudoaneurysm	1 (2.6)	3 (4.3)	0.549
Intracardiac fistula	0	0	-
Surgical indication	17 (43.6)	45 (64.3)	0.085
Surgery performed	14 (35.9)	34 (48.6)	0.201
Duration of antibiotic treatment	32 (28–42)	42 (42–45)	<0.01
Treatment with ampicillin (days)	29 (28–32)	42 (41–45)	<0.01
Treatment with ceftriaxone (days)	29 (28–30)	43 (41–45)	<0.01
Hospital stay (days)	40 (27–54)	51 (44–66)	0.001
EFIE relapse[1]	2 (5.1)	3 (4.3)	0.833
In-hospital mortality	4 (10.3)	8 (11.4)	0.851
One-year mortality	7 (17.9)	15 (21.4)	0.682

CNS: central nervous system. Quantitative variables are reported with median and interquartile range.

[1]See text for relapses.

Ramos-Martínez, A, Miró, J. M., & Grupo de Apoyo al Manejo de la Endocarditis Infecciosa en España (GAMES) (2020). PloS one,

Tanı öncesi 3 Aydan uzun süredir semptomatik olanlar
Perivalvuler abse, kapak perforasyonu gibi komplikasyonu olan hastalar uzun süre tedavi koluna dahil edilmiş



Patients at Risk

4 weeks	39	37	35	34	33	33	32
6 weeks	70	67	62	60	59	58	55

Fig 2. One-year survival according to duration of the treatment in a series of EFIE.

Ramos-Martínez, A, Miró, J. M., & Grupo de Apoyo al Manejo de la Endocarditis Infecciosa en España (GAMES) (2020). PloS one,

PLoS One. 2018 Feb 20;13(2):e0192387. doi: 10.1371/journal.pone.0192387. eCollection 2018.

Outcome of Enterococcus faecalis infective endocarditis according to the length of antibiotic therapy: Preliminary data from a cohort of 78 patients

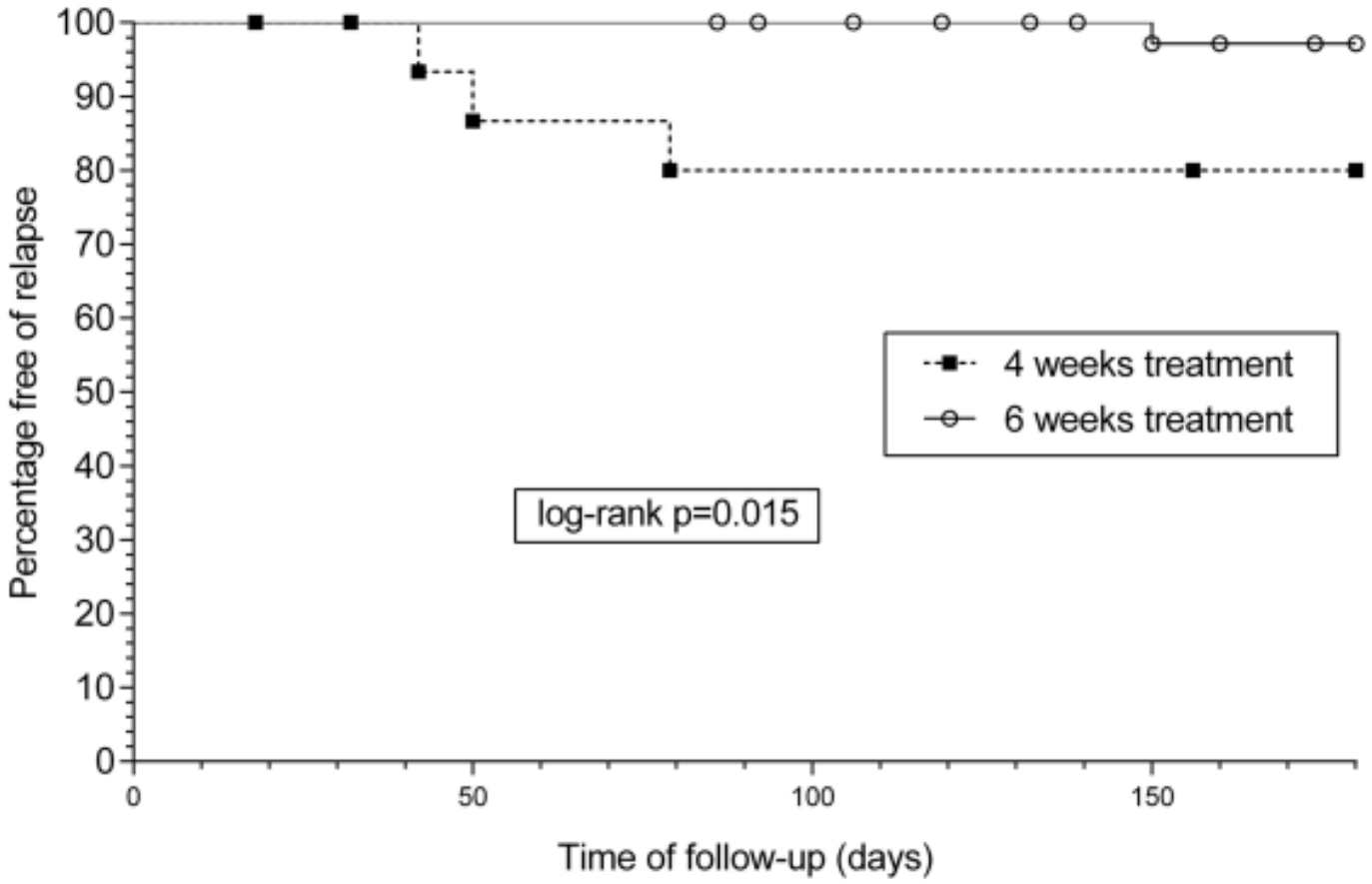
Juan M Pericàs [1], Carlos Cervera [2], Asunción Moreno [1], Cristina Garcia-de-la-Mària [1], Manel Almela [3], Carles Falces [4], Eduard Quintana [5], Bàrbara Vidal [4], Jaume Llopis [6], David Fuster [7], Carlos A Mestres [5 8], Francesc Marco [9], Jose M Miró [1]; Hospital Clinic Endocarditis Study Group

Dizayn: Retrospektif
Amaç: Amp-CRO 4w vs 6w ve Amp-Genta 4w vs 6w
Hasta popülasyonu: 78 EFİE hastası-doğal ya da yapay kapak
Primer sonlanım: Hastane içi mortalite, 1 yıllık mortalite ve relaps

Table 2. Clinical profile and outcome of 78 patients with EFIE.

	A+G (N = 32)		A+C (N = 46)		*P*
	4 wk (N = 9)	6 wk (N = 23)	4 wk (N = 14)	6 wk (N = 32)	
Type of endocarditis					0.001
Native valve	9 (100%)	14 (61%)	14 (100%)	14 (44%)	
Prosthetic valve	0	9 (39%)	0	18 (56%)	
Duration of symptoms in days, median (IQR)	2 (2-15)	30 (11-60)	7 (3-15)	10 (3-30)	0.055
Echocardiographic features					
Presence of vegetations	7 (78%)	9 (87%)	20 (64%)	22 (69%)	0.373
Size of vegetations in mm, median (IQR)	10 (4-13)	9 (5-14)	7.5 (4.5-13)	10.5 (6-16)	0.713
Periannular complications	0	6 (26%)	0	4 (13%)	0.065
Clinical complications					
Heart failure (Killip ≥3)	0	10 (44%)	1 (7%)	14 (44%)	0.008
Renal failure	5 (56%)	15 (65%)	5 (36%)	10 (31%)	0.067
Major emboli	0	7 (30%)	0	13 (41%)	0.007
Persistent bacteremia	1 (11%)	1 (4%)	3 (21%)	1 (3%)	0.143
Adverse effects related to antibiotic treatment					
Vestibular toxicity and ototoxicity	2 (22%)	1 (4%)	0	0	0.023
Myelotoxicity	0	0	1 (7%)	0	0.295
Skin rash	0	1 (4%)	1 (7%)	1 (3%)	1.000
C. difficile diarrhea	0	0	0	2 (6%)	0.499
Superinfection due to betalactam-resistant agents	0	0	0	2 (6%)	0.499
Discontinuation of antibiotic therapy	2 (22%)	9 (39%)	1 (7%)	1 (3%)	0.003
Surgical treatment	2 (22%)	14 (61%)	3 (21%)	14 (44%)	0.062
Mortality					
In-hospital mortality	3 (33%)	6 (26%)	2 (14%)	8 (25%)	0.759
One-year mortality	3 (33%)	7 (30%)	3 (21%)	8 (25%)	0.901
Relapses*	1/6 (17%)	1/17 (6%)	2/12 (17%)	0/24 (0%)	0.170

