11.00-12.00 **Terza parte:**
E' indicato abolire la profilassi antibiotica nella neutropenia post-condizionamento del trapianto autologo ed allogenico?

- Presentazione del quesito C. Girmenia (Roma)
- Le ragioni del si C. Tascini (Udine)
- Le ragioni del no A. Candoni (Modena)
- Votazione e discussione C. Girmenia (Roma)

Prof Carlo Tascini
Direttore Clinica Malattie Infettive
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Conflict of interest Disclosure

prof. Carlo Tascini has received in the last two years grants as a speaker at symposia from:

- Astrazeneca
- AVIR Pharma
- Merck
- Pfizer
- Astellas
- Angelini
- Gilead
- Novartis
- Biotest
- Thermofischer
- Correvio/Advanz Pharma
- Basilea
- Biomerieux
- Hikma
- Zambon
- Menarini
- Shionogi

Tesi di Laurea di Carlo Tascini 1989

- I chinoloni di terza generazione nella terapia delle malattie infettive (relatore prof Sergio Pauluzzi):
- Le resistenze ai chinoloni saranno rare perché bloccano la DNA girasi anche dei plasmidi!!!!

ORIGINAL ARTICLE

Molecular typing of fluoroquinolone-resistant and fluoroquinolone-susceptible *Escherichia coli* isolated from blood of neutropenic cancer patients in a single center

Clin Microbiol Infect 1999; 5: 457–461

Carlo Tascini[1], Francesco Menichetti[2], Silvia Bozza[1], Monica Fedele[1], Roberta Preziosi[1], Massimo Allegrucci[3], Albano Del Favero[4], Alessandra Micozzi[5], Piero Martino[5] and Francesco Bistoni[1]

[1]Microbiology Section, Department of Experimental Medicine and Biochemical Sciences, [2]Institute of Infectious Diseases, [3]Pharmacology Section, Department of Experimental Medicine and Biochemical Science, [4]Institute of Internal Medicine, University of Perugia, Perugia, [5]Chair of Hematology, University 'La Sapienza', Rome, Italy

Results: PFGE analysis was able to type all FQ-S isolates and most (17/19, 89%) FQ-R isolates of *E. coli*. All isolates were genotypically unrelated, with the exception of two indistinguishable FQ-R isolates from different patients in the same period. RAPD analysis typed all isolates, including those FQ-R isolates untypable by PFGE, but was unable to distinguish between some isolates that were different by PFGE. Using primer 1247, RAPD analysis identified six pairs and one triad, while primer 1283 identified seven pairs and one triad of indistinguishable isolates.

Conclusions: No spread of epidemic FQ-R or FQ-S *E. coli* isolates was documented among neutropenic patients. RAPD analysis is a powerful genotyping method, but appeared to be less reproducible and discriminatory than PFGE for investigating *E. coli* isolates.

Key words: *Escherichia coli*, fluoroquinolone resistance, neutropenic patients, PFGE, RAPD

Table 2 Ciprofloxacin MICs for *E. coli* isolates included in the study

Isolate identification	Patient identification	Isolation date	Ciprofloxacin MIC (mg/L)
L59	1	12 January 1990	0.5
L61	2	6 February 1990	0.5
L62	3	23 April 1990	2000
L64	4	25 May 1990	0.25
L66	5	4 June 1990	0.5
L67	6	23 July 1990	0.125
L68	7	13 August 1990	0.125
L69	8	7 September 1990	0.0625
L70	9	3 October 1990	0.5
L71	10	10 October 1971	0.125
L72	11	11 October 1990	0.125
L74	12	25 October 1990	0.125
L75	13	28 October 1990	0.125
L76	14	21 November 1990	0.125
L78	15	23 December 1990	0.125
L79	16	29 December 1990	0.125
L80	17	31 December 1990	2000
L82	18	25 February 1991	0.125
L83	19	16 March 1991	0.125
L87	20	2 September 1991	0.125
L90	21	17 December 1991	1000
L132	22	27 July 1991	0.125
L177	23	17 July 1991	1000
L194	24	30 July 1992	2000
L198	25	9 September 1992	0.125
L200	26	13 September 1992	0.125
L278	27	31 January 1994	0.125
L281	28	11 February 1994	2000
L282	29	7 February 1994	1000
L346	30	19 June 1995	2000
L347	23	1 October 1994	1000
L394	31	11 June 1995	1000
L402	32	19 July 1995	1000
L412	33	17 September 1995	1000
L421	34	9 October 1995	0.125
L426	35	21 October 1995	0.125
L428	36	28 October 1995	1000
L433	37	6 November 1995	0.125
L444	38	7 January 1996	1000
L445	39	9 January 1996	2000
L449	40	15 January 1996	1000
L451	41	18 January 1996	0.125
L454	42	12 February 1996	2000
L456	43	20 February 1996	2000
L457	44	20 February 1996	1000
L467	45	24 May 1996	0.125

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 8, 2005 VOL. 353 NO. 10

Levofloxacin to Prevent Bacterial Infection in Patients with Cancer and Neutropenia

Giampaolo Bucaneve, M.D., Alessandra Micozzi, M.D., Francesco Menichetti, M.D., Pietro Martino, M.D., M. Stella Dionisi, M.D., Giovanni Martinelli, M.D., Bernardino Allione, M.D., Domenico D'Antonio, M.D., Maurizio Buelli, M.D., A. Maria Nosari, M.D., Daniela Cilloni, M.D., Eliana Zuffa, M.D., Renato Cantaffa, M.D., Giorgina Specchia, M.D., Sergio Amadori, M.D., Francesco Fabbiano, M.D., Giorgio Lambertenghi Deliliers, M.D., Francesco Lauria, M.D., Robin Foà, M.D., and Albano Del Favero, M.D., for the Gruppo Italiano Malattie Ematologiche dell'Adulto (GIMEMA) Infection Program*

500 mg die (dose bassa prona a selezionare resistenza)
Esclusi i pazienti allotrapiantati
NNT febbre: 1:5

Table 1. Characteristics of the 675 Patients Whose Response to Therapy Could Be Assessed.

Characteristic	Patients with Solid Tumors or Lymphoma		Patients with Leukemia	
	Levofloxacin (N=174)	Placebo (N=171)	Levofloxacin (N=165)	Placebo (N=165)
Age — yr				
Mean	47	49	48	49
Range	19–72	18–70	18–75	18–75
Sex — no. (%)				
Male	102 (59)	93 (54)	88 (53)	87 (53)
Female	72 (41)	78 (46)	77 (47)	78 (47)
Underlying cancer — no. (%)				
Acute leukemia	—	—	164 (99)	163 (99)
Lymphoma and Hodgkin's disease	112 (64)	100 (58)	—	—
Solid tumor	24 (14)	22 (13)	—	—
Other hematologic cancers	38 (22)	49 (29)	1 (1)	2 (1)

Group and Event	Levofloxacin no./total no. (%)	Placebo no./total no. (%)	Absolute Difference in Risk (95% CI)
All treated patients			
Febrile episode	243/375 (65)	308/363 (85)	−0.20 (−0.26 to −0.14)
Death	10/373 (3)	18/363 (5)	−0.02 (−0.05 to 0.005)
All assessable patients			
Febrile episode	221/339 (65)	290/336 (86)	−0.21 (−0.27 to −0.14)
Microbiologically documented infection	74/339 (22)	131/336 (39)	−0.17 (−0.24 to −0.10)
Gram-positive	42/339 (12)	61/336 (18)	−0.06 (−0.11 to −0.003)
Gram-negative	21/339 (6)	47/336 (14)	−0.08 (−0.12 to −0.03)
Polymicrobial	11/339 (3)	23/336 (7)	−0.04 (−0.06 to −0.003)
Bacteremia	62/339 (18)	115/336 (34)	−0.16 (−0.22 to −0.09)
Gram-positive	37/339 (11)	54/336 (16)	−0.05 (−0.10 to 0.00)
Gram-negative	15/339 (4)	38/336 (11)	−0.07 (−0.10 to −0.02)
Polymicrobial	10/339 (3)	23/336 (7)	−0.04 (−0.07 to −0.01)
Clinically documented infection	30/339 (9)	33/336 (10)	−0.01 (−0.05 to 0.03)
Fever of unknown origin	117/339 (34)	126/336 (37)	−0.03 (−0.10 to 0.04)

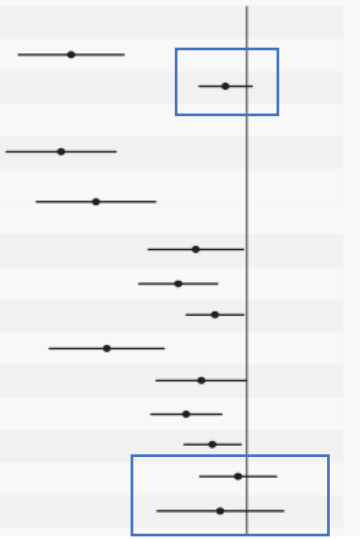

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Table 2. Characteristics of Bacterial Isolates and Number with Resistance to Levofloxacin.

