

July 1, 2021

Professor Chris Butler
Professor Richard Hobbs

Lead Investigators—*The PRINCIPLE Trial*
University of Oxford —UK
(Via email)

Dear Professors,

We write to you today with serious and urgent concerns about the randomized controlled trial of Ivermectin which you are about to begin in the UK.

At the outset, it is puzzling to understand why a trial of ivermectin would even be necessary, given the preponderance of peer-reviewed scientific evidence that has been published across the globe. This unassailable evidence includes dozens of randomized controlled trials, and a systematic review and meta analysis (using the rigorous Cochrane methods) that all show large magnitude improvements in case counts, hospitalizations and deaths using ivermectin. Therefore, it seems profoundly unethical to mount a trial designed to withhold efficacious treatment from any trial subject since it is quite possible that participants in the control arm could worsen or die without it.

Accordingly, in consideration of the above, your recent statement that, “Several small clinical studies have found that ivermectin may help to treat COVID-19. However, we need more evidence from large clinical trials, which is why we have included the treatment in the PRINCIPLE Trial,” is at best misleading, and at worst immoral.

Our catalogue of concerns also includes the design of the trial itself. If subjects are enrolled in the PRINCIPLE trial for up to 15 days after onset of symptoms, this could result in the enrolment of people with long standing symptoms, who need more intensive combination therapy including corticosteroids, and those who have already recovered. Such late enrolment would in effect be evaluating anti-inflammatory and immunomodulatory effects of ivermectin and not assessing its antiviral properties, and steroids would also be indicated. It is now well known that COVID-19 is best treated early and with combination therapy. Treating with Ivermectin far too late in the disease does little to rationalize a good study.

The low doses of ivermectin to be given in the trial—an oral dose of 0.3 mg/kg body weight for 3 days—is insufficient and will result in unreliable results data. The existing data from randomized controlled trial indicates a dose response in terms of time to viral clearance and time to symptomatic improvement, with a dose of 0.4 to 0.6 mg/kg for 5 days appearing optimal.

Another area of considerable uneasiness over your proposed trial of ivermectin is that the protocol is dated February, 2021. This means that the information in the trial consent form is both outdated and inaccurate since the latest evidence from June 2021—as previously articulated—shows that ivermectin prevents deaths from COVID-19. It is imperative that the most up-to-date evidence be provided to prospective study subjects in the consent form. The conclusions of the most recent peer-reviewed studies (below) should be integrated into the form to ensure that participants are aware of ivermectin's proof of efficacy against COVID-19.

https://journals.lww.com/americantherapeutics/abstract/9000/ivermectin_for_prevention_and_treatment_of.98040.aspx

https://journals.lww.com/americantherapeutics/fulltext/2021/06000/review_of_the_emerging_evidence_demonstrating_the.4.aspx

What is also highly ambiguous is the process that will be used to differentiate study subjects between the participants who are unvaccinated and those with post-vaccination COVID-19. If your study includes both vaccinated and unvaccinated subjects, how will you distinguish them? Furthermore, is there a plan in place for randomization to be stratified according to vaccination status?

In conclusion, it is our strong belief that The PRINCIPLE Trial is a non-essential, poorly designed study that will lead to a harvest of unreliable data concerning the utility of Ivermectin in COVID-19. Any further delays in getting safe, effective, early treatments to patients will result in additional needless illness and death.

Sincerely,



Dr. Pierre Kory, FLCCC Alliance



Dr. Tess Lawrie, The BiRD Group