P1241

Carbapenem Resistant Respiratory Tract Isolates of *Pseudomonas aeruginosa* in Europe: Comparative Antibacterial Activity (TEST 2013-2016)

IHMA, Inc.
2122 Palmer Drive
Schaumburg, IL 60173 USA
Phone: +1.847.303.5003
Fax: +1.847.303.5601
www.ihmainc.com

D. Hoban[1], D. Sahm[1], M. Renteria[1], B. Johnson[1], H. Leister-Tebbe[2] [1]International Health Management Associates, Schaumburg, IL, USA [2]Pfizer Inc., Collegeville, PA, USA

Revised Abstract

Background: *P. aeruginosa* (Pa) are virulent hospital pathogens that exhibit both intrinsic and increasingly acquired resistance to multiple classes of antibiotics. Pa isolated from the respiratory tract of at risk patients may display carbapenem resistance and frequently exhibit cross resistance to other first line therapeutic choices. The purpose of this study was to determine the *in vitro* activity of first line antibiotics against respiratory tract isolates of Pa routinely cultured from both community and hospitalized patients in European hospitals including those that exhibited carbapenem resistance. **Methods:** From 2013-2016, 2578 Pa from respiratory tract specimens were isolated from European hospitals as part of the multi-year Tigecycline European Surveillance Trial (TEST). MICs were determined by the local laboratory using supplied microdilution panels and interpreted according to EUCAST guidelines. **Results:** Percent susceptibility of comparative agents is shown below.

P. aeruginosa: % Susceptible

	2013		2014		2015		2016	
	ALL	CR	ALL	CR	ALL	CR	ALL	CR
n	793	126	686	123	596	97	503	96
Amikacin	90.7	70.6	86.6	61.0	90.4	68.0	91.3	70.8
Cefepime	76.7	37.3	73.9	28.5	76.5	24.7	74.0	28.1
Ceftazidime	78.0	45.7	77.0	41.5	80.9	29.9	76.3	38.5
Levofloxacin	59.5	14.3	56.3	7.3	61.6	8.3	62.8	22.9
Meropenem	67.3	0	67.4	0	68.3	0	68.2	0
Pip-Tazo	77.9	41.3	74.6	33.3	78.7	36.1	73.4	37.5

Alt: All isolates; CR: Carbapenem Resistant

Conclusions: Carbapenem resistant Pa demonstrates decreased susceptibility to cefepime, ceftazidime levofloxacin, amikacin and pip-tazo in each TEST study year. Carbapenem resistance in Pa is strongly associated with resistance to other first line agents used to treat *P. aeruginosa* infections. Only amikacin demonstrated % susceptible >60% against carbapenem resistant *P. aeruginosa* in each TEST study year.

Introduction

Pseudomonas aeruginosa continually represents a therapeutic challenge because of intrinsic and acquired resistance to many antimicrobial agents as well as its ability to integrate several mechanisms with the subsequent development of multi-drug resistance. Today *P. aeruginosa* is found in hospitals where reservoirs for infection can be found in intensive care units and often associated with respiratory equipment. In ICUs *P. aeruginosa* is a major pathogen in ventilator-associated pneumonia. Unfortunately there has been a global increase in strains with multiple antibiotic resistance mechanisms including AmpC beta-lactamase, extended-spectrum beta-lactamase, outer membrane porin alterations, metallo-beta-lactamase and efflux pumps. Depending upon the global region the antibiogram for *P. aeruginosa* can vary considerably to the most commonly anti-pseudomonal agents used in clinical practice.

This report documents the *in vitro* activity of commonly used first line antibiotics against *P. aeruginosa* including carbapenem resistant Pa isolated in European countries from respiratory tract infections during the Tigecycline European Surveillance Trial (TEST) program.

Materials & Methods

- Between 2013 and 2016, 817 cumulative hospital sites in 21 European countries (Belgium, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Netherlands, Poland, Portugal, Romania, Spain, Sweden, Switzerland and the United Kingdom) participated in the TEST program. For this report 2578 isolates of *P. aeruginosa* were identified to the species level and MICs determined at each participating laboratory using supplied broth microdilution panels. All isolates were derived from respiratory tract infections. Only one isolate per patient was accepted into the study.
- Organism collection, transport, confirmation of organism identification, susceptibility testing, and development and management of a centralized database were coordinated by International Health Management Associates, Inc. located in Schaumburg, IL, USA.
- Minimum inhibitory concentrations (MICs) were determined by the Clinical and Laboratory Standards Institute (CLSI) recommended broth microdilution testing method using MicroScan (Beckman Coulter, West Sacramento, CA). All antimicrobials were supplied by the panel manufacturers.
- MIC interpretive criteria followed published EUCAST guidelines [2].
- Quality controls (QC) were performed on each day of testing using appropriate ATCC control strains, following CLSI and manufacturer guidelines. Results were included in the analysis only when corresponding QC results were within the acceptable ranges [3].

