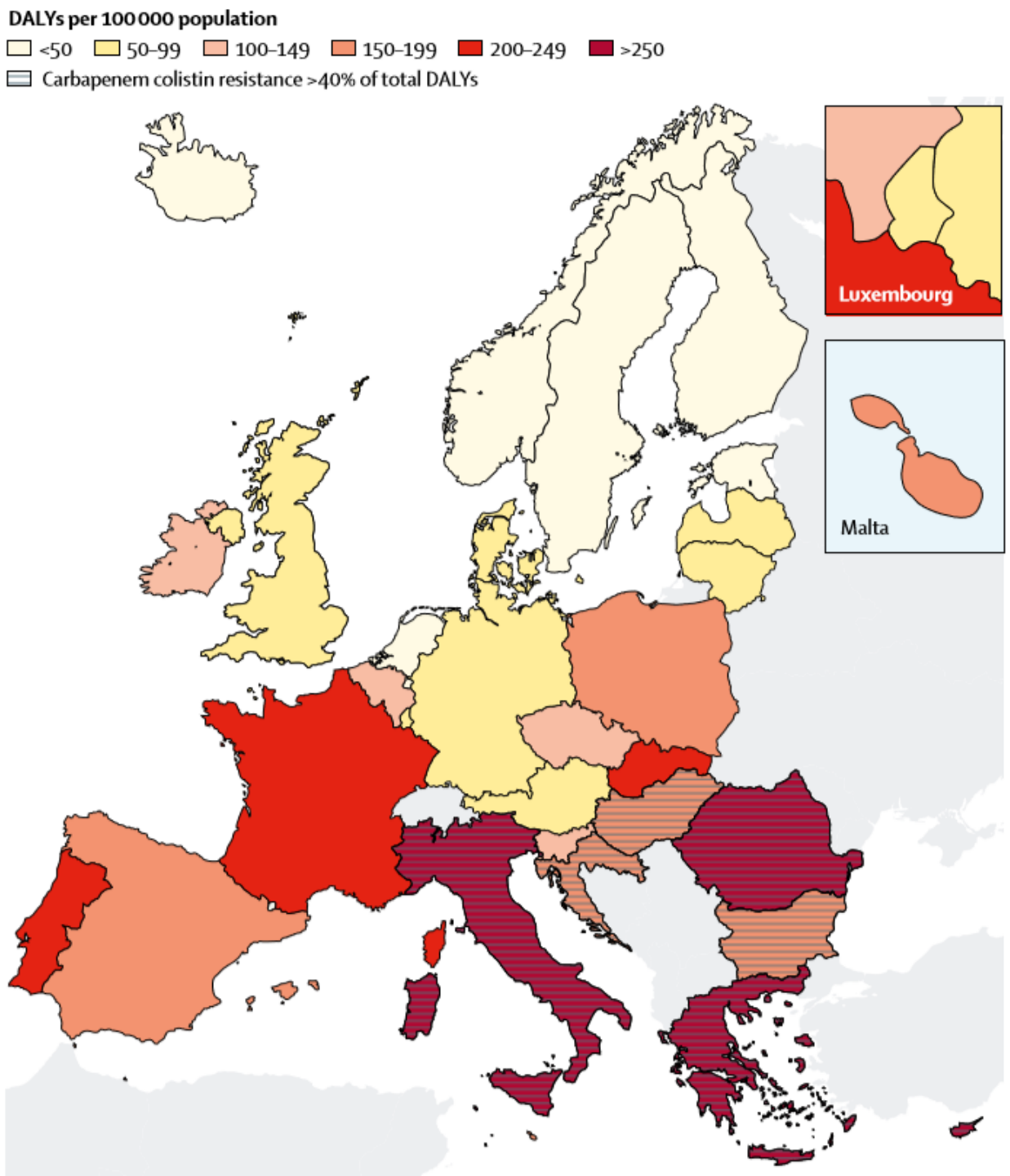
Incontri
di aggiornamento
del Dipartimento
Oncologico

