Albero decisionale nel paziente con sospetta sepsi da batteri multiresistenti

Corrado Girmenia

UOSD Pronto Soccorso e Accettazione Ematologica,
AOU Policlinico Umberto I, Roma

Key issues in the management of bacterial infections in neutropenic patients

- Changing epidemiology of MDR pathogens
- Prevention of Gram negative infections
  - Infection control
  - Antibacterial prophylaxis
- Antibacterial strategies

Bacterial infections in stem cell transplant: lesson from GITMO studies….

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).

Clinical Infectious Diseases® 2017;65(11):1884–96

The SIGNB-GITMO/AMCLI study was a prospective epidemiological survey performed in 54 transplant centers between 1 January and 31 December 2014.

A PROSPECTIVE, MULTICENTER SURVEY OF HUMAN CYTOMEGALOVIRUS (CMV) AND OTHER HERPESVIRUSES INFECTIONS AND DISEASES IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT (ALLO-HSCT) RECIPIENTS.

CLINICALTRIALS.GOV IDENTIFIER: NCT04412811

The CYTOALLO-GITMO/AMCLI study was a prospective epidemiological survey involving 40 transplant centers between 1 January 2021 and 31 March 2022 transplant

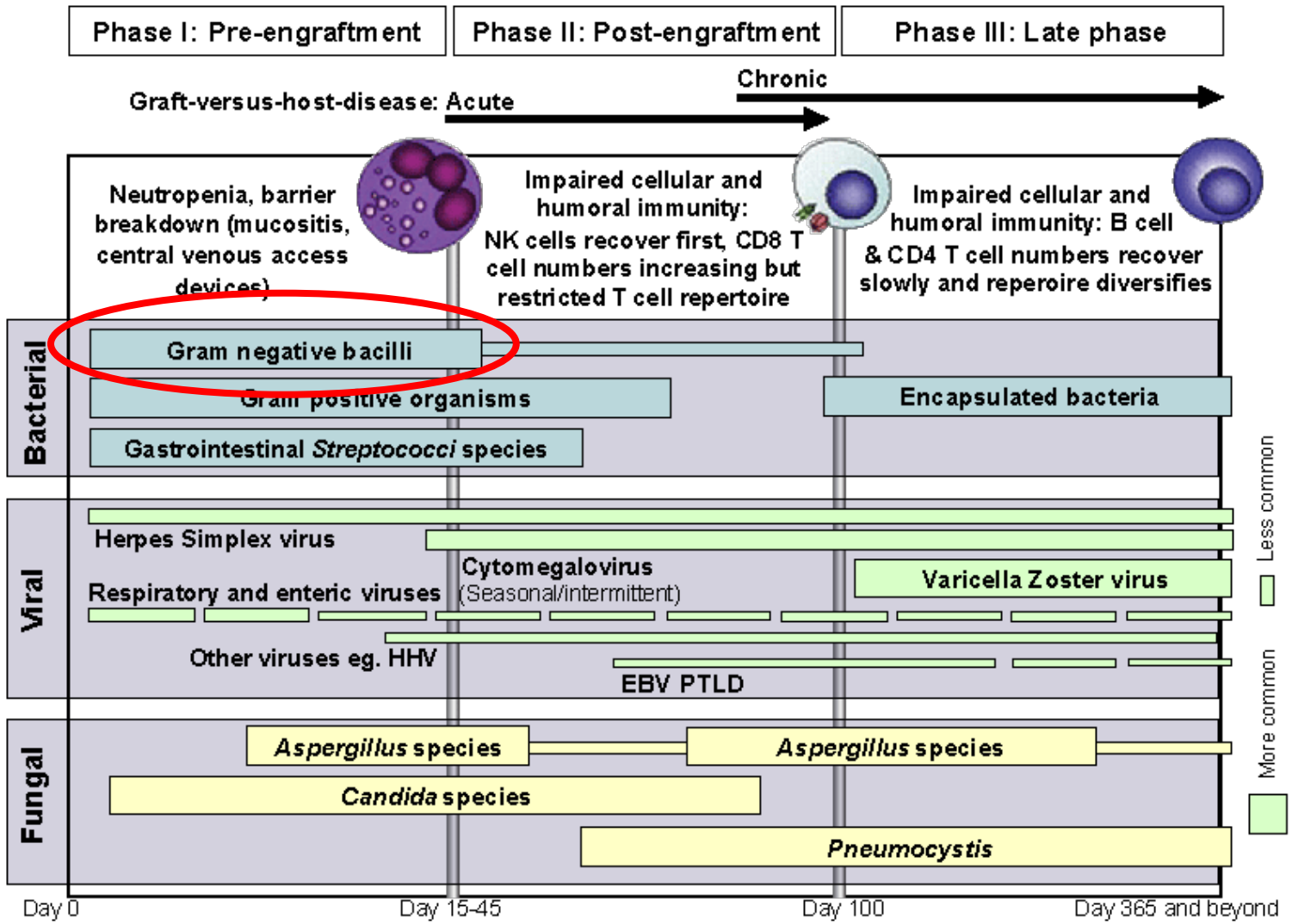
Stem Cell
Research & Therapy

Kedia et al., J Stem Cell Res Ther 2013, S3
http://dx.doi.org/10.4172/2157-7633.S3-002

Review Article Open Access

Infectious Complications of Hematopoietic Stem Cell Transplantation

Shiksha Kedia[1], Pranab Sharma Acharya[1], Farhan Mohammad[1], Huy Nguyen[1], Deepak Asti[1], Suchita Mehta[1]*, Manisha Pant[2] and Neville Mobarakai[3]



Clinical Infectious Diseases
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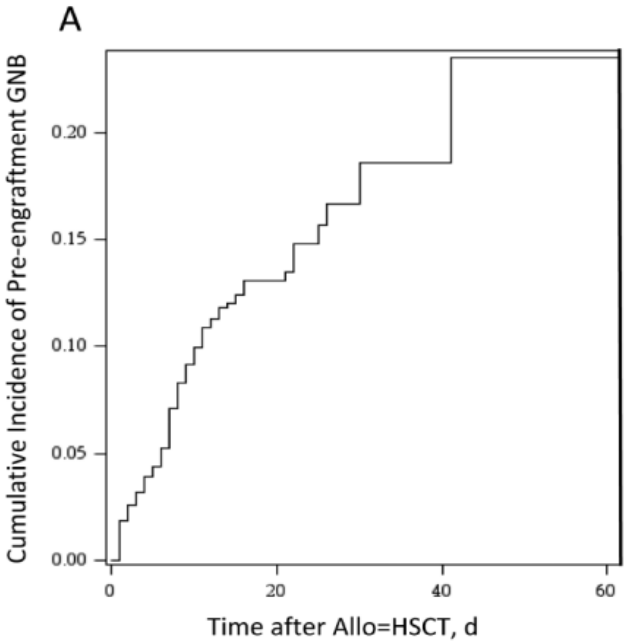
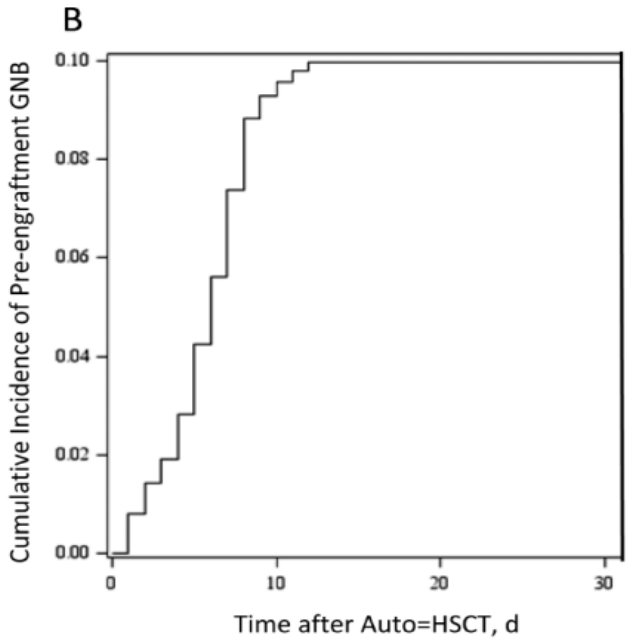
Table 2. Infections Documented Before Engraftment

Jan 2014 – Dec 2014

Infection Findings	Allo-HSCT (n = 1118)	Auto-HSCT (n = 1625)
No documented infection, No. of patients (%)		
No fever or documented infection	329 (29.5)	755 (46.5)
Fever of unknown origin only	395 (35.3)	472 (29.0)
Clinically documented infections, No. of episodes/No. of patients (%)	68/67 (6.0)	87/85 (5.2)
Pneumonia	39/39 (3.5)	53/53 (3.3)
Skin infection	14/14 (1.2)	12/12 (0.7)
GI tract infection	6/6 (0.5)	20/18 (1.1)
Other	10/9 (0.8)	2/2 (0.1)
Microbiologically documented infections, No. of episodes/No. of patients (%)	412/331 (30.1)	355/320 (19.2)
Gram-negative bacterial infection	157/148 (13.2)[a]	162/157 (9.7)[b]
Gram-positive bacterial infection	209/193 (17.3)	182/172 (10.6)
Fungal infection	24/24 (2.1)	9/9 (0.5)
Viral infection	22/22 (2.0)	2/2 (0.1)





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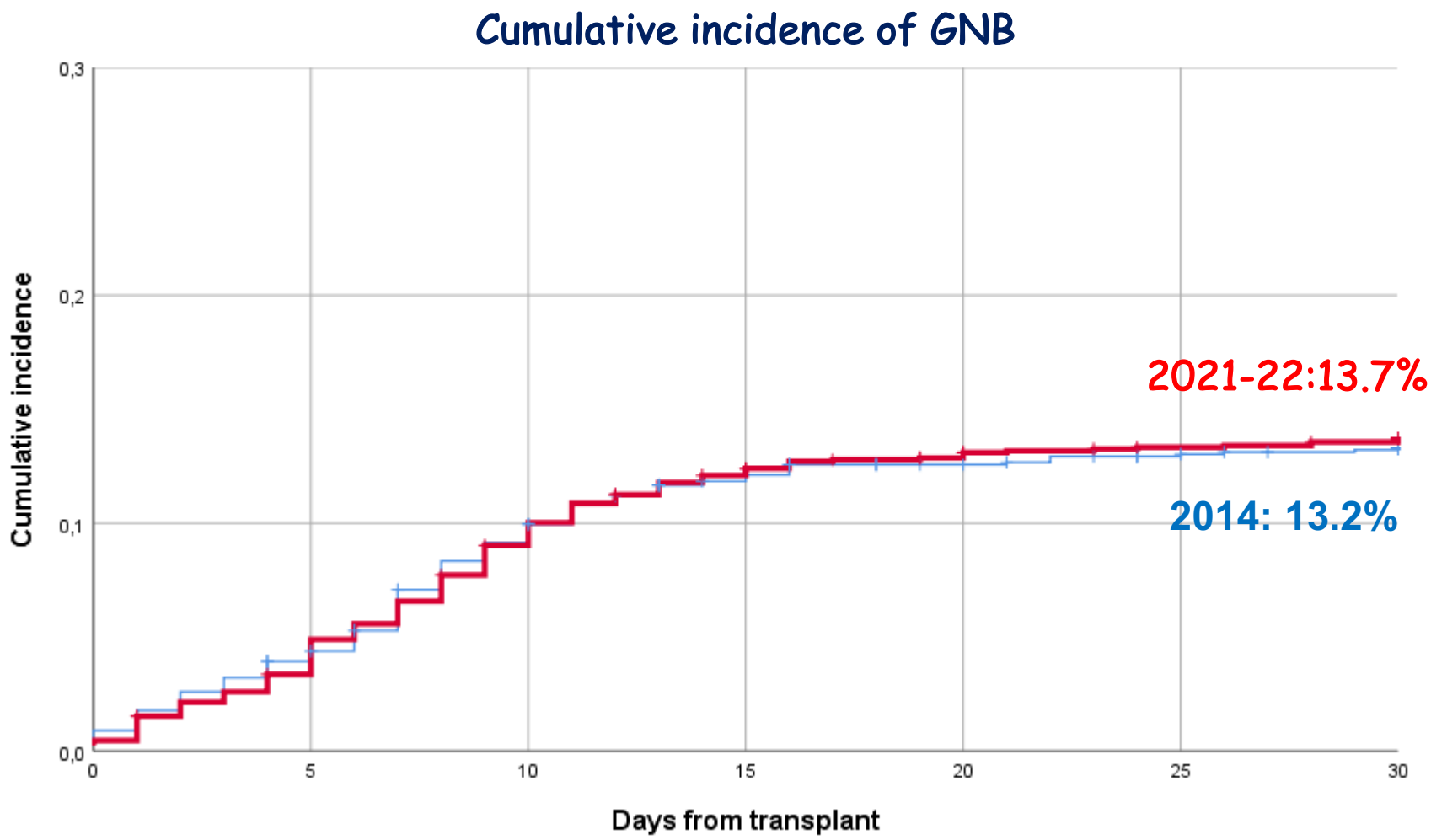
CLINICALTRIALS.GOV IDENTIFIER: NCT04412811

Girmenia et al. CYTOALLO-GITMO-AMCLI study, Jan 2021-Mar 22.

