

# The Gastrointestinal System and COVID-19

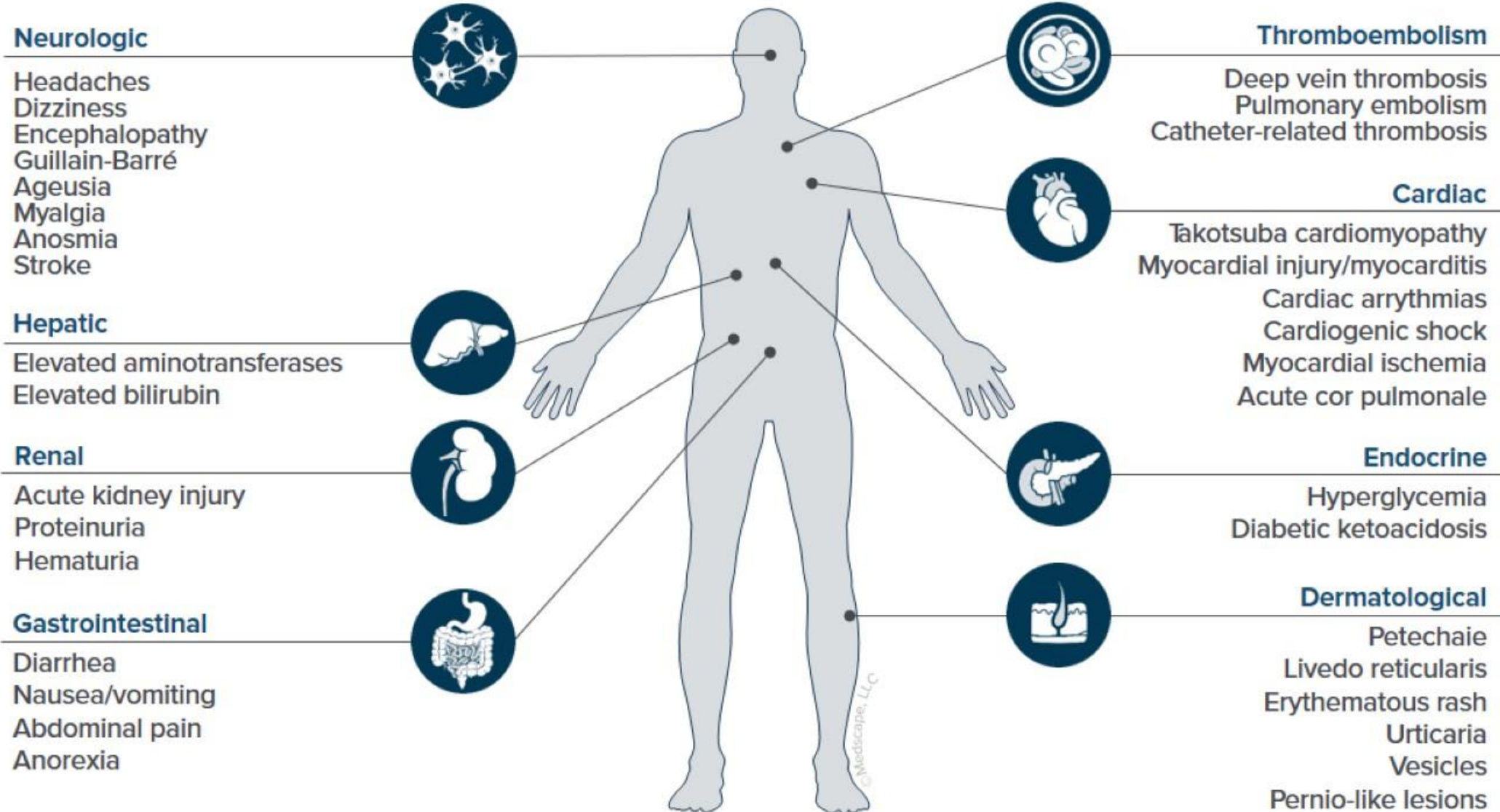
Evolving Our Understanding of the Gut  
as a Target for Therapeutics

