COVID-19 Medication Study Update

Version 5

Review of literature from May 13-27th

Vitamin D & Demographic COVID correlation

David O Meltzer, Thomas J Best, Hui Zhang, Tamara Vokes, Vineet Arora, Julian Solway

- Retrospective cohort multivariate analysis @ University of Chicago
  - N=4,314, 499 tested in past year
  - likely ***deficient*** for 127(25%) patients,
  - likely ***sufficient*** for 291(58%) patients,
  - uncertain for 81(16%) patients.
- Vitamin D deficiency thresholds:
  - most recent 25-hydroxycholecalciferol <20ng/ml before COVID-19 testing
  - 1,25-dihydroxycholecalciferol <18pg/ml within 1 year before COVID-19 testing
- Positive for COVID-19 testing was associated with:
  - Age<50 RR=1.05,p<0.021 Age≥50 RR=1.02,p<0.064,
  - non-white race RR=***2.54***,p<0.01
  - Vitamin D deficient (deficient RR=***1.77***,p<0.02) vs vitamin D sufficient(not-deficient/treatment-not-decreased),
- Predicted COVID-19 rates in the vitamin D deficient group of 21.6% (95%C) versus 12.2%(95%CI) in the vitamin D sufficient group.
  - Vitamin D deficiency declined with increasing vitamin D dose, especially of vitamin D3.
  - Vitamin D dose was not significantly associated with testing positive for COVID-19.

Remdesivir. . .finding chinks in the armor

- NEJM May 23rd N=1,063 DBPC
- 10 day course shortened hospitalization by 4 days (11 vs 15)
- Mortality 7% vs 12% (not SS)
- No benefit to survival in ventilated or ECMO patients observed