Pericas 2018



Patients at risk				
6 weeks treatment	42	42	41	35
4 weeks treatment	17	14	13	13

Sonuç olarak iyi seçilmiş, komplike olmayan İE'ler dahi olsa AMP-CRO 4 haftalık tedavi süresinin önerilmesi için daha çok veriye ihtiyaç olduğunu belirtmişler

Effectiveness of Cloxacillin with and without Gentamicin in Short-Term Therapy for Right-Sided *Staphylococcus aureus* Endocarditis

A Randomized, Controlled Trial

Esteban Ribera, MD; Jose Gómez-Jimenez, MD; Emilia Cortes, MD; Oscar del Valle, MD; Ana Planes, MD; M. Teresa Gonzalez-Alujas, MD; Benito Almirante, MD; Imma Ocaña, MD; and Albert Pahissa, MD

Background: It is often difficult to administer extended antibiotic therapy in the hospital for right-sided *Staphylococcus aureus* endocarditis. Although the effectiveness of single-drug therapy given for 4 to 6 weeks and that of two-drug therapy given for 2 weeks have been shown, no short-course therapy with penicillinase-resistant penicillin alone and therapy with combined regimens are warranted.

Ann Intern Med. 1996;125:969-974.

Dizayn: Randomize, kontrollü çalışma
Amaç: Kloksasilin (2 g IV q4hr, 14d) tek başına vs. kloksasilin (14d) +genta (7d)
Hasta popülasyonu: 90 IVDU RV İE, MSSA
Primer sonlanım: 2 hafta tedavi sonunda klinik ya da mikrobiyolojik persistan hastalık, relaps, mortalite

Table 2. Selected Baseline Characteristics of 74 Patients Evaluable for the Efficacy Analysis*

Characteristic	Cloxacillin-Only Group (n = 38)	Cloxacillin plus Gentamicin Group (n = 36)
Age, *y*	26.5 ± 4.0	27.1 ± 3.4
Men, *n (%)*	30 (79)	26 (72)
Positive for human immunodeficiency virus, *n (%)*	35 (92)	32 (89)
Duration of drug addiction, *y*	7.4 ± 3.7	7.8 ± 4.2
Duration of symptoms, *d*	7.1 ± 6.0	7.9 ± 4.8
Body temperature at hospital admission, °C	39.0 ± 0.9	38.7 ± 1.1
Dyspnea, *n (%)*	9 (24)	10 (28)
Systolic blood pressure, *mm Hg*	109 ± 15	110 ± 14
Hemoglobin level, *g/L*	122 ± 18	120 ± 18
Leukocyte count, $\times 10^9$/L	8.8 ± 4.1	10.1 ± 3.3
Neutrophil count, $\times 10^9$/L	6.9 ± 3.5	8.2 ± 3.0
CD4 count, $\times 10^6$/L†	318 ± 224	341 ± 420
Serum creatinine level, *μmol/L*	79 ± 25	106 ± 126
Serum albumin level, *g/L*	31 ± 6	30 ± 7
Chest radiographic findings, *n (%)*		
Normal	16 (42)	13 (36)
≥2 pulmonary emboli‡	8 (21)	10 (28)
Pleural effusion	6 (16)	7 (19)
Diagnostic criteria, *n (%)*		
Definite endocarditis	19 (50)	20 (56)
Probable endocarditis	13 (34)	12 (33)
Possible endocarditis	6 (16)	4 (11)
Size of vegetation ≥10 mm, *n/n (%)*§	9/19 (47)	11/20 (55)

* Unless otherwise noted, values are the mean ± SD.
† Values are only from patients with human immunodeficiency virus infection.
‡ Two or more pulmonary infiltrates or nodules, with or without cavitation.
§ Values are number of patients with vegetation greater than or equal to 10 mm/number of patients in whom the size of vegetation could be determined.

Table 3. Outcome of All Randomly Assigned Patients According to Treatment Regimen (Intention-to-Treat Analysis)

Outcome	Cloxacillin-Only Group (n = 45)	Cloxacillin plus Gentamicin Group (n = 45)
Successful therapy, *n (%)**	34 (76)	31 (69)
Failed therapy, *n (%)*	11 (24)	14 (31)
Reasons for modification of therapy (failure), *n*		
Left-sided or pulmonic valve endocarditis	3	4
Streptococcus viridans endocarditis	1	2
Osteomyelitis	1	0
Allergy to penicillin or infection with methicillin-resistant *Staphylococcus aureus*	1	2
Patient left hospital against medical advice	1	1
Death during treatment	1	2
Active infection at 14 days	3	2
Relapse	0	1

* $P > 0.2$ for comparison between groups.

Ribera, E (1996). ***Annals of internal medicine***

Table 4. Outcome of 74 Patients Evaluable for the Efficacy Analysis

Outcome	Cloxacillin-Only Group (*n* = 38)	Cloxacillin plus Gentamicin Group (*n* = 36)
Successful therapy, *n* (%)	34 (89)	31 (86)
Failed therapy		
Death during treatment, *n* (%)	1 (2.5)	2 (5.5)
Active infection at 14 days, *n* (%)	3 (8)	2 (5.5)
Positive blood cultures 2 days after the end of treatment, *n*	0	0
Relapse, *n* (%)	0	1 (3)
Outcome during treatment		

Table 5. Recurrences of *Staphylococcus aureus* Bacteremia after the End of Treatment in All Study Patients

Patient	Treatment Regimen	Days after Therapy	Intravenous Drug Use	Original Phage Group	Phage Group at Recurrence	Diagnosis
1	Cloxacillin	102	Yes	III	II	Reinfection
2	Cloxacillin plus gentamicin	54	Yes	III	95	Reinfection
3	Cloxacillin	19	Yes	II	I	Reinfection
4	Cloxacillin plus gentamicin	5	No	V	V	Relapse
5	Cloxacillin plus gentamicin	39	Yes	Reverse phage-typing:3A± *	III	Reinfection
6	Cloxacillin plus gentamicin	173	Yes	II	V	Reinfection

* Nontypable strain by routine test dilution, 100 × routine test dilution, and heat.

İn vitro ve hayvan çalışmalarında penisilinaz dirençli penisilinlerin AG ile kombinasyonunun 2 haftalık tedavisinin RVE S. aureus İE'lerinde etkinliği zaten gösterilmiş

Bu çalışmada da monoterapi ile 2 hafta tedavinin yeterliği olduğu gösterilmiş

Başka çalışmalarla kısa süreli monoterapi etkinliği değerlendirilmeli...

Ribera, E (1996). ***Annals of internal medicine***

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 31, 2019 VOL. 380 NO. 5

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. Schønheyder, 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.