Characteristic	Levofloxacin (N=339)	Placebo (N=336)
Microbiologically documented infection	74	131
No. with bacteremia	62	115
Single gram-positive isolate	37	54
S. aureus	0	10
Coagulase-negative staphylococcus	31	32
Streptococcus species	5	9
Other gram-positive organisms	1	3
Single gram-negative isolate	15	38
Pseudomonas species	6	8
E. coli	7	22
Other gram-negative organisms	2	8
Levofloxacin resistance in single-agent bacteremias — no. resistant/total no. available for analysis	41/47	32/68
Gram-positive isolate	31/34	28/44
S. aureus	0	1/7
Coagulase-negative staphylococcus	27/30	26/31
Streptococcus species	4/4	1/3
Other gram-positive organisms	0	0/3
Gram-negative isolate	10/13	4/24
Pseudomonas species	4/6	1/4
E. coli	5/5	2/16
Other gram-negative organisms	1/2	1/4

Antibiotic Prophylaxis in Neutropenic Patients

New Evidence, Practical Decisions

Leonard Leibovici, MD[1,2]
Mical Paul, MD[1,2]
Michael Cullen, MD[3]
Giampaolo Bucaneve, MD[4]
Anat Gafter-Gvili, MD[1,2]
Abigail Fraser, MPH[1]
Winfried V. Kern, MD[5]

interval [95% CI], 2–54%). Thus, 55 patients who have acute leukemia or who undergo bone marrow transplantation must receive prophylaxis to prevent 1 death. In 4 studies that included patients with solid tumors or lymphoma, prophy-

33% (95% CI, 2–54%). Because mortality during neutropenia has declined in recent years, a rate of 5.5% deaths in the control group was used (derived from studies that were performed after 2000) to estimate that 55 patients with acute leukemia or who received high-dose chemotherapy with stem cell transplantation needed to receive prophylaxis with a fluoroquinolone to prevent 1 death.

a secondary consideration. Patients who received fluoroquinolones for prophylaxis suffered more side effects than patients who received placebo or no treatment (RR, 1.41; 95% CI, 1.09–1.83), resulting in 25 as the number needed to harm.[1] However, all of those

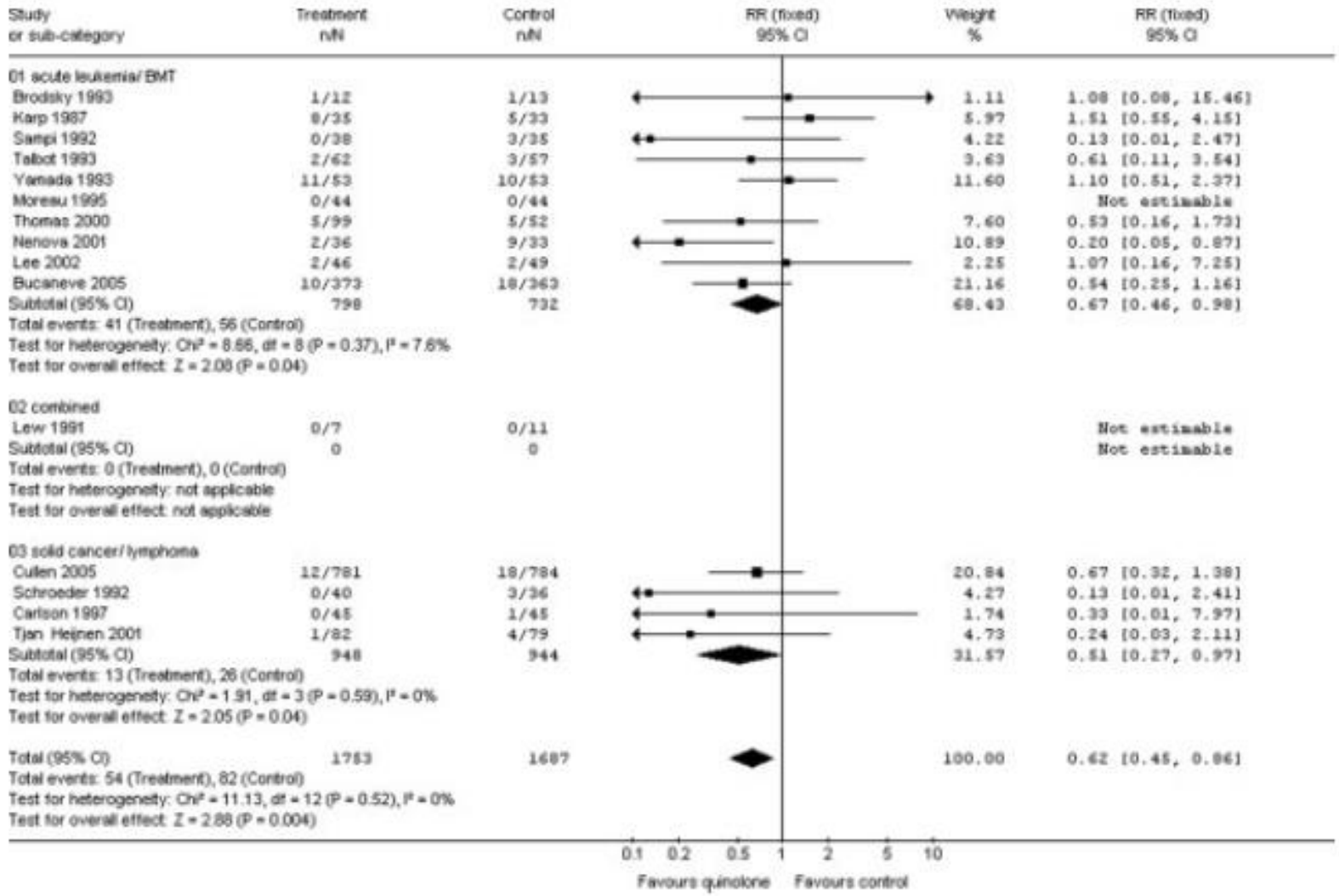

FIGURE 1. This chart illustrates the relative risks (RR) with 95% confidence intervals (95% CI) for all-cause mortality in patients who received fluoroquinolones versus patients who received either placebo or no treatment (the 2 recent trials [Bucaneve et al., 2005[2]; Cullen et al., 2005[3]] were included). Studies are listed according to lead the author and the year (see the list of References). BMT indicates bone marrow transplantation; Chi^2, chi-square test; df, degrees of freedom; I^2, test for heterogeneity.

Antibiotic Prophylaxis in Neutropenic Patients

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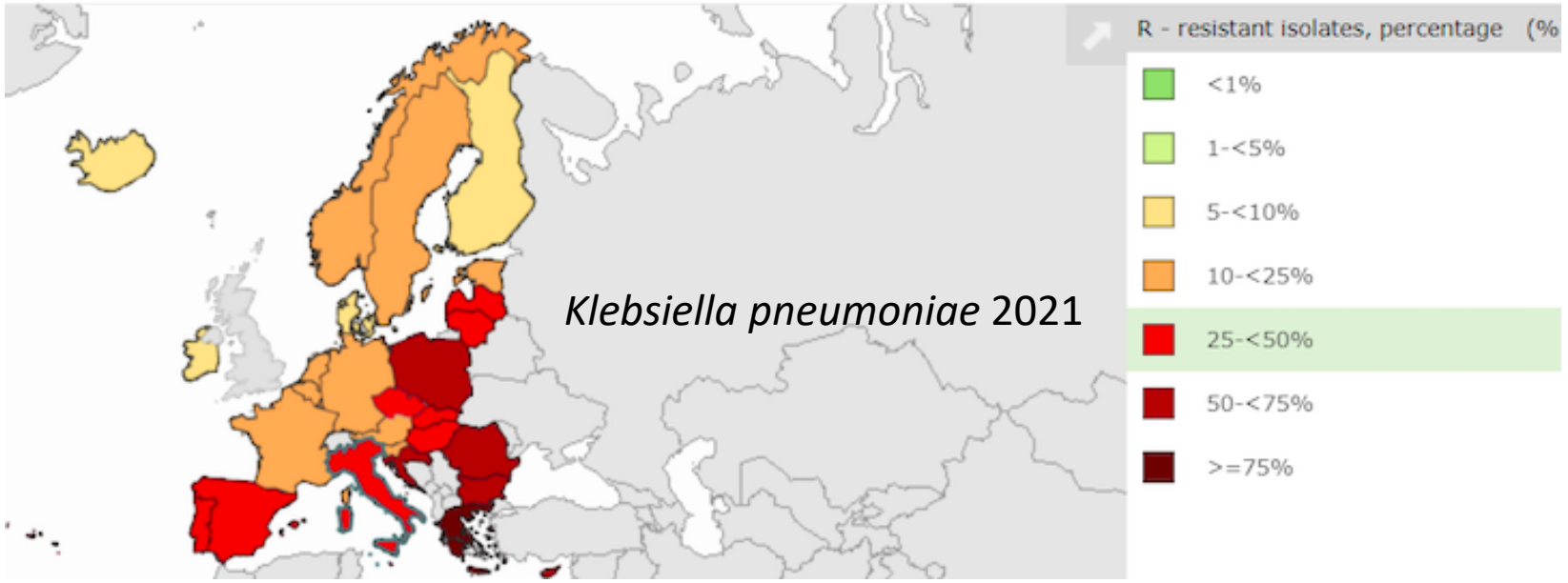
GIMEMA study[2] as it was in previous studies.[1] The GIMEMA study was conducted in a population with nearly 50% resistance to fluoroquinolones in all pathogens and 20% resistance in gram-negative isolates in the control group and in a country with a baseline resistance of approximately 20% in gram-negative isolates from the community[40] and medical departments.[41] Prophylaxis should be considered in locations that have similar or less resistance.



