From: Stan Young [redacted] (b) (6)
Sent: 3/19/2021 6:20:17 PM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: Re: [EXTERNAL] ivermectin

good. make the data public.

Stan and Pat Young [redacted] (b) (6)

On Friday, March 19, 2021, 5:36:07 PM EDT, Woodcock, Janet <janet.woodcock@fda.hhs.gov> wrote:

Yes very close but like everything in government hair-pulling-out slow! jw

From: Stan Young <[redacted] (b) (6)>
Sent: Friday, March 19, 2021 5:03 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: [EXTERNAL] ivermectin

Janet: Any progress on a large, simple RCT? Stan

Stan and Pat Young [redacted] (b) (6)

From: Stan Young [redacted]
Sent: 1/20/2021 7:37:07 PM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: Re: Congratulations

Janet: Thanks for the note. Stan

Stan and Pat Young [redacted]

On Wednesday, January 20, 2021, 5:52:06 PM EST, Woodcock, Janet <janet.woodcock@fda.hhs.gov> wrote:

No but the group previously known as "Operation Warp Speed"/therapeutics, BARDA, and NIH/ACTIV are working hard to get a pragmatic trial set up fast, I am helping as I can. jw

From: Stan Young <[redacted]>
Sent: Wednesday, January 20, 2021 5:08 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Congratulations

Janet:

Good to see that you are acting FDA Commissioner.

You must be busy. Is someone at FDA looking into ivermectin for COVID?

Stan and Pat Young [redacted]

From: Adam, Stacey (FNIH) [T] [sadam@fnih.org]
Sent: 1/15/2021 1:08:59 PM
To: Garner, Carl [garner_carlos_o@lilly.com]; Bozzette, Sam A (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8054ed74996e46c2a49cb31ec22af84b-HHS-sam.boz]; Butterton, Joan [joan_butterton@merck.com]; De Claro, R. Angelo [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=25c4631cbb7144d4a22d53c5e5fcfdce-DECLAROR]; Draghia-Akli, Ruxandra [RDraghia@ITS.JNJ.com]; Eisner, Mark [eisner.mark@gene.com]; Gottesdiener, Keith [redacted (b) (6)]; Eric Hughes [eric.hughes@novartis.com]; Judy Currier [jscurrier@mednet.ucla.edu]; Kim, Elizabeth [elkim@deloitte.com]; LaVange, Lisa [lisa.lavange@unc.edu]; Levy, Elliot [elliottl@amgen.com]; Mellors, John W [jwm1@pitt.edu]; Menon, Sandeep [Sandeep.M.Menon@pfizer.com]; Parker, Ashley S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3f43b948b59f4e679535a8a3ebc91167-HHS-ashley.]; Patel, Naimish [naimish.patel@sanofi.com]; Peppercorn, Amanda [amanda.f.peppercorn@gsk.com]; Poole, Mike [Mike.Poole@gatesfoundation.org]; Proschan, Michael A (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=820d510db037432ab1ffafcd070ee409-HHS-proscha]; Read, Sarah W (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=72ca09ea60c74100a908211e1f7c5f6a-HHS-readsa-]; Santos, Michael R (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5d410c16ad784c24a4ee47599cafec85-HHS-msantos]; Shen, Yuan Li [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=697e41cd393a4fbab78fe028b77a20fb-SHENYU]; Stein, Peter [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d30a87acb0184261961264ba984b0a51-Peter.Stein]; Wholley, David N (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=784115e9182043d48eaa9e91761c4330-HHS-dwholle]; Buchman, Tim G (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3b2ac13394e34125b8f9d36dcebd3157-HHS-Tim.Buc]; Collins, Sylva [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=751351605a0a41f1ab97cb8a8753b432-Sylva.Colli]; Amanda Peppercorn [amanda.peppercorn@gmail.com]; Higgs, Elizabeth S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0ac36dd643c04994b3161baf825cbfc3-HHS-ehiggs-]; Koroshetz, Walter J (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4d97701b01894e15a53709b9df3e08e7-HHS-koroshe]; Timothy Burgess [timothy.burgess@usuhs.edu]; Reineck, Lora A (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=311c3ebe3a4c491db44fbf671e535f76-HHS-lora.re]; Aggarwal, Neil R (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a7e4ee23a27e4699ad1d5fb0e4e240ce-HHS-neil.ag]; Rosenberg, Yves D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5a312ca63150451cb98005b27b4a0f8b-HHS-rosenbe]; Goff, David C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1fa2747f2f704a3ba1637f2febe8bc67-HHS-david.g]; Brown, Jeremy (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=6e502731145c4045b5e088df526a710b-HHS-jeremy.]; Gadbois, Ellen L (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=680ebce054324eff90ecfff770987437-HHS-gadbois]; Culp, Michelle A (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=93cef0f5bf33475c8e44a8b2a2516251-HHS-michell]; Jacqueline Kirchner [Jacqueline.Kirchner@gatesfoundation.org]; Beigel, John H (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=db2bc96f962b4661b0494e9fa6ca6bcf-HHS-jbeigel]; Phillips, L Revell CIV DTRA RD (USA) [redacted (b) (6)] Petrovick, Martha - 0449 - MITLL [petrovick@ll.mit.edu]; [redacted (b) (6)] Sizemore, Christine F (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d39a40f80fd64c1081df4a43500560b6-HHS-christi]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]

CC: Colvis, Christine M (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d3bb5ce5263c4206885ede0146e96813-HHS-christi]; Jansen, Kathrin [kathrin.jansen@pfizer.com]; Lowy, Douglas (NCI) (b) (6); Young, John [john.young.jy3@roche.com]; Biggs, Mary [biggs.mary@gene.com]; Butcher, Tina [tina_butcher@merck.com]; Demarcus [demarcus@email.unc.edu]; Macone, Erin [erinm@amgen.com]; Melencio, Cheryl L (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=baa3813b343d4f4cb949f1b990023053-HHS-cmelenc]; Salathin, Carla [carla.salathin@novartis.com]; Menetski, Joseph M (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d8ed7bcfcbc04f338026fde223a907ae-HHS-jmenets]; Dana Carluccio [dana.carluccio@roseliassociates.com]; Rose Li Central Account [FNIH@roseliassociates.com]; Lucas Smalldon [Lucas.Smalldon@roseliassociates.com]; jennifer.j.palmer@pfizer.com; Mollica, Linda /US [Linda.Mollica@sanofi.com]; Qashu, Felicia M (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3f0b71ff369f40f9bd47c1a2968585c1-HHS-felicia]; Patterson, Amy (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a842e9e8e9e84d7b8736ddaa333145d0-HHS-amy.pat]; Rubin, Daniel B. [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=aff2818c53624c0c9c406ea1ae161987-RUBIND]; Marston, Hilary D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87f32347b819459fb55d2b7e2bacc5eb-HHS-hilary.]; Chen, Helen [qingchen@deloitte.com]; Wung, Peter /US [Peter.Wung@sanofi.com]; Hoots, Keith K (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2ebb64d11ebd42f4bb63f192e1e388ac-HHS-hootswk]; Groesch, Mary E (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=78d9da4715154e1eabcf9d0178d06b88-HHS-mary.gr]; Shipp, Allan C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=04e31be85c264b16bef9602845846e60-HHS-allan.s]; Kindzelski, Andrei L (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=202c4c81c85749ee80ee895d3b4e4132-HHS-kindzel]; Hone, David M (Dave) CIV DTRA J9 (USA) (b) (6); Reisler, Ronald B CTR USARMY DOD JPEO CBRND (USA) [(b) (6); Walker, Paula J (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5230079373904be5a42bac56b97a1a3e-HHS-walkerp]; Sorosa, Alex [asorosa@deloitte.com]; Lumsden, Joanne M (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b4248b5d666d46f8a4b522b21c7a6d4d-HHS-joanne.]

Subject: The COVID-19 Treatment Guidelines Panel's Statement on the Use of Ivermectin for the Treatment of COVID-19 https://bit.ly/2N69NqB

Dear ACTIV TX-Clinical WG,

Following onto our discussion yesterday, please find below the current treatment guidelines for ivermectin.

Thanks,

Stacey

The COVID-19 Treatment Guidelines Panel's Statement on the Use of Ivermectin for the Treatment of COVID-19

Last Updated: January 14, 2021

Recommendation

- The COVID-19 Treatment Guidelines Panel (the Panel) has determined that currently there are insufficient data to recommend either for or against the use of ivermectin for the treatment of COVID-19. Results from adequately powered, well-designed, and well-conducted clinical trials are needed to provide more specific, evidence-based guidance on the role of ivermectin for the treatment of COVID-19.

Rationale

Ivermectin is an antiparasitic drug that is approved by the Food and Drug Administration (FDA) for the treatment of onchocerciasis and strongyloidiasis. Ivermectin is not FDA-approved for the treatment of any viral infection. In general, the drug is well tolerated. It is currently being evaluated as a potential treatment for COVID-19.

Antiviral and Anti-Inflammatory Effects of Ivermectin

Reports from in vitro studies suggest that ivermectin acts by inhibiting the host importin alfa/beta-1 nuclear transport proteins, which are part of a key intracellular transport process that viruses hijack to enhance infection by suppressing the host antiviral response.[1,2] In addition, ivermectin docking in vitro may interfere with the attachment of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein to the human cell membrane.[3]

Ivermectin has been shown to inhibit the replication of SARS-CoV-2 in cell culture. However, pharmacokinetic and pharmacodynamic studies suggest that ivermectin doses up to 100-fold higher than those approved for use in humans would be required to achieve the plasma concentrations necessary to duplicate the drug's antiviral efficacy in vitro.[4,5] Even though ivermectin appears to accumulate in lung tissue, with the doses used in most clinical trials, predicted systemic plasma and lung tissue concentrations are much lower than 2 μM, the half-maximal inhibitory concentration (IC_{50}) against SARS-CoV-2 in vitro.[6,7]

Ivermectin demonstrates potential anti-inflammatory properties in some in vitro studies,[8,9] properties which have been postulated to be beneficial in the treatment of COVID-19.[10]

Clinical Data

Since the last revision of the Ivermectin section of the Guidelines, the results of several randomized trials and retrospective cohort studies of ivermectin use in patients with COVID-19 have been published in peer-reviewed journals or made available as preliminary, non-peer-reviewed reports. Some clinical studies showed no benefits or worsening of disease after ivermectin use,[11-14] whereas others reported shorter time to resolution of disease manifestations attributed to COVID-19,[15-18] greater reduction in inflammatory markers,[16,17] shorter time to viral clearance,[11,16] or lower mortality rates in patients who received ivermectin than in patients who received comparator drugs or placebo.[11,16,18]

However, most of the studies reported to date had incomplete information and significant methodological limitations, which make it difficult to exclude common causes of bias. The missing information and limitations include the following:

- The sample size of most of the trials was small.
- Various doses and schedules of ivermectin were used.
- Some of the randomized controlled trials were open-label studies in which neither the participants nor the investigators were blinded to the treatment arms.
- In addition to ivermectin or the comparator drug, patients also received various concomitant medications (e.g., doxycycline, hydroxychloroquine, azithromycin, zinc, corticosteroids), confounding assessment of the true efficacy or safety of ivermectin.
- The severity of COVID-19 in the study participants was not always well described.
- The study outcome measures were not always clearly defined.

Because of these limitations, the Panel cannot draw definitive conclusions about the clinical efficacy or safety of ivermectin for the treatment of COVID-19. Results from adequately powered, well-designed, and well-conducted clinical trials are needed to provide more specific, evidence-based guidance on the role of ivermectin for the treatment of COVID-19.

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From: Gennaro D'Urso [gdurso@geneticnetworks.com]
Sent: 1/7/2021 4:23:27 PM
To: Gennaro D'Urso [gdurso@geneticnetworks.com]
Subject: Fwd: Automatic reply: Genetic Networks Update

---------- Forwarded message ---------
From: **Gennaro D'Urso** <gdurso@geneticnetworks.com>
Date: Thu, Jan 7, 2021 at 3:21 PM
Subject: Re: Automatic reply: Genetic Networks Update
To: Adam, Stacey (FNIH) [T] <sadam@fnih.org>
Cc: Chen, Helen <qingchen@deloitte.com>, Appell, Evan <eappell@deloitte.com>, Leland Hartwell <Lee.Hartwell@asu.edu>

Dear Stacey,

Thank you so much for moving this forward. Lee and I would just like to emphasize how important it is to put a meeting on the calendar to present our most recent results to the preclinical group.

We have heard through several of our contacts at different agencies throughout the govt that ivermectin is getting a great deal of attention recently. We identified ivermectin early this year soon after the pandemic occurred and identified a novel mode of action (MOA) for this drug. This MOA is shared with 7 other safe drugs we identified using our proprietary platform, some of which demonstrate more potential promise than ivermectin. We are now ready to disclose drug names for our best candidates and determine the next best steps. There is no doubt in our minds that this work will result in saving many lives.

We would suggest a one hour meeting to hear our story.

If you can help to make that happen we would be grateful.

Sincerely,

Gennaro and Lee

1951 NW 7th Ave, Suite 300
Miami, FL 33136
www.geneticnetworks.com
1-888-844-9743

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1951 NW 7th Ave, Suite 300
Miami, FL 33136
www.geneticnetworks.com
1-888-844-9743

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 1/20/2021 3:17:26 PM
To: Freire, Maria (FNIH) [T] [mfreire@fnih.org]
Subject: RE: Soo happy!

Oh dear! I am determined to get some of these repurposed drugs evaluated! jw

---

From: Freire, Maria (FNIH) [T] <mfreire@fnih.org>
Sent: Wednesday, January 20, 2021 3:08 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Re: Soo happy!

Yes, you are probably crazy but the agency desperately needs you! It can't be fun given what is going on but you are the right person.

Thanks for looking into ivermectin. It would be great to have an answer. (b) (6) in Peru right now and they dispense it like candy. The other day the headline in Spanish was "FDA approves Ivermectin for COVID treatment" and cited ScienceDirect. The medical community was elated and felt vindicated. Well, not so fast. When I went to the source article, the headline in English was "FDA-approved drug ivermectin inhibits replication of SARS-CoV-2". Go try to explain the translation glitch - I nearly got skinned alive.

Hang in! M.

From: "Woodcock, Janet" <Janet.Woodcock@fda.hhs.gov>
Date: Wednesday, January 20, 2021 at 1:43:19 PM
To: "Freire, Maria (FNIH) [T]" <mfreire@fnih.org>
Subject: RE: Soo happy!

Thanks, and great to hear from you. Hope you are well. I'm probably crazy to do this, but I think the Agency needs me at this point.

We are trying to put together a pragmatic trial that can include ivermectin. I'll do everything I can to help get that up and funded.

TX jw

From: Freire, Maria (FNIH) [T] <mfreire@fnih.org>
Sent: Wednesday, January 20, 2021 1:39 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Soo happy!

Janet, I am SO happy you will be interim FDA Commissioner. If there is anything I can do to help, let me know.

The world owes you a HUGE debt of gratitude- not only for all your work at FDA but for your super-human efforts at OWS. THANK YOU!

Onward! María

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 1/15/2021 11:47:50 AM
To: Robert Califf, M.D. (b) (6)
Subject: RE: Congrats!

Say ivermectin or fluvoxamine for COVID19 outpatients. jw

From: Robert Califf, M.D. (b) (6)
Sent: Friday, January 15, 2021 11:47 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Re: Congrats!

Totally virtual? What's the topic?

rmc

From: Janet Woodcock <Janet.Woodcock@fda.hhs.gov>
Date: Friday, January 15, 2021 at 8:01 AM
To: "Robert Califf, M.D." (b) (6)
Subject: RE: Congrats!

(b) (5) jw

From: Robert Califf, M.D. (b) (6)
Sent: Thursday, January 14, 2021 2:10 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Congrats!

(b) (5)

rmc

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 1/13/2021 1:02:09 PM
To: Alexis Lieberman [(b) (6)]
Subject: RE: Information re Covid treatment

FDA is not a funding agency. NIH, BARDA etc for these sorts of trials. And it takes a long time. The ACTIV coalition at NIH has looked at ivermectin numerous times and have not picked it up. jw

From: Alexis Lieberman <(b) (6)>
Sent: Wednesday, January 13, 2021 12:13 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Re: Information re Covid treatment

It's the funding that is an issue. Can the FDA fund? If so, I can do the rest.

Alexis Lieberman

On Jan 13, 2021, at 11:12 AM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

You can get a group of clinicians and a company to provide drug and placebo, write a protocol, get an IND from FDA and get IRB clearance. Not so easy. Jw

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From: Alexis Lieberman <(b) (6)>
Date: January 13, 2021 at 11:09:00 AM EST
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Re: Information re Covid treatment

What can I do to help set up that pragmatic trial that you mentioned?

Alexis Lieberman

On Jan 13, 2021, at 10:54 AM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

I spy is for critical patients. Not sure that is the best test case. Jw

---

From: Alexis Lieberman <(b) (6)>
Date: January 13, 2021 at 10:01:16 AM EST
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>, Robert Malone <(b) (6)>
Subject: Re: Information re Covid treatment

Is it too late to set up that study now? I am in contact w Robert Malone — he is trying to figure out funding for such a study, as he has an open arm in the I-Spy trial. Are you and he talking about it?

Alexis Lieberman

On Jan 13, 2021, at 8:38 AM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

Thank you. It is certainly being evaluated by the scientific teams at ACTIV and OWS, so it is not ignored. I wish I had set up a large pragmatic outpatient screening study at the outset of this, we have a number of approved oral agents that it would be good to test. Thanks for writing. Janet W

-----Original Message-----
From: Alexis Lieberman <(b) (6)>
Sent: Tuesday, January 12, 2021 10:00 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Re: Information re Covid treatment

Dear Dr. Woodcock,
I am writing again to urge that the FDA allow the use of ivermectin for Covid. Since I wrote in November, multiple other positive studies have been completed. Unfortunately, studies are not being completed in the United States as the monoclonal antibody studies have exclusivity contracts with the emergency departments that are doing research. I am aware that there has been a recent FDA review of the international studies showing that ivermectin reduces morbidity and mortality in for Covid especially when used as postexposure prophylaxis and early in disease. The sooner the FDA endorses this drug, the sooner a broad swath of physicians will use it. This drug, in addition to a wide vaccine strategy, has the potential to transform the pandemic in the United States.
Thank you,
Alexis Lieberman, MD

On Nov 11, 2020, at 5:58 PM, Alexis Lieberman <(b) (6)> wrote:

Dear Dr. Woodcock,
As a practicing pediatrician in Philadelphia, I am writing to request that you use your role on the Covid task force to advocate for an immediate, large-scale RCT for ivermectin early in disease. I include summaries of studies done so far on ivermectin that point to its promise.

As you know, Ivermectin is an anti-parasitic drug that is used widely throughout the world and is generally very well-tolerated with only very RARE side effects in those who do not have parasites, primarily limited to allergic reactions. The drug is proposed to prevent the virus from getting into the nucleus of the human cell. While the initial Monash in-vitro study used very high doses and the early Surgisphere study was discredited, since that time, there have been a dozen positive clinical studies. Surely there is enough evidence now to warrant a large-scale, government-funded RCT.

This inexpensive, off-patent drug will not make money for any drug company. Therefore, it falls to the government to take steps to fund a trial. I implore you to advocate for this!

STUDIES AND LINKS REGARDING IVERMECTIN:

10/29/30. India: Two doses of ivermectin, given 72 hours apart, prophylactically, was associated with a 73% reduction of COVID-19 infection among healthcare workers for the following one-month, in a case control study of 186 pairs.
https://www.medrxiv.org/content/10.1101/2020.10.29.20222661v1

10/26/30: Baghdad, Iraq: A recent study done Baghdad compared COVID patients who took ivermectin or did not. In this, 10% of the non-Ivermectin group progressed to severe disease well only 4% of the ivermectin group did. In that same study there was a 27% mortality rate for those who did not take over motion versus 18% and those who did.
https://www.medrxiv.org/content/10.1101/2020.10.26.20219345v1?fbclid=IwAR0M7sh3HnP3rDM5FRyiM34RsBFWBoXDcRfP3Nz4Yaw9Ia7YAo8FMmE4rGY

9/28/20: Bangladesh: In this retrospective study, they compared patients who received Ivermectin with those who

receive the standard of care. They found that 46% of the standard of care patients required oxygen and 8% went to the intensive care unit. This was compared to those who did receive ivermectin, in which 9% required oxygen and only 1% went to the intensive care unit. https://www.trialsitenews.com/mymensingh-medical-college-retrospective-study-ivermectin-superior-to-standard-of-care-for-covid-19-patients/

8/28/20: Preventive study from Egypt showing for the first time a large reduction in covid contraction for family members taking prophylactic dose of Ivermectin when there is an infected person in the same household. Household contacts who did not take ivermectin had a 58% rate of contracting Covid, compared to only 7% of those who did take ivermectin.
https://clinicaltrials.gov/ProvidedDocs/61/NCT04422561/Prot_SAP_000.pdf

8/26/20: Bangladesh. 400 patients were randomized to either receive ivermectin or placebo. In that study 18% of the placebo patients progressed to clinical deterioration while only 9% of those with ivermectin deteriorated. In that study they also compared percentage of patients who had early clinical improvement within a week, and of those without Ivermectin, 44% improved quickly while of those with Ivermectin, 60% improved quickly.
https://clinicaltrials.gov/ProvidedDocs/31/NCT04523831/Prot_ICF_000.pdf

7/8/20 Baghdad, Iraq: This study compared hospitalized patients with mild to moderate symptoms who took ivermectin or did not. Those who did not had a hospital stay of 12 days on average, vs 7% in those who did take ivermectin.
https://www.medrxiv.org/content/10.1101/2020.07.07.20145979v1.full.pdf

6/30/20 Dominican Republic Data:
https://www.trialsitenews.com/president-of-dominican-republic's-largest-private-health-group-discusses-the-success-of-ivermectin-as-a-treatment-for-early-stage-covid-19/

6/28/20 Bangladesh Data (mild to moderate cases, comparison with hydroxychloroquine/azithromycin). This study is not statistically significant but showed a trend of recovery in eight days with ivermectin versus nine without.
https://www.trialsitenews.com/ivermectin-study-reveals-fantastic-results-100-of-60-patients-better-in-an-average-of-just-under-6-days/

6/10/20 Florida Data (first U.S. data, on hospitalized patients). This is a retrospective intensive care unit study in which those who did not receive ivermectin had a 25% mortality rate while those who did receive ivermectin had a 15% mortality rate. It has since been published in a peer-reviewed journal.
https://journal.chestnet.org/article/S0012-3692(20)34898-4/fulltext

5/2/20 Peru Data: areas of the country where ivermectin was used have a lower case rate and lower fatality rate than areas where ivermectin was not used.
https://www.docdroid.net/J8wuZlb/ivermectin-studyesen-pdf

3/2020: Australian study that showed that high doses of ivermectin killed the Covid virus in a test tube study.
https://research.monash.edu/en/publications/the-fda-approved-drug-ivermectin-inhibits-the-replication-of-sars

The FLCC, a US based group of colleagues with over 200 years of combined experience in Critical Care and Emergency Medicine, as well as long-standing shared interests in developing effective treatments for critical illnesses including sepsis, is a working group devoted to creating a treatment protocol against COVID-19.
They developed an inpatient Covid protocol which has lead to a mortality rate of 4-10%, compared to the world average of 23%.
They have now developed a prophylactic and early outpatient combination treatment protocol for COVID-19 called I-Mask+.
https://covid19criticalcare.com/wp-content/uploads/2020/11/FLCCC-IVERMECTIN-Protocol.pdf

This protocol recommends ivermectin, vitamins C and D, Zinc, melatonin and, for adults only, aspirin.

Their rationale is based on multiple studies as well as real-world evidence comparing countries using ivermectin, such as Peru, Brazil and Haiti, to those not using it, such as the Dominican Republic and the US.

Here is the introductory video from FLCC:
https://vimeo.com/473929788/382c386d60

Thank you for your consideration,
Alexis Lieberman, MD
Advocare Fairmount Pediatrics

From: Stan Young [(b) (6)]
Sent: 1/21/2021 1:48:32 PM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: Florida study
Attachments: Rajter 2020 ivermectin propensity.pdf

Janet: The attached study looks good to me. Florida. Observation, but there was careful control of confounders. Someone might ask for the data set. Small n=~280. If you all are able to get the data set, I'm willing to give it a look also.

Stan and Pat Young (b) (6)

From: Geoffrey Taylor [redacted] (b) (6)
Sent: 3/26/2021 6:51:27 AM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: [EXTERNAL] British Ivermectin Recommendation Development Panel - Response to EMA Statement on Ivermectin for Covid-19

Janet
I thought you might be interested.
Best wishes
Geoff Taylor

https://trialsitenews.com/british-ivermectin-recommendation-development-panel-response-to-ema-statement-on-ivermectin-for-covid-19/

From: Stan Young [(b) (6)]
Sent: 3/24/2021 9:36:13 PM
To: Amar Bhat [abhat@reaganudall.org]
CC: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: [EXTERNAL] Re: COVID-19 Therapeutics/Vaccines Evidence Accelerator Weekly Update
Attachments: ivermectin meta-analysis.pdf; Ivermectin NIH.docx; Ivermectin Patel 2020.pdf

Amar: The attached items relate to ivermectin. The two studies look quite sound to me.

Stan and Pat Young (b) (6)

On Monday, March 22, 2021, 9:40:09 AM EDT, Amar Bhat <abhat@reaganudall.org> wrote:

Stan,

So far, we haven't had any discussions regarding ivermectin. I have seen in press, etc. some references to use of ivermectin, but we have not scheduled any discussions regarding repurposing of ivermectin for COVID-19 so far. If you would like to suggest something (along with potential presenters), please let me know.

Regards,
Amar

Amar Bhat, PhD
Reagan-Udall Foundation for the FDA
M: (b) (6)

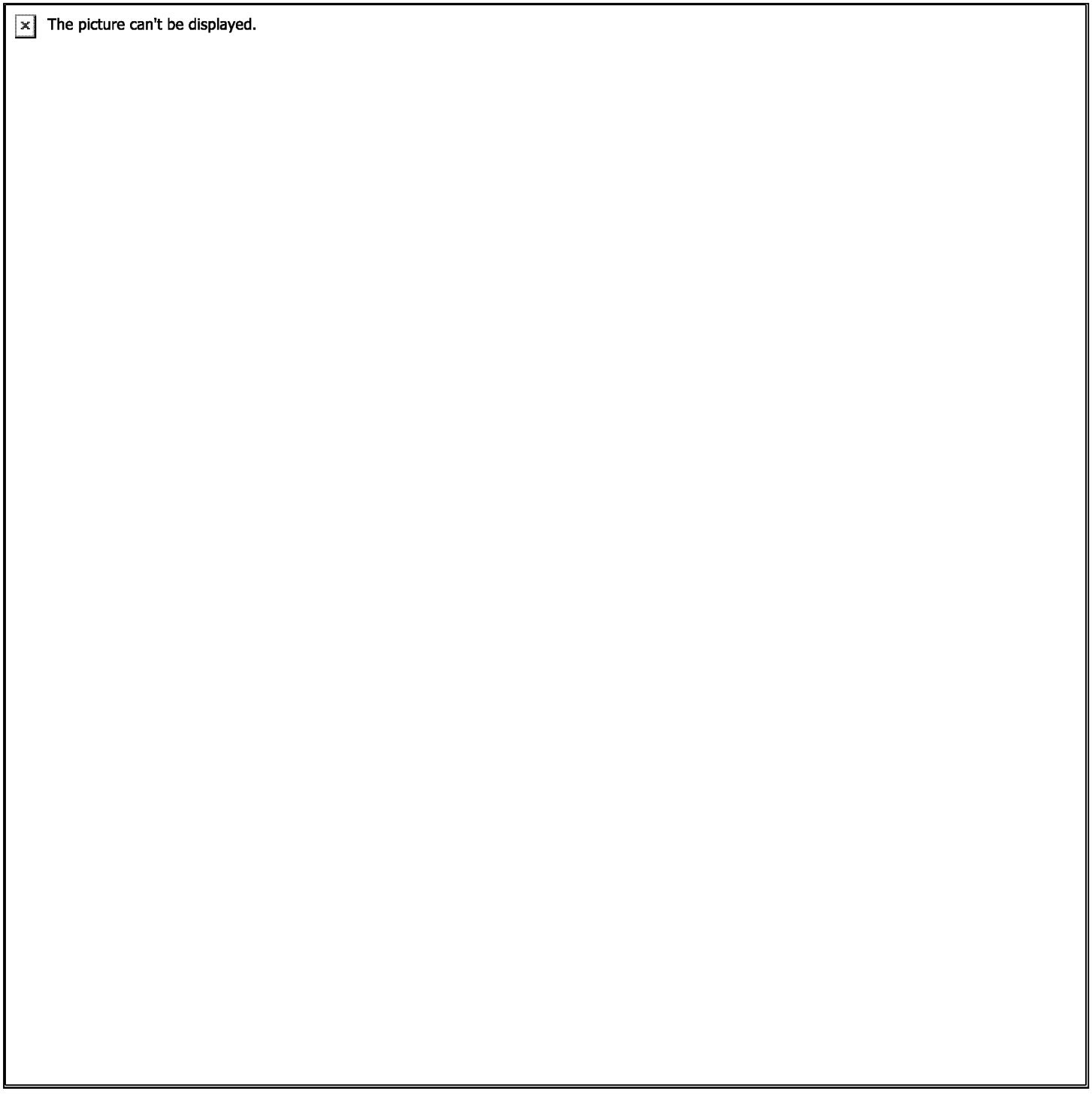
From: Stan Young <(b) (6)>
Reply-To: "(b) (6)"
Date: Friday, March 19, 2021 at 10:02 PM

To: Amar Bhat <abhat@reaganudall.org>
Subject: Re: COVID-19 Therapeutics/Vaccines Evidence Accelerator Weekly Update

Amar: I follow lots of threads. Please point me to any reganudall thread on ivermectin. Stan

Stan and Pat Young (b) (6)

On Friday, March 19, 2021, 6:44:19 PM EDT, Amar Bhat <admin@reaganudall.org> wrote:



You are receiving this message because you are noted as a participant in the Therapeutics workstream of the COVID-19 Evidence Accelerator. This communication provides a recap of the

week's activity and any requests for follow-up. If you are no longer interested in COVID-19 Evidence Accelerator activity, please let us know and we will update our distribution list.

We had a great week here at the Evidence Accelerator with the start of our Vaccines workstream. On Thursday, we expanded our discussions to include vaccine topics during our Therapeutics Lab meeting. Going forward, we will continue to feature Vaccine-specific topics alongside our Therapeutics topics, during joint Lab meetings on the 1st and 3rd Thursdays, 3-4pmET timeslot.

Note that we will shortly be extending calendar invitations for all COVID-19 Evidence Accelerator Lab meetings through the end of summer.

