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SARS-CoV-2 Vaccination and Solid Organ Transplant Patients: Data Needed to Inform Safety and Efficacy

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Solid organ transplant (SOT) recipients appear to have higher rates of mortality from COVID-19 when compared to other populations, attributed to underlying immunosuppression and concomitant co-morbidities.[1] Such findings are consistent with other respiratory viral infections that are associated with an increased risk of morbidity and mortality in immunocompromised hosts.[2] Further, these patients experience prolonged SARS-CoV-2 shedding which has been linked to emergence of viral mutants. Prolonged shedding also poses a risk of transmission and requires prolonged isolation, potentially leading to delays in medical care.

Although use of various SARS-CoV-2 vaccines is being considered for these at-risk patients, SOT recipients were specifically excluded from the completed and most ongoing vaccine trials. We expect that vaccine responses in these patients may be significantly impaired, due to both their primary underlying co-morbid conditions and immunosuppressive medications, as has been seen with other vaccines in this population.[3]

The candidate vaccines against SARS-CoV-2 utilize novel mechanisms to elicit immune responses, including mRNA and viral vectors. The safety of these vaccines has not been established in immunocompromised patients. Historically, vaccines can induce donor-specific and non-donor-specific antibodies but have not been associated with graft rejection in solid organ transplant patients.[3] How frequently donor-specific antibodies develop after SARS-CoV-2 vaccination and whether or not these antibodies may increase the risk of allograft dysfunction is unknown. Emerging protein-based vaccines utilize adjuvants that have not been widely studied in transplant recipients and also raise theoretical concerns for possible graft rejection. Although most studies of adjuvanted vaccines have not shown an increased risk of rejection, boosting of anti-HLA antibodies might occur.[3] Given the rapid uptake of vaccine proteins throughout the body, we would anticipate that any significant upregulation of the immune response might occur

within the first few weeks, as seen in the published data from completed trials, allowing us to promptly identify if rejection might occur at increased rates after vaccination.[4,5] Understanding these unique safety issues will likely build confidence in these vaccines for providers and patients.

There, too, is an urgent need to fund prospective studies to define the efficacy of the SARS-CoV-2 vaccine in SOT recipients. The immunogenicity, persistence of antibody titers, clinical efficacy data and unique adverse events need to be understood for SOT patients. The specific impact and appropriate timing of vaccine in patients chronically on co-stimulatory blockers and B-cell active therapies, like rituximab, merits additional study. Efficacy must be understood in terms of prevention of infection, hospitalization and death, as well as the reduction of SOT recipients' role in community spread. As these vaccines have different mechanisms of action, comparison of relative safety and humoral and cellular immune efficacy of these vaccines will inform appropriate dosing regimens and shape vaccine approaches for future pandemics.[4,5]

Given the growing numbers of immunosuppressed and their potential to spread infection, understanding how best to implement SARS-Co-V-2 immunization in SOT will enhance our ability to protect those at greatest risk for COVID-19 and ultimately our entire community.

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