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## FACULTY

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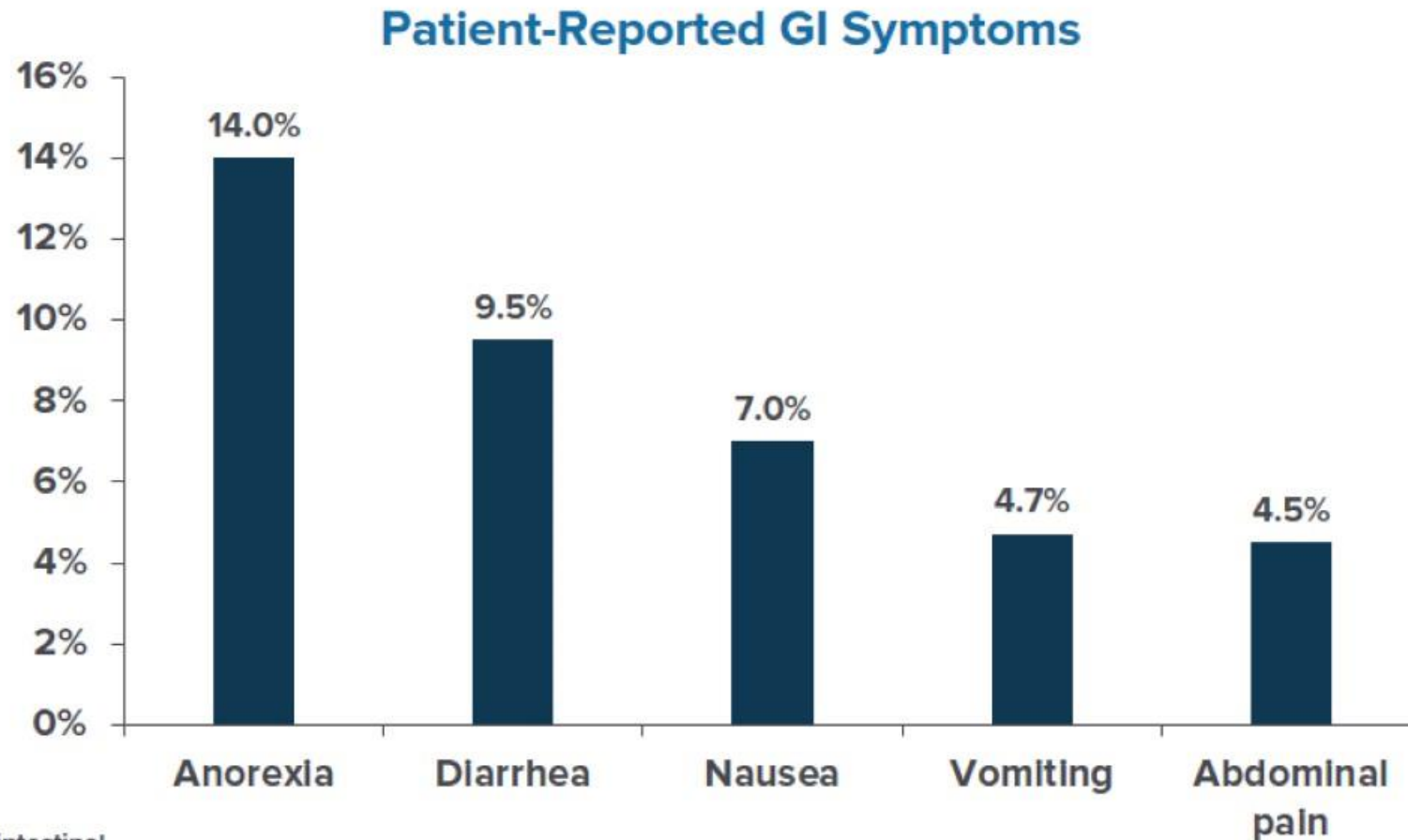
# Extrapulmonary Manifestations of COVID-19



# COVID-19 and the GI System

## Patient-Reported Symptoms

Meta-analysis of 212 studies involving 281,461 patients with COVID<sup>[a]</sup>



- The Omicron variant was the first COVID-19 variant noted to have more GI manifestations than prior variants<sup>[b]</sup>
- Children are more likely to experience (or at least to report) GI-related COVID symptoms<sup>[b]</sup>

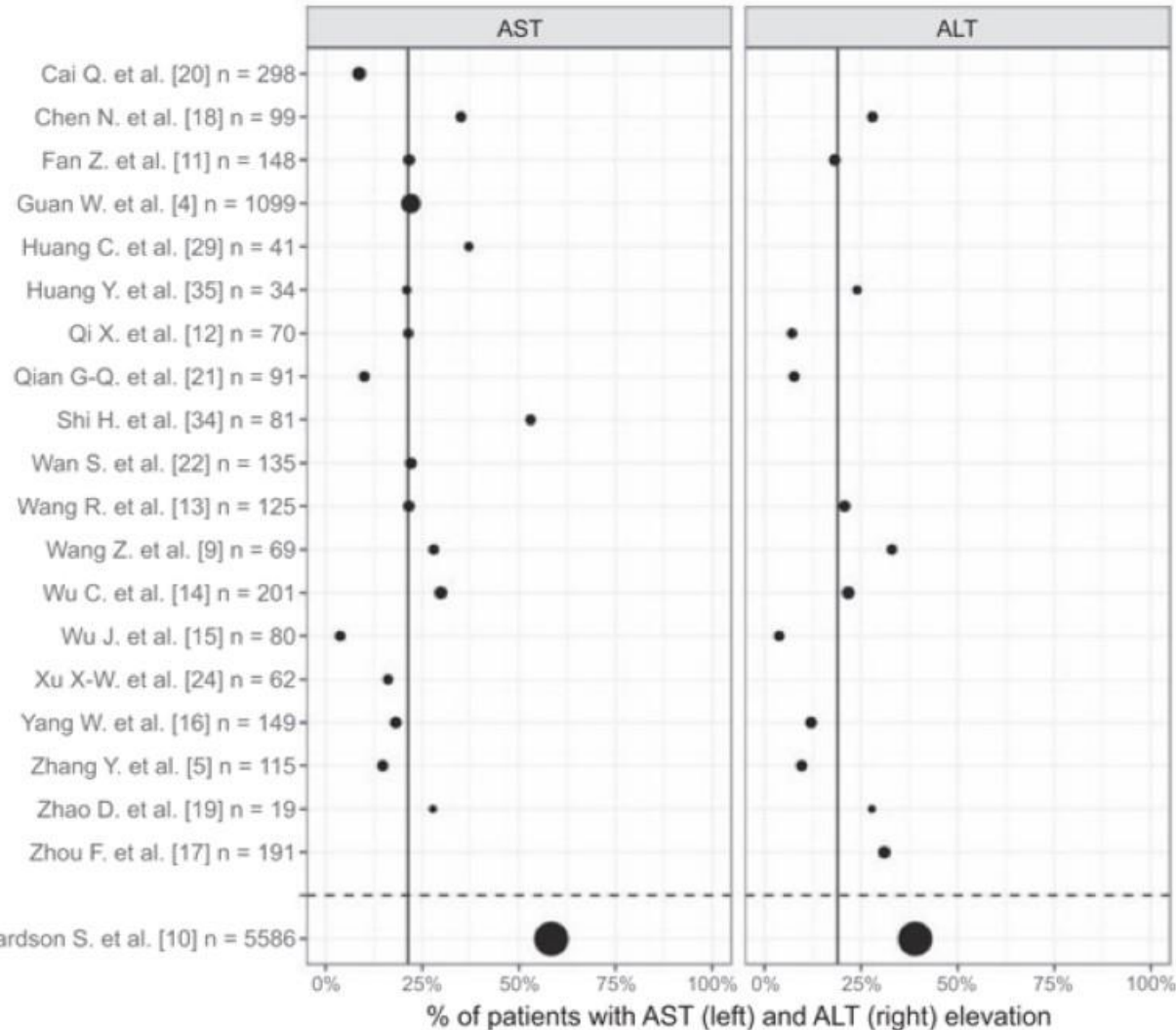
GI, gastrointestinal.

