

Activity of CEM-102 (sodium fusidate) against 40 MRSA from Cystic Fibrosis Patients

Abstract E-1558

Cynthia Todd, Pamela Mcghee, and Peter Appelbaum
Hershey Med. Ctr., Hershey, PA 17033

Background:

Infections caused by MRSA occur often in CF patients and there is a lack of new oral agents to treat them. Sodium fusidate has been successfully used in Europe to decolonize the lungs of CF patients (1, 2). This study 1) used MIC to test activity of CEM-102, vancomycin, teicoplanin, daptomycin, tigecycline, azithromycin, clarithromycin, linezolid, quinupristin/dalfopristin and trimethoprim/sulfamethoxazole against a range of recent CF MRSA strains and 2) tested CEM-102 in combination with tobramycin or amikacin by time-kill against two CF MRSA strains.

Methods:

Forty strains of MRSA were isolated from patients at Hershey Med. Ctr. CF clinic during the past 12 months. The variable number of tandem repeats (VNTR, formerly MLVA) method was done on all strains to ensure only one strain per patient. CLSI microdilution was done using commercially, or in-house, prepared trays (TREK, Inc., Cleveland, OH). Vancomycin MICs were read after 24 h. Subinhibitory concentrations of CEM-102 were combined with subinhibitory concentrations of each aminoglycoside to look for synergy or antagonism by time-kill.

Results:

MICs ($\mu\text{g/mL}$) are listed in the Table.

| Drug | Range | MIC ₅₀ | MIC ₉₀ |
|-------------------------------|-----------------|-------------------|-------------------|
| CEM-102 | 0.12-0.5 | 0.12 | 0.25 |
| Vancomycin | 0.5-1 | 0.5 | 1 |
| Teicoplanin | 0.25-1 | 0.5 | 1 |
| Daptomycin | 0.5-1 | 0.5 | 1 |
| Tigecycline | 0.12-0.25 | 0.12 | 0.25 |
| Azithromycin | 1- ≥ 32 | ≥ 32 | ≥ 32 |
| Clarithromycin | 0.25- ≥ 32 | ≥ 32 | ≥ 32 |
| Linezolid | 1-4 | 2 | 2 |
| Quinupristin/dalfopristin | 0.25-1 | 0.5 | 1 |
| Trimethoprim/sulfamethoxazole | $\leq 0.5/9.5$ | $\leq 0.5/9.5$ | $\leq 0.5/9.5$ |

Conclusions:

CEM-102, an oral antistaphylococcal agent used in other countries for many years, was very potent against all MRSA strains from CF patients (MIC range: 0.12-0.5 $\mu\text{g/mL}$). Vancomycin, teicoplanin, daptomycin, quinupristin/dalfopristin, tigecycline, linezolid and trimethoprim/sulfamethoxazole were very active. All potent drugs tested here except for linezolid and trimethoprim/sulfamethoxazole are only available intravenously. Resistance was found to azithromycin and clarithromycin with MIC₅₀ and MIC₉₀ values of ≥ 32 $\mu\text{g/mL}$. Time-kill studies showed synergy between CEM-102 and tobramycin with 1/2 strains at 24 h.