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Incidence of Disease Flare After BNT162b2 Coronavirus Disease 2019 Vaccination in Patients With Rheumatoid Arthritis in Remission

As vaccination programs against coronavirus disease 2019 (COVID-19) progress worldwide, the first data about COVID-19 vaccines' safety and immunogenicity in patients with rheumatic and musculoskeletal diseases (RMDs) have estimated an incidence of between 5% and 17% for RMD flares after COVID-19 vaccination (1,2). However, we feel that more details are needed to help inform vaccine decision-making for patients with an RMD.

We prospectively assessed flare rates in 77 consecutive patients with rheumatoid arthritis (RA) in clinical remission (28 joints disease activity score based on C reactive protein [DAS28-CRP] <2.6) in the 3 months before vaccination (Table 1.). All patients underwent vaccination with BNT162b2 (BioNTech-Pfizer) between March and April 2021 following the Italian government regulations. All patients discontinued antirheumatic therapies according to American College of Rheumatology (ACR) COVID-19 recommendations (3). We evaluated disease activity after 3 months using DAS28-CRP and defined flares as concordance between patient and rheumatologist assessment and DAS28-CRP elevation of more than 1.2.

Table 1. Clinical characteristics of patients with rheumatoid arthritis undergoing vaccination with BNT162b2 COVID-19 vaccine

Characteristics	Results
Age, years ± SD	62.2 ± 13.2
Female sex, n (%)	62 (80.5)
Seropositive (RF or ACPA), n (%)	53 (68.8)
CRP, mean ± SD, mg/dl	
Baseline	2.1 ± 1.9
3-month FU	2 ± 1.9 N/S (P = 0.81)
DAS28-CRP, mean ± SD	
Baseline	1.9 ± 0.5
3-month FU	2.1 ± 0.8 N/S (P = 0.33)
Antirheumatic drugs, n (%)	
Glucocorticoids	20 (27.4)
Mean dose of prednisone (mg/d)	1.3
Methotrexate	15 (20.5)
Leflunomide	11 (15)
Hydroxychloroquine	3 (4)
TNFα inhibitors	26 (35.6)
IL-6 inhibitors	9 (81.8)
Rituximab	10 (13.7)
JAK inhibitors	10 (13.7)

Abbreviations: ACPA, anti-citrullinated peptide antibodies; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; DAS28-CRP, 28 joints disease activity score based on C-reactive protein; FU, follow-up; IL-6, interleukin-6; JAK, Janus kinase; RF, rheumatoid factor; N/S, not significant; TNF, tumor necrosis factor.

Six patients (7.8%; 95% confidence interval: 6.9-8.7%) had one disease flare each. Most flares (5/6) occurred after the second dose (mean: 2.6 days) and all flares resolved within 2 weeks (mean: 6.4 days). One flare was classified as "severe," and the mean number of involved joints was 2.7. All patients were treated with glucocorticoids (6/6) and anti-inflammatory drugs (3/6). The patients with flares were undergoing treatment with Janus kinase inhibitors (3/6), methotrexate (2/6), intravenous abatacept (1/6), subcutaneous tumor necrosis factor α inhibitor (1/6), and rituximab (1/6). We did not record any change in antirheumatic therapy during follow-up or after flares.

Our data show a very low flare rate after the BNT162b2 COVID-19 vaccine in patients with RA in remission and are consistent with previous findings about Varicella-zoster virus (6.7%) (4) and Hepatitis B virus (2.2%) (5) vaccinations. Because remission is not commonly obtained in the real world, we are aware that our findings may not be generalizable to all patients with RA receiving COVID-19 vaccination.

Five out of six patients with flares withdrew or delayed antirheumatic therapies in the proximity of vaccination according to ACR guidelines. Even if there is no direct evidence that holding therapies could occur in a higher proportion of disease flares, we suggest that clinicians consider this possibility when counseling patients about COVID-19 vaccination.

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