DASON COVID-19 Weekly Treatment Literature Update 6/8/2020
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The following summarizes key literature pertaining to treatment of COVID-19 during the past week.
*Note: some of the data discussed below is in pre-print form that has not yet been peer-reviewed. We have noted some discrepancies in some of this data, and final printed versions may ultimately differ from what is shown here. We will update as soon as possible; caution is advised when interpreting this literature.

Retractions
Due to concerns over data validity and inability to provide public access to the data contained in the Surgisphere database, three studies were retracted last week and doubt has been cast on a 4th study regarding ivermectin from Latin America (see below for details on the hydroxychloroquine retraction).

Discussion of the concerns with the database can be found [here.](https://www.who.int/gho/coronavirus/en/)

1. Hydroxychloroquine *Lancet* study originally posted [at this link](https://www.lancet.com/journals/lancet/article/PIIS0140-6736(20)30700-0/fulltext) and the Lancet [expression of concern.](https://www.lancet.com/journals/lancet/article/PIIS0140-6736(20)30701-2/fulltext)
4. There is an additional pre-print regarding efficacy of ivermectin from the same author group that is no longer available on-line.

Remdesivir
*Remdesivir Access*: Additional shipments continue to be distributed to state health departments. Data regarding shipments to states is now being posted to the Public Health Emergency website: [https://www.phe.gov/emergency/events/COVID19/Investigation-MCM/Pages/remdesivir.aspx](https://www.phe.gov/emergency/events/COVID19/Investigation-MCM/Pages/remdesivir.aspx)

The next distribution will be based on data hospitals enter into the TeleTracking system which captures COVID-19 positive patients at your facility by **MIDNIGHT, MONDAY JUNE 8, 2020**.

On Monday, June 1st, Gilead posted a [press release](https://www.gilead.com) about the results of remdesivir for moderate disease (remdesivir 5d, vs. 10d vs. standard of care). The release includes limited information on the study for review. The data are from the first 584 enrolled patients and based on the data provided, both 5 and 10 day treatment arms had a higher percentage of patients with an improvement in the outcome scale compared with patients in the standard of care arm.

The remdesivir summary table with the information of published studies to date can be found [at this link](https://dason.medicine.duke.edu/summary-recent-clinical-data-use-remdesivir-covid-19)
This was a randomized, double-blind placebo-controlled trial conducted out of University of Minnesota that enrolled asymptomatic non-hospitalized adults across the US and Canada to evaluate hydroxychloroquine (HCQ) post-exposure prophylaxis (PEP). 821 subjects were enrolled after a high- or moderate-risk COVID-19 household or occupational exposure and within 4 days initiated oral HCQ (800 mg X1, followed by 600 mg 6-8h later, then 600 mg daily for 4 days) or placebo. Digital informed consent was obtained from all subjects, with follow-up email surveys for up to 6 weeks after enrollment. Study drug was shipped overnight to study participants via courier. Median age of study participants was 40 years; they were most commonly women (52%), health care workers (66%), with high-risk exposures (88%). 27.4% had chronic health conditions, most commonly hypertension (12.1%) and asthma (7.6%). Since patients were followed remotely and COVID-19 testing had limited availability during the study time frame, a clinical definition of COVID-19 was used based on reported symptoms. The primary outcome, new illness compatible with COVID-19, was similar in those receiving HCQ and placebo (11.8% vs 14.3%, respectively, p=0.35). There were two hospitalizations (one in each group) and no arrhythmias or deaths. Rates of PCR-confirmed COVID-19 were similar between the two treatment groups (2.7% HCQ, 2.2% placebo). 40% of HCQ patients reported side effects compared to 17% of those receiving placebo (p<0.001); these were mostly gastrointestinal side effects.

Approximately 22% and 33% of study participants also took zinc or vitamin C, respectively, but this was evenly distributed across treatment groups and did not seem to impact occurrence of COVID-19 confirmed illness in either of the treatment groups. There were no differences in incidence of COVID-19 compatible illness between the treatment groups when further stratified by subgroup including age, sex, days of exposure, type of contact, medication adherence, and days from exposure to start of study treatment. Limitations of this study include lack of SARS-CoV-2 testing in all study subjects, self-reported adherence and symptoms, and loss to follow-up for a small proportion of study patients. Also, the study subjects were recruited largely through the internet and were generally younger overall.

Following recent concerns about safety of hydroxychloroquine/chloroquine, the investigators of the Randomised Evaluation of COVID-19 thERapY (RECOVERY) trial in the UK released a statement after its Independent Data Monitoring Committee reviewed the data for the unblinded HCQ arm of this trial. The trial include 6 active treatment arms (HCQ, azithromycin, lopinavir/ritonavir, low dose dexamethasone, tocilizumab, or convalescent plasma) as well as a standard of care (SOC) arm, and has enrolled more than 11,000 patients at 175 NHS hospitals in the UK. After review of the data the investigators determined there was no beneficial effect of HCQ in hospitalized patients and stopped enrollment into the HCQ arm of the study. Among 1542 patients receiving HCQ, 28-day mortality was 25.7% compared to 23.5% in 3132 patients receiving SOC (HR 1.11 [95% CI: 0.98-1.26]). Other outcomes such as length of hospital stay were also similar for HCQ vs SOC.


Hydroxychloroquine Data: Please note, the summary table has also been updated and is available at this link: https://dason.medicine.duke.edu/summary-recent-clinical-data-use-hydroxychloroquine-and-chloroquine-covid-19