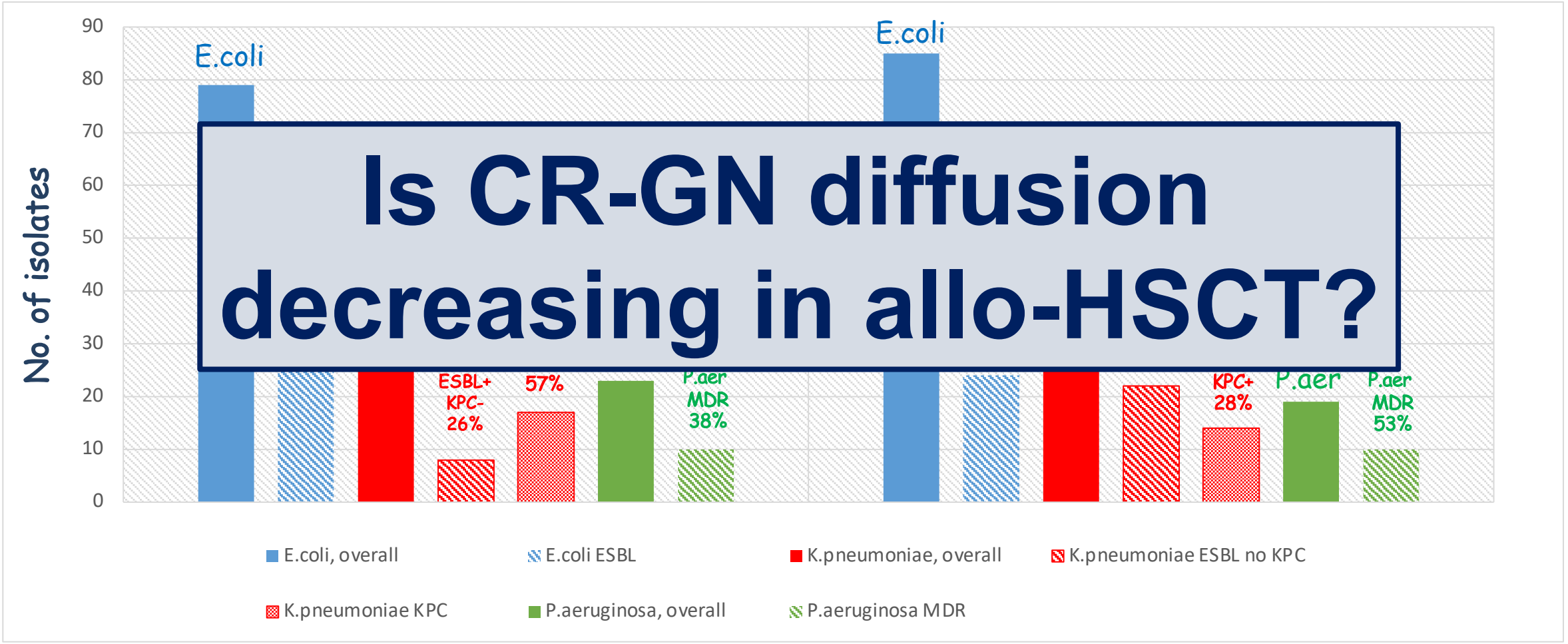
The incidence of early pre-engraftment GNB in allo-HSCT was **13.7%** (179/1310).

Gram-neg bacteremia during the engraftment period in allo-HSCT: comparison of two GITMO-AMCLI prospecive studyes



Gram-neg bacteremia during the engraftment period in allo-HSCT: comparison of two GITMO-AMCLI prospective studies

Gram-negative isolates and resistance patterns: 157 isolates in 2014, 179 isolates in 2021-22



Is CR-GN diffusion decreasing in allo-HSCT?

KP-KPC in 2014: 17 isolates from 15 of 44 centers

KP-KPC in 2021-22: 14 isolates form 8 of 42 centers

JAC Antimicrob Resist
https://doi.org/10.1093/jacamr/dlab167

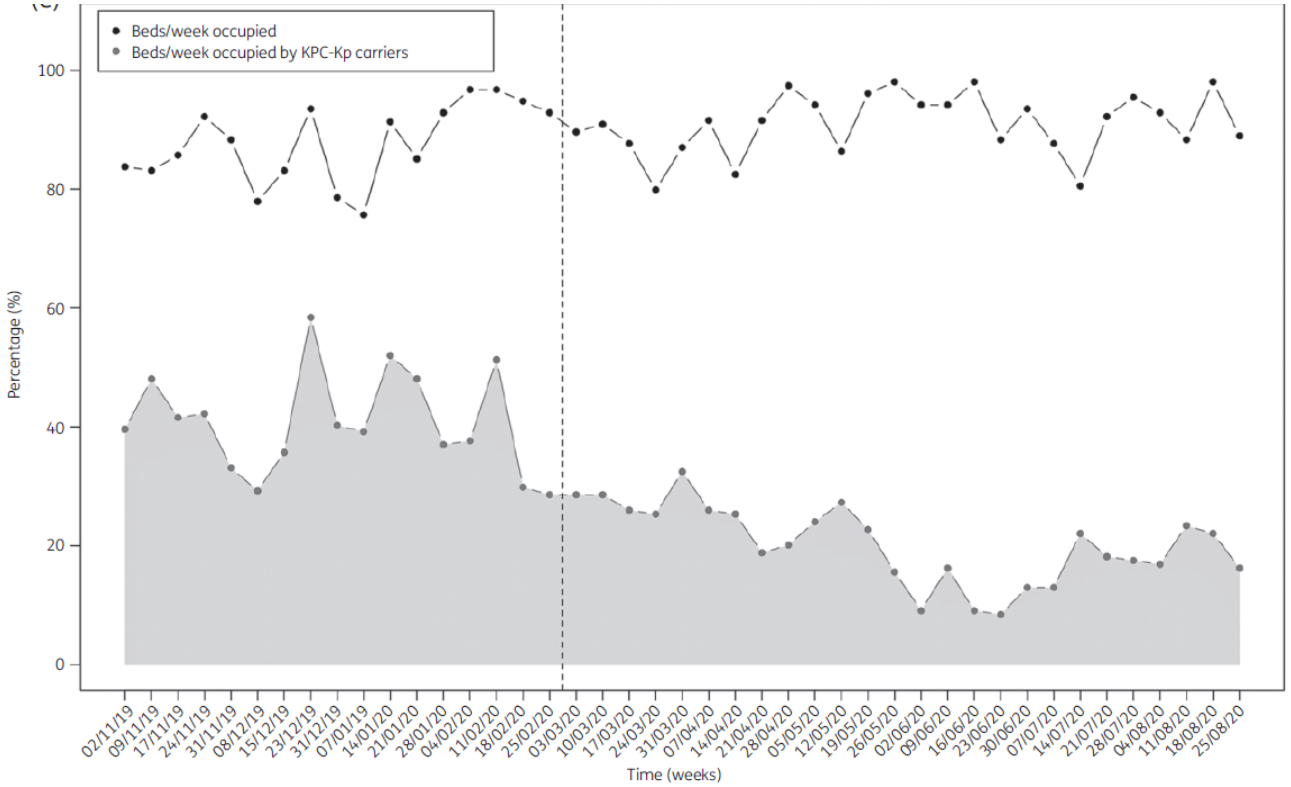
JAC-Antimicrobial Resistance

Reduced transmission of *Klebsiella pneumoniae* carbapenemase-producing *K. pneumoniae* (KPC-KP) in patients with haematological malignancies hospitalized in an Italian hospital during the COVID-19 pandemic

Alessandra Micozzi [1]*, Giovanni Manfredi Assanto[1], Laura Cesini[1], Clara Minotti[2], Claudio Cartoni[2], Saveria Capria[2], Giulia Ciotti[1], Danilo Alunni Fegatelli[3], Livia Donzelli[1], Maurizio Martelli[1] and Giuseppe Gentile[1]

[1]Department of Translational and Precision Medicine, Haematology, Sapienza University of Rome, Rome, Italy; [2]Department of Haematology, Oncology and Dermatology, Azienda Policlinico Umberto I, Rome, Italy; [3]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

We analysed KPC-KP spread among 123 patients with haematological malignancies, hospitalized between March and August 2020, who were managed using measures against COVID-19. Their outcomes were compared with those of 80 patients hospitalized during the preceding 4months (November 2019–February 2020).

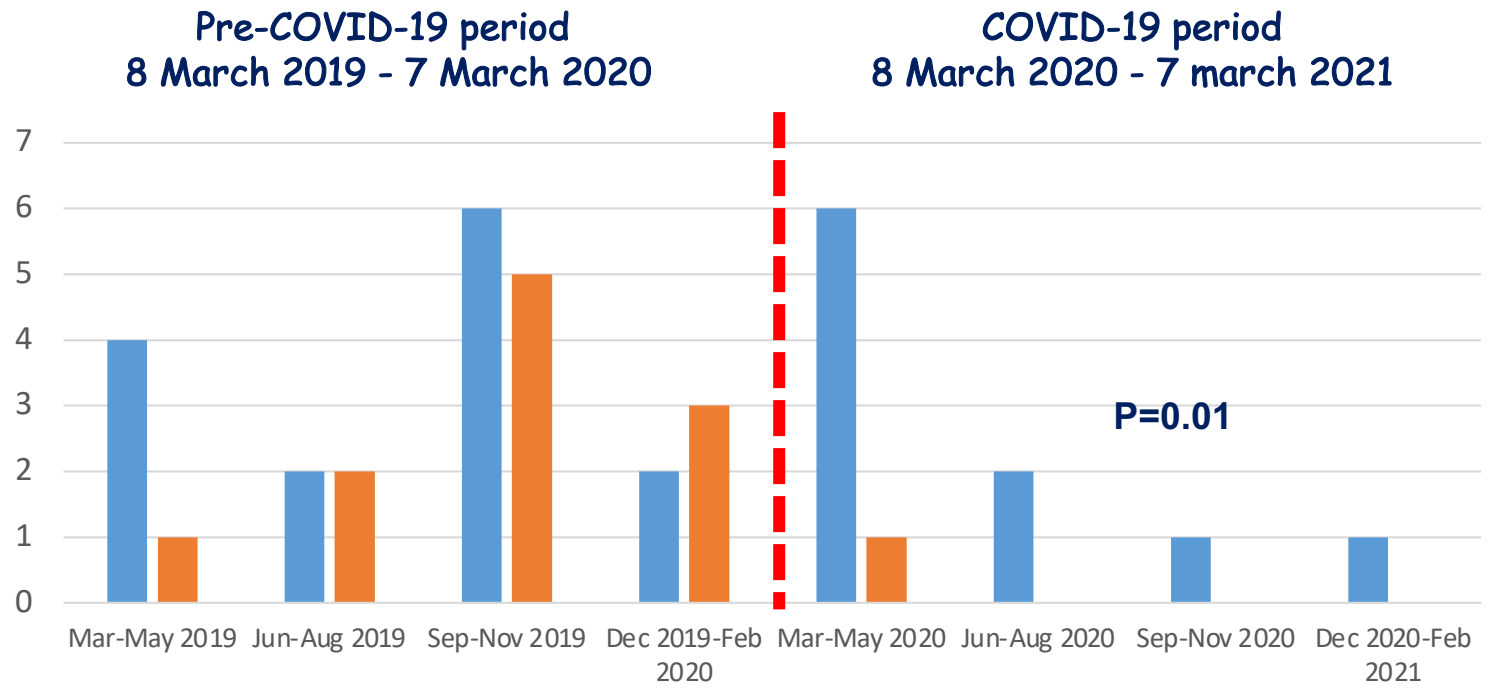


Four KPC-KP bloodstream infections (BSIs) were experienced by 123 patients (**3%**) in March–August 2020, and seven BSIs (one fatal) by 80 patients (**8%**) in November 2019–February 2020 (P=0.02). Consumption and expense of ceftazidime/avibactam administered to KPC-KP-positive patients significantly decreased in March–August 2020.

Reduced Klebsiella pneumoniae carbapenemase–producing K.pneumoniae (KPC-KP) colonization in a hematological-emergency setting during the coronavirus disease 2019 (COVID-19) pandemic

Alessandro Laganà MD, et al Infection Control & Hospital Epidemiology (2022), 1–2

UOSD Pronto Soccorso e Accettazione Ematologica, AOU Policlinico Umberto I, Sapienza University of Rome, Italy



Cases of primary KPC colonization present at the time of hospitalization

Cases of secundary KPC colonization acquired during hospitalization

Differences in the two periods:

- one more nurse
- access and spaces dedicated to patients only
- family visits not allowed
- increase in the use of alcoholic gel, masks and gloves (for both health care professionals and patients).
- COVID-19-related greater attention to patients management: the role of personal safety!!

Hematologic Emergency Unit, AOU Policlinico Umberto I, Rome

Infection control intervention against MDRO and SARS CoV-2 CDC guidelines

Type of intervention	CDC 2006 Guidelines on management of MDRO in healthcare settings, 2017 update	CDC Guidance for Public Health Strategies to Address High Levels of Community Transmission of SARS-CoV-2, December 2020
Universal use of face masks	X	XXXX
Providing the necessary number and appropriate placement of hand washing sinks and alcohol-containing hand rub dispensers in the facility	XXXX	XXXX
Physical distancing	X	XXXX
Limiting contacts	XXXX	XXXX
Avoid nonessential indoor spaces and crowded outdoor settings	X	XXXX
Increased testing, diagnosis, and isolation	XXXX	XXXX
Implementing system changes to ensure prompt and effective communications	XXXX	XXXX
Maintaining staffing levels appropriate to the intensity of care required	XXXX	XXXX
Educational campaigns to enhance adherence to contact precautions practices in conjunction with other control measures	XXXX	XXXX

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GITMO ONLUS
Gruppo Italiano per il Trapianto di Midollo Osseo, cellule staminali emopoietiche e terapia cellulare - ONLUS
Iscr. Registro Reg. Liguria – decr. n. 120 del 18/01/08 – cod. fisc. 95107000101 part. iva 01727920991

Probability of mortality at 4 months from transplant: Multivariate analysis

Allo-HSCT		Auto-HSCT	
Variable	HR (95% CI), p	Variable	HR (95% CI), p
Age (+10y)	1.10 (1.01-1.20) 0.03	Lymphoma vs other diseases	6.17 (2.78-1.6) <0.001
Other diseases vs acute leukemia	0.42 (0.29-0.63) <0.001	Phase of the und disease at transplant: noCR vs CR	4.8 (2.19-10.34), <0.001
Phase of the und disease at transplant: noCR vs CR	2.16 (1.47-3.15) <0.001	Pre transplant neutropenia	3.82 (1.80-8.12) 0.001
Pre auto-HSCT	1.76 (1.19-2.63) 0.006	Days of pre engraftment neutropenia (PMN<100/cmm)	1.07 (1.04-1.18) <0.001
Days of pre engraftment neutropenia (PMN<100/cmm)	1.03(1.01-1.04) <0.001	Gram neg bacterial infection	2.43 (1.22-4.84) 0.01
Acute II-IV GVHD	2.15 (1.21-3.82) 0.009		
Gram neg bacterial infection	2.13 (1.45-3.13) <0.001		

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Intercontinental study on pre-engraftment and post-engraftment Gram-negative rods bacteremia in hematopoietic stem cell transplantation patients: Risk factors and association with mortality

Diana Averbuch[a,*], Gloria Tridello[b], Jennifer Hoek[c], Malgorzata Mikulska[d], Thomas Pabst[e], Lucrecia Yañez San Segundo[f], Hamdi Akan[g], Tülay Özçelik[h], Irene Donnini[i], Galina Klyasova[j], Aida Botelho de Sousa[k], Tsila Zuckerman[l], Cristina Tecchio[m], Rafael de la Camara[n], Sahika Zeynep Aki[o], Per Ljungman[p], Zafer Gülbas[q], Emmanuelle Nicolas-Virelizier[r], Elisabetta Calore[s], Katia Perruccio[t], Ron Ram[u], Claudio Annaloro[v], Rodrigo Martino[w], Batia Avni[a], Peter J. Shaw[x], Alexandra Jungova[y], Katia Codeluppi[z], Tracey O'Brien[β], Anna Waszczuk-Gajda[γ], Montserrat Batlle[δ], Anastasia Pouli[ε], Catherina Lueck[λ], Lidia Gil[θ], Simona Iacobelli[μ], Jan Styczynski[π], Dan Engelhard[a,1], Simone Cesaro[b,1]

Patients in whom allogeneic or autologous HSCT was performed during February 2014-May 2015 in the participating centers were prospectively followed.

