COVID Update March 2021

Vaccination and Asymptomatic Spread

Impact of the COVID-19 Vaccine on Asymptomatic Infection Among Patients Undergoing Pre-Procedural COVID-19 Molecular Screening Clin Infect Dis. 2021 Mar 10;ciab229

- https://pubmed.ncbi.nlm.nih.gov/33704435/
- The impact of vaccines on asymptomatic SARS-CoV-2 infection is largely unknown.
- Retrospective cohort study of **39,156** within a large US health care system
- The primary outcome was the relative risk of a positive SARS-CoV-2 molecular test among those asymptomatic persons who had received at least one dose of vaccine, as compared to persons who had not received vaccine
- **Vaccination with mRNA 10 days post 1st dose have a significant reduction in asymptomatic spread of the virus**
- 39,156 within a large US health care system
- 80% reduction of asymp disease

Vaccines in the Real World:

Vaccine Effectiveness of Pfizer and moderna COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Health Care Personnel, First Responders, and Other Essential and Frontline Workers — Eight U.S. Locations, December 2020–March 2021

- https://www.cdc.gov/mmwr/volumes/70/wr/mm7013e3.htm?s_cid=mm7013e3_w
- Prospective cohort **3,950** health care workers
- Mid Dec 2020 to id March 2021
- MRNA vaccines given
- Weekly COVID tests for 13 weeks
- **80% effective 2 weeks after 1st dose**
- **90% effective 2 weeks after 2nd dose**

Vaccines in Long COVID

- **Are vaccines safe in patients with Long COVID? A prospective observational study**
- https://www.medrxiv.org/content/10.1101/2021.03.11.21253225v2
- We know that the vaccines prevent symptomatic covid but we don't really know how the vaccine affects symptoms in patients with Long Covid. *Does it make their symptoms better or worse?*
- Small study, most with severe long COVID, with 8 months of persistent symptoms (fatigue, sob and insomnia)
- Small sample size (66) **44 vaccinated (pfizer OR oxford) vs 22 non-vaccinated**
- **It was safe, more felt better with vaccine**
- 23.2% vaccinated vs 15.4%

AstraZeneca Phase 3 Read out

AZD1222 US Phase III trial met primary efficacy endpoint in preventing COVID-19 at interim analysis

- Link
- Oxford chimpanzee modified adenovirus vector
- Screwed up the PR on this puppy
- This interim safety and efficacy analysis was based on 32,449 participants accruing 141 symptomatic cases of COVID-19. The trial had a 2:1 randomisation of vaccine to placebo.
- 79% overall effective - corrected 76%
- **No deaths, no ICU admissions**
- Same results in elderly and across races
- 2 dose at 4 weeks but evidence suggest improved efficacy with longer time between doses
- Stored at normal refrigeration temperatures
- No increase in CVT or stroke compared to background rate (1 per million)
- Newly released data basically the same

BLAZE 1- Phase 3 study results published in press release

Lilly's bamlanivimab and etesevimab together reduced hospitalizations and death in Phase 3 trial for early COVID-19

- https://investor.lilly.com/news-releases/news-release-details/lillys-bamlanivimab-and-etesevimab-together-reduced

    - bamlanivimab (LY-CoV555) 700 mg and etesevimab (LY-CoV016) 1400 mg together significantly reduced COVID-19 related hospitalizations and deaths
    - This new Phase 3 cohort of BLAZE-1 included 769 high-risk patients, aged 12 and older with mild to moderate COVID-19 (therapy: n=511; placebo: n=258).
    - 4 deaths total - all in the placebo arm
    - **85% reduction in hospitalization and death**

REGENERON Cocktail

- REGEN-COV™ (CASIRIVIMAB WITH IMDEVIMAB) ANTIBODY COCKTAIL REDUCED HOSPITALIZATION OR DEATH BY 70% IN NON-HOSPITALIZED COVID-19 PATIENTS
- ttps://newsroom.regeneron.com/news-releases/news-release-details/phase-3-trial-shows-regen-covtm-casirivimab-imdevimab-antibody
- This is the largest trial to date including N = 4567 non-hospitalized patients
- **70% reduction in death and hospitalization**
- Worked on the variants as well
- Safe and appears to dramatically reduce the risk of hospitalization and death in the outpatient setting

Phase 3 COMET-ICE (COVID-19 Monoclonal antibody Efficacy Trial - Intent to Care Early)

Vir Biotechnology and GSK Announce VIR-7831 Reduces Hospitalization and Risk of Death in Early Treatment of Adults with COVID-19

- Data according to a press release: https://www.biospace.com/article/releases/vir-biotechnology-and-gsk-announce-vir-7831-reduces-hospitalization-and-risk-of-death-in-early-treatment-of-adults-with-covid-19/
- Interim analysis of data from 583 patients enrolled in the COMET-ICE trial, demonstrated an **85% (p=0.002) reduction in hospitalization or death** in patients receiving VIR-7831 as monotherapy compared to placebo, the primary endpoint of the trial. VIR-7831 was well tolerated.
- This targets a “persevered part” of the spike protein - ie: without that part of the spike it cannot enter cell and in theory could be resistant to all variants