Upcoming Meetings

- Mar 24th – Therapeutics Parallel Analysis (Accelerators-only)
- Mar 25th – Post-Acute Sequelae of SARS-CoV-2 (PASC) Infection Working Group
- **April 1st – Therapeutics/Vaccines Lab meeting (Topics: Update on Alpha-1 blockers, COVID-19 data resource)**

Evidence Accelerator in the news:

- Harnessing a watershed moment for real-world data - Fierce Healthcare
- COVID-19 Diagnostics Market - Digital Journal
- Shot in the Arm: COVID-19 Boost to RWD - PharmaVOICE

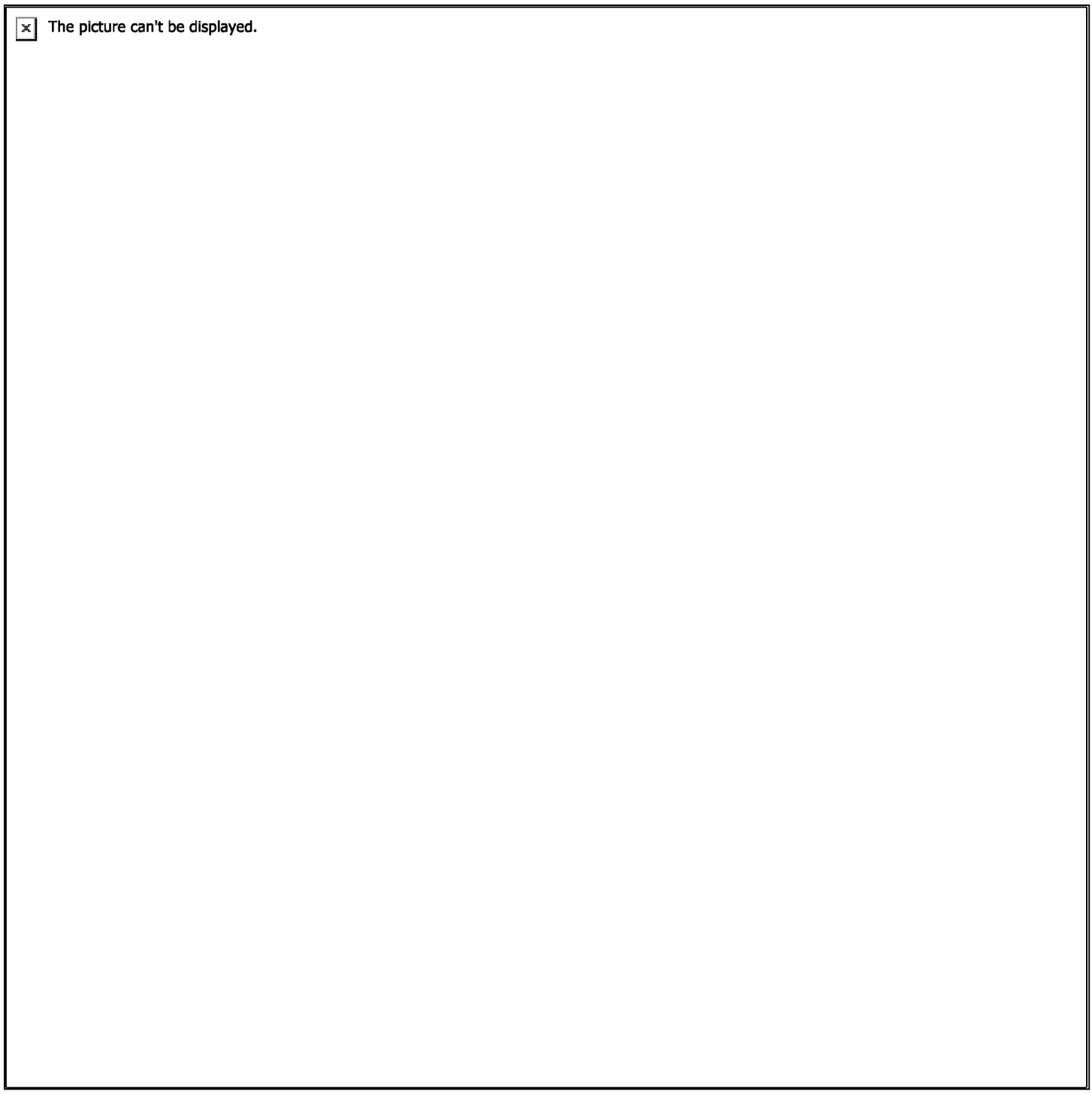
Therapeutics/Vaccines Workstream

Thursday Afternoon "Lab" Meeting

As mentioned above, we had our inaugural meeting of the new Vaccines workstream. To start us off, we had a wide-ranging conversation with Dr. Michael Osterholm of the Center for Infectious Disease Research and Policy (CIDRAP) at the University of Minnesota, facilitated by Dr. Patrick Ryan of OHDSI. In his remarks, Dr. Osterholm noted the need for nimbleness in responding to this public health crisis, whether in regard to vaccine deployment or in tracking the spread of variants. He was followed by Drs. Steve Anderson and Richard Forshee of FDA's Center for Biologicals Evaluation

Research (CBER) who provided an overview of CBER's system for vaccine safety surveillance, working in tandem with other U.S. Government agencies such as CMS, CDC and the VA. CBER's slides are available on the Evidence Accelerator website. Finally, we were introduced to Heidi the Hypothetical Patient and some of her "friends" by Dr. Donna Rivera of FDA's Oncology Center of Excellence. Participants of our Diagnostics Lab meetings will remember Heidi as our hypothetical patient whose data journey helps us illustrate data flows (or lack-of-flow and interoperability) as patients encounter the healthcare system.

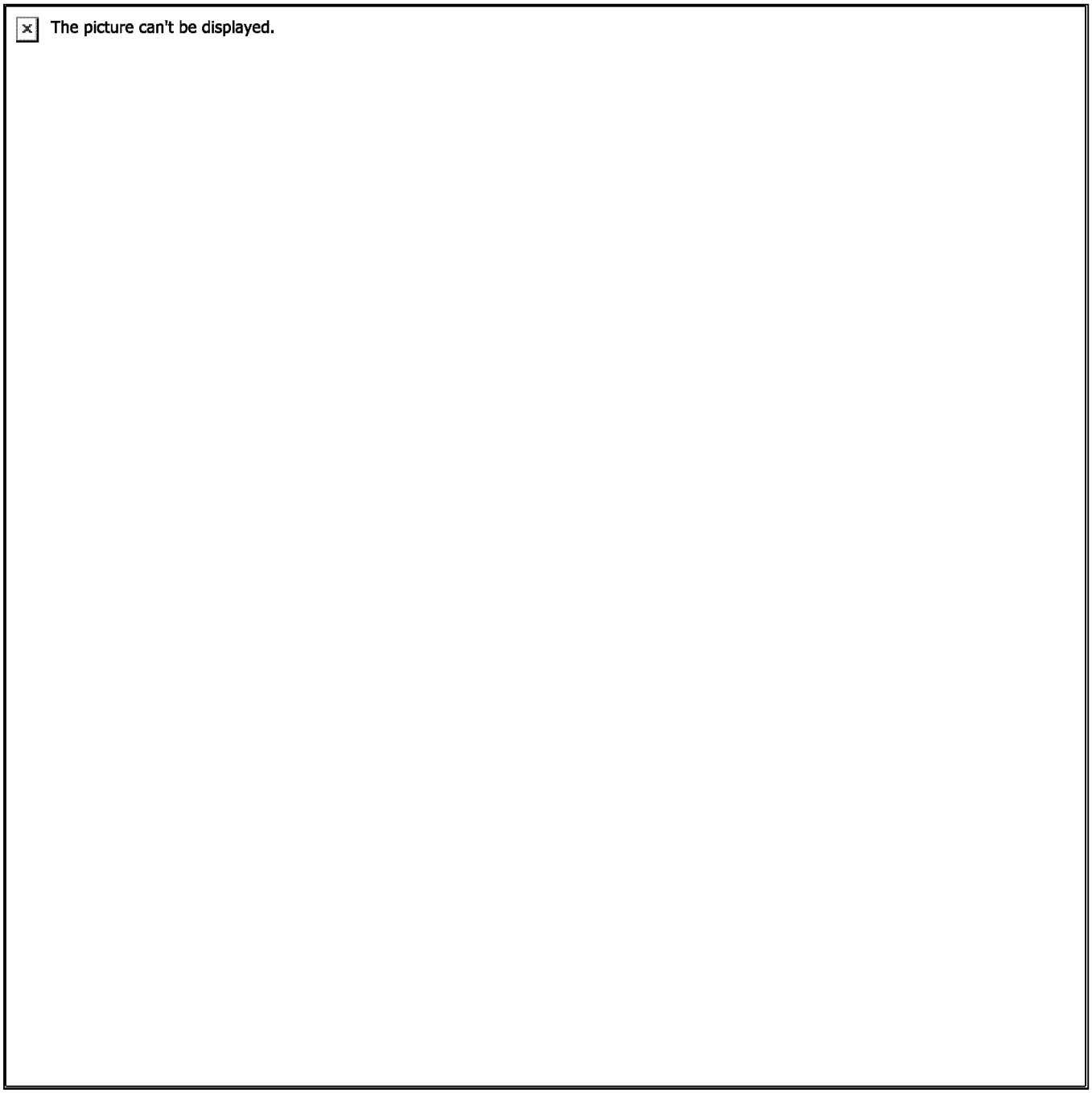
Below is our data visualization highlight, showing current status in COVID-19 vaccine rollout in the United States.



Source: Johns Hopkins Coronavirus Resource Center

Click Here for Therapeutics Lab Meeting Summaries

Therapeutics Parallel Analysis Workgroup



We are pleased to announce that the first manuscript of the Therapeutics Parallel Analysis work group has been published. The article, COVID-19 Evidence Accelerator: A parallel analysis to describe the use of Hydroxychloroquine with or without Azithromycin among hospitalized COVID-19

patients, is now available online and we invite you to take a look. Our appreciation to all who contributed to this work and we look forward to our next publications.

This week, in our Therapeutics PA Accelerators-only meeting, we met to review and finalize the approach to age coding and "small numbers" in our Natural History of Coagulopathy question set. In the remdesivir portion of the meeting, we discussed some Aim 2 protocol changes to how we handle patients with poor prognoses who were administered remdesivir as a last resort, as opposed those who were administered remdesivir in the first two days after admission.

Next week will be our Accelerators-only meeting, Wednesday, March 24th, 12-1pmET.

Post-Acute Sequelae of SARS-CoV-2 (PASC): We are preparing materials for the first larger convening of the Post-Acute Sequelae of SARS-CoV-2 (PASC) Infection Working Group (planned for March 25 at 3pmET). Preparation includes summarizing responses and themes from the survey distributed last month. Additionally, we are collecting feedback on the updated concept proposal from our Steering Committee. We will summarize the responses to the Accelerator survey and the concept proposal and present to the PASC Working Group as our call to action.

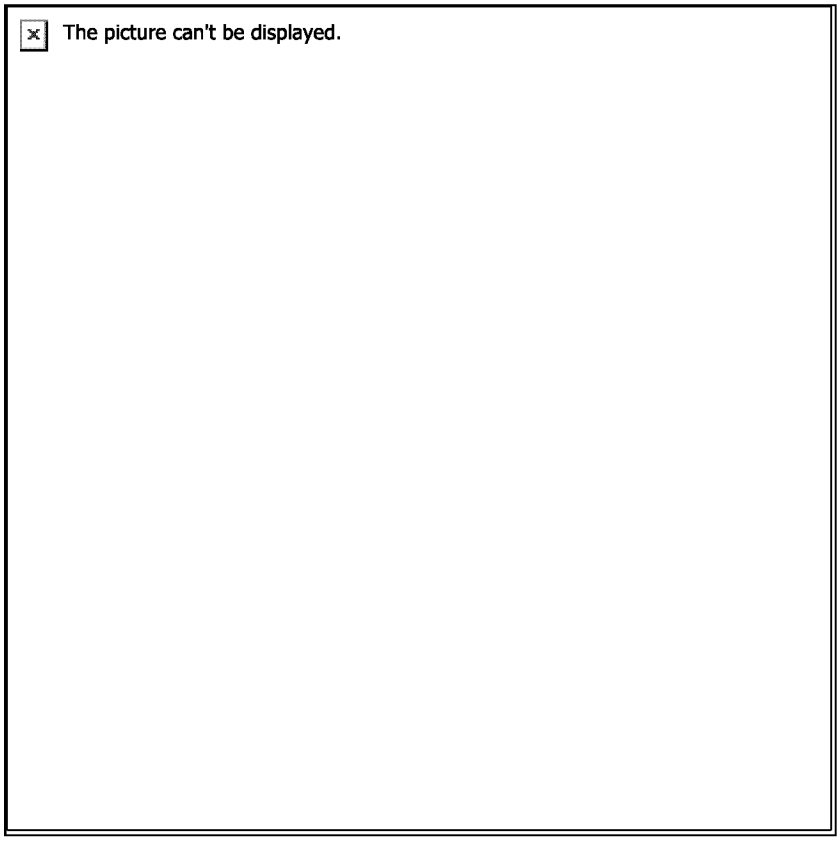
***Action Requests*:**

- Coagulopathy Accelerators: Please let Dr. Jeff Allen know if you would be interested in examining the use of oral anticoagulants within your dataset as an addendum to the natural history work underway.
- Remdesivir Accelerators: If you haven't already, please send in your Aim 1 tables so that we can finalize our Aim 2 protocol.
- PASC: If you are interested in joining the PASC Working Group, please email Dr. Alecia Clary.
- Evidence Accelerator Blog: if you have an idea for future post and/or would like to submit a post for consideration, please let me know.
- Members of our Accelerators-only meetings are invited to join our Online Community Forum. Questions or need a fresh link? Email me.

Finally, please let me know if you are no longer interested in COVID-19 Evidence Accelerator activity and we will update our distribution list.

Regards,

Amar Bhat
Chief Operating Officer
Reagan-Udall Foundation for the FDA



Contact Us

Reagan-Udall Foundation for the FDA
1900 L Street, NW Suite 835
Washington, District of Columbia 20036
202-849-2075
admin@reaganudall.org

From: Steve Kirsch [(b) (6)]
Sent: 1/25/2021 11:11:19 AM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: why some IVM outpatient studies showed no response

Of course…. All the studies I've seen were given an inadequate dose!

Once infected, the recommended dose is .2mg/kg each day for at least 3 days and ideally 5 days.

The problem was dosing was wild west until the FLCCC came out with their protocol guidelines.

Not following the guidelines is just like what happened with the Marik Sepsis Protocol. The RCTs did NOT follow the protocol (it must be given within 6 hours or it WILL fail) so they couldn't replicate his results (because they spent 24 hours to enroll) and there was NO effect. Marik was labelled a quack. Marik went 150 or so sepsis patients in a row on his sepsis protocol and never lost a single one. NOBODY is that "lucky". To this day, this is not generally known and we lose 10M people a year to unnecessary death due to it.

It you look at the studies with 3 -5 days of IVM at adequate dose I think you'll find they are all effective. I'll check with Paul.

-steve

From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Sent: Monday, January 25, 2021 4:55 AM
To: Steve Kirsch [(b) (6)]
Subject: RE: Ivermectin is being treated unfairly by the NIH panel

There have been studies in outpatients that are not encouraging. Nevertheless we are trying to set up a pragmatic trial. Janet W

From: Steve Kirsch <[(b) (6)]>
Sent: Monday, January 25, 2021 1:49 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Ivermectin is being treated unfairly by the NIH panel

Has anyone filed for an EUA for IVM?

If I had to pick another highly effective drug for COVID, that would be it. The NIH guidelines panel did a very poor job on this drug and they VERY BADLY misinterpreted one of the studies and downgraded IVM to neutral. I don't think we need more data on this. We just need another set of eyes to clearly look at the data that is out there and if they have any questions, they should email pierre or paul who are the two world experts on using this drug for COVID. They wrote a great response to the NIH which any evaluator should study.

It's not just me that believes that. Emory Med School Dean is a strong proponent of IVM and do so after a great deal of study. More recently, an independent researcher who does Cochrane reviews, Tess Lawrie in the UK, did her own independent assessment of the evidence and was so stunned by what she found she's been working unpaid to try to convince other scientists of the merit of this drug, e.g., watch at 6minutes at https://www.youtube.com/watch?v=rHPkR6QRcCc&feature=youtu.be.

This drug is getting treated unfairly. Is there any way you can help right that wrong?

-steve

From: Adam, Stacey (FNIH) [T] [sadam@fnih.org]
Sent: 1/22/2021 3:36:41 PM
To: Adrian Hernandez, M.D. [adrian.hernandez@duke.edu]
CC: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]; Eric Hughes [eric.hughes@novartis.com]; Read, Sarah W (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=72ca09ea60c74100a908211e1f7c5f6a-HHS-readsa-]; Appell, Evan [eappell@deloitte.com]; Sorosa, Alex [asorosa@deloitte.com]; Nasr, Hana [hanasr@deloitte.com]; Dr Eric Perakslis, Ph.D. [eric.perakslis@duke.edu]; Tyrus Rorick [tyrus.rorick@duke.edu]; Dana Carluccio [dana.carluccio@roseliassociates.com]; Rose Li Central Account [FNIH@roseliassociates.com]; Wholley, David N (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=784115e9182043d48eaa9e91761c4330-HHS-dwholle]; Lauren Cohen [lauren.w.cohen@duke.edu]; Chen, Helen [qingchen@deloitte.com]
Subject: RE: Summary of the Potential Pragmatic Trial Discussion with PCORnet

Thanks, Adrian,

This is great news to hear. I am working right now to find time on Janet and Cliff's calendars to plan the next larger meeting as we have a couple of other interested groups that might be able to lead as well or collaborate with your team to expand the reach of the trial. We would discuss this at the next meeting with all the groups.

Thanks for following up!

Best,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: **(301) 435-8364** | Mobile: [redacted] (b) (6)

From: Adrian Hernandez, M.D. <adrian.hernandez@duke.edu>
Sent: Friday, January 22, 2021 3:30 PM
To: Adam, Stacey (FNIH) [T] <sadam@fnih.org>
Cc: Woodcock, Janet (FDA/CDER) <Janet.Woodcock@fda.hhs.gov>; Lane, Cliff (NIH/NIAID) [E] <[redacted] (b) (6)>; Eric Hughes <eric.hughes@novartis.com>; Read, Sarah (NIH/NIAID) [E] <[redacted] (b) (6)>; Appell, Evan <eappell@deloitte.com>; Sorosa, Alex <asorosa@deloitte.com>; Nasr, Hana <hanasr@deloitte.com>; Dr Eric Perakslis, Ph.D. <eric.perakslis@duke.edu>; Tyrus Rorick <tyrus.rorick@duke.edu>; Dana Carluccio <dana.carluccio@roseliassociates.com>; Rose Li Central Account <FNIH@roseliassociates.com>; Wholley, David (FNIH) [T] <dwholley@fnih.org>; Lauren Cohen <lauren.w.cohen@duke.edu>; Chen, Helen <qingchen@deloitte.com>
Subject: Re: Summary of the Potential Pragmatic Trial Discussion with PCORnet

Stacey

We met this afternoon with the PCORnet and PCORI leadership and everyone agrees this would line up with what we've done before.

Let us know any next steps.

Adrian

From: "Adam, Stacey (FNIH) [T]" <sadam@fnih.org>
Date: Wednesday, January 20, 2021 at 10:48 AM
To: "Adrian Hernandez, M.D." <adrian.hernandez@duke.edu>, Amanda Windham <awindham@duke.edu>, Lauren Cohen <lauren.w.cohen@duke.edu>, "Chen, Helen" <qingchen@deloitte.com>
Cc: Janet Woodcock <Janet.Woodcock@fda.hhs.gov>, "Lane, Cliff (NIH/NIAID) [E]" <[redacted] (b) (6)>, Eric Hughes <eric.hughes@novartis.com>, "Read, Sarah (NIH/NIAID) [E]" <[redacted] (b) (6)>, "Appell, Evan" <eappell@deloitte.com>, "Sorosa, Alex" <asorosa@deloitte.com>, "Nasr, Hana" <hanasr@deloitte.com>, "Dr Eric Perakslis, Ph.D." <eric.perakslis@duke.edu>, Tyrus Rorick <tyrus.rorick@duke.edu>, Dana Carluccio <dana.carluccio@roseliassociates.com>, Rose Li Central Account <FNIH@roseliassociates.com>, "Wholley, David (FNIH) [T]" <dwholley@fnih.org>
Subject: Summary of the Potential Pragmatic Trial Discussion with PCORnet

Dear ACTIV and PCORnet Teams,

Please find attached the summary and action items from our call yesterday for everyone's reference. In addition, please find the meta-analysis on ivermectin that I referred to yesterday at this website: https://ivmmeta.com/.

We will be back in touch to arrange the larger meeting once I know when the ACTIV leads have availability to discuss.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Foundation for the National Institutes of Health
Direct: **(301) 435-8364** | Mobile: [redacted] (b) (6)
fnih.org
11400 Rockville Pike, Suite 600, North Bethesda, MD 20852

Sent: 3/13/2021 8:45:38 AM
To: Geoffrey Taylor [(b) (6)]
Subject: RE: [EXTERNAL] Ivermectin

Thank you for writing. The USG has known about the interest in ivermectin since last summer, and we have been reviewing data as it becomes available. What you read was FDA legal-speak roughly meaning that there are not any applications in-house, in other words, we don't have a data submission. We are not allowed to say whether or not we are reviewing applications for investigational drugs due to confidentiality concerns. I would not expect an application to be submitted for ivermectin, just as we did not get one for dexamethasone although corticosteroids have become standard of care in the US for the severe stage of COVID-19. I knew about the Ivermectin Recommendation group, although I have not reviewed their analysis in detail.

Obviously an oral product with good anti-viral activity and good safety would be a tremendous boon in this disease. There has been concern that at usual tolerated doses intracellular concentrations are not high enough with ivermectin to achieve this goal. There is an effort ongoing to formally test ivermectin in an adequately powered trial here in the US.

At the moment we have monoclonal antibodies that are highly effective in inhibiting disease progression and have been shown (although not fully FDA reviewed) in two independent trials to cut hospitalization and death by greater than 75% when administered early to high risk outpatients. There are obvious problems in administration of monoclonals but hundreds of thousands of infusions have been done..

We hope that oral direct antivirals will emerge into efficacy trials soon.

Janet Woodcock

-----Original Message-----
From: Geoffrey Taylor <(b) (6)>
Sent: Saturday, March 13, 2021 7:50 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: [EXTERNAL] Ivermectin

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Janet

I just read the following from a March 8 FDA release: " The FDA said initial research is underway, but the agency has not yet reviewed any data to support the use of ivermectin to treat or prevent COVID-19."

If that is true, and the FDA, unlike the NIH, hasn't reviewed any data after sixteen successful human trials of ivermectin that I know of, the first reporting in May 2020, then that is a matter of the utmost concern. It is truly sad for the very large numbers of US residents who have passed away, their friends and their families. And it is ongoing.

One metaanalysis, which I have just seen, records another 35 trials.

One reason people would turn to veterinary formulations, is that they are precluded by the authorities from being prescribed a cheap drug with a long history of very safe use.

So I pose the question: Cui bono?

Best wishes
Geoff Taylor, Perth

I am a member of the British Ivermectin Recommendation Development group, which held a worldwide Zoom meeting three weeks ago, with representation from every continent, and now has placed its recommendations before the UK medicines authority.

From: Steve Kirsch [redacted]
Sent: 3/14/2021 4:56:14 PM
To: Woodcock, Janet [janet.woodcock@fda.hhs.gov]
Subject: FW: [EXTERNAL] this just in.... real world result from a IVM prescriber who switched to the combo: FLV + IVM = 100% success rate in 100 patients... WAY better than IVM alone

Wow.... maybe some hope after all ☺

From: Stein, Peter <Peter.Stein@fda.hhs.gov>
Sent: Sunday, March 14, 2021 1:29 PM
To: Steve Kirsch <stk@m10.io>
Subject: RE: [EXTERNAL] this just in.... real world result from a IVM prescriber who switched to the combo: FLV + IVM = 100% success rate in 100 patients... WAY better than IVM alone

Steve,
Received – appreciate your forwarding this information,
Peter Stein

From: Steve Kirsch [redacted]
Sent: Sunday, March 14, 2021 4:08 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Cc: Lane, Henry C (NIH) [redacted]; Stein, Peter <Peter.Stein@fda.hhs.gov>; Francis Collins [redacted]; Austin, Christopher P (NIH) [redacted] Hall, Matthew D (NIH) [redacted]
Subject: [EXTERNAL] this just in.... real world result from a IVM prescriber who switched to the combo: FLV + IVM = 100% success rate in 100 patients... WAY better than IVM alone
Importance: High

I just got this just now.... I had told Dr. Haider about fluvoxamine a few weeks ago and he agreed to add it to COVID patients he treated with just IVM. He's a teledoc so prescribes nationwide (to states he's allowed to).

Boy, the FDA should be racing to approve at least fluvoxamine now if not both drugs, but our application has been at FDA for over 6 weeks with no communication at all on the merits.

So now we have:
1) lenze trial: 100% success of 80 patients,
2) seftel trial: 100% of 77 patients,
3) Haider real-world prescribing to clients all over the country: 100% out of 100 patients.

Do you see a pattern yet? In the Seftel study alone, the p-value on the symptoms was 1e-14 with 100% effect size. NOBODY has been able to explain a confounder. There isn't a single observational study on large populations that didn't show a positive effect.

Maybe time to trust the data on the table and save some lives? 😊

-steve

From: Dr. Syed Haider <thedoc@drsyedhaider.com>
Sent: Sunday, March 14, 2021 12:44 PM
To: Steve Kirsch (b) (6)
Subject: Re: Fluvoxamine status?

No one was hospitalized on ivm and fluvoxamine.

This is a change from before when using just ivermectin. I saw at least 2 patients hospitalized in the month before starting fluvoxamine out of a small cohort of about 20 acute cases, so 10% hospitalizations.

However another patient would normally have been hospitalized because their O2 sat dropped to the low 80s, but they insisted on staying home and getting home oxygen rather than going to a hospital where they would not have had access to the appropriate treatment.

Also no one has gotten worse after starting the two meds. Again a definite change from ivermectin alone when at least 20% worsened after starting, especially those who came after day 5 of illness.

So far I have not seen anyone who started in the first week of illness stay sick longer than 2 weeks - this is also a change from ivermectin alone. At least 10% of patients starting ivermectin alone between days 5 and 7 are still sick after day 14.

-Syed

On Sun, Mar 14, 2021, 2:47 PM Steve Kirsch (b) (6) wrote:

> Anyone on the combo hospitalized?
> Anyone get worse after starting?
>
> Sent from my iPhone
>
> On Mar 14, 2021, at 11:43 AM, Dr. Syed Haider <thedoc@drsyedhaider.com> wrote:
>
> There were a few patients I didn't prescribe it to because they were already on another SSRI. Oldest was probably 88 and she is doing great on it and feeling better, the youngest was in their mid 20s and also did well.
>
> My general impression is that it is rare for patients not to feel much better within 3 days of starting. Occasionally they have very mild lingering symptoms for a week.
>
> One patient so far had an adverse reaction with headaches and nerve pain, which is one of the rare side effects and went away when she stopped fluvoxamine.
>
> Everyone I prescribed it to did take it with ivermectin. It helps that it is usually covered by insurance if you prescribe the 100mg tabs and tell them to take 1/2 tab twice a day, and if not it is cheap enough to pay out of pocket.
>
> This is not the case with other things like steroid inhalers, which are too expensive if not covered and colchicine which is often not covered outside of gout and then also too expensive.
>
> -Syed

On Sat, Mar 13, 2021, 8:56 PM Steve Kirsch <(b) (6)> wrote:

Any restrictions on the Fluvoxamine where a patient wasn't able to qualify for it? Youngest and oldest patients?

Sent from my iPhone

On Mar 13, 2021, at 3:38 PM, Dr. Syed Haider <thedoc@drsyedhaider.com> wrote:

Mostly standard FLCCC protocol of 0.2mg per kg for 2-5 days til feeling better.

Probably 25-50 active cases. I'll try to get follow up from all of them on their experience.

-Syed

On Sat, Mar 13, 2021, 6:07 PM Steve Kirsch <(b) (6)> wrote:

What ivermectin dose? .2mg/kg for 3 to 5 days?

Were these with active covid cases or were they stockpiling?

Is there a way for you to email follow up on the results ? this would be REALLLLLYYYYY IMPORTANT!!!!!!!!!!!!

From: Dr. Syed Haider <thedoc@drsyedhaider.com>
Sent: Saturday, March 13, 2021 2:53 PM
To: Steve Kirsch (b) (6)
Subject: Re: Fluvoxamine status?

Probably 100 at this point, but in telemedicine I don't get great follow-up from most patients, so can't really assess the impact. Also everyone so far has been using it as an adjunct to ivermectin. There was just one patient who came mentioning the 60 minutes segment and specifically requesting it in case they got sick.

-Syed

On Sat, Mar 13, 2021, 5:07 PM Steve Kirsch (b) (6) wrote:

How many prescriptions have you given total? Any uptake since the 60 minutes story aired last Sunday?

Sent from my iPhone

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 3/16/2021 1:28:05 PM
To: Tess Lawrie [tess@e-bmc.co.uk]
Subject: RE: [EXTERNAL] URGENT: The BIRD meeting proceedings and recommendation on covid-19 prevention and treatment

Thank you for writing. We are very aware of the wide use of ivermectin, including for scabies. The concern about animal use is that people are dosing themselves with doses intended for animals and getting serious toxicities. This is not good.

Ivermectin use for COVID-19 has been evaluated multiple times by experts in the US, not just at the FDA.

Janet Woodcock

From: Tess Lawrie <tess@e-bmc.co.uk>
Sent: Tuesday, March 16, 2021 12:33 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Fwd: [EXTERNAL] URGENT: The BIRD meeting proceedings and recommendation on covid-19 prevention and treatment

Dear Janet Woodcock,

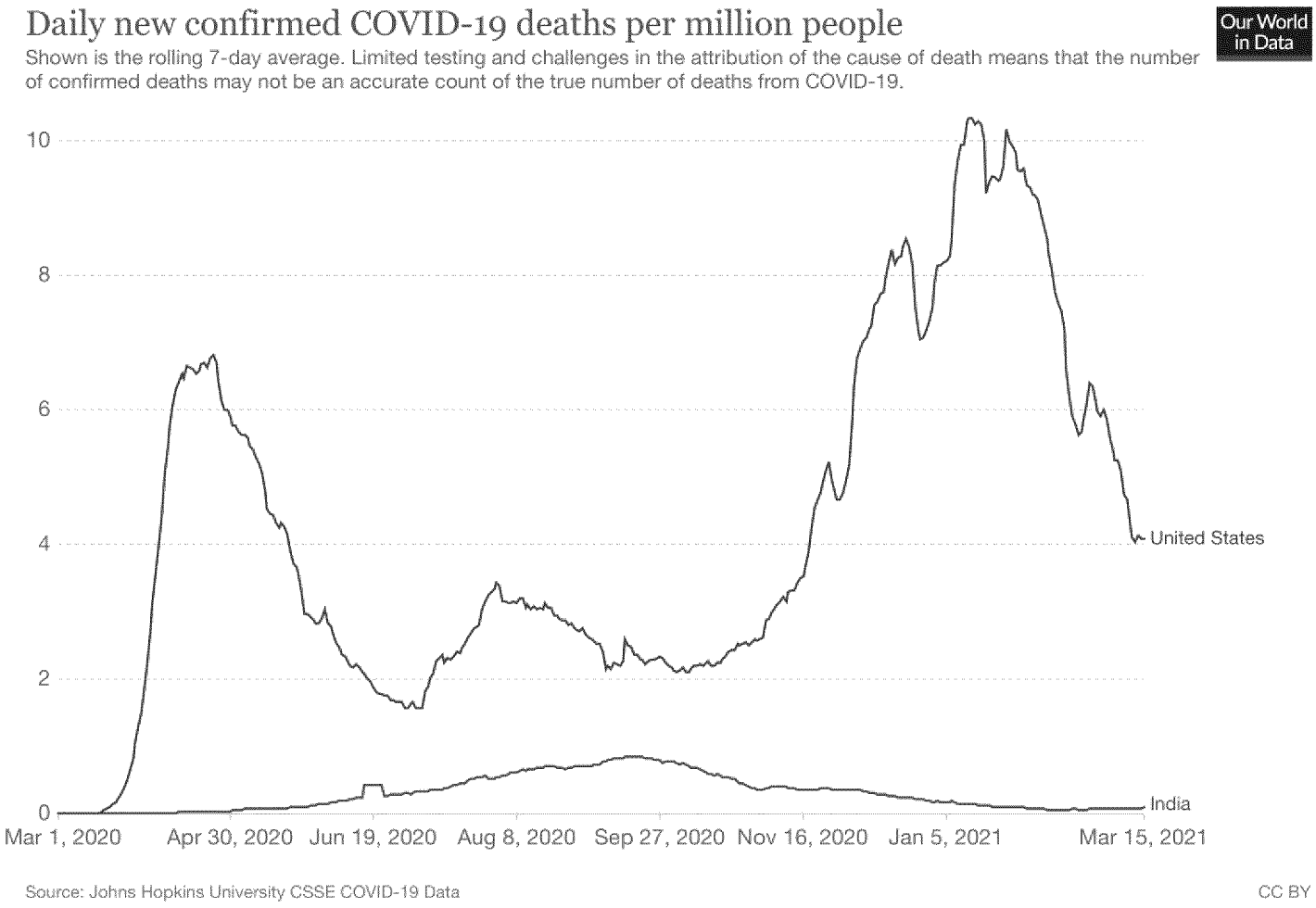
I am sharing with you the correspondence that I have had with Peter Stein and colleagues with regard to the use of ivermectin for the treatment and prevention of covid. I am concerned that they have not yet seen the evidence that we sent to them on the 26th February, as the FDA's official position on ivermectin continues to be that there is no evidence to support its use and that ivermectin is intended for animals. The latter is particularly misleading and derogatory, given that ivermectin is widely used in humans around the world, including among the elderly in the US for the treatment of scabies. In addition, the FDA (and NIH) continues to refer to the in vitro Caly study to support the erroneous notion that ivermectin cannot be effective against covid at regular doses - there are at least 22 RCTs and 5 systematic reviews that show that ivermectin could have a significant impact on the pandemic and, in particular, reduce deaths.

I ask you to pay particular attention to the country example of India, which is four times more populous that the US, and where ivermectin is freely distributed in many states.

I attach the documents that I have shared to date with members of your organization and trust that you will read them with soon, so that we can agree to start saving lives with this cheap, safe and effective generic medicine. Honestly, what does the FDA have to lose?