a. Li J, et al. J Med Virol. 2021;93:1449-1458; b. Moyer MW. What are the symptoms of Omicron? New York Times. Published Dec 21, 2021. Updated January 3, 2022. Accessed January 17, 2022. <https://www.nytimes.com/2021/12/21/well/live/omicron-variant-symptoms-covid.html>

# COVID-19 and the GI System

## Laboratory Reports

### AST or ALT Elevation Upon Hospital Admission in Patients With COVID-19



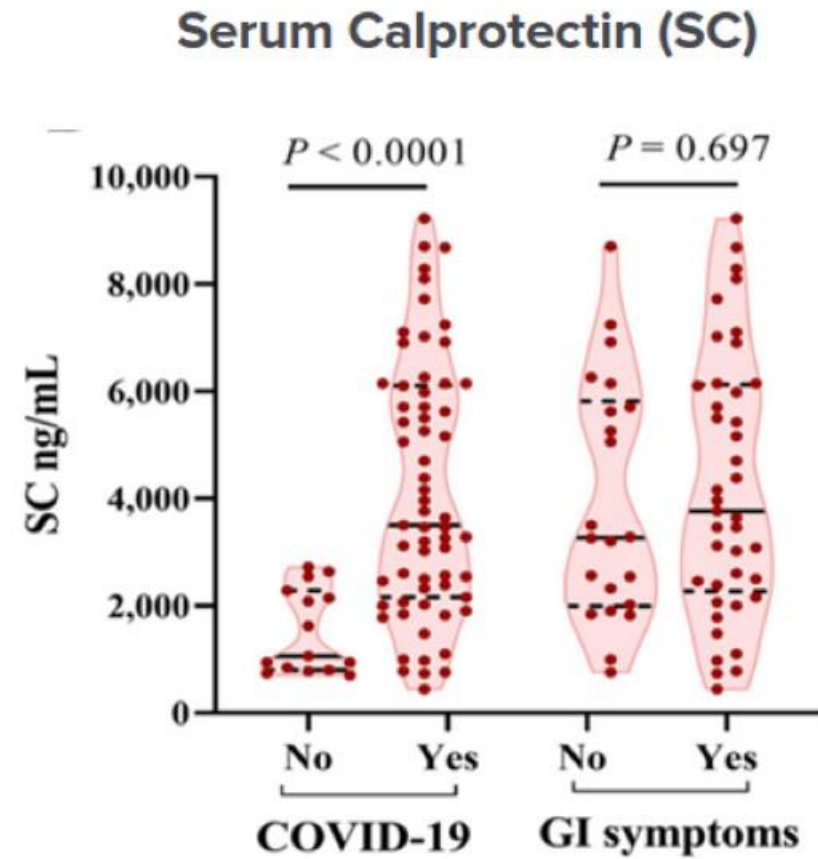
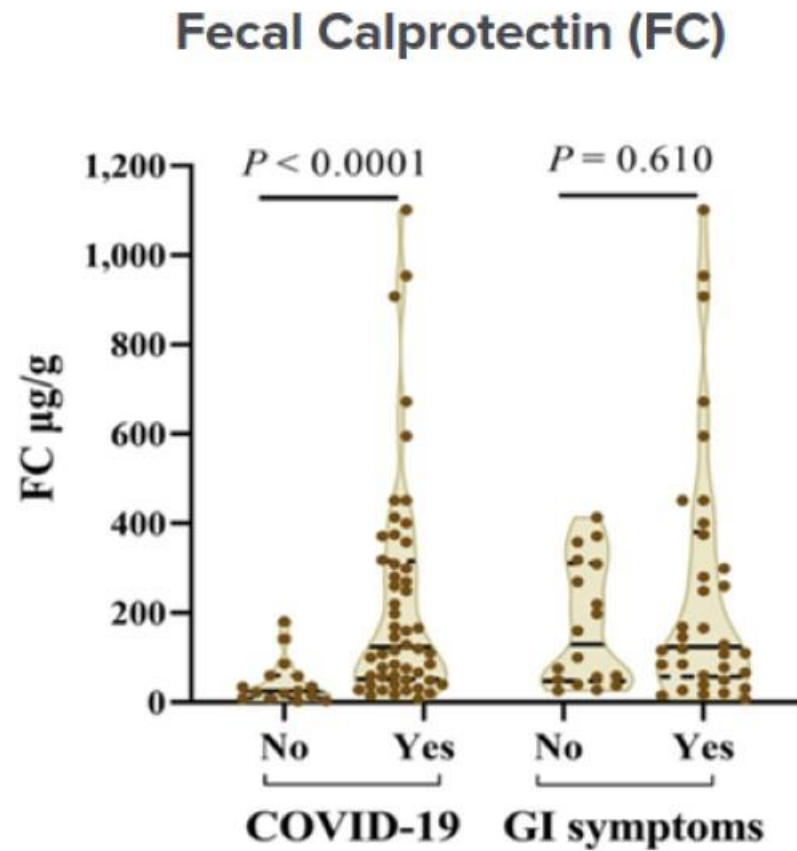
- Liver markers and abnormalities are frequently seen in patients who are hospitalized with COVID-19
- While inflammatory markers are often elevated in patients with COVID-19, this is most likely due to systemic immune response and not inflammation of the GI tract specifically