Infezioni multiresistenti in ambito oncologico

15 Maggio 2019

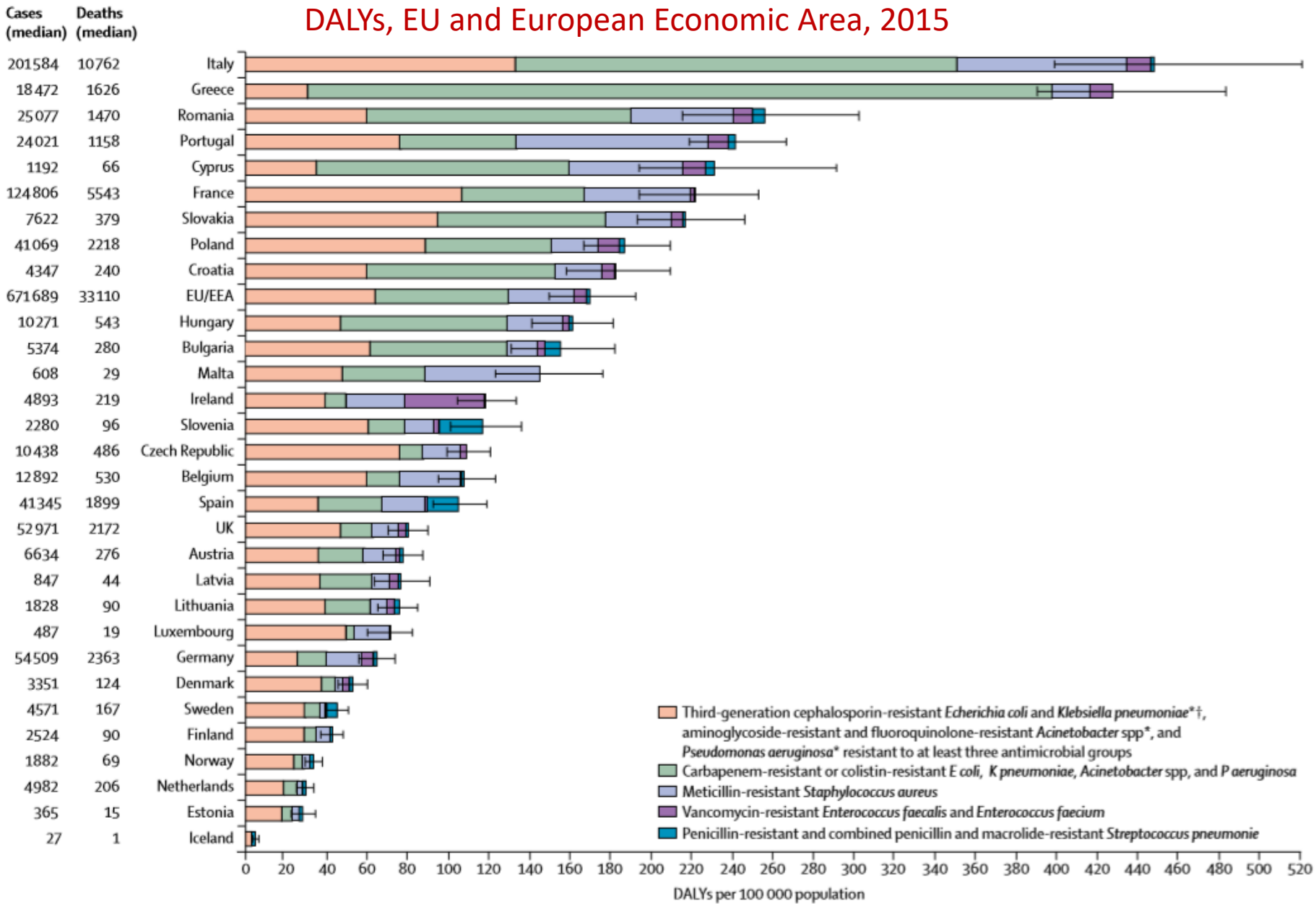
Giuseppe Marasca



Model estimates of the burden of infections with selected antibiotic-resistant bacteria of public health importance in DALYs per 100 000 population, EU and European Economic Area, 2015

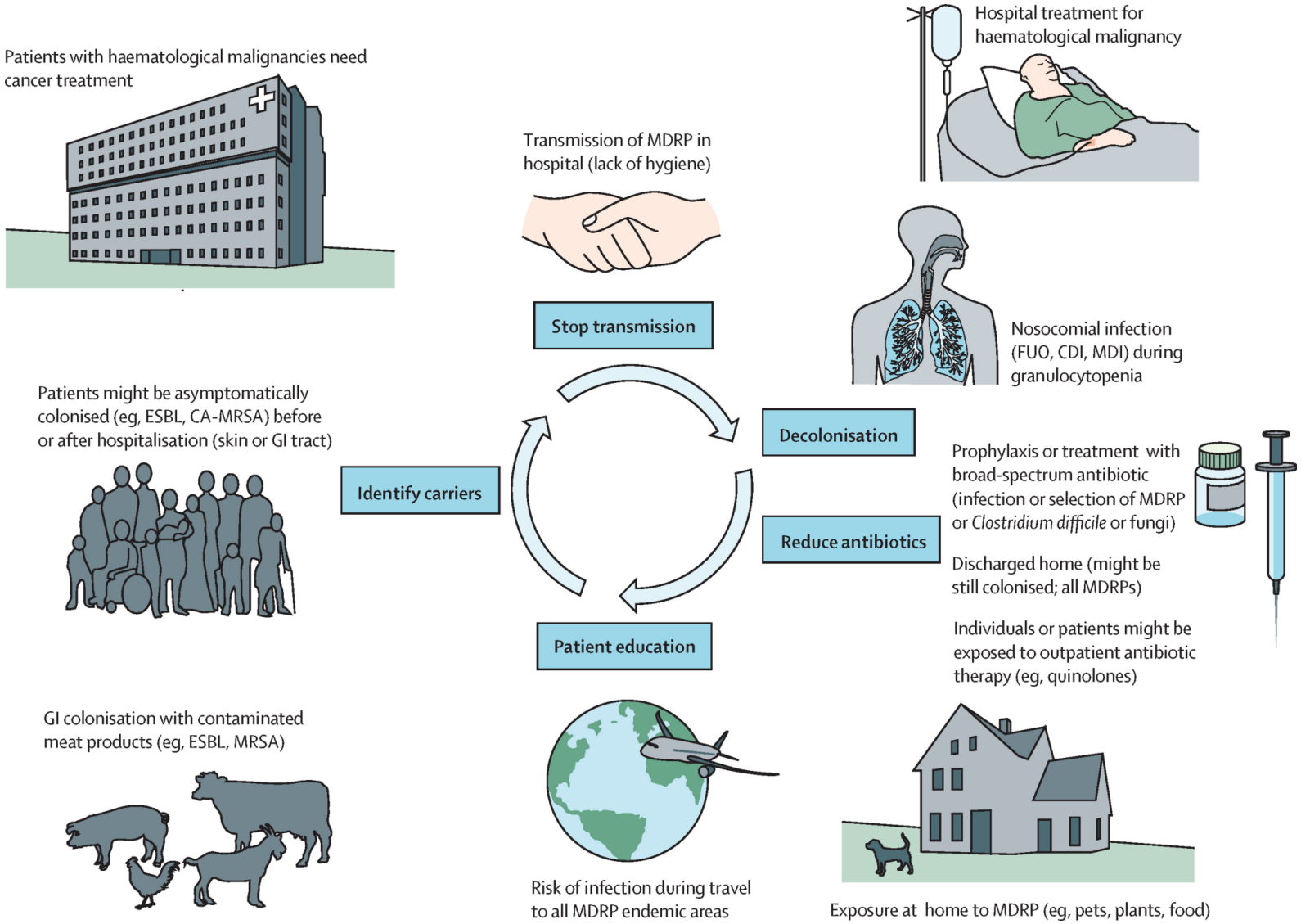
Lancet Infect Dis 2019; 19: 56–66

Burden of infections with antibiotic-resistant bacteria in DALYs, EU and European Economic Area, 2015



Lancet Infect Dis 2019; 19: 56–66

Settings contributing to transmission of MDR pathogens in patients with malignancies, and infection control interventions



