### New Study: Hydroxychloroquine Works in Monkeys, Not Humans

Thus, at this point, there is no compelling evidence to recommend the use of hydroxychloroquine for clinical use and several large organizations have suspended research involving this drug. There has been an enormous amount of valuable scientific resources which have been devoted to answering this scientific, now political, issue. These resources would have been better spent on more promising treatment modalities, such as studying Camostat mesilate or nafamostat mesylate therapy for COVID-19, a compound which has been shown to block TMPRSS2. Infection Control Today. Aug. 3, 2020. <u>https://www.infectioncontroltoday.com/view/new-study-hydroxychloroquine-works-in-monkeys-not-humans</u>

# Hydroxychloroquine Randomized Controlled Hydroxychloroquine Trials With Negative Outcomes:

• Borba, et al. (Brazil) – **RCT. Double Blinded**. **Hospitalized with severe COVID-19**. 18.9% of the patients in the high dose group developed QTc interval abnormalities compared to 11.1% in the low dosage group. The lethality in the high dose group was more than twice that of the low dose control. The study was discontinued. April 24, 2020. <u>https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2765270</u>

• Boulware, et al. (USA) – – **RCT. Double Blinded**. Prophylaxis post exposure to SARS-CoV-2 "After high-risk or moderate-risk exposure to Covid-19, hydroxychloroquine did not prevent illness compatible with Covid-19 or confirmed infection when used as **postexposure prophylaxis within 4 days** after exposure." New England Journal of Medicine. June 3, 2020. <u>https://www.nejm.org/doi/full/10.1056/NEJMoa2016638</u>

• Oxford RECOVERY Study: (UK) – **RCT. Hospitalized Patients.** "There was no significant difference in the primary endpoint of 28-day mortality (25.7% hydroxychloroquine vs. 23.5% usual care; hazard ratio 1.11 [95% confidence interval 0.98-1.26]; p=0.10). There was also no evidence of beneficial effects on hospital stay duration or other outcomes." The Trial was halted because of lack of efficacy. June 5, 2020. <u>https://www.ox.ac.uk/news/2020-06-05-no-clinical-benefit-use-hydroxychloroquine-hospitalised-patients-covid-19</u>

• Skipper, et al. (USA & Canada) – **RCT. Double Blind. Non-Hospitalized Patients.** "Hydroxychloroquine did not substantially reduce symptom severity in outpatients with early, mild COVID-19." Annals of Internal Medicine. July 16, 2020. <u>https://www.acpjournals.org/doi/10.7326/M20-4207</u>

• Cavalcanti, et al. (Brazil) – **RCT. Hospitalized Patients.** "Among patients **hospitalized with mild-to-moderate Covid-19**, the use of hydroxychloroquine, alone or with azithromycin, did not improve clinical status at 15 days as compared with standard care." New England Journal of Medicine. July 23, 2020. https://www.nejm.org/doi/full/10.1056/NEJMoa2019014

• Abella, et al. (USA) -- **RCT. Double Blind.** Efficacy and Safety of Hydroxychloroquine vs Placebo for Preexposure SARS-CoV-2 Prophylaxis Among Health Care Workers. **Prophylaxis**. Benefit not demonstrated. <u>https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2771265</u>

• WHO SOLIDARITY Trail, Pan, et. al. (WHO). **RCT**. **Adult Hospitalized Patients**. Repurposed antiviral drugs for COVID-19 –interim WHO SOLIDARITY trial results. Benefit not demonstrated. <u>https://www.medrxiv.org/content/10.1101/2020.10.15.20209817v1</u>

• Rajasingham, et al. (United States) – **RCT. Double Blind. Prophylaxis** of Healthcare Workers. Pre-exposure prophylaxis with hydroxychloroquine once or twice weekly did not significantly reduce laboratory-confirmed Covid-19 or Covid-19-compatible illness among healthcare workers. <u>https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1571/5929230</u>

• Self, et al (United States) --- RCT. Double Blind. Adult Hospitalized Patients with Respiratory Illness. The trial was stopped at the fourth interim analysis for futility with a sample size of 479 patients. ...did not significantly improve clinical status at day 14. <u>https://jamanetwork.com/journals/jama/fullarticle/2772922</u>

## **Ivermectin Negative Studies**

### 2023, January 12: Study Confirms No Benefit to Taking Ivermectin for COVID-19 Symptoms

"A study led by the Duke Clinical Research Institute (DCRI) in partnership with Vanderbilt University found no differences in relief of mild-to-moderate COVID-19 symptoms between participants taking ivermectin and participants taking a placebo. These results confirm findings from a previous arm of the study that tested a lower dose and shorter duration of ivermectin." <u>Study Confirms No Benefit to Taking Ivermectin for COVID-19 Symptoms | Duke Clinical Research Institute https://dcri.org/news/study-confirms-no-benefit-taking-ivermectin-covid-19-symptoms</u>

- RCT from Argentina -- No Effect July 2, 2021
  July 2021 Ivermectin to prevent hospitalizations in patients with COVID-19 (IVERCOR-COVID19) a
  randomized, double-blind, placebo-controlled trial
  The mean age was 42 years (SD ± 15.5) and the median time since symptom onset to the inclusion
  was 4 days. <u>https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-021-06348-5</u>
- Efficacy of Ivermectin Treatment on Disease Progression Among Adults With Mild to Moderate COVID-19 and Comorbidities The I-TECH Randomized Clinical Trial Feb. 18, 2022