Dizayn: Çok merkezli, non-inferiority randomize çalışma

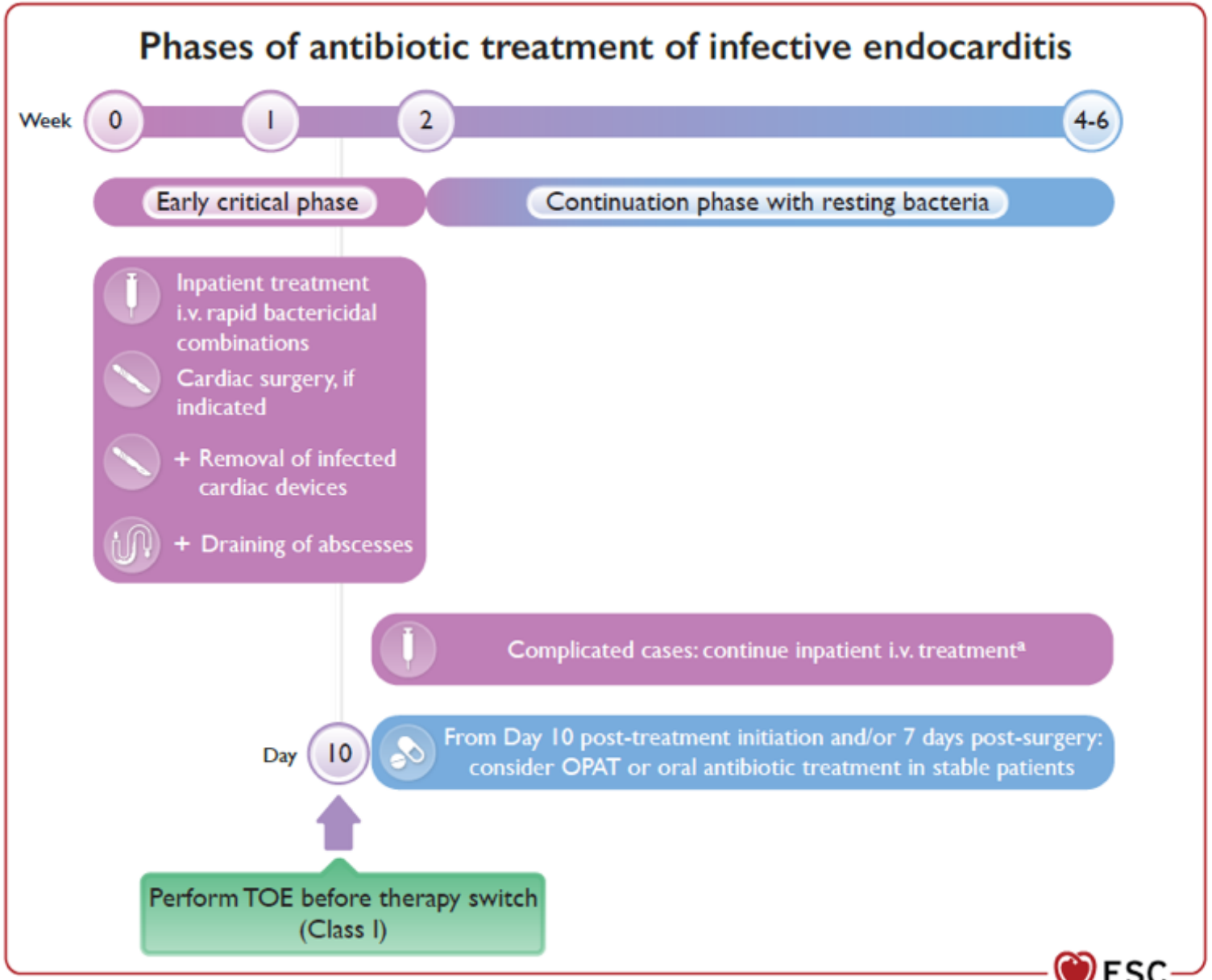
Amaç: IV antibiyotik vs. IV sonrası oral tedavi, randomize 1:1

Hasta popülasyonu: 400 hasta Sol kalp İE, NVE + PVE

(*Streptococcus* spp*, Staphylococcus aureus,* or *Enterococcus faecalis,* KNS)

Primer sonlanım: Randomizasyondan sonraki 6 ayda tüm nedenlere bağlı ölüm+plansız kardiyak cerrahi+ relaps+ embolizasyon

N: 199:201 (IV vs. oral)

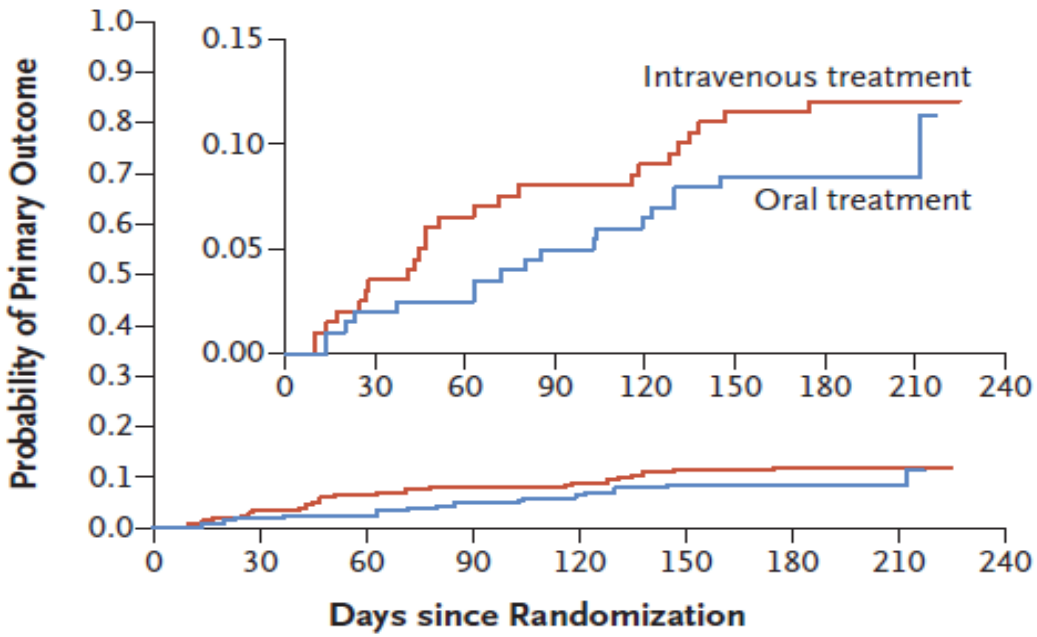

Phases of antibiotic treatment of infective endocarditis
Week
0
1
2
4-6
Early critical phase
Continuation phase with resting bacteria
Inpatient treatment i.v. rapid bactericidal combinations
Cardiac surgery, if indicated
+ Removal of infected cardiac devices
+ Draining of abscesses
Complicated cases: continue inpatient i.v. treatment[a]
Day
10
From Day 10 post-treatment initiation and/or 7 days post-surgery: consider OPAT or oral antibiotic treatment in stable patients
Perform TOE before therapy switch (Class I)
ESC

POET: ORAL TEDAVİ REJİMLERİ

PEN H+Metisilin H *S.aureus*/KNS	**MSSA/MSKNS**	**MRKNS**	***E.faecalis***	**Streptokok pen MİK<1 mg/L**	**Streptokok pen MİK≥1 mg/L**
AMOX 1g x 4 + fusidic acid 0.75g x 2	Dicloxacillin 1 g x 4 and fusidic acid 0.75 g x 2	LZD 0.6 g x 2 and fusidic acid 0.75 g x 2	AMOX 1 g x 4 and RİF 0.6 g x 2	AMOX 1 g x 4 and RİF 0.6 g x 2	LZD 0,6 g x2 and RİF 0.6 g x 2
AMOX 1 g x 4 and rifampicin 0.6 g x 2	Dicloxacillin 1 g x 4 and rifampicin 0.6 g x 2	LZD 0.6 g x 2 and rifampicin 0.6 g x 2	AMOX 1 g x 4 and MOXİ 0.4 g x 1	LZD 0.6 g x 2 and RİF 0.6 g x 2	MOXİ 0.4 g x 1 and RİF 0.6 g x 2
LZD 0.6 g x 2 and fusidic acid 0.75 g x 2	LZD 0.6 g x 2 and fusidic acid 0.75 g x 2		LZD 0.6 g x 2 and rifampicin 0.6 g x 2	LZD 0.6 g x 2 and MOXI 0.4 g x 1	MOXİ 0.4 g x 1 and KLİN 0.6 g x3
LZD 0.6 g x 2 and rifampicin 0.6 g x 2	LZD 0.6 g x 2 and rifampicin 0.6 g x 2		LZD 0.6 g x 2 and MOXI 0.4 g x 1		

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)
COPD	17 (8.5)	9 (4.5)
Liver disease	7 (3.5)	6 (3.0)
Cancer	14 (7.0)	18 (9.0)
Intravenous drug use	3 (1.5)	2 (1.0)
Pathogen — no. (%)†		
Streptococcus	104 (52.3)	92 (45.8)
Enterococcus faecalis	46 (23.1)	51 (25.4)
Staphylococcus aureus‡	40 (20.1)	47 (23.4)
Coagulase-negative staphylococci	10 (5.0)	13 (6.5)
Laboratory results at randomization		
Hemoglobin — mmol/liter	6.3±1.1	6.5±1.0
Leukocytes — $\times 10^{-9}$/liter	7.6±3.6	7.2±2.6
C-reactive protein — mg/liter	24.3±18.4	19.9±16.7
Creatinine — μmol/liter	124±112	141±164
Preexisting prosthesis, implant, or cardiac disease — no. (%)		
Prosthetic heart valve	53 (26.6)	54 (26.9)
Pacemaker	15 (7.5)	20 (10.0)
Other known valve disease	82 (41.2)	90 (44.8)
Cardiac involvement at randomization — no. (%)§		
Mitral-valve endocarditis	65 (32.7)	72 (35.8)
Aortic-valve endocarditis	109 (54.8)	109 (54.2)
Mitral-valve and aortic-valve endocarditis	23 (11.6)	20 (10.0)
Endocarditis in other locations§	2 (1.0)	0
Pacemaker endocarditis	6 (3.0)	8 (4.0)
Vegetation size >9 mm	7 (3.5)	11 (5.5)
Moderate or severe valve regurgitation	19 (9.5)	23 (11.4)
Valve surgery during current disease course	75 (37.7)	77 (38.3)



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

Figure 2. Kaplan–Meier Plot of the Probability of the Primary Composite Outcome.

