مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre

Post-HSCT Complications:

Bacterial Infections

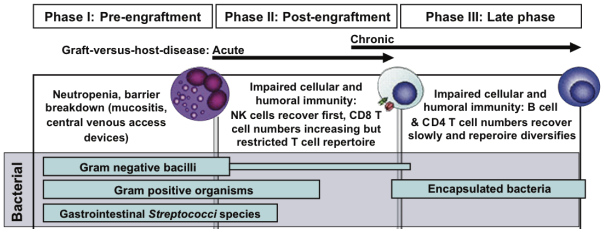
Dr Ali S. Omrani
KFSH&RC

4th WBMT Symposium - 17 January 2017, Riyadh, Saudi Arabia

Dr Ali S. Omrani MBBCh MSc FRCP FRCPath

- Consultant Infectious Diseases Physician
- Head of Section, Adult Infectious Diseases
- Deputy Chairman, Department of Medicine
- Chairman, Antimicrobial Utilization & Evaluation Committee

Hematopoietic Stem Cell Transplantation



Kedia et al. J Stem Cell Res Ther S3:002

Risk Assessment

- Type of graft
  - Allogeneic >>> autologous
- Source of stem cells
  - Cord blood >> unrelated/mismatched donor >> related/matched donor
- Conditioning
  - Myeloablative >> non-myeloablative
- GVHD

Kedia et al. J Stem Cell Res Ther S3:002

Essential Prevention Measures

- Effective hand hygiene
- Standard barrier precautions
- Exclude HCW with acute illness
- Single rooms
- High rate air exchange + HEPA

Freifeld et al. Clin Infect Dis 2011;52(4):e56–e93

Prophylactic Antibiotics

- High risk patients only
- Ciprofloxacin or levofloxacin
- Addition of a gram-positive active agent to fluoroquinolone prophylaxis is generally not recommended

Freifeld et al. Clin Infect Dis 2011;52(4):e56–e93

Febrile Neutropenia

- Neutropenia: ANC < 500/mL
- T ≥38.3 (or ≥38.5ºC) once or ≥38.0°C over 1 or 2 hours
- Up to 80% of patients with hematologic malignancies
- Clinically documented infections occur in 20-30% of febrile episodes
- Bacteremia occurs in 10-25%

Freifeld et al. Clin Infect Dis 2011;52:e56–e93
Flowers et al. J Clin Oncol 2013;31(3): 794-810
de Naurois et al. Ann Oncol 2010;21(suppl 5): v252-v256.
Averbuch et al. Haematologica 2013;98:1826-1835

FN: Risk Assessment

- Neutropenia > 7 days
- Significant co-morbidities
- Hypotension
- Pneumonia
- GI symptoms
- CNS change

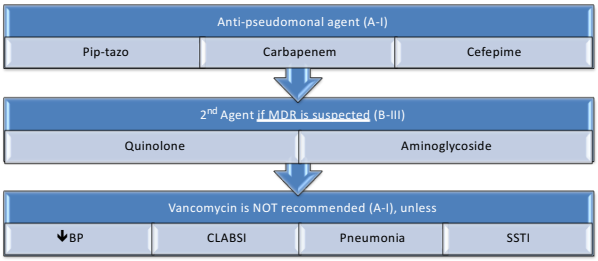
Freifeld et al. Clin Infect Dis 2011;52:e56–e93
Flowers et al. J Clin Oncol 2013;31(3): 794-810
de Naurois et al. Ann Oncol 2010;21(suppl 5): v252-v256.
Averbuch et al. Haematologica 2013;98:1826-1835

FN: Management

Clinical assessment	History and physical examination
Microbiology	Previous colonization/infections Biomarkers
Radiology	Past and new
Antimicrobials	Prophylaxis Empiric therapy Targeted therapy

Freifeld et al. Clin Infect Dis 2011;52:e56–e93
Flowers et al. J Clin Oncol 2013;31(3): 794-810
de Naurois et al. Ann Oncol 2010;21(suppl 5): v252-v256.
Averbuch et al. Haematologica 2013;98:1826-1835