Sincerely,
Tess

Dr. Theresa Lawrie
Evidence-based Medicine Consultancy Ltd
e-bmc.co.uk



Tess

Dr. Theresa Lawrie
Evidence-based Medicine Consultancy Ltd
e-bmc.co.uk

Begin forwarded message:

From: Tess Lawrie <tess@e-bmc.co.uk>
Subject: Re: [EXTERNAL] URGENT: The BIRD meeting proceedings and recommendation on covid-19 prevention and treatment
Date: 15 March 2021 at 16:30:33 GMT
To: Tess Lawrie <tess@e-bmc.co.uk>
Cc: "Stein, Peter" <Peter.Stein@fda.hhs.gov>, "Cavazzoni, Patrizia" <Patrizia.Cavazzoni@fda.hhs.gov>, "Farley, John" <John.Farley@fda.hhs.gov>

Dear Dr Stein and Colleagues,

It has been a while since we shared with you the British Ivermectin Recommendation Development (BIRD) meeting recommendation and Evidence-to-Decision Framework. I am therefore writing to enquire where you are in the process of evaluating the evidence we sent on this essential drug for covid-19.

I would also like to share with you a link to the UK-based team's systematic review and meta-analysis on ivermectin for covid-19 that underpins the BIRD recommendation: https://osf.io/k37ft/
This manuscript, which is now available on a preprint website, successfully underwent a four-peer review process for a high-impact factor journal. All four reviewers were satisfied that their queries were addressed. Our systematic review is the fifth review of ivermectin for the treatment and prevention of ivermectin (KORY et al 2021 https://t.co/B3MRnPAw5R; HILL et al 2021 https://t.co/r8fQIgbIgu; COBOS-CAMPOS et al 2021 https://t.co/EDRx8vyqoe; BRYANT et al 2021 https://t.co/u148ZUsyvy; NARDELI et al., 2021 - attached). As you know, systematic reviews are considered the highest level of evidence on effects of an intervention. All five systematic review teams are in agreement that the effect that ivermectin could have on reducing mortality and morbidity related to covid-19 is substantial. All reviewers, with the exception of Hill et al, agree that ivermectin could have a significant impact on the pandemic.

In addition, you will have seen from the BIRD Evidence to Decision framework previously shared, that the values, resource, equity, acceptability and feasibility criteria all favour the implementation of ivermectin for covid-19 as soon as possible.

You should know that the World is waiting on your team to act in the global public's interest and approve ivermectin without further delay.

We look forward to some news.

Kind regards,
Tess Lawrie, on behalf of the BIRD Steering Group and recommendation panel

Dr. Theresa Lawrie
Evidence-based Medicine Consultancy Ltd
e-bmc.co.uk

On 5 Mar 2021, at 15:58, Tess Lawrie <tess@e-bmc.co.uk> wrote:

Dear Dr, Stein,

I trust that you are well and thank you for acknowledging receipt of last week's email.

We have since written an executive summary and I attach it here for your information, with an updated BIRD proceedings document. They are still draft documents as endorsements keep flooding in and we intend to publish these with the final document. There are also the results of a public participation survey to be included. Again, please don't hesitate to contact me if you have any queries about the large body of accumulated evidence on ivermectin use for covid-19.

Kind regards,
Tess

Dr. Tess Lawrie, on behalf of the BIRD Steering Group and Recommendation Development Panel
Director
Evidence-based Medicine Consultancy Ltd

e-bmc.co.uk

<BIRD Proceedings 02-03-2021 v 1.5.1.pdf>
<BIRD Proceedings Executive Summary.pdf>

On 26 Feb 2021, at 16:42, Stein, Peter <Peter.Stein@fda.hhs.gov> wrote:

Dear Dr. Lawrie,
Thank you for forwarding this information – it's much appreciated – and clearly reflects your group's thoughtful assessment. We'll certainly review what you've provided.

Sincerely,
Peter Stein
Director, Office of New Drugs, CDER/FDA

From: Tess Lawrie <tess@e-bmc.co.uk>
Sent: Friday, February 26, 2021 10:59 AM
To: Abernethy, Amy <Amy.Abernethy@fda.hhs.gov>; Anderson, Erika <Erika.Anderson@fda.hhs.gov>; Yiannas, Frank <Frank.Yiannas@fda.hhs.gov>; james.sigg@fda.hhs.gov; Tyler, James <James.Tyler@fda.hhs.gov>; Tierney, Julia <Julia.Tierney@fda.hhs.gov>; Hinton, Denise <Denise.Hinton@fda.hhs.gov>; Raza, Mark <Mark.Raza@fda.hhs.gov>; Abdoo, Mark <Mark.Abdoo@fda.hhs.gov>; Araojo, Richardae <Richardae.Araojo@fda.hhs.gov>; McMeekin, Judith <Judith.McMeekin@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Roth, Lauren <Lauren.Roth@fda.hhs.gov>; Tantillo, Andrew <Andrew.Tantillo@fda.hhs.gov>; Vasisht, Kaveeta <Kaveeta.Vasisht@fda.hhs.gov>; Felberbaum, Michael <Michael.Felberbaum@fda.hhs.gov>; Mair, Michael <Michael.Mair@fda.hhs.gov>; Mettler, Erik <Erik.Mettler@fda.hhs.gov>; Miller, Elizabeth <Elizabeth.Miller@fda.hhs.gov>; Rogers, Michael <Michael.Rogers@fda.hhs.gov>; Cavazzoni, Patrizia <Patrizia.Cavazzoni@fda.hhs.gov>; Marks, Peter <Peter.Marks@fda.hhs.gov>; Mayne, Susan <Susan.Mayne@fda.hhs.gov>; Pazdur, Richard <Richard.Pazdur@fda.hhs.gov>;Jeffrey.shuren@fda.hhs.gov; Slikker, William <William.Slikker@fda.hhs.gov>; Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Mitch.zeller@fda.hhs.gov; Stein, Peter <Peter.Stein@fda.hhs.gov>; Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>; Sally.chloe@fda.hhs.gov
Cc: claire Mock-Muñoz de Luna <claire@e-bmc.co.uk>; Ketan Gajjar <ketan.gajjar@nhs.net>; Andy Bryant <andy.bryant@newcastle.ac.uk>; Tony Tham <(b) (6)>; Scott Mitchell <scott.mitchell@gov.gg>; Tina Peers <tina@drtinapeers.com>
Subject: [EXTERNAL] URGENT: The BIRD meeting proceedings and recommendation on covid-19 prevention and treatment

Dear Dr. Stein and FDA Colleagues,

We are writing to share with you the evidence to decision framework of the British Ivermectin Recommendation Development (BIRD) Meeting that was held on Saturday 20th February 2021 via Zoom from Bath, United Kingdom. The expert panel of health and allied professionals and other stakeholders included representatives from 16 countries, namely Argentina, Australia, Belgium, Botswana, Canada, France, Hungary, India, Ireland, Japan, Peru, Nigeria, South Africa, The Philippines,

United States, United Kingdom. The ethos of the BIRD meeting was that of scientific rigour and transparency in the spirit of international collaboration towards a common goal – that of saving lives.

The recommendation was developed according *The WHO Handbook of Guideline Development (2014).* BIRD panel conclusions are that ivermectin should be approved immediately for prevention and treatment of covid-19.

The BIRD recommendation on covid-19 prevention and treatment

The British Ivermectin Recommendation Development Panel recommends ivermectin for the prevention and treatment of covid-19 to reduce morbidity and mortality associated with covid-19 infection and to prevent covid-19 infection among those at higher risk.

The BIRD Steering Group has taken heed of the WHO statement on 'Developing global norms for sharing data and results during public health emergencies' that states that 'public disclosure of information of relevance to public health emergencies should not be delayed', and also notes the' very great risks' that can occur from 'withholding data and results arising from analyses'. We are, therefore, sharing this evidence-to decision framework within just a few days of the BIRD meeting to avoid delay.

Further, due to the urgency related to the communication and dissemination of this recommendation that is aimed at saving thousands of lives daily, please forgive the limitations of the draft proceedings document attached. Information on the process and methods can be found among the annexes. An Executive Summary is being finalised and will be available on Monday.

We look forward to hearing from you soon and would be happy meet with you via teleconference if you think this will be helpful.

Please do not hesitate to contact us with any questions.

Kind regards,

Dr. Tess Lawrie, on behalf of the BIRD Steering Group and Recommendation Development Panel
Evidence-based Medicine Consultancy Ltd
e-bmc.co.uk

From: Tom Brown [(b) (6)]
Sent: 3/18/2021 11:50:21 AM
To: Woodcock, Janet [janet.woodcock@fda.hhs.gov]
Subject: [EXTERNAL] Ivermectin

I think it's been a long time since you were a real doctor. Maybe you could show some courage and take a real look at this drug as a treatment for Covid-19.

Do something good with your "position of authority" for a change. Get out of the pocket of the pharmaceutical companies.

Just a thought.

Tom Brown
(b) (6)

Do the right thing, and do it right now.

From: Graaf, P.H. van der [p.vandergraaf@lacdr.leidenuniv.nl]
Sent: 3/8/2021 8:13:11 AM
To: Carl Peck [(b) (6)]; Ginny Schmith [gschmith@nuventra.com]
CC: Yaning Wang [(b) (6)]; Nick Holford [n.holford@auckland.ac.nz]; Mike Eldon [(b) (6)]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Zhao, Liang [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c1a1570c185440e69410afc0312b4ef1-ZhaoL]; cpteditor@ascpt.org
Subject: [EXTERNAL] RE: Validation

Dear all,

Thanks for the interesting thoughts.

I agree with Ginny that we should wait for more data to come out. The point that the standard dose was unlikely to work has already been made, but of course this doesn't mean that a higher dose/exposure will be efficacious.

Best wishes,

Piet

Piet van der Graaf, PharmD PhD
Senior Vice President, Quantitative Systems Pharmacology
Professor of Systems Pharmacology
Editor-in-Chief *Clinical Pharmacology & Therapeutics*

CERTARA

Canterbury Innovation Centre, University Road, Canterbury, CT2 7FG, United Kingdom
(+44) 1227 931625
(+1) (b) (6)

From: Carl Peck <(b) (6)>
Sent: 07 March 2021 23:28
To: Ginny Schmith <gschmith@nuventra.com>
Cc: Yaning Wang <(b) (6)>; Graaf, P.H. van der <p.vandergraaf@lacdr.leidenuniv.nl>; Nick Holford <n.holford@auckland.ac.nz>; Mike Eldon <(b) (6)>; Janet Woodcock <Janet.Woodcock@FDA.GOV>; Liang Zhao <Liang.Zhao@fda.hhs.gov>
Subject: Re: Validation

Good points, Ginny.

Carl

On Mar 7, 2021, at 2:53 PM, Ginny Schmith <gschmith@nuventra.com> wrote:

Carl-

Thanks for the feedback. I am not sure there is a need for another paper yet given the number of articles and commentaries on the subject, but I will leave that to Piet for his opinion.

As for ivermectin, our paper said that the approved dose (a single 200 mcg/kg dose or about 16-20 mg) would not work, but if the approved dose was administered daily, the lung concentrations would likely be 1/4th of the IC_{50}. Unlike hydroxychloroquine, ivermectin has a reasonable safety profile at the approved dose and doses up to 120 mg once weekly or 60 mg/kg three times weekly have been well tolerated in a small group of healthy subjects. Therefore, I wonder whether higher doses of ivermectin (120 mg once daily for 5-7 days) would result in efficacy in the treatment or prevention of COVID. In our original paper, I did not highlight this because I did not want clinicians to start using high doses off label without it being studied in a more well controlled clinical study situation. I know of several clinicians who have asked Merck to do a study at the higher doses but were not successful in getting them to do this. I also know of several companies now trying to develop an inhaled version as well. I think a paper like you suggest would be better after we hear from some of the studies with higher daily doses or inhaled administration.

Ginny

From: Carl Peck <(b) (6)>
Sent: Sunday, March 7, 2021 3:04 PM
To: Ginny Schmith <gschmith@nuventra.com>
Cc: Yaning Wang <(b) (6)>; Piet Van Der Graaf <p.vandergraaf@lacdr.leidenuniv.nl>; Nick Holford <n.holford@auckland.ac.nz>; Mike Eldon <(b) (6)>; Janet Woodcock <Janet.Woodcock@FDA.GOV>; Liang Zhao <Liang.Zhao@fda.hhs.gov>
Subject: Validation

Ginny, I just noted the piece below in Steve Shafer's Daily COVID Update *(3/6/21):

"Ivermectin was the drug du jour for several months for COVID, at least on talk radio. A study in JAMA found that "among adults with mild COVID-19, a 5-day course of ivermectin, compared with placebo, did not significantly improve the time to resolution of symptoms. The findings do not support the use of ivermectin for treatment of mild COVID-19, although larger trials may be needed to understand the effects of ivermectin on other clinically relevant outcomes" (see https://1drv.ms/b/s!AuOyHP_aTIy7s8JfmXPkeKdzWjSVFA?e=Enmi7w)."

The above may validate your excellent CPT paper "**The Approved Dose of Ivermectin Alone is not the Ideal Dose for the Treatment of COVID-19**"

Similarly, RCT's have confirmed Yaning Wang's equally excellent paper " **Connecting hydroxychloroquine in vitro antiviral activity to in vivo concentration for prediction of antiviral effect: a critical step in treating COVID-19 patients** ", which concluded:

"Under the assumption that in vivo cellular accumulation is similar to that from the in vitro studies, the calculated free lung concentrations that would result from proposed dosing regimens are well below the in vitro EC50/EC90 values, making the antiviral effect against SARS-CoV-2 not likely achievable with a safe oral dosing regimen. Well-designed clinical trials that leverage full understanding of drug pharmacology and disposition, as well as disease pathogenesis, will be necessary to definitively determine whether the risk/benefit balance is favorable for a given treatment."

Perhaps you should collaborate with Yaning to write a piece for CPT showing how good clin pharm and pharmacometrics can avert wasting resources on poorly thought out hypotheses.

Carl

From: Stephen Ditmore [redacted]
Sent: 3/5/2021 7:33:58 AM
To: [redacted] Austin, Christopher P (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=11945b8d0caf49bc84e09171ec167b3a-HHS-austinc]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Kim, Peter (NIH/NIAID) [redacted]; Hall, Matthew D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=80fd9cb35d73417388a946a421745cbf-HHS-hallma-]; Harrigan, Rachel (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7a035d32ebba4e64a02797bcfa74c1a0-HHS-Rachel.]
CC: Kim, Peter S (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2876661346ba42d7a684f7d3ae5c5b4c-HHS-peter.k]
Subject: [EXTERNAL] Stages of COVID-19 (Griffin et.al.) and response to the NIH/NCATS Antiviral Summit

Dr. Francis Collins, Director, NIH
Dr. Christopher Austin, Director, NCATS
Dr. Matthew Hall, Division of Preclinical Innovation, NCATS
Dr. Janet Woodcock, Commissioner, FDA
Dr. Rachel Harrigan, OWS
Dr. Peter S. Kim, NIAID

Dear Distinguished NIH and NDA leaders;
This letter follows on two previous messages praising ACTIV and BLAZE outpatient trials and Dr. Peter Kim's **Therapy for Early COVID-19, A Critical Need**. We applaud the **NIH-CoV2 Therapeutics Antiviral Summit** as well.

Encouraged by Dr. Woodcock's reply to our first letter, in which she agreed that a common nomenclature for the stages of COVID-19 is needed, it gives us great pleasure to inform you that **The Importance of Understanding the Stages of COVID-19 in Treatment and Trials,** Dr. Daniel Griffin, lead author, is now available.

While in many respects the **NIH-CoV2 Therapeutics Antiviral Summit** was a smashing success, an invitation was extended by Dr. Collins to say what's missing that would help forward COVID-19 therapeutics development. We'd like to address that topic.

At 4:15:35 in the video Dr. Richard Whitley makes a point worth emphasizing: that a drug, like any product, should be formulated with the intended use and method of administration in mind. In a situation in which speed of manufacture & distribution (and low cost) are critical, it would be a great shame to overlook opportunities to utilize existing therapeutics because we are jaded by high profile failures, even as we come to understand COVID-19 disease much better. We have not exhausted the available options by any means, and there's much we still don't know because the poor outcomes of some trials reflect a failure to administer antivirals promptly enough.

The need for speed in COVID-19 testing and administration of an antiviral therapeutic to infected individuals, whether for treatment's sake or as part of a clinical trial, separates the COVID-19 experience from our battle with HIV/AIDS. The two have in common, however, the need for trials

and treatment to proceed simultaneously, in parallel. For this to occur it is imperative that we involve primary care physicians and community-based outpatient clinics. What's missing, in our view, are:

- Clinics and Urgent Care Centers as primary sites of outpatient trials and treatment. In the case of SARS-CoV-2 the need for speed suggests that the personnel making the phone calls to inform patients of their positive test results should inform them of their treatment and clinical trial options on the spot. To do otherwise is to risk missing the window of opportunity.
- Therapeutics intended for distribution by pharmacists that reflect the latest medical thinking without hewing slavishly to pharmaceutical company commercial interest.
- The voices of clinicians. While the **NIH-CoV2 Therapeutics Antiviral Summit** was very good as far as it went, clinicians, including those with deep experience working in outpatient settings, need to be part of the dialogue for the enterprise of translational medicine to succeed.

If we may be allowed a criticism of the summit, the self-congratulations around the approval of remdesivir, a drug with which many clinicians are deeply unimpressed, justifiably rankled some. Success in the lab does not always translate to success in medical practice. While we all want good science, we also want pragmatic science. Enthusiasm would have been more justified for monoclonal antibody therapies. Broad implementation remains a struggle, but we are seeing positive outcomes when antibodies are administered early.

A follow-up summit is called for, this time featuring clinicians at the vanguard. We hope that Dr. Griffin, his co-authors and others might work with NCATS in planning panels. Besides discussion of specific repurposed agents for early outpatient treatment, panels could be devoted to alternative clinical trial design and to how epidemiological evidence is understood. Such a follow-on summit, emphasizing access to treatment and involving clinicians, would be in keeping with the Biden Administration's **Executive Order on Improving and Expanding Access to Care and Treatments for COVID-19**.

Concerning the matter of epidemiological evidence, positive and negative, the famotidine experience, PPI's, and ivermectin could be discussed in a single panel. The bringing together of Dr. Christopher Almario of Los Angeles and of Dr. Pierre Kory of the FLCCC, for example, could be very thought provoking. They have brought forth evidence of harm in one case, benefit in the other, that is real despite not being in the form of gold standard clinical trials.

The lack of clear guidance from U.S. health authorities in the area of COVID-19 outpatient therapeutics has consequences, from inflated exuberance about hydroxychloroquine to premature antibiotics prescription justified by a 'pneumonia' diagnosis. Scientific recommendations can be made on the basis of preponderance of the evidence; failure to do so often results in poorer medicine.

We've included our previous letter to Dr. Peter Kim, below, because we believe the six therapeutics named in it present a solid starting point for discussion. A particular point worth making where two drugs are of the same class, such as favipiravir (T-705) and molnupiravir (EIDD-2801), is that an immediate EUA for favipiravir would allow it to be utilized as an active control. Molnupiravir trials could be expanded to include ACTs, allowing reseach to proceed even as people are being treated.

While we expect the core group preparing the panels should be U.S. persons, there are physicians from other nations it would be useful to hear from as the US re-joins the WHO. The WHO SOLIDARITY trial has expressed interest in initiating more early outpatient RCTs, but that would be pointless using the list of therapeutics they have already researched, which is less up-to-date than the six discussed in the letter below (Dr. Kim's three plus our three). We also need to better evaluate

the research and field experience of other nations that has already occurred with favipiravir, ivermectin, and interferon gamma, the three therapeutics we would add to Dr Kim's list.

We do not mean to ignore drug categories other than antivirals, as those also may be important to outpatient treatment. The COLCORONA study of colchicine is worth discussing for methodology, execution, and result. There remains interest among clinicians in the uses of anticoagulants and endothelial stabilizers like tissue plasminogen activator, defibrotide, and statins in treating COVID, and we would all like to understand the latest forensics and research on the finding of megakaryocytes in places other than bone marrow. Having said that, let's not fail to research simpler solutions. Is it helpful to take aspirin and melatonin week 2? Until that's systematically investigated, we won't know. Could such a study be incorporated into a multi-agent RCT? In this instance, could matched pairing in the post-study analysis of an open label trial substitute for randomization?

The common theme running through our commentary is outpatient COVID-19 therapeutics and the role of the community based practitioner and pharmacist in addressing our current pandemic. Please consider holding a follow-on summit with that focus.

Sincerely,

Binh Ngo, MD
Associate Professor
Keck Medical School of USC
Los Angeles, CA

Marc Rendell, MD
Medical Director
Rose Salter Medical Research Foundation
Newport Beach, CA

Paul E. Marik MD, FCCP, FCCM
Eastern Virginia Medical School
Department of Internal Medicine
Chief, Pulmonary and Critical Care Medicine
Norfolk, VA

Pierre Kory, MD, MPA
Pulmonary and Critical Care Medicine
Aurora St. Luke's Medical Center
Milwaukee, WI

Stephen Ditmore
Health Reporter
Parkchester Times
Bronx, NY

---------- Forwarded message ---------
From: **Stephen Ditmore** <[redacted](b) (6)>

Date: Mon, Nov 30, 2020 at 12:47 AM
Subject: Praise and concurring recommendations for Kim et.al.; Therapy for Early COVID-19, A Critical Need; JAMA Viewpoint, November 11, 2020
To: <[redacted]>, Kim, Peter (NIH/NIAID) <[redacted]>
Cc: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>, Harrigan, Rachel (HHS/IOS) <Rachel.Harrigan@hhs.gov>, Marik, Paul E. <MarikPE@evms.edu>, Joseph E. Varon <[redacted]>, Ngo, Binh <Binh.Ngo@med.usc.edu>, marc rendell <rendell@asndi.com>, Pierre Kory <[redacted]>

Peter S. Kim, MD, corresponding author
Therapeutics Research Program, Division of AIDS
National Institute of Allergy and Infectious Diseases
National Institutes of Health,
5601 Fishers Ln, Bethesda, MD 20892
[redacted]

Drs. Janet Woodcock, Rachel Harrigan, and Robert Califf are copied on this email.
Please forward to co-authors (including Dr. Fauci), collaborators and colleagues.

[redacted]

Dear Dr. Kim:

We take great encouragement from your recent letter, **Therapy for Early COVID-19, A Critical Need**, which we support wholeheartedly. By that letter, along with the clarity of **the Bamlanivimab EUA instructions**, you and your colleagues are making it clear that antiviral therapeutics will be most effective when administered early in the course of SARS-CoV-2 infection.

We offer our comments as friendly, concurring suggestions from grateful allies, and are happy to do whatever we can to help spread the word among clinicians and policy makers. We have experienced first-hand that some clinicians remain predisposed to deny treatment before symptoms worsen. We are also concerned about reliance on I.V. administration of therapeutics further straining our hospitals and their personnel. A goal of outpatient COVID-19 therapeutics should be to relieve that strain by providing solutions that can be implemented in community based settings.

Quoting (for reference) from your letter, **Therapy for Early COVID-19, A Critical Need**:

> ***Several antivirals approved or in development for other viral infections, such as HIV, hepatitis C virus, and ebolaviruses, are under investigation for early treatment of COVID-19. These investigations have not yet yielded clinically actionable results; however, many trials are ongoing. Examples of antivirals in trials for early treatment of COVID-19 are MK-4482 (EIDD-2801), an orally bioavailable***

ribonucleoside inhibitor that was originally developed for influenza (NCT04575597); SNG001, a nebulized formulation of interferon-β1a developed for viral infections in patients with chronic obstructive pulmonary disease (NCT04385095); and camostat mesylate, a serine protease inhibitor approved for treatment of chronic pancreatitis and postoperative reflux esophagitis (NCT04353284).

We view your candidates favorably. Having said that, we would add three:

- **favipiravir**
- **interferon gamma**
- **ivermectin**

Of the six (your three+ours), only one, ivermectin, is currently FDA approved. **Please open and glance at Dr. Marik's attached slides**. A partial bibliography of the studies cited appears below.

Ivermectin is available as generic in part due to the generous policies of Merck. While we would welcome Merck advancing ivermectin for COVID-19, Merck has taken a financial interest in MK-4482 (EIDD-2801), so we believe someone else must be identified who will assess the evidence for ivermectin efficacy, champion the finalizing of research, and make necessary applications on an expedited basis.

The evidence for ivermectin efficacy far exceeds that for either famotidine or hydroxychloroquine, two previously FDA approved orally available medications that have received scrutiny. We join front-line intensivist Drs. Marik, Kory, and Varon in asking that our health authorities act on the evidence concerning ivermectin, as attached and as supported by Dr. Kory's interview at **https://youtu.be/n2MlliaLC0A**. Whether it's BARDA, NIAID, ACTIV, OWS, **NCATS**, or a private foundation, someone needs to be found to advance ivermectin in the public interest.

Under current circumstances, preponderance of the evidence, not proof, should be the applicable standard for an EUA or a broad phase 3 IND from the FDA. If necessary, risk can be quantified; actuarys do it routinely. If some risk taking is likely to minimize harm from the disease, that fact should be incorporated when discussing means and methods, including standards for FDA approval.

Finally, there is the matter of clinical trial design under the circumstance we now find ourselves, which is dire. There is no question double-blind placebo controlled clinical trials are the evidentiary gold standard, but they fail to offer patient and clinician control concerning the individual patient's wish to be treated, or not. RCTs do not allow us to both scale up, and compare treatments, in the way we need to. Attempting to do so will result in an enormous number of people who desire treatment receiving placebo, and medical staff time going into administering it. Having said all that, observational trials are unlikely to generate the quality data we need to inform our decisions. There is middle ground: **active control clinical trials (ACTs)**. Former FDA Commissioner Robert Califf, MD has spoken favorably of the potential of such trials, which would allow both randomization and integration with clinical practice. We have cc'd Dr. Califf on this message so that he might comment. Because ivermectin is already approved and widely available, it's adoption as a background therapy would open possibilities in active control clinical trial design so we can dispense with having to deny patients needed treatment because they were allocated placebo.

With respect to existing FDA approved agents, we've swung and missed twice in the cases of hydroxychloroquine and famotidine. While that may be discouraging, no batter returns to the dugout

after two strikes, and there are two more at-bats before the half-inning is over. Let's take the rest of our nine swings now, choosing wisely while acting with alacrity as we await widespread vaccination.

Sincerely,

Paul E. Marik MD, FCCP, FCCM
Eastern Virginia Medical School
Department of Internal Medicine
Chief, Pulmonary and Critical Care Medicine
Norfolk, VA

Pierre Kory, MD, MPA
Pulmonary and Critical Care Medicine
Aurora St. Luke's Medical Center
Milwaukee, WI

Joseph Veron, MD, FACP, FCCP, FCCM, FRSM
United Memorial Medical Center
University of Texas School of Medicine
Houston, TX

Binh Ngo, MD
Associate Professor
Keck Medical School of USC
Los Angeles, CA

Marc Rendell, MD
Medical Director
Rose Salter Medical Research Foundation
Newport Beach, CA

Stephen Ditmore
Health Reporter
Parkchester Times
Bronx, NY

From: Flahive, James [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=570655C122F24177BA6E9AC768A6F731-JAMES.FLAHI]
Sent: 3/4/2021 2:14:46 PM
To: Barclay, Lisa (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=18c6508b15a249799140fcd8d9ddc1ac-HHS-Lisa.Ba]; Despres, Sarah (OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8e5f3d3f26584babb7b48c3cac8bba82-HHS-Sarah.D]
CC: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Tierney, Julia [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1160d300bc4248b790ded292a082e9a8-Julia.Tiern]; Fristedt, Andi [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8ebcdc6531394636a5afcb391a6c0cc3-Andi.Friste]; Abernethy, Amy [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c84171967c724ee799bb2658197086bc-Amy.Abernet]; Raza, Mark [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5811a7d72ee34aa78ff3c8ccb59f92ee-MRaza]; Anderson, Erika [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=98606928b9a64edfb25aba1e3573fdfe-Eranders]; Roth, Lauren [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=52bfd08572694f269a20c508f3c04a03-Lauren.Roth]; Helms Williams, Emily [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=873be46f1b1a4d2b8df3fe67137cbdc8-HELMSWILLIA]; Rebello, Heidi [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2834ce193ca949799ef063e34a2cfa0b-Heidi.Rebel]; Felberbaum, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4819a643ca2945cdb1a2631b83e69673-Michael.Fel]; Tobias, Lindsay [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a4766773c717470bbc55d204b5f067b2-Lindsay.Sto]; Caccomo, Stephanie [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=950c32cebc4b4f80b302c50cf31c8524-Stephanie.C]
Subject: Internal confidential deliberative Night Note for Friday, 3/5

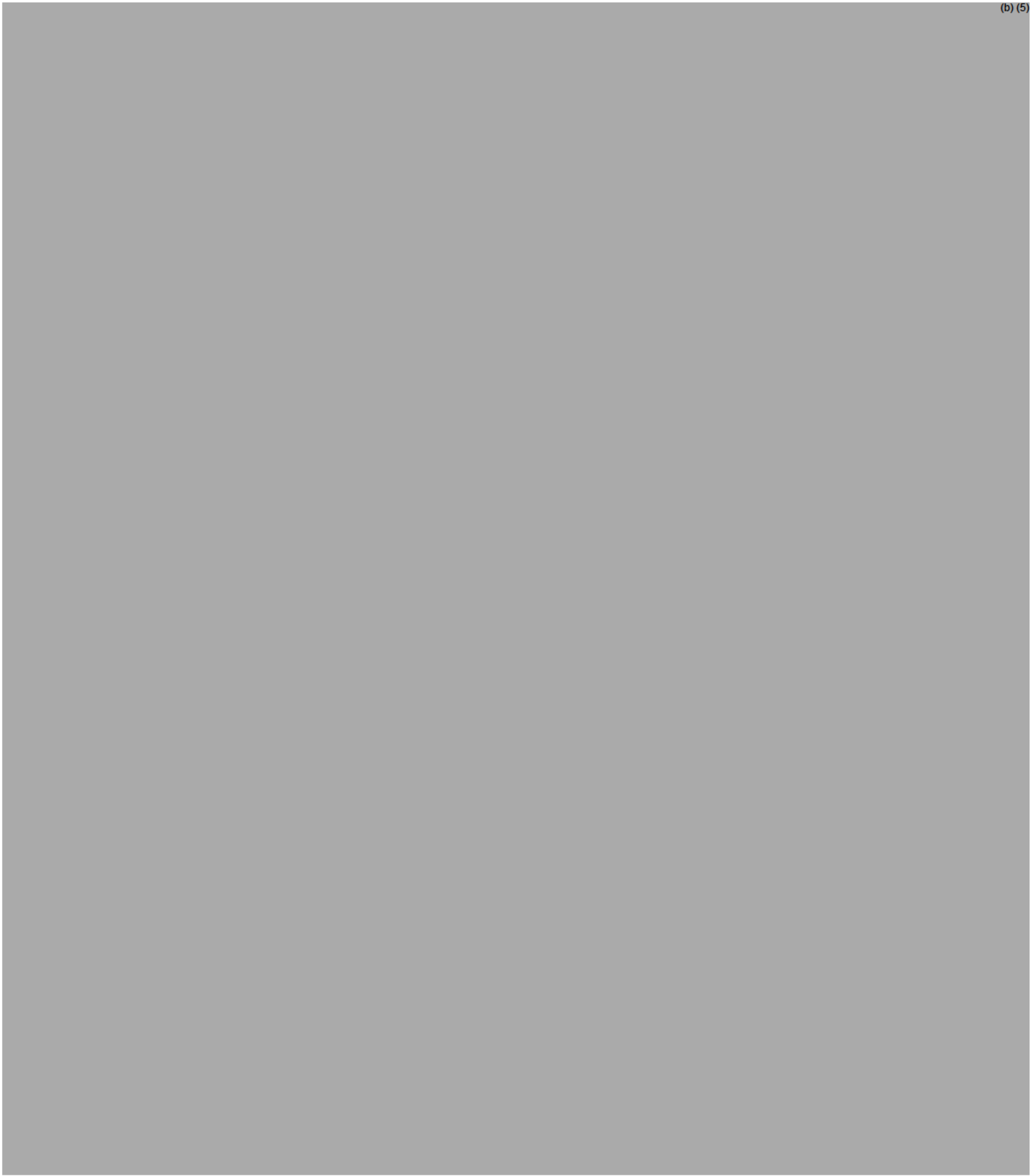
(b) (5)

[redacted]

- **Consumer Update: Why You Should Not Use Ivermectin to Treat or Prevent COVID-19**

This new Consumer Update provides information on how some consumers are looking at unconventional treatments, not approved or authorized by the FDA, to treat or prevent COVID-19. Using any treatment for COVID-19 that's not approved or authorized by the FDA can be highly dangerous, even lethal. There seems to be a growing interest in a drug called ivermectin to treat humans with COVID-19. Ivermectin is often used in the U.S. to treat or prevent parasites in animals. The FDA has received multiple reports of patients who have required medical support and been hospitalized after self-medicating with ivermectin intended for horses.

