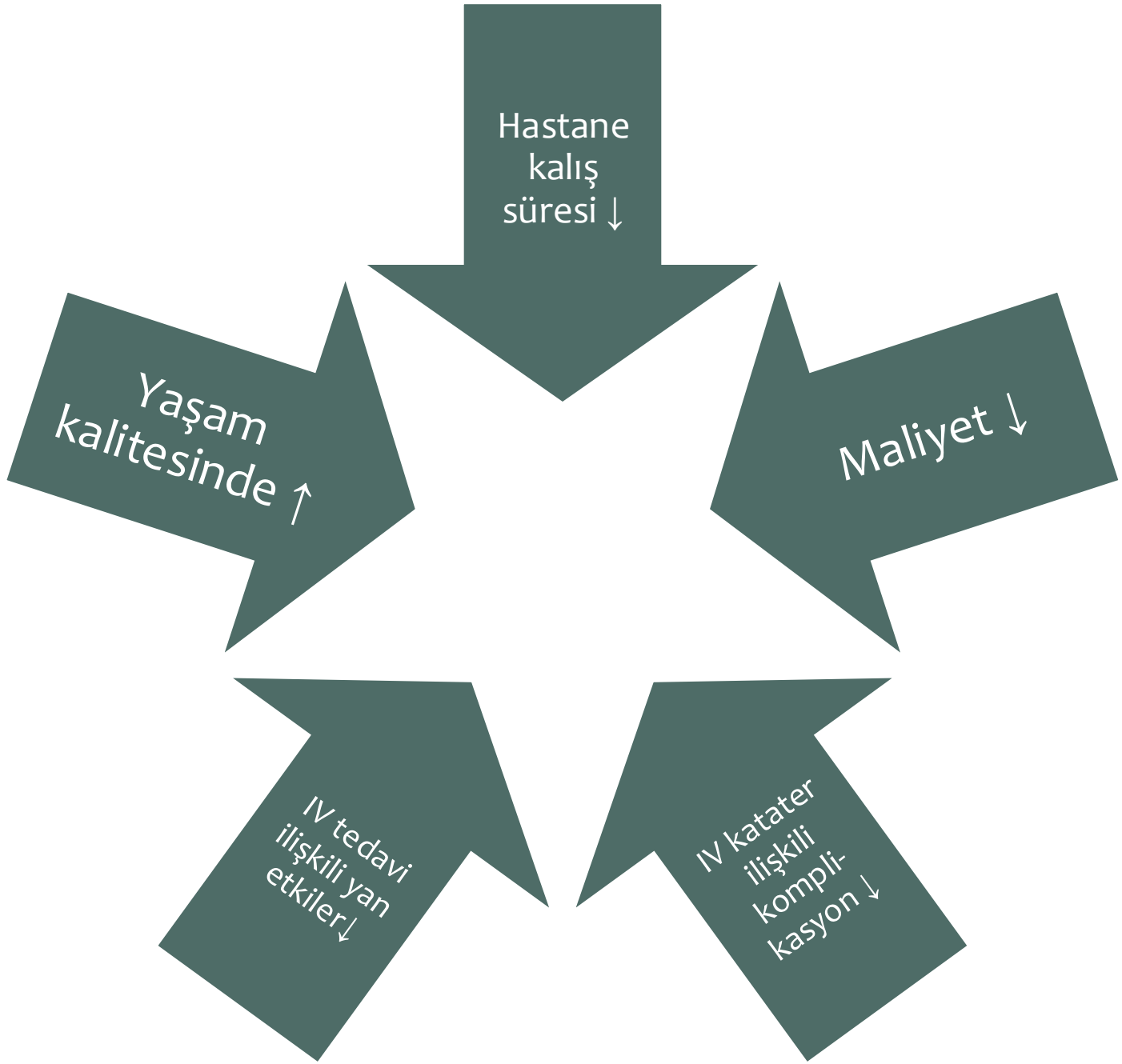
Yüksek Riskli İnfeksiyonlarda Oral Tedavi Kanıtları

Dr. Melike TÖRÜYENLER COŞKUNPINAR

Yüksek riskli infeksiyon nedir?..

ORAL TEDAVİYE ERKEN GEÇİŞ



1. Kan dolaşımı infeksiyonları
   - Gram-negatif bakteriyemi
   - Gram pozitif bakteriyemi
   - İnfektif endokardit
2. Kemik – eklem infeksiyonları
3. Beyin absesi
4. Ciddi pnömoni
5. Sepsis / yoğun bakım hastası
6. Fungal infeksiyonlar

JAMA Network | Open

Original Investigation | Infectious Diseases

Early Switch From Intravenous to Oral Antibiotics for Patients With Uncomplicated Gram-Negative Bacteremia

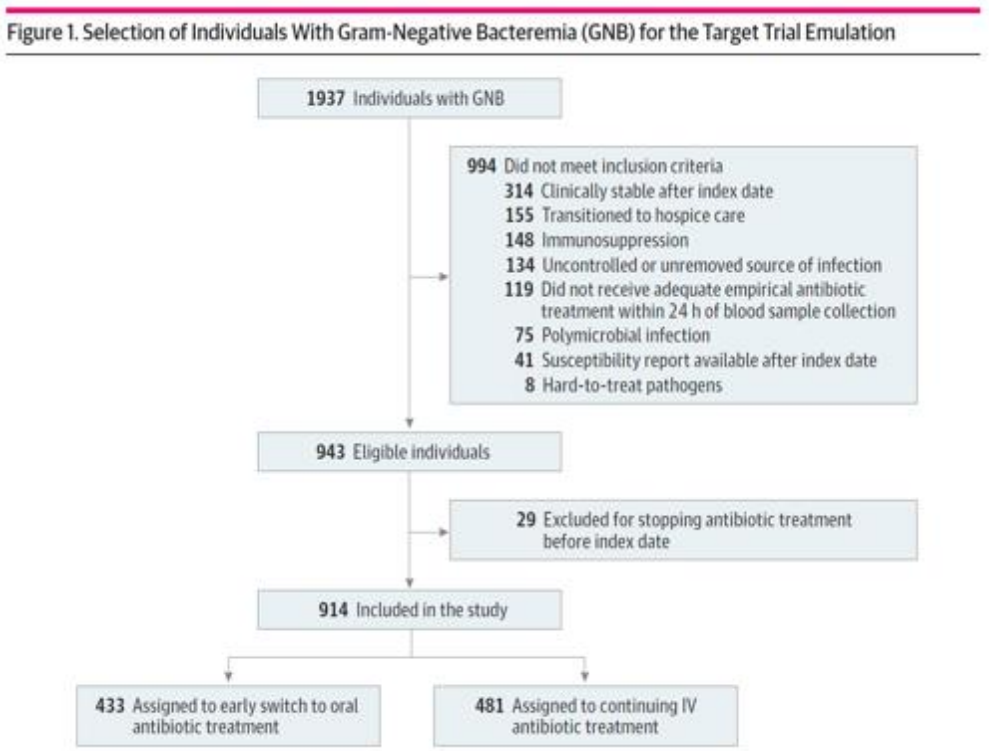
Sandra Tingsgård, MD; Simone Bastrup Israelsen, MD, PhD; Henrik Løvendahl Jørgensen, MD, PhD; Christian Østergaard, MD, DMSc; Thomas Benfield, MD, DMSc

- 914 unkomplike Gram-negatif bakteriyemi
- Çok merkezli, 3 yıllık

- İlk kan kx sonrası 4 gün içinde orale geçiş vs en az 5 gün süren parenteral tedavi
  - Kan kx pozitifliğinden sonraki 24 saatte parenteral tedavi başlanması
  - 4 gün içinde ADT sonucuna ulaşılması

- **Kan kx sonrası 4. günde klinik stabilite**

- 90 günlük mortalite

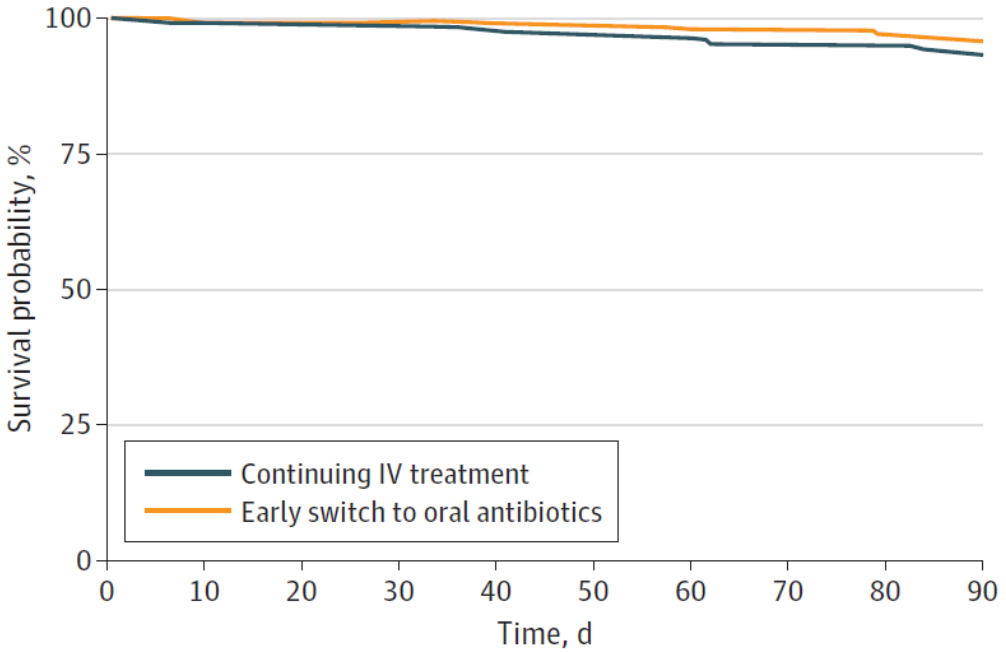


- İmmunsupresyon
- Kaynak kontrolü sağlanamaması
- *Acinetobacter*, *Burkholderia*, *Pseudomonas*, *Brucella ya da Fusobacterium* spp.
- Polimikrobiyal infeksiyon

Table 3. Inverse Probability–Weighted 90-Day Risk of All-Cause Mortality Among Individuals With Gram-Negative Bacteremia Continuing IV Antibiotic Therapy vs Early Switch to Oral Antibiotic Therapy

Analysis	90-d Risk of all-cause mortality, % (95% CI)		90-d Risk difference (95% CI)	90-d Risk ratio (95% CI)
	Early oral switch	Continuing IV treatment		
Intention-to-treat	9.1 (6.7-11.6)	11.7 (9.6-13.8)	−2.5 (−5.7 to 0.7)	0.78 (0.60 to 1.10)
Per-protocol	9.6 (6.7-12.4)	9.7 (7.6-11.8)	−0.1 (−3.4 to 3.1)	0.99 (0.70 to 1.40)

Figure 2. Weighted Survival Curves for Individuals Who Continued or Switched to Early Oral Antibiotics



No. at risk										
Continuing IV treatment	481	367	346	340	333	327	323	319	318	315
Early switch to oral antibiotics	433	381	378	375	371	370	366	365	360	360

Orale geçilen ve IV devam edilen hastalar arasında mortalite açısından fark yok.

Clinical Microbiology and Infection 30 (2024) 492–498

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journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

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

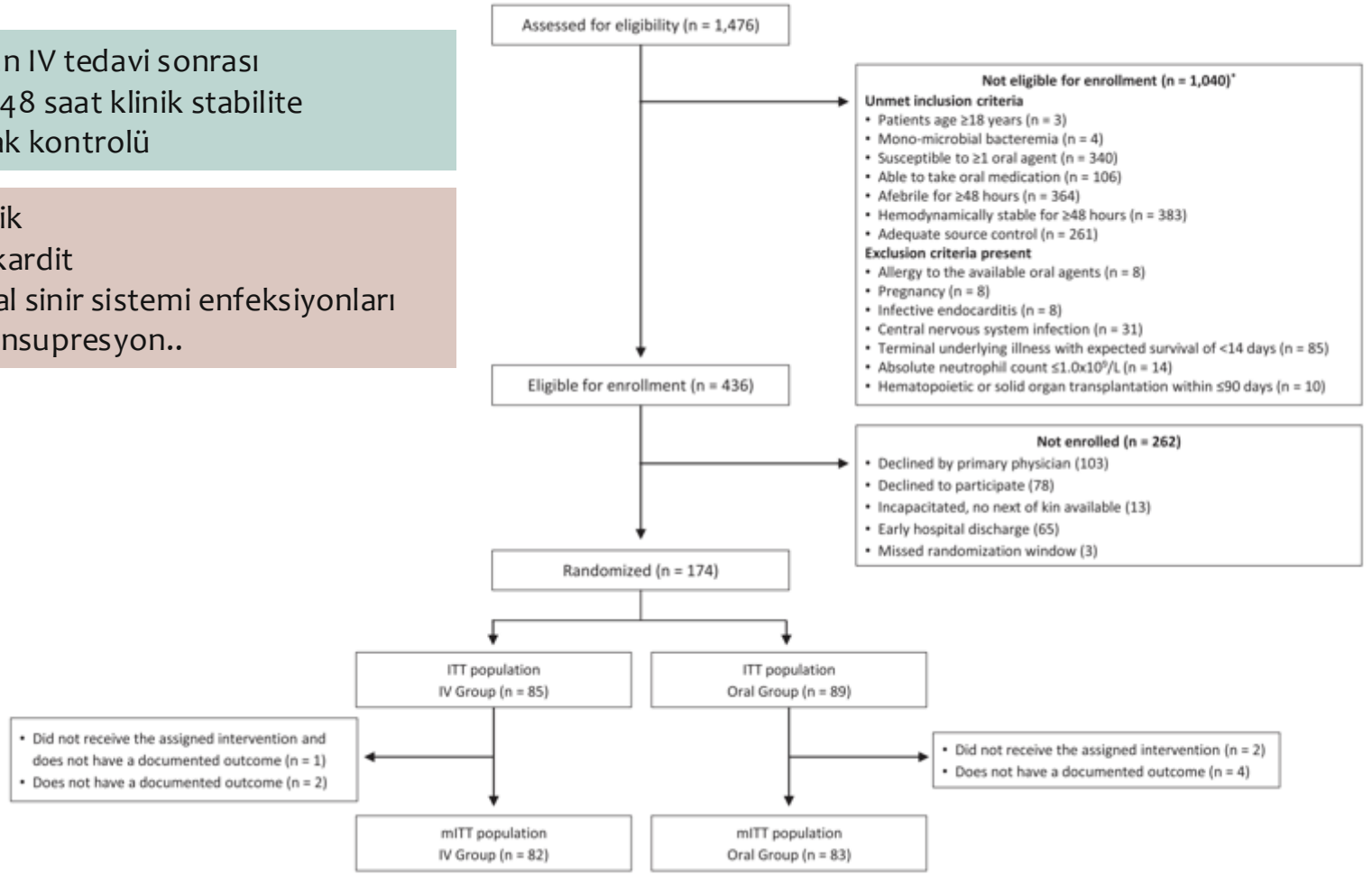
- Açık etiketli, çok merkezli, RKT, 2024
- Oral β-laktam, kinolon ya da TMP-SMX duyarlı monomikrobiyal Enterobacterales bakteriyemi

