Safety of the first dose of mRNA SARS-CoV-2 vaccines in patients with rheumatic and musculoskeletal diseases

The safety of the SARS-CoV-2 mRNA vaccines in patients with rheumatic and musculoskeletal diseases (RMD) on immunomodulatory therapy is unknown because these individuals were largely excluded from the vaccine trials. The levels of systemic reactogenicity reported with SARS-CoV-2 mRNA vaccines to date have raised concern for a more serious adverse event profile in patients with underlying immune dysregulation. There is currently no direct evidence about mRNA vaccine safety in patients with RMD and current guidance is based on expert opinion.[1] Concerns relating to the side effect profile of the SARS-CoV-2 mRNA vaccines have been identified as a primary concern of patients resulting in vaccine hesitancy.[2] To assess tolerability and peri-vaccination reactogenicity in this patient population, we studied a sample of patients with RMD on immunomodulatory therapy who underwent early vaccination.

Patients with RMD who received the SARS-COV-2 mRNA vaccine between 17 December 2020 and 11 February 2021 were recruited to participate in this observational cohort study by invitation on social media. Information on demographics, diagnoses and therapeutic regimens was collected. Participants completed an online questionnaire detailing any reactions experienced within the first week following the first vaccine dose.

We studied 325 participants with RMD, of whom 51% received Pfizer/BioNTech and 49% received Moderna vaccine. Median (IQR) age was 43 (34–54) years; 96% were female, 89% were white and 9% were Hispanic/Latino. The most common diagnoses were inflammatory arthritis (38%), systemic lupus erythematous (28%) and overlap connective tissue disease (19%). Immunomodulatory regimens included non-biologic disease modifying antirheumatic drugs (44%), biologic therapy (19%) and combination therapy (37%).

Local symptoms including pain, swelling and erythema were reported by 89%. Systemic symptoms were reported by 69%. Fatigue was the most commonly reported systemic event, with 7.4% of participants reporting severe fatigue. A detailed categorisation of reactogenicity, in comparison to reported events in the large-scale randomised trials, is noted in figure 1.[3 4] There was one case of PCR-confirmed SARS-CoV-2 and one diagnosis of peripheral neuropathy during follow-up. There were no allergic reactions requiring epinephrine, and 3% reported developing a new infection requiring treatment.

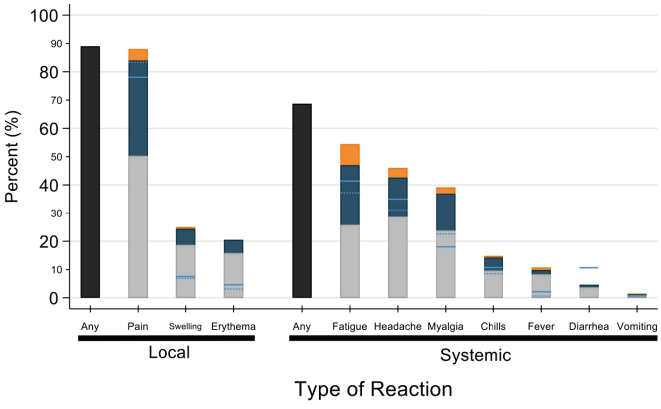

Figure 1 Local site and systemic adverse reactions in patients with rheumatic and musculoskeletal diseases within the first week following the first dose of the SARS-CoV-2 vaccination. Mild: does not interfere with activity, moderate: some interference with activity, severe: prevents daily activity. Severe, Moderate, Mild, BNT162b2, mRNA-1273.

This study represents the first available data on the safety and reactogenicity of mRNA COVID-19 vaccines in a dedicated population of patients with RMD on immunomodulatory therapy. In general, local and systemic adverse events were consistent with expected vaccine reactogenicity, mainly mild and similar in frequency to those reported in the vaccine trials.[3 4] Systemic reactions such as fatigue, headache and myalgia were common, while gastrointestinal adverse events were less common. The rate of systemic events was slightly higher than reported in solid organ transplant recipients on immunosuppression who underwent early vaccination.[5]

Strengths of this study include a national sample and novel, early data to inform major concerns among patients and their providers. Limitations include a relatively small, non-randomised sample, lack of longer-term safety data and a less granular ascertainment of side effects than the original trials. The majority of participants were female and white which may limit generalisability. Furthermore, most participants were less than 55 years of age, which likely impacted our findings given the known increased reactogenicity in this age group. The time course of this study did not allow for assessment of disease flares following vaccination and long-term follow-up is vital to further explore the safety profile of the vaccine. Additional study is warranted to examine the efficacy of SARS-CoV-2 mRNA vaccines in patients with RMD, particularly given concerns that response to vaccination may be attenuated in individuals on immunomodulatory therapy.[6]

In this sample of patients with RMD vaccinated against SARS-CoV-2, we observed expected transient local and systemic reactions that were typically mild. There were no allergic reactions requiring epinephrine. The most common adverse events were injection site pain and fatigue. These early, reassuring results may ameliorate concern among patients and provide guidance for rheumatology providers in critical discussions regarding vaccine hesitancy or refusal.

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