**INTRODUCTION**

Pseudomonas aeruginosa is a major source of morbidity in Cystic Fibrosis (CF) patients. The recurrent character of these infections requires the frequent use of anti-pseudomonal antibiotics.

As a result, multiresistance to anti-pseudomonal antibiotics is frequently observed in these strains [1].

Reviving older antibiotics and optimizing their activity may help to alleviate this burden.

Temocillin (TMO) is the 6-α-methoxy derivative of ticarcillin (Fig.1). It is highly stable to Amp-C-type cephalosporinases and most extended-spectrum β-lactamases (ESBLs). TMO was abandoned for a long time due to lack of activity against Gram-positive organisms, anaerobes and P. aeruginosa. Yet it was recently reintroduced because of its activity against ESBL-producing Enterobacteriaceae [2].

Recent studies from our group showed that intrinsic resistance of P aeruginosa to TMO was due to active efflux by the constitutively-expressed transporter MexAB-OprM and that natural mutations in the corresponding genes restored TMO activity [3].

**OBJECTIVES**

To evaluate the activity of temocillin, in comparison with other anti-pseudomonal β-lactams, against P. aeruginosa collected in four CF centers across Europe.

**METHODS**

335 isolates of *P. aeruginosa* from CF patients

99 isolates provided by Dr M. Tunney, The Queen’s University of Belfast, United Kingdom.

88 isolates provided by Drs A. Vergison / O. Denis from the Hôpital des Enfants Malades Reine Fabiola, Brussels, Belgium.

80 isolates provided by Prof. Patrick Plésiat, CHRU Besançon, Besançon, France.

68 isolates provided by Prof. Barbara Kahl, University of Münster, Münster, Germany.

Quality control strain ATCC® 27853™.

**Antibiotics used**

Temocillin (TMO); ticarcillin (TIC); piperacillin / tazobactam (TZP); ceftazidime (CAZ) and meropenem (MEM).

**Antibiotic susceptibility testing**

MICs were determined by microdilution in cation-adjusted Muller Hinton broth, according to CLSI guidelines [4] and susceptibility assessed using EUCAST interpretative criteria [5]. MICs of different antibiotics in individual strains were compared using quantile density contour analysis (JMP 10.0.2, SAS Institute Inc., Cary, NC).

**REFERENCES**


**RESULTS**

![Fig.1 structure of temocillin (6-α-methoxy-ticarcillin). The red arrow indicates the methoxy group that plays an important role in resistance to hydrolysis by β-lactamas.](image)

**CONCLUSIONS**

> According to EUCAST susceptibility breakpoints, half of the strains were susceptible to MEM, and one third to TAZ and CAZ

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> One fifth of the strains have MICs ≤ 16 mg/L for TMO and TIC

> ~10% of strains that were resistant to TIC, TAZ, CAZ, or MEM remained susceptible to temocillin

**CONCLUSIONS**

> According to EUCAST susceptibility breakpoints, half of the strains were susceptible to MEM, and one third to TAZ and CAZ in this collection.

> Interestingly, temocillin was as active as its parent compound TIC against *P. aeruginosa* isolated from cystic fibrosis patients, with 22 % of the strains displaying an MIC ≤ 16 mg/L.

> A subset of strains that were resistant to TIC, TAZ, CAZ, or MEM remained susceptible to temocillin possibly due to the expression of ESBL(s), carbapenemase(s) or other resistance mechanisms that do not affect temocillin.

> Temocillin may therefore offer a useful alternative in the treatment of *P. aeruginosa* infections in CF patients and should be included in susceptibility testing.

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