



TO: Catholic Health Medical Staff
FROM: Dr. Kevin Shiley, Infection Prevention and Control
DATE: April 24, 2020
RE: Hydroxychloroquine for Covid-19 therapy

When a physician uses a product for an indication not listed in the approved labeling ("off-label"), the physician has the responsibility to be well informed about the product and to base the proposed use on scientific rationale and medical evidence.

Reports of *in vitro* antiviral activity of hydroxychloroquine on SARS-CoV-1 prompted many medical professionals to consider this medication's use for off label use in patients infected with SARS-CoV-2 /Covid-19. Given the extraordinary influx of patients with life-threatening Covid-19 and a lack of well studied available treatments, the use of hydroxychloroquine has become commonplace in many regions. Anecdotal reports within our healthcare community and elsewhere have raised concerns for increased risk or ventricular arrhythmias and substantial QTc prolongation.

Human trials data on the use of hydroxychloroquine are now emerging. The human studies to date; many of which are yet to be published in peer reviewed journals, are limited by small numbers, study design, and varying doses and durations of therapy. Nonetheless, we feel it is important to communicate these data to providers in an effort to aid them in their decision making for individual patients. If, after reviewing a patient's case, it is felt that hydroxychloroquine may be beneficial to the patient, it is advised that the provider discuss the risks and potential benefits of the therapy with the patient or her/his proxy.

In addition, it is strongly recommended that close monitoring of the patient's QTc occurs, both before initiation and while on the medication. It is also recommended to avoid hydroxychloroquine if the patient has risk factors for QT prolongation, including concurrent medications with QT prolonging effects. Likewise, it is recommended to avoid adding other medications with potential QT prolonging effects, such as azithromycin, unless strongly indicated and then only with close monitoring for arrhythmia.

A brief patient information sheet is included with this memorandum. This may be used to help inform patients/healthcare proxies at the time of decision making regarding hydroxychloroquine use.

FDA MedWatch Advisory 4/24/2020

"If a health care professional is considering use of hydroxychloroquine or chloroquine to treat or prevent COVID-19, FDA recommends checking www.clinicaltrials.gov for a suitable clinical trial and considering enrolling the patient. Consider using resources available to assess a patient's risk of QT prolongation and mortality."

Recent Pre-publication News

Nature Medicine research brief:

"A phase IIb trial of 81 patients in Manaus, Brazil, treated with azithromycin in combination with high- or low-dose chloroquine, was reported in MedRxiv. The study, which has not yet been peer-reviewed, found no evidence of significant benefits of chloroquine–azithromycin and highlighted safety concerns, with the high-dose arm terminated early due to the incidence of QT interval prolongation. Also in MedRxiv, a multicenter open-label randomized control study of COVID-19 patients in China treated with hydroxychloroquine alone failed to show any effect on its primary endpoint, the negative conversion rate, but did exhibit a moderate reduction in lymphopenia and C-reactive protein levels. This study also has not yet been peer-reviewed." <https://www.nature.com/articles/d41591-020-00011-3>

"Outcomes of hydroxychloroquine usage in United States veterans hospitalized with Covid-19"

"In this study, we found no evidence that use of hydroxychloroquine, either with or without azithromycin, reduced the risk of mechanical ventilation in patients hospitalized with Covid-19. An association of increased overall mortality was identified in patients treated with hydroxychloroquine alone. These findings highlight the importance of awaiting the results of ongoing prospective, randomized, controlled studies before widespread adoption of these drugs."

<https://www.medrxiv.org/content/10.1101/2020.04.16.20065920v1>

Other Recent Publications and Pre-publications

1. Yao X, Ye F, Zhang M et al. **In vitro antiviral activity and projection of optimized dosing design of hydroxychloroquine for the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).** *Clin Infect Dis*. 2020; (published online March 9.) DOI:10.1093/cid/ciaa237
2. Liu J, Cao R, Xu M, et al. **Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro.** *Cell Discov*. 2020; 6: 16
3. Wang M, Cao R, Zhang L, et al. **Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro.** *Cell Res*. 2020; 30: 269-271
4. Cortegiani A, Ingoglia G, Ippolito M, Giarratano A, Einav S. **A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19.** *J Crit Care*. 2020; (published online March 10.)
5. Gautret P, Lagier JC, Parola P, et al. **Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial.** *Int J Antimicrob Agents*. 2020; (published online March 20.)
6. Gautret P, Lagier JC, Parola P, et al. **Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: an observational study.** <https://www.mediterranee-infection.com/wp-content/uploads/2020/03/COVID-IHU-2-1.pdf> Date: 2020. Date accessed: April 2, 2020
7. Alhazzani W, Moller MH, Arabi YM, et al. **Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19).** *Intensive Care Med*. 2020; (published online March 28.) DOI:10.1007/s00134-020-06022-5
8. Chen J, Liu D, Liu L, et al. **A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19).** *J Zhejiang Univ (Med Sci)*. 2020; (published online March 6.) DOI:10.3785/j.issn.1008-9292.2020.03.03
9. Chen Z, Hu J, Zhang Z, et al. **Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial.** *medRxiv*. 2020; (published online March 31.) (preprint). DOI: 10.1101/2020.03.22.20040758
10. Molina JM, Delaugerre C, Le Goff J, et al. **No evidence of rapid antiviral clearance or clinical benefit with the combination of hydroxychloroquine and azithromycin in patients with severe COVID-19 infection.** *Med Mal Infect*. 2020; (published online March 30.) DOI:10.1016/j.medmal.2020.03.006