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Antimicrobial Susceptibility Profiles for *Acinetobacter baumannii* from Europe: TEST 2014-2015

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Revised Abstract

Background: *Acinetobacter baumannii* has been recognized as an important opportunistic pathogen responsible for pneumonia, septicemia, urinary tract infections and meningitis, and is often associated with nosocomial outbreaks. Due to their capacity to acquire and accumulate resistance determinants, clinical isolates of *A. baumannii* are often multi-drug resistant and difficult to eradicate. In this study, data from the Tigecycline European Surveillance Trial (TEST) program were analyzed to evaluate the activity of tigecycline and comparator antibiotics against recent (2014-2015) clinical isolates of *A. baumannii* from Europe. **Methods**: Between 2014 and 2015, 300 cumulative sites participated in the TEST program in 19 European countries. A total of 1,343 isolates of *A. baumannii* were identified to the species level and MICs determined at each participating laboratory using supplied broth microdilution panels. Organism identification was confirmed using MALDI-TOF mass spectroscopy at a central laboratory (IHMA, Inc., Schaumburg, IL, US). EUCAST breakpoint criteria were applied to define susceptibility and resistance where available (amikacin, levofloxacin, meropenem); CLSI breakpoints were applied for cefepime, ceftazidime, ceftriaxone, minocycline, and piperacillin-tazobactam. There are no breakpoint for tigecycline. **Results**: Results are shown in the following table (MIC, $MIC_{50/90}$ in mg/L, %S=% susceptible). Minocycline was the only antimicrobial agent against which *A. baumannii* from Europe had a >50% a susceptibility rate. Although there are no interpretive criteria for tigecycline this drug did exhibit potent *in vitro* activity with $MIC_{50/90}$ values of 0.5/2 mg/L.

Antimicrobial	%S	MIC_{50}	MIC_{90}	Minimum MIC	Maximum MIC
Tigecycline	na	0.5	2	≤ 0.008	8
Amikacin	42.4	32	> 64	≤ 0.5	> 64
Levofloxacin	27.0	8	> 8	≤ 0.008	> 8
Meropenem	32.3	> 16	> 16	≤ 0.06	> 16
Cefepime	30.0	32	> 32	≤ 0.5	> 32
Ceftazidime	31.3	> 16	> 16	≤ 1	> 16
Ceftriaxone	19.2	> 32	> 32	0.12	> 32
Minocycline	68.1	2	16	≤ 0.5	> 16
Piperacillin Tazobactam	29.5	> 128	> 128	≤ 0.06	> 128

na; no breakpoints available

Conclusions: *A. baumannii* present significant treatment challenges due to lack of activity across many drug classes. Continued monitoring for emerging resistance trends is warranted, and continued search for newer more effective drugs is critical for the future management of patients with infections caused by these organisms.

Introduction

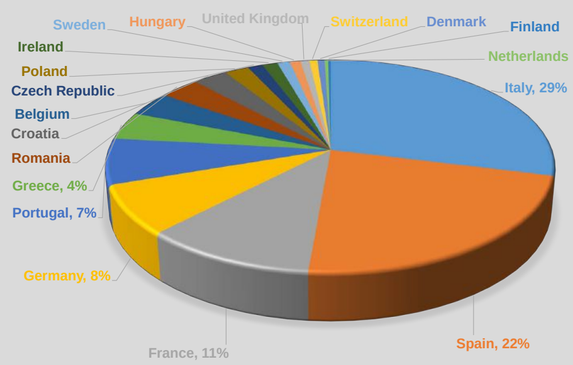
Acinetobacter baumannii has been recognized as an important opportunistic pathogen responsible for pneumonia, septicemia, urinary tract infections and meningitis, and is often associated with nosocomial outbreaks. Due to their capacity to acquire and accumulate resistance determinants, clinical isolates of *A. baumannii* are often multi-drug resistant and difficult to eradicate. In this study, data from the Tigecycline European Surveillance Trial (TEST) program were analyzed to evaluate the activity of tigecycline and comparator antibiotics against recent (2014-2015) clinical isolates of *A. baumannii* from Europe.