Klebsiella pneumoniae 2021

E. coli 2021

P. aeruginosa 2021

Tabella 6. Risultati delle rilevazioni sulle % di antibiotico resistenza di *E. coli* svolte nel 2019 dai Labora

Escherichia coli			TUTTI I MATERIALI Numero di isolati = 11.896						SANGUE E LIQUOR Numero di isolati = 918						RESPI Numero di		
Principio attivo	**Antibiotic class**	**Antibiotic subclass**	**Codice**	**Num.**	**%R**	**%I**	**%S**	**%R 95%C.I.**	**Codice**	**Num.**	**%R**	**%I**	**%S**	**%R 95%C.I.**	**Codice**	**Num.**	**%R**
Ampicilina	Penicillins	Aminopenicillins	AMP	5.760	**70,6**	**0,0**	**29,4**	69,4-71,7	AMP	451	**79,4**	0	20,6	75,6-83,1	AMP	216	**81,9**
Amoxicilina/Acido clav.	Beta-lactam+Inib.		AMC	10.153	**44,5**	0	55,5	43,5-45,5	AMC	846	**52,4**	0	47,6	49,0-55,7	AMC	640	**57,3**
Piperacilina/Tazob.	Beta-lactam+Inib.		TZP	11.143	**11,3**	2,4	86,4	10,7-11,9	TZP	910	**10,8**	4,3	84,9	8,8-12,8	TZP	692	**16,9**
Cefotaxima	Cephems	Cephalosporins III	CTX	10.705	**31,6**	0,4	68	30,7-32,4	CTX	821	**44,7**	0,5	54,8	41,3-48,1	CTX	646	**41,6**
Ceftazidima	Cephems	Cephalosporins III	CAZ	11.878	**24,8**	5,6	69,6	24,0-25,6	CAZ	917	**38,3**	5,3	56,4	35,1-41,4	CAZ	695	**32,5**
Cefepima	Cephems	Cephalosporins IV	FEP	7.485	**21,5**	7,6	70,9	20,6-22,4	FEP	516	**36,6**	6,6	56,8	32,5-40,8	FEP	291	**28,9**
Ciprofloxacina	Quinolones	Fluoroquinolones	CIP	11.873	**45,4**	4,2	50,4	44,5-46,3	CIP	915	**59,8**	2	38,3	56,6-63,0	CIP	697	**53,8**
Levofloxacina	Quinolones	Fluoroquinolones	LVX	2.352	**46**	2,8	51,2	44,0-48,0	LVX	429	**59,4**	0,5	40,1	54,8-64,1	LVX	200	**59**
Amikacina	Aminoglycosides		AMK	9.572	**1**	4,2	94,7	0,8-1,2	AMK	914	**1,6**	5,9	92,5	0,8-2,5	AMK	687	**1,9**
Gentamicina	Aminoglycosides		GEN	11.878	**19,1**	0,9	80	18,4-19,9	GEN	917	**28,1**	0,7	71,2	25,2-31,0	GEN	696	**24,3**
Imipenem	Penems	Carbapenems	IPM	6.398	**0,7**	1,5	97,8	0,5-0,9	IPM	505	**0,6**	0,6	98,8	0,0-1,3	IPM**	273	**1,1**
Meropenem	Penems	Carbapenems	MEM	11.862	**0,9**	0,5	98,6	0,7-1,1	MEM	915	**0,7**	0,3	99	0,1-1,2	MEM	692	**1,9**
Ertapenem	Penems	Carbapenems	ETP	10.864	**2,6**	0,3	97,1	2,3-2,9	ETP	902	**1,1**	0,2	98,7	0,4-1,8	ETP	684	**3,1**
Fosfomicina	Fosfomycins	Fosfomycins	FOS	10.890	**3,8**	0	96,2	3,5-4,2	FOS	839	**1,5**	0	98,5	0,7-2,4	FOS	667	**3,9**
Tigecycline	Tetracyclines	Glycylglycines	TGC	8.124	**7,1**	0,8	92,1	6,5-7,7	TGC	874	**4,3**	0,5	95,2	3,0-5,7	TGC	649	**7,9**
Nitrofurantoina	Nitrofurans		NIT	6.428	**3,3**	0	96,7	2,9-3,8									

** Numerosità insufficiente per avere una buona stima campionaria

Tabella 8. Risultati delle rilevazioni sulle % di antibiotico resistenza di *P. aeruginosa* svolte nel 2019 dai L

Pseudomonas aeruginosa			TUTTI I MATERIALI Numero di isolati = 4.330						SANGUE E LIQUOR Numero di isolati = 270						RESPI Numero di i		
Principio attivo	Antibiotic class	Antibiotic subclass	Codice	Num.	%R	%I	%S	%R 95%C.I.	Codice	Num.	%R	%I	%S	%R 95%C.I.	Codice	Num.	%R
Amikacina	Aminoglycosides		AMK	4163	8,9	3,7	87,4	8,0-9,8	AMK**	269	6,7	4,5	88,8	3,7-9,7	AMK	1751	8,3
Gentamicina	Aminoglycosides		GEN	4321	21,2	0,0	78,8	19,9-22,4	GEN**	270	17,8	0,0	82,2	13,2-22,3	GEN	1769	19,1
Piperacillina/Tazobactam	Beta-lactam+Inhib.		TZP	1246	38,0	0,0	62,0	35,3-40,7	TZP**	269	28,6	0,0	71,4	23,2-34,0	TZP	1745	31,9
Ceftazidima	Cephems	Cephalosporins III	FEP	4322	26,1	0,0	73,9	24,8-27,4	FEP**	269	23,8	0,0	76,2	18,7-28,9	FEP	1771	22,4
Cefepima	Cephems	Cephalosporins IV	CAZ	2186	30,5	0,0	69,4	28,6-32,4	CAZ**	148	27,7	0,0	72,3	20,5-34,9	CAZ	792	26,6
Ciprofloxacina	Quinolones	Fluoroquinolones	CIP	4315	35,0	0,0	65,0	33,6-36,4	CIP**	269	24,2	0,0	75,8	19,0-29,3	CIP	1767	32,6
Levofloxacina	Quinolones	Fluoroquinolones	LVX	1439	46,5	0,1	53,4	43,9-49,1	LVX**	122	32,0	0,0	68,0	23,7-40,2	LVX	520	50,6
Colistina	Lipopeptides		COL	1940	8,7	0,0	91,3	7,4-9,9	COL**	139	5,8	0,0	94,2	1,9-9,6	COL	734	10,5
Imipenem	Penems	Carbapenems	IPM	2034	24,8	4,3	70,9	23,0-26,7	IPM**	149	24,2	3,4	72,5	17,3-31,0	IPM	741	28,6
Meropenem	Penems	Carbapenems	MEM	4298	15,0	10,3	74,8	13,9-16,0	MEM**	269	12,6	10,4	77,0	8,7-16,6	MEM	1759	16,4

** Numerosità insufficiente per avere una buona stima campionaria

2020 FVG

RETE CURE SICURE FVG

Prescrivere antibiotici solo quando è veramente necessario

Trattare le infezioni (presenza di sintomi) e non le colonizzazioni (es. di ferite superficiali, delle vie aeree superiori, batteriurie asintomatiche, ecc.)

Aumentare l'adesione alle misure di controllo della trasmissione dei microrganismi, in particolare l'igiene delle mani.

L'uso di un antibiotico è sconsigliato, perché meno efficace, se la sua percentuale di resistenza è ≥20-30% nell'epidemiologia locale; la perdita dell'efficacia è documentata graficamente con la simbologia come segue:

verde	Resistente + Intermedio < 20%
giallo	Resistente + Intermedio 20-30%
rosso	Resistente + Intermedio > 30%

Principali microrganismi gram negativi isolati da tutti i materiali

	Escherichia coli			*Klebsiella spp.*			*Proteus spp.*			Altri enterobatteri			*Pseudomonas aeruginosa*		
	Testati	R+I[4]	%	Testati	R+I[4]	%	Testati	R+I[4]	%	Testati	R+I[4]	%	Testati	R+I[4]	%
Amikacina	8923	111	**1,2**	2479	51	**2,1**	1427	27	**1,9**	2055	41	**2,0**	2121	91	**4,3**
Amoxicillina/ac. clavulanico	12251	3686	**30,1**	3098	639	**20,6**	1778	348	**19,6**	-	-	-	-	-	-
Cefepima	9525	757	**7,9**	2363	226	**9,6**	1185	55	**4,6**	1733	54	**3,1**	1857	202	**10,9**
Cefotaxime	9000	900	**10,0**	2310	253	**11,0**	1427	139	**9,7**	1970	319	**16,2**	-	-	-
Ceftazidime	9950	809	**8,1**	2505	280	**11,2**	1277	87	**6,8**	1925	278	**14,4**	2123	216	**10,2**
Ciprofloxacina	12957	2825	**21,8**	3290	384	**11,7**	1866	539	**28,9**	2648	273	**10,3**	2123	350	**16,5**
Colistina	-	-	-	758	58	**7,7**	-	-	-	-	-	-	-	-	-
Gentamicina	12955	943	**7,3**	3288	135	**4,1**	1865	323	**17,3**	2646	182	**6,9**	1622	119	**7,3**
Meropenem	9702	3	**0,0**	2372	75	**3,2**	1206	1	**0,1**	1689	2	**0,1**	1915	154	**8,0**
Piperacillina/tazobactam	11408	721	**6,3**	2942	413	**14,0**	1666	21	**1,3**	2378	211	**8,9**	2091	284	**13,6**
Trimet./sulfamet.	12831	3142	**24,5**	3268	367	**11,2**	1852	873	**47,1**	2634	219	**8,3**	-	-	-

