A Phase II, Randomized, Sham-Controlled Dose-Finding Study of the RD-X19 Treatment Device in Individuals with Mild-to-Moderate COVID-19

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Presentation Outline

- Preclinical identification of 425 nm light as a variant-agnostic countermeasure against SARS-CoV-2
  - ✓Stops cell entry
  - ✓Slows viral replication

- Clinical evaluations of the RD-X19 as a therapeutic device against COVID-19
  - ✓Accelerated symptom resolution in patients age 40+ with mild COVID-19
  - ✓No disruption of oral microbiome diversity
  - ✓Decreased nasopharyngeal viral load

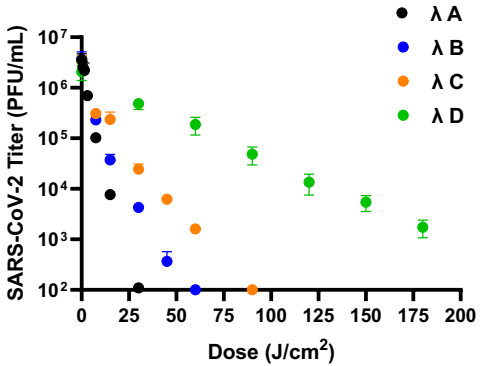
EmitBio Translational Science Paradigm

High Efficiency LEDs

Engineering

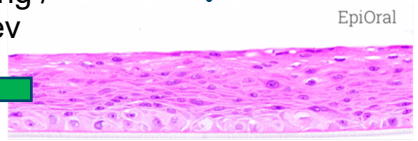
BLUs enable precise in vitro controldensity of color and energy

BSL2 / BSL3



Dose and wavelength dependent biological activity

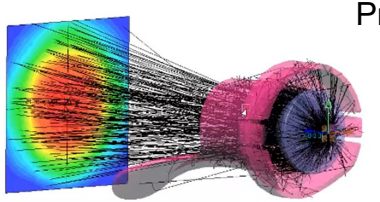
Preclinical Performance Testing



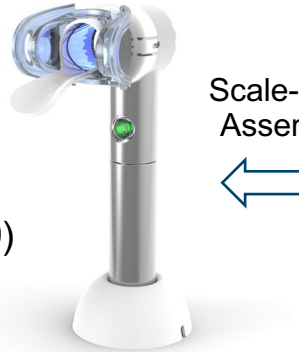
3D Human Tissue Model, Proprietary Virus Infected Tissue Protocols

Established Go-No Go Criteria

Prototyping / Adv Dev



Scale-Up & Assembly



Real World, Clinical Solutions (*e.g.* RD-X19)

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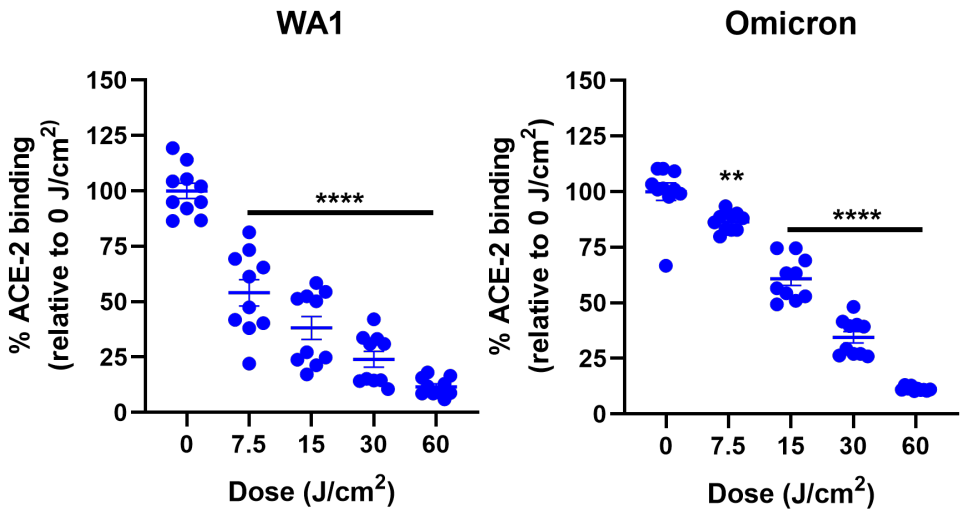
425 nm light inhibits SARS-CoV-2 spike trimer binding to ACE-2 *in vitro*