(b) (5)



From: Carl Peck [(b) (6)]
Sent: 3/8/2021 3:16:39 PM
To: Ginny Schmith [gschmith@nuventra.com]
CC: Piet Van Der Graaf [p.vandergraaf@lacdr.leidenuniv.nl]; Yaning Wang [(b) (6); Nick Holford [n.holford@auckland.ac.nz]; Mike Eldon [(b) (6)]; Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; cpteditor@ascpt.org
Subject: [EXTERNAL] Fwd: Validation

Ginny,

Apparently, FDA has weighed in - see below.

Carl

Begin forwarded message:

From: Joshua Galanter <galanter.joshua@gene.com>
Subject: **Re: Validation**
Date: March 8, 2021 at 10:13:59 AM PST
To: Stephen Ruberg <(b) (6)>
Cc: Carl Peck <(b) (6)>, Daniela Drago <drago@innovareg.com>, Joshua Galanter <galanter.joshua@gene.com>, Christine Garnett <Christine.Garnett@fda.hhs.gov>, Charles Gombar <charlie.gombar@gatesfoundation.org>, Charlie Grudzinskas <(b) (6)>, Diane K Jorkasky <(b) (6)>, Jaime Kenyon <jaime.kenyon@ucsf.edu>

The FDA has weighed in...

https://www.fda.gov/consumers/consumer-updates/why-you-should-not-use-ivermectin-treat-or-prevent-covid-19

> **There seems to be a growing interest in a drug called ivermectin to treat humans with COVID-19. Ivermectin is often used in the U.S. to treat or prevent parasites in animals. The FDA has received multiple reports of patients who have required medical support and been hospitalized after self-medicating with ivermectin intended for horses.**

Echoes of when people were using chloroquine for fish tanks.

FDA Letter to Stakeholders: Do Not Use Chloroquine ...

www.fda.gov › product-safety-information › fda-letter-...

Mar 27, 2020 — The FDA's Center for Veterinary Medicine has recently become aware that some consumers may mistake *chloroquine* phosphate used to treat disease in *aquarium fish* for FDA-approved drugs (used to treat malaria and certain other conditions in humans) that are being studied as a COVID-19 treatment for humans.

Man Dies, Wife Hospitalized From Ingesting Fish Tank ...

www.pharmacypracticenews.com › Covid-19 › Article

Mar 25, 2020 — ... *chloroquine* phosphate in the mistaken belief the additive, commonly used by *aquariums* to clean *fish tanks*, was a prophylactic for COVID-19 ...

Man dies after ingesting fish tank cleaner containing...

www.beckershospitalreview.com › public-health › man...

Mar 24, 2020 — A man in Arizona is dead and his wife is in critical care after the couple ingested a non-medication form of *chloroquine* phosphate to stave off ...

Josh

On Sun, Mar 7, 2021 at 8:33 PM Stephen Ruberg <[redacted] (b) (6)> wrote:

Thanks Carl.

I just saw 60 Minutes tonight and the story of fluvoxamine for COVID-19 - PATIENTS WITH MILDER SYMPTOMS.
Another drug being re-purposed for treatment. Positive Ph 2 results (N=152 and p=0.009), but I am skeptical.
Lots of caveats for the trial. I should have a Blog paper posted on this by tomorrow AM.

https://jamanetwork.com/journals/jama/fullarticle/2773108

In short, my prior is 0.01 (or 1%) chance that the drug works ... and honestly, that may be optimistic.
Using my favorite Bayesian formula for calculating a posterior probability, I get a posterior that the drug works of 0.081. Yes, that's right. 8% chance that it truly works.
We will see as the larger follow-on trial is due to finish in a month or so.

On Sun, Mar 7, 2021 at 3:07 PM Carl Peck <[redacted] (b) (6)> wrote:

FYI - on value of clin pharm/pharmacometrics in Covid Rx R&D.

Carl

Begin forwarded message:

From: Carl Peck <[redacted] (b) (6)>
Subject: Validation
Date: March 7, 2021 at 12:03:37 PM PST

To: Ginny Schmith <gschmith@nuventra.com>
Cc: Yaning Wang <[redacted](b) (6)>, Piet Van Der Graaf <p.vandergraaf@lacdr.leidenuniv.nl>, Nick Holford <n.holford@auckland.ac.nz>, Mike Eldon <[redacted](b) (6)>, Janet Woodcock <Janet.Woodcock@FDA.GOV>, Liang Zhao <Liang.Zhao@fda.hhs.gov>

Ginny, I just noted the piece below in Steve Shafer's Daily COVID Update *(3/6/21):

"Ivermectin was the drug du jour for several months for COVID, at least on talk radio. A study in JAMA found that "among adults with mild COVID-19, a 5-day course of ivermectin, compared with placebo, did not significantly improve the time to resolution of symptoms. The findings do not support the use of ivermectin for treatment of mild COVID-19, although larger trials may be needed to understand the effects of ivermectin on other clinically relevant outcomes"
(see https://1drv.ms/b/s!AuOyHP_aTIy7s8JfmXPkeKdzWjSVFA?e=Enmi7w)."

The above may validate your excellent CPT paper "**The Approved Dose of Ivermectin Alone is not the Ideal Dose for the Treatment of COVID-19**"

Similarly, RCT's have confirmed Yaning Wang's equally excellent paper "**Connecting hydroxychloroquine in vitro antiviral activity to in vivo concentration for prediction of antiviral effect: a critical step in treating COVID-19 patients** ", which concluded:

"Under the assumption that in vivo cellular accumulation is similar to that from the in vitro studies, the calculated free lung concentrations that would result from proposed dosing regimens are well below the in vitro EC50/EC90 values, making the antiviral effect against SARS-CoV-2 not likely achievable with a safe oral dosing regimen. Well-designed clinical trials that leverage full understanding of drug pharmacology and disposition, as well as disease pathogenesis, will be necessary to definitively determine whether the risk/benefit balance is favorable for a given treatment."

Perhaps you should collaborate with Yaning to write a piece for CPT showing how good clin pharm and pharmacometrics can avert wasting resources on poorly thought out hypotheses.

Carl

--
Make it a stellar day,

Steve Ruberg, PhD
President, Analytix Thinking
Bringing Data to Life

[redacted](b) (6)
+1 317-506-5686

AnalytixThinking.blog

--

Joshua Galanter, MD, MAS

Medical Safety Director

Early Development Safety (EDS)

Product Development Safety (PDS)

Genentech, Inc 1 DNA Way, South San Francisco, CA 94080

Mobile (b) (6) galantj1@gene.com

Administrative Assistant, Rosa Fifita

Desk +1 650-467-7468 **Mobile** (b) (6) fifitar@gene.com

The linked image cannot be displayed. The file may have been moved, renamed, or deleted. Verify that the link

Upcoming out of office dates:
No upcoming travel due to COVID-19 pandemic

From: Adam, Stacey (FNIH) [T] [sadam@fnih.org]
Sent: 2/26/2021 1:55:47 PM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: RE: [EXTERNAL] URGENT: The BIRD meeting proceedings and recommendation on covid-19 prevention and treatment

Thank you!

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: **(301) 435-8364** | Mobile: (b) (6)

From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Sent: Friday, February 26, 2021 1:44 PM
To: Adam, Stacey (FNIH) [T] <sadam@fnih.org>
Subject: RE: [EXTERNAL] URGENT: The BIRD meeting proceedings and recommendation on covid-19 prevention and treatment

I'm working on that. jw

From: Adam, Stacey (FNIH) [T] <sadam@fnih.org>
Sent: Friday, February 26, 2021 1:31 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: RE: [EXTERNAL] URGENT: The BIRD meeting proceedings and recommendation on covid-19 prevention and treatment

Thanks, Janet,

Agreed. (b) (5)

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: **(301) 435-8364** | Mobile: (b) (6)

From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Sent: Friday, February 26, 2021 1:12 PM

To: Kessler, David (HHS/IOS) <David.Kessler@hhs.gov>; Collins, Francis (NIH/OD) [E] <[redacted]>; Fauci, Anthony (NIH/NIAID) [E] [redacted]; Bugin, Kevin (FDA/CDER) <kevin.bugin@fda.hhs.gov>; Teyhen, Deydre (HHS/IOS) [redacted] Adam, Stacey (FNIH) [T] <sadam@fnih.org>
Subject: FW: [EXTERNAL] URGENT: The BIRD meeting proceedings and recommendation on covid-19 prevention and treatment

Another good reason to get ACTIV 6 up and running. Solid evidence still lacking. jw

---

From: Tess Lawrie <tess@e-bmc.co.uk>
Sent: Friday, February 26, 2021 10:59 AM
To: Abernethy, Amy <Amy.Abernethy@fda.hhs.gov>; Anderson, Erika <Erika.Anderson@fda.hhs.gov>; Yiannas, Frank <Frank.Yiannas@fda.hhs.gov>; james.sigg@fda.hhs.gov; Tyler, James <James.Tyler@fda.hhs.gov>; Tierney, Julia <Julia.Tierney@fda.hhs.gov>; Hinton, Denise <Denise.Hinton@fda.hhs.gov>; Raza, Mark <Mark.Raza@fda.hhs.gov>; Abdoo, Mark <Mark.Abdoo@fda.hhs.gov>; Araojo, Richardae <Richardae.Araojo@fda.hhs.gov>; McMeekin, Judith <Judith.McMeekin@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Roth, Lauren <Lauren.Roth@fda.hhs.gov>; Tantillo, Andrew <Andrew.Tantillo@fda.hhs.gov>; Vasisht, Kaveeta <Kaveeta.Vasisht@fda.hhs.gov>; Felberbaum, Michael <Michael.Felberbaum@fda.hhs.gov>; Mair, Michael <Michael.Mair@fda.hhs.gov>; Mettler, Erik <Erik.Mettler@fda.hhs.gov>; Miller, Elizabeth <Elizabeth.Miller@fda.hhs.gov>; Rogers, Michael <Michael.Rogers@fda.hhs.gov>; Cavazzoni, Patrizia <Patrizia.Cavazzoni@fda.hhs.gov>; Marks, Peter <Peter.Marks@fda.hhs.gov>; Mayne, Susan <Susan.Mayne@fda.hhs.gov>; Pazdur, Richard <Richard.Pazdur@fda.hhs.gov>; Jeffrey.shuren@fda.hhs.gov; Slikker, William <William.Slikker@fda.hhs.gov>; Solomon, Steven M <Steven.Solomon@fda.hhs.gov>; Mitch.zeller@fda.hhs.gov; Stein, Peter <Peter.Stein@fda.hhs.gov>; Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>; Sally.chloe@fda.hhs.gov
Cc: claire Mock-Muñoz de Luna <claire@e-bmc.co.uk>; Ketan Gajjar [redacted] Andy Bryant <andy.bryant@newcastle.ac.uk>; Tony Tham <[redacted]>; Scott Mitchell <scott.mitchell@gov.gg>; Tina Peers <[redacted]>
Subject: [EXTERNAL] URGENT: The BIRD meeting proceedings and recommendation on covid-19 prevention and treatment

Dear Dr. Stein and FDA Colleagues,

We are writing to share with you the evidence to decision framework of the British Ivermectin Recommendation Development (BIRD) Meeting that was held on Saturday 20th February 2021 via Zoom from Bath, United Kingdom. The expert panel of health and allied professionals and other stakeholders included representatives from 16 countries, namely Argentina, Australia, Belgium, Botswana, Canada, France, Hungary, India, Ireland, Japan, Peru, Nigeria, South Africa, The Philippines, United States, United Kingdom. The ethos of the BIRD meeting was that of scientific rigour and transparency in the spirit of international collaboration towards a common goal – that of saving lives.

The recommendation was developed according *The WHO Handbook of Guideline Development (2014).* BIRD panel conclusions are that ivermectin should be approved immediately for prevention and treatment of covid-19.

The BIRD recommendation on covid-19 prevention and treatment

The British Ivermectin Recommendation Development Panel recommends ivermectin for the prevention and treatment of covid-19 to reduce morbidity and mortality associated with covid-19 infection and to prevent covid-19 infection among those at higher risk.

The BIRD Steering Group has taken heed of the WHO statement on 'Developing global norms for sharing data and results during public health emergencies' that states that 'public disclosure of information of relevance to public health emergencies should not be delayed', and also notes the' very great risks' that can occur from 'withholding data and results arising from analyses'. We are, therefore, sharing this evidence-to decision framework within just a few days of the BIRD meeting to avoid delay.

Further, due to the urgency related to the communication and dissemination of this recommendation that is aimed at saving thousands of lives daily, please forgive the limitations of the draft proceedings document attached. Information on the process and methods can be found among the annexes. An Executive Summary is being finalised and will be available on Monday.

We look forward to hearing from you soon and would be happy meet with you via teleconference if you think this will be helpful.

Please do not hesitate to contact us with any questions.

Kind regards,

Dr. Tess Lawrie, on behalf of the BIRD Steering Group and Recommendation Development Panel
Evidence-based Medicine Consultancy Ltd
e-bmc.co.uk

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 3/5/2021 8:01:19 AM
To: Kimberly, Brad [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=08bc909ed76d49868a5ff92c3c70fb72-Bradley.Kim]
Subject: RE: JW TWEETS: Ivermectin // BABY FOOD

Good thanks jw

From: Kimberly, Brad <Brad.Kimberly@fda.hhs.gov>
Sent: Friday, March 5, 2021 8:00 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Cc: Felberbaum, Michael <Michael.Felberbaum@fda.hhs.gov>; Hetlage, Daniel <Daniel.Hetlage@fda.hhs.gov>; Rebello, Heidi <Heidi.Rebello@fda.hhs.gov>; Robb, Melissa <Melissa.Robb@fda.hhs.gov>; Thorpe, Valarie <Valarie.Thorpe@fda.hhs.gov>; Tierney, Julia <Julia.Tierney@fda.hhs.gov>
Subject: JW TWEETS: Ivermectin // BABY FOOD

Good morning… two items for your review this AM. Thanks! --Brad

===

CU: IVERMECTIN

Using any treatment for #COVID19 that's not approved or authorized by the FDA can be highly dangerous and potentially lethal. Don't do it! **[QRT @US_FDA]**

===

TOXIC METALS IN BABY FOOD

We take exposure to toxic elements in the food supply extremely seriously, especially when it comes to protecting the health & safety of the youngest and most vulnerable. We're committed to reducing exposure to the greatest extent feasible & further advance progress in this area. **[QRT @DrMayneFDAFood]**

Brad Kimberly
Director, Social Media

Office of Media Affairs
Office of External Affairs
U.S. Food and Drug Administration
Tel: 240-402-1002 | Cell: (b) (6)
brad.kimberly@fda.hhs.gov

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 2/17/2021 3:34:45 PM
To: Steve Kirsch [stk@m10.io]
Subject: RE: [EXTERNAL] fan mail

I hope a pragmatic trial can get going very soon, all are aligned. jw

From: Steve Kirsch <(b) (6)>
Sent: Wednesday, February 17, 2021 3:03 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: [EXTERNAL] fan mail

Hah... see red....

From: David Boulware <boulw001@umn.edu>
Sent: Wednesday, February 17, 2021 10:37 AM
To: Glenn Bunting <(b) (6)>; Steve Kirsch <(b) (6)>
Subject: RE: Timeline?

It was Sanjay Gupta's producer.

Also, FYI NIH is getting serious about repurposed drugs. Janet Woodcock has lit a fire.

DB

From: Glenn Bunting <(b) (6)>
Sent: Wednesday, February 17, 2021 12:14 PM
To: David Boulware <boulw001@umn.edu>; Steve Kirsch <(b) (6)>
Subject: Re: Timeline?

Do we know who is doing it for what program?

From: David Boulware <boulw001@umn.edu>
Sent: Wednesday, February 17, 2021 9:36:03 AM
To: Steve Kirsch <(b) (6)>
Cc: Glenn Bunting <(b) (6)>
Subject: RE: Timeline?

Steve,
CNN story is about repurposed medicines overall, and the challenges of studying them.
They are aiming for next week and plan to cover multiple drugs – metformin, fluvoxamine, ivermectin.

DB

From: Steve Kirsch <(b) (6)>
Sent: Wednesday, February 17, 2021 11:27 AM
To: David Boulware <boulw001@umn.edu>
Cc: Glenn Bunting (<(b) (6)>
Subject: RE: Timeline?

Did you talk to them? Find out any info???

From: David Boulware <boulw001@umn.edu>
Sent: Wednesday, February 17, 2021 6:03 AM
To: Steve Kirsch <(b) (6)>
Subject: RE: Timeline?

CNN is going to do story on repurposed meds for COVID, regardless of whether I am involved or not.

From: Steve Kirsch [(b) (6)]
Sent: 2/9/2021 2:07:48 AM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: A good theory as to why kids have less problems with COVID (fyi)

just read the part in red

From: Farid Jalali [(b) (6)]
Sent: Monday, February 8, 2021 10:47 PM
To: Steve Kirsch <stk@m10.io>
Subject: Re: New comment on "COVID-19: Platelets, serotonin, SSRIs, and cyproheptadine"

Thanks Steve. I won't get in the middle of conversation with Angela but you are correct and she is correct too. Kids recover but a very small subset do not and we have no way to figure out yet who that subset is. However, the same physiology applies to them as you said. One difference is the cd147 activation of platelets increases as people age, we think so there may be far less platelet activation in kids due to this virus, presumably.

Your overall thought process is similar to many of us. Why do we have to go thru massive RCTs to prescribe a relatively safe and well tolerated therapy with little harm to a healthy person with mild disease to prevent severe disease along a pathway showing benefit in smaller trials. The upsides are decent and downsides are small. But unfortunately that's not how US approaches therapies. Many other countries don't do it this way.

If a few doses of ivermectin or FLV prevents severe disease, great. If it doesn't, not much was lost while trying.

When you compare that thought process to non-judicious use in this country (more rhan anywhere else) of Remdesivir or plasma or tocilizumab (all with a large set of very very shaky data from the start until now) it really frustrates most of us.

Let's put it this way. Heparin saves lives. Proven now beyond shadow of doubt in very large RCTx3 in western world, trials run by the boys and girls who frequent our conferences as keynote speakers. YET Our covid19 guidelines in US and all major societies still recommend against full dose anticoagulant use with heparin.

The whole thing is just so bizarre and so frustrating. Many have died due to this attitude in this country.

On the cyproheptadine front, we are working with Canadian version of FDA to get the trial approved. Protocol written, proposal detailed, and met with drug company who supplies it to the hospital to submit more info to Canadian FDA equivalent.

I and Phil will keep you updated.
Thanks
Farid

Sent from my iPhone

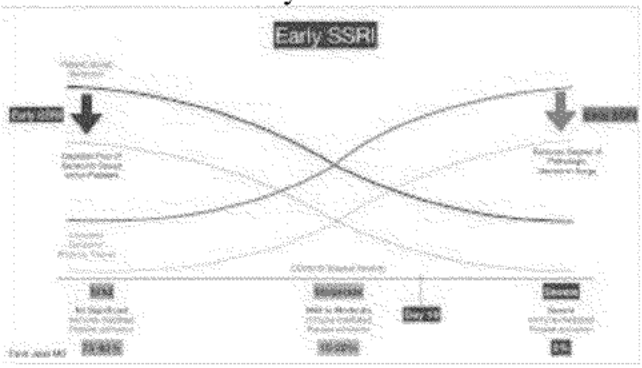
On Feb 8, 2021, at 10:12 PM, Steve Kirsch [(b) (6)] wrote:

From: YouTube <noreply@youtube.com>
Sent: Friday, February 5, 2021 4:21 AM
To: Steve Kirsch (b) (6)
Subject: New comment on "COVID-19: Platelets, serotonin, SSRIs, and cyproheptadine"

New comment on "COVID-19: Platelets, serotonin, SSRIs, and cyproheptadine"

YouTube

Al Ma commented on your video



COVID-19: Platelets, serotonin, SSRIs, and cyproheptadine

Al Ma
Great information. Thank you for sharing!

REPLY
MANAGE ALL COMMENTS

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 2/6/2021 9:08:34 AM
To: Stan Young (b) (6)
Subject: RE: off the wall

PS a lot of things kill viruses in cells in vitro but don't work in people: dose, tissue penetration, pharmacokinetics, other factors. HCQ is one of those, in vivo probably not enough in the cells at a safe dose. jw

From: Stan Young <(b) (6)>
Sent: Friday, February 5, 2021 6:02 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Re: off the wall

Janet: Is Merck giving an opinion? Do they have data? RCT? Do they have a more expensive solution? (conspiracy theory? see 1 below)

Both could be right. Ivermectin by itself might not be effective. The zinc-doxycycline-ivermectin** combination is reported to be effective in India. How effective? Maybe enough for public health, say 50%, but not a magic bullet like I hear that antibody infusion is.

(1)We have been and are in a world of smoke and mirrors. Lancet had to withdraw an HCQ paper that looked very impressive (HCQ was not effective and caused deaths) as the data appeared to have been made up. Who has the time and money to make up a study good enough to fool Lancet? Was Lancet in on the game?

**here is the storyline, as I understand it. Zinc kills viruses, but typically can not get into cells on its own. An interaction with HCQ or ivermectin lets zinc get into the cells where the zinc kills the virus. An antibiotic is added (wrongly, I think) as it is pneumonia that does most of the killing of humans with flu. COVID kills differently.

Stan and Pat Young (b) (6)

On Friday, February 5, 2021, 2:54:19 PM EST, Woodcock, Janet <janet.woodcock@fda.hhs.gov> wrote:

. Merck has just said they think ivermectin very unlikely to provide benefit (they invented it). Doxy, zinc?? Doubtful. Agree NC probably as you say!! jw

From: Stan Young <(b) (6)>
Sent: Friday, February 5, 2021 2:51 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: off the wall

Janet:

I've studied the literature fairly well now. I'm sure your statisticians have also. I think the case for zinc, doxycycline, ivermectin is strong, observational and RCTs.

I have no idea about legal/political things. Why not just give (physicians) permission in 25/50 states? Pair them so that the states within a pair are similar, then randomly assign within pairs.

I know a bit about NC, their reporting of positives, of people with symptoms, of those admitted to hospitals, of deaths is both slow and, in my opinion, not very reliable.

Stan and Pat Young (b) (6)

From: Steve Kirsch [(b) (6)]
Sent: 5/21/2021 1:08:20 PM
To: Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]
CC: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: [EXTERNAL] New data: Here's a way you can do the right thing on IVM

Cliff,

Cliff,

here's a way for you to change your recommendation on ivermectin without backtracking.

PLEASE DO THIS ASAP.

Brazil is in total denial that early treatment works this. So is Tamil Nadu.

thanks!

-steve
==========
Four new randomized controlled trials (RCTs) for ivermectin treatment (3) and prevention (1), below, have recently appeared in mainstream scientific journals over the past six weeks. There are already some 20 of those RCTs for IVM treatment of COVID-19, and for those 8 which included serious cases, pooled mortality reduction was 78%, with statistically significant benefits in 7 of these 8. What's new here is that these four recent papers are the first of these published in mainstream journals. Also, a major result on biological mechanism of IVM activity against SARS-CoV-2 is being finalized from a leading world virology lab—the PI is next door to a recent Nobel laureate.

Chaccour[1] - Patients in the ivermectin group recovered earlier from hyposmia/anosmia (76 vs 158 patient-days; $p < 0.001$). Lesser reduction in viral load. [IVM as a single agent appears in many studies, clinical and animal, to have greater reduction in morbidity v. infectivity; this may relate to greater shielding of NTD v. RBD region of viral spike protein]

Mahmud[2] – Just one dose of IVM at 12 mg, plus doxy. Several clinical benefits at p=.001, including reduction in viral load.

Shahbaznejad[3] - Duration of symptoms and of hospitalization – IVM improved by ~ p = .02 for each. Cough: p=0.02; shortness of breath, $p < 0.05$.

Seet[4] – IVM was given in **just one low dose** of 12 mg in a prevention study, with observation over 42 days. Three other prevention regions were administered **every day for 42 days**. IVM did best as to clinical benefits – it reduced symptomatic COVID by 50% (p=.003) and acute respiratory symptoms by 50% (p=.012).

1. Chaccour C, Casellas A, Blanco-Di Matteo A, 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*. 2021;32.

2. Mahmud R, Rahman MM, Alam I, et al. Ivermectin in combination with doxycycline for treating COVID-19 symptoms: a randomized trial. *Journal of International Medical Research*. 2021; 49(5):030006052110135 50.

3. Shahbaznejad L, Davoudi A, Eslami G, et al. Effect of ivermectin on COVID-19: A multicenter double-blind randomized controlled clinical trial. *Clinical Therapeutics*. 2021; https://doi.org/10.1016/j.clinthera.2021.04.007.

4. Seet RCS, Quek AML, Ooi DSQ, et al. Positive impact of oral hydroxychloroquine and povidone-iodine throat spray for COVID-19 prophylaxis: An open-label randomized trial. *International Journal of Infectious Diseases.* 2021;106:314-322.

From: Steve Kirsch (b) (6)
Sent: 5/20/2021 10:37:48 PM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: [EXTERNAL] whoa! found out why hospitals deny ivermectin

there have been 6 court cases on IVM and they all rule in favor of the plaintiff.

here's why we think hospitals are denying treatments that can save lives... if hospitals stray off the reservation, they lose liability protection (see red below).

So hospitals stay safe and people die unnecessarily.

Now just pretend you got hospitalized... even as head of the FDA and you knew all the studies are 100% positive for IVM and effect size is >65%, you would not be able to get treatment. How would you feel about that? If it were me, I'd be pretty upset, and probably die.

Is there a good way to fix this?

-steve

From: 4 <(b) (6)>
Sent: Thursday, May 20, 2021 6:44 PM
To: Steve Kirsch (b) (6)
Cc: Pierre Kory - FLCCC (pkory@flccc.net) <pkory@flccc.net>
Subject: RE: Gavin de Becker's father denied ivermectin and died: why?

Just to you and Pierre, Steve.

First, Thank You so much. You're more likely to get a reply than I. Though I confirmed Loftus received my letter and received four phone messages, he never responded in any way. And neither did the doctor. Amazing since I have power of attorney for medical stuff involving my father.

Dr. Bhandari is the actual doctor responsible for treating my father at the Desert Springs Hospital. She acknowledged by text that she received my letter ("Thank you for sending this and will read it soon") but never replied to my emails or phone calls or texts.

You are welcome to call or text her, Steve: Here is her cellphone and email address: (b) (6) (b) (6)

Perhaps this information can be valuable if you do an article: A likely reason the hospital and doctor felt comfortable ignoring me outright is that the Federal Government has cured a giant

problem for hospitals and doctors when it comes to Covid: Zero liability for hospitals but only **if** they follow govt-approved treatments:

"The PREP Act specifies four types of **covered countermeasures**:
(i) a qualified pandemic or epidemic product; (ii) a "security countermeasure"; (iii) a **drug, biological product, or device that the U.S. Food and Drug Administration (FDA) has authorized for emergency use**; and (iv) a respiratory protective device"

So if a doctor or hospital does something that the FDA didn't specifically authorize for emergency use, then the hospital wouldn't get protection against liability. And this is likely part of why most hospitals and doctors are against Ivermectin. They have been granted complete protection from liability anytime they are treating any Covid patient, so long as they use only treatments that have emergency use authorization.

In effect the Federal Government is practicing medicine for individual patients, and all patients, telling doctors what they can and cannot do.

https://crsreports.congress.gov/product/pdf/LSB/LSB10443

-----Original Message-----
From: Steve Kirsch <[redacted](b) (6)
Sent: Thursday, May 20, 2021 6:12 PM
To: Chris.loftus@uhsinc.com; [redacted](b) (6); lisa.miller@uhsinc.com
Cc: 4 <[redacted](b) (6)>; Vikas Sukhatme (vsukhatme@emory.edu) <vsukhatme@emory.edu>; Pierre Kory - FLCCC (pkory@flccc.net) <pkory@flccc.net>; Vidula Sukhatme (vidula@global-cures.org) <vidula@global-cures.org>
Subject: *EXTERNAL* Gavin de Becker's father denied ivermectin and died: why?

Hi Chris and Lisa,

I'm a writer at TrialSiteNews and I'm writing an op-ed about ivermectin being denied for hospitalized patients.

As I'm sure you are aware, ivermectin has an average 65% mortality benefit when used late in disease. There have been a total of 12 studies, all but one showing a positive benefit. The one negative study, the Shahbaznejad et al paper had a very high p-value as there was just a single death and it was a patient who was about to die at baseline.

So in denying a potentially life saving treatment, I'm sure this was based on solid data and consideration of all available evidence.

I was wondering what data the hospital relied upon that would lead you to conclude that the treatment was more likely to hurt the patient than to help the patient?

And what error have the courts been making in deciding the ivermectin treatment cases for the plaintiff?

Thanks in advance and I look forward to your response.

-steve

From: IAN GRANT-WHYTE [(b) (6)
Sent: 6/29/2021 1:47:10 AM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
CC: Berlin, Robert [robert.berlin@fda.hhs.gov]
Subject: [EXTERNAL] It is reasonable to try just about anything as long as the risk for harm is very low.
Attachments: ETOH.COVID.ARTICLE.8.21.2020.edited.final.8.28.20 (1) (1) (1) (1) (1) (1) (1) (2) (3) (1) (1) (1) (6) (1) (1) (1) (1) (1) (3) (4) (1) (7) (1) (1) (1) (3) (3).docx

Judith Tharp, MD
Emergency Medicine

Doesn't "prove" that Ivermectin helped, but in the course of an ongoing epidemic capable of severe illness and complication, almost any treatment must be called experimental (empirical). The way I look at it, it is reasonable to try just about anything as long as the risk for harm is very low. You can't wait for a randomized controlled study in the middle of a raging pandemic. Analysis of possible benefit/no-benefit from Ivermectin can be done later, but that will depend on adequate record-keeping and reporting.

From: Adam, Stacey (FNIH) [T] [sadam@fnih.org]
Sent: 4/22/2021 9:54:15 AM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: RE: [EXTERNAL] ACTIV-6

Thank you thought for looping me into the request. I really appreciate it!
Stacey

Stacey J. Adam, PhD
Associate Vice President
Research Partnerships
Direct: **(301) 435-8364** | Mobile: (b) (6)

From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Sent: Thursday, April 22, 2021 9:10 AM
To: Adam, Stacey (FNIH) [T] <sadam@fnih.org>
Subject: RE: [EXTERNAL] ACTIV-6

Of course jw

From: Adam, Stacey (FNIH) [T] <sadam@fnih.org>
Sent: Thursday, April 22, 2021 9:02 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: RE: [EXTERNAL] ACTIV-6

Hi Janet,

You are correct, but of course we are mostly completed in our prioritization for the first rounds, so I need to see how NIH/ACTIV wishes to handle/message this to them.

Thanks,
stacey

Stacey J. Adam, PhD
Associate Vice President
Research Partnerships
Direct: **(301) 435-8364** | Mobile: (b) (6)

From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Sent: Thursday, April 22, 2021 8:37 AM

To: Adam, Stacey (FNIH) [T] <sadam@fnih.org>
Subject: RE: [EXTERNAL] ACTIV-6

Thx they seem to want to help with agent selection jw

From: Adam, Stacey (FNIH) [T] <sadam@fnih.org>
Sent: Thursday, April 22, 2021 8:31 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: RE: [EXTERNAL] ACTIV-6

Hi Janet,

As Francis and a number of NIH colleagues are on here as well, I will consult with them and make sure that someone is on point to send a response.

Thanks,
Stacey

Stacey J. Adam, PhD
Associate Vice President
Research Partnerships
Direct: **(301) 435-8364** | Mobile: (b) (6)

From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Sent: Thursday, April 22, 2021 8:06 AM
To: Adam, Stacey (FNIH) [T] <sadam@fnih.org>
Subject: FW: [EXTERNAL] ACTIV-6

Maybe best for you to respond? jw

From: Stephen Ditmore <(b) (6)>
Sent: Thursday, April 22, 2021 12:44 AM
To: (b) (6) Austin, Christopher P (NIH) <(b) (6)>; Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>; Kim, Peter (NIH/NIAID) <(b) (6)>; Hall, Matthew D (NIH) <(b) (6)>; Harrigan, Rachel (OS) <Rachel.Harrigan@hhs.gov>; (b) (6)
Cc: Kim, Peter S (NIH) <(b) (6)>; research.support.services@vumc.org; dukectsi@dm.duke.edu; Renee.Pridgen@duke.deu; Joseph E. Varon <(b) (6)>; marc rendell <rendell@asndi.com>; Pierre Kory <(b) (6)>; Marik, Paul E. <MarikPE@evms.edu>; Ngo, Binh <Binh.Ngo@med.usc.edu>; Denise Brennan-Rieder <(b) (6)>; Daniel Griffin <(b) (6)>; Mika Turkia <turkia@nic.fi>
Subject: [EXTERNAL] ACTIV-6

Dr. Francis Collins, Director, NIH
Dr. Michael Gregory Kurilla, Director, Division of Clinical Innovation, NCATS
Dr. Matthew Hall, Division of Preclinical Innovation, NCATS
Dr. Janet Woodcock, Acting Commissioner, FDA

Dr. Rachel Harrigan, OWS
Dr. Peter S. Kim, NIAID
Renee Pridgen, MHA, Duke Clinical Research Institute
General Questions, Duke Clinical & Translational Science Institute
Research Support Services, Vanderbilt Institute for Clinical and Translational Research

Dear Dr. Collins and colleagues,

Your recent **announcement of the ACTIV-6 clinical trial**, investigating repurposed COVID-19 therapeutics for early-stage disease, is the best reply our previous letters could have received. We are excited at the prospect of having answers that will allow outpatient clinicians throughout the United States and the world to effectively treat COVID-19. NCATS is the right agency to undertake this; the participation of Duke and Vanderbilt is reason for further optimism.

