Journal Club:
Key findings from recent publications in antimicrobial R&D

Guest speakers: Melis Anahtar, Nicole Scangarella-Oman, David Paterson

Moderator: Florian Maurer

Host: Victor Kouassi

26 March 2026

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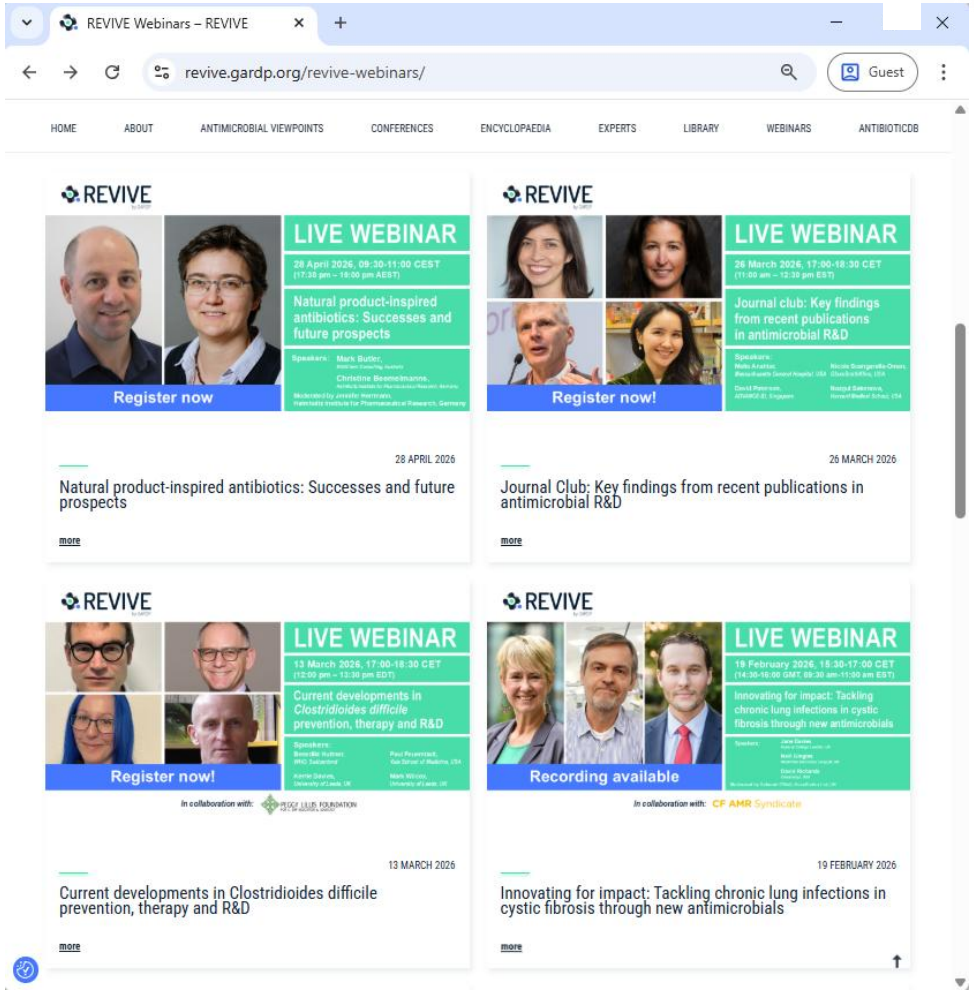

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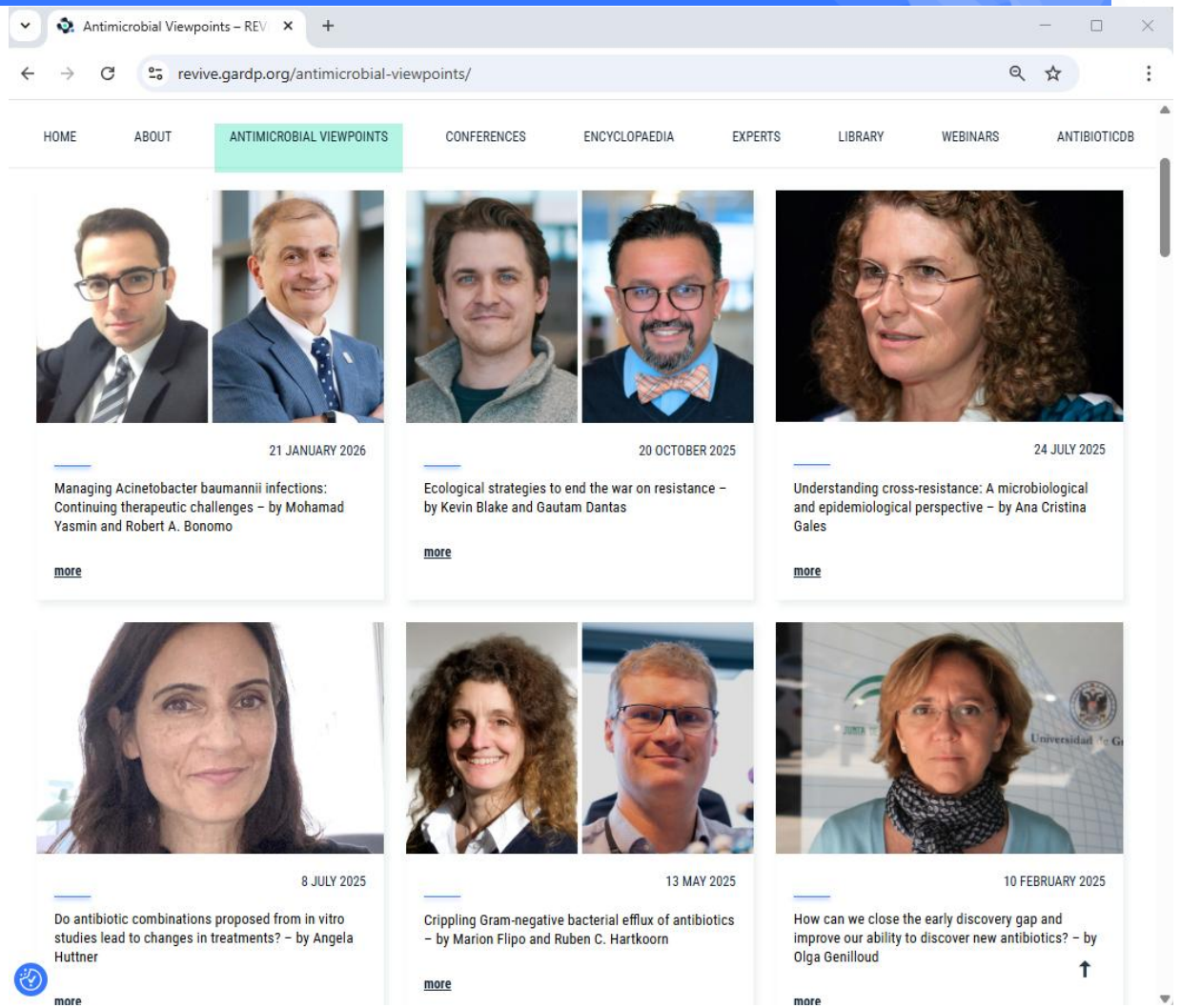

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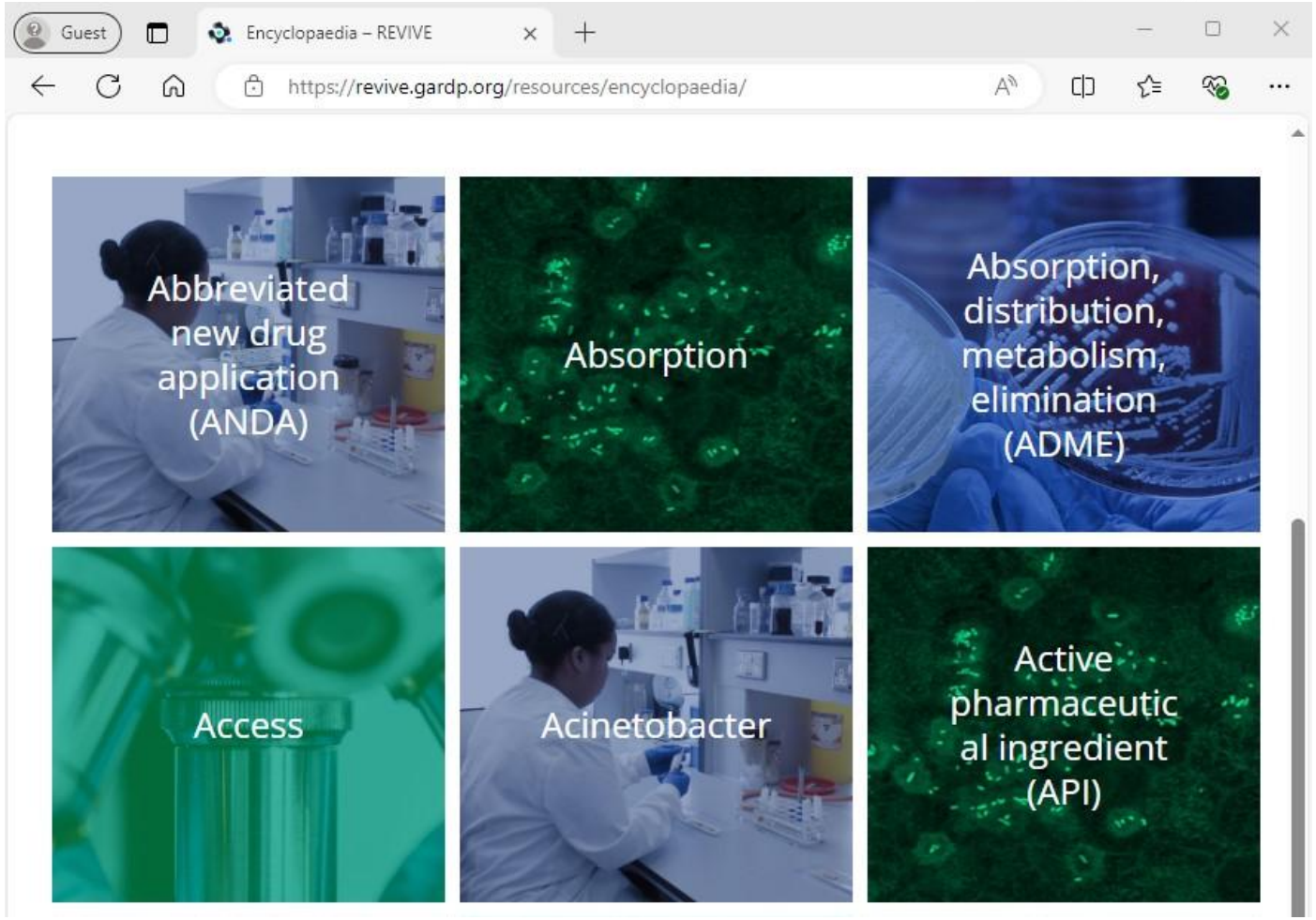

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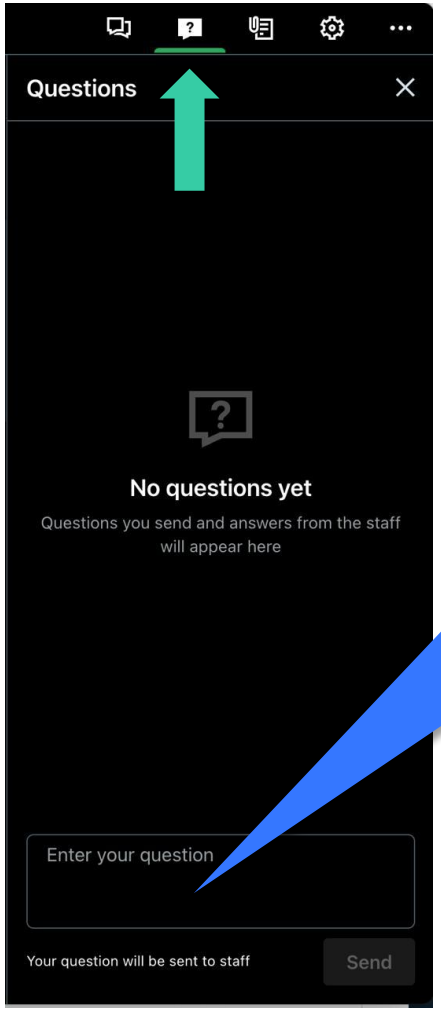

Please submit your questions through the box provided after clicking the ‘questions’ button. We will review all questions and respond to as many as possible after the presentation.

Today's speakers

REVIVE by GARDP

Journal Club: Key findings from recent publications in antimicrobial R&D

Moderator:
Florian Maurer
Basilea Pharmaceuticals, Switzerland

David Paterson
ADVANCE-ID, Singapore

Nicole Scangarella-Oman
GlaxoSmithKline, USA

Melis Anahtar
Massachusetts General Hospital, USA

David Paterson

David Paterson is Director of ADVANCE-ID (ADVANcing Clinical Evidence for Infectious Diseases) at Saw Swee Hock School of Public Health and Yong Loo Lin School of Medicine at National University of Singapore.

ADVANCE-ID is a clinical trials network comprising more than 100 hospitals across 20 countries in Asia. This network is jointly funded by the Wellcome Trust and a number of Singaporean institutions with an aim to conduct clinically important trials in the field of antimicrobial resistance (AMR). This comprises trials of antibiotics, diagnostics and prevention strategies.

David is also an Honorary Professor at the University of Queensland and has more than 600 peer-reviewed publications predominantly in AMR. His research focuses on the molecular and clinical epidemiology of infections with antibiotic-resistant organisms, with the intent of translating knowledge into optimal prevention and treatment of these infections. Multi-country clinical trials are the major component of his research portfolio, and the predominant focus of ADVANCE-ID.

THE UNIVERSITY OF QUEENSLAND
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CREATE CHANGE

Game Changer Trial

Investigator-Initiated Randomised Controlled Trial of Cefiderocol versus Standard of Care Antibiotics

David Paterson
Co-Director, ADVANCE-ID
National University of Singapore

Disclosures

SAB AMR Action Fund and Consultant to CARB-X and GARDP

Grants from Shionogi, Pfizer, Merck, bioMerieux, Gilead

Consultant to Innoviva, Aurobac, BioVersys, Menarini, Gangagen, Kinvard, Basilea, Advanz Pharma, Tamrisa, Antabio

BACTERIAL AND FUNGAL INFECTIONS NEWSLETTER

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Randomised Controlled Trials

Citation of Articles	PICO	Main Results	Risk of Bias
Baghdadi JD, Harris AD, Pineles L, Al-Shanqeeti S, Palacio D, Charles DW, et al. Using probability of community-acquired pneumonia to tailor antimicrobials among inpatients: a pragmatic, randomized trial. Clin Infect Dis. 2026 Mar 13; doi:10.1093/cid/ciag126	**P:** 107 hospitalized adults receiving antibiotics for suspected respiratory infection with either low procalcitonin (65%), positive respiratory virus testing (30%), or both (5%) at 2 hospitals. **I:** Antimicrobial stewardship–guided interpretation of test results via a templated electronic health record note providing post-test probability of bacterial pneumonia and antibiotic decision recommendations.	Stewardship-guided interpretation significantly reduced antibiotic exposure, with mean in-hospital antibiotic days of therapy of 7.5 vs 11.6 in usual care (difference −4.1 days, P = .006). Respiratory antibiotics were discontinued within 5 days for 76% of intervention patients vs 49% in the usual care group (P = .004). There were no statistically significant differences in hospital length of	Moderate risk: The pragmatic design enhances real-world applicability but the relatively small sample size and proof-of-concept nature limit statistical power and generalizability. Lack of blinding could introduce performance bias in prescribing behavior. However, randomized allocation and objective antibiotic utilization outcomes strengthen internal validity.


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PBPs
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IRON
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MDR GRAM
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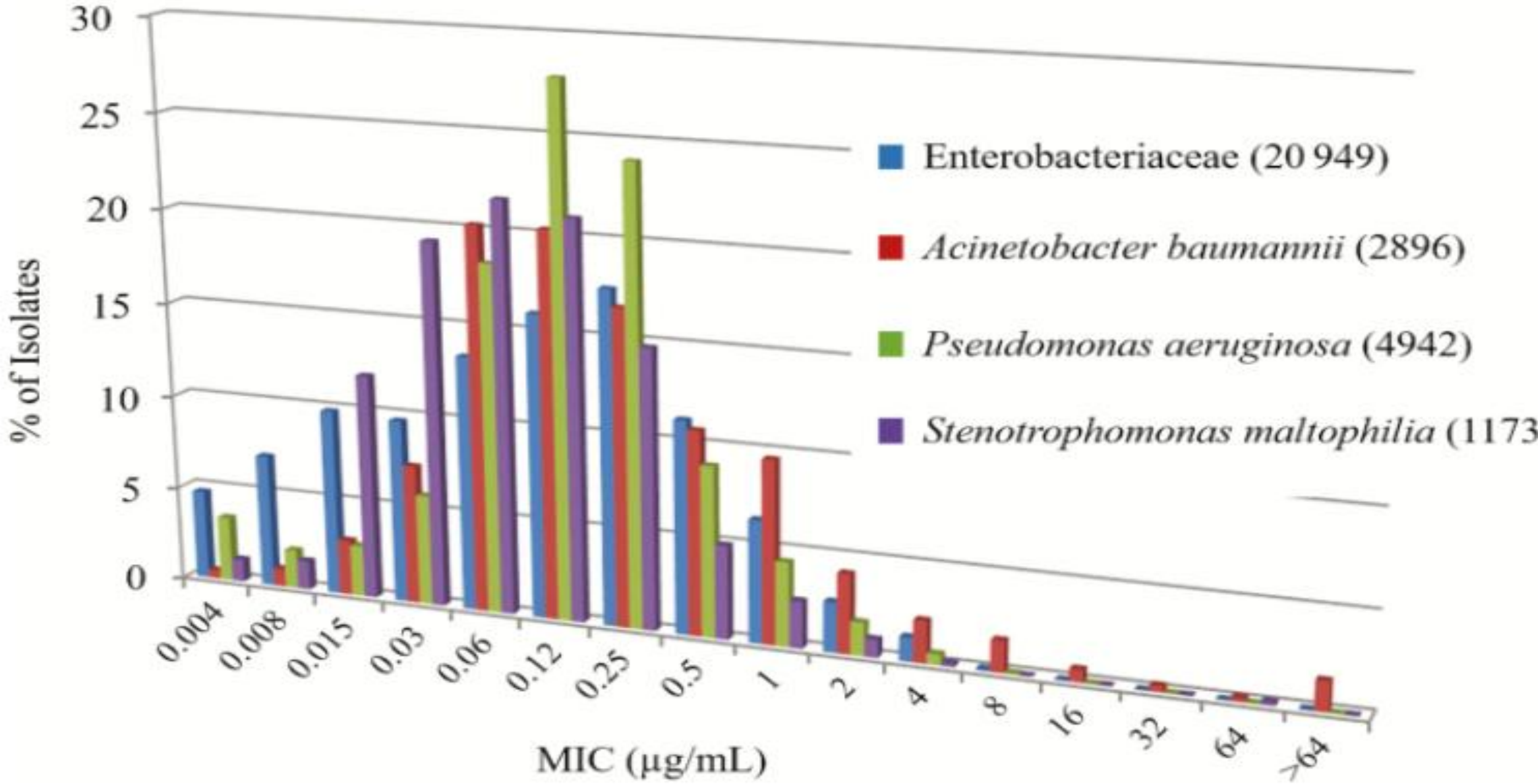
ME