- Illuminated spike trimers and assessed binding to ACE-2
- Dose-dependent reduction in spike trimers binding to ACE-2 *in vitro*
- **Reductions consistent across multiple variants, including those heavily mutated in spike**



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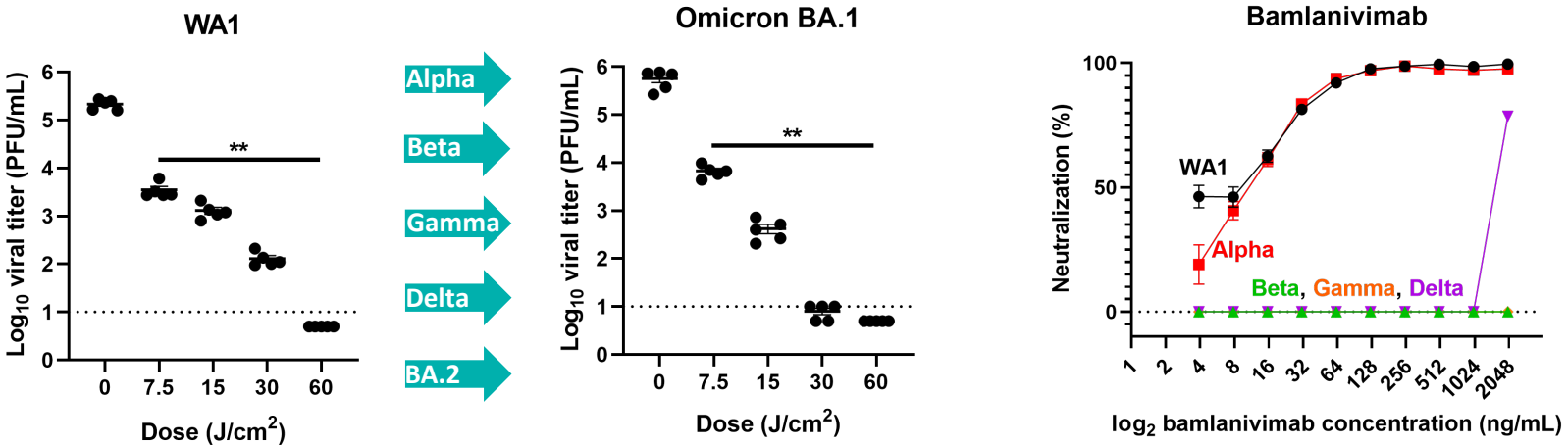
425 nm light inactivates cell-free SARS-CoV-2

- 425 nm light demonstrates consistent inactivation of SARS-CoV-2 variants regardless of mutations
- Monoclonal antibodies (*e.g.* bamlanivimab) have reduced neutralization against Beta, Gamma, or Delta variants



1. Stasko N, Cockrell A, Kocher J, et al. A randomized, controlled, feasibility study of RD-X19 in subjects with mild-to-moderate COVID-19 in the outpatient setting. Clin Trans Sci. 2022;15:1291-1303.

2. Kocher J, Arwood L, Roberts RC, Henson I, Annas A, Emerson D, Stasko N, Fulcher ML, Brotton M, Randell SH, Cockrell AS. Visible blue light inactivates SARS-CoV-2 variants and inhibits Delta replication in differentiated human airway epithelia. bioRxiv. 2022.01.25.477616; doi: https://doi.org/10.1101/2022.01.25.277616