We are a group of correspondents and co-authors of two recent papers:

The Importance of Understanding the Stages of COVID-19 in Treatment and Trials
Daniel O Griffin et al.

The Time to Offer Treatments for COVID-19
Binh Ngo et al.

In particular, Drs. Binh Ngo and Marc Rendell of Los Angeles, around whose efforts the rest of us have formed, have been consistent seekers of repurposed outpatient COVID-19 antivirals. We wonder if there is a way one or both might be nominated to advise the ACTIV-6 clinical trial.

While there's much to be said about where the US and the world stand concerning COVID-19 therapeutics, we'd like to take this opportunity to summarize our thoughts concerning:

Selection of agents

First, a question: Is it the intent of ACTIV-6 to focus on agents thought to have antiviral activity, or should we take the word "symptoms" to imply something else?

Either way, we hope the need for answers concerning ivermectin is at or near the top of your agenda. The volume of in vivo data from around the world, most of it supporting the hypothesis of ivermectin efficacy against COVID-19, is considerable. Noted physicians in the U.S. and abroad, including members of our group, stand ready to present that data & their meta-analysis of it. Ivermectin skeptics, some of them equally noted, often question the quality of said data, leading to the necessity of a government or foundation funded clinical trial such as ACTIV-6.

Other agents with antiviral activity we suggest might be included are **budesonide**, **niclosamide**, and **nitric oxide nasal spray**.

The centrality of timing

If it's antivirals you wish to trial, we're concerned that a window of 7 days from symptom onset may be excessive relative to the initiation of treatment. It's our understanding that the BLAZE trials initiated therapy within a shorter time-frame, as did the COLCORONA study of colchicine (for other reasons, since that is not an antiviral). In fact, many of us would suggest that procedure &

process refinements that result in the minimizing of time to treatment in an outpatient setting, if undertaken, could be an enormous contribution of your study apart from or in addition to the identification of an effective antiviral drug.

On the other hand, if what you're considering are anti-inflammatories and anticoagulants, it might be better to wait until week 2. The centrality of timing relative to the specific therapeutic being considered is a matter about which prominent physicians within our group, who might disagree concerning other matters, speak with one voice, and about which we would urge you to consider Griffin et. al, mentioned above. Many previous trials have made mistakes of timing. Trial size and statistical sophistication cannot compensate if the timing of drug administration is improper relative to disease course.

The U.S.N.I.H. and U.S. pharmaceutical companies have scored important wins with respect to mRNA vaccines, and some would say monoclonal antibodies. We're grateful; the world is grateful. Yet even in the area of vaccines, noted tropical disease specialist Peter Hotez recently said in an interview:

> ***There were policy decisions focused exclusively around innovation, not sufficiently considering which vaccines were going to be needed in resource poor countries.***

Abroad, ***and*** here in the U.S., this pandemic is far from over. Our search for self-administered outpatient therapeutics has ***not*** been successful to date (with the possible exception of recent evidence for aspirin's efficacy in reducing progression to severe disease). But we do know more than we did a year ago. Screening programs and independent researchers are pointing us toward possible answers, and some are medicines with which physicians have had long experience. Ivermectin remains in-the-running, and there are signals other medicines are forthcoming. Comparative trials are needed; we have great hope ACTIV-6 will make a positive contribution.

Sincerely,

Binh Ngo, MD
Associate Professor
Keck Medical School of USC
Los Angeles, CA

Marc Rendell, MD
Medical Director
Rose Salter Medical Research Foundation
Newport Beach, CA

Paul E. Marik MD, FCCP, FCCM
Eastern Virginia Medical School
Department of Internal Medicine
Chief, Pulmonary and Critical Care Medicine
Norfolk, VA

Pierre Kory, MD, MPA
Pulmonary and Critical Care Medicine
Aurora St. Luke's Medical Center

Milwaukee, WI

Stephen Ditmore
Health Reporter
Parkchester Times
Bronx, NY

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 5/14/2021 7:57:50 AM
To: h.rees@pharmaflowltd.com
Subject: RE: [EXTERNAL] UK Initiative on COVID-19 - brief update

Thx Janet W

From: h.rees@pharmaflowltd.com <h.rees@pharmaflowltd.com>
Sent: Friday, May 14, 2021 7:08 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Re: [EXTERNAL] UK Initiative on COVID-19 - brief update

Dear Janet,

Again, sending the attached privately, in case it may or may not be of interest. Also, a link to a recent press release from the Front Line COVID-19 Critical Care Alliance:

https://covid19criticalcare.com/videos-and-press/flccc-releases/flccc-alliance-statement-on-the-irregular-actions-of-public-health-agencies-and-the-widespread-disinformation-campaign-against-ivermectin/

If you are curious why I am following this, it's because the 'ROADMAP TO A BETTER FUTURE' has Healthcare professionals, along with patients, front and center of drug development.

In the same way pilots are crucial in developing aircraft (and making sure they are safe for passengers), physicians/doctors/clinicians should undertake an analogous role in medicines (IMHO). Jenner, Banting et al, Fleming, Salk, were all medically qualified – and that is not the case today.

Me thinks the integration of the CPI, GMPs for the 2st Century and the principles of evidence based medicine would be a potent combination, along with a strategic approach to building supply chains to patient markets.

Hope all is still good.

Kind regards,

Hedley

:>)

Sent from my iPhone

On 11 May 2021, at 17:40, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

Thanks! You've been productive. Janet W

From: h.rees@pharmaflowltd.com <h.rees@pharmaflowltd.com>
Sent: Tuesday, May 11, 2021 12:14 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: RE: [EXTERNAL] UK Initiative on COVID-19

Thanks Janet – good to hear you are driving it – there seems to be a growing body of evidence out there now!

All good here, hope same with you.

Really believing now that COVID has raised public awareness of the crucial importance of the manufacturing supply chain in properly satisfying the needs of patients for safe, effective, high quality (and affordable) drugs. I have covered your work in the final chapter of *What Patients Need to Know About Pharmaceutical Supply Chains,* titled 'ROADMAP TO A BETTER FUTURE'.

Drug Development for Research Scientists is next on the agenda – hopefully you will consider contributing some thoughts, short or long as you like?

Finally, Industrial Pharmacy kindly published a two part article of mine on COVID supply chains in the last fall, see both editions here:

Part 1 https://www.dropbox.com/s/edbj61w6opl95j2/IP66%20FIP%20Sept%202020.pdf?dl=0

Part 2 https://www.dropbox.com/s/2v2rfcz1pq8oyue/IP67_2_FIP.pdf?dl=0

That's it from me!

With kind regards,

Hedley

From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Sent: 11 May 2021 15:50
To: h.rees@pharmaflowltd.com
Subject: RE: [EXTERNAL] UK Initiative on COVID-19

Thanks, ACTIV at FNIH/NIH at my urging is launching a large simple trial with ivermectin as the first agent. Hope you are well. jw

From: h.rees@pharmaflowltd.com <h.rees@pharmaflowltd.com>
Sent: Tuesday, May 11, 2021 5:53 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: [EXTERNAL] UK Initiative on COVID-19

Dear Janet,

This may be of no interest whatsoever, and this is just an informal observation for you to ignore as you see fit.

As I have been developing patient-physician focussed models of drug development (aligned with the CPI), I happened across this initiative here. The lady behind it is Tess Lawrie. I had a Zoom call with her today and she has some very interesting ideas on building evidence of a drugs' potential in terms of safety, efficacy and quality.

I will leave that with you in case the initiative that Tess is fronting would be useful information within FDA.

With kind regards,

Hedley

Hedley Rees
Managing Consultant PharmaFlow Ltd
T: +44 1656 655664
M: (b) (6)

Author
Book: *Supply Chain Management in the Drug Industry: Delivering Patient Value for Pharmaceuticals and Biologics* (2011) - Read Me
Book: *FIND IT, FILE IT, FLOG IT: Pharma's Crippling addiction and How to Cure It (2015)* - Read me
Book: *Taming the BIG PHARMA MONSTER by Speaking Truth to Power* – (2019) - Read me
Book: *What Patients Need to Know About Pharmaceutical Supply Chains – (2021)* – Read me
Video: *Supply Chain Management in the Drug Industry: Delivering Patient Value for Pharmaceuticals and Biologics* (2011) – Watch it
Video: *MEDICINES FOR THE 21st CENTURY: Safe, Better, Cheaper (2019)* – Watch it

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 5/10/2021 2:18:32 PM
To: Cole Sommers [(b) (6)]
Subject: RE: [EXTERNAL] Why aren't we using Ivermectin for covid?

Thank you. I am familiar with the ivermectin data. I believe it soon will be tested in a large trial to get a definitive idea of its effectiveness in early treatment. Janet Woodcock

From: Cole Sommers <(b) (6)>
Sent: Monday, May 10, 2021 2:11 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: [EXTERNAL] Why aren't we using Ivermectin for covid?

Dear Dr. Woodcock,

I am sure that you are aware of the numerous studies showing the efficacy of Ivermectin in both the prophylaxis and treatment of covid-19.

I recommend that you to review the meta analysis by Dr. Tess Lawrie as well as the work of Paul Marik, MD.
Countries that have adopted Ivermecitn have seen a large decrease in both cases and CFR.

We need all the tools in the tools shed to battle this terrible pandemic. That includes mass vaccinations as well as safe and effective early treatment such as Ivermectin. People are dying that simply don't have to die.

If you are not familiar with all of the literature on Ivermectin I will be happy to send it to you.
We must think our way out of this pandemic using first principles reasoning and work up form known medical principles rather than reasoning form analogy.

Thank you,
Cole Sommers

"Your Deeds Are Your Monuments"

NULLIUS IN VERBA

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 7/1/2021 3:12:56 PM
To: Paul Elias Alexander [(b) (6)]
Subject: RE: [EXTERNAL] Real World Evidence and non-randomized research.

Thanks. To my knowledge, there is no reliable evidence that hydroxychloroquine is effective in treating or preventing COVID-19 and we are testing ivermectin. Janet W

From: Paul Elias Alexander <(b) (6)>
Sent: Thursday, July 1, 2021 10:24 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>; Marks, Peter <Peter.Marks@fda.hhs.gov>
Subject: [EXTERNAL] Real World Evidence and non-randomized research.

Hi Dr. Woodcock, good morning. I have read your good publication with Dr. Marks on using real world evidence and also Dr. Friedan's paper on using non-randomized research. I also know of the CURES ACT 2016 section 3022 that confines and constrains the FDA to use real world non randomized evidence to make regulatory decisions. 'All evidence is fair game'!

Short of randomized controlled evidence that is time consuming and costly to mount especially within the throes of a pandemic emergency, then we have to consider real world evidence, anecdotal evidence, case series...everything.

Via the precautionary principle we do all we can to not cause harm and to yield some benefit, until more is known. If a drug or drugs have even the modest of possible benefit, and no harms, then we are obligated to consider it. 'First do no harm'. We have these drugs with regulatory approval, used for 70 years, for other conditions, safe, effective, available etc., then why not use it if it 'could' help. If it can possibly help, should we not at least try? This is the mind boggling issue, these drugs 'may well work'. Why not try it?

Thus I am arguing that you consider HCQ and IVM etc. from this lens. Can you? Let us remove the prior politics from this situation and try to consider these as a way to save lives. Always. This has been politicized and biased wrongfully and people are scared and do not want to believe in other things. They have been confused and told things that make no sense. It seems that our premier agencies are not being served by the persons assessing the therapeutics and many often are conflicted.

We can treat our way out of this along with vaccines (if not harmful). I am against these vaccines for children, anyone under 30...

I wrote to you as the top most decision-makers. I ask careful consideration.

Happy 4th of July, 2021! In the greatest nation.

Best,

Paul E. Alexander, PhD
Health Research Methodologist
Evidence-Based-Medicine
Clinical epidemiologist

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 4/11/2021 1:19:28 PM
To: Steve Kirsch [(b) (6)]
Subject: RE: [EXTERNAL] ivermectin will be tested in ACTIV-6

Yes I can't comment. jw

From: Steve Kirsch <(b) (6)>
Sent: Sunday, April 11, 2021 11:09 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: [EXTERNAL] ivermectin will be tested in ACTIV-6

hah.... I have it on VERY good authority that IVM is being tested in ACTIV-6.

I bet you know that too (just can't tell me due to secrecy reasons).

😉

> -----Original Message-----
> From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
> Sent: Sunday, April 11, 2021 6:35 AM
> To: Steve Kirsch <(b) (6)>
> Subject: RE: [EXTERNAL] Ivermectin: better outcomes in the ivm cohort in
> 49/49 studies
>
> Hopefully this will be tested in a large RCT very soon. jw
>
> -----Original Message-----
> From: Steve Kirsch <(b) (6)>
> Sent: Saturday, April 10, 2021 2:51 PM
> To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
> Subject: [EXTERNAL] Ivermectin: better outcomes in the ivm cohort in 49/49
> studies
>
> CAUTION: This email originated from outside of the organization. Do not click
> links or open attachments unless you recognize the sender and know the
> content is safe.
>
>
> 49 studies, 45 of which published in peer reviewed journals, 25 are RCTs.
>
> In 100% of these, the cohort that included the ivermectin ALWAYS did better.
> NOT A SINGLE COUNTER EXAMPLE (including the very flawed JAMA study).
>
> Nobody I talked with can cite a single instance where a drug with 49/49
> batting average was found to be a dud.

>
> can you or anyone at the FDA?
>
> -steve

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 6/22/2021 12:46:06 PM
To: LARRY ROSENFELD [(b) (6)]
Subject: RE: [EXTERNAL] Treatment for covid

There is an EUA for Regeneron and hundreds of thousands of doses have been administered to early, high risk patients. Ivermectin is under study. Janet Woodcock

-----Original Message-----
From: LARRY ROSENFELD <(b) (6)>
Sent: Monday, June 21, 2021 11:26 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: [EXTERNAL] Treatment for covid

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Why aren't physicians prescribing
Regeneron and Ivermectin for early stage covid? There is evidence that these medications are effective to prevent viral replication. What is the F D A doing to save lives during this pandemic?

From: Steve Kirsch [redacted] (b) (6)
Sent: 5/28/2021 12:47:29 PM
To: Lane, Henry C (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d904337536cf41719032a9359a1ec2ab-HHS-CLANE-n]
CC: Daniel O'Connor [doconnor@trialsitenews.com]
Subject: [EXTERNAL] **URGENT** What you are doing is unethical and costing THOUSANDS of lives every day

Importance: High

Hi Cliff,

I'm sure you know by now that Together showed that both IVM and FLV work. Gates Foundation knows. The WHO knows and they aren't saying anything.

You may even know that the numbers from the washU trial showed the same effect size. Waiting an extra day for drug delivery dramatically lowers the effect size which is why it was lower in this trial, but still above the 20% threshold Francis Collins mentioned on 60 Minutes.

These drugs MUST be given EARLY for the largest effect. Wait 5 days before treatment and efficacy goes down. Every virologist knows that.

The public must be told to take these drugs ASAP. You can't find a single doctor who has used these drugs who will tell you otherwise. Not one.

there isn't a shred of evidence that both drugs are neutral or net harmful. NO study shows that. I simply cannot find a single doctor anywhere in the world who have used these drugs that believes these drugs are neutral or harmful.

You can change the NIH Guidelines for these two drugs based on expert opinion easily. You don't even need a vote, as we learned from Peter Yim's efforts where the NIH refused to disclose whether there was a vote on ivermectin and none of the panelists would say anything.

Keeping whether or not there was a vote secret, even after a FOIA request, is NOT IN THE PUBLIC INTEREST. How do you explain avoid answering even a single question like that?

I offered $2M to anyone in the world who could provide a decent argument that the NIH or WHO guidelines either 1) fit the evidence or 2) minimized # of lives lost.
https://trialsitenews.com/if-you-can-prove-that-the-nih-and-who-got-their-treatment-guidelines-right-you-could-win-2m/

Guess what? NOT ONE SINGLE TAKER. I even make it easy. There were two independent ways to win: you could prove it EITHER way. NO TAKERS. Nobody qualified even attempted to enter.

This article published 2 days ago in TSN show even more evidence.
https://trialsitenews.com/five-rcts-recently-published-in-mainstream-scientific-journals-that-confirm-major-statistically-significant-benefits-of-ivermectin-against-covid-19-as-reported-in-several-prior-rcts/

How do you explain all this? All these studies are positive and your recommendations are NEUTRAL?

NEUTRAL is when half the studies are positive, half are negative. That's NEUTRAL. When you have 22 studies that are positive, with only 1 study which CALCULATED the effect size (and did not directly measure it) with a VERY insigificant p value of .54 (not .054), that's basically 22 positive studies and one very statistically random result that was no better than a random guess. So the only negative study was the lowest quality data in the lot. Clearly, that's the ONLY study you believe. That's ridiculous.

If you had a basketball team with a 22-0 win loss record, would you call that a winning team, losing team, or neutral? I get it... that's neutral.

I clearly point out in TSN op-ed discussing IVM, HCQ, and FLV that it is IMPOSSIBLE to justify that all three drugs don't work. The hypothesis doesn't fit any of the facts. Apparently everyone agrees with my analysis since nobody tried to get the $2M reward for showing I was wrong.
https://trialsitenews.com/do-the-nih-and-who-covid-treatment-recommendations-need-to-be-fixed/

The only way to prove these drugs don't work is to transpose the treatment and control arm data to make your study look correct as Adrian Hernandez attempted before he got caught just hours later:
https://twitter.com/Covid19Crusher/status/1397214174766325765

After they pointed his error out on Twitter, Hernandez then corrected his paper, republished it to medrxiv, but by cherry picking studies, left his conclusion intact. He basically worked backwards from the conclusion he wanted. That's the ONLY way you can show IVM doesn't work.

So ONLY study that proved his point reversed, and he doesn't change the conclusions. Are you kidding me?!?! NOBODY IS BUYING ANY OF THIS. Except your committee.

There have been ZERO takers to my $2M offer. NOBODY CAN DEFEND YOU. NOBODY IN THE WORLD. I've even reached out to IVM bashers pleading with them to take my money. They never respond. Hard to give away $2M nowadays.

I request that you change both guidelines for FLV and IVM to "FOR" IMMEDIATELY as your failure to do so is costing tens of thousands of lives every day.

If you want to also change the guidelines on HCQ for use *EARLY* that would also correct another error. I argue that 29 positive studies, 0 negative studies is compelling in my op-ed in TSN as noted above.

We have a lot of data on HCQ in practice. Telemed and numerous clinical practices across the US have been using hydroxychloroquine for most of the year to treat early outpatient Covid and have treated more than 120,000 Americans by now: 70,000 in one telemed group, 20,000 in another; 20,000 in a large Texas practice; 4,000 in a southern California practice; 3,000 in another Texas practice, 3,000 by Dr. Zelenko, etc., with literally a handful of deaths in total. Estimated that 40% of these patients have been high-risk. So something like 50,000 patient lives saved by HCQ, a drug that your Guidelines say should be avoided, even for early treatment (except in clinical trials). After 29 positive clinical trials for early treatment, isn't it time to call this one based on expert opinion.

The effect size of HCQ is clearly lower than IVM and FLV. The HCQ real-world data FURTHER aids the case of FLV and IVM.

Surely you are aware of the Precautionary Principle since it was used to justify mask wearing. See https://www.bmj.com/content/369/bmj.m1435

If not, let me summarize: in a pandemic, if an intervention causes no harm, and MIGHT be helpful, we should use it. Ivermectin is arguably one of the safest drugs every created. Fluvoxamine is also extremely safe when properly prescribed per FDA guidelines on interactions. There is no evidence that when given EARLY, either of these drugs causes harm.

As further evidence that the precautionary principle applies, please listen to this one-minute video of the head of the WHO COVID-19 response: https://twitter.com/skynews/status/1238504143104421888?lang=en.

You and your committee are doing exactly the opposite. You are afraid to take any action because you are afraid of making a mistake. You should be focused on minimizing the number of deaths.

I have been urging you to do the right thing for at least 5 months now.

My patience is at an end.

If you fail to immediately change the guidelines to reflect reality, I will ramp up my efforts to expose the truth so that lives can be saved. I have the capital to do that.

I will start by making this email public. It is being bcc'ed to three dozen key influencers. You will be asked to explain why you did nothing to the US Congress and the mainstream media. Failing to correct these mistakes will destroy the credibility of the NIH Guidelines.

Please let me know **TODAY** what you plan to do. This isn't a tough call. If you cannot figure it out in a few hours, I think you should resign.

All of this data has been hiding in plain sight for months and neatly summarized for you on c19early.com. It has been obvious for at least 7 months for both drugs when I started calling publicly for the use of both drugs. It's about time for you to do the same.

If you have any questions, you can email me or call me at 650-279-1008.

I look forward to hearing back from you. TODAY.

Thank you for your attention to this urgent matter.

-steve

From: Steve Kirsch (b) (6)
Sent: 5/20/2021 10:59:37 AM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: Re: [EXTERNAL] outpatient treatments must be delivered early, but rarely do patients present within 48 hrs of symptoms!

Thanks. That is a KEY insight. This is why so many people have died.

Have u read my op-ed on TrialSiteNews yet? Long but tells the story really well.

Sent from my iPhone

On May 20, 2021, at 6:47 AM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

Don't know. jw

From: Steve Kirsch <(b) (6)>
Sent: Thursday, May 20, 2021 9:44 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Re: [EXTERNAL] outpatient treatments must be delivered early, but rarely do patients present within 48 hrs of symptoms!

As in show me the phase 3 study data driven I presume?

If I show him 50 phase 2 lower quality studies all consistent it won't move needle?

Sent from my iPhone

On May 20, 2021, at 6:41 AM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

Very unlikely to happen, he is completely data-driven. jw

From: Steve Kirsch (b) (6)
Sent: Thursday, May 20, 2021 1:43 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: [EXTERNAL] outpatient treatments must be delivered early, but rarely do patients present within 48 hrs of symptoms!

This is the reality… patients present late. (see below)

If we can get patients EARLY, zero deaths and hospitalizations. LOTS of treatments will work… flv only, ivm only, etc.

How can we get Dr. Fauci to deliver this message? (hint, hint)

-steve

From: Dr. Syed Haider <thedoc@drsyedhaider.com>
Sent: Wednesday, May 19, 2021 5:29 PM
To: Steve Kirsch [redacted (b) (6)]
Cc: Miguel Antonatos, MD <[redacted (b) (6)]>; Bob Apter [redacted (b) (6)]
[redacted (b) (6)]>; David Seftel <dseftel@enablebiosciences.com>
Subject: Re: doxycycline?

Within 2 days I have not seen anyone fail to improve. Coming to me within 2 days happens rarely, and even then getting the meds from the pharmacy can be a hurdle, which is why patients should have these medications on hand and ready to go.

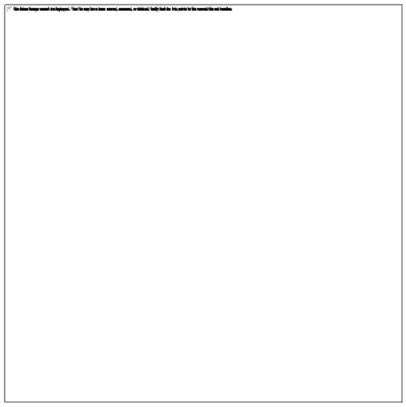
On Wed, May 19, 2021 at 8:24 PM Steve Kirsch <[redacted (b) (6)]> wrote:

> do you have 100% success rate when FLV + IVM are given within 2 days of symptoms?
>
> Looks like if 5 days or more success rate is only a 50% reduction.
>
> Timing is EVERYTHING.
>
> Only 3 failures reasons: started LATE, bad drug, patient didn't take meds.

> **From:** Miguel Antonatos, MD [redacted (b) (6)]
> **Sent:** Wednesday, May 19, 2021 5:21 PM
> **To:** Steve Kirsch [redacted (b) (6)]
> **Cc:** Syed Haider (thedoc@drsyedhaider.com) <thedoc@drsyedhaider.com>
> **Subject:** Re: doxycycline?
>
> Yes I prescribe doxycycline but not upfront only for certain situations when a patient is not improving with ivermectin/fluvoxamine after 8-10 days then I recommend adding an antibiotic and my preference is doxycycline.

Best,

Miguel Antonatos, MD
Board Certified Internal Medicine Physician



On Wed, May 19, 2021 at 7:06 PM Dr. Syed Haider <thedoc@drsyedhaider.com> wrote:

> No, I don't prescribe doxycycline to anyone.

On Wed, May 19, 2021 at 12:49 AM Steve Kirsch [redacted] (b) (6) wrote:

> do you prescribe this up front for your patients? if so, how much of a difference does it make?

From: Steve Kirsch [redacted] (b) (6)
Sent: 5/21/2021 2:01:22 AM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: [EXTERNAL] india is going to be a big RCT for IVM

Just three weeks after adding Ivermectin, Delhi now leads India out of the deadly second surge of the COVID pandemic. Cases that had peaked at 28,395 on April 20 plummeted nearly 80% to just 6,430 on May 15. Deaths peaked May 4, and now they are also down 25%

https://www.thedesertreview.com/opinion/letters_to_editor/ivermectin-crushes-delhi-cases/article_31f3afcc-b7fa-11eb-9585-0f6a290ee105.html

Since we know IVM doesn't really work per the NIH, I wonder what caused such a massive drop? Can anyone at NIH explain that? Boy, I'd love to be a fly on the wall for THAT conversation.

From: Steve Kirsch [(b) (6)]
Sent: 5/20/2021 1:26:43 PM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: [EXTERNAL] We'll get Punjab and others to lead the way here...My op-ed will be published in Times of India!

Hopefully, both the op-ed in the Times of India and changing treatment guidelines in Punjab will start to move the needle.

Thanks for the insights on Dr. Fauci... Incredibly valuable

-steve

From: Steve Kirsch
Sent: Thursday, May 20, 2021 10:21 AM
To: (b) (6); Sandhu Gurpal Jaya <(b) (6)>
Cc: Amol Kothalkar (b) (6) <(b) (6)>; Vikas Sukhatme (vsukhatme@emory.edu) <vsukhatme@emory.edu>; Arjun Bhagat <(b) (6)>
Subject: COVID treatment

Thanks Arjun.

Nice to meet you Gurpal! If you can get this information to the right people, that would be wonderful. Vikas and I are available 24x7 for questions and happy to speak with you at any time.

My goal is to have the COVID Treatment Guidance changed in Punjab, prove that that reduces the hospitalization and death rate to near zero, and then repeat in other states in India.

The message we need to get incorporated is simple:
1) everyone should get treated for COVID **ASAP**. This is THE most important advice. Today, people wait too long to be treated and even with perfect drugs, treatment can fail.
2) do not wait for symptoms if you have a positive test get treated. If you think you have a covid symptom, get treated. SOONER IS ALWAYS BETTER.
3) NOBODY is exempt from treatment, all ages.
4) Have the drugs "on hand" so you can start immediately if you get sick
5) The two most important drugs are Fluvoxamine and ivermectin. Everyone should get at least these two drugs.
6) If you start late, you will need higher dosages of the core drugs and more drugs, e.g, 100mg BID of fluvoxamine vs. 50mg BID if you are treated early
7) Lower dosing of fluvoxamine for teenagers and children

The treatment principles are explained in this document:
India op-ed

Why the WHO and NIH are wrong about ivermectin and fluvoxamine is explained in this long document
Do the NIH and WHO COVID treatment recommendations need to be fixed?

Dr. Sukhatme, Dean of the Emory School of Medicine, and other docs are available for a zoom call whenever you would like to discuss.

Amol Kothalkar, a physician in Buldhana India has treated hundreds of patients with this protocol and swears by it. The protocol is based on solid science and published studies. Not only does it work in studies published in peer reviewed journals, and in clinical practice all over the world, but it works on the ground in India. Dr. Kothalkar will tell you these methods are transformative. He will tell you it is unethical to withhold these drugs.

-steve

From: Arjun Bhagat <(b) (6)>
Sent: Thursday, May 20, 2021 9:46 AM
To: (b) (6); Sandhu Gurpal Jaya <(b) (6)>
Cc: Steve Kirsch (b) (6)
Subject: Introduction

Hi Gurpal and Steve,

I have talked to both of you, so you have context. This email is to get you both connected.

As discussed, Steve, please send over some of your white paper(s) which you think would allow the professionals to understand what you are suggesting/propagating. Once they have had a chance to read it all, and if they have questions, they can reach out to you for further clarifications or details.

I really hope we can get some traction on this, and save lives in Punjab as soon as possible.

Cheers,

Arjun
(b) (6)

From: Steve Kirsch [redacted]
Sent: 5/12/2021 12:46:36 AM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: [EXTERNAL] there is better supply of IVM in a third world country

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this is ridiculous don't you think?

-----Original Message-----
From: John Halbleib <[redacted]>
Sent: Tuesday, May 11, 2021 9:30 PM
To: Steve Kirsch <stk@m10.io>
Subject: Re: IVM + FLV

I will press and see what answers they come up with.

So far:

CVS said they didn't have either medicine in stock and were out and checking with Walgreen's was a good idea.

Walgreen's told me they'd call CVS and let me know when they were ready. Walgreen's only got back to me two days later about Fluvoxamine and the pharmacist had no record of the Ivermectin at all and said "she'd have someone call CVS." I've not heard back since.

Sent from my iPad

> On May 11, 2021, at 9:18 PM, Steve Kirsch <[redacted]wrote:
>
> can you press them on it. I'm curious how it goes. I will write this up as a case study.
>
> so NONE of the pharmacies could provide you with ivermectin? what are they telling you?
>
>> -----Original Message-----
>> From: John Halbleib <[redacted]>
>> Sent: Tuesday, May 11, 2021 8:51 PM
>> To: Steve Kirsch <stk@m10.io>
>> Subject: Re: IVM + FLV
>>
>> Walgreen's Pharmacy never followed up on Ivermectin.
>>
>> Sent from my iPad
>>
>>>> On May 7, 2021, at 5:45 PM, Steve Kirsch [redacted]wrote:
>>>
>>> were you able to get both drugs?
>>>
>>>> -----Original Message-----
>>>> From: John Halbleib <[redacted]>
>>>> Sent: Thursday, May 6, 2021 9:24 AM
>>>> To: Steve Kirsch <[redacted]>
>>>> Subject: Re: IVM + FLV
>>>>
>>>> Walgreen's texted saying Fluvoxamine was ready with no mention of
>>>> Ivermectin so my guess is they're holding that one up.
>>>>
>>>> I had 9 IVM pills to start and have taken 7 so far. I didn't get
>>>> the impression that the pharmacies were going to let me have it.
>>>>
>>>> I could go and try Costco and Safeway. I'm a Kaiser Member but
>>>> would expect them to be the most uncooperative of all.
>>>>
>>>> Sent from my iPhone
>>>>
>>>>>> On May 6, 2021, at 9:06 AM, Steve Kirsch <[redacted]> wrote:
>>>>>
>>>>> how is the ivermectin fill going?
>>>>>

>>>>>> -----Original Message-----
>>>>>> From: John Halbleib <[redacted]>
>>>>>> Sent: Thursday, May 6, 2021 9:05 AM
>>>>>> To: Steve Kirsch <[redacted]>
>>>>>> Subject: Re: IVM + FLV
>>>>>>
>>>>>> Walgreen's has Fluvoxamine ready. You said Prozac was even better
>>>>>> so my plan was to see if CVS will just fill Prozac while I wait
>>>>>> and if they seem to be holding it up I'll go to Walgreen's where
>>>>>> Fluvoxamine is already waiting for me now.
>>>>>>
>>>>>> Sent from my iPhone
>>>>>>
>>>>>>>>>> On May 6, 2021, at 6:12 AM, Steve Kirsch [redacted] wrote:
>>>>>>>
>>>>>>> were you able to get the meds from the US pharmacies?
>>>>>>>
>>>>>>>>>> -----Original Message-----
>>>>>>>>>> From: John Halbleib <[redacted]>
>>>>>>>>>> Sent: Thursday, May 6, 2021 1:57 AM
>>>>>>>>>> To: Steve Kirsch <[redacted]>
>>>>>>>>>> Subject: Re: IVM + FLV
>>>>>>>>>>
>>>>>>>>>> All symptoms are less now. Cough almost gone, full body unwell
>>>>>>>>>> feeling way less including the "I feel like I should have a
>>>>>>>>>> fever but don't" feeling. The tongue thing had felt like I
>>>>>>>>>> burnt my tongue without actually having done that and has
>>>>>>>>>> lessened a lot and may be gone
>>>>>>>> soon.
>>>>>>>>>>
>>>>>>>>>> I told Dr Apter I took a Covid Test (NAAT) and he had already
>>>>>>>>>> said even if it comes back negative the safest thing was still
>>>>>>>>>> to continue treatment. It did comeback negative from a test on
>>>>>>>>>> May 3 and I have continued IVM and FLU with a prescription of
>>>>>>>>>> Prozac electronically sent also to finish up after Fluvoxamine is gone.
>>>>>>>>>>
>>>>>>>>>> I've lost some sleep in recent days and haven't 100% had my
>>>>>>>>>> wits about me but later I have a story to tell of how the 60
>>>>>>>>>> Minutes Segment influenced me to push for a friend's mother in
>>>>>>>>>> Egypt to get Fluvoxamine for her Covid diagnosed back in March.
>>>>>>>>>> Spoiler alert...she successfully made her way through despite
>>>>>>>>>> some scary
>>>>>>>> vulnerabilities.
>>>>>>>>>>
>>>>>>>>>> I'll tell the whole story later,
>>>>>>>>>>
>>>>>>>>>> Thank you,
>>>>>>>>>> John
>>>>>>>>>>
>>>>>>>>>> Sent from my iPad
>>>>>>>>>>
>>>>>>>>>>>>>> On May 6, 2021, at 12:35 AM, Steve Kirsch [redacted] wrote:
>>>>>>>>>
>>>>>>>>>> you should be getting better and better each day?
>>>>>>>>>>
>>>>>>>>>> were you able to fill the prescriptions???
>>>>>>>>>>
>>>>>>>>>>>>>> -----Original Message-----
>>>>>>>>>>>>>> From: John Halbleib <[redacted]>
>>>>>>>>>>>>>> Sent: Wednesday, May 5, 2021 6:09 PM
>>>>>>>>>>>>>> To: Steve Kirsch <[redacted]>
>>>>>>>>>>>>>> Subject: Re: IVM + FLV
>>>>>>>>>>>>>>
>>>>>>>>>>>>>> Doing well, thanks. Exchanged emails with Robert also.
>>>>>>>>>>>>>>
>>>>>>>>>>>>>> Sent from my iPhone
>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>>> On May 5, 2021, at 4:59 PM, Steve Kirsch <[redacted]> wrote:
>>>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>>> How are you doing?