High Risk FN *(IDSA 2011)*



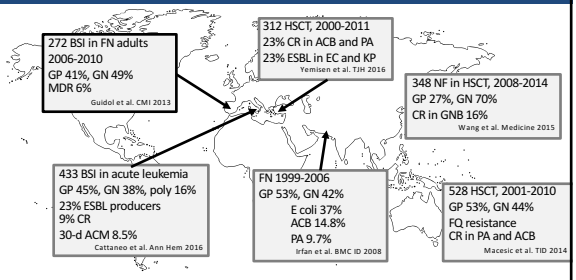
Freifeld et al. Clin Infect Dis 2011;52(4):e56–e93

High Risk FN *(ECIL-4)*

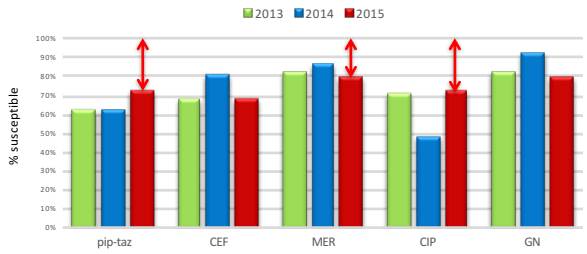
Cefepime, ceftazidime Piperacillin-tazobactam Ticarcillin-clavulanate Cefoperazone-sulbactam Piperacillin + gentamicin	A-I
Carbapenem	B-II
Anti-pseudomonal BL + AG or FQ Colistin + β-lactam ± rifampicin	B-III

Averbuch et al. Haematologica 2013;98:1826-1835

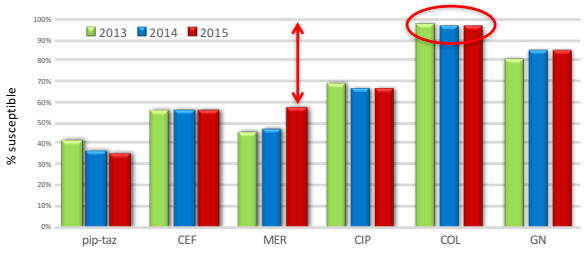
Epidemiology

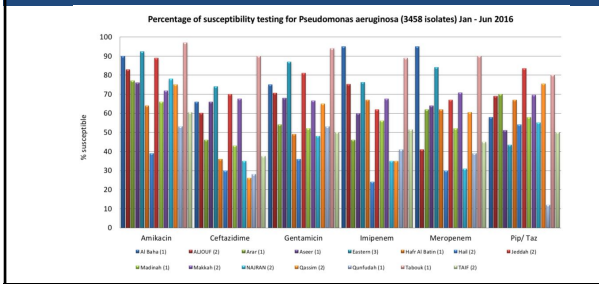


K. pneumoniae from KFSHRC Hematology



P. aeruginosa from KFSHRC Hematology





Courtesy of Dr Hail Alabdaly, Saudi MoH

High Risk FN (IDSA & ECIL-4)

- Initial empirical therapy should be modified if the patient is at risk for MDR infection (B-III)
  - Previous infection or colonization
  - Hospital epidemiology

MRSA	vancomycin, linezolid or daptomycin (B-III)
VRE	linezolid or daptomycin (B-III)
ESBL-producers	carbapenems (B-III)
CRE	colistin or tigecycline (C-III)

Freifeld et al. Clin Infect Dis 2011;52(4):e56–e93 Averbuch et al. Haematologica 2013;98:1826-1835

Land of the Unknowns!

HSCT - FN → Empiric Antibiotics → What's next?

HSCT - FN → Empiric Antibiotics → What's next?

Defined focus ± microbiology → treat accordingly (A-I)

Freifeld et al. Clin Infect Dis 2011;52(4):e56–e93 Averbuch et al. Haematologica 2013;98:1826-1835

Spiraling Confusion

HSCT - FN → Empiric Antibiotics → What's next?

