Evidence Update on COVID-19
Treatments Version 1

This is a summary of the latest evidence available on the treatments being testing *in vitro* and *in vivo* for COVID-19. It is not comprehensive and will be updated as more treatments and data is published.

Ivermectin

Anti-parasitic drug that has some anti-viral properties.
Inhibits HIV-1 integrase protein and importin heterodimer to inhibit viral replication
Good safety profile

- In vitro
  - Caly - Vero cells + SARS-CoV2 2hours, then ivermectin.
    - After 24 hours reduced viral RNA in supernatant
    - After 48 hours all viral material lost

Convalescent plasma

Plasma from recovered patients contains antibodies and may reduce viral load/reduce hospital time

- Shen - 5 patients on IMV received plasma on day 10 or 22
  - Plasma contained IgG and IgM anti-SARS-CoV2 antibodies
  - Viral loads became negative after 12 days, SOFA scores decreased (2-10 down to 1-4), patients improved
  - No control group - only 5 patients - also on antivirals - not clear if beneficial
- Duan - 10 patients safety study - no adverse effects

Anti-virals - None proven to work in humans

Lopinavir-Ritonavir - Part of RECOVERY trial

- Cao - 199 patients (99 L+R, 100 standard care) non-blinded trial
  - No difference in viral load, clinical improvement or mortality
- Li - 44 patients (21 L+R, 16 arbidol, 7 standard care) - underpowered trial
  - No difference in viral load, clinical improvement or mortality
- Ye - 47 patients (42 L+R or 5 control)
  - Suggest positive effect but no statistics and underpowered

Monoclonal antibodies

IL-6 levels are associated with worse outcomes, 2.9 higher levels in severe disease (n-1302) Coomes
Tocilzumab - anti-IL-6 receptor antibody

- Xiaoling - 21 severe patients showed sig change lymphocyte count, CRP levels and reduced oxygen intake - suggest positive outcome (no control group, also on various antivirals, bias)

Siltuximab - anti-IL-6 receptor antibody

- Gritti - 21 patients showed reduced CRP levels, 33% showed clinical improvement, 43% stabilised, 24% worsened after 8 days - no evidence of benefit and no controls

Hydroxychloroquine and chloroquine (rapid review) - Part of RECOVERY trial

- In vitro
  - Studies show HCQ is more potent against SARS-CoV2, but both drugs inhibit viral replication (Yao, Liu, Wang)
  - Wang - Chloroquine + remdesivir inhibited viral infection when used as pre-treatment (not clinically relevant for treating those already infected)
- In vivo
  - Gautret - 36 patients, 20 HCQ, 16 standard care
    - HCQ had increased viral clearance on day 6 (70% vs. 12.5%)

        - HCQ + azithromycin all had viral clearance on day 6
        - Underpowered, no follow up, no randomisation - bias
- Safety
    - Lane - <200,000 users of HCQ + sulfasalazine, azithromycin or amoxicillin
        - No risk of serious adverse events after 30 days for HCQ + sulf
        - HCQ + azithromycin increased cardiovascuilar mortality, angina and heart failure - combination may not be beneficial in SARS-CoV2

Multiple RCT ongoing for HCQ and CQ

Corticosteroids - Low dose dexamethasone in RECOVERY trial

- No clinical data exists to indicate a benefit from steroids in RSV, influenza, SARS or MERS - potential for harm is increased - greater viraemia, increased risk of diabetes and avascular necrosis and psychosis (Russell)
- Low dose dexamethasone may reduce duration of mechanical ventilation and mortality in ARDS (Villar)

ACE inhibitors

SARS-CoV2 binds to the ACE2 receptor for cell entry

- 205 patients in UK - lower rate of death or ICU admittance within 7 days if patient on ACE inhibitor (OR 0.29) - No evidence ACE inhibitors increase severity of COVID Bean