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De-escalation antibiotica dopo trapianto allogenico nei pazienti colonizzati con germi MDR

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PALERMO

No Disclosures

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

AGENDA

Problema MDR nel trapianto allogenico

De-escalation

Nostra esperienza

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De-escalation

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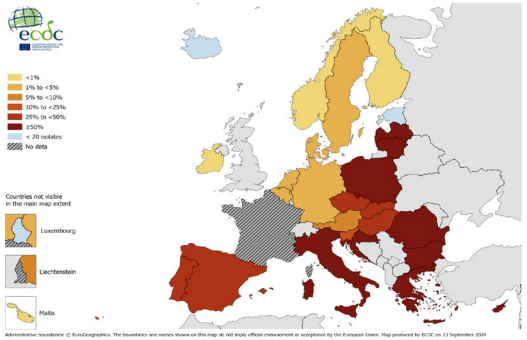
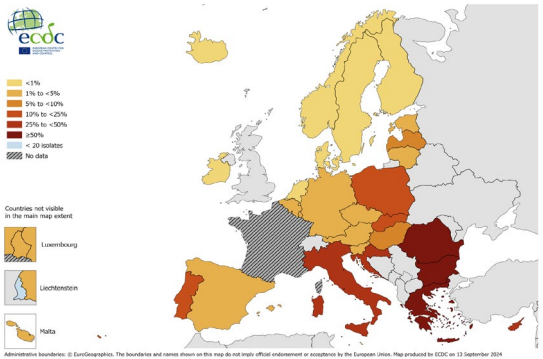
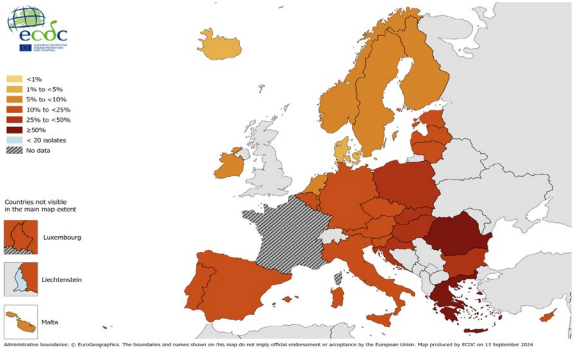
MDR nel trapianto allogenico



