Home-based Treatment of Nontuberculous Mycobacteria Pulmonary Disease Via a Novel Nitric Oxide Generator and Delivery System

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Disclosure

- Study Sponsored by Beyond Air and a Cystic Fibrosis Foundation TDA Grant
- Attendance in Conference Sponsored by Beyond Air

- Data presented in this presentation is of an ongoing study, and therefore subject to change

Inhaled Nitric Oxide for the Treatment of NTM

- Nontuberculous mycobacterial pulmonary disease (NTM-PD) poses a particular threat to patients with cystic fibrosis (CF) and other underlying pulmonary conditions.
- Intermittent inhaled nitric oxide (iNO) has demonstrated bactericidal activity against NTM and shown to be synergistic with standard antibiotic therapy *in vitro.*
- NO has potentially beneficial anti-inflammatory, anti-microbial and direct pulmonary vasodilatory effects.
- Early clinical data suggest iNO treatment to be beneficial for the treatment of NTM-PD[1,2]

1. Bentur L, *et al.* Pilot study to test inhaled NO in CF patients with refractory Mycobacterium abscessus lung infection. J Cyst Fibros. 2020Mar;19(2):225-231
2. R. Thomson , A.R. Colin , L. Morgan , Home-Based Intermittent Inhaled High-Dose Nitric Oxide in Nontuberculous Mycobacterial Pulmonary Disease Using a Novel Nitric Oxide Generator and Delivery System Is Safe and Well Tolerated. https://doi.org/10.1164/ajrccm-conference.2022.205.1_MeetingAbstracts.A3876

Study Objectives

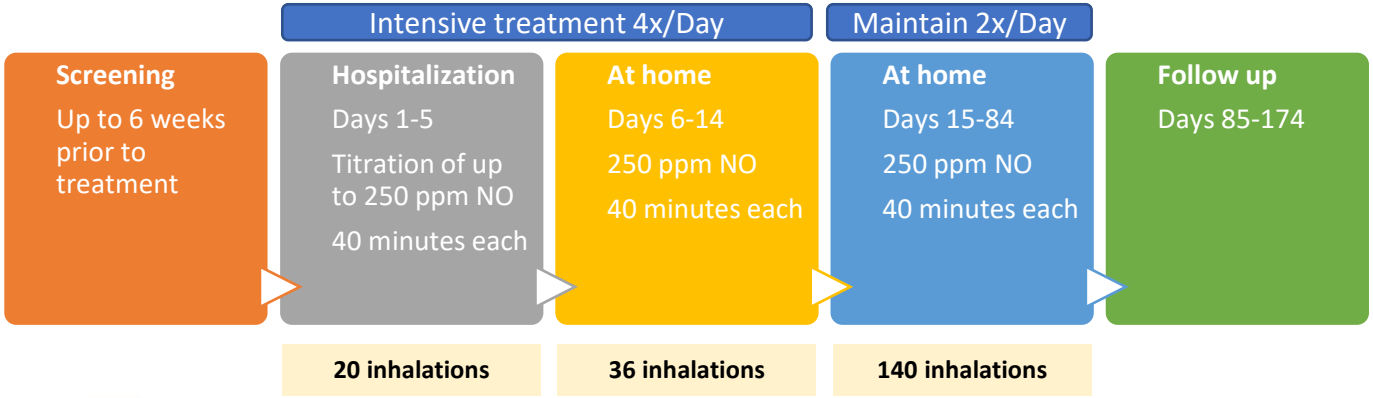
Primary Objective

To assess the safety of high dose intermittent iNO in CF and non-CF patients with treatment refractory NTM infection

Secondary Objectives

To assess the evidence of efficacy of high dose intermittent iNO given in conjunction with standard therapy for treatment refractory NTM infection as measured by clinical, physical, microbiological and change from baseline in QOL