   In this open-label randomized clinical trial of high-risk patients with COVID-19 in Malaysia, a 5-day course of oral ivermectin administered during the first week of illness did not reduce the risk of developing severe disease compared with standard of care alone. Among 490 patients included in the primary analysis (mean [SD] age, 62.5 [8.7] years; 267 women [54.5%]), 52 of 241 patients (21.6%) in the ivermectin group and 43 of 249 patients (17.3%) in the control group progressed to severe disease
- Effect of Early Treatment with Ivermectin among Patients with Covid-19 Brazil May 4, 2022

(This article was published on March 30, 2022, and updated on April 5, 2022, at NEJM.org.) A total of 3515 patients were randomly assigned to receive ivermectin (679 patients), placebo (679), or another intervention (2157). "Treatment with ivermectin did not result in a lower incidence of medical admission to a hospital due to progression of Covid-19 or of prolonged emergency department observation among outpatients with an early diagnosis of Covid-19. " https://www.nejm.org/doi/10.1056/NEJMoa2115869

• RCT - Effect of Ivermectin vs Placebo on Time to Sustained Recovery in Outpatients With Mild to Moderate COVID-19 A Randomized Clinical Trial. In this double-blinded, randomized, placebocontrolled platform trial conducted in the US during a period of Delta and Omicron variant predominance, and that included 1591 adult outpatients with COVID-19. Among outpatients with mild to moderate COVID-19, treatment with ivermectin, compared with placebo, did not significantly improve time to recovery. These findings do not support the use of ivermectin in outpatients with mild to moderate COVID-19. JAMA Network: https://jamanetwork.com/journals/jama/fullarticle/2797483  Effect of Higher-Dose Ivermectin for 6 Days vs Placebo on Time to Sustained Recovery in Outpatients With COVID-19 - A Randomized Clinical Trial "Among outpatients with mild to moderate COVID-19, treatment with ivermectin, with a maximum targeted dose of 600 µg/kg daily for 6 days, compared with placebo did not improve time to sustained recovery. These findings do not support the use of ivermectin in patients with mild to moderate COVID-19." double-blind, randomized, placebo-controlled platform trial including 1206 US adults https://jamanetwork.com/journals/jama/fullarticle/2801827

• COVID-OUT Trails

"Ivermectin and fluvoxamine, meanwhile, showed no benefit in randomized COVID-OUT study" "Bramante and colleagues also tested ivermectin and fluvoxamine, but found no reduction in long COVID risk with either drug versus placebo (ivermectin: HR 0.99, 95% CI 0.59-1.64; fluvoxamine: HR 1.36, 95% CI 0.78-2.34)." <u>https://clinicaltrials.gov/ct2/show/NCT04510194</u> <u>https://www.medpagetoday.com/infectiousdisease/longcovid/103450</u>

- Randomized Trial of Metformin, Ivermectin, and Fluvoxamine for Covid-19 "None of the three medications that were evaluated prevented the occurrence of hypoxemia, an emergency department visit, hospitalization, or death associated with Covid-19." https://www.nejm.org/doi/10.1056/NEJMoa2201662
- Efficacy and safety of ivermectin in patients with mild COVID-19 in Japan and Thailand (Randomized double blind trial)

"The results show that ivermectin (0.3–0.4 mg/kg), as a treatment for patients with mild COVID-19, is ineffective; however, its safety has been confirmed for participants, including minor participants of 12 years or older" <u>https://www.jiac-j.com/article/S1341-321X(23)00316-1/fulltext</u>

## Ivermectin Retracted Studies

- Large Ivermectin Study Retracted -- Made by Surgisphere

   Preprint publisher finds evidence of plagiarism, problems with raw data
   July 20, 2021. <u>https://www.medpagetoday.com/special-reports/exclusives/93658</u>
   Efficacy and Safety of Ivermectin for Treatment and prophylaxis of COVID-19
   Pandemic <u>https://www.researchsquare.com/article/rs-100956/v4</u>
- Surgisphere Retracted Studies on ACE Inhibitors & COVID, Hydroxychloroquiin and Ivermecitn. Surgisphere database, however, and the retractions followed on 4 June. But of the 200 papers examined by Science—all published after the retractions—105 inappropriately cited one of the disgraced studies. <u>https://www.science.org/content/article/many-scientists-citing-two-scandalouscovid-19-papers-ignore-their-retractions</u>
- Another Ivermectin-COVID-19 Paper Is Retracted
   A paper on the potential use of ivermectin to treat Covid-19 has been retracted for a litany of flaws, joining at least 10 other articles on the therapy, some liked to promote without evidence, to fall. "...statistical analysis, and presents unclear data interpretation.
   The conclusions and statements of the authors cannot be readily supported by the information presented in the paper." <u>Another Ivermectin-COVID-19 Paper Is Retracted (medscape.com)</u>
   Use of ivermectin in the treatment of Covid-19: A pilot trial <a href="https://www.sciencedirect.com/science/article/pii/S2214750021000445">https://www.sciencedirect.com/science/article/pii/S2214750021000445</a>