



# COVID-19 Treatment Update

Version #7



## Tocilizumab (IL-6) reduced mortality

- › <https://www.sciencedirect.com/science/article/pii/S2665991320301739?via%3Dihub>
- › All patients (n=544) received: supplemental oxygen, hydroxychloroquine, azithromycin, antivirals, LMWH
  - 179 received tocilizumab IV(88) or subQ (91)
  - 73 deaths in standard therapy arm
  - 13 deaths in tocilizumab (p<0.0001)
  - Lower risk of mechanical ventilation and death in the IL-6 arm
    - › Adjust Hazard ratio 61% p=0.02



## Remdesivir Price Set

- › Gilead press release:

- 5 Day therapies
- 200mg load then 100mg daily X4
  - › \$2,340 per 5 day course for US Government
  - › \$3,120 per 5 day course for private insurance

- › Remdesivir had positive study data on decreasing length of stay

- Did not show statistical significance on overall survival.





## Dexamethasone-MedRxiv

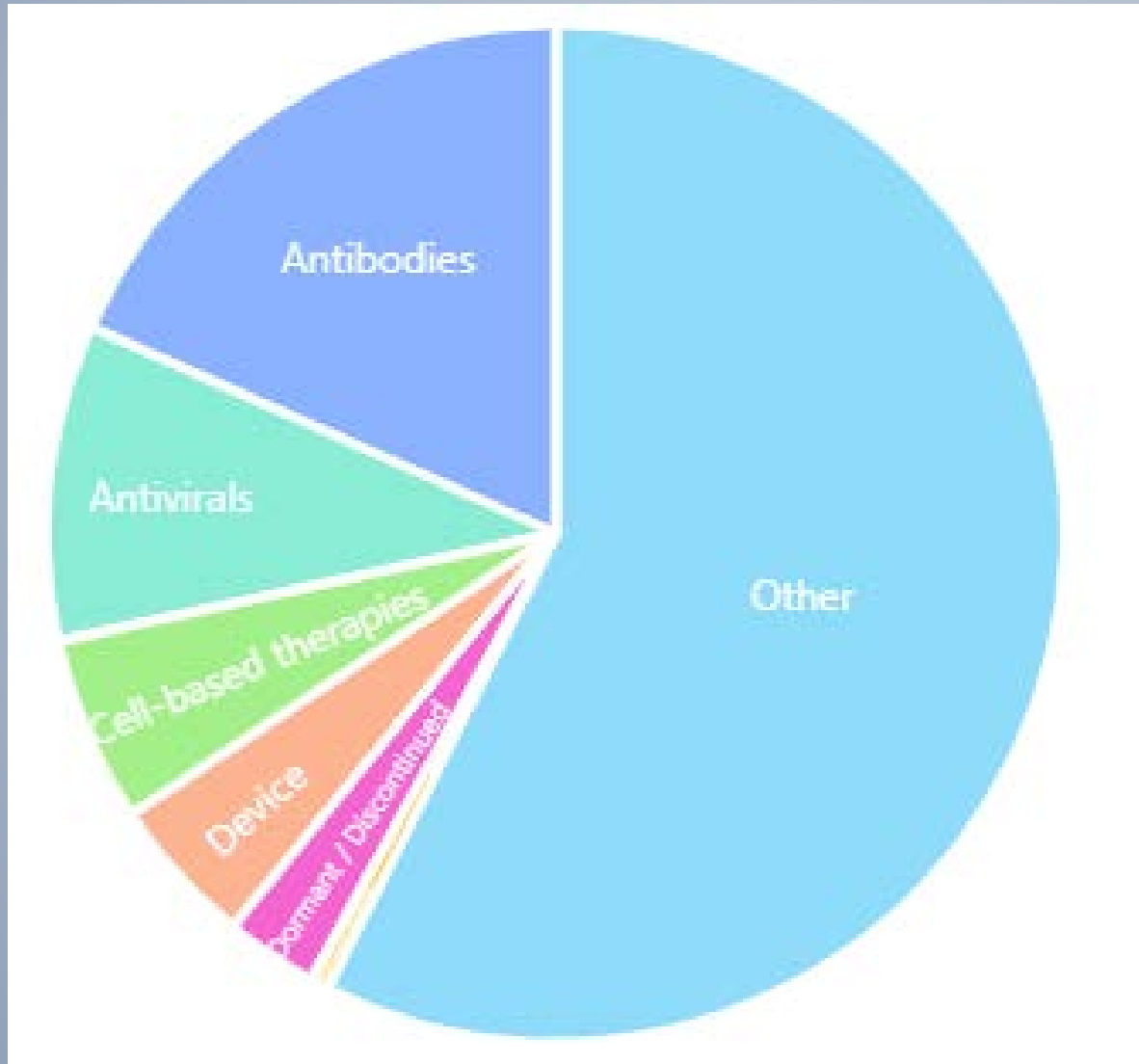
- › March advice- Steroids make COVID worse, do not use them in early stage
- › June- Dexamethasone improves survival in critical cases, may not help mild disease
- › RECOVERY Trial-looked at many therapies used in treating hospitalized COVID-19 patients, 28 day mortality
  - 2,104 patients received dexamethasone compared to 4321 who received standard therapies
- › Dexamethasone
  - Decreased ventilator deaths by 33%  $p < 0.001$
  - Decreased O2 w/o vent by 20%  $p = 0.002$
  - No benefit in milder disease