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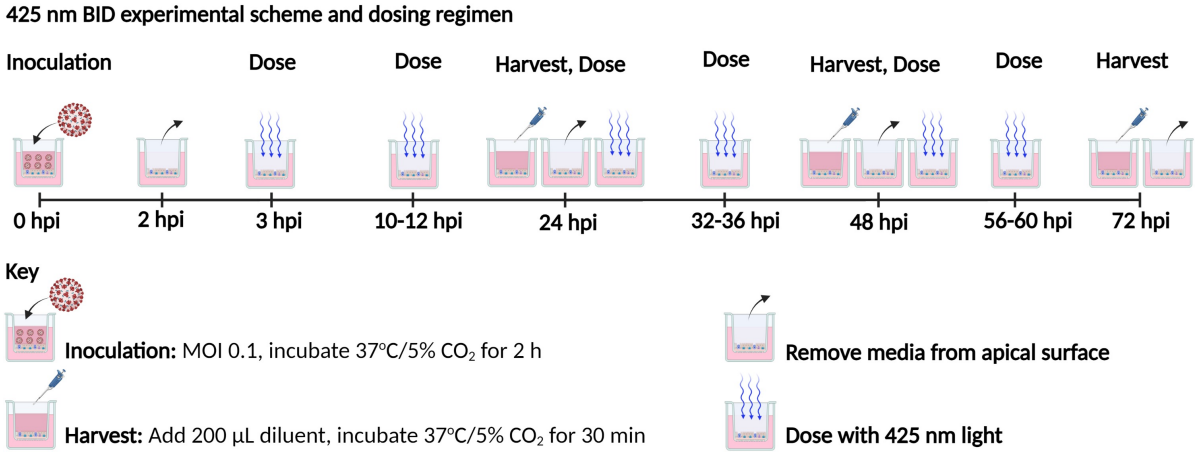
425 nm light reduces viral titers in a well-differentiated model of the human airway

- Primary tracheobronchial cells cultured at the air-liquid interface differentiate and mimic airway *in vivo*
  - Cilia beating
  - Mucus production
- Model used for preclinical testing of:
  - Remdesivir (Veklury)
  - Nirmatrelvir/ritonavir (Paxlovid)
  - Molnupiravir (Lagevrio)



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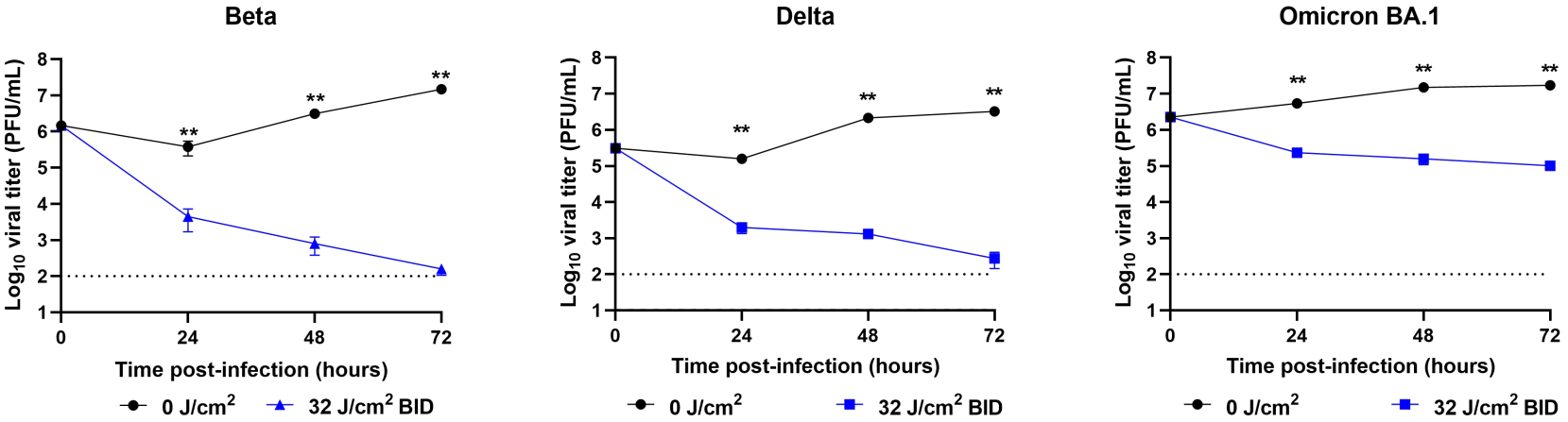
425 nm light reduces SARS-CoV-2 titers in a well-differentiated model of the human airway at non-cytotoxic doses



72 h (3 BID)	Beta	Delta	Omicron BA.1
Log_{10} reduction relative to 0 J/cm^2	5.1	4.2	2.2

