Ciddi İnfeksiyonlarda Ayaktan Ardışık Oral Kombine Antimikrobiyal Tedavi Mi?

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KLiMiK 2024

Endokardit

S. aureus bakteremisi

Gram-negatif bakteremiler

Endokardit

POET

Randomized Controlled Trial > N Engl J Med. 2019 Jan 31;380(5):415-424.
doi: 10.1056/NEJMoa1808312. Epub 2018 Aug 28.

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen [1], Nikolaj Ihlemann [1], Sabine U Gill [1], Trine Madsen [1], Hanne Elming [1],

- ✓ Danimarka, 2011-2017, RKÇ, açık etiketli, non-inferiorite

Sol kapak endokarditi

- ✓ Klinik olarak stabil
- ✓ En az 10 gün iv uygun tedavi (cerrahi sonrası 7 gün)
- ✓ TÖE'da cerrahi gerektirecek apse veya kapak anomalisi olmaması

→ Oral ardışık (n=201)

→ Klasik iv tedavi (n=199)

POET

Randomized Controlled Trial > N Engl J Med. 2019 Jan 31;380(5):415-424.
doi: 10.1056/NEJMoa1808312. Epub 2018 Aug 28.

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen [1], Nikolaj Ihlemann [1], Sabine U Gill [1], Trine Madsen [1], Hanne Elming [1],

Characteristic	Intravenous Treatment (N=199)	Oral Treatment (N=201)
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)

Hepsi MSSA

Characteristic	Intravenous Treatment (N=199)	Oral Treatment (N=201)
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)

POET – Oral tedavi rejimleri

Tüm rejimler kombine !

	Oral regimens	Frequency n (%)
Staphylococcus aureus	Dicloxacillin and rifampicin	15 (22)
	Amoxicillin and rifamp	
	Moxifloxacin and rifam	
	Amoxicillin and fusidic	
	Dicloxacillin and fusidi	
	Fusidic acid and linezo	
	Rifampicin and linezoli	
	Penicillin and rifampic	
	Amoxicillin and clinda	
	Ampicillin and rifampi	
	Moxifloxacin and fusid	
	Moxifloxacin and linez	
	Linezolid and clindamy	
Enterococcus faecalis	Amoxicillin and moxifl	
	Amoxicillin and linezol	
	Amoxicillin and rifamp	
	Moxifloxacin and linez	
	Amoxicillin and ciprofl	
	Amoxicillin	
	moxicillin and rifampicin	47 (52)
	moxicillin and moxifloxacin	12 (13)
	fampicin and linezolid	8 (9)
	oxifloxacin and linezolid	8 (9)
	moxicillin and linezolid	7 (8)
	nicillin	3 (3)
	mpicillin and moxifloxacin	1 (1)
	mpicillin and rifampicin	1 (1)
	cloxacillin and moxifloxacin	1 (1)
	oxifloxacin and clindamycin	1 (1)
	oxifloxacin and vancomycin	1 (1)
	sidic acid and linezolid	5 (38)
	fampicin and linezolid	4 (31)
	moxicillin and linezolid	1 (8)
	cloxacillin and rifampicin	1(8)
	oxifloxacin and linezolid	1(8)
	fampicin and Fusidic acid	1(8)

Amoksisilin

Dikloksasilin

Rifampisin

Fusidik asit

Moksifloksasin

Linezolid

Kasper Iverson et al. NEJM, 2019; Magnus Bock et al. Clin Infect Dis, 2023

Sonlanım noktaları

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)
Composite outcome	**24 (%12.1)**	**18 (%9)**	**3.1 (-3.4 to 9.6)**	**0.72 (0.37 to 1.36)**

Kasper Iverson et al. NEJM, 2019

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

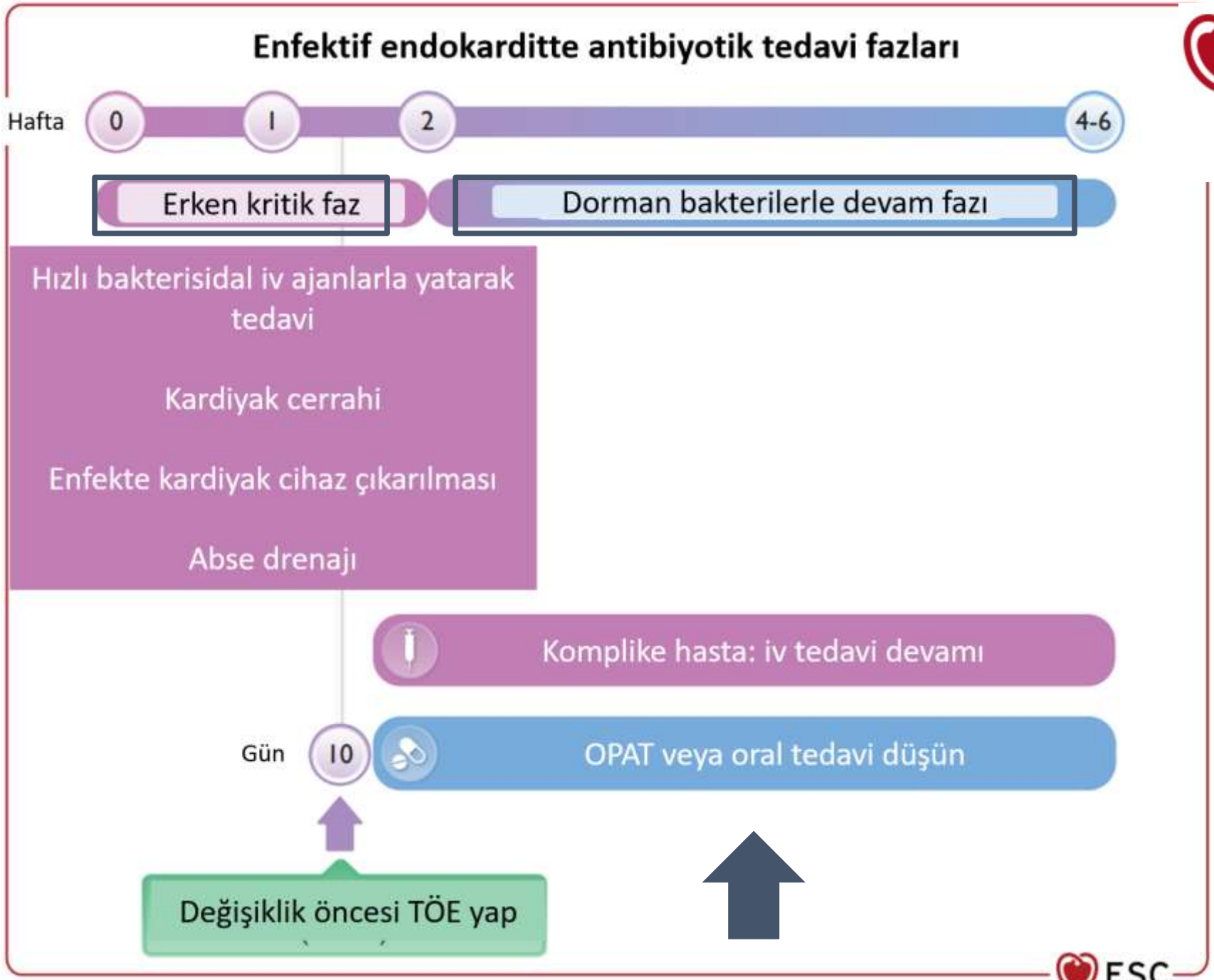
Mia M Pries-Heje [1], Christoffer Wiingaard [1], Nikolaj Ihlemann [1], Sabine U Gill [2], Niels E Bruun [3],

