ORIGINAL ARTICLE
LUNG INFECTION

SHAREABLE PDF

# Antibiotic efficacy varies based on the infection model and treatment regimen for *Pseudomonas aeruginosa*

Cristina Cigana[1,2], Serena Ranucci[1], Alice Rossi[1], Ida De Fino[1], Medede Melessike[1] and Alessandra Bragonzi[1,2]

**Affiliations**: [1]Infections and Cystic Fibrosis Unit, Division of Immunology, Transplantation and Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milano, Italy. [2]Both authors contributed equally and share senior authorship.

**Correspondence**: Alessandra Bragonzi, Infections and Cystic Fibrosis Unit, Division of Immunology, Transplantation and Infectious Diseases, San Raffaele Scientific Institute, Milano, Italy.
E-mail: bragonzi.alessandra@hsr.it

@ERSpublications
**Disease-specific animal models and treatment regimens are essential in order to optimise anti-*Pseudomonas* drug testing** http://bit.ly/2ISfBiB

**Cite this article as:** Cigana C, Ranucci S, Rossi A, *et al*. Antibiotic efficacy varies based on the infection model and treatment regimen for *Pseudomonas aeruginosa*. *Eur Respir J* 2020; 55: 1802456 [https://doi.org/10.1183/13993003.02456-2018].



ABSTRACT Antibiotic discovery and preclinical testing are needed to combat the *Pseudomonas aeruginosa* health threat. Most frequently, antibiotic efficacy is tested in models of acute respiratory infection, with chronic pneumonia remaining largely unexplored. This approach generates serious concerns about the evaluation of treatment for chronically infected patients, and highlights the need for animal models that mimic the course of human disease.

In this study, the efficacy of the marketed antibacterial drugs tobramycin (TOB) and colistin (COL) was tested in murine models of acute and chronic *P. aeruginosa* pulmonary infection. Different administration routes (intranasal, aerosol or subcutaneous) and treatment schedules (soon or 7 days post-infection) were tested.

In the acute infection model, aerosol and subcutaneous administration of TOB reduced the bacterial burden and inflammatory response, while intranasal treatment showed modest efficacy. COL reduced the bacterial burden less effectively but dampened inflammation. Mice treated soon after chronic infection for 7 days with daily aerosol or subcutaneous administration of TOB showed higher and more rapid body weight recovery and reduced bacterial burden and inflammation than vehicle-treated mice. COL-treated mice showed no improvement in body weight or change in inflammation. Modest bacterial burden reduction was recorded only with aerosol COL administration. When treatment for chronic infection was commenced 7 days after infection, both TOB and COL failed to reduce *P. aeruginosa* burden and inflammation, or aid in recovery of body weight.

Our findings suggest that the animal model and treatment regimen should be carefully chosen based on the type of infection to assess antibiotic efficacy.