DASON COVID-19 Update 11/20/2020

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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*Note: some of the data discussed below may be in pre-print form that has not yet been peer-reviewed.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.

Guideline Updates

There were 3 guideline updates this week:

Earlier today (11/20), the WHO guideline committee recommended against using remdesivir

NIH treatment guidelines were updated 11/18 to include statement on bamlanivimab

Based on the available evidence, the Panel has determined the following:

- At this time, there are insufficient data to recommend either for or against the use of bamlanivimab for the treatment of outpatients with mild to moderate COVID-19.
- Bamlanivimab should not be considered the standard of care for the treatment of patients with COVID-19.
- An interim analysis of the BLAZE-1 study, a Phase 2, randomized, placebo-controlled trial, suggested a potential clinical benefit of bamlanivimab for outpatients with mild to moderate COVID-19. However, the relatively small number of participants and the low number of hospitalizations or emergency department visits make it difficult to draw definitive conclusions about the clinical benefit of bamlanivimab.
- More data are needed to assess the impact of bamlanivimab on the disease course of COVID-19 and to identify those people who are most likely to benefit from the drug. Health care providers are encouraged to discuss participation in bamlanivimab clinical trials with their patients.
- Given the possibility of a limited supply of bamlanivimab, as well as challenges distributing and administering the drug, patients at highest risk for COVID-19 progression should be prioritized for use of the drug through the EUA. In addition, efforts should be made to ensure that communities most affected by COVID-19 have equitable access to bamlanivimab.
- Bamlanivimab should not be withheld from a pregnant individual who has a condition that poses a high risk of progression to severe COVID-19, and the clinician thinks that the potential benefit of the drug outweighs potential risk (see the criteria for EUA use of bamlanivimab below).
- Patients who are hospitalized for COVID-19 should not receive bamlanivimab outside of a clinical trial.

IDSA Treatment Guidelines were updated 11/18

Recommendation 13: Among ambulatory patients with COVID-19, the IDSA guideline panel suggests against the routine use of bamlanivimab. (Conditional recommendation, Very low certainty of evidence)

- Remark: In patients at increased risk (as defined by the FDA EUA [122]), bamlanivimab is a reasonable treatment option if, after informed decision-making, the patient puts a high value on the uncertain benefits and a low value on uncertain adverse events.
Therapeutic/Regulatory Information

Yesterday, FDA approved an EUA for baricitinib (a JAK1/JAK2 inhibitor, brand name Olumiant) in combination with remdesivir (Veklury) for COVID-19. This is for hospitalized adults and children >= 2 years of age requiring supplemental oxygen, invasive mechanical ventilation, or ECMO.

This was largely on the basis of data from the ACTT-2 trial in the US, which is being run by the NIH. (Here is the link of the results previously shared from 9/14 press release) https://investor.lilly.com/news-releases/news-release-details/baricitinib-combination-remdesivir-reduces-time-recovery and subsequent data from 10/8 in press release) https://investor.lilly.com/news-releases/news-release-details/baricitinib-has-significant-effect-recovery-time-most-impactful.

The initial findings reported a median one day improvement in recovery time in the overall study population when baricitinib was given in combination with remdesivir to hospitalized patients. The updated findings from 10/8 reported a numerical (35%) but not statistically significant reduction in mortality (5.1 vs. 7.8%, p=0.09) that was more pronounced among patients requiring oxygen.

Additional data presented as part of the EUA include two additional outcomes. First, patients receiving baricitinib had improved clinical status (on 8-point ordinal scale) at day 15 compared with those receiving placebo (p=0.044). Secondly, the proportion of patients who died or progressed to non-invasive or invasive mechanical ventilation was lower in the group receiving remdesivir plus baricitinib 23% vs. 28% in patients receiving remdesivir plus placebo (p=0.039). For the 21% of patients requiring non-invasive ventilation and 11% requiring invasive mechanical ventilation or ECMO at baseline, disease progression was considered a worsening of at least 1 point on the ordinal scale for this outcome.

The baricitinib covered by this authorization will be used only by healthcare providers, in combination with remdesivir, to treat suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or ECMO; and

The use of baricitinib covered by this authorization must be in accordance with the dosing regimens as detailed in the authorized Fact Sheets. Here are links to all of the materials:

- FDA authorization letter
- Press release
- FAQ document
- HCP fact sheet (please note, this includes dosing guidance and administration instructions for patients unable to take po medications)
- Patient and family fact sheet

Vaccine Information This Week

It has been a busy week for vaccine news:

DHHS has partnered with several community pharmacies to provide public vaccinations once supplies are available (please note: this will be after the first wave of vaccine and is not anticipated until at least late winter 2021). You can read more in this press release.
Current Status of Vaccine Data:
Pfizer (mRNA, 2 doses 21 days apart)

- 11/9 press release on Pfizer vaccine - interim analysis - 90% efficacy for 7 day endpoint
- 11/18 Update on the data-phase III study is complete, efficacy estimate increased to 95% for 7 day endpoint (170 active cases (162 were in placebo, only 8 in vaccinated patients, a total of 10 severe cases (included in the 170) and of those, 9 received placebo)
- EUA has been filed (anticipated turn around is 2 weeks)
- Cold chain requirements: -70 (+/- 10-15 degrees) - good for 5 days in the refrigerator, Pfizer has developed a thermal shipper that will keep vaccine frozen on dry ice for 15 days (will need dry ice replenishment)

Moderna (mRNA, 2 doses 28 days apart)

- 11/16 press release on Moderna vaccine - Phase III study is complete, 94.5% effective at 14 day endpoint - (95 active cases (90 in placebo, 11 severe cases, all in placebo)) and accompanying NIH Press release
- Cold chain requirements - good under refrigeration for 30 days

Astra Zeneca (adenovirus vector vaccine, initially studied as 2 doses)

- New trial started this week with a 2 dose schedule

New Treatment Information This Week

Yesterday (11/19), results of the REMAP-CAP studied that was a large trial modified to address COVID-19 treatments released results of the tocilizumab treatment arm in a press release. On the recommendation of the DSMB, efficacy of tocilizumab is being declared with an OR of 1.87 for combination of survival and length of time organ support in ICU was received. The data are based on the first 303 patients. In a press conference, investigators highlighted that this is a sicker patient population than the previously published NEJM data.

Treatment Summary Tables

NIH Treatment Guidelines Summary: https://dason.medicine.duke.edu/nih-covid-19-treatment-guideline-updates

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

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

All FAQs available here: https://dason.medicine.duke.edu/covid-19-novel-coronavirus-resources