POET

5. yıl sonuçları

	Intravenous Treatment (n=199)	Oral Treatment (n=201)	HR	95% CI
Primary composite outcome, n (%)	90 (45.2)	66 (32.8)	0.65	0.48 - 0.90
All-cause mortality, n (%)	70 (35.2)	47 (23.4)	0.61	0.42 - 0.88
Unplanned cardiac surgery, n (%)	21 (10.6)	13 (6.5)	0.57	0.29 - 1.14
Embolic event, n (%)	6 (2.5)	8 (4.0)	1.23	0.43 - 3.54
Relapse of positive blood culture, n (%)	11 (5.5)	8 (4.0)	0.69	0.28 - 1.71
Composite outcome	90 (45.2)	66 (%32.8)	0.65	0.47-0.90

ESC 2023



ESC European Society of Cardiology

2023 ESC Guidelines for the management of endocarditis

Recommendations	Class[a]	Level[b]
APAT veya **ORAL ARDIŞIK** tedavi 1. Sol kapak endokarditi olan 2. *Streptococcus* spp. , *E. faecalis*, *S. aureus*, KNS 3. En az 10 gün iv uygun tedavi (cerrahi sonrası 7 gün) 4. Klinik olarak stabil 5. TÖE'da cerrahi gerektirecek apse veya kapak anomalisi olmaması	IIa 	A
1. Tedavisi zor mo.larla gelişen İE 2. Sirotik hasta (Child Pugh B veya C) 3. Ciddi SSS embolisi 4. Tedavisiz geniş ekstrakardiyak abse 5. Kapak komplikasyonları 6. Diğer cerrahi gerektirecek ciddi komplikasyonlar 7. Cerrahi sonrası ciddi komplikasyonlar 8. Damar içi ilaç kullanımına bağlı İE	III 	C

- MRSA
- VRE (LNZ, DAP dirençli)
- MDR, XDR Gram-negatif bakteri
- Yüksek düzey penisilin direnci olan oral streptokoklar
- Candida dışı mantarlar

2023 ESC Guidelines for the management of endocarditis

Diğer prospektif k ç

First Author & Year	N	Inclusion and Exclusion Criteria	Regimen Oral vs IV	Success Oral vs IV	Complications Oral vs IV, n (%)	
Stamboulian 1991[50]	30	Included: native valve IE due to penicillin-susceptib	2 weeks ceftriaxone then	100% (15/15)	Relapse	0/15 (0%) vs.
Totals (N=3 RCTs) + 1 quasi-experimental	474 815			Success: Oral 77% (179/233) vs. IV 67% (162/241) Success: Oral 78% (317/404) vs. IV 68% (281/411)		

Penisilin duyarlı streptokoklar

eysel

iv

alite ↓

Relaps benzer

ESC 2023- Sağ kapak endokarditi

ESC European Society of Cardiology

- Ana etken *S. aureus* / KNS

✓Ankomplike hastalarda
✓Tedavi uyumu iyi olacaksa
✓Mo. her ikisine de duyarlı ise
✓İv tedavi verilemiyorsa

Oral siprofloksasin
(2x750mg)
+
Rifampisin
(2x300mg)

IE- Wikiguideline consensus statement, 2023

Monoterapi?

First Author & Year	N	Inclusion and Exclusion Criteria	Regimen Oral vs IV	Success Oral vs IV	Complications Oral vs IV, n (%)	
Stamboulian 1991[50]	30	Included: native valve IE due to penicillin-susceptib Exclusion cardiovas factors, p	2 weeks ceftriaxone then	100% (15/15)	Relapse	0/15 (0%) vs.
Heldman 1996[51]	44	Included: drug user sided stap (95% MS Excluded prosthetic pregnant,				
Tissot-Dupont[‡] 2019[63]	341	Included: valve, inc prosthetic *aureus* (i MRSA)				
Totals (N=3 RCTs) + 1 quasi-experimental	474 815			Success: Oral 77% (179/233) vs. IV 67% (162/241) Success: Oral 78% (317/404) vs. IV 68% (281/411)		

Penisilin duyarlı streptokoklar

CRO→Amoksisilin vs. **CRO**

Relaps 0/15 vs. 1/15

İVDU, sağ-kapak, %95 MSSA

CİP+RA vs. **standart İV**

Başarı 18/19 vs 22/25

S. aureus'a bağlı endokardit, yarı-deneysel

İV **SXT+DA →oral SXT** vs. **standart İV**

Hastane içi mortalite ve 30 günlük mortalite ↓

Relaps benzer

IE- Wikiguideline consensus statement, 2023

İE'de monoterapi

Clin Microbiol Infect. 2016 Jul;22(7):607-12. doi: 10.1016/j.cmi.2016.04.003. Epub 2016 Apr 16.

