Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

anti-rheumatic drugs (DMARDs) is not only associated with suppression of active inflammation, but also allows the repair of initial joint damage. However, little is known about the further course of these patients under sustained therapy: can we prevent structural changes with biological DMARDs over a longer period of time at a clinically meaningful level? Can structural lesions, especially new bone formation, develop independently from active inflammation? Are the mechanical and physiological properties of this healing tissue (ie, backfill) sufficient to sustain the joint function and to impede degeneration in the long term? Furthermore, in view of the existing evidence,[7,8] the clinical implications of these findings remain unclear, as we do not know whether these rather small changes in the sacroiliac joint are relevant on an individual patient level. All these factors necessitate further investigations with clinical and imaging studies in the future.

However, the presented study results provide evidence that healing effects can be seen not only in patients treated with TNF inhibitors but also in those receiving therapeutic IL-17A inhibition. The comparison of results of different RCTs indicate a similar effect for TNF and IL-17A inhibition, although we need to be aware that such comparisons based on diverse study populations, varying inclusion and exclusion criteria, and different MRI assessors need to be interpreted with caution. Therefore, the results of the first double blind randomised, controlled, head-to-head SURPASS trial in axial spondyloarthritis (adalimumab *vs* secukinumab)[9] that focuses particularly on radiographic spinal progression are eagerly awaited.

Altogether, the presented work by Maksymowych and colleagues marks an important milestone in spondyloarthritis research and provides relevant findings for a better understanding of treatment effects in axial spondyloarthritis that will certainly inspire further research.

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Breakthrough SARS-CoV-2 infections, morbidity, and seroreactivity following initial COVID-19 vaccination series and additional dose in patients with SLE in New York City

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Patients with systemic lupus erythematosus (SLE) are at high risk of severe disease from COVID-19, due to inherent immune perturbations and frequent use of immunosuppressants.[1,2] These medications also affect clinical and serological responses to vaccination against SARS-CoV-2, with higher rates of breakthrough hospitalisations and attenuated seroreactivity in patients with immunosuppressed rheumatic disease after the initial vaccination series compared with controls.[3–5] Vaccine responses were investigated in

New York City (NY, USA) between December, 2021, and February, 2022, during a surge of the highly infectious omicron (B.1.1.529) BA.1 variant of SARS-CoV-2, which resulted in a considerable increase in cases of and hospitalisations from COVID-19. In the general population, vaccine efficacy following two mRNA vaccine doses was lower against severe disease caused by the omicron variant than that caused by earlier variants (ie, alpha [B.1.1.7] and delta [B.1.617.2]), but efficacy was regained in individuals who received a third dose.[6] In patients with rheumatic disease, an additional vaccine dose elicited increased humoral responses relative to the initial vaccination series; however, clinical and serological efficacy has not yet been reported specifically among patients with SLE.[7]

In this study, we evaluated clinical efficacy and seroreactivity of vaccination against SARS-CoV-2 in previously reported patients from the New York University Lupus Cohort who had received an initial vaccination series with or without an additional vaccination dose, with particular attention to events occurring during the surge of the omicron BA.1 variant in New York City.[1,4,8] A full list of participant inclusion criteria are provided in the appendix (p 1).

The occurrence of breakthrough SARS-CoV-2 infections after vaccination were evaluated in 163 participants from patient encounters and chart review, with follow-up for at least 6 months after the initial vaccination series or until breakthrough infection. The initial vaccine series consisted of two doses of an mRNA (BNT162b2 [Pfizer–BioNTech] or mRNA-1273 [Moderna]) vaccine or one dose of a vector-based vaccine (Ad26.COV2.S [Johnson & Johnson]). 125 (77%) of 163 participants received one additional vaccine dose after the initial series. Clinical follow-up was required after Feb 4, 2022 (when the number of COVID-19 cases in New York City returned to baseline levels before the omicron BA.1 variant surge), with follow-up of the last patient recorded on April 24, 2022. Positive PCR or antigen-based testing was required for confirmation of a breakthrough infection, either performed at the clinical site or self-reported. All patients signed an informed consent form that was available in English, Spanish, and Mandarin. Patients consented to participation in the study as approved by the institutional review board at New York University (#s14–00487).

57 (35%) patients receiving an additional vaccine dose were evaluated longitudinally for antibodies against the SARS-CoV-2 spike receptor binding domain (R&D Systems, Minneapolis, MN, USA). Samples were available at a mean of 30·2 days (SD 20·1) after the initial vaccine series (timepoint 2) and 44·7 days (31·7) after the additional dose (timepoint 4). A subset of 26 (46%) patients had a blood sample taken before their initial vaccine dose (timepoint 1; baseline) and before their additional dose (timepoint 3; 176·6 days [41·8] after initial series). Low antibody response following vaccination was defined as up to 100 units/mL, which was the lowest value observed in control participants in our previous study.[4] Two group comparisons were performed using the χ^2 test or Fisher's exact test for categorical variables (including breakthrough SARS-CoV-2 infections) and the two-sample Mann-Whitney test for continuous variables (including antibody titres for SARS-CoV-2 spike protein).

