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The in-vitro activity of cefiderocol, a novel siderophore cephalosporin, against a global collection of Stenotrophomonas maltophilia

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Background: *S. maltophilia* is a gram-negative, non-fermentative, environmental bacterium that has emerged as important cause of nosocomial infections in immunocompromised hosts. *S. maltophilia* colonizes humid surfaces such as the tubes used in mechanical ventilation and urinary catheters. *S. maltophilia* infections pose a serious clinical problem as clinical therapeutic options for *S. maltophilia* infections are scarce or limited to sulfamethoxazole-trimethoprim and colistin. Cefiderocol (formerly S-649266) is a novel siderophore cephalosporin for injection discovered by Shionogi & Co., Ltd. An important biological feature of cefiderocol is it's potent activity against a variety of gram-negative pathogens including multi-drug resistant strains of *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. However, until now the antibacterial activity of this new drug against *S. maltophilia* has not been reported to date. In this study, the *in vitro* antibacterial activity of cefiderocol was evaluated against a global collection of *S. maltophilia* clinical isolates.

Material/methods: MIC was determined by broth microdilution method according to Clinical and Laboratory Standard Institute guidelines. For the MIC determination of cefiderocol iron-depleted CAMHB was used. Cefepime, ceftazidime-avibactam, ceftolozane-tazobactam, ciprofloxacin, colistin

and meropenem were included as comparator compounds. All testing was done at IHMA, Inc. using isolates collected through global surveillance initiatives (SIDERO-WT-2014, SIDERO-CR-2014/16). In all 645 *S. maltophilia* isolates were analyzed (30 % from sputum specimens, 22 % from endotracheal specimens, 11 % bronchoalveolar lavage specimens, 4 % from urine, 6 % from peritoneal fluid, and 27% from other).

Results: Cefiderocol showed potent *in vitro* activity against *S. maltophilia* with MIC90 of 0.25 mg/L, and suppressed the growth of all strains at 4 mg/L. Other β-lactams such as ceftazidime-avibactam, ceftolozane-tazobactam or meropenem were not effective (MIC50/MIC90: 16/64, 8/>64, >64/>64 mg/L, respectively). The MIC50/90 of colistin was 1/>8 mg/L, and 28% of the isolates showed MIC of >2 mg/L to colistin.

Conclusions: Cefiderocol showed potent *in vitro* antimicrobial activity against *S. maltophilia* including isolates with relatively low susceptibility to colistin. These data suggest that cefiderocol is a promising siderophore cephalosporin antibiotic for the treatment of infections caused by this problematic pathogen.