UC Davis COVID-19 Treatment Protocol

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Treatment Algorithm	
Step down/ICU level care • Radiographic infiltrates by imaging OR • Clinical assessment (crackles on exam) AND SpO2≤94% OR • Requiring supplemental O2/mechanical ventilation Additional criteria to consider if COVID-19 confirmed • Age >60 • Co-morbid conditions: COPD, ILD, CF, Lung Transplant/BMT	• Start chloroquine or hydroxychloroquine (call ASP pager for approval prior to use) AND • Obtain consent for Remdesivir study; or via compassionate use for severely hypoxemic (high PEEP, FiO2 requirements >40%, PaO2/FiO2<300) Avoid steroids if possible, known to cause prolonged viral shedding in related disease states

Floor level care (i.e. SpO2 >94% or not on supplemental O2)
• Comorbid conditions (lung disease, SOT, chemotherapy, immunosuppressed) AND
  ○ Febrile, unclear source, with negative RVP- Send COVID-19 PCR
  ○ Evidence of URTI/LRTI - Send COVID-19 PCR with RVP
	• Start hydroxychloroquine only if COVID-19 positive (call ASP pager for approval prior to use)
	• Monitor closely, telemetry, continuous O2 monitor

Outpatient care Fever and/or URI/LRTI symptoms PLUS • Lung disease (COPD, CF, ILD) • Lung Transplant	• Consider hydroxychloroquine if COVID PCR positive • Advise patients on return precautions/self-isolation

Therapeutic Agents

**NOTE: These agents are not FDA-approved for treatment of COVID-19; Supportive care is crucial for management of cases

	Agent	Dosing
Preferred	Remdesivir[a] (Clinical Trial or Compassionate Use Only)	200mg IV x1, followed by 100mg q24h for duration of hospitalization; 10 day total max *for pediatric patients, please consider compassionate use only, NIAID study is only for patients >18
	Chloroquine[b] (restricted)	≥50kg: 500mg PO BID x 7-10 days <50kg: 500mg PO BID x 2 days, then 500mg PO daily x 5-8 days *Please note that <50kg regimen should not be used for pediatric patients. *** Peds dosing
	Hydroxychloroquine[b] (restricted)	400mg PO BID, then 200mg BID x 4 days *no adjustment with renal failure *** Peds dosing
Not recommended	Oseltamivir[c]	Not recommended
	Ribavirin[c]	Not recommended

Notes:

a. Preferred agent for severe cases; Remdesivir is a prodrug metabolized via CYP3A4, concomitant CYP3A4 inhibitors should be avoided if possible. Possible Clinical Trials:
   a. NCT04280705 – Adaptive COVID-19 study (NIH)
   b. NCT04292899 – Severe cases (SpO2 <94% on screening) 5 vs. 10 days vs. SOC (Gilead)
   c. NCT04292730 – Moderate cases (SpO2 ≥ 94% on screening) 5 vs. 10 days vs. SOC (Gilead)

b. hydroxychloroquine is the preferred oral agent for mild, moderate, and severe cases; Chloroquine phosphate can be used as an alternative for supply concerns. Dosing from Chinese National Health Commission guideline and expert consensus on chloroquine and ongoing hydroxychloroquine clinical trial.

c. Oseltamivir and other neuraminidase inhibitors do not appear to have activity against other coronaviruses (SARS), and should be reserved for treatment of influenza.

Enteral Administration in Patients Unable to Swallow

Chloroquine

a. Non-sterile compounding available:
   i. Trissel's 6th ed. page 129-131
b. Commercial Liquid: None available

Hydroxychloroquine

a. Non-sterile compounding available:
   i. Trissel's 6th ed. page 291
   ii. McHenry AR et al.
b. Commercial Liquid: None available

Safety Considerations

***Monitoring/Lab Recommendations in Addition to Routine Clinical Monitoring*

1) Remdesivir
    a) Tolerability/Adverse Effects
        i) Remdesivir has been generally well tolerated in preclinical and clinical studies to date. Self-limiting, reversible hepatotoxicity has been observed, which resolved after therapy cessation. Nephrotoxicity has been observed in preclinical studies.
    b) Exclusion Criteria
        i) ALT/AST >5x ULN; exclusion for compassionate use >5x ULN
        ii) eGFR < 50 or requiring dialysis; exclusion for compassionate use eGFR < 30
        iii) Pregnancy/breastfeeding
        iv) Allergy
        v) Anticipated transfer to non-study site hospital within 72hrs
    c) Monitoring/Labs
        i) Per NIAID study protocol
2) Chloroquine
    a) Tolerability/Adverse Effects
        i) Chloroquine is generally well tolerated.
        ii) Cardiovascular: Prolonged QT interval, Torsades de pointes, AV block, and ventricular fibrillation/tachycardia (typically in prolonged therapy)
        iii) Dermatologic: Erythema multiforme
        iv) Endocrine: Hypoglycemia
        v) Hematologic: Hemolytic anemia
        vi) Neurologic: Extrapyramidal symptoms and seizure
    b) Monitoring/Labs
        i) CBC, ECG, BMP
3) Hydroxychloroquine
    a) Tolerability/Adverse Effects
        i) Cardiovascular: Prolonged QT interval, Torsades de pointes, AV block, and ventricular arrhythmia
        ii) Dermatologic: Erythroderma, skin pigmentation disorder
        iii) Endocrine: Hypoglycemia (Severe)
        iv) Hematologic: Agranulocytosis, Aplastic anemia, Thrombocytopenia
        v) Musculoskeletal: Myopathy/muscle weakness
        vi) Psychiatric: Anxiety, hallucination
        vii) Respiratory: Bronchospasm has been reported in post-marketing data
        viii) Ocular: retinal disorder only with prolonged use (7.5%)
    b) Monitoring/Labs
        i) CBC, ECG, BMP

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