30
25
20
15
10
5
0
% of Isolates
Enterobacteriaceae (20 949)
Acinetobacter baumannii (2896)
Pseudomonas aeruginosa (4942)
Stenotrophomonas maltophilia (1173
0.004
0.008
0.015
0.03
0.06
0.12
0.25
0.5
1
2
4
8
16
32
64
>64
MIC (µg/mL)

Cefiderocol versus imipenem-cilastatin for the treatment of complicated urinary tract infections caused by Gram-negative uropathogens: a phase 2, randomised, double-blind, non-inferiority trial

Simon Portsmouth, David van Veenhuyzen, Roger Echols, Mitsuaki Machida, Juan Camilo Arjona Ferreira, Mari Ariyasu, Peter Tenke, Tsutae Den Nagata

APEKS-UTI Results

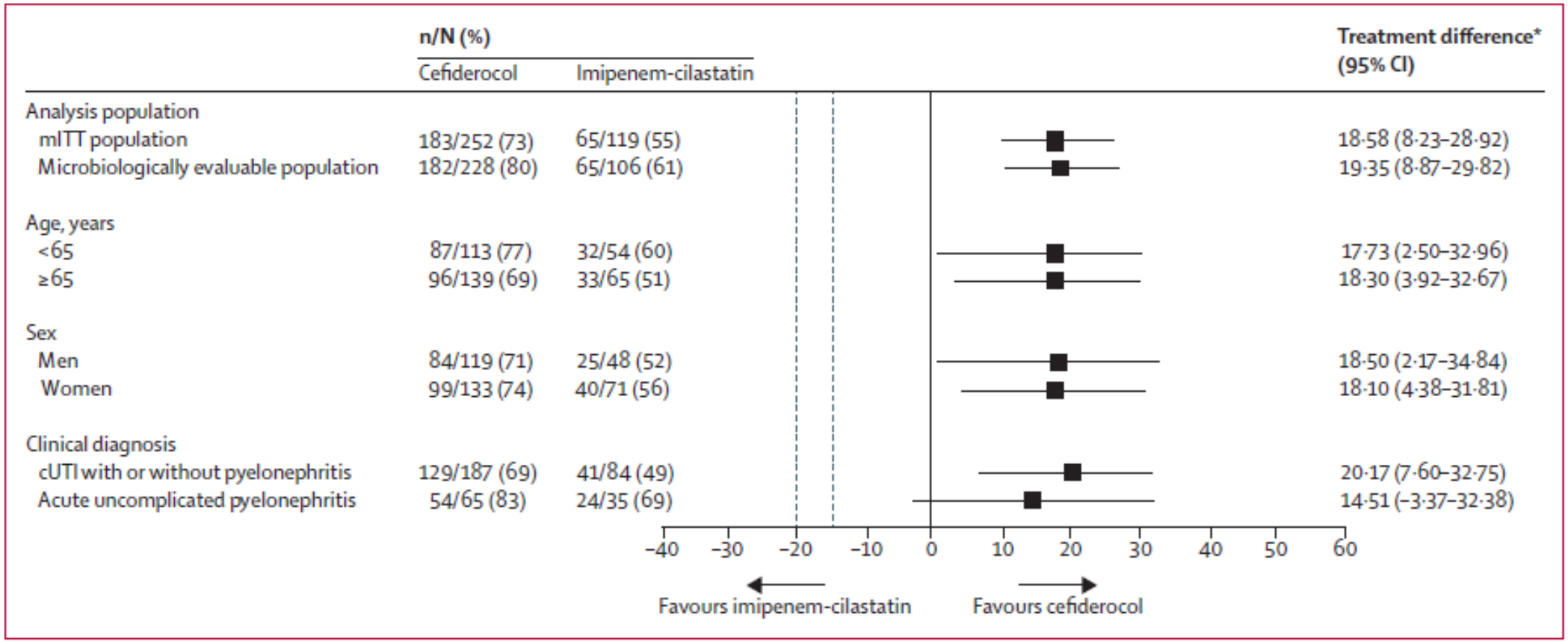
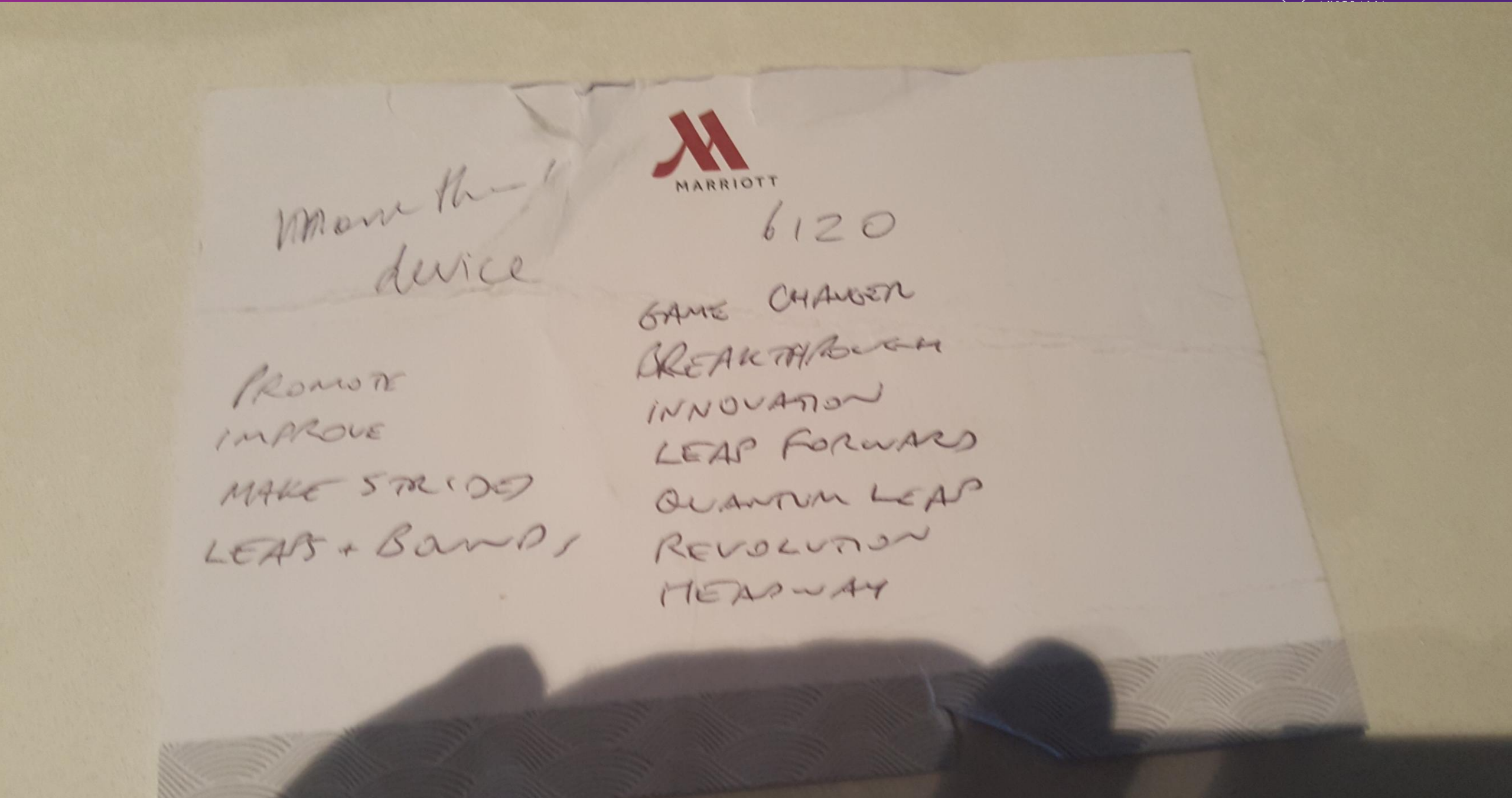


Figure 3: **Composite outcome at test of cure by predefined subgroups**


MARRIOTT
6120
GAME CHANGER
BREAKTHROUGH
INNOVATION
LEAP FORWARD
QUANTUM LEAP
REVOLUTION
MEADWAY
PROMOTE
IMPROVE
MAKE STRIDES
LEAPS + BOUNDS

Cefiderocol versus standard therapy for hospital-acquired and health-care-associated Gram-negative bacterial bloodstream infection (the GAME CHANGER trial): an open-label, parallel-group, randomised trial

*David L Paterson, Helmi Sulaiman, Po-Yu Liu, Mark D Chatfield, Mesut Yilmaz, Zeti Norfidiyati Salmuna, Mohd Zulfakar Mazlan, Siriluck Anunnatsiri, Rujipas Sirijatuphat, Darunee Chotiprasitsakul, David C Lye, Jyoti Somani, Shirin Kalimuddin, Abdullah T Aslan, Visanu Thamlikitkul, Yi-Tzu Lee, Ya-Sung Yang, Yi-Tsung Lin, Wan Nurliyana Wan Ramli, Chien-Hao Tseng, Sophia Archuleta, Yvonne Fu Zi Chan, Brian M Forde, Hugh Wright, Adam G Stewart, Kay A Ramsay, Weiping Ling, Vicki Rossi, Tiffany M Harris-Brown, Patrick N A Harris, on behalf of the GAME CHANGER Trial Investigators**

Overview

- Review of study design
- Study Population
- Primary outcome
- Secondary outcomes

- Discussion points

Study Design

- Multicentre, randomised, non-inferiority, open-label trial comparing cefiderocol with standard of care antibiotics for Gram negative bacterial bloodstream infection that is hospital-acquired or healthcare-associated

- Cefiderocol dosage regimen: 2 grams IV over 3 hours, every 8 hours for 5-14 days
  - Dosage adjustment for ARC and decreased renal function
  - The use of a second antibiotic with activity against a Gram-negative organism was allowed in the first 72 hours post randomisation until the susceptibility of cefiderocol was confirmed

Standard of care antibiotics

- One, two or three antibiotics with activity against Gram negative bacteria
- Can be adjusted according to susceptibility results or changes in the patient's condition

- For both arms, additional antibiotics can be given for Gram positive or anaerobic organisms or fungi

Inclusion Criteria

Inclusion Criteria

- Bloodstream infection with a Gram-negative organism from at least one blood culture draw.
- No more than 48 hours has elapsed from the time of positive blood culture's collection
- Hospital-acquired bloodstream infection (>48 hours from hospital admission) OR
- Healthcare associated bloodstream infection (infections presenting at admission or within 48 hours of admission AND line infection OR hospital clinic in last 30 days OR overnight hospitalization in last 90 days OR nursing home OR home IV antibiotics or wound care)
- Adults

Exclusion Criteria

- Refractory shock or comorbid condition such that not expected to survive more than 7 days
- History of moderate to severe hypersensitivity reaction to a cephalosporin
- Polymicrobial bloodstream infection with a significant Gram-positive pathogen
- Line-related and line unable to be removed
- Treatment is not with intent to cure the infection
- Pregnancy or breast-feeding
- On peritoneal dialysis
- Prior inclusion in the trial

Randomisation

- 1:1 cefiderocol or standard of care antibiotics
- Random sequence generated using random permuted blocks of unequal length
- Stratification by:
  (a) Charlson co-morbidity index (≥4 or less than 4)
  (b) Region (Australia, Asia, Europe/Turkey)

- The online electronic data capture platform REDCap© was used to manage randomisation

Primary Outcome Measure

- **14-day all-cause mortality**, with day 1 being the day of randomisation
- Hypothesis: Cefiderocol is non-inferior to SOC
- Sample size calculations: Considering a mortality rate of 10% in the control group, and a non-inferiority margin of 10% difference in the two groups, the study would require 284 patients in total to achieve 80% power with a 2-sided alpha level of 0.05

Main Analysis Population

Main analysis population: all patients randomised except where:

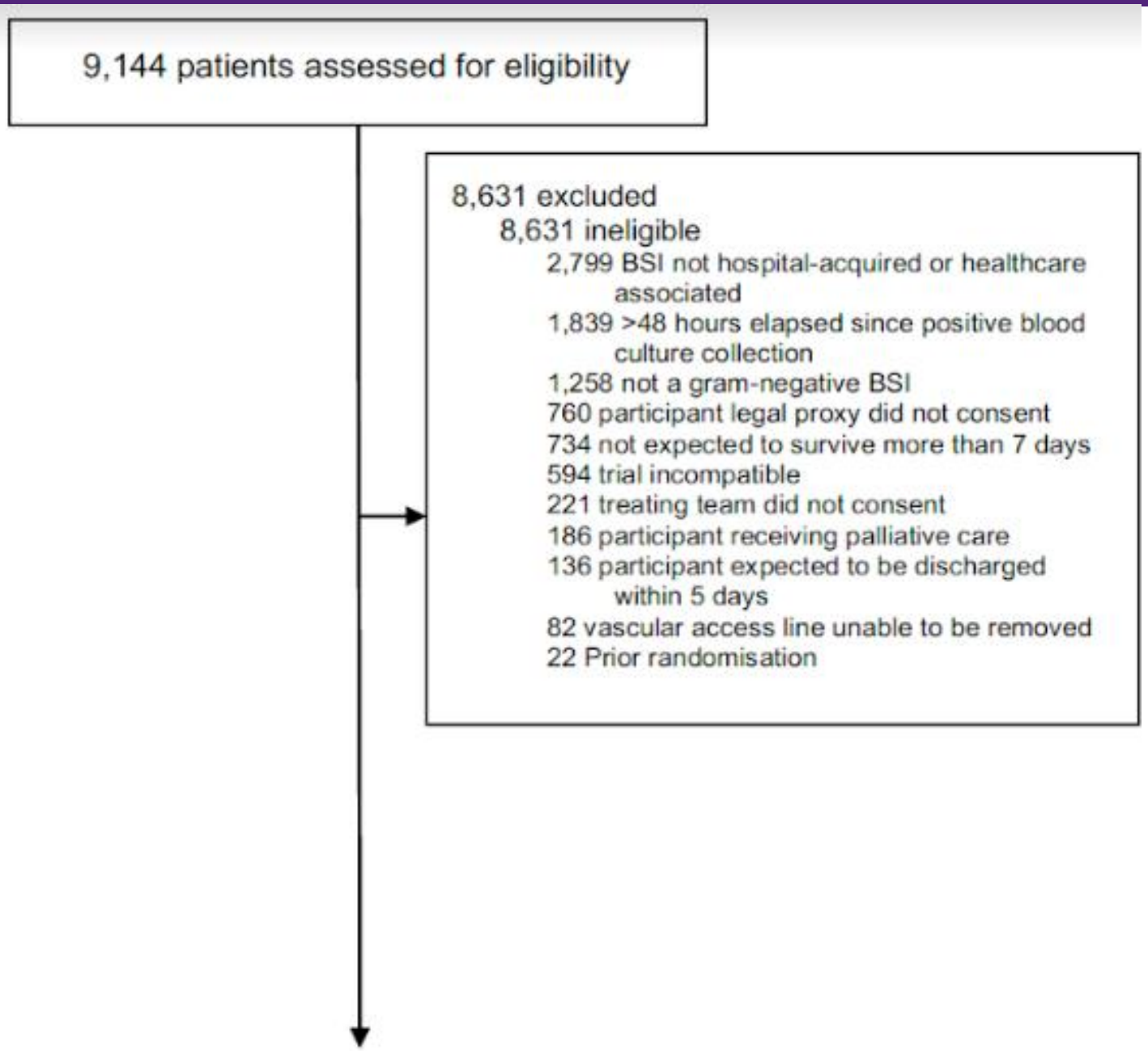
- No aerobic Gram-negative bacilli grew from a patient's index blood culture
- Post-randomisation, patient did not receive at least one dose of cefiderocol (if randomised to cefiderocol arm) or an agent with activity against GNBs (if randomised to SOC)
- Patient withdrew consent before day 14

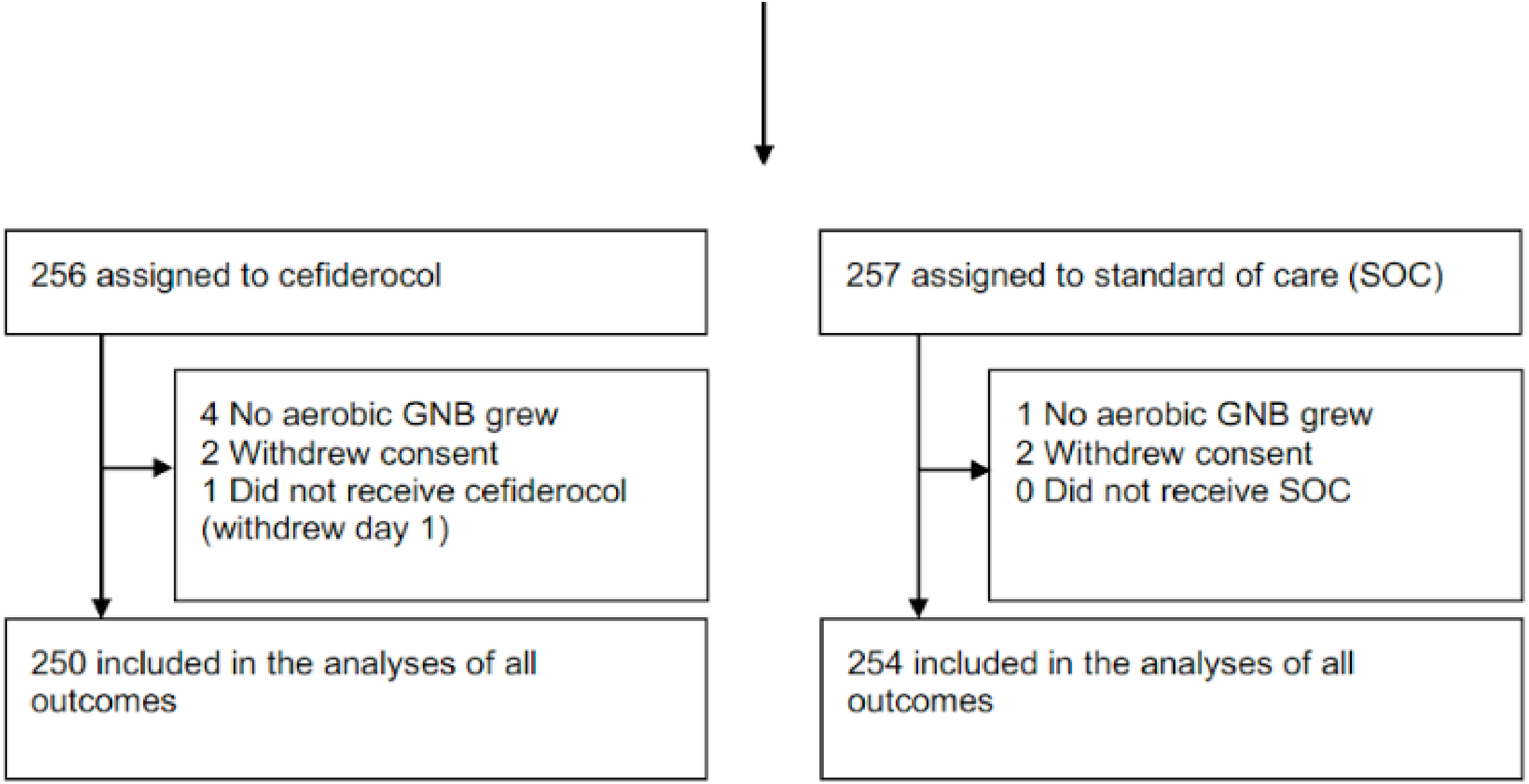
Carbapenem Resistant Subset

- All analyses (including the primary analysis of 14-day ACM) were also be performed on the patients with carbapenem resistant organisms in their index blood cultures