Switch to oral antibiotics in the treatment of infective endocarditis is not associated with increased risk of mortality in non-severely ill patients

A Mzabi [1], S Kernéis [2], C Richaud [2], I Podglajen [2], M-P Fernandez-Gerlinger [2], J-L Mainardi [3]

- 2000-2012, retrospektif kohort, n=426
- Streptokoklar (%40), *S. aureus* (%19), Enterokok (%12)

Oral ardışık
n= 214

İntravenöz
n= 212

%50 monoterapi

(çoğu oral amoksisilin)

Oral tedavi etkin

Mortalite iv tedavi kolunda daha yüksek

Relaps ve reinfeksiyon benzer

S. aureus bakteremisi (SAB)

> Lancet Infect Dis. 2024 Jan 17:S1473-3099(23)00756-9.
doi: 10.1016/S1473-3099(23)00756-9. Online ahead of print.

Efficacy and safety of an early oral switch in low-risk Staphylococcus aureus bloodstream infection (SABATO): an international, open-label, parallel-group, randomised, controlled, non-inferiority trial

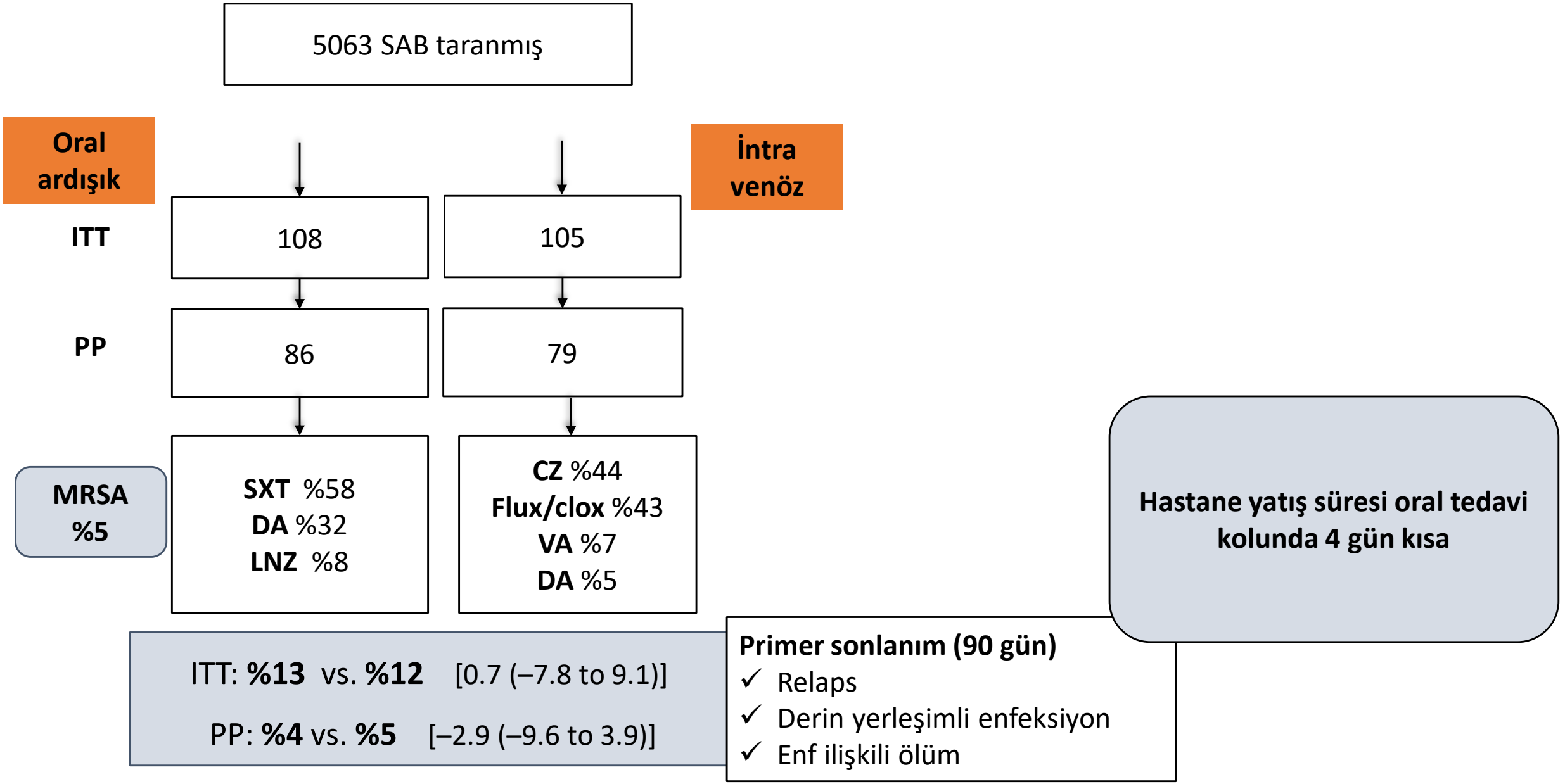
Achim J Kaasch [1], Luis Eduardo López-Cortés [2], Jesús Rodríguez-Baño [2],

- Uluslararası, açık etiketli, RKÇ, non-inferiorite çalışması

Düşük riskli SAB

5-7 gün iv tedavi sonrası ardışık oral tedavi

- Derin yerleşimli enfeksiyon olmaması (endokardit, pnömoni, enfekte implant, drene edilmemiş apse, ampiyem, osteomiyelit yok)
- Son 4 gün içinde septik şok olmaması
- Persistan bakteriyemi olmaması
- İlk 4 gün içinde kateterin çekilmesi


