10.20 Antibiotico-resistenza in Italia: i problemi di oggi e le soluzioni per il domani
Carlo Tascini, Azienda Ospedaliera dei Colli Napoli

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XI CONGRESSO
NAZIONALE ANIPIO

Roma, 18-19 ottobre 2019

Il sottoscritto Carlo Tascini
ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg. Applicativo dell'Accordo Stato-Regione del 5 novembre 2009,

dichiara

che negli ultimi due anni ha avuto rapporti diretti di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

- *Merck*
- *Pfizer*
- *Astellas*
- *Angelini*
- *Gilead*
- *Novartis.*
- *Thermofischer*
- *Biotest*
- *Zambon*
- *Biomerieux*

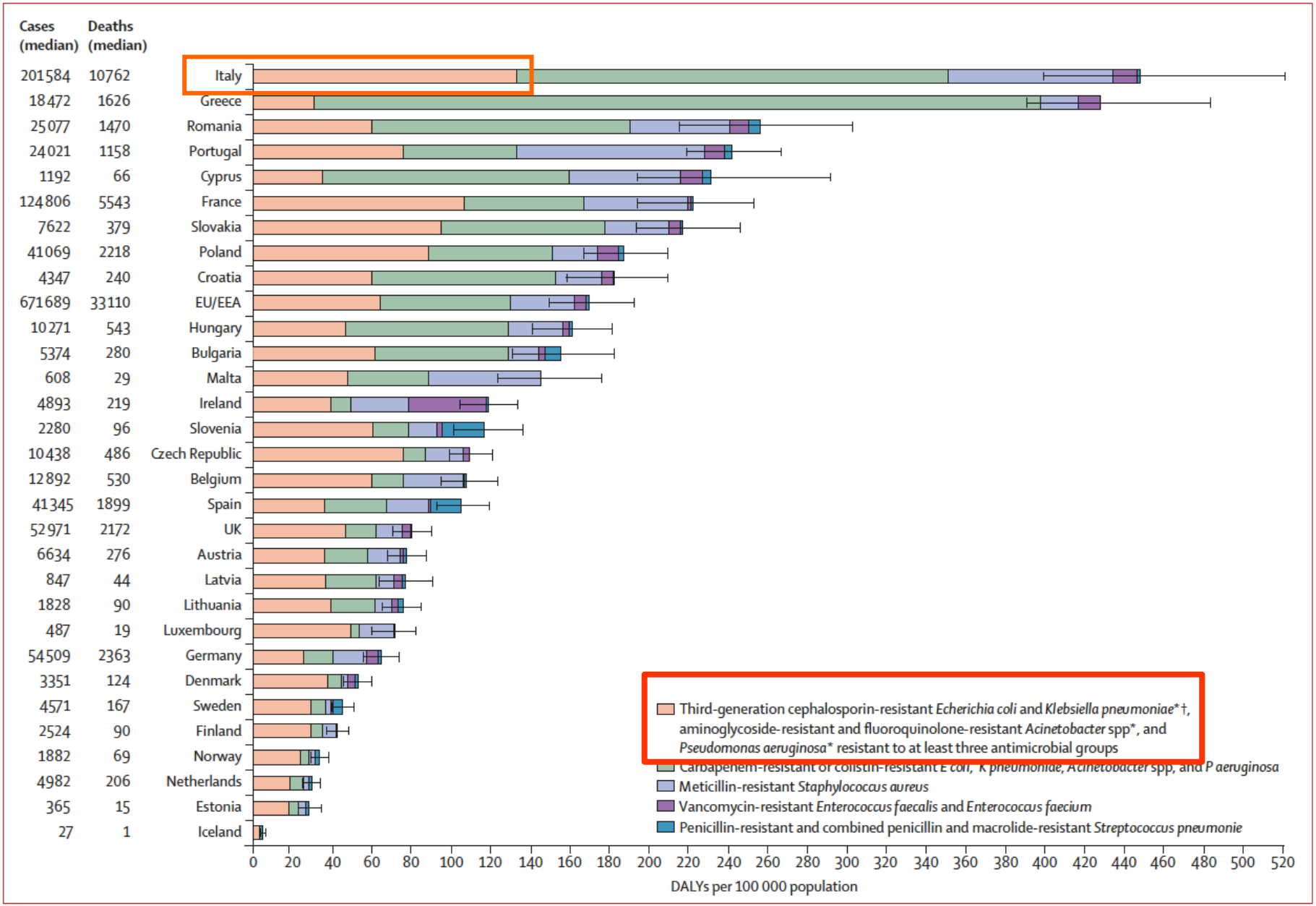


Figure 3: **Burden of infections with antibiotic-resistant bacteria in DALYs, EU and European Economic Area, 2015**

Error bars are 95% uncertainty intervals. Greece did not report data on *S pneumoniae* isolates to the European Antimicrobial Resistance Surveillance Network in 2015. DALY rates are age-standardised to limit the effect of demographic differences across countries; numbers of cases and deaths are not age-standardised. DALYs=disability-adjusted life-years. *Excludes those resistant to carbapenem or colistin. †In 2015, most of the third-generation cephalosporin-resistant *E coli* (88·6%) and *K pneumoniae* (85·3%) isolates reported to the European Antimicrobial Resistance Surveillance Network produced an extended-spectrum β-lactamase.[9]

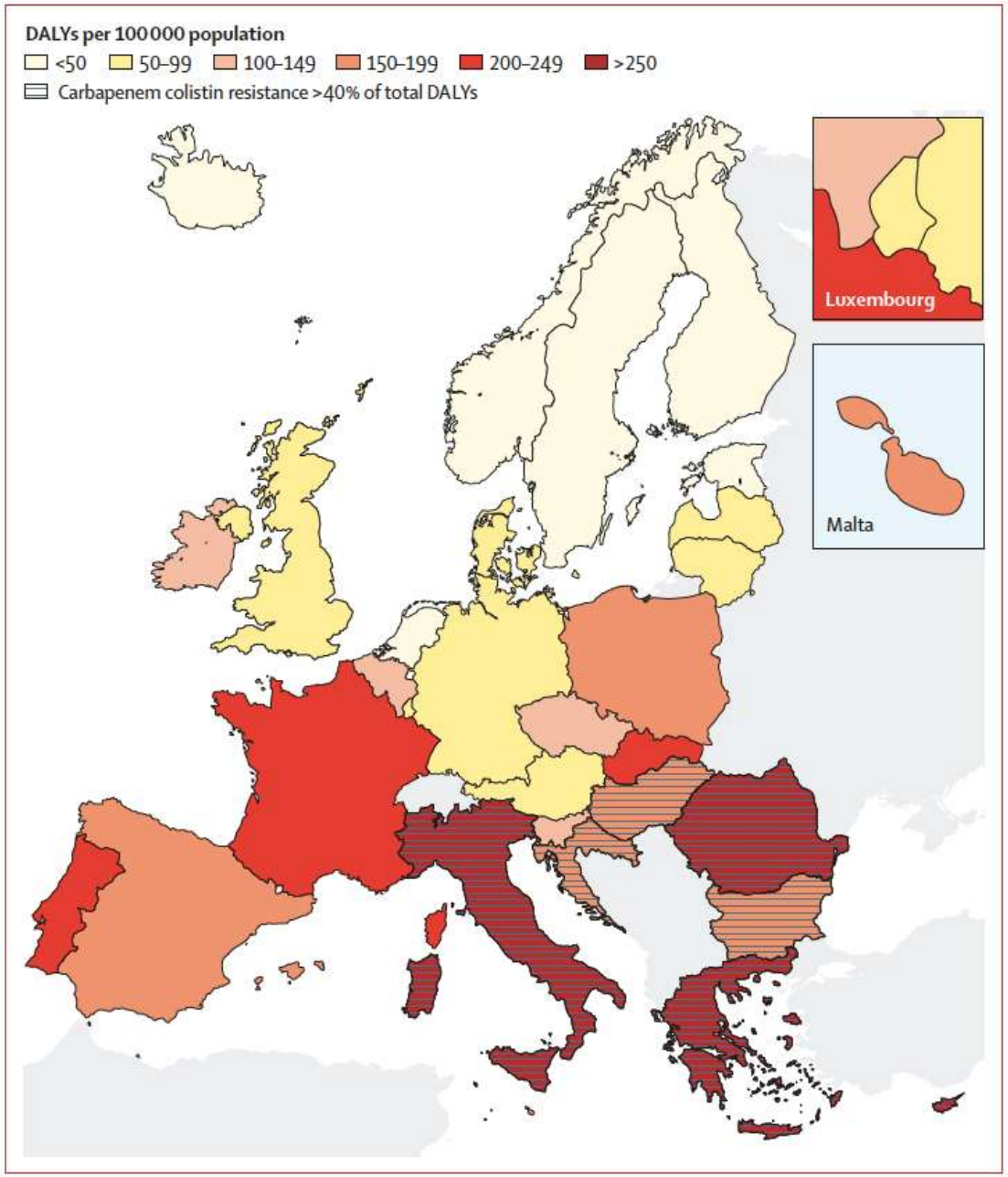


Figure 4: **Model estimates of the burden of infections with selected antibiotic-resistant bacteria of public health importance in DALYs per 100 000 population, EU and European Economic Area, 2015**
Greece did not report data on *S pneumoniae* isolates to the European Antimicrobial Resistance Surveillance Network in 2015. DALYs=disability-adjusted life-years.

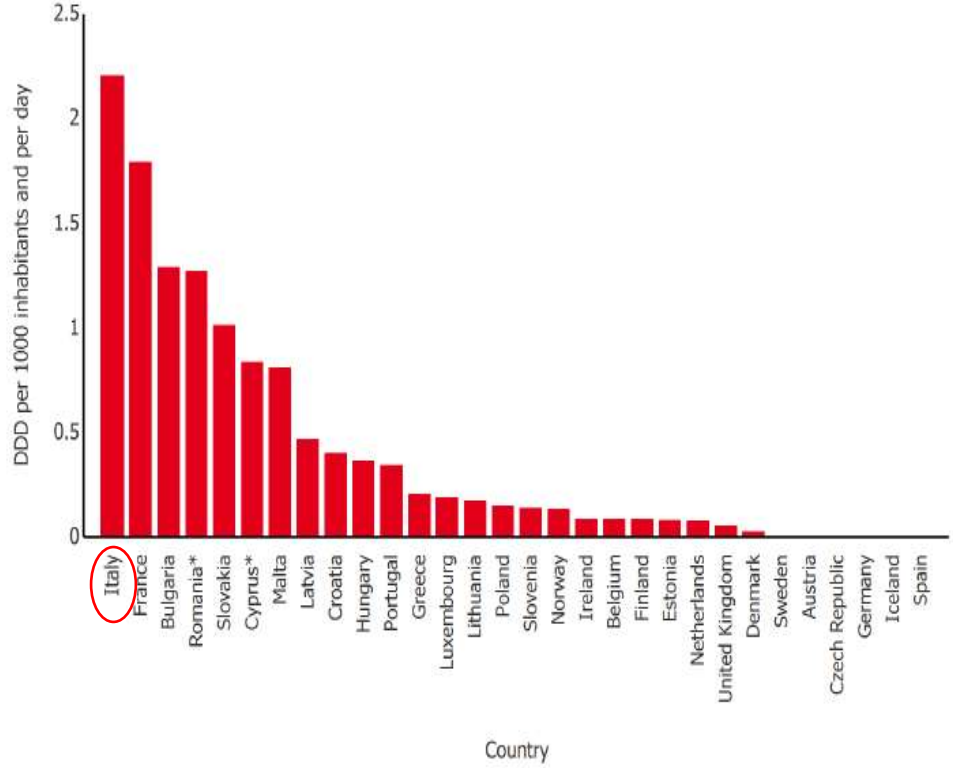
Morti per ESBL

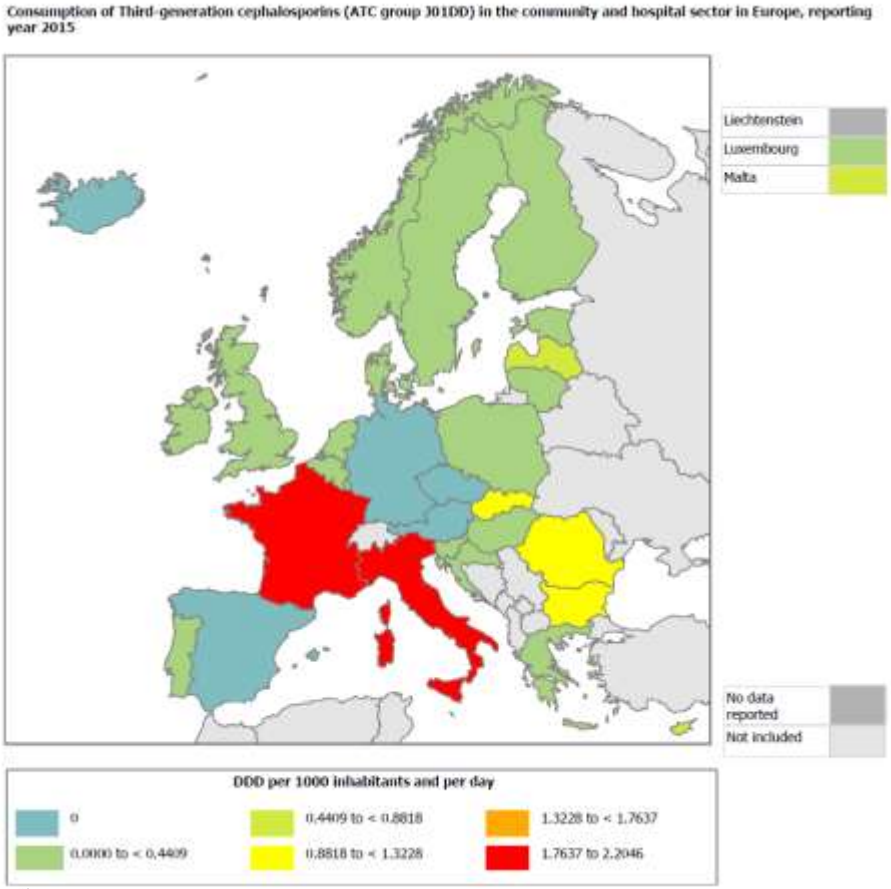
- Ma siamo sicuri di questo dato
- Vi risulta dalla vostra esperienza personale
- Non sarà ora di misurare le sepsi da ESBL e CPE a livello nazionale?

Consumption of Third-generation cephalosporins (ATC group J01DD) in the community and hospital sector in Europe, reporting year 2015

*No data are shown for those countries only reporting data for the community

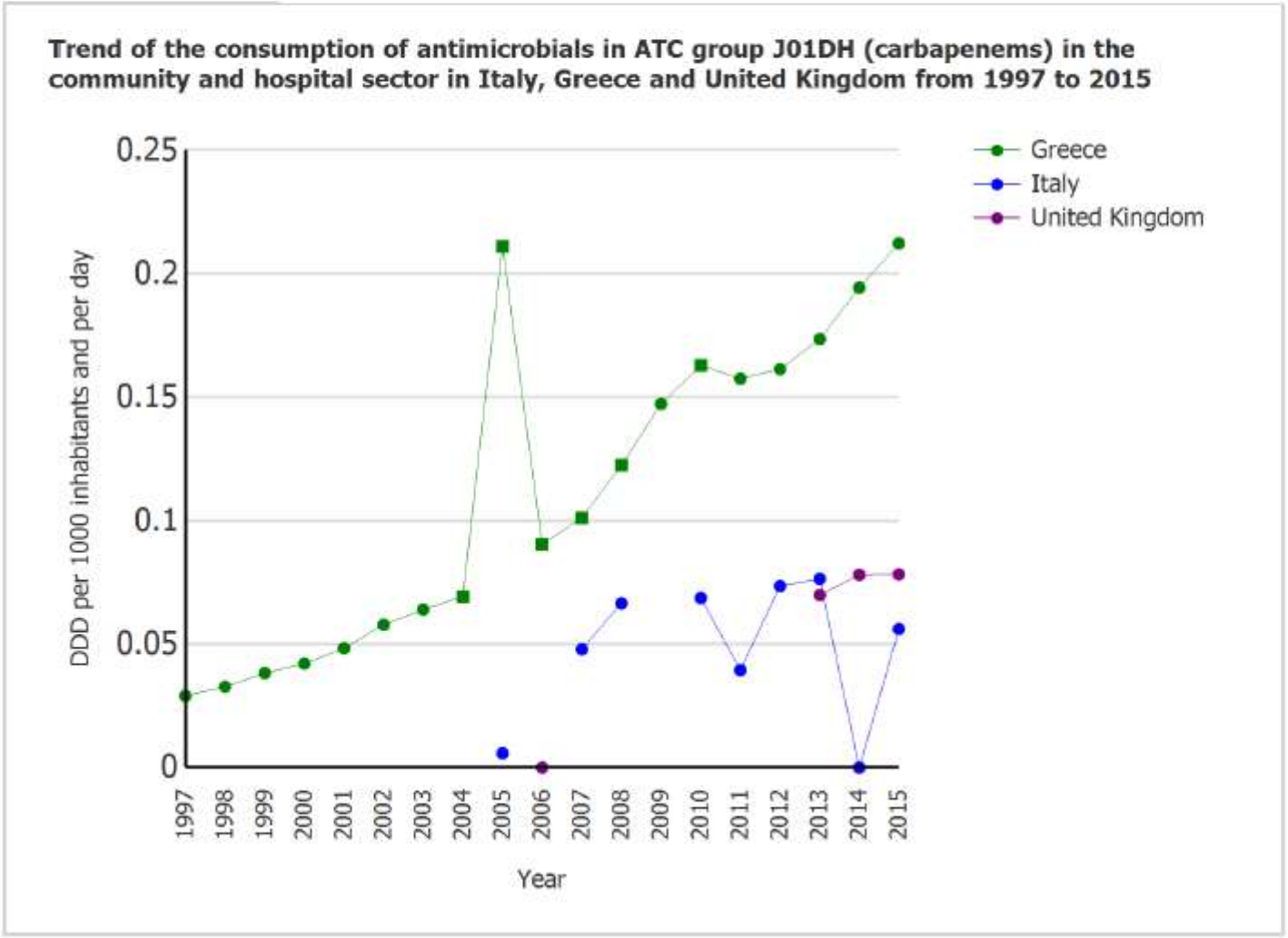
* Country provided only total care data.





* Country provided only total care data.