The GNRB cumulative incidence among 2818 allo-HSCT was: pre-engraftment (pre-eng-allo- HSCT), 8.4 (95% CI 7–9%), post-engraftment (post-eng-allo-HSCT), 5.8% (95%CI: 5–7%); among 3152 auto- HSCT, pre-eng-auto-HSCT, 6.6% (95%CI: 6–7%), post-eng-auto-HSCT, 0.7% (95%CI: 0.4–1.1%). GNRB, especially MDR, was associated with increased mortality.

Table 2
Factors associated with mortality in allogeneic HSCT (multivariate analysis).

Parameter	Number (%)	Pre-engraftment mortality		Post-engraftment mortality	
		HR (95% C.I.)	*P* value	HR (95% C.I.)	*P* value
Pre-engraftment GNR bacteremia					
No	2563 (93.1)	1.00		1.00	
Yes, MDR	88 (3.2)	1.97 (1.34–2.88)	0.0005	2.05 (1.21–3.48)	0.008
Yes, non-MDR	101 (3.7)	1.37 (0.93–2.04)	0.11	1.33 (0.74–2.38)	0.34
Missing data	45				
Post-engraftment GNR bacteremia			Not relevant		
No	2561 (96.1)			1.00	
Yes, MDR	45 (1.7)			7.48 (4.14–13.51)	<0.0001
Yes, non-MDR	59 (2.2)			2.73 (1.19–6.23)	0.017
Missing data	132				

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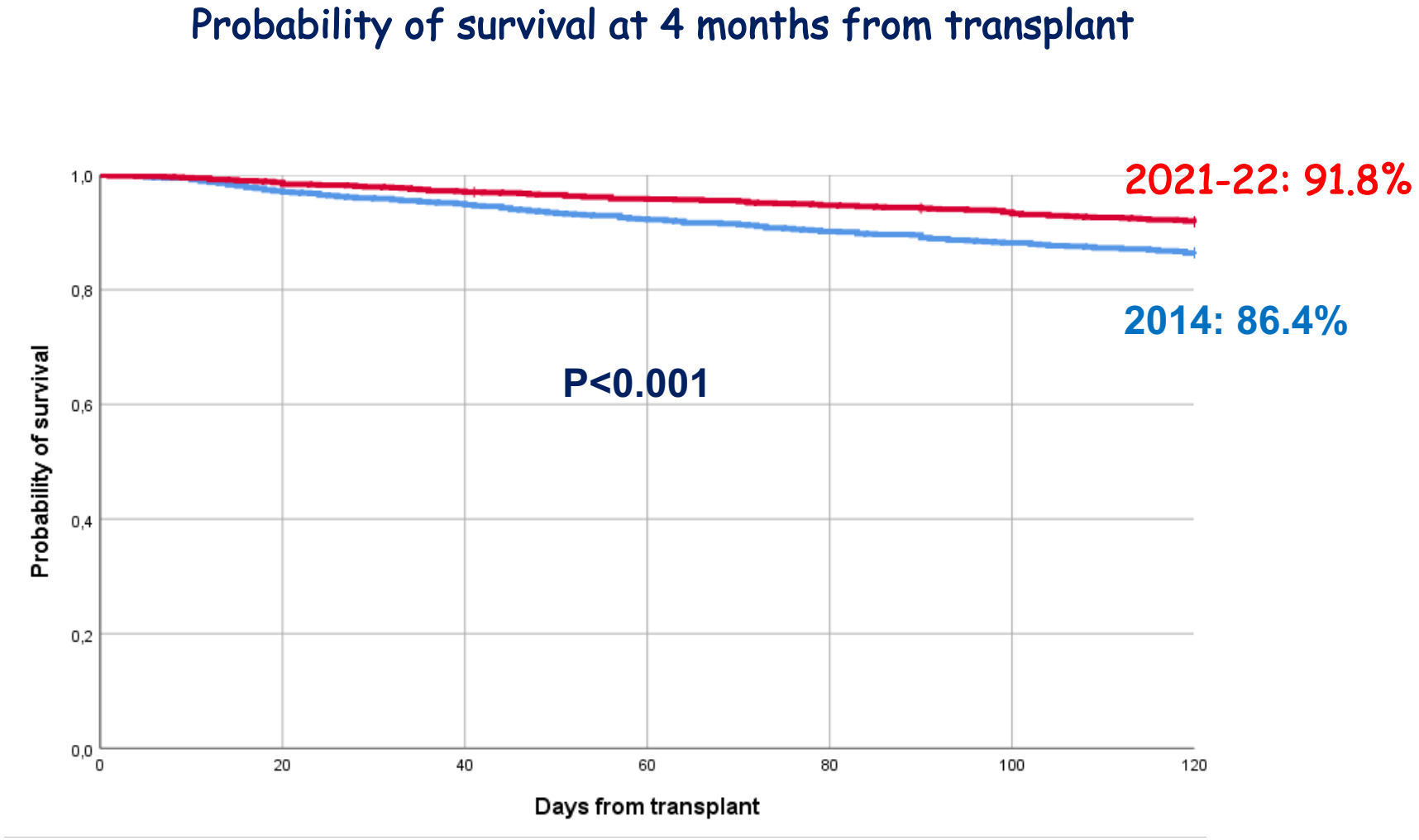
CLINICALTRIALS.GOV IDENTIFIER: NCT04412811

Probability of mortality at 12 months from transplant

Variables		Univariate		Multivariate	
		HR (95% CI)	p	HR (95% CI)	p
Sex	Male vs female	1.07 (0.83-1.39)	0.58		
Age (increased by 10 years)		1.02 (1.01-1.02)	<0.001	1.01 (1.01-1.02)	<0.001
Underlying hematologic disease	Diseases other than acute leukemia	1.00			
	Acute leukemia	1.43 (1.09-1.86)	0.009	1.77 (1.28-2.45)	<0.001
Phase of the underlying disease at transplant	Complete remission	1.00			
	Chronic phase	0.92 (0.62-1.36)	0.68	1.41 (0.91-2.19)	0.13
	No complete remission	1.42 (1.05-1.91)	0.022	1.86 (1.32- 2.62)	<0.001
Previous HSCT	No	1.00			
	Previous auto-HSCT	1.18 (0.74-1.86)	0.49		
	Previous allo-HSCT	1.50 (0.87-2.57)	0.14		
Recipient/donor HCMV serology	Negative/negative	1.00			
	Negative/positive	1.10 (0.54-2.25)	0.80		
	Positive/Negative	1.38 (0.79-2.41)	0.26		
	Positive/Positive	1.42 (0.84-2.42)	0.19		
ECOG performance status at transplant	0-1	1.00			
	>1	2.18 (1.39-3.41)	<0.001	2.22 (1.40-3.51)	<0.001
HCT comorbidity index at transplant	Score 0	1.00			
	Score 1-2	1.34 (0.99-1.83)	0.062	1.10 (0.80-1.50)	0.6
	Score >=3	2.0 (1.48-2.70)	<0.001	1.52 (1.11-2.10)	0.010
Stem Cell Source	Peripheral blood	1.00			
	Bone marrow	0.59 (0.39-0.90)	0.014		
	Cord blood	1.56 (0.64-3.77)	0.33		
Donor type	Matched related	1.00			
	Mismatched related	1.10 (0.56-2.17)	0.77		
	Haploidentical	1.17 (0.82-1.68)	0.38		
	Matched unrelated	0.76 (0.52-1.11)	0.16		
	Mismatched unrelated	1.37 (0.94-1.99)	0.10		

Variables		Univariate		Multivariate	
		HR (95% CI)	p	HR (95% CI)	p
Conditioning regimen	Myeloablative	1.00			
	Non myeloablative/ reduced intensity	1.04 (0.80-1.34)	0.79		
T cell depletion	No	1.00			
	Yes	0.72 (0.55-0.93)	0.012		
Use of post transplant cyclophosphamide as GVHD prophylaxis	No	1.00			
	Yes	0.82 (0.64-1.06)	0.12		
Letermovir prophylaxis	No	1.00			
	Yes	1.01 (0.77-1.32)	0.93		
Days to engraftment	<=20 days	1.00			
	>20 days	1.55 (1.20-1.99)	<0.001	1.40 (1.08-1.82)	0.011
Acute GVHD	Grade 0-1	1.00			
	Grade 2-4	1.57 (1.17-2.09)	0.002		
CS-HCMV DNAemia	Yes	1.00			
	No	0.70 (0.49-1.00)	0.049		
EBV DNAemia	Neg- < 1000 copies/ml	1.00			
	>=1000 copies /ml	1.08 (0.80-1.47)	0.60		
Gram negative bacteremia	No	1.00			
	Yes	2.27 (1.72-2.99)	<0.001	2.23 (1.68-2.97)	<0.001
Invasive fungal disease	No	1.00			
	Yes	2.33 (1.55- 3.49)	<0.001	2.01 (1.33-3.04)	<0.001

Gram-neg bacteremia during the engraftment period in allo-HSCT: comparison of two GITMO-AMCLI prospective studies



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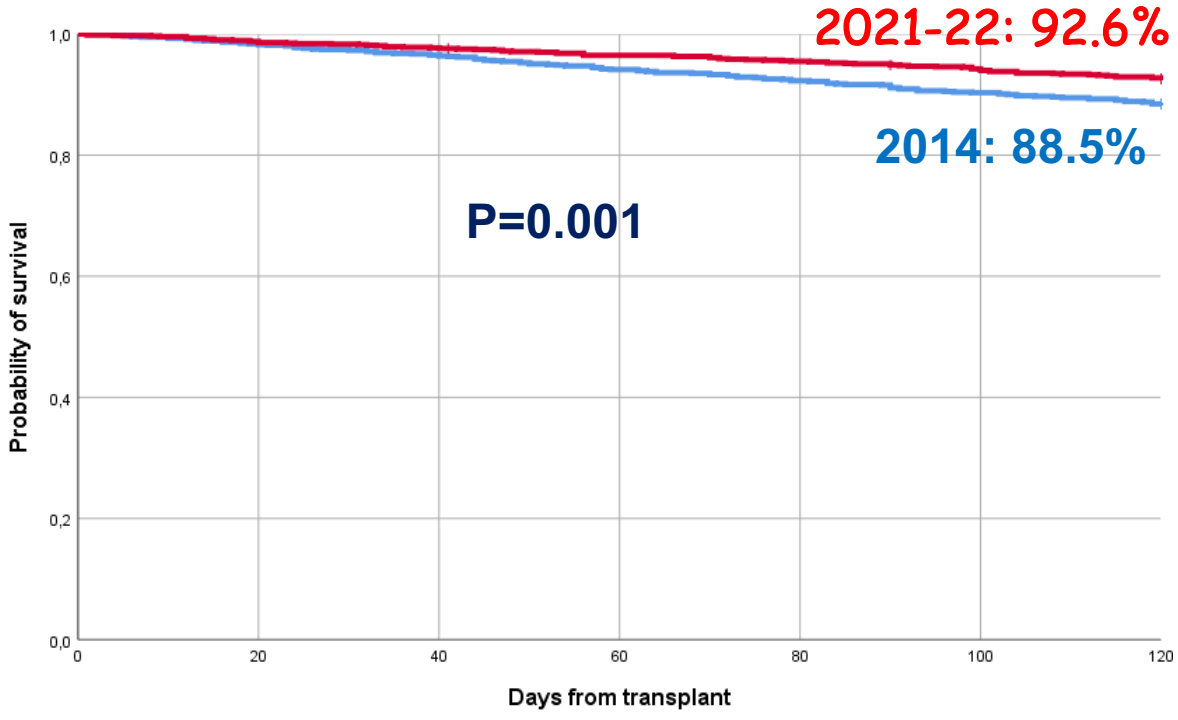
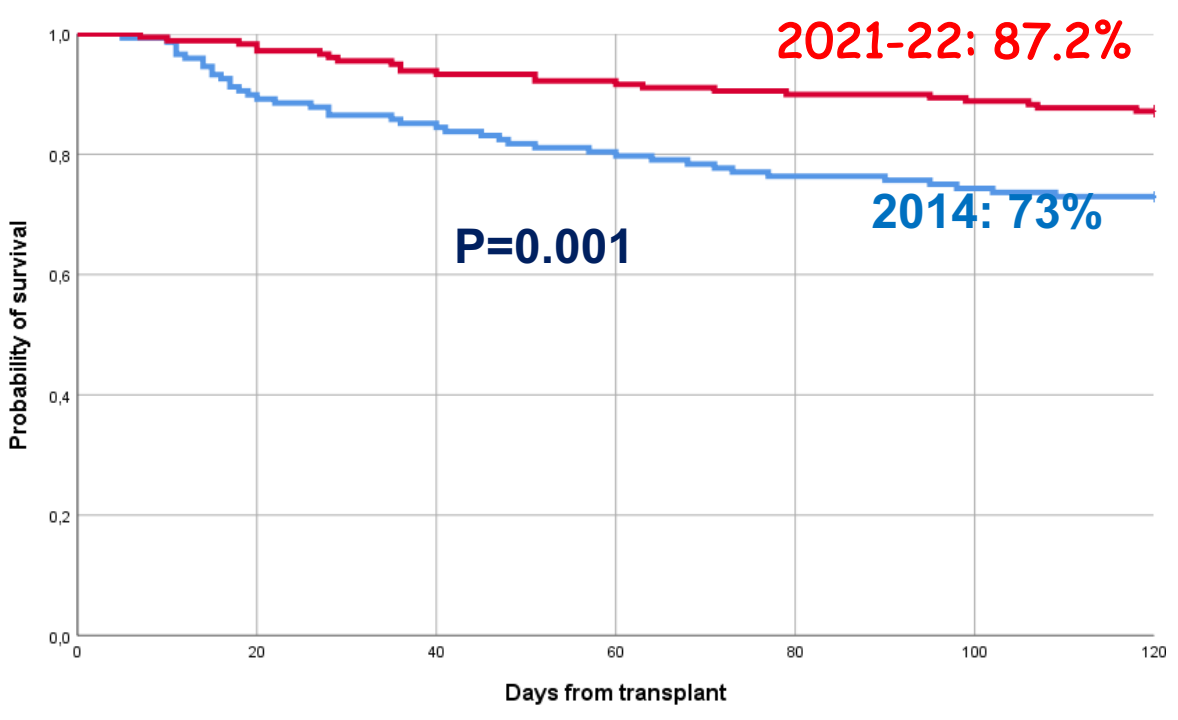
Probability of survival at 4 months from transplant according to GNB

