











If this presented hypothesis is true, the timing of IVM administration should be just prior to or at the cytokine storm. Seriously affected SARS-CoV-2-infected patients develop a cytokine storm alongside hypoxemia around Days 10–14, referred to as the “Second week crash” (Bernstein and Cha, 2020; Zayet et al., 2020; Mehta and Fajgenbaum, 2021; “Second-week crash” is time of peril for some patients with COVID-19). Our study on IVM combination therapy initiated therapy around Day 10, as patients typically presented to the study hypoxic at Day 9 (mean time from the symptom onset to treatment initiation was 9.2 days). This timing resulted in successful treatment, with all 24 severely hypoxic patients, recovering without hospitalizations (Hazan et al., 2022a). In short, IVM should typically be administered at the point of an SpO<sub>2</sub> drop, the cytokine storm onset, and/or approximately Days 10–14.

## CONCLUSION

We are hypothesizing the IVM mechanism of action as a therapeutic for COVID-19 is through feeding of *Bifidobacterium*, which then inhibits cytokine function and tames the cytokine

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storm (Figure 1). As such, IVM should be administered at the time of the cytokine storm.

## DATA AVAILABILITY STATEMENT

The original contributions presented in this study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

## AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for publication.

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**Conflict of Interest:** SH declares that she has a pecuniary interest in Topelia Pty Ltd in Australia, and Topelia Pty Ltd in United States where the development of COVID-19 preventative/treatment options are being pursued. She has also filed patents relevant to Coronavirus treatments. She is the founder and owner of Microbiome Research Foundation, ProgenaBiome, and Ventura Clinical Trials.

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