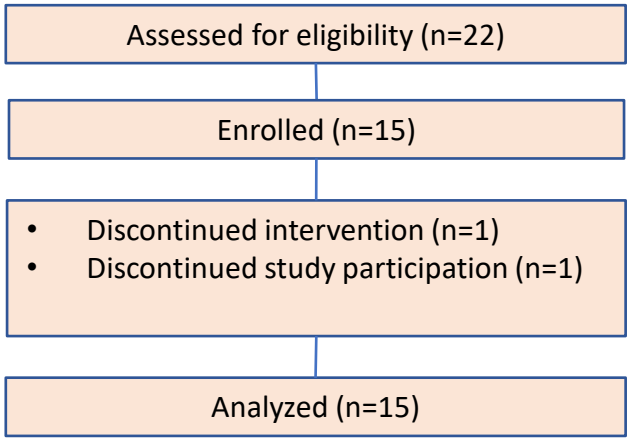
Study design and study treatment



Inhalations administered *via* **LungFit GO™**

- A novel investigational medical device (Beyond Air, NY, USA)
- Generates NO from room air
- Allows NO delivery via a breathing circuit and standard CPAP face mask, both at clinical and home setting

Subject Disposition and Baseline Demographics



- Mean Age: 62.1 yrs (SD 15; range 22-82)
- 75% female

Baseline conditions	N
Cystic fibrosis	2
Primary ciliary dyskinesia	1
Bronchiectasis	7
Chronic obstructive pulmonary disease	1

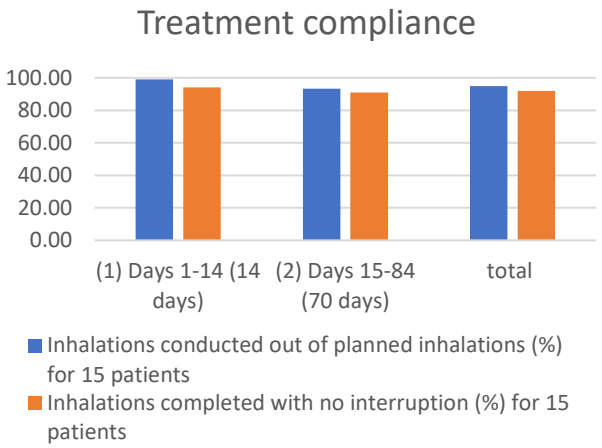
NTM species as per medical history	N
Mycobacterium abscessus	4
Mycobacterium avium	9
Other *Mycobacterium (simiae, triplex)*	2
Total	15

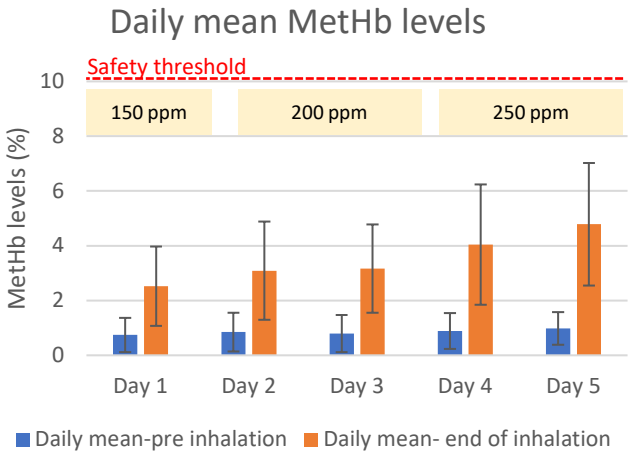
High Compliance Rate with No SAEs that led to Discontinuation of Treatment

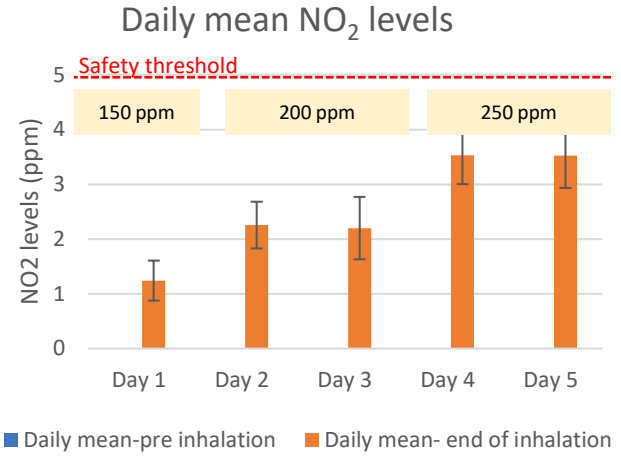
Total N (Intent-to-treat Population) = 15	N	%
Any AE	15	100
Any AE related to study treatment *	9	60.0
Any AE related to study treatment classified as Severe *	0	0
Any Serious Adverse Event (SAE)	6	40.0
Any SAE occurring during treatment period	3	20
Any SAE related to study treatment *	1	6.7