From: Kurt Stockbauer [(b) (6)]
Sent: 7/23/2021 10:30:48 PM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: [EXTERNAL] Covid 19 protocol

Do the right thing Janet Ivermectin should be part of US protocol!

India saw a dramatic fall in cases after the ICMR and AIIMS added Ivermectin to their protocols on April 20, 2021. Daily COVID-19 cases, which peaked at 414,188, are now down to 84,332, representing a drop of 80% overall in the country of India.

What seemed to be an impending humanitarian crisis at the end of April has now been brought under control, not with mass vaccination, but instead with an inexpensive repurposed drug, Ivermectin.

Kurt

From: Michael Morrison [(b) (6)]
Sent: 10/20/2021 11:51:44 AM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: Re: [EXTERNAL] Your opinion, please

Thank you (or your staff) - sincerely - for your replies.

On Oct 20, 2021, at 7:53 AM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

NIH is doing a study on outpatient treatment with ivermectin. It is an RCT. Janet Woodcock

From: Michael Morrison <(b) (6)>
Sent: Tuesday, October 19, 2021 10:27 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Re: [EXTERNAL] Your opinion, please

Yet your FDA is why I'm being denied access to a profilaxis which has proven to be effective in other studies. My pharmacist is refusing to fill a prescription by referring to your agency's guidance.

Another NIH publication:

https://pubmed.ncbi.nlm.nih.gov/33592050/

"Two-dose ivermectin prophylaxis was associated with a 73% reduction of SARS-CoV-2 infection among healthcare workers."

Certainly an NIH follow up study is justified.

On Oct 19, 2021, at 8:30 AM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

Need to see results from RCTs, as the authors say. These types of studies are hypothesis generating, not confirmatory. Janet Woodcock

From: Michael Morrison <(b) (6)>
Sent: Monday, October 18, 2021 9:39 PM

To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: [EXTERNAL] Your opinion, please

You'll no doubt find this interesting:

https://pubmed.ncbi.nlm.nih.gov/33065103/

From: rihrih wfuma.org [rihrih@wfuma.org]
Sent: 9/11/2021 11:02:10 AM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: Re: [EXTERNAL] Consider human-use OTC ivermectin &

If that can benefit public health - sure.

R.

On Sep 11, 2021, at 10:03 AM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

That is a matter for the Center for Drug Evaluation and Research at the FDA to consider. Would you like me to direct your inquiry to them? Janet Woodcock

From: rihrih wfuma.org <rihrih@wfuma.org>
Sent: Friday, September 10, 2021 4:58 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Re: [EXTERNAL] Consider human-use OTC ivermectin &

… currently available data, as presented in the below figures, seems to support public use?

R.

On Sep 10, 2021, at 11:36 AM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

Yes must be later, and not published. jw

From: rihrih wfuma.org <rihrih@wfuma.org>
Sent: Friday, September 10, 2021 11:16 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Cc: rihrih wfuma.org <rihrih@wfuma.org>
Subject: RE: [EXTERNAL] Consider human-use OTC ivermectin &

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2779044

Did TOGETHER assess ivermectin?

From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Sent: Friday, September 10, 2021 10:55 AM
To: rihrih wfuma.org <rihrih@wfuma.org>
Subject: RE: [EXTERNAL] Consider human-use OTC ivermectin &

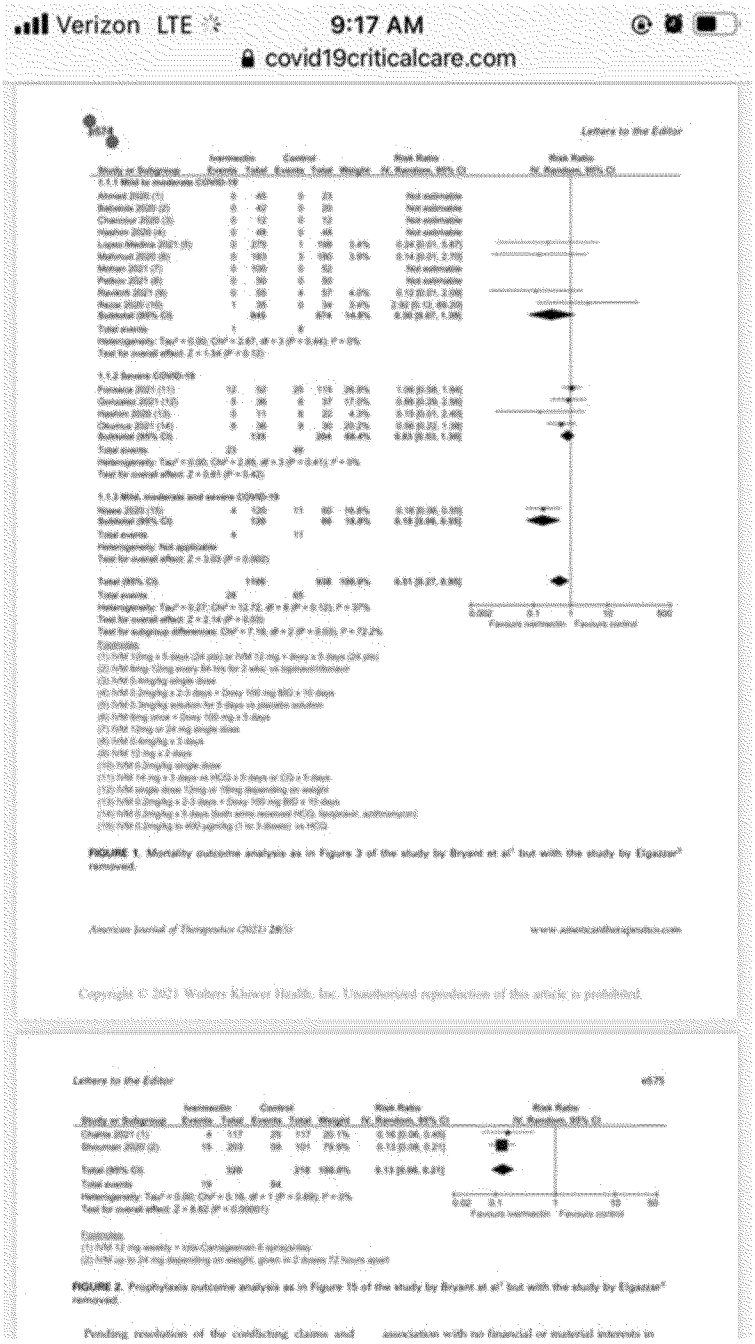
Did this include the TOGETHER results? Very small numbers of events in many of these studies. jw

---

From: rihrih wfuma.org <rihrih@wfuma.org>
Sent: Friday, September 10, 2021 9:17 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Re: [EXTERNAL] Consider human-use OTC ivermectin &

Thank you - figures 1 and 2 here list studies and outcomes:

https://covid19criticalcare.com/wp-content/uploads/2021/09/Response-to-Elgazzar.pdf



R.

On Sep 10, 2021, at 8:14 AM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

The current evidence of effectiveness of ivermectin and HCQ against COVID-19 is negative. The ACTIVE 6 trial is testing a higher dose/longer duration of ivermectin in outpatients. I'm unaware of data on nitazaxanide. Janet Woodcock

From: rihrih wfuma.org <rihrih@wfuma.org>
Sent: Friday, September 10, 2021 6:43 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: [EXTERNAL] Consider human-use OTC ivermectin &

Dear Dr. Woodcock,

Considering the potential public health value, including potential benefit in early / home use treatment of COVID-19, safety history and profiles of current OTC products, might it be now appropriate for ivermectin and nitazaxanide, and even hydroxychloroquinine, to be available OTC in the US?

https://covid19criticalcare.com/wp-content/uploads/2020/11/FLCCC-Alliance-I-MASKplus-Protocol-ENGLISH.pdf

With sincere respect,

Roxolana Horbowyj, MD, FACS

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 8/31/2021 7:44:13 AM
To: Ashley, Donald [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=40241a76230349cbb195ab1721092196-Donald.Ashl]
Subject: RE: [EXTERNAL] Fox News Ivermectin and Consumer Deaths from Reckless Medical Advice

Thx! jw

From: Ashley, Donald <Donald.Ashley@fda.hhs.gov>
Sent: Tuesday, August 31, 2021 7:41 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: FW: [EXTERNAL] Fox News Ivermectin and Consumer Deaths from Reckless Medical Advice

Janet: I'll arrange for an appropriate reply. Don

From: BRUCE JOHNSON <(b) (6)>
Sent: Monday, August 30, 2021 10:57 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>; Ashley, Donald <Donald.Ashley@fda.hhs.gov>
Subject: [EXTERNAL] Fox News Ivermectin and Consumer Deaths from Reckless Medical Advice

Why hasn't the fda warmed Fox News of its reckless conduct with respect to invermectin?

Like below
https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-warns-seller-marketing-dangerous-chlorine-dioxide-products-claim

Bruce Johnson
(b) (6)

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 8/9/2021 7:11:10 AM
To: Stan Young [(b) (6)]
Subject: RE: [EXTERNAL] soy protein

Not so simple. I don't think ivermectin works well enough It is a large simple no touch trial though. jw

From: Stan Young <(b) (6)>
Sent: Sunday, August 8, 2021 11:00 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: [EXTERNAL] soy protein

Janet: I've been following virus somewhat closely. I'm quite distrustful of CDC numbers. You mentioned that you were considering an FDA experiment on ivermectin; large simple trial. What is going on there? Rank the states by population. At random, one of each pair allows ivermectin. ?? Stan

Stan and Pat Young (b) (6)

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 8/17/2021 2:16:27 PM
To: Adv Nadkarni [(b) (6)]
Subject: RE: [EXTERNAL] How state of Uttar Pradesh, India contained Delta Variant nCoV

Thank you for the information. Janet Woodcock

From: Adv Nadkarni <(b) (6)>
Sent: Tuesday, August 17, 2021 2:08 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: [EXTERNAL] How state of Uttar Pradesh, India contained Delta Variant nCoV

Dear Dr. Woodcock,

I have the evidence from the respective State officials (India) on how Uttar Pradesh (UP), India with population 240 million contained the infections due to Delta variant nCoV that has the most efficient mutation ever, the L452R (R=Arginine - Hydrophilic, Positively charged side chain with the highest pKa3 semi-essential amino acid) in the RBD. The ACE2 is negatively charged.

In the first week of April 2021, when the Second wave in India shot up, a pilot program was conducted in the City of Agra, UP, by the city's Chief Medical Officer Dr. Anshul Pareek. He gave Ivermectin 12 mg, 1 tablet a day for 3 days to every person with mild/moderate symptoms, who was tested nCoV positive through RT/PCR test. In addition, he also gave Ivermectin 12 mg to every family member and other persons who came in contact with the person found nCoV positive. Dr. Pareek observed very good outcome, and that's when the Uttar Pradesh state govt. decided to replicate this model state-wide which started in the 3rd week of April is still being followed. For the last month, Uttar Pradesh has recorded less than 50 cases daily among its population of 240 million people. This model of using Ivermectin as a therapeutic and prophylactic agent was then used by other states viz. Delhi, Madhya Pradesh, Gujarat, Uttarakhand, Bihar, Rajasthan, Punjab to my knowledge and the evidence I have gained so far. You may check the results at https://www.covid19india.org/
May be you can contact with the IDSP (Integrated Disease Surveillance Program) India officials and confirm this information by yourself. I hope the information I shared with you is helpful to you in saving the people from your country.

Best Regards,

Adv. Nadkarni, B.Sc.(Physics), MS (Computer Engg), MBA, LL.B.
India

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 7/15/2021 10:10:30 AM
To: Karla [(b) (6)]
Subject: RE: [EXTERNAL] Thank You for Your Bold Move

Thank you for writing. We will look at all the evidence on ivermectin. Janet Woodcock

From: Karla <(b) (6)>
Sent: Thursday, July 15, 2021 9:31 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: [EXTERNAL] Thank You for Your Bold Move

Dear Dr. Woodcock,

Thank you for your bold move in asking the independent Office of the Inspector General to investigate how the FDA and representatives of Biogen interacted prior to the FDA's approval of the company's Aduhelm (aducanumab) for Alzheimer's disease.

I am writing to ask for your help, as the US is in need of another bold move. Currently, the FDA recommends against the use of ivermectin to treat or prevent COVID-19 (https://www.fda.gov/consumers/consumer-updates/why-you-should-not-use-ivermectin-treat-or-prevent-covid-19). This post also states, "The FDA has not reviewed data to support use of ivermectin in COVID-19 patients to treat or to prevent COVID-19; however, some initial research is underway."

Dr. Woodcock, the data has been reviewed by the NIH which then upgraded its standing on ivermectin from "not recommended" to "neutral." The data has been reviewed through meta-analyses by Dr. Tess Lawrie, a WHO independent research consultant, who then stated, "I independently reviewed 27 studies presented by the Front Line COVID-19 Critical Care (FLCCC) alliance as evidence of ivermectin's effectiveness. The resulting evidence is consistent and unequivocal. Ivermectin works well both in preventing COVID infections and in preventing deaths at the same doses used to treat lice and other parasitic infections," (https://www.youtube.com/watch?v=M8RMBa1UfsE). The data has been reviewed through meta-analysis by Dr. Andrew Hill from University of Liverpool, England, supported by The WHO Access to COVID-19 Tools (ACT) Accelerator, who also found ivermectin produces large statistically significant reductions in mortality, time to clinical recovery, and time to viral clearance (https://www.youtube.com/watch?v=yOAh7GtvcOs).

Dr. Woodcock, I am asking you for another bold move. I am asking you to review the data presented to the NIH January 6, 2021 (https://covid19criticalcare.com/wp-content/uploads/2021/01/FLCCC-PressRelease-NIH-C19-Panel-FollowUp-Jan7-2021.pdf https://www.youtube.com/watch?v=eeYoXGoh96w). I am confident you too will find ivermectin produces large statistically significant improvement in COVID-19 patients and that it would be unconscionable to continue to withhold the FLCCC ivermectin protocols, as pediatric COVID-19 cases begin to surge, long-hauler COVID-19 cases continue to mount and COVID deaths are on the rise.

I am asking you to immediately align the FDA position on ivermectin with that data.

My prayer is that you are honest. I am praying for your strength.

Sincerely,
Karla Q. Harris
Baltimore MD

A Guide to Home-Based COVID Treatment
https://aapsonline.org/covidpatientguide/

The 411 on COVID - Ask Your Doc'!
https://www.youtube.com/watch?v=QAHi3lX3oGM&t=928s
https://www.youtube.com/watch?v=d8o58HB8uYE&t=429s

From: Larry Kayser [redacted] (b) (6)
Sent: 9/3/2021 11:18:29 AM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: [EXTERNAL] I am here again

Good morning Dr. Woodcock,

I sit here still in amazement that we are approaching 100 days since the EUA submission for Aviptadil and not a sound from the FDA apart from another declaration that it is safe. In the meantime, we pound away at vaccines, shame people who don't want to get it for valid reasons and do virtually nothing to equip our hospitals with any therapeutics that can give any kind of hope for critically ill patients while thousands die each week and we are simply scolded for not getting the vaccination.

We still don't have any reliable public data for vaccination side effects. We hear that Ivermectin is harming people, yet there are many doctors who are using it despite the FDA refusal. Now we have lawsuits trying to force hospitals to administer Ivermectin because people keep reading from places all around the world that doctors are using it and it helps. We don't even have a right to try for that drug so people take matters into their own hands and do harm to themselves with wrong dosing or who knows what else they might be doing wrong.

Now the FDA has granted right to try for Aviptadil, which I am grateful for. Why would the FDA grant permission for them to try it at all if it is not worthy of an EUA in this time of emergency? It is simply beyond my comprehension that the FDA does not know if Aviptadil is safe and "may be effective" at this point. I cannot understand how this agency withholds this and other drugs that might be the only hope critically ill people have to recover. Or that it might be used to prevent people from getting to that stage. The FDA has again reiterated that it is safe, so it will not do serious harm to people. Yet here we sit week after week while people die. I had another dear friend die yesterday. I tried to get the Right to Use application to him and his doctors, but it takes too long for the overwhelmed medical staff to even respond, and very few doctors have ever heard of Aviptadil, so they are understandably skeptical of the request. Somehow it has been deemed safe and effective enough to be granted an EUA in Georgia, and I suspect some other Caucasus countries to follow. But here we sit paralyzed while people keep dying.

I know that I will receive the standard reply that you cannot comment on drugs you have been involved with. I simply don't know where else to turn to vent my frustrations. I don't think people who are sitting in offices at the FDA or the CDC understand how deeply these agencies have broken trust with the American people during this pandemic, and how this process has exposed the bureaucratic pace of the drug approval process except of course for vaccines. So the strategy that has dominated our world is to get hundreds of millions of shots into healthy people while we have so little emphasis and development on therapies for the sick and dying. I have tried so hard in the last 18 months to not grow cynical about money, about large Pharma control, about who is funding clinical trials…I am losing my battle with cynicism.

I know you can't help. If you took the time to read this, thank you. If you have an assistant read it and respond, I guess it really doesn't matter.

Sincerely,
Larry

Larry Kayser

From: Bernstein, Ilisa [IBernstein@aphanet.org]
Sent: 9/1/2021 5:16:52 PM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Solomon, Steven M [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e49ac6a056dc4f299ea269945e962e82-SSOLOMON]; Cavazzoni, Patrizia [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c42abd33834044ecbaa03d075cc0a5d2-Patrizia.Ca]
Subject: [EXTERNAL] APhA/ASHP/AMA joint statement against ivermectin

Today, APhA, AMA, and ASHP joined together to help FDA and the public health community in efforts to prevent the prescribing and dispensing of ivermectin for COVID-19. Pasted below is the press release. Thanks so much for all that you and my former colleagues are doing during these tough times.

https://www.pharmacist.com/APhA-Press-Releases/ama-apha-ashp-call-for-immediate-end-to-prescribing-dispensing-and-use-of-ivermectin-to-prevent-or-treat-covid-19-outside-clinical-trials

Thanks. Be well.
ilisa

ILISA BG BERNSTEIN, PharmD, JD, FAPhA
Senior Vice President, Pharmacy Practice and Government Affairs
American Pharmacists Association
2215 Constitution Avenue, NW
Washington, DC 20037
202-429-7533 (O) | [redacted] (b) (6) (M)
www.pharmacist.com

PRESS RELEASE PUBLISHED ON WEDNESDAY, SEPTEMBER 1, 2021

AMA, APhA, ASHP Call for Immediate End to Prescribing, Dispensing, and Use of Ivermectin to Prevent or Treat COVID-19 Outside Clinical Trials

WASHINGTON, DC – The American Medical Association (AMA), American Pharmacists Association (APhA), and American Society of Health-System Pharmacists (ASHP) **strongly oppose the ordering, prescribing, or dispensing of ivermectin to prevent or treat COVID-19 outside of a clinical trial.**

Ivermectin is approved by the U.S. Food and Drug Administration (FDA) for human use to treat infections caused by internal and external parasites. It is not approved to prevent or treat COVID-19. Ivermectin is also available to treat certain veterinary conditions; medications formulated or intended for use in animals should not be used by humans. We are alarmed by reports that outpatient prescribing for and dispensing of ivermectin have increased 24-fold since before the pandemic and increased exponentially over the past few months. As such, we are calling for an immediate end to the prescribing, dispensing, and use of ivermectin for the prevention and treatment of COVID-19 outside of a clinical trial. In addition, we are urging physicians, pharmacists, and other prescribers — trusted healthcare professionals in their communities — to warn patients

against the use of ivermectin outside of FDA-approved indications and guidance, whether intended for use in humans or animals, as well as purchasing ivermectin from online stores. Veterinary forms of this medication are highly concentrated for large animals and pose a significant toxicity risk for humans.

The U.S. Centers for Disease Control and Prevention (CDC) and the FDA have issued advisories indicating that ivermectin is not authorized or approved for the prevention or treatment of COVID-19. The National Institutes of Health, World Health Organization, and Merck (the manufacturer of the drug) all state there is insufficient evidence to support the use of ivermectin to treat COVID-19. The Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19 also recommend against the use of ivermectin outside of a clinical trial.

Use of ivermectin for the prevention and treatment of COVID-19 has been demonstrated to be harmful to patients. Calls to poison control centers due to ivermectin ingestion have increased five-fold from their pre-pandemic baseline. A recent CDC Health Alert Network Advisory recommends that healthcare professionals should counsel patients against use of ivermectin as a treatment for COVID-19, including emphasizing the potentially toxic effects of this drug, including "nausea, vomiting, and diarrhea. Overdoses are associated with hypotension and neurologic effects such as decreased consciousness, confusion, hallucinations, seizures, coma, and death."

For more information, we encourage patients and healthcare providers to consult the FDA's Consumer Update on Why You Should Not Use Ivermectin to Treat or Prevent COVID-19 and the CDC Health Alert Network Advisory on the Rapid Increase in Ivermectin Prescriptions and Reports of Severe Illness Associated with Products Containing Ivermectin to Prevent or Treat COVID-19.

Patients are encouraged to talk to their physicians, pharmacists, and other prescribers about currently available therapies authorized or approved for the treatment or prevention of COVID-19. The most effective ways to limit the spread of COVID-19 are to get vaccinated, wear a face mask, stay at least six feet from others in public places, wash hands frequently, and avoid large crowds of people. Our organizations strongly urge eligible unvaccinated individuals to get vaccinated.

AMA COVID-19 Resource Center for Physicians
APhA COVID-19 Resource Center
ASHP COVID-19 Resource Center

About the American Medical Association
The American Medical Association is the physicians' powerful ally in patient care. As the only medical association that convenes 190+ state and specialty medical societies and other critical stakeholders, the AMA represents physicians with a unified voice to all key players in health care. The AMA leverages its strength by removing the obstacles that interfere with patient care, leading the charge to prevent chronic disease and confront public health crises and, driving the future of medicine to tackle the biggest challenges in health care.
About the American Pharmacists Association
The American Pharmacists Association is only organization advancing the entire pharmacy profession. Our expert staff, and strong volunteer leadership, including many experienced pharmacists, allow us to deliver vital leadership to help pharmacists, pharmaceutical scientists, student pharmacists and pharmacy technicians find success and satisfaction in their work, while advocating for changes that benefit them, their patients and their communities. For more information, please visit www.pharmacist.com.
About ASHP
ASHP is the collective voice of pharmacists who serve as patient care providers in hospitals, health systems, ambulatory clinics, and other healthcare settings spanning the full spectrum of medication use. The organization's 58,000 members include pharmacists, student pharmacists, and pharmacy technicians. For 79 years, ASHP has been at the forefront of efforts to improve medication use and enhance patient safety. For more information about the wide array of ASHP activities and the many ways in which pharmacists advance healthcare, visit ASHP's website, ashp.org, or its consumer website, SafeMedication.com.
Contacts:
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Frank Fortin
American Pharmacists Association
ffortin@aphanet.org
Amy Ruth Cole
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Thanks. Be well

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202-429-7533 (O) | (b) (6) (M)
www.pharmacist.com

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 4/6/2020 10:25:37 AM
To: Hugh Taylor [h.taylor@unimelb.edu.au]; Jonathan Javitt [jjavitt@neurorxpharma.com]; Alfred Sommer [asommer@jhu.edu]
CC: Andy Harris [(b) (6)]
Subject: RE: Ivermectin CoronaVirus Data

Thank you. jw

From: Hugh Taylor <h.taylor@unimelb.edu.au>
Sent: Monday, April 6, 2020 5:14 AM
To: Jonathan Javitt <jjavitt@neurorxpharma.com>; Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>; Alfred Sommer <asommer@jhu.edu>
Cc: Andy Harris <(b) (6)>
Subject: Re: Ivermectin CoronaVirus Data

Thanks Jonathan,
It is good to hear from you and I trust that you and your family are all safe and well.
For background I have attached the recent paper and a few thoughts of mine.
I hope this helps some, but I would be happy to try to answer any further questions.
Best wishes,
Hugh

Professor Hugh R Taylor AC,
Immediate Past President, The International Council of Ophthalmology,
Melbourne Laureate Professor, Harold Mitchell Chair of Indigenous Eye Health Melbourne School of Population and Global Health, University of Melbourne, 207 Bouverie Street, Carlton, 3053. Ph: +61 3 8344 9320 Mobile (b) (6) (b) (6)

www.iehu.unimelb.edu.au
'I respectfully acknowledge Traditional Owners and Custodians of the Country on which I work'

From: Jonathan Javitt <jjavitt@neurorxpharma.com>
Date: Monday, 6 April 2020 at 6:30 pm
To: "Woodcock, Janet" <Janet.Woodcock@fda.hhs.gov>, Hugh Taylor <h.taylor@unimelb.edu.au>, Al Sommer <asommer@jhu.edu>
Cc: Andy Harris <(b) (6)>
Subject: Ivermectin CoronaVirus Data

Adding Al Sommer to this thread. Al was head of the International Center for Epidemiology and Preventive Ophthalmology when the human Ivermectin work was done.

Dear Janet,

Please forgive me if I'm telling you things you already know.

If I can be helpful in any way, please use me. I have zero financial connection to Ivermectin. I was involved with Executive leadership at Merck in the 1980's when Hugh Taylor at Johns Hopkins proved that Ivermectin eradicates Onchocerciasis in Humans and Merck donated sufficient Ivermectin to eradicate human onchocerciasis and, therefore, River Blindness.

The veterinary division of FDA obviously has 100's of millions of animals worth of safety data on this drug. I have fed it to 9 dogs over 35 years. WHO probably has the human safety data. Likely the most knowledgeable living researcher (unfortunately (b) (6) passed away) is Prof. Hugh Taylor in Melbourne, who led the research effort at JHU. (b) (4)

Dr. Vagelos would almost certainly be an expert or spokesperson for FDA because the human ivermectin donation program was one of his crowing achievements at Merck

(b) (4)

Coronavirus Can be Stopped in 48 Hours Using a Simple Anti-Parasitic Drug: Monash University
News18 News185 April 2020

Amid a barrage of research on finding treatment for new coronavirus, Australian scientists have found that a common anti-parasitic drug killed SARS-CoV-2 virus, growing in cell culture, within 48 hours in lab settings. Ivermectin is an FDA-approved anti-parasitic drug that has also been shown to be effective in vitro against a broad range of viruses including HIV, dengue, influenza and Zika virus.

Published in the journal Antiviral Research, the study from Monash University showed that a single dose of Ivermectin could stop the coronavirus growing in cell culture -- effectively eradicating all genetic material of the virus within two days. "We found that even a single dose could essentially remove all viral RNA by 48 hours and that even at 24 hours there was a really significant reduction in it," said study lead author Dr Kylie Wagstaff.

Dr Wagstaff, however, cautioned that the tests conducted in the study were in vitro and that trials needed to be carried out in people. "Ivermectin is very widely used and seen as a safe drug. We need to figure out now whether the dosage you can use it at in humans will be effective - that's the next step," Wagstaff informed. In times when we're having a global pandemic and there isn't an approved treatment, "if we had a compound that was already available around the world then that might help people sooner".

"Realistically it's going to be a while before a vaccine is broadly available," she said. Although the mechanism by which Ivermectin works on the virus is not known, it is likely, based on its action in other viruses, that it works to stop the virus 'dampening down' the host cells' ability to clear it. Dr Wagstaff made a previous breakthrough finding on Ivermectin in 2012 when she identified the drug and its antiviral activity with Monash Biomedicine Discovery Institute's Professor David Jans, also an author on this paper. Professor Jans and his team have been researching Ivermectin for more than 10 years with different viruses.

Dr Wagstaff and Professor Jans started investigating whether it worked on the SARS-CoV-2 virus as soon as the pandemic was known to have started. The use of Ivermectin to combat COVID-19 depends on pre-clinical testing and clinical trials, with funding urgently required to progress the work, the researchers noted.https://in.news.yahoo.com/coronavirus-stopped-48-hours-using-103100205.html?soc_src=social-sh&soc_trk=fb

--

From: Freire, Maria (FNIH) [T] [mfreire@fnih.org]
Sent: 6/18/2020 5:27:44 PM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: RE: Ivermectin

Nope, I was wrong. They are using the regular dose: 0.2mg/Kg. I have reached out to colleagues to see if the results still stand. What I can tell you is that the ivermectin supply is Peru is being wipped out because it is being use as a prophylactic. I'll pass along any more information. M.

From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Sent: Thursday, June 18, 2020 4:45 PM
To: Freire, Maria (FNIH) [T] <mfreire@fnih.org>
Subject: RE: Ivermectin

Yes would like to know if possible. Thanks. jw

From: Freire, Maria (FNIH) [T] <mfreire@fnih.org>
Sent: Thursday, June 18, 2020 4:43 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: RE: Ivermectin

I will try to find out from my Peruvian contacts. My guess – only a guess – is that they would have been pretty high doses. M.

From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Sent: Thursday, June 18, 2020 4:36 PM
To: Freire, Maria (FNIH) [T] <mfreire@fnih.org>
Subject: RE: Ivermectin

I'm following up. Certainly is a very safe drug, not sure what levels achieved in vivo. jw

From: Freire, Maria (FNIH) [T] <mfreire@fnih.org>
Sent: Thursday, June 18, 2020 11:44 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: RE: Ivermectin

David tells me there is a paper that just came out about the in vitro activity. I've not seen it but pretty dramatic results. M.

From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Sent: Thursday, June 18, 2020 10:08 AM
To: Freire, Maria (FNIH) [T] <mfreire@fnih.org>
Subject: RE: Ivermectin

Thanks for the information. Have not forgotten what you told me about this. wj

From: Freire, Maria (FNIH) [T] <mfreire@fnih.org>
Sent: Thursday, June 18, 2020 10:00 AM

To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Ivermectin

Dear Janet,

Below is the curve I mentioned for the city of Iquitos, in the Peruvian Amazon. The health system collapsed almost immediately; it was terrible. They had ivermectin and used it to treat patients. Clearly, these are empirical results, not a clinical trial, but the source is reputable and the data comes from the Ministry of Health (MINSA). The use of Ivermectin was approved by MINSA for COVID-19 treatment on May 8th. The same has been reported for other regions in Peru and in Honduras. BTW – Ivermectin fared rather well in the prioritization by the ACTIV WG in the second wave of potential therapeutic compounds. Best, Maria

Fuente: Aguirre Chang, Gustavo A.*; Trujillo Figueredo, Aurora N.*; Segovia-Juárez, José L.** COVID-19: Impacto del uso de la Ivermectina en la reducción del número de fallecidos. *Médicos de la UNMSM, Perú. ** Ph.D., Universidad Nacional de Ingeniería (UNI). 29 de Mayo 2020.