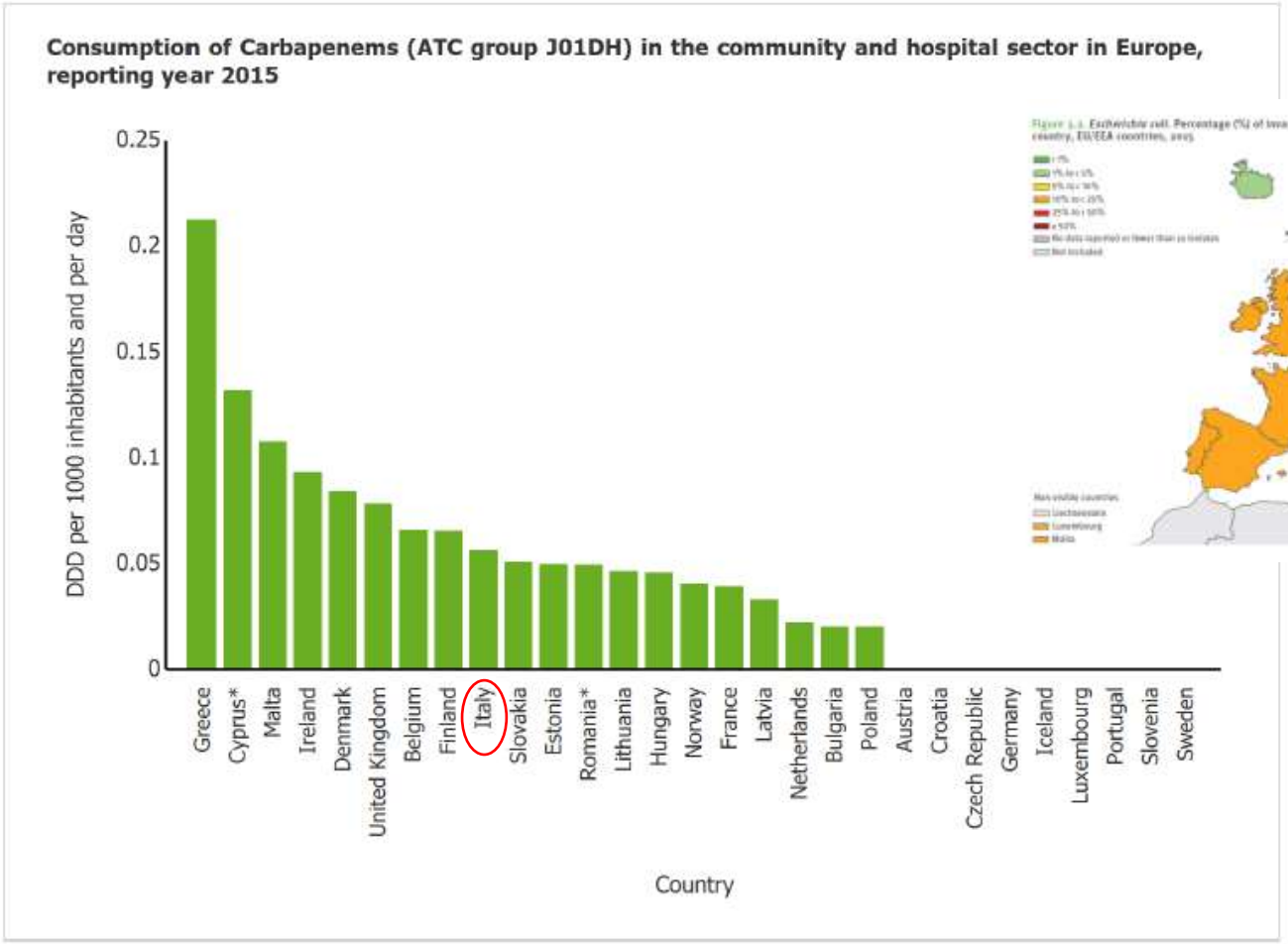
Trend of the consumption of Carbapenems (ATC group J01DH) in the community and hospital sector in Italy, Greece and United Kingdom from 1997 to 2015



Consumption of Carbapenems (ATC group J01DH) in the community and hospital sector in Europe, reporting year 2015

*No data are shown for those countries only reporting data for the community

* Country provided only total care data.



* Country provided only total care data.

Clinical Infectious Diseases

MAJOR ARTICLE

Increased Relative Abundance of *Klebsiella pneumoniae* Carbapenemase-producing *Klebsiella pneumoniae* Within the Gut Microbiota Is Associated With Risk of Bloodstream Infection in Long-term Acute Care Hospital Patients

Teppei Shimasaki,[1,a] Anna Seekatz,[2] Christine Bassis,[2] Yoona Rhee,[1] Rachel D. Yelin,[1] Louis Fogg,[3] Thelma Dangana,[1] Enrique Cornejo Cisneros,[1,4] Robert A. Weinstein[1], Koh Okamoto,[1,5] Karen Lolans,[1] Michael Schoeny,[3] Michael Y. Lin,[1] Nicholas M. Moore,[1] Vincent B. Young,[2] and Mary K. Hayden[1]; for the Centers for Disease Control and Prevention Epicenters Program

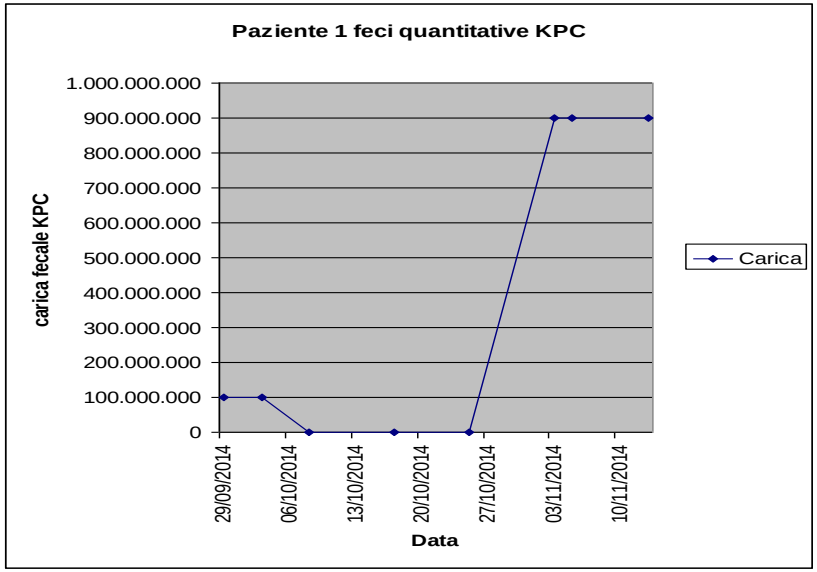
[1]Department of Internal Medicine, Division of Infectious Diseases, Rush University Medical Center, Chicago, Illinois; [2]Department of Internal Medicine, Division of Infectious Diseases, University of Michigan Medical School, Ann Arbor; [3]Department of Nursing, Rush University Medical Center, Chicago, Illinois; [4]Hospital Nacional Cayetano Heredia, Lima, Peru; and [5]University of Tokyo Hospital, Japan

Table 3. Risk Factors Associated With ≥22% Relative Abundance of *Klebsiella pneumoniae* Carbapenemase-producing *Klebsiella pneumoniae* in the Gut Microbiota

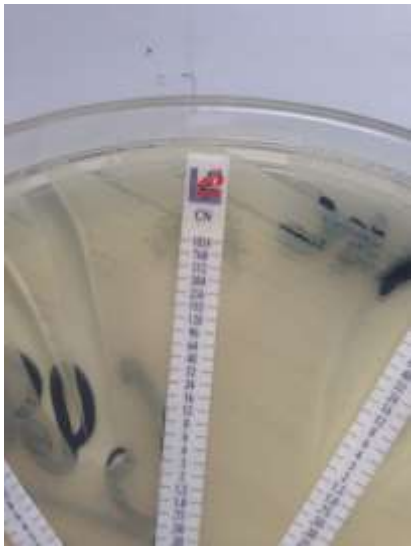
Clinical Predictor	Hazard Ratio (95% Confidence Interval)	*P* Value
Age, years	0.99 (0.97–1.02)	.549
Charlson comorbidity index	0.90 (0.74–1.09)	.277
Any medical device use	1.05 (0.25–4.48)	.943
Mechanical ventilation	0.82 (0.39–1.71)	.588
Gastrostomy tube	0.62 (0.30–1.29)	.204
Central line	1.17 (0.55–25)	.689
Hemodialysis	0.77 (0.23–2.54)	.666
Urinary catheter	0.73 (0.34–1.55)	.409
Any antibiotic exposure	0.70 (0.24–2.07)	.519
Carbapenem	2.19 (1.06–4.55)	.036
Beta-lactam/beta-lactamase inhibitor	0.66 (0.23–1.90)	.436
Vancomycin (intravenous)	0.79 (0.38–1.66)	.537
Metronidazole	0.50 (0.12–2.12)	.351

KPC outbreak pediatric haematologic unit Pisa

- 27/9/2014: 17 year-old girl with LLA (a diseases treatable with SCT)
- Whole body radiation, induction chemotherapy for SCT
- During neutropenia; fever and severe sepsis
- Admission to ICU
- 29/9/2014: KPC septic shock: death
- In the pediatric ward other 4 cases were identified: isolation procedure and oral gentamicin four times a day to decontaminate the gut

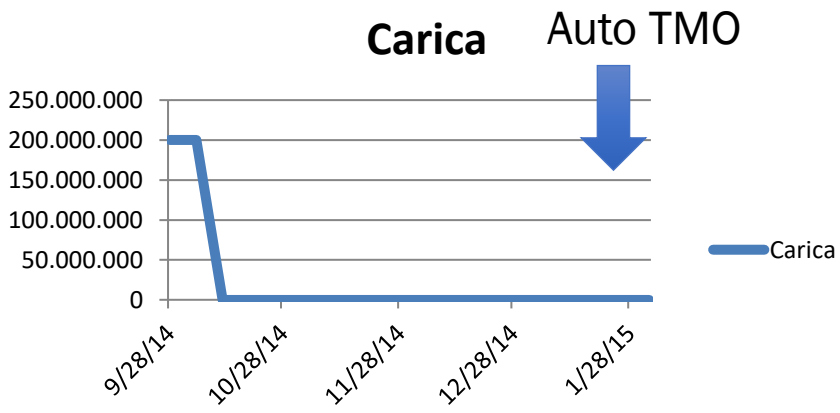


Ceppo Genta R dalle feci

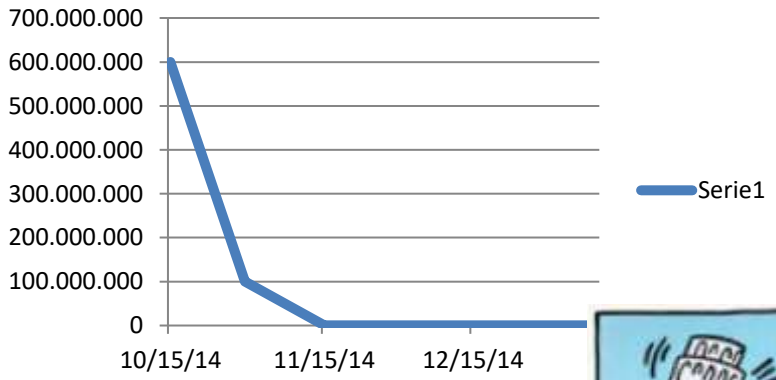


Ceppo genta S dal sangue trattata con successo

Paziente 2 con LLA, sottoposto a TMO con feci negative anche alla PCR



Paziente 3 LLA feci negative anche alla PCR



AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy

mcr-1.2, a New *mcr* Variant Carried on a Transferable Plasmid from a Colistin-Resistant KPC Carbapenemase-Producing *Klebsiella pneumoniae* Strain of Sequence Type 512

Vincenzo Di Pilato,[a] Fabio Arena,[b] Carlo Tascini,[c] Antonio Cannatelli,[b] Lucia Henrici De Angelis,[b] Simona Fortunato,[c] Tommaso Giani,[b] Francesco Menichetti,[c] Gian Maria Rossolini[b,d,e,f]

Clin Microbiol Infect 2012; 18: 941–945

REVIEW 10.1111/j.1469-0691.2012.03956.x

Bed occupancy rates and hospital-acquired infections—should beds be kept empty?

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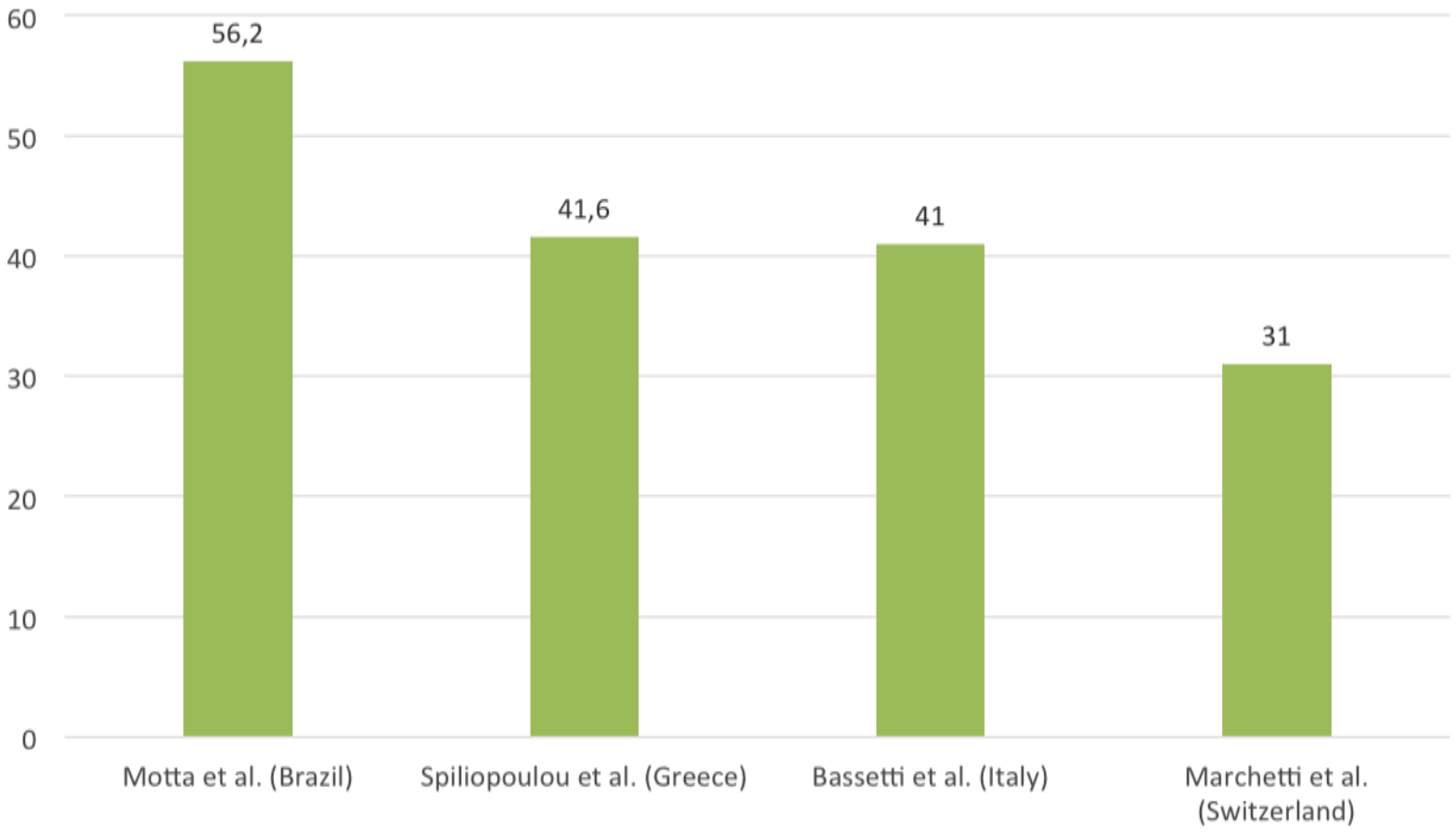
Abstract

There is growing evidence that bed occupancy (BO) rates, overcrowding and understaffing influence the spread of hospital-acquired infections (HAIs). In this article, a systematic review of the literature is presented, summarizing the evidence on the adverse effects of high BO rates and overcrowding in hospitals on the incidence of HAIs. A Pubmed database search identified 179 references, of which 44 were considered to be potentially relevant for full-text review. The majority (62.9%) focused on methicillin-resistant *Staphylococcus aureus*-associated infection or colonization. Only 12 studies were found that provided a statistical analysis of the impact of BO on HAI rates. The median BO rate of the analysed studies was 81.2%. The majority of studies (75%) indicated that BO rates and understaffing directly influence the incidence of HAIs. Only three studies showed no significant association between BO rates and the incidence of HAIs. Interestingly, only one of the included studies detected a seasonal trend in the BO rate. The present review shows an association between BO rates and the spread of HAIs in various settings. Because the evidence on this topic is limited, we conclude that further research is needed in order to analyse the rationale of a threshold BO rate, because keeping beds empty is comparatively costly.

