Background: Pseudomonas aeruginosa (PA) an important nosocomial pathogen. Unfortunately, increasing occurrences of multidrug-resistant (MDR) and extensively drug-resistant (XDR) isolates remain limited. Ceftolozane-tazobactam (C/T) and ceftazidime-avibactam (CZA) are two newer antimicrobials with antipseudomonal activity. The purpose of this study was to directly compare the in vitro activity of C/T and CZA versus antimicrobial non-susceptible (NS) PA clinical isolates as obtained from the CANWARD study.

Methods: Annually from 2007 to 2017, sentinel hospitals across Canada submitted blood, respiratory, urine, and wound isolates (consentive, one per patient/infection site) from patients attending ERs, medical and surgical wards, hospital clinics, and ICUs (CANWARD). Susceptibility was performed using broth microdilution as described by CLSI. MDR PA were defined as isolates that tested NS to at least one antimicrobial from ≥3 classes. XDR PA were defined as isolates that tested NS to at least one antimicrobial from ≥5 classes.

Results: 4224 PA clinical isolates were obtained as part of the CANWARD study. 628 (14.9%) were MDR, and 129 (3.1%) were XDR. The in vitro activity of C/T and CZA (plus relevant comparators) is presented in the accompanying table and figures.

Conclusions: The in vitro activity of C/T was superior versus antimicrobial NS PA clinical isolates (including MDR and XDR isolates) recovered from patients across Canada.

In total, 4224 PA clinical isolates were obtained as a part of the CANWARD Study between January 2007 and December 2017. Isolates were collected from patients on medical wards (n = 1437, 34.0%), hospital clinics (n = 1035, 24.5%), intensive care units (n = 933, 22.1%), emergency rooms (n = 511, 12.1%), and surgical wards (n = 309, 7.3%). The distribution of isolates by species were: P. aeruginosa (2829 (67.6%) respiratory, 765 (18.1%) blood, 432 (10.2%) wound, and 198 (4.7%) urine. The in vitro activity of ceftolozane-tazobactam, ceftazidime-avibactam, and comparators versus all isolates and antimicrobial non-susceptible subsets is presented in Table 1 and Figure 1. The MIC distribution of ceftolozane-tazobactam and ceftazidime-avibactam versus all isolates, and the MDR and XDR subsets is presented in Figures 2 and 3, respectively.

Materials and Methods

Bacterial isolates: From January 2007 to December 2017, inclusive, 10 to 15 sentinel hospitals across Canada submitted clinical isolates from patients attending emergency rooms, medical and surgical wards, hospital clinics, and intensive care units (CANWARD). On an annual basis, each centre was asked to submit clinical isolates (consecutive, one patient/infection site) from blood, respiratory, urine, and wound infections. The medical centers submitted clinically significant isolates, as defined by their local site criteria. Isolate identification was performed by the submitting site and confirmed at the reference site as required (i.e., when morphological characteristics and antimicrobial susceptibility patterns did not fit the reported identification). Isolates were shipped on Amos semi-solid transport media to the coordinating laboratory (Health Sciences Centre, Winnipeg, Canada), subcultured onto appropriate media, and stocked in skim milk at 4°C until minimum inhibitory concentration (MIC) testing was carried out.

Antimicrobial Susceptibilities: Following 2 subcultures from frozen stock, the in vitro activity of ceftolozane-tazobactam, ceftazidime-avibactam, and relevant comparators was determined by broth microdilution in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines.1,4 In-house prepared broth microdilution panels were used to test all antimicrobial agents. Antimicrobial MICs were interpreted using CLSI breakpoints.5 MDR PA isolates were defined as isolates testing non-susceptible to at least one antimicrobial from ≥3 or more different classes. Extensively drug-resistant (XDR) PA isolates were defined as a subset of MDR isolates that tested non-susceptible to at least one antimicrobial from ≥5 different classes. For the purpose of this study, two different cut-off MICs were used for PA isolates: (i) ≥MIC90 (i.e., ≥32 mg/L for cefepime, amikacin), fluoroquinolones (ciprofloxacin), aminoglycosides (gentamicin, kanamycin, amikacin), quinolones (ciprofloxacin), aminoglycosides (gentamicin, amikacin), and polypeptide antibiotics (teicoplanin, vancomycin, and teichoic acid bacteriostatic antibiotics). This cut-off was chosen to provide a reasonable balance between efficacy and clinical relevance.

Conclusions: The CANWARD study is supported in part by the University of Manitoba, National Microbiology Laboratory, Achaogen, Astellas, Merck Canada Inc., Paratek, Pfizer, Sunovion Pharmaceuticals, The Medicines Company, and Tetraphase.

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Abstract

In total, 4224 PA clinical isolates were obtained as a part of the CANWARD Study between January 2007 and December 2017. Isolates were collected from patients on medical wards (n = 1437, 34.0%), hospital clinics (n = 1035, 24.5%), intensive care units (n = 933, 22.1%), emergency rooms (n = 511, 12.1%), and surgical wards (n = 309, 7.3%). The distribution of isolates by species were: P. aeruginosa (2829 (67.6%) respiratory, 765 (18.1%) blood, 432 (10.2%) wound, and 198 (4.7%) urine. The in vitro activity of ceftolozane-tazobactam, ceftazidime-avibactam, and comparators versus all isolates and antimicrobial non-susceptible subsets is presented in Table 1 and Figure 1. The MIC distribution of ceftolozane-tazobactam and ceftazidime-avibactam versus all isolates, and the MDR and XDR subsets is presented in Figures 2 and 3, respectively.

Table 1: In Vitro Activity of Ceftolozane-Tazobactam, Ceftazidime-Avibactam, and Relevant Comparators Versus Multidrug-Resistant Non-Susceptible P. aeruginosa Clinical Isolates

Results

Figure 1: In Vitro Activity of Ceftolozane-Tazobactam and Ceftazidime-Avibactam Versus Antimicrobial Non-Susceptible P. aeruginosa Clinical Isolates

Figure 2: MIC Distribution of Ceftolozane-Tazobactam and Ceftazidime-Avibactam versus P. aeruginosa Clinical Isolates

Figure 3: MIC Distribution of Ceftolozane-Tazobactam and Ceftazidime-Avibactam versus MDR and XDR P. aeruginosa Isolates

References