US Cohort →

# COVID-19 and the GI System

## Laboratory Reports (cont)

Comparison of Intestinal Inflammation Markers Based on COVID-19 Infection, GI Symptoms



# COVID Transmission

## *What We Know for Sure*



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# COVID Transmission

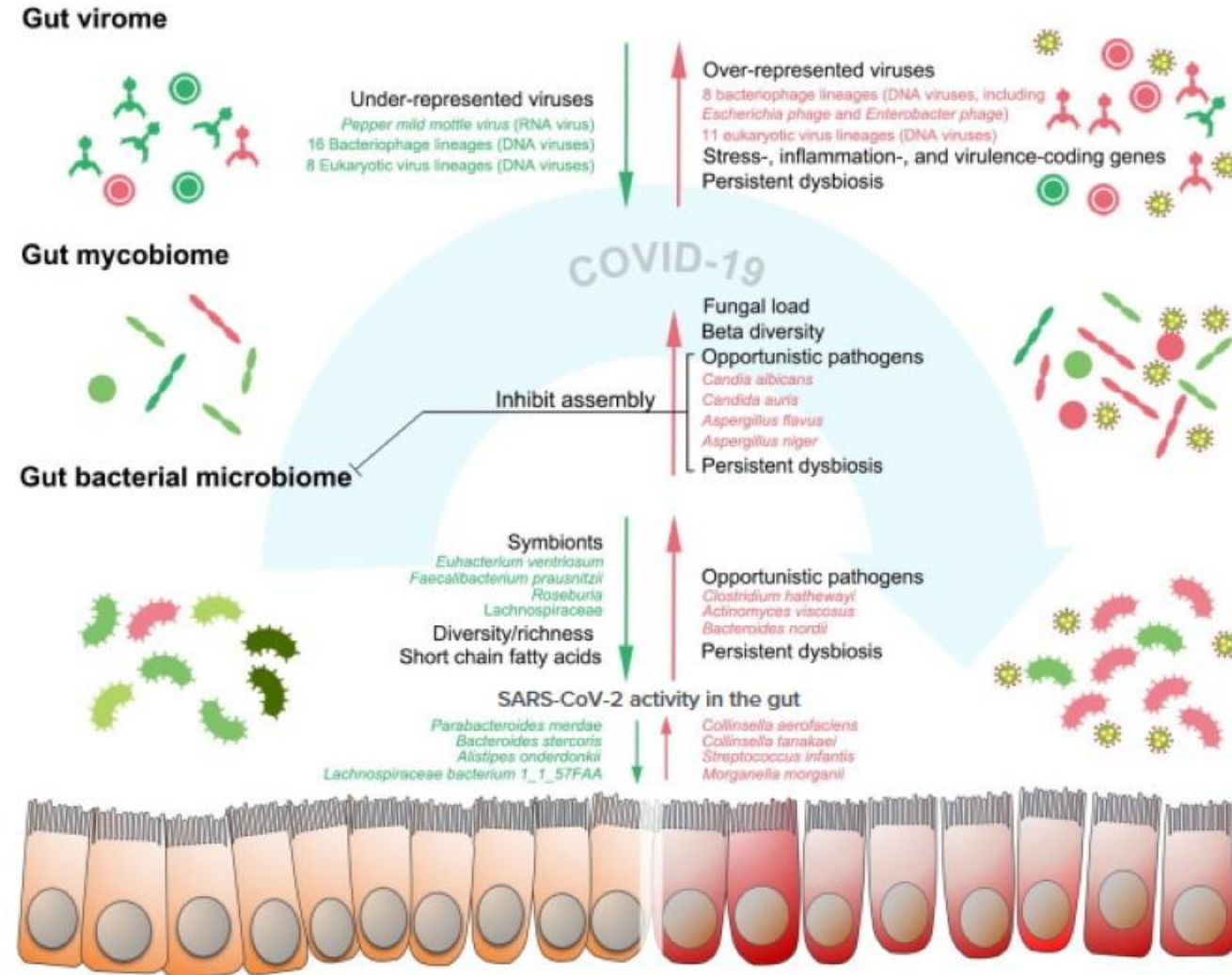
## *Investigating Nonrespiratory Routes*



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# SARS-CoV-2 and the Gut Microbiome

