P1153 In vitro activity of aztreonam-avibactam and comparator agents against Enterobacteriaceae from Europe collected during the ATLAS Global Surveillance Program 2015-2017

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Background: Avibactam (AVI) is a non-β-lactam β-lactamase inhibitor with activity against class A, class C, and some class D β-lactamases, including extended-spectrum β-lactamases (ESBLs) and KPCs. Aztreonam (ATM) is stable to hydrolysis by metallo-β-lactamases (MBL). ATM-AVI is being developed for use against carbapenem-resistant Enterobacteriaceae, especially those producing MBLs that often co-carry serine β-lactamases. This study evaluated the in vitro activity of ATM-AVI and comparators against Enterobacteriaceae collected in 2015-2017 in Europe.

Materials/methods: Non-duplicate clinical isolates were collected from Northern/Western Europe (Belgium, Denmark, France, Germany, Italy, Netherlands, Portugal, Spain, Sweden, United Kingdom) and Central/Eastern Europe (Austria, Czech Republic, Greece, Hungary, Poland, Romania, Russia, Turkey). Susceptibility testing was performed using CLSI broth microdilution and interpreted using EUCAST 2018 breakpoints. ATM-AVI was tested at a fixed concentration of 4 mg/L avibactam. PCR and sequencing were used to determine the β-lactamase genes present in all isolates with meropenem (MEM) MIC >1 mg/L, and Escherichia coli, Klebsiella spp. and Proteus mirabilis phenotypically positive for ESBL activity (2015) or with ATM or ceftazidime MIC >1 mg/L (2016-2017).

Results: % susceptibility for ATM and MEM varied slightly for the regions, but ATM-AVI demonstrated good activity against Enterobacteriaceae, with MIC90 values of 0.12-0.5 mg/L in both European regions for all subsets of isolates (Table). In both regions, >99.9% of isolates, including all that produced MBLs, were inhibited by ≤8 mg/L of ATM-AVI. The percentages of MEM-non-susceptible isolates in Northern/Western and Central/Eastern Europe were 2.5 and 5.6%, respectively, and the percentages of MBL-positive isolates were 0.4 and 1.9%, respectively. 109 NDM- and 104 VIM-type MBLs were found in 13 species and 15 countries. No IMP-type MBLs were found. The majority of MBL-producing Enterobacteriaceae isolates co-carried one or more plasmid- or chromosomally-mediated serine β-lactamases, including CTX-M-15 and OXA-48.

Conclusions: ATM-AVI had good activity against Enterobacteriaceae isolated in Europe, including those that produced ESBLs and MBLs. ATM-AVI was highly active against all MBL-containing Enterobacteriaceae, regardless of species or country of isolation. The promising in vitro activity of ATM-AVI against carbapenem-resistant Enterobacteriaceae, especially those producing MBLs that are disseminating around the globe, warrants further development of this combination.