Effective vaccines mean that the COVID-19 pandemic may be more controlled in the coming months, but the SARS-CoV-2 virus will likely remain a part of our everyday lives. That makes it important for physicians to have therapeutics in their toolbox to treat patients at all stages of disease progression—today, as well as in the future.

The “COVID-19: What Physicians Need to Know” webinar series features AMA physician leaders hosting installments that aim to gain fact-based insights from the nation’s highest-ranking subject matter experts working to protect the public’s health.

Three physician leaders from the Food and Drug Administration (FDA) recently met virtually with AMA President Susan R. Bailey, MD, to discuss the therapeutics being used in the United States, the state of therapeutic clinical trials worldwide, the challenges of obtaining robust therapeutic data, and potential areas of investigation and discovery.

There have been more than 2,000 registered clinical trials involving more than a half million people worldwide. However, of all those trials, only about 5% are adequately powered to yield actionable information, said Janet Woodcock, MD, the FDA’s acting director.

So, what has been authorized for physicians to treat COVID-19?

More than 100,000 patients hospitalized in the U.S. have been treated with convalescent plasma. It’s a plausible answer for a disease for which you don’t have any treatment and a huge number of individual emergency access requests came in for that early on in the pandemic, Dr. Woodcock said.

But there are still numerous questions about it, she said.
An FDA Center for Biologics Evaluation and Research (CBER) analysis showed there was an advantage to using the treatment early in the course of a COVID-19 patient’s hospitalization. But other studies have not seen an advantage and there is ongoing research looking at whether the intervention neutralizes the virus, when it is most beneficial, and plasma virus titers necessary.

Treatments for mild COVID-19

Since the earliest days of the pandemic, a few options for treating patients with mild to moderate COVID-19 have been discovered and they are aimed at keeping high-risk patients out of the hospital and preventing mortality, said John Farley, MD, director of the FDA’s infectious diseases office in the FDA Center for Drug Evaluation and Research (CDER).

Monoclonal antibodies (mAbs) are designed to block SARS-CoV-2 viral attachment and entry into human cells, neutralizing the virus. At this article’s deadline, there were three emergency use authorized products:

- Bamlanivimab.
- Bamlanivimab and etesevimab administered together.
- REGN-COV: casirivimab and imdevimab administered together.

The mAbs have been authorized to use for mild to moderate COVID-19 and can be used in adults and children 12 or older and weighing at least 40 kilograms who are at high risk of developing severe COVID-19 or progressing to hospitalization.

These treatments are not authorized for patients who are already hospitalized for COVID-19 or those who require oxygen therapy. At least two trials have suggested using the treatment on patients already on ventilators may do more harm than good, Dr. Farley said.

In a phase 3 trial for patients receiving the bamlanivimab and etesevimab versus placebo, there was a 70% reduction in patients who required hospitalization or died after 29 days, he said. There were 10 deaths for patients who received a placebo and no deaths among those who received the treatment.
Some challenges have emerged for treating patients with these mAB infusions and the uptake of their use has been limited, including the need to administer the mABs via infusion and short window of time to administer them—treatment must be given within 10 days of symptom onset. Additionally, research has indicated that circulating SARS-CoV-2 viral variants may be associated with resistance to mABs. Information on resistance can be found in the FDA fact sheets and from state and local public health authorities.

Learn more with this HHS digital toolkit on mAbs.

### Treatments for sicker patients

**Remdesivir.** This intravenous drug can be used in hospitalized adult patients and children 12 years or older who weigh at least 40 kilograms.

**Imnomodulators.** Several immunomodulator therapies have also been used with some success, said Sally Seymour, MD, the deputy director for safety in the pulmonary, allergy and rheumatology products division at CDER. They are dexamethasone, baricitnib and tocilizumab.

**Dexamethasone** can be used for hospitalized patients on oxygen or a ventilator after a study published in *The New England Journal of Medicine* found that, overall, the treatment resulted in a 3% reduction in mortality. For those on a ventilator, there was 12% reduction in mortality, Dr. Seymour said.

**Baricitnib** was authorized for emergency use in November for COVID-19 patients in combination with remdesivir for patients 2 and older on supplemental oxygen, a mechanical ventilator or extracorporeal membrane oxygenation machine. A National Institutes of Health (NIH)-sponsored study showed it reduced recovery time by one day, to seven days, and that it reduced the odds of a patient dying or going on a mechanical ventilator.

**Tocilizumab** trials have had mixed results, but recently released data in a nonpeer-reviewed preprint article shows absolute mortality reduced by 4%. NIH issued a statement for use in certain patients.

Early in the pandemic, researchers turned to existing drugs to determine whether they could effectively treat COVID-19. While research continues on that front, scientists are also looking at new or repurposed, never approved antivirals that can treat COVID-19 early in the disease, Dr. Woodcock said.

Dr. Farley said it’s important to look for treatments that have clinical benefit for the patient. For example, there are companies working medication that would improve symptoms faster. The idea is...
to obtain drugs to help alleviate COVID-19 symptoms in the way that oseltamivir (marketed as Tamiflu) can help treat patients with influenza.

The priority, he said, is “to keep our highest-risk patients out of the hospital right now, and hopefully we are getting those high-risk patients vaccinated as quickly as possible.”

The NIH has developed and regularly updates its COVID-19 treatment guidelines.

The AMA's COVID-19 vaccines guide for physicians contains background and actions, evidence-based messaging guidance and best practices for consideration in external communications on COVID-19 vaccine topics.