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Email Dr. Susanna Naggie 10/18/21 Principal Investigator ACTIV-6
Re: Underdosing of Ivermectin in ACTIV-6

Mon, Oct 18, 2021 6:27 pm
(doctrumpet@aol.com)To:susanna.naggie@duke.edu Details
Dr. Susanna Naggie
Principal Investigator ACTIV-6
Duke Medical Center

Dear Dr. Naggie,
Below are emails to the FDA and all members of the Duke IRB regarding what I believe to be underdosing of ivermectin in ACTIV-6. I believe that giving less than in Together where ivermectin showed insignificant benefit is hard to rationalize. I was in contact with Dr. Nina Gentile at the Temple site who was open to discussing a change in dose. I have sent them my thoughts. She told me that giving it on an empty stomach came from the FDA and I see that it has always been given that way for parasites but I provided you with a reference suggesting blood levels are 2.6 times higher when taken with food. That is how the FLCCC Alliance has recommended it be used. There may well be other data on ivermectin's pharmacokinetics.

I am also concerned that Merck will be supplying the stromectol. They came out with a fraudulent public statement 2/4/21.

[Merck on Ivermectin](#) while they had terrible conflict of interest, having gotten \$356 million from HHS to develop a competitor therapeutic which turned out to be mutagenic molnupiravir which they are aggressively marketing. They cosponsored the heavily criticized Lopez Medina JAMA study in which the final conclusions said ivermectin was ineffective in "adults" with mild COVID, not mentioning that the patients averaged 37 years old. Their actions with viox were terrible.

[merck's deadly viox playbook](#) I worry they will come after me for saying that. Given their terrible conflict of interest and track record, the stromectol being used in ACTIV-6 should be assayed or a different product should be considered.

Sincerely,
Michael B. Goodkin MD, FACC
doctrumpet@aol.com

-----Original Message-----

From: doctrumpet@aol.com

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Sent: Mon, Oct 18, 2021 3:57 pm

Subject: Underdosing of Ivermectin in ACTIV-6

Duke Institutional Review Board

Dear Sirs,

Below is an email I sent to Clinicaltrialconduct-COVID19@fda.hhs.gov. I believe the ivermectin arm of the ACTIV-6 is underdosing ivermectin in the treatment arm. Patients are being randomized to 0.3 or 0.4 mg/kg of ivermectin on an empty stomach for 3 days or placebo. In the Together Trial, reported in August, patients were randomized to ivermectin 0.4 mg/kg on an empty stomach for 3 days or placebo. The study failed show convincing evidence of benefit of ivermectin. Giving patients the same or less than what was used in Together where it didn't show significant benefit or placebo seems unfair to patients and has little chance to answer the question of whether ivermectin should be used in early COVID. The dosing should be amended to something similar to that which is recommended by the FLCCC Alliance, a treatment strategy used by many of those around the world most involved with ivermectin. Much higher doses of ivermectin have proven safe. Giving ivermectin 0.4-

0.6 mg/kg with food for 5 days would be very safe. Dr. Pierre Kory, clearly the main proponent of ivermectin in the world, who has testified before the US senate and published a meta analysis, has by far the most experience with those around the world using ivermectin, pierrekory@icloud.com, 212-518-1420.

This study has major implications for the entire world where safe, cheap repurposed drugs to treat COVID are not being used. This study is much too important to fail because ivermectin was underdosed.

Sincerely,

**Michael B. Goodkin MD, FACC
doctrumpet@aol.com
484-433-8283**

Dear FDA,

I have some concerns regarding dosing of ivermectin in ACTIV-6, It is a very important issue. If ivermectin is proven to be of unequivocal value in treating early COVID-19 it would have a profound effect on the entire planet. Ivermectin appears to have nearly eliminated COVID in Uttar Pradesh, 230 million people but there are still skeptics. [COVID nearly eliminated in Uttar Pradesh](#) Many discount observational data but if true, ivermectin could be applicable to many poor countries who will not see the vaccines any time soon. Randomized trial data for ivermectin which appears more important to the vast majority of scientists, clinicians and epidemiologists, is a mess. Unfortunately I think ACTIV-6, COVID-OUT and PRINICIPLE, which give patients the same dose or less ivermectin than in Together, will not answer the question of whether early COVID patients should be treated with ivermectin. These trials should have their ivermectin

dosing altered substantially to reflect that dosing in Together was too low..

IVERMECTIN DOSING FOR COVID IN MAJOR COVID TRIALS TOGETHER, ACTIVE-6, COVID-OUT AND PRINCIPLE

How should ivermectin be administered?

All of these studies give ivermectin on an empty stomach which is how it is normally given for parasites because the FDA has recommended it. Taking it with food increases absorption 2.6 times for a 30 mg dose. The vast majority of ivermectin experts give it with food for COVID.

J Clin Pharmacology 2002 42:1122

What dose of ivermectin should be used to treat early COVID in the ongoing large randomized trials since the results of Together were reported, not clearly showing statistically significant benefit? There were problems with the trial. [Together Ivermectin Analysis](#)

It is safe to say that dosing should be something greater than the 0.4 mg/kg on an empty stomach for 3 days which was used in Together. Given the at most mild benefit in Together, it would seem that a higher dose, longer duration of therapy and/or giving it with food would be likely to show benefit, a result that would benefit everyone except drug companies. There is no significant risk of toxicity from giving it with food, giving up to 0.6 mg/kg or extending dosing to 5 days as recommended by the FLCCC Alliance who has more experience with ivermectin than any other group in the world.

ACTIVE-6

**Experimental: Arm A - Ivermectin
Ivermectin - 7-mg tablets**

Participant will be instructed to take a pre-specified number of tablets for 3 consecutive days based on their weight for a daily dose of approximately 300-400 µg/kg. One site confirmed it is given on an empty stomach on advice of the FDA.

COVID-OUT

Drug: Ivermectin

An antiparasitic medication administered as 390mcg/kg for weight category <104 kg, and 470mcg/kg for weight category >104 kg for 3 days. Site confirmed given on empty stomach

PRINCIPLE

Ivermectin is being given on an empty stomach for 3 days

Weight 45-64 kg Ivermectin 18 mg Average dose 0.32 mg/kg

Weight 65-84 kg Ivermectin 24 mg. Average dose 0.32 mg/kg

Weight >84 kg. Ivermectin 30 mg

In ACTIV-6, COVID-OUT and PRINCIPLE half the patients are getting a similar dose to Together and half are getting less.

This is from the FLCCC website. Treatment for early COVID Ivermectin¹

0.4–0.6 mg/kg per dose (take with or after a meal) — one dose daily, take for 5 days or until recovered.

Use upper dose if: 1) in regions with aggressive variants (e.g. Delta); 2) treatment started on or after day 5 of symptoms or in pulmonary phase; or 3) multiple comorbidities/risk factors

Dr. Kory's protocol seems to make a lot more sense if one wants a true test of ivermectin in early COVID. I hope you will consider altering how ivermectin is administered in ACTIV-6

Michael B. Goodkin MD, FACC