Candidemia: Proportion of Patients in Medicine Departments



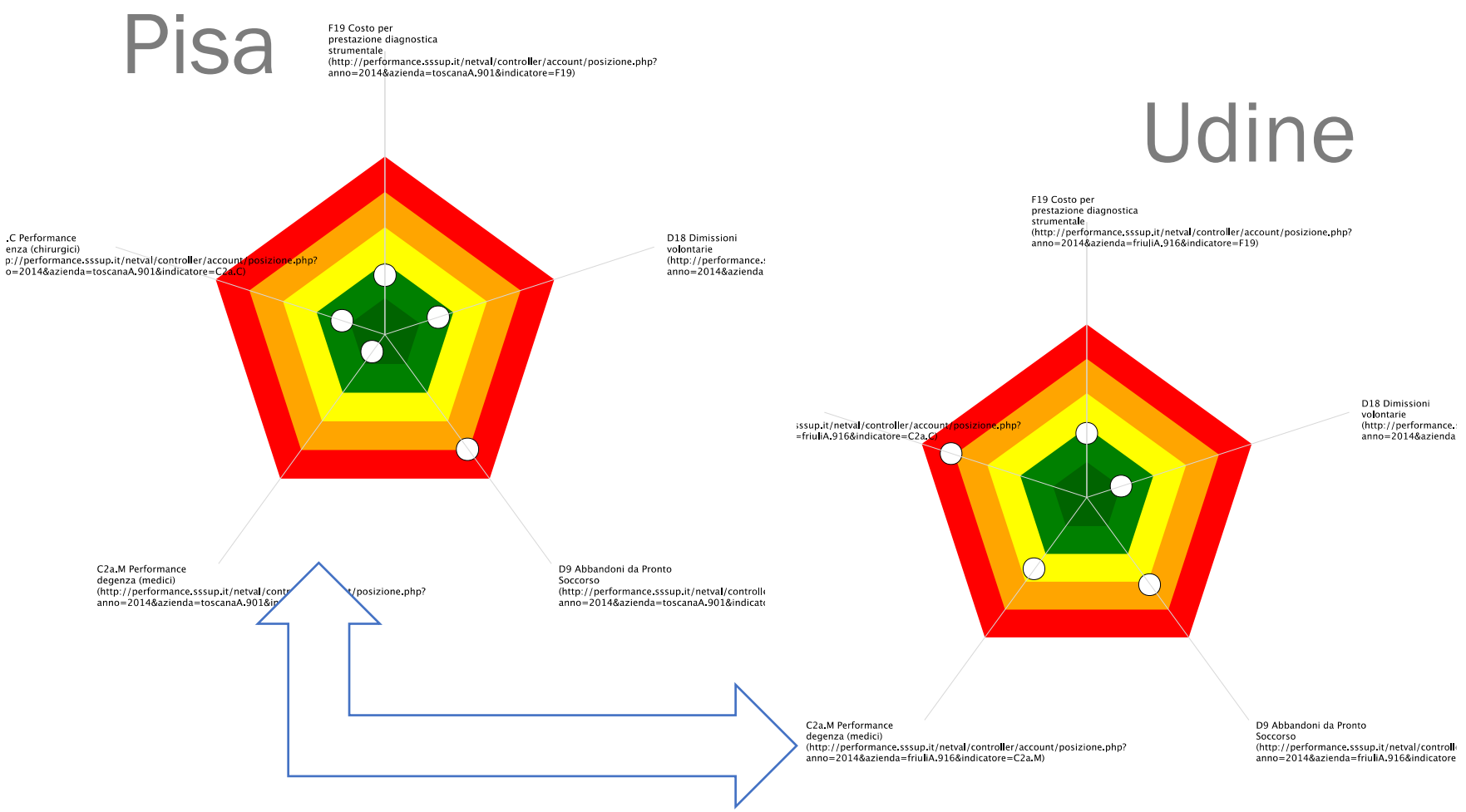
Braz J Infect Dis 2010;14:441-448; Clin Microbiol Infect 2010; 16: 1378–1381; PLoS One. 2011;6(9):e24198; Clin Infect Dis 2004;38:311-20

Candidemie Pisa/Udine/Firenze

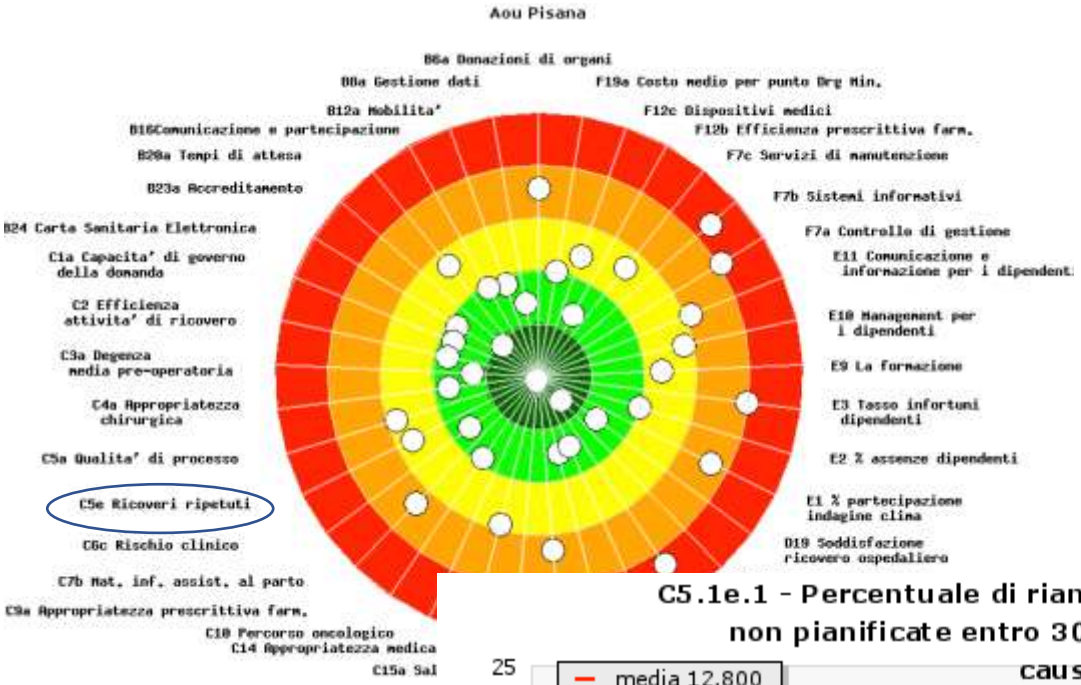
Ward	Mean length of stay (Days) PISA	Rate/ 10000 days admission PISA	Mean length of stay (Days) UDINE	Rate/ 10000 days admissio n UDINE	Mean length of stay (Days) FIRENZE	Rate/ 10000 days admission FIRENZE
All Hospital patients	5,95	3,59	9,76	1,44	6,86	3,70
General + Specialized Medicine	6,29	4,37	12,72	0,95	4,67	11,70
ICU	5,7	9,95	18,3	2,16	6,08	1,13
Surgery	4,05	2,48	9,76	4,7	5,71	5,71
Internal medicine alone	5	10,38	8,7	1,04	6,15	2,60

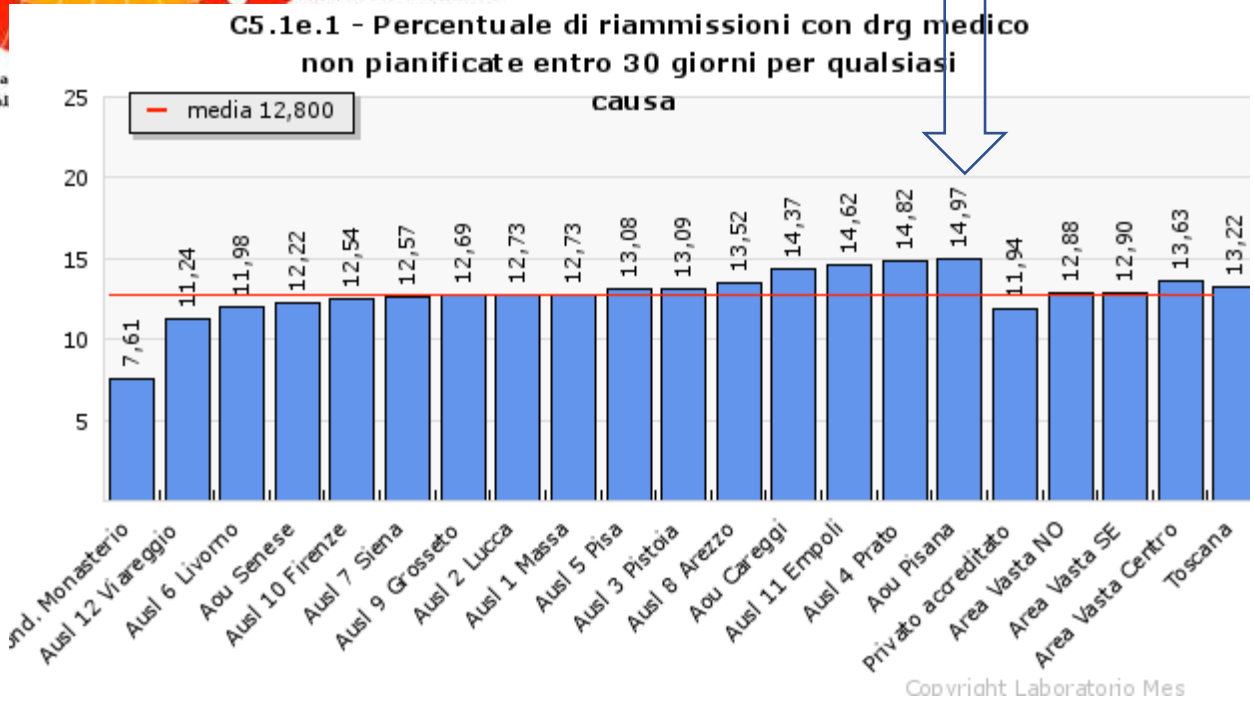
Tascini C et al., *Variable incidence of candidemia in patients admitted to ICUs or medical wards of large tertiary-care Italian hospitals,* Clinical Microbiology and Infection (2015), http://dx.doi.org/10.1016/j.cmi.2015.05.019

Target S. Anna School Pisa 2014 – Performance Lenght of stay in Internal Medicine



Target S. Anna School Pisa 2014 –





PICC and Candida

Intensive Care Med
DOI 10.1007/s00134-015-3892-0

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Peripherally inserted central catheter as a predominant risk factor for candidemia in critically ill patients in Internal Medicine wards in Italy

Accepted: 19 May 2015

Electronic supplementary material
The online version of this article (doi: 10.1007/s00134-015-3892-0) contains supplementary material, which is available to authorized users.

Table 1 Comparison of clinical characteristics and outcomes of patients in the general internal medicine wards versus those in the intensive care units

Clinical characteristics and outcomes of patients	All patients (n = 72)	Patients in General Internal Medicine wards (n = 50)	Patients in Intensive Care Units (n = 22)	p value
Clinical characteristics				
Age (years)	73 ± 14	78 ± 13	66 ± 12	<0.05
Charison score	6.82 ± 2.70	6.69 ± 2.52	7.16 ± 3.14	ns
Admission from home	36/72 (50 %)	34/50 (68 %)	2/22 (9 %)	≤0.001
Transfer from surgical ward	14/72 (19 %)	1/50 (2 %)	13/22 (59 %)	≤0.001
Hospital stay (days)	15 [8–35]	11 [6–20]	40 [30–72]	≤0.001
Time to onset of candidemia (days)	7 [2–17]	4 [1–11]	21 [9–36]	≤0.001
Very early onset candidemia (<48 h from admission)	24/72 (34 %)	23/50 (46 %)	1/22 (5 %)	≤0.001
Early onset candidemia (2–10 days from admission)	19/72 (26 %)	13/50 (26 %)	6/22 (27 %)	ns
Late onset candidemia (>10 days from admission)	29/72 (40 %)	14/50 (28 %)	15/22 (68 %)	<0.05
Patient therapy and outcomes				
Therapy with azole	39/72 (54 %)	33/50 (66 %)	6/22 (27 %)	<0.05
Therapy with echinocandins	17/72 (22 %)	2/50 (4 %)	14/22 (64 %)	≤0.001
No treatment	17/72 (24 %)	15/50 (30 %)	2/22 (9 %)	ns
Continuous infusions	48/72 (67 %)	29/50 (58 %)	19/22 (86 %)	<0.05
Nasogastric tube	33/72 (46 %)	16/50 (32 %)	17/22 (77 %)	≤0.001
Central venous catheter	26/72 (36 %)	9/50 (18 %)	17/22 (77 %)	≤0.001
Peripherally inserted central catheter	37/72 (52 %)	36/50 (72 %)	1/22 (5 %)	≤0.001
Overall mortality	31/72 (43 %)	17/50 (34 %)	14/22 (64 %)	≤0.001

Data are presented as the mean ± standard deviation, number with the percentage in parenthesis, or the median with the interquartile range in square brackets, as appropiate
ns Not significant

MES: Management e Sanità
Scuola Sant'Anna di Pisa

il **Laboratorio Management e Sanità (MeS)** dell'Istituto di Management della **Scuola Superiore Sant'Anna**, che dal 2008 ha sviluppato il "Sistema di Valutazione dei Sistemi sanitari regionali", oggi condiviso da **dieci regioni italiane** (Basilicata, Calabria, Friuli Venezia Giulia, Liguria, Lombardia, Marche, Puglia, Toscana, Umbria, Veneto) e dalle **due province autonome** di Trento e Bolzano. Il progetto ha permesso negli anni la condivisione e l'evoluzione di un sistema di valutazione delle "performance" dei sistemi sanitari regionali, che oggi si compone di quasi 400 indicatori, per monitorare la capacità di miglioramento nella gestione dei servizi sanitari. Queste

L'analisi dei circa 390 indicatori del Sistema di Valutazione mostra come le Regioni del Network, malgrado le complessità, siano sistemi capaci di miglioramento. Le aree che hanno registrato gli **avanzamenti più significativi** sono le **vaccinazioni** (per quanto le coperture registrate ancora non raggiungano gli standard desiderati), i **tempi di attesa per la chirurgia oncologica** (in particolare, per il trattamento di utero e mammella) e in generale la **capacità dei sistemi di indirizzare l'utenza** verso i *setting* di offerta più appropriati, evitando **ospedalizzazioni inutili**.

e rosolia, che a **Trento** si fermava all'84.5% nel 2015, nel 2018 raggiunge il 94.3%; se in **Liguria** si dovevano mediamente attendere circa 35 giorni per un'operazione chirurgica per un tumore maligno alla mammella, nel 2018 il valore scende a 28 giorni; in **Puglia** il tasso di ospedalizzazione era del 170.4 per mille residenti nel 2013, scendeva a 128.8 nel 2017, per calare ulteriormente a 124 nel 2018. Si riducono in particolare i ricoveri ad alto rischio di inappropriatezza: in **Veneto** ad esempio, *best practice* del Network, il tasso cala ulteriormente dai 111 ricoveri (per 10.000 residenti) del 2017 a 104 del 2018. Ancora critica tuttavia **l'appropriatezza nell'uso dei servizi di diagnostica per immagini** e in aumento **i tempi di attesa al pronto soccorso**, per i casi meno gravi (aumentano leggermente, ad esempio, i tempi di attesa in pronto soccorso per i codici verdi, in pressoché tutte le Regioni del Network).

Indicatori

- Dove sono le sepsi?
- Le sepsi da MRSA?
- L sepsi da ESBL/AmpC?
- Le sepsi da KPC?
- Le sepsi da NDM?
- Siamo pronti?

ASPECT-NP

- DBRCT, non-inferiority trial
- Ventilated nosocomial pneumonia
  - Ventilator-associated pneumonia (VAP)
  - Ventilated hospital-acquired pneumonia (Ventilated HAP)
- Interventions
  - Meropenem 1gm q8
  - C/T 3 gm q8
- All patients underwent lower airway sampling
- Stratified by
  - Age (≥65 or <65)
  - VAP vs Ventilated HAP
- N=726

DBRCTs = Double Blind Randomized Controlled Trial

Kollef MH, et al. ECCMID 2019 #P1917

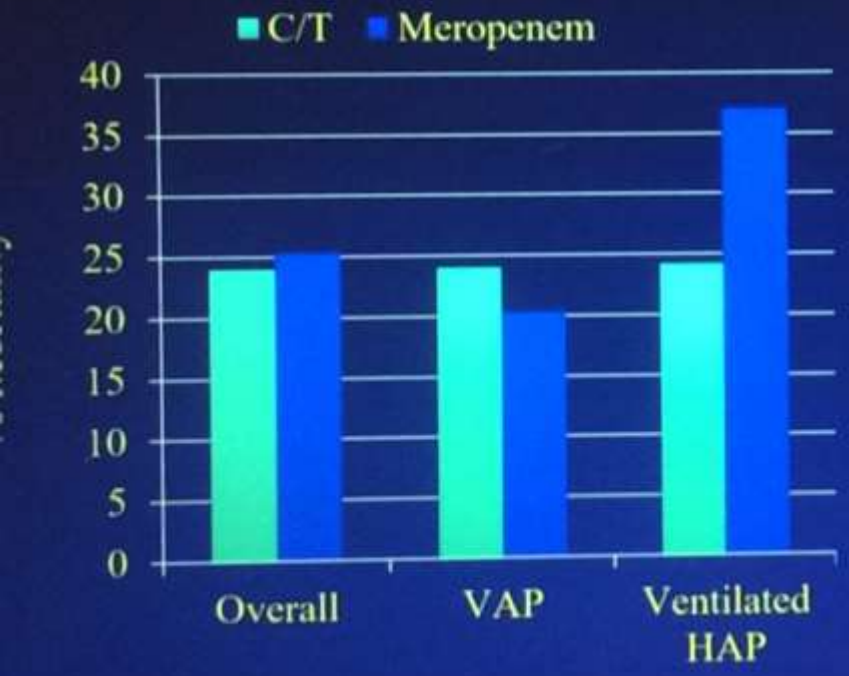
Table 3. Baseline LRT Pathogens (≥10 Isolates) in the mITT Population

	C/T (N=264)	Meropenem (N=247)
Gram-negative pathogens, n (%)	259 (98.1%)	240 (97.2%)
Pseudomonas aeruginosa, n (%)	63 (23.9%)	65 (26.3%)
MDR, n (%)	24 (9.1%)	11 (4.5%)
XDR, n (%)	10 (3.8%)	5 (2.0%)
Enterobacteriaceae, n (%)[a]	195 (73.9%)	185 (74.9%)
ESBL+ Enterobacteriaceae, n (%)	84 (31.8%)	73 (29.6%)
Enterobacter cloacae, n (%)	17 (6.4%)	16 (6.5%)
Escherichia coli, n (%)	51 (19.3%)	42 (17.0%)
Klebsiella oxytoca, n (%)	14 (5.3%)	12 (4.9%)
Klebsiella pneumoniae, n (%)	86 (32.6%)	91 (36.8%)
Proteus mirabilis, n (%)	24 (9.1%)	20 (8.1%)
Serratia marcescens, n (%)	18 (6.8%)	12 (4.9%)
Acinetobacter baumannii, n (%)	24 (9.1%)	14 (5.7%)
Haemophilus influenzae, n (%)	22 (8.3%)	16 (6.5%)
Streptococcus spp., n (%)[b]	14 (5.3%)	18 (7.3%)
Monomicrobial, n (%)	164 (62.1%)	158 (64.0%)
Polymicrobial, n (%)	100 (37.9%)	89 (36.0%)

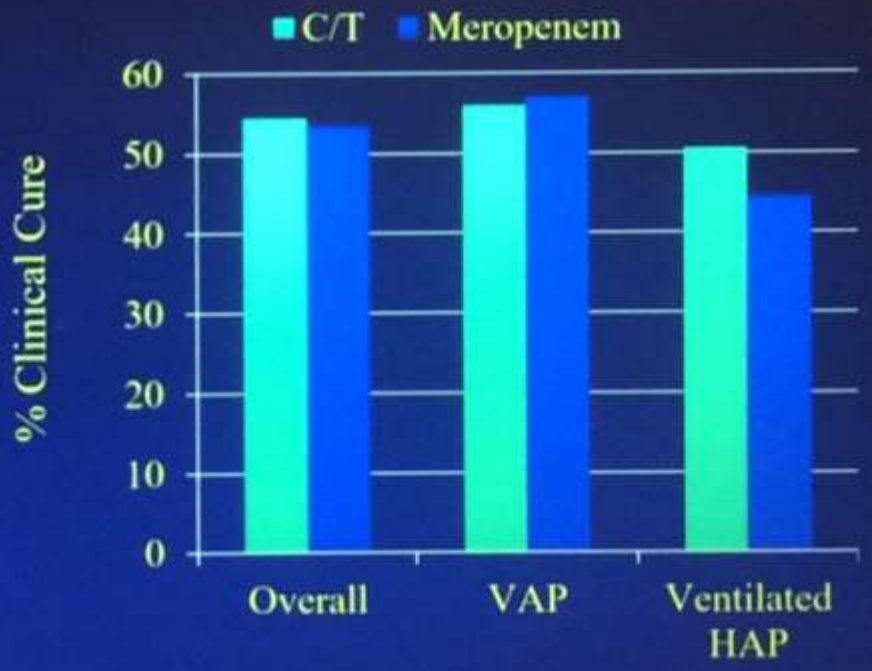
C/T, ceftolozane/tazobactam. ESBL, extended-spectrum beta-lactamase. LRT, lower respiratory tract. MDR, multidrug resistant. mITT, microbiologic intent-to-treat. XDR, extensively drug resistant.

