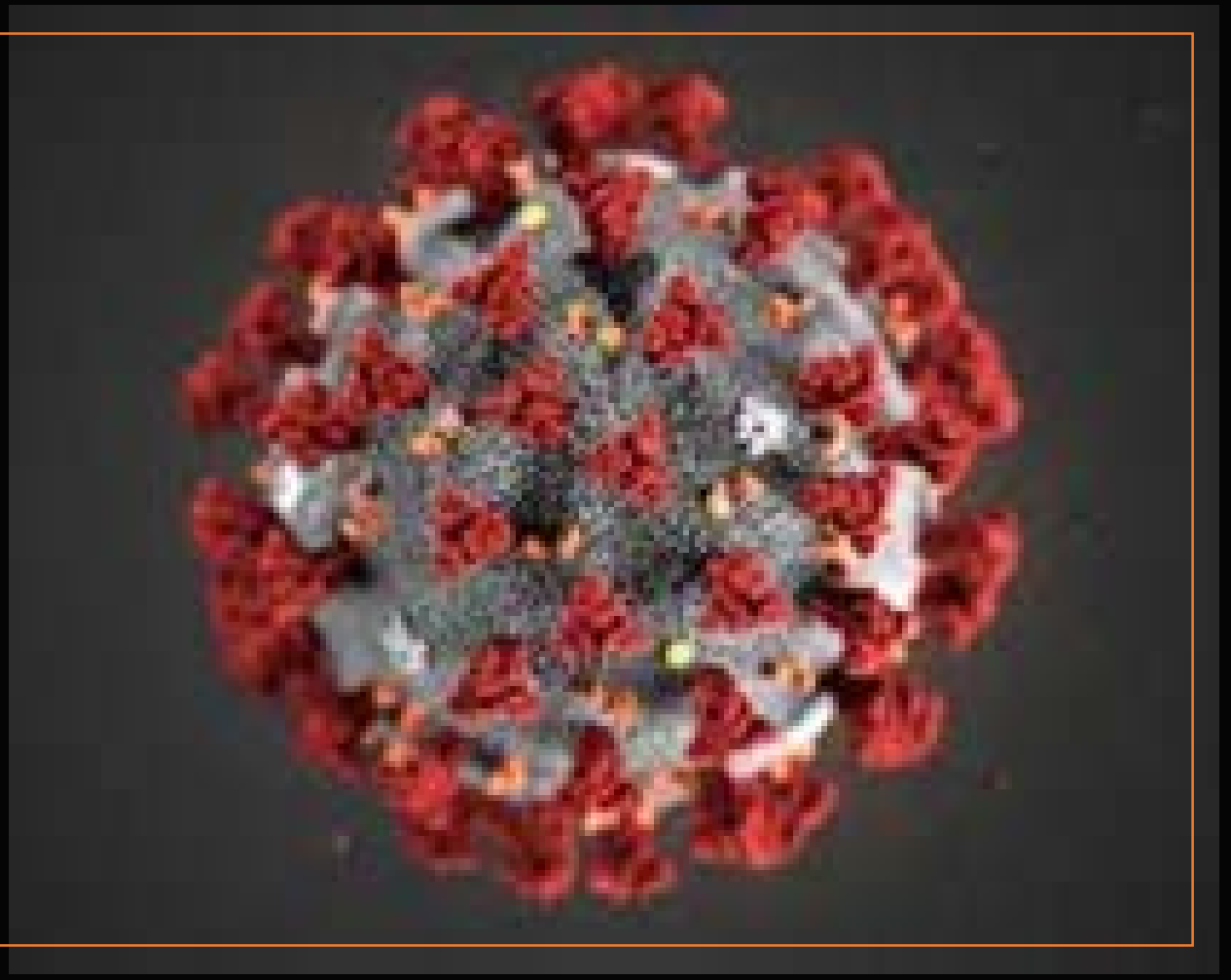
Covid-19

Medications in the News Volume 4

Week of May 4th – 11th 2020



Disclosures

- **No llamas were harmed during the development of this slide presentation**

Major medication trials (1,169) per clinicaltrials.gov

Remdesivir

- Trial results have been released. This was approved for emergency use in COVID-19 May 1st by FDA. 607,000 dose donated to treat vented patients.
  - HHS is coordinating the distribution of this through Amerisource Bergan Specialty only
  - State Dept of Health will decide which hospitals receive supply
- Remdesivir in Adults with Severe COVID-19 : A Randomised, doubleblind, placebo-controlled, multicentre trial. **The Lancet**. https://doi.org/10.1016/S0140- 6736(20)31022-9
  - Rnd DBPC trial n=237 participants (158 randomized to remdesivir, 79 to placebo)
  - Time to clinical improvement did not differ by study arm, 21 vs 23 days (HR 1.23, 95% CI 0.87 – 1.75).
  - Overall frequency of adverse events was similar in both groups;
  - Treatment cessation due to adverse events was higher in the remdesivir (12%) than placebo (5%) group.

