CEM-102 (Fusidic Acid) in vitro activity and evaluation of molecular resistance mechanisms among European Gram-positive isolates (2008-2009)

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Objectives: To evaluate the activity of fusidic acid (FA) among Gram-positive bacteria collected in European medical centers in the 2008-2009 period and to analyze the prevalence of FA resistance (R) mechanisms among staphylococci (2008).

Methods: A total of 7,504 strains collected from 29 European (EU) medical sites located in 13 countries were susceptibility (S) tested by CLSI reference broth microdilution against FA and comparator agents. 336 Staphylococcus spp. (2008 only) displaying FA MIC at >=2 mg/L were tested for the presence of fusB, fusC and fusD and mutations on fusA and fusE (FA primary and secondary active site).

Results: FA was very active against all staphylococci displaying a MIC50 of 0.12 mg/L regardless of methicillin-resistant (MR) profile. Applying EUCAST breakpoints (none available for CLSI), 90.7% of S. aureus (SA) strains were S to FA, with lower rates observed among MRSA (77.9%). Coagulase-negative staphylococci (CoNS) demonstrated 36.7% R against FA (14/867 S. saprophyticus with intrinsically elevated FA MIC). MRCoNS displayed 40.5% of FA-R. FA demonstrated marginal activity against enterococci and streptococci, with MIC50 values for beta-haemolytic, group A, B and viridians group streptococci, S. pneumoniae and enterococci ranging from 4 to 8 mg/L. Among 336 staphylococci (FA MIC, >=2 mg/L), the presence of acquired FA-R genes was detected in 64.9% of the strains (36.6% fusB and 28.3% fusC). fusB and fusC rates among FA-R strains were 10.4 and 17.3% for SA and 26.1 and 11.3% for CoNS, respectively. fusA mutations were detected in 57 of 62 FA-R SA, most common being aminoacid alterations on position 461 (Leu to Lys/Ser). One SA showed a mutation on fusE (Q140L). Ireland and Greece showed the highest SA FA-R rates with high prevalence of L461K fusA mutation (clinical outbreaks). Low staphylococci FA-R rates (1.4-3.1%) were observed in Israel, Italy, Poland, Spain and Sweden.

Conclusions: FA appears to be a valuable alternative to other anti-MRSA oral agents in the treatment of serious staphylococci infections. Despite the long term of FA clinical use in European countries, staphylococci R rates are still remarkably low except in clonal occurrences in a minority of institutions.