No GNB



GNB



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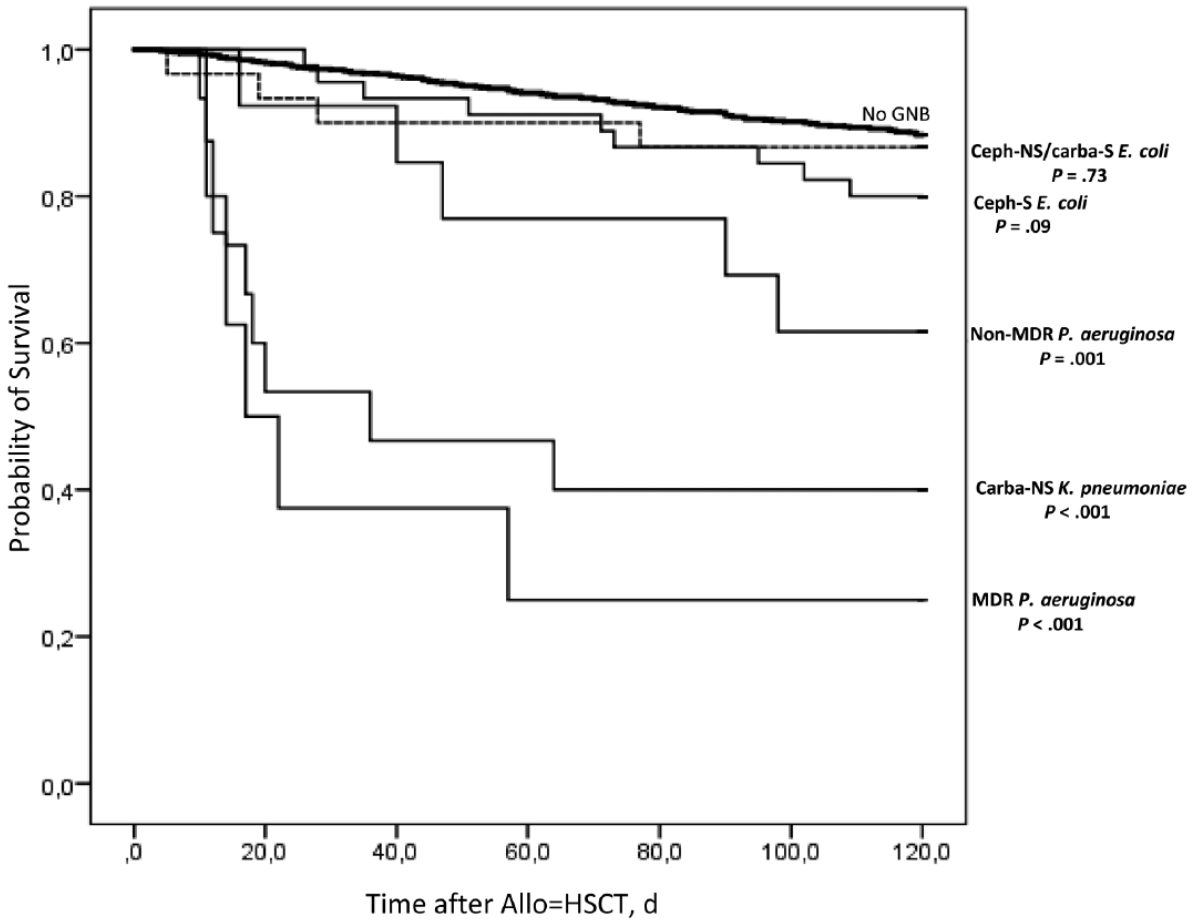

Jan- Dec 2014

The mortality rate 30 days after the diagnosis of GNB was **17.9%** (25 of 140 patients), and in 96% of patients (24 of 25) the infection was considered the primary cause of death. Of 46 patients who died before engraftment, **the cause of death was a GNB in 18 (39.1%).**

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CLINICALTRIALS.GOV IDENTIFIER: NCT04412811

Jan 2021-Mar 2022

The mortality rate 30 days after the diagnosis of GNB was **6.1%** (11 of 179 patients). Of 27 patients who died before engraftment, **the cause of death was a GNB in 5 (19%).**

GITMO
GRUPPO ITALIANO PER IL TRAPIANTO DI MIDOLLO OSSEO, CELLULE STAMINALI EMOPOIETICHE E TERAPIA CELLULARE

AMCLI associazione microbiologi clinici italiani

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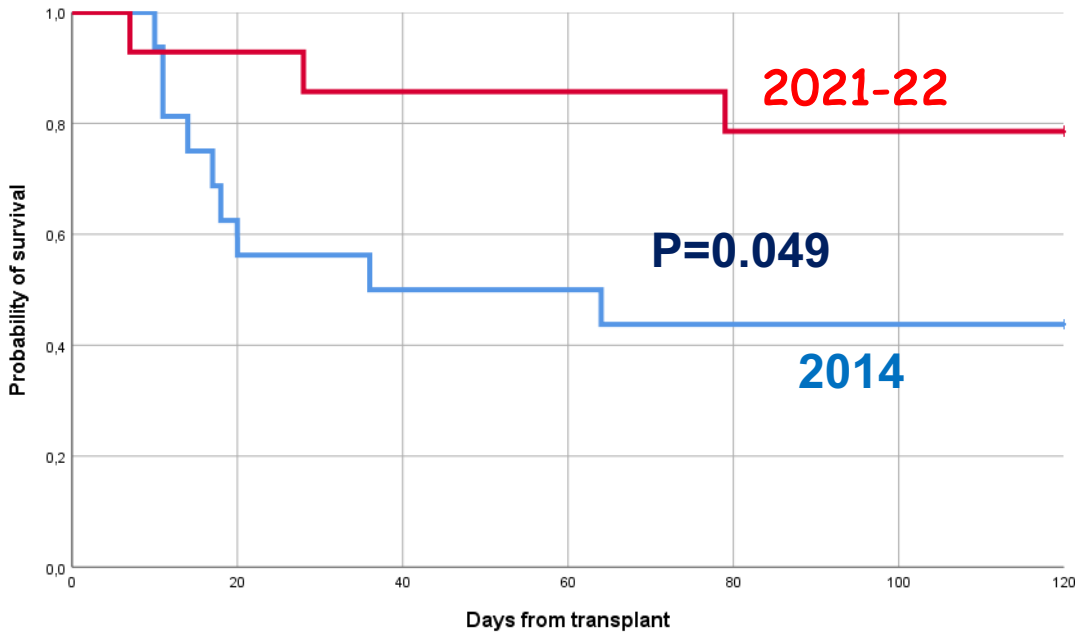
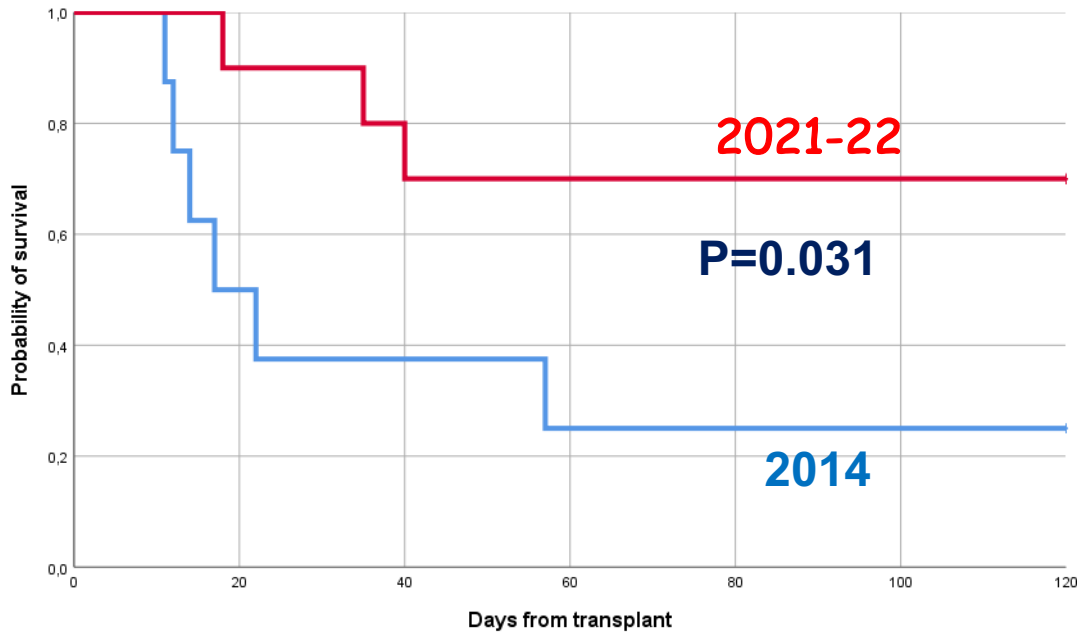
Probability of survival at 4 months from transplant according to GNB

KP-KPC

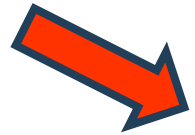
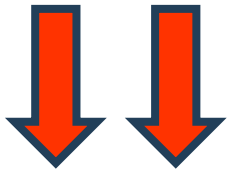


PA MDR



Gram-neg bacteremia during the engraftment period in allo-HSCT: comparison of two GITMO-AMCLI prospective studies

2014 vs 2021-22

- Incidence of GNB during the engraftment period 
- Incidence of MDR GNB 
- Overall mortality at 1 year from allo-HSCT 
- Mortality in patients with pre-engraftment GNB 
- Mortality in patients with pre-engraftment MDR GNB 

Prevention of GNB in neutropenic patients

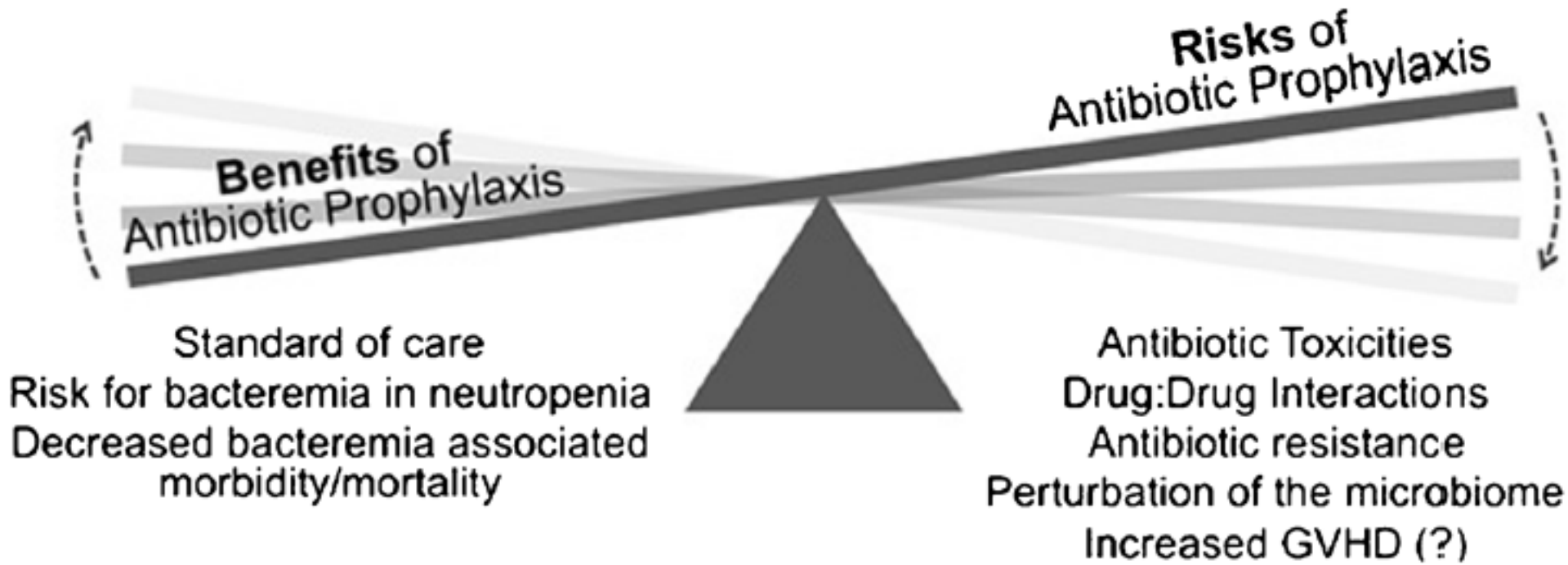
- Infection control: the lesson from COVID-19
- Antibacterial prophylaxis (fluoroquinolones)

Current Hematologic Malignancy Reports (2018) 13:59–67
https://doi.org/10.1007/s11899-018-0435-0

STEM CELL TRANSPLANTATION (R MAZIARZ, SECTION EDITOR)

Rethinking Antimicrobial Prophylaxis in the Transplant Patient in the World of Emerging Resistant Organisms—Where Are We Today?

Lucy E. Horton[1] · Nina M. Haste[2] · Randy A. Taplitz[1]



Clinical Infectious Diseases
MAJOR ARTICLE
IDSA Infectious Diseases Society of America hivma hiv medicine association OXFORD
2017;65(11):1884–96

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).