- Carbapenem non-susceptibility was defined as any isolate testing resistant (R) or “susceptible increased exposure” (I) to meropenem or imipenem (or ertapenem for Enterobacterales) according to results of broth microdilution performed at the central study laboratory using EUCAST breakpoints[1].
- Imipenem resistance in *Proteus*, *Providencia* and *Morganella* species (intrinsic resistance) or *Pseudomonas* (no susceptibility breakpoint) was insufficient to define CR alone.
- If an organism was not received by the central laboratory or was non-viable on sub-culture, susceptibility was defined as per the site laboratory testing, i.e. locally reported as “R” or “I” to meropenem or imipenem (or ertapenem in Enterobacterales).
- Stenotrophomonas maltophilia, Aeromonas spp (except A. caviae) and Elizabethkingia were always regarded as carbapenem resistant because of intrinsic carbapenemases

Results


9,144 patients assessed for eligibility
8,631 excluded
8,631 ineligible
2,799 BSI not hospital-acquired or healthcare associated
1,839 >48 hours elapsed since positive blood culture collection
1,258 not a gram-negative BSI
760 participant legal proxy did not consent
734 not expected to survive more than 7 days
594 trial incompatible
221 treating team did not consent
186 participant receiving palliative care
136 participant expected to be discharged within 5 days
82 vascular access line unable to be removed
22 Prior randomisation


256 assigned to cefiderocol
4 No aerobic GNB grew
2 Withdrew consent
1 Did not receive cefiderocol (withdrew day 1)
250 included in the analyses of all outcomes
257 assigned to standard of care (SOC)
1 No aerobic GNB grew
2 Withdrew consent
0 Did not receive SOC
254 included in the analyses of all outcomes

Baseline characteristics well matched

Characteristic	Cefiderocol (N = 250)	Standard of Care (N = 254)
Age, mean (SD), y	62 (15)	61 (16)
Female sex, No. (%)	108 (43)	102 (40)
Body Mass Index, mean (SD), kg/m^2	23 (21-27)	24 (21-27)
Country, No. (%)		
Australia	20 (8)	20 (8)
Malaysia	75 (30)	62 (24)
Singapore	40 (16)	30 (12)
Taiwan	38 (15)	55 (22)
Thailand	50 (20)	59 (23)
Turkey	27 (11)	28 (11)
Charlson Comorbidity Score, median (IQR) [a]	5 (3-7)	5 (3-7)
Comorbidity, No. (%)		
Congestive heart failure	12 (5)	21 (8)
Chronic pulmonary disease	14 (6)	17 (7)
Diabetes mellitus	91 (36)	112 (44)
Moderate or severe renal disease	69 (28)	76 (30)
Moderate or severe liver disease	19 (8)	18 (7)
Solid tumor	71 (28)	66 (26)
Hematologic malignancy	60 (24)	48 (19)
AIDS	3 (1)	4 (2)
Immunosuppressed, No. (%) [b]	152 (61)	147 (58)
Neutropenia, No. (%)	48 (19)	42 (17)

Severity of illness and source well matched

Acquisition, No. (%)		
Hospital-acquired	156 (62)	153 (60)
Healthcare-associated	94 (38)	101 (40)
Surgery within 14 days of index blood culture, No. (%)	23 (9)	41 (16)
ICU admission, No. (%)	43 (17)	50 (20)
On mechanical ventilation at randomization, No. (%)	37 (15)	51 (20)
On inotropic support at randomization, No. (%)	37 (15)	42 (17)
Baseline SOFA score, median (IQR)	4 (2-6)	4 (3-7)
Presumed source of BSI, No. (%)		
Urinary tract infection	52 (21)	46 (18)
Intra-abdominal infection	40 (16)	48 (19)
Line-related infection	40 (16)	53 (21)
Pneumonia	33 (13)	30 (12)
Skin and soft tissue infection	13 (5)	10 (4)
Other	26 (10)	15 (6)
Unknown	46 (18)	52 (20)

Baseline Microbiology well matched

Polymicrobial BSI, No (%)	25 (10)	27 (11)
Organisms in index blood culture, No (% patients)		
Escherichia coli	90 (36)	77 (30)
Klebsiella pneumoniae	73 (29)	80 (31)
Enterobacter spp.	19 (8)	21 (8)
Pseudomonas aeruginosa	27 (11)	24 (9)
Acinetobacter spp.	18 (7)	25 (10)
Stenotrophomonas maltophilia	5 (2)	3 (1)

Outcomes by Treatment Allocation

Primary Analysis Population

	Cefiderocol (N=250)	Standard of care (N=254)	Absolute risk difference, % (95% CI)	Risk ratio (95% CI)
Full population				
Day 14	20 (8%)	17 (7%)	1% (−3 to 6)	1·20 (0·64 to 2·23)
Day 30	42 (17%)	38 (15%)	2% (−5 to 8)	1·12 (0·75 to 1·68)
Day 90	73 (29%)	75 (30%)	0% (−8 to 8)	0·99 (0·75 to 1·30)
Carbapenem-resistant subset				
Day 14	9/64 (14%)	6/63 (10%)	5% (−7 to 16)	1·48 (0·56 to 3·91)
Day 30	21/64 (33%)	16/63 (25%)	7% (−8 to 23)	1·29 (0·75 to 2·24)
Day 90	31/64 (48%)	30/63 (48%)	1% (−17 to 18)	1·02 (0·71 to 1·46)

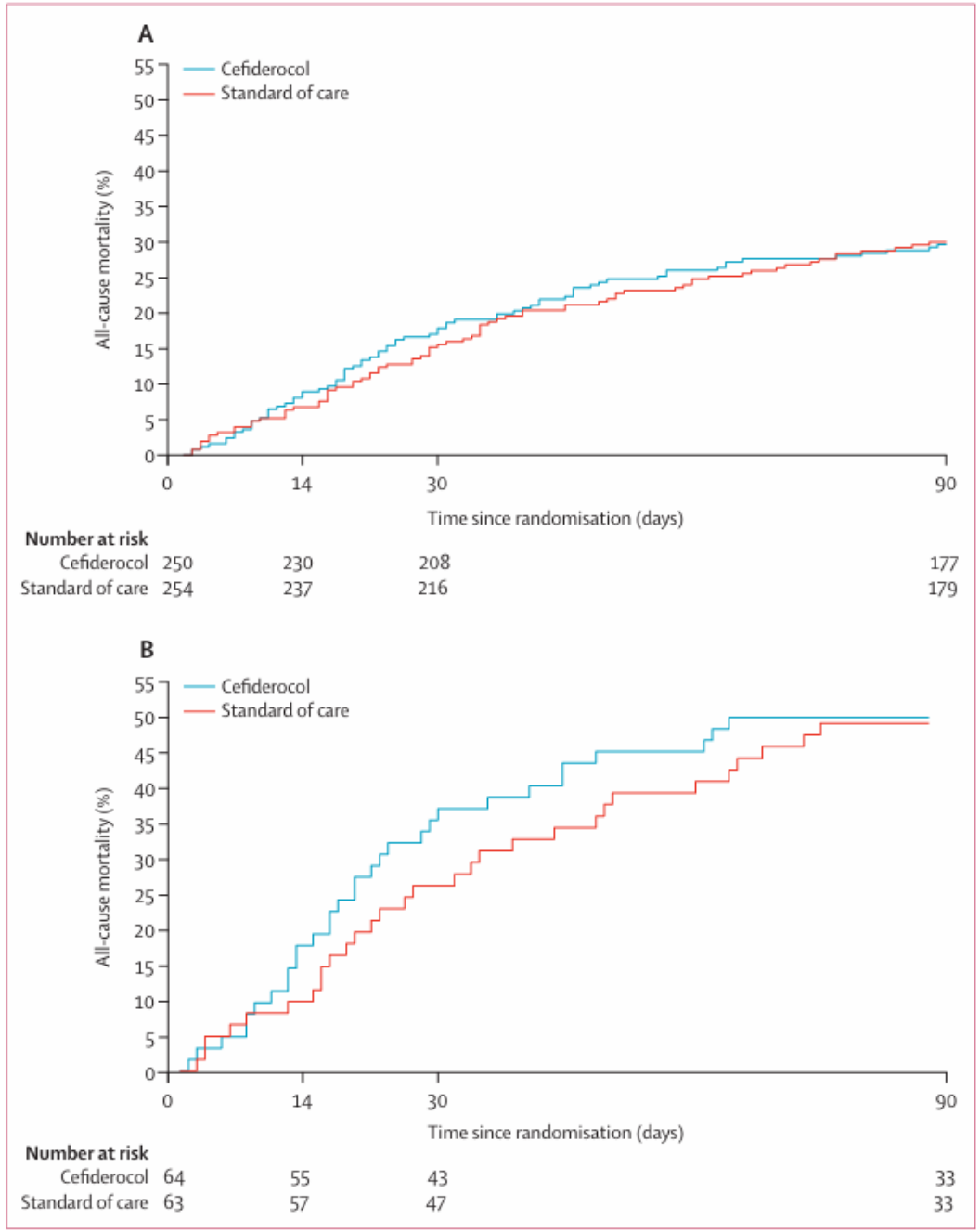


***Figure 2*: Kaplan–Meier plot of all-cause mortality up to day 90**

Cumulative incidence of mortality in the main analysis population (A) and in the carbapenem-resistant subset (B).

	Randomized to Cefiderocol			**Randomized to SOC**		
	Day 14	Day 30	Day 90	Day 14	Day 30	Day 90
MBL+ CRE	5/16 (31%)	8/16 (50%)	12/16 (75%)	0/11 (0%)	2/11 (18%)	5/11 (45%)
Other CRE	1/16 (6%)	2/16 (12%)	4/16 (25%)	1/21 (5%)	4/21 (19%)	10/21 (48%)
CRAB	1/11 (9%)	5/11 (45%)	6/11 (55%)	3/14 (21%)	7/14 (50%)	10/14 (71%)
CR-PA	2/7 (29%)	2/7 (29%)	2/7 (29%)	1/7** (14%)	2/7** (29%)	3/7** (43%)
Stenotrophomonas	0/5* (0%)	2/5* (40%)	2/5* (40%)	0/3** (0%)	0/3** (0%)	0/3** (0%)
Other CR non-fermenters	0/4* (0%)	0/4* (0%)	1/4* (25%)	1/6 (17%)	1/6 (17%)	2/6 (33%)
Aeromonas with intrinsic carbapenemase	0/6 (0%)	2/6 (33%)	4/6 (67%)	0/2 (0%)	0/2 (0%)	0/2 (0%)
TOTAL	**9/64 (14%)**	**21/64 (33%)**	**31/64 (48%)**	**6/63 (10%)**	**16/63 (25%)**	**30/63 (48%)**

Discussion Points

- Cefiderocol was non-inferior to SOC in total analysis population
  - Populations well matched at baseline
  - Large sample size

- Cefiderocol was not superior to SOC for CR subset
  - CR population was small (126 in total)
  - Poor outcomes in MBL+ strains (acknowledging small sample size)
  - Acceptable outcomes in CRAB, KPC and OXA-48 producers, Stenotrophomonas, CR-PA

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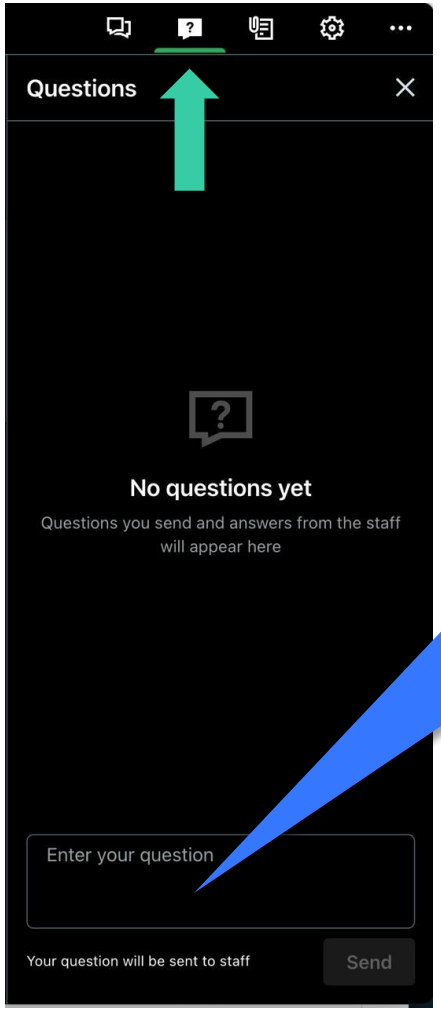

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Melis Anahtar

Melis Anahtar is a physician-scientist whose research and clinical work focus on developing novel therapeutic and diagnostic approaches to combat the rising threat of infectious diseases.

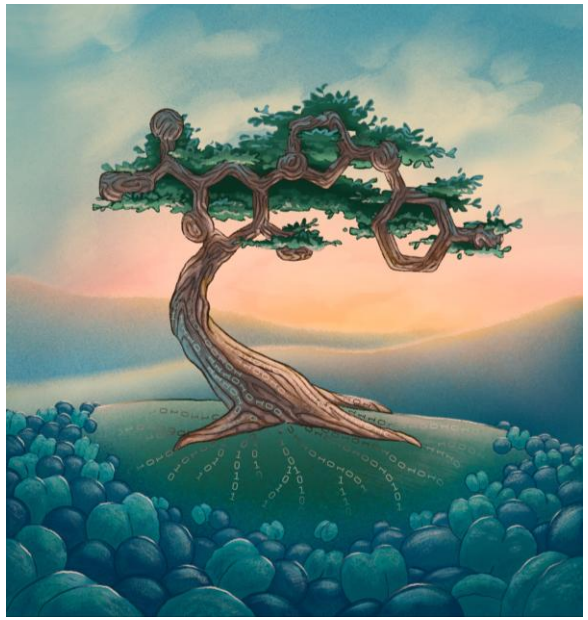
She is an Assistant Professor in Pathology at Harvard Medical School, USA with joint appointments in the Massachusetts General Hospital (MGH) Departments of Pathology and Medicine. Melis leads a research lab in the Division of Infectious Diseases and serves as an Assistant Director of the MGH Clinical Microbiology lab. She previously co-founded Day Zero Diagnostics, a sequencing-based infectious disease diagnostic company, which was recently acquired.

Article

A generative deep learning approach to *de novo* antibiotic design

Cell

Aarti Krishnan,[1,2,3,4,25] Melis N. Anahtar,[1,2,4,5,25] Jacqueline A. Valeri,[1,2,4,25] Wengong Jin,[6,7] Nina M. Donghia,[4] Leif Sieben,[1,2,4,8] Andreas Luttens,[1,2] Yu Zhang,[1,2,4] Seyed Majed Modaresi,[1,2,4] Andrew Hennes,[1,4] Jenna Fromer,[9] Parijat Bandyopadhyay,[1,2] Jonathan C. Chen,[1,2] Danyal Rehman,[10] Ronak Desai,[1,11,12] Paige Edwards,[1,2] Ryan S. Lach,[13] Marie-Stéphanie Aschtgen,[14] Margaux Gaborieau,[14] Massimiliano Gaetani,[15,16] Samantha G. Palace,[17] Satotaka Omori,[13] Lutete Khonde,[18] Yurii S. Moroz,[19,20,21] Bruce Blough,[22] Chunyang Jin,[22] Edmund Loh,[14,23] Yonatan H. Grad,[17] Amir Ata Saei,[14] Connor W. Coley,[9,24] Felix Wong,[1,2,13] and James J. Collins[1,2,4,26,*]



Melis Anahtar, MD PhD

Assistant Professor of Pathology, Harvard Medical School
Assistant Director, Clinical Microbiology Lab,
Massachusetts General Hospital (MGH)

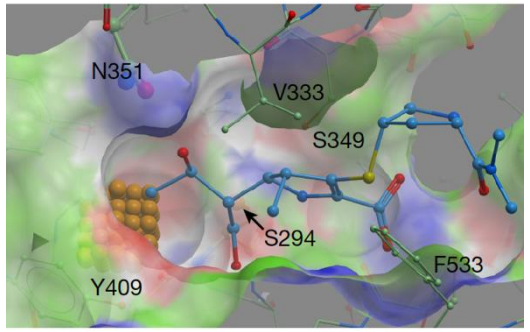
manahtar@mgh.harvard.edu

BROAD INSTITUTE

Mass General Brigham

Modern approaches to antibiotic discovery

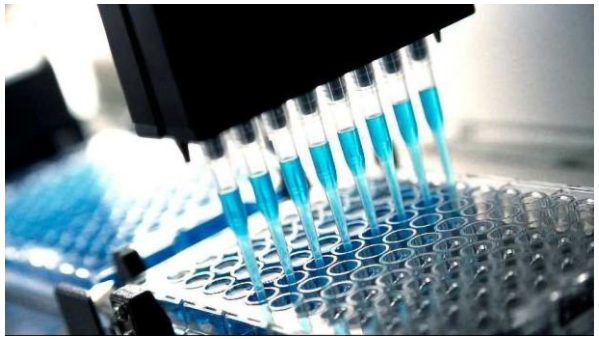
Rational design



e.g. ETX-0462 (β-lactamase inhibitor)

Durand-Reville et al., *Nature,* 2021

High throughput screening (HTS)

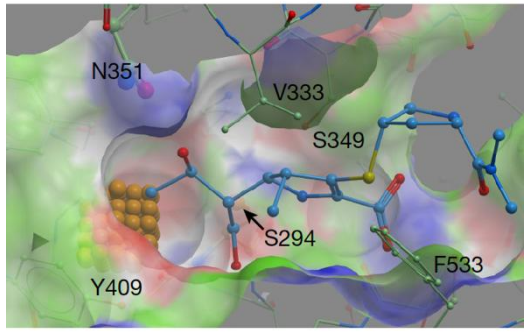


e.g. zoliflodacin (whole cells of *E. coli, S. aureus)*

Payne et al., *Nature Reviews Drug Discovery,* 2007

Modern approaches to antibiotic discovery

Rational design



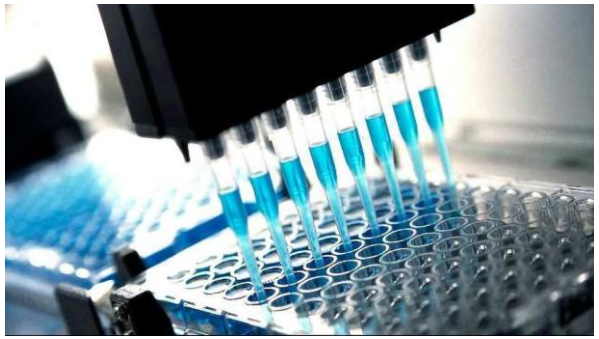
Durand-Reville et al., *Nature,* 2021

A Deep Learning Approach to Antibiotic Discovery

Use a deep learning model to computationally predict antibiotic efficacy from a chemical structure

