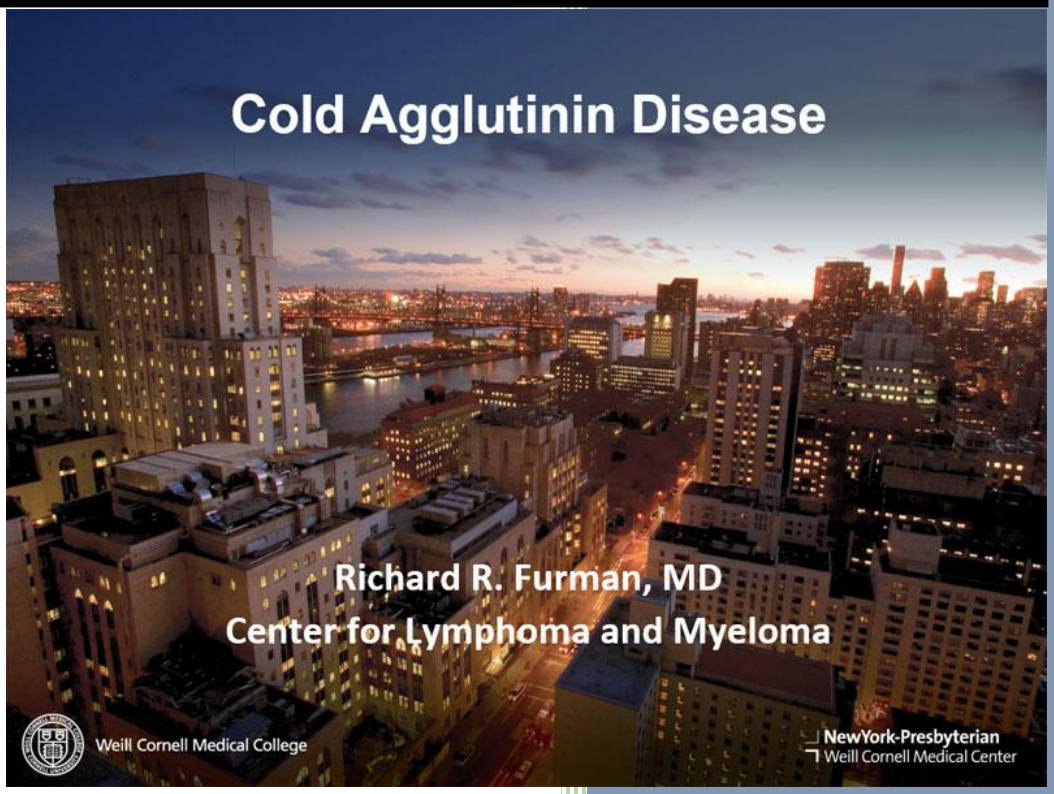
1/19/221

Covid-19 Vaccine Information



Dr Richard Furman

COVID-19 Vaccine Information.

1. While these vaccines have been developed and approved quicker than any vaccine in history, and have used novel technologies, we do not have any reason at this time to question their safety. The RNA vaccine technology (more later) has been used for years in animal vaccines, just not human vaccines, and are extremely well studied. They really represent a major step forward in generating vaccines rapidly. They really are only limited by the need for cold temperatures for storage.
2. While the timelines for these vaccines have been very short, these vaccines are studied in large number of patients. (Pfizer: 40,000 in total in the pivotal trial: 20,000 vaccine vs 20,000 placebo; Moderna: 30,000 in total in the pivotal trial: 15,000 vaccine vs 15,000 placebo.) Most of our oncology drugs are approved using studies of 150-300 patients.
3. The RNA vaccines use RNA encapsulated in a lipid vesicle to deliver it to cells where it is taken up and transcribed (processed) like normal RNA into a protein that is placed on the surface of the cell for the immune system to see and recognized as foreign. This really replicates what the virus itself does. There is no means for the RNA to be changed into DNA, make it into the nucleus, or enter the cell's normal DNA. The Pfizer/BioNTech and Moderna vaccines are RNA vaccines.
4. The AstraZeneca/Oxford vaccine, approved in the United Kingdom is different in that it uses a replication deficient virus. The virus infects cells and places its immunogenic proteins on the surface of cells for the immune system to react to. Even though this is not a killed virus vaccine, this vaccine should still be safe from the perspective of a patient with immunosuppression. The one issue with the AstraZeneca/Oxford vaccine is that there were some errors in the conduct of the clinical trial which might make the data suspect. One group of patients received a half-dose of vaccine. Interesting, these patients seem to be better protected when looking at the numbers. There are several theoretical reasons why this might occur, but it is counterintuitive. There were some differences in spacing the vaccine doses, which may also explain some of the benefit. The efficacy in the majority of the patients is lower, approximately 60%. What we are missing are the data with statistics to assess whether these are meaningful differences or possibly due to chance.
5. We have no reason to believe there is any advantage of the Pfizer/BioNTech or the Moderna vaccine over the other. Both vaccines did numerically very close (which is very reassuring) and none of the differences in outcomes is statistically meaningful.
6. We currently do not have efficacy or safety data for these vaccines in patients with immunosuppression. With this being said, we do not have any reason to expect the safety to be any different in patients with immunosuppression. While we do have theoretical reasons for why the vaccine might be less effective, and therefore alter a risk-benefit assessment, these vaccines are very immunogenic and will hopefully be equally efficacious. We also know how dangerous COVID-19 infection is and therefore any steps that could be taken to lessen the risk of morbidity or mortality is critical.

7. We should also remember that the vaccines were shown to reduce illness, but this does not mean that patients cannot get infected and still be contagious. The vaccines may lessen the duration of viral shedding, and therefore risk of spreading the virus, but may not limit it altogether. As such, people previously infected and people who have been vaccinated, still need to follow all of the safety protocols until "masks off" if declared.
8. Many patients are on different treatments during this period. We don't know whether any of these treatments will impair the immune response to the COVID-19 vaccine. While we have some anecdotal evidence of BTK inhibitors helping prevent severe COVID-19 illness, the clinical trial data are still emerging. The acalabrutinib trial in COVID-19 (non-CLL patients) did not show a benefit, but there were some issues with that trial that might not make it generalizable to everyone. I suspect that BTK inhibitors do help and have been continuing my patients on them. With regard to the vaccine, any temporary interruption will likely not be sufficient to make a difference and I would recommend just continuing the inhibitor. I am also recommending the same for the PI3K inhibitors and venetoclax. Anti-CD20 monoclonal antibodies would be different, and it might make sense to defer vaccination until after therapy is completed if there is an option.