



BLUE SKY FACULTY FOLIO

IMPACT

Transcendent Effort

How a physician-scientist became a leader in COVID-19 treatment research

Long before the COVID-19 pandemic emerged, Adit Ginde, MD, MPH, Professor of Emergency Medicine and Vice Chair for Research at the University of Colorado School of Medicine, was well into a productive clinical and research career. He had published numerous peer-reviewed articles, secured extensive federal funding, and led acute and critical care trials focusing on respiratory infections including pneumonia, sepsis, respiratory failure, and acute respiratory distress syndrome (ARDS).

This impressive research portfolio propelled Ginde to take on a significant role responding to the largest global public health crisis in generations. When the federal government launched Operation Warp Speed, he helped design and conduct multiple vaccine trials as part of the \$18 billion initiative

to accelerate international COVID-19 vaccine research and development through public-private partnership.

Joining the international sprint to quell the virus' impact, Ginde was also involved in early therapeutic trials, including Passive Immunity for our Nation (PassITON) which studied convalescent plasma as treatment, and ORCHID, which determined that hydroxychloroquine was not effective for COVID-19 inpatients.

AN ACTIV ROLE

National Institutes of Health formed the Accelerating Covid-19 Therapeutic Interventions and Vaccines (ACTIV) platforms in mid-April 2020 to lead a coordinated response strategy. ACTIV brought together sibling agencies including Operation Warp Speed and other leading experts from



emergency medicine, critical care, and infectious diseases to study six categories of therapies for COVID-19 patients.

Ginde joined the ACTIV-3 leadership team, which designed the platform for trials of antiviral drugs to treat COVID-19 inpatients, including monoclonal antibodies – laboratory-produced infection fighters, delivered by infusions.

“THIS WORK HAS FELT LIKE A CULMINATION OF WHAT I HAD PREPARED FOR MY ENTIRE CAREER,” HE SAYS. “YOU WORK TO TRY TO MAKE AN IMPACT ON PATIENT CARE AND OUTCOMES AND TO LEARN HOW TO BETTER TREAT PATIENTS. THIS WAS PUTTING THAT GOAL ON OVERDRIVE BECAUSE THERE WAS SUCH A PUBLIC HEALTH NEED AND SO MUCH AT STAKE.”

In 18 grueling months, ACTIV-3 completed six clinical trials of antiviral treatments. Ginde experienced a satisfying post-trial payoff as co-lead author of a study that compared the effectiveness of one of the monoclonal antibody treatments to a placebo in hospitalized COVID-19 patients. The study concluded that while

the treatment did not shorten hospital stays, it did reduce deaths by 30 percent.

Continuing his work, Ginde led the University of Colorado’s arm of ACTIV-4, which investigated the effectiveness of drugs designed to prevent secondary damage to heart, lung and blood vessel tissue caused by COVID-19. He’s also part of the ACTIV-6 trial, which is studying existing drugs, such as ivermectin, to see if they can prevent severe disease in COVID-19 outpatients.

Beyond ACTIV, Ginde took on a novel challenge as the national principal investigator of the six-site TREAT NOW trial, funded by the Department of Defense to investigate the effectiveness of repurposing two anti-HIV drugs as combination therapy for COVID-19 outpatients.

The work was challenging because it had to be completed without “any physical interaction with the participant,” Ginde says.

Demonstrating that “no-touch trials” are feasible and effective with careful design, integrated information systems and “fail safes” to protect patient privacy and safety, TREAT NOW offers just one example of how clinicians and researchers can apply the lessons learned from the first few years responding to the COVID-19 pandemic and beyond, Ginde believes.

“We are in a stage now that we are able to be a little bit reflective, while seeing that there is a mountain of work still ahead of us,” he says.

AN EXTRAORDINARY OPPORTUNITY

The pandemic underscored the need for governments, public health experts, and healthcare systems to remain flexible in their response to an ever-changing virus, Ginde says.

For example, while monoclonal antibodies produced mixed results with COVID-19 inpatients, they proved very effective in treating outpatients with moderate to severe symptoms.

But this good news was met with multiple barriers to patient access. Authorized by the FDA in November 2020, supplies of monoclonal antibodies were limited, many providers didn't know about them, and patients who wanted them often lacked timely access to an ordering provider. And while the medications were free from the federal government, there was no guarantee that the infusions could be administered without cost.

Ginde and other COVID-19 response leaders "strongly recommended centralized resources to order and access treatment to overcome these barriers," championing state-run facilities to administer the treatments free of charge. Later that month, a standing order from the State of Colorado's chief medical officer allowed eligible patients to receive the treatments for free at sites run by the Colorado Department of Public Health and the Environment.

This decision helped Colorado manage healthcare resources and save lives during the peaks of the Delta and Omicron variants and eased access to care among individuals who have been disproportionately affected by the pandemic, Ginde noted.

Despite these wins, Ginde warns, "The virus is always ahead. We just try to minimize the amount we are behind. Treatment- and vaccine-resistant variants cause us to re-evaluate current strategies and develop new countermeasures as the virus mutates and adapts."

Each medical advance creates a new set of challenges and



assumptions about all treatments – including how equitably they can be administered – are susceptible to change with each new variant.

"One of the main issues is that the evidence for COVID-19 therapeutics evolves so rapidly, from initial knowledge of efficacy to the changes that occur as variants have evolved," Ginde says. "For providers, it's been challenging to keep up with all the new and ever-changing treatments, as well as where and how to access them.

Aiming to do just that, he created the real-world evidence platform, mAb Colorado. This led him to start directly informing decisions by the Food and Drug Administration, White House COVID-19 Response Team, and U.S. Government inter-agency therapeutic advisory groups.

Now recognized as a national and global leader in the ongoing fight against COVID-19, Ginde has added nearly 100 publications to his C.V. since the pandemic began, with more in progress.

"WHAT HAPPENED IN A LITTLE MORE THAN TWO YEARS IS EXTRAORDINARY IN TERMS OF HOW QUICKLY SCIENCE CAN MOVE TO ANSWER QUESTIONS AND PROVIDE ACTIONABLE DATA THAT HAS SAVED MANY MILLIONS OF LIVES THROUGH VACCINES AND THERAPEUTICS," HE SAYS. "IT IS TRULY AN HONOR TO CONTRIBUTE TO THIS TRANSCENDENT EFFORT. HOW LIKELY IS IT IN A LIFETIME TO HAVE SUCH AN OPPORTUNITY?" ■