No defined focus of infection

No positive microbiology

Persistent FN

- More clinical evaluation
- More investigations
- ?add/switch antibiotics → spiraling empiricism
- ?non-infectious etiologies

Neutropenia + Febrile

"Patients who **remain hemodynamically unstable** after initial doses with standard agents for NF should have their antimicrobial regimen **broadened** to include coverage for resistant gram-negative, gram-positive, and anaerobic bacteria and fungi (A-III)"

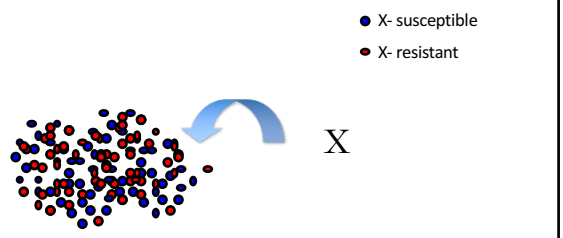
Freifeld et al. Clin Infect Dis 2011;52(4):e56–e93 Averbuch et al. Haematologica 2013;98:1826-1835

Neutropenia + Febrile

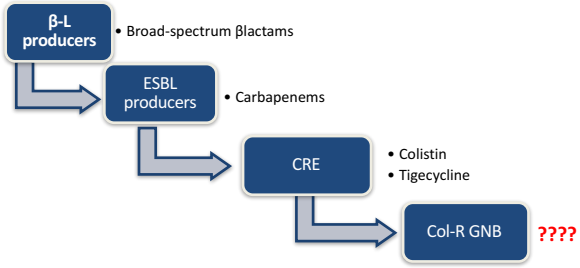
"Unexplained persistent fever in a patient whose condition is **otherwise stable** rarely requires an empirical change to the initial antibiotic regimen"

Freifeld et al. Clin Infect Dis 2011;52(4):e56–e93

Selection Pressure



Selection Pressure



KFSH&RC – Dec 2016

Micro Reports | Susceptibilities | Specimen | Action List

	A	B	C	D	E
1	Klebsiella pneumoniae				
2		MDIL	MINT	EDIL	EINT
3	Ampicillin	>=32	R		
4	Amoxicillin/Clavulanate	>=32	R		
5	Piperacillin/Tazobactam	>=128	R		
6	Cephalothin	>=64	R		
7	Cefuroxime		R		
8	Cefoxitin	>=64	R		
9	Ceftazidime	>=64	R		
10	Ceftriaxone	>=64	R		
11	Cefepime	>=64	R		
12	Ciprofloxacin	>=4	R		
13	Gentamicin	>=16	R		
14	Amikacin	>=64	R		
15	Tobramycin		R		
16	Meropenem	>=16	R		
17	Imipenem	>=16	R		
18	Nitrofurantoin	256	R		
19	Trimethoprim/Sulfamethoxazole	>=320	R		
20	Carbapenem Resistant Enterobacteriaceae*		Identified		
21	Fosfomycin			1024	R
22	Aztreonam	>=64	R		
23	Colistin*	2			
24	Netilmicin		R		
25	Ampicillin/Sulbactam	>=32	R		
26	Levofloxacin	>=8	R		
27	Minocycline	>=16	R		

K. pneumoniae

Quinolones	**R**
Aminoglycosides	**R**
Pip-tazo	**R**
Cephalosporins	**R**
Carbapenems	**R**
Colistin	**R**
Fosfomycin	**R**

Spiraling Confusion

HSCT - FN → Empiric Antibiotics → What's next?

No defined focus of infection, no positive microbiology

When to Stop?

Neutropenia + Afebrile *(IDSA 2010)*

- Documented infections/unexplained fever → antibiotics until ANC is > 500 cells/mm³ or longer if clinically necessary **(B-III/BII)**

ALTERNATIVELY

- Resolved infection + persistent neutropenia → resume oral prophylaxis **(C-III)**

Freifeld et al. Clin Infect Dis 2011;52(4):e56–e93

Neutropenia + Afebrile *(ECIL4)*

Empirical antibiotics can be discontinued:

a) after ≥72h

b) hemodynamically stable

c) afebrile for ≥48h

irrespective of their neutrophil count or expected duration of neutropenia **(BII)**

Averbuch et al. Haematologica 2013;98:1826-1835

Conclusion: Post-HSCT Bacterial Infections

- **Hand hygiene and standard IPC are essential**
- Location, location, location!
- Prompt ACTION is essential

Post-HSCT Bacterial Infections

- **PROMPT ACTION**
  - PROMPT assessment +
  - PROMPT therapy +
  - PROMPT rationalization +
  - PROMPT discontinuation of unnecessary therapy


مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre
Gen Org مؤسسة عامة
Thank you
asomrani@kfshrc.edu.sa