DASON COVID-19 Weekly Treatment Literature Update 7/10/2020
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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*Note: some of the data discussed below is in pre-print form that has not yet been peer-reviewed.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.

Treatment Updates
Remdesivir- The Society of Infectious Diseases Pharmacists have created a new FAQ document clarifying some aspects of the new acquisition process for remdesivir that will begin in the coming weeks. This link has been added to the DASON COVID-19 updates site: https://sidp.org/resources/Documents/SIDP_RDV%20Commercial%20Allocation%20FAQ_Press%20Release_2020.07.07_FINAL.pdf

On Friday, July 10, 2020 additional data on remdesivir were presented at a virtual COVID-19 conference and summarized in a press release from Gilead. This is an additional analysis of the Phase 3 SIMPLE Severe study which was previously described in NEJM (https://www.nejm.org/doi/full/10.1056/NEJMoa2015301). This new analysis compares patients who received remdesivir as part of the trial with an external group of 818 patients receiving standard of care. The reported results suggest a mortality benefit in the remdesivir treated patients. We eagerly await the ability to review the data and will continue to provide updates as more data become available. The press release can be found at this link: https://www.gilead.com/news-and-press/press-room/press-releases/2020/7/gilead-presents-additional-data-on-investigational-antiviral-remdesivir-for-the-treatment-of-covid-19

Sarilumab- In a press release last week, Sanofi and Regeneron Pharmaceuticals announced that the Phase 3 trial of sarilumab failed to meet primary and secondary endpoints. The press release can be found at this link: https://www.sanofi.com/en/media-room/press-releases/2020/2020-07-02-22-30-00

New Literature This Week

This was a multicenter retrospective observational study of 2,541 adults with a confirmed positive SARS-CoV-2 test admitted to 6 hospitals in the Henry Ford Health System in Michigan between 3/10/2020- 5/2/2020. Patients were treated according to standardized hospital protocols with either hydroxychloroquine (HCQ) (400 mg BID for 1 day, followed by 200 mg BID on days 2-5) (47.3% of patients), azithromycin (AZ) (500 mg X 1 followed by 250 mg QD x 4 days) (5.8% of patients), a combination of HCQ + AZ (for severe COVID-19 with minimal cardiac risk factors) (30.8% of patients) or neither drug (16.1% of patients). 68% of patients received adjunctive corticosteroids
(methylprednisolone/prednisone) and 4.5% also received tocilizumab. Median age of study participants was 64 years (IQR: 53-76 years), with 51% male and 56% African American. The study endpoint was inpatient mortality; other endpoints were not reported. Overall unadjusted in-hospital mortality was 18.1% overall, 13.5% HCQ, 20.1% HCQ+ AZ, 22% AZ, and 26.4% for no HCQ/AZ (p<0.001). In Kaplan Meier and Cox Proportional Hazard models adjusting for a number of covariates (age, gender, cardiovascular disease, lung disease, mSOFA and oxygen saturation), use of HCQ + AZ (HR 0.29 [95% CI 0.22-0.40]) or HCQ alone (HR 0.34 [95% CI 0.25-0.46]) was associated with significantly lower in-hospital mortality than neither medication. Other significant predictors of mortality included age >= 65 years, BMI >=30, Chronic Kidney Disease, O2 saturation <95%, and mechanical ventilation. In a propensity matched analysis of 190 HCQ and 190 non-HCQ recipients, HCQ was associated with lower mortality (HR 0.49 [95% CI 0.29-0.83]). Potential limitations of this study include the lack of mSOFA score for 25% of the study population (and lack of information about how these patients were handled in the analysis), lack of apparent adjustment or evaluation of clustering by hospital, retrospective nature of the study, inclusion of multiple post-admission covariates in the risk-adjustment and propensity-score, lack of adjustment for time (as patients may have had better outcomes over time with more clinician experience with managing COVID), and other measures of disease severity (ie ferritin, d-dimer, etc were not considered).

An editorial comment has been published on this paper as well, discussing strengths and limitations of the study: Lee TC, MacKenzie LJ, McDonald E, Tong SYC. An Observational Cohort Study of Hydroxychloroquine and Azithromycin for COVID-19: (Can’t get no) Satisfaction. Int J Infec Dis 2020. https://doi.org/10.1016/j.ijid.2020.06.095

Treatment Summary Tables
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

The hydroxychloroquine summary table is available at this link: https://dason.medicine.duke.edu/summary-recent-clinical-data-use-hydroxychloroquine-and-chloroquine-covid-19

The tocilizumab 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-tocilizumab-covid-19