Fluorochinoloni possono selezionare ceppi resistenti

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0066-4804/10/$12.00 doi:10.1128/AAC.01131-09

Treatment with Fluoroquinolones or with β-Lactam–β-Lactamase Inhibitor Combinations Is a Risk Factor for Isolation of Extended-Spectrum-β-Lactamase-Producing *Klebsiella* Species in Hospitalized Patients▽

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Clinical Infectious Diseases
MAJOR ARTICLE

Fluoroquinolone Prophylaxis Selects for Meropenem-nonsusceptible *Pseudomonas aeruginosa* in Patients With Hematologic Malignancies and Hematopoietic Cell Transplant Recipients

Morgan Hakki,[1] Romney M. Humphries,[2] Peera Hemarajata,[3] Gregory B. Tallman,[4] Ryan K. Shields,[5] Roberta T. Mettus,[5] Yohei Doi,[5,6] and James S. Lewis ..

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Results. We analyzed 55 episodes of *P. aeruginosa* bacteremia among 51 patients. Breakthrough bacteremia while on fluoroquinolone prophylaxis was associated with nonsusceptibility to meropenem, but not to antipseudomonal β-lactams or aminoglycosides. The receipt of fluoroquinolone prophylaxis was independently predictive of bacteremia with a meropenem-nonsusceptible isolate. All meropenem-nonsusceptible isolates analyzed by WGS contained *oprD* inactivating mutations, and all meropenem-nonsusceptible isolates tested demonstrated reductions in the meropenem minimum inhibitory concentration in the presence of an efflux pump inhibitor. A phylogenetic analysis based on WGS revealed several clusters of closely related isolates from different patients.

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Original article

Effect of outpatient antibiotics for urinary tract infections on antimicrobial resistance among commensal *Enterobacteriaceae*: a multinational prospective cohort study

A.J. Stewardson [1, 2, 3, *], J. Vervoort [4], N. Adriaenssens [4, 5], S. Coenen [4, 5], M. Godycki-Cwirko [6, 7], A. Kowalczyk [7], B.D. Huttner [1, 8], C. Lammens [4], S. Malhotra-Kumar [4], H. Goossens [4], S. Harbarth [1, 8] on behalf of SATURN WP1 Study Group, SATURN WP3 Study Group[9]

Chinoloni aumentano i ceppi resistenti tra i conviventi di pazienti trattati con chinoloni

Results: We included 300 households (205 exposed, 95 non-exposed) with 716 participants. Most exposed patients received nitrofurans (86; 42%) or fluoroquinolones (76; 37%). CIP-RE were identified in 16% (328/2033) of samples from 202 (28%) participants. Fluoroquinolone treatment caused transient suppression of *Enterobacteriaceae* (S2) and subsequent two-fold increase in CIP-RE prevalence at S3 (adjusted prevalence ratio (aPR) 2.0, 95% CI 1.2–3.4), with corresponding number-needed-to-harm of 12. Nitrofurans had no impact on CIP-RE (aPR 1.0, 95% CI 0.5–1.8) or NIT-RE. ESBL-PE were identified in 5% (107/2058) of samples from 71 (10%) participants, with colonization not associated with antibiotic exposure. Household exposure to CIP-RE or ESBL-PE was associated with increased individual risk of colonization: aPR 1.8 (95% CI 1.3–2.5) and 3.4 (95% CI 1.3–9.0), respectively.

Conclusions: These findings support avoidance of fluoroquinolones for first-line UTI therapy in primary care, and suggest potential for interventions that interrupt household circulation of resistant *Enterobacteriaceae*. **A.J. Stewardson, Clin Microbiol Infect 2018;24:972**

Profilassi nel trapianto di midollo

Journal of Infection (2014) 69, 13–25

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BIAM British Infection Association

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REVIEW

Antibiotic prophylaxis in hematopoietic stem cell transplantation. A meta-analysis of randomized controlled trials.

Shun-ichi Kimura, Yu Akahoshi, Hirofumi Nakano, Tomotaka Ugai, Hidenori Wada, Ryoko Yamasaki, Yuko Ishihara, Koji Kawamura, Kana Sakamoto, Masahiro Ashizawa, Miki Sato, Kiriko Terasako-Saito, Hideki Nakasone, Misato Kikuchi, Rie Yamazaki, Shinichi Kako, Junya Kanda, Aki Tanihara, Junji Nishida, Yoshinobu Kanda*

Results: Seventeen trials with 1453 autologous and allogeneic HSCT recipients were included. Systemic antibiotic prophylaxis was compared with placebo or no prophylaxis in 10 trials and with non-absorbable antibiotics in two trials. Systemic antibiotics other than fluoroquinolones were evaluated in five of these 12 trials. Four trials evaluated the effect of the addition of antibiotics for gram-positive bacteria to fluoroquinolones. One trial compared two different systemic antibiotic regimens: fluoroquinolones versus trimethoprim-sulfamethoxazole. As a result, systemic antibiotic prophylaxis reduced the incidence of febrile episodes (OR 0.16; 95%CI 0.09–0.30), clinically or microbiologically documented infection (OR 0.38; 95%CI 0.22–0.63) and bacteremia (OR 0.31; 95%CI 0.16–0.59) without significantly affecting all-cause mortality or infection-related mortality.

Conclusions: Systemic antibiotic prophylaxis successfully reduced the incidence of infection. However, there was no significant impact on mortality. The clinical benefits of prophylaxis with fluoroquinolones were inconclusive because of the small number of clinical trials evaluated.

Clinical Infectious Diseases

MAJOR ARTICLE

Incidence, Risk Factors and Outcome of Pre-engraftment Gram-Negative Bacteremia After Allogeneic and Autologous Hematopoietic Stem Cell Transplantation: An Italian Prospective Multicenter Survey

Corrado Girmenia,[1] Alice Bertaina,[2] Alfonso Piciocchi,[3] Katia Perruccio,[4] Alessandra Algarotti,[5] Alessandro Busca,[6] Chiara Cattaneo,[7] Anna Maria Raiola,[8] Stefano Guidi,[9] Anna Paola Iori,[1] Anna Candoni,[10] Giuseppe Irrera,[11] Giuseppe Milone,[12] Giampaolo Marcacci,[13] Rosanna Scimè,[14] Maurizio Musso,[15] Laura Cudillo,[16] Simona Sica,[17] Luca Castagna,[18] Paolo Corradini,[19] Francesco Marchesi,[20] Domenico Pastore,[21] Emilio Paolo Alessandrino,[22] Claudio Annaloro,[23] Fabio Ciceri,[24] Stella Santarone,[25] Luca Nassi,[26] Claudio Farina,[27] Claudio Viscoli,[28] Gian Maria Rossolini,[29,30] Francesca Bonifazi,[31,a] and Alessandro Rambaldi,[5,32,a] for the Gruppo Italiano Trapianto di Midollo Osseo (GITMO) and Associazione Microbiologi Clinici Italiani (AMCLI).