ASPECT-NP (Clinical Outcomes)

28-Day All-Cause Mortality (ITT)



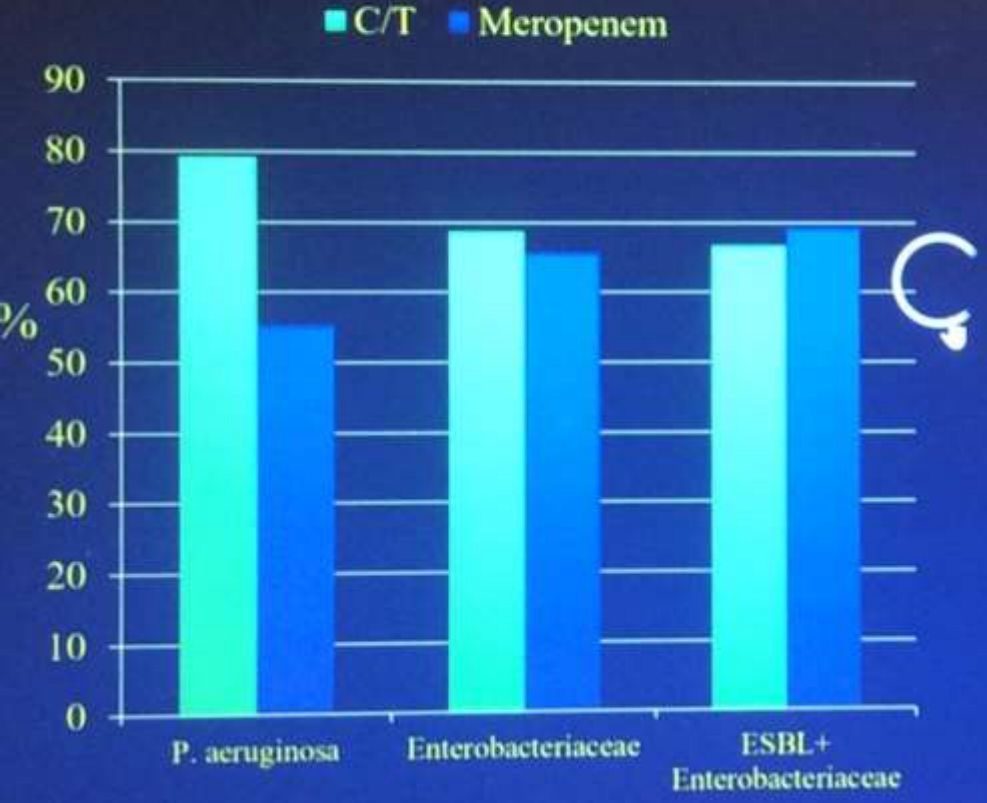
Clinical Cure at TOC (ITT)



Kollef MH, et al. ECCMID 2019. #P1917

ASPECT-NP (Micro Outcomes)

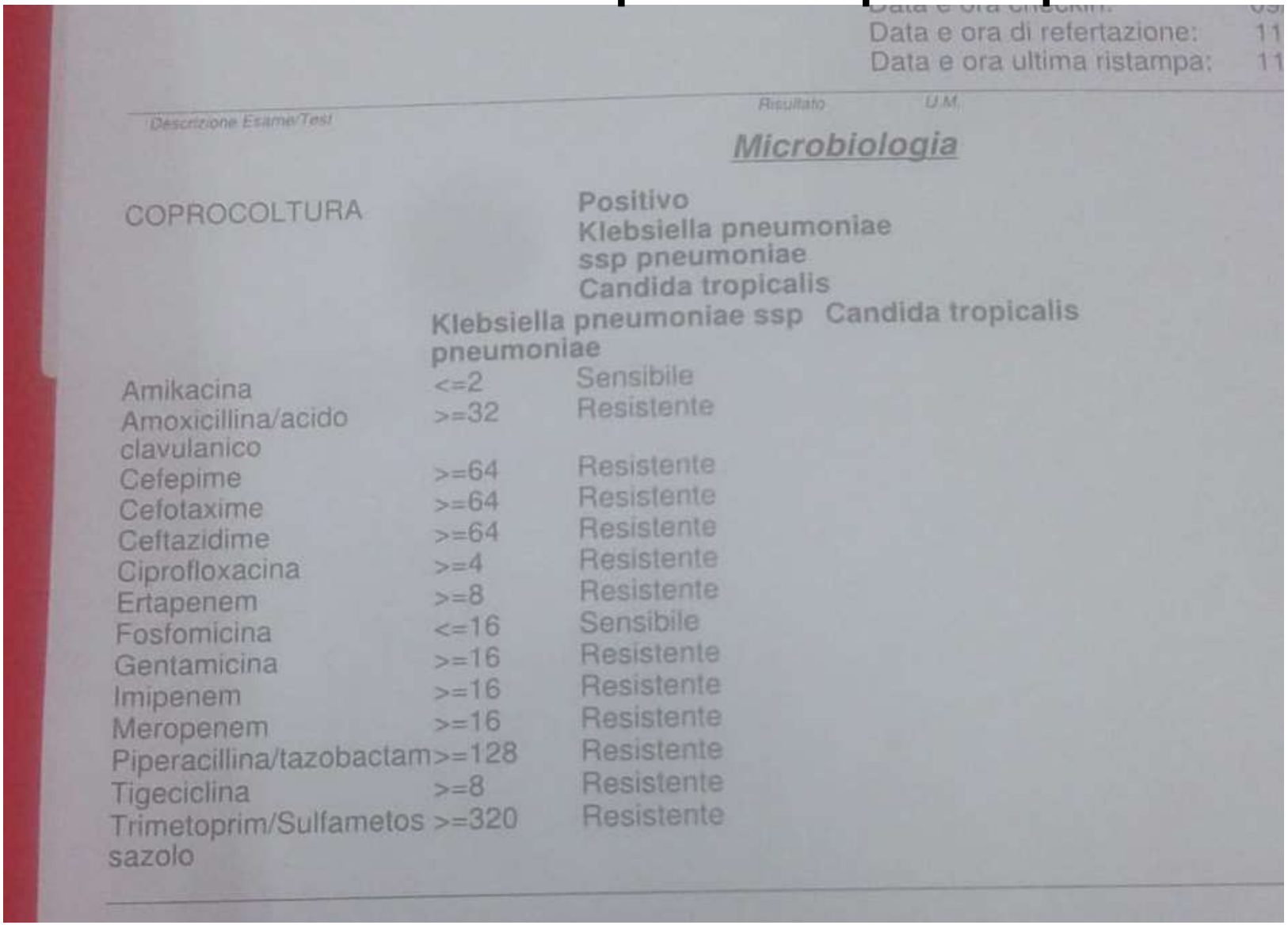
Microbiologic Eradication



	C/T	Mero
P. aeruginosa	79% (23/29)	55% (21/38)
K. pneumoniae	71% (30/42)	67% (32/48)
ESBL+ K. pneumoniae	67% (20/30)	67% (18/27)
E. Coli	78% (18/23)	73.9% (17/23)
ESBL+ *E. coli*	83% (10/12)	86% (6/7)
H. Influenzae	92% (11/12)	50% (4/8)

Martin-Loeches I et al. ECCMID 2019, #O0302

Bambina leucemica Osp. Pausillipon Napoli



Data e ora di refertazione: 11
Data e ora ultima ristampa: 11

Microbiologia

Descrizione Esame/Test		Risultato	U.M.
COPROCOLTURA		**Positivo** **Klebsiella pneumoniae ssp pneumoniae** **Candida tropicalis**	
	Klebsiella pneumoniae ssp pneumoniae	**Candida tropicalis**	
Amikacina	<=2	Sensibile	
Amoxicillina/acido clavulanico	>=32	Resistente	
Cefepime	>=64	Resistente	
Cefotaxime	>=64	Resistente	
Ceftazidime	>=64	Resistente	
Ciprofloxacina	>=4	Resistente	
Ertapenem	>=8	Resistente	
Fosfomicina	<=16	Sensibile	
Gentamicina	>=16	Resistente	
Imipenem	>=16	Resistente	
Meropenem	>=16	Resistente	
Piperacillina/tazobactam	>=128	Resistente	
Tigeciclina	>=8	Resistente	
Trimetoprim/Sulfametossazolo	>=320	Resistente	

CPE

- Manca colistina
- Manca ceftazidime/avibactam
- Manca genotipo o fenotipo di resistenza

Caso clinico

- Paziente trapiantato in Toscana ad ottobre 2018
- Ictus post intervento con emi-sindrome sinistra (ricovero un mese in UTI)
- Due mesi in riabilitazione dimesso gennaio 2019
- Ricovero in un ospedale periferico a Napoli giugno 2019 (PCT 70, GB 18.000, 91% neutrofili; Lattati 3,5)
- **Inizia meropenem edema delle labbra**
- Trasferito al Cotugno con ciprofloxacina 200 mg x 2 die (sulla lettera di dimissione di Pisa si dice colonizzato da KPC)

Caso clinico

- Telefonata ai colleghi rianimatori di Pisa per avere antibiogramma

Ricerca Klebsiella carbapenemasi produttrice **positivo** *feci*

1 ° microrganismo: ***Klebsiella pneumoniae***

MIC = Minima concentrazione
S = Sensibile; I = Intermedio;

Antibiotico	*MIC (µg/ml)*	*SIR*
>> BRODODILUIZIONE IN MICROPIASTRA <<		
Amikacina	>16	**R**
Amoxicillina/Clavulanato	>8	**R**
Ampicillina/sulbactam	>32	**R**
Cefepime	>32	**R**
Cefotaxime	>4	**R**
Ceftazidime	>128	**R**
Ciprofloxacina	>2	**R**
Colistina	>8	**R**
Doripenem	>8	**R**
Ertapenem	>1	-
Fosfomicina	32	S
Gentamicina	2	S
Imipenem	>16	**R**
Levofloxacina	>4	**R**
Meropenem	>64	**R**
Nitrofurantoina	>64	-
Piperacillina/Tazobactam	>128	**R**
Tigeciclina	1	S
Trimetoprim-sulfametossazolo	>4	**R**

Caso clinico

- Ceppo dalle feci fatto antibiogramma (Io considero assolutamente appropriato)
- Ma non si parla di genotipo o fenotipo
- NDM (epidemia area vasta toscana) o KPC o Oxa 48 (sarà utile per vaborbactam)?
- Non viene testato ceftazidime/avibactam?

Caso clinico

- Test rapido molecolare su feci: KPC
- Terapia con ceftazidime avibactam e fosfomicina
- PCT: 8 poi 5 in seconda e terza giornata

Screening per le carbapenemasi

- In un contesto di KPC lo screening per le carbapenemasi diventa fondamentale per la gestione delle epidemie e dei nuovi farmaci

Ambretti *et al. Antimicrobial Resistance and Infection Control* (2019) 8:136
https://doi.org/10.1186/s13756-019-0591-6

Antimicrobial Resistance and Infection Control

REVIEW Open Access

Screening for carriage of carbapenem-resistant Enterobacteriaceae in settings of high endemicity: a position paper from an Italian working group on CRE infections

Simone Ambretti[1*], Matteo Bassetti[2], Pierangelo Clerici[3], Nicola Petrosillo[4], Fabio Tumietto[5], Pierluigi Viale[5] and Gian Maria Rossolini[6]

Subsequently, the Italian Ministry of Health produced an Act [43] for the implementation of national surveillance of bloodstream infections by carbapenem resistant *Escherichia coli* and *Klebsiella pneumoniae.* The Act recommends active screening in all contacts of CRE-positive patients, in all patients with a previous colonization/infection that are admitted to hospital, and in all patients coming from endemic areas. Moreover, screening was suggested for patients admitted or transferred to high-risk units and in patients transferred from another hospital or with a history of recent hospitalization or coming from long term care facilities. Ministry of Health recommended also contact precautions and isolation for all colonized/infected individuals, including cohorting strategies, strengthening hand hygiene procedures and education.

antimicrobial stewardship. In particular, in certain categories of colonized patients who are at high-risk for invasive infections (e. g. neutropenic patients), knowledge of CRE colonization can be relevant to the selection of empiric antimicrobial chemotherapy covering the colonizing pathogen in case of emergence of a septic status In this case, knowledge of the resistance mechanism of the colonizer is particularly important, given the different spectrum of activity of anti-CRE agents for example, the empirical use of ceftazidime-avibactam could be considered in case of a CPE producing KPC but not in case of a CPE producing a metallo-β-lactamase [44].

44. Wright H, Bonomo RA, Paterson DL. New agents for the treatment of infections with gram-negative bacteria: restoring the miracle or false dawn? Clin Microbiol Infect. 2017 Oct;23(10):704–12. https://doi.org/10.1016/j.cmi.2017.09.001.

Intensive Care Med
https://doi.org/10.1007/s00134-018-5360-0

ORIGINAL

Mortality attributable to different *Klebsiella* susceptibility patterns and to the coverage of empirical antibiotic therapy: a cohort study on patients admitted to the ICU with infection

GiViTI Steering Committee, Guido Bertolini[1], Giovanni Nattino[1], Carlo Tascini[2], Daniele Poole[3], Bruno Viaggi[4], Greta Carrara[1*], Carlotta Rossi[1], Daniele Crespi[1], Matteo Mondini[1], Martin Langer[5], Gian Maria Rossolini[6,7] and Paolo Malacarne[8]

Figure 1. Flow chart of the study

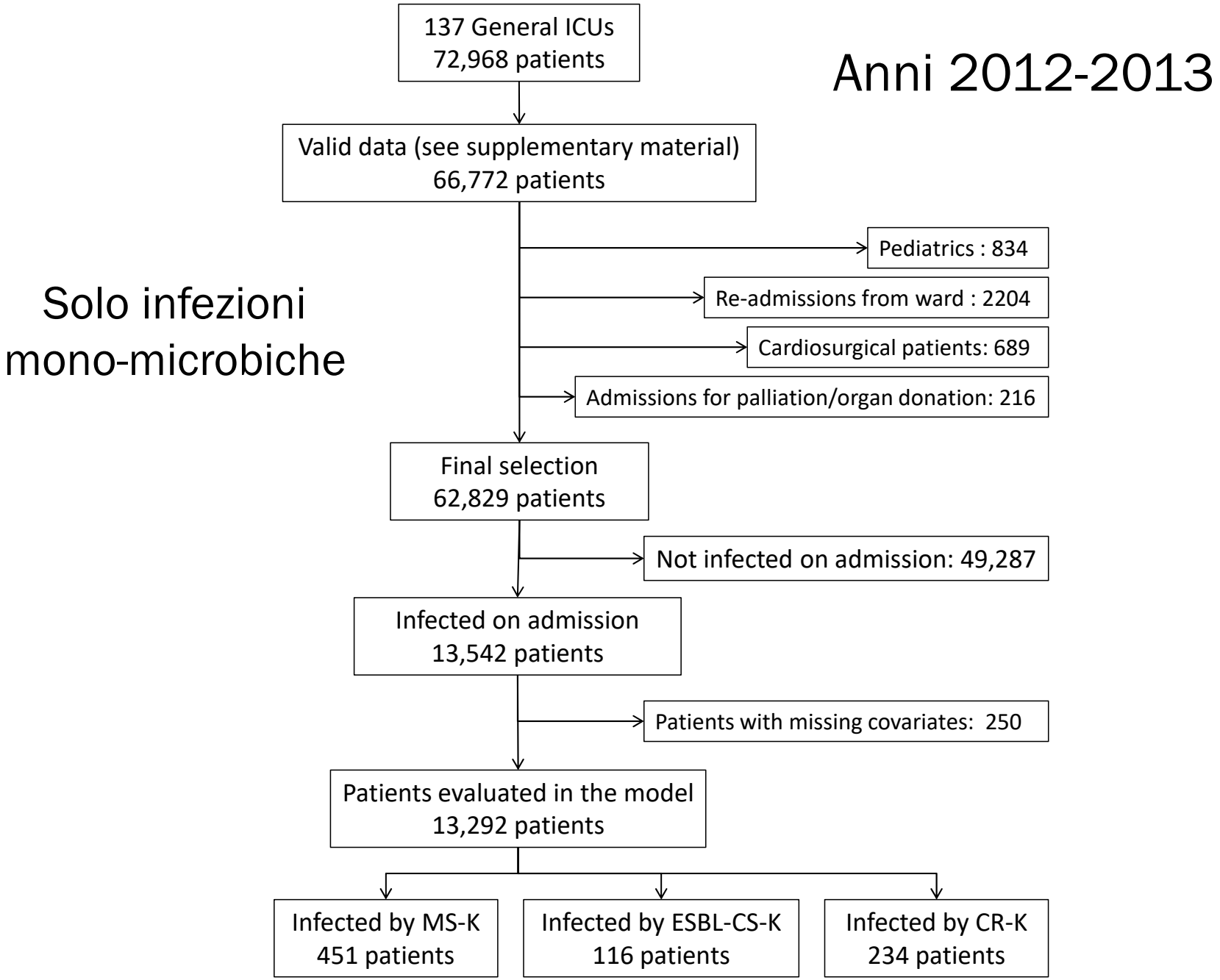
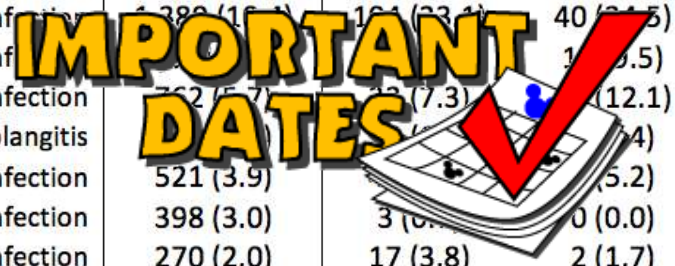


