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In the last two decades the epidemiology of the infections in neutropenic cancer patients has progressively changed: Bacteremic infections due to gram-negative bacilli decreased and those due to gram-positive organisms increased. Today, around 70% of bacteremia documented during febrile neutropenia are caused by gram-positive cocci. Several factors played an important role in this epidemiological modification: The extended use of CVC, the prophylactic use of fluoroquinolones and the oral and gastrointestinal mucositis, all favoring the direct entry of the colonizing microorganisms into the bloodstream. Among the gram-positive organisms, the most frequently isolates are represented by coagulase-negative staphylococci and viridans streptococci. It is noteworthy that many gram-positive organisms responsible of infections in febrile neutropenia are resistant to the antibiotic routinely used as empirical treatment, i.e. ceftazidime and amikacin. It should also be stressed that the majority of staphylococci, both coagulase-negative and coagulase-positive, are resistant to methicillin, being susceptible only to glycopeptide antibiotics.

Several factors should be considered for including in the empiric antibiotic regimen from the beginning a glycopeptide antibiotic or reserving this as rescue therapy after the microbiological documentation of a gram-positive infection. In a setting of high rate of methicillin-resistant staphylococci, especially in patients with acute leukemia or undergoing BMT, with CVC and severe mucositis, seems to be rational to include in the empirical antibiotic regimen a glycopeptide antibiotic from the beginning.

It should also be stressed that infections caused by gram-positive cocci may have an indolent course (i.e. those caused by CNS) or a fulminant course (i.e. some infections caused by VS or *Staphylococcus aureus*).

Rescue therapy may be efficacious in controlling an indolent infection but initial glycopeptide antibiotic is certainly preferred for fulminant infections. Partially implantable CVC of Hickman-Broviac type are largely used in neutropenic patients with hematologic malignancies. Infection related to these devices are relatively frequent and mainly caused by gram-positive organisms. Among the gram-positive infections potentially responsible of a

fulminant course are those caused by viridans streptococci. Bacteremia caused by viridans streptococci are most often documented in patients receiving high-dose of cytosine-arabioside developing severe mucositis. Acute respiratory distress syndrome may be a complication of VS bacteremia in as much as 30% of the patients and often have a lethal outcome.

Teicoplanin was used to empirically treat febrile neutropenia in combinations with several antibiotics, most frequently with a combination of a beta-lactam antibiotic (penicillin or cephalosporin) and an aminoglycoside. The comparator regimens were represented by beta-lactams and aminoglycoside with or without vancomycin. Several studies have been conducted with teicoplanin in febrile neutropenia and the response rate was always good or ten comparative studies have been conducted with teicoplanin combined with other antibiotics for the empirical treatment of febrile neutropenia enrolling around one-thousand and five-hundred patients. A meta-analysis of these studies clearly shows that regimen including teicoplanin gave better results than comparators.

The Gimema study was a comparative study of teicoplanin and vancomycin, both combined with amikacin and ceftazidime. The overall response to therapy as well the response in FUO, clinically documented and microbiologically documented infections was similar for the two treatment groups. It is noteworthy that the response to therapy in gram-positive bacteremia was excellent for any single pathogen and similar for the two treatment groups. However, not unexpectedly, the tolerability of the regimen including teicoplanin was better, namely for a lower rate of skin rashes.

The pharmaco-economic analysis of this study including acquisition cost, administration cost, cost of failure and cost of adverse events, showed similar results.

As far as the comparison with vancomycin is concerned, a meta-analysis of all the performed studies show similar efficacy, according to the Gimema study results. Furthermore, the meta-analysis of adverse events confirms that teicoplanin have a better tolerability.

However, it should be remembered that the final outcome of any febrile neutropenic episode in patients with hematologic malignancies is related not only to antineoplastic therapy but mostly to the rise of granulocyte count.