TREATMENT OF COVID-19 WITH INHALED NITRIC OXIDE USING A NOVEL NITRIC OXIDE GENERATOR

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- COVID-19 caused over 6.6 million hospitalizations and over 5 million deaths worldwide as of November 2021.
- While new variants of COVID-19 emerge continuously, posing a challenge for immunization strategies, treatment options of COVID-19 remain limited, highlighting the need for innovative solutions.
- Inhaled Nitric Oxide (iNO) has proven antimicrobial, anti-inflammatory and vasodilator properties.
- iNO was previously tested for various lower respiratory infections (LRI), where intermittent administration at 150-250 ppm, was well tolerated and safe, and demonstrated positive efficacy trends.

This poster summarizes an ongoing, randomized, open label, multi-center pilot study, to evaluate the safety and efficacy of iNO for the treatment of hospitalized adults with COVID-19 or other viral LRI.

STUDY DESIGN AND STUDY POPULATION

- 40 subjects hospitalized for COVID-19 or viral pneumonia [n=40 (COVID-19, n=39; viral pneumonia, n=1)] , were randomized 1:1 to either iNO [treated with 150 ppm iNO for 40 minutes, 4 times daily, up to 7 days in addition to standard supportive treatment (SST)], or control [receiving SST alone].
- iNO was delivered by LungFit™, an innovative portable device under development (Beyond Air, NY, USA) that generates NO from room air.
- Enrolled patients are followed for a 180-day follow-up period.
- Study endpoints include safety and time on oxygen supplementation, among others.
- Intent To Treat (ITT) population included 35 subjects with 16 in the iNO group and 19 in the SST

Control group

Standard Supportive Treatment (SST)

Treatment group

iNO at 150 ppm delivered with the LungFit™ device
40 minutes 4 times daily for up to 7 days
+
SST

Demographics		SST	LungFit- 150 ppm NO+SST	All
Age (years)	N	19	16	35
	Mean	53.2	50.5	51.9
	Std	11.9	16.1	13.8
	Min	20.0	23.0	20.0
	Max	71.0	78.0	78.0
Gender	Male [n (%)]	17 (89.5)	9 (56.3)	26 (74.3)
	Female [n (%)]	2 (10.5)	7 (43.8)	9 (25.7)

Baseline characteristics	SST	LungFit- 150 ppm NO+SST
o_2 required at baseline (%)	68.4	62.5
Cardiac disorders (%)	10.5	12.5
Metabolic disorders(%)	47.4	43.8
Resp. disorders (%)	21.1	12.5
Vascular disorders (%)	21.1	50.0

ADVERSE EVENTS AND TREATMENT SAFTEY PARAMTERES

<u>iNO treatment was well tolerated overall</u>

<u>Adverse events</u>

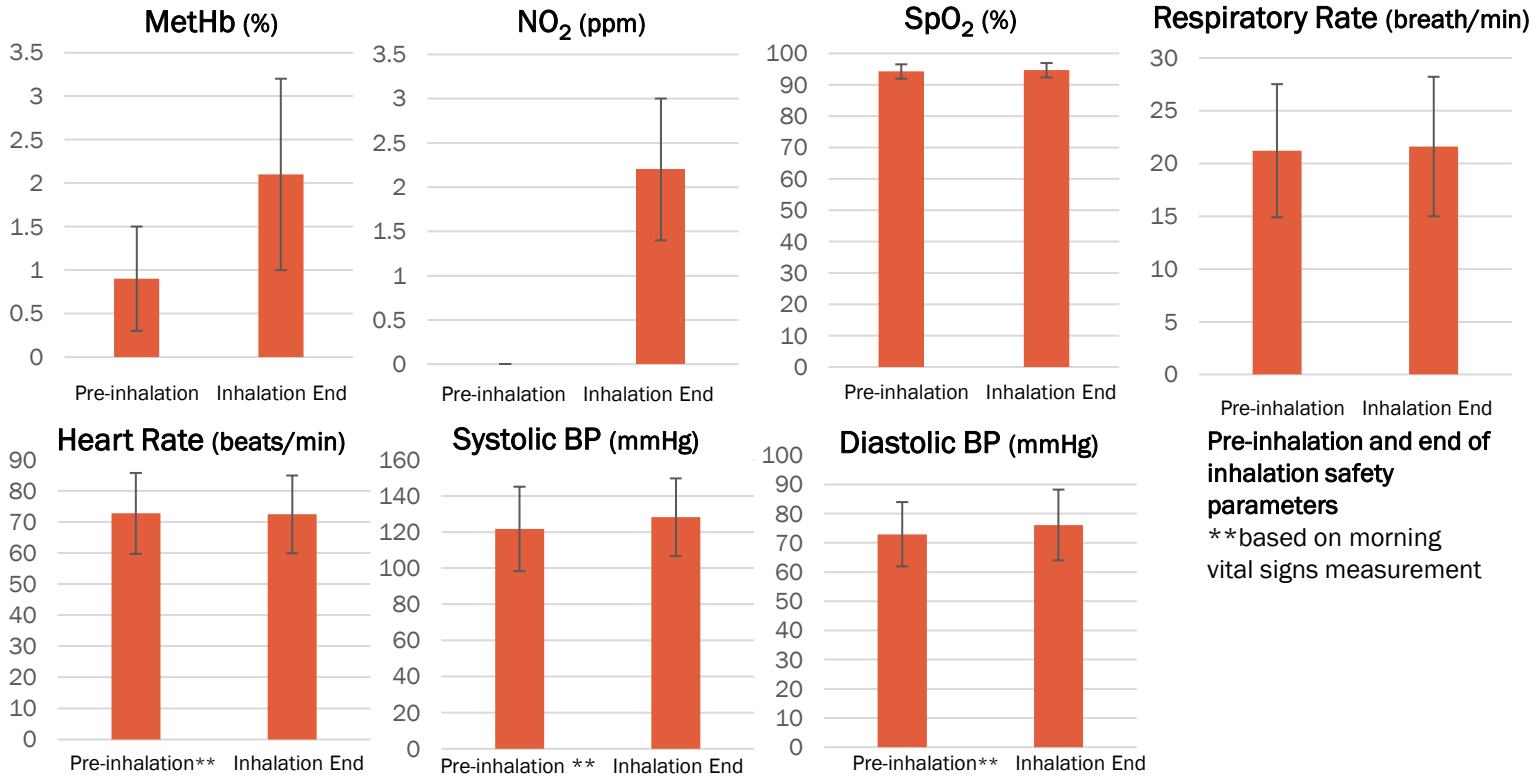
- A total of 34 AEs were reported in 17 subjects
- **None of the AEs assessed by the investigators were treatment related**
- Two SAEs were reported in iNO + SST group; both were related to underlying condition and were determined to be unrelated to study drug/device.