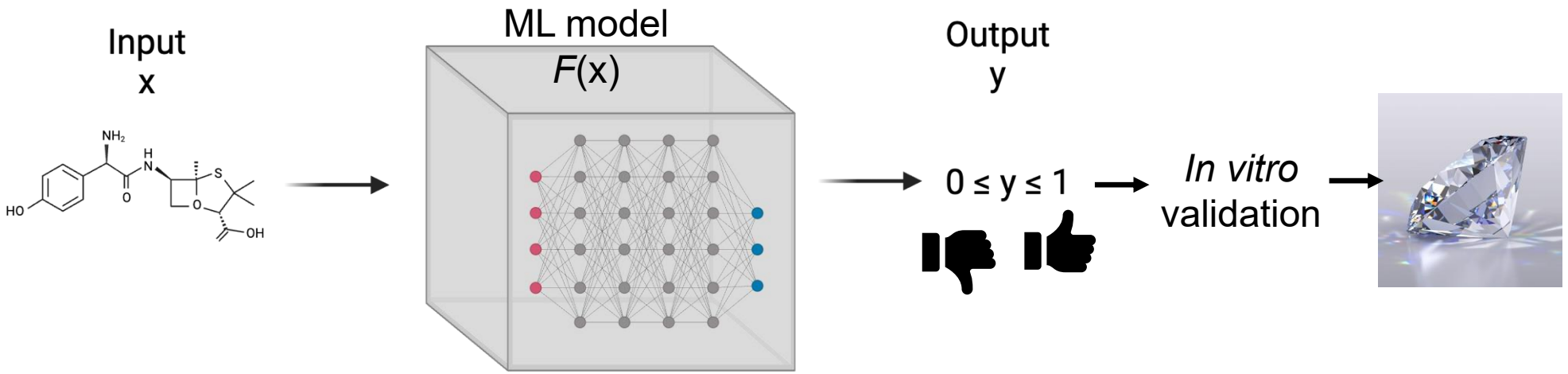
Stokes et al., *Cell*, 2020

High throughput screening (HTS)



Payne et al., *Nature Reviews Drug Discovery,* 2007

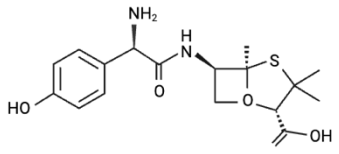
Deep learning for antibiotic discovery



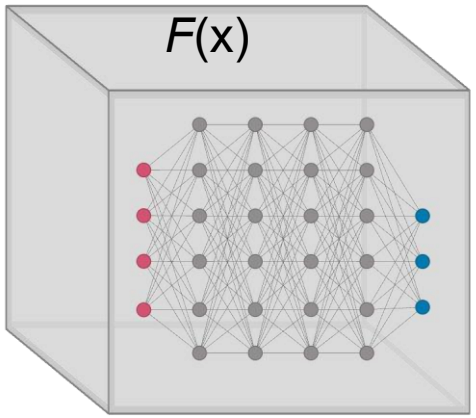
Deep learning for antibiotic discovery

Trained on *phenotypic* screens
Mechanism agnostic

Input
x



ML model
F(x)



Output
y

$0 \leq y \leq 1$

In vitro
validation

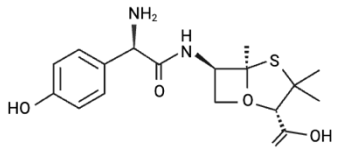
Organism specific,
e.g. N. gonorrhoeae,
S. aureus

Anahtar*, Valeri*, Modaresi*, et al., under review
Wong*, Zheng*, et al., *Nature,* 2024

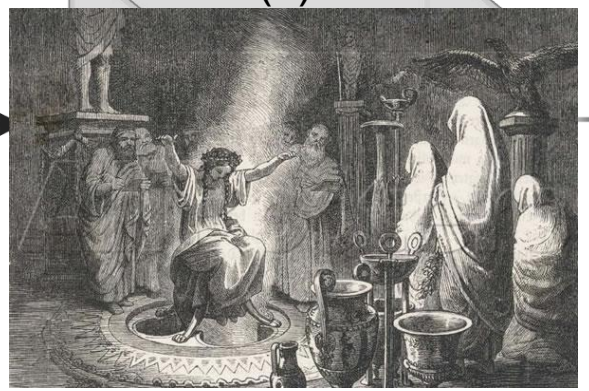
Deep learning for antibiotic discovery

Trained on *phenotypic* screens
Mechanism agnostic

Input
x



ML model
F(x)



Output
y

$0 \leq y \leq 1$

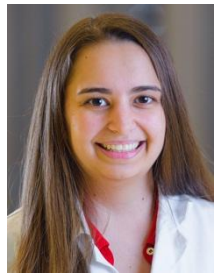
In vitro
validation

Organism specific,
e.g. N. gonorrhoeae,
S. aureus

Anahtar*, Valeri*, Modaresi*, et al., under review
Wong*, Zheng*, et al., *Nature,* 2024

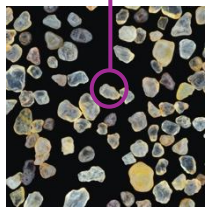
Can we use deep learning models to design new antibiotics *de novo*?


Aarti Krishnan


Jackie Valeri

# of molecules:

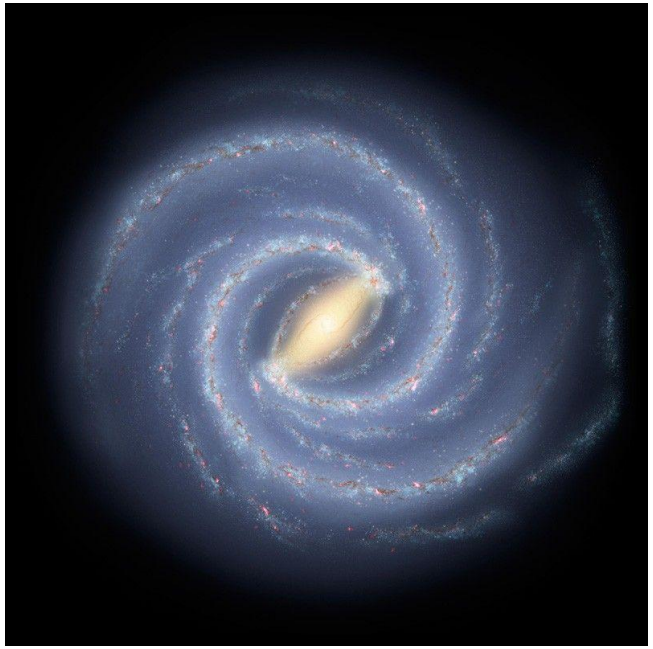
1



Commercially-available today

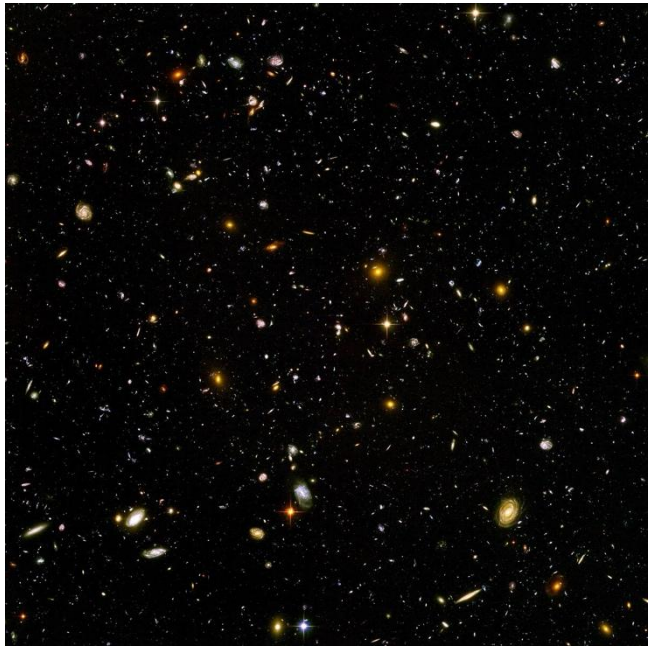
10^{11}

10^{48}



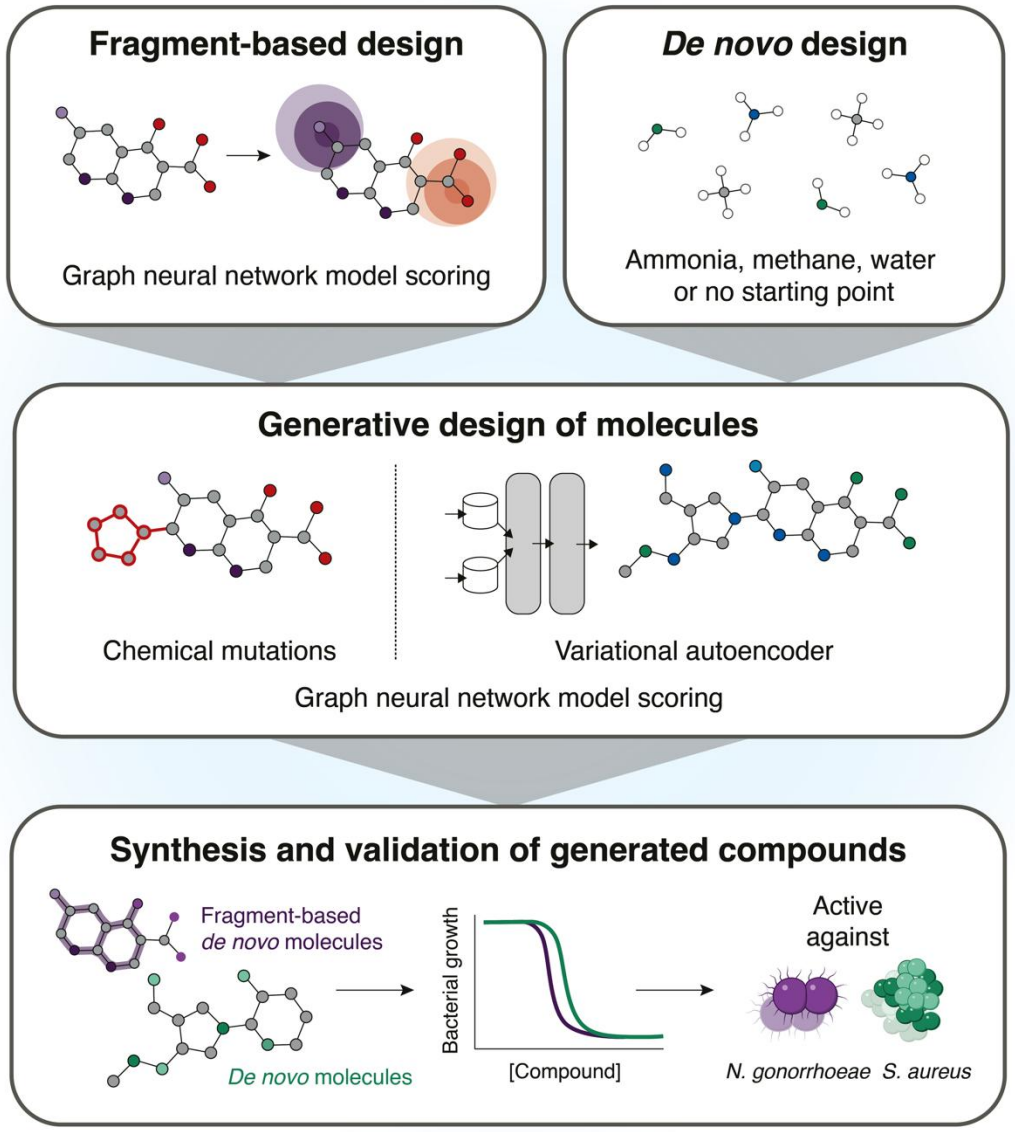
Theoretical drug-like chemical space

10^{60}



Reymond *et al.*, *Acc. Chem. Res.*, 2015

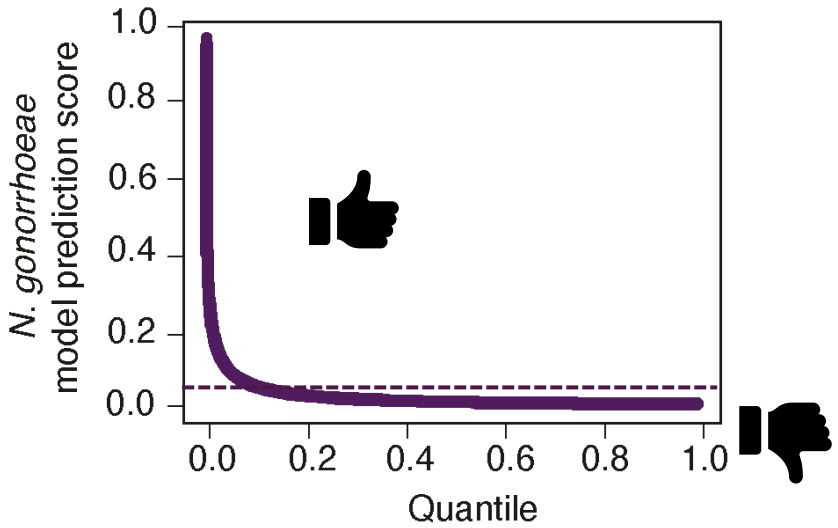
Applying generative AI methods to antibiotic design



Krishnan*, Anahtar*, Valeri*, et al.,
Cell, 2025

1. Fragment identification

45,858,026 fragments scored with the *N. gonorrhoeae* model



Krishnan*, Anahtar*, Valeri*, et al., *Cell,* 2025

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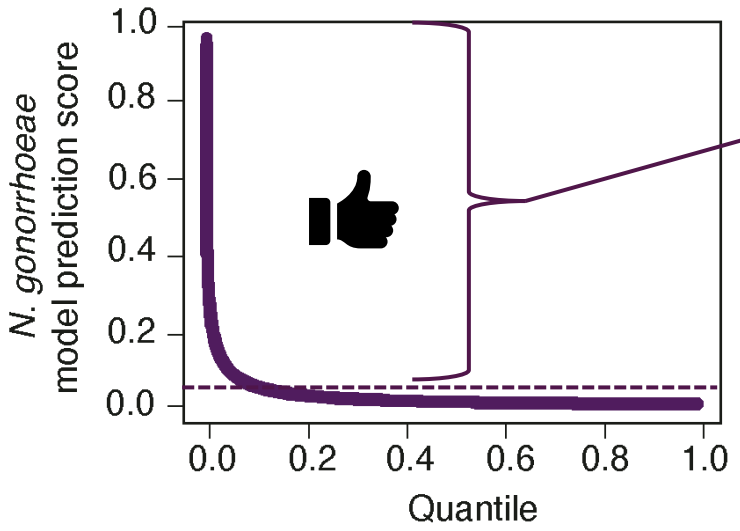

45,858,026 fragments

Predicted antibiotic activity against *N. gonorrhoeae*

3,844,505 fragments

Predicted low cytotoxicity and no PAINS or Brenk alerts

1,159,284 fragments

Structurally dissimilar

1,156,945 fragments

Cytotoxicity models from Wong*, Zheng*, et al. *Nature* 2024

1. Fragment identification

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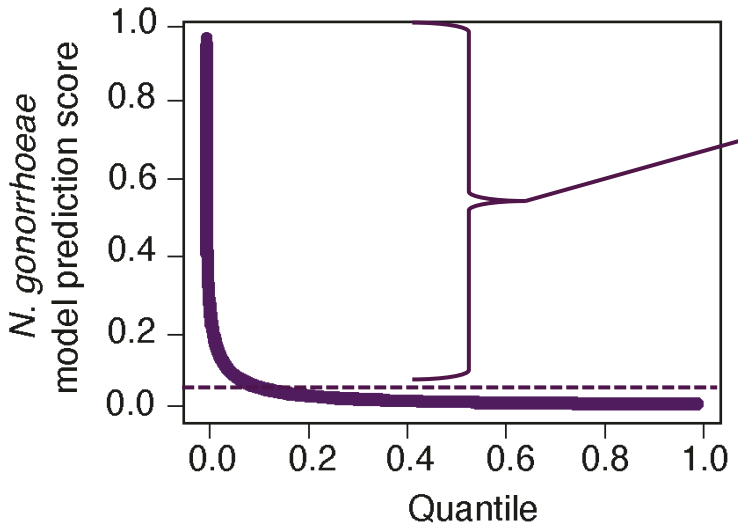

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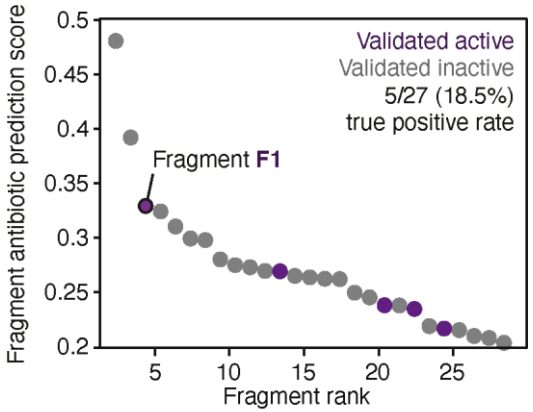

