

The role of investigator initiated clinical trials in advancing antimicrobial use

Guest speakers: Anouk G. Overdeest, Jesús Rodríguez-Baño & Nicholas A. Turner
Moderator: Steven Tong
Host: Victor Kouassi

29 September 2026

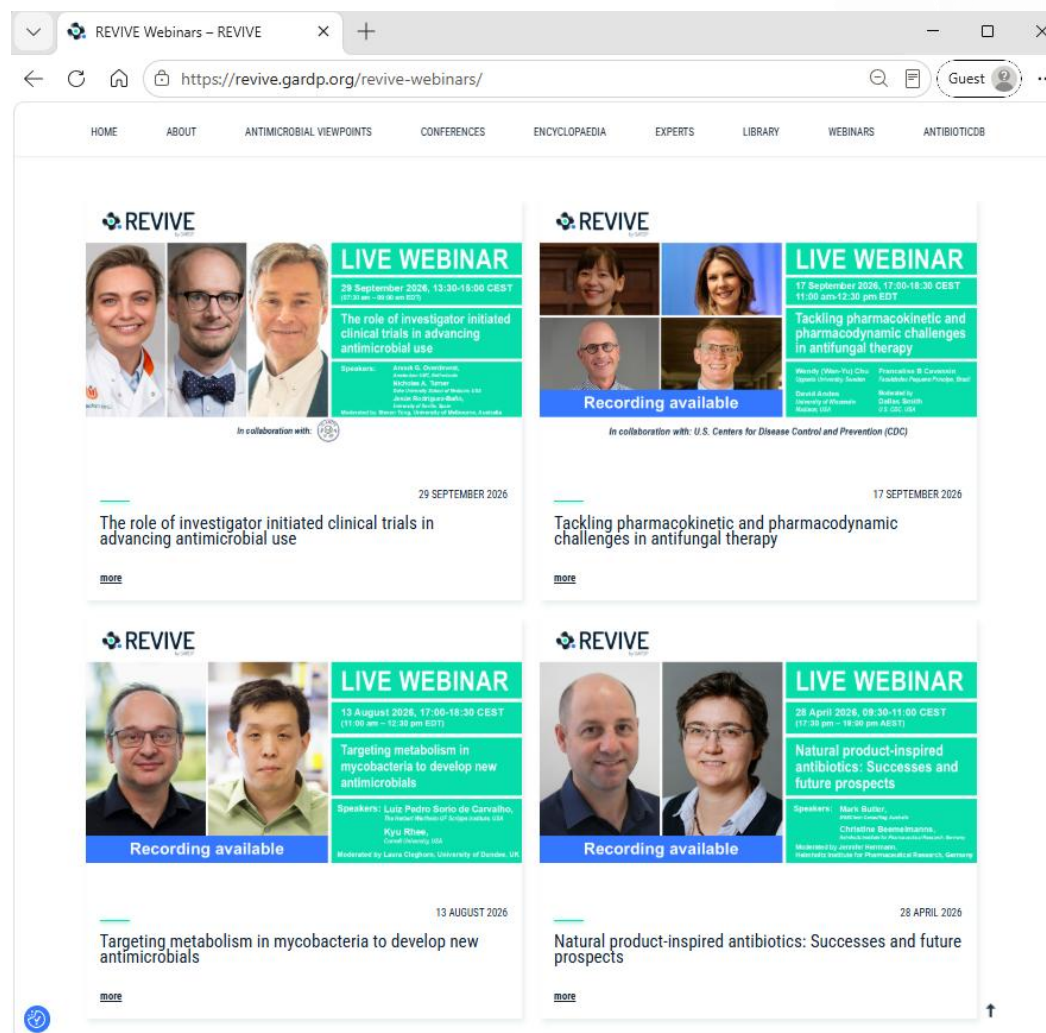


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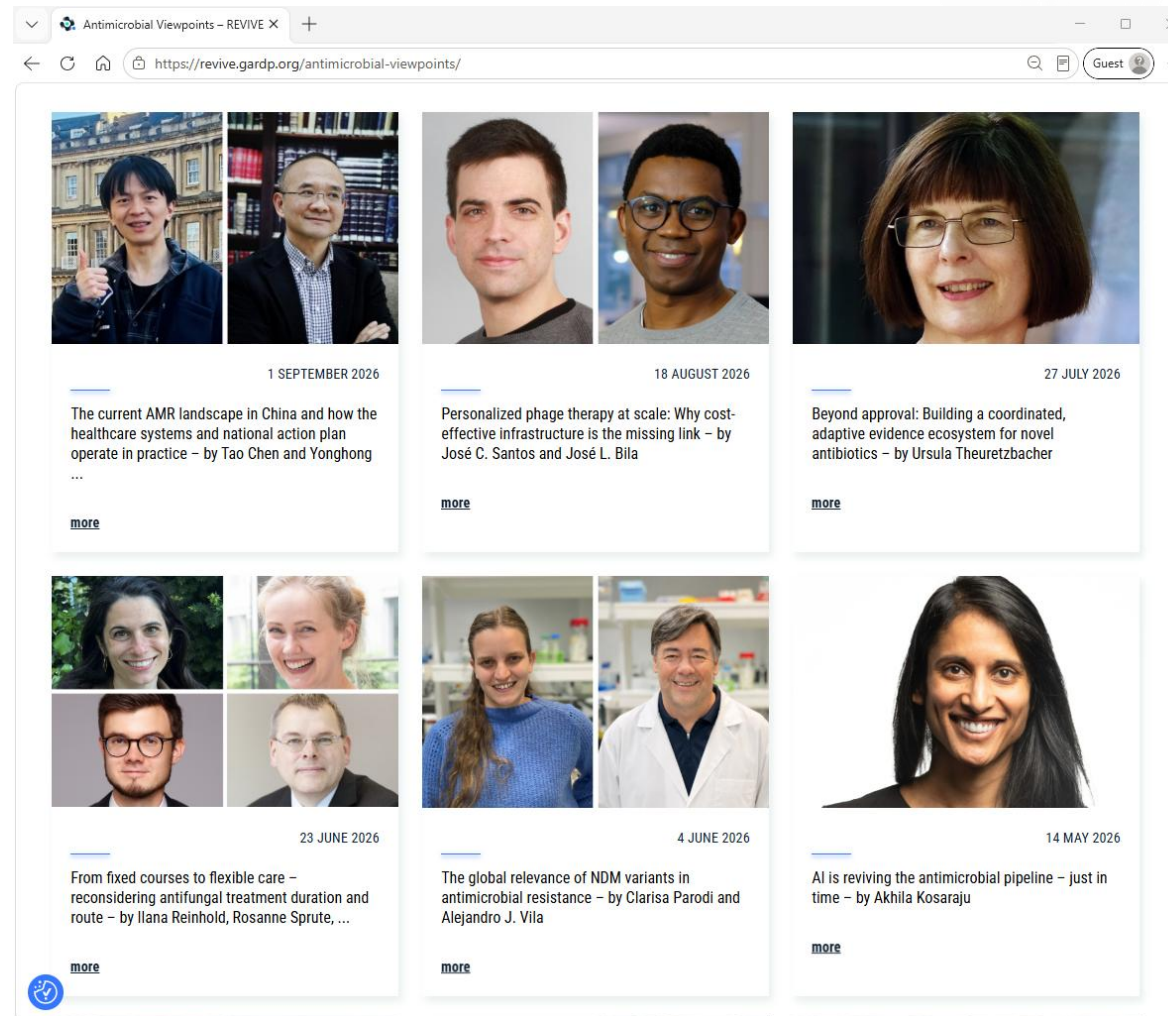


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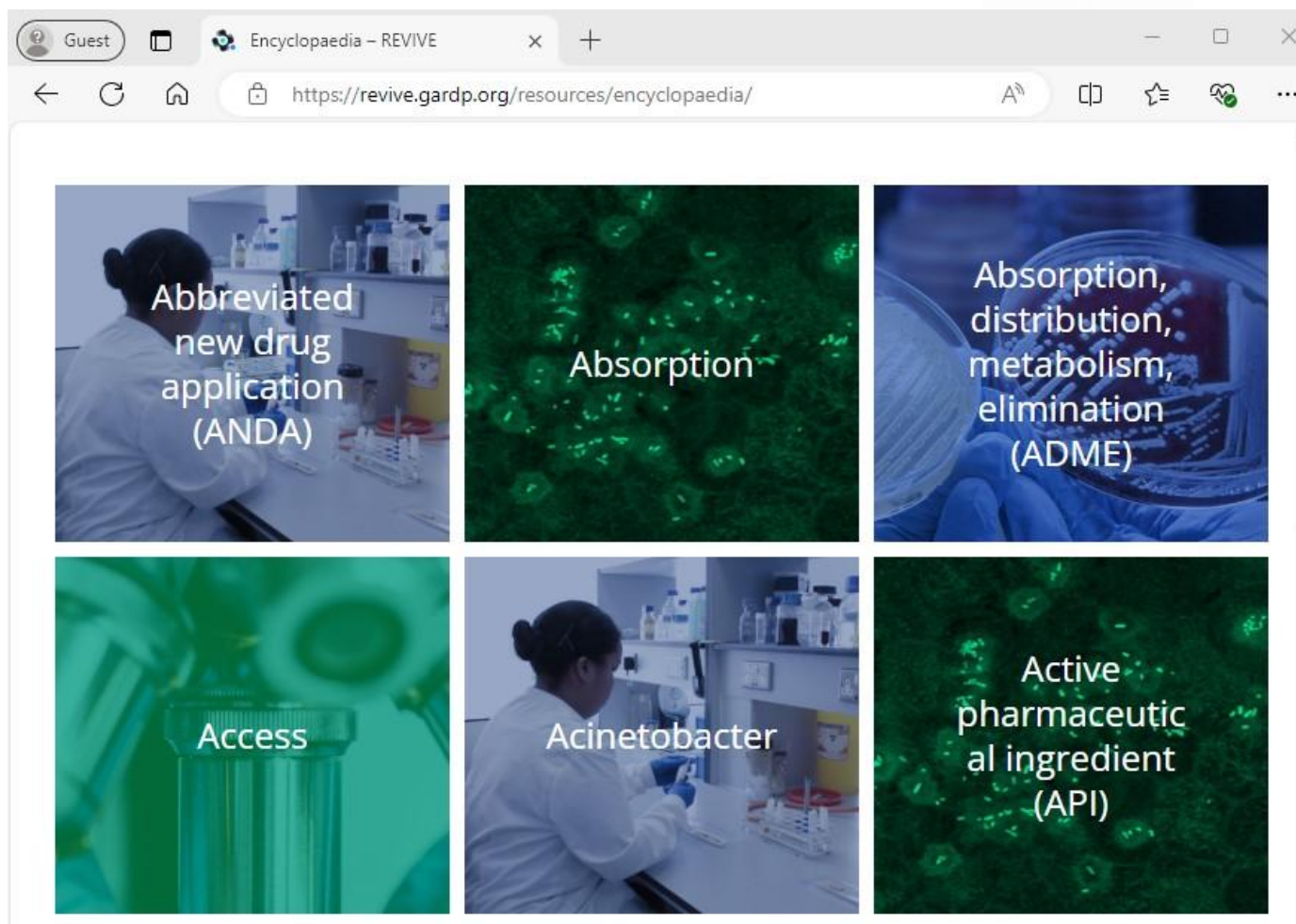
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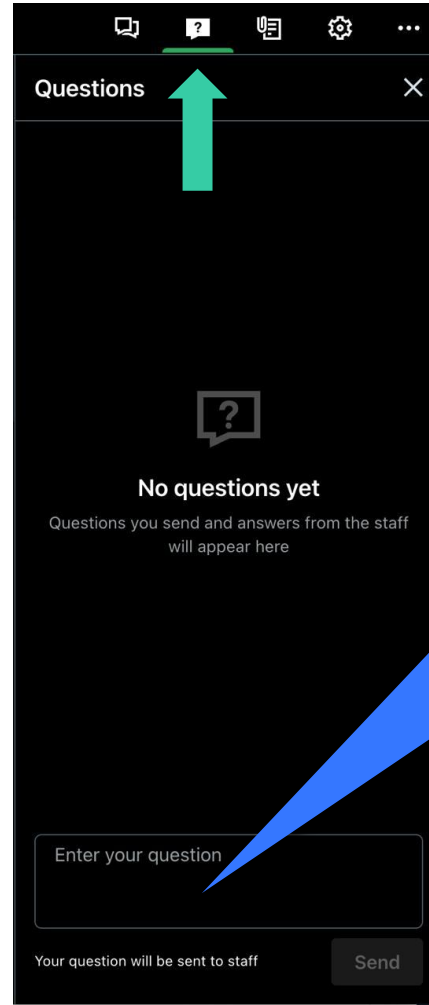
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Please submit your questions through the box provided after clicking the 'questions' button. We will review all questions and respond to as many as possible after the presentation.

This webinar was developed in collaboration with



Today's speakers



The role of investigator initiated clinical trials in advancing antimicrobial use



Moderator:
Steven Tong
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Australia



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Erin K. McCreary, PharmD (1), Ahmad Mourad, MD MHS (2, 3)

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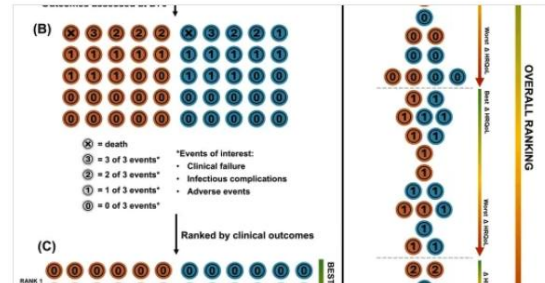


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Do's and DOTS: contextualizing the DOTS clinical trial

Jonas Tverring, PhD and Sean W. X. Ong, MBBS

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Sean W. X. Ong, MBBS and Jonas Tverring, PhD

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Reframing success: lessons on noninferiority trials from GAME CHANGER

Ahmad Mourad^{1,2} · Erin K. McCreary³

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Show Outline

Keywords

Noninferiority · Clinical trials · Methods · Antimicrobial resistance

Key Messages

- Noninferiority trials are an ethical and feasible option to study use of antimicrobials for patients with antimicrobial-resistant infections but require careful design and rigorous trial conduct.
- Clinical interpretation of results depends on both the noninferiority margin and CI, not just the p value alone, as bias and wide margins can obscure important losses in efficacy.
- Noninferiority does not imply equivalence or clinical acceptability, and results must be interpreted in the context of real-world consequences to avoid misinterpretation by clinicians and policymakers.