Table 2
Infection and antimicrobial therapy variables

Variable	IV Group ($n = 85$)	Oral Group ($n = 89$)
Pitt bacteraemia score[a]	1 (0–1)	1 (0–1)
Source of bacteraemia		
Urinary tract	51 (60%)	54 (61%)
Intra-abdominal	14 (16%)	8 (9%)
Biliary	4 (5%)	8 (9%)
Primary bacteraemia	8 (9%)	7 (8%)
Respiratory tract	2 (2%)	8 (9%)
Skin and soft tissue	2 (2%)	0 (0%)
Vascular line	1 (1%)	2 (2%)
Other	3 (4%)	2 (2%)
Enterobacterales species		
E. coli	55 (65%)	61 (69%)
Klebsiella species	22 (26%)	20 (22%)
Enterobacter species	6 (7%)	6 (7%)
Citrobacter species	1 (1%)	0 (0%)
Proteus species	0 (0%)	1 (1%)
Serratia marcescens	1 (1%)	1 (1%)
ESBL-producing organism[b]	17/84 (20%)	11/88 (13%)
Device in place at the time of bacteraemia		
None	67 (80%)[c]	66 (75%)[c]
Urinary device	13 (15%)	12 (14%)
Central venous access	2 (2%)	5 (6%)
Biliary stent or drain	1 (1%)	5 (6%)
Tracheostomy	1 (1%)	0 (0%)
Source control required[d]	18 (21%)	28 (31%)
Days of pre-randomisation active IV antimicrobial therapy[e]	4 (3–5)	4 (3–5)
Pre-randomization antimicrobial therapy[f]		
β-lactam/β-lactamase inhibitor combination	19 (22%)	27 (30%)
Carbapenem	40 (47%)	27 (30%)
Cephalosporin	26 (31%)	34 (38%)
Fluoroquinolone	0 (0%)	1 (1%)
Trimethoprim/sulfamethoxazole	0 (0%)	0 (0%)
Post-randomization antimicrobial therapy[g]		
β-lactam/β-lactamase inhibitor combination	15 (18%)	27 (30%)
Carbapenem	23 (27%)	0 (0%)
Cephalosporin	44 (52%)	31 (35%)
Fluoroquinolone	2 (8%)	17 (19%)
Trimethoprim/sulfamethoxazole	1 (1%)	14 (16%)
Total duration of antimicrobial therapy (d)[e]	11 (8–14)	14 (11–16)

- 3-5 gün IV tedavi sonrası
- En az 48 saat klinik stabilite
- Kaynak kontrolü

- Gebelik
- Endokardit
- Santral sinir sistemi enfeksiyonları
- İmmunsupresyon..



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Original article

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

Kaynak kontrolü ve klinik stabilite varlığında
Enterobacterales bakteriyemi tedavisinde
Orale geçiş IV tedavi devamına göre NON-INFERIOR

Table 3
Primary and secondary outcomes

Outcome	Population	IV Group	Oral Group	Difference (95% CI)[a]
Treatment failure within 90 d	ITT[b]	24 (28.2%)	22 (24.7%)	−3.7% (−16.6% to 9.3%)
	mITT[c]	21 (25.6%)	18 (21.7%)	−3.7% (−16.6% to 9.2%)
90-d all-cause mortality	ITT[b]	6 (7.1%)	7 (7.9%)	0.8% (−7.0% to 8.6%)
	mITT[c]	3 (3.7%)[d]	3 (3.6%)[e]	−0.04% (−5.8% to 5.7%)
Additional antimicrobial therapy	ITT[b]	13 (15.3%)	8 (9.0%)	−6.8% (−16.1% to 2.6%)
	mITT[c]	10 (12.2%)	4 (4.8%)	−7.1% (−15.5% to 1.3%)
Microbiological relapse	ITT[b]	13 (15.3%)	10 (11.2%)	−4.1% (−14.1% to 5.9%)
	mITT[c]	10 (12.2%)	6 (7.2%)	−4.8% (−14.0% to 4.3%)
Infection-related re-admission	ITT[b]	12 (14.1%)	19 (21.3%)	7.2% (−4.0% to 18.3%)
	mITT[c]	9 (11.0%)	15 (18.1%)	7.5% (−3.1% to 18.1%)

ITT, intention-to-treat; IV, intravenous; mITT, modified intention-to-treat.

[a] Group differences expressed as the Oral Group minus the IV Group, adjusted for urinary source of bacteraemia.

[b] ITT IV Group ($n = 85$), Oral Group ($n = 89$).

[c] mITT IV Group ($n = 82$), Oral Group ($n = 83$).

[d] Gastrointestinal bleeding ($n = 1$), COVID-19 ($n = 1$), and cancer ($n = 1$).

[e] End-stage liver disease ($n = 1$), and COVID-19 ($n = 2$).

Pseudomonas spp. bakteriyemisi

Infection (2018) 46:365–373
https://doi.org/10.1007/s15010-018-1131-7

ORIGINAL PAPER

CrossMark

Is fluoroquinolone monotherapy a useful alternative treatment for *Pseudomonas aeruginosa* bacteraemia?

Ping-Feng Wu[1,2] · Yi-Tsung Lin[1,3] · Fu-Der Wang[1,2] · Tsuey-Ching Yang[4] · Chang-Phone Fung[5]

Received: 23 October 2017 / Accepted: 13 March 2018 / Published online: 20 March 2018

- Bakteriyemi tedavisinde β-laktam vs kinolon
- Klinik sonlanımlar benzer

- **Kinolon grubunda hastalar median 6 günden sonra oral tedaviye geçmişler**

antibiotics

MDPI

Article

Beta-Lactam vs. Fluoroquinolone Monotherapy for *Pseudomonas aeruginosa* Infection: A Systematic Review and Meta-Analysis

Eric Reid [1,*], Ryan W. Walters [1] and Christopher J. Destache [1,2]

- Kinolon kullanımı, orale geçiş yapılsa bile β-laktamlardan daha kötü sonuçlara yol açmamış.

STUDY PROTOCOL Open Access

Early oral stepdown antibiotic therapy versus continuing intravenous therapy for uncomplicated Gram-negative bacteraemia (the INVEST trial): study protocol for a multicentre, randomised controlled, open-label, phase III, non-inferiority trial

I. Russel Lee[1*], Steven Y. C. Tong[2], Joshua S. Davis[3], David L. Paterson[4], Sharifah F. Syed-Omar[5], Kwong Ran Peck[6], Doo Ryeon Chung[6], Graham S. Cooke[7], Eshele Anak Libau[1], Siti-Nabilah B. A. Rahman[8], Mihir P. Gandhi[8], Luming Shi[8], Shuwei Zheng[9], Jenna Chaung[10], Seow Yen Tan[11], Shirin Kalimuddin[12,13], Sophia Archuleta[14,15] and David C. Lye[1,15,16,17*]

- Uluslararası, açık etiketli, faz 3, RKT
- Non-inferiority
- 1:1 dağılım
- Primer sonlanım; 30 günlük mortalite
- **Sekonder sonlanım;** Yaşam kalitesi ve kurtarılmış sağlık yıllarının incelendiği **sağlık ekonomisi değerlendirmesi**

Unknown status

Verified 2023-11 by Tan Tock Seng Hospital

Last known status was: Recruiting

Early Oral Step-down Antibiotic Therapy for Uncomplicated Gram-negative Bacteraemia

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, Luis Eduardo López-Cortés, Jesús Rodríguez-Baño, José Miguel Cisneros, M Dolores Navarro, Gerd Fätkenheuer, Norma Jung, Siegbert Rieg, Raphaël Lepeule, Laetitia Coutte, Louis Bernard, Adrien Lemaignen, Katrin Kösters, Colin R MacKenzie, Alex Soriano, Stefan Hagel, Bruno Fantin, Matthieu Lafaurie, Jean-Philippe Talarmin, Aurélien Dinh, Thomas Guimard, David Boutoille, Tobias Welte, Stefan Reuter, Jan Kluytmans, Maria Luisa Martin, Emmanuel Forestier, Hartmut Stocker, Virginie Vitrat, Pierre Tattevin, Anna Rommerskirchen, Marion Noret, Anne Adams, Winfried V Kern, Martin Hellmich, Harald Seifert, for the SABATO study group*

- 31 merkez, 2024
- >5000 hasta taranmış → 213 hasta alınmış
- **Düşük riskli / komplike olmayan SAB**
- 5-7 gün IV tedavi sonrası orale geçiş

Gruplar dengeli
KİKDE / DYDE

MRSA oranı iki grupta da düşük

	Intention-to-treat population		Clinically evaluable population	
	Oral switch group (n=108)	Intravenous group (n=105)	Oral switch group (n=86)	Intravenous group (n=79)
Age, years	64·4 (16·8)	62·6 (17·6)	62·4 (17·1)	62·1 (17·8)
Sex				
Male	71 (66%)	77 (73%)	59 (69%)	58 (73%)
Female	37 (34%)	28 (27%)	27 (31%)	21 (27%)
BMI, kg/m²	27·6 (6·7)	25·6 (5·4)	27·4 (6·5)	26·1 (5·3)
Time in hospital before randomisation, days	10 (7–14)	11 (7–15)	10 (7–13)	10 (7–13)
Intervention to remove or drain infective focus	9 (8%)	14 (13%)	5 (6%)	10 (13%)
Echocardiography (TTE or TEE, or both) performed within 7 days before or after randomisation	69 (64%)	60 (57%); 1	55 (64%)	46 (58%)
CRP at baseline visit, mg/L*	35 (13–70); 13	23 (10–59); 15	35 (14–64); 11	20 (11–52); 13
Resistance of *Staphylococcus aureus* isolate				
Meticillin	6 (6%)	10 (10%)	4 (5%)	5 (6%)
Clindamycin	12 (12%); 4	11 (11%); 5	10 (12%); 4	7 (10%); 5
Co-trimoxazole	1 (1%); 2	3 (3%); 1	0 (0%); 2	2 (3%)
Focus of infection				
Peripheral venous catheter	47 (44%)	46 (44%)	41 (48%)	35 (44%)
Central venous catheter	24 (22%)	25 (24%)	18 (21%)	16 (20%)
Skin and soft-tissue infection	26 (24%)	22 (21%)	19 (22%)	19 (24%)
Other†	5 (5%)	4 (4%)	4 (5%)	3 (4%)
Not identified	6 (6%)	8 (8%)	4 (5%)	6 (8%)
Comorbidities				
Moderate or severe liver disease	11 (10%)	4 (4%)	8 (10%)	2 (3%)
Chronic renal failure	17 (16%); 1	18 (17%)	10 (12%); 1	12 (15%)
End-stage renal disease	9 (8%); 1	5 (5%)	5 (6%); 1	4 (5%)
Chronic lung disease	14 (13%); 1	17 (16%)	10 (12%)	11 (14%)
Diabetes without end-organ damage	25 (23%)	18 (17%)	21 (24%)	11 (14%)
Diabetes with end-organ damage	19 (18%)	10 (10%)	13 (15%)	9 (11%)
Any immunosuppression‡	16 (15%)	16 (15%); 1	12 (14%)	14 (18%); 1
Charlson Comorbidity Index	3 (1–5)	3 (1–4)	2 (1–4)	3 (1–4)
Intravenous antimicrobials before randomisation, days	6 (6–7)	6 (5–7)	7 (6–7)	6 (5–7)

SABATO çalışması

Düşük riskli SAB'ta ayrıntılı klinik değerlendirme ve yakın izlem sağlandığında erken oral geçiş, standart IV tedaviye göre **non-inferior**

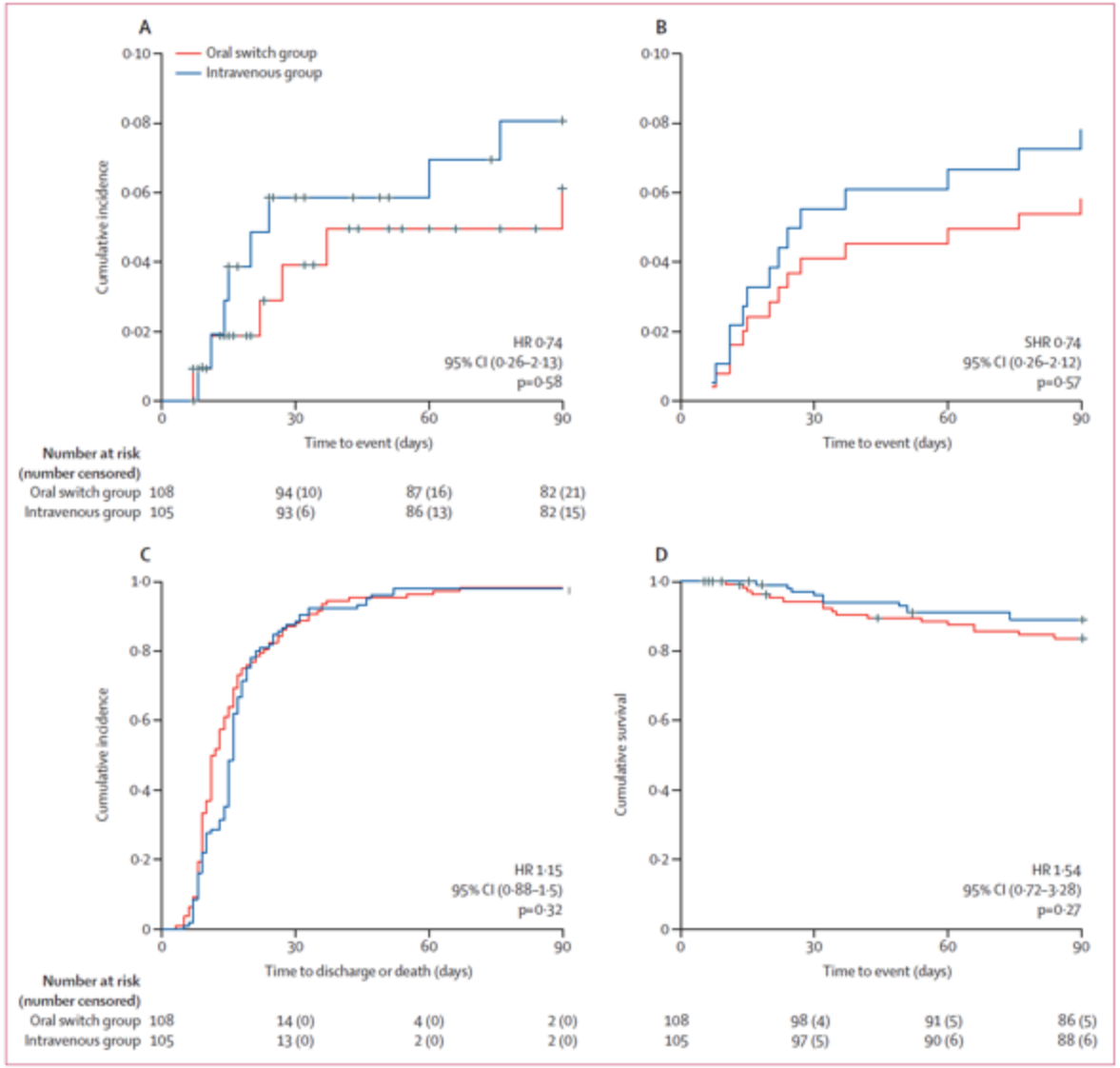


Figure 2: Estimates of cumulative incidence from the date of the first positive blood culture for the intention-to-treat population