Pseudomonas CR e CRE possono essere profilassati dai chinoloni? No

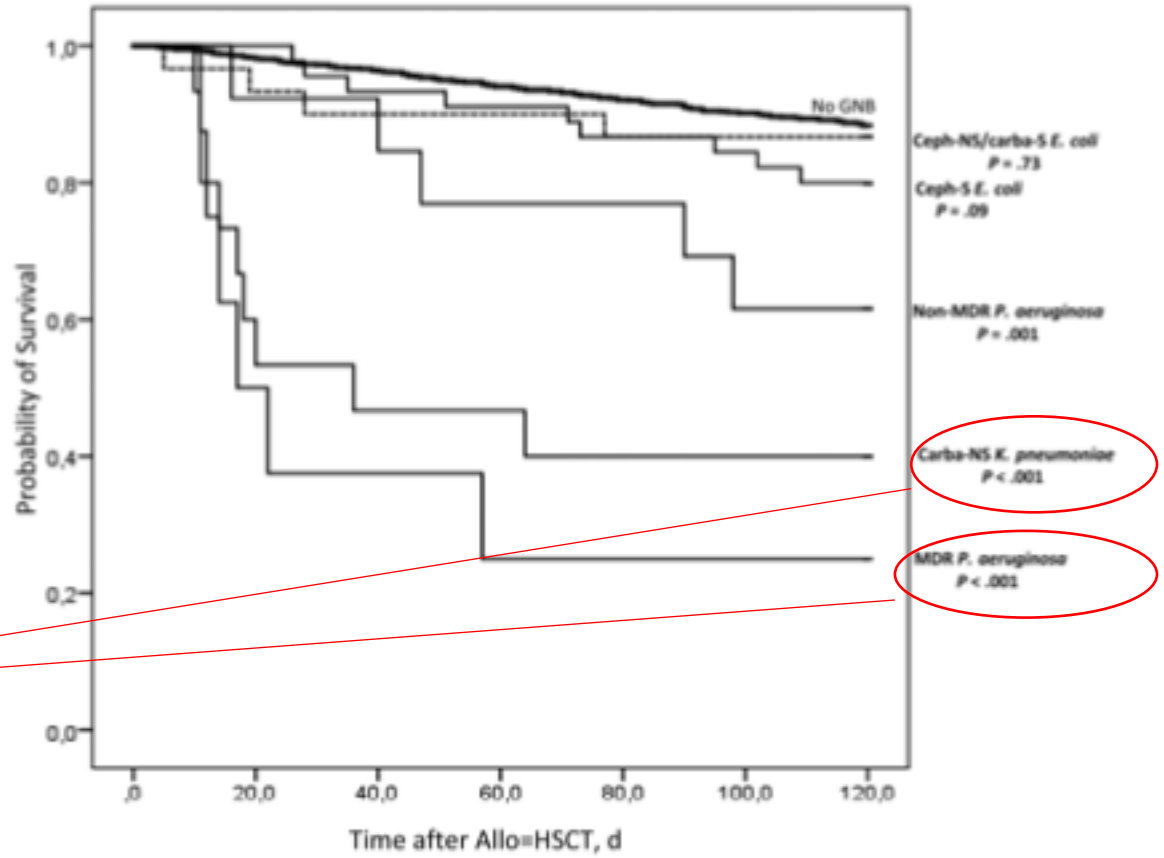


Figure 4. Probability of survival 4 months after allogeneic hematopoietic stem cell transplantation (allo-HSCT) according to the development of pre-engraftment gram-negative bacteremia caused by different species. (The probability of survival was not calculated for other pathogens, for which the number of episodes was very low.) Abbreviations: Carba-NS, nonsensitive to carbapenems; carba-S, sensitive to carbapenems; ceph-NS, nonsensitive to the third-generation cephalosporin ceftazidime; ceph-S, sensitive to ceftazidime; *E. coli, Escherichia coli*; *K. pneumoniae, Klebsiella pneumoniae*; MDR, multidrug-resistant; *P. aeruginosa, Pseudomonas aeruginosa*.

SEIFEM: Italian epidemiology

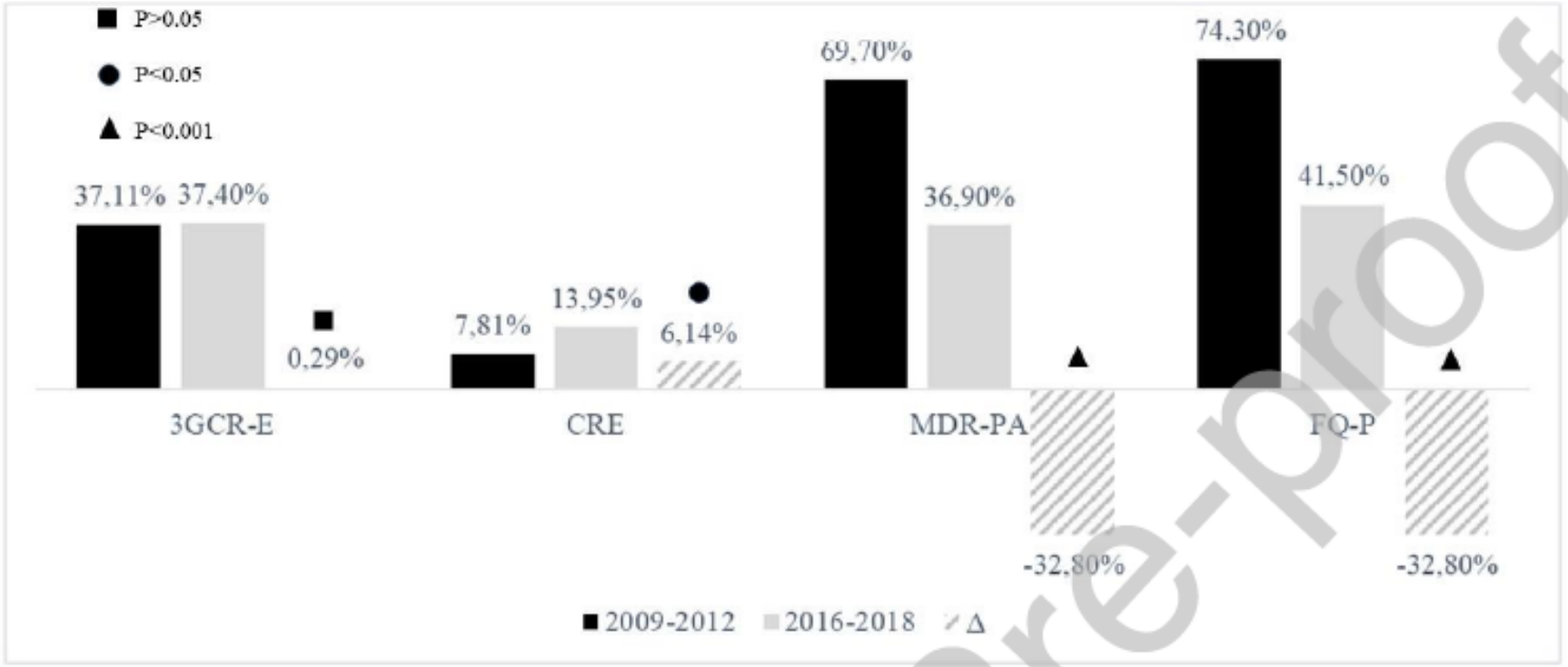
- Most frequently isolated bacteria and susceptibility profiles

Microorganisms	Total							MDR isolates
		Ceftazidime	Ciprofloxacin	Meropenem	Amikacin	Gentamicin	Piperacillin/ tazobactam	
Total	834	516 (61.9)	335 (40.2)	675 (80.9)	663 (79.5)	606 (72.6)	555 (66.5)	256 (30.7)
Escherichia coli	440	315 (71.6)	147 (33.4)	436 (99.1)	394 (89.6)	355 (80.7)	360 (81.8)	75 (17.1)
Klebsiella pneumoniae	160	57 (35.6)	48 (30.0)	78 (48.7)	100 (62.5)	86 (53.7)	55 (34.4)	101 (63.1)
Pseudomonas aeruginosa	122	81 (66.4)	73 (59.8)	80 (65.6)	89 (72.9)	86 (70.5)	74 (60.6)	45 (36.9)
Enterobacter cloacae	31	23 (74.2)	24 (77.4)	29 (93.5)	31 (100)	28 (90.3)	23 (74.2)	4 (12.9)
Acinetobacter baumannii	14	1 (7.1)	5 (35.7)	5 (35.7)	5 (35.7)	6 (42.8)	3 (21.4)	9 (64.3)
Stenotrophomonas maltophilia[a]	14	NA	NA	NA	NA	NA	NA	14 (100)
Others	53	39 (73.6)	38 (71.7)	47 (88.7)	44 (83.2)	45 (84.9)	40 (75.5)	8 (15.1)
MDR isolates	256	20 (7.8)	7 (2.7)	99 (38.7)	106 (41.4)	72 (28.1)	36 (14.1)	-

Trecarichi et al IJAA 2023 https://doi.org/10.1016/j.ijantimicag.2023.106806

SEIFEM: Italian Epidemiology-resistance

Correlation between % of third-generation cephalosporin-resistant *Enterobacterales* (3GCR-E), carbapenem-resistant *Enterobacterales* (CRE), MDR *P. aeruginosa* (MDR-PA) isolates and fluoroquinolone prophylaxis (FQ-P) during the periods 2009-2012 and 2016-2018 and their % differences (Δ).



Trecarichi et al IJAA 2023 https://doi.org/10.1016/j.ijantimicag.2023.106806

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Commentary

Fluoroquinolone prophylaxis during neutropenia: what can we expect nowadays?

M. Mikulska [1,*], C. Cordonnier [2]

Two recent guidelines invite the readers to interpret the data in the light of the lack of significant benefit on mortality, and despite a possible reduction in the rate of infection and fever episodes in some settings, they do not recommend FQ prophylaxis [15,16]. This cautious policy is in agreement with what we, on behalf of the ECIL group, have recently published [8].

In conclusion, it is unlikely that FQ prophylaxis would reduce mortality, because (1) infections by susceptible strains are easily treated with standard empirical therapy, and (2) mortality is mainly driven by infections caused by pathogens resistant to standard therapy employed in febrile neutropenia and to FQs. In the era of increasing antibiotic resistance, even in settings with low prevalence of MDR bacteria so far, routine use of FQ prophylaxis should be reconsidered. Further research should focus on rapid

incidence, risk factors and outcome of pre-engraftment gram-negative bacteremia after allogeneic and autologous hematopoietic stem cell transplantation: an Italian prospective multicenter survey. Clin Infect Dis 2017;65:1884–96.

[13] Trecarichi EM, Tumbarello M, Spanu T, Caira M, Fianchi L, Chiusolo P, et al. Incidence and clinical impact of extended-spectrum-beta-lactamase (esbl) production and fluoroquinolone resistance in bloodstream infections caused by escherichia coli in patients with hematological malignancies. J Infect 2009;58:299–307.