~100% viability in time-matched, uninfected controls

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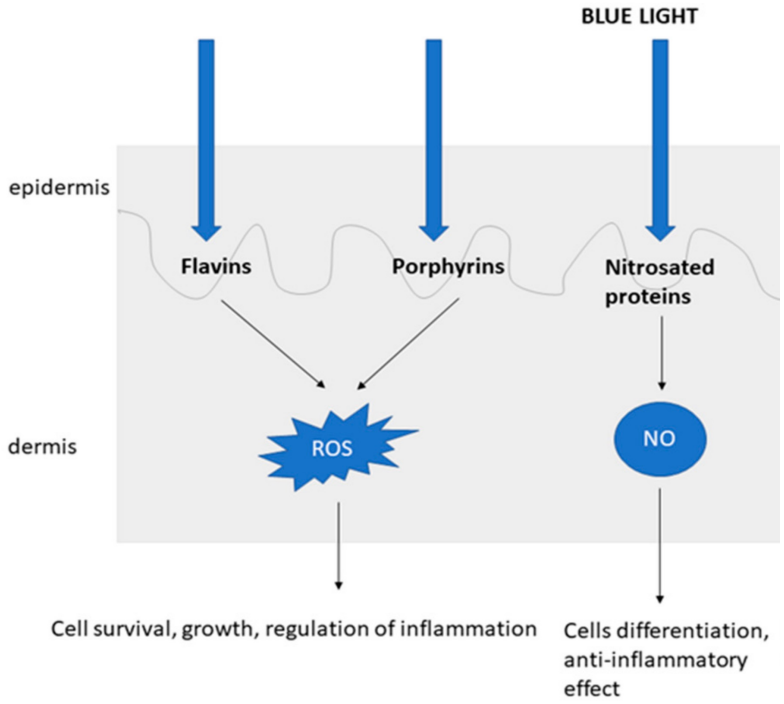
How does High Energy Visible Light Work?



- Generation of reactive oxygen species (ROS)[1]
- Release of nitric oxide (NO)
- Endoplasmic Reticulum (ER) stress and impaired RNA translation to protein[2]

[1] *Sadowska M, Narbutt J, Lesiak A. Blue Light in Dermatology. Life. 2021; 11(7):670.*
[2] *Nakato, R. et al. Regulation of the unfolded protein response via S-nitrosylation of sensors of endoplasmic reticulum stress. Sci. Rep.* ***5****, 14812; doi: 10.1038/srep14812 (2015).*

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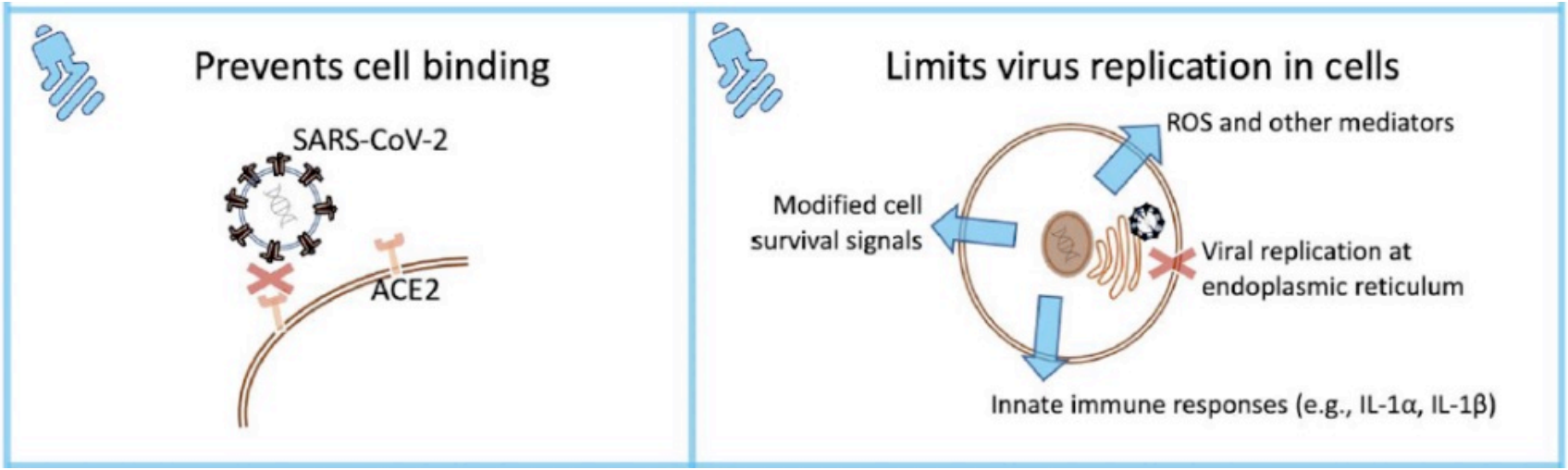
Antiviral Light Mechanism of Action