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 12/20/2020 1:45:35 PM
To: Wholley, David (FNIH) [T] [dwholley@fnih.org]
Subject: RE: Further Summary on Ivermectin ACTIV Review

Thanks, very helpful. wj

From: Wholley, David (FNIH) [T] <dwholley@fnih.org>
Sent: Saturday, December 19, 2020 9:35 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Cc: Adam, Stacey J (NIH) <sadam@fnih.org>; Freire, Maria C (NIH) <mfreire@fnih.org>; Collins, Francis S (NIH) (b) (6)
Subject: FW: Further Summary on Ivermectin ACTIV Review

Hi Janet—there have been a number of inquiries from the Hill regarding ivermectin. Thought you should know about the information regarding ACTIV review of this agent that we have sent to Francis earlier this evening. Thanks, David

---

From: Wholley, David (FNIH) [T]
Sent: Saturday, December 19, 2020 8:42 PM
To: Collins, Francis (NIH/OD) [E] <(b) (6)>
Cc: Adam, Stacey (FNIH) [T] <sadam@fnih.org>; Freire, Maria (FNIH) [T] <mfreire@fnih.org>
Subject: Further Summary on Ivermectin ACTIV Review

Hi Francis,

In case it is of use in your interactions with Senator Johnson or other future inquiries, below and attached is a complete description of the review of ivermectin by the ACTIV team, courtesy of Stacey Adam of course. If OK with you I would like to share this with Janet Woodcock so everyone is in sync. David

1. Ivermectin was first reviewed in Wave 1. It made it through the initial triage of 400 agents by ACTIV and was scored in the antiviral subteam of the Therapeutics Clinical Working Group assigned to look at such agents. It scored moderately well due to the anecdotal data from its use in the clinic in Peru and other countries, and several early, though inadequately powered and inconclusive, case studies. However, the preclinical data for ivermectin's mechanism of action were very weak, and since none of the clinical information was from controlled trials, the review team felt more information was needed in order to place it into a large confirmatory trial. In addition, the group felt there were higher priority repurposed agents to pursue at the time (a continuing theme; see attached slides for review meeting summary)
2. Inhaled ivermectin was reviewed in Wave 2. But in this instance the formulation that was submitted to ACTIV for consideration was significantly lacking in the PK/PD data needed to suggest that it would indeed be effective in patients. It did not score well in the clinical antiviral subteam, so the ACTIV Preclinical Working Group then took it up to see if there could be a match for preclinical testing resources in NIAID. The prior/ongoing studies for both the inhaled and the oral formulation of ivermectin; these are currently pending and will be reviewed by ACTIV as soon as they are available (see attached slides review meeting and agent review summary).
3. Oral ivermectin was reviewed by the ACTIV team yet again, as part of our 3rd Round of Wave 3 review of agents. (It is worth noting here that these reviews are part of a very urgent but also intensive effort, having taking place virtually on a weekly basis since May, often on weekends.) At this point, the group determined that the preclinical data showing any potential antiviral mechanism of action of ivermectin was still weak, and that they would be far more comfortable waiting to see the results of the NIAID preclinical studies that were set up through the ACTIV Preclinical WG (and which are still ongoing). In addition, it was noted that a number of Phase 2 randomized clinical trials across the world had been begun by other groups: at least one here in the US (UPenn), one in the EU (sponsored by Gates), and

one in Japan. These studies should be complete or nearly completed soon, although we have yet to see any public release of their results.

4. Given the impending availability of preclinical NIAID testing data and the data from the existing clinical studies—which would provide further and better controlled experimental results to more definitively either reinforce or contradict the suggestions from the earlier case studies that ivermectin might be an effective treatment for COVID-19--the team from ACTIV that studies antiviral agents decided to defer further consideration of the agent until those data are available and able to be reviewed. (see attached slides review meeting and agent review summary)

5. Furthermore, since this review by the ACTIV antiviral team, data has very recently emerged in the scientific literature and from some other presentations to the ACTIV team that suggest that the effects of ivermectin might in fact not be antiviral, but could be instead related to host-targeted/immune-modulatory mechanisms of action. In consequence of this, the ACTIV TX-Clinical WG co-chairs have recommended that the data on ivermectin be yet again further reviewed by the ACTIV team that evaluates immune modulators to make doubly sure whether there is any value in the agent from that perspective, given that group's specific scientific expertise. This review is expected to take place by January 15.

As you know, ACTIV has reviewed literally hundreds of drugs since its inception in April in order to select those agents that are most promising for further study, and as a result has numerous immune modulators, antiviral drugs (including monoclonal antibodies), anti-inflammatory agents, and anti-thrombotics currently in clinical testing in the various ACTIV master protocols. While we are still assessing whether ivermectin is at all effective in treating COVID-19 and why, the ultimate question is of course whether ivermectin is sufficiently more effective against COVID19 than those treatments already being tested through ACTIV or other potential treatments we are in the process of assessing, and therefore why it should be worth not just the considerable cost of such testing in terms of USG financial resources, but probably more importantly why it could be worth the additional allocation of increasingly scarce resources to conduct crucial clinical trials of COVID-19 agents within our already overburdened U.S. healthcare system.

Please let me know if you have further questions. Thanks, David

From: Steve Kirsch (b) (6)
Sent: 12/8/2020 12:00:17 AM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]; Austin, Christopher P (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=11945b8d0caf49bc84e09171ec167b3a-HHS-austinc]
CC: Hall, Matthew D (NIH) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=80fd9cb35d73417388a946a421745cbf-HHS-hallma-]
Subject: HSGAC hearing on repurposed drugs

Wow. These people are absolutely incompetent. they are doing a huge disservice here.

From: Steve Kirsch
Sent: Monday, December 7, 2020 8:57 PM
To: Mulkins, Christopher (HSGAC) <Christopher_Mulkins@hsgac.senate.gov>
Cc: Petry, Megan (HSGAC) <Megan_Petry@hsgac.senate.gov>; Tsilker, Yelena (HSGAC) <Yelena_Tsilker@hsgac.senate.gov>; Ryan, Corban (HSGAC) <Corban_Ryan@hsgac.senate.gov>; McLeod, Josh (HSGAC) <Josh_McLeod@hsgac.senate.gov>; Rosenstock, Shani (HSGAC) <Shani_Rosenstock@hsgac.senate.gov>; Ashish Jha - Harvard (ashish_jha@brown.edu) <ashish_jha@brown.edu>
Subject: RE: why there isn't an EUA for fluvoxamine

I saw the list of witnesses for your hearing. It seems to be a mix of ivermectin, HCQ, favipiravir, and anti-vax.

None of those drugs those witnesses will talk about has anywhere close to the p value and quality of evidence as Fluvoxamine. That's why it was the lead story in JAMA when it was published. More importantly, the patients report that this drug turns covid into a "mild cold". While that is anecdotal, it is verifiable in a VERY large cohort. I know because I talked to the physician treating all the cases. He just reported the people who previously opted out are all changing their minds and opting in.

Ivermectin is arguably the second best drug. There is only one RCT published in a peer reviewed journal on Ivermectin (Podder et al) and that was far smaller than the fluvoxamine trial (less than half the size). here's what it said:
There were 30 patients in the control arm and 32 patients in the intervention arm. Total recovery time from the onset of symptoms to complete resolution of symptoms of the patients in the intervention arm was 10.09 ± 3.236 days, compared to 11.50 ± 5.32 days in the control arm (95% CI -0.860,3.627, p>. 05) and was not significantly different. The mean recovery time after enrolment in the intervention arm was 5.31 ± 2.48 days, which also did not differ significantly from the control arm of 6.33 ± 4.23 days (95% CI −0.766, 2.808, p> 0.05). Results of negative repeat RT- PCR were not significantly different between control and intervention arms (control 90% vs intervention 95%, p>.05). Conclusion: Ivermectin **had no beneficial effect on the disease course** over usual care in mild to moderate COVID-19 cases.

Most doctors basically only use high quality data, so there is really no comparison here. There are certainly a lot more studies on Ivermectin, but again, these is dismissed by doctors if it isn't double blind RCT published in a peer reviewed journal. The Ivermectin meta analysis wasn't published in a journal, wasn't peer reviewed. I asked the 12 medical experts on the CETF SAB what they thought of the meta analysis and they said Garbage IN, Garbage out. It is not debatable: the highest quality evidence for ivermectin said IT HAS NO BENEFIT.

I'm very familiar with Favipiravir and I love the Fujifilm people. We are great friends. But the fact is that drug doesn't work either. I was very disappointed but it is what it is. That's why the UCLA trial never got started. the PI lost interest because the data showed there was nothing there. This data is all in plain sight.

You are focusing your entire hearing on junk science and you are giving repurposed drugs a bad name. Instead of helping the cause and saving lives, you are hurting it by featuring these drugs where the highest quality evidence shows

they have no effect and then compounding that error by ignoring the only drug that is proven in both high quality evidence and in subsequent use in the field to be game changing for this disease.

I am baffled by your decision-making process.

-steve

From: Mulkins, Christopher (HSGAC) <Christopher_Mulkins@hsgac.senate.gov>
Sent: Monday, December 7, 2020 11:14 AM
To: Steve Kirsch (b) (6)
Cc: Petry, Megan (HSGAC) <Megan_Petry@hsgac.senate.gov>; Tsilker, Yelena (HSGAC) <Yelena_Tsilker@hsgac.senate.gov>; Ryan, Corban (HSGAC) <Corban_Ryan@hsgac.senate.gov>
Subject: RE: why there isn't an EUA for fluvoxamine

Steve, thanks so much for keeping us up to date on the Fluvoxamine developments. We very much appreciate it. We have decided to take a different tact with the hearing tomorrow, but we would very much like to know the progress in regards to Fluvoxamine and its benefits for treating COVID patients.

Thanks again!
Chris

From: Steve Kirsch (b) (6)
Sent: Friday, December 4, 2020 4:02 AM
To: Mulkins, Christopher (HSGAC) <Christopher_Mulkins@hsgac.senate.gov>
Cc: Petry, Megan (HSGAC) <Megan_Petry@hsgac.senate.gov>; Tsilker, Yelena (HSGAC) <Yelena_Tsilker@hsgac.senate.gov>; Ryan, Corban (HSGAC) <Corban_Ryan@hsgac.senate.gov>
Subject: why there isn't an EUA for fluvoxamine

Normally the drug maker has to apply. There are >12 manufacturers of the drug and none were cooperative. We had to purchase the drug to do the study. There's no money for them to do apply.

There is a citizen's route to apply for an EUA but it is slow and rarely used. I don't know who I could hire for this since the talent all works full time for drug companies.

There is clearly sufficient body of evidence for an EUA. I've shown this evidence to top doctors and they all find it compelling and would take the drug if they got sick. That's well beyond the standard.

So this is a HUGE loophole in the system that needs to be addressed by HSGAC. In cases like this (generic drug many manufacturers, pandemic), the FDA itself should assemble the case for the EUA.

So you now have two repurposed drugs, Fluvoxamine and Ivermectin. Both have a 10X reduction in hospitalization rate.

If you don't call me as a witness, may I suggest Dr. David Seftel or the Dean of the Medical School at Emory University?

From: Mulkins, Christopher (HSGAC) <Christopher_Mulkins@hsgac.senate.gov>
Sent: Thursday, December 3, 2020 8:37 AM
To: Steve Kirsch (b) (6)>
Cc: Petry, Megan (HSGAC) <Megan_Petry@hsgac.senate.gov>; Tsilker, Yelena (HSGAC) <Yelena_Tsilker@hsgac.senate.gov>; Ryan, Corban (HSGAC) <Corban_Ryan@hsgac.senate.gov>
Subject: RE: i'm on the call now....<music waiting for organizer>

My apologies again, Mr. Kirsch, for not being able to stay on the call this morning. Really appreciate your time and insight!

Chris

From: Steve Kirsch [(b) (6)]>
Sent: Thursday, December 3, 2020 10:32 AM
To: Mulkins, Christopher (HSGAC) <Christopher_Mulkins@hsgac.senate.gov>
Cc: Petry, Megan (HSGAC) <Megan_Petry@hsgac.senate.gov>; Tsilker, Yelena (HSGAC) <Yelena_Tsilker@hsgac.senate.gov>; Ryan, Corban (HSGAC) <Corban_Ryan@hsgac.senate.gov>
Subject: i'm on the call now....<music waiting for organizer>

From: Mulkins, Christopher (HSGAC) <Christopher_Mulkins@hsgac.senate.gov>
Sent: Wednesday, December 2, 2020 4:48 PM
To: Steve Kirsch [(b) (6)]>
Cc: Petry, Megan (HSGAC) <Megan_Petry@hsgac.senate.gov>; Tsilker, Yelena (HSGAC) <Yelena_Tsilker@hsgac.senate.gov>; Ryan, Corban (HSGAC) <Corban_Ryan@hsgac.senate.gov>
Subject: RE: Connection

We have a conflict at 10, but can do 10:30. We can use [(b) (6)] and the passcode of [(b) (6)] Looking forward to the discussion tomorrow.

Chris

From: Steve Kirsch [(b) (6)]>
Sent: Wednesday, December 2, 2020 6:29 PM
To: Mulkins, Christopher (HSGAC) <Christopher_Mulkins@hsgac.senate.gov>
Cc: Petry, Megan (HSGAC) <Megan_Petry@hsgac.senate.gov>; Tsilker, Yelena (HSGAC) <Yelena_Tsilker@hsgac.senate.gov>; Ryan, Corban (HSGAC) <Corban_Ryan@hsgac.senate.gov>
Subject: RE: Connection
Importance: High

I'm free from 9am EST to 11am EST... would 10am EST work?

From: Mulkins, Christopher (HSGAC) <Christopher_Mulkins@hsgac.senate.gov>
Sent: Wednesday, December 2, 2020 2:52 PM
To: Steve Kirsch [(b) (6)]>
Cc: Petry, Megan (HSGAC) <Megan_Petry@hsgac.senate.gov>; Tsilker, Yelena (HSGAC) <Yelena_Tsilker@hsgac.senate.gov>; Ryan, Corban (HSGAC) <Corban_Ryan@hsgac.senate.gov>
Subject: RE: Connection

Thanks Josh. Appreciate the connection. Moving you to bcc to save you inbox.

Mr. Kirsch, would be great to connect. I have copied my colleagues here as well. Would you have time to chat tomorrow?

Thanks,
Chris

From: McLeod, Josh (HSGAC) <Josh_McLeod@hsgac.senate.gov>
Sent: Wednesday, December 2, 2020 5:37 PM

To: Mulkins, Christopher (HSGAC) <Christopher_Mulkins@hsgac.senate.gov>; (b) (6)
Cc: Rosenstock, Shani (HSGAC) <Shani_Rosenstock@hsgac.senate.gov>
Subject: Connection

Chris,

Connecting you with Steve Kirsch, who created the COVID-19 Early Treatment Fund https://www.treatearly.org/overview

We spoke with Steve earlier today and think he can provide valuable information in preparation for the hearing Tuesday.

Thanks,
Josh

From: Adam, Stacey (FNIH) [T] [sadam@fnih.org]
Sent: 11/17/2020 12:02:42 PM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: RE: Ivermectin and an IND

I know. The results out of Peru sold her. They did not originally sell our reviewers... 😊

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (301) 435-8364 | Mobile: (b) (6)

From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Sent: Tuesday, November 17, 2020 11:55 AM
To: Adam, Stacey (FNIH) [T] <sadam@fnih.org>
Subject: RE: Ivermectin and an IND

Yes if possible. You know Maria is very interested in this. jw

From: Adam, Stacey (FNIH) [T] <sadam@fnih.org>
Sent: Tuesday, November 17, 2020 11:51 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>; Kilgore, Nicole R CIV USARMY (USA) <(b) (6)>
Subject: RE: Ivermectin and an IND

Thanks, Janet,

As with Cyclosporin, would you like ACTIV to review this for prioritization? We did so twice already, but in earlier rounds when the data was not so developed. Would you like us to take another look?

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (301) 435-8364 | Mobile: (b) (6)

From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Sent: Tuesday, November 17, 2020 9:25 AM
To: Kilgore, Nicole R CIV USARMY (USA) <(b) (6)>; Adam, Stacey (FNIH) [T] <sadam@fnih.org>
Subject: FW: Ivermectin and an IND

Potentially more information on Ivermectin use. Janet W

From: Marik, Paul E. <MarikPE@EVMS.EDU>
Sent: Tuesday, November 17, 2020 8:01 AM

To: [redacted] (b) (6); Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Cc: Pierre Kory <[redacted] (b) (6)>
Subject: Ivermectin and an IND

Dear Drs. Lieberman and Woodcock:

I was sent this communication below. Two points in response.
1. As this is a FDA approved drug an IND may not be required. Please see the ACTS Vitamin C trial. As the product used (IV Vitamin C) was FDA approved for the treatment of "scurvy" the FDA provided a waiver of an IND.
2. There is now overwhelming evidence that Ivermectin is useful for prophylaxis, postexposure Rx, early symptomatic treatment and late treatment of COVID-19. To ignore this exceedingly safe, effective and cheap medication is immoral. URGENT action is required.

Please see attachments and links below.

Kindly

Paul Marik. MD

U-Tube Channel
https://www.youtube.com/channel/UCz9Pvn15m4Rv1uY-aBYRVuw

https://www.trialsitenews.com/real-world-evidence-i-mask-protocol-ivermectin-key-for-prophylaxis-and-early-treatment-of-covid-19/?fbclid=IwAR33nTE-TJ1fzO87s12DNqWN0cTZ9YBz-m-Nt4haNWOvlKURRJBG6ZO9l1U

https://www.trialsitenews.com/why-isnt-ivermectin-being-widely-researched-and-utilized/

FLCCC
https://covid19criticalcare.com/

Here is a happy email exchange w the FDA
Thanks, I will definitely follow up. jw
-----Original Message-----
From: Alexis Lieberman <[redacted] (b) (6)>
Sent: Monday, November 16, 2020 8:15 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Re: Information re Covid treatment
Good morning, Dr Woodcock,
I wanted to follow up about the IND for the [redacted] (b) (4) study. I also learned that the [redacted] (b) (4) [redacted] (b) (4) study and the [redacted] (b) (4) study are each also waiting for an IND. While it looks like many trials are occurring in the US for ivermectin use for Covid, I believe only the [redacted] (b) (4) has an IND. The others are all waiting. I greatly appreciate your assistance with this!
Alexis Lieberman, MD
On Nov 13, 2020, at 2:11 PM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:
Is this study with an inhaled or oral formulation? Thanks jw
-----Original Message-----
From: Alexis Lieberman <[redacted] (b) (6)>
Sent: Thursday, November 12, 2020 4:55 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Re: Information re Covid treatment

Thank you. I understand that part of the reason the drug has not been pursued is that it was considered that there are enough studies already underway. I would like to bring to your attention that the study in Philadelphia that has been listed with clinicaltrials.gov at [redacted] (b) (4) has not yet begun because the investigators have been waiting for an IND from the FDA for nearly 5 months already. I wonder if there is any way to facilitate them getting the IND rapidly so that their study can begin during the current surge in cases in Philadelphia? Any assistance with this would be greatly appreciated.

Sincerely,

Alexis Lieberman, MD

On Nov 12, 2020, at 10:23 AM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

Thank you. We have considered this drug before, will refer these references to the assessment team for further evaluation. Janet Woodcock

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

From: Alexis Lieberman <[redacted] (b) (6)>

Sent: Wednesday, November 11, 2020 5:58 PM

To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>

Subject: Information re Covid treatment

Dear Dr. Woodcock,

As a practicing pediatrician in Philadelphia, I am writing to request that you use your role on the Covid task force to advocate for an immediate, large-scale RCT for ivermectin early in disease. I include summaries of studies done so far on ivermectin that point to its promise.

As you know, Ivermectin is an anti-parasitic drug that is used widely throughout the world and is generally very well-tolerated with only very RARE side effects in those who do not have parasites, primarily limited to allergic reactions. The drug is proposed to prevent the virus from getting into the nucleus of the human cell. While the initial Monash in-vitro study used very high doses and the early Surgisphere study was discredited, since that time, there have been a dozen positive clinical studies. Surely there is enough evidence now to warrant a large-scale, government-funded RCT.

This inexpensive, off-patent drug will not make money for any drug company. Therefore, it falls to the government to take steps to fund a trial. I implore you to advocate for this!

STUDIES AND LINKS REGARDING IVERMECTIN:

10/29/30. India: Two doses of ivermectin, given 72 hours apart, prophylactically, was associated with a 73% reduction of COVID-19 infection among healthcare workers for the following one-month, in a case control study of 186 pairs.
https://www.medrxiv.org/conte.../10.1101/2020.10.29.20222661v1

10/26/30: Baghdad, Iraq: A recent study done Baghdad compared COVID patients who took ivermectin or did not. In this, 10% of the non-Ivermectin group progressed to severe disease well only 4% of the ivermectin group did. In that same study there was a 27% mortality rate for those who did not take over motion versus 18% and those who did.
https://www.medrxiv.org/cont.../10.1101/2020.10.26.20219345v1...

9/28/20: Bangladesh: In this retrospective study, they compared patients who received Ivermectin with those who receive the standard of care. They found that 46% of the standard of care patients required oxygen and 8% we nt to the intensive care unit. This was compared to those who did receive ivermectin, in which 9% required oxygen and only 1% went to the intensive care unit. https://www.trialsitenews.com/mymensingh-medical-college-r.../

8/28/20: Preventive study from Egypt showing for the first time a large reduction in covid contraction for family members taking prophylactic dose of Ivermectin when there is an infected person in the same household. Household contacts who did not take ivermectin had a 58% rate of contracting Covid, compared to only 7% of those who did take ivermectin.
https://clinicaltrials.gov/.../61/NCT04422561/Prot_SAP_000.pdf

8/26/20: Bangladesh. 400 patients were randomized to either receive ivermectin or placebo. In that study 18% of the placebo patients progressed to clinical deterioration while only 9% of those with ivermectin deteriorated. In that study they also compared percentage of patients who had early clinical improvement within a week, and of those without Ivermectin, 44% improved quickly while of those with Ivermectin, 60% improved quickly.
https://clinicaltrials.gov/.../31/NCT04523831/Prot_ICF_000.pdf

7/8/20 Baghdad, Iraq: This study compared hospitalized patients with mild to moderate symptoms who took ivermectin or did not. Those who did not had a hospital stay of 12 days on average, vs 7% in those who did take ivermectin.
https://www.medrxiv.org/.../10.../2020.07.07.20145979v1.full.pdf

6/30/20 Dominican Republic Data:
https://www.trialsitenews.com/president-of-dominican-repub.../
6/28/20 Bangladesh Data (mild to moderate cases, comparison with hydroxychloroquine/azithromycin). This study is not statistically significant but showed a trend of recovery in eight days with ivermectin versus nine without.
https://www.trialsitenews.com/ivermectin-study-reveals-fan.../
6/10/20 Florida Data (first U.S. data, on hospitalized patients). This is a retrospective intensive care unit study in which those who did not receive ivermectin had a 25% mortality rate while those who did receive ivermectin had a 15% mortality rate. It has since been published in a peer-reviewed journal.
https://journal.chestnet.org/.../S0012-3692(20)34898.../fulltext
5/2/20 Peru Data: areas of the country where ivermectin was used have a lower case rate and lower fatality rate than areas where ivermectin was not used.
https://www.docdroid.net/J8wuZlb/ivermectin-studyesen-pdf
3/2020: Australian study that showed that high doses of ivermectin killed the Covid virus in a test tube study.
https://research.monash.edu/.../the-fda-approved-drug-ivermec...
The FLCC, a US based group of colleagues with over 200 years of combined experience in Critical Care and Emergency Medicine, as well as long-standing shared interests in developing effective treatments for critical illnesses including sepsis, is a working group devoted to creating a treatment protocol against COVID-19.
They developed an inpatient Covid protocol which has lead to a mortality rate of 4-10%, compared to the world average of 23%.
They have now developed a prophylactic and early outpatient combination treatment protocol for COVID-19 called I-Mask+.
https://covid19criticalcare.com/.../FLCCC-IVERMECTIN-Protocol...
This protocol recommends ivermectin, vitamins C and D, Zinc, melatonin and, for adults only, aspirin.
Their rationale is based on multiple studies as well as real-world evidence comparing countries using ivermectin, such as Peru, Brazil and Haiti, to those not using it, such as the Dominican Republic and the US.
Here is the introductory video from FLCC:
https://vimeo.com/473929788/382c386d60
Thank you for your consideration,
Alexis Lieberman, MD
Advocare Fairmount Pediatrics

Paul E. Marik MD, FCCP, FCCM|
Eastern Virginia Medical School|
Department of Internal Medicine|
Chief, Pulmonary and Critical Care Medicine|
825 Fairfax Ave, Rm 575, Norfolk, VA 23507|
☎ 757.446.8910| 🖷 757.446.5242 |
✉ marikpe@evms.edu| 🖳 www.evms.edu|

Teaching. Discovering. Caring.

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 12/15/2020 7:47:40 AM
To: John P. Hussman, Ph.D. [(b) (6)]
Subject: RE: COVID-19: Pandemic trajectory; Repurposed therapeutics; Vaccine considerations (antigens, rare occurence of Bell's palsy, dose sparing, immune correlates); Public health messaging

Thank you. I've tried to talk people into testing ivermectin formally but other agents keep getting prioritized higher. Cys-A is being pushed by some but is placed lower for testing given other priorities. Appreciate your input. jw

From: John P. Hussman, Ph.D. <(b) (6)>
Sent: Monday, December 14, 2020 11:19 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Cc: John P. Hussman, Ph.D. <hussman@hussmanfoundation.org>; Brooke Steinau <bsteinau@hussmanfoundation.org>
Subject: RE: COVID-19: Pandemic trajectory; Repurposed therapeutics; Vaccine considerations (antigens, rare occurence of Bell's palsy, dose sparing, immune correlates); Public health messaging

Thank you for your note. Of course – I'm glad for these to be circulated further, and hope that some part is helpful.

The finding that the mAbs aren't helpful in late disease is understandable. By that point, my impression is that the maladaptive inflammatory response dominates any cytopathic effect of the virus itself, and the pathology seems to persist despite antibody response. Blunting the inflammatory tissue damage from infiltrating neutrophils and macrophages (including thrombosis and damage to blood vessels from barrier degradation and extravasation) seems to be important.

With regard to cyclosporine A, I've seen a number of letters to editors suggesting potential benefit, but only one small trial (33274479) in COVID-19. There may be more I haven't seen. While there are some in-vitro reports of SARS-CoV-2 inhibition, as well as inhibition of other hCoVs, my impression is that the main argument favoring cyclosporine is that it's been relatively well-studied in macrophage activation syndrome (secondary hemophagocytic lymphohistiocytosis HLH). One protocol (HLH-2004 modified for adults) includes cyclosporine A in combination with glucocorticoids and etoposide – the basic target being suppression and apoptosis of hyperproliferating T-cells.

As I am not a clinician, I would defer to intensivists in their choice of cyclosporine as part of a protocol to address macrophage activation / cytokine storm. However, my impression is that in the context of COVID-19, inflammatory monocytes/macrophages and neutrophils appear dominant. Severe patients already show lymphopenia (though typically with virus-reactive T-cells among the depressed population that remains), so the main potential benefit of cyclosporine would seem to be indirect reduction of cytokine transcription and possibly a reduction in ROS-induced oxidative stress.

Despite the immunosuppressive effects of cyclosporine, there don't seem to be broad reports of increased infection resulting from short-term use, and it is already among clinical options for HLH. So the interest in cyclosporine seems reasonable. The question is whether there are other reports of specific benefit in COVID-19.
In HLH that is refractory to glucocorticoids and cyclosporine, there are reports that more direct inhibition of cytokine response may have potential benefit, including IL-1 blockade (e.g. anakinra) and IL-6 blockade (e.g. tocilizumab). As I noted in my prior email, the EUA for barcitinib was welcome, and there are also favorable reports for ruxolitinib, another JAK 1/2 inhibitor.

Finally, among well-tolerated options even in moderate cases, before the point of clinical deterioration, I do believe that doxycycline (excluding pregnant patients) may have pleiotropic benefits, particularly in reducing inflammatory extravasation and tissue damage (via MMP inhibition among other mechanisms). I suspect that this may be part of what's going on in so-called "long-COVID." Given that some of our global health work has been on river blindness with

the Carter Center, I've got enough familiarity with the pleiotropic effects of mectizan (ivermectin) to be unsurprised by various reports of benefit in COVID-19, with few side effects. Though adequate RCTs are lacking, both of these – particularly doxycycline – make sense for consideration or additional investigation among the repurposed therapeutics above.

Hope this helps! (especially for a fellow Northwestern alum). Best - John

John P. Hussman, Ph.D.
Director, Hussman Foundation

HUSSMAN FOUNDATION

6021 University Blvd, Suite 490 | Ellicott City, MD 21043
443.465.4814 | hussman@hussmanfoundation.org

From: Woodcock, Janet [mailto:Janet.Woodcock@fda.hhs.gov]
Sent: Monday, December 14, 2020 6:33 PM
To: John P. Hussman, Ph.D.
Subject: RE: COVID-19: Pandemic trajectory; Repurposed therapeutics; Vaccine considerations (antigens, rare occurence of Bell's palsy, dose sparing, immune correlates); Public health messaging

Thanks very much. I will circulate again with your permission. It does appear that the monoclonal neutralizing antibodies are not helpful in late disease.

Given the immune pathology, what do you think about cyclosporine as a repurposed agent? I getting a lot of push on that one! Thanks jw

---

From: John P. Hussman, Ph.D. [redacted (b) (6)]
Sent: Thursday, December 10, 2020 11:53 AM
To: Auchincloss, Hugh (NIH) <[redacted (b) (6)]>; Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>; Bozick, Brooke A (NIH) [redacted (b) (6)]; Harris, Kara M (NIH) <[redacted (b) (6)]>; Conrad, Patricia L (NIH) <[redacted (b) (6)]>; CVH <cvh@vanhollen.org>; Tricia_Russell@vanhollen.senate.gov; Burrow, David <David.Burrow@fda.hhs.gov>; Cruse, Alonza <Alonza.Cruse@fda.hhs.gov>; [redacted (b) (6)]; 'mom@martinomalley.com' <mom@martinomalley.com>; Kenny Thompson Jr. ([redacted (b) (6)] <[redacted (b) (6)] pslavin@partners.org; Clemmens, Michael (mclemmens@aahs.org) <mclemmens@aahs.org>; Jarrell, Bruce (bjarrell@umaryland.edu) <bjarrell@umaryland.edu>; Ford, Henri (hford@med.miami.edu) <hford@med.miami.edu>; jeffrey.duerk@miami.edu; Jay Perman (jperman@usmd.edu) <jperman@usmd.edu>; Chris Elias (chris.elias@gatesfoundation.org) <chris.elias@gatesfoundation.org>; Chris Karp (Chris.Karp@gatesfoundation.org) <Chris.Karp@gatesfoundation.org>; Pericak-Vance, Margaret A. <MPericak@med.miami.edu>
Cc: Brooke Steinau <bsteinau@hussmanfoundation.org>; John P. Hussman, Ph.D. <hussman@hussmanfoundation.org>
Subject: COVID-19: Pandemic trajectory; Repurposed therapeutics; Vaccine considerations (antigens, rare occurence of Bell's palsy, dose sparing, immune correlates); Public health messaging

Good morning all,

Given the recent acceleration in the trajectory of COVID-19 fatalities, and the likelihood that widespread vaccination may not be achieved until mid-year, I am writing to share a few perspectives that may be useful in the interim. As with all of these periodic notes since February, they are offered as input for consideration, in hope that some part of this may be helpful in your own thinking, or that of your staff, on one or more of these issues.

With gratitude for all of your dedicated efforts on so many fronts of this pandemic.

Wishing you and yours well. Best – John

John P. Hussman, Ph.D.
Director, Hussman Foundation

Key Points:

(additional charts, references, and links below):

- **Pandemic trajectory**: While post-inauguration improvements in containment practices will certainly be helpful, the recent shift in the trajectory of the pandemic suggests that U.S. fatalities are actually likely to *peak* close to January 20, suggesting the urgency of more immediate containment efforts, if even more comprehensive public health messaging relating to limits on group size and unmasked conversation in indoor public airspace. A conservative estimate of the current trajectory (which short-run figures exceed) suggests the potential for U.S. fatalities to reach 385,000 by January 20, with a subsequently declining pace still potentially contributing to 530,000 U.S. fatalities by March 15. Having modeled the trajectory of the pandemic since early February, probably the most striking aspect, from a mathematical perspective, is how profoundly sensitive this trajectory can be to small improvements or relaxations in the estimated "tightness" of containment behavior. Charts below.