Ruhnke M, Arnold R, Gastmeier P. *Lancet Oncol* 2014; 15: e606–19

Multidrug-resistant pathogens in patients with cancer

	Drug resistance	Risk factors
Staphylococcus aureus	Meticillin (and more commonly used oxacillin)	Previous or prolonged stay in hospital; ≥65 years of age; recent surgery within past 4 weeks; enteral feeding; open skin lesions; skin graft-versus-host disease (allogeneic haemopoietic stem-cell transplant); and previous antibiotics (quinolones, glycopeptides, and cephalosporins)
Vancomycin-resistant *Enterococci* spp	Vancomycin and all glycopeptides	Neutropenia >7 days; severe mucositis; *Clostridium difficile*-associated diarrhoea; colonisation with vancomycin-resistant *Enterococci* spp on admission to hospital (risk factor for fatal bacteraemia); and previous antibiotics (oral vancomycin, extended-spectrum cephalosporins, and metronidazole)
Extended-spectrum β-lactamase-producing *Enterobacteriaceae* (eg, *E coli* and *K pneumoniae*)	Penicillin, and third-generation cephalosporin (eg, cefotaxime, ceftriaxone, and ceftazidime)	Admission to intensive-care unit; nosocomial acquisition; hospital stay 21 days or longer; severe illness; central venous catheter; urinary catheter; ventilatory assistance; haemodialysis; emergency abdominal surgery; gastrostomy or jejunostomy tube; gut colonisation; previous broad-spectrum antibiotic treatment; travel to endemic areas (eg, eastern or southern Europe; Middle-East, Africa, southeast Asia); and contaminated meat products
Carbapenemase-producing Enterobacteriaceae (eg, *K pneumoniae*)	Carbapenems (eg, imipenem, meropenem, and ertapenem)	Exposure to antibiotic therapy (carbapenems); ≥65 years of age; hospital stay 21 days or longer (in acute care hospitals); and travel and stay in endemic areas[*]
P aeruginosa	Three or more classes of anti-pseudomonal active drugs	Acute myeloid leukaemia; previous antibiotics (quinolones, metronidazole; third-generation cephalosporins, and carbapenems); endogenous source; and water sources (shower etc)
A baumannii	More than two of following five drug classes: cephalosporins (ceftazidime, cefepime, or antipseudomonal); carbapenems (imipenem or meropenem); penicillin (ampicillin–sulbactam); fluoroquinolones (ciprofloxacin or levofloxacin); and aminoglycosides (gentamicin, tobramycin, or amikacin)	Intravascular catheters[*]; trauma or burns[*]; chronic lung disease[*]; and travel and stay in endemic areas[*]

Ruhnke M, Arnold R, Gastmeier P. *Lancet Oncol* 2014; 15: e606–19

Infection control measures for specific pathogens

	MRSA	ESBL (*E coli* and *K pneumoniae*)	VRE
Before admission	Search and destroy strategy for elective admission to hospital	Search and destroy strategy not proven to be effective Screening of patients at high risk from high-prevalence areas or countries before elective admission	Search and destroy strategy not proven effective (enterococcal infections mostly from endogenous infection or colonisation of gastrointestinal tract) Screening patients at high risk from high-prevalence areas or countries before elective admission
After admission	Screening patients at high risk of infection	Screening patients at high risk (swabs from rectum)	Screening patients at high risk (swabs from rectum)
Isolation during hospital stay	Isolation dependent on screening results if MRSA is known from previous hospital stay Single-room isolation preferable if MRSA-positive Otherwise isolation with other MRSA-positive patients	Isolation dependent on patient screening results if ESBL is known from previous hospital stay Single-room isolation preferable, otherwise isolation with other ESBL-positive patients	Isolation dependent on screening results if VRE is known from previous hospital stay Single-room isolation preferable, otherwise isolation with other VRE-positive but not MRSA or ESBL-positive patients if VRE-positive
Hospital stay in shared room	Shared rooms with strict hand hygiene, use of coat and gloves (for non-medical and medical staff) if neither single-room nor cohort isolation is feasible. Labels indicating restrictions to room access for non-medical staff Avoid person-to-person contact with other patients Patients should apply hand disinfectant regularly When leaving the room, the patient should protect infected body regions (eg, wear a mask to protect infected areas of the mouth and nose)	Shared rooms with strict hand hygiene, use of coat and gloves (for non-medical and medical staff) if neither single-room nor no cohort isolation is feasible Labels indicating restrictions to room access for non-medical staff Avoid person-to-person contact with other patients Infected patients should use strict hand hygiene regularly	Shared rooms with strict hand hygiene, use of coat and gloves (for non-medical and medical staff) if neither single-room nor cohort isolation is feasible Labels indicating restrictions to room access for non-medical staff Avoid person-to-person contact with other patients Infected patients should apply strict hand hygiene regularly
Decolonisation	Mupirocin (nasal ointment) Gargling (chlorhexidine) Daily bathing of skin and wounds (chlorhexidine and octenidine)	No effective decolonisation known	No effective decolonisation known
Clearance of colonisation	Three negative results on surveillance series (swabs from known MRSA-positive sites—nose, throat, rectum, and groin) 24 h apart	Three negative results on surveillance series (swabs from known ESBL-positive sites—stool, rectum, and urine) 1 week apart	Three negative results on surveillance series (swabs from known VRE-positive sites—stool, rectum, and urine) 1 week apart
Patient discharge	Information on MRSA colonisation status sent to outpatient facilities	Information on ESBL colonisation status sent to outpatient facilities	Information on VRE colonisation status sent to outpatient facilities

Ruhnke M, Arnold R, Gastmeier P. *Lancet Oncol* 2014; 15: e606–19

Antibiotici

JAMA | Original Investigation

Effect of Piperacillin-Tazobactam vs Meropenem on 30-Day Mortality for Patients With *E coli* or *Klebsiella pneumoniae* Bloodstream Infection and Ceftriaxone Resistance

A Randomized Clinical Trial

JAMA. 2018;320(10):984-994. doi:10.1001/jama.2018.12163

The study will use a **randomised, controlled phase III non-inferiority trial design** comparing two drug regimens (*carbapenem vs. carbapenem-sparing*) for bloodstream infections caused by **third-generation cephalosporin non-susceptible** *E. coli* or Klebsiella spp.

Blinding will not be performed as the two antibiotics have different pharmacokinetics.

Follow-up will be for 30 days post enrollment.