*including possibly, probably and definitely related

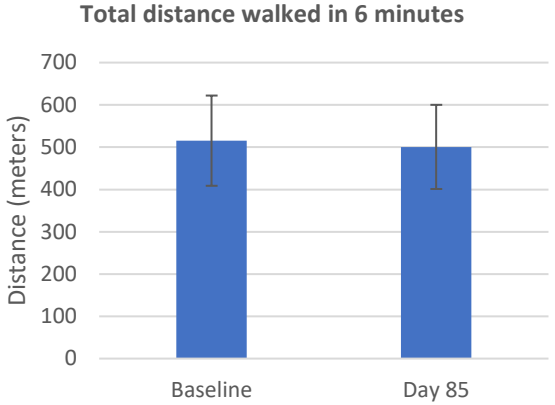
- Related AEs included: Hemoptysis (SAE), vomiting, balance difficulty, dry mouth, fatigue, headache, paresthesia and hypotension
- Methemoglobin and NO_2 elevation are both associated with iNO exposure, therefore these two parameters were monitored during treatments in hospitalization period, with safety thresholds set to 10% and 5 ppm respectively

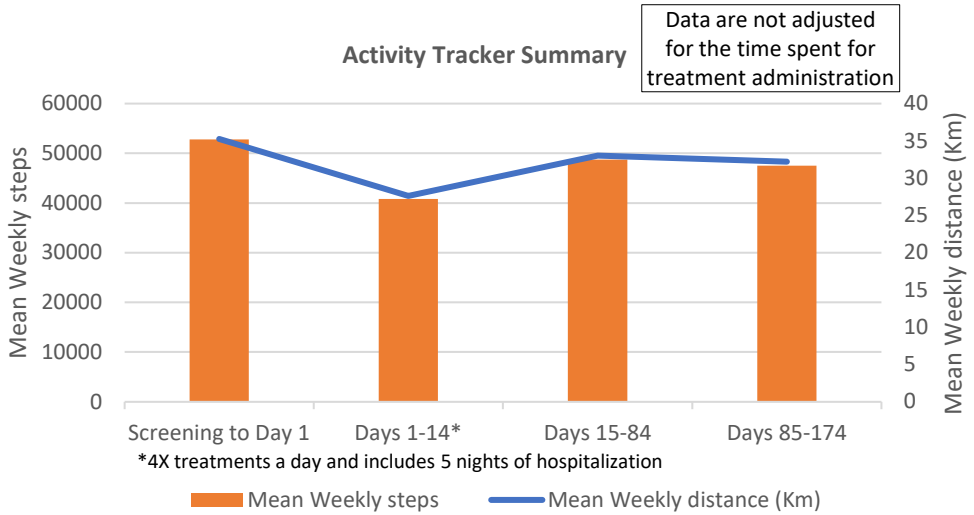


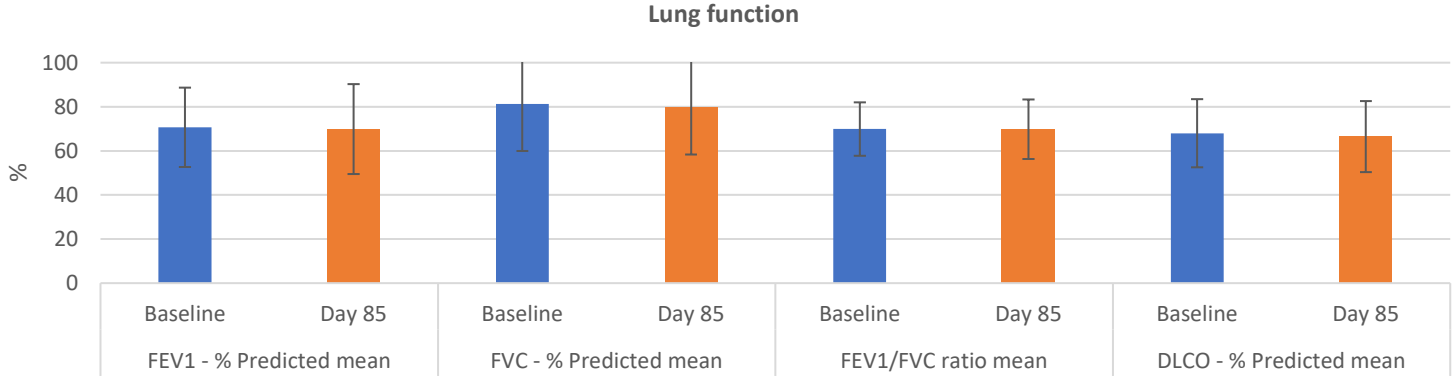




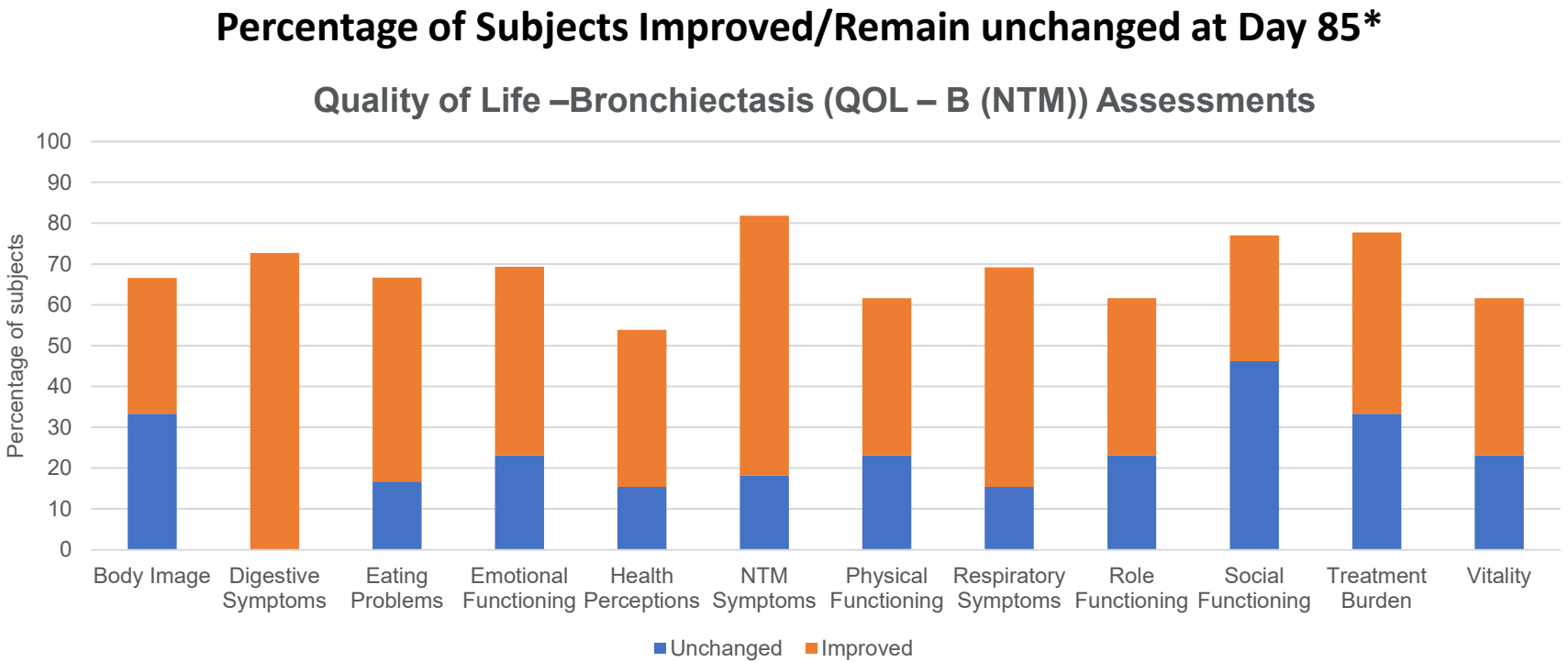
Comparable Lung Function Throughout Treatment







Improvement in patient reported outcomes



*The denominator for the percentages is the number of subjects with both a non-missing baseline value and a non-missing value at Study Day 85.

