Comparative in vitro activity of Temocillin, Meropenem, Ceftazidime, and Piperacillin/Tazobactam against panel strains and clinical isolates of *Burkholderia cepacia* complex from 9 different genomovars

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Background - B. cepacia infections treatment

- **Treatment of B. cepacia infections is hampered by their intrinsic resistance to many antimicrobial agents such as :**
  - **aminoglycosides**
  - **polymyxins**
  - **anti-pseudomonal penicillins**
- **Conventional therapy include combination of drugs active in vitro against the isolate with (when possible) different mechanisms of action**

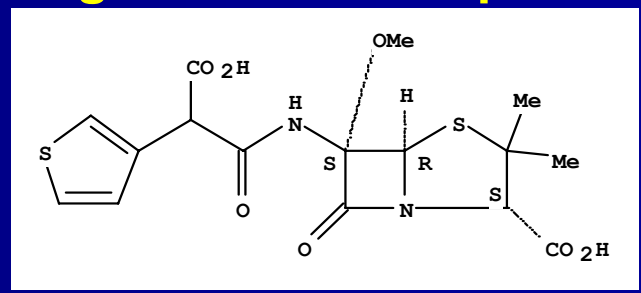
Döring & Hoiby, *JCF* 2004; UK CF TRUST Antibiotic group, 2002

Background - Temocillin

- 6-α-methoxy-ticarcillin
- spectrum directed only on gram negative bacteria without non-fermenters (*Pseudomonas aeruginosa*, *Acinetobacter* spp.)
- active against all β-lactamases including ESBL and AmpC producers
- <u>Main Indications</u> :

  - urinary tract infections

  - gram negative nosocomial infections



- Adverse Effects : hypersensitivity to penicillins
- Recognized Orphan Drug for the treatment of B. cepacia infection by the EMEA and the FDA

Aim of the study

- **Although temocillin has already been used in a pilot clinical studies (Taylor, *JAC* 1992) with success for the treatment of *Bcc* infections in CF patients, only a few *in vitro* susceptibility data are available**
- **Our aim was, therefore, to determine the MICs of β-lactams used in CF patients**

  - meropenem

  - ceftazidime

  - piperacillin/tazobactam

  - temocillin

  towards a well characterized panel of laboratory strains and clinical isolates of *B. cepacia complex*