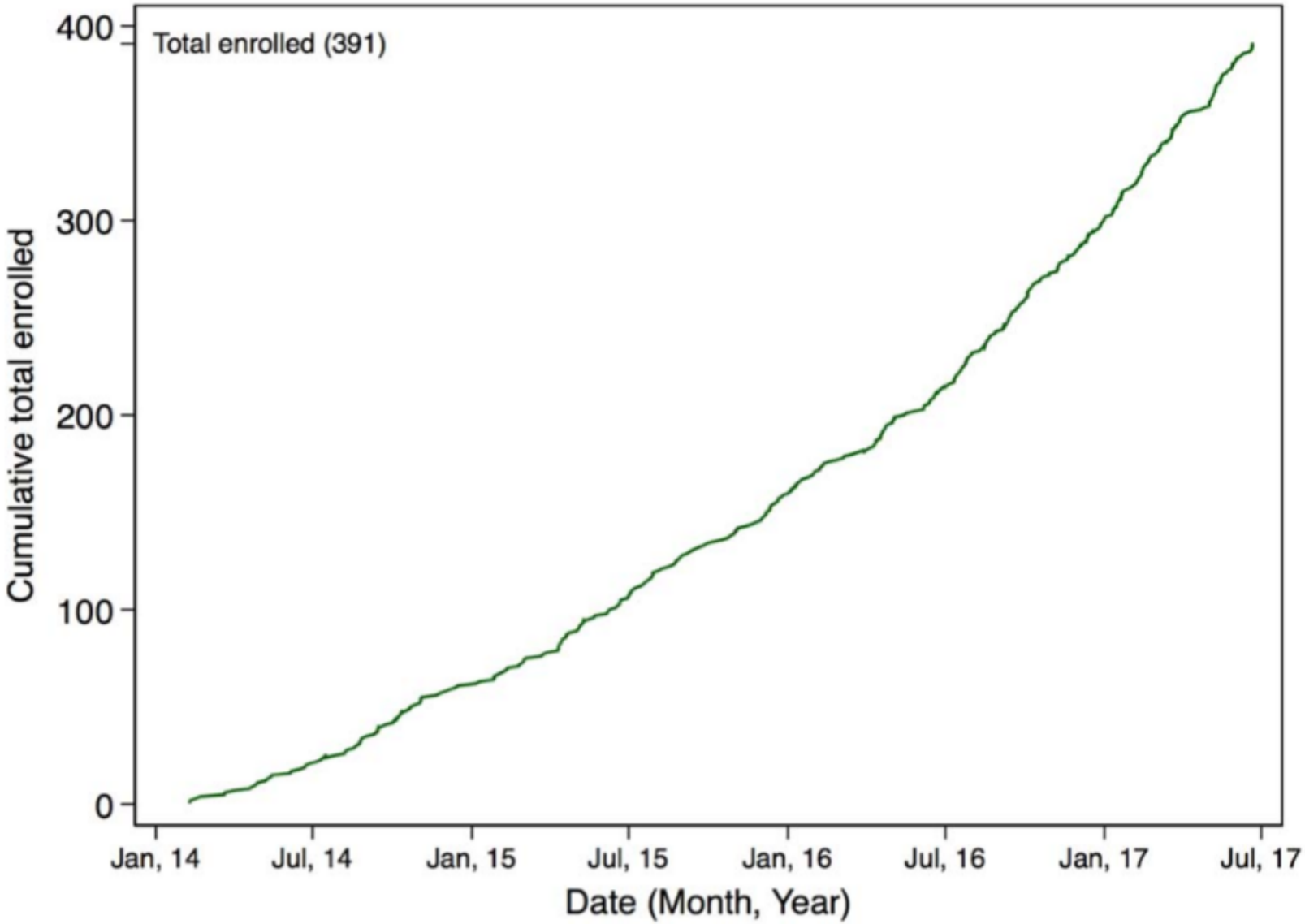
Direct patient contact will be brief and last for 5 days only

Summary of Protocol changes

Date	Summary of changes
8th May 2013	Trial Protocol Finalised
11th Feb 2014	First Patient enrolled (Singapore)
7th April 2014	Addition of Australian recruiting sites, site investigators updated
18th June 2014	Amendments • Age >=18 years as inclusion (for non-Singapore sites where age of majority is 21 years) • Secondary outcome 5 amended to "**Superinfection with a carbapenem or piperacillin-tazobactam resistant organism or *Clostridium difficile*"** *(i.e. addition of piperacillin-tazobactam resistance and C. difficile)* • Data management system changed from OpenClinica to REDCap • Sample size re-calculated (reconsidered by new trial statistician); revised to 454 patients • Addition of details for SAE / "SUSAR" definitions and reporting to align with Australian NHMRC guidelines
21st Sept 2014	Trial protocol submitted for publication BMC Trials (published online 27th Jan 2015)
26th March 2015 (Final protocol version)	• Removal of requirement for daily blood cultures for first 3 days post randomization. ○ Changed to: "*Blood cultures will be drawn on day 3, or on other days up to day 5 if the patient is febrile (temp >38°C) or if previous day blood culture is positive*" • Addition in trial schedule of stipulation to collect daily FBC until white cell count <=12 x10^9/L • Further details provided on the statistical ruling for interim analyses, along with the interval timing of DSMB reviews and clarification of stopping rules (Peto rule)

The study protocol was published in BMC Trials in Jan 2015 and can be accessed here: https://www.ncbi.nlm.nih.gov/pubmed/25623485

Cumulative Enrollment



Primary aim:
30-day mortality will be assessed by clinical record review and direct patient interview/phone consultation, if applicable

Secondary aims:
(**1**) **Time to clinical and microbiologic resolution of infection** – defined as number of days from randomisation to resolution of fever (temperature > 38.0 ◦C) and leucocytosis (white blood cell count >12x10^9/L) **PLUS** sterilisation of blood cultures.
This endpoint is relevant given that it uses highly objective criteria to determine resolution of infection. Given this is an unblinded study, we sought only to use objective criteria rather than other clinically defined criteria, such as “resolution of symptoms and signs of infection”, which may be subjective in interpretation.