Materials & Methods

- Between 2014 and 2015, 300 cumulative sites participated in the TEST program in 19 European countries. A total of 1,343 isolates of *A. baumannii* were identified to the species level and MICs determined at each participating laboratory using supplied broth microdilution panels.
- Organism collection, transport, confirmation of organism identification, and development and management of a centralized database were coordinated by International Health Management Associates, Inc. located in Schaumburg, IL, USA. Organism identification was confirmed using MALDI-TOF mass spectroscopy.
- Minimum inhibitory concentrations (MICs) were determined by the Clinical and Laboratory Standards Institute (CLSI) recommended broth microdilution testing method [1].
- EUCAST breakpoint criteria were applied to define susceptibility and resistance where available (amikacin, levofloxacin, meropenem); CLSI breakpoints were applied for antimicrobials for which there are no EUCAST breakpoints (cefepime, ceftazidime, ceftriaxone, minocycline, and piperacillin tazobactam) [2,3]. There are no breakpoint criteria for tigecycline when tested against *A. baumannii*.
- Quality control testing was performed on each day of testing using appropriate ATCC control strains and following CLSI and manufacturer guidelines. Results were included in the analysis only when corresponding QC results were within the acceptable ranges [2].
- MDR was defined as non-susceptibility to amikacin, meropenem, and piperacillin-tazobactam utilizing CLSI breakpoint criteria.

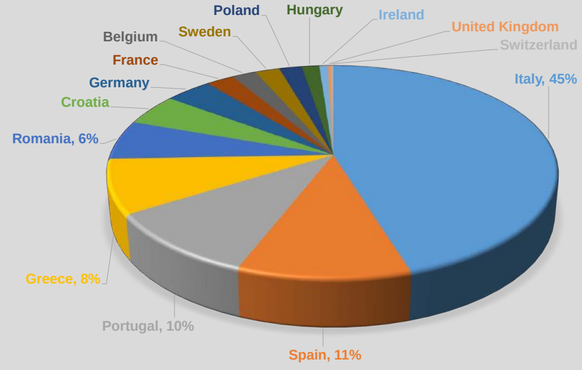
Results

Figure 1. Countries Contributing *A. baumannii* Isolates.*



* Italy, Spain, France, Germany, Portugal, and Greece contributed >80% of all isolates.

Figure 2. Countries Contributing MDR *A. baumannii* Isolates.*



* Italy, Spain, Portugal, Greece, and Romania contributed 80% of the MDR isolates.

Table 1. *In Vitro* Activity of Tigecycline and Comparator Antimicrobial Agents Against 1,343 *A. baumannii* Isolates.

Antimicrobial Agent	MIC_{50}	MIC_{90}	MIC Range	% Susceptible	% Intermediate	% Resistant
Tigecycline	0.5	2	≤ 0.008 - 8	na[a]	na	na
Amikacin	32	> 64	≤ 0.5 - >64	42.4	4.3	53.3
Levofloxacin	8	> 8	≤0.008 - >8	27.0	1.7	71.3
Meropenem	> 16	> 16	≤.0.06 - >16	32.3	3.7	64.0
Cefepime	32	> 32	≤ 0.5 - >32	30.0	7.7	62.3
Ceftazidime	> 16	> 16	≤ 1 - >16	31.3	5.4	63.3
Ceftriaxone	> 32	> 32	0.12 - >32	19.2	14.5	66.3
Minocycline	2	16	≤ 0.5 - >16	68.1	18.4	13.5
Piperacillin-tazobactam	> 128	> 128	≤ 0.06 - >128	29.5	3.7	66.8

na; no breakpoints available

Table 2. Tigecycline MIC Cumulative Frequency Distributions (%) Among *A. baumannii* Isolates from 19 European Countries.