Method and Strains

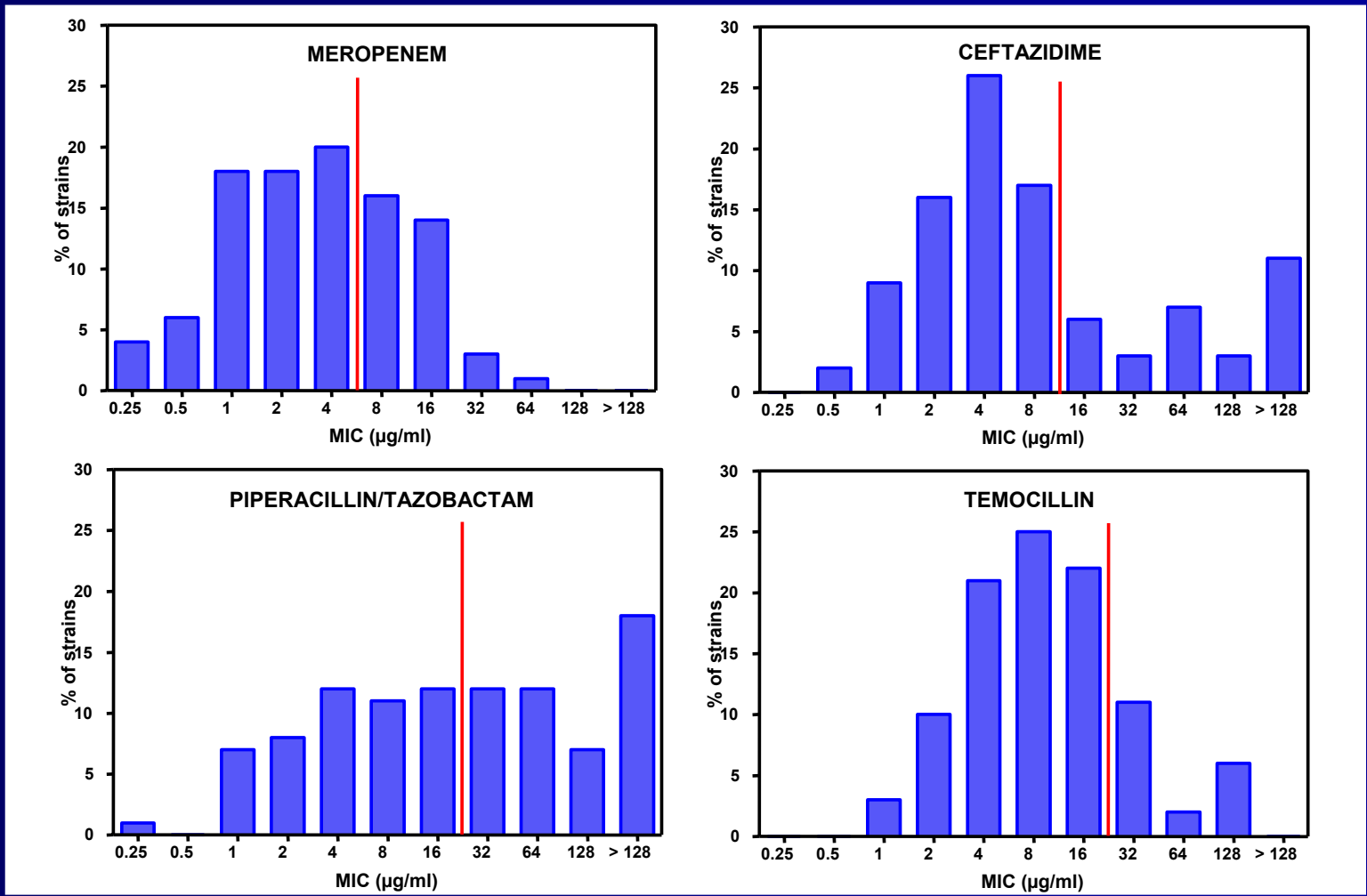
- **MICs were determined using the CLSI broth microdilution technique including *E. coli* ATCC 25923 and *P. aeruginosa* ATCC 27853 as quality control strains**
- **CLSI breakpoint for GNB non-Pseudomonas were applied for MER, CTZ, and PTZ; and that of Fuchs et al. (EJCM 1985) fro temocillin for categorization**
- **100 strains from 9 different species of Bcc were used with repartition between panel strains and clinical isolates**

