Can Cancer Drugs Be Used to Treat COVID-19?

Studies suggest BTK inhibitors and hormone therapy might lessen disease severity and speed recovery.

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Certain types of targeted therapy and hormone therapy used to treat cancer could potentially also be used as treatments for people with COVID-19, according to research presented this week at the American Association for Cancer Research (AACR) COVID-19 and Cancer virtual meeting.

BTK inhibitors, a class of targeted drugs for leukemia and lymphoma that includes Calquence (acalabrutinib) and Imbruvica (ibrutinib), may help people with advanced COVID-19 by reducing excessive inflammation that can lead to lung and other organ damage, researchers reported. Androgen-blocking hormone therapy could also help speed COVID-19 recovery—perhaps especially in men—and clinical trials are underway.

As the global COVID-19 pandemic continues unabated, scientists are studying a wide range of existing drugs as potential treatments for the new coronavirus, officially known as SARS-CoV-2. Among these are medications used for HIV and for hepatitis C.

The severe lung damage and other manifestations of COVID-19 are attributable in part to the coronavirus itself and in part to the immune system's response to it. Some people develop an immune overreaction known as a cytokine storm, in which a flood of immune system chemical messengers lead to excessive inflammation and organ failure. During the early stages of illness, antivirals that directly target the virus may be most beneficial, while therapies that calm the excessive immune response may be needed later on.

Some drugs commonly used by cancer patients have already proved useful in the treatment of COVID-19, including the anti-inflammatory steroid dexamethasone and Actemra (tocilizumab), which is used to manage side effects of cancer immunotherapy.

But drugs designed to treat cancer itself may also play a role.

BTK Inhibitors

At the AACR meeting, Louis Staudt, MD, PhD, of the National Cancer Institute, and Steven Treon, MD, PhD, of Dana-Farber Cancer Institute in Boston, described the rationale for and findings from

early studies of BTK inhibitors for patients with severe COVID-19.

BTK inhibitors block the activity of Bruton's tyrosine kinase, which is important for the development of B cells that grow out of control in people with leukemia and lymphoma. BTK also plays a role in regulating the activity of immune cells known as macrophages that produce inflammatory cytokines.

Staudt, Mark Roschewski, MD, PhD, and colleagues conducted an observational study of 19 patients hospitalized with severe COVID-19, including 11 on supplemental oxygen and eight on mechanical ventilators. They were treated off-label with Calquence for 10 to 14 days.

A majority of the patients had improved oxygen levels, often within a few days after starting Calquence, the researchers reported in Science Immunology. By the end of treatment, eight people on supplemental oxygen (73%) were able to breathe room air and were discharged from the hospital. Half of the patients on ventilators were taken off and two of them (25%) could breathe room air and were discharged.

Comparing blood samples from the COVID-19 patients and healthy volunteers, the researchers found that the former showed greater BTK activity and production of the cytokine interleukin 6 (IL-6). After treatment with Calquence, levels of IL-6 and C-reactive protein (another biomarker of inflammation) returned to normal levels in most patients, and low lymphocyte levels rose.

"Activation of monocytes and macrophages is key to hyperinflammation. It appears that clinical improvement is related to improvement in inflammatory markers," said Staudt, who noted that as an oncologist, he was surprised to be presenting research on an infectious disease.

Although Calquence can cause side effects, including low blood cell counts, when used for cancer treatment, the short course used in this study was well tolerated.

A Phase II trial of Calquence for hospitalized COVID-19 patients, known as CALAVI, is underway in the United States (ClinicalTrials.gov number NCT04380688), and a companion trial in other countries will start soon (NCT04346199).

Treon's team looked at outcomes among six COVID-19 patients with Waldenstrom macroglobulinemia (a rare blood cancer) who were being treated with Imbruvica, another BTK inhibitor. As described in the journal Blood, the five patients on standard doses of Imbruvica had fevers and coughs, but they did not develop shortness of breath and did not require hospitalization.

The sixth patient, who was on a reduced dose of Imbruvica, experienced worsening shortness of breath and was hospitalized. He was taken off the drug and his symptoms worsened, necessitating supplemental oxygen and ultimately ventilation. In light of the favorable outcomes among the other patients, he was restarted on a full dose of Imbruvica and experienced rapid improvement, allowing him to come off the ventilator the next day and be discharged from the hospital two days later.

Clinical trials of Imbruvica for people with severe COVID-19 are also underway (NCT04375397 and NCT04439006). The BTK inhibitor Brukinsa (zanubrutinib) is being evaluated in another study (NCT04382586).

Hormone Therapy

Catherine Marshall, MD, MPH, of Johns Hopkins University School of Medicine in Baltimore, described a different approach to COVID-19 treatment using androgen-blocking hormone therapy.

It has been widely observed that men with COVID-19 are more likely than women to develop severe disease and have a higher mortality rate, suggesting sex hormones may play a role.

SARS-CoV-2 uses a receptor known as ACE2 to bind to human cells and must be activated or "primed" by an enzyme called TMPRSS2. The TMPRSS2 gene is mostly highly expressed in the prostate and it is upregulated by androgens, or male hormones. But it is also expressed in the lungs.

Although research is still early and data are mixed, some studies have shown that men have higher ACE2 and TMPRSS2 levels in their lungs, which could make them more susceptible to the coronavirus. What's more, androgens may increase these levels while estrogens lower them.

Testosterone and other androgens can stimulate prostate tumor growth, and men with prostate cancer are often treated with androgen deprivation therapy (ADT) to halt production of these hormones or stop them from working.

Researchers previously observed that among 118 men with prostate cancer who contracted SARS-CoV-2, the four who were using ADT had a slightly lower rate of severe disease than men not on ADT and none of them died. But these numbers are too small to draw any definitive conclusions.

Marshall and her colleagues therefore designed the RECOVER trial to evaluate whether bicalutamide (Casodex and generic versions), a drug that blocks androgen receptors and leads to an increase in estradiol, could help promote recovery in people with COVID-19.

This Phase II study (NCT04374279) aims to enroll 60 patients with COVID-19 who are hospitalized with mild to moderate respiratory symptoms and do not yet require mechanical ventilation. The trial will enroll people who have not yet developed severe disease because hormone therapy is unlikely to help during the most advanced inflammatory stage of the disease, Marshall explained.

The study will enroll women—who sometimes have high testosterone levels—as well as men. Exclusion criteria include current use of hormone therapy, poor liver function and recent heart problems.

The study participants will be randomly assigned to receive bicalutamide plus standard-of-care treatment for seven days or standard treatment alone. The main study endpoint will be clinical improvement after a week of treatment according to a World Health Organization scale. The

researchers will also look at the effect of bicalutamide on viral infectivity.

Another trial, known as COVIDENZA (NCT04475601), is evaluating the newer anti-androgen medication Xtandi (enzalutamide) as a treatment for COVID-19. However, Marshall said her team selected bicalutamide because generic versions cost less than $200 a course, whereas more expensive patented drugs might not be widely available on a global scale.

Click here to see the AACR COVID-19 and Cancer program.

Click here to see Cancer Health's coverage of the new coronavirus and COVID-19.
