## 新冠肺炎感染症在免疫相關發炎性疾病突破性感染 COVID-19 breakthrough infection in immune-mediated inflammatory diseases 盧俊吉

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Because of dysregulated autoimmunity and the use of immunosuppressants, host responses targeting SARS-CoV-2 virus and variants have altered in immune-mediated inflammatory diseases (IMID) patients. The immunogenicity, longevity, and safety of vaccination are different from those in healthy controls. Mounted evidence challenged the antibody neutralization targeting new virus variants and indicated the increased susceptibility to earlier breakthrough infections in these groups. Raised concerns about the reduced humoral immunogenicity of vaccines against SARS-CoV-2 in IMID and the increased risk of breakthrough infections have been argued since the development of varied kinds of vaccines. Most of the studies have demonstrated the declined humoral immune responses in IMID patients in the emergent COVID era, almost all 6 months within the vaccination.

Nonetheless, longitudinal follow-up data are scarce or unpublished in determining the immunogenicity and safety of SARS-CoV-2 vaccines. Considering that the levels of SARS-CoV-2 specific IgG correlate with infection risk and vaccine efficacy, investigating the long-term immunogenicity and safety of SARS-CoV-2 vaccines and identifying the breakthrough infection in IMID patients are warranted.

Data showed that the antibody responses in patients with IMID after two doses of SARS-CoV-2 vaccination had both lower intensity and reduced durability compared with healthy controls. Elders with IMID lose their humoral response to vaccination over time and are likely to benefit from an additional vaccination. Risks including older age, male sex, and the presence of comorbidities have a critical contribution to the outcomes of COVID-19 infection. T-cell and B cell targeting therapies contribute to the strongest negative effect on the immunogenicity of SARS-CoV-2 vaccines. B cell depletion therapy treated IMID patients, regardless of vaccine status, appear to be vulnerable to SARS-CoV-2 breakthrough infection, and were associated with severe outcomes. However, another data demonstrated that the incidence and severity of delta ((B.1.617.2) SARS-CoV-2 breakthrough infections in IMID patients on immunosuppressants was similar to that in controls. A Netherland national prospective multicenter cohort indicated that the cumulative incidence of reported SARS-CoV-2 omicron breakthrough infections was high, but similar between IMID patients on immunosuppressants and controls, and disease severity of breakthrough infection was mostly

mild. Additional vaccinations and prior SARS-CoV-2 infections contributed to the reduced the incidence of breakthrough infections.

Characterizing the variations in the time course of SARS-CoV-2 specific antibody responses associated with individual IMID diagnoses, the use of immunosuppressants, and additional vaccine doses is critical to guide vaccination recommendations. More frequent booster vaccinations for patients IMID to ensure effective immunization to prevent breakthrough infections is recommended.