Potential repurposed therapeutic candidates for SARS-CoV-2 infection (COVID-19)

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Overview (Hussman 32848776): Cellular and molecular pathways of COVID-19 and potential points of therapeutic intervention
See also Baylor University Medical Center: Clinical outcomes after early ambulatory multidrug therapy for high-risk COVID-19

NOTE: This list does not comprise a set of recommendations, but includes generally well-tolerated medications with potential empiric benefit in COVID-19. These candidates include medications approved by the FDA for other conditions, or represent over-the-counter supplements. While their mode of action is consistent with suspected cellular and molecular disease mechanisms, and beneficial outcomes have been indicated in research studies and clinical reports with few adverse side-effects, their use in COVID-19 has generally not been evaluated in large-scale randomized controlled trials. Typical contraindications apply. Provided strictly to share and discuss with a physician, not as medical advice.

Prophylaxis (all over-the-counter, at common recommended dosages):

- **Quercetin**: anti-inflammatory properties, potential synergy with vitamin D and melatonin, zinc ionophore
- **Zinc**: Reduced in-hospital mortality in combination with a zinc ionophore
- **Vitamin D**: attenuated TLR-mediated cytokine induction, reduced cytopathic effect
- **DHA/EPA**: inhibition of NF-kB-mediated adhesion of inflammatory cells to vascular endothelia
- **Melatonin**: inhibition of NF-kB mediated MMP9 expression, reduced hypoxic stress, inhibition of TNF, IL6, VEGF
- **Artemisinin**: in-vitro inhibition of SARS-CoV-2 infection and RBD binding

Confirmed infection (not for self-medication: ask about and discuss with physician):

- **Doxycycline**: Typical dosage - 100mg bid, 5-7 days. Contraindicated if known/intended pregnancy during treatment. Broad spectrum, pleiotropic effects against pneumonia; antiviral, cardioprotective, anti-inflammatory properties, IL6, MMP9, and NF-kB inhibition, as well as SARS-CoV-2 main protease (Mpro) required for replication. SOCS (suppressor of cytokine signaling) induction. May interfere with TLR hyperactivation and cytokine induction mediated by dsRNA intermediates, and recruitment and extravasation of inflammatory leukocytes. Photosensitivity.
- **Ivermectin**: 200ug/kg, single dose (~12mg for 132lb, 18mg for 198lb patient). Warning: avoid products intended for animal use. Pleiotropic anti-inflammatory effects with in-vitro inhibition of SARS-CoV-2 nuclear import and binding of nonstructural proteins including RdRp. Lower mortality observed in patients requiring ventilation. However, no high-quality RCTs despite multiple reports of benefit with acceptable tolerability.
- **FDA EUAs issued for Bamlanivimab and Casirivimab/Imdevimab mAbs for patients at risk of severe progression.**

Clinical worsening (not for self-medication: ask about and discuss with physician):

- **Ruxolitinib**: (JAK1/2 inhibitor) 20mg bid first 2 days, de-escalated to 10mg bid and 5mg bid over following 12 days. Rapid clinical response in RESPIRE study with no serious side effects. Improved tomographic findings, discharge, pulmonary function, well-tolerated in compassionate use trials.
- **FDA EUAs for Baricitinib, Remdesivir and convalescent plasma.**

Acute respiratory distress (not for self-medication: ask about and discuss with physician):

- **Dexamethasone**: (corticosteroid). Reduced mortality in patients requiring invasive ventilation in large RCT study.
- **Tocilizumab**: (IL6 receptor inhibitor). Combination with dexamethasone reported to increase survival in some groups.
- **Dornase alfa**: administration reported to improve respiration via degradation of neutrophil extracellular traps (NETs)

Additional references (PMID)

(Benefit) Clinical benefit; (M) Mode of action; (C) Contraindication or ineffective context

**General discussion**: 32848776 Ambulatory care 33388006 Melatonin (Benefit) 33083812 Zinc (Benefit) 33140042 Artemisinin (M) 32786284, 32696720 Doxycycline: (Benefit) 32873175, 32802622, 32742970, MRx, 33388006 (M) 32314492, 32752944, 33142770, 32653520, 32758890, 32696730 (C) transient autoimmune response to Minocycline 30345250, Ivermectin: (Benefit) 33065103 MRx MRx2 MRx3 MRx4 MRx5 AB (M) 33032231, 32251768, 32752944, 32736876, 32895293, 33131430, 33341233 (C) no benefit observed in severe patients receiving immunosuppressant drugs 33175880, Ruxolitinib (Benefit) 32850921, 32470486, 32814839, 33173161 (M) 32636055, 32702726, Dornase alfa (Benefit) 32922804, 32993479 (M) 32355564