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[16] Klastersky J, de Naurois J, Rolston K, Rapoport B, Maschmeyer G, Aapro M, et al. Management of febrile neutropenia: ESMO clinical practice guidelines. Ann Oncol 2016;27:v111–8.

Cosa fare allora

Journal of Infection (2009) 58, 299–307

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Incidence and clinical impact of extended-spectrum-β-lactamase (ESBL) production and fluoroquinolone resistance in bloodstream infections caused by *Escherichia coli* in patients with hematological malignancies

Enrico M. Trecarichi [a], Mario Tumbarello [a,*], Teresa Spanu [b], Morena Caira [c], Luana Fianchi [c], Patrizia Chiusolo [c], Giovanni Fadda [b], Giuseppe Leone [c], Roberto Cauda [a], Livio Pagano [c]

Multivariate analysis				
Inadequate initial antimicrobial treatment	—	—	0.009	14.96 (1.95–114.51)
ESBL production	—	—	0.01	8.84 (1.48–52.91)
Prolonged neutropenia (≥10 days)	—	—	0.02	8.10 (1.29–50.57)

Unless otherwise noted in column 1, results represent number (%) of patients.

[a] During the 3 months prior to collection of the index blood culture.

Impact of a Multiplex PCR Assay for Bloodstream Infections With and Without Antimicrobial Stewardship Intervention at a Cancer Hospital

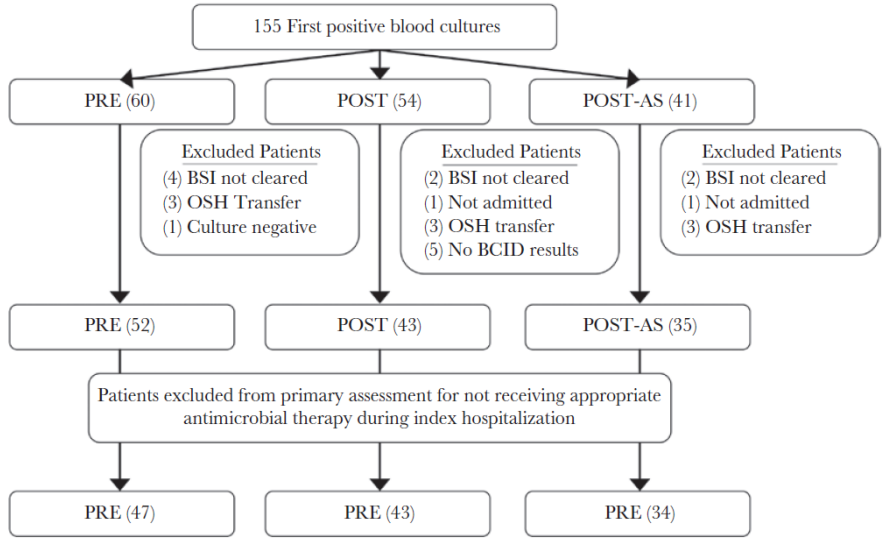
- Pre-post intervention study (2014-2016)
- Evaluate impact of BCID with and without ASP intervention

- **BCID improved median time to organism identification** from positive Gram stain **by > 40 hours** between the BCID and non-BCID arms (**44 hours, 2.8 hours, 1.5 hours; *P* < .001**).

Table 3. Primary and Secondary Outcomes

	PRE (n = 52), No. (%)[a]	POST (n = 43), No. (%)[a]	POST-AS (n = 35), No. (%)[a]	*P* Value[b]
Appropriate antimicrobial therapy	47 (90)	43 (100)	34 (97)	.071
Time to appropriate antimicrobial therapy,[c] median (IQR), h	30 (0–59)	17 (0–41)	20 (0–43)	.432
Time to organism identification, median (IQR), h	44 (30–57)	2.8 (1.4–5.1)	1.5 (1.3–2.0)	<.001
In-hospital mortality	2 (3.9)	3 (7.0)	2 (5.7)	.793
30-d mortality	5 (9.6)	6 (14)	5 (14)	.747
30-d readmission	15 (29)	8 (19)	11 (31)	.374
30-d readmission with bacteremia episode	2 (3.9)	1 (2.3)	3 (8.6)	.401

- **…urs POST-AS),** with and without AS intervention in a **multivariable regression analysis**,
- no significance in primary analysis (time to appropriate therapy: 13 hours POST and 10 hours POST-AS) when compared with the PRE intervention cohort.



- **The addition of AS** in both analyses **did not significantly affect the time to appropriate antimicrobial therapy.**
- **Interventions not associated** with **any increase in in-hospital or 30-day mortality.**

Many neutropenic patients on apprpriate empirical therapy
Epidemiology? Mainly Gram pos no great impact of res
BCID not BCID2,
no new molecules

Buss et al CID 2018

Impact of a Rapid Molecular Test for Klebsiella pneumoniae Carbapenemase and Ceftazidime-Avibactam Use on Outcomes after Bacteremia Caused by Carbapenem-Resistant Enterobacterales

*Study Design: observational study, 137 patients with CRE bacteremia enrolled from 2016 -2018 at 8 academic medical centers in NY/NJ → 3/8 used BCID testing.
*106 patients (77%) infected with CP-CRE (64% K. pneumoniae, 15% E. coli, 11% E. cloacae) → 89 (65%) with blaKPC, 8 (6%) with blaOXA-48 and 7 (5%) with blaNDM.

❖ **BCID ASSAY**

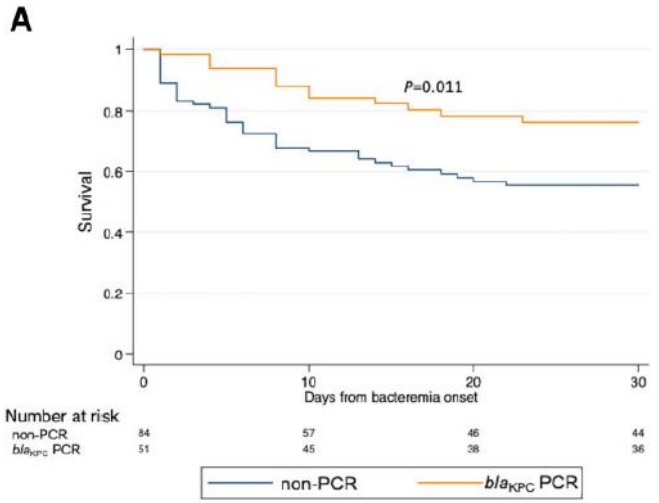
- **blaKPC in 32/33 patients where gene detected by WGS of bloodstream isolates (no other gene detection systems used)**

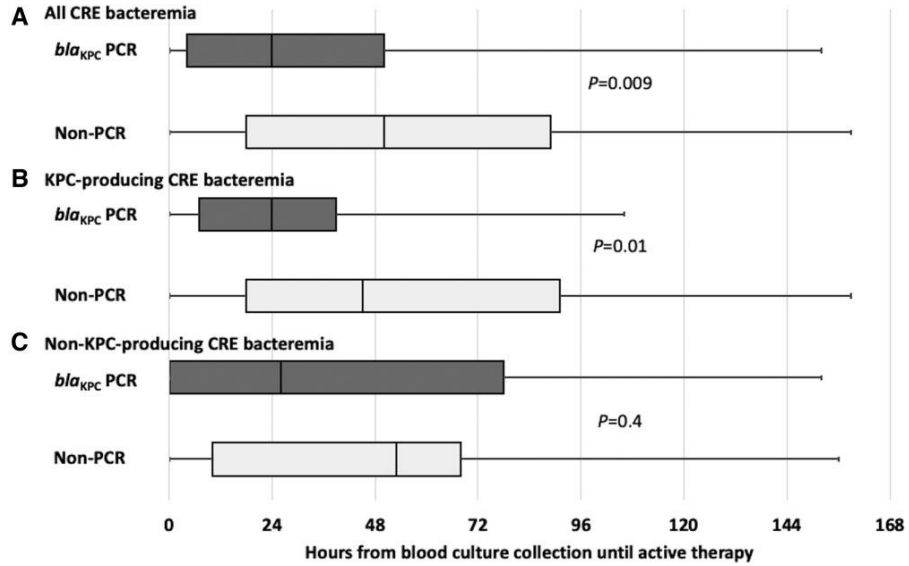
❖ **MORTALITY**

- **14 and 30-day mortality lower in PCR-patients vs non-PCR patients** (14-day: 16% vs. 37%, *P=0.007*; 30-day: 24% vs. 47%, *P=0.007*).
- **Mortality drop** in PCR patients only **observed in patients with KPC-producing CRE bacteremia.**

❖ **TIME TO RESULT and intervention**

- blaKPC PCR testing = **median of 22 hours from BC collection to detection of CRE bacteremia, vs 67 hours in non-PCR patients (*P<0.0001*).**
- **BCID-patients: more likely to receive active antimicrobial therapy within 24 hours** (43% vs.24%; *P=0.02*) **and 48 hours** (63% vs. 37% *P=0.004*) after bacteremia onset.
- **Median time from BC to active therapy = 24 hours in PCR-patients vs 50 hours in non-PCR patients** *(P=0.009)*.