  35 *B. multivorans*

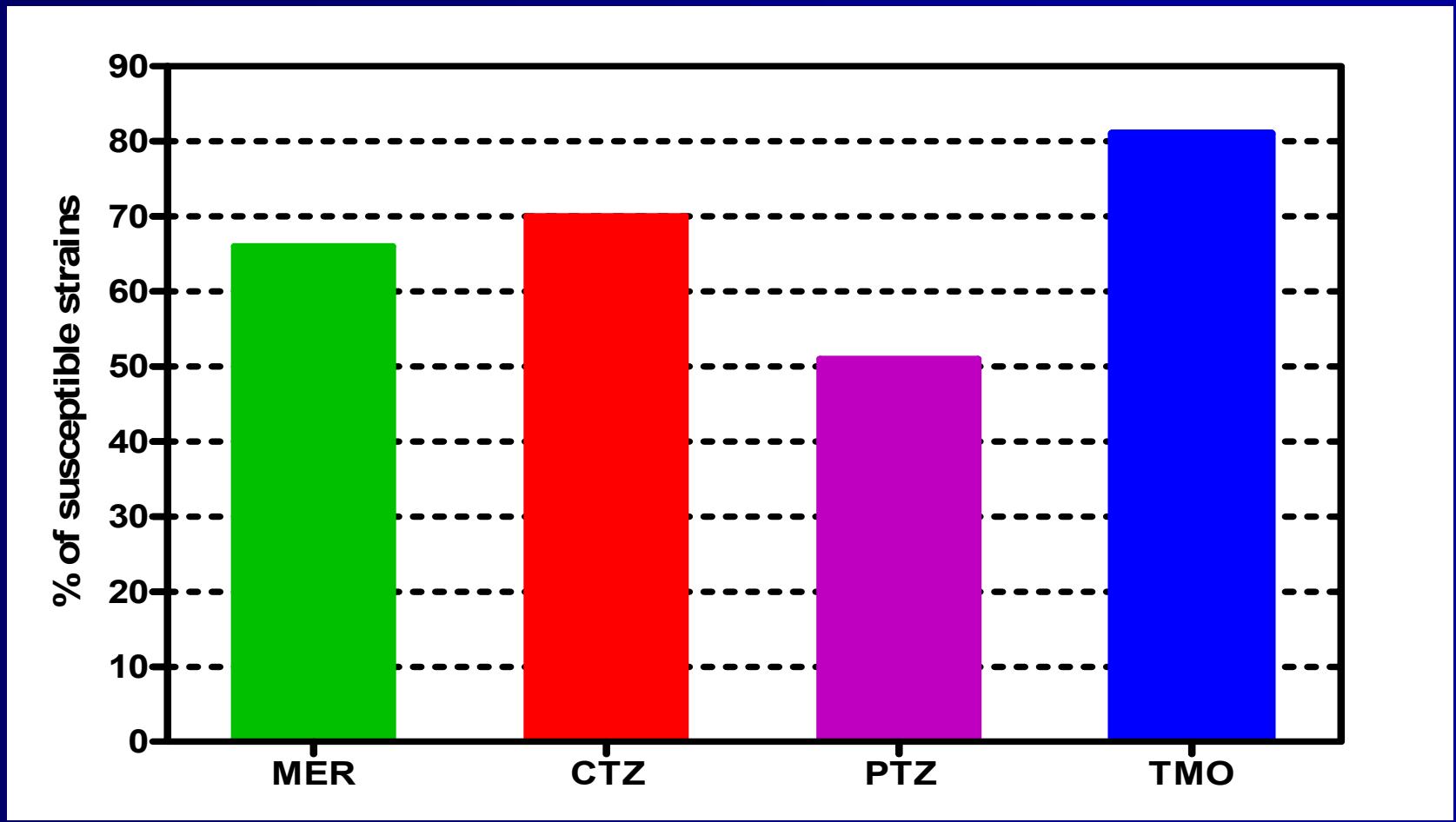
  30 *B. cenocepacia*

  5 *B. cepacia, ambifria, pyrrocinia, vietnamensis, dolosa, stabilis, anthinia*

Results – MIC distributions



Results – Global Susceptibility



Results

Comparison between species

% of susceptible strains

	B. multivorans (n = 35)	*B. cenocepacia* (n = 30)
MER	46	60
CTZ	77	43
PTZ	51	30
TMO	68	77

Results – Particular Strains

