From: Fauci, Anthony (NIH/NIAID) [E]
Sent: Tue, 11 Feb 2020 13:12:28 +0000
To: Cassetti, Cristina (NIH/NIAID) [E]
Subject: FW: coronaviruses

Please handle. Thanks.

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-----Original Message-----
From: (b) (6)
Sent: Tuesday, February 11, 2020 8:01 AM
To: (b) (6)
; Holbrook, Michael (NIH/NIAID) [C] < (b) (6) >; Fauci, Anthony (NIH/NIAID) [E] (b) (6)
Subject: coronaviruses

Hello,

Working as an occupational physician in France, I would like to draw your attention to the antiviral activity of proton pump inhibitors, including for the Gibbon Ape Leukemia virus, a virus which does not require acidification of endosomes for entry into cells, as is the case with coronaviruses.

Indeed, in 2015 Long et al. (1) found that « …The commonly used proton pump inhibitors, Omeprazole and Esomeprazole were also able to inhibit entry of all PVs tested but at higher drug concentrations than may be achieved in vivo… ».
Using omeprazole and esomeprazole magnesium hydrate, prepared in sterile DMSO (Sigma), they concluded that « … OM and ESOM appeared to decrease fluorescence, and therefore increase endosomal pH, only at a concentration of 200µM, higher than that required to inhibit PV entry. Moreover cellular toxicity was observed at this concentration after 24 hours… ».

In 2016, Dowall et al. (2) found : « …Whereas omeprazole and esomeprazole demonstrated in vitro activity against EBOV, the results were in line with a previous report using pseudotyped viruses where the values of drug concentration causing 50% inhibition (IC50) were in the region of 50 µM [10]. This suggested that doses required for potent inhibition would be difficult to achieve without concomitant and significant toxicity (the licenced dosing for 40 mg esomeprazole, 20 mg esomeprazole and 20 mg omeprazole generates median maximum plasma concentrations of 1.59–9.61 µM, 0.51–4.78 µM and 0.15–3.51 µM, respectively… ».

However, omeprazole is marketed in a non-ionized form and must be ionized (in acidic environment) to be