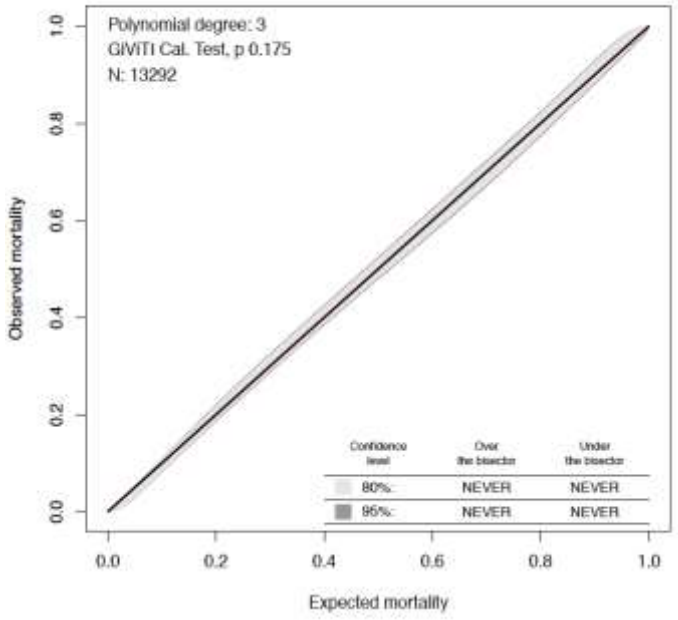
Table 1. Description of patients

	Infected at admission	MS-Kp	ESBL-CS-Kp	CR-Kp	*p*-value[1]
N	13,292	451	116	234	-
Age - Mean (SD)	67.9 (15.1)	68.0 (14.8)	68.7 (13.1)	64.4 (15.3)	0.003
Gender - N (%)					
Male	7,994 (60.1)	272 (60.3)	76 (65.5)	149 (63.7)	0.49
Female	5,298 (39.9)	179 (39.7)	40 (34.5)	85 (36.3)	
BMI - N (%)					
Underweight	911 (6.9)	32 (7.1)	12 (10.3)	17 (7.3)	
Normal	5,827 (43.8)	199 (44.1)	40 (34.5)	111 (47.4)	0.21
Overweight/obese	6,554 (49.3)	220 (48.8)	64 (55.2)	106 (45.3)	
Comorbidities - N (%)					
Hypertension	6,753 (50.8)	232 (51.4)	64 (55.2)	113 (48.3)	0.47
Arrhythmia	2,510 (18.9)	71 (17.3)	18 (15.5)	42 (17.9)	0.73
Moderate COPD	2,502 (18.8)	72 (16.0)	17 (14.7)	47 (20.1)	0.30
Cerebrovascular disease	1,768 (13.3)	70 (15.5)	28 (24.1)	38 (16.2)	0.083
Diabetes type II (no insulin treatment)	1,758 (13.2)	78 (17.3)	15 (12.9)	26 (11.1)	0.080
Pre-ICU hospital stay - Median (IQR)	1 (0-7)	2 (0-11)	8 (1-18)	9 (1-25)	<0.001
SAPSII[1] **-** Mean (SD)	46.6 (8.9)	49.0 (18.6)	46.6 (18.5)	45.5 (18.5)	0.037
SOFA[1] **-** Mean (SD)	7.4 (4.2)	8.3 (4.3)	7.5 (4.2)	7.9 (4.3)	0.15
ICU length of stay - Median (IQR)	6 (2-13)	10 (5-18)	8 (3-17)	11 (4-19)	0.26
ICU outcome - N (%)					
Alive	9,734 (73.2)	347 (76.9)	84 (72.4)	135 (57.7)	<0.001
Dead	3,558 (26.8)	104 (23.1)	32 (27.6)	99 (42.3)	
Hospital outcome - N (%)					
Alive	8,349 (62.8)	286 (63.4)	70 (60.3)	109 (46.6)	<0.001
Dead	4,943 (37.2)	165 (36.6)	46 (39.7)	125 (53.4)	

Table 2. Details of infections

	Infected at admission	MS-Kp	ESBL-CS-Kp	CR-Kp	*p*-value[1]
N	13,292	451	116	234	-
Type of infection[2] **-** N (%)					
Extrahospital	8,213 (61.8)	223 (49.4)	38 (32.8)	48 (20.5)	
Hospital (not ICU) /long-term rehabilitation unit	4,310 (32.4)	158 (35.0)	56 (48.3)	137 (58.5)	<0.001
Other ICU	769 (5.8)	70 (15.5)	22 (19.0)	49 (20.9)	
Severity of infection on admission - N (%)					
Simple infection	4,946 (37.2)	154 (34.1)	42 (36.2)	81 (34.6)	
Severe sepsis	3,973 (29.9)	118 (26.2)	33 (28.4)	71 (30.3)	0.70
Septic Shock	4,373 (32.9)	179 (39.7)	41 (35.3)	82 (35.0)	
Max severity of infection during the stay - N (%)					
Simple infection	4,190 (31.5)	123 (27.3)	36 (31.0)	69 (29.5)	
Severe sepsis	4,070 (30.6)	117 (25.9)	37 (31.9)	67 (28.6)	0.38
Septic Shock	5,032 (37.9)	211 (46.8)	43 (37.1)	98 (41.9)	
Site of infection (top 10) - N (%)					
Pneumonia	5,595 (42.1)	170 (37.7)	47 (40.5)	96 (41.0)	0.66
Peritonitis	2,814 (21.2)	88 (19.5)	20 (17.2)	42 (17.9)	0.80
Urinary tract infection	[illegible]	[illegible]	40 [illegible]	65 (27.8)	0.035
Lower respiratory tract infection	[illegible]	[illegible]	[illegible].5)	25 (10.7)	0.41
Skin and soft tissue infection	[illegible]	[illegible] (7.3)	[illegible] (12.1)	21 (9.0)	0.25
Cholecystitis/cholangitis	[illegible]	[illegible]	[illegible].4)	3 (1.3)	0.010
Primary bloodstream infection	521 (3.9)	[illegible]	[illegible].2)	13 (5.6)	0.51
CNS infection	398 (3.0)	3 [illegible]	[illegible] 0 (0.0)	3 (1.3)	0.18
Upper respiratory tract infection	270 (2.0)	17 (3.8)	2 (1.7)	10 (4.3)	0.50
Gastroenteritis	261 (2.0)	8 (1.8)	0 (0.0)	9 (3.8)	0.048
Hospital mortality by severity on admission - N deaths (Mortality)					
Simple infection	1,248 (25.2)	56 (36.4)	9 (21.4)	30 (37.0)	0.16
Severe sepsis	1,329 (33.5)	35 (29.7)	13 (39.4)	32 (45.1)	0.093
Septic Shock	2,366 (54.1)	74 (41.3)	24 (58.5)	63 (76.8)	<0.001





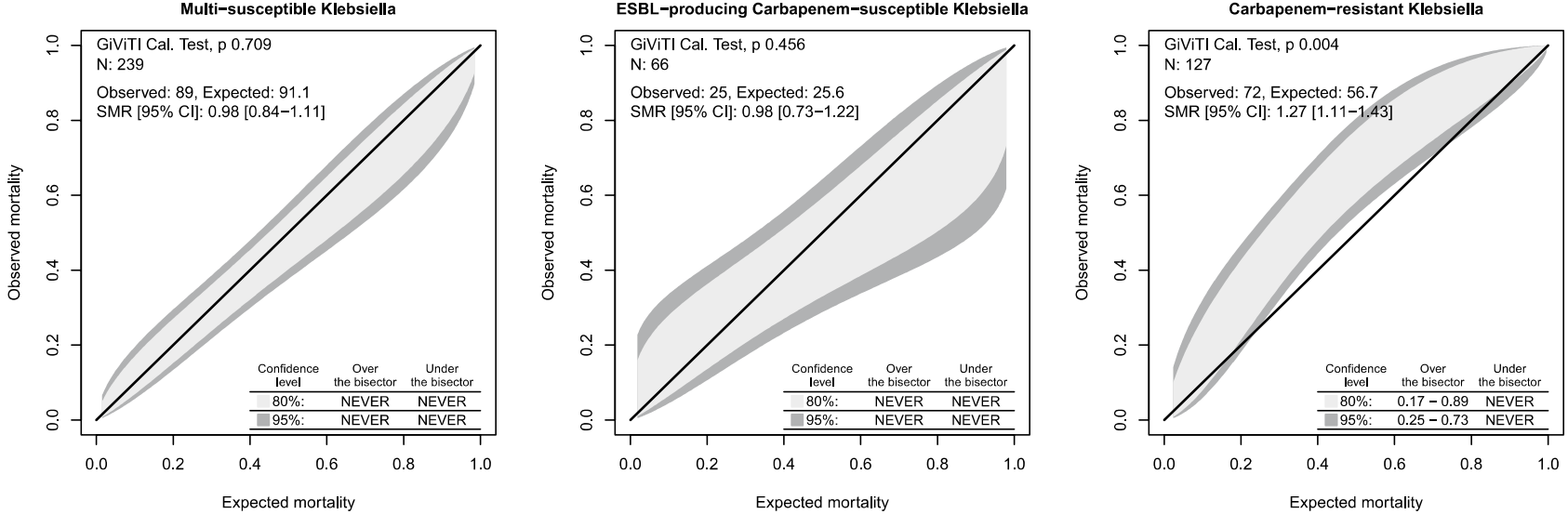
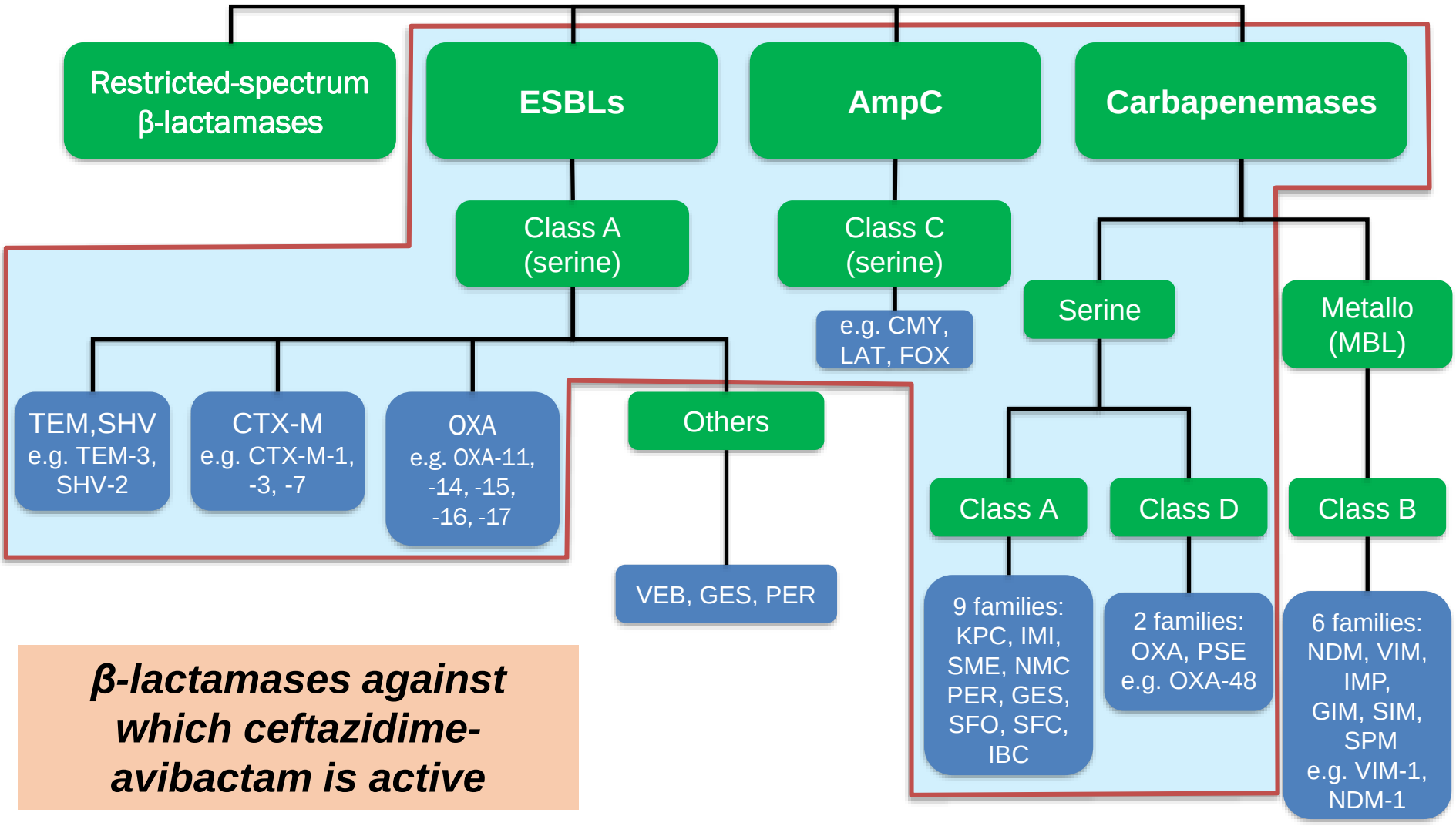


Fig. 3 Calibration of the model in monomicrobial infection, according to the different antibiotic resistance profile. **a** Multi-susceptible Klebsiella. **b** ESBL-producing Carbapenem-susceptible Klebsiella. **c** Carbapenem-resistant Klebsiella

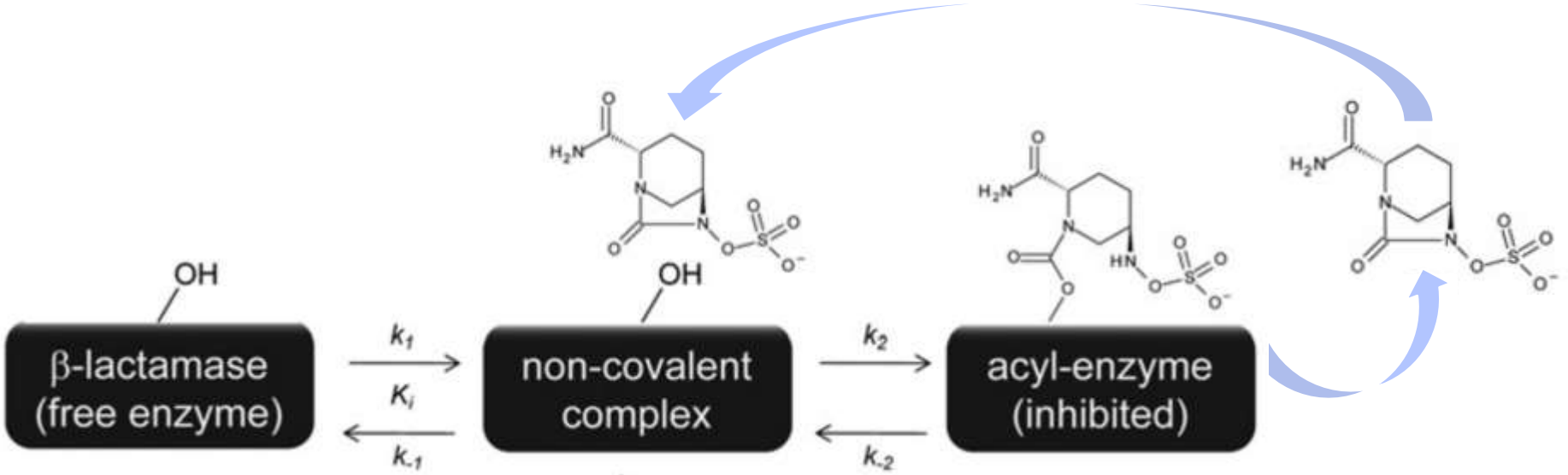
Ceftazidime avibactam sinergismo con meropenem e gentamicina

Microbiology lab Azienda Ospedaliera dei Colli, Naples Italy

In vitro activity of ceftazidime-avibactam against specific β-lactamases



β-lactamases against which ceftazidime-avibactam is active



		acylation ($M^{-1}s^{-1}$)	t permanence (min)
A	ESBL	$x10^5$	40±10
	KPC	$x10^4$	82±6
C	AmpC (E)	$x10^3$	300±20
	AmpC (PA)	$x10^3$	6±2 T > Ct 100%
D	OXA 48	$x10^3$	1000±300

Ehmann DE, et al. J Biol Chem 2013; 39: 27960-71

Seven prospective, international, multicentre, randomised Phase III studies

RECLAIM 1, 2 and 3: Adults with cIAI

Double-blind randomisation (1:1):
- CAZ 2000 mg + AVI 500 mg + metronidazole 500 mg IV q8h *or*
- MER 1000 mg IV + placebo q8h

Primary objective:
- RECLAIM 1 and 2:
- Assess non-inferiority of CAZ-AVI re: clinical cure at TOC visit in patients with ≥1 identified pathogen (mMITT populations)
- RECLAIM 3:
- Proportion of patients with clinical cure at TOC visit (CE populations)

RECAPTURE 1 and 2: Adults with cUTI (including acute pyelonephritis)

Double-blind randomisation (1:1) :
- CAZ 2000 mg + AVI 500 mg q8h IV *or*
- DOR 500 mg + placebo q8h IV

Primary objective:
Assess non-inferiority of CAZ-AVI on co-primary endpoints in mMITT analysis set:
1) Resolution of UTI-specific symptoms
2) Resolution/improvement of flank pain
3) Per-patient microbiol eradication and symptomatic resolution

REPRISE Adults with CAZ-resistant pathogens

Open-label randomisation (1:1) :
- CAZ 2000 mg + AVI 500 mg + metronidazole 500 mg q8h IV *or*
- Best available therapy

Primary objective:
Estimate per-patient clinical response to CAZ-AVI and best available therapy at TOC visit in cUTI and cIAI caused by CAZ-resistant Gram-negative pathogens

REPROVE Adults with nosocomial pneumonia (including VAP)

Double-blind randomisation (1:1) :
- CAZ 2000 mg + AVI 500 mg q8h IV *or*
- MER 1000 mg + placebo q8h IV

Plus open-label empiric linezolid + aminoglycoside

Primary objective:
Assess non-inferiority of CAZ-AVI on clinical cure rate at TOC visit in cMITT and CE populations

AVI, avibactam; CAZ, ceftazidime; CE, clinically evaluable; cIAI, complicated intra-abdominal infection; cMMIT, clinically modified intent-to-treat; cUTI, complicated urinary tract infection; DOR, doripenem; IV, intravenous; MER, meropenem; mMITT, microbiological modified intent-to-treat; q8h, every 8 h; TOC, test of cure; UTI, urinary tract infection; VAP, ventilator-associated pneumonia.

