



Eli Lilly Neutralizing Antibodies: Breakthrough for COVID-19

Treatment?

September 21, 2020

[Kevin Kavanagh, MD](#)

Eli Lilly stated LY-CoV555 was “well tolerated” without the observation of any drug-related serious events. And that adverse events were similar to placebo. However, the exact incidence of milder drug reactions which could affect patient acceptance were not given.

Today we finally had some good news in our fight against coronavirus disease 2019 (COVID-19). Eli Lilly announced preliminary results to their SARS-CoV-2 neutralizing antibody product, LY-CoV555, which was reported to have [spectacular results](#). In an investor news release they stated that in a Phase 2 randomized double-blind controlled trial they observed a 72% decrease in hospitalizations or ER visits with LY-CoV555.

This is excellent news after the mediocre findings of the recent randomized trial of remdesivir which found outcome differences of “[uncertain clinical importance](#)”.

Eli Lilly stated LY-CoV555 was “well tolerated” without the observation of any drug-related serious events. And that adverse events were similar to placebo. However, the exact incidence of milder drug reactions which could affect patient acceptance were not given in the news release.

Eli Lilly also observed that most hospitalizations occurred in patients who had an increased age or BMI. Underscoring the importance of the co-morbidities of age and obesity in COVID-19 disease.

A related product, convalescent serum, was found to have clinical efficacy when it was given within 3 days of diagnosis and in high concentration. And although given an FDA emergency authorization, its overall benefit has since been panned in the news media.

One may ask, why are the Eli Lilly results different from the positive, but somewhat disappointing, results of convalescent serum? The short answer is, they are not. LY-CoV555 targets the same clinical sweet spot where convalescent serum was found to be most effective.

In the Eli Lilly trial, LY-CoV555 was given to patients with mild to moderate symptoms and within 3 days of their diagnosis. In other words, similar to convalescent serum, initial results demonstrate that LY-CoV555 is effective if given in the early stages of the disease, soon after diagnosis. In addition, Eli Lilly’s product is designed to be composed of highly effective neutralizing antibodies.

Meeting these patient administration requirements on a mass scale is almost an impossible task with convalescent serum. There just is not enough to have it in everyone's urgent treatment center. But the Eli Lilly product is composed of a high concentration of highly effective neutralizing antibodies, which hopefully can be manufactured in great enough quantities to become a bridge to a vaccine.



Kevin Kavanagh, MD

One cautionary note was a statement: “Viral RNA sequencing revealed putative LY-CoV555-resistance variants in placebo and all treatment arms. The rate of resistance variants was numerically higher in treated patients (8 percent) versus placebo (6 percent).”

Thus, as with any anti-viral agent, viral resistance might possibly develop. This is to be expected. Nature adapts and RNA viruses are known to have a proclivity to mutate. This is often observed in phage therapy where there is described a dance of mutations between the bacteria and [attacking virus](#). However, in this instance, the viral mutations are beneficial when you are wanting to kill an evolving bacteria, but are detrimental when targeting the virus itself.

LY-CoV555 targets an “epitope in the SARS-CoV-2 spike region”. This is the same region many vaccines are targeting. So far, SARS-CoV-2 has not appeared to mutate at a very fast rate regarding its spike protein region. However, the development of resistance to LY-CoV555 will still need to be carefully monitored, since the emergence of a new resistant viral strain could impact the efficacy of not only monoclonal antibodies but also of future vaccines.

There would be less of a concern if LY-CoV555 was targeted and effective in the few who were severely sick, but it appears its application is most beneficial when given early and possibly to the masses. But, it is probably not realistic that LY-CoV555 can be produced in high enough volume to be available to all. No SARS-CoV-2 product to date has been able to even approach this goal. As observed in the Eli Lilly study, those newly diagnosed patients who are obese or have advanced age are the most likely to become hospitalized, and I feel initially this innovative product should be targeted toward these high-risk patients.