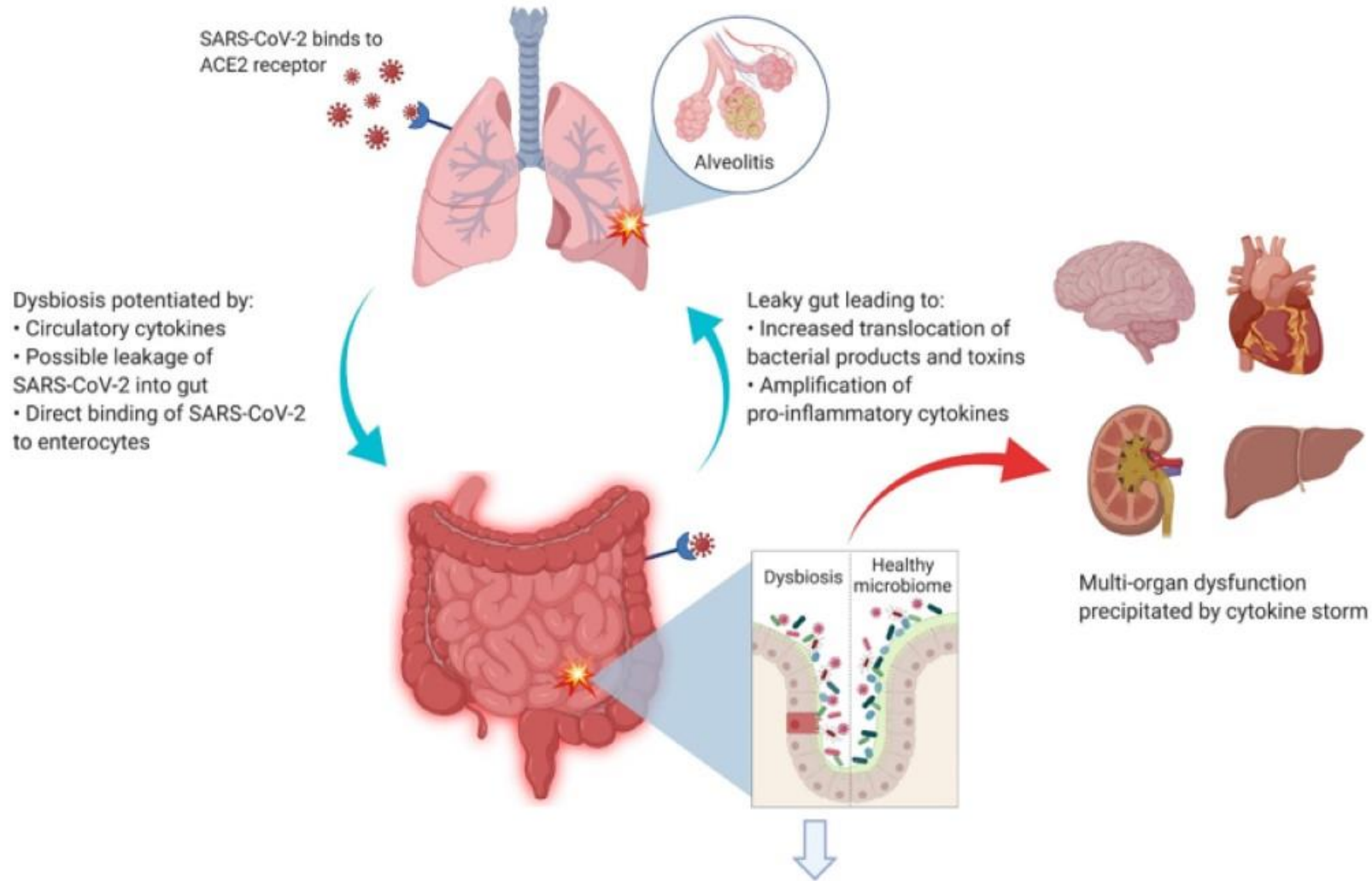
## What's Going On?



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 Zuo T et al. Genom Proteom Bioinform.  
 Published online 2021.  
 doi:10.1016/j.gpb.2021.09.004

