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Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy (APECED) or Autoimmune Polyglandular Syndrome type-1 (APS-1) is a rare monogenic disorder caused by mutations in the *AIRE* gene that manifests with multi-organ autoimmunity involving a wide spectrum of endocrine and non-endocrine tissues. At NIH, we currently follow the world's largest population of APECED/APS-1 and we have extensive experience in the management of affected patients.

Through the course of the SARS-CoV-2 pandemic, we have acquired knowledge indicating that a proportion of APECED/APS-1 patients are at increased risk for severe COVID-19 pneumonia resulting in prolonged hospitalization, mechanical ventilation, and mortality (Bastard *et al.*, *J Exp Med*, 2021).

The CDC has now recognized that individuals with moderate to severe immune compromise due to a medical condition and/or immunosuppressive treatment could benefit from a third dose of an mRNA COVID-19 vaccine. Research conducted at NIAID/NIH (Delmonte *et al*, *under revision*) found that a significant proportion of patients with APECED/APS-1 either did not produce antibodies against SARS-CoV-2 following vaccination (primarily in the setting of immunosuppressive treatment such as with rituximab) or produced very low titers of antibodies that were just above the threshold of positivity. This information coupled with the favorable safety profile of the vaccine in this patient population support our recommendations for an additional dose of mRNA COVID-19 vaccine following an initial 2-dose primary mRNA COVID-19 vaccine series in patients with APECED/APS-1.

Therefore, it is advised that patients with APECED/APS-1 are within this vulnerable high-risk patient population for COVID-19 complications and should be prioritized for a booster mRNA vaccine (Pfizer or Moderna) against SARS-CoV-2 infection. Per ACIP guidelines, a booster should be given no sooner than 28 days after completion of the 2-dose primary mRNA COVID-19 vaccination series.

The NIH would be interested in obtaining a blood sample prior to the booster COVID-19 vaccine and another blood sample 1 month after the booster COVID-19 vaccine to evaluate patient responses to the booster. The results of the individual patient antibody titers will not be shared with the individual patient as the tests used are not clinically certified; however, the results will greatly improve our understanding of mRNA vaccine responses in patients with APECED as a group and that information will be communicated to the scientific and medical community and to the patient group.