Characterization of Inhaled Nitric Oxide (iNO) for the treatment of Viral Community Acquired Pneumonia (CAP)

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Background

- COVID-19 infections are over 600 million cases and over 6.5 million deaths worldwide, as of September 2022
- Continuously emerging COVID-19 variants pose a serious challenge for immunization strategies. This highlights the need for innovative treatment solutions.
- Inhaled Nitric Oxide (iNO) has proven antimicrobial, anti-inflammatory, and vasodilator properties
- Previous iNO therapy at 150-250 ppm for various Lower Respiratory Tract Infections (LRTI) was shown to be well tolerated and safe and demonstrated positive efficacy trends.

Methods

Study Design:

- Randomized, open label, multi-center pilot study
- Evaluate the safety and efficacy of iNO for the treatment of hospitalized adults with COVID-19 or other viral LRTI

Treatment group:
iNO at 150 ppm delivered with the LungFit™ PRO device, 40 minutes, 4 times daily for up to 7 days

Control group:
Standard Supportive Treatment (SST)

- Enrolled patients are followed for up to 180-day follow-up period
- Study endpoints include safety and time on oxygen supplementation, among others

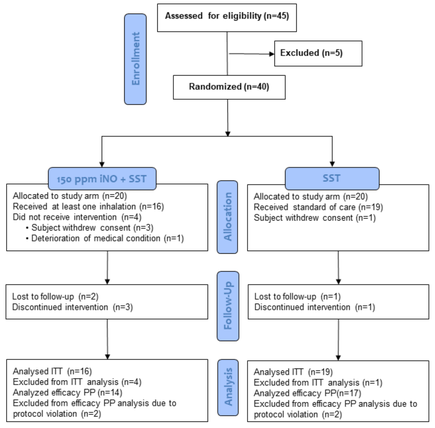
Study Device:

- iNO was delivered by LungFit™ PRO, an innovative portable device (Beyond Air®, NY, USA) that generates NO from room air

Results

Study Population

40 subjects hospitalized for viral pneumonia, incl. COVID-19 were randomized 1:1 to receive iNO at 150 ppm vs. SST.
Intent To Treat (ITT) population included 35 subjects with 16 in the iNO group and 19 in the SST



Demographics

Demographics		150 ppm NO + SST	SST	All
Number of patients	N (%)	16 (45.7)	19 (54.3)	35 (100)
Age (years)	Mean ,std	50.5, 16.1	53.2, 11.9	51.9, 13.8
Gender	Male, n (%)	9 (56.3)	17 (89.5)	26 (74.3)
	Female, n (%)	7 (43.8)	2 (10.5)	9 (25.7)
BMI (kg/m^2)	Mean, std	28.8, 5.2	29.7, 2.5	29.3, 3.9
Viral infection	SARS-CoV2, n (%)	15 (93.8)	19 (100)	34 (97.1)
	Other, n (%)	1 (3.6)	0 (0)	1 (2.9)

Baseline Characteristics

Medical History		150 ppm NO + SST	SST
Chronic Medication, n (%)		10 (62.5)	11 (57.9)
Tobacco Use n (%)	No	12 (75.0)	17 (89.5)
	Former	2 (12.0)	1 (5.3)
	Current	2 (12.0)	1 (5.3)
Cardiac disorders, n (%)		2 (12.5)	2 (10.5)
Metabolic disorders, n (%)		7 (43.8)	9 (47.4)
Respiratory disorders, n (%)		2 (12.5)	4 (21.1)
Vascular disorders, n (%)		8 (50.0)	4 (21.1)

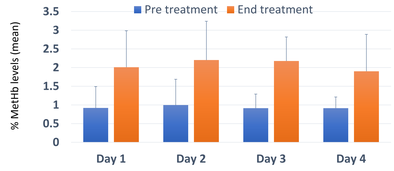
Disease-Related Baseline Characteristics		150 ppm NO + SST	SST
O2 required at baseline, n (%)	No	6 (37.5)	6 (31.6)
	Yes	10 (62.5)	13 (68.4)
COVID-related drugs, n (%)	Remdesivir	7 (43.8)	6 (31.6)
	Dexamethasone	11 (68.8)	14 (73.7)
	Baricitinib	1 (6.0)	1 (5.3)
	Dexacort forte	0 (0)	2 (10.5)

Safety

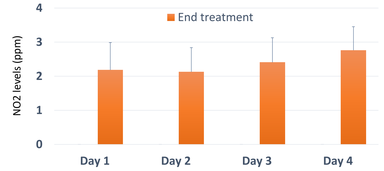
Adverse Events	150 ppm NO + SST		SST	
	n	%	n	%
Any AE	9	56.3	8	42.1
Any AE Classified as Moderate or Severe	4	25.0	3	15.8
Any AE Drug/Device-Related*	0	0	0	0
Any AE leading to early treatment termination**	2	12.5	1	5.3
Any SAE	2	12.5	0	0
Any SAE Drug/Device-Related*	0	0	0	0