Satlin et al, Clinical Infectious Disease, 2022, https://doi.org/10.1093/cid/ciac354

Eseguita procedura di trapianto allogenico di cellule staminali emopoietiche da sangue periferico da donatore familiare aploidentico (fratello), AB0 incompatibile maggiore (Paziente 0 pos, Donor A pos), con condizionamento mieloablativo secondo schema Thiotepa-Busulfano-Fludarabina (TBF).

Data trapianto: 8-9/08/2023.

Paziente 27 anni: storia clinica, 9 agosto allo-TMO

- Puntata febbrile (TC 39°) senza alterazione dei parametri vitali in data 09/08/23, g+0dalla reinfusione per cui venivano eseguite emocolture da PICC e da vena periferica, e veniva avviata terapia antibiotica ad ampio spettro con Piperacillina/Tazobactam, 18 g infusione continua in data 09/08/23. Il giorno successivo comparsa inoltre di scariche di feci semi-liquide associate a dolore emorroidario per cui venivano eseguite test molecolare su feci con riscontro di positività per *E. coli* produttore di Shiga toxin 1 e 2. Valutato dai colleghi infettivologi, proseguiva terapia in atto e stretto monitoraggio degli indici di funzionalità renale.

Paziente 27 anni: storia clinica

BATTERIOLOGIA

Materiale: Feci

Ag Clostridium difficile (GDH)	**Negativo**
Ricerca diretta molecolare multiplex - Batteri	
Campylobacter spp	**Non rilevata**
Clostridium difficile toxin B	**Non rilevata**
Salmonella spp	**Non rilevata**
Shigella spp / EIEC	**Non rilevata**
Vibrio spp	**Non rilevata**
Yersinia enterocolitica	**Non rilevata**
Aeromonas spp	**Non rilevata**
Clostridium difficile hypervirulent	**Non rilevata**
E.coli O157	**Non rilevata**
STEC (stx 1 / 2)	**Rilevata**

Positività al test molecolare per Sgia toxins 1, 2 di E.coli (STEC/EHEC) - da valutarsi clinicamente.

EPEC (eaeA)	**Non rilevata**
ETEC (lt / st)	**Non rilevata**
EAEC (aggR)	**Non rilevata**

PIPERACILLINA: Concentrazione pre-dose	**32.24**	mg/L
Data in cui ripetere il monitoraggio	**giovedì**	
Commento	**Concentrazione al di sotto del range terapeutico**	

In considerazione di una CLCr stimata di 2.5 mL/min/kg, in empirico si suggerisce di aumentare la posologia a 20.25 gr nelle 24 ore in infusione endovenosa continua.

Dopo iniziale lieve miglioramento della curva termica, dal 16/08/23 nuovamente febbrile con puntate fino a 39,8°C, pertanto si eseguiva *escalation* su base empirico-ragionata della terapia antibiotica avviando Meropenem, Amikacina e Caspofungina (questa in sostituzione di Ambisome al fine di ridurre la tossicità renale).

Emocolture positive 16 agosto 2023
Un secondo film array, positive anche per
Candida tropicalis

T2 MR (Risonanza Magnetica)	
T2 Batteria	**Negativa**
	T2Batteria panel ESKAPE: Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Escherichia coli.
T2 Candida	**Negativa**
	T2Candida 1.1 panel: Candida albicans/tropicalis, Candida parapsilosis, Candida krusei/glabrata.

Ricerca diretta molecolare multiplex	
GRAM NEGATIVI	
Acinetobacter calcoaceticus-baumannii complex	**Negativa**
Bacteroides fragilis	**Negativa**
Enterobacterales	**Positiva**
Enterobacter cloacae complex	**Negativa**
Escherichia coli K1	**Positiva**
Klebsiella aerogenes	**Negativa**
Klebsiella oxytoca	**Negativa**
Klebsiella pneumoniae group	**Negativa**
Proteus spp.	**Negativa**
Salmonella spp	**Negativa**
Serratia marcescens	**Negativa**
Haemophilus influenzae	**Negativa**
Neisseria meningitidis	**Negativa**
Pseudomonas aeruginosa	**Negativa**
Stenotrophomonas maltophilia	**Negativa**
Ricerca diretta molecolare multiplex	
GENI DI RESISTENZA ANTIMICROBICA	
CTX-M	**Negativa**
IMP	**Negativa**
KPC	**Negativa**
mcr-1	**Negativa**
NDM	**Negativa**
OXA-48	**Negativa**
VIM	**Negativa**
LIEVITI	
Candida albicans	**Negativa**
Candida auris	**Negativa**
Candida glabrata	**Negativa**
Candida krusei	**Negativa**
Candida parapsilosis	**Negativa**
Candida tropicalis	**Positiva**
Cryptococcus neoformans/gattii	**Negativa**

Emocolture del 16 agosto 2023: Candida tropicalis non presente nelle colture; MIC tol/taz 8 mg/L

Ceppo 1	Escherichia coli		

Ceppo produttore di cefalosporinasi Amp-C.

Antibiogramma

	Ceppo 1	
ANTIBIOTICO		*MIC*
Amikacina	S	<=4
Amoxicillina-clavulanato	R	>64
Ceftazidime	R	>64
Ceftazidime-avibactam	S	<=1
Ceftriaxone	R	>4
Ceftriaxone Meningitidis	R	>4
Ciprofloxacina	S	0.25
Ertapenem	S	<=0.5
Fosfomicina c/G6P	S	<=16
Gentamicina	S	<=1
Meropenem	S	<=0.125
Meropenem Meningitidis	S	<=0.125
Piperacillina-tazobactam	R	>128
Tigecyclina	S	<=0.25
Trimetoprim-sulfametoxazolo	I	4

< R = Resistente, S = Sensibile, I = Intermedio >

Risposta telefonica MIC ceftolozano Tazobactam 8 mg/L R

17 agosto, venite chiamati in consulenza
Allo trapianto in 2 settimana, senza attecchimento
Precedente VIM dal tampone rettale, *E. coli* dal sangue
probabile AmpC? Pip/tazo R, C. tropicalis DNA nel sangue ma non nella coltura (al momento).
Che fate?

Original Investigation | Hematology

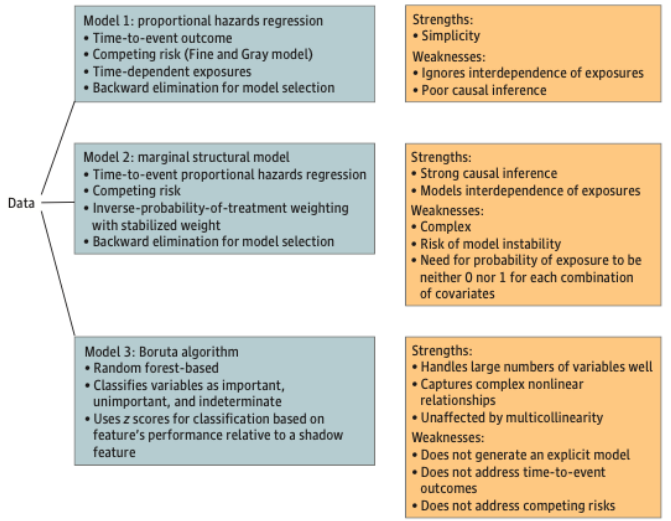
Analysis of Antibiotic Exposure and Development of Acute Graft-vs-Host Disease Following Allogeneic Hematopoietic Cell Transplantation

Armin Rashidi, MD, PhD; Fei Gao, PhD; David N. Fredricks, MD; Steven A. Pergam, MD, MPH; Marco Mielcarek, MD; Filippo Milano, MD, PhD; Brenda M. Sandmaier, MD; Stephanie J. Lee, MD, MPH

RESULTS A total of 2023 patients (median [range] age, 55 [18-78] years; 1153 [57%] male) were eligible. Weeks 1 and 2 after HCT were the highest-risk intervals, with multiple antibiotic exposures associated with higher rates of subsequent aGVHD. In particular, exposure to carbapenems during weeks 1 and 2 after allo-HCT was consistently associated with increased risk of aGVHD (minimum hazard ratio [HR] among models, 2.75; 95% CI, 1.77-4.28), as was week 1 after allo-HCT exposure to combinations of penicillins with a β-lactamase inhibitor (minimum HR among models, 6.55; 95% CI, 2.35-18.20).

CONCLUSIONS AND RELEVANCE In this cohort study of allo-HCT recipients, antibiotic choices and schedules in the early course of transplantation were associated with aGVHD rates. These findings should be considered in antibiotic stewardship programs.

Figure 1. Summary of the 3 Statistical Methods



Lo studio ipotizza che Carbapenemico nelle prime due settimane dopo allo-TMO induce aGVHD
Piperacillina/tazobactam nella prima settimana prima del trapianto segnale debole
In questa popolazione dobbiamo essere ancora più restrittivi?

Voi cosa avreste fatto?