Risk factors for pre-engraftment Gram negative infections: multivariate analysis

Allo-HSCT		Auto-HSCT	
Variable	HR (95% CI), p	Variable	HR (95% CI), p
Age (+10y)	1.16 (1.06-1.27), 0.001	Age (+10y)	1.20 (1.06-1.36), 0.004
Other diseases vs acute leukemia	0.65 (0.46-0.92), 0.01	Lymphoma vs other diseases	1.86 (1.30-2.66), <0.001
Donor MMR MMU CB	 4.14 (2.31-7.42), <0.001 2.92 (1.47-5.81), 0.002 3.50 (1.32-9.29), 0.01	Antibacterial prophylaxis vs no prophylaxis	0.50(0.34-0.75), <0.001
Ex vivo T-cell depletion	0.13 (0.03-0.53). 0.004		
Days of pre-engraftment neutropenia	1.02 (1.01-1.03), <0.001		

Journal of Infection 77 (2018) 68–74

Contents lists available at ScienceDirect

Journal of Infection

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

Impact of fluoroquinolone prophylaxis during neutropenia on bloodstream infection: Data from a surveillance program in 8755 patients receiving high-dose chemotherapy for haematologic malignancies between 2009 and 2014

Winfried V. Kern[a,*], Susanne Weber[b], Markus Dettenkofer[c,1], Klaus Kaier[b], Hartmut Bertz[d], Michael Behnke[e], Maja Weisser[f], Tim Götting[c], Andreas F. Widmer[f], Christian Theilacker[f,a,2], the Hospital Infection Surveillance System for Patients with Haematologic/Oncologic Malignancies Study Group (ONKO-KISS)

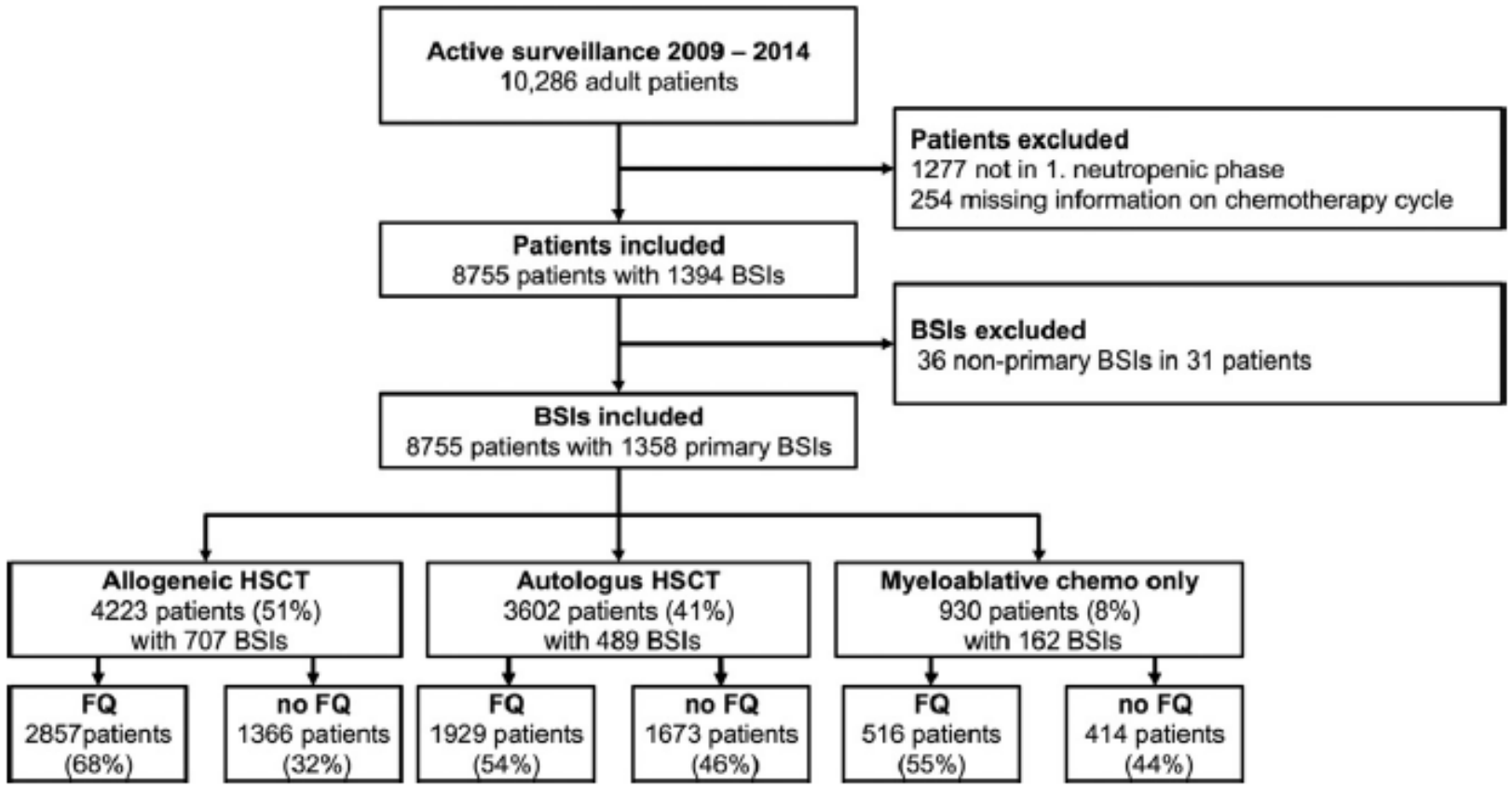


Fig. 1. Flow chart patients included in the study.

Journal of Infection 77 (2018) 68–74

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Impact of fluoroquinolone prophylaxis during neutropenia on bloodstream infection: Data from a surveillance program in 8755 patients receiving high-dose chemotherapy for haematologic malignancies between 2009 and 2014

Winfried V. Kern[a,*], Susanne Weber[b], Markus Dettenkofer[c,1], Klaus Kaier[b], Hartmut Bertz[d], Michael Behnke[e], Maja Weisser[f], Tim Götting[c], Andreas F. Widmer[f], Christian Theilacker[f,a,2], the Hospital Infection Surveillance System for Patients with Haematologic/Oncologic Malignancies Study Group (ONKO-KISS)

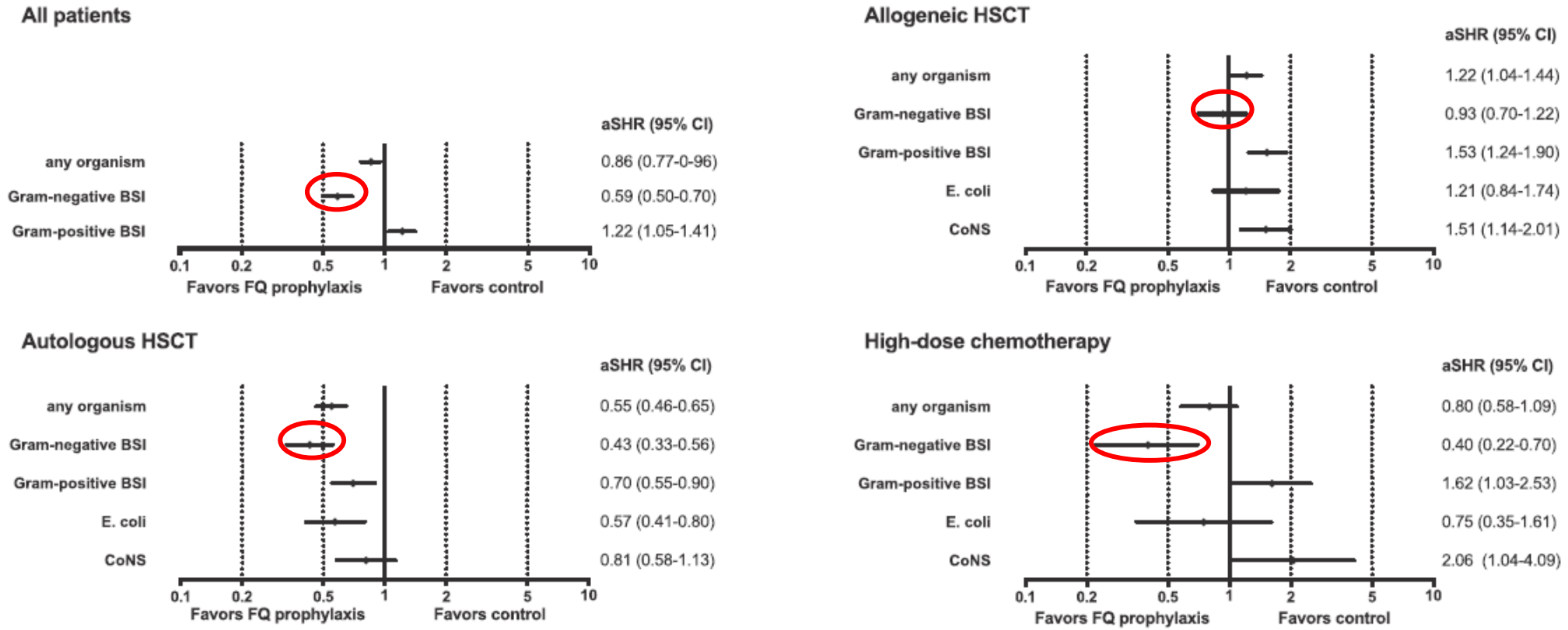


Fig. 3. Adjusted subdistribution ratios (aSHR) for BSI in neutropenic patients receiving fluoroquinolone prophylaxis versus those receiving no prophylaxis.

Effect of Levofloxacin Prophylaxis on Bacteremia in Children With Acute Leukemia or Undergoing Hematopoietic Stem Cell Transplantation

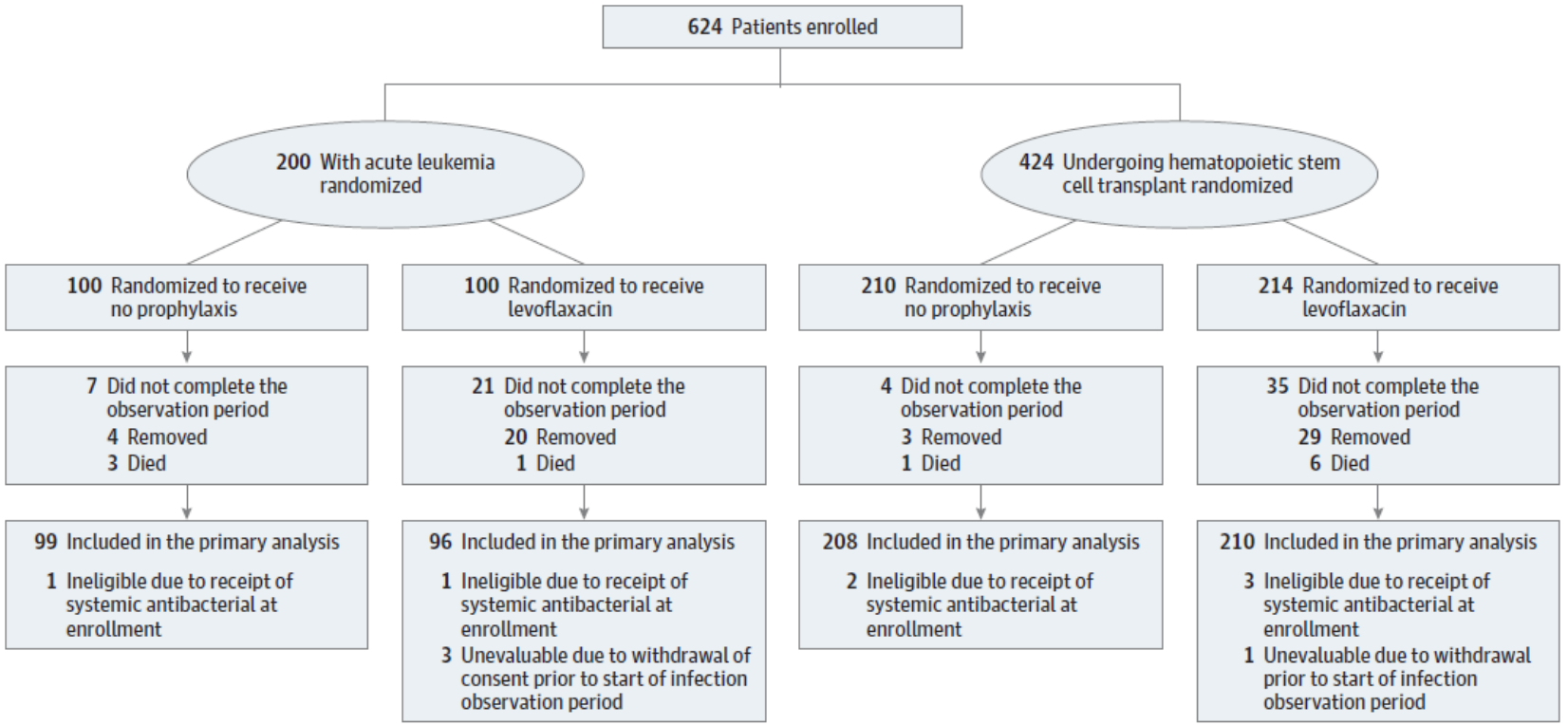
A Randomized Clinical Trial

Sarah Alexander, MD; Brian T. Fisher, DO, MSCE; Aditya H. Gaur, MD; Christopher C. Dvorak, MD; Doojduen Villa Luna, MS; Ha Dang, PhD; Lu Chen, PhD; Michael Green, MD, MPH; Michael L. Nieder, MD; Beth Fisher, MSN; L. Charles Bailey, MD, PhD; John Wiernikowski, Pharm D; Lillian Sung, MD, PhD; for the Children's Oncology Group

JAMA. 2018;320(10):995-1004.

multicenter, randomized, open-label phase 3 trial conducted by the Children's Oncology Group.