		Tigecycline MIC (mg/L)											
Country	N	≤0.008	0.02	0.03	0.06	0.12	0.25	0.5	1	2	4	8	≥16
Belgium	50			2.0	10.0	36.0	64.0	82.0	**100**				
Croatia	39				2.6	2.6	12.8	28.2	64.1	**94.9**	100		
Czech Republic	17				11.8	64.7	**94.1**	94.1	100				
Denmark	8				12.5	50.0	87.5	87.5	87.5	**100**			
Finland	3						66.7	**100**					
France	146			0.7	16.4	51.4	69.2	79.5	**90.4**	100			
Germany	101	1.0	2.0	4.0	26.7	54.5	74.3	85.1	**97.0**	100			
Greece	57						8.8	63.2	**94.7**	100			
Hungary	12					8.3	8.3	25.0	75.0	**100**			
Ireland	17				11.8	29.4	35.3	52.9	82.4	**94.1**	100		
Italy	388	0.5		1.0	2.8	8.2	20.9	45.1	77.3	**97.4**	99.5	100	
Netherlands	4					25.0	**100**						
Poland	27				3.7	11.1	25.9	51.9	85.2	**92.6**	100		
Portugal	94			1.1	1.1	7.4	18.1	44.7	84.0	**98.9**	100		
Romania	45						2.2	11.1	71.1	82.2	**100**		
Spain	302	0.7		1.3	8.3	21.9	37.4	58.6	86.8	**97.4**	100		
Sweden	14					7.1	64.3	**92.9**	100				
Switzerland	9				22.2	88.9	**100**						
United Kingdom	10				30.0	40.0	60.0	80.0	**100**				

a. MIC_{90} values in bold.

Table 3. *In Vitro* Activity of Tigecycline and Comparator Antimicrobial Agents Against 688 MDR *A. baumannii* Isolates.

Antimicrobial Agent	MIC_{50}	MIC_{90}	MIC range	% Susceptible	% Intermediate	% Resistant
Tigecycline	1	2	≤ 0.008 - 8	na[a]	na	na
Amikacin	> 64	> 64	32 - >64	0.0	7.6	92.4
Levofloxacin	> 8	> 8	1 - >8	1.2	5.2	93.6
Meropenem	> 16	> 16	4 - >16	0.0	1.3	98.7
Cefepime	> 32	> 32	1 - >32	1.3	6.4	92.3
Ceftazidime	> 16	> 16	≤ 1 - >16	3.8	5.1	91.1
Ceftriaxone	> 32	> 32	4 - >32	0.9	4.8	94.3
Minocycline	4	16	≤ 0.5 - >16	47.7	29.8	22.5
Piperacillin-tazobactam	> 128	> 128	32 - >128	0.0	2.6	97.4

na; no breakpoints available

Table 4. Tigecycline MIC Cumulative Frequency Distributions (%) Among 688 MDR *A. baumannii* Isolates from European Countries.

	Tigecycline MIC (mg/L)										
	≤0.015	**0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**≥16**
N	**1**	2	0	11	74	172	270	134	22	2	
Cum%	**0.1**	0.4	0.4	2.0	12.8	37.8	77.0	96.5	99.7	100	

Conclusions

- Among the European countries that contributed *A. baumannii* for the TEST study, the tigecycline MIC_{90} value was 2 mg/L (Table 1). MIC_{90} values varied from 0.25 to 4 mg/L between countries (Table 2).
- Over 50% of the *A. baumannii* collected from patients in Europe were MDR (688 isolates).
- Only tigecycline demonstrated appreciable activity against *A. baumannii* from patient infections in Europe, including MDR isolates (Table 3). More than 96% of the MDR *A. baumannii* isolates had MIC values ≤ 2 mg/L (Table 4).
- *A. baumannii* is a significant opportunistic pathogen with resistance mechanisms and requires continued monitoring of susceptibility to antimicrobial agents through surveillance efforts such as the TEST program.

References and Acknowledgments:

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2. Clinical and Laboratory Standards Institute. 2015. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Sixth Informational Supplement. CLSI Document M100S. Wayne, PA.
3. European Committee on Antimicrobial Susceptibility Testing (EUCAST). 2015. *Breakpoint tables for interpretation of MICs and zone diameters*, version 5.0 http://www.eucast.org.

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