Stops Entry

Slows Replication

1. *Zupin L, Gratton R, Fontana F, et al. Blue photobiomodulation LED therapy impacts SARS-CoV-2 by limiting its replication in Vero cells. J. Biophotonics. 2021;14: e202000496.*
2. *Stasko N, Kocher JF, Annas A, et al. Visible blue light inhibits infection and replication of SARS-CoV-2 at doses that are well-tolerated by human respiratory tissue. Sci Rep. 2021 Oct 18;11(1):20595.*

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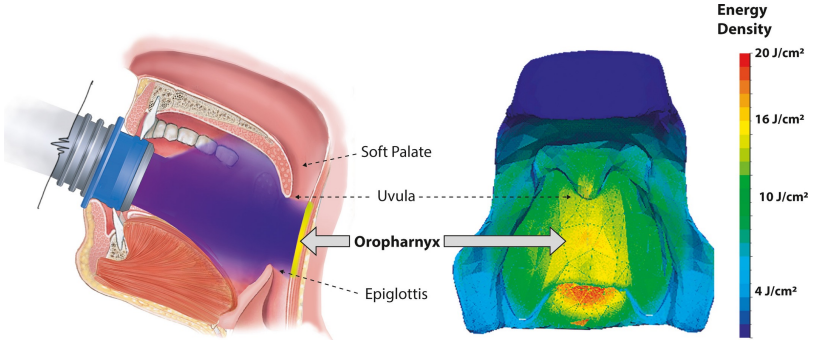
RD-X19 Therapeutic Device Overview

RD-X19: Handheld medical device that delivers 425 nm light to the oropharynx.[1]



Duration: 5-minute treatment, twice daily for 7 days.

Use: Intended for at-home use.

[1]*Stasko N, Cockrell A, Kocher J, et al. A randomized, controlled, feasibility study of RD-X19 in subjects with mild-to-moderate COVID-19 in the outpatient setting. Clin Trans Sci. 2022;15:1291-1303.*

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Clinical overview

Trial	Purpose		# Subjects	Completion Dates	Key Findings
1	**Safety**	P10	25	September 2020	RD-X19 is well-tolerated → no serious adverse events
2	**Early Feasibility**	P12	31	January 2021	RD-X19 treatment clinically meaningful → more rapid symptom resolution and viral load reduction
3	**Dose ranging**	P20	216	June 2022	Clear treatment benefit, symptom resolution established in target populations to be confirmed by pivotal trial (P30)
4	**Pivotal (ongoing)**	**P30**	**326**	***December 2023***	**With time to symptom resolution repeated from P20, FDA approval targeted in 2024**

Clinical Trial Overview EB-P20-01 (NCT04966013)

- **Population**
  - 216 adults, 18-65 years old with mild-to-moderate COVID-19
    - Full analysis set (FAS) or Safety Population: 176 adults in Cohort B treated with 32 J/cm^2
- **Co-primary efficacy endpoint**
  - Time to sustained resolution of all eight COVID-19 signs and symptoms in subjects with **mild-to-moderate COVID-19** **or** **mild COVID-19**
    - Mild (no lung involvement)
    - Moderate (lung involvement)
- **Other endpoints**
  - Microbiome impact
  - Mean change in nasopharyngeal viral load

