COVID-19 Use Causes Tocilizumab Shortage

The IL6-blocking drug tocilizumab (Actemra; Genentech) is used for managing rheumatologic diseases and cytokine release syndrome (CRS) in people treated with chimeric antigen receptor (CAR) T-cell therapies. But following mounting evidence that tocilizumab improves survival in critically ill COVID-19 patients, the FDA granted it an emergency use authorization for COVID-19 treatment in June (Lancet 2021;397:1637–45).

In August the FDA added tocilizumab to its shortage list, where it remains.

"I think that Genentech was not prepared for the unprecedented demand; normally tocilizumab is a pretty predictable product," says Erin Fox, PharmD, of the University of Utah in Salt Lake City. This, combined with a surging Delta variant wave that has led to more hospitalizations than previous variants, and a lower-than-hoped-for uptake of COVID-19 vaccinations, seemingly caught the manufacturer off-guard.

"The shortage is an ongoing area of concern and is impacting both access to CAR T-cell therapies as well as our ability to administer them safely to our patients," says Navneet Majhail, MD, MS, of the Sarah Cannon Transplant and Cellular Therapy Network in Nashville, TN. CAR T-cell therapies are provided under an FDA Risk Evaluation and Mitigation Strategies program, which due to the acutely life-threatening nature of CRS, requires all institutions administering CAR T cells to have a minimum of two doses of tocilizumab on site for each patient. Several CAR T-cell clinical trials are under way, and they require having tocilizumab on hand to maintain trial protocols and timelines.

Another IL6 inhibitor, siltuximab (Sylvant; EUSA Pharma), and anakinra (Kineret; Sobi), an IL1 inhibitor, are plausible alternatives to treat CRS, but "the majority of data around treatment of CRS following CAR T-cell therapy is with tocilizumab," notes Majhail, who has worked to boost supplies of siltuximab and anakinra at his institution as a backup option to treat CRS.

The supply of tocilizumab was better in October than in September, but the University of Utah Health academic healthcare system chose to "reserve supply needed for CAR T patients," only then allocating the remainder for COVID-19 patients. "It was just a balance of trying to make sure that we had enough of everything. When we did not, for COVID-19 patients, we used drugs such as baricitinib [a JAK1/2 inhibitor] to try to conserve the supply," adds Fox.

The shortage of tocilizumab is "highly unusual," notes Fox, who says that shortages normally involve low-cost generic drugs, not expensive, brand-name products. In September, Genentech said that replenishment of stock has begun, but warned that "additional intermittent periods of stockouts" are expected in the months ahead, "especially if the pandemic continues at the current pace."

Majhail agrees: "The situation of tocilizumab shortage is unpredictable and is completely dependent on the prevalence of COVID in our communities."

Furthermore, a new variant of COVID-19 could stymie Genentech's efforts to restore the supply of tocilizumab, but Fox remains optimistic that future surges in hospitalization rates can be avoided, and that Genentech "has a good plan for continued production and supply," having learned from the slowly ending shortage. –*Victoria Forster* ■

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NIH Director Will Leave Lasting Mark on Cancer

After 12 years at the helm of the NIH, geneticist Francis Collins, MD, PhD, announced on October 5 that he will step down as the agency's director by the end of the year. When he does, Collins will leave a lasting mark on the cancer research enterprise.

Collins helped launch the Cancer Moonshot Initiative, which provided $1.8 billion in additional funding to the NCI over 7 years. He also spearheaded the creation of a 5-year, $220 million collaboration with pharmaceutical companies, the Partnership for Accelerating Cancer Therapies, centered around validating biomarkers for immunotherapy treatments (Cancer Discov 2017;8:OF7).

Even though most Collins-led undertakings did not explicitly focus on cancer, they often contained substantial funds earmarked for the NCI, or they affected cancer research indirectly.

Take, for example, the Precision Medicine Initiative, later renamed the All of Us Research Program. The effort's cornerstone is a massive longitudinal cohort study that combines health data with biospecimen collection and analysis; many of the million or so participants invariably have or will develop cancer, providing a window into the etiology of the disease (Cancer Discov 2015;5:1230).

But with $70 million set aside for the NCI, the initiative also helped fund studies such as the Molecular Analysis for Therapy Choice (NCI-MATCH) trial. Plus, it supported efforts to create precision oncology resources, such as cancer genomic data repositories and a collection of tumor-derived tissue models.

"Taking big difficult problems and bringing lots of people, money, and resources to bear on them is a signature thing that Francis does," says Lawrence Brody, PhD, of the National Human Genome Research Institute (NHGRI), who has shared lab space with Collins for nearly 30 years.

To make such large-scale programs happen, Collins needed to ensure buy-in from multiple stakeholders across government, academia, industry, and elsewhere—a skill that comes naturally to the politically savvy physician-scientist, according to Greg Simon, JD, a former policy adviser to Vice President Al Gore who later led the White House Cancer Moonshot Task Force and the Biden Cancer Initiative.

"Francis is the master diplomat," Simon says. "He has always been really good about organizing complicated large science projects."

Collins has also proven adept at securing money. During his tenure, the NIH budget increased from $29.5 billion to $43 billion; around one sixth of those funds consistently went to the NCI. Such a steadily rising budget commitment owes a lot to Collins and his "consummate skill in explaining the science to the Congress and making a compelling case" for biomedical research, according to David