US Committee on Homeland Security and Governmental Affairs

Early Outpatient Treatment: An Essential Part of the COVID-19 Solution, Part II

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Honorable Senators of the Committee on Homeland Security,

My name is Jean-Jacques Rajter, MD. It is an honor and privilege to stand here in front of this committee providing first-hand experience on the early treatment for COVID-19. I am a pulmonary, critical, and sleep specialist residing in Broward County, Florida. My practice, Pulmonary and Sleep Consultants of Florida is made up of myself, my wife and business partner Dr. Juliana Cepelowicz Rajter, 2 full time Advanced Registered Nurse Practitioners, and 1 part time Advanced Registered Nurse Practitioner. We have a thriving inpatient and outpatient practice providing care to thousands of patients annually.
My team has extensive experience with treatment of COVID-19 in both inpatients and outpatients.
Although the first human cases of COVID-19 were originally reported in Wuhan in December of 2019, the first confirmed US cases of COVID-19 were in mid-January. It was not until March were confirmed cases of COVID-19 started appearing in Florida. Early on in the pandemic, most US physicians and health care facilities were caught off guard, as no proper diagnostic testing, protective equipment, and treatment algorithms were readily available.
During that first wave of COVID-19, hydroxychloroquine based regimens were considered appropriate, as no alternative options had been proven to be effective. I am not here to debate the merits or short comings of hydroxychloroquine based regimens, as this has already extensively been done by all parties involved. By early April, it became quite apparent that those hydroxychloroquine regimens did not work well in patients with more advanced COVID-19, as many of them ended up in ICU on ventilators and subsequently died.
In early April, Dr. Kylie Wagstaff and a team of researchers at Monash University in Australia published data indicating that Ivermectin was effective at reducing COVID-19 viral loads by 5000 fold within 48 hours in their cell culture models. The very next day, a COVID-19 patient of mine was rapidly deteriorating. She had gone from room air, to nasal cannula, to 50% oxygen over a few hours and

was continuing to deteriorate. She would likely be intubated shortly with its associated high mortality. After discussing her care with her family, I was implored to look for any other possible alternative to avoid further clinical deterioration. The patient's son was literally pleading with me to find some alternative to save his mother's life. We discussed the results of the in-vitro study using Ivermectin. Even though the drug has a great safety record, the patient's son was advised that no dosing trials had been completed. After extensive discussion we agreed that Ivermectin had other approved indications and he requested that I attempt use of an approved dosing regimen. Since no other options were available at the time, informed consent was obtained and Ivermectin administered. The patient deteriorated as expected for about 12 more hours, but stabilized by 24 hours and improved by 48 hours. Subsequent to this, 2 more patients had similar issues and were treated with the Ivermectin based protocol. Based on past experience, these patients should have done poorly, yet they all survived. This laid the foundation for the ICON study (Use of Ivermectin is Associated With Lower Mortality in Hospitalized Patients With Coronavirus Disease 2019) which was peer reviewed and published in CHEST, a major US based medical journal. Even though I did a lot of peer reviewed published research in my earlier years, I am currently a clinical physician who prior to this pandemic had no interest or inclination to do further research. Yet, I could not stand idly by as I have seen more people die in the past 6 months than I have in my entire medical career combined. Extraordinary times called for extraordinary measures.

The ICON study is a retrospective propensity matched observational study looking at the effect of ivermectin on hospitalized patients. Propensity matching is aimed at reducing the likelihood of selection bias and reducing the effects of confounding variables. Our propensity matched pairs were assessed based on age, gender, pulmonary condition, hypertension, HIV status, severe pulmonary disease at presentation, exposure to steroids, hydroxychloroquine, azithromycin, race, WBC count, absolute lymphocyte count, and need for mechanical ventilation at the time of study entry. We were limited to enrolling 300 patients into the study based on the limitation imposed on us by the Institutional Review Board. 107 patients received conventional care and 173 patients received conventional care plus Ivermectin. The overall mortality was 25% in the conventional care, whereas it dropped to 15% in the Ivermectin treated group. This was statistically significant difference in favor of Ivermectin use. In those patients with severe pulmonary disease at onset, the mortality benefit was even more staggering at 80.7% versus 38.8%. We concluded that further studies were needed to confirm those preliminary findings.