At the time of initial vaccination, 82 (50%) of 163 patients were on at least one immunosuppressant and 26 (16%) were on more than one immunosuppressant (appendix p 5). The mean follow-up time from the initial vaccine series was 11·2 months (SD 1·8).

See Online for appendix

Of the 125 patients who received an additional COVID-19 vaccine dose, 28 (22%) had a breakthrough infection, compared with 16 (42%) of 38 who did not receive an additional dose (appendix p 9). In other words, 28 (64%) of 44 patients with a breakthrough infection had received an additional vaccination compared with 97 (82%) of 119 without a breakthrough infection (p=0·022; table). The mean time from the last vaccine dose to infection was 142·1 days (SD 87·8), and 164·7 days (88·8) from last vaccine dose to last follow-up in individuals without breakthrough infection. Of the 44 breakthrough SARS-CoV-2 infections, only two infections occurred before the start of the omicron wave in New York City (Dec 2, 2021), both in patients who did not receive the additional dose. No deaths related to COVID-19 were reported. Two patients were hospitalised due to COVID-19 (appendix p 7); both improved clinically and were subsequently discharged. Two non-hospitalised patients were treated with monoclonal antibodies, and three with ritonavir-boosted nirmatrelvir (Paxlovid; Pfizer, New York City, NY, USA). 13 (30%) of 43 patients taking mycophenolate mofetil at the time of the initial vaccination series and

	SARS-CoV-2 infection (n=44)	No SARS-CoV-2 infection (n=119)	p value
Received additional vaccine dose	28 (64%)	97 (82%)	0·022
Time from terminal vaccine dose to infection or last follow-up, days	142·1 (87·8)	164·7 (88·8)	0·14
Age, years	42·6 (12·6)	44·7 (13·9)	0·43
Sex			
Female	41 (93%)	108 (91%)	0·76
Male	3 (7%)	11 (9%)	..
Race			
White	26 (59%)	38 (32%)	0·0020
Black	5 (11%)	34 (29%)	..
Asian	9 (20%)	30 (25%)	..
Other	4 (9%)	17 (14%)	..
Ethnicity			
Hispanic or Latinx	17 (39%)	39 (33%)	0·58
Non-Hispanic or Latinx	27 (61%)	80 (67%)	..
Initial mRNA COVID-19 vaccine	42 (95%)	115 (97%)	0·66
Initial vector-based vaccine	2 (5%)	4 (3%)	..
History of lupus nephritis	22 (50)	58 (49%)	1·0
Medications at time of last vaccine			
Hydroxychloroquine	40 (91%)	100 (84%)	0·32
Glucocorticoids	14 (32%)	42 (35%)	0·85
≥1 immunosuppressant	24 (55%)	59 (50%)	0·60
Glucocorticoids plus immunosuppressant	13 (30%)	34 (29%)	1·00
Combination of immunosuppressants	11 (25%)	17 (14%)	0·16
COVID-19 treatment			
Monoclonal antibodies	3 (7%)	NA	..
Ritonavir-boosted nirmatrelvir	3 (7%)	NA	..
Remdesivir	1 (2%)	NA	..

Data are n (%) or mean (SD). SLE=systemic lupus erythematosus. NA=not applicable.

Table: **Factors associated with SARS-CoV-2 infection after vaccination in patients with SLE**

two (50%) of four patients who received rituximab in the 6 months before the initial series had a breakthrough SARS-CoV-2 infection. Among the 28 patients with a history of COVID-19 before vaccination, five (18%) had another infection following vaccination, compared with 39 (29%) of 135 patients without a history of COVID-19.

26 patients with blood samples available at all four timepoints showed a pattern of increased antibody titres after the initial vaccination series, a decrease over time, and a subsequent increase after the additional dose (appendix p 10).

Among the 57 patients who were serologically evaluated after the initial vaccination series and additional dose, median antibody titre at timepoint 2 was 397·0 units/mL (IQR 57·0–753·0), and was higher at timepoint 4 (1036·0 [517·0–1338·5]; appendix p 10). Five patients had an antibody titre at timepoint 4 that was more than 100 units/mL lower than at timepoint 2. After the initial vaccination series, 21 (37%) patients had low ELISA responses, with antibody titres up to 100 units/mL; however, only four (7%) patients continued to have low responses after the additional dose (each patient was taking at least one immunosuppressant and three were on combination therapy, with one having an asymptomatic breakthrough infection on Jan 5, 2022).