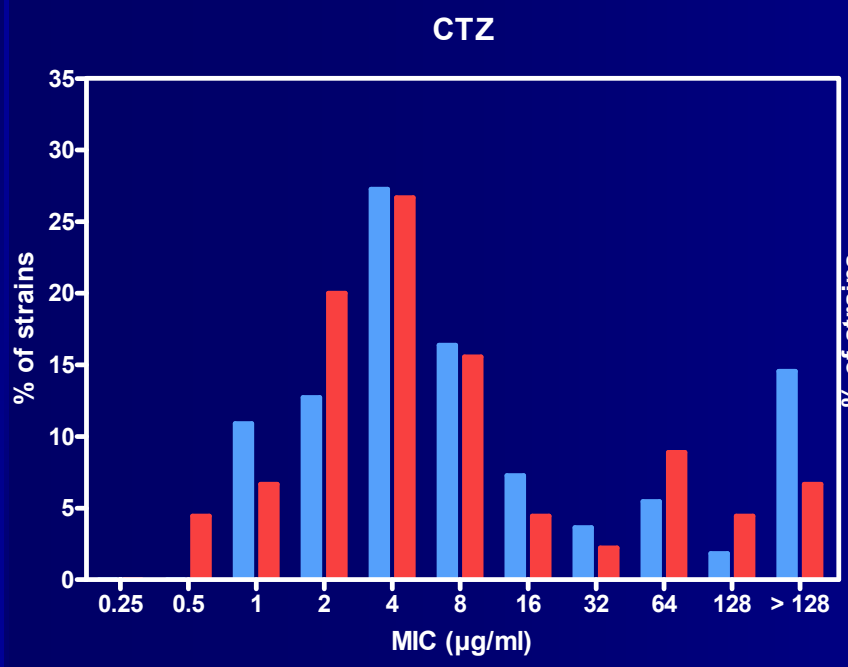
Strains	nbr of strains	Species
resistant to all antibiotics	13	*B. multivorans* (6) *B. cenocepacia* (7)
susceptible only to		
TMO	7	*B. cepacia* (1) *B. cenocepacia* (5) *B. dolosa* (1)
CTZ	3	*B. multivorans*
MER	1	*B. vietnamensis*
PTZ	1	*B. multivorans*

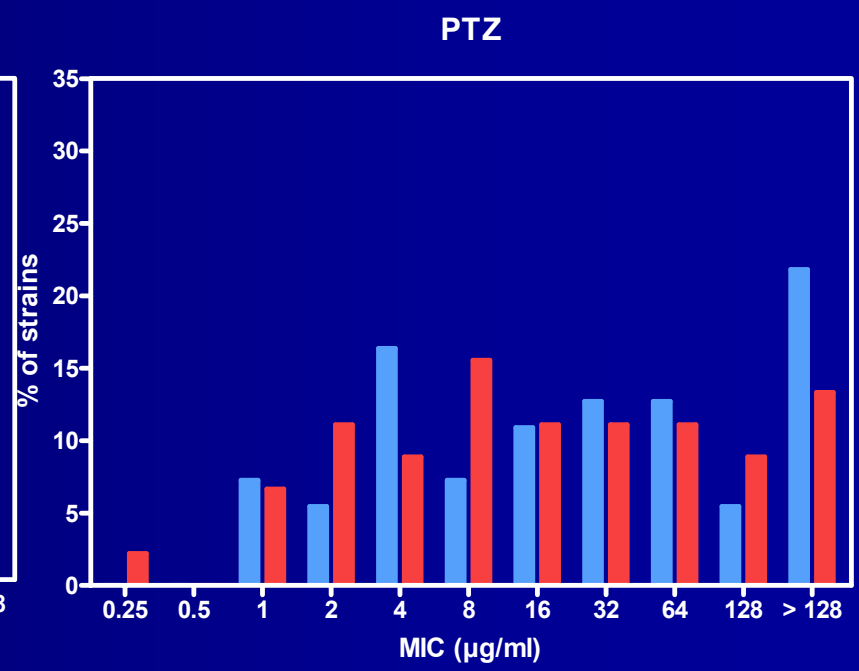
Results

Comparison : Panel Strains vs. Clinical Isolates

Panel strains (n = 45)

Clinical isolates (n = 55)