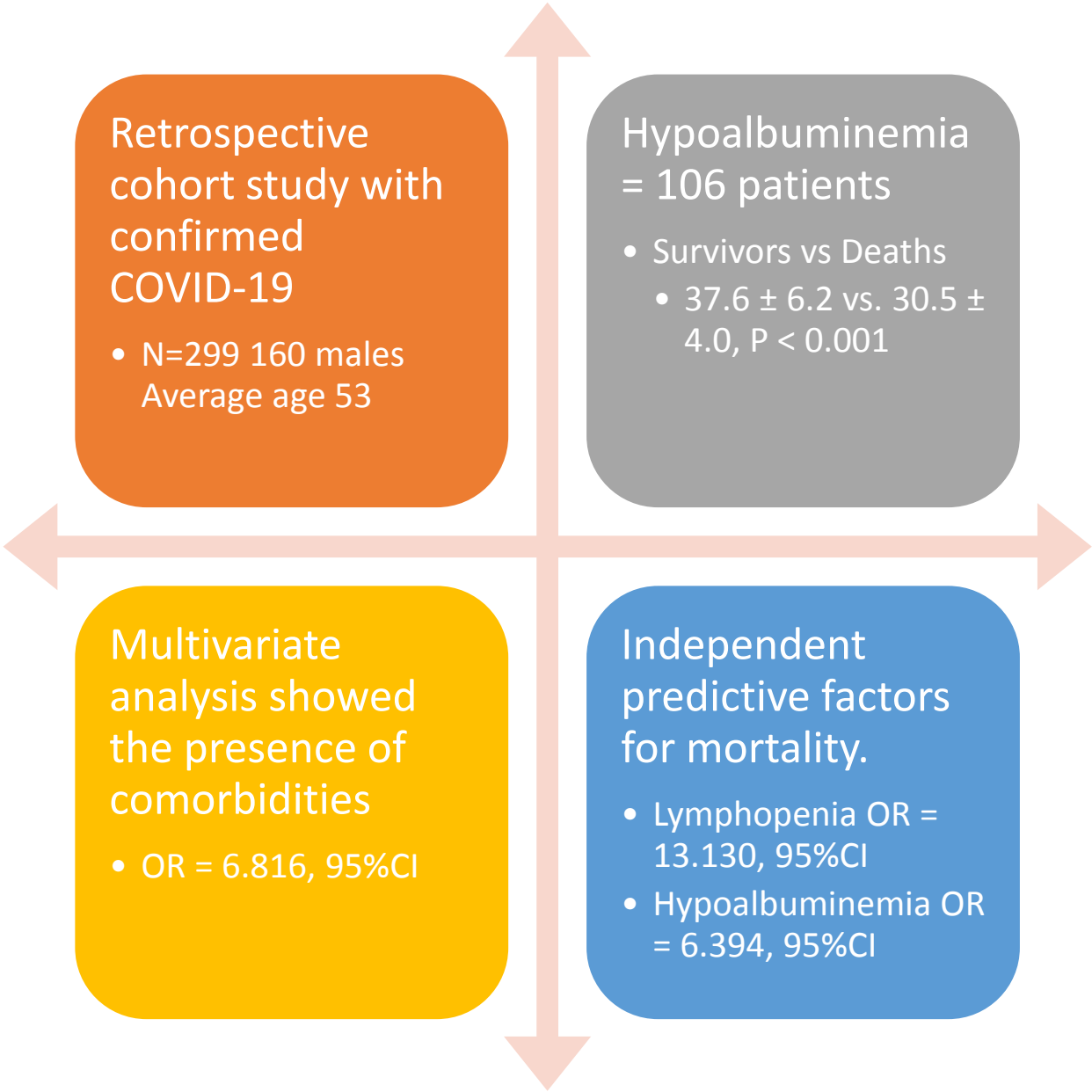
Remdesivir Trial Methods

- Severity of illness scale:
  - 1 (not hospitalized) to 8 (dead).
- Study demographics
  - Lowest enrolled= 4, denoting hospitalization, but no need for extra oxygen.
    - 38% benefit to recovery
  - Most enrollees = 5, meaning they did need oxygen.
    - 47% benefit
  - Score = 6 Receiving high flow oxygen
    - 20% benefit
  - Score =7 ventilated or ECMO
    - 0.05% benefit
- Trial was stopped too early, study goals were adjusted midway

Convalescent Plasma—Safety Study

- The incidence serious adverse events (SAEs) in the ***first four hours*** after transfusion was <1%. Mortality in that time period 0.3%
- N= 5,000 66% of patients were in ICU setting
- 36 reported SAEs overall—I interpreted these to manifest > 4 hrs post infusion
  - 25 reported incidences of related SAEs,
    - Mortality (n=4),
    - Transfusion-associated circulatory overload (TACO; n=7),
    - Transfusion-related acute lung injury (TRALI; n=11),
    - Severe allergic transfusion reactions (n=3).
    - Only 2 of 36 SAEs were judged as definitely related to the transfusion by the treating physician.
  - The seven-day mortality rate was 14.9%.
- Conclusion: Given the deadly nature of COVID-19 and the large population of critically-ill patients included in these analyses, the mortality rate does not appear excessive. These early indicators suggest that transfusion of convalescent plasma is safe in hospitalized patients with COVID-19.
- Michael Joyner, R. Scott Wrigh et al

Albumin as a predictor of COVID 19 outcomes



Nerds of the world. . .Ready Warp engines. . .

Vaccine Development—Operation Warp Speed

- Moderna Pharmaceuticals- Phase 1 clinical trial reported
  - N=45, Participants received doses of 25mcg, 100mcg, 250mcg
- All showed seroconversion by day 15
- At day #43, after 2 doses
  - 25mcg-anti body titers were proportionate to patients w/ (+) COVID 19 test
  - 100mcg- antibody exceeded convalescent plasma
  - ADR- highest in the 250mcg group, typically injection site reaction
- Neutralizing antibodies data released on only 8 participants.
  - 4 from the 25mcg/ 4 from 100mcg ?? Why not everyone?
  - Is this intentional? Is data being withheld? Stock price manipulation?
- Phase 2 trial with n= 1,000+ is the next stage for this product (July?)
  - Will focus on 25mcg and 10mcg doses
- President Trump tweeting that we will have a vaccine by December 2020. . .optimistic or realistic?
  - US Gov't paid AstraZeneca $1B to ecure COVID-19 vaccine doses when available