Olumiant- Immune suppressant for RA (Eli Lilly)

- NIAID is conducting a placebo controlled trial currently
- Study data expected to be available in the next 2 months

Hydroxychloroquine link to intubation or death NEJM n=1,376

- 58.9% in hydroxy arm, 180 intubated
- Conclusion: No significant association between hydroxychloroquine use and intubation or death.
- Over 100 other hydroxychloroquine trials still under way

No timeline set for results

- Convalescent plasma, colchicine, Calquence (lymphoma),

Tocolizumab—(aka Actemra)IL-6 inhibitor

- Case report n=25 patients severe COVID-19
- 14 days of follow-up, tocilizumab was associated with dramatic decline in inflammatory markers, radiological improvement, and reduced ventilator support requirements.
- majority (92%) of patients experienced at least one adverse event.
- Adequately powered trials are needed to confirm efficacy.
    - Phase 3 trials underway results by early summer

Alattar et al. (May 5, 2020). Tocilizumab for the Treatment of Severe COVID-19. Journal of medical virology. https://doi.org/10.1002/jmv.25964

Favipiravir—aka Avigan

- Currently not FDA approved or available in US
- Open-label, prospective, randomized, n=236 adults w COVID pneumonia in China
  - 1600 mg twice daily on day 1, then 600 mg twice daily thereafter for 7–10 days)
  - Better clinical recovery rate at 7 days (61 vs 52%) vs control group (umifenovir)
  - Stratified by disease severity, 2x had severe disease in FVR arm. Clinical recovery:
    - 71% vs 56%
    - Severe pneumonia recovery 6% vs 0%
- Nonrandomized study in patients with non-severe COVID19 in China 14 day
  - (n=35) ; viral clearance (4 vs 11 days)
  - Improvement rate on chest CT imaging on day 14 (91 vs 62%) compared with the control group receiving lopinavir/ritonavir
    - both groups also received aerosolized interferon α-1b.

Medication Updates

Corticosteroids

- Still not recommended for routine use
- The Surviving Sepsis Campaign COVID-19
  - Gives an unenthusiastic suggestion to use low dose, low duration in ARDS
  - This follows the NIH practice guideline

Vitamin D—Northwestern University

- Study reviewed large populations and prominent Vitamin D level trends
- No individual data collected
- Noticed a correlation between countries with low Vitamin D and poor COVID outcomes
  - Low vitamin D correlates to hyper active immune systems
  - Theory: pediatrics have lower COVID 19 mortality—immune system us not fully developed
- No recommendations at this time to take mega doses of Vitamin D

ACE/ARB

- ACE was associated with a statistical significant improvement in outcomes
- ARB had an associated trend, but not statistical in nature
- No benefit in alternating therapies of these meds.

Anticoaglants—More likely to clot than bleed

- Coagulation abnormalities observed in COVID 19 :
  - prothrombotic disseminated intravascular coagulation (DIC), a high incidence of venous thromboembolism, elevated D-dimer levels, high fibrinogen levels, and microvascular and macrovascular thrombosis.
- markedly elevated levels of D-dimer (>6 x ULN) have decreased mortality when given prophylactic doses of LMWH or UFH
- A randomized open-label clinical trial is currently being conducted to evaluate prophylactic- and therapeutic-dose
- Additional study is needed to understand the anticoagulant needs of COVID -19 patients.
- Several organizations have published interim guidance for the management of COVID-19-associated coagulopathy
  - The International Society for Thrombosis and Haemostasis (ISTH)
  - American Society of Hematology (ASH) recommend that all hospitalized COVID19 patients, including non-ICU patients, receive prophylactic-dose LMWH unless contraindicated (e.g., active bleeding, platelet count <50K)
    - Studying a therapeutic treatment arm currently

Epoprostenol

- Selective pulmonary vasodilator, administered by inhalation
  - similar efficacy, lower potential for systemic adverse effects, lower cost, and ease of delivery compared to nitric oxide.
- Lacks clinical trial data showing benefit in ARDS
- Goal is to increase Pa02 + reduce pulmonary artery pressure
  - Dosages up to 50 ng/kg per minute have been used (titrated to response).
  - Most effective and safe dosage appears to be 20-30 ng/kg per minute in adults
  - 30 ng/kg per minute in pediatric patients
- Surviving Sepsis Campaign neither endorses or condemns its use pending more trial data
  - They do endorse short trial of niric oxide in ARDS. If Pa02 does not respond quickly taper off.

DARE-19 Trial

- Medscape Medical News April 30th 2020
- Safety of dapagliflozin (Farxiga) in COVID-19 disease
  - Prior reports had suggested halting therapy from all SGLT2 inhibitors metabolic acidosis was deemed prevalent
  - Has FDA approval for improved CV outcomes
- Phase 3 trial, Double blinded, placebo controlled focusing on use in respiratory failing patients
  - N=900, (+) COVID test and O2 sats >94%
  - Excludes kidney disease and current SGLT2 therapy
  - Does it decrease disease progression, clinical complications and death in COVID-19

• Llama antibodies save the world?

Say What???

- May 28, 2020 version of Cell
  - details the findings of researchers inoculating llamas with COVID-19 proteins
  - isolating antibodies that deactivate the cell binding capabilities of SARS-CoV-2
- This research may lead to future therapeutic break thrus