

A novel device for gaseous nitric oxide to treat antibiotic resistant bacterial and fungal lung infections in patients with cystic fibrosis

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Introduction: Lower respiratory infections will be the fourth leading cause of death in 2020 globally. However, antibiotic therapies for patients with lung infections are hampered by drug-resistant bacteria which are now ubiquitous in hospital settings and the community. A typical example are patients with the hereditary disease cystic fibrosis (CF) who are at a higher risk of suffering from lung infections caused by drug-resistant bacterial and fungal pathogens (2). Here we investigate a novel broad-spectrum treatment strategy for pulmonary infections caused by drug-resistant pathogens, based on gaseous nitric oxide (NO) because NO is highly bactericidal and fungicidal at concentrations of 160-200 ppm, and virtually no microorganism can develop resistance to NO at this dose.

Methods: In an ongoing first-in-human open-label, standard care-controlled phase 1 trial, six adult CF patients chronically infected with various drug-resistant bacterial and fungal pathogens including *P. aeruginosa*, *Mycobacterium abscessus* and *Aspergillus fumigatus* receive 160 ppm of NO for 2x5 days trice daily for 30 min with 3.5 h recreation time by inhalation via a NO device (Linde AG, Munich, Germany). The primary endpoint is safety secondary endpoints are change of bacterial and or fungal load after completion of the treatment compared to baseline, change in lung function (FEV1) from baseline.

Results: Preliminary data from 4 patients revealed that antibiotic-resistant bacteria and fungi such as *Pseudomonas aeruginosa* *Escherichia coli* (ESBL), *Mycobacterium abscessus* und *Aspergillus fumigatus* had been eradicated after therapy or had been reduced to several orders of magnitude. Lung function relative to baseline increased to approx. 15%.

Conclusion: Provided further data confirm these preliminary results, the novel NO therapeutic strategy will be an alternative to current antibiotic therapy designed for pulmonary infections, avoid adverse effects caused by repeated antibiotic treatment courses in patients, improve quality of life, prognosis and life expectancies for infected patients, make convenient home therapy possible, reduce health care costs of treatment and hospital stay.