5063 SAB taranmış
Oral ardışık
İntra venöz
ITT
108
105
PP
86
79
MRSA %5
SXT %58
DA %32
LNZ %8
CZ %44
Flux/clox %43
VA %7
DA %5
ITT: %13 vs. %12 [0.7 (–7.8 to 9.1)]
PP: %4 vs. %5 [–2.9 (–9.6 to 3.9)]
Primer sonlanım (90 gün)
✓ Relaps
✓ Derin yerleşimli enfeksiyon
✓ Enf ilişkili ölüm
Hastane yatış süresi oral tedavi kolunda 4 gün kısa

5063 hasta taranmış → Çalışmaya dahil edilen 213

Signs and symptoms of complicated *S. aureus* bloodstream infection present	
- Deep seated focus present (e.g. endocarditis, pneumonia, undrained empyema, and osteomyelitis)	
- Septic shock within 4 days before randomization	
- Prolonged bacteraemia (positive follow-up blood culture more than 72 hours after start of adequate antimicrobial therapy)	560 (20%)
- Body temperature >38 °C on two separate days within 48h before randomization	124 (4·5%)
Presence of non-removable foreign body (prosthetic heart valves, deep-seated vascular grafts with foreign material, ventriculo-atrial shunt); haemodialysis shunts are accepted	847 (26·4%)
Intravascu	169 (5·9%)

Enfeksiyon kaynağı

% 44 PVK

% 22 SVK

% 24 Cilt-yumuşak doku

Komplike olmamış SAB klinik pratiğimizin ne kadarı oluşturuyor??

AJ Kaasch et al. Lancet Infect Dis, 2024

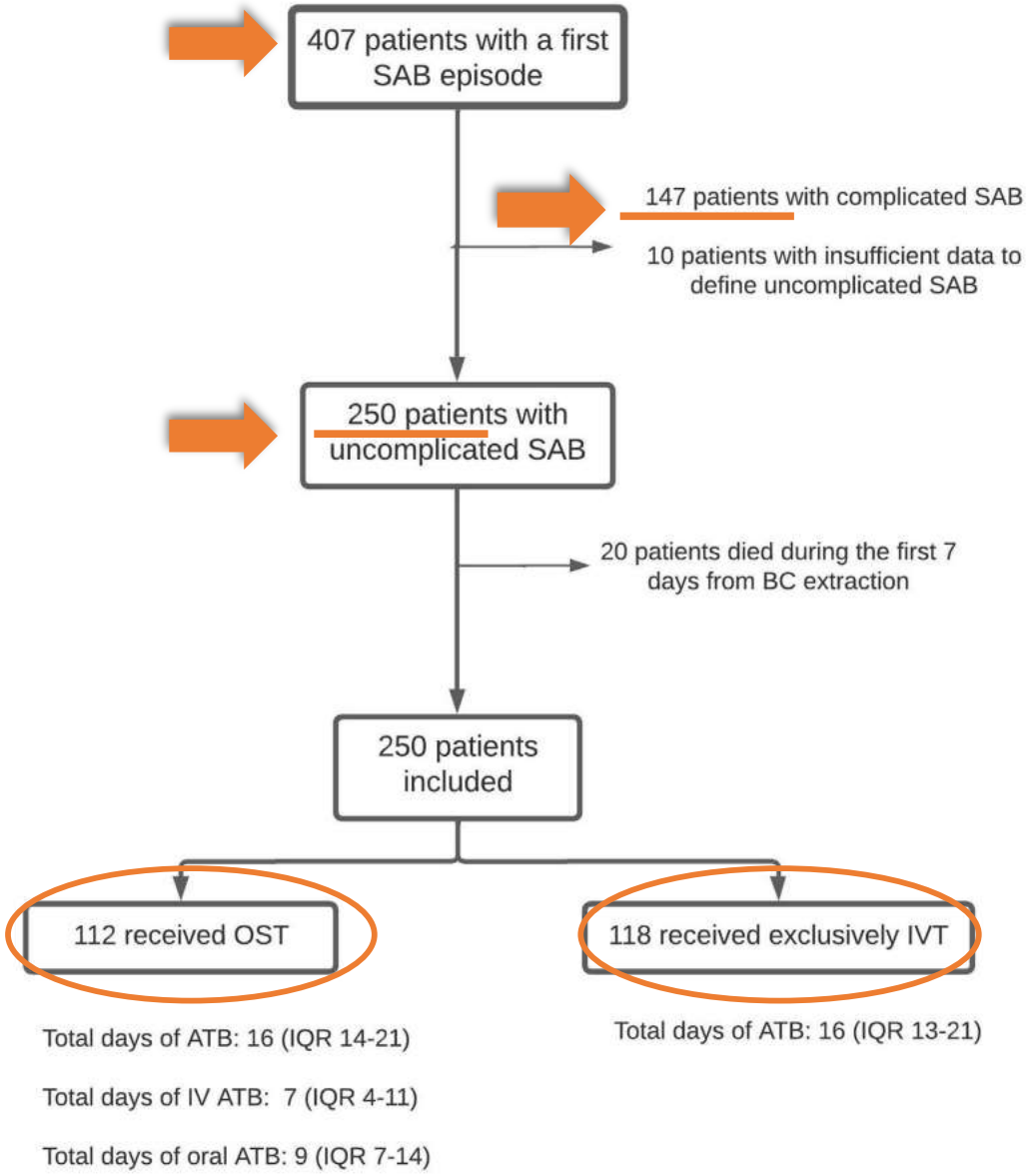
Ankomplike bakteriyemi bu kadar az mı?

Observational Study > Clin Microbiol Infect. 2023 Jun;29(6):744-750.
doi: 10.1016/j.cmi.2023.02.001. Epub 2023 Feb 10.

