







## LETTER

# Clinical outcomes of breakthrough COVID-19 after booster vaccination in patients with systemic rheumatic diseases

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Vaccines for SARS-CoV-2 are effective in patients with systemic rheumatic disease (SRD) without exhibiting significant safety issues or causing disease flares,<sup>1–3</sup> whereas two doses of mRNA vaccines lead to significantly better outcomes of breakthrough (ie, despite vaccination) COVID-19 compared with unvaccinated patients.<sup>4</sup> Since a third (booster) dose is deemed necessary for better immunisation,<sup>5</sup> we aimed to examine hospitalisation rates and mortality of breakthrough COVID-19 in patients with SRD who had received three doses of the vaccine (booster-vaccinated), compared with those who received two doses (fully vaccinated) or were unvaccinated. We also comparatively assessed breakthrough COVID-19 outcomes in booster-vaccinated individuals with or without SRDs.

We prospectively recorded date/type of vaccination, demographic, clinical and COVID-19-related features (date of infection,

duration of self-reported symptomatology, hospitalisation, need for non-invasive ventilation and death), in consecutive SARS-CoV-2-infected patients followed up in our department from March 2020 (onset of pandemic) to February 2022. We also included as controls consecutive booster-vaccinated healthcare workers and patients' friends/relatives without SRD. Only individuals in whom breakthrough COVID-19 occurred  $\geq 14$  days after the second or third vaccination were enrolled in the study. Mean $\pm$ SD was used for continuous variables and percentages (%) for categorical variables. Fisher's exact test and Mann-Whitney test were used.

A total of 65 booster-vaccinated, 36 fully vaccinated and 60 unvaccinated patients with SRD, as well as 80 booster-vaccinated individuals without SRD, were enrolled. Demographic, clinical and treatment characteristics were similar across groups compared, except

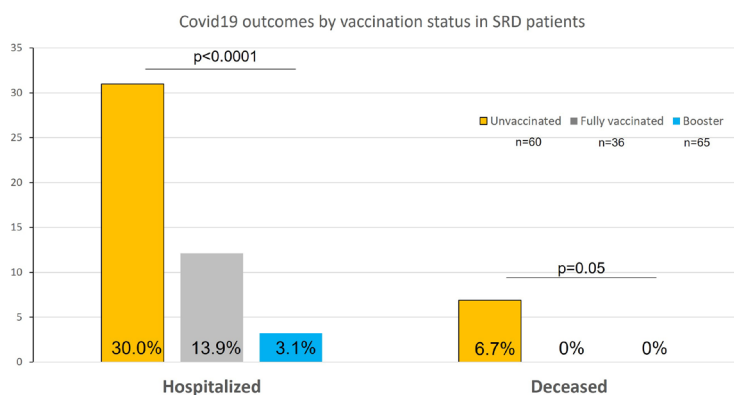


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**Figure 1** Better outcomes for booster-vaccinated compared with fully vaccinated or unvaccinated patients with SRDs. SRD, systemic rheumatic disease.

for lung disease, which was more common in the fully vaccinated patients compared with the other patient groups and the control group (online supplemental tables 1 and 2). COVID-19-related hospitalisations were less common in booster-vaccinated (2/65, 3.1%) than in fully vaccinated (5/36, 13.9%,  $p=0.09$ ) or unvaccinated patients (18/60, 30.0%,  $p<0.0001$ ). While 4/60 (6.7%) unvaccinated patients died, there were no deaths in the booster-vaccinated and fully vaccinated patient groups (figure 1). Moreover, clinical outcomes of breakthrough COVID-19 were comparable between booster-vaccinated patients with SRD and individuals without SRD (deaths: 0% for both groups, hospitalisations: 1.25% for individuals without SRD vs 3.1% for patients with SRD), except for duration of COVID-19 symptomatology, which was longer in patients with SRD than in controls ( $6.1\pm 3.2$  vs  $4.9\pm 3.1$  days,  $p=0.01$ ) (online supplemental table 2).

Therefore, in concert with studies examining data from the general population,<sup>6</sup> we show that booster vaccination further reduces the frequency of COVID-19-related hospital admissions and deaths in people with SRDs. Notably, comparisons in small-scale, breakthrough infections following booster vaccination in individuals with and without SRDs show that outcomes are comparable between the two groups. This was true, despite the higher frequency of adverse prognostic factors for COVID-19, like age and lung disease, in SRD patients compared with the group of individuals without SRD. Our study has certain limitations. First, COVID-19 in this cohort occurred at different time points of the pandemic; thus, the possibility that different variants of SARS-CoV2 have infected our patients over the entire study period cannot be excluded. Of note, booster-vaccinated patients were enrolled during the same time period when both Delta and Omicron variants were prevalent. Second, antibody response, which might have been affected by immunosuppressive/immunomodulatory treatments,<sup>2</sup> was not measured.

To conclude, these results suggest that booster COVID-19 vaccination has beneficial effects in patients with SRDs, on par with what has been shown for the general population.<sup>6</sup> This, in combination with the

reassuring results about the safety of vaccines,<sup>1–3</sup> argues in favour of booster vaccination in patients with SRD.

**Correction notice** This article has been corrected since it was first published online. Maria G Tektonidou was incorrectly listed as Maria GG Tektonidou.

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#### REFERENCES

- 1 Fragoulis GE, Bournia V-K, Mavrea E, *et al*. COVID-19 vaccine safety and nocebo-prone associated hesitancy in patients with systemic rheumatic diseases: a cross-sectional study. *Rheumatol Int* 2022;42:31–9.
- 2 Furer V, Eviatar T, Zisman D, *et al*. Immunogenicity and safety of the BNT162b2 mRNA COVID-19 vaccine in adult patients with autoimmune inflammatory rheumatic diseases and in the general population: a multicentre study. *Ann Rheum Dis* 2021;80:1330–8.
- 3 Connolly CM, Ruddy JA, Boyarsky BJ, *et al*. Disease flare and Reactogenicity in patients with rheumatic and musculoskeletal diseases following two-dose SARS-CoV-2 messenger RNA vaccination. *Arthritis Rheumatol* 2022;74:28–32.
- 4 Papagoras C, Fragoulis GE, Zioga N, *et al*. Better outcomes of COVID-19 in vaccinated compared to unvaccinated patients with systemic rheumatic diseases. *Ann Rheum Dis* 2021. doi:10.1136/annrheumdis-2021-221539. [Epub ahead of print: 10 Nov 2021].
- 5 Speer C, Töllner M, Benning L, *et al*. Third COVID-19 vaccine dose with BNT162b2 in patients with ANCA-associated vasculitis. *Ann Rheum Dis* 2022. doi:10.1136/annrheumdis-2021-221747. [Epub ahead of print: 10 Jan 2022].
- 6 Arbel R, Hammerman A, Sergienko R, *et al*. BNT162b2 vaccine booster and mortality due to Covid-19. *N Engl J Med* 2021;385:2413–20.