There was no association between antibody titre after the additional dose and breakthrough SARS-CoV-2 infection (appendix p 10). The median titre at timepoint 4 for the 13 individuals with breakthrough infections was 1135·0 units/mL (IQR 675·0–1378·5; mean 90·4 days [SD 56·3] from the additional vaccine dose to infection), compared with 994·5 units/mL (436·3–1306·8) in the 44 patients without breakthrough infection (141·6 days [53·6] from the additional dose to last follow-up; appendix p 8).

Patients with SLE from a multiethnic cohort of patients in New York City who had received an additional dose of COVID-19 vaccine were significantly less likely to have a subsequent SARS-CoV-2 infection than were those who had only received the initial vaccine series. The rarity of severe clinical disease in vaccinated patients with SLE and COVID-19 exemplifies the considerable protective effect of vaccination in patients at high baseline risk, particularly compared with earlier in the pandemic.[1,2] There have been reports of decreased severity of infections with the omicron variant compared with the delta variant, but it has been difficult to ascertain the role of previous infection and vaccination in comparing virulence, and the omicron variant remains deadly in areas with less robust vaccination rates (eg, Hong Kong).[9]

Patients with SLE showed an overall improvement in serological response after an additional dose of COVID-19 vaccine compared with that observed following the initial vaccination series. However, five patients had lower antibody titres at timepoint 4 than at timepoint 2, possibly due to variable timing of the serological evaluation at timepoint 2 relative to vaccination, which might have been shorter. Of note, SARS-CoV-2 spike antibody titre was not associated with breakthrough SARS-CoV-2 infection, potentially indicating the known immune evasion of the omicron variant or a plateau

effect beyond a particular antibody titre. Although the mild nature of COVID-19 cases among the study cohort of vaccinated patients with SLE could still represent an effect of humoral immunity, it is also likely to be a result of prolonged T-cell immunity, which is retained against the omicron variant.[10] Given the correlation between anti-SARS-CoV-2 spike protein antibody titres and antigen-specific production of interferon-γ (representing T-cell responses), it is assumed that the additional dose accentuates both responses, providing the benefit against severe disease reported.[4]

Limitations of this study include the study population, which represents a convenience sample that might be biased regarding patients presenting for clinical follow-up or COVID-19 treatment, and the absence of a serially followed healthy control group. All patients were required to have a positive SARS-CoV-2 test to document infection, although these results were self-reported in many cases. Albeit unlikely, it remains possible that patients did not disclose a breakthrough infection through follow-up. Associations related to medication adjustments at the time of vaccinations were not evaluated, given evolving recommendations throughout the pandemic, and neither were associations between infection, hospitalisation, and antibody titre related to medication adjustments. There remains no defined ELISA threshold of anti-SARS-CoV-2 spike protein antibody titre known to confer protection against COVID-19. Likewise, exposure risk was not captured, which could confound results.

To our knowledge, this study represents the first report of the clinical efficacy of the initial vaccination series and an additional dose against COVID-19, inclusive of the omicron BA.1 wave in New York City, and the first known longitudinal documentation of antibody responses to vaccination against COVID-19 in a cohort of patients with SLE. Protection from infection in patients receiving an additional vaccine dose and the low hospitalisation rate of vaccinated patients is reassuring, given the inherent risks in this patient population.

AS, AJE, JPB, and PMI contributed equally to this work. AS, AJE, NF, RMC, JPB, and PMI conceived the study. AS, BB, GHa, and PMI performed the literature search. AS, AJE, BB, GHa, NF, DZ, MM, GHo, JL, PR, C-ET, HMB, RMC, JPB, and PMI performed data collection. AS, AJE, JPB, and PMI created the figures and wrote the original draft. All authors performed interpretation and analysis of data, reviewed or edited the manuscript, approved the final version for publication, and agree to be accountable for all aspects of the work. AS, AJE, and PMI verified the underlying data. AS, AJE, JPB, and PMI had final responsibility for the decision to submit for publication. AS has received consulting fees from AstraZeneca, Bristol-Myers Squibb, Eli Lilly and Company, GlaxoSmithKline, and Kezar Life Sciences. RHH has received consulting compensation from Janssen. JUS has served as a consultant for Janssen, Amgen, Pfizer, Sanofi, UCB, Bristol-Myers Squibb, and Abbvie; and has received funding for investigator-initiated studies from Pfizer and Janssen. RMC has received consulting fees from Momenta–Janssen. JPB has received consulting fees and served on data and safety monitoring boards for Momenta–Janssen, Ventus, Equillium, and GlaxoSmithKline. PMI has received consulting fees from GlaxoSmithKline and Momenta–Janssen. All other authors declare no competing interests. Deidentified participant data will be made available upon request by email to the corresponding author. This work was supported by the National Institutes of Health–National Institute of Arthritis and Musculoskeletal and Skin Diseases (P50 AR07059) to JPB and PMI and Bloomberg Philanthropies COVID-19 Response Initiative Grant to JUS and PMI. The funders of the study had no role in study design, data collection, data analysis, data interpretation, writing of the report, or decision to submit for publication.

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