	Intention-to-treat population			Clinically evaluable population		
	Oral switch group (n=108)	Intravenous group (n=105)	Percentage-point difference (95% CI)	Oral switch group (n=86)	Intravenous group (n=79)	Percentage-point difference (95% CI)
Primary endpoint						
SAB-related complication within 90 days	14 (13%)	13 (12%)	0·7 (−7·8 to 9·1)	3 (4%)	4 (5%)	−2·9 (−9·6 to 3·9)
Reason primary outcome was met						
SAB-related complication	6 (6%)	8 (8%)	−2·1 (−9·7 to 5·5)	3 (4%)	4 (5%)	−1·6 (−9·0 to 5·8)
Relapsing SAB	3 (3%)	4 (4%)	−1·0 (−6·8 to 4·7)	2 (2%)	2 (3%)	−0·2 (−5·1 to 4·7)
Deep-seated infection with *S aureus*	5 (5%)	8 (8%)	−3·0 (−10·4 to 4·4)	3 (4%)	4 (5%)	−1·6 (−9·0 to 5·8)
Death attributable to SAB	2 (2%)	0	1·9 (−1·6 to 5·3)	1 (1%)	0	1·2 (−2·3 to 4·6)
Missing outcome data	8 (7%)	5 (5%)	2·7 (−4·7 to 10·0)	..	..	..
Attributability of death non-evaluable	3 (3%)	1 (1%)	1·8 (−2·7 to 6·4)	..	..	..
Secondary endpoints						
Length of hospital stay from SAB onset, days	12 (9–19)	16 (10–19)	−2 (−4 to 0); p=0·043*	11 (9–16)	15 (10–18)	−2 (−5 to 0); p=0·020*
Participants with complications of intravenous administration†						
Any complication	9 (9%); 11	17 (17%); 5	−7·9 (−17·6 to 1·9)	6 (7%); 3	13 (17%); 2	−9·5 (−20·5 to 1·5)
Chemical phlebitis	7	9	−2·1 (−10·1 to 5·9)	5	8	−4·3 (−13·8 to 5·2)
Infectious thrombophlebitis or phlebitis	0	2	−1·9 (−5·5 to 1·7)	0	2	−2·5 (−7·2 to 2·2)
Other‡	2	6	−3·9 (−9·9 to 2·2)	1	3	−2·6 (−8·6 to 3·4)
Participants with *Clostridium difficile* infection§	2 (2%); 8	2 (2%); 7	−0·1 (−3·8 to 3·6)	2 (2%); 7	1 (1%); 5	1·1 (−4·0 to 6·1)
Survival						
14 days	98·1% (1·3); 2	100·0% (0); 0	−1·9 (−4·5 to 0·7)	98·8% (1·2); 1	100·0% (0); 0	−1·2 (−3·4 to 1·1)
30 days	94·3% (2·3); 6	96·0% (2·0); 4	−1·7 (−7·6 to 4·2)	98·8% (1·2); 1	98·7% (1·3); 1	0·1 (−3·3 to 3·5)
90 days	83·6% (3·6); 17	89·0% (3·1); 11	−5·4 (−14·8 to 4·0)	92·9% (2·8); 6	94·8% (2·5); 4	−1·9 (−9·3 to 5·5)

Data are n (%), median (IQR), n (%); missing, or Kaplan-Meier estimate (SE); number of deaths, unless specified otherwise. SAB=*Staphylococcus aureus* bloodstream infection. *Data are median difference (95% CI). †Complications of intravenous administrations might be caused by study drug or other intravenous medications. ‡In the intention-to-treat population, other complications of intravenous therapy were haematoma (n=1) and inflammation at a previous peripheral catheter insertion site (n=1) in the oral switch group and extravasation (n=1), refusal of renewed catheter placement (n=3), and clogged intravenous access (n=2) in the intravenous group. §Missing participants were those with diarrhoea that did not undergo *C difficile* testing and were considered negative for statistical analysis.

Table 2: Primary and secondary outcome variables for the intention-to-treat and clinically evaluable populations

Open Forum Infectious Diseases
REVIEW ARTICLE

A Narrative Review of Early Oral Stepdown Therapy for the Treatment of Uncomplicated *Staphylococcus aureus* Bacteremia: Yay or Nay?

Michael Dagher,[1] Vance G. Fowler Jr.,[1] Patty W. Wright,[2] and Milner B. Staub[2,3]

[1]Division of Infectious Diseases, Duke University School of Medicine, Durham, North Carolina, USA, [2]Division of Infectious Diseases, Vanderbilt University Medical Center, Nashville, Tennessee, USA, and [3]Geriatric Research, Education and Clinical Center (GRECC), Tennessee Valley Healthcare System, Veterans Health Administration, Nashville, Tennessee, USA

Unkomplike SAB

- İlk kan kxden 48-96 saat sonra alınan takip kan kültürlerinin negatif olması
- Uygun tedavi sonrası 72 saat içinde ateşin düşmesi
- İE ekartasyonu
- Protez/implante cihazların bulunmaması
- Metastatik enfeksiyon odaklarının olmaması

Table 2. Details of Study Arms, Outcomes, and Antibiotic Administration for Published Studies Describing Oral Antibiotic Therapy for *S. aureus* Bacteremia

Author & Year	Study Arm	Study Arm Outcome	Standard Therapy Arm	Standard Therapy Outcome	Outcome Analysis	Days IV Before PO Switch
Linezolid						
Stevens et al. [29] 2002	Linezolid 600 mg IV twice daily → change to linezolid 600 mg PO twice daily at investigator discretion, at least 7 days	9/15 (60.0%) of evaluable MRSA bacteremia achieved clinical cure	Vancomycin 1 g IV twice daily	7/10 (70.0%) of evaluable MRSA bacteremia achieved clinical cure	—	Specific inform… linezolid ro… istration o… not given
Moise et al. [30] 2002	Linezolid oral or IV 600 mg twice daily (adult); 10 mg/kg oral or IV (pediatric or <40 kg)	18/21 (85.7%) clinically evaluable bacteremic patients achieved clinical cure	—			
Birmingham et al. [31] 2003	Linezolid oral or IV 600 mg twice daily (adult); 10 mg/kg oral or IV (pediatric or <40 kg)	16/31 evaluable; 12/16 (63.2%) achieved clinical cure; 10/14 (71.4%) microbiological cure	—			
Wilcox et al. [32] 2004	Linezolid (IV→PO) 600 mg twice daily	13/15 (86.7%) SAB patients achieved clinical cure with linezolid	Teicoplanin (IV→IM)	9/18 (50% … ical cu…		
Shorr et al. [33] 2005	Linezolid IV or IV→PO 600 mg twice daily	28/74 (36%) of ITT SAB achieved clinical cure; 14/25 (56%) of evaluable MRSA bacteremia achieved clinical cure; 41/59 (69%) achieved microbiological cure	Vancomycin 1 g IV twice daily	25/70 (36… ical cu… remia … (73%)		
Wilcox et al. [34] 2009	Linezolid 600 mg (route not specified)	38/52 (75.0%) SAB and 22/25 (88.0%) MRSA bacteremia achieved clinical cure; 46/56 (82.1%) SAB; 21/26 (80.8%) MRSA bacteremia achieved microbiological cure	Vancomycin 1 g twice daily with option to change to oxacillin 2 g IV or dicloxacillin 500 mg oral every 6 hours for MSSA	29/42(69… MRSA bacteremia achieved clinical cure; 35/42 (83.3%) SAB; 18/21 (85.7%) MRSA bacteremia achieved microbiological cure	was −12.3 to 24.2 for MRSA bacteremia, −10.4 to 34.0 for SAB, −16.3 to 13.9 for MRSA bacteremia, −26.2 to 16.4 for microbiological cure; *P* values for these analyses not provided	linezolid route of administration or duration was not given for SAB patients
Usery et al. [35] 2015	Linezolid 600 mg twice daily (IV or PO not specified)	12/15 (80%) had complicated bacteremia; 9/15 (60%) achieved clinical cure; 14/14 linezolid (100%) achieved microbiological cure; 6/15 (40%) linezolid died	Vancomycin IV	48/54 (88.9%) of vancomycin and 51/53 (96.2%) daptomycin patients had complicated bacteremia; 31/53 (58.5%) daptomycin and 33/54 (61.1%) vancomycin achieved clinical cure; 44/47 (93.56%) daptomycin and 45/50 (90%) vancomycin achieved microbiological cure; 10/53 (18.9%) daptomycin and 5/54 (9.3%) vancomycin died	*P* = .9624 for clinical cure; *P* = .6777 for microbiological cure; *P* = .0186 for mortality	—

Statik?
ama
Yüksek biyoyararlanım**

LİNEZOLİD

Unkomplike SAB tedavisine klinik ve mikrobiyolojik kür

IV tedavi sonrası linezoild PO verilen hastalar
NON-İNFERİOR
Tedavisi parenteral tamamlanan hastalar

Open Forum Infectious Diseases
REVIEW ARTICLE

A Narrative Review of Early Oral Stepdown Therapy for the Treatment of Uncomplicated *Staphylococcus aureus* Bacteremia: Yay or Nay?

Michael Dagher,[1] Vance G. Fowler Jr.,[1] Patty W. Wright,[2] and Milner B. Staub[2,3]
[1]Division of Infectious Diseases, Duke University School of Medicine, Durham, North Carolina, USA, [2]Division of Infectious Diseases, Vanderbilt University Medical Center, Nashville, Tennessee, USA, and [3]Geriatric Research, Education and Clinical Center (GRECC), Tennessee Valley Healthcare System, Veterans Health Administration, Nashville, Tennessee, USA

Unkomplike SAB

- IVOS → Kinolon yada kinolon+rif
  - Kanıtlar linezolid çalışmaları kadar güçlü değil
  - Sekonder sonlanımlar yeterince değerlendirilmemiş
  - **Kinolonlar için monoterapide direnç gelişim ihtimali !!**

Linezolid ya da konvansiyonel IV tedaviyi tolere edemeyen hastalarda kinolon+ rifampisin alternatif olabilir!

			IV for MRSA			
Fluoroquinolones						
Bouza et al. [37] 1989	Ciprofloxacin IV, IV→ PO or PO; for IV, doses ranged from 200 to 400 mg daily; for PO, doses ranged from 1000 to 1500 mg daily	2/2 (100%) achieved clinical cure	—	—	—	
Dworkin et al. [8] 1989	Ciprofloxacin 300 mg IV + rifampicin 300 mg PO twice daily for 7 days changed to ciprofloxacin 750 mg PO + rifampicin 300 mg PO twice daily for 21 days	5 patients were lost to follow-up without record of readmission; 5 patients readmitted with other infections or re-infection	—	—	95% CI for clinical 76%–100%	ays
Heldman et al. [9] 1996	Ciprofloxacin 750 mg PO + rifampin 300 mg PO twice daily	18/19 (94.7%) achieved microbiological cure	Oxacillin 2 g IV every 4 hours or vancomycin 1 g IV twice daily + gentamicin IV for first 5 days	22/25 (80.0%) achieved microbiological cure	Odds ratio for microbiological treatment failure (oral vs SPT) was 0.4 (95% CI, 0.01 to 5.5; $P = .6$)	Oral ciprofloxacin + rifampin began on admission
Schrenzel et al. [38] 2004	Fleroxacin 400 mg PO daily + rifampicin 600 mg PO daily	15/19 (79%) catheter-related SAB; 10/11 (91%) primary SAB achieved clinical cure; 15/19 (79%) catheter-related SAB and 10/10 (100%) primary SAB achieved microbiological cure	Flucloxacillin 2 g IV every 6 hours or vancomycin 1 g IV twice daily	10/11 (91%) catheter-related SAB, 4/5 (80%) primary SAB achieved clinical cure; 9/10 (90%) catheter-related SAB and 5/5 (100%) primary SAB achieved microbiological cure	Relative risk was 0.8 (95% CI, 0.4 to 1.3; $P = .81$), 1.4 (95% CI, 0.3 to 5.9; $P = .54$), 0.8 (95% CI, 0.5 to 1.3; $P = .63$), and undefined ($P = .33$)	Fleroxacin + rifampicin oral therapy was started on admission or after up to 24 hours of IV fleroxacin + rifampin therapy
Beganovic et al. [39] 2019	Levofloxacin or moxifloxacin (administration route and dose unknown)	Of 32 patients for whom patient characteristics were balanced, there was no difference in time to mortality	Nafcillin, oxacillin, or cefazolin IV (dose unknown)	Of 32 patients for which patient characteristics were balanced, there was no difference in time to mortality	Hazard ratio of 1.33, with 95% CI of 0.30 to 5.96	Specific information about levofloxacin or moxifloxacin route of administration or duration was not given

S. aureus bakteriyemilerinde (SAB) oral tedaviye geçiş

- Öneriler unkomplike SAB için
  - Unkomplike / komplike ayrımı?
  - Unkomplike tanımı ne kadar güçlü?
  - Sonradan saptanan metastatik odaklar?
    - *Rassumen ve ark.* → RKT, unkomplike değerlendirilen hastaların 1/3'ünde sonradan fark edilen metastatik odaklar
    - Görüntüleme yöntemleri yeterli mi?

SAB'ta sorun oral tedaviye geçiş değil;
Hastanın 'unkomplike' olmadığını güvenle söyleyememek

Clinical Infectious Diseases
MAJOR ARTICLE

Early Oral Antibiotic Switch in *Staphylococcus aureus* Bacteraemia: The *Staphylococcus aureus* Network Adaptive Platform (SNAP) Trial Early Oral Switch Protocol

Dana de Kretser,[1,a] Jocelyn Mora,[2,a] Max Bloomfield,[3,a] Anita Campbell,[4,a] Matthew P. Cheng,[5,a,b] Stephen Guy,[6,7,a] Marjolein Hensgens,[8,9,a,b] Shirin Kalimuddin,[10,11,a] Todd C. Lee,[12,a,b] Amy Legg,[13,14,a] Robert K. Mahar,[15,16,a] Michael Marks,[17,18,19,a] Julie Marsh,[20,a,b] Anna McGlothin,[21,a,b] Susan C. Morpeth,[22,a,b] Archana Sud,[23,a] Jaap Ten Oever,[24,a] Dafna Yahav,[25,a,b] Marc Bonten,[8,b] Asha C. Bowen,[20,b] Nick Daneman,[26,b] Sebastiaan J. van Hal,[27,28,b] George S. Heriot,[2,b] Roger J. Lewis,[21,b] David C. Lye,[29,30,31,32,b] Zoe McQuilten,[7,33,b] David L. Paterson,[34,b] J. Owen Robinson,[35,36,37,38,b] Jason A. Roberts,[14,34,39,40,41,b] Matthew Scarborough,[42,b] Steve A. Webb,[42,b] Lynda Whiteway,[5] Steven Y. C. Tong,[2,43,a,b] Joshua S. Davis,[44,a,b] Genevieve Walls,[22,a,b,c] Anna L. Goodman,[1,42,45,a,b,c]; the SNAP Early Oral Switch Domain-Specific Working Group[a] and SNAP Global Trial Steering Committee[b] for the SNAP Trial Group

- Klinik stabil SAB hastaları
- 77 merkez, hedef ≥1000 katılımcı
- Primer sonlanım; 90 günlük mortalite

- **Komplike** ve unkomplike SAB
- Antibiyotik seçimi
- Kombinasyon tedavisi..