Figure. Study Participation and Flow Through the Trial[a]



Effect of Levofloxacin Prophylaxis on Bacteremia in Children With Acute Leukemia or Undergoing Hematopoietic Stem Cell Transplantation

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MAIN OUTCOMES AND MEASURES The primary outcome was the occurrence of bacteremia during 2 chemotherapy cycles (acute leukemia) or 1 transplant procedure (HSCT). Secondary

Table 2. Comparison of Bacteremia Incidence per Patient During the Infection Observation Period and Bacteremia Rate per 1000 Patient-Days Between Randomized Groups for Acute Leukemia and HSCT Groups (N = 613)

	Bacteremia Incidence, No./Total (%)		Risk Difference, % (95% CI)	Risk Ratio (95% CI)	*P* Value
	Levofloxacin	No Prophylaxis			
Primary Analysis[a]					
Total acute leukemia	21/96 (21.9)	43/99 (43.4)	21.6 (8.8-34.4)	0.50 (0.32-0.78)	.001
AML	15/64 (23.4)	25/63 (39.7)	16.3 (0.3-32.2)	0.59 (0.35-1.01)	.05
Relapsed ALL	6/32 (18.8)	18/36 (50.0)	31.2 (10.1-52.5)	0.38 (0.17-0.83)	.007
Total HSCT	23/210 (11.0)	36/208 (17.3)	6.3 (0.3-13.0)	0.63 (0.39-1.03)	.06
Autologous	3/79 (3.8)	9/78 (11.5)	7.7 (0.51-16.0)	0.33 (0.09-1.17)	.07
Allogeneic	20/131 (15.3)	27/130 (20.8)	5.5 (3.8-14.8)	0.74 (0.43-1.24)	.25
Post hoc Analysis[b]					
	Bacteremia Rate/1000 Patient-Days (95% CI)			Adjusted Rate Ratio (95% CI)[c]	
Total acute leukemia	4.9 (3.3-7.3)[c]	9.4 (7.1-12.3)[c]	4.3 (1.3-7.4)	0.52 (0.32-0.85)	.008
Person-days of observation, No.	5327	5973			
Total HSCT	5.3 (3.5-8.0)[c]	10.0 (6.6-14.8)[c]	5.2 (1.1-9.3)	0.53 (0.32-0.88)	.02
Person-days of observation, No.	4042	3766			

CONCLUSIONS AND RELEVANCE Among children with acute leukemia receiving intensive chemotherapy, receipt of levofloxacin prophylaxis compared with no prophylaxis resulted in a significant reduction in bacteremia. However, there was no significant reduction in bacteremia for levofloxacin prophylaxis among children undergoing HSCT.

Impact of Fluoroquinolone Prophylaxis on Neutropenic Fever, Infections, and Antimicrobial Resistance in Newly Diagnosed AML Patients

Jessica Caro,[1,*] Rafael Madero-Marroquin,[2,*] Nicole Zubizarreta,[3] Erin Moshier,[3] Douglas Tremblay,[3] Alex Coltoff,[3] Guido Lancman,[3] Risa Fuller,[4] Meenakshi Rana,[4] John Mascarenhas,[3] Samantha E. Jacobs[4]

Clinical Lymphoma, Myeloma and Leukemia, Vol. 22, No. 12, 903–911 © 2022 I

We evaluated the effectiveness of primary fluoroquinolone prophylaxis in an area with high fluoroquinolone resistance. We performed a retrospective chart review of newly diagnosed adult AML patients who received frontline therapy at Mount Sinai Hospital in New York, NY, between 2012 and 2019. Primary outcome was development of neutropenic fever. Secondary outcomes were development of systemic bacterial infections and infections with multidrug-resistant organisms and Clostridioides difficile

Table 2 Incidence of Neutropenic Fever and Mortality by Antibiotic Prophylaxis Group

Outcomes	No Prophylaxis N = 34	Prophylaxis N = 87	*P*-value
Neutropenic Fever, N (%)	28 (82.4%)	56 (64.4%)	
Crude Time-Varying HR [95% CI] – Post Induction	*Reference*	0.73 [0.45-1.18]	.193
Multivariable[a] Time-Varying HR [95% CI] – Post Induction	*Reference*	0.59 [0.36-0.97]	.039
Mortality, N (%)	17 (50.0%)	48 (55.2%)	
Crude Time-Varying HR [95% CI] – Post Induction	*Reference*	0.98 [0.56-1.71]	.939
Multivariable* Time-Varying HR [95% CI] – Post Induction	*Reference*	0.95 [0.54-1.68]	.860

Table 3 Systemic Bacterial Infections Per Patient During Induction Therapy and 6-month Follow-up by Antibiotic Prophylaxis Group

Outcome	Induction		Relative Risk	*P*-value	Six-Month Follow Up		Relative Risk	P-value
	No Prophylaxis N = 34	Prophylaxis N = 87			No Prophylaxis[a] N = 33	Prophylaxis N = 87		
Any BSI	12 (35.3%)	15 (17.2%)	0.4885	.030	17 (51.5%)	27 (31.0%)	0.6024	0.029
Gram-negative BSI	6 (17.7%)	5 (5.8%)	0.3257	.049	10 (30.3%)	15 (17.2%)	0.5690	0.111
Gram-positive BSI	9 (26.5%)	10 (11.5%)	0.4342	.043	12 (36.4%)	17 (19.5%)	0.5374	0.050
Fluoroquinolone-resistant gram-negative bacteria	2 (5.9%)	4 (4.6%)	0.7816	.770	6 (18.2%)	9 (10.3%)	0.5690	0.246
Other multidrug-resistant bacteria[b]	4 (11.8%)	11 (12.6%)	1.0747	.895	9 (27.3%)	18 (20.7%)	0.7586	0.434
Any CDI	19 (55.9%)	26 (29.9%)	0.5348	.005	21 (63.6%)	37 (42.5%)	0.6683	0.026
Any MDI or CDI	26 (76.5%)	38 (43.7%)	0.5712	.001	27 (81.8%)	55 (63.2%)	0.7727	0.026
C. difficile infection	3 (8.8%)	4 (4.6%)	0.5211	.376	5 (15.2%)	6 (6.9%)	0.4552	0.167

BSI= bloodstream infection; CDI= clinically documented infection; MDI= microbiologically documented infection
[a] One patient was lost to follow-up after induction and was therefore not included in the 6-month follow-up period
[b] Includes infections due to methicillin-resistant Staphylococcus aureus, Vancomycin-resistant Enterococcus, extended-spectrum beta-lactamase producing Enterobacterales, carbapenem-resistant Enterobacterales, or multidrug-resistant gram-negative bacteria (defined as non-susceptibility to at least one agent in ≥ 3 antimicrobial categories)

Figure 1 Predicted probabilities for neutropenic fever by prophylaxis group before and after receiving induction chemotherapy.

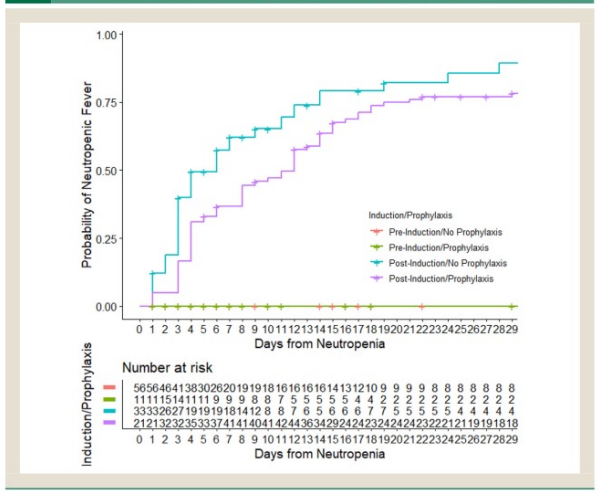
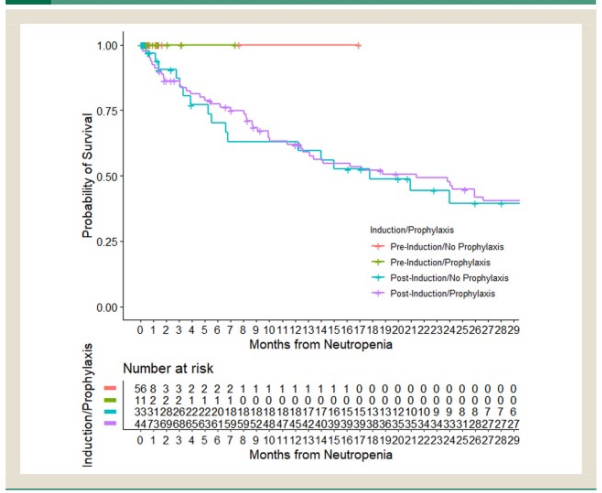


Figure 2 Predicted probabilities for overall survival by prophylaxis group before and after receiving induction chemotherapy.



In an area with high fluoroquinolone resistance, primary fluoroquinolone prophylaxis in newly diagnosed AML patients reduced the risk of neutropenic fever and systemic bacterial infections without increased antimicrobial resistance. Prospective, randomized studies are needed to confirm these observations.

VOLUME 36 · NUMBER 30 · OCTOBER 20, 2018

JOURNAL OF CLINICAL ONCOLOGY ASCO SPECIAL ARTICLE

Check for updates

Antimicrobial Prophylaxis for Adult Patients With Cancer-Related Immunosuppression: ASCO and IDSA Clinical Practice Guideline Update

Randy A. Taplitz, Erin B. Kennedy, Eric J. Bow, Jennie Crews, Charise Gleason, Douglas K. Hawley, Amelia A. Langston, Loretta J. Nastoupil, Michelle Rajotte, Kenneth V. Rolston, Lynne Strasfeld, and Christopher R. Flowers

CLINICAL QUESTION 1

Antibacterial Prophylaxis. Does antibacterial prophylaxis with a fluoroquinolone, compared with placebo, no intervention, or another class of antibiotic, reduce the incidence of and mortality as a result of febrile episodes in patients with cancer?

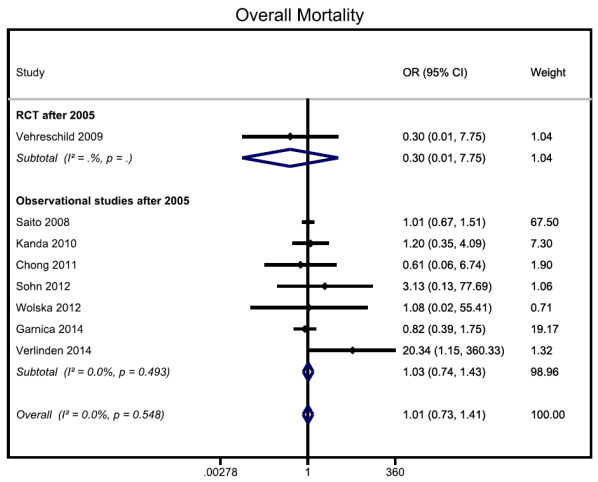
Recommendation 1.2. Antibiotic prophylaxis with a fluoroquinolone is recommended for patients who are at high risk for FN or profound, protracted neutropenia—for example, patients with acute myeloid leukemia/myelodysplastic syndromes (AML/MDS) or HSCT treated with myeloablative conditioning regimens.

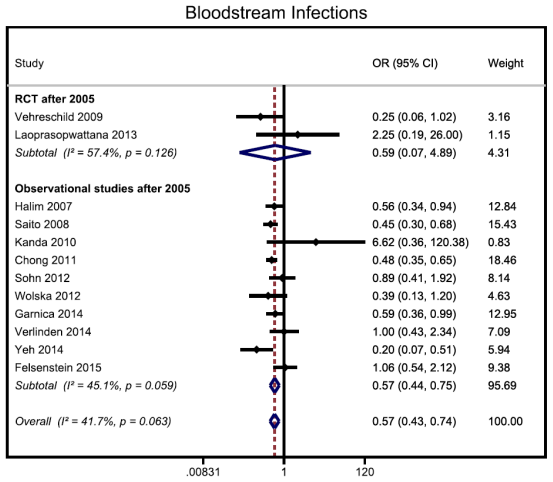
Fluoroquinolone prophylaxis in haematological cancer patients with neutropenia: ECIL critical appraisal of previous guidelines

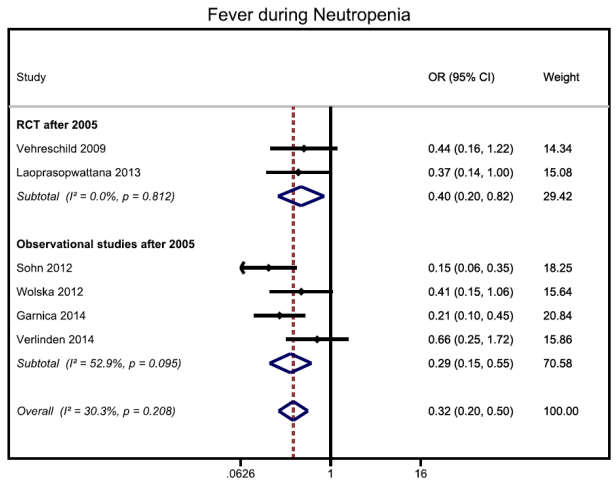
Malgorzata Mikulska [a,*], Diana Averbuch [1,b], Frederic Tissot [1,c], Catherine Cordonnier [d], Murat Akova [e], Thierry Calandra [f], Marcello Ceppi [g], Paolo Bruzzi [g], Claudio Viscoli [a] on behalf of the European Conference on Infections in Leukemia (ECIL), a joint venture of the European Group for Blood and Marrow Transplantation (EBMT), the European Organization for Research and Treatment of Cancer (EORTC), the International Immunocompromised Host Society (ICHS) and the European Leukemia Net (ELN)

Journal of Infection (2018) **76**, 20–37

Fluoroquinolone (FQ) prophylaxis was recommended in 2005 by European Conference on Infections in Leukemia (ECIL) for patients with prolonged neutropenia. In consideration of a worldwide increase in antibiotic resistance, the issue of FQ prophylaxis during neutropenia was re-evaluated.







No effect of the background rate of FQ resistance on the efficacy of FQ prophylaxis was observed. In few studies, FQ prophylaxis resulted in an increased colonisation or infection with FQ- or multi-drug resistant strains.

Use of antibacterial prophylaxis for patients with neutropenia

M. A. Slavin,[1,2] S. Lingaratnam,[1] L. Mileshkin,[1,3] D. L. Booth,[2] M. J. Cain,[4] D. S. Ritchie,[1,2] A. Wei[5] and K. A. Thursky[1,2,6]

[1]Peter MacCallum Cancer Centre, East Melbourne, Victoria, [2]The Royal Melbourne Hospital, Melbourne, Victoria, [3]University of Melbourne, Melbourne, Victoria, [4]Sir Charles Gardiner Hospital, Perth, Western Australia, [5]The Alfred Hospital, Melbourne, Victoria, and [6]St Vincent's Hospital, Melbourne, Victoria, Australia

Internal Medicine Journal **41** (2011) 102–109

Table 1 Key practice points – prophylaxis

- There is currently insufficient evidence to recommend routine use of FQ prophylaxis in patients at low risk of developing neutropenic fever (grade C)
- FQ prophylaxis should also not be routinely used in high-risk haematology patients (grade C)
- FQ prophylaxis could be considered in outpatient SCT and palliative patients with bone marrow failure (grade C)
- Appropriate surveillance (detailed within text) should be undertaken by centres using FQ prophylaxis (grade C)
- When the prevalence of FQ resistance in *E. coli* in internal medicine patients at an institution approaches 20%, FQ prophylaxis is unlikely to be effective (grade C)

SCT, stem cell transplant; FQ, fluoroquinolone.