The primary composite outcome was all-cause mortality, unplanned cardiac surgery, embolic events, or relapse of bacteremia with the primary pathogen, from randomization until 6 months after antibiotic treatment was completed. The oral treatment group shifted from intravenously administered antibiotics to orally administered antibiotics at a median of 17 days after the start of treatment. The inset shows the same data on an enlarged y axis.

POET-1:

- Oral koldaki hastalar, IV tedavinin 17.gününde geçiş yapmış
- Alt grup analizlerinde sonuçlar benzer (kalp kapağı, etken, cerrahi-cerrahisiz)
- Çalışma dizaynında asıl endişe gastrointestinal biyoyararlanımla ilgili
- İki ayrı mekanizmayla etki eden, farklı gruplardan iki ayrı antibiyotik kombinasyonu
- Tedavi seçildikten sonra farmakokinetik sonuçlara göre değişiklik yapılmamış

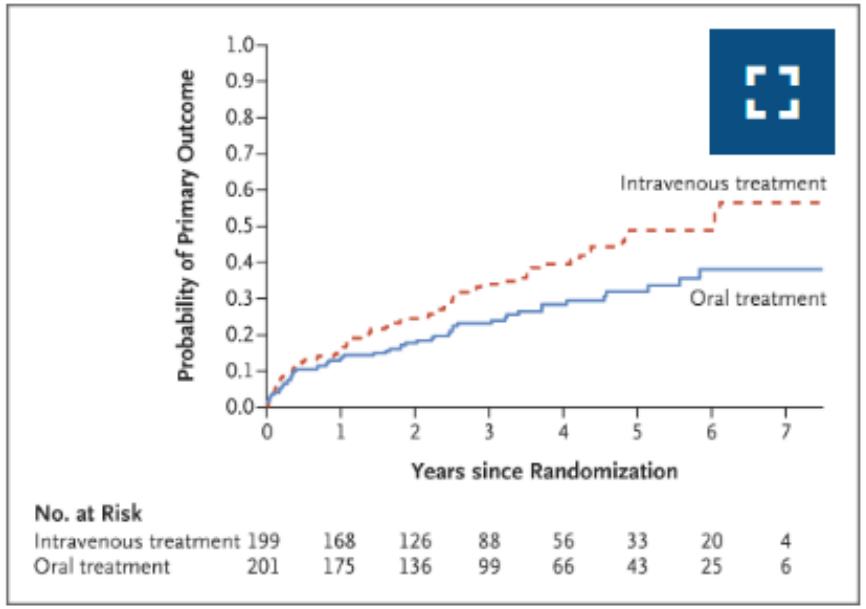
- **SONUÇ OLARAK; SOL KAPAK İE'LERİNDE SEÇİLMİŞ HASTALARDA ORAL TEDAVİYE GEÇİŞ ETKİN VE GÜVENLİ**

N Engl J Med. 2019 Apr 4;380(14):1373-1374. doi: 10.1056/NEJMc1902096. Epub 2019 Mar 17.

Long-Term Outcomes of Partial Oral Treatment of Endocarditis

Henning Bundgaard [1], Nikolaj Ihlemann [1], Sabine U Gill [2], Niels E Bruun [3], Hanne Elming [4], Trine Madsen [5], Kaare T Jensen [6], Kurt Fursted [7], Jens J Christensen [8], Martin Schultz [3], Lauge Østergaard [3], Flemming Rosenvinge [2], Henrik C Schønheyder [5], Jannik Helweg-Larsen [9], Emil L Fosbøll [9], Lars Køber [9], Christian Torp-Pedersen [5], Niels Tønder [10], Claus Moser [9],

FIGURE 1



Cumulative Incidence Plot of the Primary Composite Outcome.

Mortalite IV kolda n:54 (%27) vs. Oral kol n:33 (%16)
HR 0.57, 95% CI, 0.37 to 0.87)

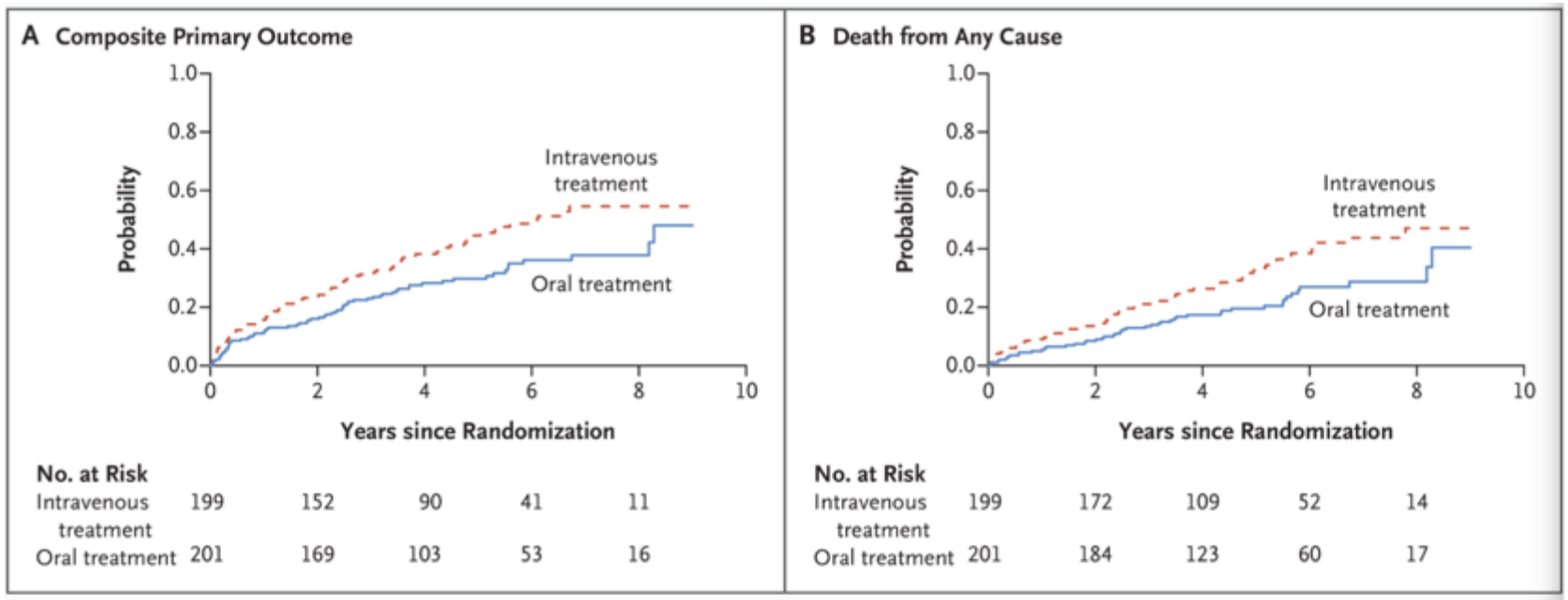
Klinik olarak stabil, sol kalp İE'sinde erken oral tedaviye geçiş gecikmiş tedavi başarısızlığı ile ilişkili DEĞİL

Randomized Controlled Trial > N Engl J Med. 2022 Feb 10;386(6):601-602.
doi: 10.1056/NEJMc2114046.