Acinetobacter



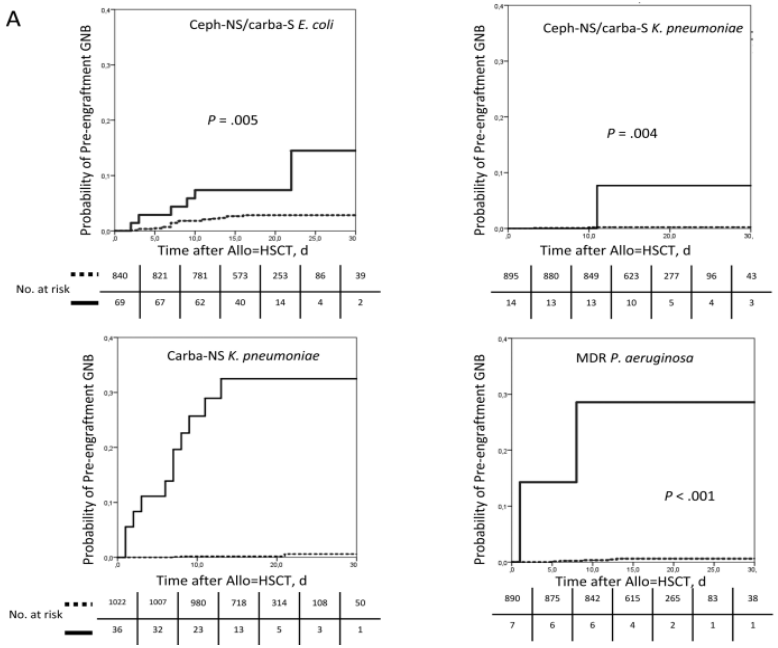
K.Pneumoniae

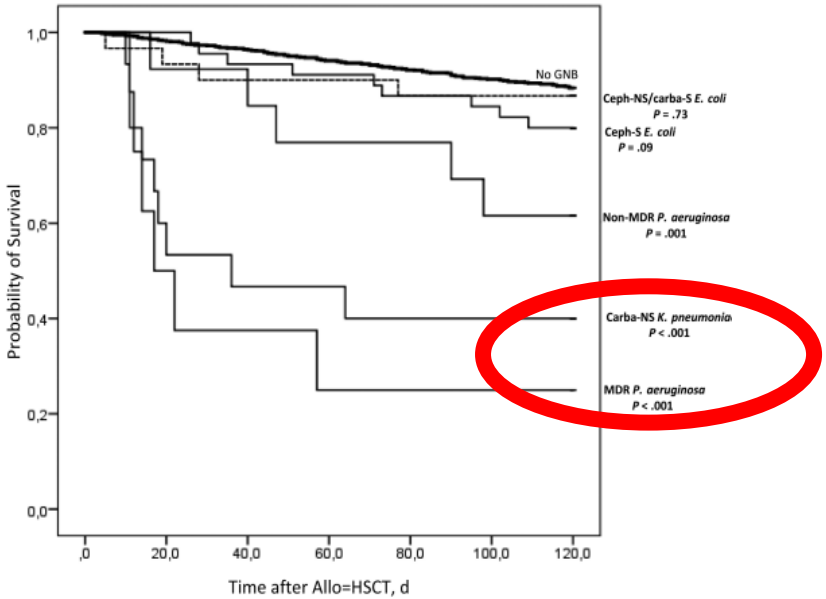


P.Aeruginosa

ECDC, 2023
Antimicrobial resistance in the EU/EEA (EARS-Net)

MDR nel trapianto allogenico





Correlazione tra colonizzazione e infezione pre-engrafment
(E. coli, K. pneumoniae, and P. aeruginosa)

Girmenia C, Clin Inf Dis 2017

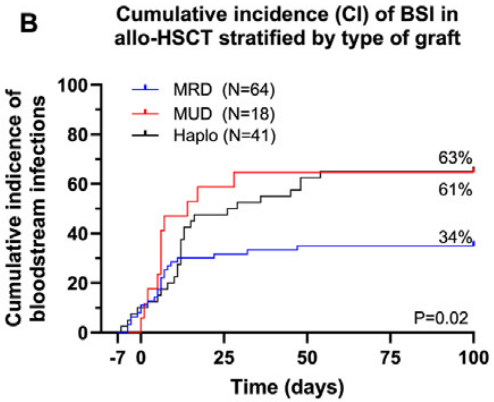
MDR nel trapianto allogenico

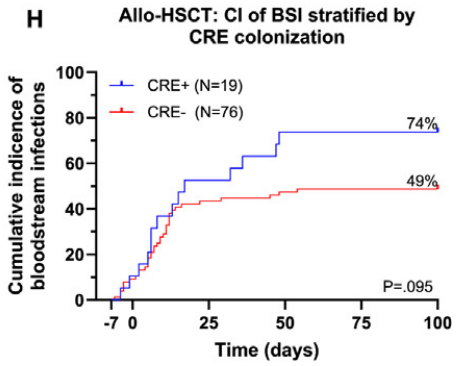
	HR (95% CI)	p
Age (+10y)	1,15 (1.05-1.25)	0.016
Other disease vs AL	0.64 (0.46-0.89)	0.009
Donor (vs MRD) MMR MUD CB	 3.7 (2.15-6.50) 2.91 (1.50-5.64) 3.77 (1.5-9.45)	 <0.0001 0.001 0.005
Days of pre-engraftment neutropenia	1.02 (1.01-1.03)	0.004

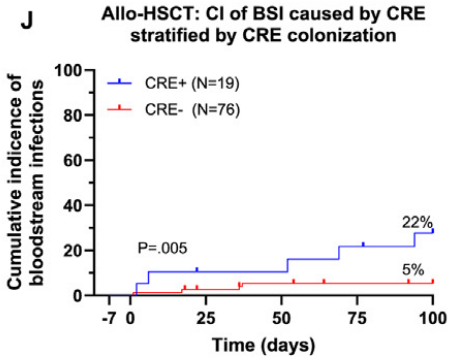
Fattori di rischio per GNI pre-engrafment
Analisi multivariata

