Supplement

Prophylaxis and antimicrobial treatment; old protocol

Before January 2011, prophylaxis during an episode of prolonged neutropenia consisted of oral ciprofloxacin 500 mg BID and oral fluconazole 150 mg QD. When patients were colonized with ciprofloxacin resistant Gram-negative bacteria, cotrimoxazole (960 mg BID orally) combined with colistin (200 mg TID orally) was used as prophylaxis. Streptococcal prophylaxis was added when patients received high dose cytarabine (clindamycin 300 mg TID orally) or busulfan/cyclophosphamide (cefazolin 1000 mg TID i.v.). In case of colonisation with *Candida glabrata* or *Candida krusei*, patients received amphotericin B deoxycholate orally (200 mg QID), instead of fluconazole. When a patient developed fever, defined as a single temperature measurement > 38.6°C or > 38.3°C for more than a hour, EAT with imipenem 500 mg QID i.v., was administered. Antibiotic prophylaxis was either stopped or continued during EAT depending on the preference of the treating physician. If fever persisted, empirical vancomycin was added according to the physician's judgment. Imipenem was continued until patients were afebrile for at least five days. If blood cultures became positive, EAT was continued for at least ten days, and depending on the pathogen/clinical suspicion, targeted antibiotics were added (e.g. vancomycin). In case of neurological disease / neurological involvement or symptoms, patients received meropenem (1000 mg TID i.v.) instead of imipenem because of an increased probability of convulsions (14).

Prophylaxis and antibiotic treatment; new protocol

In January 2011, a protocol on restrictive EAT use was implemented. Bacterial prophylaxis did not change except that streptococcal prophylaxis consisted of cefazolin only (1000 mg TID i.v.). Fluconazol was given, but in case of colonisation with *C. glabrata* or *C. krusei* no antifungal prophylaxis was administered. In case of febrile neutropenia, imipenem was started and discontinued after three days if blood cultures remained negative, irrespective of fever, on condition

that the patient was hemodynamically stable and there was no suspicion of pulmonary infection with an (at that moment) unknown etiology. When blood cultures became positive, therapy was targeted on the pathogen and EAT was discontinued. During EAT, antibacterial prophylaxis was discontinued. If a patient became febrile for a second time during the same neutropenic episode, imipenem was restarted (after collection of blood cultures and repeated physical examination) and stopped as described above. According to the protocol, EAT was not restarted for additional 3rd febrile episodes during the same neutropenic period, provided that the patient remained hemodynamically stable.