Figures (1)

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Do's and DOTS: contextualizing a clinical trial evaluating dalbavancin use in *Staphylococcus aureus* bacteraemia

Jonas Tverring^{1,2,*} · Sean W.X. Ong^{3,4,5,6,*}

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Show Outline

Keywords

Clinical trial · Certainty of evidence · Dalbavancin · Generalisability · Noninferiority margin · *Staphylococcus aureus* bacteraemia

As practicing infectious disease physicians, clinical trialists, and regular prescribers of dalbavancin, we read the recently published dalbavancin as an option for treatment of *Staphylococcus aureus* bacteraemia (DOTS) trial by Turner *et al.* [1] with great interest. We can expect to see an increased use of long-acting lipoglycopeptides in the future, based on the number of real-world reports that are being published [2–4], the fact that the patent for dalbavancin is expiring in the European Union in February 2026 (Anna Flodgren, Medical Advisor Nordics at ADVANZ PHARMA, 1 October 2025, personal communication), and that the expected compound annual growth rate is 12.5% for dalbavancin from 2026 to 2033 [5]. High-quality randomised controlled trials for off-label indications are therefore highly warranted, and we applaud the authors for their effort. But, how should we interpret the results from the DOTS trial and are they enough to support or oppose widespread use of dalbavancin for *S. aureus* bacteraemia (SAB)?

Article metrics

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Breaking down the Desirability of *Staphylococcus aureus* bacteraemia



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Clinical trials: from generating the initial idea to reporting final results and everything in between

ESCMID Course
Valletta, Malta
November 19-21 2026

Clinical trials: from generating the initial idea to reporting final results and everything in between

Valletta, Malta



Day 1 Thursday, 19 November 2026

PART I - DEVELOPING THE IDEA Chair: Angela Huttner	
10:30 – 10:40	Welcome and introduction
10:40 – 11:20	How to generate and frame clinical trial ideas Josh Davis
11:20 – 12:00	How to write a clinical trial protocol Steven Tong
12:00 – 12:40	Successful grant-writing: how to apply for and secure funding Marc Bonten
12:40 – 13:30	Lunch break
PART II - MAKING THE IDEA A REALITY Chair: Josh Davis	
13:30 – 14:10	How to create a budget for a clinical trial Julia Bielicki
14:10 – 14:50	Choosing a trial design: from individual randomised to cluster randomised and platform designs Julia Bielicki
14:50 – 15:30	How to get ethics and regulatory approval Mo Yin
15:30 – 15:50	Break
WORKSHOP I – PITCH YOUR CLINICAL TRIAL IDEA AND GET FEEDBACK FROM THE FACULTY AND DELEGATES (10 minutes pitch, 10 minutes faculty feedback, 10 minutes delegate feedback/discussion) Chair: Steven Tong	
15:50 – 16:20	Trial proposal 1
16:20 – 16:50	Trial proposal 2
16:50 – 17:20	Trial proposal 3
17:20 – 17:30	Closing remarks

Clinical trials: from generating the initial idea to reporting final results and everything in between

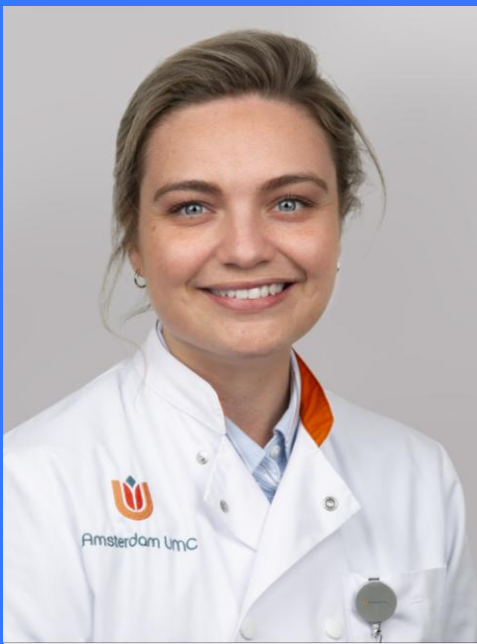
Valletta, Malta



Day 2 Friday, 20 November 2026

PART III - GETTING DOWN TO BUSINESS Chair: David Paterson	
08:40 – 09:20	How to create CRFs/eCRFs and a clinical trial database Josh Davis
09:20 – 10:00	How to create great participant information-and-consent materials Steven Tong
10:00 – 10:40	How to use AI in trial planning, design and analysis Sanjat Kanjilal
10:40 – 11:00	Break
PART IV - ANALYSING TRIAL RESULTS Chair: Marc Bonten	
11:00 – 11:40	Basics of frequentist analysis for RCTs Henri van Werkhoven
11:40 – 12:20	Basics of Bayesian analysis for RCTs Sarah Walker
12:20 – 13:00	What the hell is an “estimand”?! Using the estimand framework, including approach to intercurrent events and missing data Sarah Walker
13:00 – 14:00	Lunch break
PART V - CHOOSING THE RIGHT DESIGN TO ANSWER YOUR QUESTION(S) Chair: Julia Bielicki	
14:00 – 14:40	Choosing the optimal primary outcome for your trial David Paterson
14:40 – 15:20	Adaptive trial designs: when, why and how to use them Henri van Werkhoven
15:20 – 16:00	Industry-sponsored vs investigator-initiated trials Tom Holland
16:00 – 16:20	Break
WORKSHOP II – LEARNING FROM OUR MISTAKES Chair: Tom Holland	
16:20 – 16:50	I wish I knew what I know now when I was younger
16:50 – 17:20	Get me out of this hot mess! How to deal with it when it all goes wrong
17:20 – 17:30	Closing remarks

Anouk G. Overdevest



Anouk G. Overdevest is currently completing her PhD at Amsterdam UMC, Netherlands and received her medical degree in 2022.

Her research focuses on optimizing treatment strategies for benign biliary disease, with the main focus of this being the multicentre nationwide COBRA trial. She aspires to become a gastroenterologist and has a special interest in interventional endoscopy and hepatobiliary disorders.

One day of antibiotic treatment is non-inferior to 4 - 7 days in patients with acute cholangitis after adequate biliary drainage (COBRA): a multicentre randomized controlled trial

A.G. Overdevest, E. Sieswerda, S. Haal, J.A. Bogaards, K.S. Boparai, F. Ter Borg, M.A. Brink, F. Van Delft, V.K. Dik, L.P. Gilissen, M. Hadithi, W.L. Hazen, F. Van Der Heide, W.J. Den Hollander, A. Inderson, P.J.F. De Jonge, S.D. Kuiken, J.M. Munneke, B. Opsteeg, L. Perk, A.C. Poen, J.W. Poley, R. Quispel, R. Scheffer, D.W. Schölvink, E.J. Soest, A.C. Tan, W.J. Thijs, N.G. Venneman, F.P. Vleggaar, W. Van De Vrie, J.M. Vrolijk, R.L.J. Van Wanrooij, P.W. Weijnenborg, M.G. Dijkgraaf, J.M. Prins, R.P. Voermans

PhD candidate
Amsterdam UMC
Department of Gastroenterology and Hepatology





Disclosures

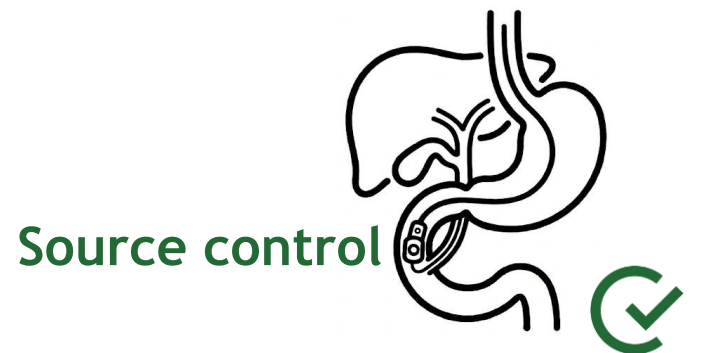
- Personal: nothing to disclose.
- This work was funded by an investigator-initiated research grant from ZonMw (GGG-project 10140022010013)
 - Government-funded, designs programmes on behalf of the Ministry of Health, Welfare and Sport, the Dutch Research Council (NWO) and other organisations



Background

Acute cholangitis is a serious infection where bile flow obstruction allows micro-organisms to accumulate

Treatment of acute cholangitis is based on two pillars¹:



Endoscopic biliary
drainage (ERCP)



Antibiotic treatment

Optimal antibiotic
treatment
duration after
ERCP?



Background



Antibiotic stewardship

To treat patients with appropriate antibiotics while minimising harm and patient burden¹⁻².



United Nations

Member states at the 2024 UNGA reaffirmed antimicrobial stewardship and rational antibiotic use as urgent global priorities³.



Target

Acute cholangitis is a common infection and an actionable target for reducing unnecessary antibiotic use worldwide.



Background

The international Tokyo Guidelines recommend 4 - 7 days of antibiotic treatment after adequate endoscopic biliary drainage¹

However, observational data suggest shorter treatment may be sufficient²



To assess whether 1 day of antibiotic treatment is non-inferior to 4 - 7 days in achieving clinical cure for acute cholangitis after adequate endoscopic biliary drainage



Study design



Open-label multicentre non-inferiority randomized controlled trial



31 participating centres across the Netherlands



Patients with acute cholangitis after adequate biliary drainage and fever resolution



Randomization 1:1 ratio 1-day vs. 4 – 7 days after ERCP
Stratification: aetiology and blood culture result



Blinded outcome assessment by independent adjudication committee





Methods - study population



Acute cholangitis with a distal obstruction, with clinical signs of source control



Concurrent infections requiring antibiotic treatment

Neutropenia ($< 500/\mu\text{L}$)

Use of specific immunosuppressants

Blood culture with *Staphylococcus aureus*, *Pseudomonas aeruginosa* or yeasts



Methods - outcomes



Clinical cure* 

*Symptom-free by day 14 without relapse or death occurring by day 30



Relapse by day 90 

(Cholangitis-related) mortality by day 90 

Reported AB-related adverse events



Total follow-up time of 90 days



Methods - primary outcome

Non-inferiority margin of -7.5%

- The one-sided 95% CI for the absolute risk difference (1-day minus 4-7 days) must be greater than -7.5%

Sample size

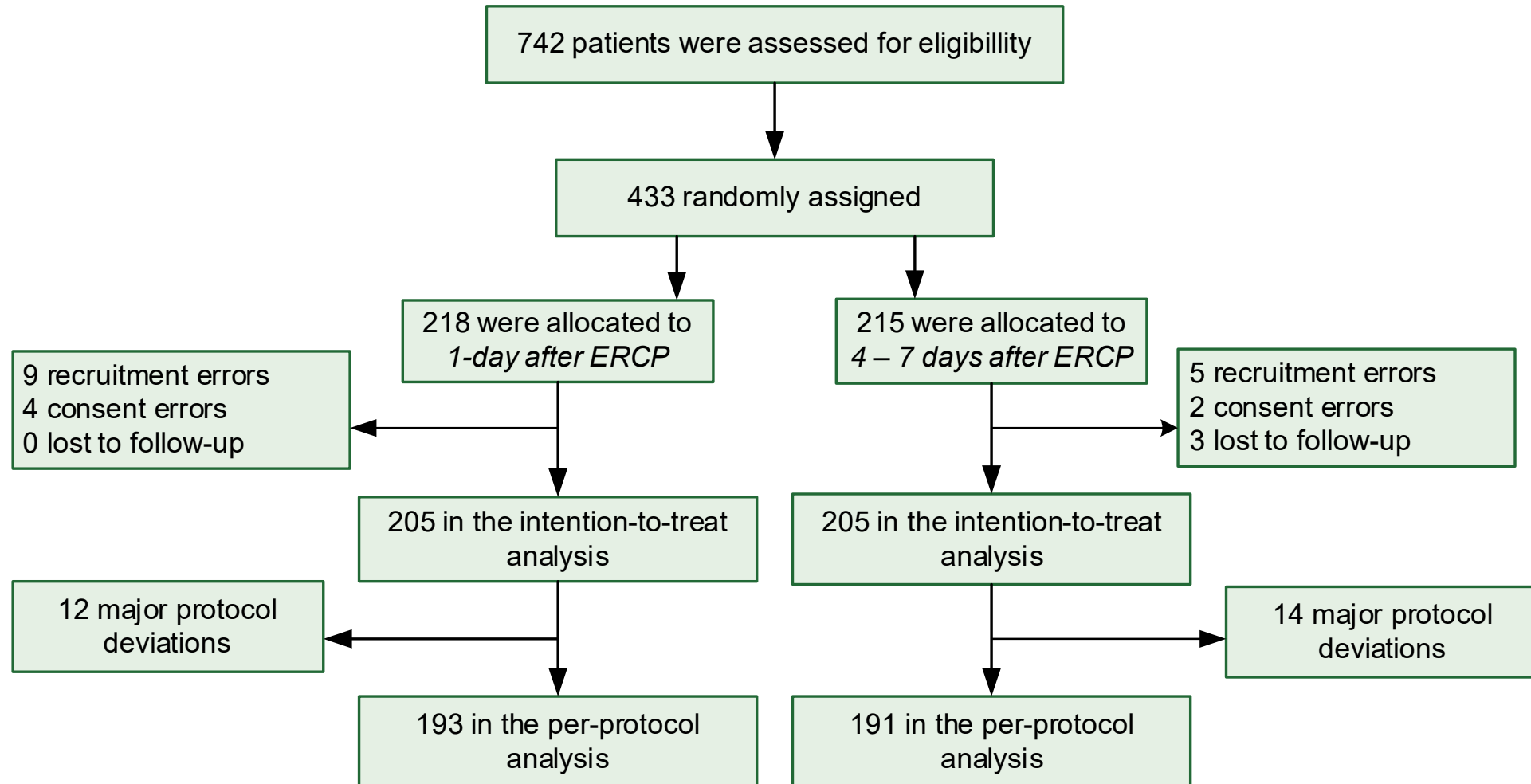
- 90% clinical cure in both groups, a one-sided 5% alpha, 80% power, 5% drop-out
- $n = 416$

