Dignity Health - Mercy San Juan Medical Center
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COVID-19 Treatment Options

Coronaviruses are a large family of viruses that are common in people and many different species of animals, including camels, cattle, cats, and bats. Although rare, animal coronaviruses can infect people as with MERS-CoV, SARS-CoV and now with SARS-CoV-2. This virus originated in bats early on, many of the patients at the epicenter of the outbreak in China had some link to a large seafood and live animal market, which ultimately led to person-to-person spread.

There are no FDA approved treatments for coronavirus disease 2019 (COVID-19) but a number of drugs are under investigation and some medications are being used based on their in-vitro activity against COVID-19 or experience with humans in either COVID-19 or SARS and/or MERS.

Remdesivir

- Nucleotide analog that has shown in-vitro activity to COVID-19 in preliminary trials. It is not FDA approved and currently available for compassionate use through Gilead Pharmaceuticals
- **Dosing**: 200mg IV on day 1 followed by 100mg IV once daily on days 2-5 or 2-10.
- **SE**: renal insufficiency, acidosis, elevated transaminases, co-formulated with sulfobutyether B-cyclodextrin (SBECD), potential for accumulation in renal failure
- **Drug interactions**: Prodrug of CYP3A4, potential for reduced conversion in the presence of CYP3A4 inhibitors (lopinavir, ritonavir, darunavir or cobicistat)

Clinical Trials:

- **Inclusion criteria**: documented SARS-CoV-2, hospitalized with fever, and mechanical ventilation
- **Exclusion criteria**: evidence of multi-organ failure, pressors to maintain BP, ALT/AST >5x ULN, Crcl <30ml/min or HD, concurrent treatment with other agents with potential antiviral activity against SARS-CoV-2 <24hrs prior to Remdesivir

Hydroxychloroquine or Chloroquine

- The patient will not be approved for the clinical trial and compassionate use of remdesivir if used <24 hrs prior to initiation of first dose of remdesivir.
- In vitro data suggests it's more potent than chloroquine against COVID-19
- **Hydroxychloroquine dosing**: 400mg po daily x 5 days OR 400mg PO BID on day 1 followed by 200mg PO BID on days 2-5
- 2020 French study demonstrated the combination of hydroxychloroquine + azithromycin significantly reduced viral load and duration of infection
- Hydroxychloroquine 600mg PO daily x 5 days + azithromycin 500mg PO day 1 then 250mg PO x 4 days
- **Chloroquine dosing**: 500mg PO BID x7 days, if wt <50kg, then 500mg BID for day 1 and 2, then 500mg daily for day 3 through 7
- Tablet cannot be split or crushed but may be prepared into an oral suspension
- No renal/hepatic dose adjustments
- **AE**: cardiotoxicity, QTc prolongation, hematologic toxicity, G6PD deficiency
- **SE**: dizziness, HA, nausea, vomiting, abdominal pain, diarrhea, tinnitus, irritability

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Lopinavir/Ritonavir (Kaletra)

- Significant interaction with remdesivir, strongly consider before initiation of therapy, may exclude use of remdesivir
- Lopinavir is an HIV protease inhibitor that has been reported to have activity against 2019-nCoV.
- **Dosing**: 400/100mg PO BID for up to 10 days
- Liquid formulation available, if crushing tablets this decreases AUC by 45-47%, consider doubling dose either 800/200mg PO BID or 400/100mg PO QID. BID dosing may have better GI tolerance
- **SE**: Nausea, diarrhea hyperglycemia, increased liver transaminases or lipids, hypertension and prolonged QT interval

Studies:

- 2020 NEJM study showed in adults with severe disease, lopinavir/ritonavir had no benefit beyond standard of care
- Singapore study: 5 patients received lopinavir/ritonavir and progressive disease only occurred in two patients
- 4 patients, 2 with mild, 2 with severe COVID-19 in Shanghai who received 400/100mg PO BID x 6-15 days. 3 improved with 2 of them having negative viral testing at end of data collection. The fourth patient showed signs of improvement.
- Randomized control trial is currently pending from china

Other Medications

- Brilacidin, a defensing mimetic drug candidate. It has shown antibacterial, anti-inflammatory and immunomodulatory properties in several clinical trials.
- CytoDyn-leronlimab, a CCR5 antagonist, currently in phase two clinical trials as a treatment for HIV
- BXT-25, treatment for Acute Respiratory Distress Syndrome (ARDS) in late-stage patients infected with COVID-19.
- Actemra, ability to prevent cytokine storms or overreaction of the immune system

Adjunctive Therapy

- Adjunctive corticosteroids have not shown clinical benefit and delayed viral RNA clearance in other coronavirus diseases (SARS and MERS)
- Open labelled, randomized, controlled trial of 48 patients will be conducted in China comparing methylprednisolone 1-2 mg/kg/day IV for 3 days to a control group in patients with severe COVID-19.
- Favilavir, first approved coronavirus drug in china

Vaccines

- Altimmune's intranasal corona virus vaccine, design and synthesis of the vaccine has been completed and animal testing will follow
- INO-4800 by Inovio Pharmaceuticals, supported by a $9million grant from the Coalition for Epidemic Preparedness Innovations (CEPI). Company has prepared 3,000 doses for human clinical trials planned to be conducted across the US, China and South Korea. **Plans to produce one million doses of the vaccine by the end of 2020.**
- NP-120 (Ifenprodil) by Algernon Pharmaceuticals, has demonstrated efficacy in improving survivability in mice infected with **H5N1.**
- APN01 by University of British Columbia and APEIRON biologics is being tested in China in a phase one pilot trial as a treatment for COVID-19. The clinical trial will test the drugs efficacy in reducing the viral load in patients.
- mRNA-1273 vaccine by Moderna and Vaccine research center, targeting the Spike (S) protein of the coronavirus.
- Avian Coronavirus Infectious Bronchitis Virus (IBV) vaccine by MIGAL Research Institute, modified to treat COVID-19, originally created for the avian coronavirus
- TNX-1800: modified horsepox virus
- Recombinant subunit vaccine developed based on the trimeric S protein (S-Trimer) of the COVID-19, which is responsible for binding with the host cell and causing a viral infection
- Vaxart oral recombinant vaccine, based on genome of COVID-19
- Linear DNA vaccine, PCR-based DNA manufacturing technology