Zavicefta EMA EPAR. April 2016. Accessed Nov 2017 (www.ema.europa.eu, ceftazidime-avibactam PI)

Sternbach N, et al. Efficacy and safety of Ceftazidime-Avibactam: a systematic review and meta-analysis. *J Antimicrob Chemother 2018; 73: 2021-9*

Time of follow-up	No. of trials	No. of patients	Response rate	
			CAZ/AVI	comparator
EOT				
UTI				
IAI				
TOC				
UTI				
IAI				
pneumo				
LFU				
UTI				
IAI				

Indications approved by EMA:

1. **complicated UTI**
2. **complicated IAI**
3. **HAP or VAP**
4. **Infections due to aerobic Gram-negative organisms in patients with limited treatment options**

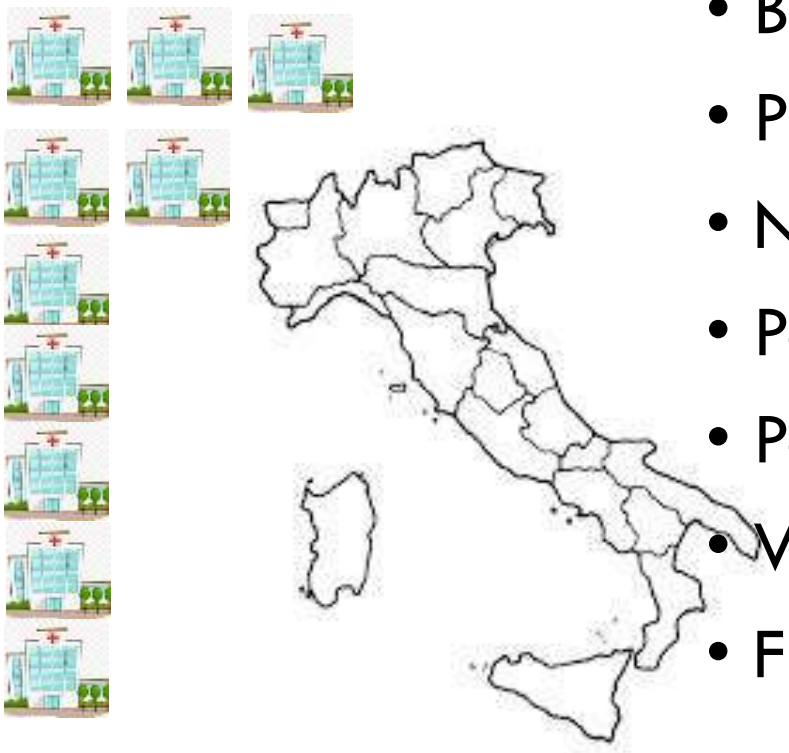
Clinical Infectious Diseases

MAJOR ARTICLE

Efficacy of Ceftazidime-Avibactam Salvage Therapy in Patients With Infections Caused by *Klebsiella pneumoniae* Carbapenemase–producing *K. pneumoniae*

Mario Tumbarello,[1,a] Enrico Maria Trecarichi,[1,a] Alberto Corona,[2] Francesco Giuseppe De Rosa,[3] Matteo Bassetti,[4] Cristina Mussini,[5] Francesco Menichetti,[6] Claudio Viscoli,[7] Caterina Campoli,[8] Mario Venditti,[9] Andrea De Gasperi,[10] Alessandra Mularoni,[11] Carlo Tascini,[12] Giustino Parruti,[13] Carlo Pallotto,[14] Simona Sica,[15] Ercole Concia,[16] Rosario Cultrera,[17] Gennaro De Pascale,[18] Alessandro Capone,[19] Spinello Antinori,[20] Silvia Corcione,[3] Elda Righi,[4] Angela Raffaella Losito,[1] Margherita Digaetano,[5] Francesco Amadori,[6] Daniele Roberto Giacobbe,[7] Giancarlo Ceccarelli,[9] Ernestina Mazza,[10] Francesca Raffaelli,[1] Teresa Spanu,[21] Roberto Cauda,[1] and Pierluigi Viale[8]

- Roma
- Milano
- Torino
- Udine
- Modena
- Pisa
- Genova

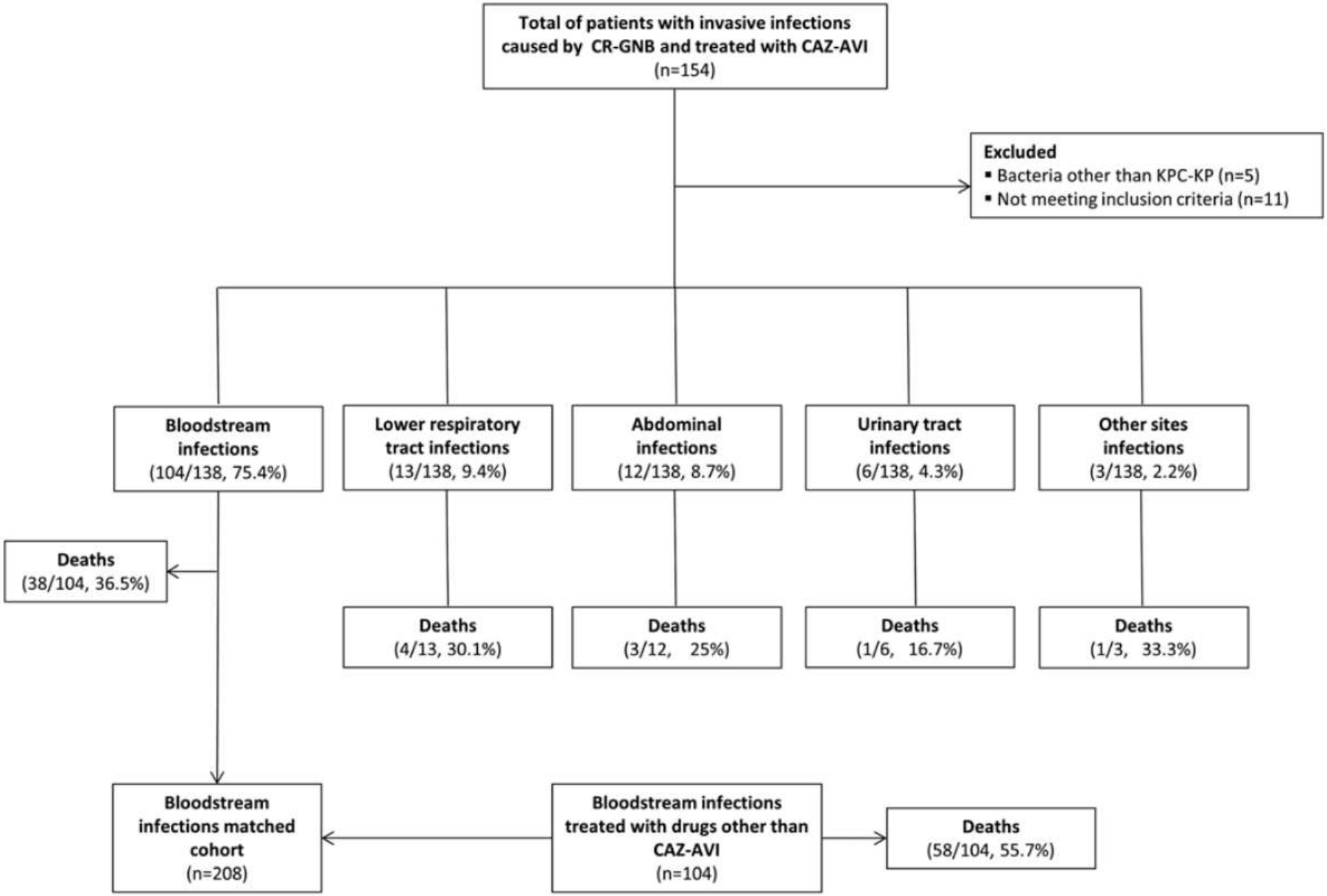


- Bologna
- Palermo
- Napoli
- Pescara
- Perugia
- Verona
- Ferrara

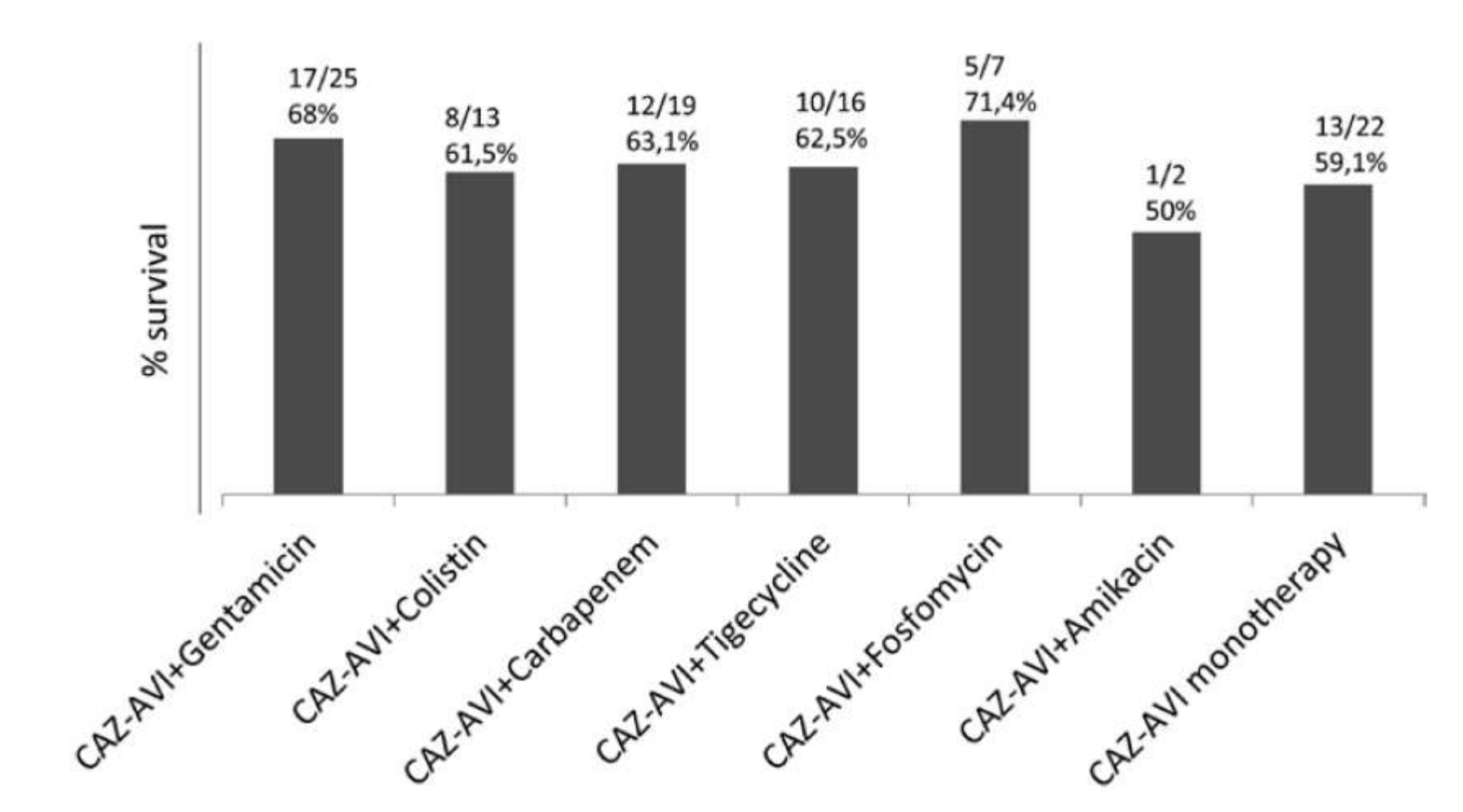
Tumbarello M, Trecarichi EM, Corona A, De Rosa FG, Bassetti M, Mussini C, Menichetti F, Viscoli C, Campoli C, Venditti M, De Gasperi A, Mularoni A, Tascini C, Parruti G, Pallotto C, Sica S, Concia E, Cultrera R, De Pascale G, Capone A, Antinori S, Corcione S, Righi E, Losito AR, Digaetano M, Amadori F, Giacobbe DR, Ceccarelli G, Mazza E, Raffaelli F, Spanu T, Cauda R, Viale P.
Efficacy of Ceftazidime-Avibactam Salvage Therapy in Patients With Infections Caused by *Klebsiella pneumoniae* Carbapenemase–producing *K. pneumoniae*. Clin Infect Dis. 2018 Jun 9. doi: 10.1093/cid/ciy492. [Epub ahead of print]

- **METHODS:** We retrospectively reviewed 138 cases of infections caused by Klebsiella pneumoniacarbapenemase-producing (KPC-Kp) in adults who received CAZ-AVI in compassionate-use programs in Italy. Case features and outcomes were analyzed, and survival was then specifically explored in the large subcohort whose infections were bacteremic.
- **RESULTS**:The 138 patients started CAZ-AVI salvage therapy after a first line treatment (median: 7 days) with other antimicrobials. CAZ-AVI was administered with at least one other active antibiotic in 109 (78.9%) cases. Thirty days after infection onset, 47 (34.1%) of the 138 patients had died. Thirty-day mortality among the 104 patients with bacteremic KPC-Kp infections was significantly lower than that of a matched cohort whose KPC-Kp bacteremia had been treated with drugs other than CAZ-AVI (36.5% vs. 55.7%, p=0.005). Multivariate analysis of the 208 cases of KPC-Kp bacteremia identified septic shock, neutropenia, Charlson comorbidity index >3, and recent mechanical ventilation as independent predictors of mortality, whereas receipt of CAZ-AVI was the sole independent predictor of survival.
- ***CONCLUSIONS: CAZ-AVI appears to be a promising drug for treatment of severe KPC-Kp infections, especially those involving bacteremia.***

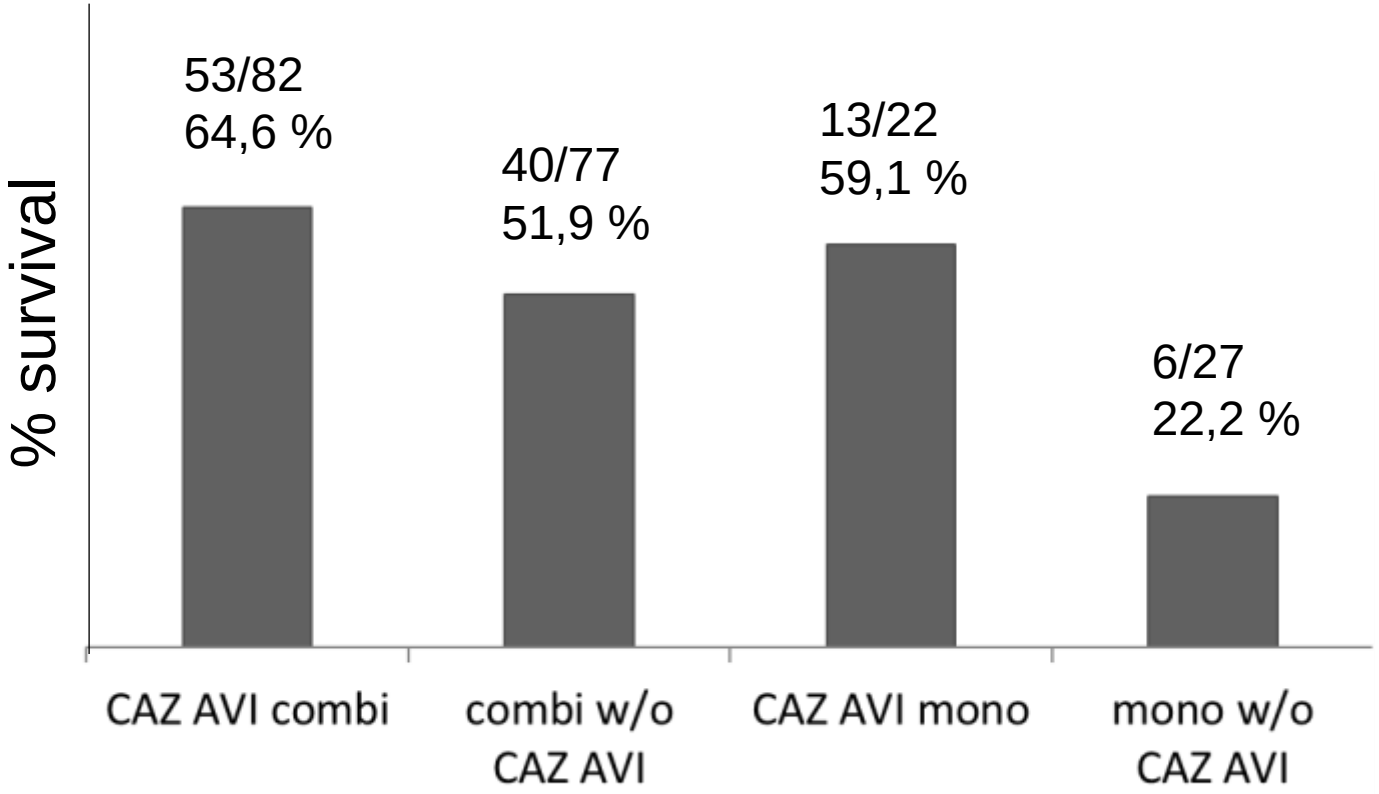
Apr 2016 – Dec 2017



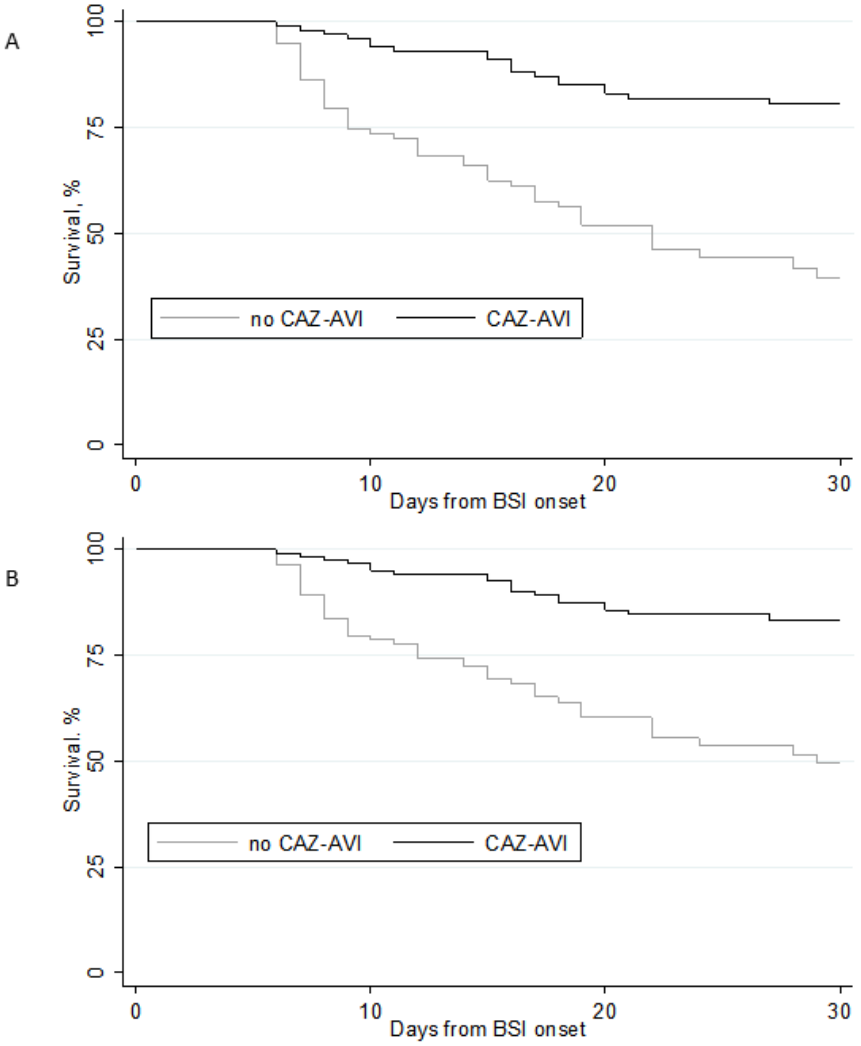
Thirty-day survival rates of CAZ-AVI treated bacteremic patients according to concomitant drugs used as combitation therapy or to CAZ-AVI monotherapy.