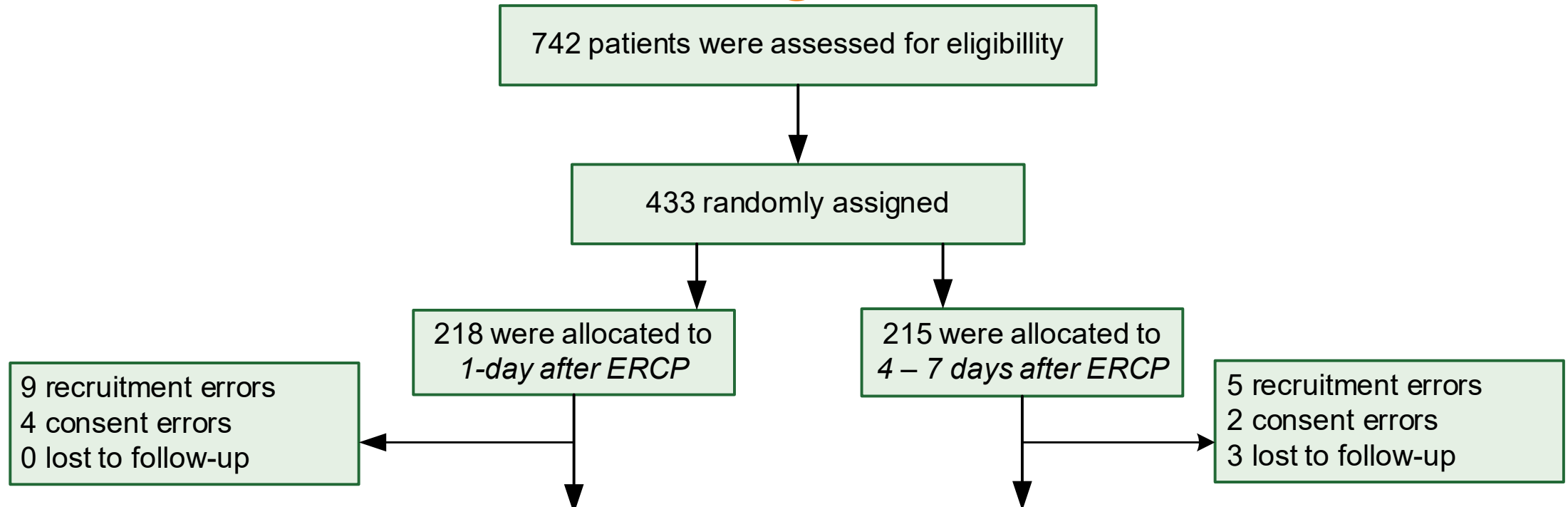
Primary analysis

- Intention-to-treat (in case of >90% protocol adherence)



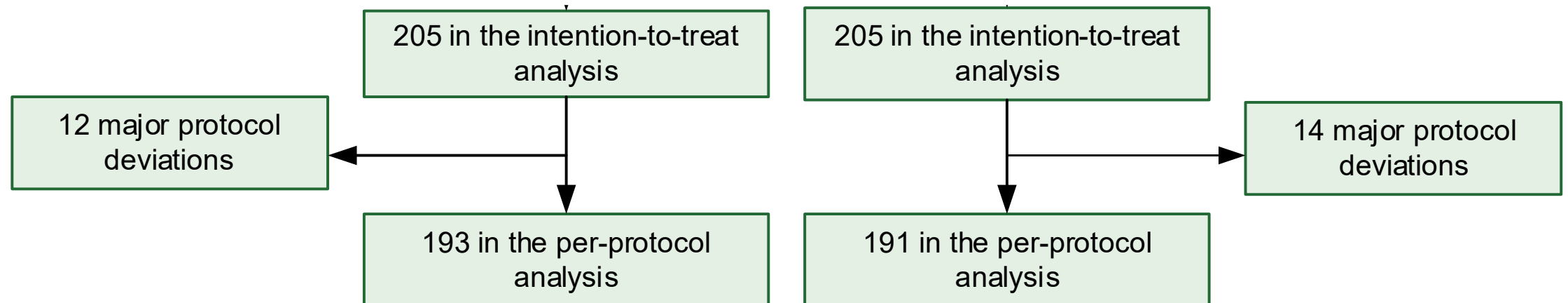
Results - flowchart







Results - flowchart



Results - baseline



	1-day group (n=205)	4-7-day group (n=205)
Female - no, (%)	93 (45)	85 (41)
Age - years, median (IQR)	75 (65 - 81)	74 (66 - 81)
Severity grade - no, (%)		
Mild	87 (42)	87 (42)
Moderate	101 (49)	97 (47)
Severe	17 (8)	21 (10)



Results - primary analysis

Analysis	1 day	4-7 days
	<i>clinical cure/total</i>	
Intention-to-treat (n = 410)	195/205 (95%)	192/205 (94%)
Per-protocol (n = 384)	184/193 (95%)	191/191 (95%)



Secondary outcomes - non-inferiority

1 day after ERCP

4-7 days after ERCP

Diff (95% CI)



All-cause mortality
by day 90

3%

1%

1.5% (-1.1 to ∞)



Cholangitis-related
mortality by day 90

1%

0%

1.0% (-0.6 to ∞)



Secondary outcomes - superiority

1-day group

4-7-day

Diff (95% CI)



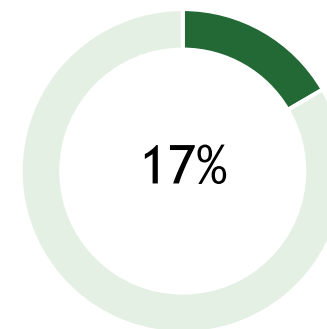
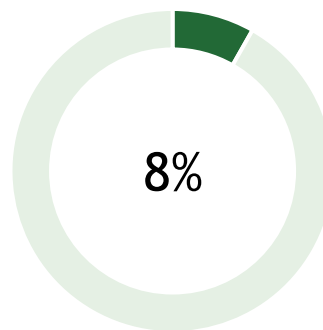
AB treatment
by day 30



4 (4 to 4)



Reported AB-related
AE by day 14



-8% (-15 to -2)



Results - subgroup analysis



Subgroup analysis	1 day	4-7 days
	<i>clinical cure/total</i>	
Gram-negative bacteraemia	67/72 (93%)	67/74 (91%)
Other positive, negative or unkown BC	128/133 (96%)	125/131 (95%)



Conclusions and implications



1-day of antibiotic treatment after adequate endoscopic biliary drainage is non-inferior to 4 - 7 days in adults with acute cholangitis



Non-inferiority was consistent across sensitivity analyses and several subgroups, including gram-negative bacteraemia



Patients reported more AB-related adverse events in the 4-7-day group



A 1-day course after source control is sufficient and can be the standard treatment duration for acute cholangitis



Acknowledgements

We like to thank the patients for their participation and all physicians who contributed to the study by enrolling patients.

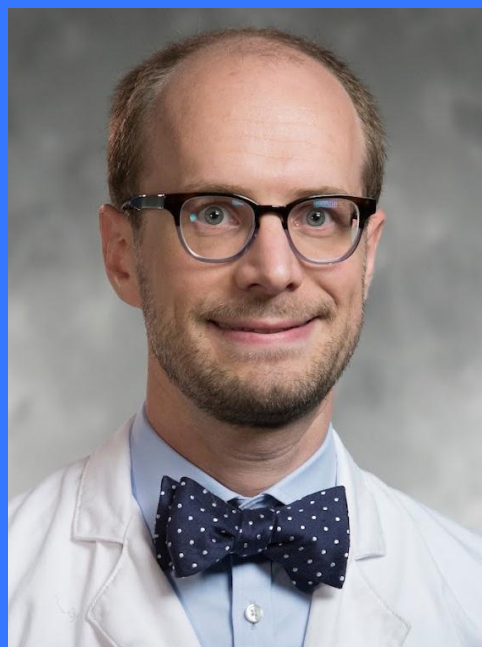


A special thanks to the trial core team:

- Prof. Jan Prins, infectious disease physician Amsterdam UMC
- Dr. Elske Sieswerda, clinical microbiologist Julius Centre
- Dr. Hans Bogaards, statistician Amsterdam UMC
- Dr. Rogier Voermans, principal investigator & gastroenterologist Amsterdam UMC



Nicholas A. Turner



Nicholas A. Turner is an Assistant Professor of Infectious Diseases at Duke University School of Medicine.

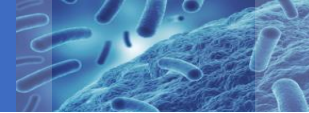
As a physician-researcher, he has participated in multiple large-scale clinical trials focused on bacteremia and antibacterials - including DOTS (dalbavancin), ERADICATE (ceftobiprole), PALACE (penicillin allergy), and iNAAN (penicillin allergy). He also has an active K23 grant studying the role of the microbiome in preventing progression to C. difficile disease.

Dalbavancin as an Option for Treatment of *Staphylococcus aureus* Bacteremia

The DOTS Trial

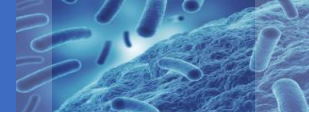
NA Turner, T Hamasaki, S Evans, SB Doernberg, TP Lodise, H King, V Ghazaryan, SE Cosgrove, TC Jenkins, C Liu, S Sharma, S Zaharoff, L Wahid, P Cook, I Raad, R Hachem, A Chaftari, M Sims, C DeMarco, LG Miller, MW McCarthy, CG Morse, C Lucasti, G Forrest, K Cherabuddi, C Polk, T Fazili, ME Rupp, GR Thompson, K Kim, L Strnad, AE Schnee, JA McKinnell, M Ramesh, FP Silveira, TP McCarty, TC Lee, EG McDonald, K Paolino, K Wiegand, A Wall, T Riccobene, R Patel, U Rappo, HF Chambers, VG Fowler, Jr., TL Holland on behalf of the **Antibacterial Resistance Leadership Group**





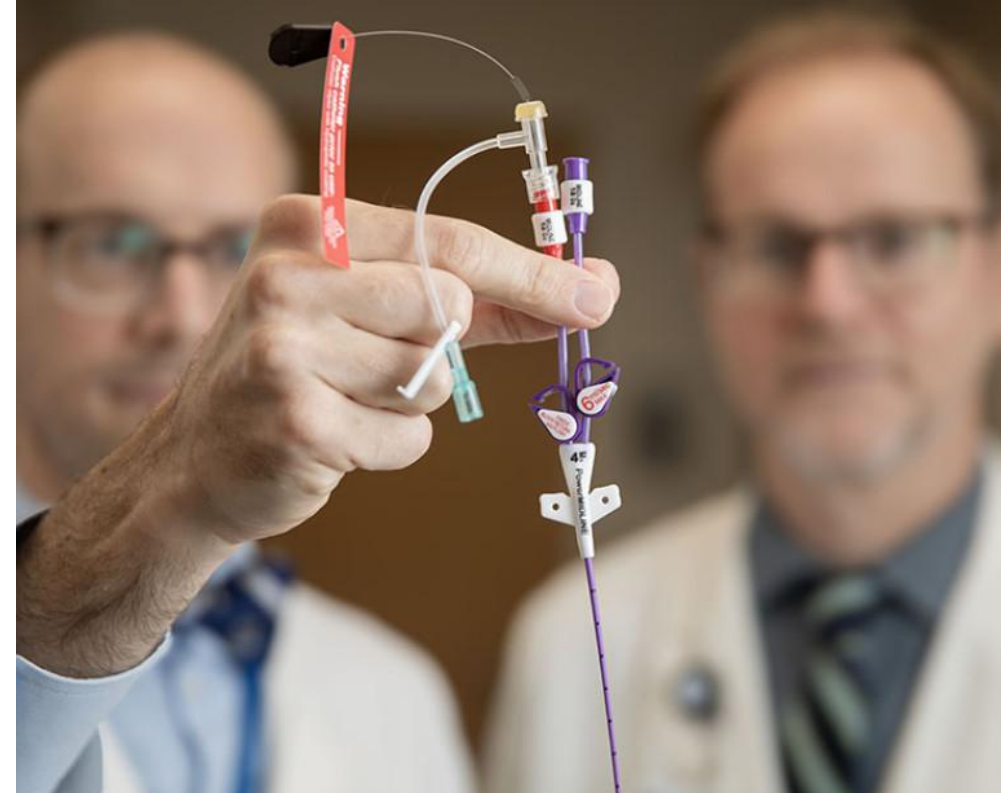
DISCLOSURES

- Support: NIH (NIAID Award No. 5UM1AI104681-09).
- Study drug supplied by Abbvie.
- The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.
- Dalbavancin is not currently approved by the FDA or EMA for the treatment of complicated SAB or endocarditis.