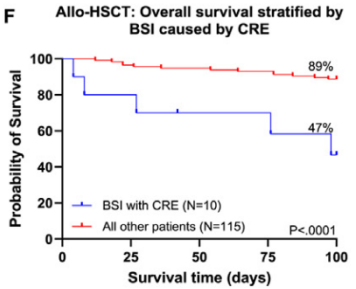
Girmenia, Cin Inf Dis 2017

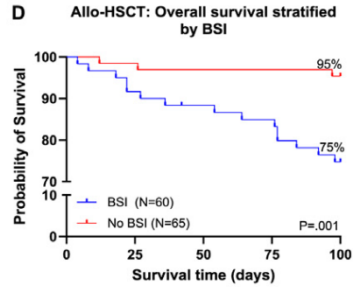
MDR nel trapianto allogenico

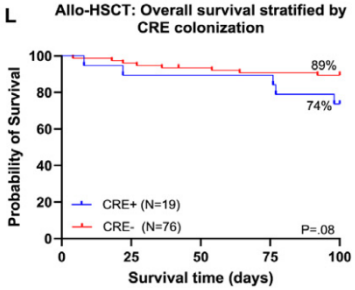












Van Leeuwen, TCT 2025

AGENDA

Problema MDR nel trapianto allogenico

De-escalation

Nostra esperienza

De-escalation: ECIL approach

	De-escalation approach ECIL 4	De-escalation approach ECIL 10
Indication	1) Complicated presentations **BII** 2) Known colonization with resistant bacteria **BII** 3) Previous infection with resistant bacteria **BII** 4) In centers where resistant pathogens are regularly seen at the onset of febrile neutropenia **BII**	1) Sepsis/Septic shock 2) Known colonization with resistant bacteria; 3) Previous infection with resistant bacteria; 4) In centers where resistant pathogens are regularly seen at the onset of febrile neutropenia.
Options for initial antibiotic therapy	1) Carbapenem monotherapy **BII** 2) Combination of anti-pseudomonal beta-lactam + aminoglycoside or quinolone (with carbapenem as the beta- lactam in seriously ill-patients) **BIII** 3) Colistin + beta-lactam +/- rifampicin (for PsA, AB, SM) **BIII** 4) Early coverage of resistant-Gram-positives with a glycopeptide or newer agent (If risk factors for Gram-positives present) **CIII**	1) Carbapenem monotherapy 2) Combination of anti-pseudomonal beta-lactam + aminoglycoside 3) Beta lactam targeting the suspected colonizing pathogen based on susceptibility testing 4) Early coverage of resistant-Gram-positives with a glycopeptide or newer agent if risk factors for Gram-positives present

Averbuch D, ECIL 2024

De-escalation (2)

- ✓ KPC-carriers è un fattore predittivo per KPC-KpBSI.
- ✓ Mortalità in aplasia da CT in leucemie acute si riduce con terapia EAT MDR-driven.
- ✓ De-escalation è praticata solo nel 35% dei centri trapianto secondo una survey del 2020
- ✓ Poco studiato nel setting trapianto allogenico
- ✓ In 1 studio, tasso di de-escalation 55.9% (early and late) dopo allo, ma pazienti non colonizzati.
- ✓ La mediana di durata della terapia MDR-driven è lunga (12.8 gg in 1 studio).

Micozzi, Infect Dis 2021
Verlinden, Bone marrow Transplant 2020
Gustinetti, Biol Blood Marrow Transplant 2018
Micozzi, Infect Drug Resist 2023

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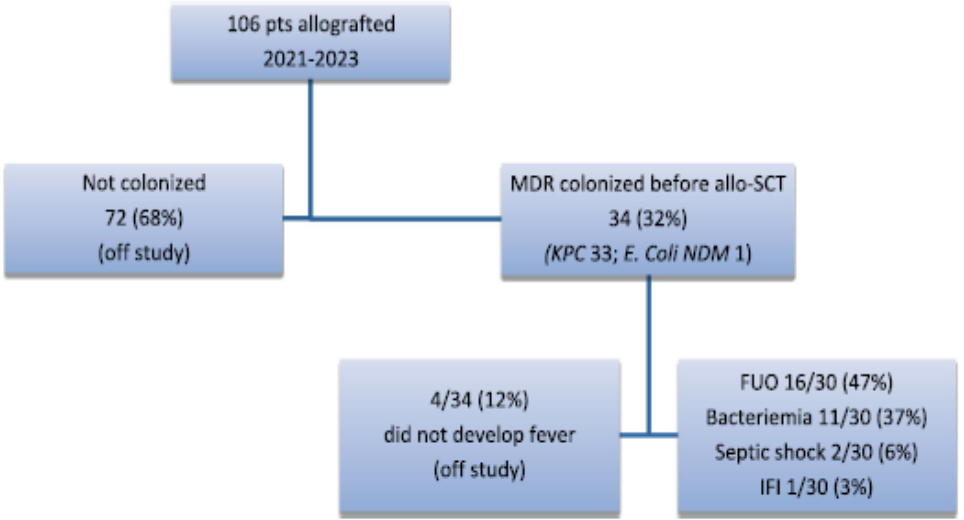