Consulenza MI: ceftazidime avibactam 2,5 g ogni 8 ore, caspofungina ed ambisome

Concentrazione Ceftazidime pre-dose	**29.57**	mg/L
Concentrazione Avibactam pre-dose	**5.52**	mg/L
Dose consigliata	**2.5 gr ev IC**	mg
Intervallo di somministrazione	**8**	Ore
Data in cui ripetere il monitoraggio	**lunedì**	
Commento	***Concentrazione ai limiti inferiore del range terapeutico in empirico, ma in range terapeutico per una MIC =<1 mg/L.***	

Candida tropicalis mai cresciuta: contaminazione dei brodi di emocoltura?
Continuato ceftazidime avibactam per 10 gg totali senza recidiva, attecchimento

Paziente di 27 anni: lettera di dimissione

- Emesi alimentare lontano dai pasti in assenza di nausea associata, insorta in g+22 (31/08/23), per cui nel sospetto di inizale GVHD acuta intestinale alta veniva programmata EGDS. In data 05/09/23 eseguita EGDS che escludeva quadro di GVHD acuta ma che evidenziava petecchie gastroduodenali ed angio-displasia. Il quadro sintomatologico si è progressivamente risolto con terapia sintomatica (antiacidi e levosulpiride).
- **NO aGVHD**

Strain	ARGs	Chromosomal mutations	MLST (Achtman)	Plasmids	pMLST	Mobile Genetic Elements	Serotype	CHType
EC_JS	bla_{DHA-1} mphA macrolidi qnrB4 Chinoloni Sul1 sulfa dfrA7 Trimetoprim qacE Ammonio		ST442	IncFIB (AP001918) IncFII	FIB_28	IS6100 (IS6 family) MITEEc1 IS100 (IS21 family) ISEc31 (IS3 family) IS421 (IS4 family) IS26 (IS6 family)	O174:H9	fimH32 fumC95

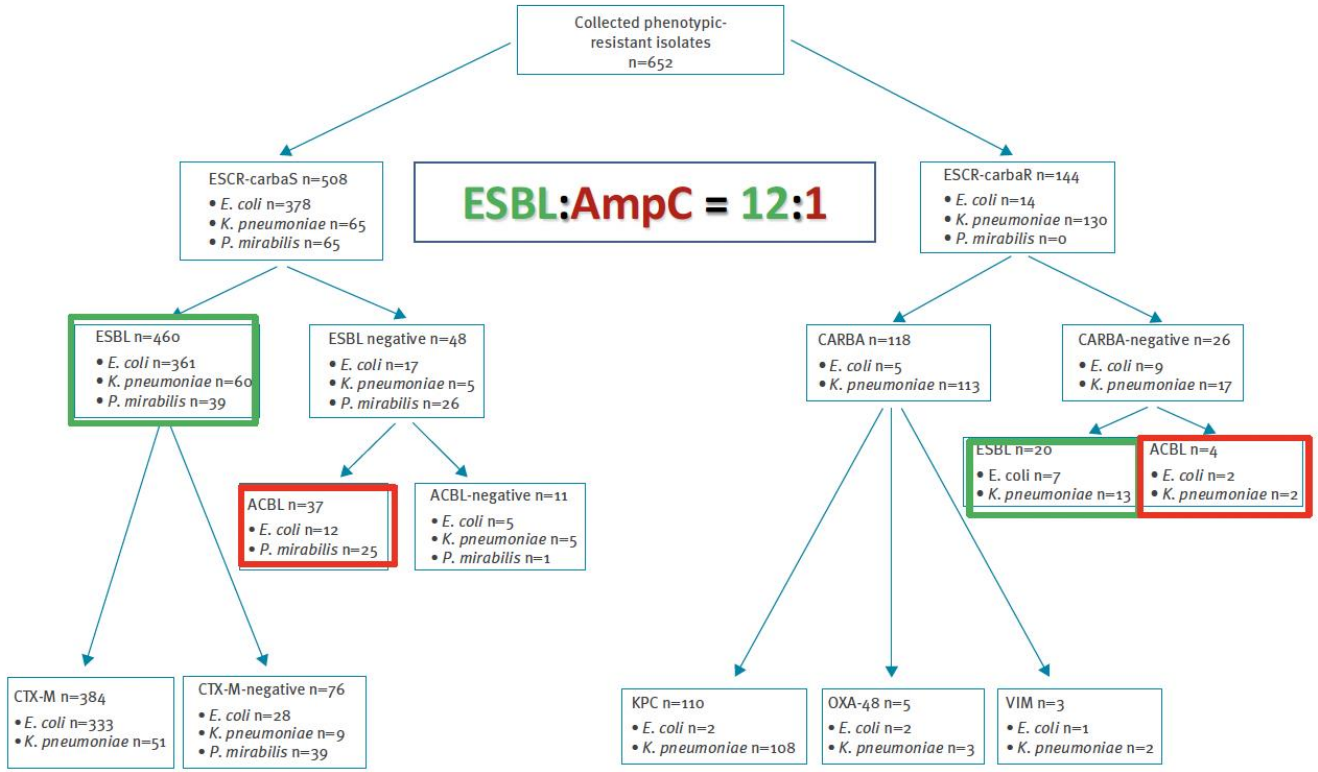
Euro Surveill. 2017;22(31):pii=30583.

Evolving beta-lactamase epidemiology in *Enterobacteriaceae* from Italian nationwide surveillance, October 2013: KPC-carbapenemase spreading among outpatients

T Giani [1,2], A Antonelli [2,3], M Caltagirone [4], C Mauri [5], J Nicchi [3], F Arena [1], E Nucleo [4], S Bracco [5], A Pantosti [6], The AMCLI-CoSA survey participants [7], F Luzzaro [5], L Pagani [4], GM Rossolini [1,3,8]

FIGURE 2

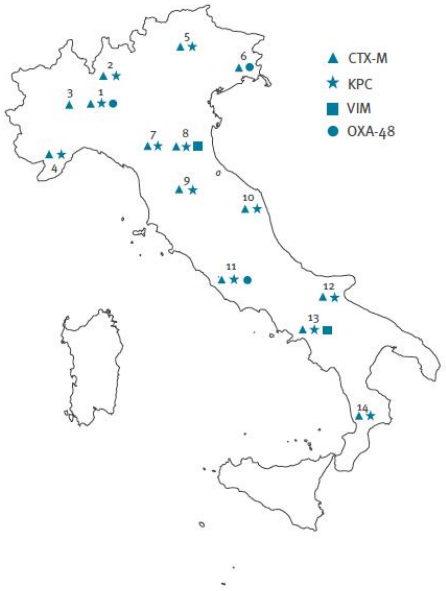
Distribution of *Escherichia coli*, Klebsiella pneumoniae and *Proteus mirabilis* isolates according to resistance phenotypes and genotypes, nationwide surveillance survey, Italy, October 2013 (n=652 isolates)



ACBL: isolates producing acquired class C beta-lactamase; CARBA: carbapenemase producing isolates; *E. coli: Escherichia coli*; ESBL: isolates producing extended spectrum beta-lactamase; ESCR-carbaS: isolates non-susceptible to extended-spectrum cephalosporins but susceptible to carbapenems; ESCR-carbaR: isolates non-susceptible to extended-spectrum cephalosporins and non-susceptible to carbapenems; *K. pneumoniae: Klebsiella pneumoniae; P. mirabilis: Proteus mirabilis*.

FIGURE 1

Distribution of the centers participating in the survey, Italy, October 2013 (n=14)



For each centre the presence of CTX-M extended-spectrum beta-lactamase and carbapenemase genes is also indicated.

Centers listed as follows: 1-Milano; 2-Lecco; 3-Novara; 4-San Remo; 5-Bolzano; 6-Udine; 7-Modena Bg; 8-Modena Pc; 9-Firenze; 10-Ancona; 11-Roma; 12-San Giovanni Rotondo; 13-Avellino; 14-Cosenza.

For each isolate, information on the type of clinical specimen and of patient (inpatient or outpatient) were provided. Isolates from patients from nursing homes or other long-term care facilities, and isolates from surveillance specimens, were excluded. Each laboratory also provided information on the total number of non-replicate clinical isolates of *Enterobacteriaceae* of the same species observed during the collection period from inpatients and outpatients.

CURRENT OPINION

Neutropenia and antibiotics: when, what, how and why?

Jana Dickter[a], *Cathy Logan*[b] *and Randy Taplitz*[a]

Volume 36 • Number 4 • August 2023

ogy [8]. And most recently, updated ECIL guidelines from 2021 reviewed the risk of infections and FN associated with other agents including immunotherapy and molecular therapies for the treatment of AML and acute lymphocytic leukemia (ALL). They conclude that most agents do not pose a significant infection risk when used as monotherapy, but caution is recommended when combining agents. Antibacterial prophylaxis is only recommended when hypomethylating agents are combined with venetoclax [22▪▪].

While the guidelines recommend risk-assessment, in general they do not account for inpatient versus outpatient status with regards to prophylaxis. Perhaps the need for antimicrobial prophylaxis should take into consideration how quickly antibiotics can be initiated. New approaches to risk stratification for prophylaxis are needed.

Conclusioni

- La profilassi antibiotica non impatta sulla mortalità
- Dipende dalla percentuale di resistenza ai chinoloni (>20%)
- La profilassi potrebbe selezionare ceppi MDR
- La profilassi alterando il microbioma, induce la GVHD?
- La diagnosi rapida potrebbe essere l'alternativa alla terapia semi-targeted
- Pertanto i fattori di rischio dovrebbero essere riveduti: ho la biologia molecolare disponibile?, il paziente è ricoverato?