Percentages of 30 day survival in patients with BSI across treatment regimens



Kaplan-Meier survival analyses in the cohorts with KPC Kp bloodstream infections (BSIs)

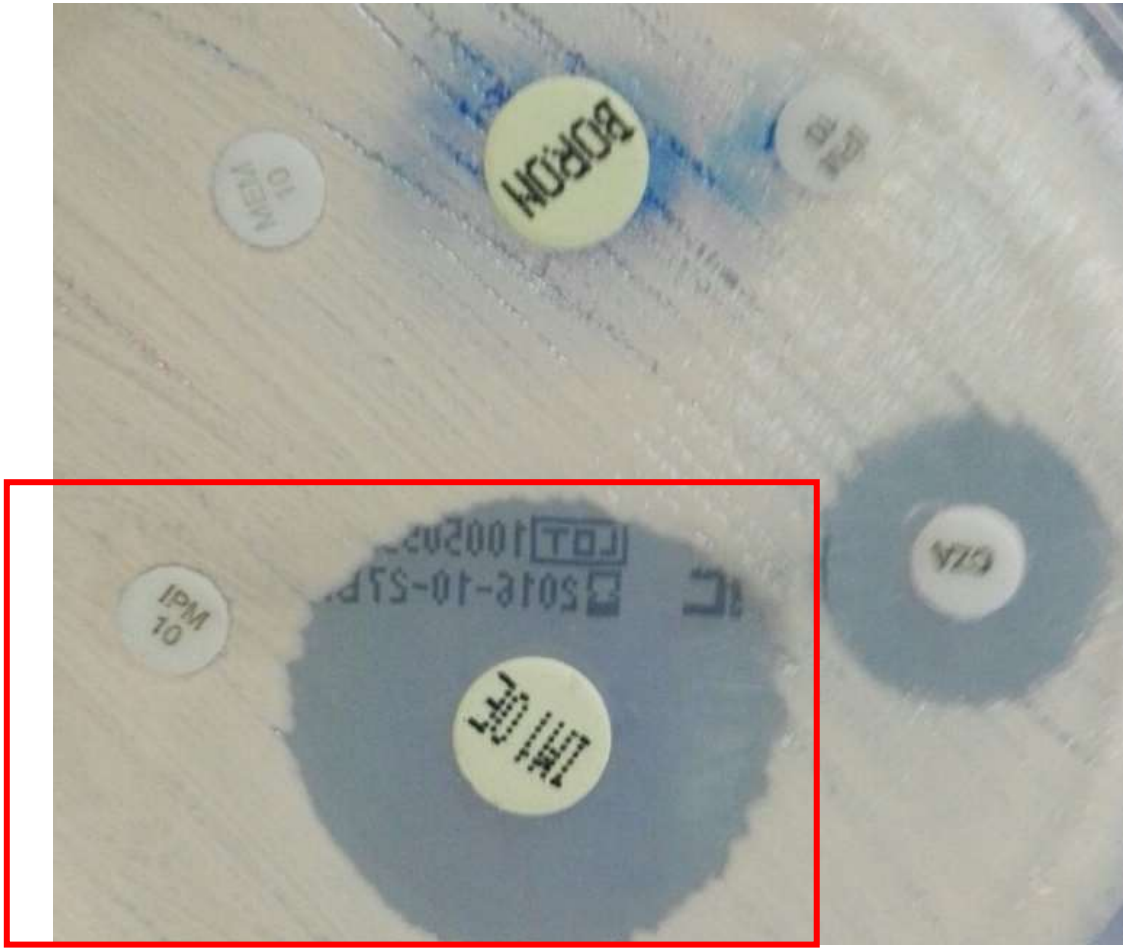


P<0.001

P<0.001

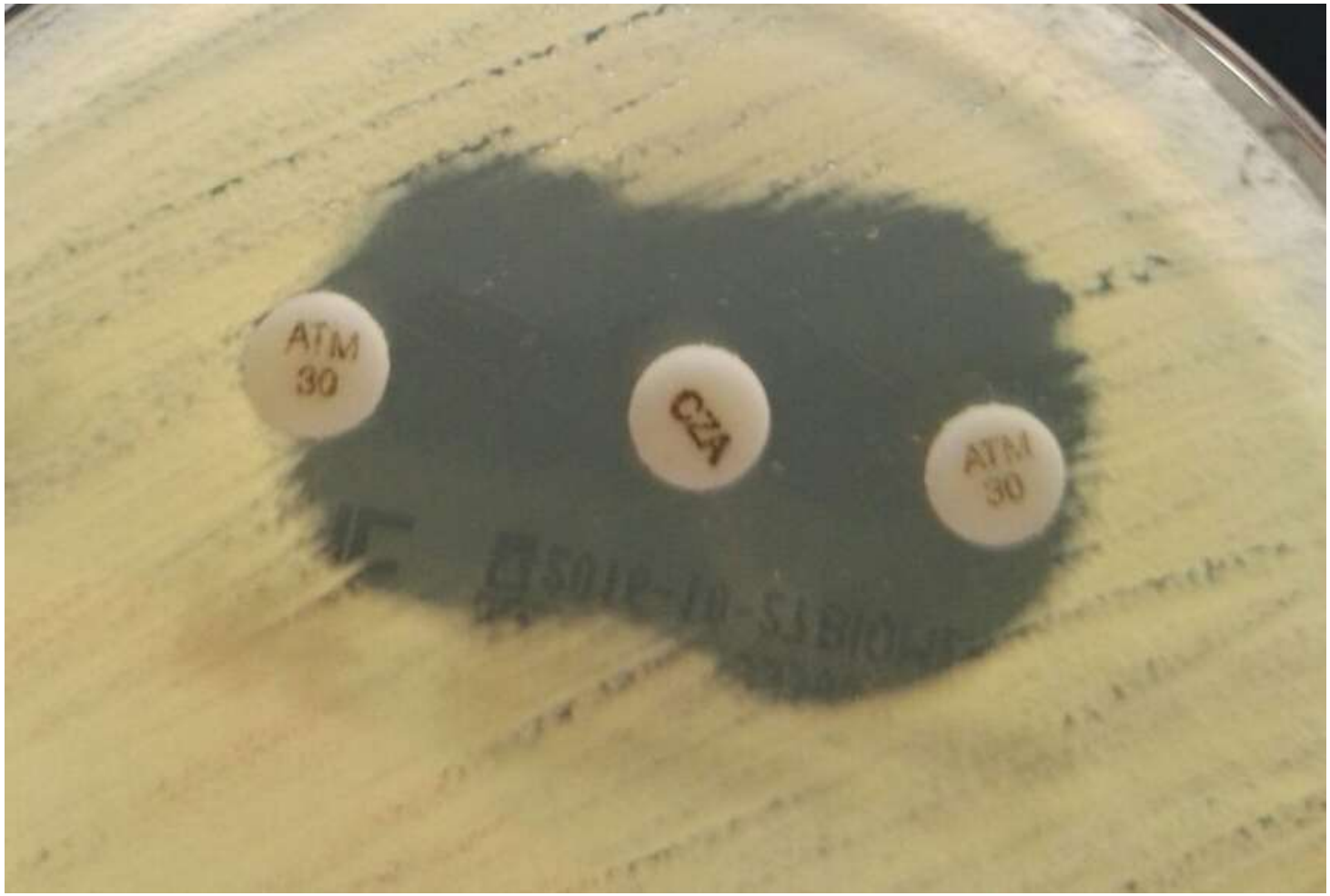
after adjustment for the presence of septic shock at the start of salvage treatment

Test EDTA positivo, boronico negativo: metallo enzima, no KPC



Laboratorio Microbiologia Azienda Ospedaliera dei Colli

Sinergismo cazavi ed aztreonam contro *Klebsiella* matallo-enzima



Laboratorio Microbiologia Azenda Ospedaliera dei Colli

Ceftazidime ed aztreonam da soli

Laboratorio Microbiologia Azienda Ospedaliera dei Colli

Aztreonam avibactam

- In fase di studio
- Fare scorte di aztreonam (in India)

Efficacy and Safety of Meropenem–Vaborbactam Versus Best Available Therapy for the Treatment of Carbapenem-Resistant *Enterobacteriaceae* Infections in Patients Without Prior Antimicrobial Failure: A Post Hoc Analysis

Matteo Bassetti · Daniele Roberto Giacobbe · Niki Patel · Glenn Tillotson · Jill Massey

Received: March 6, 2019

Table 2 Efficacy results in patients without prior antimicrobial failure in the mCRE-MITT population

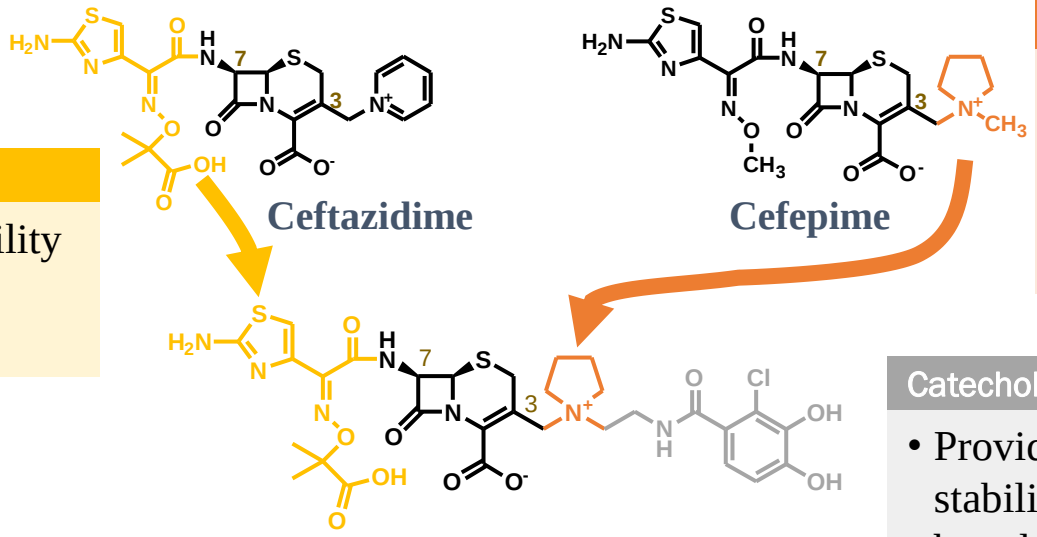
Efficacy endpoints (mCRE-MITT)	Meropenem–vaborbactam (n = 23)	Best available therapy (n = 15)	Absolute difference (95% CI)
Clinical cure at TOC	16 (69.6)	4 (26.7)	+ 42.9 (+ 13.7 to + 72.1)
Clinical cure at EOT	19 (82.6)	5 (33.3)	+ 49.3 (+ 20.8 to + 77.7)
Microbiologic cure[a] at EOT	19 (82.6)	6 (40.0)	+ 42.6 (+ 13.4 to + 71.8)
Microbiologic cure[a] at TOC	16 (69.6)	5 (33.3)	+ 36.2 (+ 5.9 to + 66.6)
Day 28 mortality	1 (4.3)	5 (33.3)	− 29.0 (− 54.3 to − 3.7)

CI confidence intervals, *EOT* end of therapy, *mCRE-MITT* microbiologic carbapenem-resistant *Enterobacteriaceae* modified intent-to-treat, *TOC* test of cure

[a] Microbiologic cure was defined as microbial eradication or presumed eradication

Unique structure of cefiderocol

Cefiderocol incorporates features of other cephalosporin antibiotics, but is distinct from other beta-lactam antibiotics due to its beta-lactamase resistance and iron chelation[1]



C-7 side chain[3]

- Enhances stability against beta-lactamases

C-3 side chain[2]

- Facilitates penetration of the Gram-negative outer membrane
- Confers low affinity for beta-lactamases

Catechol moiety

- Provides additional stability against beta-lactamases[4]
- Binds to free iron[5]

1. Ito A, et al. *Antimicrob Agents Chemother* 2016;60:7396–40; 2. Hancock RE, et al. *J Chemother* 1996;8 Suppl 2:31–6;
3. Craig WA et al. *Principles and Practice of Infectious Diseases (Eighth Edition)* 2015; Chapter 21:278–292;
4. Ito-Horiyama T, et al. *Antimicrob Agents Chemother* 2016;60:4384–6; 5. Ito A, et al. *J Antimicrob Chemother* 2016;71:670–7.

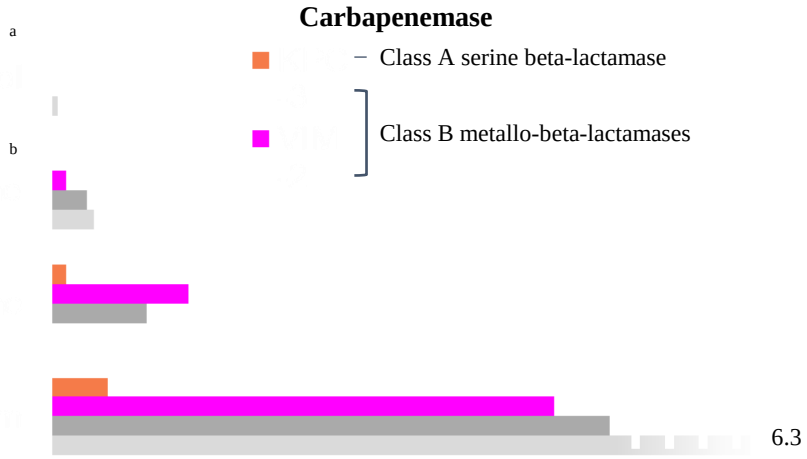
Cefiderocol mechanism of action

- Cefiderocol is a beta-lactam antibiotic and therefore inhibits bacterial cell wall synthesis[1]
- Cefiderocol is highly resistant to hydrolysis by various types of carbapenemases[2]
- Trojan horse mechanism of entry into the bacterial cell circumvents efflux pump- and porin-mediated mechanisms of resistance[3]

1. Bush K, et al. *Cold Spring Harb Perspect Med* 2016;6:a025247; 2. Ito A, et al. *J Antimicrob Chemother* 2016;71:670–7;
3. Ito A, et al. *Antimicrob Agents Chemother* 2016;60:7396–401; 4. Tsuji M, et al. Poster P0808 ECCMID 2016; Amsterdam, Netherlands.

Stability of cefiderocol against carbapenemases

Various carbapenemases show very limited *in vitro* activity against cefiderocol, showing that cefiderocol is highly stable against these enzymes



Cefiderocol's stability against carbapenemases enables it to overcome carbapenemase-mediated resistance

[a]Slight hydrolysis of cefiderocol by KPC-3 was observed, but was too weak for calculation of k_{cat};
[b]Hydrolysis observed, but k_{cat} could not be determined because K_m was too high.
k_{cat}, catalyst rate constant; K_i, inhibitor constant; K_m, Michaelis-Menten constant.
Ito-Horiyama T, et al, *Antimicrob Agents Chemother* 2016;60:4384–6.

Cefiderocol in the context of newer BLIs

	Antibiotic	MIC_{50}, mg/L	MIC_{90}, mg/L	Resistant, %[a]
KPC positive (n=75)	Cefiderocol	1	2	
	Ceftazidime/avibactam	1	4	4.0
	Ceftolozane/tazobactam	64	>64	97.3
	Colistin	1	>8	40.0
VIM positive (n=27)	Cefiderocol	1	4	
	Ceftazidime/avibactam	>64	>64	88.9
	Ceftolozane/tazobactam	>64	>64	100
	Colistin	0.5	>8	18.5
NDM positive (n=12)	Cefiderocol	4	8	
	Ceftazidime/avibactam	>64	>64	100
	Ceftolozane/tazobactam	>64	>64	100
	Colistin	0.5	>8	25.0
OXA-48-like positive (n=32)	Cefiderocol	0.5	4	
	Ceftazidime/avibactam	1	4	9.4
	Ceftolozane/tazobactam	>64	>64	93.8
	Colistin	0.5	>8	21.9

Kazmierczak KM, et al. *Int J Antimicrob Agents* 2019;53:177–84.

External *in vitro* study summary: MDR isolates from Italy

TABLE 1. Percentage of isolates susceptible (%S) to Cefiderocol, grouped for *Enterobacterales*, *A. baumannii*, *P. aeruginosa* and *Aeromonas* spp with their resistance mechanisms.