Five-Year Outcomes of the Partial Oral Treatment of Endocarditis (POET) Trial

Mia M Pries-Heje [1], Christoffer Wiingaard [1], Nikolaj Ihlemann [1], Sabine U Gill [2], Niels E Bruun [3], Hanne Elming [3], Jonas A Povlsen [4], Trine Madsen [5], Kaare T Jensen [4], Kurt Fursted [6], Martin Schultz [7], Lauge Østergaard [1], Jens J Christensen [8], Ulrik Christiansen [5], Flemming Rosenvinge [2], Jannik Helweg-Larsen [1], Emil L Fosbøl [1], Lars Køber [1], Christian Torp-Pedersen [9], Niels Tønder [9], Claus Moser [1], Kasper Iversen [7], Henning Bundgaard [10]

POET çalışmasının 5. yıl analizleri



Primer sonlanım;

Oral kol %33 vs IV kol %45 patients HR 0.65; 95% [CI], 0.47 to 0.90)

Fark özellikle herhangi bir nedene bağlı mortaliteden kaynaklanıyor (oral kolda 47 hasta %23; IV kol 70 hasta %35)

Accelerated treatment of endocarditis—The POET II trial: Rationale and design of a randomized controlled trial

Lauge Østergaard, MD,[a,1] Mia Marie Pries-Heje, MD,[a,1] Rasmus Bo Hasselbalch, MD,[b] Magnus Rasmussen, MD, PhD,[c] Per Åkesson, MD,[c] Robert Horvath, MD,[d] Jonas Povlsen, MD, PhD,[e] Sabine Gill, MD, PhD,[f] Niels Eske Bruun, MD, DMSc,[g] Katrine Müllertz, MD, PhD,[h] Christian Ditlev Tuxen, MD, PhD,[i] Nikolaj Ihlemann, MD, PhD,[a] Jannik Helweg-Larsen, MD, DMSc,[j] Claus Moser, MD, PhD,[k] Emil Loldrup Fosbøl, MD, PhD,[a] Henning Bundgaard, MD, DMSc,[a,2] and Kasper Iversen, MD, DMSc[b,2] *Copenhagen, Aarhus, Odense, Roskilde, Hillerød, Denmark; Lund, Sweden; and Brisbane, Australia*

Dizayn: Çok merkezli, multinasyonel, non-inferiority RKÇ

Amaç: Hızlandırılmış tedavi (2-4w) vs. standard tedavi süresi (4-6w), randomize 1:1

Hasta popülasyonu: Kesin sol kalp İE (*Streptococcus* spp*, Staphylococcus aureus,* or *Enterococcus faecalis*)

Primer sonlanım: Randomizasyondan sonraki 6 ayda tüm nedenlere bağlı ölüm+plansız kardiyak cerrahi+ relaps+ embolizasyon

Table I. Criteria for randomization

1. No further cardiac surgery planned during IE admission
2. Neutrophil leucocytes <10 * 10^9/L and less than 15% increment in 3 consecutive blood samples or neutrophil leucocytes <50% of the highest measured value; however, <13*10^9/L and less than 15% increment in 3 consecutive blood samples
3. CRP <40 mg/L and less than 15% increment in 3 consecutive blood samples or CRP <50% of the highest measured value; however, <40 mg/L
4. Procalcitonin <0.5 µg/L
5. Body temperature (morning) <38.0°C for 2 consecutive days
6. Transesophageal echocardiography within 96 h without signs of disease progression

Disease progression on TEE may include increased vegetation size, increased valve regurgitation, or formation of abscess.
CRP, C-reactive protein.

Accelerated treatment of endocarditis—The POET II trial: Rationale and design of a randomized controlled trial

Lauge Østergaard, MD,[a,1] Mia Marie Pries-Heje, MD,[a,1] Rasmus Bo Hasselbalch, MD,[b] Magnus Rasmussen, MD, PhD,[c] Per Åkesson, MD,[c] Robert Horvath, MD,[d] Jonas Povlsen, MD, PhD,[e] Sabine Gill, MD, PhD,[f] Niels Eske Bruun, MD, DMSc,[g] Katrine Müllertz, MD, PhD,[h] Christian Ditlev Tuxen, MD, PhD,[i] Nikolaj Ihlemann, MD, PhD,[a] Jannik Helweg-Larsen, MD, DMSc,[j] Claus Moser, MD, PhD,[k] Emil Loldrup Fosbøl, MD, PhD,[a] Henning Bundgaard, MD, DMSc,[a,2] and Kasper Iversen, MD, DMSc[b,2] *Copenhagen, Aarhus, Odense, Roskilde, Hillerød, Denmark; Lund, Sweden; and Brisbane, Australia*

- Çalışma hala devam ediyor olarak görünüyor
- Sonuçları henüz yayımlanmadı

Open access Protocol

BMJ Open

Oral switch versus standard intravenous antibiotic therapy in left-sided endocarditis due to susceptible staphylococci, streptococci or enterococci (RODEO): a protocol for two open-label randomised controlled trials

Adrien Lemaignen ,[1,2] Louis Bernard ,[1] Pierre Tattevin,[3] Jean-Pierre Bru,[4] Xavier Duval,[5,6] Bruno Hoen,[7] Solène Brunet-Houdard,[8] Jean-Luc Mainardi,[9] Agnes Caille,[8,10] On behalf of the RODEO (Relais Oral Dans le traitement des Endocardites à staphylocoques ou streptOcoques) and AEPEI (Association pour l'Etude et la Prévention de l'Endocardite Infectieuse) study groups

RODEO-1 ve RODEO-2

RODEO-1 ve RODEO-2

- **Dizayn:** non-inferiority prospektif randomize paralel çalışmalar
- **Amaç:** Sol kalp İE'de erken oral tedaviye geçişin sonuçlarını değerlendirmek
- **Hasta popülasyonu: 10 gün IV tedavi sonrasında iki çalışmada da 324 hasta randomize edilecek**
  - **RODEO-1:** Sol kalp İE (*Staphylococcus aureus*)
  - **RODEO-2 :***Streptococcus* spp, *Enterococcus* spp
- **Primer sonlanım:** Tedavi bittikten sonraki 3 ay içinde tedavi başarısızlığı (mortalite+ plansız kardiyak cerrahi + relaps)

RODEO-1 ve RODEO-2

- **Müdahale:**
  - **RODEO-1; MSSA,**
    - ≤70 kg LEVO 500 mg/d + RİF 600 mg/d
    - >70 kg LEVO 750 mg/d + RİF 900 mg/d
  - **RODEO-2; *Streptococcus* spp or *Enterococcus* spp (AMOX MIC ≤0.5 mg/L)**
    - ≤70 kg Amoksisilin 3x1500 mg
    - >70 kg Amoksisilin 3x 2000 mg

- **Çalışma statüsü:** Haziran 2023'te tamamlanmış, **sonuçlar hala yayımlanmadı**

Clinical Trial > Rev Infect Dis. 1991 Jan-Feb:13 Suppl 2:S160-3.
doi: 10.1093/clinids/13.supplement_2.s160.

Antibiotic management of outpatients with endocarditis due to penicillin-susceptible streptococci

D Stamboulian [1], P Bonvehi, C Arevalo, R Bologna, I Cassetti, V Scilingo, E Efron

Dizayn: Prospektif, randomize

Hasta popülasyonu: Sol kalp İE Streptokok Penisilin MIC <*0.2* µg/ml

Amaç: Tek doz CRO 4 hafta (n:15) vs. CRO 2hafta+ Amoksisilin oral 2 hafta (n:15)

Sonuçlar: Klinik kür iki kolda da benzer (%100)

Tek IV kolda 1 relaps

Clinical Trial > Am J Med. 1996 Jul;101(1):68-76. doi: 10.1016/s0002-9343(96)00070-8.

Oral antibiotic treatment of right-sided staphylococcal endocarditis in injection drug users: prospective randomized comparison with parenteral therapy

A W Heldman [1], T V Hartert, S C Ray, E G Daoud, T E Kowalski, V J Pompili, S D Sisson, W C Tidmore, K A vom Eigen, S N Goodman, P S Lietman, B G Petty, C Flexner

Dizayn: Prospektif, randomize

Hasta popülasyonu: Olası RVE+IVDU; n: 44

Amaç: Oral (Cipro+RİF) vs. IV (oksasilin ya da vankomisin)

Primer sonlanım: Test of cure blood culture (antibiyotik kesildikten sonra 6. ve 7. ve 35. gün steril kan kültürü)

Tedavi başarısızlığı: AB'ye rağmen LVİE, kalp yetmezliği, hemodinamik bozulma, MV gerektiren solunum sıkıntısı, 10 gün tedavi sonrasında bakteriyemi nüksü, metastatik infeksiyon

TABLE III

Efficacy of Oral Versus Parenteral Antibiotics

	Oral	Intravenous
a. Bacteriologic evaluation of outcome		
Cured	18	22
Failed	1	3($P = 0.6$)
b. Combined bacteriologic and projected clinical evaluations of outcome		
Cured	26	30
Failed	3	3($P = 0.9$)