# COVID-19 Tracking tool

- › Milken Institute has a tracking tool of many vaccines and treatments
  - app-<https://covid-19tracker.milkeninstitute.org/>
  - Broken down into treatments—currently tracking 257
    - › Antivirals--Remdesivir
    - › Antibodies- Convalescent Plasma
    - › Cell based therapies-, stem cells
    - › Devices
    - › RNA Based therapies
    - › Repurposed medications-hydroxychloroquine, dexamethasone
  - Vaccines
    - › Vaccine tracking website--<https://www.covid-19vaccinetracker.org/>
    - › 172 in development, 13 in clinical trials



# Milken Institute







## Methylprednisolone GLUCOCOVID --medrxiv

- › Would a 6 day course of IV methylprednisolone improve outcomes in ARDS?
- › N=85, looking for death, ICU admit, ventilator placement
  - CRP decrease in MP group  $p=0.0003$
  - Hyperglycemia more frequent in MP group
  - reduced risk in age-stratified analysis RR- 0.55  $p=0.024$
  - In the per-protocol analysis,  $p=0.0037$ 
    - › RR = 0.11 in patients aged 72 yr or less,
    - › RR= 0.61 age >72 yr
    - › RR= 0.37 for the entire group

# How are therapies usually developed?

- › Pre Clinical Phase
  - Collect data, non human testing
  - Toxicology and pharmacology data gathered
- › Phase I clinical testing
  - Small study of healthy people
  - Evaluate safety and immune response at varies doses
  - Short time periods 1-2 years, COVID 3 months
- › Phase II Clinical trial
  - Study 100's of people
  - More in depth review of safety, efficacy, targets optimal dosing
  - Moderate time 2-3 years, COVID 6-8 months
- › Phase III Clinical trial
  - Study 1000's of people
  - Fine tune safety and efficacy
- › Regulatory approval
  - FDA reviews trial data and licenses
  - Manufacturer can produce product while this occurs, just cannot sell it or market it
  - Normally takes 2 years, COVID- few months







# Metformin for COVID?

- › Observational Study
  - n=6,200 adults with diabetes or obesity and commercial insurance who were hospitalized with COVID-19,
- › Sorry guys this won't help you 😞
  - fewer deaths among women taking metformin vs naïve
  - adjusting for other risk factors, 21% to 24% less likely to die from COVID
  - The benefit was not seen in men
- › Study coauthor Carolyn Bramante of the University of Minnesota
  - “We know that metformin has different effects between men and women. In the diabetes prevention trial, metformin reduced C-reactive protein twice as much in women as men,”
  - “Metformin also decreases levels of TNF-alpha, an inflammation protein that appears to make COVID-19 worse.
    - › Studies have suggested metformin may bring down TNF-alpha levels to a greater extent in women than in men.
- › "The fact that we saw the benefit in women only, and the fact that metformin lowers TNF-alpha in female mice, might suggest that the TNF-alpha effects of metformin are why it helps in COVID-19
- › Unfortunately this news was given the label “MORE STUDIES ARE NEEDED”