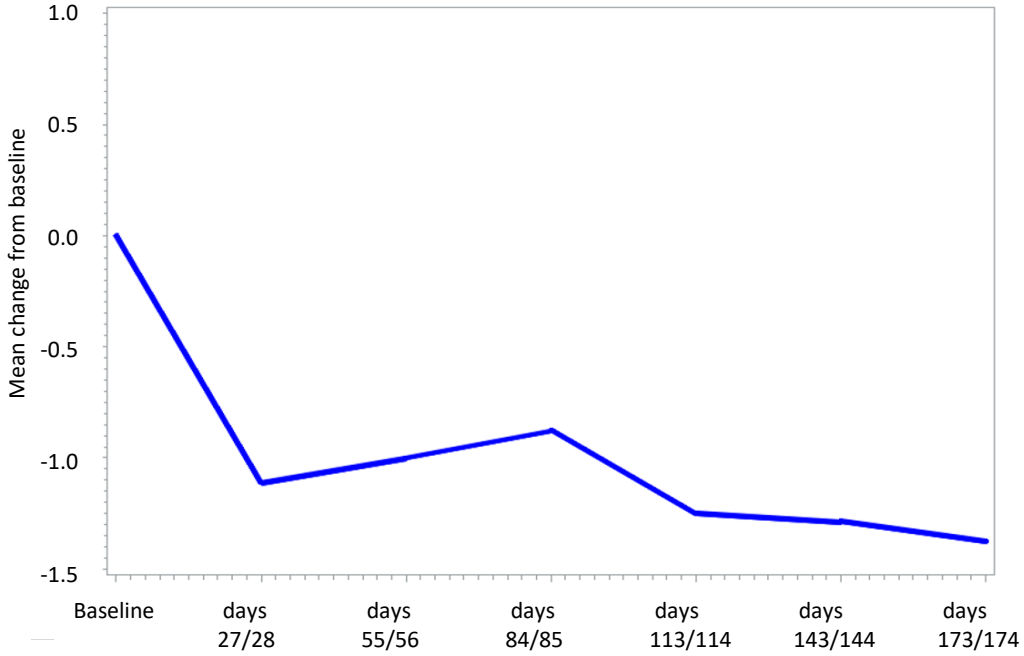
Reduction in Microbial Load

- The changes reach statistical significance at study day 113/114, and a trend in favor of decrease in mycobacterial load was observed at the other time points.
- One subject achieved culture conversion with 3 consecutive negative cultures
- One subject was positive at baseline and tested only negative after NO treatments began, but was unable to produce three sputum samples throughout the 24 weeks of the study

Semiquantitative scale for mycobacterial culture growth at baseline

Score		N	%
0	no growth in broth/solid medium	3	23.08
1	broth medium growth only	4	30.77
2	< 50 countable colonies on solid medium	0	0
3	1+ growth on solid medium	2	15.38
4	2+ growth on solid medium	1	7.69
5	3+ growth on solid medium	0	0
6	4+ growth on solid medium	3	23.08
All		13	100.00

Mean change from baseline on the semiquantitative scale for mycobacterial culture growth



Discussion

- Intermittent high dose NO treatment was safe and well-tolerated in both the hospital and home settings
  - No treatment related SAEs leading to study discontinuation
  - All patients demonstrated ability to self-administer therapies at home using the easy-to-operate and compact novel NO generator – LungFit GO™
- Respiratory function and physical function were maintained during treatment and follow-up
- Improvement seen in the majority of QOL-B (NTM) domains
- Trends in the reduction of microbial load were noted