My team has multiple study protocols in place, ready to be implemented in short order. We have established relationships with international teams to complete such randomized controlled trials, yet funding for such studies has been elusive at best.

During the second wave of the pandemic, it was common for my team to treat in excess of 40 patients with COVID-19 on a daily basis. This ICON protocol has been optimized over the months as more information regarding treatment

successes and failures became apparent. The success rate of the Ivermectin based protocol is now far superior to what it was in its early days. The current ICON protocol is as follows:

- Ivermectin 200 mcg/kg orally on day 1 and 2. May redosed on day 8 and 9, 15, 22, and 29 as needed if patients remain symptomatic.
- Doxycycline 100 mg orally twice daily for 5 days or azithromycin 250 mg orally daily for 5 days if unable to take doxycycline.
- Vitamin C 1000 mg twice daily.
- Vitamin D3 1000 units daily.
- Zinc sulfate 220 mg daily or 50 mg of elemental zinc daily.
- Famotidine 20 mg twice daily.
- Atorvastatin 40 mg daily.
- If hypoxic dexamethasone 6 mg daily for 10 days.
- If mildly hypoxic, will need supplemental oxygen at home.
- If D dimer elevated, will need anticoagulation.
- If more severe and requires hospitalization, will consider convalescent plasma transfusion x2 and remdesivir with or without baricitinib.

Ivermectin based protocols have now been studies across the world, yet no major large scale randomized control study has been completed.

A meta-analysis of 21 studies looking at the effectiveness of Ivermectin in COVID-19 was released on November 26. The results of this study is attached below. This included:

3 early treatment studies from Espitia-Hernandez, Carvallo, and Cadegiani.

12 late treatment studies from Gorial, Podder, Khan, Chachar, Mahmud, Rajter, Hashim, Camprubi, Elgazzar, Spoorthi, Budhiraja, and Niaee.

4 pre-exposure prophylaxis studies from Behera, Carvallo, Hellwig, and Bernigaud.

2 post exposure prophylaxis studies from Shounan and Elgazzar

Treatment time	Number of studies reporting positive results	Total number of studies	Percentage of studies reporting positive results	Probability of an equal or greater percentage of positive results from an ineffective treatment	Random effects meta-analysis results
Early treatment	3	3	100%	0.13 1 in 8	91% improvement RR 0.09 [0.02-0.40] p = 0.0016

Late treatment	12	12	100%	0.00024 1 in 4 thousand	60% improvement RR 0.40 [0.24-0.66] p = 0.00038
Pre-Exposure Prophylaxis	4	4	100%	0.063 1 in 16	98% improvement RR 0.02 [0.00-1.27] p = 0.065
Post-Exposure Prophylaxis	2	2	100%	0.25 1 in 4	87% improvement RR 0.13 [0.05-0.39] p = 0.00027
All studies	21	21	100%	0.00000048 1 in 2 million	75% improvement RR 0.25 [0.16-0.40] p = <0.0001

Some detractors of Ivermectin use point to the fact that Wagstaff and team used supratherapeutic levels of Ivermectin in her cell lines. They obviously miss the fact that the original study in cell lines was merely a proof of concept and not a dosing trial. Subsequent studies completed by the very same research team in lung cells indicated that a cumulative dose of 350-450 mcg/kg would achieve effective tissue levels of Ivermectin. We came to the same conclusion based on clinical experience and have been a 200 mcg/kg on 2 consecutive days dosing regimen since May. Of the hundreds of outpatients treated by my team, only 2 were admitted to the hospital, one due to heart failure, the other due to symptomatic delay of over 1 week before seeking medical attention. Neither of them died, neither of them needed intubation.