Sequential oral antibiotic in uncomplicated Staphylococcus aureus bacteraemia: a propensity-matched cohort analysis

Itziar Diego-Yagüe [1], Alberto Mora-Vargas [1], Jose Manuel Vázquez-Comendador [1],

- Retrospektif, tek merkez, İspanya
- Medyan 7 günden sonra oral tdv
- AMC (%37), FQ (%31), SS (%16)



Baseline and clinical characteristics between groups. Continuous variables are expressed as median (interquartile range)

Variable		OST ($N = 112$)	IVT ($N = 118$)	p
Demographic and comorbidities				
Age (y)		68 (52–80)	68 (58–81)	0.525
Gender (female)		34.8% (39)	30.5% (36)	0.574
Charlson index		2 (0–4) (111/112)	2 (1–5)	0.599
Arterial hypertension		42.0% (47)	61.0% (72)	0.005
Diabetes mellitus		22.3% (25)	32.2% (38)	0.105
Chronic cardiac failure		19.6% (22)	33.9% (40)	0.017
Ischemic cardiopathy		13.4% (15)	23.7% (28)	0.062
Natural valvular disease		10.7% (12)	16.9% (20)	0.187
Chronic renal failure		15.2% (17)	23.7% (28)	0.134
Renal replacement therapy		4.5% (5)	6.8% (8)	0.310
Liver cirrhosis		2.7% (3/111)	2.5% (3)	1.000
Solid organ malignancy		27.0% (30/111)	18.6% (22)	0.156
Clinical presentation				
Acquisition	Community	28.6% (32)	29.7% (35)	0.472
	Nosocomial	50.9% (57)	55.9% (66)	
	HA	20.5% (23)	14.4% (17)	
Primary focus	Unknown	20.6% (22/107)	32.8% (38/116)	0.049
	Central catheter	13.1% (14/107)	9.4% (11/116)	0.526
	Peripheral catheter	25.2% (27/107)	21.5% (25/116)	0.527
	SSTIs	21.5% (23/107)	14.6% (17/116)	0.222
	Respiratory	7.5% (8/107)	18.1% (21/116)	0.027
	Other	12.2% (13/107)	5.1% (6/116)	0.153
Fever		92.9% (104/112)	88.0% (103/117)	0.265
Fever during first 48 h		36.5% (38/104)	33.0% (34/103)	0.662
Septic shock		14.3% (16)	28.2% (33/117)	0.015
SOFA score		1 (0–2) (111/112)	3 (1–4)	<0.001
Acute renal failure		28.4% (31/109)	36.8% (43/117)	0.203
Acute cardiac failure		9.0% (10/111)	18.8% (22/117)	0.037
Microbiology and management				
Methicilin-resistant SA		12.5% (14)	24.6% (29)	0.027
Vancomycin MIC >1,5		10.7% (12)	14.4% (17)	0.433
Time to positivity (h)		13 (10–17)	13 (10–16)	0.667
Positive control BC during first 48 h		18.3% (15/96)	20.8% (20/82)	0.709
Echocardiography (any)		64.3% (72/112)	71.3% (82/115)	0.320
Transoesophageal echocardiography		22.3% (25/112)	21.7% (25/115)	1.000
Source control procedures		53.6% (59)	48.2% (54)	0.425

Itziar Diego-Yagüe et al. Clin Microbiol Infect, 2023

Variable	OST ($N = 77$)	IVT ($N = 77$)	p
Demographic and comorbidities			
Age (y)	69 (53-80)	67 (57-78)	0.665
Gender (female)	31.2% (24)	28.6% (22)	0.860
Charlson index	2 (0-4) (76/77)	2 (0-4)	0.605
Arterial hypertension	49.4% (38)	53.2% (41)	0.747
Diabetes mellitus	24.7% (19)	24.7% (19)	1.000
Chronic cardiac failure	24.7% (19)	24.7% (19)	1.000
Ischemic cardiopathy	14.3% (11)	22.1% (17)	0.296
Natural valvular disease	14.3% (11)	15.6% (12)	1.000
Chronic renal failure	14.3% (11)	22.1% (17)	0.296
Renal repl			0.719
Liver ci			0.681
Solid			1.000
Immu			1.000
Vascu			
Perip			1.000
Short			0.639
Long			1.000
Clinic			
Acqui			0.712
Prima			0.857
			0.811
			0.849
			0.309
			0.022
			0.442
			0.620
Septic			0.835
SOFA sc			0.507
Acute renal			0.394
Acute cardiac failure	11.7% (9)	11.7% (9)	1.000
Microbiology			
Methicillin-resistant *Staphylococcus aureus*	15.6% (12)	13.0% (10)	0.818
Time to positivity (h)	13 (10–17)	12 (10–16)	0.417
Management before oral therapy			
Initial combination antibiotic	44.2% (34)	39.2% (29/74)	0.621
Initial appropriate antibiotic	86.5% (64/74)	82.9% (58/70)	0.645

Primer sonlanım

(90 günlük mortalite ve mikrobiyolojik başarısızlık)

↓

Oral - iv: %10.4 - %32.5, RR: 0.42 (0.22-0.79)

Itziar Diego-Yagüe et al. Clin Microbiol Infect, 2023

Komplike SAB

Clin Infect Dis. 2021 Sep 7;73(5):895-898. doi: 10.1093/cid/ciab156.