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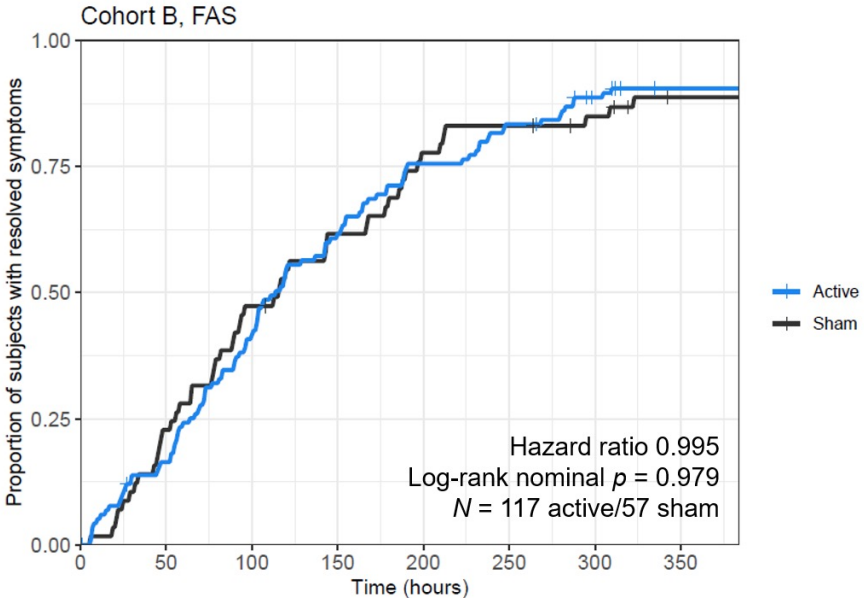
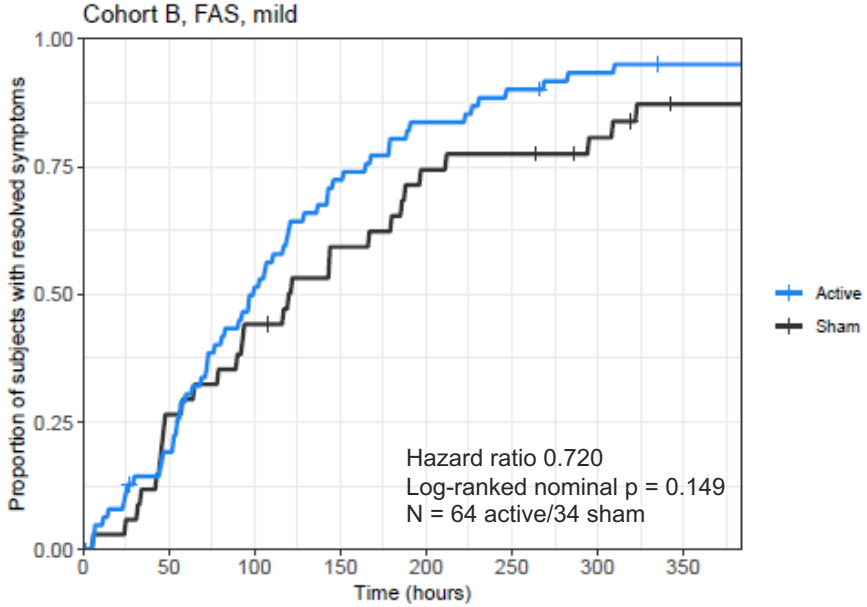
EB-P20-01 Co-Primary Endpoint (NCT04966013)



Cohort B ("Final Cohort") time to sustained resolution in the full analysis set (FAS) which includes subjects with **mild (no lung involvement) to moderate (lung involvement) disease** at baseline



Cohort B ("Final Cohort") time to sustained resolution in the full analysis set (FAS) which includes subjects with **mild (no lung involvement) disease** at baseline

