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# LOW INDUCTION OF ANTIBIOTIC RESISTANCE BY TWO NEW DRUGS AGAINST *PSEUDOMONAS AERUGINOSA* IN A CLINICAL COHORT OF CYSTIC FIBROSIS PATIENTS

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## INTRODUCTION

**Pulmonary exacerbations in cystic fibrosis (CF) patients with chronic *Pseudomonas aeruginosa* infection are associated with increased morbidity. Ceftolozane/tazobactam (C/T) and ceftazidim/avibactam (CZA) are both combination intravenous (IV) antibiotics with activity against multi-drug-resistant Gram-negative bacteria. This is a retrospective study of respiratory cultures positive for *P. aeruginosa* that underwent susceptibility testing for (C/T), (CZA), and other commonly used antibiotics. Isolates were collected from CF patients aged ≥18 years between January 1, 2015, and June 1, 2020.**

## AIM

**Objective: To evaluate the susceptibility of *P. aeruginosa isolates to* two new antibiotics and whether treatment with these new antibiotics increased the resistance of *P. aeruginosa* isolates to other commonly used antibiotics.**

## CONCLUSIONS

**In an era of increasing antimicrobial resistance, we find that C/T and CZA adds a significantly higher proportion of in vitro susceptibility than other commonly used antibiotics for treatment of *P. aeruginosa* isolates from CF patients.**

**Thirty CF patients were treated with C/T among which 20 patients continued having susceptible *P. aeruginosa* isolates after initiation of treatment. No patients were treated with CZA.**

**Treatment with C/T for *P. aeruginosa* infection had no significant impact on resistance development against other commonly used antibiotics.**

## CONTACT INFORMATION

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## RESULTS

**Table 1. Susceptibility data for cephalosporins tested in 6332 *Pseudomonas aeruginosa* isolates from 276 cystic fibrosis patients sampled from 2015-2020**

| | No. of isolates | | | | | |
|---|---|---|---|---|---|---|
| Species and antimicrobial agent(s) | EUCAST Zone diameter breakpoints (mm) | Resistant (n) | Intermediate (n) | Susceptible (n) | No test | Proprotion of susceptible isolates (%) |
| ***Pseudomonas aeruginosa* (n=6332)** | | | | | | |
| Ceftazidime | <17 to > 50 | 2521 | 1013 | 2774 | 22 | 44 |
| Ceftolozan+tazobactam | <24 to > 24 | 618 | 1 | 1802 | 3911 | 74* |
| Ceftazidime+avibactam | <17 to > 17 | 509 | NA | 995 | 4828 | 66* |

Abbreviations: NA: Not available
* p<0.0001 by Chi-square test

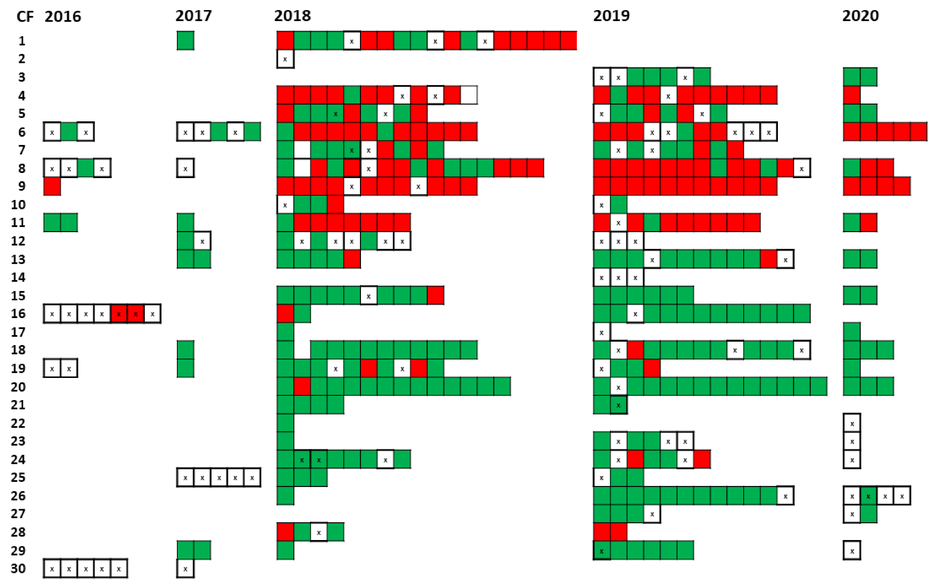
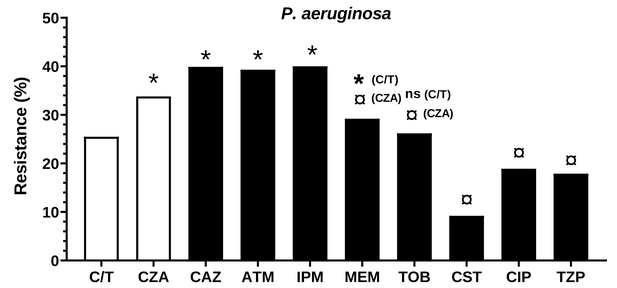