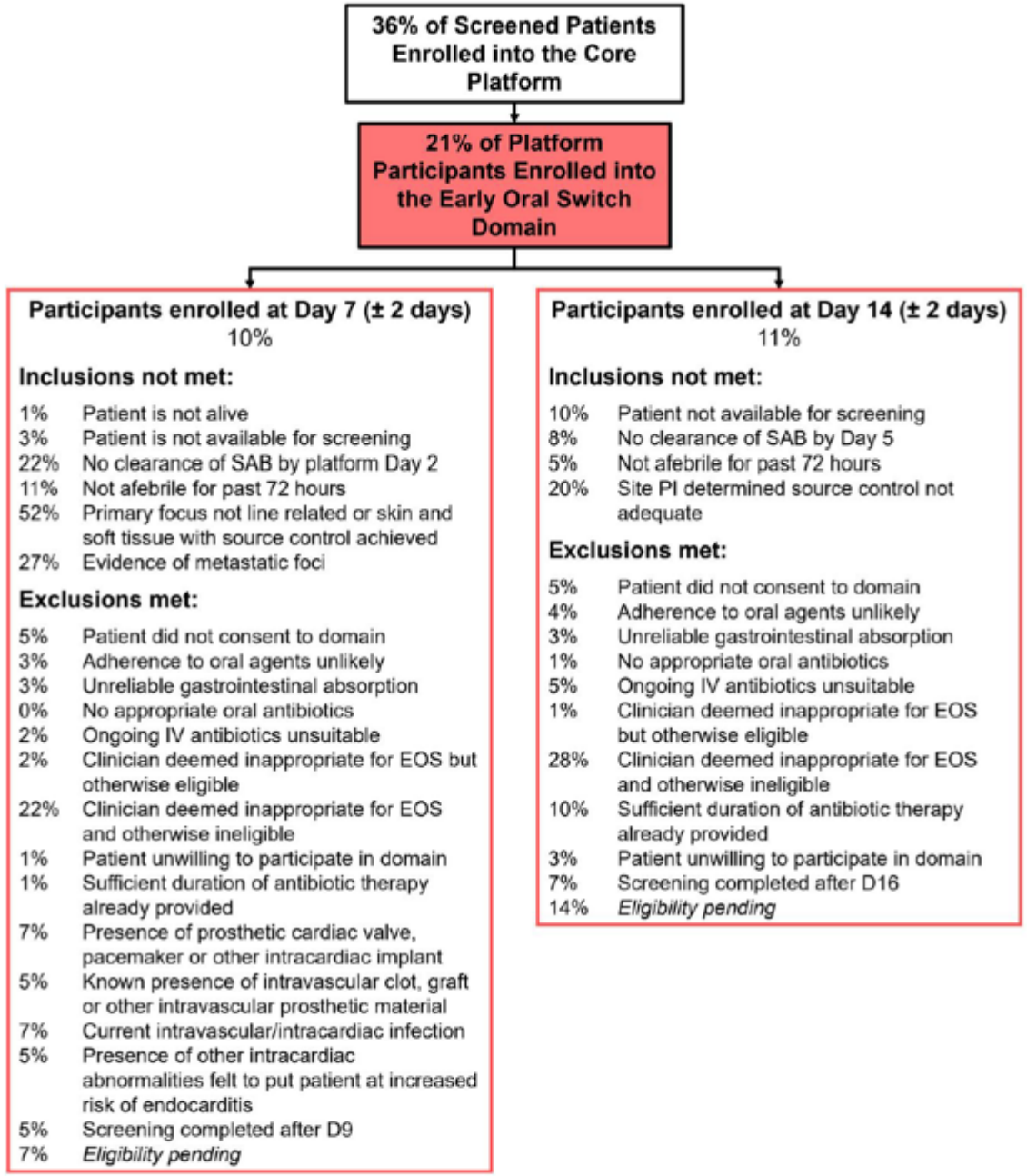


Figure 1. SNAP CONSORT as of 21 August 2023. Abbreviations: CONSORT, Consolidated Standards of Reporting Trials; EOS, early oral switch; IV, intravenous; PI, principal investigator; SAB, *S. aureus* bacteraemia; SNAP, *S. aureus* Network Adaptive Platform.

JAC Antimicrob Resist
https://doi.org/10.1093/jacamr/dlaf004

JAC-Antimicrobial Resistance

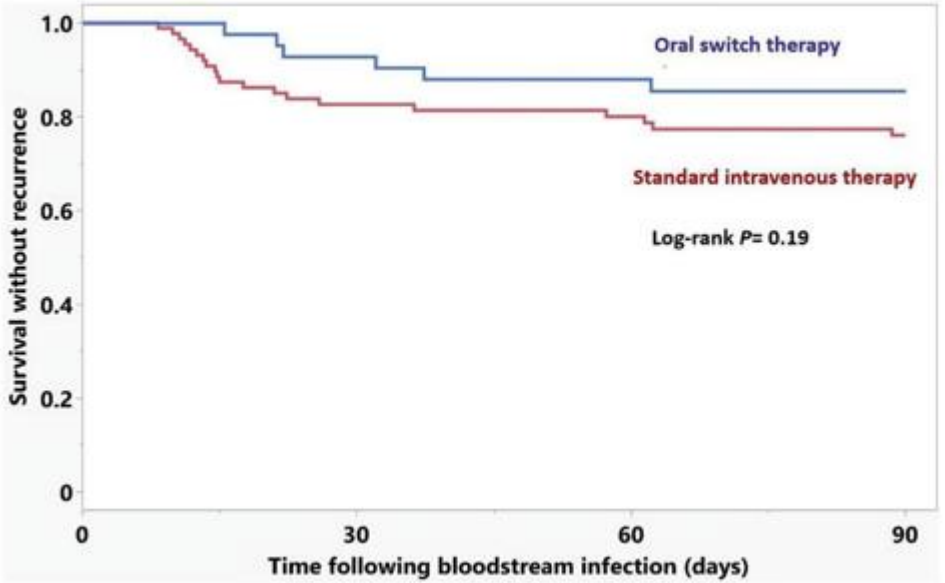
Oral switch antibiotic therapy in uncomplicated *Enterococcus faecalis* bloodstream infection

Sarah Al Mansi [1,2*], Margaret Pokalsky[1], Katherine Turnley[1], Andrew Freeman[1], P. Brandon Bookstaver [3,4], Joseph Kohn[4], Hana R. Winders [4], Sarah Withers[5] and Majdi N. Al-Hasan [1,2]

[1]University of South Carolina School of Medicine, Columbia, SC 20203, USA; [2]Department of Internal Medicine, Division of Infectious Diseases, Prisma Health Midlands, Columbia, SC, USA; [3]Department of Clinical Pharmacy and Outcomes Science, University of South Carolina College of Pharmacy, Columbia, SC, USA; [4]Department of Pharmacy, Prisma Health Midlands, Columbia, SC, USA; [5]Department of Pharmacy, Prisma Health Upstate, Greenville, SC, USA

- 131 unkomplike *E. faecalis* bakteriyemisi
- Üriner odak → %35

- Tüm nedenlere bağlı mortalite ve tedavi başarısızlık oranları arasında FARK YOK



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. Fosbøl, 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.

- Randomize, çok merkezli, noninferiorite
- Stabil kliniği olan 400 sol kalp endokarditi
  - *Streptococus* spp.
  - *E. faecalis*
  - *S. aureus*
  - KNS

MRSA yok*

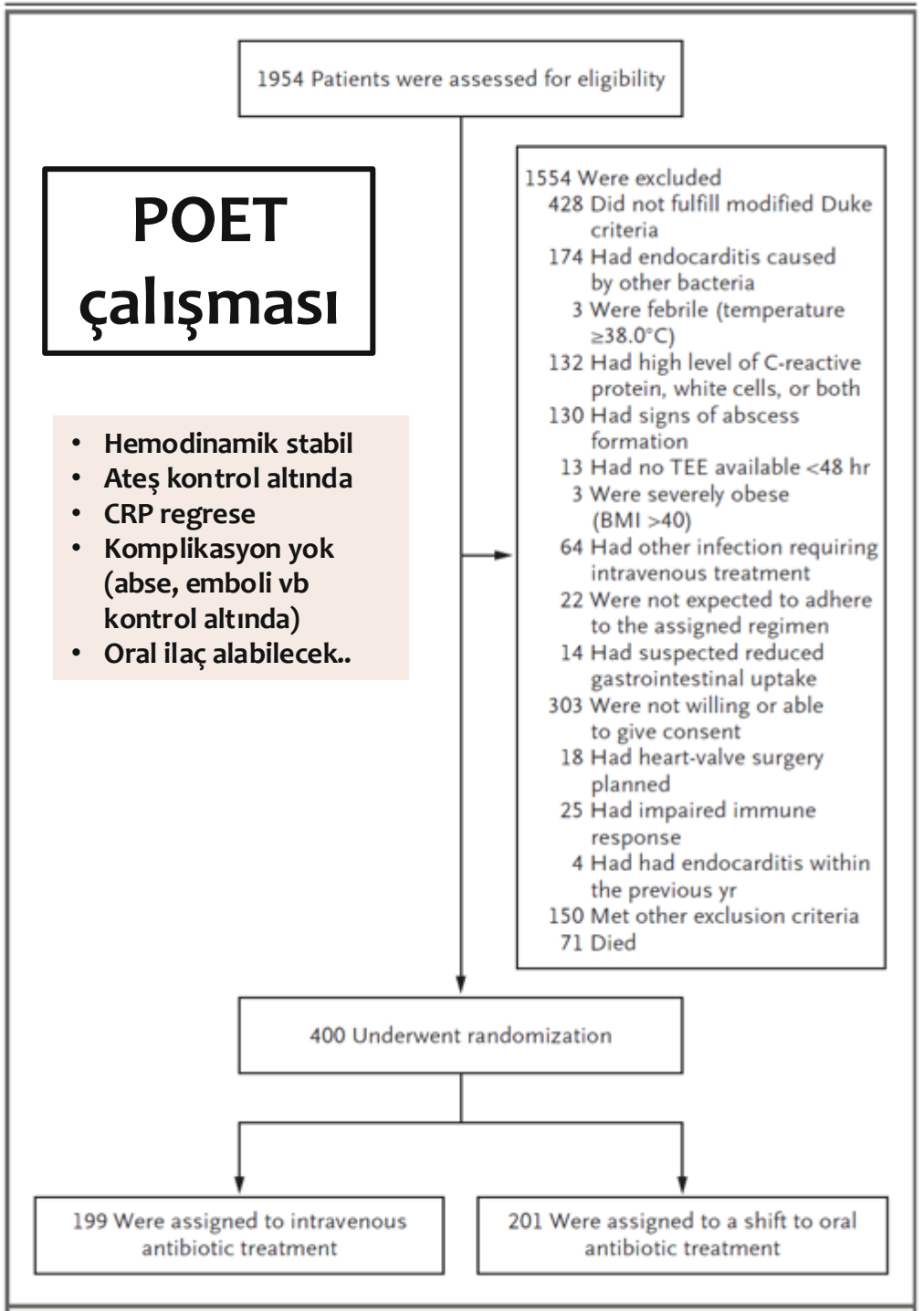
- En az 10 gün IV tedavi → oral (201 hasta)
  - Biyoyararlanımı iyi ajanlar (amox+rif, LNZ, moksif.)

- **Primer sonlanım**
  - Tüm nedenlere bağlı mortalite
  - Planlanmayan kardiyak cerrahi
  - Embolik olaylar
  - Primer patojenle bakteriyemi relapsı

} Tedavi tamamlandıktan sonra 6 ay takip

POET çalışması

- **Hemodinamik stabil**
- **Ateş kontrol altında**
- **CRP regrese**
- **Komplikasyon yok (abse, emboli vb kontrol altında)**
- **Oral ilaç alabilecek..**



POET çalışması

IV vs IVOS

Mortalite ve relapsta FARK YOK

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)

* Six patients, three in each group, had two outcomes.
† For details about relapse of the positive blood culture, see the Supplementary Appendix.

KISITLILIKLAR

- Çok seçilmiş hasta grubu
- MRSA yok
- Kritik hasta yok
- Danimarka modeli → ayaktan hastaya da çok yakın takip

PRATİK DEĞİŞTİREN ÇALIŞMA!

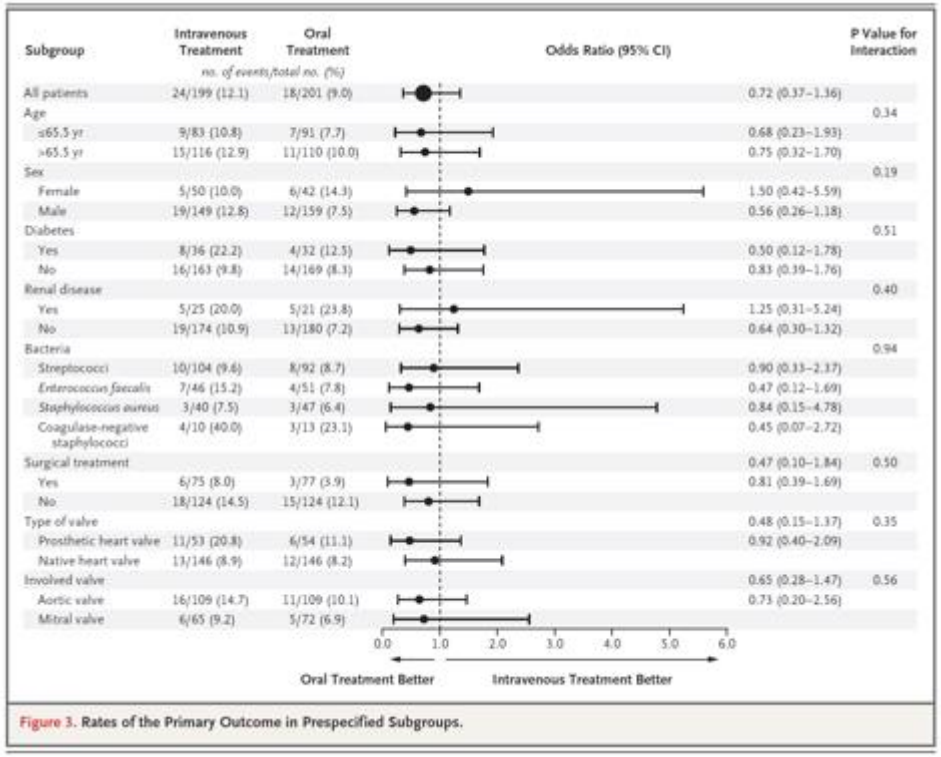


Figure 3. Rates of the Primary Outcome in Prespecified Subgroups.

