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Research Letter

# Safety Profile and Low Risk of Disease Relapse After BNT162b2 mRNA SARS-CoV-2 Vaccination in Patients With Rare Rheumatic Diseases

*To the Editor:*

Vaccination today represents the first defense against the effects of the coronavirus disease 2019 (COVID-19), mainly in patients with rheumatic diseases (RDs), where an increased risk for hospitalization and death has been reported.[1,2] The previous studies on the safety and tolerability of the BNT162b2 mRNA SARS-CoV-2 vaccine[3] in patients affected with RDs predominantly included patients with inflammatory arthritis.[4,5,6] The aim of our present study was to assess the safety of the BNT162b2 mRNA SARS-CoV-2 vaccine and the occurrence of possible disease flares after vaccination in patients with rare RDs or systemic lupus erythematosus (SLE).

We performed an observational study including patients with rare RDs and SLE vaccinated at the Rheumatology Unit of Bari with the BNT162b2 mRNA SARS-CoV-2 vaccine during a vaccination campaign launched in April 2021. All clinical and demographic data of the overall population are reported in Table 1, whereas more specific data on the individual diseases are reported in the Supplementary Tables (available from the authors on request). The patient global assessment (PtGA) was measured on a 0–10 visual analog scale (VAS) before the first dose (baseline), at the time of the second vaccine dose, and 4 weeks after the second dose. Antirheumatic drugs were managed according to the current recommendations by the American College of Rheumatology.[7] After the first and second shots, a paper survey was distributed to all patients. All patients could contact our center by phone or email, and patients reporting a worsening of the disease were seen promptly in the outpatient clinic. Data collection for this study was approved by the local ethics committee (study no. 5277, approval no. 83233, 09/08/2017). Patients' written informed consent to participate in the study was obtained.

Among 452 patients with rare RDs and SLE followed in our outpatient clinics, 287 (63.5%) agreed to be vaccinated during our vaccination campaign and were included in the study. After the first dose of the BNT162b2 mRNA SARS-CoV-2 vaccine, 152 (53%) patients reported at least 1 adverse event (AE). Data regarding AEs are shown in detail in Table 2. The number of AEs increased after the administration of the second dose, as reported by 176 (64.7%) patients. Among the AEs, a condition of flu-like symptoms was significantly increased after the second dose. We observed a growth of prevalent patients who suffered from arthralgias or myalgias, fatigue, and fever. No major AEs, such as major cardiovascular events, thrombosis, or anaphylaxis, were observed. All AEs were self-limiting and no patients needed hospitalization. Excluding injection site pain, multiple regression analysis showed that female sex (hazard ratio [HR] 2.34,

*Table 1.* Population vaccinated with BNT162b2 mRNA SARS-CoV-2 vaccine during the vaccination campaign carried out at the Rheumatology Unit of Bari (n = 287).

| | Mean ± SD or n (%) |
|---|---|
| Age, yrs | 53 ± 14 |
| Female | 239 (83.3) |
| No. of comorbidities | 2.4 ± 2 |
| PtGA | 3.8 ± 2.5 |
| PGA | |
| High | 1 (0.3) |
| Moderate | 50 (17.4) |
| Low | 161 (56.1) |
| Remission | 75 (26.1) |
| Rheumatic disease | |
| SSc | 90 (31.4) |
| SLE and primary APS | 68 (23.7) |
| Idiopathic inflammatory myositis | 47 (16.4) |
| Behçet disease | 39 (13.6) |
| Vasculitis | 27 (9.4) |
| MCTD | 9 (3.1) |
| UCTD | 7 (2.4) |
| Treatment | |
| Glucocorticoids | 143 (49.8) |
| ≥ 1 csDMARD | 209 (72.8) |
| Hydroxychloroquine | 84 (29.3) |
| Methotrexate | 55 (19.2) |
| Mycophenolate mofetil | 45 (15.7) |
| Azathioprine | 44 (15.3) |
| Colchicine | 10 (3.5) |
| Cyclophosphamide | 7 (2.4) |
| Leflunomide | 6 (2.1) |
| Salazopyrin | 4 (1.4) |
| IVIG | 2 (0.7) |
| Cyclosporine | 1 (0.3) |
| Tacrolimus | 1 (0.3) |
| bDMARD and tsDMARD | 72 (25.1) |
| TNFi | 26 (9.1) |
| Rituximab | 16 (5.6) |
| Tocilizumab | 8 (2.8) |
| Belimumab | 8 (2.8) |
| Benralizumab | 5 (1.7) |
| Apremilast | 3 (1.0) |
| Abatacept | 2 (0.7) |
| Anakinra | 2 (0.7) |
| Ustekinumab | 2 (0.7) |