(**2**) **Clinical and Microbiologic Success** – defined as survival **PLUS** resolution of fever and leucocytosis **PLUS** sterilisation of blood cultures. All of these criteria will be assessed on day 4, counted from the day of randomisation (day 1) in order to determine a rapid response from the trial drug

- 379 were randomized modified intention to treat (mITT) population (**piperacillin-tazobactam=188, meropenem=191**)
- The majority of patients were enrolled in **Singapore (40.5%),** Australia (22.5%) and Turkey (12.1%)
- BSIs were most frequently **healthcare-associated (56.4%),** of urinary tract origin (60.9%) and caused by *E.coli* (86.5%)
- A total of **23/187** (**12.3%**) patients randomized to piperacillin-tazobactam met the primary outcome of mortality at 30 days, compared with **7/191** (**3.7%**) randomized to meropenem (risk difference 8.6%, 95% CI 3.4% to 14.5%; RR 3.4, 95% CI 1.5 to 7.6; p=0.002)

- There were no significant differences in subsequent infection with carbapenem resistant gram-negative organisms or *C.difficile* between treatment arms

JAMA. 2018;320(10):984-994. doi:10.1001/jama.2018.12163

Kaplan-Meier Failure Estimates for Primary Outcome

@Merino Trial Comment 1: “Most deaths were not due to infection - we all know as clinicians that assigning cause of death is difficult. In our study design we took the view that all-cause mortality was the most appropriate endpoint for our trial. Clearly some will die from non-ID causes.”

@Merino Trial. “We believe that inadequately treated infection (as may have been provided by PTZ), pushed people with significant comorbidities over the edge. While these people may have been destined to die from that underlying comorbidity, their death was hastened by suboptimal BSI Rx..”

Could be, and their believe would be supported by rapid disappearance of the difference at day-60 and day-90

Median observation time for both meropenem (MER) and piperacillin-tazobactam (PTZ) groups = 30 days; includes primary analysis population

JAMA. 2018;320(10):984-994. doi:10.1001/jama.2018.12163

Sample Size Calculation

"Because no randomized clinical trials have previously compared treatment options for ESBL producers causing BSI, the sample size estimation was derived from the largest retrospective study available at the time. ***The overall 30-day mortality in this observational study was 16.7%*** in those receiving a carbapenem (Rodriguez-Bano J CID 2012).

Based on a mortality rate of 14% in the control group (assuming mortality in observational cohorts may be greater than in trials with exclusion criteria) and a non inferiority margin of 5%, 454 patients were needed in total to achieve 80% power with a 1-sided α level of .025, allowing for 10% dropout."

The actual overall 30-day mortality in the Merino Trial was 30/391 (7.7%)!!

- Given the mortality rate in the trial (7.7%), **the 5% non-inferiority margin originally planned for the trial is too high**.

- The **sample size required** to show non-inferiority with the trial's mortality rate and a conservative non-inferiority margin of **2.5% is 2882 patients**.

- The interim analysis, including 13% of the required sample size to show non-inferiority (379 patients with 30 deaths), might have occurred at a time-point where **random overestimate of the truth** might happen.

- In a systematic review comparing trials **stopped early for benefit vs. trials testing the same interventions but completing recruitment**, large differences in treatment effect size (ratio of relative risks <0.75) between terminated vs. completed RCTs **were observed in RCTs that had fewer than 500 events** (Bassler D, JAMA 2010).

- Another systematic review reached a similar conclusion that **trials stopped early for benefit exaggerate effects especially when the number of events is small** (Montori VM, JAMA 2005).

- A review of RCTs performed subsequent to a trial stopped for benefit assessing the same intervention found that **49% truncated RCTs were followed by a subsequent RCT. Only half of the subsequent RCTs confirmed the terminated trial's benefit while the other half found no difference or significance in the opposite direction** (Murad MH, J Clin Epidemiol 2017).

- The bulk of the observational data to date show no difference between empiric or definitive treatment with beta-lactams beta-lactamase inhibitors vs. carbapenems (Muhammed M, Open Forum Infect Dis 2017)

The MERINO trial has important implications for clinicians, clinical microbiologists, and antibiotic stewards.

•The study results provide clear evidence that piperacillin/tazobactam **should not be used for definitive treatment of blood stream infections due to ceftriaxone-resistant *E coli* or *K pneumoniae***, regardless of the patient population, source of infection, bacterial species, or response to initial empirical piperacillin-tazobactam therapy.

•In addition, the study suggests that reporting of piperacillin-tazobactam susceptibility for ceftriaxone-resistant *E coli* and *K pneumoniae* should include a caveat against its use in bacteremias

Mary K.Hayden and Sarah Y. Won (*Rush University Medical Center, Chicago, Illinois*)
JAMA, 2018;320,(10): 979-81

How, then, can the use of carbapenems be decreased?

- First, as noted by the authors, the study results **should not be extrapolated to newer BLBLIs**, which require specific investigation of efficacy in randomized clinical trials.

- Second, studies of short-duration antibiotic treatment and non carbapenem options for empirical and step-down therapy are needed to identify safe and effective regimens that limit carbapenem exposure. (Chotiprasitsakul, CID 2018). New tools may soon be available, such as electronic decision support for antibiotic selection that calculates the estimated likelihood of antibiotic-resistant bacterial infection for each patient at the time of hospital admission.(Harvard Pilgrim Healthcare Institute. INSPIRE 2018)

- Third, prevention of infection should be emphasized so as to reduce the need for antibiotic treatment altogether.

Mary K.Hayden and Sarah Y. Won (*Rush University Medical Center, Chicago, Illinois*)
JAMA, 2018;320,(10): 979-81

Ceftazidime/Avibactam

Zavicefta®

Classificazione del medicinale per uso umano «Zavicefta» ai sensi dell'art. 8, comma 10, della legge 24 dicembre 1993, n. 537. (Determina n. 10/2018). (18A00325) (GU Serie Generale n.16 del 20-01-2018)

«Zavicefta» e' indicato per il trattamento delle seguenti infezioni negli adulti:

- infezione intra-addominale complicata (cIAI);
- infezione complicata del tratto urinario (cUTI), inclusa pielonefrite;
- polmonite acquisita in ospedale (HAP), inclusa polmonite associata a ventilazione meccanica (VAP)
- e' inoltre indicato per il trattamento di infezioni causate da microrganismi Gram-negativi aerobi in pazienti adulti nei quali vi siano opzioni terapeutiche limitate