**Including 'possibly related'*
*** AEs leading to early treatment termination:*
SST group - 1 subject suffered from hypoxemia
NO group- 1 subject experienced bradycardia (pre-existing);
1 subject experienced hypoxemia (unrelated to study treatment)
AE – Adverse Event; SAE – Serious Adverse Event

Mean MetHb levels (%) at pre- and end of inhalation

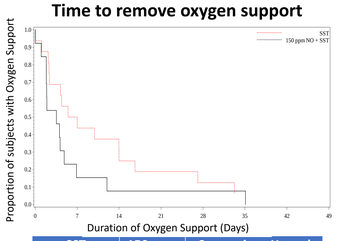


Mean NO_2 levels (ppm) at end of inhalation



Efficacy – Intent to Treat (ITT)

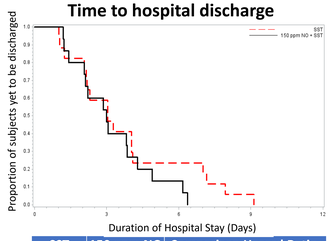
Time to remove oxygen support



SST N = 19	150 ppm NO + SST N = 16	Comparison Hazard Ratio, 150 NO + SST vs SST
Median	Median	HR[1] ,p-value[2] ,[95% CI]
6.3	3.6	2.8 , 0.034, [1.1, 7.1]

[1]With adjustment to gender and age group.
[2]P-value derived from Cox proportional hazard model.

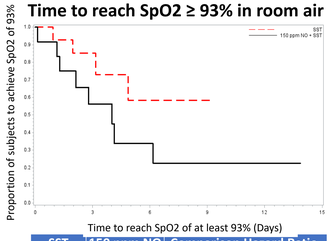
Time to hospital discharge



SST N = 19	150 ppm NO + SST N = 16	Comparison Hazard Ratio, 150 NO + SST vs SST
Median	Median	HR[1] ,p-value[2] ,[95% CI]
3.0	3.0	1.7, 0.239, [0.7, 4.2]

[1]With adjustment to gender and age group.
[2]P-value derived from Cox proportional hazard model.

Time to reach SpO2 ≥ 93% in room air

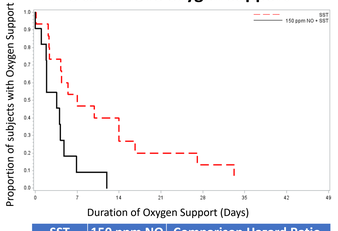


SST N = 15	150 ppm NO + SST N = 13	Comparison Hazard Ratio, 150 NO + SST vs SST
	Median	HR[1] ,p-value[2] ,[95% CI]
NA[3]	4.0	5.4, 0.049, [1.0, 28.8]

Only subjects with low saturation at entry are included.
[1]With adjustment to age group.
[2]P-value derived from Cox proportional hazard model.
[3]Not calculable.

Efficacy – Per Protocol (PP)

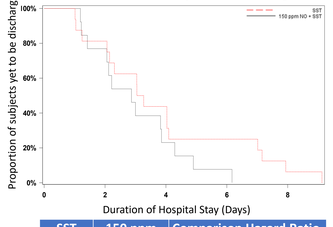
Time to remove oxygen support



SST N = 17	150 ppm NO + SST N = 14	Comparison Hazard Ratio, 150 NO + SST vs SST
Median	Median	HR[1] ,p-value[2] ,[95% CI]
7.0	3.6	6.3 , 0.0035, [1.8, 21.8]

[1]With adjustment to gender and age group.
[2]P-value derived from Chi-square.

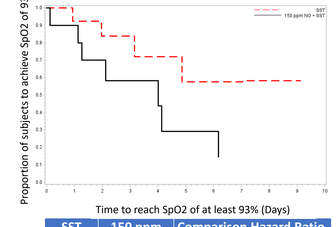
Time to hospital discharge



SST N = 17	150 ppm NO + SST N = 14	Comparison Hazard Ratio, 150 NO + SST vs SST
Median	Median	HR[1] ,p-value[2] ,[95% CI]
3.2	2.9	1.9 , 0.203, [0.7, 4.9]

[1]With adjustment to gender and age group.
[2]P-value derived from Chi-square.

Time to reach SpO2 ≥ 93% in room air



SST N = 14	150 ppm NO + SST N = 10	Comparison Hazard Ratio, 150 NO + SST vs SST
	Median	HR[1] ,p-value[2] ,[95% CI]
NA[3]	4.0	4.9 , 0.067, [0.9, 27.3]

Only subjects with low saturation at entry are included.
[1]With adjustment to age group.
[2]P-value derived from Chi-square.
[3]Not calculable.

CRP	150 ppm NO + SST	SST
Change from Baseline, Mean, std	-6.1, 7.2	-3.9, 3.9

Summary

1) iNO treatment delivered with LungFit PRO in patients with viral community-acquired pneumonia (97% COVID-19) was safe and well tolerated
2) There were indications of improved efficacy on multiple parameters in the iNO treatment group vs. the SST control group with a significant reduction in the duration of oxygen support
3) A larger study in this patient population is warranted to confirm these results