**Figure 2: Overview of in vitro susceptibility to C/T for non-mucoid *P. aeruginosa* isolates from the first intravenous treatment of C/T 2016-2020. Red: resistant, green; sensitiv and X: treatment with C/T.**




2421 *P. aeruginosa* isolates were tested against C/T, 1504 *P. aeruginosa* isolates were tested against CZA and 6310 *P. aeruginosa* isolates isolates were tested against ceftazidime (CAZ), aztreonam (ATM), imipenem (IMP), meropenem (MEM), tobramycin (TOB), colistin (CST), ciprofloxacin (CIP) and piperacillin/tazobactam (TZP).

**Figure 1: Percentage of non-mucoid *P. aeruginosa* isolates resistant to C/T and CZA and other commonly used anti-pseudomonal antibiotics**. Statistical significance between C/T and CZA against the other commonly used antibiotics was assessed using Fisher's exact test.
*: percentage of resistance for C/T and CZA lower than for other antibiotics, P ≤ .05
¤: percentage of resistance for C/T and CZA higher than for other antibiotics, P ≤ .05

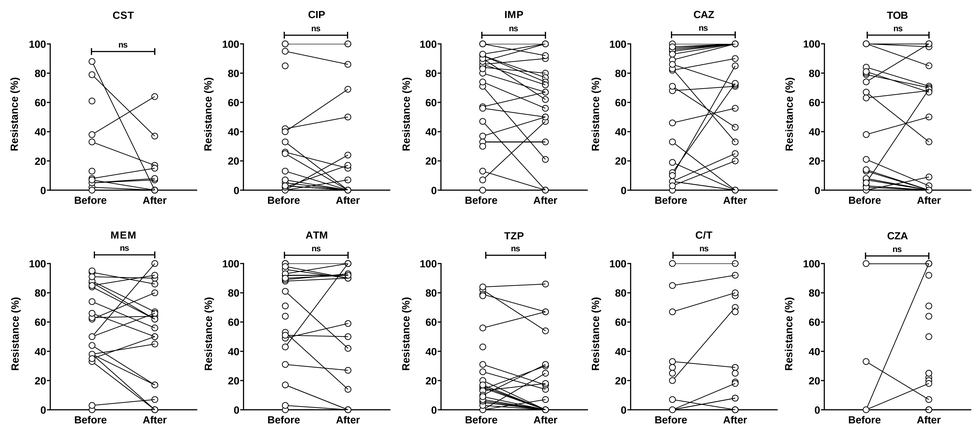



**Figure 3: Distribution of resistant non-mucoid *P. aeruginosa* isolates before and after the first intravenous treatment of C/T from 28 CF patients.** Statistical significance was assessed using Wilcoxon test.

## METHODS

**This study is a retrospective observational study that was performed on pseudonymized collection of bacterial isolates from 276 patients with CF attending the CF center at Rigshospitalet, Copenhagen, Denmark from 2015-2020. 6332 *P. aeruginosa* isolates were cultures from CF sputum samples between January 2015 and June 2020. Antimicrobial susceptibility was determined by disc diffusion methodology following the EUCAST criteria where zone diameter results were used to determine susceptible, intermediate, and resistant category. Antimicrobial content in Oxoid discs were ceftolozan/tazobactam (C/T) (40 µg), ceftazidime/avibactam (CZA) (14 µg), ceftazidime (CAZ) (10 µg), aztreonam (ATM) (30 µg), imipenem (IPM) (10 µg), meropenem (MEM) (10 µg), tobramycin (TOB) (10 µg), colistin (CST) (50 µg), ciprofloxacin (CIP) (5 µg) and piperacillin/tazocabtam (TZP) (? µg). Thirty CF patients received intravenous treatment with C/T from 2016-2020.**