DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

are highly conserved among viral strains. On March 25, 2021, NIAID launched a Phase 1 clinical trial in healthy adults to assess the safety and immunogenicity of second-generation COVID-19 vaccine candidates developed by Gritstone Oncology, Inc. Gritstoneôs COVID-19 vaccine candidates utilize a strategy aimed at inducing both neutralizing antibodies and T cell responses to elicit a broad immune response against conserved viral antigens. NIAID also is conducting early-stage research on pan-coronavirus vaccines designed to provide broad protective immunity against multiple coronaviruses, especially SARS-

a stabilized SARS-CoV-2 spike protein for use in COVID-19 vaccine development. This crucial breakthrough in structure-based vaccine design led to the development of safe and effec1t3.00000912 0 612 792 r

based vaccines continue to display high levels of effectiveness.

antibodies against SARS-CoV-2 variants compared to levels in individuals who received just the primary regimen, and early clinical data still being evaluated suggest these boosted individuals are, at least initially, well-protected against the current Delta and Omicron variants, particularly against severe disease.

FDA amended the EUAs for the Moderna and Johnson & Johnson/Janssen COVID-19 vaccines, respectively, to allow for use of a single booster dose for individuals 18 years of age and older. FDA also amended the EUA for the Pfizer/BioNTech COVID-19 vaccine to allow for the use of a single booster dose for individuals 12 years of age and older. CDC recommends receiving a booster dose of the COVID-19 vaccine at least 5 months after completion of the primary series of

On April 23, 2021, NIAID launched an observational study at the NIH Clinical Center assessing how people with immune system deficiencies or dysregulations respond to COVID-19 vaccination. NIAID investigators also will gather information about COVID-19 illness in these individuals. This study will inform decision-making about COVID-19 vaccination in people with immune deficiencies and dysregulation conditions. In August 2021, NIAID launched multiple additional studies to assess and enhance the immune response to COVID-19 vaccines in immunocompromised individuals with autoimmune diseases as well as solid organ transplant recipients. This effort features a study with a multicenter, adaptive design to assess the immune responses to an additional dose of the COVID-19 vaccine in immunocompromised individuals. Data from this research will inform future considerations of additional doses of COVID-19 vaccines for these populations. CDC has made a recommendation, after review of the available scientific data, that people with moderately to severely compromised immune systems receive an additional dose of mRNA COVID-19 vaccine at least 28 days after a second dose of Pfizer/BioNTech COVID-19 vaccine or Moderna COVID-19 vaccine.

Clinical Trials of COVID-19 Vaccine Candidates in Special Populations

To effectively end the COVID-19 pandemic, it will be important to vaccinate as many people as possible, including those in special populations, such as pregnant and lactating women

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developers have begun, or are planning to begin, trials to test their vaccine candidates in children, adolescents, and other special populations.

Other COVID-19 Vaccine Candidates

NIAID also is supporting Phase 3 clinical trials of COVID-19 vaccine candidates from AstraZeneca (AZD1222) and Novavax (NVX-CoV2373). FDA has not yet authorized either of these vaccine candidates for emergency use.

Understanding the Nature of Immunity to SARS-CoV-2

NIAID is conducting and supporting research to enhance our knowledge of immunity against SARS-CoV-2 and to identify components of the immune response that provide protection against COVID-19. NIAID also is

up to 8 months in patients after mild to moderate COVID-19. NIAID also supported two separate studies examining T cell responses in recovered COVID-19 patients and individuals vaccinated against COVID-19. They found robust immune responses to the original strain as well as multiple variants of SARS-CoV-2 in both groups. Additional work by NIAID researchers and grantees showed that most individuals with existing T

The Adaptive COVID-19 Treatment Trial

Early in the outbreak, NIAID launched a multicenter, randomized placebo-controlled clinical trial, the Adaptive COVID-19 Treatment Trial (ACTT), to evaluate the safety and efficacy of multiple investigational therapeutics for COVID-19. ACTT-1 examined the antiviral drug remdesivir for treatment of severe COVID-19 in hospitalized adults. Based on positive data from ACTT-1, the FDA approved the use of remdesivir for treatment in adults and children 12 years of age and older and weighing at least 40 kg hospitalized due to COVID-19. ACTT-2 evaluated the anti-inflammatory drug baricitinib in combination with remdesivir, and based on favorable data from ACTT-2, the FDA issued an EUA for the use of baricitinib in combination with remdesivir for treatment of adults and children older than 2 years hospitalized with COVID-19 and requiring supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation. The FDA subsequently revised the EUA for baricitinib to remove the requirement that baricitinib be administered in combination with remdesivir. ACTT-3 evaluated the treatment of hospitalized COVID-19 patients with remdesivir plus interferon beta-1a, which is used to treat individuals with multiple sclerosis, and found no clinical benefit from the addition of interferon beta-1a. ACTT-4 assessed baricitinib plus remdesivir versus the glucocorticoid dexamethasone plus remdesivir in adults hospitalized with COVID-19 and requiring oxygen, showing that these two regimens led to similar outcomes.

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effort, the Collaboration to Assess Risk and Identify Long-term Outcomes for Children with COVID (CARING for Children with COVID), will permit data to be shared across studies to determine the spectrum of illness and predict long-term consequences of infection.

Addressing the Long-term Effects of COVID-19

Many people who have had COVID-19 experience continued symptoms or other sequelae as they transition from the acute to post-acute phases of the disease, and we continue to learn more about the duration and manifestations of COVID-19 as we hear from these patients.

NIH has announced the Researching COVID to Enhance Recovery (RECOVER) Initiative, a trans-NIH effort to address PASC, including targeted funding for research in this critical area. The NIH RECOVER Initiative will complement ongoing NIAID studies to better understand the various post-acute manifestations of COVID-19 in various populations. On June 10, 2021, NIH announced awards to New York University (NYU) to build the RECOVER research consortium, harmonize and coordinate data within the consortium, and develop methods for monitoring protocols; and to Massachusetts General Hospital to provide statistical analyses and coordinate data standardization, access, and sharing among RECOVER projects. On September 15, 2021, NIH announced, through NHLBI and the National Institute of Neurological Disorders and Stroke, awards to NYU to develop the RECOVER Cohort with funding from the American Rescue Plan Act of 2021 (P.L. 117-2). NYU is engaging more than 100 researchers at more than 30 institutions to build a diverse national study population and support large-scale studies on the long-term effects of COVID-19.

NIAID intramural scientists initiated the Longitudinal Study of COVID-19 Sequelae and Immunity to better understand PASC and determine the extent to which people who have recovered from acute SARS-CoV-2 infection develop an immune response that provides protection against reinfection. NIAID-supported investigators also have established the Immunophenotyping Assessment in a COVID-19 Cohort (I