Heldman, 1996

CMI COMMUNICATIONS 2 (2025) 105063

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journal homepage: www.elsevier.com/locate/cmicom

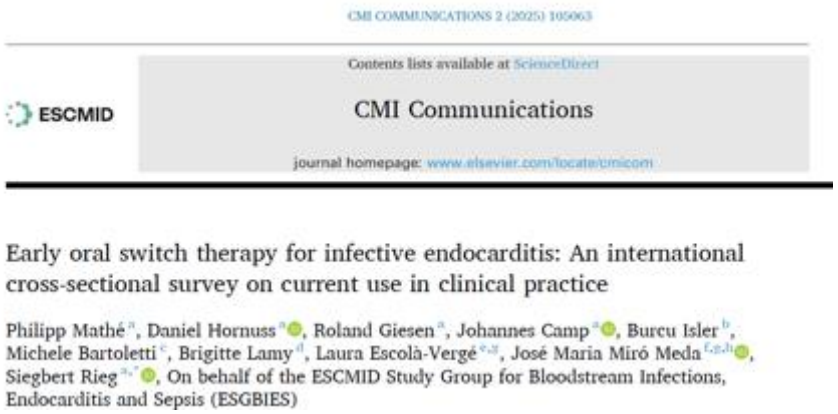
Early oral switch therapy for infective endocarditis: An international cross-sectional survey on current use in clinical practice

Philipp Mathé [a], Daniel Hornuss [a], Roland Giesen [a], Johannes Camp [a], Burcu Isler [b], Michele Bartoletti [c], Brigitte Lamy [d], Laura Escolà-Vergé [e,g], José Maria Miró Meda [f,g,h], Siegbert Rieg [a,*], On behalf of the ESCMID Study Group for Bloodstream Infections, Endocarditis and Sepsis (ESGBIES)

74 EHU

%80'i 2.-3. seviye merkez

Katılım yeri: Avrupa n:54, Asya n: 10



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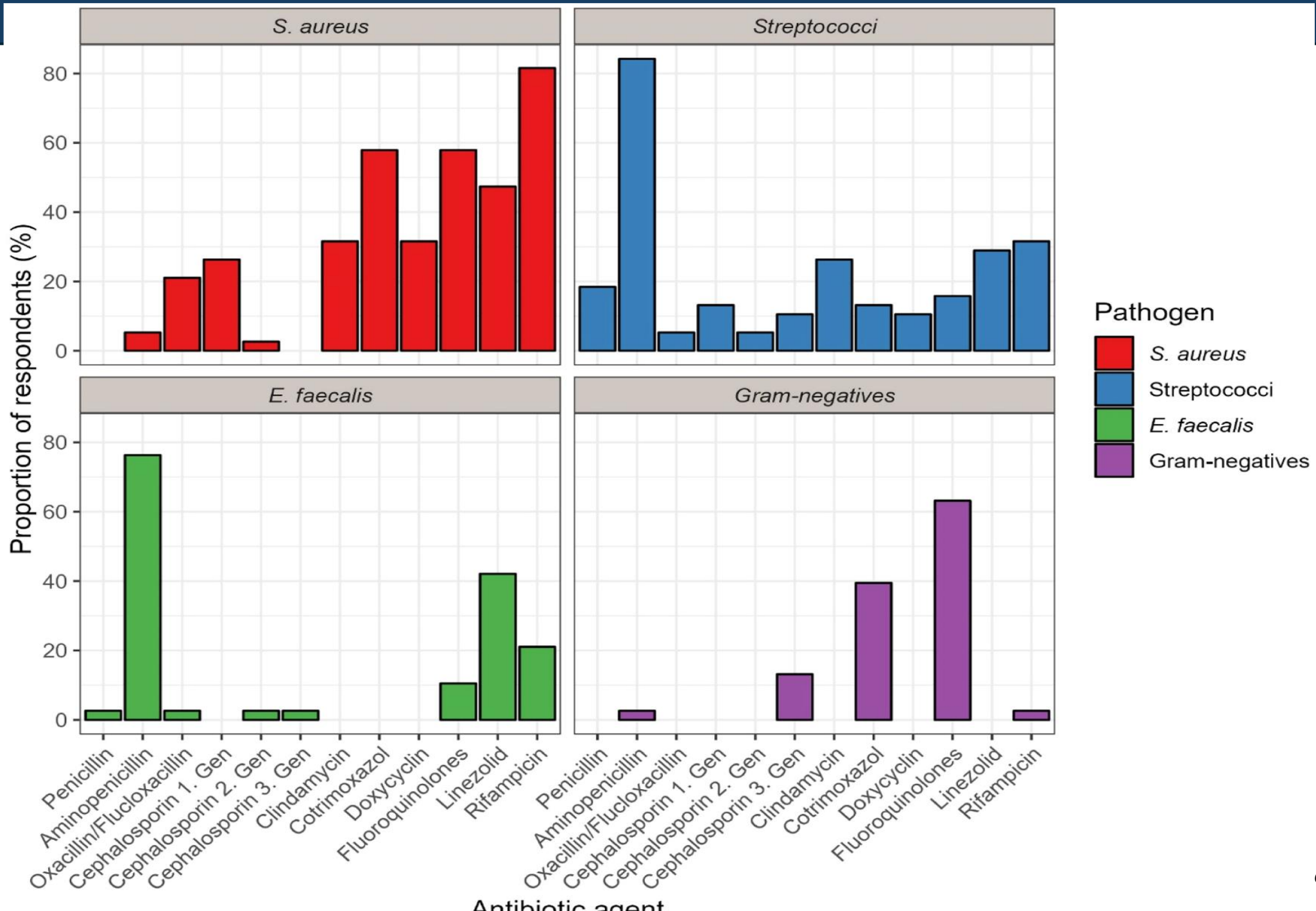
- 74 katılımcının %50'si , sol IE'de EOS'u **hiç kullanmadıklarını** belirtti (36/74, %49)

- EOS kullanan katılımcılardan (n = 38) sadece 5'i olguların >%30'unda

- NV-IE'ye kıyasla PV-IE'li hastalarda daha az sıklıkla kullanılmakta
- EOS en sık streptokokal NVE'de ve en az *S. aureus* PV-IE'li hastalarda
- ***Endocarditis Team varlığında*** EOS kullanımında anlamlı bir fark YOK


S. aureus
Streptococci
E. faecalis
Gram-negatives
Proportion of respondents (%)
0
20
40
60
80
Penicillin
Aminopenicillin
Oxacillin/Flucloxacillin
Cephalosporin 1. Gen
Cephalosporin 2. Gen
Cephalosporin 3. Gen
Clindamycin
Cotrimoxazol
Doxycyclin
Fluoroquinolones
Linezolid
Rifampicin
Antibiotic agent
Pathogen
S. aureus
Streptococci
E. faecalis
Gram-negatives

ey. 2025

Clinical Infectious Diseases

MAJOR ARTICLE

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 Spellberg[1]

[1]Department of Medicine and Infectious Diseases, Los Angeles County + University of Southern California Medical Center, Los Angeles, California, USA; [2]Department of Medicine, Keck School of Medicine–University of Southern California, Los Angeles, California, USA; [3]Department of Integrative Anatomical Sciences, Keck School of Medicine–University of Southern California, Los Angeles, California, USA; and [4]Department of Pharmacy, University of Southern California Mann School of Pharmacy and Pharmaceutical Sciences, Los Angeles, California, USA

Background. We sought to compare the outcomes of patients treated with intravenous (IV)-only vs oral transitional antimicrobial therapy for infective endocarditis (IE) after implementing a new expected practice within the Los Angeles County Department of Health Services (LAC DHS).

Dizayn: Çok merkezli, retrospektif, 2023

Amaç: IV tek başına vs. IV→Oral

Primer sonlanım: 90. günde klinik başarı (mortalite olmaması ve bakteriyemi nüksü ya da tedaviye sekonder komplikasyon olmaması)

Table 1. Demographics by Treatment Arm

Demographic	Intravenous Therapy (n = 211)	Oral Therapy (n = 46)	*P* Value
Race			.18
Asian	13 (6.2)	2 (4.3)	
Black	16 (7.6)	7 (15.2)	
White	31 (14.7)	5 (10.9)	
Hispanic	129 (61.1)	29 (63.0)	
Other[a]	22 (10.4)	3 (6.5)	
Gender			
Female	59 (28.0)	14 (30.4)	.22
Male	152 (72.0)	32 (69.6)	
Median age (IQR), y	55 (42–65)	39 (30.5–61.8)	.01
Key features			
Endocarditis definite	128 (60.7)	28 (60.9)	.98
Endocarditis possible, total	83 (39.3)	18 (39.1)	.98
Clinical	44 (20.9)	12 (26.1)	.29
Duke's criteria	39 (18.5)	6 (13.0)	.29
Prosthetic valve[b]	31 (14.7)	4 (8.7)	.28
PPM or ICD[b]	20 (9.5)	1 (2.2)	.08
CVC[b]	26 (12.3)	1 (2.2)	.03
PPM and CVC	1 (0.5)	0 (0.0)	>.99

Freling. CID, 2023.