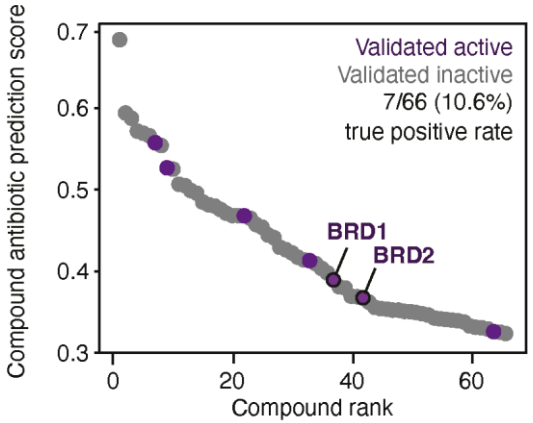

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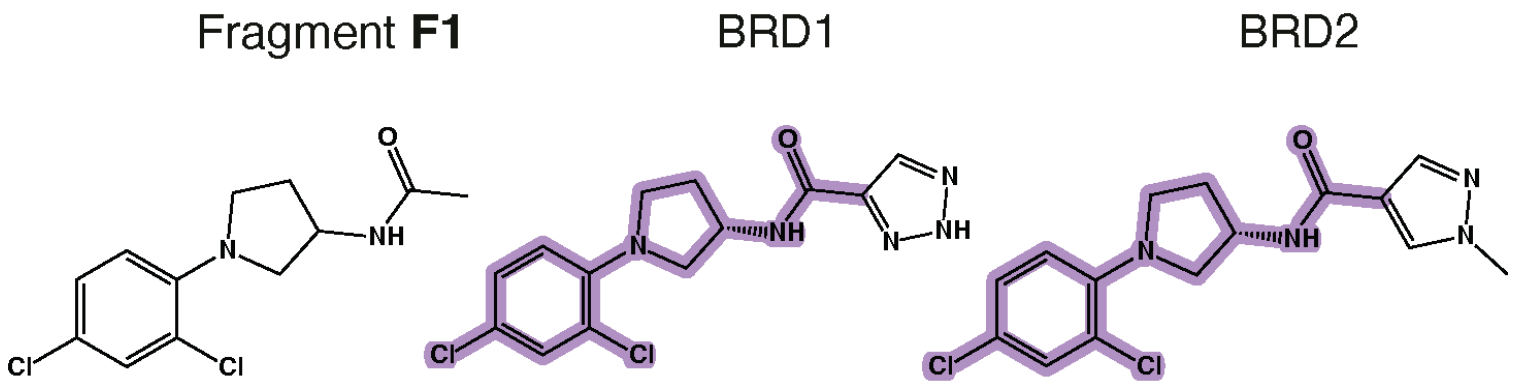
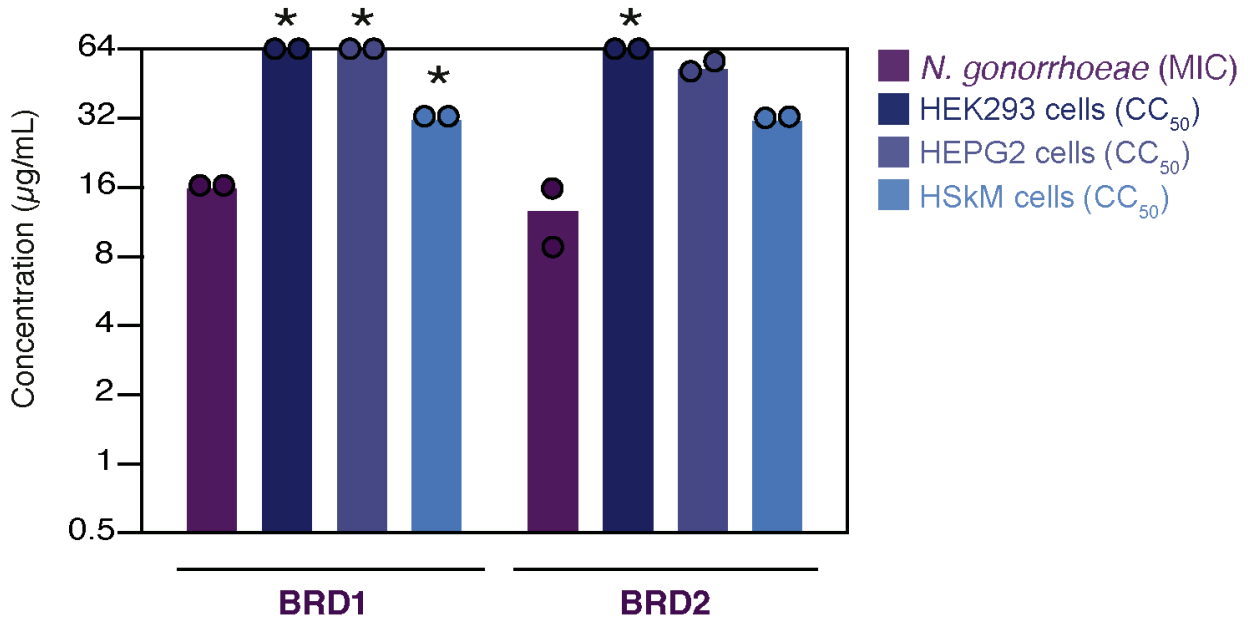
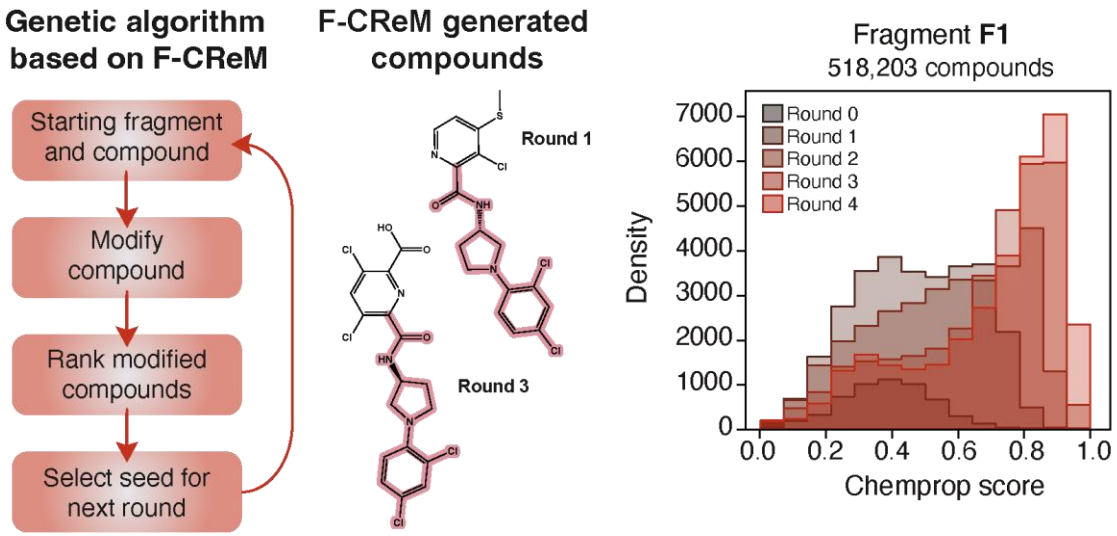
1. Fragment identification





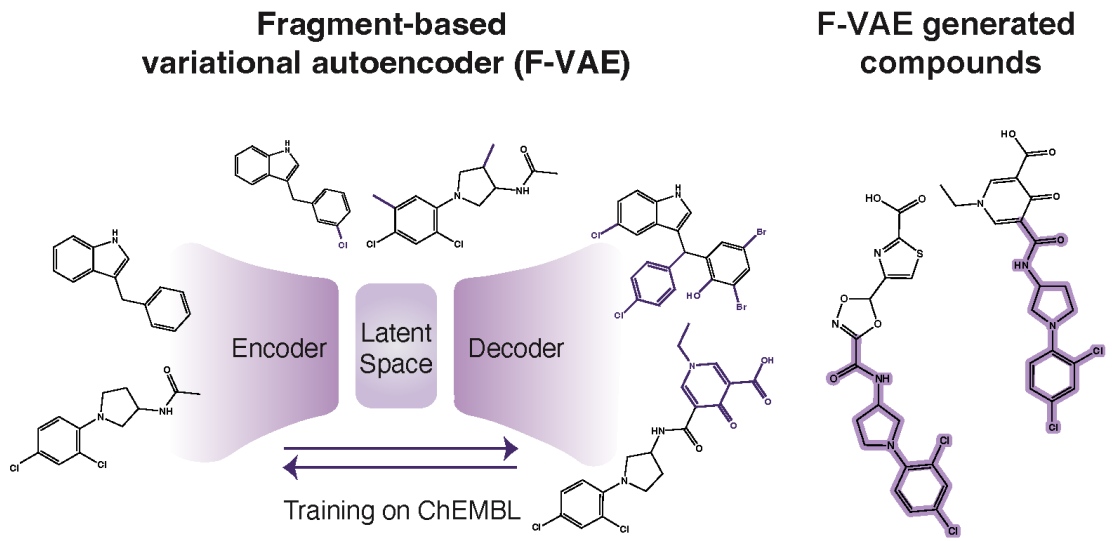
2. Generative design

Fragment-based Chemically Reasonable Mutations (F-CReM)



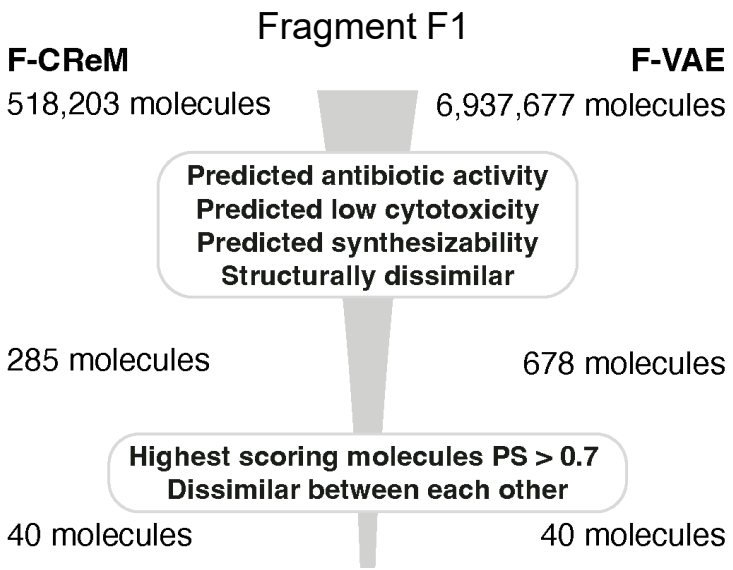
Polishchuk et al. *J. Cheminform*. 2020

Fragment-based Variational Autoencoder (F-VAE)



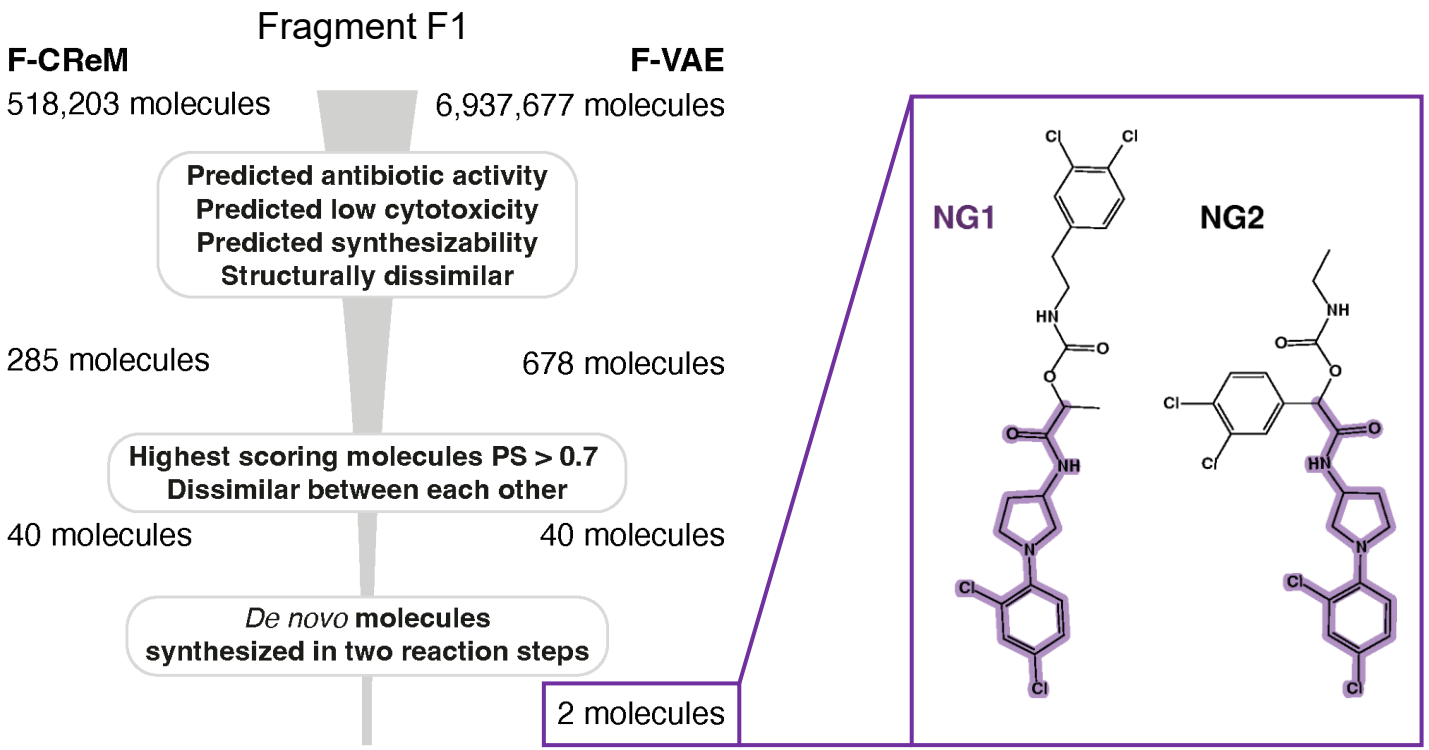
With Wengong Jin
Jin et al., *arXiv*, 2018

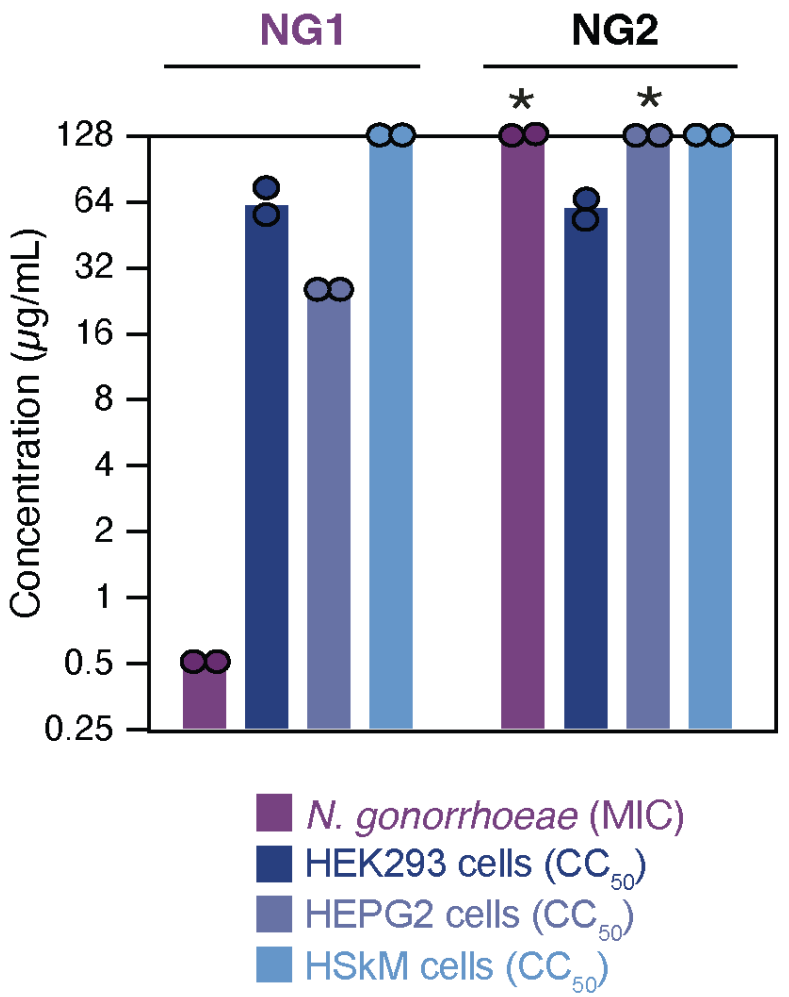
2. Generative design



Krishnan*, Anahtar*, Valeri*, et al., *Cell,* 2025

3. Synthesis and validation of designed compounds





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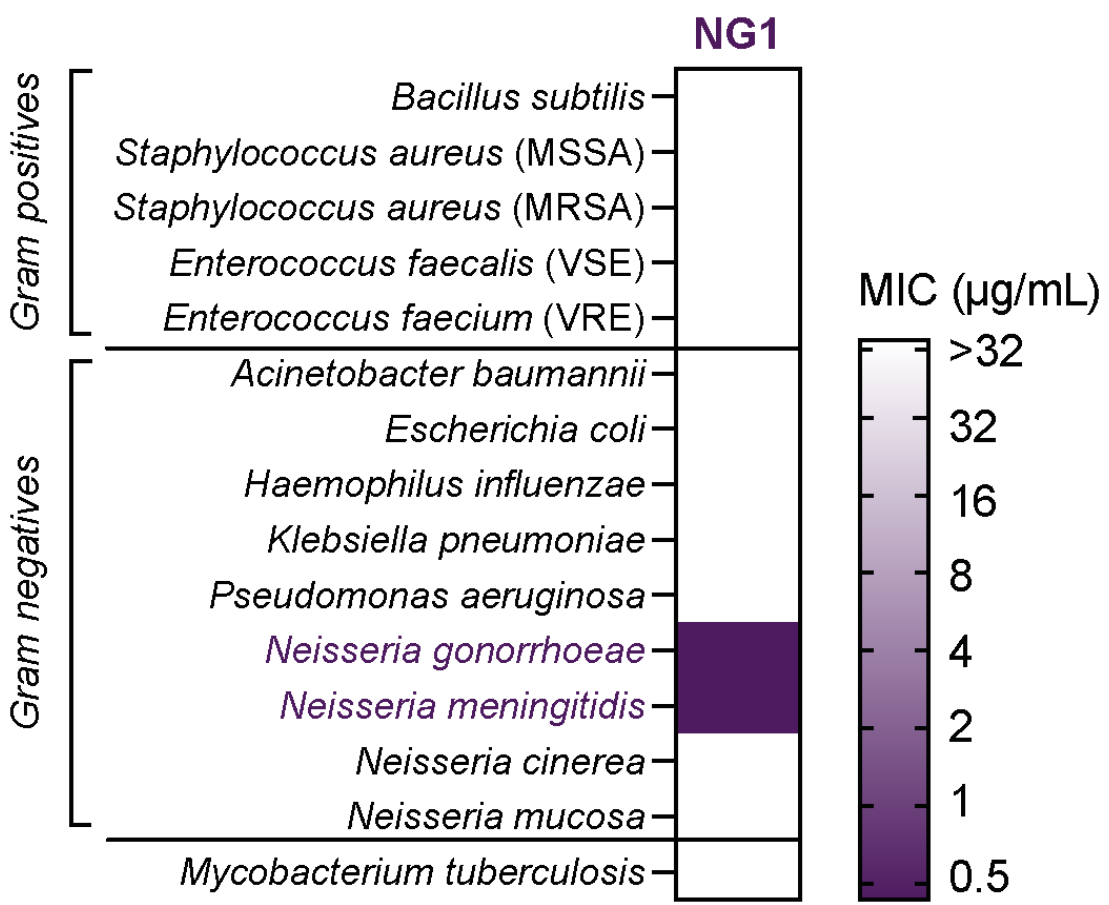
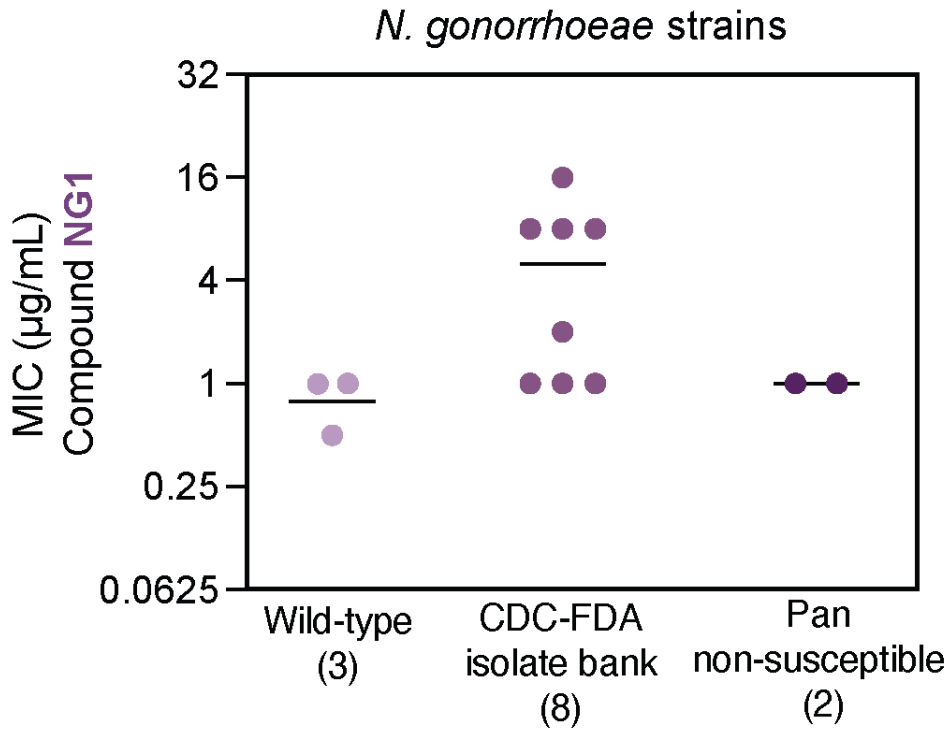
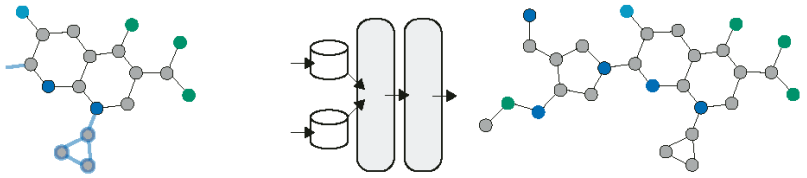




What if we don't start from a fragment? "Truly *de novo*"