Detractors of Ivermectin use would also point to some fabricated or extravagant safety concerns for Ivermectin use. Ivermectin is widely used with in excess of 3.7 billions doses administered wordwide. It is part of the WHO efforts to eliminate onchocerciasis and lymphatic filariasis as a public health problem in much of Africa. In APOC countries (Angola, Burundi, Cameroon, Central African Republic, Chad, Congo, Democratic Republic of Congo, Ethiopia, Equatorial Guinea, Gabon, Kenya, Liberia, Malawi, Mozambique, Nigeria, Rwanda, Sudan, Tanzania and Uganda), it is estimated that 65% of the total population living in an endemic area need to take ivermectin annually to eliminate onchocerciasis and lymphatic filariasis as a public health problem. It is currently also approved for treatment of strongyloidiasis and scabies. Because of this, Ivermectin is part of the WHO Model List of Essential Medications. The ICON dosing regimen is based on a currently accepted dosing regimen for Norwegian scabies. This dosing regimen has long standing safety data. Safety of a medication is due to its pharmacokinetics and possible interactions, but not its intended use. Hence, these safety concerns are significantly exaggerated. Remdesivir for example is known to cause renal insufficiency and failure, yet has been considered the standard of care. Yet no study has documented a survival benefit for this

medication. As of November 20, the WHO recommends against the use of remdesivir in COVID-19 patients. WHO has issued a conditional recommendation against the use of remdesivir in hospitalized patients, regardless of disease severity, as there is currently no evidence that remdesivir improves survival and other outcomes in these patients.

As is the case with any infections, early intervention has been proven time and again to be of critical importance. The same is true for COVD-19.

- Early intervention increases the likelihood of keeping people out of the hospital and hence decreasing the pressure on the Health Care system.
- Early intervention is cost effective as it decreases the overall Health Care expenditure.
- Early intervention and treatment decrease viral shedding and viral transmission in the home setting which is currently believed to me a major site of transmission.
- Early intervention increases survival.
- Early intervention decreases the economic impact.

Other treatment modalities have also not shown to be extremely effective. As discussed above, remdesivir has not been shown to impact mortality. Convalescent plasma has not been widely documented as improving survival either. Steroids improve survival by several percentage points only.

Even if vaccines are 80% successful (debatable but subject of another senate hearing I'm sure), we still need to treat the 20% of people who become ill with COVID-19 notwithstanding vaccination. Some people may not be able to receive the vaccine for a variety of reasons. Vaccines may not be widely available for many months. Vaccines may no provide long term immunity. Based on these factors, treatment for COVID-19 will need to remain on the forefront even after vaccination programs are initiated.

To summarize, based on the facts as presented above, Ivermectin is effective in early disease, late disease, post exposure prophylaxis, and pre exposure prophylaxis. The response to Ivermectin has been well documented. Ivermectin is an oral medication requiring no monitoring. It is safe and has a long track record of such safety. It is inexpensive and widely available.
The US has spend billions of dollars on a multitude of treatment options. My team is ready to proceed with the needed randomized control trials to address any such residual doubt related to Ivermectin use. Yet we are unable to proceed due to lack of funding and support. A few hundred thousand dollars, may definitively proof or disprove the effectiveness of Ivermectin for early treatment with a properly designed and implemented randomized control trial. More funding could look at the effectiveness of pre and post exposure prophylaxis using Ivermectin. A couple million dollars could complete a multi-center double blind, placebo control trial with Ivermectin. Based on the John Hopkins COVID Resource Center, our beautiful country has over 266,000 people dead to date

with a mortality of 82 people per 100,000 population. Norway and Finland have a mortality of 6.2 and 7.2 per 100,000. If this were extrapolated to the US, our mortality to date would only be 20 to 23,000 people. Australia with 3.6 per 100,000 would extrapolate to 12,000. Ladies and gentlemen, I implore you as a front line provider of COVID-19 to do better. To provide us the answers we need as health care providers to help your constituents survive this horrible pandemic in great number. May G'd bless you and the United States of America.