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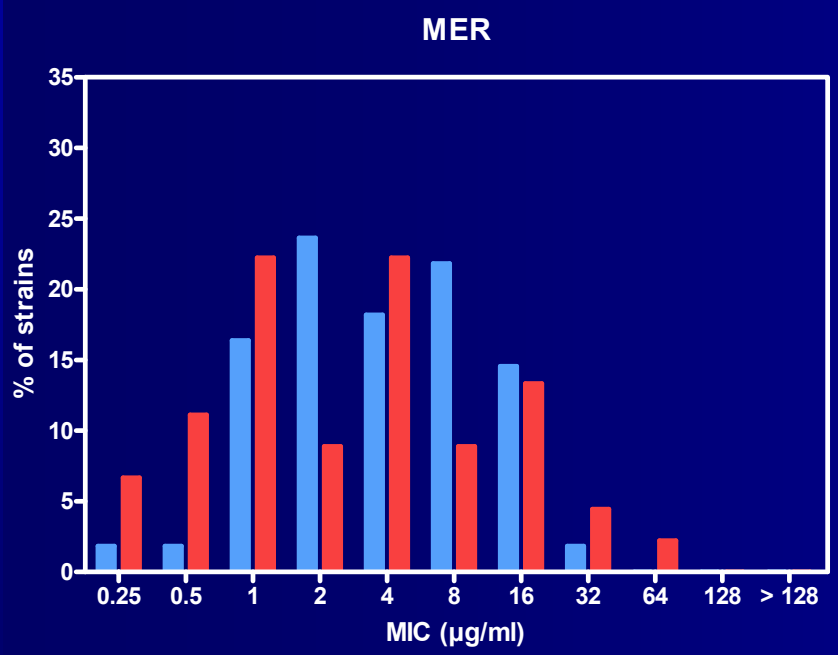

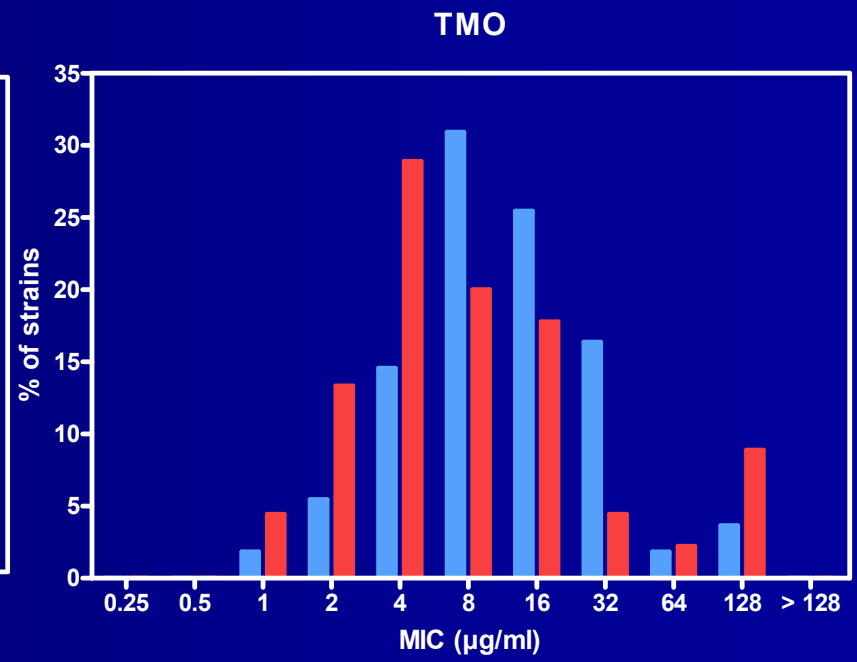

Conclusions - Perspectives

- **Temocillin was the most active β-lactam tested against these strains of *B. cepacia***
- **There might be a slightly different susceptibility pattern between *B. multivorans* and *B. cenocepacia* (especially for ceftazidime).**
- **There was no significant differences between panel strains and clinical isolates**

These results combined with those of the pilot study suggest a potential advantage of temocillin in *B. cepacia* infected CF patients