APS: antiphospholipid syndrome; bDMARD: biologic DMARD; csDMARD: conventional synthetic DMARD; DMARD: disease-modifying antirheumatic drug; IVIG: intravenous Ig; MCTD: mixed connective tissue disease; PGA; physician global assessment; PtGA; patient global assessment; SSc: systemic sclerosis; SLE: systemic lupus erythematosus; TNFi: tumor necrosis factor inhibitor; tsDMARD: targeted synthetic DMARD; UCTD: undifferentiated connective tissue disease; VAS: visual analog scale.

*Table 2.* Adverse events recorded after the first and second doses of BNT162b2 mRNA SARS-CoV-2 vaccine.

| | First Dose, n = 287 | Second Dose, n = 272 |
|---|---|---|
| Patients with ≥ 1 AE | 152 (53.0) | 176 (64.7) * |
| Injection site pain | 124 (43.2) | 127 (46.7) |
| Headache | 45 (15.7) | 55 (20.2) |
| Arthralgias or myalgias | 29 (10.1) | 76 (27.9) *** |
| Fatigue | 12 (4.2) | 46 (16.9) *** |
| Fever | 11 (3.8) | 48 (17.6) *** |
| Allergic reaction | 5 (1.7) | 9 (3.3) |
| GI disorders | 6 (2.1) | 9 (3.3) |
| Other AEs | 10 (3.5) | 11 (4.0) |

Data are expressed as n (%). * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ vs first dose. AE: adverse event; GI: gastrointestinal.

95% CI 1.51–4.76), a high/moderate disease activity according to physician global assessment (HR 2.89, 95% CI 1.24–6.74), and older age (HR 0.95, 95% CI 0.93–0.97) were statistically significant predictors for AEs (data not shown).

No differences in PtGA VAS during the vaccination period were observed. The PtGA [median (IQR)] was 4 (2.0–5.5) at baseline; prior to the second dose and 4 weeks after, the PtGA remained at 4 (2.0–6.0). Although 7 patients reported worsening of PtGA after the first vaccine dose, this was negligible (≤ 2), with no clear signs of clinical reactivation of the disease. After the second dose, all patients were evaluated during a routine follow-up visit, at a mean of 7.1 ± 2.8 weeks. Only 6 of 287 (2.1%) patients reported a worsening of disease activity during the follow-up visit. Of these, 2 patients with SLE complained of a relapse of arthralgias, and the other 2 patients with SLE reported a cutaneous flare. One patient with systemic sclerosis reported an increase in the frequency of Raynaud phenomenon, while 1 patient with Behçet disease (BD) reported an erythema nodosum relapse. These patients did not show significant evidence of worsening disease activity at the follow-up visit.

Patients with SLE showed no worsening of the Systemic Lupus Erythematosus Disease Activity Index 2000 score (median [IQR]) at follow-up visit after vaccination (baseline 2 [0–4] vs follow-up 2 [0–2], $P = 0.6$). Behçet's Disease Current Activity Form remained stable in patients with BD (baseline 1 [0–1] vs follow-up 1 [0–1], $P = 0.1$). Finally, in patients with idiopathic inflammatory myopathies, we did not find an increase of creatine kinase (baseline 96 [65–166] IU/L vs follow-up 125 [69–275] IU/L, $P = 0.6$) or a worsening of Manual Muscle Testing 8 (baseline 80 [75–80] IU/L vs follow-up 80 [75–80], $P = 0.5$).

In conclusion, our study supports the safety of the BNT162b2 mRNA SARS-CoV-2 vaccine in patients with rare RDs and SLE, in whom we highlighted mild AEs and no disease relapse.

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The authors declare no conflicts of interest relevant to this article.

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## DATA AVAILABILITY STATEMENT

The complete dataset is available upon request and has received local ethics committee approval for sharing.

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