

P1853 Cefiderocol susceptibility and geographical analysis against globally isolated meropenem non-susceptible Gram-negative bacteria containing serine- and metallo-carbapenemase gene

Masakatsu Tsuji*¹, Krystyna Kazmierczak², Meredith Hackel², Mark Wise², Roger Echols³, Dan Sahm², Christopher Longshaw⁴, Davide Manissero⁴, Yoshinori Yamano¹

¹ SHIONOGI & CO., Ltd, OSAKA, Japan, ² IHMA, Inc., Schaumburg, United States, ³ ID3C, Easton, United States, ⁴ Shionogi Ltd., London, United Kingdom

Background: Cefiderocol (CFDC) is a novel parenteral siderophore cephalosporin active against Gram-negative pathogens including carbapenem-resistant (CR) isolates. Previously, we reported that CFDC showed potent activity (MIC₉₀ = 4 mg/L) against a total of 1873 meropenem non-susceptible strains (1021 CR Enterobacteriaceae and 852 multi-drug resistant non-fermenters) that were collected in Europe (EU) (53%), Latin America (21%), North America (12%), Asia (8%), and South Pacific/Africa/Middle East (6%) in 2014 to 2016. We screened for the presence of carbapenemase genes in isolates of Enterobacteriaceae (N=1021), *Pseudomonas aeruginosa* (N=368) and *Acinetobacter baumannii* (N=262) by PCR and analyzed their distribution by geography.

Materials/methods: MICs were determined by broth microdilution and interpreted according to CLSI guidelines. The test isolates were selected from all over the world (213 medical centers in 51 countries). Conventional PCR was used to screen for the presence of the following carbapenemase genes: KPC, NDM, IMP, VIM, SPM, GIM, OXA-48, OXA-23, OXA-24/40, and OXA-58.

Results: Against 569 KPC-producing Enterobacteriaceae, 345 metallo-β-lactamase producers (200 VIM, 130 NDM, and 15 IMP), and 480 OXA producers (136 OXA-48, 227 OXA-23, 109 OXA-24/40, and 8 OXA-58), CFDC MIC₉₀ was 4, 4, and 2 mg/L, respectively. In case of CRE, KPC producers were detected most frequently in North and South America, and NDM producers were detected most frequently in Asia and South Pacific countries. In EU, KPC, OXA-48 and VIM producers were all detected, although the frequency was different among countries. KPC, OXA-48, and VIM were dominant in Italy, Russia/Spain/Turkey, and Greece, respectively. In the case of *P. aeruginosa*, VIM producers were the most common MBLs observed on a global basis, however for some Asian countries IMP was common. The majority of VIM harboring *P. aeruginosa* came from Greece and Belgium. For *A. baumannii*, OXA-23 group producers were isolated globally, but OXA-24/40 producers were detected at high rates in Latin America and EU. In EU countries, *A. baumannii* harboring OXA-24/40 were frequently isolated in Spain, Russia, Romania, and Serbia.

Conclusions: CFDC demonstrated the potential to be effective against a global collection of CR Enterobacteriaceae, *A. baumannii*, and *P. aeruginosa*, regardless of the presence of serine- or metallo-type carbapenemases.