ESC European Society of Cardiology
European Heart Journal (2023) **44**, 3948–4042
https://doi.org/10.1093/eurheartj/ehad193

2023 ESC Guidelines for the management of endocarditis

Developed by the task force on the management of endocarditis of the European Society of Cardiology (ESC)

Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Nuclear Medicine (EANM)

Table S9 Combinations of antibiotics for oral step-down treatment

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

CoNS, coagulase-negative staphylococci.

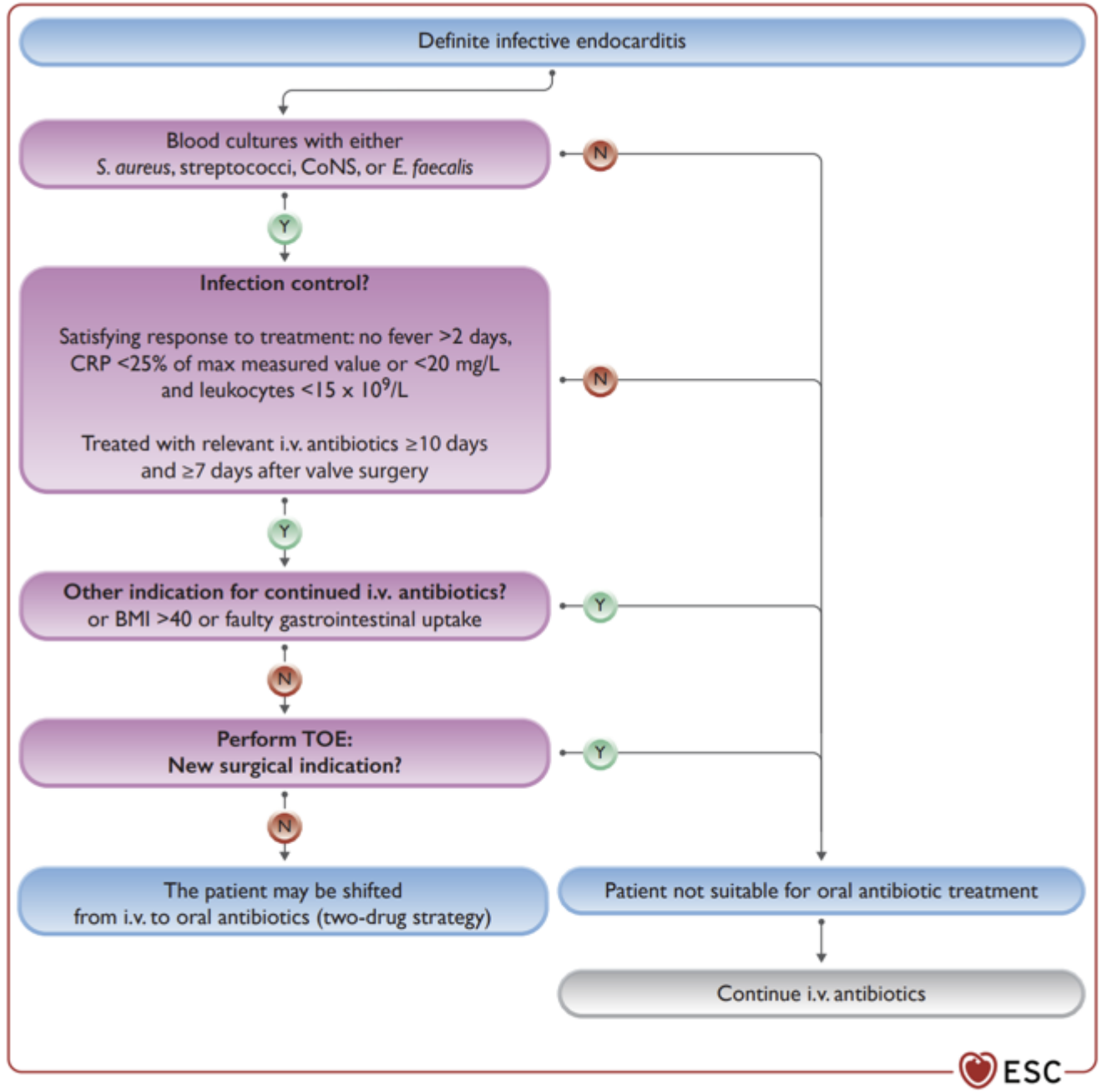


Figure 9 Flowchart to assess clinical stability based on the Partial Oral Treatment of Endocarditis trial. BMI, body mass index; CoNS, coagulase-negative staphylococci; CRP, C-reactive protein; i.v., intravenous; TOE, transoesophageal echocardiography. Adapted with permission from Iversen *et al.*[43]

POET ve ESC rehberi sonrası gerçek yaşam verileri ne diyor?

JAC Antimicrob Resist
https://doi.org/10.1093/jacamr/dlaf032

JAC-Antimicrobial Resistance

Switching from intravenous to oral antibiotic therapy in the treatment of infective endocarditis: a case series and literature review of real-world data

Lorenzo Brando Lundgren [1†], Lorenzo Albertini [1†], Anna De Bona[1], Camilla Tincati [1], Matteo Augello [1*] and Giulia Marchetti [1]

Table 3. Observational studies assessing the switch to partial oral

Study (year)	Study design (country)	Population	Sample size
Dworkin *et al.* (1989)[10]	Pilot non-randomized clinical trial (USA)	Definite right-side endocarditis in PWID	14
Colli *et al.* (2007)[9]	Retrospective observational study (Italy)	Definite left-side IE after cardiac surgery	14
Dernonchy *et al.* (2011)[8]	Retrospective observational study (France)	Definite or possible IE	66 [POT (19) ver IV (47)]
Mzabi *et al.* (2016)[7]	Retrospective observational study (France)	Definite or possible IE	426 [POT (214) versus IV (21
Tissot-Dupont *et al.* (2019)[6]	Retrospective observational	Definite *S. aureus* IE	341 [POT (171) versus IV (17
Marks *et al.* (2020)[11]			
Lewis *et al.* (2022)[14]	study (USA)	including endocarditis	
Wildenthal *et al.* (2022)[15]	Retrospective observational study (USA)	Complicated *S. aureus* bacteraemia and incident IE in PWID	238 (154 IE) [partial IV (22 versus POT (3 versus total I (90)]

Table 4. Case series/reports assessing the switch to partial oral antibiotic therapy in the treatment of IE

Study (year)	Patients (*n*)	Age (years)	Male sex, *n*, (%)	CCI (median) or comorbidities	Surgery (%)	Type of IE	Complications, *n* (%)	Aetiology (*n*)	IV therapy (days)	POT (days)	Total therapy (days)			
Miller *et al.* (2022)[20]	11	Median: 32	7 (63.6)	0	5 (55)	NVIE (4), PVIE (7)	7 (77)	MSSA (3), viridans group streptococci (3), *E. faecalis* (2), negative bacterial culture (2), *Candida albicans* (1)	Median: 13 (IQR: 4–22)	Median: 23 (IQR: 12–38)	N/A			
Parker and Fossieck (1980)[21]	35	Median: 31	35 (100)	Unknown; 29 (93%) were PWID	0	NVIE (35)	0	MSSA (35)	Mean: 16.4 (SD: 4–33)	Mean: 26 (SD: 14–58)	Mean: 42.4 (SD: 34–69)	clindamycin, penicillin V		
Attanasio *et al.* (2020)[22]	5	Median: 61	4 (80)	2	0	PVIE (5)	4 (80)	*E. faecalis* (5)	Median: 28 (IQR: 18–41)	Median: 120 (IQR: 78–174)	N/A	Amoxicillin/clavulanate (5), cefditoren (5)	Cured at discharge and negative FU (6 months)	Unknown
Alsaeed *et al.* (2023)[23]	1	17	1 (100)	0	0	NVIE	1	MSSA	17	51	68	Linezolid, rifampicin	Cured at discharge and negative FU (6 months)	Patient's family decision
Archuleta	1	64	1	5 (HIV/HCV coinfection	0	NVIE	0	VRE	17	25	42	Linezolid	Cured at	Unknown
Colkesen (2021)[26]	1	83	0 (0)	4	0	NVIE	0	MSSA	14	28	42	Moxifloxacin	Cured at discharge and negative FU (6 months)	Unknown
Guntheroth (1984)[27]	1	23	0 (0)	2 (cognitive deficit, ventricular septal defect)	0	NVIE	0	*Streptococcus sanguinis*	0	30	30	Amoxicillin	Cured at discharge and negative FU (12 months)	Patient and family's wish
Mahmoud *et al.* (2020)[28]	1	65	1 (100)	4 (chronic kidney disease, ischaemic and valvular heart disease)	0	PVIE	1	*E. faecalis*	0	365	365	Amoxicillin/clavulanate	Cured at discharge and negative FU (12 months)	Patient's wish

MRSA endokarditi
Sağ kapak endokarditi
Komplike olgular..
Gram-negatifler yok

Gerçek yaşam koşullarında klinik stabil olan İE hastalarında oral tedaviye geçiş etkili ve güvenlidir.

Daha kısa hastane yatış süreleri, yaşam kalite artışı ve maliyetin azalması ile de ilişkilidir.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Oral versus Intravenous Antibiotics for Bone and Joint Infection

OVIVA

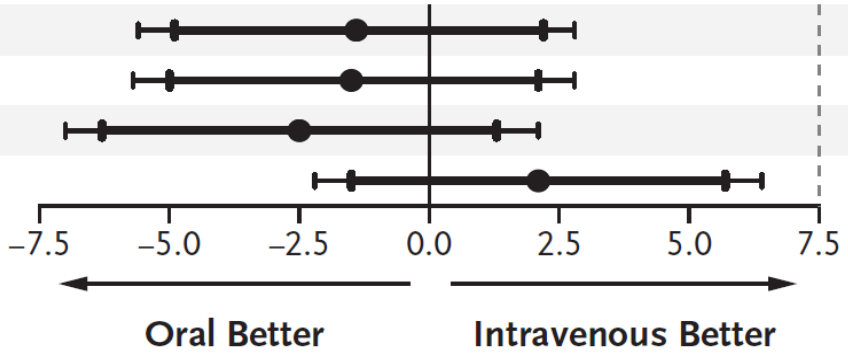
- RKT, açık etiketli, noninferiorite, 2019
- 1015 hasta
- Tedavi grupları
  - Oral → tedavi başlangıcı veya cerrahiden 7 gün sonra orale geçiş
  - IV → 6 hafta boyunca IV
- Primer sonlanım noktası; randomizasyondan 1 yıl sonra tedavi başarısızlığı

Figure 1. Enrollment, Randomizati

Table 1. Baseline Characteristics of the Trial Participants.*

Characteristic	Intravenous Group (N=527)	Oral Group (N=527)	Total (N=1054)
Age — yr			
Median (interquartile range)	61 (49–70)	60 (49–70)	60 (49–70)
Range	18–92	18–91	18–92
Male sex — no. (%)	320 (60.7)	358 (67.9)	678 (64.3)
Baseline surgical procedure — no. (%)			
No implant or device present; débridement of chronic osteomyelitis performed	153 (29.0)	169 (32.1)	322 (30.6)
No implant or device present; débridement of chronic osteomyelitis not performed	25 (4.7)	29 (5.5)	54 (5.1)
Débridement and implant retention	124 (23.5)	123 (23.3)	247 (23.4)
Removal of orthopedic device for infection	89 (16.9)	78 (14.8)	167 (15.8)
Prosthetic joint implant removed	68 (12.9)	67 (12.7)	135 (12.8)
Prosthetic joint implant, one-stage revision	47 (8.9)	43 (8.2)	90 (8.5)
Surgery for diskitis, spinal osteomyelitis, or epidural abscess; débridement performed	8 (1.5)	5 (0.9)	13 (1.2)
Surgery for diskitis, spinal osteomyelitis, or epidural abscess; débridement not performed	13 (2.5)	13 (2.5)	26 (2.5)
Deep-tissue histologic result — no. (%)			
Infected	266 (50.5)	277 (52.6)	543 (51.5)
Equivocal	13 (2.5)	17 (3.2)	30 (2.8)
Uninfected	31 (5.9)	32 (6.1)	63 (6.0)
Not done or missing†	217 (41.2)	201 (38.1)	418 (39.7)
Microbiologic diagnostic sampling — no. (%)			
Two or more samples positive for same organism	357 (67.7)	338 (64.1)	695 (65.9)
Two or more samples taken but only one positive for a given pathogenic organism	20 (3.8)	32 (6.1)	52 (4.9)
Only one sample taken, which was found to be positive for a pathogenic organism by closed biopsy	25 (4.7)	30 (5.7)	55 (5.2)
Two or more samples taken but only one positive for a given nonpathogenic organism	21 (4.0)	25 (4.7)	46 (4.4)
Sampling undertaken but no organisms identified	77 (14.6)	78 (14.8)	155 (14.7)
Not done or missing‡	27 (5.1)	24 (4.6)	51 (4.8)
Organisms identified — no./total no. (%)§			
Staphylococcus aureus MRSA da var	196/500 (39.2)	182/503 (36.2)	378/1003 (37.7)
Coagulase-negative staphylococcus	137/500 (27.4)	135/503 (26.8)	272/1003 (27.1)
Streptococcus species	72/500 (14.4)	73/503 (14.5)	145/1003 (14.5)
Pseudomonas species	28/500 (5.6)	23/503 (4.6)	51/1003 (5.1)
Other gram-negative organisms	84/500 (16.8)	84/503 (16.7)	168/1003 (16.7)
Culture negative	77/500 (15.4)	78/503 (15.5)	155/1003 (15.5)

Subgroup	Oral Group	Intravenous Group	Risk Difference (90% CI; 95% CI)
	patients with treatment failure/ total no. of participants		
Intention-to-treat population	70.0/527	77.3/527	−1.4 (−4.9 to 2.2; −5.6 to 2.9)
Modified intention-to-treat population	67/509	74/506	−1.5 (−5.0 to 2.1; −5.7 to 2.8)
Per-protocol population	61/466	69/443	−2.5 (−6.3 to 1.3; −7.0 to 2.1)
Worst-case sensitivity analysis	85/527	74/527	2.1 (−1.5 to 5.7; −2.2 to 6.4)



Eksik verileri olan katılımcılar için;

- IVOS grubunun tümünde **tedavi başarısızlığı olduğu**
- IV grubunun hiçbirinde **tedavi başarısızlığı olmadığı** varsayılmış

ORAL STRATEJİYE AİT EN KÖTÜ ALTERNATİF

Oral tedaviler;

- Yüksek biyoyararlanım
- İyi kemik penetrasyonu
- Çoğunlukla kombinasyon rejimleri

