10 YEARS OF BREAKTHROUGHS A HEALTHIER FUTURE

iABC inhaled Antibiotics in Bronchiectasis and Cystic Fibrosis

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In vitro antimicrobial activity of tobramycin, colistin, aztreonam and the new antibiotic murepavadin (POL7080) against cystic fibrosis *Pseudomonas aeruginosa* growing in biofilms

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Facts & Figures

Start date:	01/08/2015
End date:	31/12/2021
Contributions	
IMI funding:	24 331 609 €
EFPIA in kind:	30 213 513 €
Other:	4 117 897 €
Total Cost:	58 663 019 €
Project website:	www.iabcproject.com

Challenge

Pseudomonas aeruginosa is a major cause of morbidity and mortality in chronically infected cystic fibrosis (CF) patients. The most frequently used inhaled antibiotics are tobramycin (TOB), colistin (COL) and aztreonam (AZT). Murepavadin is an outer-membrane protein targeting novel antibiotic with antipseudomonal activity. In this study, we analysed the effect of these antimicrobials against *P. aeruginosa* growing in biofilms

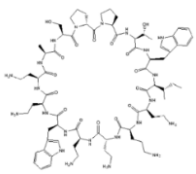


Figure 1: Murepavadin *chemical structure*

Approach & Methodology

- **53 *P. aeruginosa*** recovered from Spain, The Netherlands, Northen Ireland and Australia were used
- **Morphotyes**:18 smooth, 11 mucoid, 11 rough, 10 metallic, and 3 small colony variant
- **Biofilm models**:

Close static system: The ***Calgary*** device was used to determine the minimal biofilm inhibitory concentration (MBIC), the minimal biofilm eradication concentration (MBEC) and the minimal biofilm bactericidal concentration (MBBC) of TOB, COL, AZT and POL7080. Results were compared to MIC values obtained with standard reference broth microdilution.

Open model: ***Bioflux*** is an open biofilm model based on microfluidics, 3 strains (1 reference and 2 clinical) were used to test the activity of murepavadin. Biofilms were stained with the **LIVE/DEAD® BacLight** and fluorescence images were analysed with *Image J* program.

Results

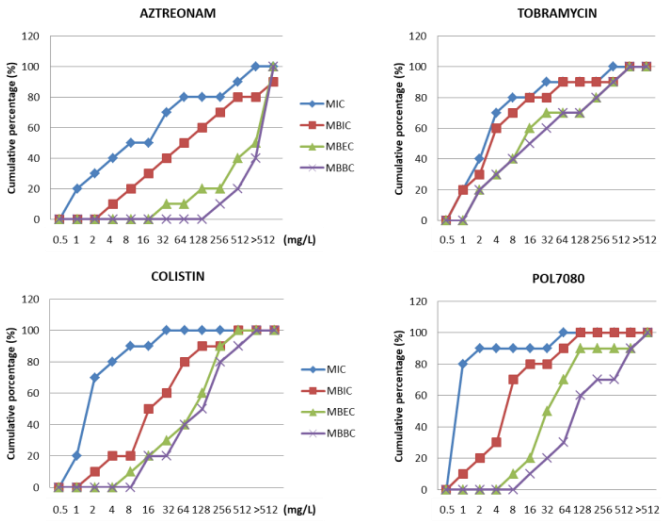
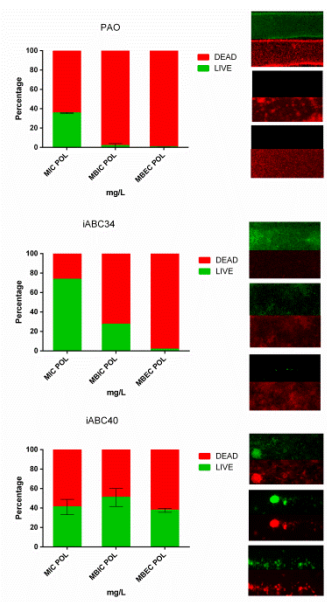


Figure 2: *Calgary results*

Thirty-two of the isolates were biofilm producers; 8 of them were weak (<25 percentile), 16 moderate (25-75 percentile) and 8 strong (>75 percentile) producers. Murepavadin and COL presented similar antimicrobial activity against both planktonic (POL7080 MIC_{50}=0,5 mg/L, colistin MIC_{50}= 1 mg/L) and biofilm growing bacteria ($MBBC_{50}$=64 mg/L for both antibiotics). Aztreonam showed a large difference between the MIC and the biofilm PD parameters (MIC_{50}=4 mg/L vs. $MBBC_{50}$ >512 mg/L) while tobramycin showed the best efficacy against biofilm growth (MIC_{50}=2 mg/L vs. $MBBC_{50}$=8 mg/L).



Bioflux results:
Biofilms of the PAO reference and the iABC34 smooth clinical strain treated with the MBEC of murepavadin, emitted 98.3-99.5% of dead signal, while it was of 61-63.8% for the iABC40 mucoid clinical strain.

Figure 3: Bioflux results
Percentage of live and dead signal emitted by the biofilm at each antibiotic concentration

Impact & take home message

Murepavadin is a promising new antibiotic with activity against biofilms of *P.aeruginosa*

This work has received support from the EU/EFPIA/[Novartis,Polyphor] Innovative Medicines Initiative [2] Joint Undertaking (iABC) grant no 115721-2.