Si devono considerare le linee-guida ufficiali sull'uso appropriato degli agenti antibatterici

Ambler Class	Active Site	β-lactamases	Examples of enzymes	Typical Producers	Effective inhibitors	Substrate
A	Serine	Pencillinases	TEM, SHV, CTX-M	*Enterobacteriaceae*	Clavulanate, tazobactam, sulbactam,	Pencillins, cephalosporins
A	Serine	Carbapenemases	KPC, GES	*Enterobacteriaceae*	Vaborbactam, avibactam, relebactam	β-lactams
B	Metal ions (usually Zinc)	Metallo-β-lactamases	NDM, VIM, IMP, L1	*S. maltophilia, A. baumannii, Enterobacteriaceae, Pseudomonas* spp.		β-lactams except aztreonam
C	Serine	Cephalosporinases	AmpC, CMY	SPICE organisms*, *Pseudomonas* spp., *A. baumannii*	Vaborbactam, avibactam, relebactam	Cephalosporins, penicillins
D	Serine	Oxacillinases	OXA	*Enterobacteriaceae, A. baumannii*	Avibactam, relebactam (variable inhibition)	β-lactams to varying degrees

* *Serratia*, *Providencia*, "Indole-positive" *Proteus* species, *Citrobacter*, and *Enterobacter* species.

Type	Ambler Molecular Class	Characteristics	Examples of Enzymes
Narrow-spectrum β-lactamases[12,18,19]	A	Hydrolyze penicillin; produced primarily by *Enterobacteriaceae*	Staphylococcal penicillinase, TEM-1, TEM-2, SHV-1
Extended-spectrum β-lactamases[20]	A	Hydrolyze narrow and extended-spectrum β-lactam antibiotics	SHV-2, CTX-M-15, PER-1, VEB-1
Serine carbapenemases[20]	A	Hydrolyze carbapenems	KPC-1, IMI-1, SME-1
Metallo-β-lactamases[21,22]	B	Hydrolyze carbapenems	VIM-1, IMP-1, NDM-1
Cephalosporinases[10,23,24]	C	Hydrolyze cephamycins and some oxyimino β-lactams; inducible; chromosomally mediated	AmpC, P99, ACT-1, CMY-2, FOX-1, MIR-1
OXA-type enzymes[25-27]	D	Hydrolyze oxacillin, oxyimino β-lactams, and carbapenems; produced by *Pseudomonas aeruginosa* and *Acinetobacter baumannii*	OXA enzymes

Studi registrativi

Clinical Infectious Diseases

MAJOR ARTICLE

Ceftazidime-avibactam Versus Doripenem for the Treatment of Complicated Urinary Tract Infections, Including Acute Pyelonephritis: RECAPTURE, a Phase 3 Randomized Trial Program

Florian M. Wagenlehner,[1] Jack D. Sobel,[2] Paul Newell,[3] Jon Armstrong,[3] Xiangning Huang,[4] Gregory G. Stone,[5] Katrina Yates,[3,a] and Leanne

RECLAIM

Clinical Infectious Diseases

MAJOR ARTICLE

Efficacy and Safety of Ceftazidime-Avibactam Plus Metronidazole Versus Meropenem in the Treatment of Complicated Intra-abdominal Infection: Results From a Randomized, Controlled, Double-Blind, Phase 3 Program

John E. Mazuski,[1] Leanne B. Gasink,[2] Jon Armstrong,[5] Helen Broadhurst,[5] Greg G. Stone,[3] Douglas Rank,[4] Lily Llorens,[4] Paul Newell,[5] and Jan Pachl[6]

Ceftazidime-avibactam or best available therapy in patients with ceftazidime-resistant Enterobacteriaceae and *Pseudomonas aeruginosa* complicated urinary tract infections or complicated intra-abdominal infections (REPRISE): a randomised, pathogen-directed, phase 3 study

Yehuda Carmeli, Jon Armstrong, Peter J Laud, Paul Newell, Greg Stone, Angela Wardman, Leanne B Gasink

Ceftazidime-avibactam versus meropenem in nosocomial pneumonia, including ventilator-associated pneumonia (REPROVE): a randomised, double-blind, phase 3 non-inferiority trial

Antoni Torres, Nanshan Zhong, Jan Pachl, Jean-François Timsit, Marin Kollef, Zhangjing Chen, Jie Song, Dianna Taylor, Peter J Laud, Gregory G Stone, Joseph W Chow

Lancet Infect Dis 2018; 18: 285–95

Findings: Between April 13, 2013, and Dec 11, 2015, 879 patients were randomly assigned. 808 patients were included in the safety population, 726 were included in the clinically modified intention-to-treat population, and 527 were included in the clinically evaluable population. Predominant Gram-negative baseline pathogens in the microbiologically modified intention-to-treat population (n=355) were *Klebsiella pneumoniae* (37%) and *Pseudomonas Aeruginosa* (30%); 28% were ceftazidime-non-susceptible.

In the clinically modified intention-to-treat population, 245 (**68·8%)** of 356 patients in the ***ceftazidime-avibactam*** group were clinically cured, compared with 270 (**73·0%)** of 370 patients in the ***meropenem*** group (difference –4·2% [95% CI –10·8 to 2·5]).

In the clinically evaluable population, 199 (**77·4%**) of 257 participants were clinically cured in the ***ceftazidime-avibactam*** group, compared with 211 (**78·1%**) of 270 in the ***meropenem*** group (difference –0·7% [95% CI –7·9 to 6·4]).

Adverse events occurred in 302 (75%) of 405 patients in the ceftazidime-avibactam group versus 299 (74%) of 403 in the meropenem group (safety population), and were mostly mild or moderate in intensity and unrelated to study treatment.

Serious adverse events occurred in 75 (**19%**) patients in the ***ceftazidime-avibactam*** group and 54 (**13%**) patients in the ***meropenem*** group. Four serious adverse events (all in the ceftazidime-avibactam group) were judged to be treatment related.

Ceftazidime-avibactam was non-inferior to meropenem in the treatment of nosocomial pneumonia. These results support a role for ceftazidime-avibactam as a potential alternative to carbapenems in patients with nosocomial pneumonia (including ventilator-associated pneumonia) caused by Gram-negative pathogens.