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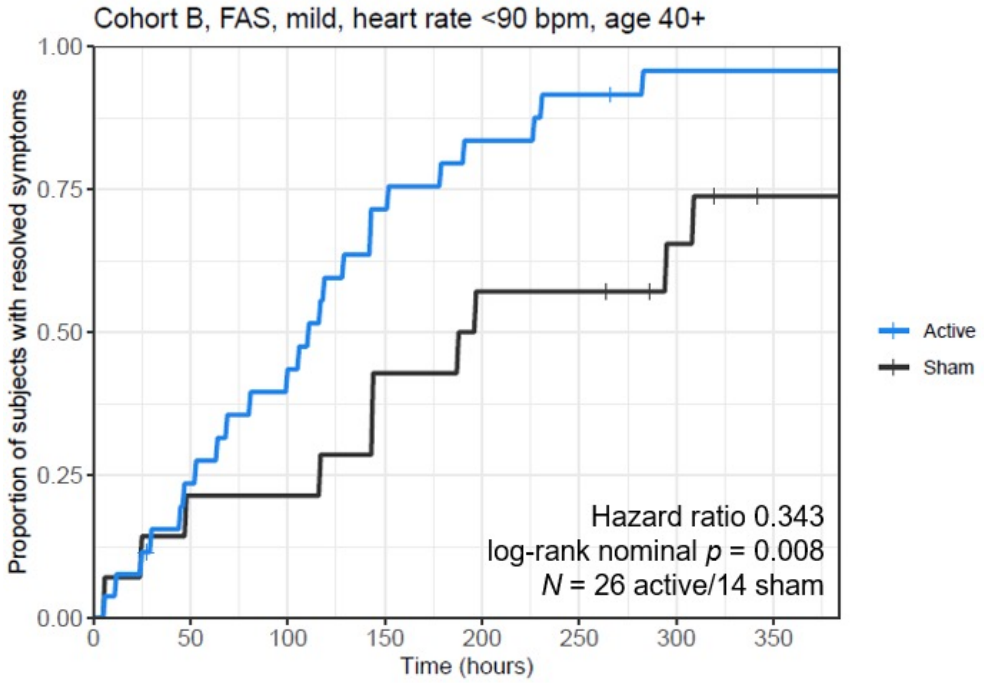
EB-P20-01 Post Hoc Endpoint Analysis (NCT04966013)

- **Post Hoc Analysis:** subset of subjects ages 40 years and older with mild COVID-19 and heart rate less than 90 beats per minute showed a **77-hour difference** in symptom resolution.
  - Median times to sustained symptom resolution: 111 hours for the RD-X19 active treatment vs. 188 hours for the sham treatment
- **Learnings:** Use this population for evaluation of the 32 J/cm^2 device in the pivotal trial.
- **Safety:** No serious treatment-related adverse events.



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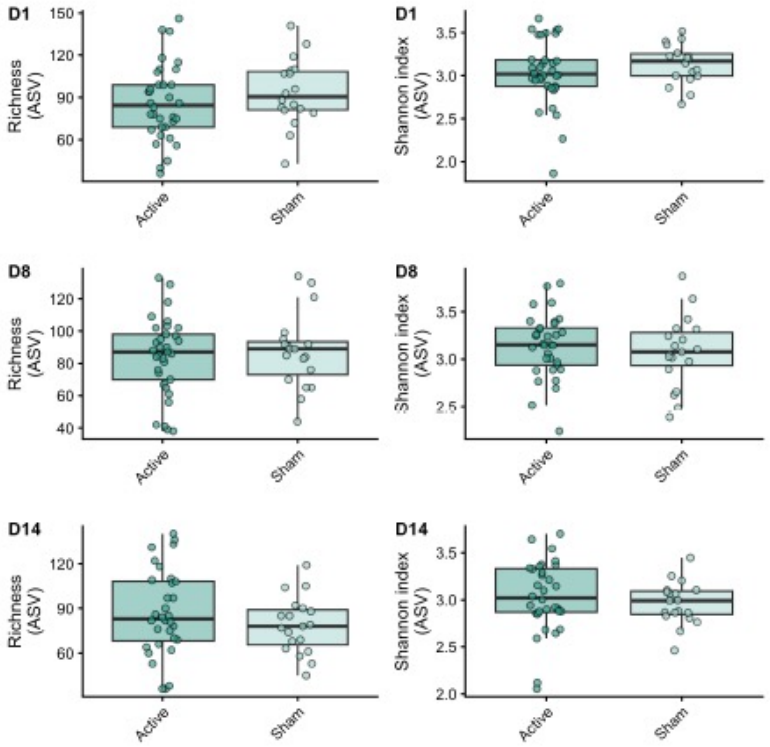
The RD-X19 does not appear to impact the α-diversity of the oral microbiome

- Salivary samples collected at Days 1, 8, and 14. Microbiome analyzed by 16S rRNA sequencing[1].
- Alpha diversity evaluated by sequence richness (left) and Shannon index (right).
- Similar results observed when accounting for disease, baseline severity, or age.



