Email from WAYNE WEART, PharmD, April 7, 2020

Dear Beth, here are some Facebook posts I have made in response to questions from my collogues which might be helpful? Stay safe and have a wonderful and blessed week! Wayne Weart

March 23, 2020

Dear Colleagues, Here is a link to the most recent CDC Information for Clinicians on Therapeutic Options for COVID-19 Patients

https://www.cdc.gov/.../2019-ncov/hcp/therapeutic-options.html

It reviews the two old meds chloroquine and hydroxychloroquine and what is currently underway. I want to add that both drugs can cause QT prolongation so be careful and with chloroquine remember that it can cause hemolytic anemia in patients with G6PD deficiency which is the second most common human enzyme defect, affecting some 400 million people world-wide (primarily Mediterranean and African). It affects 1 in 10 African American males in the US. Hydroxychloroquine does appear to be more effective to date and is also safer, but the data is far from convincing and the dosage is still to be worked out as well as the very limited 6 patients who had a better response when azithromycin was added to hydroxychloroquine in the French case reports. “There are no currently available data from Randomized Clinical Trials (RCTs) to inform clinical guidance on the use, dosing, or duration of hydroxychloroquine for prophylaxis or treatment of SARS-CoV-2 infection.”

This update also covers Gilead's investigational IV antiviral remdesivir and the on-going trials. This agent is no longer going to made available under the compassionate use policy as they are redirecting the supply to the ongoing clinical trials as of 3-22-2020 according to the company. Very limited data to date.

They also state “ Lopinavir-ritonavir did not show promise for treatment of hospitalized COVID-19 patients with pneumonia in a recent clinical trial in China [8]. This trial was underpowered, and lopinavir-ritonavir is under investigation in a World Health Organization study.”

Stay tuned as this will be a very rapidly changing area as other than slowing down the curve our best hope is probably a pharmacotherapy option as a vaccine is likely still a year to 18 months away at best.

Please stay safe and if possible, stay at home and practice all of the recommended non-pharmacologic recommendations. I wish everyone a wonderful and blessed week

Coronavirus disease 2019 (COVID-19) is a virus (more specifically, a coronavirus) identified as the cause of an outbreak of respiratory illness first detected in China.

CDC.GOV

Coronavirus Disease 2019 (COVID-19)

Coronavirus disease 2019 (COVID-19) is a virus (more specifically, a…

Coronavirus di

sease 2019 (COVID-

March 30, 2020

Dear Colleagues, we now have more observational data not a controlled trial, from the French experience with the combo of hydroxychloroquine and azithromycin in the first 80 patients including the original 6 patients we mentioned last week. This is pre-publication data from the authors and many countries including

the France and the US have made a decision to allow hydroxychloroquine to be used for COVID-19. These results should they prove to be reliable suggest that many patients have been able to be discharged within 5 days? They were considered noncontagious 80-90% by day 7-8? We eagerly await the on-going clinical trials. I believe that even MUSC has this combo as one of its protocols for selected patients.

Yesterday the FDA granted an Emergency Use Authorization for hydroxychloroquine and chloroquine and Sandoz donated 30 million doses of hydroxychloroquine to the National Stockpile. The FDA will allow these medications to be distributed and prescribed by doctors to hospitalized teen and adult patients with COVID-19, as appropriate, when a clinical trial is not available or feasible," Novartis Chief Executive Vas Narasimhan told a Swiss newspaper that hydroxychloroquine is our biggest hope in combating COVID-19. (Novartis owns Sandoz). Stay tuned as we are going to learn much more in record time! Please take all necessary precautions and stay safe! God Bless!!

Wayne Weart

April 7, 2020

Dear Colleagues, there is very limited data primarily from a non-controlled recent trial from France where 65 of 80 COVID-19 patients were successfully treated with a combo of hydroxychloroquine plus azithromycin. Its being widely studied in many countries including the US but the data is limited but promising. The risk of G6PD deficiency causing hemolytic anemia is with chloroquine and the risk of retinopathy including blindness is with both antimalarials but tends to be with higher doses and long term use (IE ~ 5years or more). QTc prolongation is a concern especially when added to other agents which also cause it like azithromycin but the folks with the Arizona CERT experts on QTc prolongation suggest that most patients ~90% can use the regimen and about 1% are at risk from arrhythmias. We probably do need to check for QT prolongation at base-line and if the baseline QTc is less than 460 ms in prepubescent males < 470 ms in postpubescent males and <480 ms in females we are probably OK but we will need to monitor the electrolytes and Keep potassium at 4.0 or higher, Mg at 2.0 or more and stop any other meds that can increase QTc if they are not required. I have previously posted on the SC Pharmacists Facebook Page the data from the French experience with this regimen. I am happy to e-mail you any further information is you will send me your e-mail address. Stay safe and have a great and a blessed week! Wayne

Additional information about Investigational Meds showing promise?

IL-6 receptor blockade with monoclonal antibodies may benefit patients with COVID-19 induced pneumonitis ?

Tocilizumab (Actemra) specifically has data from the frontlines of the pandemic that indicate that the agent might offer lifesaving benefit for patients with COVID-19 in respiratory distress. Currently, tocilizumab is FDA approved to manage cytokine release syndrome (CRS) in patients receiving CAR T-cell therapy.

Investigators in Italy and China who have used tocilizumab to treat patients infected with COVID-19 at doses comparable to those used for the management of CRS have reported rapid improvement in both intubated and non-intubated patients. In these reports, the expedited administration of anti-IL-6R therapy for patients in acute respiratory distress has been essential.