BACKGROUND: *Staphylococcus aureus*

- Leading cause of death by bloodstream infection worldwide
- Treatment traditionally involves prolonged intravenous antibiotics
- Complications from long-term intravenous antibiotics are common
- Better treatments are needed

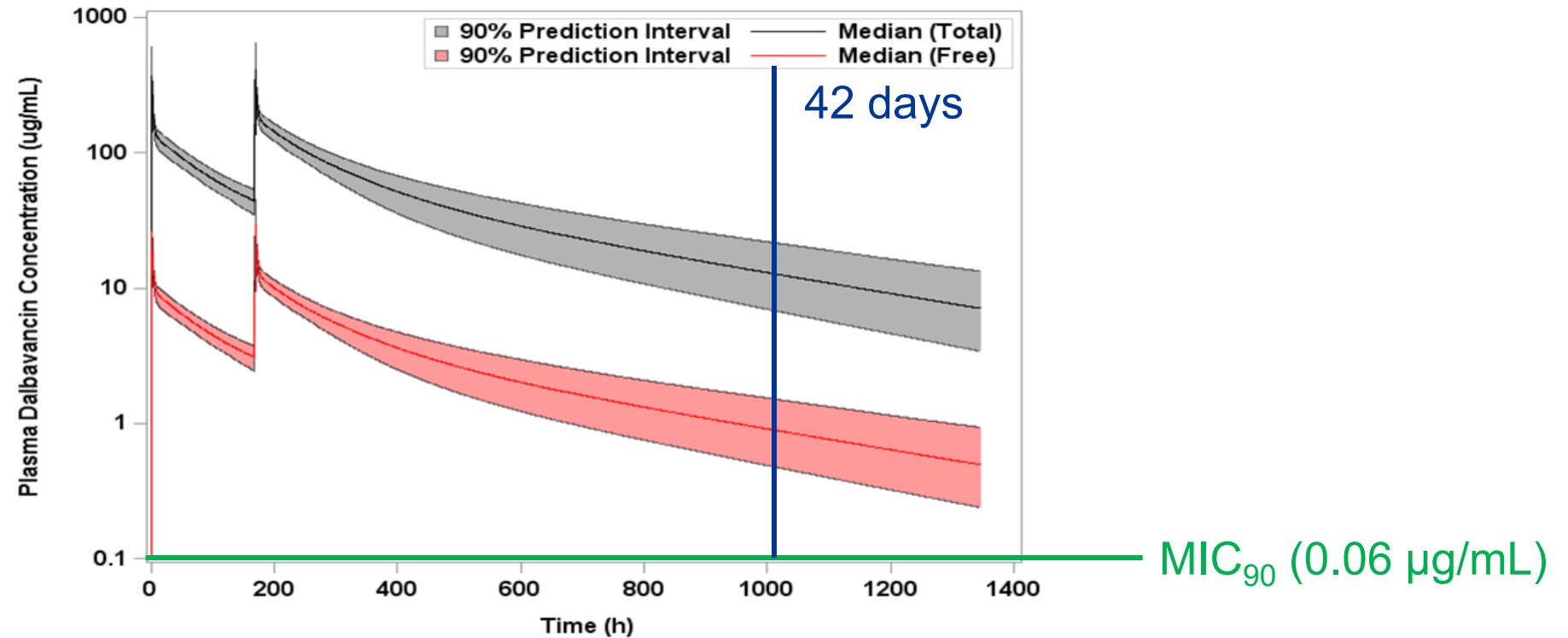


Bai et al *Clin Microbiol Infect* 2022

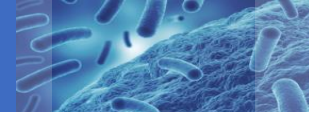
Suzuki et al *OFID* 2018

Global Burden of Disease 2019 Lancet 2022

BACKGROUND: Dalbavancin

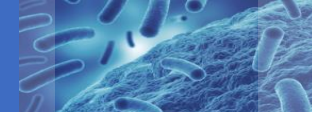


- Lipoglycopeptide with potent *S. aureus* activity (including MRSA)
- Two weekly infusions of 1500 mg provides effective levels for 6 weeks
- FDA/EMA approved for acute bacterial skin & skin structure infection

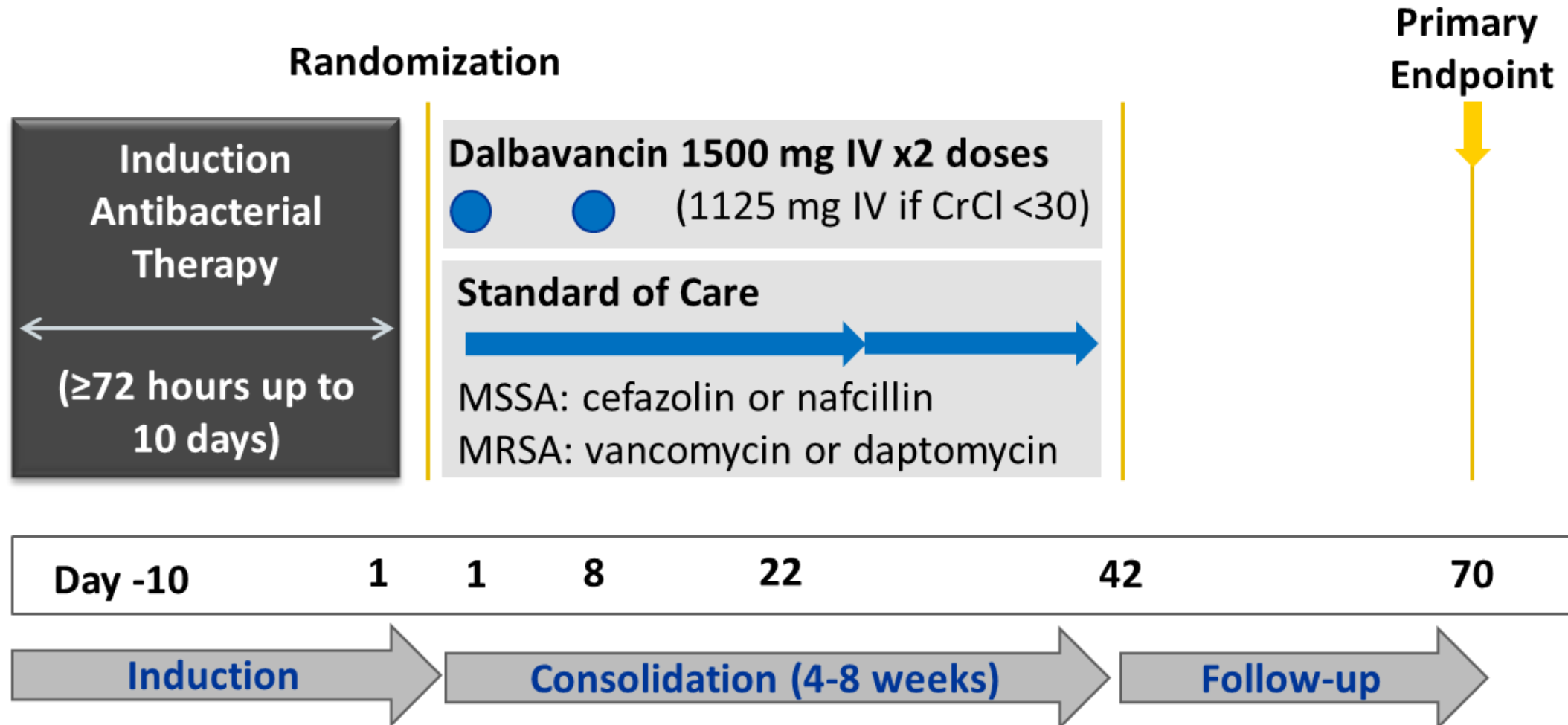


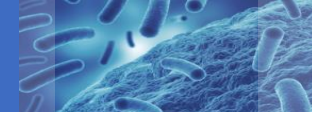
Study Hypothesis

- We hypothesized dalbavancin would have:
 - Similar clinical efficacy
 - Fewer treatment-associated adverse events
- Resulting in dalbavancin being superior to standard of care



METHODS: DOTS Study Design

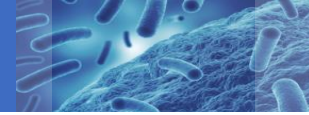




METHODS: Primary Outcome

▪ Desirability of Outcome Ranking (DOOR) at day 70, by ITT

Rank	Alive	How many of: 1) Clinical failure 2) Infectious complications 3) SAE or AE leading to study drug discontinuation	Quality of Life
1	Yes	0 of 3	Tiebreaker based on quality of life score
2	Yes	1 of 3	
3	Yes	2 of 3	
4	Yes	3 of 3	
5	No (dead)	Any	



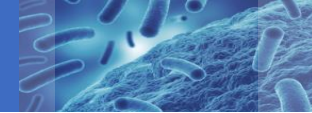
METHODS: Secondary Outcomes & Power

- **Secondary Outcomes**

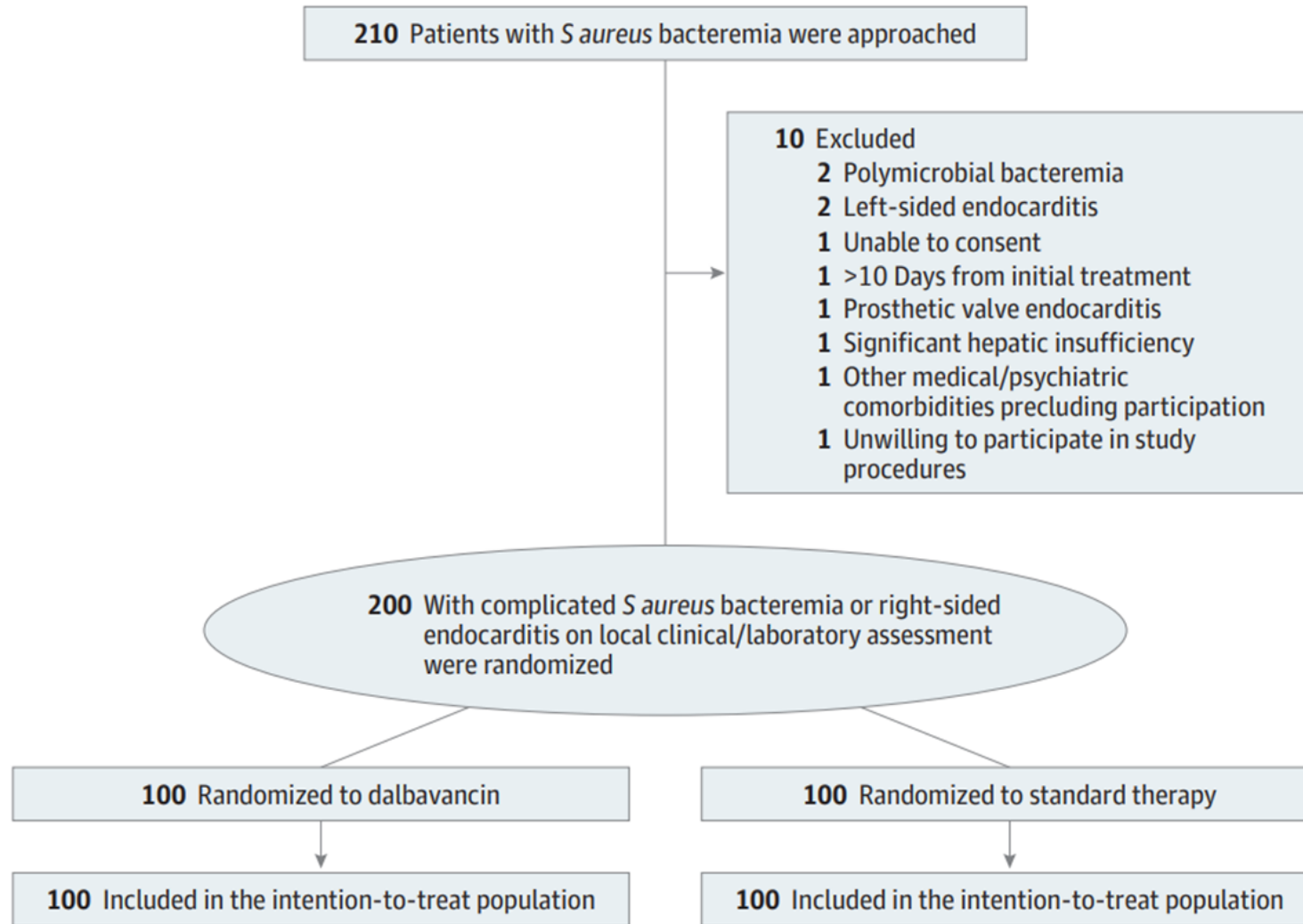
- Day 70 clinical efficacy (assessed by blinded committee)
- Adverse events by modified ITT (receipt of ≥ 1 study dose)

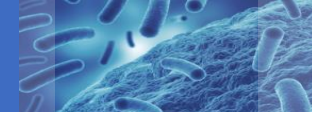
- **Power considerations**

- Powered for primary outcome
- 95% power for $n=200$ (with up to 12% loss to follow-up)
- Similar power for secondary outcome (20% NI margin)



RESULTS: Subject Disposition





RESULTS: Trial Population

Median age 56

~15% PWID

Pretty typical comorbidities

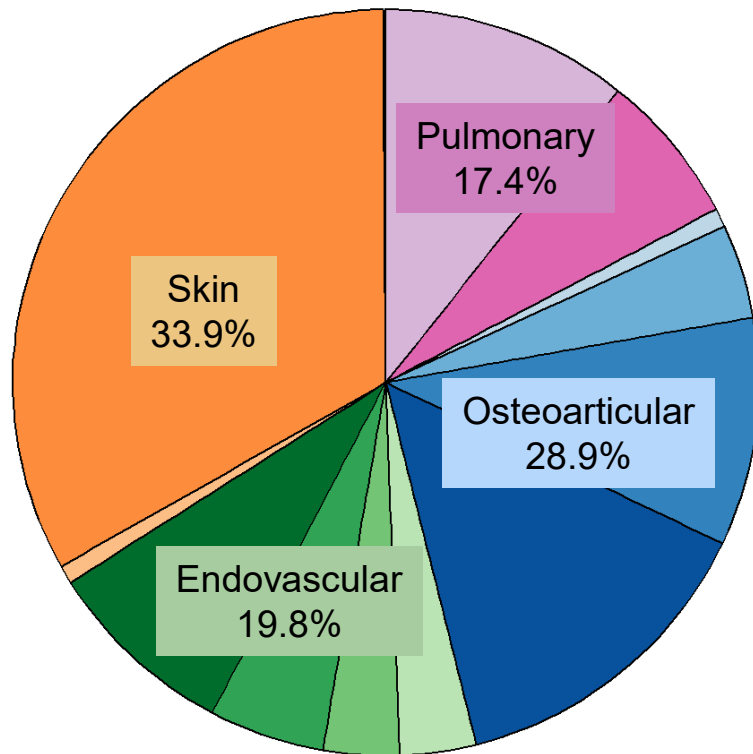
Table 1. Baseline Characteristics of Participants in the DOTS Trial^a

