Febrile Neutropenia

General points

Neutropenia = Neutrophil Count < 1.0 x 10^9 /L

Severe Neutropenia = Neutrophil Count < 0.5 x10^9 /L

Fever = Temp ≥38 ^{o} C

Febrile Neutropenia / Neutropenic sepsis is a medical emergency. IV antimicrobial therapy should be started without delay.

N.B. Check previous microbiology results for history of **MDROs** e.g. ESBL, MRSA, and CPE, as these pathogens may not be covered by all empiric regimes - contact microbiology for advice if required.

Blood cultures – send one set from each lumen of CVC and a peripheral set if possible OR peripheral X 2 if no CVC is present.

Respiratory tract swab for covid +/- other viruses if suspected, MSU/CSU for culture, sputum culture, stool sample if diarrhoea, wound swabs if applicable.

Many chemotherapeutic agents can cause nephrotoxicity and a review of renal function in active malignancy should be done when using aminoglycosides in these patients.

Antibiotics

First Line:

Piperacillin-tazobactam 4.5 g **QDS** IV

Add **Gentamicin** once daily IV (see Gentamicin dosing schedule) (**OR** in multiple myeloma/cisplatin-based therapy **Ciprofloxacin** 400mg q8-12 hourly IV) if any features of haemodynamic instability e.g. tachycardia, hypotension, or hypothermia.

Add **Teicoplanin** (please see Teicoplanin dosing schedule) if history of **MRSA** colonization/infection OR suspected line-related sepsis OR critically ill OR active mucositis.

NOT IgE-mediated/anaphylaxis/severe penicillin allergy:

Ceftazidime 2g TDS IV (adjust dose in renal impairment).

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Teicoplanin (please see Teicoplanin dosing schedule)

Add **Gentamicin** once daily IV (please see Gentamicin dosing schedule) (**OR** in multiple myeloma/cisplatin-based therapy **Ciprofloxacin** 400mg q8-12 hourly IV) if any features of haemodynamic instability e.g. tachycardia, hypotension, or hypothermia.

IgE-mediated/anaphylaxis/severe penicillin allergy :

Ciprofloxacin 400 mg 8 to 12 hourly IV

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Teicoplanin (please see Teicoplanin dosing schedule)

Add **Amikacin** once daily IV if any features of haemodynamic instability eg. tachycardia, hypotension, or hypothermia (please see Amikacin dosing schedule).

If known colonisation or previous infection with **ESBL** - producing OR gram negative bacteria resistant to piperacillin-tazobactam or cephalosporins use **Meropenem** 1g TDS IV. Note restricted antimicrobial agent, discuss with microbiology.

*In severe illness, haemodynamic instability, OR if history of infection/colonisation with gentamicin resistant Gram-negative bacteria replace gentamicin with **Amikacin** once daily in all combinations. (please see Amikacin dosing schedule)

** In a haemodynamically unstable patient, the benefit of gentamicin/amikacin may outweigh the risk – discuss with haematology consultant.

***** Please read the HPRA Drug Safety Alert issued in 2018 and the HPRA Drug Safety Newsletter issued in 2023 highlighting restrictions on use of fluoroquinolones (eg. ciprofloxacin, levofloxacin) due to the risk of disabling, long-lasting and potentially irreversible side effects (including tendon damage, QT prolongation, neuropathies and neuro psychiatric disorder). Use of fluoroquinolones in older patients, those with renal impairment, solid organ transplantation or on systemic corticosteroids increases the risk of tendon damage.

Comments

- Consider stopping Gentamicin/Amikacin at 24-72 hours if afebrile, and no gram negative pathogen isolated from blood cultures. Other antimicrobials may need to be continued.
- If pathogen identified, target therapy in accordance with susceptibility test results.

If persistent fever on empiric antimicrobials and evidence of clinical deterioration:

- Re-evaluate patient for potential focus of infection.
- Contact microbiology for advice –may require escalation of **gram negative cover** +/- gram positive cover.
- Consider addition of **anti-fungal agent** if fever persists beyond 4 days.
- Consider investigations for opportunistic pathogens such as PJP, mycobacteria, viruses, fungi etc. as applicable.

References

Averbach et al. European guidelines for empirical antibacterial therapy for febrile neutropenic patients in the era of growing resistance: summary of the 2011 4 th European Conference on Infections in Leukaemia. Haematologica 2013:98(12): 1826-1835.