8th European Conference on Infections in Leukaemia: 2020 guidelines for the use of antibiotics in paediatric patients with cancer or post-haematopoietic cell transplantation

Thomas Lehrnbecher, Dina Averbuch, Elio Castagnola, Simone Cesaro, Roland A Ammann, Carolina Garcia-Vidal, Jukka Kanerva, Fanny Lanternier, Alessio Mesini, Malgorzata Mikulska, Dorothea Pana, Nicole Ritz, Monica Slavin, Jan Styczynski, Adilia Warris, Andreas H Groll, on behalf of the 8th European Conference on Infections in Leukaemia

Lancet Oncol 2021; 22: e270–80

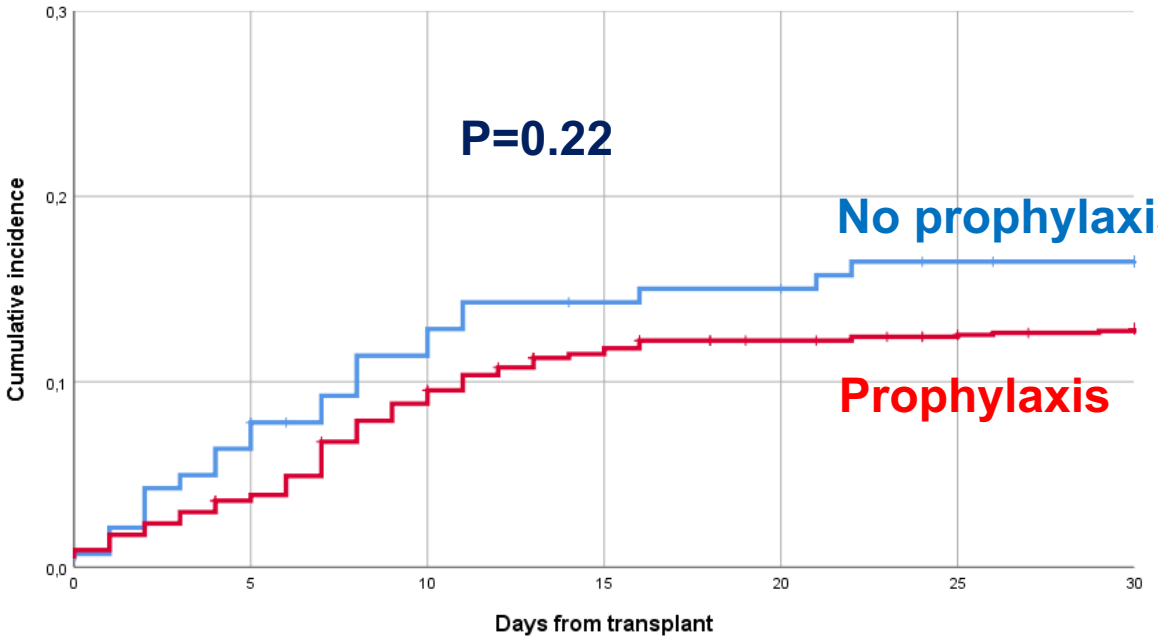
Prophylaxis of bacterial infections

the ECIL-8 group does not recommend routine antibacterial prophylaxis for paediatric patients with lymphoma, acute leukaemia, relapsed acute leukaemia, or patients with neutropenia during the pre-engraftment stage of HCT (grade D recommendation, level of evidence III). This recommendation is based on data from randomised trials and meta-analyses, information from long-term observational studies on resistance, and European Medicines Agency recommendations.

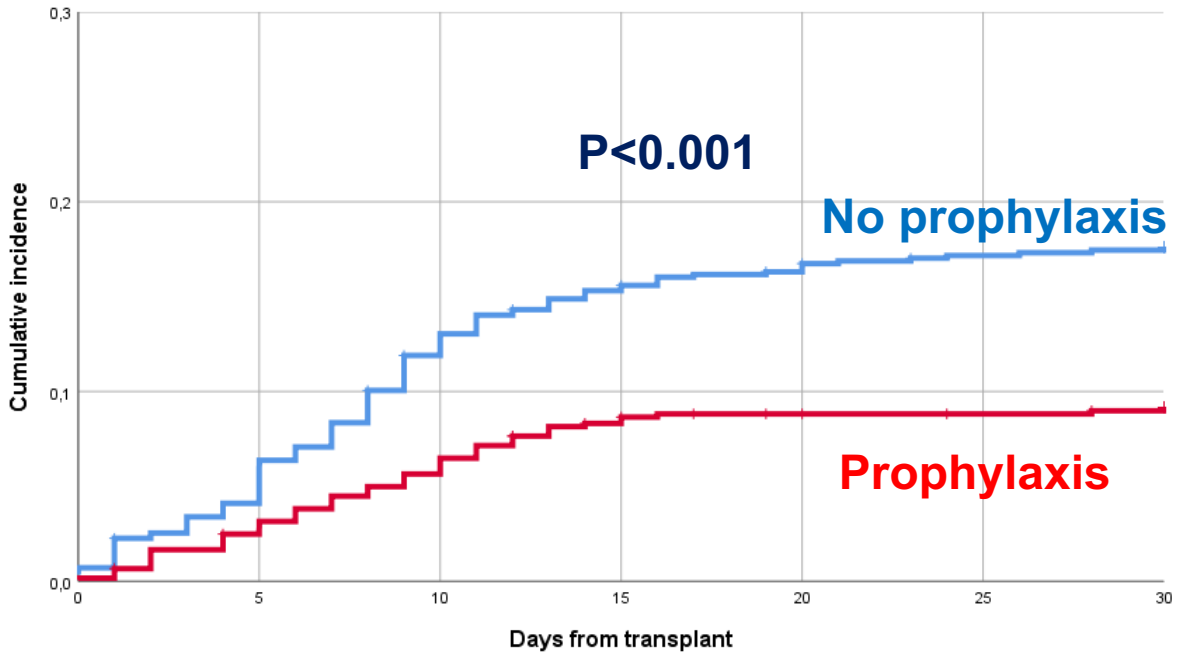
Gram-neg bacteremia during the engraftment period in allo-HSCT: comparison of two GITMO-AMCLI prospective studies

Cumulative incidence of GNB according to antibacterial prophylaxis

Study 2014



Study 2021-22



Study 2014: no prophylaxis 141/1118 pts (12.6%)

Study 2021-22: no prophylaxis 707/1310 pts (54%)

Gram-neg bacteremia during the engraftment period in allo-HSCT: comparison of two GITMO-AMCLI prospective studies

Efficacy of ATB prophylaxis according to GNB susceptibility pattern

GNB susceptibility pattern, n	No ATB prophylaxis, n (%)	ATB Prophylaxis, n (%)	p
Enterobacteria no ESBL, 146	75/848 (8.8)	71/1580 (4.5)	<0.0001
Enterobacteria ESBL ,83	33/848 (3.9)	50/1580 (3.2)	0.35
Enterobacteria KPC, 30	10/848 (1.2)	20/1580 (1.3)	1
P.aeruginosa no MDR, 23	11/848 (1.3)	12/1580 (0.8)	0.2
P.aeruginosa MDR, 18	8/848 (0.8)	12/1580 (0.8)	1
Other, 25	10/848 (1.2)	15/1580 (0.9)	0.7
Total, 327	147/848 (17.3)	180/1580 (11.4)	0.0001

ATB prophylaxis during the engraftment after allo-HSCT:

- **Significantly prevents GNB by not MDR strains**
- **Does not increase the risk GNB by MDR strains**

Appropriate management of MDR-GNB infections in neutropenic patients

The antibiotic therapy in febrile high-risk neutropenic patients should be:

- Early
- Targeted

Impact of Empirical Antibiotic Regimens on Mortality in Neutropenic Patients with Bloodstream Infection Presenting with Septic Shock

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

February 2022 Volume 66 Issue 2 e01744-21

Mariana Chumbita,[a] Pedro Puerta-Alcalde,[a] Carlota Gudiol,[b,c,d] Nicole Garcia-Pouton,[a] Júlia Laporte-Amargós,[b,d] Andrea Ladino,[e] Adaia Albasanz-Puig,[b,d] Cristina Helguera,[f] Alba Bergas,[b] Ignacio Grafia,[e] Enric Sastre,[b] María Suárez-Lledó,[g] Xavier Durà,[b,d] Carlota Jordán,[a] Francesc Marco,[h,i] Maria Condom,[j] Pedro Castro,[k] Jose A. Martínez,[a] Josep Mensa,[a] Alex Soriano,[a] Jordi Carratalà,[b,d] Carolina Garcia-Vidal[a]

We analyzed risk factors for mortality in febrile neutropenic patients with bloodstream infections (BSI) presenting with septic shock and **assessed the impact of empirical antibiotic regimens**. A multicenter retrospective study (2010 to 2019) of two prospective cohorts compared BSI episodes in patients with or without septic shock

TABLE 3 Mortality according to active empirical antibiotic coverage administered in Gram-negative bloodstream infection with septic shock[a]

Active antibiotic(s)	Survival, *n* (%)	Death, *n* (%)
Only 1 β-lactam was active (*n* = 64)	22 (34)	42 (66)
Only amikacin was active (*n* = 10)	1 (10)	9 (90)
Combined β-lactam and amikacin were both active (*n* = 101)	62 (61)	39 (39)
Combined β-lactam, quinolone, and amikacin were all active (*n* = 4)	2 (50)	2 (50)
Combined β-lactam and quinolone were both active (*n* = 6)	4 (67)	2 (33)
No active empirical antibiotic was administered (*n* = 22)	3 (14)	19 (86)

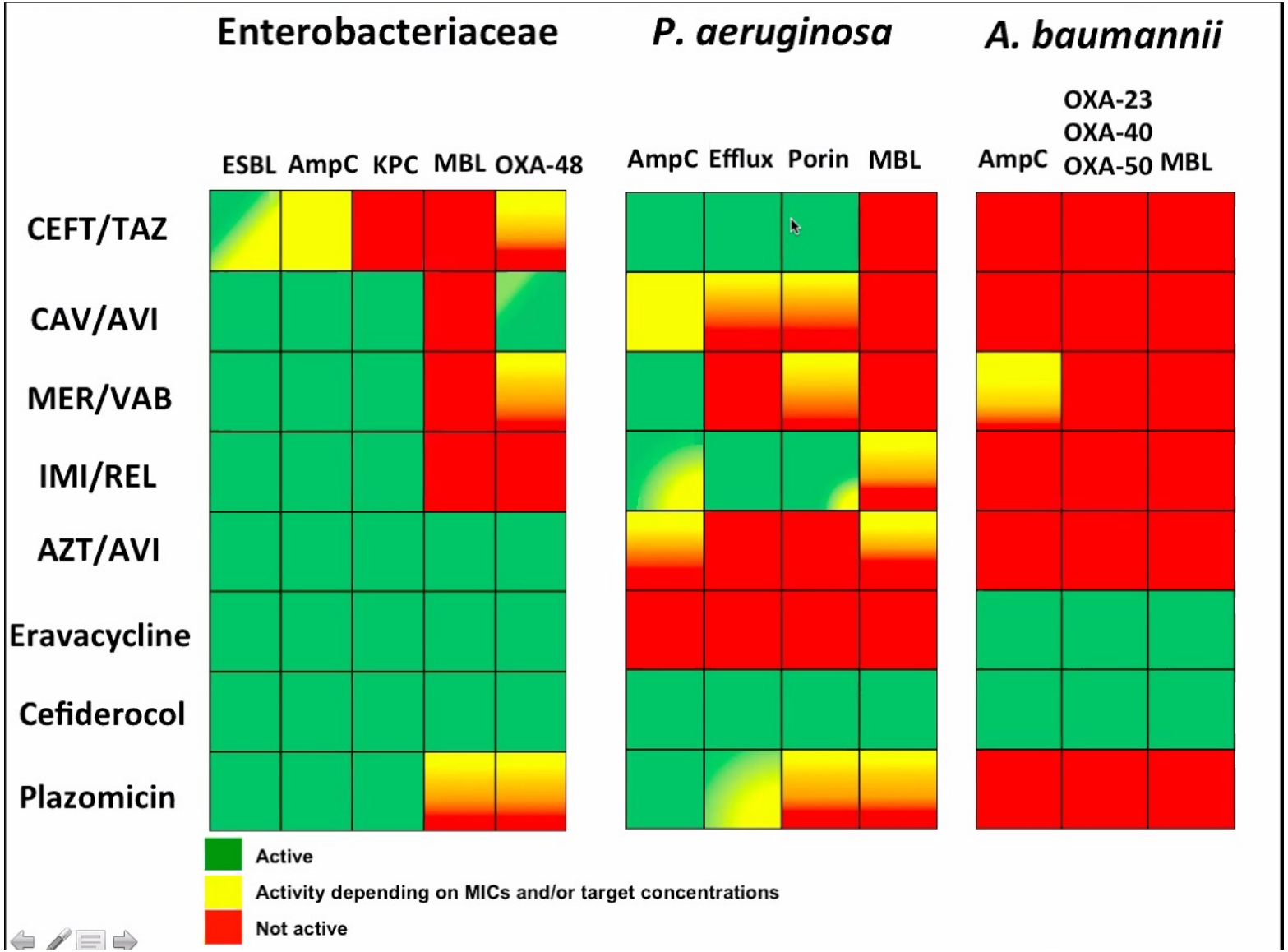
[a]*P* value for all data is <0.001.

Age of .70 years (odds ratio [OR], 2.3; 95% confidence interval [CI], 1.2 to 4.7), **IEAT for Gram-negative bacilli** (OR, 3.8; 95% CI, 1.3 to 11.1), acute kidney injury (OR, 2.6; 95% CI, 1.4 to 4.9), and **amikacin as the only active antibiotic** (OR, 15.2; 95% CI, 1.7 to 134.5) were independent risk factors for mortality, while **the combination of b-lactam and amikacin was protective** (OR, 0.32; 95% CI, 0.18 to 0.57).