NON-İNFERİOR

6 haftalık IV tedavi

****Yabancı cisim retansiyonu ya da patojen özelinde alt grup analizlerinde de sonuçlar benzer**

Oral tedavi → Daha kısa hastane yatışı ve daha az komplikasyon

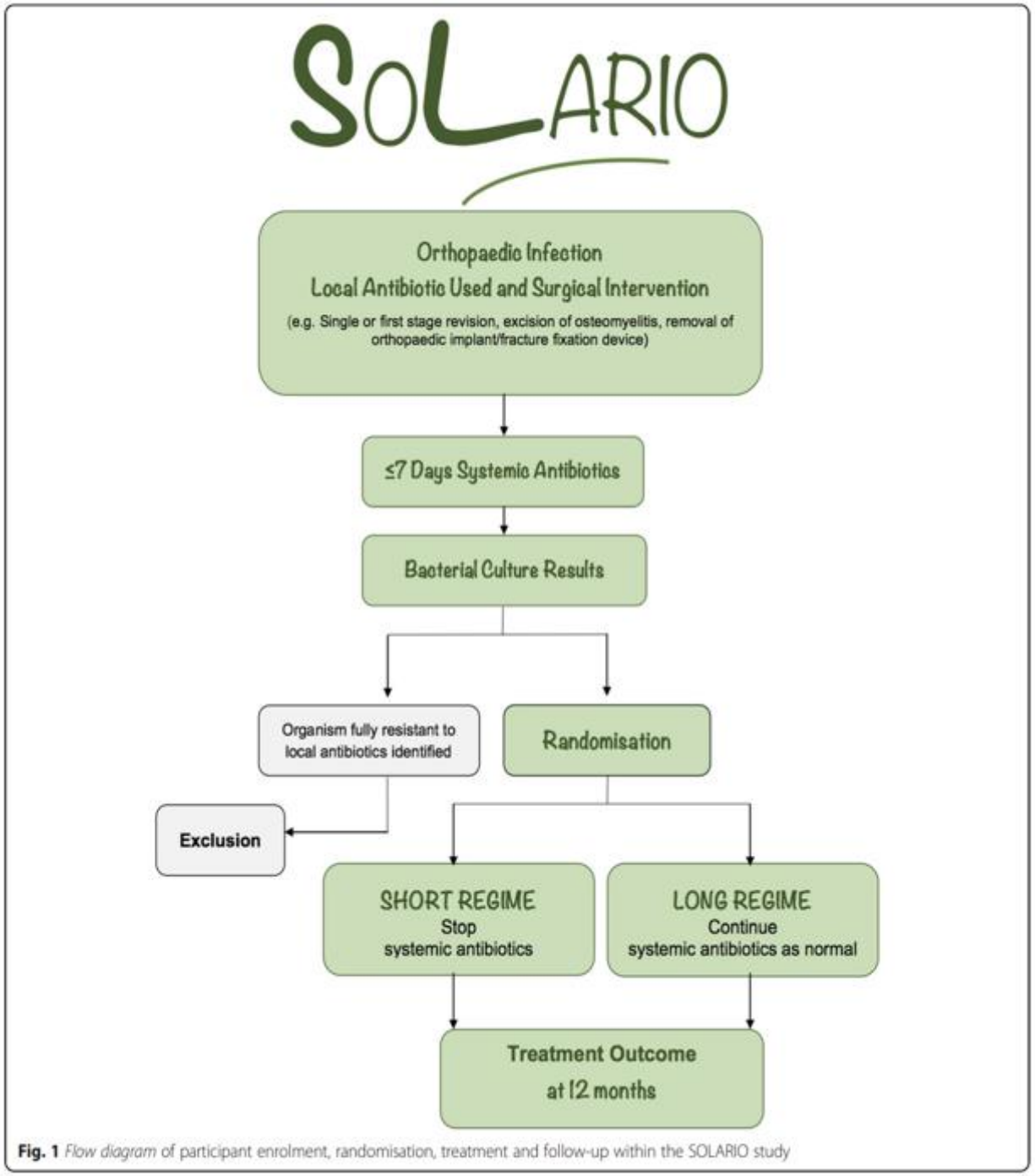


Fig. 1 *Flow diagram* of participant enrolment, randomisation, treatment and follow-up within the SOLARIO study

- RKT, açık etiketli, çok merkezli, non-inferiorite
- ESCMID Global 2026,
  - Yayınlanmamış sonuçlar, Marjan Wouthuyzen-Bakker
  - 500 hasta
  - Protez enf, septik artrit, OM
  - DAIR dışlanmış

n (%)	Başarı	Kesin başarısızlık
Uzun rejim	207 (85.9)	34 (14.1)
Kısa rejim	208 (88.9)	26 (11.1)

p=0.324

Boclé et al. BMC Musculoskeletal Disorders (2021) 22:315
https://doi.org/10.1186/s12891-021-04191-y

BMC Musculoskeletal Disorders

RESEARCH ARTICLE Open Access

Effectiveness of early switching from intravenous to oral antibiotic therapy in *Staphylococcus aureus* prosthetic bone and joint or orthopedic metalware-associated infections

Hélène Boclé[1], Jean-Philippe Lavigne[2,3], Nicolas Cellier[4], Julien Crouzet[1], Pascal Kouyoumdjian[4], Albert Sotto[1,2] and Paul Loubet[1,2*]

- Retrospektif, Fransa, tek merkez, 2008-2015
- 140 hasta, %81 MSSA
- 2 yıl boyunca tedavi başarısızlığı açısından takip

- **Erken IVOS (<5 gün) tedavi başarısızlığı ile ilişkili bulunmamış.**

Infectious Diseases Now 53 (2023) 104739

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ELSEVIER

Short communication

Early switching from intravenous to oral antibiotic therapy in bone and joint infections associated with methicillin-susceptible *Staphylococcus aureus* bacteremia

Maïwenn Petithomme-Nanrocki[a], Véronique Vernet-Garnier[b], Delphine Lebrun[a], Odile Bajolet[c], Morgane Bonnet[d], Maxime Hentzien[a], Xavier Ohl[e], Saidou Diallo[e], Firouzé Bani-Sadr[a,*]

- Retrospektif, Fransa, tek merkez, 2016-2021
- MSSA bakteriyemisi ilişkili kemik eklem infeksiyonu, 79 hasta
- %50.6 → 14. günden önce oral tedaviye geçiş

- **Erken IVOS yapılan hastalarla IV devam edilenler arasında fark yok**

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Original Article

Early switch to oral antimicrobials in brain abscess: a narrative review

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Geleneksel yaklaşım; 6-8 hafta parenteral

- Kan-beyin bariyeri
- Relaps korkusu
- Yüksek mortalite riski

KANIT DÜZEYİ DÜŞÜK!

Table 1
Overview of studies describing the use of early transition from intravenous (IV) to oral antimicrobials in the treatment of brain abscess

Author, year	Country	Study design	Overall case-fatality rate	Early orals		Standard IV treatment	
				Case-fatality rate	Recurrence	Case-fatality rate	Recurrence
Brown, 1993 [19]	England	Retrospective, single-centre	1/12	1/12	0/12	—	—
Jamjoom, 1996 [20]	England and Saudi Arabia	Bi-directional, multi-centre	0/26	0/26	0/26	—	—
Jamjoom, 1997 [22]	Saudi Arabia	Retrospective, single-centre	5/37	—	—	—	—
Srinivasan, 1999 [30]	India	Retrospective, single-centre	1/37	1/37	0/37	—	—
Skoutelis, 2000 [21]	Greece	Bi-directional, single-centre	0/8	0/8	0/8	—	—
Babu, 2002 [27]	India	Retrospective, single-		5/45	—	—	—
Jansson, 2004 [25]	Sweden	Prospective, sing		—	—	—	—
Sichizya, 2005 [26]	South Africa	Retrospective, s		—	—	—	—
Carpenter, 2007 [34]	England	Retrospective, s		0/21	—	5/28	—
Sharma, 2009 [36]	England	Retrospective, sing		—	—*	—	—
Qasim, 2010 [28]	Pakistan	Retrospective, single-centre		0/40	—	—	—
Madhugiri, 2011 [23]	India	Retrospective, single-centre	5/139	—	—	—	—
Felsenstein, 2012 [32]	England	Retrospecitive, multi-centre	7/118	—	—	—	—
Ndubuisi, 2017 [24]	Nigeria	Retrospective, multi-centre	8/79	—	—	—	—
Kafle, 2018 [29]	Nepal	Retrospective, single-centre	2/51	2/51	—	—	—
Udayakumaran, 2019 [31]	India	Retrospective, single-centre	1/48	—	—	—	0/29
Asquier-Khati, 2020 [33]	France	Retrospective, single-centre	13/108	7/48**	—	23/60**	—
Lauda-Maillen, 2021 [35]	France	Retrospective, multi-centre	13/101	1/24	1/24	12/77	4/77

RKT YOK

* 5/8 recurrences had been switched to early oral antimicrobials of first or second generation cephalosporin.
** Unfavourable outcome assessed by Glasgow Outcome Scale Score <4 was used as proxy for case-fatality.

ESCMID 2024 Beyin absesi rehberi hazırlık aşamasında yazılmış

✓

- Klinik stabil
- Nörolojik olarak iyi
- Görüntüleme ile absede küçülme gösterilen
- Gerekliyse uygun drenaj yapılmış
- Etken bilinen / hedefe yönelik tedavi mümkün olan
- Beyin penetrasyonu ve biyorarlanımı iyi oral ajana duyarı etken

X

- Multiple/ büyük abse
- Kontrolsüz infeksiyon
- Nörolojik kötüleşme
- Drenaj yapılamayan olgular
- Güvenilir taikip yapılamayacaksa

Komplikasyonsuz beyin abseli hastalarda erken oral tedaviye geçiş uzun süreli hastaneye yatış ve IV tedavi ilişkili komplikasyonları azaltabilir.

FAYDA- RİSK ORANI BELİRSİZ

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journal homepage: www.clinicalmicrobiologyandinfection.com

Guidelines

European society of Clinical Microbiology and Infectious Diseases guidelines on diagnosis and treatment of brain abscess in children and adults

Jacob Bodilsen [1, 2, 3, *], Quintino Giorgio D'Alessandris [4, 5], Hilary Humphreys [6], Mildred A. Iro [7], Matthias Klein [3, 8, 9], Katharina Last [3, 10], Inmaculada López Montesinos [11, 12], Pasquale Pagliano [3, 13, 14], Oğuz Reşat Sipahi [3, 15, 16], Rafael San-Juan [12, 17, 18], Pierre Tattevin [3, 19], Majda Thurnher [20], Rogelio de J. Treviño-Rangel [21, 22, 23, 24], Matthijs C. Brouwer [3, 25], for the ESCMID Study Group for Infections of the Brain (ESGIB)

Recommendations Assessment, Development and Evaluation approach was applied to classify strength of recommendations (strong or conditional) and quality of evidence (high, moderate, low, or very low).

Veri eksikliği nedeniyle erken oral tedaviye geçiş önerilmiyor.

recommended whenever feasible, except for cases with toxoplasmosis (strong and low). Recommended empirical antimicrobial treatment for community-acquired brain abscess in immuno-competent individuals is a 3rd-generation cephalosporin and metronidazole (strong and moderate) with the addition of trimethoprim-sulfamethoxazole and voriconazole in patients with severe immuno-compromise (conditional and low). Recommended empirical treatment of post-neurosurgical brain abscess is a carbapenem combined with vancomycin or linezolid (conditional and low). The recommended duration of antimicrobial treatment is 6–8 weeks (conditional and low). No recommendation is offered for early transition to oral antimicrobials because of a lack of data, and oral consolidation treatment after ≥6 weeks of intravenous antimicrobials is not routinely recommended (conditional and very low). Adjunctive glucocorticoid treatment is recommended for treatment of severe symptoms because of perifocal oedema or impending herniation (strong and low). Primary prophylaxis with antiepileptics is not recommended (conditional and very low). Research needs are addressed. **Jacob Bodilsen, Clin Microbiol Infect 2024;30:66**

Bodilsen et al. Trials (2021) 22:796
https://doi.org/10.1186/s13063-021-05783-8

Trials

STUDY PROTOCOL Open Access

Partial oral antibiotic treatment for bacterial brain abscess: an open-label randomized non-inferiority trial (ORAL)

Jacob Bodilsen[1,2*], Matthijs C. Brouwer[2,3], Diederik van de Beek[2,3], Pierre Tattevin[2,4,5], Steven Tong[6,7], Pontus Naucler[8] and Henrik Nielsen[2,9]

RKT, açık etiketli, uluslararası çalışma

Device associated brain abscess, severe immuno-compromise or concomitant brain abscess treatment for nocardia, tuberculosis, *Pseudomonas spp.*, fungi, parasites

No

NCT04140903 Recruiting

Partial Oral Antibiotic Treatment for Bacterial **Brain Abscess**

Conditions

Cerebral Abscess | Brain Abscess

Locations

Aalborg, Denmark
Aarhus, Denmark
Copenhagen, Denmark
Odense, Denmark

Follow-up after randomisation (months +/-10 days):	0	1	3	6	12
Extended Glasgow Outcome Scale score		x	x	x	x*
Clinical examination	x	x	x	x	x*
Cranial imaging	x	x	x		
Blood tests	x	x	x		
SF36 + EQ-5D-5L + MoCA	x	x	x	x	x
Screening for immuno-compromise (blood sample)	x			x	

*Other drug regimens may be chosen according to international or local guidelines, regional epidemiology of brain abscess bacteria, susceptibility of the causative pathogen(s), or in case of drug interactions, intolerability or toxicity.
**Can be replaced by telephone consultation if needed

2008

Early Switch to Oral Treatment in Patients with Moderate to Severe Community-Acquired Pneumonia

A Meta-Analysis

Zoe Athanassa,[1] Gregory Makris,[1] George Dimopoulos[1,2] and Matthew E. Falagas[1,3]

- TKP'de IVOS önerisi mevcut
- **Ciddi olgular?**

- 6 RKT, 1219 hasta

- Erken IVOS → IV tedaviden 2-4 gün sonra orale geçiş

- **Erken IVOS yapılanlarla IV devam edilenler arasında**
  - **Tedavi başarısı** (OR 0.76; 95% GA, 0.36-1.59)
  - **Rekürrens** (OR 1.81; 95% GA 0.70, 4.72)
  - **Mortalite** (OR 0.81; 95% GA 0.49, 1.33) **açısından fark yok**

- **IV devam edilen grupta daha uzun hastane yatış süreleri**

Early switch from intravenous to oral antibiotic therapy in patients with cancer who have low-risk neutropenic sepsis: the EASI-SWITCH RCT

Vicky Coyle,[1*] Caroline Forde,[1] Richard Adams,[2] Ashley Agus,[3] Rosemary Barnes,[4] Ian Chau,[5] Mike Clarke,[6] Annmarie Doran,[3] Margaret Grayson,[7] Danny McAuley,[8] Cliona McDowell,[3] Glenn Phair,[3] Ruth Plummer,[9] Dawn Storey,[10] Anne Thomas,[11] Richard Wilson[12] and Ronan McMullan[8]

- Randomize, çok merkezli, açık etiketli, non-inferiority çalışması
- Amaç; **düşük riskli nötropenik sepsis** hastalarında erken oral antibiyotiğe geçişin klinik ve maliyet etkinliğini değerlendirmek
  - MASCC ≥21
  - Akut lösemi ve KİT dışlanmış
- Müdahale; 12-24 saat içinde orale geçiş (AMC + siprofloksasin), toplam tedavi süresi 5 gün
- Starndart bakım; en az 48 saat IV, sonrası klinisyen kararı

Yetersiz hasta sayısı nedeniyle erken sonlanım* (n=129)

TABLE 19 Analyses for the primary outcome in the ITT and PP populations

	Standard care (*n* = 64)	Intervention (*n* = 61)	Risk difference (90% CI)	*p*-value
Treatment failure ITT (*N* = 125)				
Yes	9 (14.1%)	15 (24.6%)	0.11 (−0.01 to 0.22)	0.14
No	55 (85.9%)	46 (75.4%)		
Treatment failure PP (*N* = 113)				
Yes	8 (13.3%)	9 (17.0%)	0.04 (−0.07 to 0.148)	0.59
No	52 (86.7%)	44 (83.0%)		

NON-İNFERİORİTE GÖSTERİLEMEMİŞ

YORUM

Ancak bazı hastalar için kabul edilebilir bir strateji olabilir; bunun karşılığında artmış tedavi başarısızlığı ve yeniden yatış riski göze alınmalıdır.