FIGURE 1
Flowchart of patients included in this study. MDR, multidrug-resistant; KPC, *klebsiella pneumoniae carbapemenase*; IFI, invasive fungal infection; NDM, New Delhi metallo-beta-lactamase 1.

Bono, Frontiers in Microbiol 2025

Caratteristiche dei pazienti

Dicembre 2021-Giugno 2023

N	106 (100%)	34 (32%)	18 (17%)
Cohort	All patients	MDR cohort	MDR-colonized at allo-SCT
M/F	61/45	23/11	13/5
Median age (y)	52 (range)	58 (range 19–74)	59 (range 20–74)
Disease			
Acute myeloid leukemia	56 (53%)	25 (74%)	16 (89%)
Acute lymphoblastic leukemia	20 (19%)	5 (15%)	1 (5%)
Myelodisplastic syndrome	8 (8%)	/	1 (5%)
Lymphoma	9 (8%)	1 (3%)	/
Myeloproliferative neoplasms	10 (9%)	1 (3%)	/
Multiple myeloma	1 (1%)	/	/
Blastic plasmocytoid dendritic cell neoplasm	1 (1%)	1 (3%)	/
Aplastic anemia	1 (1%)	1 (3%)	/

Donor			
HAPLO	38 (36%)	16 (47%)	6 (33%)
MUD	33 (31%)	8 (24%)	5 (28%)
HLAid	19 (18%)	7 (21%)	4 (22%)
mMUD	16 (15%)	3 (9%)	3 (17%)
Stem cell source			
PBSC	103 (97%)	33 (99%)	18 (100%)
BM	3 (3%)	1 (1%)	/
Conditioning regimens			
MAC	79 (73%)	23 (68%)	13 (72%)
RIC	29 (27%)	11 (32%)	5 (28%)
GVHD prophylaxis			
CSA + MTX + ATG	44 (42%)	23 (68%)	12 (58%)
PTCY+CSA + MMF	62 (58%)	11 (32%)	6 (42%)

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Principali Outcomes e terapie MDR-driven

EAT	*N* = 30
CAZAVI	5 (17%)
CAZAVI + aminoglycoside	10 (30%)
Cefiderocol	1 (3%)
MEVA	1 (3%)
MEVA + aminoglycoside	4 (13%)
MEVA + glycopeptide	1 (3%)
TAZO	5 (17%)
TAZO+ aminoglycoside	1 (3%)
Meropenem	2 (6%)

	Whole population	Not colonized	Colonized
N	106	72	34
OS@1y	69%	69%	72%
PFS@1y	59%	60%	56%
NRM@100d	13%	15%	10%
NRM@1y	22%	25%	15%
G2-4 aGVHD	20%	21%	17%
G3-4 aGVHD	7%	7%	6%

OS, overall survival; PFS, progression-free survival; NRM, no relapse mortality; aGVHD, acute graft versus host disease.

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Risultati

Nel pre-attecchimento

- ✓ Nessun paziente ha presentato una traslocazione MDR
- ✓ CI di de-escalation è 79%
- ✓ Dopo la de-escalation, nessun paziente ha sviluppato una batteriemia
- ✓ AMR è stata assente
- ✓ Mediana di EAT-MDR driven 3.5 gg (range 2-8)

Bono, Frontiers in Microbiol 2025

Conclusioni

- ✓ La de-escalation si è dimostrata sicura in un setting di pazienti ad alto rischio
- ✓ Rappresenta una strategia per combattere l'elevata incidenza di KPC
- ✓ Minore utilizzo di antibiotici KPC-driven: minore pressione selettiva

GRAZIE PER LA VOSTRA ATTENZIONE