Lancet Infect Dis 2018; 18: 285–95

E riguardo le CRE..?

Clinical Infectious Diseases

MAJOR ARTICLE

Colistin Versus Ceftazidime-Avibactam in the Treatment of Infections Due to Carbapenem-Resistant Enterobacteriaceae

David van Duin,[1] Judith J. Lok,[2] Michelle Earley,[2] Eric Cober,[3] Sandra S. Richter,[4] Federico Perez,[5,6] Robert A. Salata,[6] Robert C. Kalayjian,[7] Richard R. Watkins,[8,9] Yohei Doi,[10] Keith S. Kaye,[11] Vance G. Fowler Jr,[12,13] David L. Paterson,[14] Robert A. Bonomo,[5,6,15,16] and Scott Evans[2]; for the Antibacterial Resistance Leadership Group

Clinical Infectious Diseases

BRIEF REPORT

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

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

Clinical Outcomes, Drug Toxicity, and Emergence of Ceftazidime-Avibactam Resistance Among Patients Treated for Carbapenem-Resistant Enterobacteriaceae Infections

Ryan K. Shields,[1,3,4,a] Brian A. Potoski,[1,2,3,a] Ghady Haidar,[1] Binghua Hao,[4] Yohei Doi,[1] Liang Chen,[6] Ellen G. Press,[1] Barry N. Kreiswirth,[6] Cornelius J. Clancy,[1,4,5] and M. Hong Nguyen[1,3,4]

Clinical efficacy of ceftazidime/avibactam versus other active agents for the treatment of bacteremia due to carbapenemase-producing Enterobacteriaceae in hematologic patients

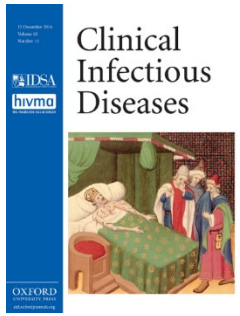
Juan J. Castón[a], Isabel Lacort-Peralta[b], Pilar Martín-Dávila[c], Belén Loeches[d], Salvador Tabares[e], Liz Temkin[f], Julián Torre-Cisneros[a,*], José R. Paño-Pardo[d,g]

Clinical Outcomes, Drug Toxicity, and Emergence of Ceftazidime-Avibactam Resistance Among Patients Treated for Carbapenem-Resistant Enterobacteriaceae Infections

Ryan K. Shields,[1,3,4,a] Brian A. Potoski,[1,2,3,a] Ghady Haidar,[1] Binghua Hao,[4] Yohei Doi,[1] Liang Chen,[6] Ellen G. Press,[1] Barry N. Kreiswirth,[6] Cornelius J. Clancy,[1,4,5] and M. Hong Nguyen[1,3,4]

[1]Department of Medicine, [2]Department of Pharmacy and Therapeutics, University of Pittsburgh, [3]Antibiotic Management Program, [4]XDR Pathogen Laboratory, University of Pittsburgh Medical Center, and [5]VA Pittsburgh Healthcare System, Pennsylvania; and [6]Public Health Research Institute Tuberculosis Center, New Jersey Medical School, Rutgers University, Newark

Thirty-seven carbapenem-resistant Enterobacteriaceae (CRE) infected patients were treated with ceftazidime-avibactam. Clinical success and survival rates at 30 days were 59% (22/37) and 76% (28/37), respectively. In 23% (5/22) of clinical successes, CRE infections recurred within 90 days. Microbiologic failure rate was 27% (10/37). Ceftazidime-avibactam resistance was detected in 30% (3/10) of microbiologic failures.



Clinical Infectious Diseases 2016;63(12):1615–8

Clinical Infectious Diseases

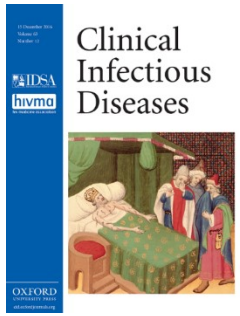
EDITORIAL COMMENTARY

Ceftazidime-Avibactam and Carbapenem-Resistant Enterobacteriaceae: "We're Gonna Need a Bigger Boat"

Brad Spellberg[1,2] and Robert A. Bonomo[3]

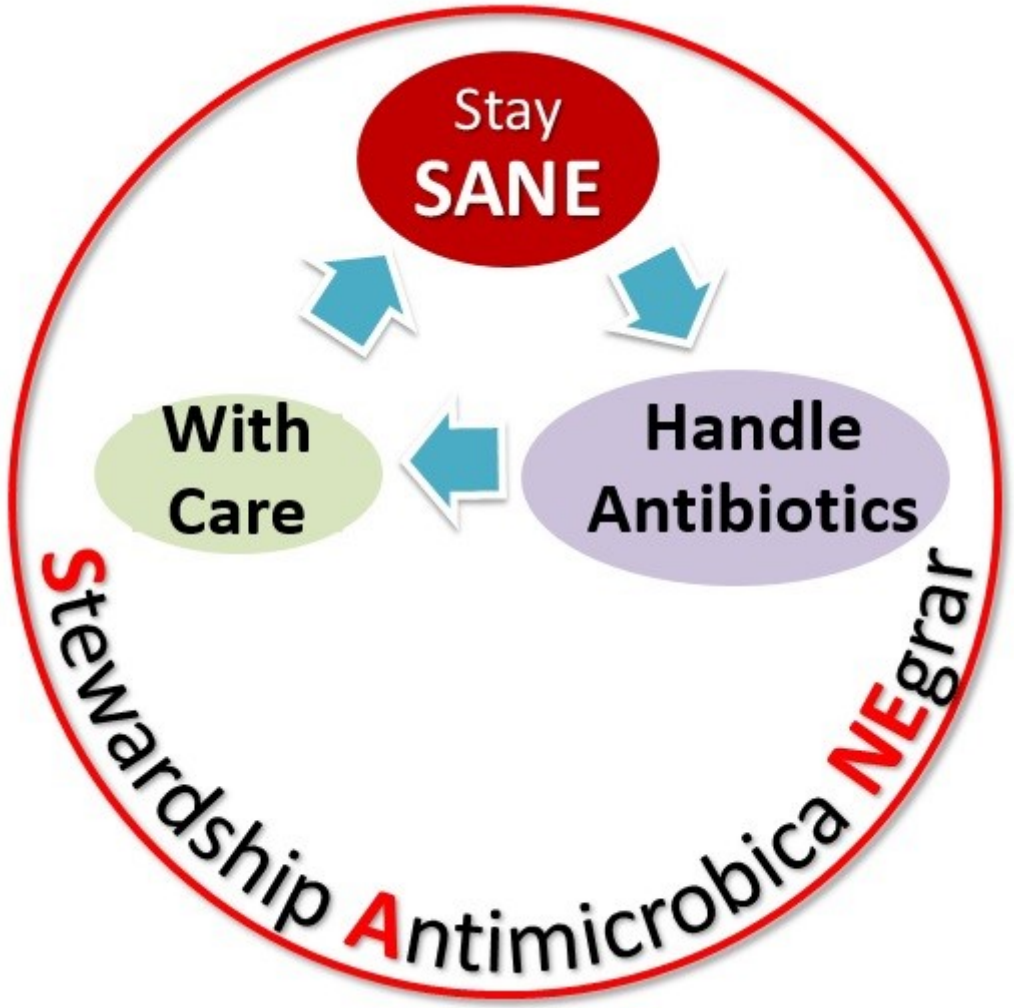
[1]Los Angeles County-University of Southern California Medical Center, and [2]Division of Infectious Diseases, University of Southern California Keck School of Medicine, Los Angeles; and [3]Departments of Medicine, Pharmacology, and Molecular Biology and Microbiology, Louis Stokes Cleveland Department of Veterans Affairs Medical Center, Case Western Reserve University, Ohio