Intravenous to Oral Switch in Complicated Staphylococcus aureus Bacteremia Without Endovascular Infection: A Retrospective Single-Center Cohort Study

Ilse J E Kouijzer [1], Eline J van Leerdam [1], Michelle Gompelman [1, 2],

HASTANE PROTOKOLÜ

Komplike bakteriyemilerde endokardit dışlanması

↓

2 hf intravenöz flukloksasilin

↓

Oral klindamisin 3x600mg

(%26'sında **RA kombinasyonu)**

			P
Male, n (%)			.193
Mean age, years			.926
Charlson comorbidity index			.446
Community acquisition, n (			.883
Persistent fever (>72 hours			.043
Persistent positive blood cu			.001
Signs of infection >48 hou			.832
MRSA, n (%)			1.000
Metastatic infection, n (%)			
Vertebral osteomyelitis			.044
Nonvertebral osteomyeli			.091
Infected osteosynthesis			.089
Arthritis			.291
Prosthetic joint infection			.954
Splenic abscess			.224
Soft tissue abscess			.883
Pulmonary foci			.039
Total, n			
Relapse	0	0	
3-Month mortality, n (%)	6 (13.3)	4 (6.6)	.242
Drainage, radiologically or surgically, n (%)	26 (57.8)	31 (50.1)	.666
Hospital admission duration, median (IQR), days	29 (33)	17 (11)	.001
Treatment duration, median (IQR), days	45 (44)	45 (49)	.355
Addition of rifampicin, n (%)	15 (33.3)	16 (26.2)	.643

GN bakteremiler

SOAB çalışması

› Clin Microbiol Infect. 2023 Oct 18:S1198-743X(23)00522-0.
doi: 10.1016/j.cmi.2023.10.014. Online ahead of print.

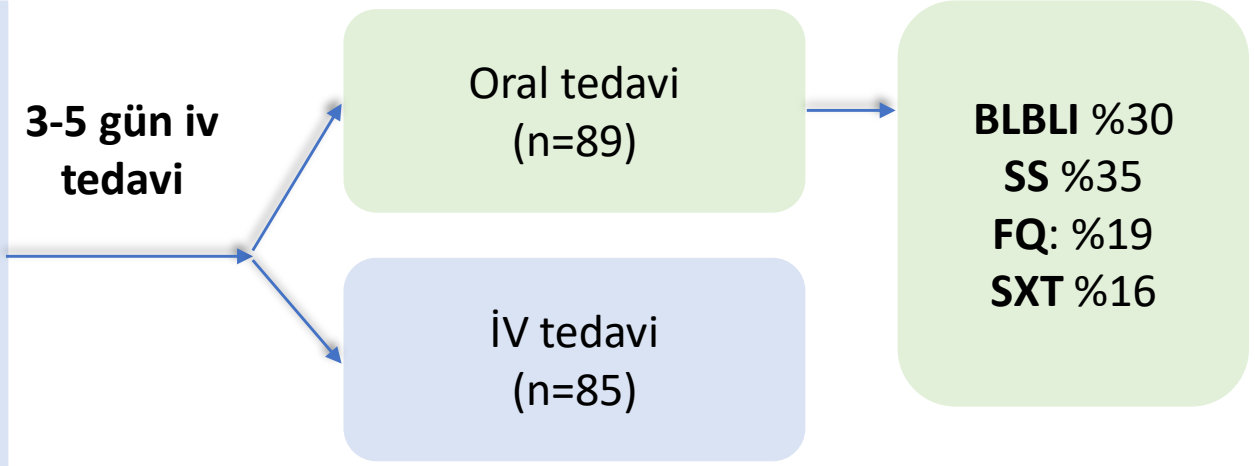
Switch to oral antibiotics in Gram-negative bacteraemia: a randomized, open-label, clinical trial

Ali S Omrani [1], Sulieman H Abujarir [2], Fatma Ben Abid [3], Shahd H Shaar [4],

- 2019-2022, Bahreyn, Kuveyt, Katar, Türkiye
- Randomize, kontrollü, açık etiketli, non-inferiorite

Enterobacterales bakteriyemisi +

- 3-5 gün iv tedaviyi tamamlamış
- Klinik olarak stabil
- Kaynak kontrolü ihtiyacı olmayan/yapılmış olan
- Etken en az bir oral **beta laktam/kinolon/SXT** duyarlı



- Enfeksiyon kaynağı: %60 üriner, %16 abdominal
- Etken: %65-69 *E.coli*, %22-26 *Klebsiella* spp.
- **Direnç durumu: 3. kuşak SS: %70-80 duyarlı**

Tedavi başarısızlığı:

Ölüm
Ek tedavi ihtiyacı
Mikrobiyolojik relaps
Enfeksiyon ilişkili başvuru

✓ Her iki grupta tedavi başarısızlığı benzer (IV vs oral: % 25.6 vs. %21.7)

✓ Oral tdv: Hastane yatışı kısa, total ab süresi uzun

AS Omrani et al. Clin Microbiol Infect, 2023

GN-KDİ: Retrospektif çalışmalar

«İntravenöz» vs «**oral»** ardışık tedavi ?

- Çoğunlukla üriner sistem enfeksiyonları, daha az sıklıkla GİS ve SVK ilişkili enfeksiyonlar
- Kaynak kontrolü yapılmış hastalar
- Orale geçiş aşamasında klinik cevap alınmış

Çalışma sonlanım noktaları:

- IV antibiyotiklerin tekrar başlanması
- Rekürrens (30-90gün)
- Bakteriyemi ilişkili ölüm

✓ Gruplar arasında tedavi başarısızlığı açısından fark yok

✓ Genelde hastane yatış süreleri daha kısa, damar yolu ile ilişkili yan etkiler az

Thurber et al. J Glob. Antimicrob. Resist. 2019, Tamma et al. JAMA Intern Med, 2019
Rieger et al. Pharmacotherapy, 2017, Nisly et al. J Glob Antimicrob Resist, 2020