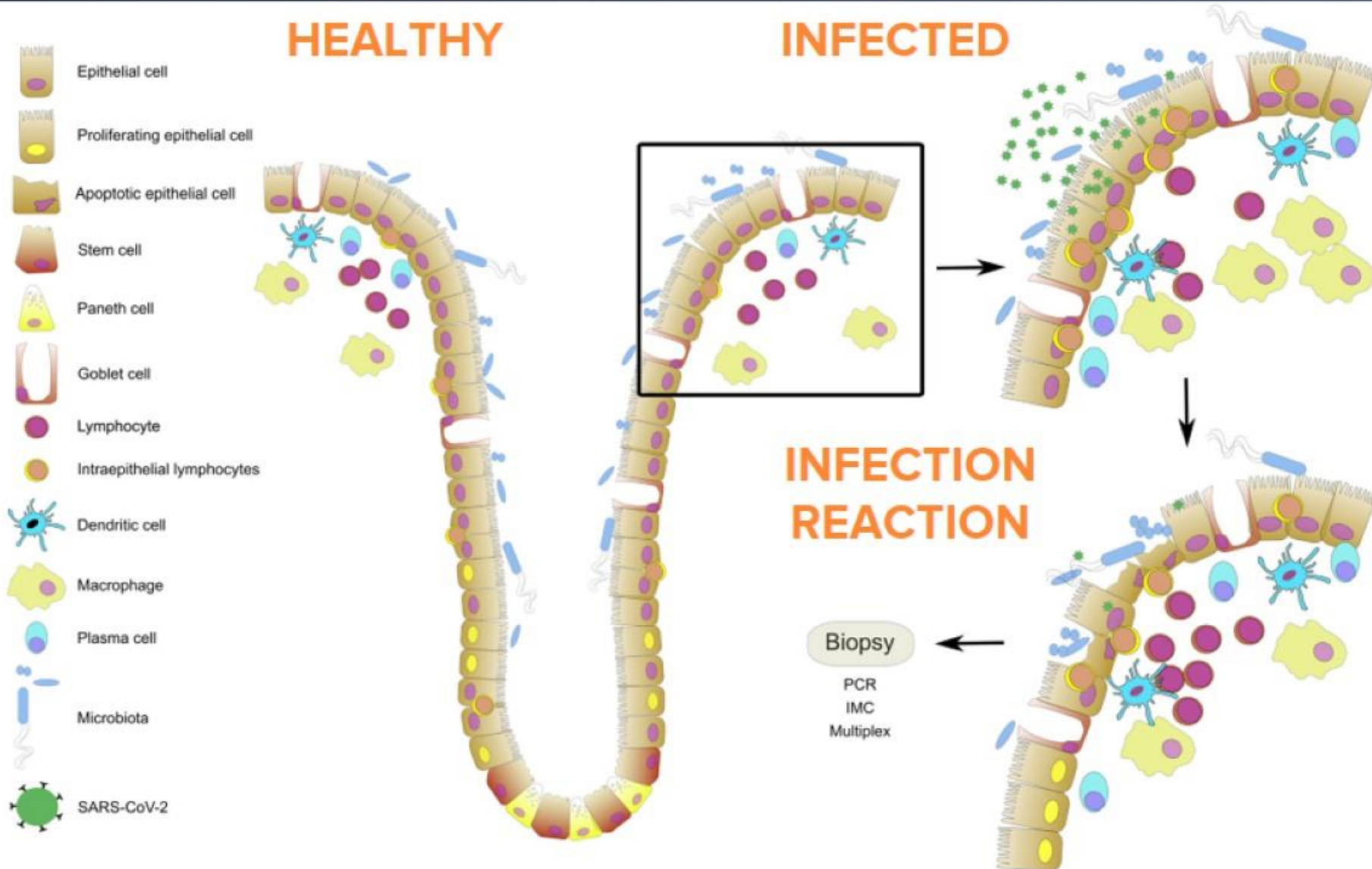


# The Gut-Lung Axis and COVID-19



- ↑ Pathobionts, ↓ symbiotic microbiome
- ↑ GI symptoms
- ↑ Stool calprotectin
- ↑ Markers of SARS-CoV-2 replicative activity

# Mechanism of SARS-CoV-2 Infection in the GI Tract



# Pharmacotherapies for COVID-19 Treatment



JAK, Janus kinase.

U.S. Food and Drug Administration (FDA). Drugs and non-vaccine biological products. Accessed March 15, 2022. <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs>; FDA. Know your treatment options for COVID-19. Updated January 27, 2022. Accessed March 15, 2022. <https://www.fda.gov/consumers/consumer-updates/know-your-treatment-options-covid-19>

# COVID-19 Treatment Recommendations

## FDA Guidance for Adult Outpatient Care – Current as of March 2022

### PATIENT DISPOSITION

Does Not Require  
Hospitalization or  
Supplemental Oxygen

### PANEL'S RECOMMENDATIONS

All patients should be offered symptomatic management **(AIII)**.

For patients who are at high risk of progressing to severe COVID-19 (treatments are listed in order of preference based on efficacy and convenience of use):

- **Ritonavir-boosted nirmatrelvir (AIIa)**
- **Sotrovimab (AIIa)**
- **Remdesivir (BIIa)**
- **Molnupiravir (CIIa)**

The Panel **recommends against** the use of **dexamethasone** or **other systemic corticosteroids** in the absence of another indication **(AIII)**.

**Remdesivir is approved by the FDA for treatment of COVID-19; the other drugs listed here are available for use via the FDA Emergency Use Authorization act.**