It is important not to draw firm conclusions from an uncontrolled, retrospective case series. Nevertheless, this is a very important study, as it is the first meaningful clinical evaluation of the efficacy of ceftazidime-avibactam when treating CRE infections, and among a fairly large number of patients with CRE. The results are quite concerning. Mortality continues to be high, and resistance seems to emerge rapidly



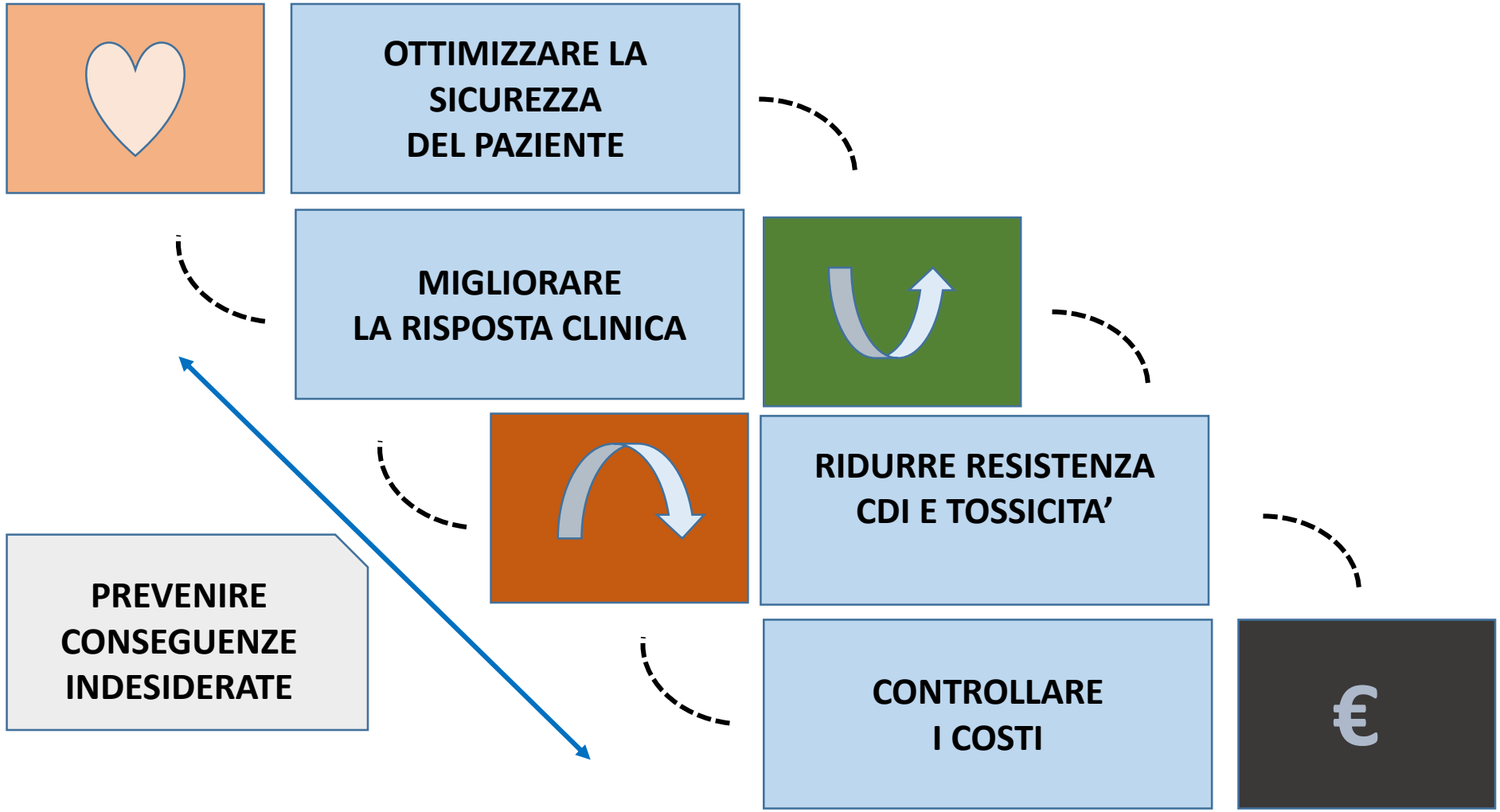
Clinical Infectious Diseases
2016;63(12):1619–21

In conclusione


Stay
SANE
Handle
Antibiotics
With
Care
Stewardship Antimicrobica NEgrar

SANE

SANE: Gli obbiettivi



Il Team

2 FTE

- **Infettivologo**
- **Microbiologo**
- **Farmacista**
- **Informatico**
- **Direzione Sanitaria**

Grazie