Preemptive Antibody Therapy for Vaccine Breakthrough SARS-CoV-2 Infection in Immunocompromised Patients

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There is increasing evidence that COVID-19 vaccination regimens applied to the general population do not adequately protect a significant proportion of immunocompromised patients. Indeed, a recent study to be published in this journal reported a 82-fold higher risk of breakthrough infection in a large cohort of fully vaccinated solid organ transplant recipients.[1] Even more strikingly, breakthrough infection in these patients was 485-fold more likely to lead to hospitalization or death.[1] These impressive clinical data corroborate poor antibody and T-cell responses elicited by 2 mRNA vaccine doses in this population.[2,3] Similarly, impaired antibody response to mRNA vaccination has been observed in patients with hematologic malignancies, those treated with anti-CD20 antibodies, and after stem cell transplantation.[4] Although a third vaccine dose could help regain a better level of immunization in some of these immunocompromised individuals,[2,3] there is a clear need to consider alternative strategies to protect this highly vulnerable patient population from developing severe COVID-19 disease.

Anti-SARS-CoV-2 antibody therapies were proved to be efficient to prevent hospitalization in unvaccinated high-risk patients when administered early after PCR diagnosis or contact with infected individuals.[5] Herein, we report our preliminary real-life experience in 2 Belgian centers in which immunocompromised patients with vaccine breakthrough infection were treated with the combination of casirivimab and imdevimab (Regeneron).

Since May 15, 2021, 9 immunocompromised adult patients (5 renal and 1 lung transplant recipients, 2 recipients of allogeneic stem cell transplant, and 1 patient with acute lymphoblastic leukemia on maintenance chemotherapy) presented with breakthrough infection developing within a range of 7–126 d (median 54 d) after a full vaccination regimen with 2 doses of BNT162b2mRNA vaccine (Pfizer-BioNTech). SARS-CoV-2 infection was established by a positive PCR test performed because of mild suggestive symptoms, which could include asthenia, cough, fever, chills, anosmia, myalgias, or headache. One patient had mild hypoxemia (Po_2: 71 mm Hg). Antibody therapy with casirivimab combined with imdevimab was initiated 8–240 h (median 8 h) after PCR diagnosis, according to manufacturer's recommendations. Injections were well tolerated with no allergic reaction reported. Seven out of 9 patients were discharged within 8 h after the antibody injection. One patient was maintained at the hospital for 16 d because of acute bacterial pyelonephritis and another for 8 d for adaptation of immunosuppressant dosing. Two patients received transient oxygen supplementation within 48 h after antibody therapy. Clinical outcome was favorable in all patients with relief of initial COVID-19-related symptoms within 2–3 d. In 5 out of 9 patients in which repeated nasopharyngeal swabs were performed, PCR tests demonstrated a rapid drop in viral RNA levels ($<10^3$ copies/mL) by a median time of 7 d (range 5–17). Viral genotyping was available for 7 out of 9 patients. Three patients were carrying the Alpha variant (lineage B.1.1.7), 3 patients the Delta variant (lineage B.1.617.2), and 1 patient the Gamma variant (lineage P.1) according to WHO nomenclature.

Although interpretation of these observations is limited by the small number of patients, we suggest that preemptive antibody therapy with casirivimab and imdevimab is safe and effective to prevent hospitalization and death following vaccine breakthrough SARS-CoV-2 infection in immunocompromised patients, regardless of the variant involved.

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