De novo molecule generation

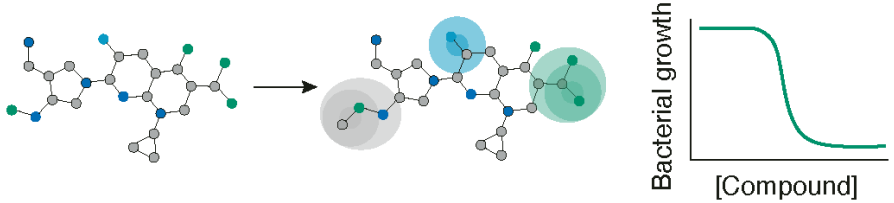
Without the need for a fragment as a starting point



Chemical mutations Variational autoencoder

Score with antibacterial prediction model

Synthesis and validation of generated compounds



JT-VAE

28,534,490 molecules

Predicted antibiotic activity

Structural dissimilarity to known antibiotics

Synthesizability (RA score)

4,831 molecules

Manually inspected

90 molecules

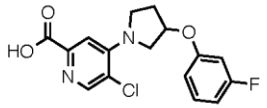
Received and tested

22 molecules

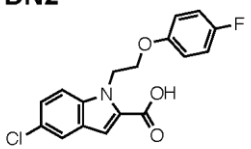
Active at ≤ 64 μg/mL

6 molecules
(27.27%)

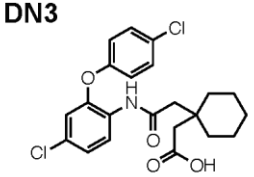
DN1



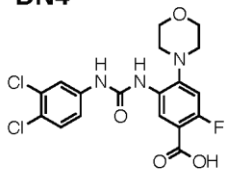
DN2



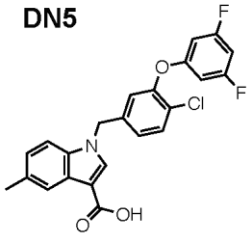
DN3



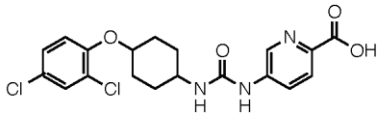
DN4



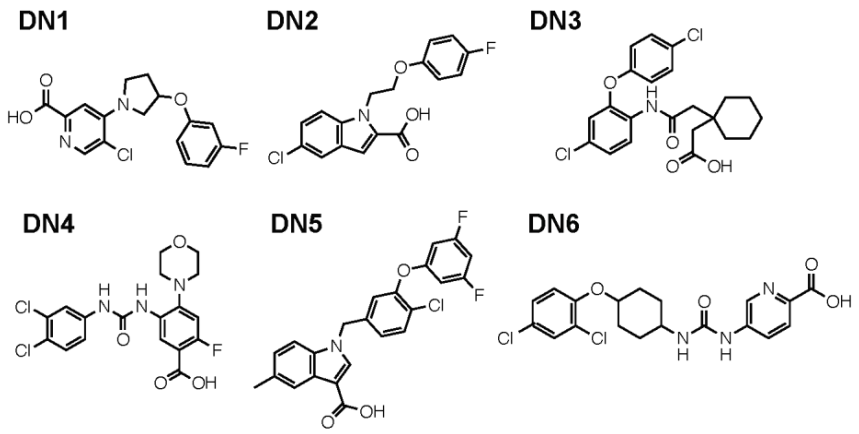
DN5

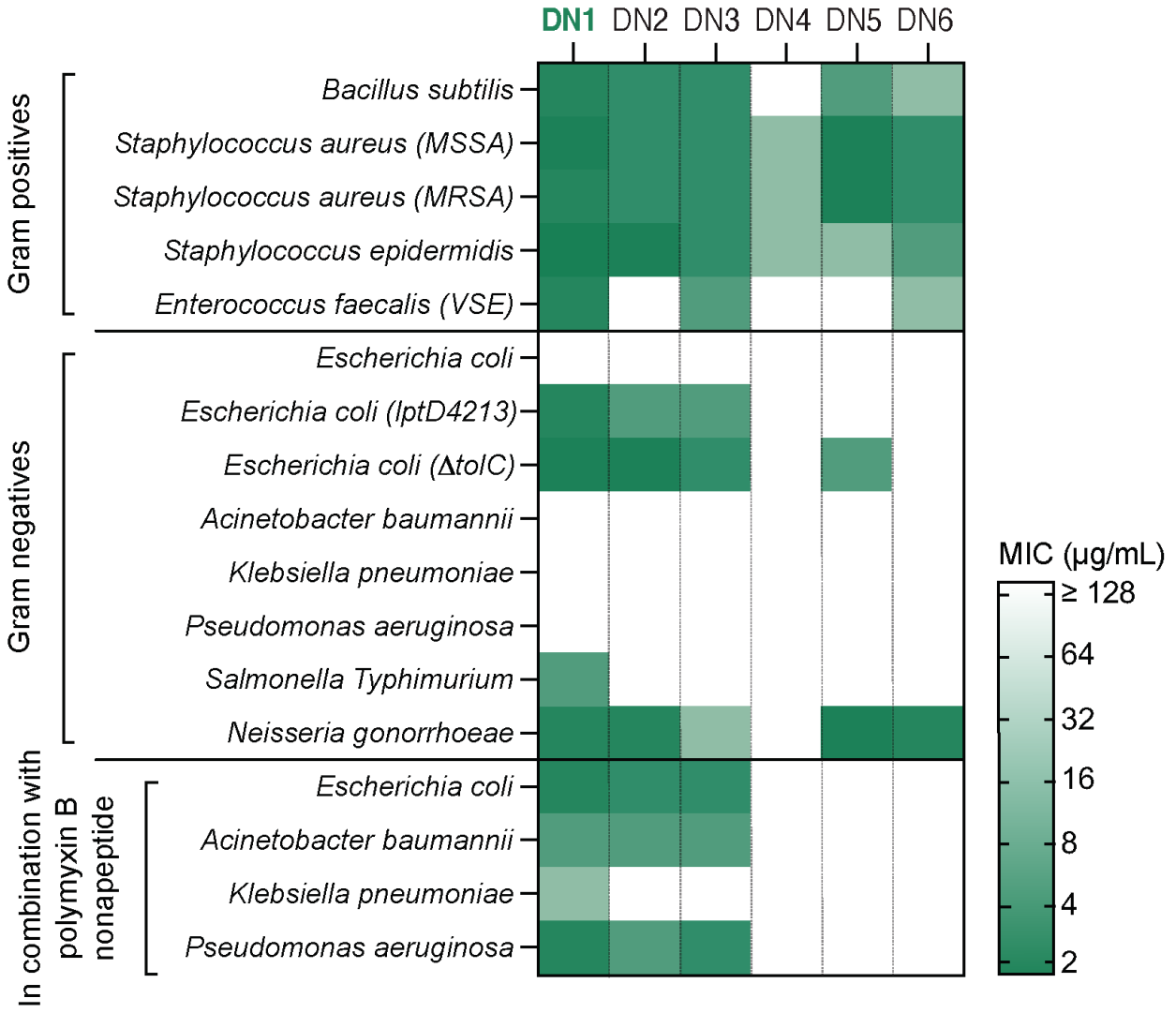


DN6



What if we don't start from a fragment? "Truly *de novo*"





How do these AI-discovered compounds work?

Morphological changes

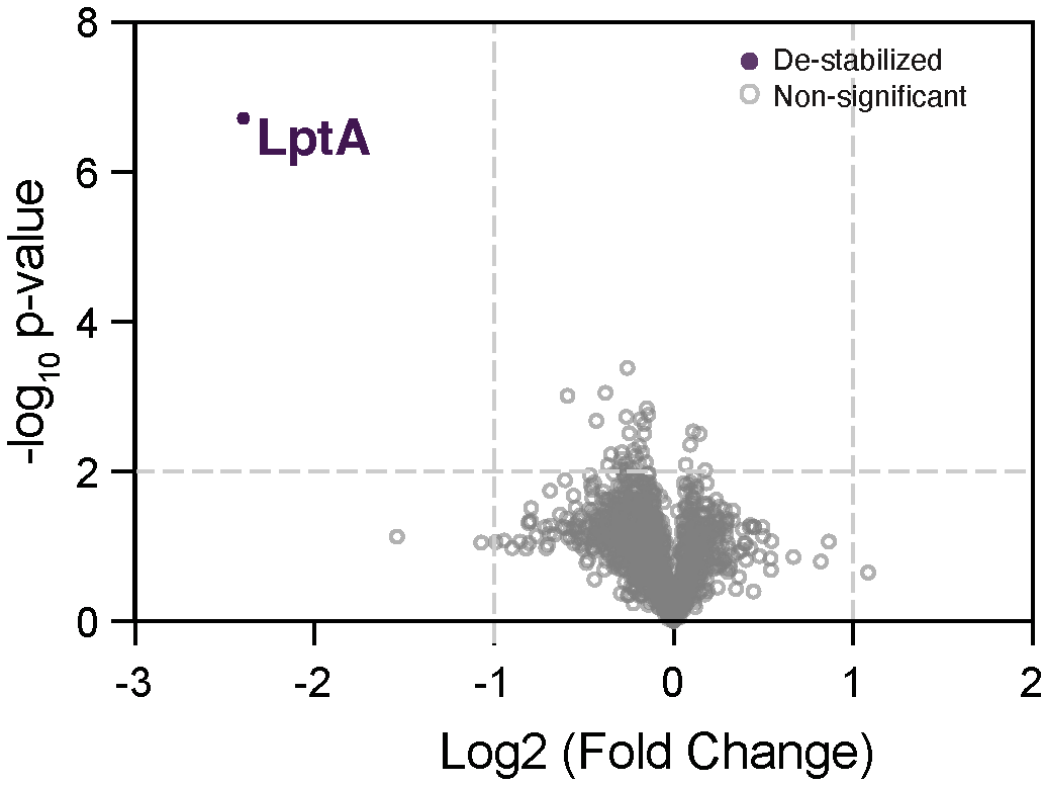
Membrane-specific fluorescent dyes

In vitro resistance evolution

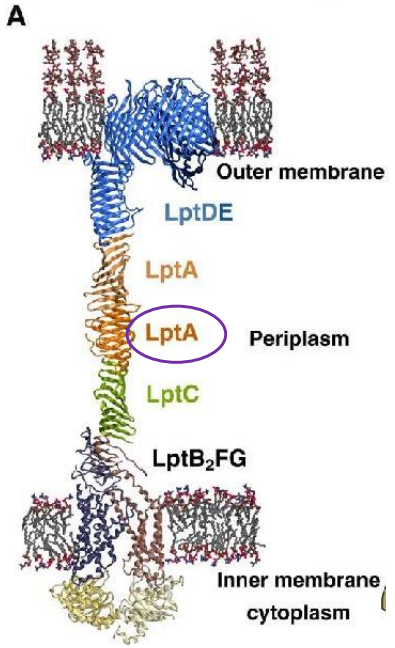
RNAseq

PISA

Protein target ID with PISA



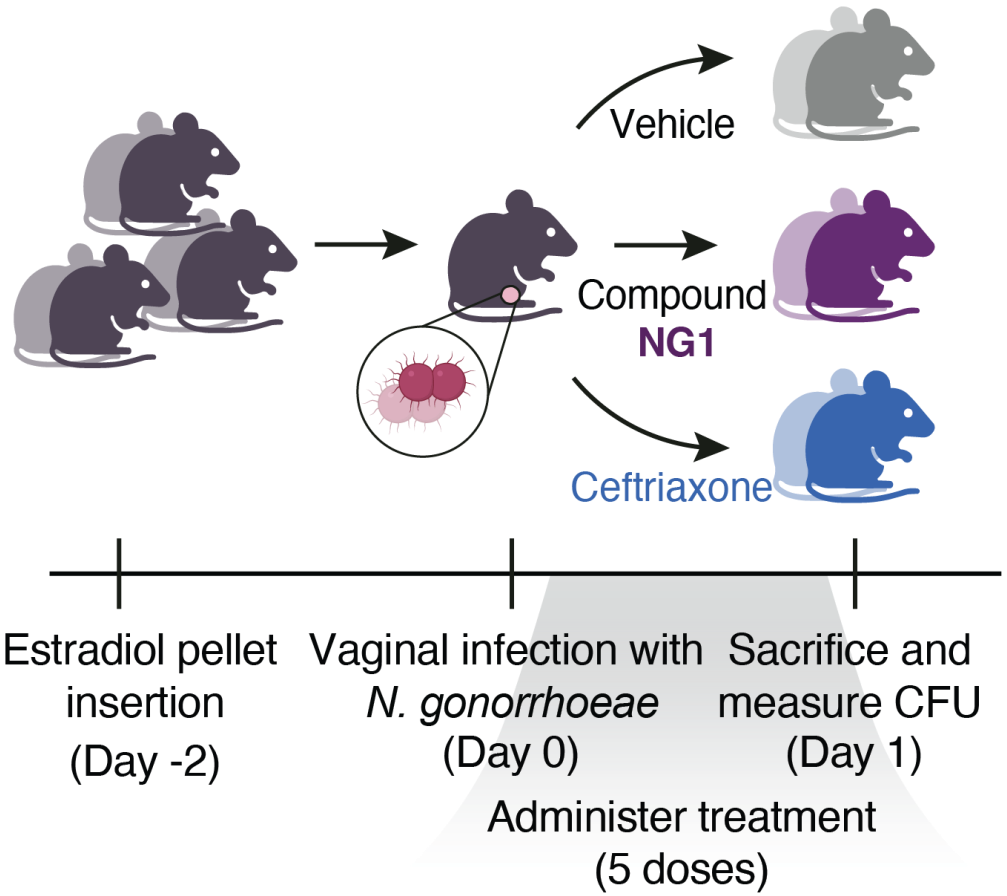
Lipopolysaccharide (LPS) transport system protein LptA: significantly destabilized by NG1



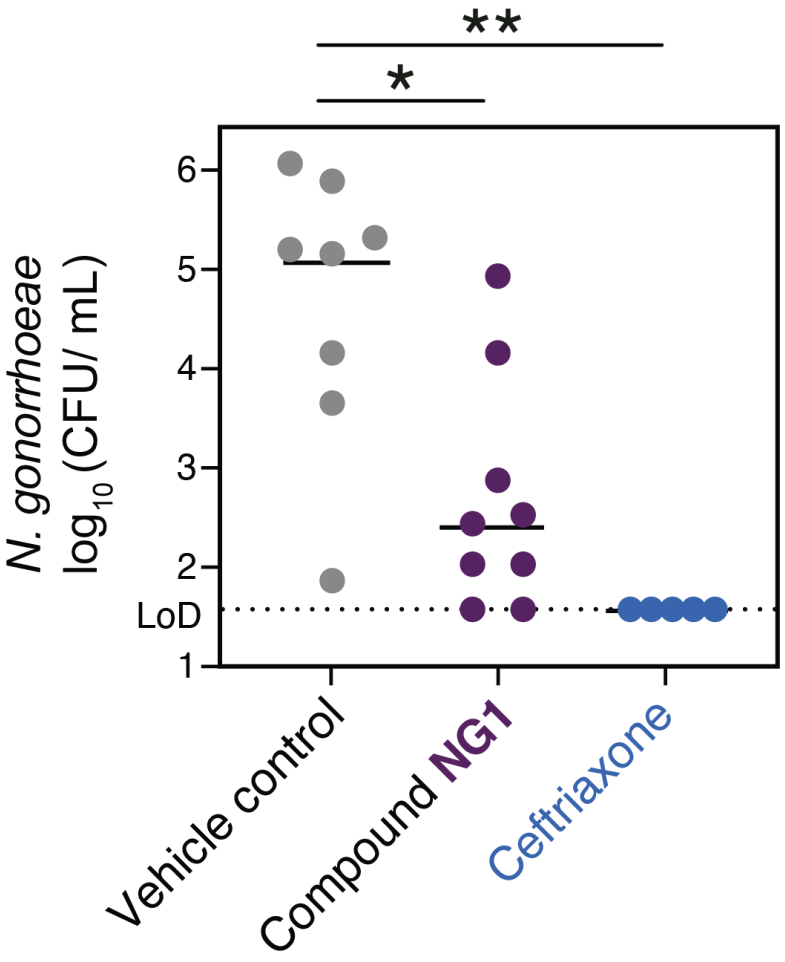
Modified from Schuster *et al. Science Advances,* 2023

Majed Modaresi, Marie-Stéphanie Aschtgen, Margaux Gaborieau, Massimiliano Gaetani, Amir Ata Saei, Edmond Loh

Efficacy in an *in vivo* mouse vaginal infection model

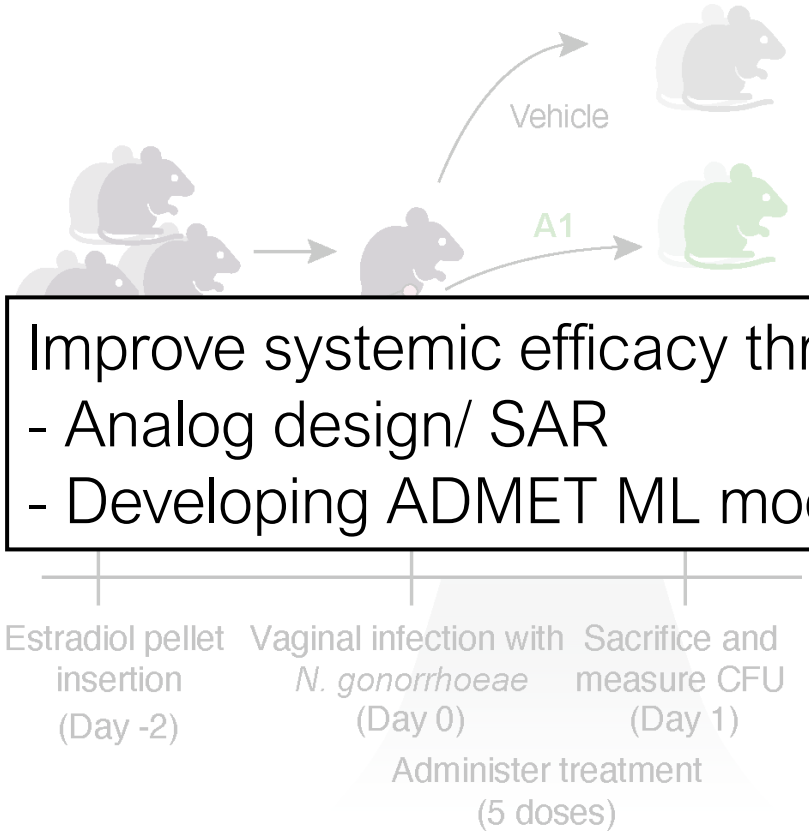


Topical delivery:



