



Adverse events and disease flares after SARS-CoV-2 vaccination in patients with systemic lupus erythematosus

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Key Points

- Over 91% of patients with SLE did not report disease flares post-SARS-CoV-2 vaccination.

Dear Editor,

Vaccination against SARS-CoV-2 is particularly important for patients with systemic lupus erythematosus (SLE), who may be at increased risk of hospitalization from COVID-19 [1]. However, the most common reason for vaccine refusal is fear of SLE flare [2]. While SARS-CoV-2 mRNA vaccines could potentially induce interferon production and increase SLE activity [3], it is unclear if SARS-CoV-2 vaccines are poorly tolerated in SLE.

In March 2021, we surveyed 466 SLE outpatients from a Rheumatology Division in New York City. SLE was defined using ICD-10 algorithms. Patients reported adverse events (AE) within 7 days of vaccination. Separately, patients reported “typical” disease flares within two weeks of vaccination. The study was approved by Hospital for Special Surgery Institutional Review Board.

183 patients with SLE responded (39.3%); mean age 52.5 [SD 14.2] years; 94% female; 65.6%; White 15.9%; Hispanic/Latinx. 136 (74.3%) reported SARS-CoV-2 vaccination. Eighty-one (59.6%) received Pfizer, 48 (39.3%) received Moderna, (72/129 received both doses) and 4

(2.9%) received Janssen. Three vaccines manufacturers were unidentified.

One hundred patients (74%) reported AEs: 61% after the first dose and 71% after the second. Most common were pain at injection site (54%), fatigue (45%), headache (36%), sore shoulder (34%), and muscle aches (26%) (Supplement). No patients reported anaphylactic symptoms.

Eleven patients (8.1%) reported flares (Table 1). These patients were older (59.8 [14.3] versus 54.2 [13.9] years) and more likely to be White (90.9% versus 65.6%). Only 1 patient who flared reported previous suspected/confirmed COVID-19 (9.1% vs. 8% in the non-flare group). Flares occurred in 12.5% receiving Moderna ($N=6$) and 6.2% receiving Pfizer ($N=5$); 1/7 patients who received both doses flared both times (Table 1). Of 12 total flares, 8 occurred after the first dose and 4 after the second. Medications to prevent or treat side effects were used by both flare and non-flare groups (Supplement). Most flares after the first dose were “mild” (87.5%), whereas most after the second were “moderate” (75%). Only one flare, after the 1st dose, was severe and characterized by joint pain and brain fog, lasting 20 days (Table 1). Six of 12 flares started 1 day after vaccination, 4/12 started 4–7 days later, and none started > 7 days later. Most flares resolved within 7 days; however, 3/12 lasted 8–21 days and 2/12 lasted > 21 days.

We acknowledge possible misclassification of AEs as flares in the absence of confirmatory laboratory studies. However, we specifically asked patients to report symptoms concordant with their typical flares, separately from AEs. Although 100 patients reported AEs, only 11 reported a flare. This method for identifying flares is supported by data showing that SLE patients are reliable narrators of their disease experience and that self-reported SLE flares are associated with clinically meaningful outcomes [4, 5]. Given that the majority of patients reported AEs, whereas few reported flares, it does not appear that side effects alone explain our results. To prevent over interpretation of these data, we did not perform statistical testing.

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Table 1 Characteristics of patients with systemic lupus erythematosus reporting “typical” flares (11 patients reported 12 flares (1 patient flared at 2/2 vaccine doses)) after COVID-19 vaccination

Study ID	Vaccine type	Flare onset (days after vaccine dose)	Flare severity (mild, moderate, severe)	Flare duration (days)	Flare symptoms*							Adverse Events (AE)			
					Fever	Joint pain	Joint swelling	Skin rash	Fatigue	Muscle aches	Other flare	Any AE	Non-flare AE symptoms		
Typical flare after vaccine dose #1															
1	Moderna	1	Mild	1 days	0	1	0	0	0	1	1	1	1	1	Pain at injection site
2	Moderna	1	Mild	4 days	0	1	1	0	0	0	0	0	1	1	Hand pain, pain at injection site, sore shoulder
3	Pfizer	1	Severe	20 days	0	1	0	0	0	1	0	0	1	1	Chills, flushing/feeling hot, headache, pain at the injection site, sore shoulder
4	Moderna	1	Mild	21 days	0	1	0	1	1	1	1	1	1	1	Headache, itching, rash at injection site, redness or swelling at injection site
5	Moderna	3	Mild	22 days	1	0	0	0	0	1	0	0	1	1	Pain at the injection site, sore shoulder
6	Moderna	4	Mild	6 days	0	0	0	0	0	1	1	1	1	1	Pain at the injection site, sore shoulder
7	Pfizer	4	Mild	22 days	1	0	0	0	0	1	1	1	1	1	Pain at injection site, Redness or swelling at the injection site, sore shoulder
8	Pfizer	7	Mild	7	0	0	0	1	0	0	0	0	1	1	Tiredness/fatigue
Typical flare after vaccine dose #2															
5	Moderna	1	Mild	4	1	0	0	0	0	1	0	0	1	1	Pain at the injection site, sore shoulder
9	Moderna	1	Moderate	3 days	0	1	1	0	1	1	1	1	1	1	Headache, pain at the injection site, redness or swelling at the injection site, sore shoulder
10	Pfizer	3	Moderate	8 days	0	1	1	0	1	1	1	1	1	1	Muscle weakness, neck pain, numbness and/or tingling in hand

Table 1 (continued)

Study ID	Vaccine type	Flare symptoms*				Flare symptoms*				Adverse Events (AE)			
		Flare onset (days after vaccine dose)	Flare severity (mild, moderate, severe)	Flare duration (days)	Fever	Joint pain	Joint swelling	Skin rash	Fatigue	Muscle aches	Other flare	Any AE	Non-flare AE symptoms
I1	Pfizer	7	Moderate	2 days	0	1	0	1	1	1	1	1	Chest pain, chills, headache, nausea/vomiting, numbness and/or tingling in hand

*0 = None, 1 = Yes

Our results are similar to a recent international study on outcomes after COVID-19 vaccination in patients with self-reported SLE [6]. Considering their US data for comparability, SLE patients in that study had a higher prevalence of flares (7/60; 11.6%) and AEs (66.7% after 1st vaccine; 76.9% after 2nd vaccine). Interestingly, they similarly found a higher prevalence of flares after the Moderna (8.8%) than the Pfizer vaccine (2.0%). Since validation of self-reported SLE can be as low as 11% [7], their different findings may reflect misclassified cases.

Our data suggest > 91% of SLE patients did not flare post-SARS-CoV-2 vaccination, and most flares were mild or moderate. Seventy-four percent reported a vaccine related AE, similar to the prevalence of AEs in the landmark Pfizer SARS-CoV-2 vaccine trial [8]. Whether factors such as vaccine manufacturer, or modifying immunosuppressive medications to enhance vaccine efficacy, independently predict flares in patients with SLE will need to be determined in larger cohorts. This information demonstrating that when flares occur, they are not severe, is reassuring. These data can help inform vaccine decision-making for patients with SLE.

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Data availability All data generated or analyzed during this study are included in this published article and its supplementary information files.

Declarations

Disclosures None.

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