<u>Other safety related items:</u>

- MetHb levels were below 6.8 % at all times (safety threshold is 10%)
- NO_2 levels were below 4.4 ppm at all timepoints (safety threshold is 5 ppm)
- No clinically significant differences were noted in respiratory rate, heart rate or blood pressure when compared between pre and end of inhalation.
- No treatment was discontinued due to discomfort or AE

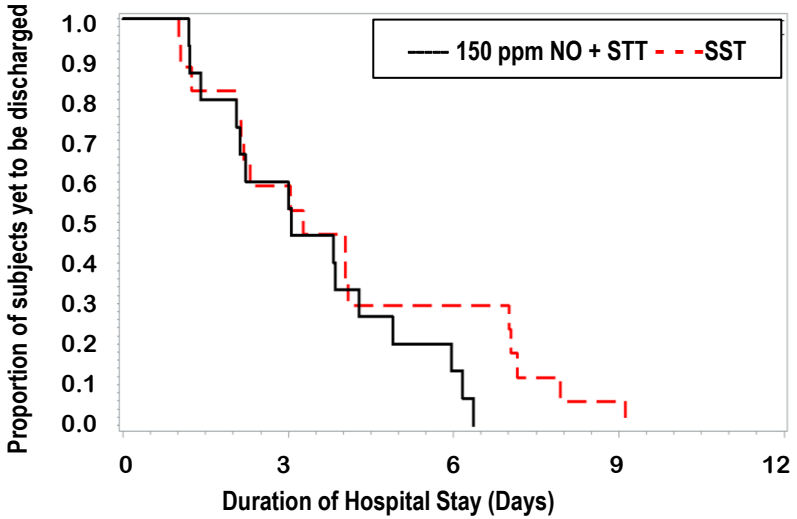
	SST				LungFit- 150 ppm NO+SST			
	Up to discharge:		Post-Discharge		Up to discharge:		Post-Discharge	
	n	%	n	%	n	%	n	%
Any AE	5	26.3	4	21.1	8	50.0	5	31.3
Any AE Drug/Device-Related*	0	0	0	0	0	0	0	0
Any SAE	0	0	0	0	1	6.3	1	6.3
Any SAE Drug/Device-Related*	0	0	0	0	0	0	0	0
Any AE Classified as Moderate or Severe	3	15.8	0	0	3	18.8	0	0
Any AE Drug/Device-Related Classified as Moderate or Severe*	0	0	0	0	0	0	0	0