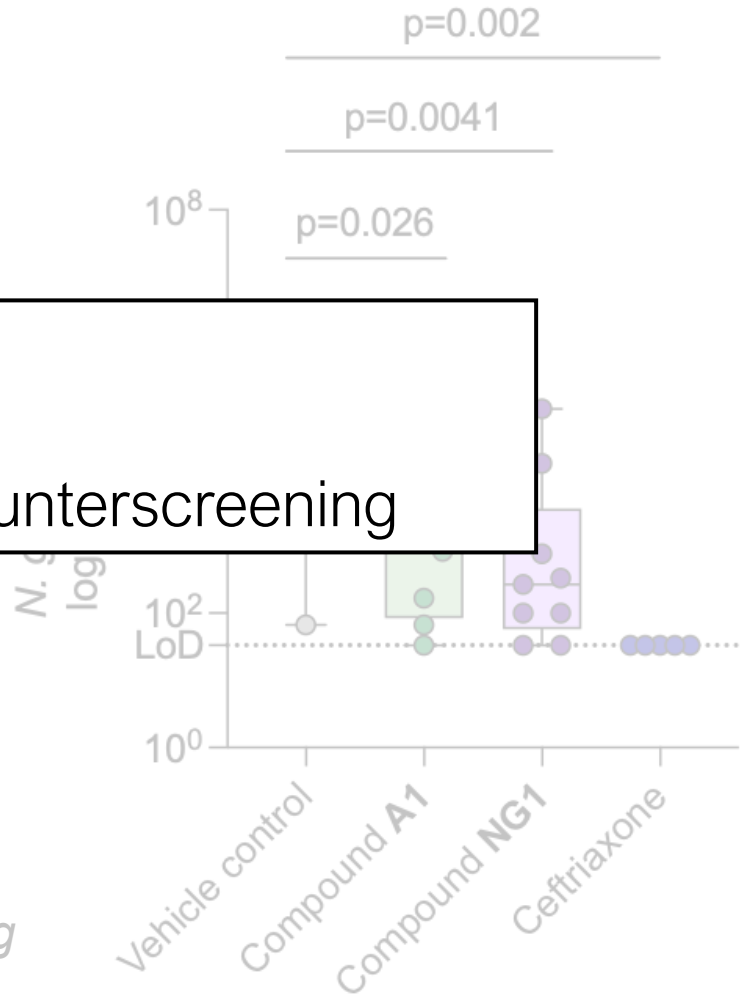
When delivered systemically: no significant decrease in vaginal *N. g*

Efficacy in an *in vivo* mouse vaginal infection model



Improve systemic efficacy through:
- Analog design/ SAR
- Developing ADMET ML models for counterscreening

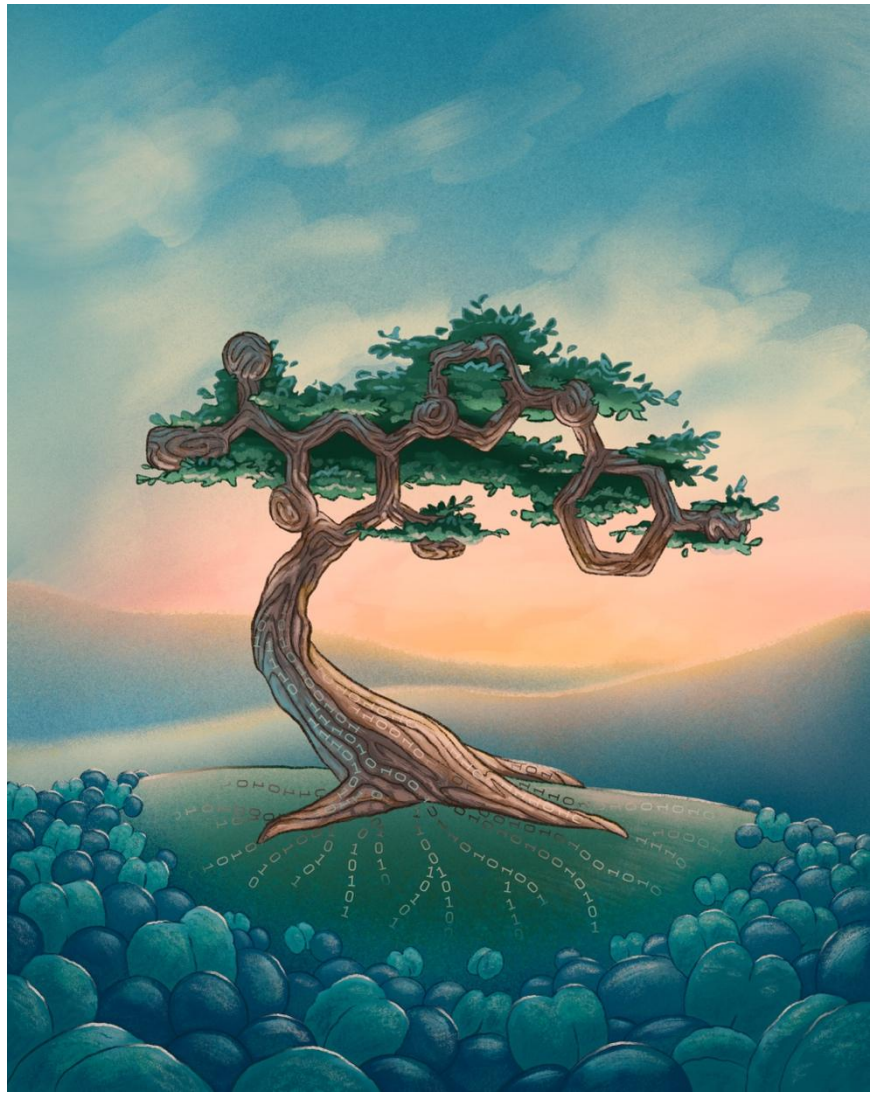
Topical delivery:



When delivered systemically: no significant decrease in vaginal *N. g*

Take-aways

- A deep learning model trained on phenotypic antibacterial data enables efficient discovery and design of novel small molecules with
  - potency even against the most highly resistant strains
  - unique mechanisms of action
- Fragment-based generative design enables more systematic exploration of chemical space
- VAE made more drug-like and synthesizable molecules than CReM
- Synthesis is a challenge that can be improved
- Deep learning affords major efficiency gains in hit identification, but hit-to-lead optimization is still necessary in current paradigm. Can be augmented with additional AI models.
- So much chemical space is left to explore!



Illustrated by Caitlin Rausch

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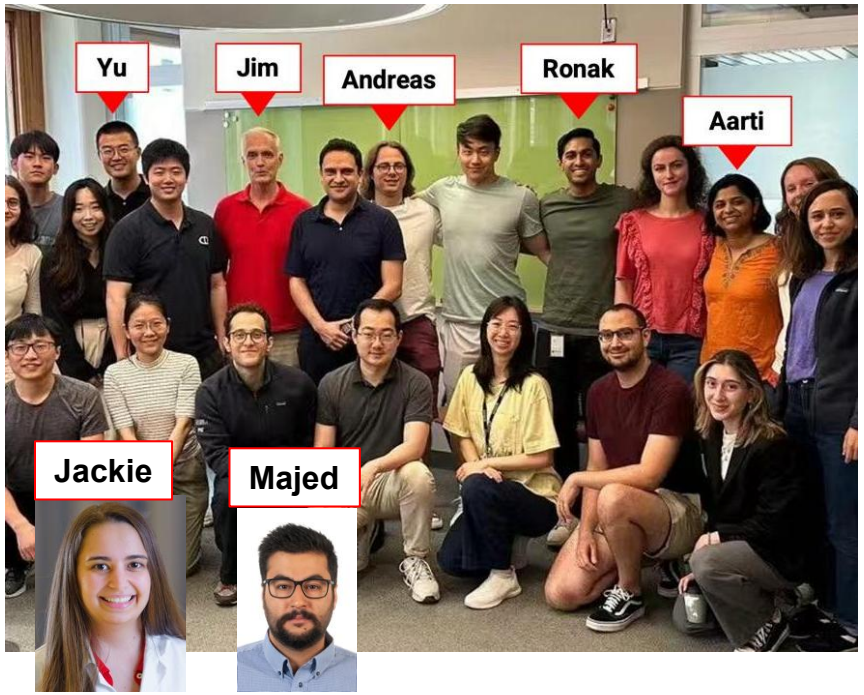
Aarti Krishnan
Majed Modaresi
Wengong Jin
Nina Donghia
Andreas Luttens
Felix Wong
Leif Sieben
Erica Zheng
Ryan Lach



For questions:
manahtar@mgh.harvard.edu

For more info:
anahtarlab.mgh.harvard.edu

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Margaux Gaborieau
Massimiliano Gaetani
Edmund Loh

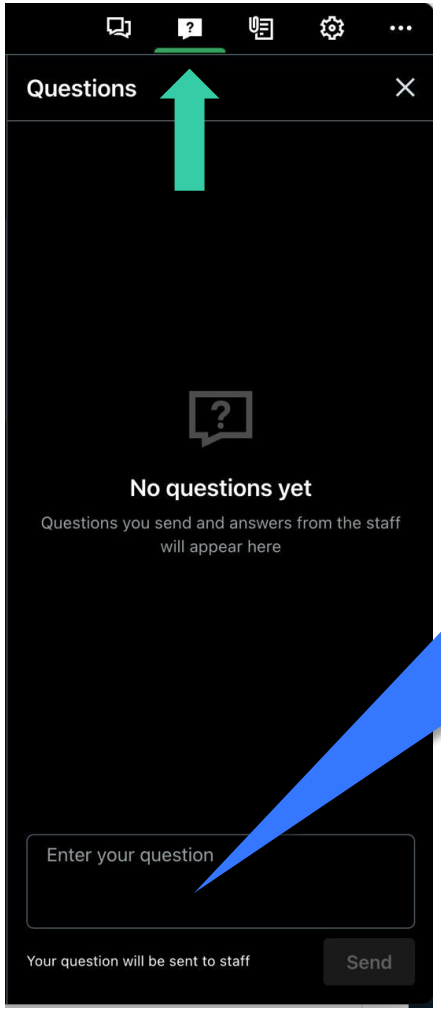
HSPH:
Yonatan Grad
Samantha Palace
Tatum Mortimer

MGH:
Infectious Diseases Division
Pathology Department

How to submit your questions

REVIVE by GARDP

If your question is addressed to a specific speaker, please include their name when submitting the question.



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.

Nicole Scangarella-Oman

Nicole Scangarella-Oman is Scientific Director in Infectious Diseases Research at GlaxoSmithKline (GSK) in Collegeville, Pennsylvania, USA. She joined the clinical microbiology group at GSK and, for over 2 decades, has focused on clinical microbiology and the development of GSK antibacterials. She is currently leading microbiology for a late-stage antibacterial.

Nicole is a member of the CLSI AST subcommittee, ESCMID and ASM and is the author of over 50 peer-reviewed scientific publications and approximately 140 scientific abstracts.

Efficacy and *in vitro* activity of gepotidacin against bacterial uropathogens, including drug-resistant phenotypes, in females with uncomplicated urinary tract infections: results from two global, pivotal, phase 3 trials (EAGLE-2 and EAGLE-3)

Antimicrobial Agents and Chemotherapy, 2025

Thursday March 26, 2026

Presenter: Nicole E. Scangarella-Oman

NX-GBL-GPT-PPT-260009
Date of preparation: March 2026

Disclosures and disclaimers

Nicole E. Scangarella-Oman

- Employed by GSK

Disclaimers

- The information is scientific and non-promotional in nature
- Content is protected by copyright and cannot be reproduced (photo, recording, or screenshots), nor disclosed or transmitted to any third party by any means, without the written authorization of GSK
- Gepotidacin is approved by the FDA for the treatment of female adults and adolescents (≥12 years) weighing ≥40 kg with uncomplicated urinary tract infections, and by the FDA for adults and adolescents (≥12 years) weighing ≥45 kg with uncomplicated urogenital gonorrhea
- EAGLE-2 was funded in part by GSK and in part with Federal funds form the US Office of the Assistant Secretary for preparedness and Response, Biomedical Advanced Research and Development Authority (HHSO100201300011C)
- EAGLE-3 was funded by GSK

Gepotidacin is a novel oral treatment option for patients with uUTI

- UTIs are among the most common bacterial infections worldwide[1]
- Approximately **50–60% of adult females will experience ≥1 UTI(s)** in their lifetime[2]
- The diversity of virulence factors and evolving resistance mechanisms in uropathogens contribute to **rising AMR in uUTI treatment**[1]

New oral treatments for UTIs are needed to battle evolving AMR among uropathogens[3]

- Gepotidacin is a novel, bactericidal, first-in-class triazaacenaphthylene antibacterial that inhibits bacterial DNA replication by a **distinct binding site, unique mechanism of action** and, for most pathogens, provides well-balanced inhibition of two different Type II topoisomerase enzymes[4–6]
- This provides **activity against most uropathogens**, including isolates resistant to current antibacterials[7,8]

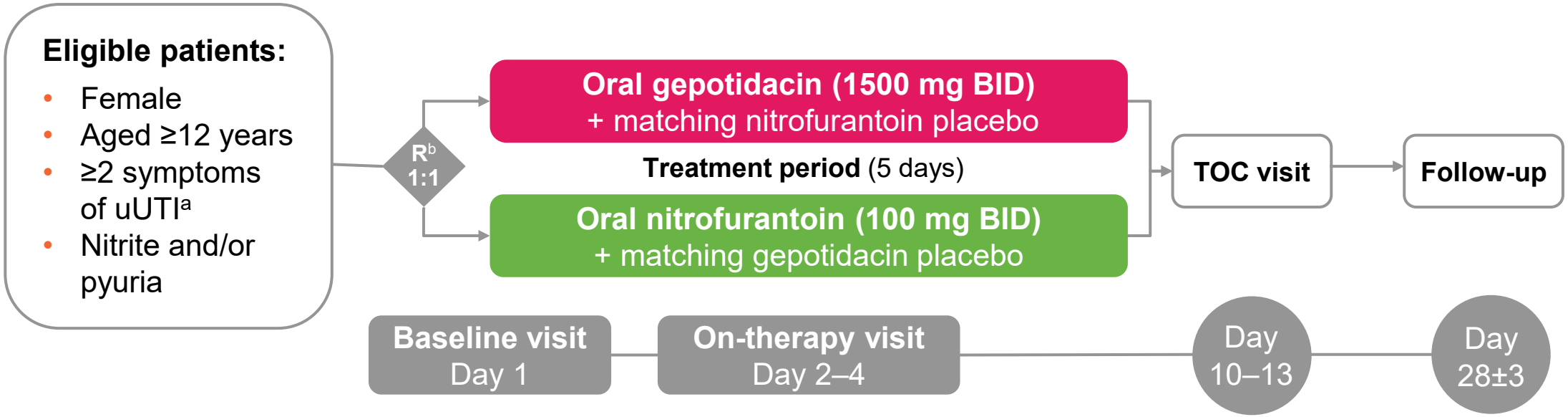
Phase 3 studies (2019–2023): EAGLE-2 and EAGLE-3 (Global uUTI studies)[9]

FDA approval for uUTI (2025)[10]

AMR = antimicrobial resistance; DNA = deoxyribonucleic acid; *E. coli* = *Escherichia coli*; FDA = US Food and Drug Administration; UTI = urinary tract infection; uUTI = uncomplicated urinary tract infection.

1. Mancuso G, et al. Pathogens. 2023;12:623; 2. Medina M, Castillo-Pino E. Ther Adv Urol. 2019;11:1756287219832172; 3. Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924; 4. Gibson EG, et al. ACS Infect Dis. 2019;5:570–581; 5. Bax BD, et al. Nature. 2010;446:935–940; 6. Oviatt AA, et al. ACS Infect Dis. 2024;10:1137–1151; 7, Arends SJR, et al. Antimicrob Agents Chemother. 2023;67:e0152522; 8. Mushtaq S, et al. Presented at ECCMID 2019, Amsterdam, the Netherlands. Poster P1849; 9. Wagenlehner FME, et al. Lancet. 2024;403:1047–1059; 10. GSK. Blujepa (gepotidacin) approved by US FDA for uUTIs. 2025. Accessed March 2026.

EAGLE-2 and EAGLE-3 were global, Phase 3 double-blind, non-inferiority randomized controlled trials



Primary endpoint analysis:
Therapeutic response (success or failure) at TOC visit (micro-ITT NTF-S [IA Set])

Therapeutic success at TOC = **Clinical success at TOC** full symptom resolution and no new signs and symptoms[c] + **Microbiological success at TOC** all baseline qualifying uropathogens eradicated; $\geq 10^5$ to $<10^3$ CFU/mL[c]

Gepotidacin demonstrated **non-inferiority to nitrofurantoin** across EAGLE-2 and EAGLE-3, and **superiority** in EAGLE-3

[a] Dysuria, frequency, urgency, or lower abdominal pain. [b] Stratified by age group and history of uUTI recurrence. [c] Without additional antibiotic use.
BID = twice daily; CFU = colony-forming unit; micro-ITT NTF-S (IA Set) = microbiological intent-to-treat nitrofurantoin-susceptible interim analysis set population; R = randomized; TOC = test-of-cure; uUTI = uncomplicated urinary tract infection.
Wagenlehner F, et al. Lancet. 2024;403:1047–1059.

Pooled microbiology results and efficacy observations from the global EAGLE-2 and EAGLE-3 trials have been analyzed

Here, we present pooled microbiology results and efficacy observations with a focus on the overall incidence of recovered drug-resistant uropathogens, **gepotidacin *in vitro* activity against drug-resistant phenotypes**, and by-pathogen efficacy responses against drug-resistant phenotypes

Data are based primarily on the **micro-ITT population,** which includes:

- All randomized participants who received ≥1 dose(s) of study treatment and had a baseline qualifying (growth ≥10^5 CFU/mL) uropathogen regardless of its susceptibility to nitrofurantoin
- A higher number of participants and uropathogen data compared with the primary analysis population, thus providing a **broader and more clinically relevant data set**

Microbiological assessments

- Quantitative urine culture and uropathogen identification were performed using standard methods
- Antimicrobial susceptibility testing was conducted according to CLSI procedures
- All microbiological assessments were conducted at a central laboratory

CLSI = Clinical & Laboratory Standards Institute; CFU = colony-forming unit; MIC = minimum inhibitory concentration; micro-ITT = microbiological intent-to-treat.

Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924.

E. coli (78%), was the most common identified baseline qualifying uropathogen, followed by *K. pneumoniae* (8%), *P. mirabilis* (5%), and *S. saprophyticus* (2%)

Incidence of baseline qualifying uropathogens for pooled EAGLE-2 and EAGLE-3 data (micro-ITT population)

Qualifying uropathogen[a]	Gepotidacin n (%)[b] N=732	Nitrofurantoin n (%)[b] N=689	Total n (%)[b] N=1,421
Total number of qualifying uropathogens, n	764	722	1486
Escherichia coli	598 (78)	561 (78)	1,159 (78)
Klebsiella pneumoniae	56 (7)	58 (8)	114 (8)
Klebsiella oxytoca/ Raoultella ornithinolytica	5 (<1)	4 (<1)	9 (<1)
Klebsiella aerogenes	2 (<1)	5 (<1)	7 (<1)
Klebsiella variicola	3 (<1)	2 (<1)	5 (<1)
Proteus mirabilis	34 (4)	33 (5)	67 (5)
Enterobacter cloacae complex	6 (<1)	11 (2)	17 (1)
Citrobacter freundii complex	13 (2)	6 (<1)	19 (1)
Citrobacter koseri	2 (<1)	6 (<1)	8 (<1)
Citrobacter amolonaticus group	2 (<1)	0	2 (<1)
Morganella morganii	8 (1)	5 (<1)	13 (<1)

Qualifying uropathogen[a]	Gepotidacin n (%)[b] N=732	Nitrofurantoin n (%)[b] N=689	Total n (%)[b] N=1,421
Serratia marcescens	0	3 (<1)	3 (<1)
Providencia rettgeri	1 (<1)	1 (<1)	2 (<1)
Serratia liquefaciens	1 (<1)	0	1 (<1)
Pseudomonas aeruginosa	2 (<1)	3 (<1)	5 (<1)
Pseudomonas putida group	1 (<1)	1 (<1)	2 (<1)
Acinetobacter baumannii nosocomialis group	0	1 (<1)	1 (<1)
Weeksella virosa	0	1 (<1)	1 (<1)
Staphylococcus saprophyticus	15 (2)	14 (2)	29 (2)
Enterococcus faecalis	14 (2)	7 (<1)	21 (1)
Enterococcus faecium	1 (<1)	0	1 (<1)

[a] All drug-resistant phenotypes were determined per CLSI or EUCAST guidelines as described in Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924. Additional uropathogens and drug-resistant phenotypes are shown in Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924. [b] Percentage of each qualifying uropathogen was calculated using the total number of baseline qualifying uropathogens at baseline as the denominator.