Characteristic	Dalbavancin (n = 100)	Standard therapy (n = 100)
Age, median (IQR), y	56 (41-66)	56 (41-68)
Age ≥80, No. (%)	1 (1)	4 (4)
Sex, No. (%)		
Male	70 (70)	68 (68)
Female	30 (30)	32 (32)
Race, No. (%)		
Asian	5 (5)	1 (1)
American Indian or Alaska Native	2 (2)	0
Black or African American	20 (20)	29 (29)
White	68 (68)	69 (69)
Not reported	5 (5)	1 (1)
Hispanic or Latino, No. (%)	11 (11)	14 (14)
Body mass index, median (IQR) ^b	27.6 (24.3-31.7)	26.9 (23.3-33.5)
Persons who inject drugs, No. (%)	16 (16)	13 (13)
Medical comorbidities, No. (%)		
Diabetes	44 (44)	48 (48)
Immunosuppressed condition ^c	35 (35)	26 (26)
Chronic kidney disease	20 (20)	30 (30)
Heart failure	21 (21)	19 (19)
Cancer	21 (21)	17 (17)
Receiving dialysis	12 (12)	13 (13)
Liver disease	14 (14)	8 (8)

RESULTS: Infection Characteristics

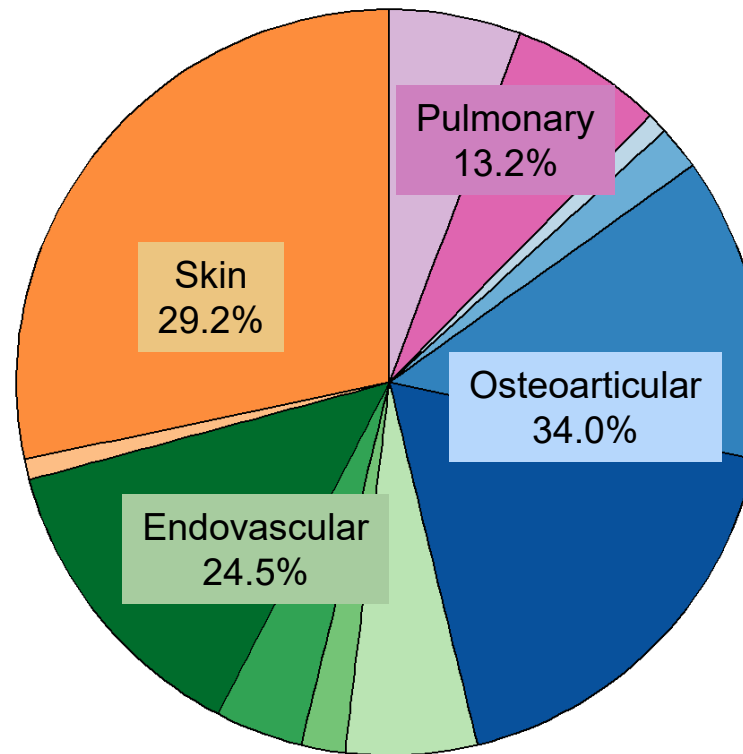
Dalbavancin

n=121 total infections among 100 subjects



Standard of Care

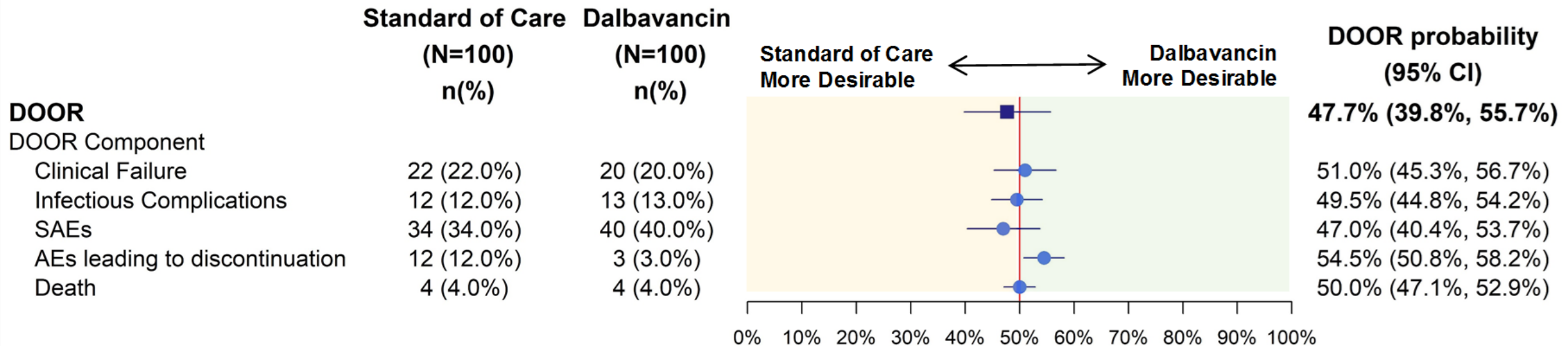
n=106 total infections among 100 subjects



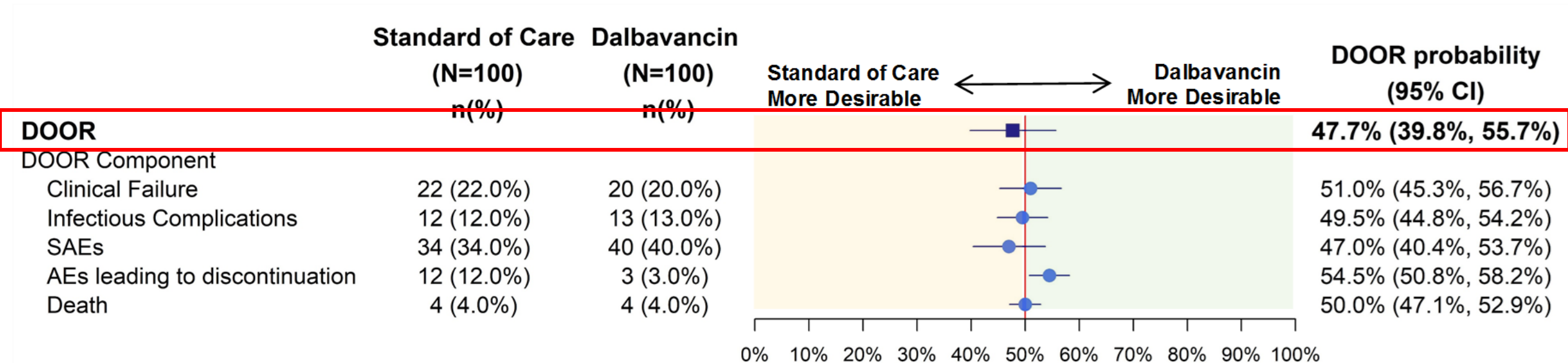
Infection

- Acute bacterial skin/skin structure infection
- Visceral abscess/septic emboli
- Septic thrombophlebitis
- Right sided native valve endocarditis
- Cardiac device infection
- Vascular graft infection / mycotic aneurysm
- Osteomyelitis, non-vertebral
- Septic arthritis of native joint
- Vertebral osteomyelitis
- Prosthetic joint infection
- Septic pulmonary emboli
- Pneumonia / empyema

RESULTS: DOOR Components at Day 70



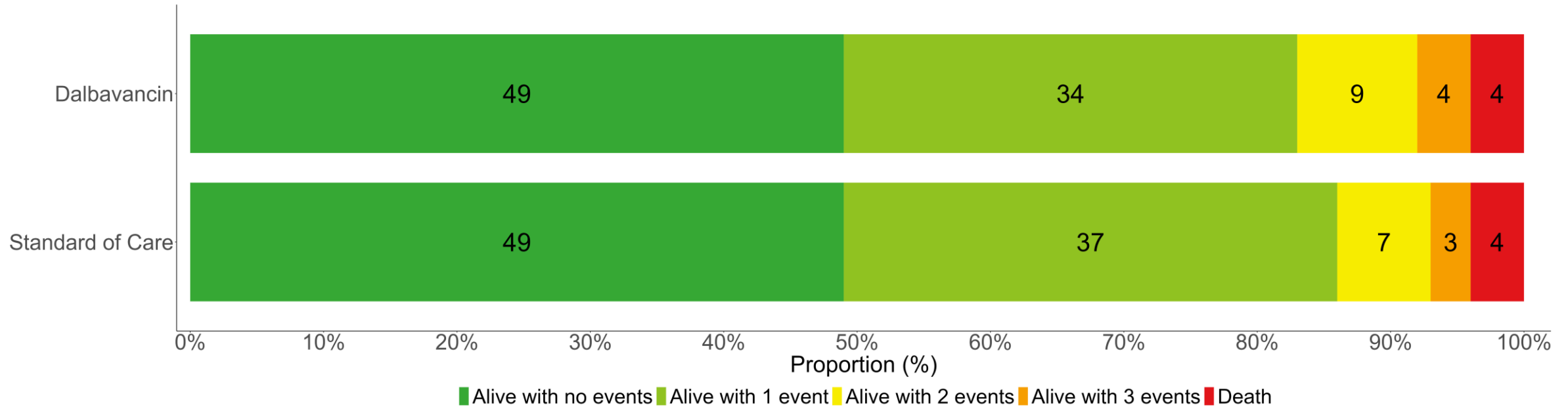
RESULTS: DOOR Components at Day 70



**Conclusion: Similar rates of survival and clinical success,
with fewer AEs leading to dalbavancin discontinuation**

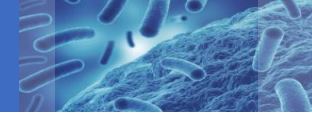
RESULTS: Primary Outcome

Overall DOOR Distribution



DOOR probability: 47.7% (95% CI: 39.8%-55.7%)

Conclusion: Benefits/risks similar with dalbavancin vs SOC

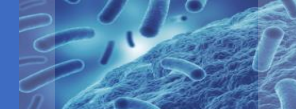


RESULTS: Secondary Outcomes

Non-inferiority Analysis

	Dalbavancin (n=100)	Standard of Care (n=100)
Clinical efficacy (95% CI)	73% (64-82)	72% (63-81)
Difference (95% CI)	+1% (-12 to +14%)	

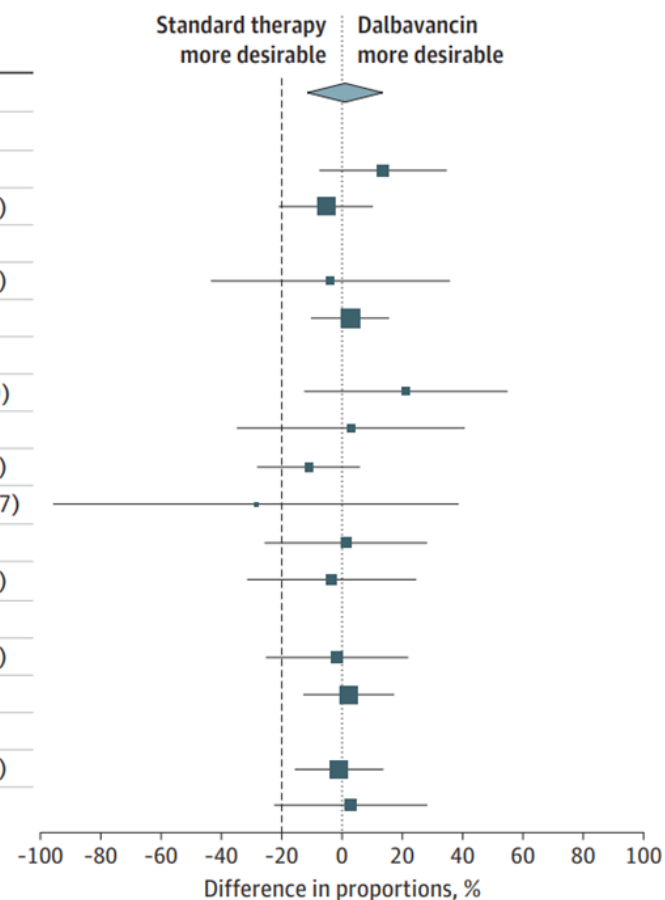
**Conclusion: Dalbavancin is non-inferior to
SOC by traditional clinical efficacy**

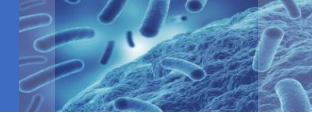


RESULTS: Efficacy by Subgroup

B Clinical efficacy at day 70

Subgroup	Participants, No./total (%)		Difference in proportions, % (95% CI)
	Dalbavancin (n = 100)	Standard therapy (n = 100)	
Overall	73/100 (73)	72/100 (72)	1.0 (-11.5 to 13.5)
Pathogen			
Methicillin-resistant <i>S aureus</i>	28/34 (82.4)	22/32 (68.8)	13.6 (-7.5 to 34.7)
Methicillin-susceptible <i>S aureus</i>	45/66 (68.2)	50/68 (73.5)	-5.3 (-21.0 to 10.3)
Persons who inject drugs			
Yes	8/16 (50.0)	7/13 (53.8)	-3.8 (-43.5 to 35.8)
No	65/84 (77.4)	65/87 (74.7)	2.7 (-10.3 to 15.6)
Infection type			
Endovascular only	12/15 (80.0)	10/17 (58.8)	21.2 (-12.5 to 54.9)
Osteoarticular only	9/16 (56.2)	8/15 (53.3)	2.9 (-34.9 to 40.7)
Skin only	16/18 (88.9)	15/15 (100.0)	-11.1 (-28.2 to 6.0)
Pulmonary only	5/7 (71.4)	3/3 (100.0)	-28.6 (-95.8 to 38.7)
Other or unknown infection only	14/19 (73.7)	21/29 (72.4)	1.3 (-25.7 to 28.2)
Multiple infections	17/25 (68.0)	15/21 (71.4)	-3.4 (-31.5 to 24.6)
Immunocompromised			
Yes	25/35 (71.4)	19/26 (73.1)	-1.6 (-25.3 to 22.0)
No	48/65 (73.8)	53/74 (71.6)	2.2 (-12.9 to 17.3)
Bacteremia duration, d			
<2	57/77 (74.0)	48/64 (75.0)	-1.0 (-15.7 to 13.7)
≥2	16/23 (69.6)	24/36 (66.7)	2.9 (-22.5 to 28.3)