A recent study protocol to evaluate the efficacy of tocilizumab in COVID-19 induced pneumonitis was able to accrue over 300 patients worldwide in less than 24 hours. Genentech also indicated that they will provide 10,000 vials of the agent to the US Strategic National Stockpile. In China, tocilizumab was approved in March 2020 for the treatment of patients infected with COVID-19 who experienced serious lung damage and elevated IL-6.

The use of IL-6 or IL-6 receptor blocking antibodies like tocilizumab (Actemra), sarilumab (Kevzara), and siltuximab (Sylvant) that are FDA approved for various conditions including rheumatologic disease and the lymphoproliferative disorder Castleman's syndrome could potentially be used to treated hospitalized critically ill patients with COVID-19-induced hypoxia, according to the researchers.

In the US, a trial of sarilumab in the COVID-19 setting remains ongoing.

March 24, 2020. sitcancer.org/research/covid-19-resources/il-6-editorial

The FDA has approved a randomized, double-blind, placebo-controlled phase III clinical trial to evaluate the safety and efficacy of intravenous (IV) tocilizumab (Actemra) plus standard of care in hospitalized adult patients with severe coronavirus disease 2019 (COVID-19) pneumonia, according to Genentech, the agent's developer.

The clinical trial, called COVACTA, is being conducted in collaboration with the Biomedical Advanced Research and Development Authority (BARDA). COVACTA is anticipated to start as early as April 2020, with a target accrual of 330 patients across the US and other countries.

The primary and secondary endpoints of the phase III study include clinical status, mortality, mechanical ventilation, and intensive care unit (ICU) variables. Researchers will follow patients for 60 days post-randomization, and an interim analysis will be conducted to look for early evidence of efficacy.

Remdesivir

Gilead Sciences Treatment: Remdesivir (GS-5734) Nucleotide prodrug

Status: The NIH announced February 25 it will run the first U.S. clinical trial evaluating an experimental treatment for COVID-19, by assessing remdesivir in patients at the University of Nebraska Medical Center in Omaha, where some Americans with the disease are being cared for or are under quarantine. Remdesivir showed "no adverse events" when administered to the first American confirmed to be infected with SARS-CoV-2 (35 y/o male with atypical pneumonia who tested positive and had recently returned from China), members of the Washington State 2019-nCoV Case Investigation Team reported in a case study. N Engl J Med 2020; 382:929-936

In China, clinical trials of Gilead Sciences' remdesivir have begun after China's National Medical Products Administration approved applications by the China-Japan Friendship Hospital and the Chinese Academy of Medical Sciences to conduct the studies. Remdesivir and chloroquine phosphate were "highly effective in the control of 2019-nCoV infection in vitro," a team of Chinese researchers reported in a study published February 4 in Cell Research.

Remdesivir is an investigational nucleotide analog with broad-spectrum antiviral activity – it is not approved anywhere globally for any use. Remdesivir has demonstrated in vitro and in vivo activity in animal models against the viral pathogens MERS and SARS, which are also coronaviruses and are structurally similar to COVID-19.

Recent data suggests remdesivir and chloroquine are highly effective in the control of 2019-nCoV infection in vitro. Cell Research (2020) 30:269–271

The Gilead studies will evaluate two dosing durations of remdesivir. One study will randomize approximately 400 patients with severe clinical manifestations of COVID-19 to receive either five or 10 days of remdesivir.

Approximately 400 participants will be randomized in a 1:1 ratio to receive remdesivir 200 mg on day one, followed by remdesivir 100 mg each day until day 5 or 10, in addition to standard of care. The primary objective of this study is to evaluate the effect of remdesivir, as measured by the normalization of fever and oxygen saturation [T < 36.6 C armpit, < 37.2 C oral, < 37.8 C rectal; and Sp02 > 94%, sustained for at least 24 hours through Day 14].

The second study will randomize approximately 600 patients with moderate clinical manifestations of disease to receive five or 10 days of remdesivir or standard of care alone. The primary endpoint of both studies is clinical improvement.

Approximately 600 participants will be randomized in a 1:1:1 ratio to receive remdesivir 200 mg on day one, followed by remdesivir 100 mg in addition to standard of care each day until day 5 or 10, compared with standard of care alone. The primary objective of this study is to evaluate the effect of remdesivir, as measured by the proportion of participants in each group discharged by day 14.

Health authorities in China have initiated two clinical trials in patients who have been infected with COVID-19 to determine the safety and efficacy of remdesivir as a potential treatment for the coronavirus. The two studies are being coordinated by the China-Japan Friendship Hospital and are being conducted at multiple sites in Hubei province.

One study is evaluating remdesivir in patients with confirmed disease who have developed more severe clinical manifestations such as a requirement for supplemental oxygen. The other study is evaluating remdesivir in patients with confirmed COVID-19 infection who have been hospitalized but are not displaying significant clinical manifestations of disease such as an oxygen requirement. The study in patients with severe disease began enrolling patients on February 6. The study in patients with moderate disease began enrolling patients on February 13. Clinical trial results are anticipated in April.

Gilead is providing study drug at no charge and provided input on study design and conduct.

Compassionate Use (Now on Hold as company has been overwhelmed and wants the supply to go to clinical trials 3-22-2020)

Gilead is working with government and non-government organizations and regulatory authorities to provide remdesivir to patients with COVID-19 for emergency treatment in the absence of any approved treatment options.

Compassionate use requests must be submitted by a patient's treating physician. Gilead is currently assessing requests on an individual basis and require, at a minimum, that the patient be hospitalized with confirmed COVID-19 infection with significant clinical manifestations.