# COVID-19 Treatment Agents

## Ineffective Against Omicron Variant<sup>[a]</sup>

- Bamlanivimab + etesevimab
- Casirivimab + imdevimab

## New Kids on the (Treatment) Block

- Nirmatrelvir + ritonavir
- Molnupiravir
- Bebtelovimab

## For Prevention in High-Risk Patients<sup>[b]</sup>

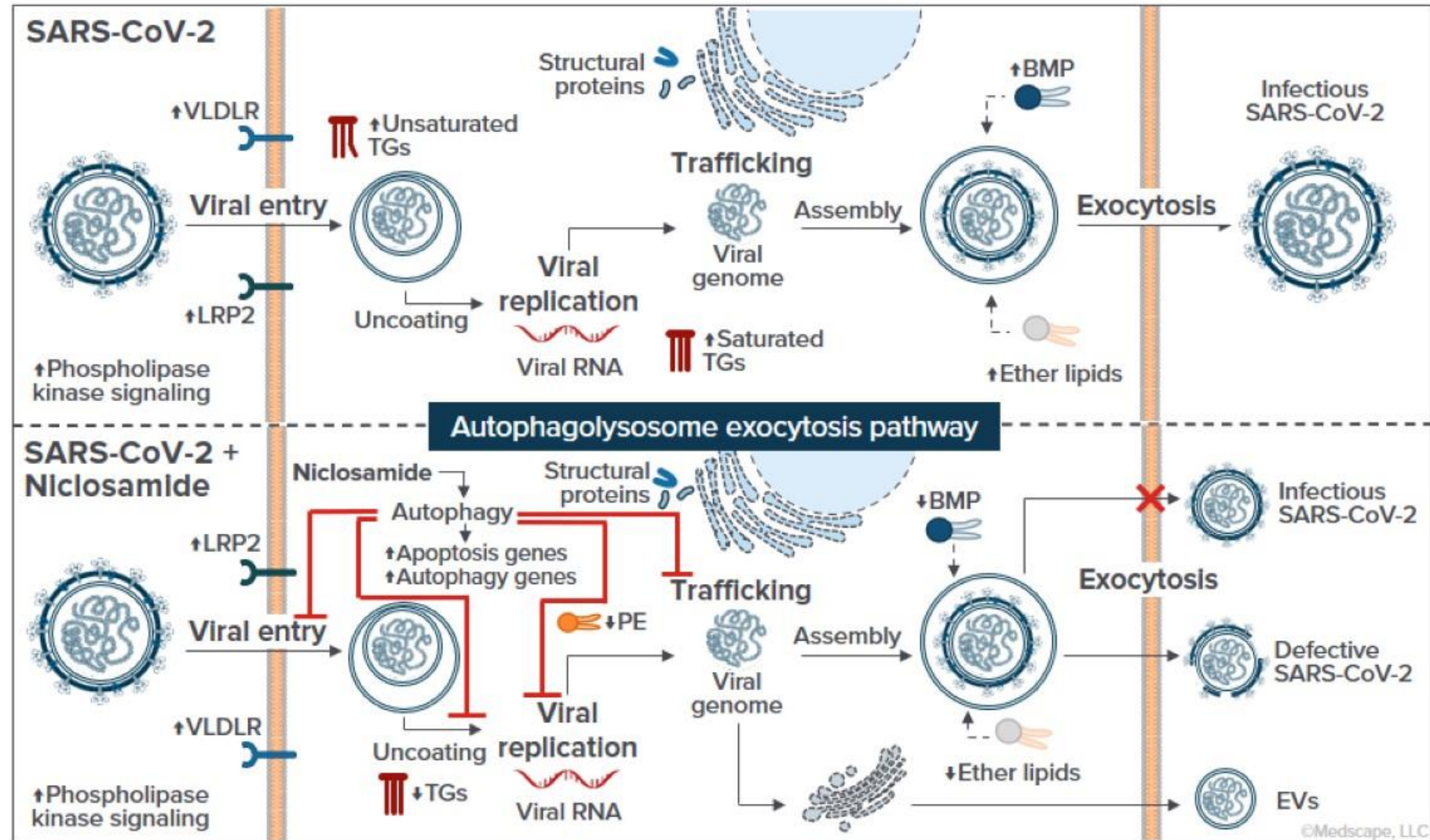
- Tixagevimab + cilgavimab

## For Management of GI Symptoms in COVID

- Niclosamide

# Mechanism of Novel COVID-19 Treatment *Nicosamide*

- Nicosamide is a prescription small molecule drug known for its anti-inflammatory and anti-viral properties
- Nicosamide is already approved in the United States for treatment of intestinal tapeworms



# Data on Novel COVID-19 Treatment *Niclosamide (RESERVOIR)*

## Study Aim

- To confirm the safety of niclosamide and assess the drug's ability to remove the SARS-CoV-2 virus from the digestive tract, as measured by the rate of SARS2 clearance from stool samples assessed by PCR test

**Inclusion criteria:  
patients with a primary  
diagnosis of COVID-19,  
with or without  
pneumonia**

**Niclosamide**  
400 mg 3 times daily

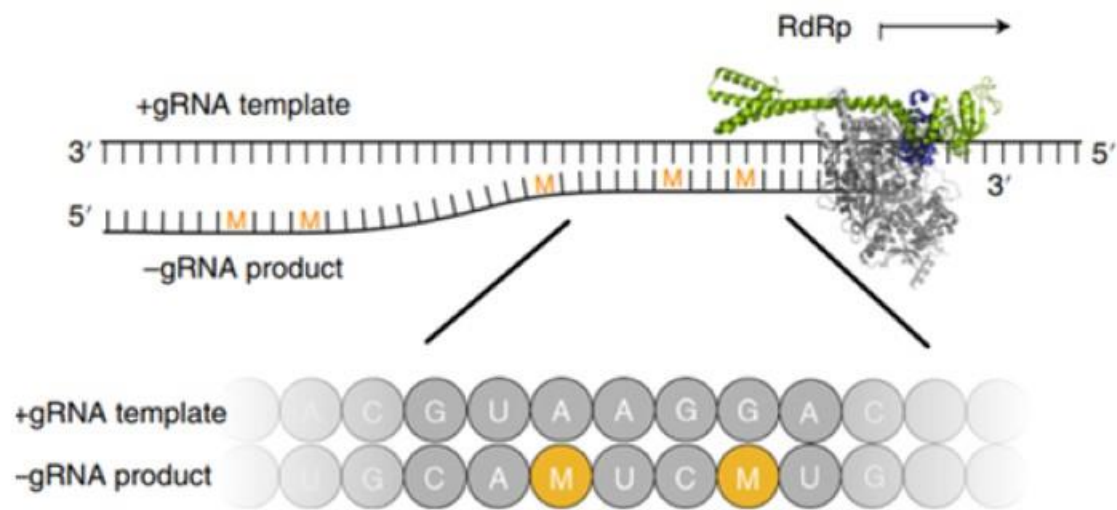
**Placebo**  
400 mg 3 times daily

After 14 days, patients will  
cease treatment but remain  
under observation for up to  
6 weeks

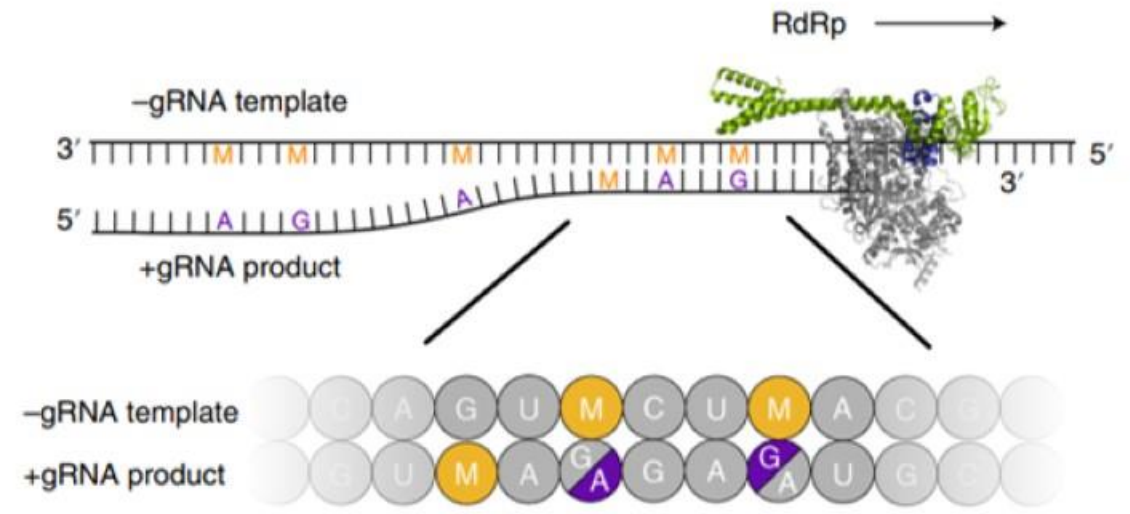
# Mechanism of Novel COVID-19 Treatment *Molnupiravir*