*including possibly and probably related

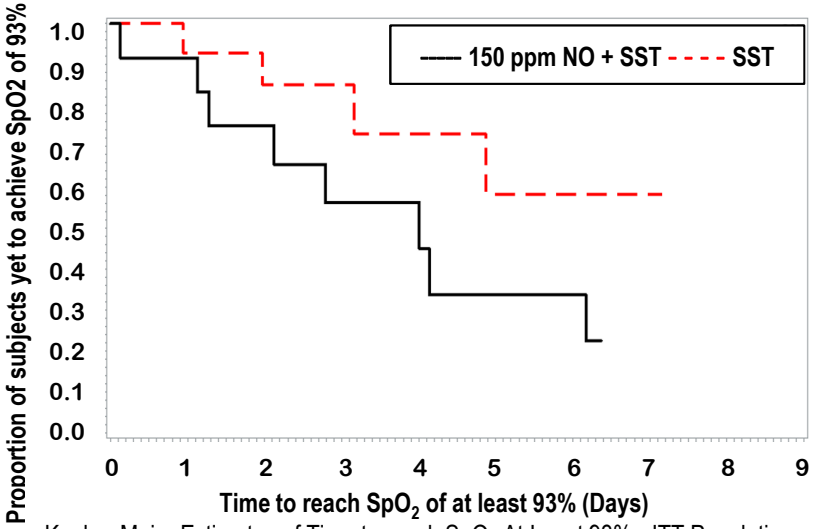


Pre-inhalation and end of inhalation safety parameters
**based on morning vital signs measurement

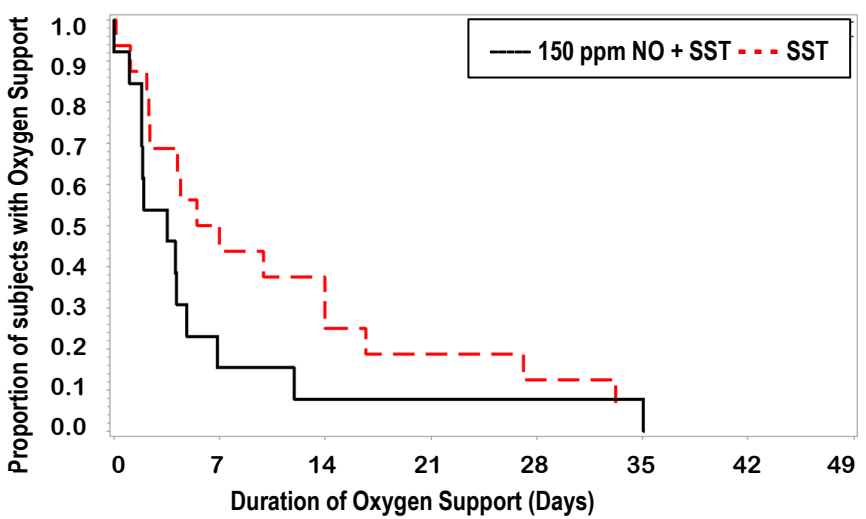
EFFICACY RESULTS AND CONCLUSION



Kaplan-Meier Estimates of Time of Hospital Stay - ITT Population
P-value=0.1991 based on Cox proportional hazard model



Kaplan-Meier Estimates of Time to reach SpO_2 At Least 93% - ITT Population
P-value=0.0490 based on Cox proportional hazard model
Kaplan-Meier curve was truncated at 7 days to reflect clinically meaningful assessment of SpO_2 ; Only subjects for which saturation dropped below 93% during hospitalization were included



Kaplan-Meier Estimates of Time duration of Oxygen Support - ITT Population
P-value=0.0339 based on Cox proportional hazard model
Kaplan-Meier curve was truncated at 35 days to reflect clinically meaningful assessment of oxygen support; Duration of oxygen support includes the need for oxygen during treatment at home

SST N = 19	150 ppm NO + SST N = 16	Comparison Hazard Ratio, 150 NO + SST vs SST
Median (Days)	Median (Days)	HR p-value [95% CI]
3.0	3.0	1.8 0.1991 [0.7,4.4]

- Trend of shortening of Length of Stay by a factor of **1.8** in favor of the iNO treatment group

SST N = 15	150 ppm NO + SST N = 12	Comparison Hazard Ratio, 150 NO + SST vs SST
Median (Days)	Median (Days)	HR p-value [95% CI]
NA	4.0	5.4 0.0490 [1.0, 28.8]

- Of subjects with unstable saturation during hospitalization, **66.7%** of iNO treatment group reached stable saturation of ≥93% during hospital stay vs. **26.7%** in the SST group

SST N = 19	150 ppm NO + SST N = 16	Comparison Hazard Ratio, 150 NO + SST vs SST
Median (Days)	Median (Days)	HR p-value [95% CI]
6.3	3.6	2.8 0.0339 [1.1, 7.1]

- Duration of oxygen support including home oxygen support **was significantly shorter** for iNO-treated subjects

iNO Treatment in patients with COVID-19 and other viral pneumonia was overall well tolerated, safe, with improved efficacy parameters in the iNO treatment group as compared to the SST control group