Gasparetto et al. BMC Infectious Diseases (2019) 19:650
https://doi.org/10.1186/s12879-019-4280-0

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Intravenous-to-oral antibiotic switch therapy: a cross-sectional study in critical care units

Juliano Gasparetto[1], Felipe Francisco Tuon[2*], Dayana dos Santos Oliveira[2], Tiago Zequinao[1], Gabriel Rammert Pipolo[1], Gabriel Velloso Ribeiro[1], Paola Delai Benincá[1], June Alisson Westarb Cruz[3] and Thyago Proenca Moraes[1]

- Retrospektif, 2 YBÜ, kesitsel
- 2016-2018
- YBÜ yatışı sepsis ya da septik şok olan 349 hasta
  - Tüm hastalar en az 24 saat parenteral tedavi almış
  - IVOS grubu; 111 (%31)
    - Klinik iyileşme gözlenir gözlenmez

- Dışkama kriterleri
  - GIS kanama, diyet intoleransı gibi oral biyoyararlanımı etkileyebilecek durumlar
  - Son 24 saat içinde klinik kötüleşme

- Primer sonlanım; tüm nedenlere bağlı mortalite

Table 2 Isolated bacteria by intervention group

	No oral switch (*n* = 238)		Oral switch (*n* = 111)		All (*n* = 349)		*P*-value
	N	%	N	%	N	%	
Negative	129	54%	76	69%	205	59%	0.024
Gram-negative	72	30%	17	15%			0.027
Enterobacter spp.	23	10%	4	4%	16	5%	0.139
Multisusceptible	7		4		11		
ESBL-producing	16		0		16		
Escherichia coli	14	6%	4	4%	18	5%	0.531
Multisusceptible	14		4		18		
Klebsiella spp.	12	5%	3	3%	15	4%	0.468
Multisusceptible	4		3		7		
Carbapenemase-producing	8		0		8		
Pseudomonas aeruginosa	11	5%	2	2%	13	4%	0.332
Multisusceptible	11		2		13		
Serratia spp.	6	3%	1				
Multisusceptible	6		1				
Acinetobacter baumannii	0	0%	1				
Proteus spp.	1	0%	1				
Multisusceptible	1	0%	1				
Burkholderia cepacia	2	1%	0				
Aeromonas hydrophila	1	0%	1				
Citrobacter spp.	1	0%	0				
Haemophilus spp.	1	0%	0				
Gram-positive	26	11%	15	14%			0.027
Stenotrophomonas maltophilia	1	0%	1	1%	2	1%	0.433
Listeria monocytogenes	1	0%	0	0%	1	0%	–
CN Staphylococcus	0	0%	1	1%	1	0%	0.433
Staphylococcus aureus	14	6%	6	5%	20	6%	0.372
MSSA	5	2%	3	3%	8	2%	
MRSA	9	4%	3	3%	12	3%	
Streptococcus pneumoniae	4	2%	4	4%	8	2%	0.097
Enterococcus spp.	4	2%	1	1%	4	1%	0.403
Streptococcus spp.	1	0%	1	1%	2	1%	0.433
Others							
Pneumocystis jirovecii	0	0%	1	1%	1	0%	–
Candida albicans	1	0%	0	0%	1	0%	–
Polymicrobial	2	1%	0	0%	2	1%	–
Total	238	100%	110	100%	348		

ESBL Extended-spectrum beta-lactamases, *MSSA* Methicillin-susceptible *Staphylococcus aureus*, *MRSA* Methicillin-resistant *Staphylococcus aureus*, *CN* Coagulase negative

ESBL ya da karbapenemaz varlığı
Burkholderia cepacia
Listeria monocytogenes
Candida albicans
Polimikrobiyal infeksiyonlar

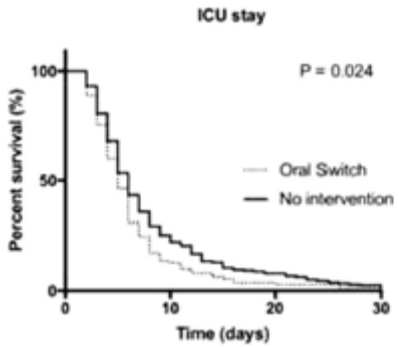
ORALE GEÇİLMEMİŞ

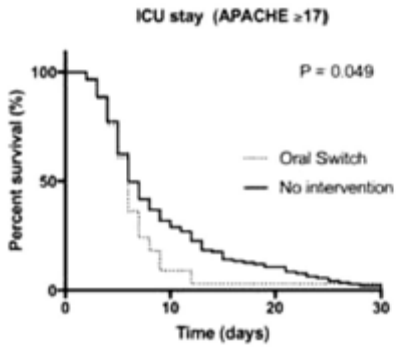
Table 1 Characteristics of patients in the oral switch stewardship program

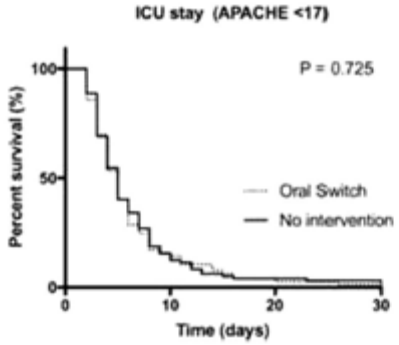
Data	All ($n = 349$)		No oral switch ($n = 238$)		Oral switch ($n = 111$)		*P*-value	Odds ratio	Multivariable analysis
	N	%		%		%			
Male	208	59.7%	132	56%	77	69%	0.010	1.79 (1.11–2.89)	NS
Female	140	40.3%	106	45%	34	31%			
Heart failure class IV	41	12%	25	11%	16	15%	0.181		
Immunosuppression	27	8%	17	7%	10	9%	0.324		
Cirrhosis	7	2%	5	2.1%	2	1.8%	0.662		
Site of infection									
Respiratory	189	54.3%	122	51.3%	67	60.9%			
Urinary	38	10.9%	32	13.4%	6	5.5%			
Abdominal	45	12.9%	37	15.5%	8	7.3%			
Bloodstream	24	6.9%	22	9.2%	2	1.8%			
Skin and soft tissue	25	7.2%	11	4.6%	14	12.7%			
Central nervous system	4	1.1%	4	1.7%	0	0%			
Others	7	2.4%	0	0%	7	6.3%			
Undefined	15	4.3%	10	4.2%	5	4.5%			
Vasoactive drug									
Vasopressin	71	20.4%	62	26.1%	9	8.2%	< 0.001	0.25 (0.12–0.53)	NS
Noradrenalin	205	58.9%	137	57.6%	68	61.8%	0.264		
Dobutamine	153	44%	117	49.2%	36	32.7%	–		
Acute Kidney Injury	69	19.8%	54	22.6%	15	13.5%	0.032		NS
Antibiotic									
Aminoglycoside	75	21.6%	31	26.1%	22	11.8%	0.002	0.38 (0.19–0.72)	0.014
Polymyxin	12	3.4%	11	4.6%	1	0.9%	0.065		
Cefazolin	8	2.3%	1	0%	7	6.4%	0.002	16.1 (1.97–132.59)	0.004
Ceftriaxone	112	32.2%	82	34.5%	30	27.3%	0.113		
Cefepime	122	34.2%	82	34.5%	40	36.4%	0.409		
Carbapenem	39	11.2%	37	15.5%	2	1.8%	< 0.001	0.10 (0.02–0.42)	NS
Quinolone	77	22.1%	10	4.2%	67	60.9%	< 0.001	40.71 (19.76–83.89)	< 0.001
Vancomycin	95	27.3%	86	36.1%	9	8.2%	< 0.001	0.15 (0.07–0.32)	NS
SMX/TMP	24	6.9%	16	6.7%	8	7.3%	0.506		
Metronidazole/clindamycin	50	14.3%	37	15.5%	13	11.8%	0.226		
Macrolide	24	6.9%	15	6.0%	9	8.2%	0.332		
Penicillin	39		8	3.4%	31	28.2%	< 0.001	11.28 (4.97–25.56)	0.001
Mortality	44	12.6%	35	14.7%	9	8.2%	0.060		
Age	64 (53–73)		65 (55–74)		64 (51–73)		0.327		
APACHE II score	15.5 (12–19)		16.5 (13–19)		15 (14–17)		0.061		0.003
SOFA score	3 (2–5)		3 (2–5)		3 (2–4)		0.112		
IV antibiotic duration (days)	5 (4–7)		7 (5–10)		3 (2–4)		< 0.001		NS
Oral antibiotic duration (days)			0		4 (3–5)		–		
Mechanical ventilation (days)	3 (2–4)		3 (2–4)		3 (1.75–4)		0.008		NS
Total hospitalization (days)	13 (8–21)		13 (8–22)		13(8–20)		0.665		
Days in the ICU	6 (4–9)		6 (4–10)		5 (3–7)		0.029		NS

Penicillins – ampicillin/sulbactam; amoxicillin; amoxicillin/clavulanate
SOFA Sequential organ failure assessment, *IV* Intravenous, *ICU* Intensive care unit, *SMX/TMP* Sulfamethoxazole/trimethoprim, *APACHE* Acute physiologic assessment and chronic health evaluation

- RKT değil
- Daha kritik hastada IV tedavide kalınmış olabilir







ICU süresindeki kısalma daha ağır hastalarda daha belirgin

Table 3 Patient costs by intervention group

Costs	No oral switch		Oral switch		*P*-value
	Median	IQR (25–75)	Median	IQR (25–75)	
Ward	474.7	(172.6–1122.1)	517.9	(258.9–1122.1)	0.099
Total hospital	3010.6	(2090.3–5032.1)	2742.3	(2003.9–3847.2)	0.063
ICU	2358.5	(1572.3–3930.9)	1965.4	(1474.1–2849.9)	0.027
Antibiotics	22.7	(10.1–64.6)	10.2	(6.4–36.4)	< 0.001
Workload	8.6	(6.1–12.3)	3.6	(2.4–4.9)	< 0.001
Consumables	23.0	(2.7–52.3)	1.75	(0.8–4.9)	< 0.001

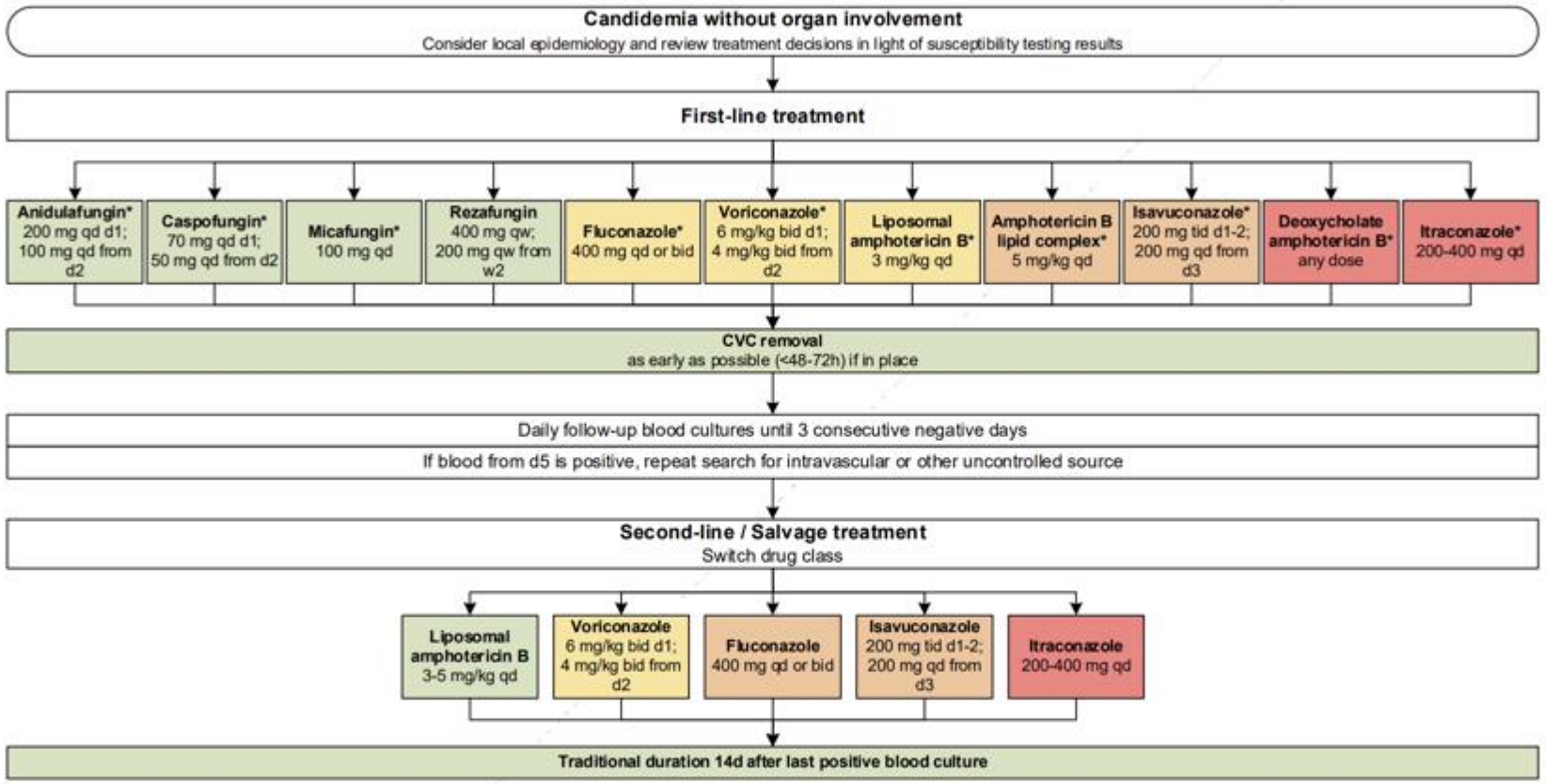
ICU Intensive care unit, *IQR* Interquartile range 25 to 75%

IVOS; maliyetleri azaltıyor !