MIS-C and severe disease in children

Covid-Linked Syndrome in Children Is Growing, and Cases Are More Severe

- https://www.nytimes.com/2021/02/16/health/covid-children-inflammatory-syndrome.html
- There are **increasing reports** of severe disease and MIS-C in children
- There is concern that newer variants are more severe in children than the wild type though is currently conjecture
  - Daniel Griffin, MD Clinical Update 53 https://www.microbe.tv/twiv/

CDC and Schools

COVID-19 in Primary and Secondary School Settings During the First Semester of School Reopening — Florida, August–December 2020

- Limited U.S. data have been reported regarding COVID-19 in students and school staff members as schools open up
- 3 million registered students
- ½ get full time in-person instruction
- Case investigation and contract tracing
- **< 1% got school related COVID-19**
- **High community spread = more school spread**
- COVID-19 school-related disease incidence among Florida students was correlated with community incidence
- Masks mandate reduced infection
- So masks, 3 feet, ventilation, testing, school can open if community spread is not crazy
- https://www.cdc.gov/mmwr/volumes/70/wr/mm7012e2.htm?s_cid=mm7012e2_x

Intermediate dose heparin vs Standard dose for ICU admitted patients the INSPIRATION randomized trial

Effect of Intermediate-Dose vs Standard-Dose Prophylactic Anticoagulation on Thrombotic Events, Extracorporeal Membrane Oxygenation Treatment, or Mortality Among Patients With COVID-19 Admitted to the Intensive Care Unit

The INSPIRATION Randomized Clinical Trial

- https://jamanetwork.com/journals/jama/fullarticle/2777829
- Intermediate-dose (enoxaparin, 1 mg/kg daily) (n = 276) vs standard prophylactic anticoagulation (enoxaparin, 40 mg daily) (n = 286), with modification according to body weight and creatinine clearance. The assigned treatments were planned to be continued until completion of 30-day follow-up
- Intermediate-dose prophylactic anticoagulation, compared with standard-dose prophylactic anticoagulation, did not result in a significant difference in the primary outcome of a composite of adjudicated venous or arterial thrombosis, treatment with extracorporeal membrane oxygenation, or mortality within 30 days.

Aspirin

- Aspirin Use Is Associated With Decreased Mechanical Ventilation, Intensive Care Unit Admission, and In-Hospital Mortality in Hospitalized Patients With Coronavirus
- https://journals.lww.com/anesthesia-analgesia/fulltext/2021/04000/aspirin_use_is_associated_with_decreased.2.aspx
- We know that Coronavirus is associated with hypercoagulability and increased thrombotic risk in critically ill patients - this paper studied whether or not aspirin was use was associated with decreased mech vent, icu admit and mortality
- Retrospective observational study of adults hospitalized with covid between march-july 2020
- 412 patients enrolled, **314 did not get aspirin vs 98 that received aspirin**
- Aspirin within 24 hours of admission or had taken aspirin 7 days before admission
- **Aspirin use was independently associated with decreased risk of mechanical ventilation, ICU admission, and in-hospital mortality**
- There were no differences in major bleeding
- Small, retrospective, needs larger randomized control trial

Post-acute-COVID

- Great review
- https://www.nature.com/articles/s41591-021-01283-z

Risk score for intubation and mortality

- https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00045-6/fulltext#tbl0003

Variable	Odds Ratio (95% CI)	P-Value
Mechanical Ventilation		
Diabetes mellitus	2.114 (1.340–3.337)	0.001
SpO_2:FiO_2 Ratio (for every 100 increase)	0.423 (0.336–0.532)	<0.001
C-Reactive Protein‡ (mg/L)	1.328 (1.120–1.574)	0.001
Lactate Dehydrogenase‡ (U/L)	2.083 (1.341–3.234)	0.001
Mortality		
Age (for every 10 years)	2.953 (2.227–3.916)	<0.001
Male Sex	3.026 (1.534–5.969)	0.001
Coronary Artery Disease	2.792 (1.351–5.770)	0.006
Diabetes mellitus	2.159 (1.175–3.967)	0.013
Statin (chronic use)	0.467 (0.237–0.920)	0.028
SpO_2:FiO_2 Ratio (for every 100 increase)	0.475 (0.362–0.622)	<0.001
Body Mass Index	1.067 (1.017–1.120)	0.008
Neut:Lymph Ratio (for 10x increase)	1.323 (1.001–1.441)	0.045
Platelets (for every 50×10^9/L increase)	0.775 (0.635–0.947)	0.013
Procalcitonin‡ (ng/mL)	1.238 (1.064–1.441)	0.006

The constant value in the ventilation regression analysis was $\beta_0 = -5.62$.
The constant value in the mortality regression analysis was $\beta_0 = -8.26$.
‡ Log base 2 transformed value.