Table 1. Demographics by Treatment Arm

Demographic	Intravenous Therapy (n = 211)	Oral Therapy (n = 46)	*P* Value
Valves involved			
AV	47 (22.3)	3 (6.5)	.01
MV	46 (21.8)	9 (19.6)	.74
PV	4 (1.9)	0 (0.0)	.85
TV	13 (6.2)	16 (34.8)	<.0001
AV + MV	17 (8.1)	2 (4.3)	.31
AV + TV	1 (0.5)	1 (2.2)	>.99
MV + TV	4 (1.9)	0 (0.0)	.85
AV + MV + TV	2 (0.9)	0 (0.0)	>.99
Unknown/presumed	57 (26.9)	15 (32.6)	.44
ICD	12 (5.7)	0 (0.0)	.12
Other[c]	8 (3.8)	0 (0.0)	.30
Any left-sided involvement	117 (55.5)	15 (32.6)	.004
Surgical management, total	51 (24.2)	14 (30.4)	.73
Early valve replacement or ICD removal[d]	39 (18.4)	13 (28.3)	
Post-Tx valve replacement or ICD removal	8 (3.8)	1 (2.2)	
Early valve repair	3 (1.4)	0 (0.0)	
Post-Tx valve repair	1 (0.5)	0 (0.0)	
Stable housing during treatment	191 (90.5)	40 (87.0)	.47
Comorbidity			
Diabetes mellitus	75 (35.5)	9 (19.6)	.04
Chronic kidney disease [e]	41 (19.4)	9 (19.6)	.98
End-stage renal disease dialysis-dependent[b]	42 (19.9)	1 (2.2)	.001
Chronic obstructive pulmonary disease	10 (4.7)	1 (2.2)	.42
Liver disease	39 (18.5)	14 (30.4)	.07
Cancer	18 (8.5)	5 (10.9)	.80
Injection drug use	38 (18.0)	17 (37.0)	.01
Median time to last follow-up (IQR), d	204 (51–495)	93.5 (26–279)	.02

Data are presented as number (%) unless otherwise indicated.

Abbreviations: AV, aortic valve; CVC, central venous catheter; ICD, implantable cardiac defibrillator or pacemaker; IQR, interquartile range; MV, mitral valve; PPM, permanent pacemaker; PV, pulmonary valve; TV, tricuspid valve; Tx, treatment.

[a]Specifics not reported, not Hispanic/Latino, Middle Eastern, Armenian, Native American.

[b]Present on admission.

[c]Right atrial vegetation/suspected infected thrombi (4), left ventricular outflow tract vegetation (1), superior vena cava echo density (2), right ventricle mid-septum vegetation (1).

Freling. CID, 2023.

	IV GRUP n:211	ORAL GRUP n:46	*p*
S. aureus	%52.1	%63	.18
MRSA	%20.4	%38.1	.04
Streptococcus spp.	%28.4	%21.7	
Klinik başarı 90.gün	%84.4	%87	.66
Klinik başarı son vizitte	%82.0	%76	.36
Readmissions within 90 days	%34	%26	.29
KC hastalığı olanlarda son vizitte klinik başarı	%87	%57	.02
Tedaviyi tamamlayamama	%7	%6.5	
İstenmeyen etki	%27	%9	.004

Freling. CID, 2023.

KESİN İE TANISI ALANLARDA PRİMER SONLANIM VERİSİ

	IV GRUP n:128	ORAL GRUP n:28	*p*
90.Gün klinik başarı	%82	%89	.27
Alive	%91.5	%96.4	.56
Nüks bakteriyemi	%96	%96	>.99
Tedaviye sekonder komplikasyon olmaması	%88	%96	.13

Sonuç: İyi seçilmiş hasta grubunda MRSA İE'si dahil oral tedavi ile klinik başarı sağlanabilir

LZD en çok kullanılan oral tedavi; STATİK vs. SİDAL konusu.... ???
Oral ardışık tedavi kolunda daha uzun Süre IV lead-in periyotu klinik sonlanıma olumlu katkı sağlamamış- yani oral tedaviye geçmeden önce IV tedavinin gereksiz uzatılmamalı; tecrübeyle IV LEAD-in süresi ters orantılı

Freling. CID, 2023.

> Int J Antimicrob Agents. 2019 Aug;54(2):143-148. doi: 10.1016/j.ijantimicag.2019.06.006. Epub 2019 Jun 8.

High-dose trimethoprim-sulfamethoxazole and clindamycin for Staphylococcus aureus endocarditis

Hervé Tissot-Dupont [1], Frédérique Gouriet [1], Leopold Oliver [2], Matthieu Jamme [3], Jean-Paul Casalta [1], Marie-Thérèse Jimeno [4], Florent Arregle [5], Cécile Lavoute [5], Sandrine Hubert [5], Mary Philip [5], Hélène Martel [5], Alberto Riberi [6], Gilbert Habib [5], Didier Raoult [7]

İE TANISI

TMP-SMZ 960/4800 mg IV

+

Klindamisin 1800mg IV

7 gün

TMP-SMZ 160/800 mg PO

günde 6 tablet

5 hafta

I. Klinik olarak Stabil ve acil kardiyak cerrahi planlanmıyor
II. IV tedaviyle bakteriyemi control altında
III. GİS emilimi problemi yok
IV. IV tedavinin daha iyi olabileceğini düşündüren pSikoSoSyal faktörler yok
V. In vitro duyarlı oral Seçenek mevcut

T&C vs. Standard tedavi (oksasilin+genta ya da vanko+genta)

	T&C n:171	STANDARD n:170	ITT analizi *p*
Vejetasyon +	%64	%82	.001
Ort. Hastane yatışı	30 gün±3	39 gün±5	.0007
MRSA			7
Doğal kapak AV TV			
Toplam mortali			024
Hastane içi mo			49
30.Gün mortali			46
90.Gün mortalite	%16	%21	.32
Bakteriyemi relapsı	%4	%6	.46
Erken relaps (<30 GÜN)	1 hasta	9 hasta	.004

Kontrol grubunda hastane yatışına sekonder komplikasyonlar, çoklu organ yetmezliği daha sık

Oral tedavi seçeneklerinin birçok etkende standard tedavilerden başarısız olduğunu gösteren veri yok

TMP-SMZ tedavisi de S. aureus İE'lerinde alternatif olarak akılda bulunmalı

Dupont, IJAA 2019

JAMA Network Open

Consensus Statement | Infectious Diseases

Guidelines for Diagnosis and Management of Infective Endocarditis in Adults
A WikiGuidelines Group Consensus Statement

Emily G. McDonald, MD, MSc; Gloria Aggrey, MD; Abdullah Tarık Aslan, MD; Michael Casias, PharmD, BCIDP, AAHIVP; Nicolas Cortes-Penfield, MD; Mei Qin (Denise) Dong, PharmD; Susan Egbert, PharmD; Brent Footer, PharmD; Burcu Isler, MD; Madeline King, PharmD; Mira Maximos, PharmD, MSc, ACPR; Terence C. Wuerz, MD, MSc; Ahmed Abdul Azim, MD; Jhongert Alza-Arcila, MD; Anthony D. Bai, MD; Michelle Blyth, MD, MSPH; Tom Boyles, MD; Juan Caceres, MD; Devin Clark, MD; Kusha Davar, MD, MBA, MS; Justin T. Denholm, BMed, PhD; Graeme Forrest, MBBS; Bassam Ghanem, PharmD, MS, BCPS; Stefan Hagel, MD, MS; Alexandra Hanretty, PharmD; Fergus Hamilton, MD; Philipp Jent, MD; Minji Kang, MD; Geena Kludjian, PharmD, BCIDP; Tim Lahey, MD, MMSc; Jonathan Lapin, PharmD; Rachael Lee, MD, MSPH; Timothy Li, MD; Dhara Mehta, PharmD, BCIDP; Jessica Moore, PharmD, MS; Clayton Mowrer, DO, MBA; Georges Ouellet, MD; Rebecca Reece, MD; Jonathan H. Ryder, MD; Alexandre Sanctuaire, PharmD, MSc; James M. Sanders, PharmD, PhD; Bobbi Jo Stoner, PharmD, BCPS; Jessica M. So, MD, MS, MPH; Jean-François Tessier, BSc, MSc; Raghavendra Tirupathi, MD; Steven Y. C. Tong, MBBS, PhD; Noah Wald-Dickler, MD; Arsheena Yassin, PharmD; Christina Yen, MD; Brad Spellberg, MD; Todd C. Lee, MD, MPH