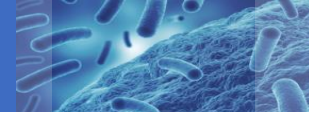




RESULTS: Safety

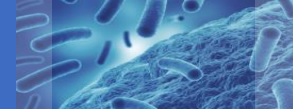
Adverse Events (AEs)	Dalbavancin (n=100)	Standard of care (n=100)
Serious adverse events (SAEs)	43	37
Related serious AEs	2	4
AEs leading to discontinuation	3	12

- Overall similar AE rates
- Slightly more AEs leading to discontinuation with SOC



DOTS CONCLUSIONS

- Dalbavancin had **similar risk/benefit** to SOC, but was not superior by DOOR
- Dalbavancin was **non-inferior to SOC by clinical efficacy**
- **Safety was overall similar** between dalbavancin and SOC
- Dalbavancin is a **viable treatment option for complicated SAB**



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Temocillin versus meropenem for the treatment of bacteraemia due to third-generation cephalosporin-resistant Enterobacterales (ASTARTÉ trial)

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Temocillin versus carbapenems for bacteraemia due to third-generation cephalosporin-resistant Enterobacterales in Spain (ASTARTÉ): a multicentre, phase 3, open-label, non-inferiority, randomised clinical trial



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Lancet 2026; 408: 430–39

Disclosures

No conflicts of interests

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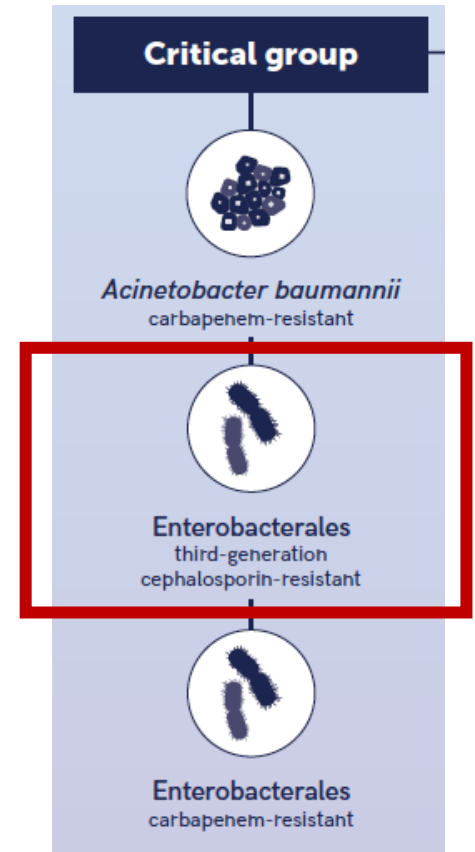
Temocillin provided by Eumedica Pharmaceuticals AG (Switzerland), through partner company Belpharma SA (Luxembourg) – no influence in design, conduction or analyses

RESEARCH QUESTION

- Is temocillin as efficacious as carbapenems for the treatment of bacteraemia due to 3rd generation cephalosporin-resistant Enterobacterales (3GCR-E)?

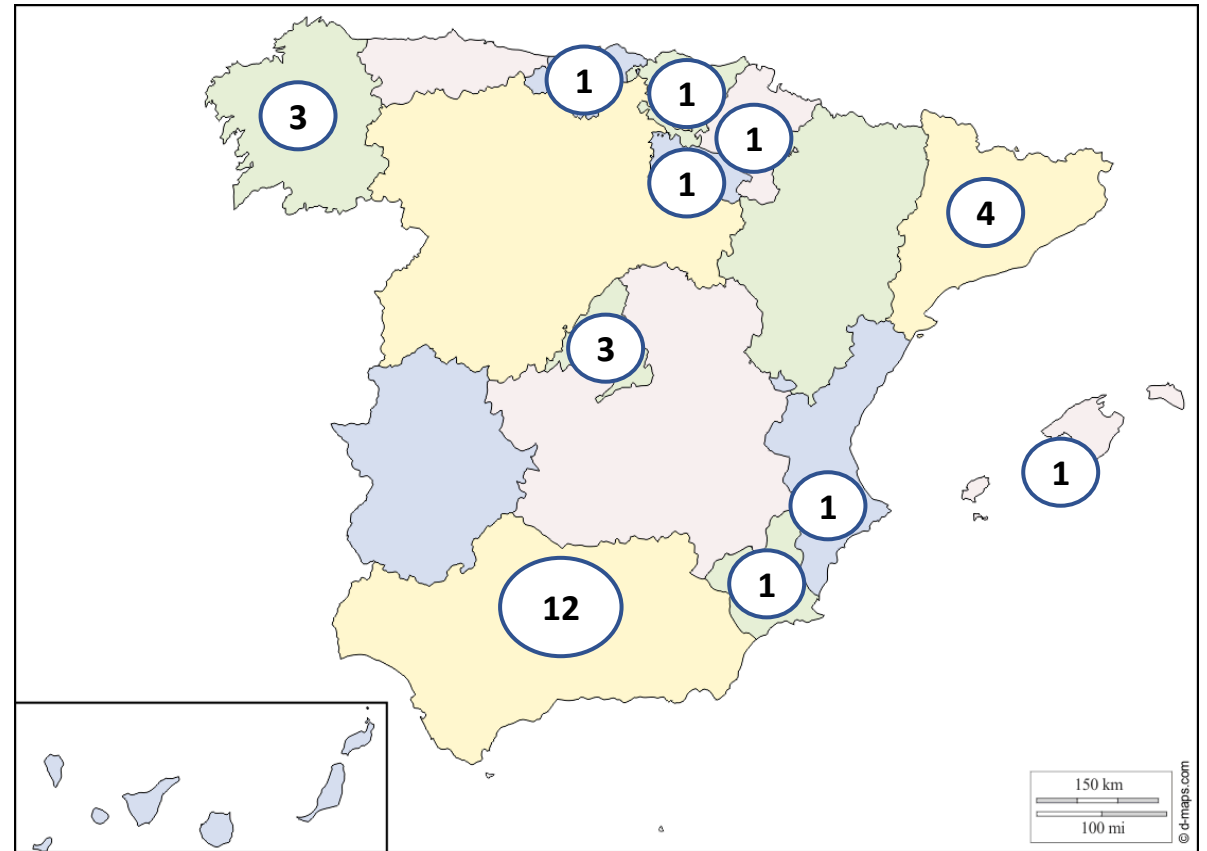
WHY THIS QUESTION

- 3GCR-E: WHO “critical group” and drivers for increasing carbapenem consumption worldwide → need for alternatives
- So far, no drug showed to be non-inferior to carbapenems in RCT
 - Piperacillin-tazobactam (MERINO trial)
 - Fosfomycin (FOREST trial)
- Temocillin is a β -lactam, stable against ESBL and AmpC enzymes
 - Narrower spectrum than carbapenems: no activity against *Pseudomonas*, *Acinetobacter* or anaerobes



HOW DID WE DO (1)

- Multicentre, open-label, phase 3, pragmatic, investigator-initiated randomized clinical trial
- 29 Spanish hospitals
- Between 2020-2024



HOW DID WE DO (2)

Inclusion criteria

1. Hospitalised adult patients with **monomicrobial bacteraemia due to *Enterobacterales***
2. **Resistant to cephalosporins** (cefotaxime, ceftriaxone; and/or ceftazidime)
3. **Susceptible to temocillin** (MIC ≤ 8 mg/L; ≤ 16 mg/L if urinary source) **and meropenem**
4. Planned duration of **IV treatment ≥ 4 days**

Exclusion criteria

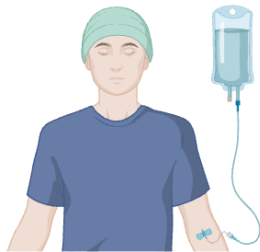
1. Pregnancy or breast feeding
2. Palliative care or life expectancy < 30 days
3. Allergy to beta-lactams
4. **> 48 h after susceptibility data available**
5. **Active empirical therapy for ≥ 96 h**
6. Infections typically needing > 14 days or meningitis
7. Peritoneal dialysis or continuous hemofiltration

HOW DID WE DO (3)

Randomisation (1:1) once susceptibility is available (<48h)
Stratified according to empirical therapy and source of BSI



Temocillin, 2 g IV TID



**Meropenem, 1 g IV TID
or ertapenem 1 g IV QD**



**Oral switch allowed if active oral
drug available, after 4 days**



- Ciprofloxacin
- TMP-SMX
- Amox-clav
- Fosfomycin



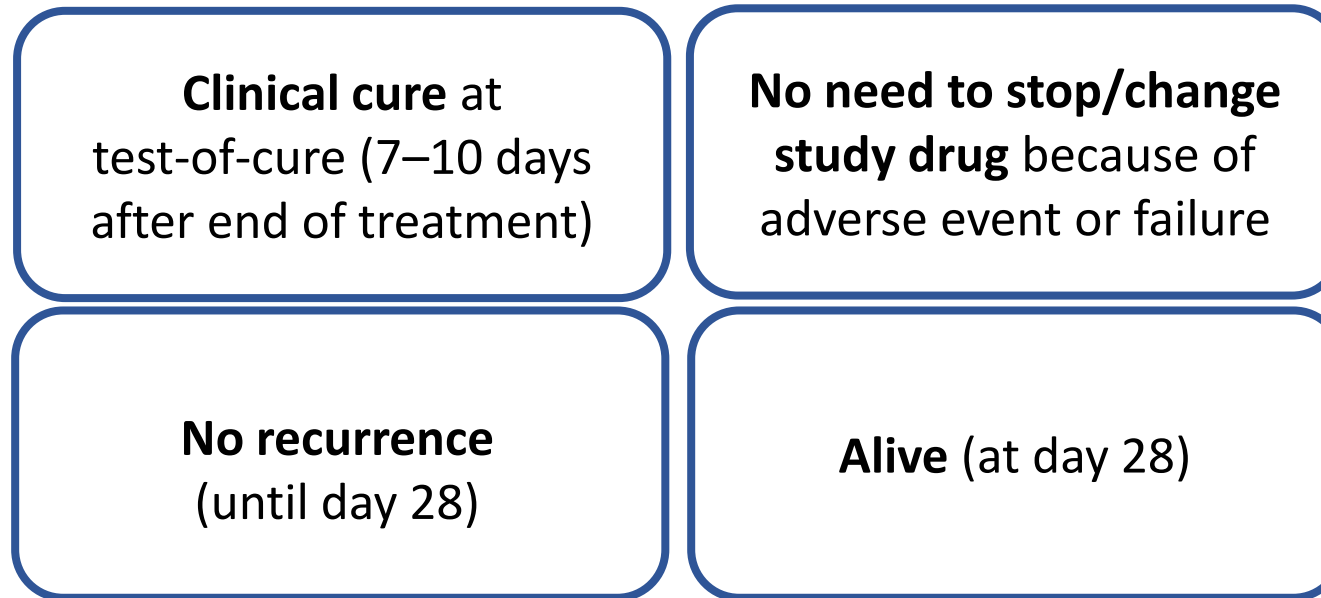
8-10 days
after end of
treatment:
Test of cure



28 days:
**Mortality,
recurrence**

HOW DID WE DO (4)

Primary endpoint: **clinical success** in the modified intention-to-treat (mITT) population



Secondary endpoints: clinical cure, mortality, recurrence, reinfections, microbiological cure, length of hospital stay, change in SOFA and adverse events

HOW DID WE DO (5)