Molnupiravir is a nucleoside analogue that is thought to halt SARS-CoV-2 replication via a 2-step mechanism

## Step 1: Incorporation



## Step 2: Mutagenesis



**Molnupiravir was fast-tracked through drug development during the COVID-19 pandemic.**

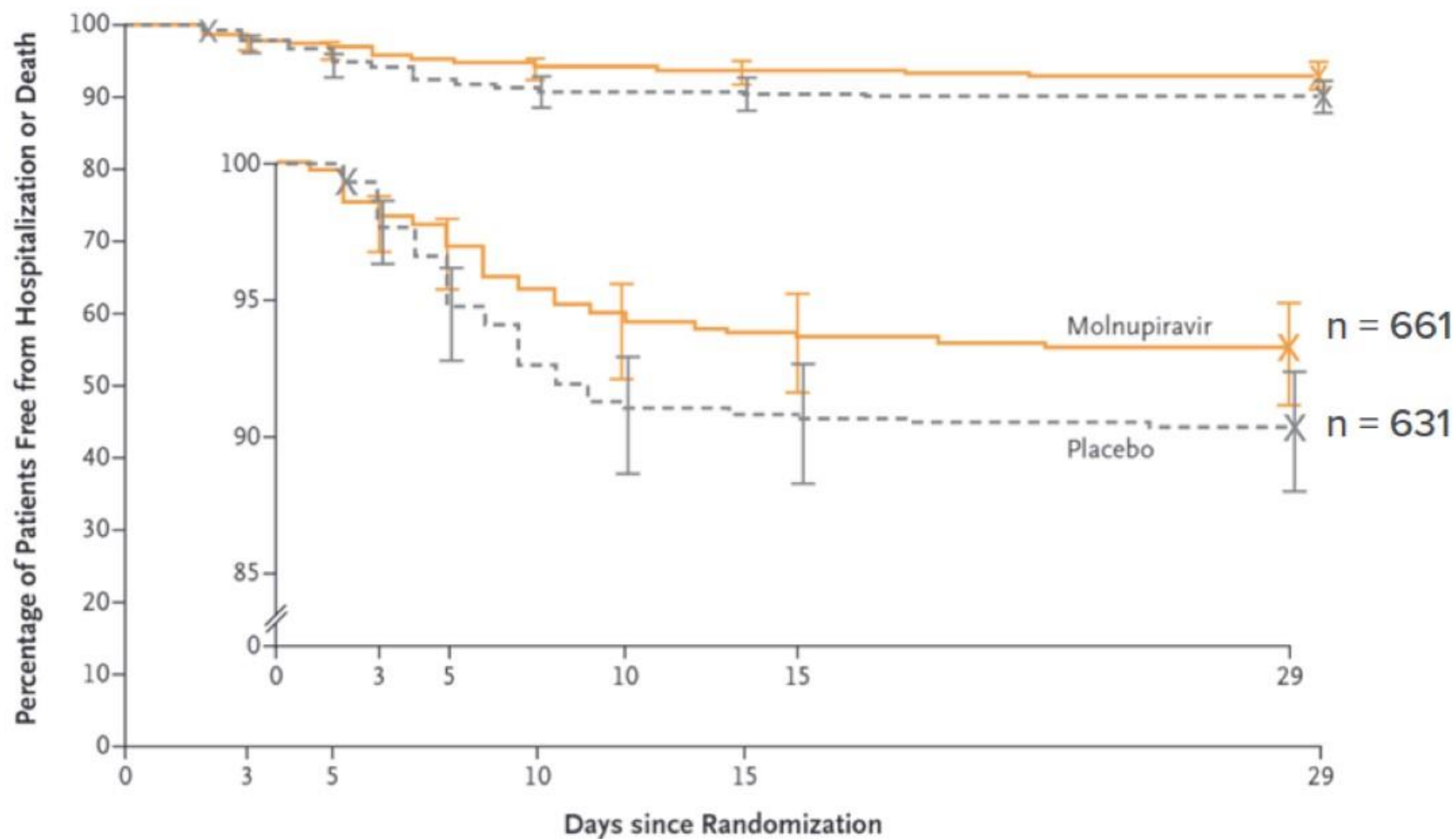
-gRNA, negative-strand genomic; +gRNA, positive-strand genomic; RdRp, RNA-dependent RNA polymerase.

Kabinger F, et al. Nat Struct Mol Biol. 2021;28:740-746.



# Data on Novel COVID-19 Treatment *Molnupiravir (MOVE-OUT)*

## Rate of Hospitalization or Death Through Day 29: Molnupiravir vs Placebo



# Considerations for the Gastroenterologist

**Might modulation of gut microbiota improve COVID-19 symptoms and speed recovery?**

Probiotics have been shown to reduce disease course in other respiratory infections, including coronaviruses<sup>[a]</sup>

## Possible Pre- or Probiotic Mechanisms Effective Against COVID-19<sup>[b]</sup>