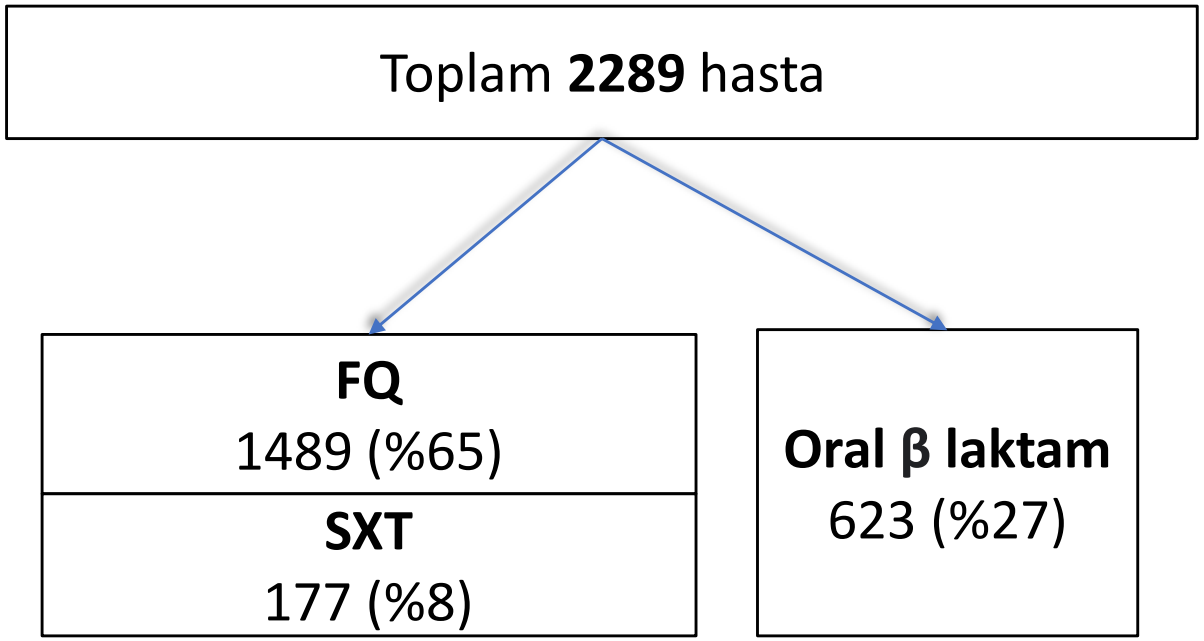
Oral tedaviler arasında fark var mı?

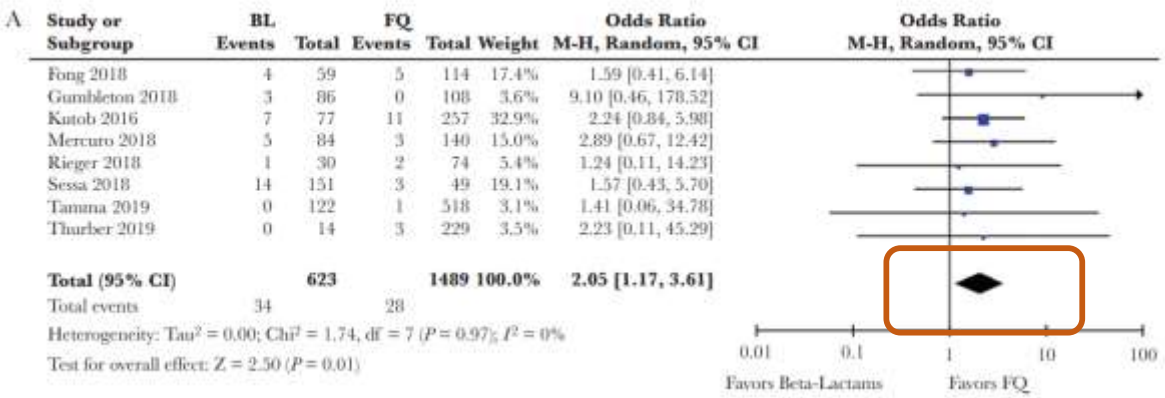
› Open Forum Infect Dis. 2019 Aug 14;6(10):ofz364. doi: 10.1093/ofid/ofz364. Online ahead of print.

Oral Fluoroquinolone or Trimethoprim-sulfamethoxazole vs. ß-lactams as Step-Down Therapy for Enterobacteriaceae Bacteremia: Systematic Review and Meta-analysis

Chitra Punjabi [1], Vivian Tien [1], Lina Meng [2], Stan Deresinski [1], Marisa Holubar [1]

- 8 retrospektif kohort çalışma
- FQ/SXT vs β laktam
- SXT'nin temsili az
- Enf kaynağı: %40-100 ÜSİ, %0-20 İAİ, bir çalışmada %18 KİKDE





Study or Subgroup	Beta-Lactams Events	Total	FQ/TMP-SMX Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Fong 2018	1	59	4	114	5.1%	0.47 [0.05, 4.34]
Gumbleton 2018	2	86	1	119	4.3%	2.81 [0.25, 31.49]
Kutob 2016	3	77	9	285	14.1%	1.24 [0.33, 4.71]
Mercuro 2018	1	84	1	140	3.2%	1.67 [0.10, 27.13]
Rieger 2018	0	30	2	84	2.7%	0.54 [0.03, 11.59]
Sessa 2018	0	151	0	57		Not estimable
Tamma 2019	15	122	68	617	70.5%	1.13 [0.62, 205]
Thurber 2019	0	14	0	250		Not estimable
Total (95% CI)		**623**		**1666**	**100.0%**	**1.13 [0.69, 1.87]**
Total events	22		85			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.46$, df = 5 ($P = 0.92$); $I^2 = 0\%$

Test for overall effect: Z = 0.49 ($P = 0.63$)

Odds Ratio M-H, Random, 95% CI

0.01 0.1 1 10 100

Favors Beta-Lactams Favors FQ/TMP-SMX

Mortalite

A

Study or Subgroup	BL Events	Total	FQ Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Fong 2018	4	59	5	114	17.4%	1.59 [0.41, 6.14]
Gumbleton 2018	3	86	0	108	3.6%	9.10 [0.46, 178.52]
Kutob 2016	7	77	11	257	32.9%	2.24 [0.84, 5.98]
Mercuro 2018	5	84	3	140	15.0%	2.89 [0.67, 12.42]
Rieger 2018	1	30	2	74	5.4%	1.24 [0.11, 14.23]
Sessa 2018	14	151	3	49	19.1%	1.57 [0.43, 5.70]
Tamma 2019	0	122	1	518	3.1%	1.41 [0.06, 34.78]
Thurber 2019	0	14	3	229	3.5%	2.23 [0.11, 45.29]
Total (95% CI)		**623**		**1489**	**100.0%**	**2.05 [1.17, 3.61]**
Total events	34		28			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.74$, df = 7 ($P = 0.97$); $I^2 = 0\%$