CLSI = Clinical & Laboratory Standards Institute; *E. coli* = *Escherichia coli*; EUCAST = European Committee on Antimicrobial Susceptibility Testing; *K. pneumoniae* = *Klebsiella pneumonia*; micro-ITT = microbiological intent-to-treat; *P. mirabilis* = *Proteus mirabilis*; *S. saprophyticus* = *Staphylococcus saprophyticus*.

Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924.

High prevalence of key drug-resistant phenotypes among baseline qualifying *E. coli* and *K. pneumoniae* isolates

Incidence of baseline qualifying uropathogens and selected drug-resistant phenotypes for pooled EAGLE-2 and EAGLE-3 data (micro-ITT population)

Qualifying uropathogen/ phenotype[a]	Gepotidacin n (%)	Nitrofurantoin n (%)	Total n (%)
Escherichia coli	598 (78)	561 (78)	1,159 (78)
Amoxicillin-clavulanic acid-R	29 (5)	20 (4)	49 (4)
Ampicillin--R	289 (48)	261 (47)	550 (47)
Cefadroxil-R	95 (16)	73 (13)	168 (14)
Cefazolin-R	107 (18)	85 (15)	192 (17)
Ceftriaxone-R	85 (14)	71 (13)	156 (13)
FQ-R	179 (30)	151 (27)	330 (28)
Mecillinam-R	18 (3)	14 (2)	32 (3)
Nitrofurantoin-R	6 (1)	8 (1)	14 (1)
Nitroxoline-R	12 (2)	12 (2)	24 (2)
SXT-R	172 (29)	149 (27)	321 (28)
ESBL+	94 (16)	76 (14)	170 (15)
MDR	175 (29)	148 (26)	323 (28)
FQ-R and ESBL+	70 (12)	53 (9)	123 (11)
FQ-R and ESBL+ and SXT-R	38 (6)	28 (5)	66 (6)
FQ-R and SXT-R	80 (13)	71 (13)	151 (13)
SXT-R and ESBL+	54 (9)	36 (6)	90 (8)

Qualifying uropathogen/ phenotype[a]	Gepotidacin n (%)	Nitrofurantoin n (%)	Total n (%)
Klebsiella pneumoniae	56 (7)	58 (8)	114 (8)
Amoxicillin-clavulanic acid-R	5 (9)	5 (9)	10 (9)
Cefadroxil-R	10 (18)	7 (12)	17 (15)
Cefazolin-R	10 (18)	8 (14)	18 (16)
Ceftriaxone-R	8 (14)	7 (12)	15 (13)
FQ-R	9 (16)	9 (16)	18 (16)
Nitrofurantoin-R	13 (23)	15 (26)	28 (25)
SXT-R	13 (23)	13 (22)	26 (23)
ESBL+	11 (20)	7 (12)	18 (16)
MDR	14 (25)	13 (22)	27 (24)
FQ-R and ESBL+	8 (14)	6 (10)	14 (12)
FQ-R and ESBL+ and SXT-R	3 (5)	4 (7)	7 (6)
FQ-R and SXT-R	3 (5)	4 (7)	7 (6)
SXT-R and ESBL+	5 (9)	5 (9)	10 (9)

[a] All drug-resistant phenotypes were determined per CLSI or EUCAST guidelines as described in Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924. Additional uropathogens and drug-resistant phenotypes are shown in Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924.

CLSI = Clinical & Laboratory Standards Institute; *E. coli* = *Escherichia coli*; ESBL+ = extended-spectrum β-lactamase positive; EUCAST = European Committee on Antimicrobial Susceptibility Testing; FQ-R = fluoroquinolone resistant; *K. pneumoniae* = *Klebsiella pneumonia*; MDR = multidrug resistant; micro-ITT = microbiological intent-to-treat; R = resistant; SXT-R = trimethoprim-sulfamethoxazole-resistant.

Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924.

Most qualifying uropathogens (93.1–100%) were susceptible to gepotidacin, with %S generally maintained across isolates with drug-resistant phenotypes (96.9–100% for *E. coli* and 85.7–100% for *K. pneumoniae*)

***In vitro* activity of gepotidacin against selected baseline qualifying uropathogens and *E. coli* and *K. pneumoniae* drug-resistant phenotypes for pooled EAGLE-2 and EAGLE-3 data (micro-ITT population)**

Uropathogen/ Phenotypic subcategory[a]	Number of isolates	Gepotidacin MIC (µg/mL)			
		Range	MIC50	MIC90	%S[b]
Escherichia coli	1,159	≤0.03–32	1	4	>99.9
Amoxicillin/clavulanic acid-R	49	0.5–16	2	4	100
Ampicillin-R	550	0.12–32	1	4	99.8
Cefadroxil-R	168	0.12–16	2	4	100
Cefazolin-R	192	0.12–16	2	4	100
Ceftriaxone-R	156	0.12–16	2	4	100
FQ-R	330	≤0.03–16	1	4	100
Mecillinam-R	32	0.25–32	2	4	96.9
Nitrofurantoin-R	14	0.5–4	2	4	100
Nitroxoline-R	24	0.5–8	2	8	100
SXT-R	321	0.12–16	1	2	100
ESBL+	170	0.12–16	2	4	100
MDR	323	0.12–16	1	4	100
FQ-R and ESBL+	123	0.12–16	2	4	100
FQ-R and ESBL+ and SXT-R	66	0.12–16	1	4	100
FQ-R and SXT-R	151	0.12–16	1	4	100

Uropathogen/ Phenotypic subcategory[a]	Number of Isolates	Gepotidacin MIC (µg/mL)			
		Range	MIC50	MIC90	%S[b]
Klebsiella pneumoniae	114	1–32	4	16	96.5
Amoxicillin/clavulanic acid-R	10	4–32	4	16	90.0
Cefadroxil-R	17	2–32	4	16	94.1
Cefazolin-R	18	2–32	4	16	94.4
Ceftriaxone-R	15	2–16	4	16	100
FQ-R	18	2–32	4	32	88.9
Nitrofurantoin-R	28	2–32	4	16	96.4
SXT-R	26	1–32	8	16	92.3
ESBL+	18	2–32	4	32	88.9
MDR	27	2–32	8	16	92.6
FQ-R and ESBL+	14	2–32	4	32	85.7
Proteus mirabilis	67	1–32	8	16	95.5
Enterobacter cloacae complex	17	2–4	4	4	100
Citrobacter freundii complex	19	0.5–8	2	8	100
Morganella morganii	13	1–16	4	16	100
Staphylococcus saprophyticus	29	0.06–0.5	0.12	0.25	93.1
Enterococcus faecalis	21	0.5–4	1	2	100

[a] All drug-resistant phenotypes were determined per CLSI or EUCAST guidelines as described in Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924. Additional uropathogens and drug-resistant phenotypes are shown in Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924. [b] Gepotidacin susceptibility defined by FDA breakpoints (FDA, 2026).

CLSI = Clinical & Laboratory Standards Institute; *E. coli* = *Escherichia coli*; ESBL+ = extended-spectrum β-lactamase positive; EUCAST = European Committee on Antimicrobial Susceptibility Testing; FDA = US Food and Drug Administration; FQ-R = fluoroquinolone resistant; *K. pneumoniae* = *Klebsiella pneumonia*; MDR = multidrug resistant; MIC = minimum inhibitory concentration; micro-ITT = microbiological intent-to-treat; SXT-R = trimethoprim-sulfamethoxazole resistant; R = resistant; S = susceptible.

Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924.

Therapeutic success rates at TOC were similar across phenotypic subcategories for each species (micro-ITT population)

Therapeutic success at TOC by baseline qualifying uropathogen and selected drug-resistant phenotypes (micro-ITT population)

Uropathogen/ phenotypic subcategory[a]	Gepotidacin N=732 n/N1 (%; 95% CI)	Nitrofurantoin N=689 n/N1 (%; 95% CI)
Escherichia coli	322/591 (54.5)	241/556 (43.3)
Amoxicillin-clavulanic acid-R	12/28 (42.9)	7/20 (35.0)
Ampicillin-R	146/288 (50.7)	115/261 (44.1)
Cefadroxil-R	48/95 (50.5)	26/73 (35.6)
Cefazolin-R	55/107 (51.4)	30/85 (35.3)
Ceftriaxone-R	43/85 (50.6)	22/71 (31.0)
FQ-R	82/174 (47.1)	54/151 (35.8)
Mecillinam-R	8/18 (44.4)	4/14 (28.6)
Nitroxoline-R	6/12 (50.0)	6/12 (50.0)
SXT-R	92/171 (53.8)	60/147 (40.8)
ESBL+	48/94 (51.1)	26/76 (34.2)
MDR	88/174 (50.6)	57/148 (38.5)
FQ-R and ESBL+	38/70 (54.3)	16/53 (30.2)
FQ-R and ESBL+ and SXT-R	23/38 (60.5)	7/28 (25.0)
FQ-R and SXT-R	39/79 (49.4)	22/71 (31.0)
SXT-R and ESBL+	30/54 (55.6)	10/36 (27.8)
Klebsiella pneumoniae	21/54 (38.9)	16/57 (28.1)
Cefadroxil-R	4/10 (40.0)	1/7 (14.3)
Cefazolin-R	4/10 (40.0)	1/8 (12.5)
Nitrofurantoin-R	5/13 (38.5)	6/15 (40.0)
SXT-R	4/13 (30.8)	1/13 (7.7)
ESBL+	5/11 (45.5)	1/7 (14.3)
MDR	6/14 (42.9)	3/13 (23.1)
Proteus mirabilis	24/34 (70.6)	9/33 (27.3)
FQ-R	7/11 (63.6)	1/3 (33.3)
SXT-R	8/12 (66.7)	1/5 (20.0)
MDR	11/16 (68.8)	1/5 (20.0)
FQ-R and SXT-R	6/10 (60.0)	1/3 (33.3)

[a] All drug-resistant phenotypes were determined per CLSI or EUCAST guidelines as described in Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924. Additional uropathogens and drug-resistant phenotypes are shown in Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924.

CI = confidence interval; CLSI = Clinical & Laboratory Standards Institute; ESBL+ = extended-spectrum β-lactamase positive; EUCAST = European Committee on Antimicrobial Susceptibility Testing; FQ-R = fluoroquinolone resistant; MDR = multidrug resistant; micro-ITT = microbiological intent-to-treat; SXT-R = trimethoprim-sulfamethoxazole resistant; TOC = test-of-cure.

Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924.

Clinical success rates at TOC were similar across phenotypic subcategories for each species (micro-ITT population)

Clinical success at TOC by baseline qualifying uropathogen and selected drug-resistant phenotypes (micro-ITT population)

Uropathogen/ phenotypic subcategory[a]	Gepotidacin N=732 n/N1 (%; 95% CI)	Nitrofurantoin N=689 n/N1 (%; 95% CI)
Escherichia coli	402/591 (68.0)	356/556 (64.0)
Amoxicillin-clavulanic acid-R	18/28 (64.3)	10/20 (50.0)
Ampicillin-R	190/288 (66.0)	160/261 (61.3)
Cefadroxil-R	63/95 (66.3)	42/73 (57.5)
Cefazolin-R	72/107 (67.3)	47/85 (55.3)
Ceftriaxone-R	57/85 (67.1)	38/71 (53.5)
FQ-R	118/174 (67.8)	91/151 (60.3)
Mecillinam-R	9/18 (50.0)	8/14 (57.1)
Nitroxoline-R	7/12 (58.3)	8/12 (66.7)
SXT-R	118/171 (69.0)	90/147 (61.2)
ESBL+	63/94 (67.0)	42/76 (55.3)
MDR	119/174 (68.4)	87/148 (58.8)
FQ-R and ESBL+	49/70 (70.0)	29/53 (54.7)
FQ-R and ESBL+ and SXT-R	27/38 (71.1)	16/28 (57.1)
FQ-R and SXT-R	52/79 (65.8)	44/71 (62.0)
SXT-R and ESBL+	37/54 (68.5)	20/36 (55.6)
Klebsiella pneumoniae	27/54 (50.0)	29/57 (50.9)
Cefadroxil-R	6/10 (60.0)	2/7 (28.6)
Cefazolin-R	6/10 (60.0)	3/8 (37.5)
Nitrofurantoin-R	6/13 (46.2)	11/15 (73.3)
SXT-R	5/13 (38.5)	4/13 (30.8)
ESBL+	7/11 (63.6)	2/7 (28.6)
MDR	8/14 (57.1)	6/13 (46.2)
Proteus mirabilis	27/34 (79.4)	16/33 (48.5)
FQ-R	9/11 (81.8)	2/3 (66.7)
SXT-R	10/12 (83.3)	3/5 (60.0)
MDR	13/16 (81.3)	3/5 (60.0)
FQ-R and SXT-R	8/10 (80.0)	2/3 (66.7)

[a] All drug-resistant phenotypes were determined per CLSI or EUCAST guidelines as described in Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924. Additional uropathogens and drug-resistant phenotypes are shown in Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924.

CI = confidence interval; CLSI = Clinical & Laboratory Standards Institute; ESBL+ = extended-spectrum β-lactamase positive; EUCAST = European Committee on Antimicrobial Susceptibility Testing; FQ-R = fluoroquinolone resistant; MDR = multidrug resistant; micro-ITT = microbiological intent-to-treat; R = resistance; SXT-R = trimethoprim-sulfamethoxazole resistant; TOC = test-of-cure.

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Microbiological success rates at TOC were similar across phenotypic subcategories for each species (micro-ITT population)

Microbiological success at TOC by baseline qualifying uropathogen and selected drug-resistant phenotypes (micro-ITT population)

Uropathogen/ phenotypic subcategory[a]	Gepotidacin N=732 n/N1 (%; 95% CI)	Nitrofurantoin N=689 n/N1 (%; 95% CI)
Escherichia coli	431/598 (72.1)	339/561 (60.4)
Amoxicillin-clavulanic acid-R	18/29 (62.1)	11/20 (55.0)
Ampicillin-R	199/289 (68.9)	160/261 (61.3)
Cefadroxil-R	62/95 (65.3)	41/73 (56.2)
Cefazolin-R	69/107 (64.5)	47/85 (55.3)
Ceftriaxone-R	55/85 (64.7)	38/71 (53.5)
FQ-R	116/179 (64.8)	80/151 (53.0)
Mecillinam-R	13/18 (72.2)	6/14 (42.9)
Nitroxoline-R	7/12 (58.3)	9/12 (75.0)
SXT-R	129/172 (75.0)	91/149 (61.1)
ESBL+	60/94 (63.8)	43/76 (56.6)
MDR	116/175 (66.3)	84/148 (56.8)
FQ-R and ESBL+	46/70 (65.7)	27/53 (50.9)
FQ-R and ESBL+ and SXT-R	29/38 (76.3)	14/28 (50.0)
FQ-R and SXT-R	58/80 (72.5)	36/71 (50.7)
SXT-R and ESBL+	38/54 (70.4)	20/36 (55.6)
Klebsiella pneumoniae	38/56 (67.9)	27/58 (46.6)
Cefadroxil-R	6/10 (60.0)	3/7 (42.9)
Cefazolin-R	6/10 (60.0)	3/8 (37.5)
Nitrofurantoin-R	8/13 (61.5)	7/15 (46.7)
SXT-R	8/13 (61.5)	4/13 (30.8)
ESBL+	7/11 (63.6)	3/7 (42.9)
MDR	10/14 (71.4)	6/13 (46.2)
Proteus mirabilis	32/34 (94.1)	21/33 (63.6)
FQ-R	9/11 (81.8)	2/3 (66.7)
SXT-R	10/12 (83.3)	4/5 (80.0)
MDR	14/16 (87.5)	4/5 (80.0)
FQ-R and SXT-R	8/10 (80.0)	2/3 (66.7)

[a] All drug-resistant phenotypes were determined per CLSI or EUCAST guidelines as described in Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924. Additional uropathogens and drug-resistant phenotypes are shown in Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924.

CI = confidence interval; CLSI = Clinical & Laboratory Standards Institute; ESBL+ = extended-spectrum β-lactamase positive; EUCAST = European Committee on Antimicrobial Susceptibility Testing; FQ-R = fluoroquinolone resistant; MDR = multidrug resistant; micro-ITT = microbiological intent-to-treat; R = resistance; SXT-R = trimethoprim-sulfamethoxazole resistant; TOC = test-of-cure.

Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924.

Conclusion

***E. coli* was the most common qualifying uropathogen** recovered from the pooled data
Resistance to current treatment options for UTIs was observed, with some drugs showing **drug resistance rates >10%**

For all **uropathogen drug-resistant phenotypes**, gepotidacin MIC_{90} values and percent susceptibilities were generally similar compared with the MIC_{90} and percent susceptibilities of the overall species, demonstrating the ***in vitro* activity of gepotidacin**

Therapeutic, clinical and microbiological success rates for gepotidacin at TOC were generally similar across phenotypic subgroups of *E. coli*, *K. pneumoniae,* and *P. mirabilis*

E. coli = *Escherichia coli*; *K. pneumoniae* = *Klebsiella pneumoniae*; MIC = minimum inhibitory concentration; *P. mirabilis* = *Proteus mirabilis*; TOC = test-of-cure; UTI = urinary tract infection.
Scangarella-Oman NE, et al. Antimicrob Agents Chemother. 2025;69:e0163924.

Thank you for joining us!

Any questions?

How to submit your questions

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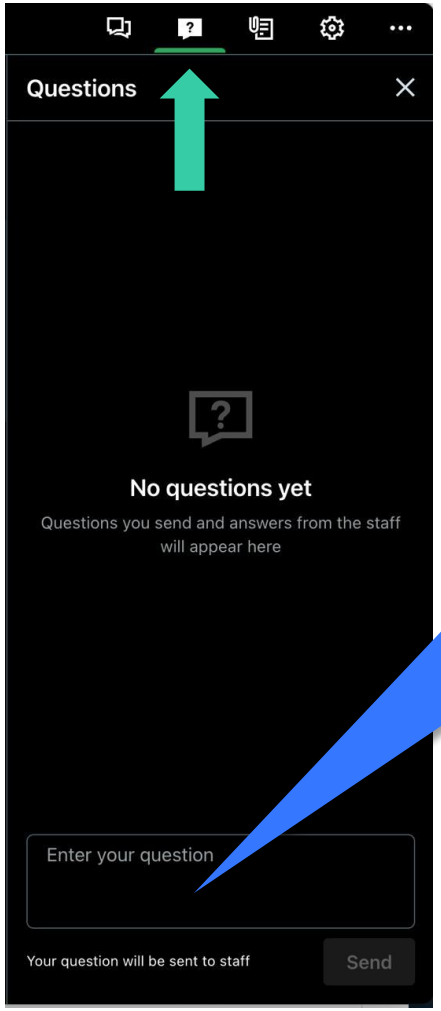
If your question is addressed to a specific speaker, please include their name when submitting the question.



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Today's speakers

REVIVE by GARDP

Journal Club: Key findings from recent publications in antimicrobial R&D

Moderator:
Florian Maurer
Basilea Pharmaceuticals, Switzerland

David Paterson
ADVANCE-ID, Singapore

Nicole Scangarella-Oman
GlaxoSmithKline, USA

Melis Anahtar
Massachusetts General Hospital, USA

Upcoming webinars

Natural Product-inspired antibiotics: Successes and future prospects

- With Mark Butler & Christine Beemelmanns
- 28 April 2026, 09:30-11:00 CEST

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