- Seçim biası !!!
- Gerçek yaşam verisi uygun YBÜ hastasında IVOS'u destekliyor
- Ancak verinin kanıt düzeyi RKT'ler kadar güçlü değil

Global guideline for the diagnosis and management of candidiasis: an initiative of the ECMM in cooperation with ISHAM and ASM

Figure 11. Optimal treatment pathway for candidaemia without organ involvement in adults when all treatment modalities and antifungal drugs are available.



Birinci basamak tedaviden **en az 5 gün sonra;**

- **Hemodinamik stabil**
- ***Candida* için kan kültür negatifliği**
- **Non-nötropenik**
- **Kaynak kontrolü sağlanmış (örn; SVK çekilmiş)**
- **Oral azollere duyarlılık konfirme edilmiş**
- **Oral azoller için hasta tolerasyonu**

Garnacho-Montero J et al.

- 294 kandidemili hasta
- Propensity score adjusted analiz
- **Ekinokandinden flukonazole geçiş zamanın mortalite ya da komplikasyon üzerine etkisi yok**

AmarCAND2 çalışması

- 5. günde oral flukonazole geçiş (%22)
- **28 günlük mortalitede fark yok**

Vazquez J et al.

- Oral flukonazole geçiş, prospektif, açık etiketli, RKT
- İlk 24 saatte SVK çıkarılmış
- Non-nötropenik
- Kan kültür negatifliği görülmüş
- Azol duyarlı
- **Küresel tedavi başarı oranları ve yan etkiler açısından fark yok.**

Kurtarma tedavisi ve dirençli izolatlar

- *C. glabrata / N. glabratus*
  - Yüksek flukonazol MİK'leri
  - Tedavi altında flukonazol direnç gelişimi
  - MİK 18 mg/L'ye kadar olan izolarlarda yüksek doz (800 mg) flukonazol kullanımı güvenli
- *C. krusei*
  - İntrensek flukonazol dirençli
  - Vorikonazol alternatif olabilir
- Ancak vorikonazol daha geniş spekturumlu olsa da **çapraz direnç riski**
  - **Flukonazol dirençli olan izolatlarda vorikonazol kullanımı açısından da dikkatli olunmalı**

Table 33. Recommendations on second-line or salvage treatment of invasive candidiasis and candidaemia in adults.

Population	Intention	Intervention	SoR	QoE	Original Source	Annotation
Any	To cure	L-AMB 3-5 mg/kg qd	A	I	Walsh CID 1998 [884]	Reasonable, if there is intolerance, limited availability, or resistance to other antifungal agents
		VCZ	B	I	Ostrosky EJCMID 2003 [838]	Limited spectrum compared to echinocandins, drug-drug interactions, iv in renal impairment, need for TDM. Non-inferiority to CASPO not investigated
					Perfect CID 2003 [839]	
					Kullberg Lancet 2005 [830]	
					Pascual CID 2008 [882]	
		ISA	C	I	Kulberg CID 2019 [731]	
		FCZ	C	I	Rex NEJM 1994 [828]	Limited spectrum (inactive against *C. krusei* and considered to be hardly active against *C. glabrata/N. glabratus*), inferior to ANID
					Anaissie CID 1996 [829]	
					Abele-Horn Infect 1996 [843]	
					Philips EJCMID 1997 [841]	
					Rex CID 2003 [840]	
					Tuil CC 2003 [842]	
					Reboli NEJM 2007 [834]	
					Leroy CCM 2009 [844]	
		ICZ	D	IIa	Tuil CC 2003 [842]	Inferior compared to FCZ

ANID, anidulafungin; CASPO, caspofungin; d, days; FCZ, fluconazole; ICZ, itraconazole; ISA, isavuconazole; L-AMB, liposomal amphotericin B; qd, daily; QoE, quality of evidence; SoR, strength of recommendation; TDM, therapeutic drug monitoring; VCZ, voriconazole.
When dosage is not specified, the standard dosing (including potential loading doses) according to the label is recommended.

Journal of Fungi

MDPI

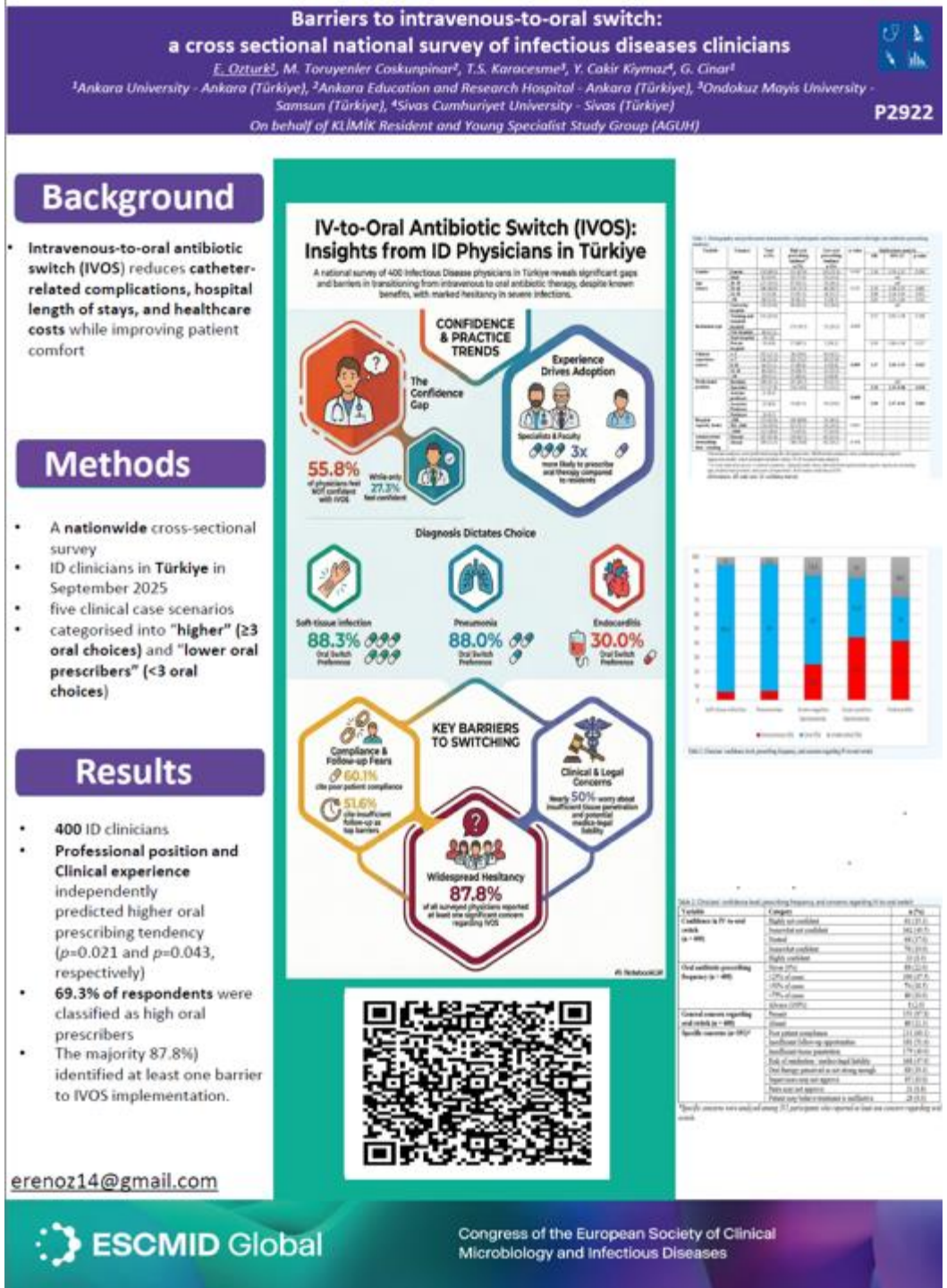
Review

Early Antifungal Treatment in Immunocompromised Patients, Including Hematological and Critically Ill Patients

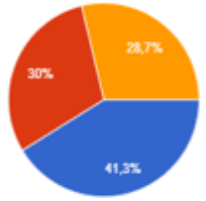
Galina Klyasova [1], Galina Solopova [2], Jehad Abdalla [3], Marina Popova [4], Muhlis Cem Ar [5], Murat Sungur [6], Riad El Fakih [7,8], Reem S. Almaghrabi [9] and Murat Akova [10,*]

Q6. What is the best time to switch from intravenous (IV) to per os (PO) antifungal therapy? What are the clinical signs and symptoms that may trigger a switch from IV to PO?			
36.	Switching from IV to PO antifungal therapy should be considered in centers where drug monitoring is available and in patients who show satisfactory clinical and/or microbiological response, have good enteric absorption	*100%*	V
Invasive Aspergillosis			
37.	Voriconazole, posaconazole, and isavuconazole can be used interchangeably based on the availability of therapeutic drug monitoring	*78%*	V
38.	Switching from intravenous to oral therapy should be recommended for patients who are clinically stable and have a reliable enteric absorption	*100%*	V
Invasive Candidiasis			
39.	Switching from echinocandin to oral fluconazole or voriconazole is considered in non-neutropenic patients with hemodynamic stability, who are afebrile for more than 24 h, can tolerate oral therapy, and have *Candida* cleared from the bloodstream, and when the isolate is confirmed susceptible to the chosen azole agent	*78%*	V
40.	It is recommended to step down to oral azole as early as possible once the patient is clinically stable and blood cultures have become negative	*89%*	V
Invasive Mucormycosis			
41.	Intravenous treatment with high-dose (5–10 mg/kg/day) liposomal amphotericin B is recommended until the disease is stable. When switching to oral therapy, the use of isavuconazole or posaconazole is recommended	*100%*	V

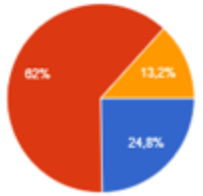
- Spesifik infeksiyon
- Hasta stabilitesi
- Terapötik ilaç monitörizasyonu
- Hasta uyumu/ takibi
- Biyoyararlanım



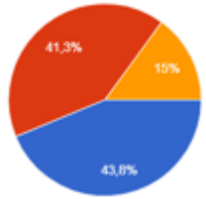
1. Komplike olmayan, kan kültür negatifliği görülen penisiline duyarlı *Streptococcus mitis* endokarditi, 16 gün penisilin tedavisi sonrası klinik stabil



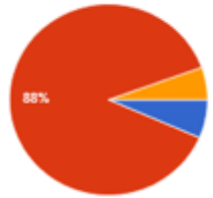
2. Üriner sistem infeksiyonuna sekonder *E. coli* bakteriyemisi, abse ya da hidronefroz yok, 3 gün seftriakson almış



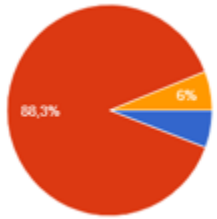
3. MSSA bakteriyemisi, komplikasyon yok, İE yok, SVK 3. günde çekilmiş, klinik olarak stabil, 5 gün IV tedavi sonrası stabil



4. Pnömokok pnömonisi, CURB-65; 1, 3 gün IV tedavi sonrası klinik yanıt var, oral seçenekler duyarlı



5. *S. pyogenes* komplike olmayan selülit, penisilin-klindamisin duyarlı, 4 gün IV tedavi sonrası klinik yanıt var



- IV antibiyotikle tedaviye devam
- Oral antibiyotiğe geçiş
- Klinik karara göre değişir / kararsızım

AGUH

PRIMUM NON NOCERE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Review
Choosing patients over placebos: oral transitional therapy vs. IV-only therapy for bacteraemia and infective endocarditis
Matthew C. Phillips [1,2,*], Noah Wald-Dickler [3], Kusha Davar [3], Rachael Lee [4], Rachel Baden [3], Paul Holtom [3], Brad Spellberg [3]
[1] Division of Infectious Diseases, Department of Medicine, Massachusetts General Hospital, Boston, MA, United States
[2] Harvard Medical School, Boston, MA, United States
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- IV tedavi daha güçlü algısı → *hasta güvenliği* mi, *klinisyen konforu* mu?
- Sadece IV tedavi verilen hastalarda;
  - Daha uzun hastane yatış süreleri
  - Daha yüksek hastane içi mortalite

IVOS'a uygun hastada oral tedavi ısrarı →
«Fonksiyonel plasebo»
Gereksiz zarar

IV Katater komplikasyonları;
- %60'a kadar genel komplikasyon
- Venöz tromboz; %38
- Katater ilişkili KDİ; %2–17.6 (mortalite %12–25)

APAT sırasında;
- %60 advers olay
- %25 yeniden yatış
- %17 ilaç yan etkisi

Hasta yaşam kalitesi
- %26: günlük yaşam kısıtlılığı
- %14: sosyal aktivite kısıtlılığı
- %55: günde >1 saat tedaviyle uğraş
- %10: tedaviye uyumsuzluk
- Sosyoekonomik eşitsizlikler ↑

Eve götürülecek mesajlar

- Yüksek riskli infeksiyonlarda soru artık ‘orale geçilir mi?’ değil, ‘**kime güvenle geçilir**?’
- Unkomplike *Enterobacterales* bakteriyemilerinde klinik olarak uygun, kaynak kontrolü sağlanmış ve oral ajanlara duyarlılık mevcutsa **3-5 gün sonra orale geçiş** yapılabilir.
- Nonfermenterler için kanıt düzeyi yüksek çalışma henüz yok
- **SOBATO** çalışması; **düşük riskli, unkomplike SAB’ta 5-7 gün sonra oral tedaviye** geçilebilir.
  - Burada sorun unkomplike olduğundan emin olmak.
- SAB orale geçişte linezolid veya kinolon+rifampisin güvenilir alternatifler
- POET çalışması; İE tedavisinde IVOS’ta **pratik değiştiren çalışma!**
  - Klinik stabil, unkomplike, kültürü negatifleşmiş; MSSA, Streptokok, *E. faecalis,* KNS
  - Orale geçiş kombinasyon tedavileri ile
- OVIVA çalışması; kemik-eklem infeksiyonlarında orale geçişte **pratik değiştiren çalışma!**
- Beyin absesi, nötropenik sepsis ya da YBÜ hastalarında IVOS için **henüz kanıt düzeyi yeterince yüksek çalışma yok**
- Kandidemik hastada; **Hemodinamik stabil, *Candida* için kan kültür negatifliği, Non-nötropenik, Kaynak kontrolü, oral azollere duyarlı ve hasta tolere edebiliyorsa 5 gün sonra azoller ile orale geçiş yapılabilir.**
- IVOS’a uygun hastada IV tedavi ısrarı → zarar > yarar

TEŞEKKÜRLER...