- **Sample size**

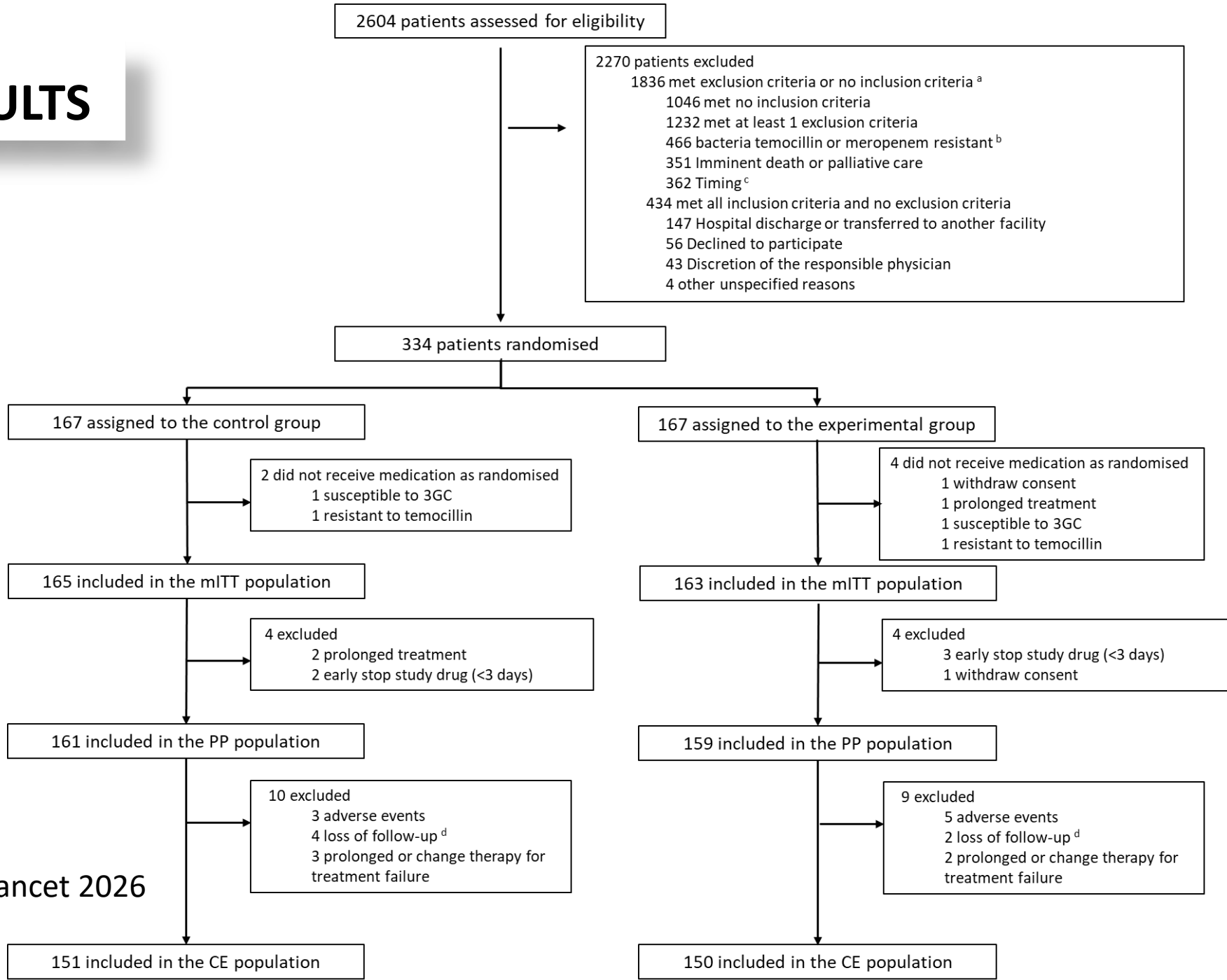
- Non-inferiority margin: 10%; estimated clinical success (both groups): 85%
- Power 80%, one-sided alpha 5%; 5% missed patients → 334 patients

- **Primary analysis:** absolute difference with 95% CI in mITT population

- **Secondary analyses**

- Secondary endpoints
- Pre-defined subgroups
- DOOR analysis

MAIN RESULTS



Baseline characteristics (mITT population)

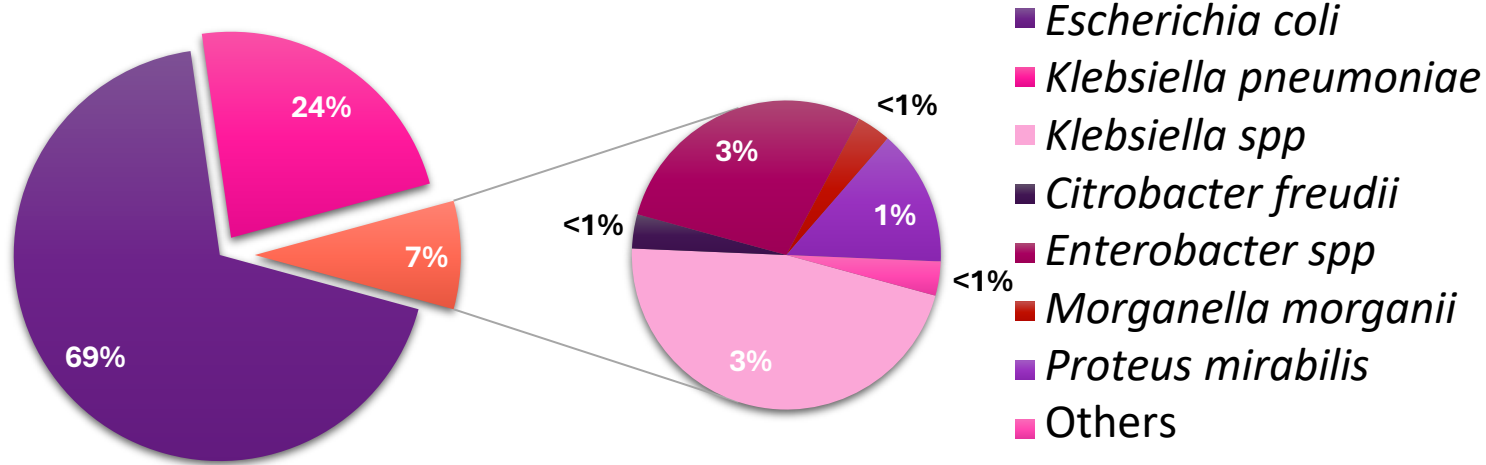
	Receiving temocillin (n=163)	Receiving carbapenem* (n=165)
Age, median (IQR), years	74 (65-82)	71 (66-77)
Female gender	59 (36.2)	47 (28.5)
Underlying conditions		
Charlson Comorbidity Index, median (IQR)	2 (1-4)	2 (0-3)
Diabetes mellitus	55 (33.7)	35 (21.2)
Chronic pulmonary disease	20 (12.3)	21 (12.7)
Cancer	40 (24.5)	36 (21.8)
Chronic renal disease, moderate-severe	30 (18.4)	27 (16.4)
Chronic liver disease	12 (7.4)	11 (6.7)
Immunosuppressive therapy	40 (24.5)	37 (22.4)
Source of bacteraemia		
Urinary tract	123 (75.5)	123 (74.5)
Biliary tract	17 (10.4)	15 (9.1)
Intraabdominal, non-biliary	8 (4.9)	9 (5.5)
Others	15 (9.2)	18 (10.9)
SOFA score, median (IQR)	2 (1-3)	2 (1-3)
Strict community acquisition	63 (38.7)	59 (35.8)
Treatment variables		
First drug administered, appropriate	103 (63.2)	103 (62.2)
Previous days of appropriate therapy, median (IQR)	2 (1-3)	2 (1-3)
Days of IV treatment with study drug, median (IQR)	6 (4-8)	6 (4-8)
Days of therapy from randomization, median (IQR)	7.5 (6-10)	7 (6-11)
Switched to oral treatment	60 (36.8)	64 (38.8)



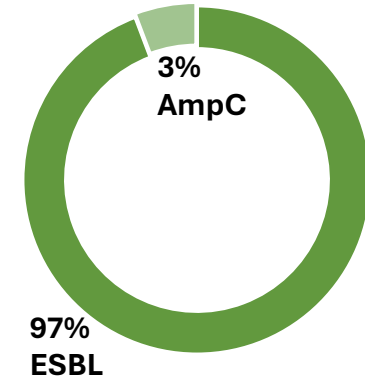
Meropenem, n=99
Ertapenem, n=66

Cogliati Dezza et al, Lancet 2026

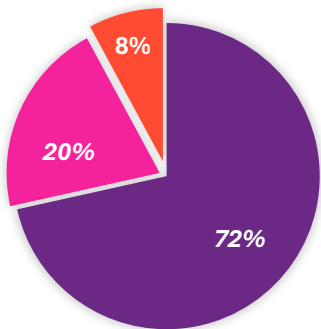
Aetiology



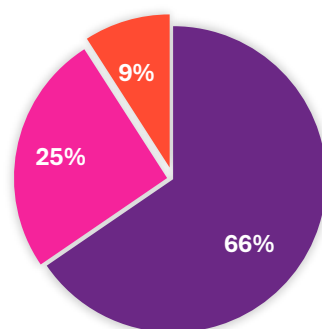
Mechanism of cephalosporin-resistance



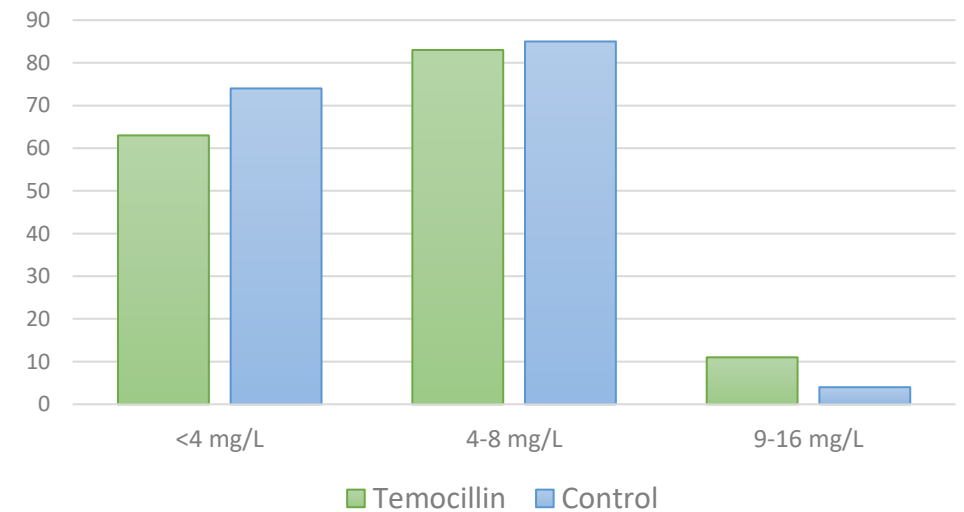
Temocillin



Control

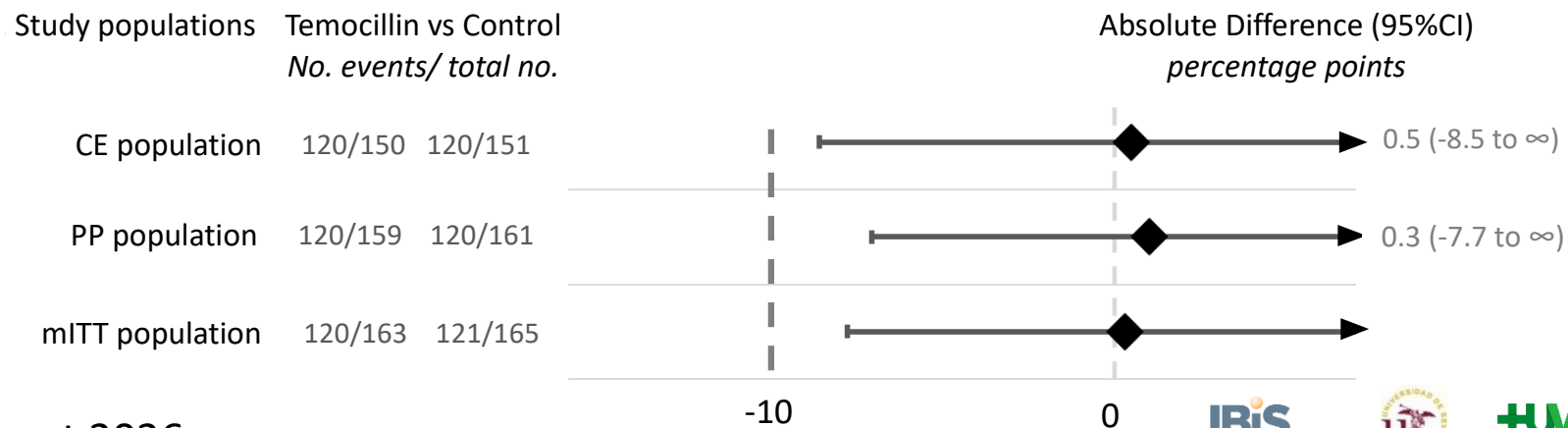


Temocillin CMI (%)



Outcomes

	Temocillin (n=163)	Carbapenem (n=165)	Difference (one- sided 95% CI)	One-sided p value*
Primary outcome				
Clinical success	120 (74%)	121 (73%)	0.3 (-7.7 to ∞)	0.017
Components of the primary outcome and secondary outcomes				
Clinical cure	130 (80%)	135 (82%)	-2.0 (-9.2 to ∞)	0.032
Stop or change study drug for any reason	10 (6%)	8 (5%)	1.3 (-∞ to 5.4)	0.0016
Recurrence until day 28	6 (4%)	10 (6%)	-2.4 (-∞ to 1.5)	<0.0001
Death, any cause at day 28	4 (2%)	6 (4%)	-1.2 (-∞ to 1.9)	<0.0001
Other outcomes				
Microbiological cure (only urinary tract infection) at TOC	37/82 (45%)	35/81 (43%)	1.9 (-10.9 to ∞)	0.063
Changes in SOFA score†	-1.4 (-1.7)	-1.2 (-1.5)	0.2 (-9.1 to ∞)	<0.0001
Reinfection until day 28	2 (1%)	2 (1%)	0.0 (-∞ to 2.0)	<0.0001
Length of hospital stay‡, days	8.9 (8.5)	9.7 (10.6)	-0.8 (-∞ to 9.5)	<0.0001