- **Repurposed therapeutics**: Expanded guidance regarding repurposing of FDA-approved therapeutics may be helpful, particularly those that are well-tolerated, supported by clinical evidence, and are informed by consideration of relevant targets in the COVID-19 pathway. I have advocated similar guidance since March, and I recognize the temerity of this proposal in the absence of definitive RCTs. By restricting the guidance to well-tolerated candidates supported by multiple lines of evidence, I trust that the FDA might find an acceptable balance between safety and potential benefit.
  - I've attached a draft example of well-tolerated, pathway-informed therapeutics that might be suggested as "options to discuss with your physician."
  - The EUA for barcitinib (which might reasonably be extended to ruxolitinib) was welcome. If there is a short list of candidates that I believe could be beneficial in limiting damage from extravasation of inflammatory leukocytes, it would include doxycycline (except in pregnancy), which might also be protective against vascular damage (possibly in synergy with a low-dose NOS/ROS inhibitor).
  - Please dismiss these views if they run counter to evidence to which I might not have access, or if your clinical experience with any of these therapeutics differs from my inferences. My research background includes biological pathways of complex disease with a focus on translational targets, but I am not a clinician.

- **Vaccine-related considerations**:
  - **Antigen design**: The leading mRNA vaccine candidates, based on a full-length spike stabilized in pre-fusion conformation, are encouraging as they are not strictly reliant on the spike receptor binding domain, and such designs have been reported to increase the breadth and potency of neutralizing antibodies in studies of SARS-CoV and MERS-CoV candidates. Designs allowing greater access to the immunodominant S-RBD can be expected to induce neutralizing antibodies but could potentially be more permissive of antibody-escape mutations and certain forms of immune-enhancement via Fc-receptor interactions. The final section of my attached paper on clinical worsening discusses some of these considerations. All of these reservations can be dismissed, of course, based on sufficient clinical evidence, so my objective is only to suggest points for examination.
  - **Bell's palsy**: My impression is that certain rare, temporary vaccine side-effects such as Bell's palsy (idiopathic facial paralysis) may be related to a brief inflammatory response that may feature an elevated neutrophil-lymphocyte ratio. Elevated NLR is a marker in Bell's as well as COVID-19, and the coronavirus spike itself can promote an inflammatory response including macrophage and neutrophil chemokines. In response to such rare side-effects, NLR might be examined as a clinical marker, and short-term corticosteroid use coupled with an antiviral medication (possibly even remdesivir in this context) could be a mitigating strategy, ideally after seroconversion. Please see additional references below.
  - **Dose sparing**: My understanding is that the incidence curve for the Pfizer vaccine largely mirrors placebo in the initial 10 days, and then flattens dramatically. Table 13 (p 32) indicates 52% efficacy (~ 1-39/82) even between dose 1 and 2, already exceeding the 50% target endpoint, with 90.5% efficacy in the 7-day period following the second dose. Moreover, most vaccine-associated cases appear to have occurred during the initial 10 days following dose 1. The

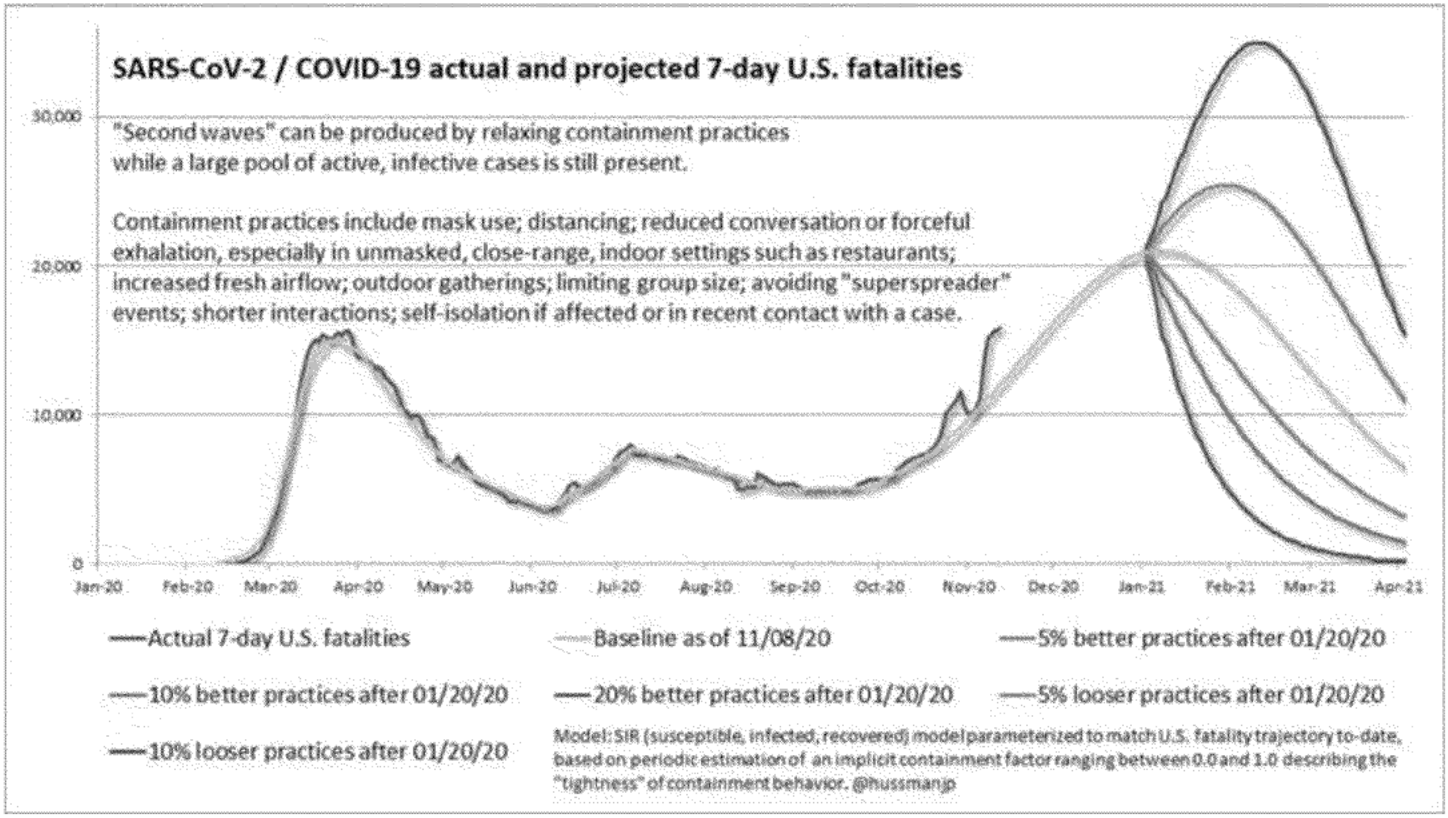
incidence curve is effectively horizontal even between days 10-28, which can be best ascribed to the first dose. In the absence of sufficient quantities of vaccine, a dose-sparing strategy might be considered, targeting a larger number of single dose recipients initially, followed by a second dose upon broader availability. A single-dose arm might be initiated immediately (perhaps publicly funded) if current data are insufficient to support that alternative. The results could, in any event, be available for evaluation to address potential mid-year supply constraints.

- **Immune correlates**: It may be useful to evaluate the extent to which various vaccine candidates induce T-cell responses (particularly in CD4+ populations, which may correlate with protection in elderly individuals), as well as the induction of antibodies to conserved epitopes or predicted escape loci.

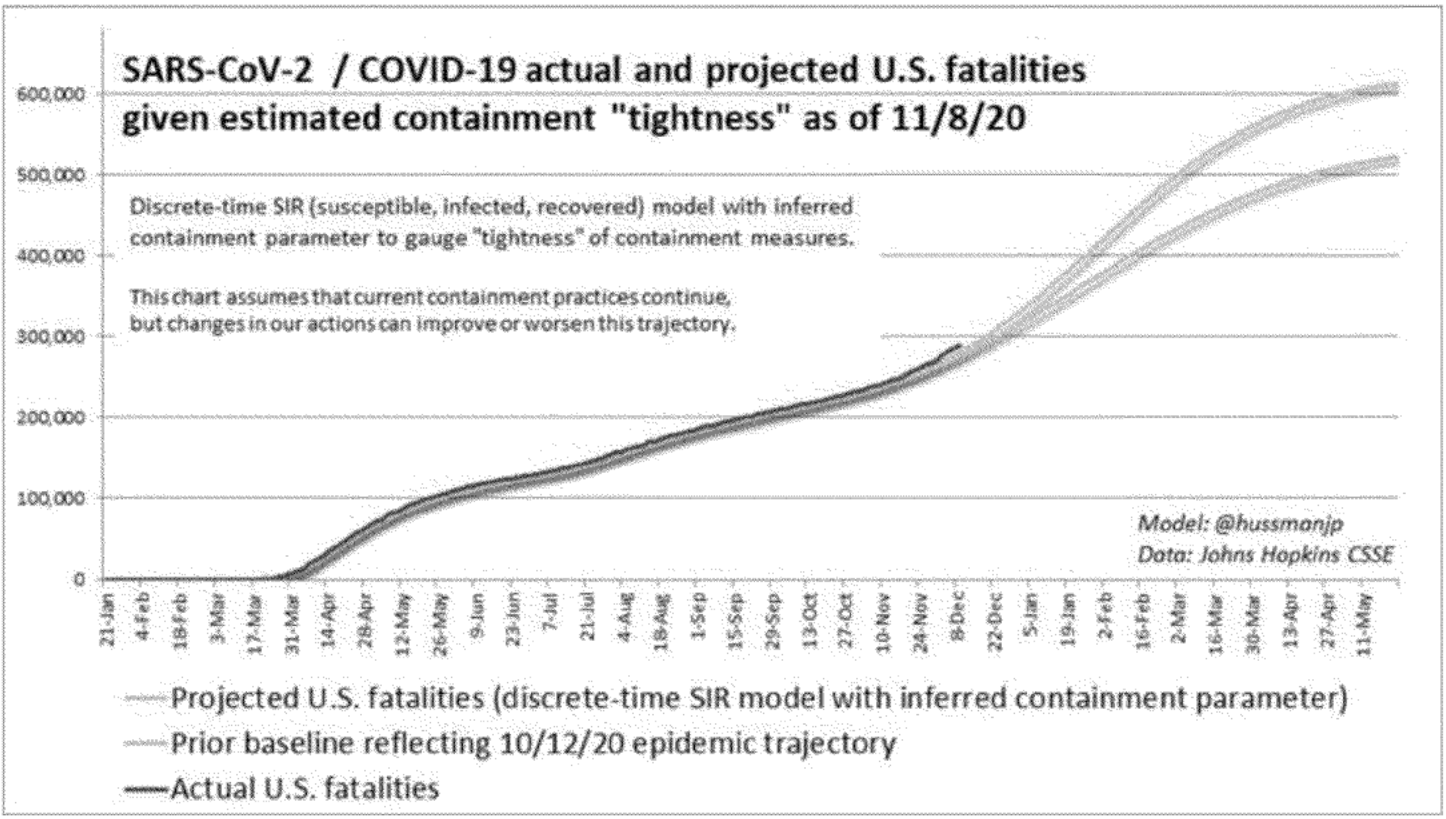
- **Public health messaging**: Given public fatigue for standard containment advice such as mask use, it may be helpful to shift messaging toward not one or two but a "menu" of practices, each that acts as a temporary and partial substitute for immunity, and each accompanied by a "why" – a logical relationship to one of the three drivers of epidemic spread:
  - 1) reducing the *probability* that contact with an infected person will result in transmission (mask use, distancing, hygiene, fresh airflow, outdoor settings, limiting interactions and unmasked indoor conversation in public);
  - 2) reducing the *number* of daily contacts (smaller and more stable groups, avoiding hub and super-spreader events) and;
  - 3) reducing the *duration* of infectivity (self-isolation, testing, contact-tracing).
  - An updated draft of possible messaging is available to the transition team.

Charts, references, and links

1. U.S. 7-day COVID-19 fatalities and implied trajectory based on estimated containment as of 11/8/20. The chart also shows the sensitivity of prospective 7-day U.S. fatalities to changes in containment practices after January 20, but not prior to that date. The model is briefly described in the chart text. Additional charts and computational details are available on request.



2. Impact of the current pandemic trajectory on potential U.S. fatalities, which can be strongly modified by changes in containment behavior.



3. Cellular and molecular pathways of COVID-19 and potential points of therapeutic intervention (Hussman, 2020, Frontiers in Pharmacology). Candidate therapeutics described in the paper include remdesivir, doxycycline, ivermectin, dexamethasone, inhibitors of JAK1/2 and IL-6, as well as various prophylactics, but are investigational, not prescriptive.

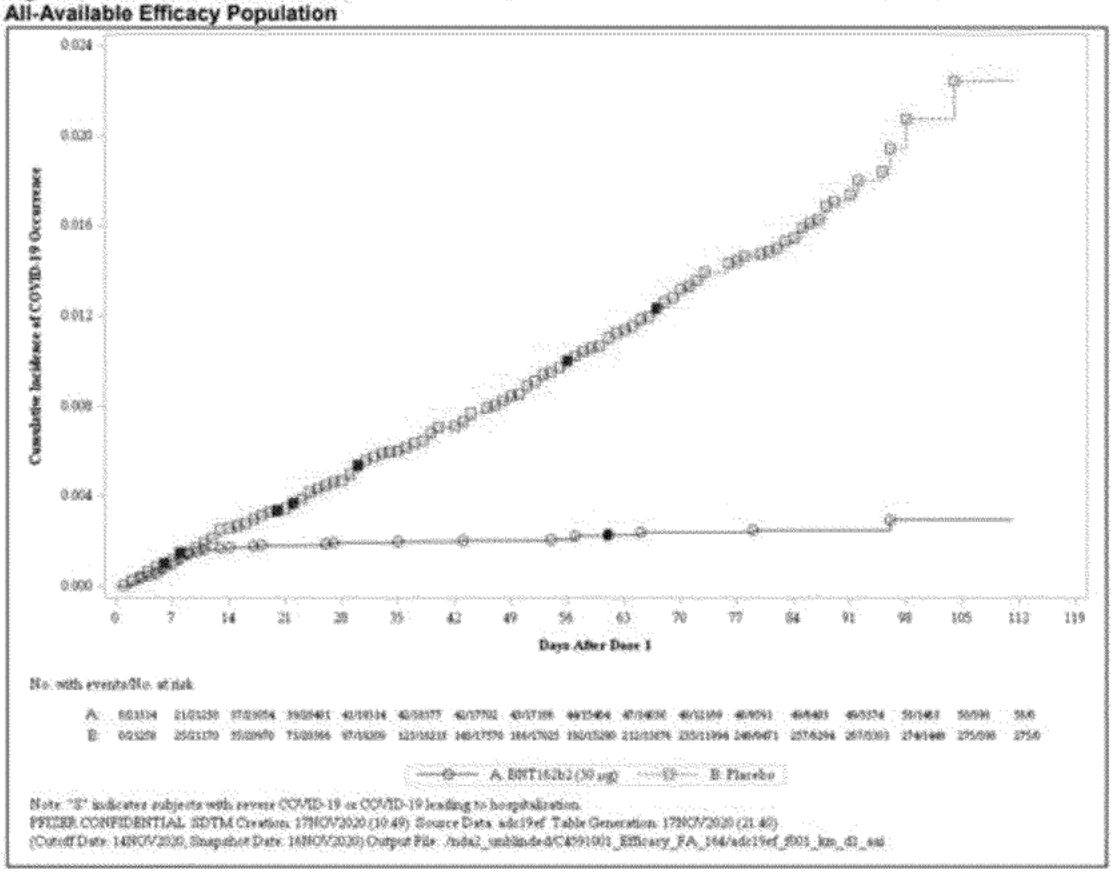
4. Attachment: COVID19_RepurposedTherapeutics. Draft guidance (example) relating to repurposing of well-tolerated, FDA-approved, pathway-informed therapeutics. Links to additional references are embedded in the PDF.

5. Attachment: Severe clinical worsening in COVID-19 and implications for antibody-based therapeutics. Currently in review. Reflects recent edits (reordering of sections, additional headers).

6. Notes on Bell's Palsy: Given that a high neutrophil-to-lymphocyte ratio (NLR) is a central feature of COVID-19 and also a correlate of Bell's palsy (which also features disruptions of smell and taste), it is possible that NLR may be a useful clinical marker in the evaluation of these cases. A few references in this regard: NLR 32364446, 33136021, 30545211; Spike protein induction of neutrophil/macrophage infiltration 16809289; Bell's Palsy in association with active COVID-19: 33159420, 32950319, 33006717, 33128540; Mitigation: NBK482290.

7. Pfizer mRNA vaccine: Cumulative incidence curve. Second dose administered after 3 weeks.

Figure 2. Cumulative Incidence Curves for the First COVID-19 Occurrence After Dose 1, Dose 1 All-Available Efficacy Population



John P. Hussman, Ph.D.
Director, Hussman Foundation

HUSSMAN FOUNDATION

6021 University Blvd, Suite 490 | Ellicott City, MD 21043
443.465.4814 | hussman@hussmanfoundation.org

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 12/7/2020 8:33:51 AM
To: Cavazzoni, Patrizia [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c42abd33834044ecbaa03d075cc0a5d2-Patrizia.Ca]
Subject: RE: To the FDA and NCATS concerning ivermectin for the treatment of COVID-19

Thx jw

From: Cavazzoni, Patrizia <Patrizia.Cavazzoni@fda.hhs.gov>
Sent: Monday, December 7, 2020 8:34 AM
To: Hahn, Stephen <SH1@fda.hhs.gov>; Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Cc: Lenihan, Keagan <Keagan.Lenihan@fda.hhs.gov>
Subject: RE: To the FDA and NCATS concerning ivermectin for the treatment of COVID-19

I will refer to CDER ExecSec
Patrizia

From: Hahn, Stephen <(b) (6)>
Sent: Monday, December 7, 2020 8:24 AM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Cc: Cavazzoni, Patrizia <Patrizia.Cavazzoni@fda.hhs.gov>; Lenihan, Keagan <Keagan.Lenihan@fda.hhs.gov>
Subject: Re: To the FDA and NCATS concerning ivermectin for the treatment of COVID-19

Keagan
Would you refer to Exec Sec?
Thx
Steve

Sent from my iPhone

On Dec 7, 2020, at 8:04 AM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

Per request below. OWS and ACTIV have evaluated several times. jw

From: Stephen Ditmore <(b) (6)>
Sent: Sunday, December 6, 2020 2:03 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Cc: Paul E. <MarikPE@evms.edu>; Joseph E. Varon <(b) (6)>; Binh <Binh.Ngo@med.usc.edu>; marc rendell <rendell@asndi.com>; Pierre Kory <(b) (6)>; Harrigan, Rachel (OS) <Rachel.Harrigan@hhs.gov>; Kim, Peter (NIH/NIAID) <(b) (6)>; robert.califf@duke.edu
Subject: To the FDA and NCATS concerning ivermectin for the treatment of COVID-19

Dr. Janet Woodcock
Director, Center for Drug Evaluation and Research
Food and Drug Administration

Please forward to:

Dr. Stephen Hahn

Commissioner of Food and Drugs

Food and Drug Administration

Dr. Patrizia Cavazzoni
Acting Director, Center for Drug Evaluation and Research
Food and Drug Administration

Dr. Christopher Austin
Director
National Center for Advancing Translational Sciences
National Institutes of Health

CTAP officials and others as deemed appropriate.
Please consider this an open, shareable communication.

Dear Dr. Woodcock et. al.:

Evidence supporting the efficacy of ivermectin for the treatment of COVID-19 continues to come to light. At this point, the need is not for the initiation of further research, but for the evaluation of available data to inform national guidance on ivermectin's use. Documentation is now available at:

- **Ivermectin-press-conference-material**
- **Epidemiologic-analyses-on-covid19-and-ivermectin**
- **Ivermectin-in-the-prophylaxis-and-treatment-of-COVID-19 (manuscript)**
- **Meta-analysis-of-COVID-19-therapeutics (slide presentation)**

We request an FDA advisory committee be convened without delay to evaluate ivermectin use for the treatment of COVID-19, as Dr. Pierre Kory suggested at time **44:15** of **a recent FLCCC press conference**, and that the members of the **Front Line Covid-19 Critical Care Alliance (FLCCC)** be recognized as stakeholders with standing to advance the case for ivermectin in a transparent, open forum, welcoming other organizations into the process as opportunities present. We understand the gatekeeper role of the FDA, and are not experienced in these matters, so would appreciate the support of the **National Center for Advancing Translational Sciences (NCATS)** and all other relevant government agencies.

After an admittedly hasty reading of **Emergency Use Authorization of Medical Products and Related Authorities Guidance for Industry and Other Stakeholders**, we wonder if our most immediate concerns could be addressed as described starting on page 30 under **IV. EMERGENCY USE OF ELIGIBLE FDA-APPROVED MCMs WITHOUT AN EUA**. Your counsel in these matters will be most appreciated. For reference, a previous message to Dr. Peter Kim is quoted below.

Sincerely,

Paul E. Marik MD, FCCP, FCCM

Eastern Virginia Medical School

Department of Internal Medicine
Chief, Pulmonary and Critical Care Medicine

Norfolk, VA

Pierre Kory, MD, MPA
Pulmonary and Critical Care Medicine
Aurora St. Luke's Medical Center
Milwaukee, WI

Joseph Veron, MD, FACP, FCCP, FCCM, FRSM
United Memorial Medical Center
University of Texas School of Medicine
Houston, TX

Binh Ngo, MD
Associate Professor
Keck Medical School of USC
Los Angeles, CA

Marc Rendell, MD
Medical Director
Rose Salter Medical Research Foundation
Newport Beach, CA

Stephen Ditmore
Health Reporter
Parkchester Times
Bronx, NY

On Mon, Nov 30, 2020 at 12:47 AM Stephen Ditmore <(b) (6)> wrote:

> Peter S. Kim, MD, corresponding author
> Therapeutics Research Program, Division of AIDS
> National Institute of Allergy and Infectious Diseases
> National Institutes of Health,
> 5601 Fishers Ln, Bethesda, MD 20892
> (b) (6)
>
> Drs. Janet Woodcock, Rachel Harrigan, and Robert Califf are copied on this email.
> Please forward to co-authors (including Dr. Fauci), collaborators and colleagues.

(b) (4)

(b) (4)

Dear Dr. Kim:

We take great encouragement from your recent letter, **Therapy for Early COVID-19, A Critical Need**, which we support wholeheartedly. By that letter, along with the clarity of **the Bamlanivimab EUA instructions**, you and your colleagues are making it clear that antiviral therapeutics will be most effective when administered early in the course of SARS-CoV-2 infection.

We offer our comments as friendly, concurring suggestions from grateful allies, and are happy to do whatever we can to help spread the word among clinicians and policy makers. We have experienced first-hand that some clinicians remain predisposed to deny treatment before symptoms worsen. We are also concerned about reliance on I.V. administration of therapeutics further straining our hospitals and their personnel. A goal of outpatient COVID-19 therapeutics should be to relieve that strain by providing solutions that can be implemented in community based settings.

Quoting (for reference) from your letter, **Therapy for Early COVID-19, A Critical Need**:

> ***Several antivirals approved or in development for other viral infections, such as HIV, hepatitis C virus, and ebolaviruses, are under investigation for early treatment of COVID-19. These investigations have not yet yielded clinically actionable results; however, many trials are ongoing. Examples of antivirals in trials for early treatment of COVID-19 are MK-4482 (EIDD-2801), an orally bioavailable ribonucleoside inhibitor that was originally developed for influenza (NCT04575597); SNG001, a nebulized formulation of interferon-β1a developed for viral infections in patients with chronic obstructive pulmonary disease (NCT04385095); and camostat mesylate, a serine protease inhibitor approved for treatment of chronic pancreatitis and postoperative reflux esophagitis (NCT04353284).***

We view your candidates favorably. Having said that, we would add three:

- **favipiravir**
- **interferon gamma**
- **ivermectin**

Of the six (your three+ours), only one, ivermectin, is currently FDA approved. **Please open and glance at Dr. Marik's attached slides**. A partial bibliography of the studies cited appears below.

Ivermectin is available as generic in part due to the generous policies of Merck. While we would welcome Merck advancing ivermectin for COVID-19, Merck has taken a financial interest in MK-4482 (EIDD-2801), so we believe someone else must be identified who will assess the evidence for ivermectin efficacy, champion the finalizing of research, and make necessary applications on an expedited basis.

The evidence for ivermectin efficacy far exceeds that for either famotidine or hydroxychloroquine, two previously FDA approved orally available medications that have received scrutiny. We join front-line

From: Woodcock, Janet [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7B0453354A9A427DB0A66A86C7A36F3D-JANET.WOODC]
Sent: 12/27/2020 11:47:48 AM
To: Steve Kirsch [(b) (6)]
Subject: RE: appropriate contact at CDC

Yes I believe it is co-chaired by Cliff Lane and another doc. jw

From: Steve Kirsch [(b) (6)]
Sent: Thursday, December 24, 2020 2:44 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: RE: appropriate contact at CDC

Apparently, it is the NIH panel that creates the guidelines for the CDC:
https://www.covid19treatmentguidelines.nih.gov/panel-roster/

From: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Sent: Thursday, December 24, 2020 6:28 AM
To: Steve Kirsch [(b) (6)]
Subject: RE: appropriate contact at CDC

No I don't have any connections there, sorry. Janet W

From: Steve Kirsch [(b) (6)]
Sent: Wednesday, December 23, 2020 5:15 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: FW: appropriate contact at CDC

Got a contact?

From: Austin, Christopher (NIH/NCATS) [E] <[(b) (6)]>
Sent: Wednesday, December 23, 2020 2:14 PM
To: Steve Kirsch <[(b) (6)]>
Subject: RE: appropriate contact at CDC

I don't unfortunately sorry

From: Steve Kirsch [(b) (6)]
Sent: Wednesday, December 23, 2020 5:07 PM
To: Austin, Christopher (NIH/NCATS) [E] <[(b) (6)]>
Subject: appropriate contact at CDC

The CDC has very out of date info on Ivermectin and has no info on fluvoxamine on their website.

Do you know who we could reach out to there that you can refer me so I don't end up in a black hole?

Thanks.

-steve

From: Alexis Lieberman (b) (6)
Sent: 11/13/2020 7:32:42 PM
To: Woodcock, Janet [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7b0453354a9a427db0a66a86c7a36f3d-Janet.Woodc]
Subject: Re: Information re Covid treatment

Oral. It's being run by Nina Gentile, and Joseph Herres. 0.2 mg/kg ivermectin up to 12 mg.

Alexis Lieberman

On Nov 13, 2020, at 2:11 PM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

Is this study with an inhaled or oral formulation? Thanks jw

-----Original Message-----
From: Alexis Lieberman (b) (6)
Sent: Thursday, November 12, 2020 4:55 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Re: Information re Covid treatment

Thank you. I understand that part of the reason the drug has not been pursued is that it was considered that there are enough studies already underway. I would like to bring to your attention that the study in Philadelphia that has been listed with clinicaltrials.gov at Albert Einstein Medical Center and Temple University Hospital has not yet begun because the investigators have been waiting for an IND from the FDA for nearly 5 months already. I wonder if there is any way to facilitate them getting the IND rapidly so that their study can begin during the current surge in cases in Philadelphia? Any assistance with this would be greatly appreciated.
Sincerely,
Alexis Lieberman, MD

On Nov 12, 2020, at 10:23 AM, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov> wrote:

Thank you. We have considered this drug before, will refer these references to the assessment team for further evaluation. Janet Woodcock

-----Original Message-----
From: Alexis Lieberman (b) (6)
Sent: Wednesday, November 11, 2020 5:58 PM
To: Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>
Subject: Information re Covid treatment

Dear Dr. Woodcock,
As a practicing pediatrician in Philadelphia, I am writing to request that you use your role on the Covid task force to advocate for an immediate, large-scale RCT for ivermectin early in disease. I include summaries of studies done so far on ivermectin that point to its promise.

As you know, Ivermectin is an anti-parasitic drug that is used widely throughout the world and is generally very well-tolerated with only very RARE side effects in those who do not have parasites, primarily limited to allergic reactions. The drug is proposed to prevent the virus from getting into the nucleus of the human cell. While the initial Monash in-vitro study used very high doses and the early Surgisphere study was discredited, since that time, there have been a dozen positive clinical studies. Surely there is enough evidence now to warrant a large-scale, government-funded RCT.

This inexpensive, off-patent drug will not make money for any drug company. Therefore, it falls to the government to take steps to fund a trial. I implore you to advocate for this!

STUDIES AND LINKS REGARDING IVERMECTIN:

10/29/30. India: Two doses of ivermectin, given 72 hours apart, prophylactically, was associated with a 73% reduction of COVID-19 infection among healthcare workers for the following one-month, in a case control study of 186 pairs.
https://www.medrxiv.org/content/10.1101/2020.10.29.20222661v1

10/26/30: Baghdad, Iraq: A recent study done Baghdad compared COVID patients who took ivermectin or did not. In this, 10% of the non-Ivermectin group progressed to severe disease well only 4% of the ivermectin group did. In that same study there was a 27% mortality rate for those who did not take over motion versus 18% and those who did.
https://www.medrxiv.org/content/10.1101/2020.10.26.20219345v1?fbclid=IwAR0M7sh3HnP3rDM5FRyiM34RsBFWBoXDcRfP3Nz4Yaw9Ia7YAo8FMmE4rGY

9/28/20: Bangladesh: In this retrospective study, they compared patients who received Ivermectin with those who receive the standard of care. They found that 46% of the standard of care patients required oxygen and 8% went to the intensive care unit. This was compared to those who did receive ivermectin, in which 9% required oxygen and only 1% went to the intensive care unit.
https://www.trialsitenews.com/mymensingh-medical-college-retrospective-study-ivermectin-superior-to-standard-of-care-for-covid-19-patients/

8/28/20: Preventive study from Egypt showing for the first time a large reduction in covid contraction for family members taking prophylactic dose of Ivermectin when there is an infected person in the same household. Household contacts who did not take ivermectin had a 58% rate of contracting Covid, compared to only 7% of those who did take ivermectin.
https://clinicaltrials.gov/ProvidedDocs/61/NCT04422561/Prot_SAP_000.pdf

8/26/20: Bangladesh. 400 patients were randomized to either receive ivermectin or placebo. In that study 18% of the placebo patients progressed to clinical deterioration while only 9% of those with ivermectin deteriorated. In that study they also compared percentage of patients who had early clinical improvement within a week, and of those without Ivermectin, 44% improved quickly while of those with Ivermectin, 60% improved quickly.
https://clinicaltrials.gov/ProvidedDocs/31/NCT04523831/Prot_ICF_000.pdf

7/8/20 Baghdad, Iraq: This study compared hospitalized patients with mild to moderate symptoms who took ivermectin or did not. Those who did not had a hospital stay of 12 days on average, vs 7% in those who did take ivermectin.
https://www.medrxiv.org/content/10.1101/2020.07.07.20145979v1.full.pdf

6/30/20 Dominican Republic Data:
https://www.trialsitenews.com/president-of-dominican-republic's-largest-private-health-group-discusses-the-success-of-ivermectin-as-a-treatment-for-early-stage-covid-19/

6/28/20 Bangladesh Data (mild to moderate cases, comparison with hydroxychloroquine/azithromycin). This study is not statistically significant but showed a trend of recovery in eight days with ivermectin versus nine without.
https://www.trialsitenews.com/ivermectin-study-reveals-fantastic-results-100-of-60-patients-better-in-an-average-of-just-under-6-days/

6/10/20 Florida Data (first U.S. data, on hospitalized patients). This is a retrospective intensive care unit study in which those who did not receive ivermectin had a 25% mortality rate while those who did receive ivermectin had a 15% mortality rate. It has since been published in a peer-reviewed journal.
https://journal.chestnet.org/article/S0012-3692(20)34898-4/fulltext

5/2/20 Peru Data: areas of the country where ivermectin was used have a lower case rate and lower fatality rate than areas where ivermectin was not used.
https://www.docdroid.net/J8wuZlb/ivermectin-studyesen-pdf

3/2020: Australian study that showed that high doses of ivermectin killed the Covid virus in a test tube study.
https://research.monash.edu/en/publications/the-fda-approved-drug-ivermectin-inhibits-the-replication-of-sars

The FLCC, a US based group of colleagues with over 200 years of combined experience in Critical Care and Emergency Medicine, as well as long-standing shared interests in developing effective treatments for critical illnesses including sepsis, is a working group devoted to creating a treatment protocol against COVID-19.
They developed an inpatient Covid protocol which has lead to a mortality rate of 4-10%, compared to the world average of 23%.
They have now developed a prophylactic and early outpatient combination treatment protocol for COVID-19 called I-Mask+.
https://covid19criticalcare.com/wp-content/uploads/2020/11/FLCCC-IVERMECTIN-Protocol.pdf
This protocol recommends ivermectin, vitamins C and D, Zinc, melatonin and, for adults only, aspirin.

Their rationale is based on multiple studies as well as real-world evidence comparing countries using ivermectin, such as Peru, Brazil and Haiti, to those not using it, such as the Dominican Republic and the US.

Here is the introductory video from FLCC:
https://vimeo.com/473929788/382c386d60

Thank you for your consideration,
Alexis Lieberman, MD
Advocare Fairmount Pediatrics