Antibiotic armamentarium against Gram negative bacteria

Piperacillin-tazobactam
Ceftazidime
Cefepime
Meropenem
Colistin
Fosfomycin
Tygecicline
Aminoglycosides

Targeted
in documented infections
vs
empiric



The choice of empiric antibiotic therapy in febrile neutropenia in the era of MDR

- Inappropriate empiric beta-lactam therapy is predictive of higher mortality in severe G-neg BSI
- In conditions at high risk of MDR infection an advanced beta-lactam should be considered in the first line empiric therapy

Clinical Infectious Diseases

MAJOR ARTICLE

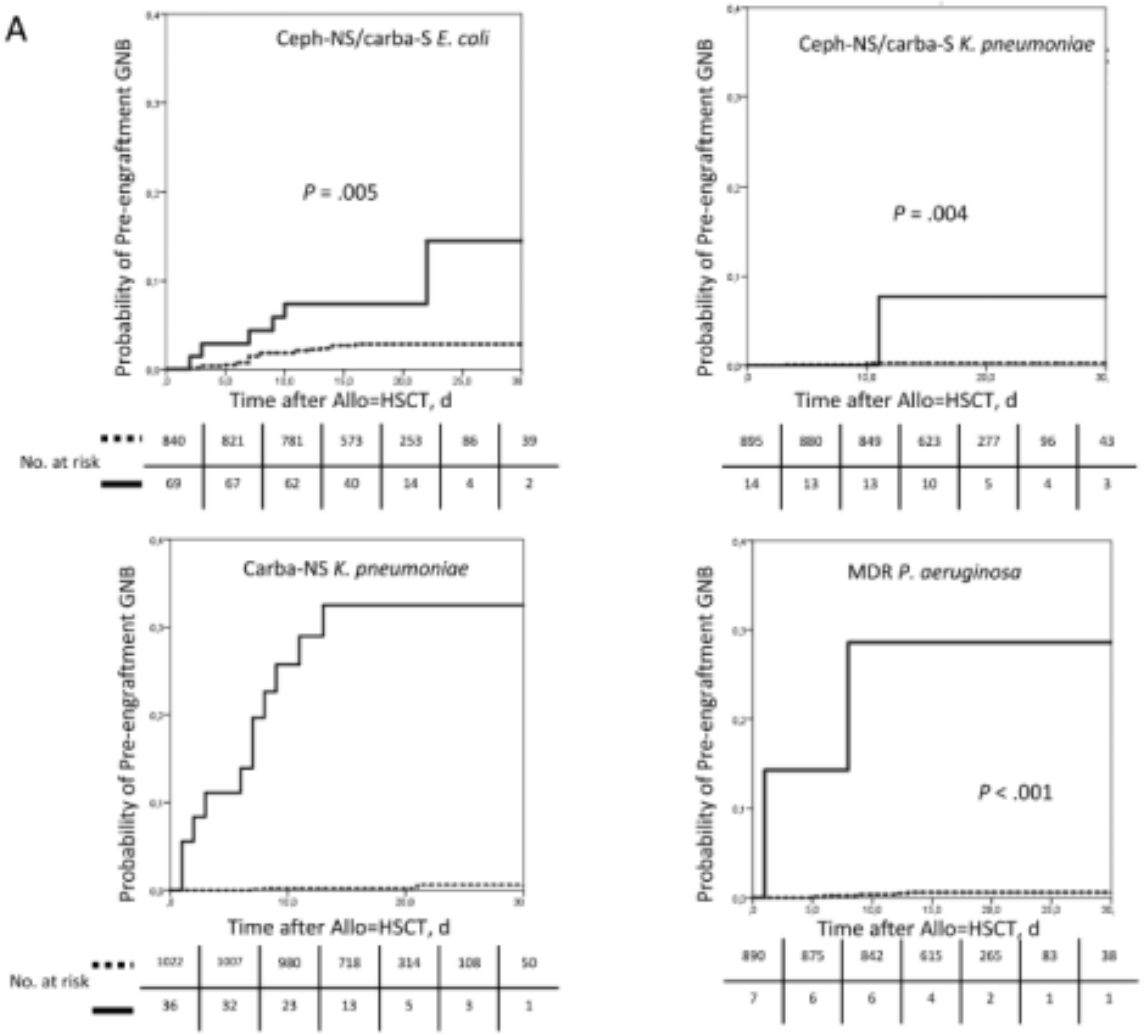
IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

2017;65(11):1884–96

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 (G Microbiologi Clinici Italiani (AMCLI).

MDR/XDR GNB colonization and risk of pre-engraftment bacteremia



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MDR/XDR GNB colonization and risk of pre-engraftment bacteremia

Table 5. Correlation Between Rectal Colonization by Resistant Gram-Negative Bacteria and Pre-Engraftment Gram Negative Bacteremia Caused by a Pathogen With the Same Susceptibility Phenotype

	Allo-HSCT		Auto-HSCT	
Microorganism	Colonized/Evaluable Patients, No. (%)	Pre-engraftment GNB Colonized/Not Colonized, % (P Value)	Colonized/Evaluable Patients, No. (%)	Pre-engraftment GNB Colonized/Not colonized, % (P Value)
Ceph-R/carba-S *Escherichia Coli*	69/909 (7.6)	8.7/1.3 (.001)	89/1307 (6.8)	9.0/4.3 (.06)
Ceph-R/carba-S *Klebsiella pneumoniae*	14/909 (1.5)	7.1/0.4 (.07)	21/1307 (1.6)	19.0/0.3 (<.001)
Carba-R *K. pneumoniae*	36/1058 (3.4)	27.8/0.4 (<.001)	21/1432 (1.5)	19.0/0.007 (<.001)
MDR *Pseudomonas aeruginosa*	7/897 (0.8)	28.6/0.6 (.001)	2/1307 (0.15)	50/0.007 (.003)

Abbreviations: Allo-HSCT and auto-HSCT, allogeneic and autologous hematopoietic stem cell transplantation; carba-R, resistant to carbapenems; carba-S, sensitive to carbapenems; ceph-R, resistant to the third-generation cephalosporin ceftazidime; GNB, gram-negative bacteremia; MDR, multidrug-resistant.

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Management of carbapenem resistant *klebsiella pneumoniae* infections in stem cell transplant recipients: an italian multidisciplinary consensus statement

by Corrado Girmenia, Claudio Viscoli, Alfonso Piciocchi, Laura Cudillo, Stefano Botti, Antonio Errico, Loredana Sarmati, Fabio Ciceri, Franco Locatelli, Maddalena Giannella, Matteo Bassetti, Carlo Tascini, Letizia Lombardini, Ignazio Majolino, Claudio Farina, Francesco Luzzaro, Gian Maria Rossolini, and Alessandro Rambaldi

- CRKp carriers, at onset of febrile neutropenia or other signs of possible infection.
  - CTAT based on the susceptibility pattern of the colonizing isolate with the inclusion of at least two active agents, if possible, is strongly recommended (**AII**).
  - The use of standard empiric antibiotic therapy, not including CRKp-active drugs, is discouraged (**AII**).
  - In SCT centers with an ongoing outbreak of CRKp, the choice of empiric CTAT may be considered also in febrile patients who are not colonized, or with an unknown colonization status. (**BII**). Prompt withdrawal of CTAT with downgrading to more traditional drugs is recommended if cultures come back negative for CRKp, also taking into consideration the clinical findings (**AII**).

Susceptibility pattern of the colonizing isolate

At least two active agents

Standard empiric antibiotic therapy discouraged in patients with colonization by MDR bacteria

Consider active empiric therapy also in noncolonized patients during an ongoing outbreak

Micozzi et al. BMC Infect Dis (2021) 21:1079
https://doi.org/10.1186/s12879-021-06747-8

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Reduced mortality from KPC-*K.pneumoniae* bloodstream infection in high-risk patients with hematological malignancies colonized by KPC-*K.pneumoniae*

Alessandra Micozzi[1*], Giuseppe Gentile[1], Stefania Santilli[2], Clara Minotti[3], Saveria Capria[3], Maria Luisa Moleti[3], Walter Barberi[3], Claudio Cartoni[3], Silvia Maria Trisolini[3], Anna Maria Testi[1], Anna Paola Iori[3], Giampaolo Bucaneve[4] and Robin Foà[1]

We compared the outcomes of KPC-KpBSIs occurring in high-risk hematological patients known to be colonized with KPC-KP, during two time periods: Mar2012-Dec2013 (Period 1, initial approach to KPC-K.pneumoniae spread) and Jan2017-Oct2018 (Period 2, full application of the preemptive strategy).

- Period 1: standard empiric antibiotics (pip/tazo)
- Period 2: empiric antibiotics active against KPC-KP (coli+tige±genta; HD MEM, MEM+ERTA; CAZ-AVI+tige±genta)

- KPC-KpBSI-related mortality in hematological patients identified as KPC-K.pneumoniae carriers dropped from 50% in Period 1 to 6% in Period 2 ($p < 0.01$).
- Overall, KPC-KpBSI-related mortality was 88% with no initial active treatment, 11.5% with at least one initial active antibiotic ($p < 0.01$), 9% with initial active combination. **Only the initial active treatment resulted independently associated with survival**.

Table 4 Multivariate Models of risk factors for 30 days crude mortality in patients population (Forward Stepwise logistic regression)

	OR (CI 95%)	p-value
MODEL 1		
KPC-*K.pneumoniae* BSI developing during inactive antibiotic treatment[a]	28 (3.9 to 199)	0.001
Acute myeloid leukemia	Not included in the Model	
Shock at onset	Not included in the Model	
Intensive chemotherapy	Not included in the model	
MODEL 2		
Initial active treatment	0.019 (0.002 to 0.20)	0.001
KPC-*K.pneumoniae* BSI developing during inactive antibiotic treatment[a]	Not included in the model	
Acute myeloid leukemia	Not included in the model	
Shock at onset	Not included in the model	
Intensive chemotherapy	Not included in the model	

[a] Developing in KPC-*K.pneumoniae* carriers receiving standard empiric antibiotic treatment

Infection and Drug Resistance

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ORIGINAL RESEARCH

Infection and Drug Resistance 2023:16 695–704

Benefits and Safety of Empiric Antibiotic Treatment Active Against KPC-*K. pneumoniae* in Febrile Neutropenic Patients with Acute Leukemia Who are Colonized with KPC-*K. pneumoniae*. A 7-Years Retrospective Observational Cohort Study

Alessandra Micozzi[1], Clara Minotti[2], Saveria Capria[2], Claudio Cartoni[2], Silvia Maria Trisolini[2], Giovanni Manfredi Assanto[1], Walter Barberi[2], Maria Luisa Moleti[2], Stefania Santilli[3], Maurizio Martelli[1], Giuseppe Gentile[1]

A 7-year (2013–2019) retrospective observational cohort study was conducted at the Haematology, Sapienza Rome University (Italy) on 94 febrile neutropenia episodes (FNE) in AL patients KPC-K. pneumoniae carriers treated with active EAT

Table 2 Response to Empiric Antibiotic Treatment (EAT)

	Total EAT n. 94 (%)	CAZAVI-Based EAT n. 56 (%)	Colistin-Based EAT n. 38 (%)	p-value (OR) [CI 95%]
Overall successful response	88 (94)	55 (98)	33 (87)	0.037 (0.26) [0.044–1.608]
Combination regimens, success of total (%)	76 of 82 (93)	43 of 44 (98)	33 of 38 (87)	0.01 (0.29) [0.049–1.78]
Failure:	6 (6.3)	1 (1.7)	5 (13)	0.037 (0.45) [0.28–0.70]
Death as a result of primary infection	4 (4.2)	–	4 (10.5)	0.024 (0.37) [0.29–0.49]
- Early death between 1 week	2 (2.1)	–	2 (2.6)	0.161 (0.131) [0.303–0.404]
KPC-KpBSI persistence or developed under EAT	2 (2.1)	1 (1.7)	1 (2.6)	0.64
Microbiologically documented infections, success of total	46 of 49 (94)	29 of 30 (97)	17 of 19 (89)	0.44
Blood stream infections (BSI)	36 of 39 (92)	22 of 23 (96)	14 of 16 (87.5)	0.54
Gram-negative BSI	24 of 27 (89)	13 of 14 (93)	12 of 14 (86)	0.23
KPC-KpBSI	19 of 22 (86)	10 of 11 (91)	9 of 11 (82)	0.21
Gram-positive BSI	12 of 12 (100)	9 of 9	3 of 3	0.19
Without BSI	10 of 10 (100)	7 of 7	3 of 3	0.46
Due to KPC-*K. pneumoniae*	9 of 9 (100)	6 of 6	3 of 3	0.32
Clinically documented infections, success of total (%)	14 of 16 (88)	12 of 12 (100)	2 of 4 (50)	0.049 (0.43) [0.078–2.37]
Fever of unknown origin, success of total (%)	24 of 25 (96)	11 of 11 (100)	13 of 14 (93)	0.56
Success without modification of EAT	61 (65)	41 (73)	20 (53)	0.034 (0.71) [0.51–1.1]
All combination regimens, success of total (%)	56 of 82 (68)	36 of 44 (82)	20 of 38 (53)	0.01 (1.27) [1.11–1.45]
Combination regimens including tigecycline plus gentamicin, success of total (%)	41 of 60 (68)	32 of 39 (82)	9 of 21 (53)	0.003 (0.79) [0.56–1.1]
Monotherapy, success of total (%)	5 of 12 (5)	5 of 12 (5)	–	

- All deaths occurred in patients treated with colistin-based EAT (4/38 vs 0/56, p = 0.02).
- CAZAVI-containing EAT was the only independent factor for an overall successful response (HR 0.058, CI 0.013–1.072, p = 0.058)

The choice of antibacterial therapy in febrile neutropenic patients in the era of MDR infections

- *Right first time* still represent a challenge in the choice of antibiotic therapy in febrile neutropenia
- New molecules active against MDR-GNB should be included in the empiric therapy of febrile neutropenia in patients at high-risk
- Biologic markers (i.e.PCR, PCT) are not able to predict the cause of febrile neutropenia in the early phase when first empiric therapy should be decided
- Colonization and local diffusion of MDR pathogens are criteria for the choice of active early empiric antibiotic therapy.
- HOWEVER, de-escalation strategy is still a debated issue of the antimicrobial stewardship in high-risk febrile neutropenia patients.