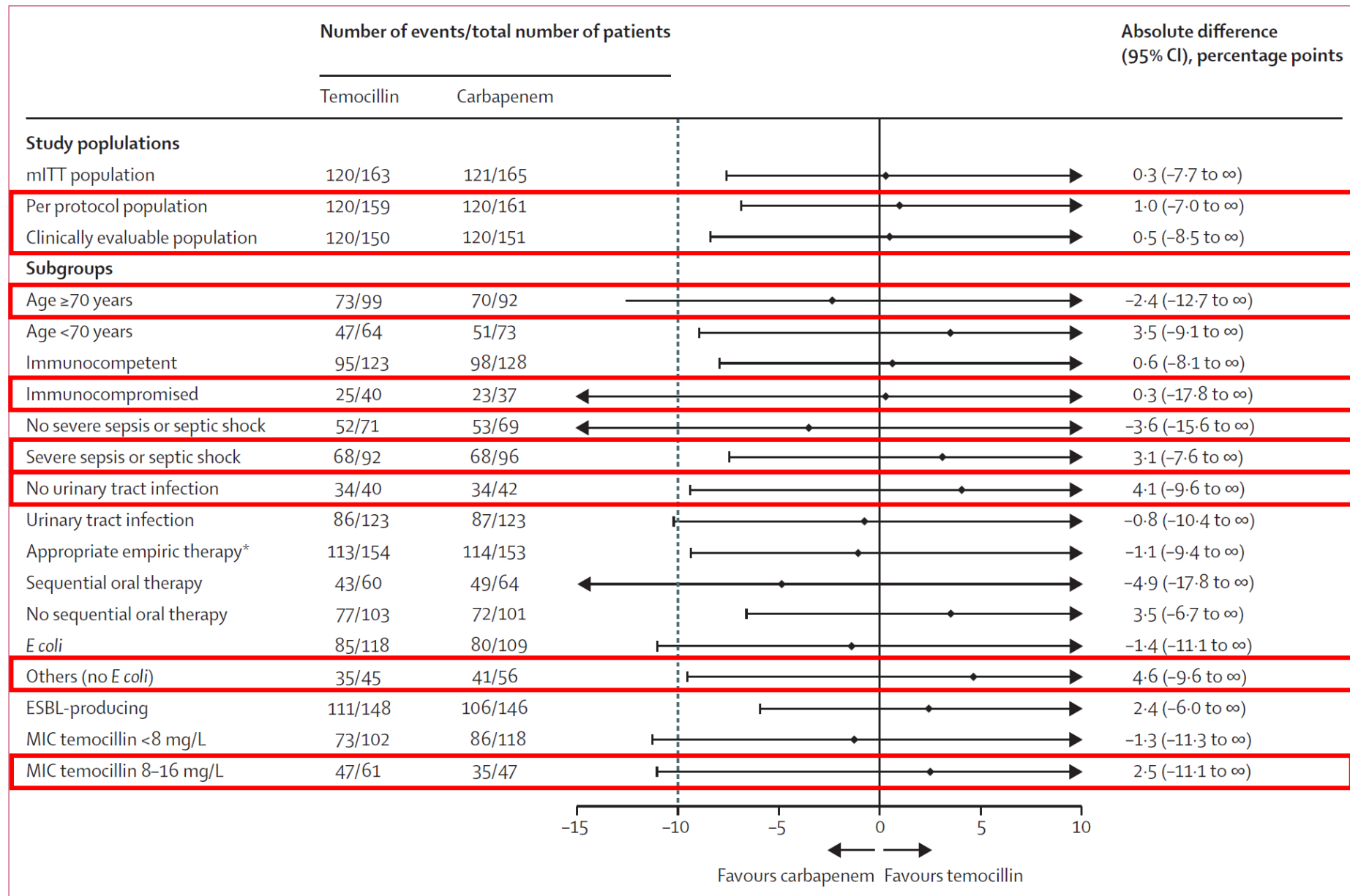
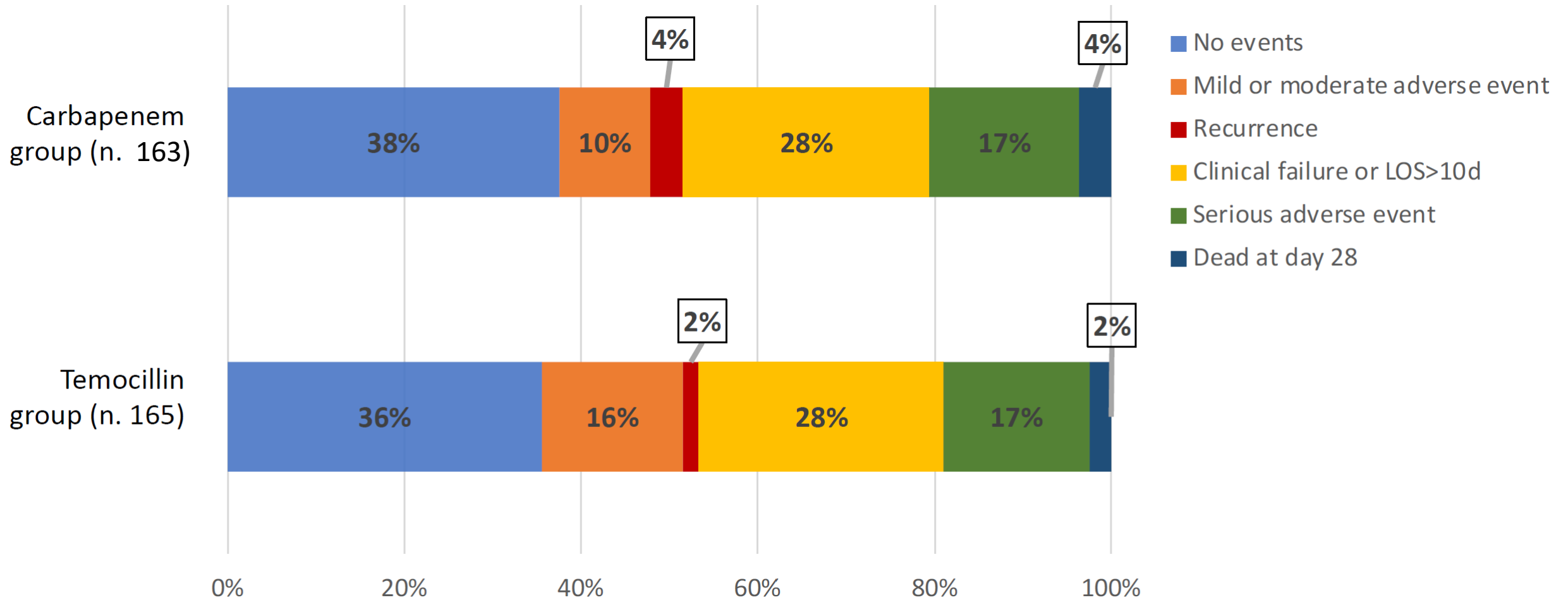


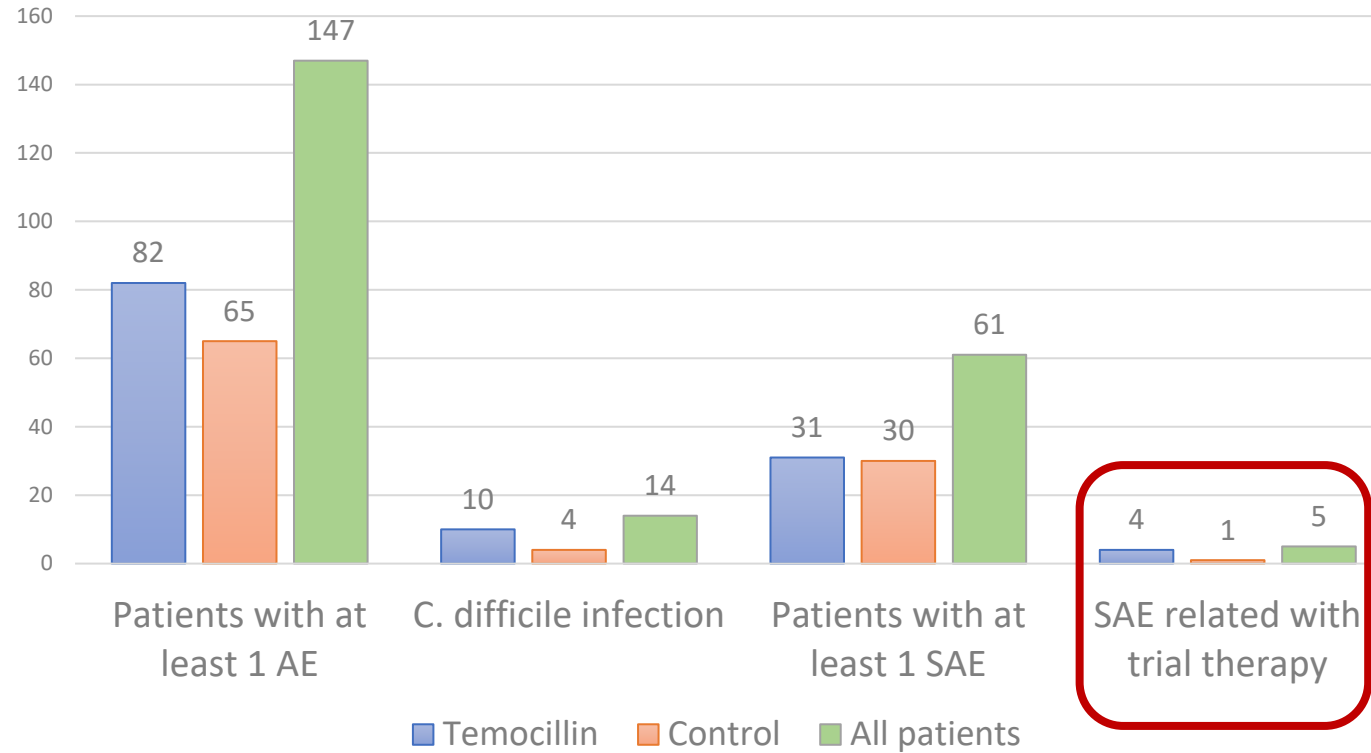
Figure 2: Forest plot of study populations and subgroups for clinical success

DOOR analysis



Probability for temocillin group to have a better DOOR: **50.0%** (95% CI 44.6 to 55.4)

ADVERSE EVENTS (absolute no.)



Temocillin	2 infections due to <i>C. difficile</i> 1 diffuse itching 1 increased transaminases
Carbapenems	1 infection due to <i>C. difficile</i>

CONCLUSION

- **Temocillin was non-inferior** to carbapenems for the targeted treatment of bacteremia due to cephalosporin-resistant Enterobacterales → alternative to carbapenems
 - Majority of UTI and biliary tract infections caused by *E. coli* and *Klebsiella* spp.
 - However, subgroups analysis were consistent with the overall effect

WHAT DID THIS STUDY NOT ANSWER

- Frequency of temocillin-resistance
- Empirical treatment with temocillin
- AmpC-producers (low numbers) - but no reason to doubt if S

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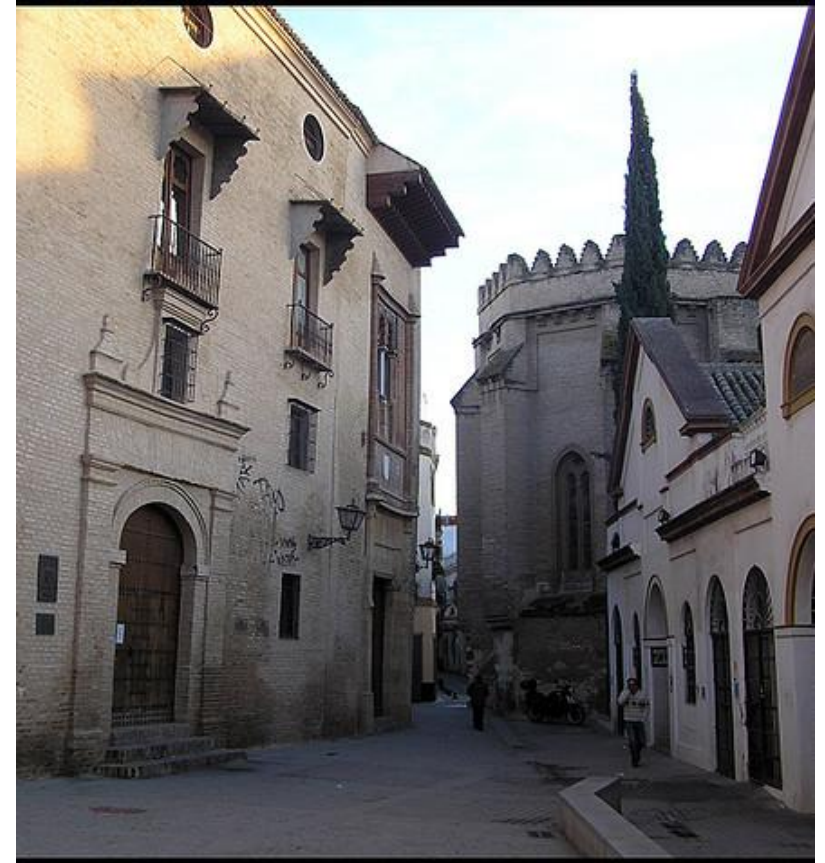
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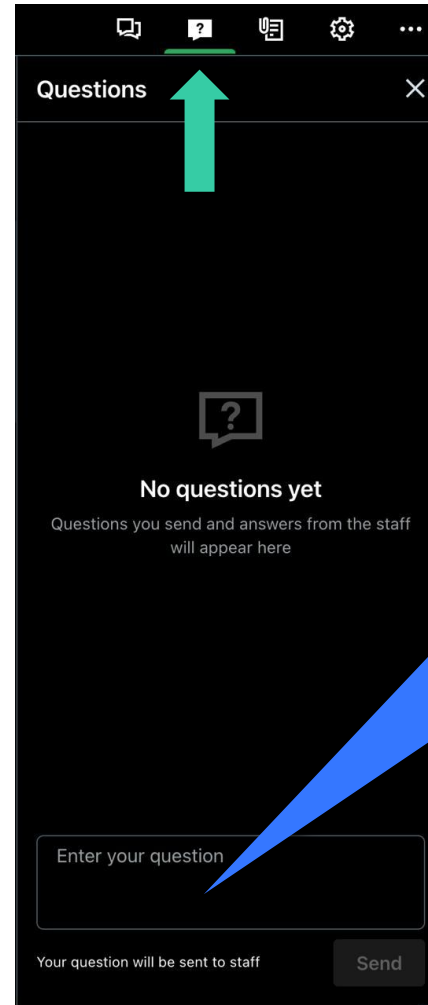


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The role of investigator initiated clinical trials in advancing antimicrobial use



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University of Melbourne,
Australia



Anouk G. Overdeest
Amsterdam UMC,
Netherlands



Nicholas A. Turner
Duke University
School of Medicine,
USA



Jesús Rodríguez-Baño
University of Seville,
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Aislinn Cook
Senior Research Fellow
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Pierre Daram
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Executive Chair
ADVANCE-ID


Pinyo Rattanaumpawan
Professor of Medicine
Mahidol University

Moderated by Regina Osih, Global Access Director, GARDP



From approval to access: A new model for delivering effective antibiotics

With Aislinn Cook, Pierre Daram, David Paterson, Pinyo Rattanaumpawan and moderated by Regina Osih

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