Results

Table 1. *In vitro* activity of β-lactams and comparator agents tested against 2,578 *P. aeruginosa* isolates collected in Europe

Drug	%S	%I	%R	MIC_{50}	MIC_{90}	MIC range
Amikacin	89.6	4.2	6.2	4	16	≤0.5 - >64
Cefepime	75.4	0	24.6	4	32	≤0.5 - >32
Ceftazidime	78.5	0	21.5	2	>16	≤1 - >16
Levofloxacin	59.8	0	40.2	1	>8	≤0.008 - >8
Meropenem	67.7	15.1	17.2	1	16	≤0.06 - >16
Pip-Tazo	76.3	0	23.7	4	128	≤0.06 - >128

Table 2. *In vitro* activity of β-lactams and comparator agents tested against 442 Carbapenem Resistant *P. aeruginosa* isolates collected in Europe

Drug	%S	%I	%R	MIC_{50}	MIC_{90}	MIC range
Amikacin	67.4	9.5	23.1	8	64	≤0.5 - >64
Cefepime	30.1	0	69.9	16	>32	1 - >32
Ceftazidime	38.7	0	61.3	16	>16	2 - >16
Levofloxacin	12.9	0	87.1	>8	>8	0.06 - >8
Meropenem	0	0	100	16	>16	16 - >16
Pip-Tazo	37.1	0	62.9	64	>128	1 - >128

Figure 1. *P. aeruginosa* and Carbapenem Resistant *P. aeruginosa* Distribution by Country

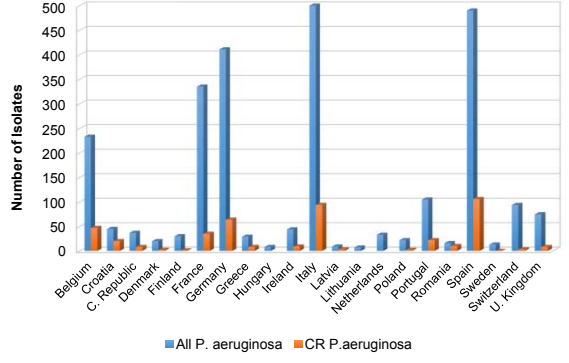


Figure 2. MIC Distribution of β-lactams against *P. aeruginosa* isolates in Europe

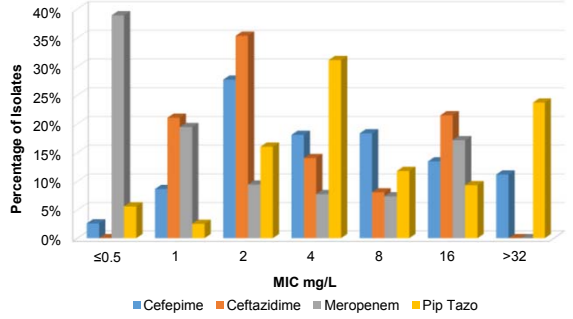
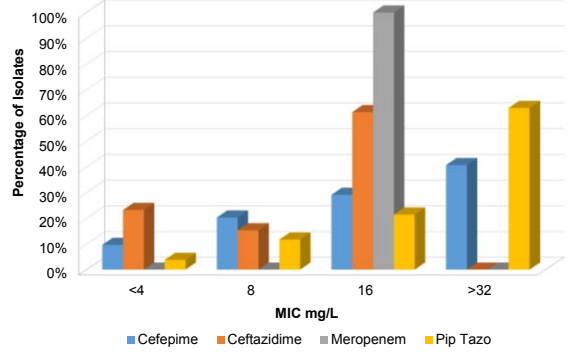


Figure 3. MIC Distribution of β-lactams against Carbapenem Resistant *P. aeruginosa*



Conclusions

- **Amikacin was the only studied antibiotic to exhibit >89% susceptibility to all Pa isolates from Europe.**
- **Carbapenem resistant isolates of Pa demonstrated significantly reduced susceptibility to all tested agents with only Amikacin again showing percent susceptible of 67%.**
- **The presence of carbapenem resistant in Pa dramatically reduced the activity of all studied agents.**
- **Continued monitoring of the resistance profiles of Pa in Europe is warranted.**

References

1. Clinical Laboratory Standards Institute (CLSI), 2015. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standards – Tenth Edition. CLSI document M07-A10 (ISBN 1-56238-887-4). CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.
2. The European Committee on Antimicrobial Susceptibility Testing–EUCAST Clinical Breakpoints 2017; http://www.eucast.org/clinical_breakpoints/
3. Clinical and Laboratory Standards Institute (CLSI), 2017. Performance Standards for Antimicrobial Susceptibility Testing – Twenty-Seventh Informational Supplement. CLSI Document M100S (ISBN 1-56238-923-8). CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.

Acknowledgments

We gratefully acknowledge the contribution of the investigators, laboratory personnel, and all members of the Tigecycline European Surveillance Trial group. This study was sponsored by Pfizer Inc. IHMA is a clinical research organization that has been contracted by Pfizer to manage the TEST program. DH, DS, MR and BJ are employees of IHMA, Inc., which was paid by Pfizer to manage this study and to prepare this poster. HL-T is an employee of Pfizer.