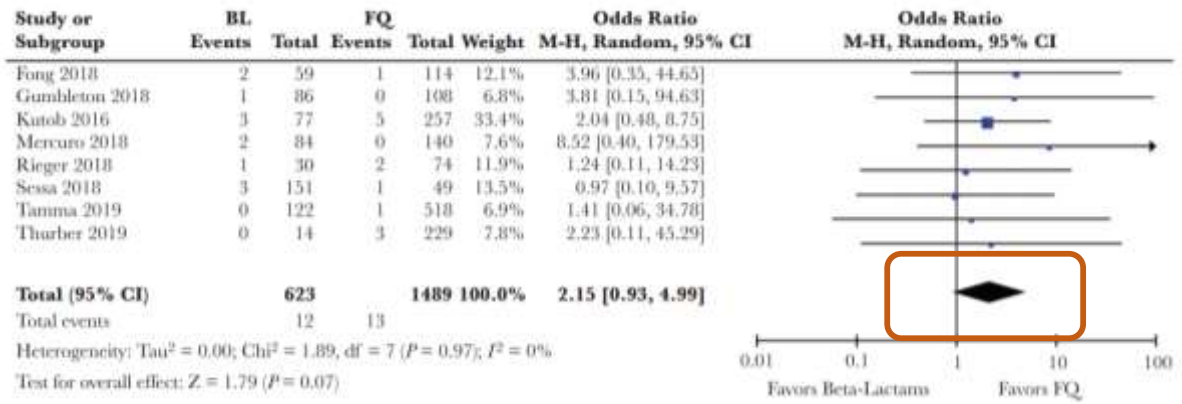
Test for overall effect: Z = 2.50 ($P = 0.01$)

Odds Ratio M-H, Random, 95% CI

0.01 0.1 1 10 100

Favors Beta-Lactams Favors FQ

Rekürrens



B

Study or Subgroup	BL Events	Total	FQ Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Fong 2018	2	59	1	114	12.1%	3.96 [0.35, 44.65]
Gumbleton 2018	1	86	0	108	6.8%	3.81 [0.15, 94.63]
Kutob 2016	3	77	5	257	33.4%	2.04 [0.48, 8.75]
Mercuro 2018	2	84	0	140	7.6%	8.52 [0.40, 179.53]
Rieger 2018	1	30	2	74	11.9%	1.24 [0.11, 14.23]
Sessa 2018	3	151	1	49	13.5%	0.97 [0.10, 9.57]
Tamma 2019	0	122	1	518	6.9%	1.41 [0.06, 34.78]
Thurber 2019	0	14	3	229	7.8%	2.23 [0.11, 45.29]
Total (95% CI)		**623**		**1489**	**100.0%**	**2.15 [0.93, 4.99]**
Total events	12		13			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.89$, df = 7 ($P = 0.97$); $I^2 = 0\%$

Test for overall effect: Z = 1.79 ($P = 0.07$)

Odds Ratio M-H, Random, 95% CI

0.01 0.1 1 10 100

Favors Beta-Lactams Favors FQ

Rekürrens (bakteriyemi)

Table 1. Oral antibiotic dosages for bacteremia and infective endocarditis/beta-lactams.

Oral Antibiotic	Microorganism	MIC (mg/L)	Dosage	Dose Adjustment for Special Populations	References
Amoxicillin	*Enterobacterales* *Streptococci*; *Enterococci*	≤1 1–2 >2	1 g tid 1 g qid Avoid	eGFR ≤ 10 mL/min or dialysis-dependent patients: 1 g bid	[40,44–47]
AMX/CLAV	*Enterobacterales*	≤2 >2	1000/125 mg tid Avoid	eGFR ≤ 10 mL/min or dialysis-dependent patients: 1000/125 or 875/125 mg bid	[42,46,48]
Cefalexin	*Enterobacterales*	≤1.5 ≤3 >3	1 g tid 1 g qid Avoid	eGFR 10–30 mL/min: 1 g tid eGFR ≤ 10 mL/min or dialysis-dependent patients: 1 g bid	[43,49]
Cefuroxime axetil	*Enterobacterales* *Streptococci*	≤0.5 >0.5	500 mg tid Avoid	None	[41]
Cefixime - Cefpodoxime	*Enterobacterales* *Streptococci*	≤0.5 >0.5	400 mg bid Avoid	None	[40,41]

G Eleftheriotis et al. Microorganisms, 2023

ÖZET

Literatür her 3 endikasyonda da oral ardışık tedavi kullanımını destekliyor

Çalışmaların kısıtlılıkları→ Gözlemsel çalışmalarda karşılaştırma gruplarında hasta ağırlıkları benzer değil

Hasta grubunun seçimi önemli:

- ✓ Komplike olmayan
- ✓ İV tedavi ile kliniği stabilleşen
- ✓ Odak kontrolü yapılan hastalar

Endokarditte kombine, bakteremilerde monoterapi

ÖZET

Oral tedaviler hastane yatış süresini kısaltıyor, damar yolu/kateter ile ilişkili komplikasyonları azaltıyor

Çalışmalarda biyoyararlanımı yüksek olarak bilinen ajanların yanı sıra beta laktamlar da kullanılmış → Oral seçeneklerin birbirlerine üstünlüklerini değerlendirmek için daha çok çalışmaya ihtiyaç var

Hastalara oral tedavi vermek için onları taburcu etmeyi beklememize gerek yok, yatarken de verebiliriz ☺

IV to PO Worksheet

★★★★★ BEFORE COMPLETING, MAKE SURE ANTIBIOTICS ARE NEEDED ★★★★★

…and remember: *The bug does not know how the drug gets there!... So: If the gut works, use it!*

Factor	Yes	No	Notes/ Comments

Dikkatiniz için teşekkür ederim …