High-quality, hypothesis-confirming data: ≥1 yeterli güçte RKÇ ile ≥1 diğer uyumlu, prospektif, kontrollü klinik çalışmaya (ikinci bir RKÇ YA DA yarı deneysel çalışma YA DA pragmatik klinik çalışma YA DA tarihsel kontrollü çalışma)

Question 3: Can Oral Antimicrobial Therapy Be Used to Treat IE? (Clear Recommendation)

We can provide a clear recommendation for this question. Three randomized clinical trials have established that transition from initial intravenous therapy to oral therapy is at least as effective as

- 3 RKÇ *(Iversen 2019, POET. Stamboulian 1991. Heldman 1996.*)
- Çok sayıda oral ab'nin serum konsantrasyonunun hedef m.o MİK'inin üzerinde olduğunu destekleyen farmakolojik veri
- Çok sayıda gözlemsel çalışma
- Hiçbir klinik ya da gözlemsel çalışmada " sadece IV tedavinin" "modern oral tedaviye" üstün olduğu ***GÖSTERİLEMEMİŞ***

Wikiguideline consensus statement 2023.

Table 3. Summary of Oral Transitional Antibiotics Used in Published Clinical Studies[a]

Drug	Organism	Dose	References
Amoxicillin	• Sensitive streptococci (with or without combination treatment) • Enterococci (only in combination with rifampin or linezolid)	1 g 4 times daily	Iversen et al,[55] 2019; Stamboulian et al,[61] 1991
Dicloxacillin	Sensitive staphylococci (data from RCT only in combination with rifampin)	1 g 4 times daily	Iversen et al, 2019[55]
Levofloxacin[b]	Sensitive staphylococci (only in combination with rifampin)	750 mg once daily	Iversen et al,[55] 2019; Heldman et al,[62] 1996
Moxifloxacin	Sensitive streptococci, enterococci, or staphylococci (only in combination with amoxicillin, rifampin, or linezolid)	400 mg once daily	Iversen et al,[55] 2019
TMP-SMX	Sensitive staphylococci	960 mg or 4800 mg daily in divided doses	Tissot-Dupont et al,[46] 2019; Freling et al,[47] 2023
Linezolid	Sensitive gram-positive cocci (alone or in combination with rifampin, moxifloxacin, or amoxicillin)[c]	600 mg twice daily	Iversen et al,[55] 2019; Tascini et al,[68] 2011; Falagas et al,[69] 2006; Colli et al,[70] 2007; Muñoz et al,[71] 2007; Freling S et al,[47] 2023
Rifampin	Only as adjunctive agent (as previously described)	600 mg once or twice daily	Iversen et al,[55] 2019; Heldman et al,[62] 1996; Acocella G,[72] 1983; Freling et al,[47] 2023

Abbreviations: RCT, randomized clinical trial; TMP-SMX, trimethoprim-sulfamethoxazole.

[a] Combination regimens were used in the largest RCT; other published regimens have included either monotherapy or combination therapy regimens.[3]

[b] The study used ciprofloxacin rather than levofloxacin, the latter of which was not yet clinically available. However, in ensuing years, ciprofloxacin experienced rapid emergence of staphylococcal resistance. Levofloxacin or moxifloxacin are preferred to ciprofloxacin due to enhanced in vitro activity against staphylococci, but generally only in combination with a second agent.

[c] For most patients in published studies, linezolid was used alone; but in some references,[3,4,12] linezolid was given in combination with rifampin, moxifloxacin, or amoxicillin.

Wikiguideline consensus statement 2023.

Question 4: If Oral Antimicrobial Therapy Is Used in the Treatment of IE, Are There Preferred Agents, Is a Specific Duration of Intravenous Lead-In Therapy Necessary, and What Are Reasonable Clinical Criteria for Patient Selection? (Clinical Review)

Not all oral antimicrobial agents are likely candidates for treatment of IE. Historical experience suggests that older sulfonamides, tetracyclines, and macrolides may lead to poor outcomes perhaps

- Kotrimoksazol; başlangıç IV tedavisi olarak 2 RKÇ'de inferior bulunmuştur
- POET çalışmasındaki gbi kombinasyon tedavisi şart mı??? Bazı seçenekler için monoterapinin etkinliğini gösteren veriler mevcut
- IV başlangıç tedavi süresi ne kadar olmalı ? Bir RKÇ'de hiç IV tedavi önerilmemiş!!!

Wikiguideline consensus statement 2023.

Question 4: If Oral Antimicrobial Therapy Is Used in the Treatment of IE, Are There Preferred Agents, Is a Specific Duration of Intravenous Lead-In Therapy Necessary, and What Are Reasonable Clinical Criteria for Patient Selection? (Clinical Review)

Not all oral antimicrobial agents are likely candidates for treatment of IE. Historical experience suggests that older sulfonamides, tetracyclines, and macrolides may lead to poor outcomes perhaps

Hasta Seçimi:

1. Klinik olarak stabil ve kaynak kontrolü için acil cerrahi endikasyon bulunmaması; ve
2. Bakteriyeminin kaynak kontrolüne gerek kalmaksızın düzelmiş/ düzelmekte olması; ve
3. Etkenin in vitro olarak duyarlı olduğubir oral antibiyotik rejiminin mevcut olması; ve
4. Gis emilimi sorunu olmaması

Wikiguideline consensus statement 2023.

Question 5: What Is the Recommended Duration of Antimicrobial Therapy for IE? (Clinical Review)

Left-Sided IE | Evidence to support durations of treatment for IE are almost entirely observational, and most durations are based on historical practice. One RCT[78] established that penicillin-susceptible streptococcal endocarditis treated with 2 weeks of combination therapy with ceftriaxone

Sol kapak İE

- Çalışmalar genellikle gözlemsel
- 1 RKÇ ***(Sexton, 1998);*** Pen S Streptokok **Genta+CRO 2w = CRO 4w**
- Diğer m.o'lar için veri yok, tedavi prensipleri tarihsel gözlemsel çalışmalara dayanıyor
  - **Stafilokok; 6w**
  - **Enterokok; 6w**
  - **HACEK; 4w**
- **PVE; 6w;** kanıt düzeyi yüksek verilerden ziyade uzman görüşlerine dayanmaktadır
- **SATIE ve POET 2 çalışmalarının sonuçları beklenmekte**

Question 5: What Is the Recommended Duration of Antimicrobial Therapy for IE? (Clinical Review)

Left-Sided IE | Evidence to support durations of treatment for IE are almost entirely observational, and most durations are based on historical practice. One RCT[78] established that penicillin-susceptible streptococcal endocarditis treated with 2 weeks of combination therapy with ceftriaxone

Sağ kapak İE

- Komplike olmayan MSSA, prospektif gözlemsel ve RKÇ
  - 2w tedavi yeterli ***(Ribera 1996);*** **bu çalışma süreyi değil kombi vs. monoterapiyi değerlendiren bir çalışma**
- **Optimal tedavi süreleri için yüksek kanıt düzeyi olan veriler yok**
- **Komplike Sağ kalp İE'lerinde tedavi süresini belirleyebilecek veri yok, kanıt olmasa da daha uzun tedaviler kullanılıyor**

26. TÜRK KLİNİK MİKROBİYOLOJİ VE İNFEKSİYON HASTALIKLARI KONGRESİ

KLİMİK 2026

29 NİSAN–3 MAYIS 2026

İEÇG

KLİMİK DERNEĞİ İNFEKTİF ENDOKARDİT VE DİĞER KARDİYOVASKÜLER İNFEKSİYONLAR ÇALIŞMA GRUBU

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KLİMİK DERNEĞİ İNFEKTİF ENDOKARDİT VE DİĞER KARDİYOVASKÜLER İNFEKSİYONLAR ÇALIŞMA GRUBU

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İLGİNİZ İÇİN TEŞEKKÜR EDERİM

İEÇG

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