[1]FAS, all analyzable samples

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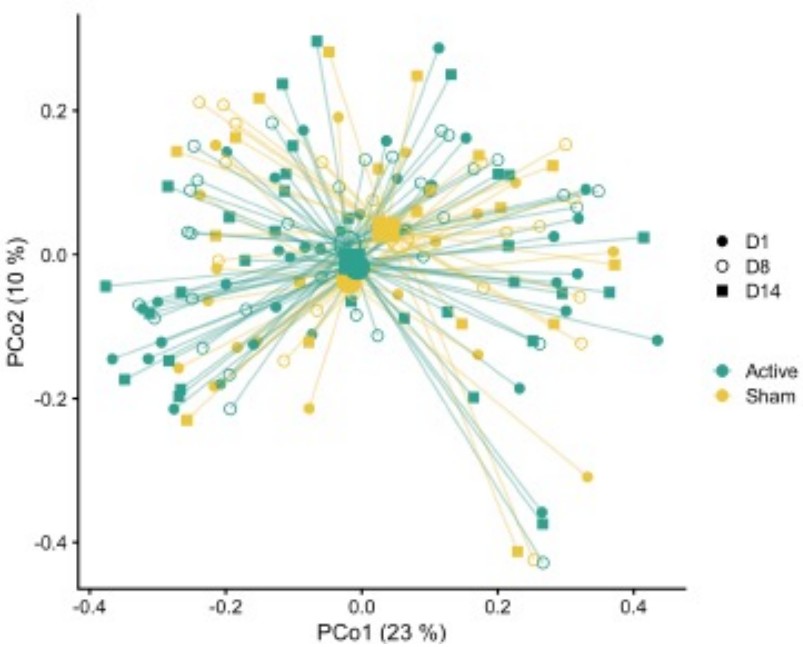
The RD-X19 does not appear to impact the β-diversity of the oral microbiome

- Salivary microbiome β-diversity analyzed via Bray-Curtis dissimilarity[1].
- Similar results observed when accounting for nasopharyngeal viral load.



[1]FAS, all analyzable samples

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RD-X19 reductions in nasopharyngeal viral load compared to other COVID-19 therapeutics

NP Viral Load via RT-qPCR	Mean Change Vs. Control Arm (log_{10})	Timepoint	Trial Number/ Reference
Sotrovimab	-0.23	Day 8	COMET-ICE (NCT04545060)
Bamlanivimab	-0.27	Day 11	BLAZE-1 (NCT04427501)
RD-X19 (FAS)	-0.56	Day 5	EB-P20-01 (NCT04966013)
Bamlanivimab + etesevimab	-0.57	Day 11	BLAZE-1 (NCT04427501)
Molnupiravir	-0.75	Day 5	MOVe-OUT (NCT04575597)
Nirmatrelvir/ritonavir (Paxlovid)	-0.87	Day 5	EPIC-HR (NCT04960202)

Clinical Trial Overview EB-P30-01 (NCT05817045)

Evaluation of the RD-X19 Treatment Device in Individuals with mild COVID-19

- **Population**
  - 40+ years of age meeting the FDA/NIH definition of mild COVID-19
    - Enrollment: 326 subjects across the US
- **Primary endpoint**
  - Time to sustained resolution of COVID-19 signs and symptoms without subsequent symptom recurrence or disease progression until the end of the study
- **Other endpoints**
  - Time to the first of two consecutive negative SARS-CoV-2 antigen tests without subsequent virological rebound

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Summary

- 425 nm light is a variant-agnostic approach against SARS-CoV-2.
- The RD-X19 does not disturb the richness or diversity of the oral microbiome.
- There is clinical evidence that the RD-X19 reduces the severity of COVID-19 symptoms.
- Further clinical investigation with the RD-X19 is ongoing.

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