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Statement on the Use of Ivermectin As Treatment for COVID-19

Evidence reviewed by the Philippine COVID-19 Living CPG Reviewers of the UP-NIH ICE and Consensus Panel Representatives of FDA-DOH, PMA, PCP, PAFP, POGS, PCEM, PSGIM, PCCP, PSPHP and PSMID.

Ivermectin

Ivermectin is an anti-helminthic drug repurposed as a potential therapy for COVID-19 because of its anti-viral properties and immunomodulatory effects. Based on in vitro studies, it prevents viruses from suppressing the host's antiviral response. As an immunomodulator, ivermectin may reduce cytokine secretion.[1-2]

A systematic review of 6 randomized controlled trials[3-8] of good methodological quality showed that:

- **Ivermectin DID NOT SIGNIFICANTLY REDUCE the risk of mortality (Relative Risk 0.74 [0.33, 1.63]) among patients with mild to severe COVID-19 disease.**
- **Ivermectin was NOT ASSOCIATED with a definite benefit in terms of other clinically important outcomes such as clinical improvement at Day 6-10 (RR 1.01 [0.87, 1.16])[3,5,9-10], clinical deterioration (RR 0.70 [0.37, 1.33])[3-6,10], and need for mechanical ventilation (RR 0.42 [0.10, 1.86])[4-5,11].**
- **Ivermectin DID NOT SIGNIFICANTLY REDUCE the duration of hospitalization (Mean Difference 0.83 [-0.86, 2.52])[6,8], and the time to resolution of symptoms (MD -0.32 [-1.51, 0.87])[3-4].**
- **The rate of hospital discharge at Day 10-14 DID NOT DIFFER SIGNIFICANTLY between the ivermectin group and the standard of care or placebo group (RR 1.04 [0.95, 1.14]) [4,5,8].**

The adverse events reported with the use of ivermectin, although not significantly increased (RR0.99 [0.73, 1.32]), include dizziness, headache, rash, and gastrointestinal symptoms such as nausea.

Based on the current evidence from randomized control trials, WE DO NOT RECOMMEND the use of Ivermectin for the treatment of COVID-19. It has not been proven to significantly reduce mortality or improve other clinical outcomes. This recommendation will be updated as more evidence is generated from ongoing trials.

REFERENCES:

1.Yang SNY, Atkinson SC, Wang C, et al. The broad spectrum antiviral ivermectin targets the host nuclear transport importin alpha/beta1 heterodimer. Antiviral Res. 2020;177:104760. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32135219.

2.Kalfas S, Visvanathan K, Chan K, Drago J. The therapeutic potential of ivermectin for COVID-19: a review of mechanisms and evidence [Internet]. MedRxiv. 2020. Available from: https://www.medrxiv.org/content/10.1101/2020.11.30.20236570v1?rss=1'

3.López-Medina E, López P, Hurtado IC, et al. Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19: A Randomized Clinical Trial [published online ahead of print, 2021 Mar 4]. JAMA. 2021;10.1001/jama.2021.3071. doi:10.1001/jama.2021.3071

4.Mohan A, Tiwari P, Suri T, Mittal S., et al. Ivermectin in mild and moderate COVID-19 (RIVETCOV): a randomized, placebo-controlled trial. Research Square Preprint. 2021.

5.Ravikirti, Ranjini, R.,Chandrima, P., et al. Ivermectin as a potential treatment for mild to moderate COVID-19 – A double blind randomized placebo-controlled trial. 2021.

6.Ahmed S Ross AG, Hossain MS,Clemens JD,Sumiya MK,Phru CS,Rahman M,Zaman K,Somani J,Yasmin R,Hasnat MA,Kabir A,Aziz AB,Khan WA,Karim M M. A five day course of ivermectin for the treatment of COVID-19 may reduce the duration of illness. International journal of infectious diseases; 2020.

7.Chaccour, C., Casellas, A., Blanco-Di Matteo, A., Pineda, I., et al. The effect of early treatment with ivermectin on viral load, symptoms and humoral response in patients with non-severe COVID-19: A pilot, double-blind, placebo-controlled, randomized clinical trial. EClinicalMedicine, p.100720; 2021.

8.Gonzalez JLB, Gámez MG, Enciso EAM, Maldonado RJE, et al. Efficacy and safety of Ivermectin and Hydroxychloroquine in patients with severe COVID-19. A randomized controlled trial. Available from: medRxiv 2021.02.18.21252037; doi: https://doi.org/10.1101/2021.02.18.21252037

9.Chachar, K., Rabia, B., Aijaz, Z., Khurshid, A., et al. Effectiveness of Ivermectin in SARS-CoV-2/COVID-19 Patients. International Journal of Sciences; 2020.

10.Okumus, N.,Demirtürk, N., Çetinkaya, R., et al. The Effectiveness and Safety of Ivermectin as add-on Therapy in Severe COVID-19 Management. Clinical trials.gov. 2021

11.Królewiecki, A., Lifschitz, A., Moragas, M., Travacio, M., et al. Antiviral Effect of High-Dose Ivermectin in Adults with COVID-19: A Pilot Randomised, Controlled, Open Label, Multicentre Trial. SSRN Electronic Journal; 2020.

12.Elgazzar A, Hany B, Youssef S, Hany B, Hafez M, Moussa H. Efficacy and Safety of Ivermectin for Treatment and prophylaxis of COVID-19 Pandemic. Research Square; 2020.

13.Niaee, M. S., Gheibi, N., Namdar, P., et al. Ivermectin as an adjunct treatment for hospitalized adult COVID-19 patients: A randomized multi-center clinical trial. Research Square; 2020.