Species	Resistance mechanisms	Cefiderocol MIC range (mg/L)	Cefiderocol S%
Enterobacterales (N=29)	EBLS/Carbapenemase producers (KPC, OXA-48, VIM, NDM, NMC/A, IMI-2, CTX-M, PER, VEB, TEM-52, TEM-92, CMY, FOX-7)	≤0.03 - >64	93.1
Pseudomonas aeruginosa (N=6)	Carbapenemase producers (VIM-1, VIM-2, IMP-13, GES-5, FIM)	0.12 - 0.5	100
Acinetobacter baumanii (N=6)	Carbapenemase producers (OXA-23, OXA-24, OXA-58, IS*Aba1*-OXA-51)	0.06 - >64	83.3
Aeromonas spp. (N=1)	ESBL (PER)	>64	0

Cefiderocol was less active against FOX-7-producing *K. pneumoniae* (MIC 8 mg/L), NDM-5-producing *E. coli* (MIC >64 mg/L), OXA-23-producing *A. baumannii* (MIC >64 mg/L) and PER-producing *Aeromonas* spp. (MIC >64 mg/L)

Copi M, et al. *Abstract submitted to ECCMID* 2019

Summary of cefiderocol Phase 2 and Phase 3 studies

Study	NCT number	Study design	Study population	Objectives	Recruitment status
APEKS-cUTI Phase 2[1]	NCT02321800	Multicentre (multinational), randomised, double-blind, parallel-group, active-controlled, non-inferiority	cUTI patients with or without pyelonephritis, or patients with AUP who have a Gram-negative uropathogen likely to be susceptible to IPM	Efficacy and safety	Completed
CREDIBLE-CR Phase 3[2]	NCT02714595	Multicentre (multinational), randomised, open-label, parallel-group, active-controlled	Patients with HAP/VAP/HCAP, cUTI, or BSI/sepsis caused by a carbapenem-resistant Gram-negative pathogen	Efficacy and safety	Completed
APEKS-NP Phase 3[3]	NCT03032380	Multicentre (multinational), randomised, double-blind, parallel-group, active-controlled	Patients with HAP/VAP/HCAP caused by Gram-negative pathogens	Efficacy and safety	Completed

1. Portsmouth S, et al. *Lancet Infect Dis* 2018;18:1319–28. 2. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02714595. Accessed May, 10 2019. 3. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/record/NCT03032380. Accessed May, 10, 2019.

Compassionate Use Programme: report of two cases

Clinical Infectious Diseases

BRIEF REPORT

Compassionate Use of Cefiderocol as Adjunctive Treatment of Native Aortic Valve Endocarditis Due to Extremely Drug-resistant *Pseudomonas aeruginosa*

Jonathan D. Edgeworth,[1] Domenico Merante,[2] Sanjay Patel,[2] Christopher Young,[3] Paul Jones,[4] Seema Vithlani,[5] Duncan Wyncoll,[3] Peter Roberts,[3] Andrew Jones,[3] Tsutae Den Nagata,[6] Mari Ariyasu,[6] David M Livermore,[7,8] and Richard Beale[9]

[1]Department of Infectious Diseases, Guy's Hospital, Kings College London, [2]Shionogi Limited, Global Clinical Development Unit, [3]Intensive Care Unit, London Bridge Hospital, HCA International, [4]Microbiology Department, HCA International, [5]Pharmacy Department, London Bridge Hospital, HCA International, London, United Kingdom; [6]Shionogi & Co., Ltd., Kitaku, Osaka, Japan; [7]Norwich Medical School, University of East Anglia, [8]Antimicrobial Resistance & Healthcare Associated Infections Reference Unit, Public Health England, Colindale, London, and [9]School of Medicine, Guy's Hospital, Kings College London, United Kingdom

CID 2019:68 (1 June) • BRIEF REPORT

Successful treatment with cefiderocol for compassionate use in a critically ill patient with XDR *Acinetobacter baumannii* and KPC-producing *Klebsiella pneumoniae*: a case report

Enrico Maria Trecarichi[1]*, Angela Quirino[2], Vincenzo Scaglione[1], Federico Longhini[3], Eugenio Garofalo[3], Andrea Bruni[3], Eugenio Biamonte[3], Rosaria Lionello[1], Francesca Serapide[1], Maria Mazzitelli[1], Nadia Marascio[2], Giovanni Matera[2], Maria Carla Liberto[2], Paolo Navalesi[3] and Carlo Torti[1] on behalf of the IMAGES Group†

[1]Unit of Infectious and Tropical Diseases, Department of Medical and Surgical Sciences, 'Magna Graecia' University, Catanzaro, Italy; [2]Unit of Clinical Microbiology, Department of Health Sciences, 'Magna Graecia' University, Catanzaro, Italy; [3]Unit of Intensive Care, Department of Medical and Surgical Sciences, 'Magna Graecia' University, Catanzaro, Italy

J Antimicrob Chemother
doi:10.1093/jac/dkz318

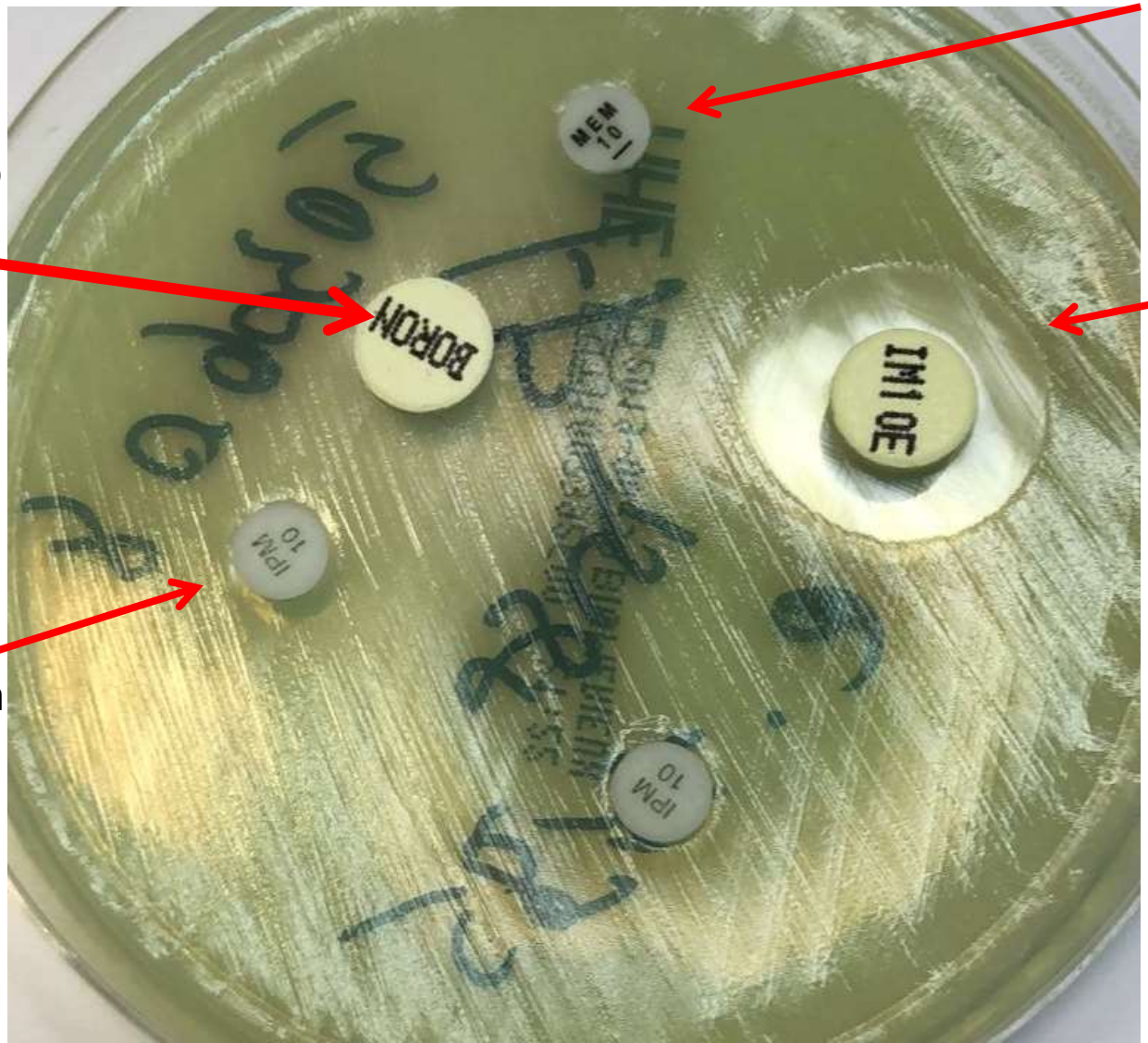
P. aeruginosa MDR: MBL

MEM: meropenem

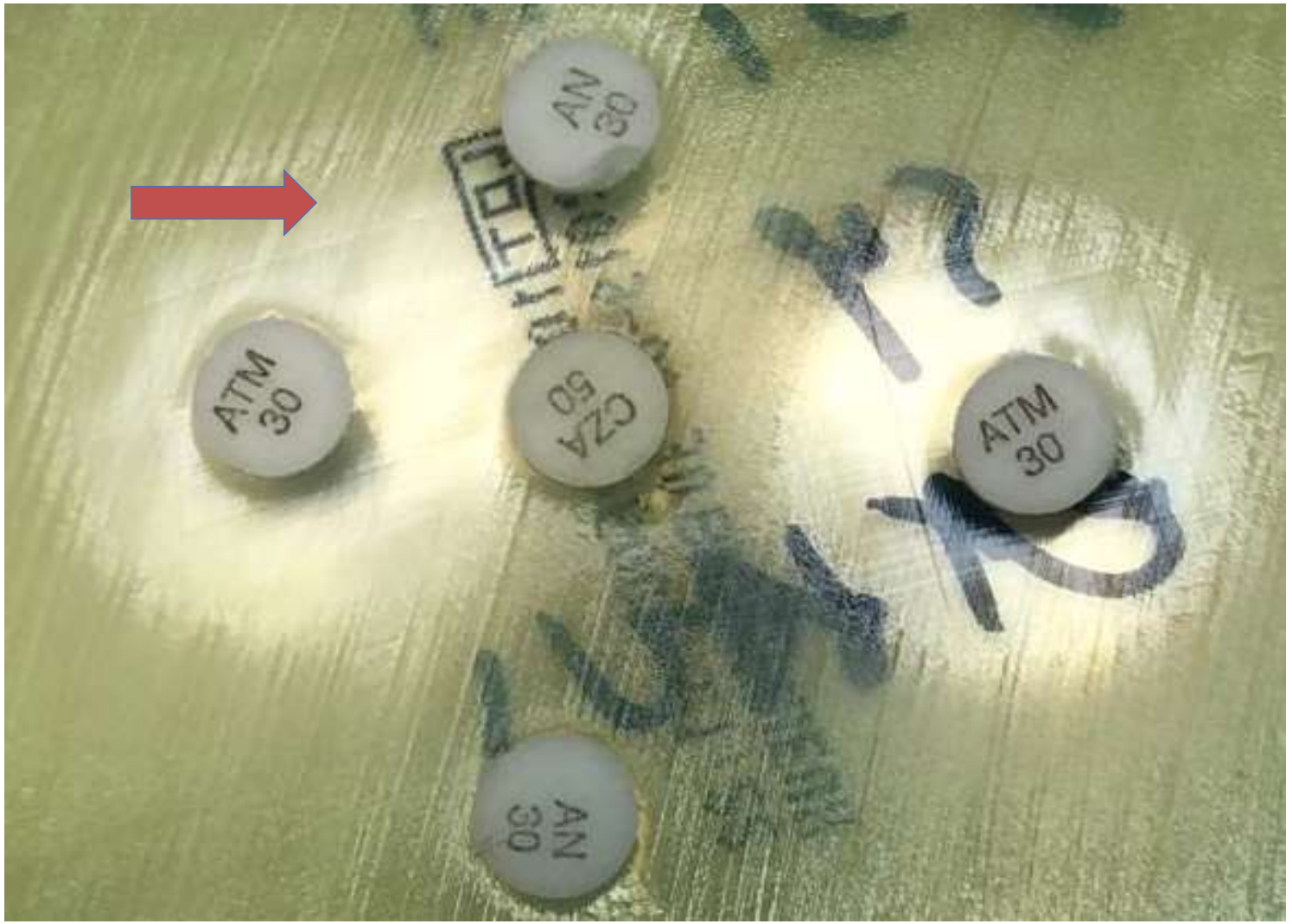
Boron: Acido boronico

IMIE: EDTA + Imipenem

IPM: imipenem



P. aeruginosa MDR

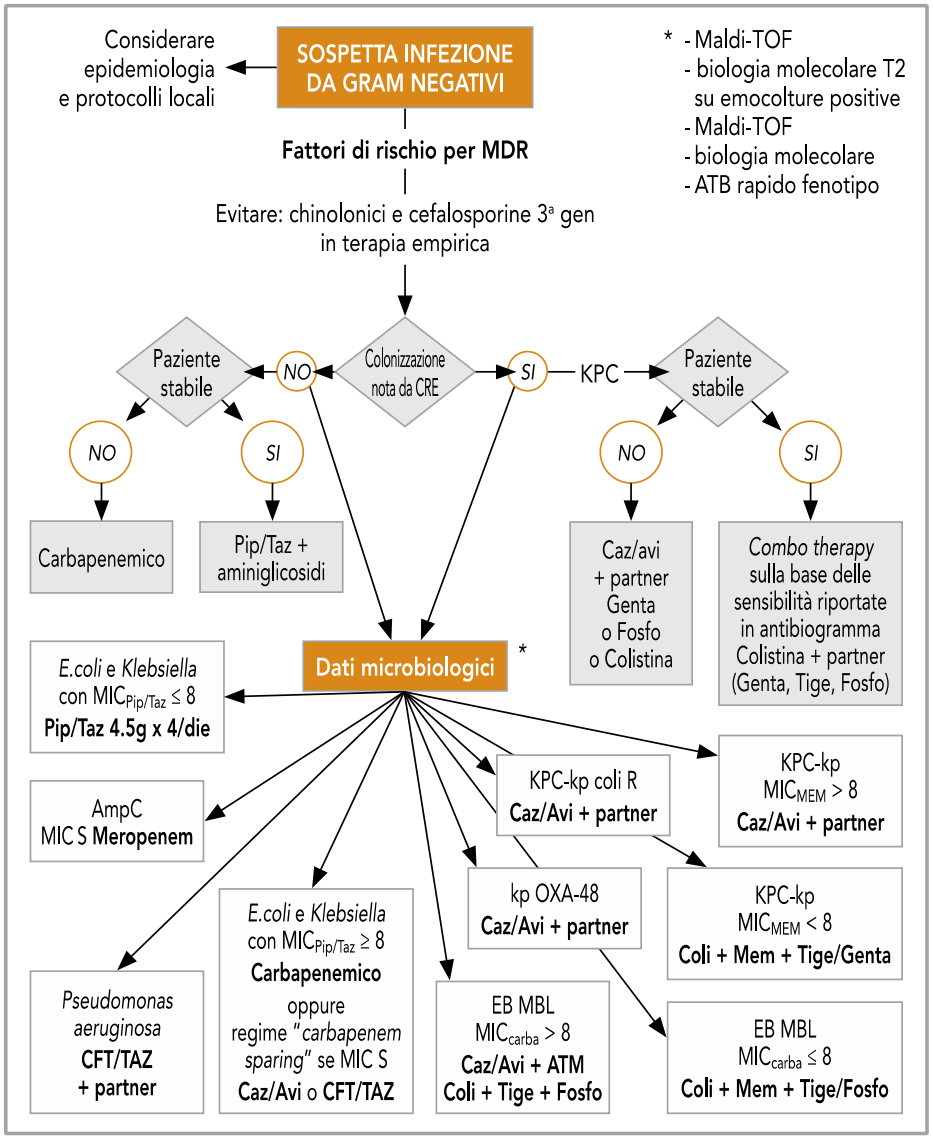


Paziente di 12 anni

- LAM
- Neutropenia profonda e prolungata
- Sepsi da P. aeruginosa
- Ectima gangrenosa genitale e fascite della pelvi
- Fallimento di cazavi, aztreonam d amikacina
- Fallimento di cefiderocol, aztreonam e meropenem
- Decesso

Algoritmo trattamento infezioni da GN MDR

Dove metto Meropenem/ Vaborbactam? Cefiderocol?

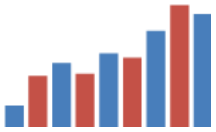


LEGENDA: **CRE**=Carbapenem-resistant Enterobacteriaceae
CFT/TAZ=Ceftolozano/Tazobactam – **Caz/Avi**=Ceftazidime/Avibactam
ATM=Aztreonam – **MEM**=Meropenem.
NOTA: *in paziente non colonizzato da CRE e stabile in caso di non disponibilità di Pip/Taz valutare se cIAI/cUTI CFT/TAZ o Caz/Avi.*

Conclusioni

- Le regole della valutazione degli ospedali devono cambiare
- Bisogna curare lo staf sanitario e l'occupazione dei letti
- Terapie innovative per germi MDR

Diagnostic and Therapeutic approach in critically ill patient with severe infection



daily monitoring of dynamic change of pct

THERAPEUTIC UP-DOWN GRADING

Clinical parameters

Severity of sepsis syndrome

- SOFA Score
- PITT Score
- CPIS Score
- MDR Score

HIGH RISK PATIENT

empirical antimicrobial therapy

targeted antimicrobial therapy

5h

personalized antimicrobial therapy

24h

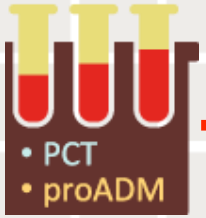
COMMUNICATE INFO AMONG CLINICIAN/LABO/MICRO

sinergy test + tdm

rapid diagnostic test
- Mass spectometry (maldi-tof)
- Phenotypic & molecular methods

Laboratory parameters

Critically ill Patient



- PCT
- proADM

BIOSCORE

SELECTED NEW ANTIBIOTICS (Companion Diagnostics) CDX

MEDIUM RISK PATIENT

empirical antimicrobial therapy

targeted antimicrobial therapy

INTERMEDIATE EVALUATION (optional)
- Bacterioscopic examination
- Rapid Identification by MALDI-ToF

LOW RISK PATIENT

empirical antimicrobial therapy

targeted antimicrobial therapy

Microbiological classic method (72-84 h)

RISK STRATIFICATION

COMBATTING MULTI DRUG RESISTANCE STATUS

antimicrobial stewardship program

reduce antibiotic duration

reduce
H length of stay
Mortality
Pharmacy cost