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Covid vaccination in patients with autoimmune diseases treated with mycophenolate: Let's think back to the recommendations

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Dear Editor,

The impact of the Covid-19 pandemic in patients with rheumatic diseases (RMDs) has been shown to have an excess of risk compared to the general population. Rheumatic diseases, steroids, immunosuppressants and comorbidities are risk factors favoring infection [1]. The possibility of vaccination however also raises a lot of questions, especially for patients with inflammatory RMDs and patients who have been treated with drugs influencing their immune system [2,3]. A task force comprising 9 rheumatologists / immunologists, 2 infectious disease specialists and 2 public health physicians was assembled and declared moderate consensus in delaying vaccination for SARS-CoV-2 in patients treated with mycophenolate in the RMDs [4]. In the documents of the Italian Society of Rheumatology of March-13-2021 and the Italian Society of Dermatology and Venereology of February 24–2021, reference is made to the clinician's decisions in delaying or suspending immunosuppressive therapies with the exception of rituximab (RTX), translating some concepts that have emerged from the international literature [3–4]. Vaccination in the Italian population initially involved health service operators and religious professions as well as elderly people hospitalized in institutionalized structures. The mRNA vaccines of Moderna and Pfizer / BioNTech do not include adjuvants of any sort, thus decreasing the probability for any unwanted immune modulation [4]. In Table 1 we report detailed informations of two nuns suffering from Systemic Lupus Erythematosus (patients 1–2), and a hospital nutritionist suffering from Pemphigus (patient-3), in clinical-laboratory remission (SELENIA/SLEDAI and PDAI) in treatment with mycophenolate and vaccinated with SARS-CoV-2 mRNA BNT162b2. Patients underwent evaluation of the lymphocyte subpopulations with determinations of the B lymphocyte population (CD27 - naive, CD27 + memory, CD38 +, CD20 +, CD19 +) evaluated by flow cytometry (FACS CANTO II, BD Biosciences), before the vaccination and 2 weeks after the second dose of vaccine. Only the nutritionist had received treatment

Table 1
Demographic, clinical and laboratory characteristics of patients before and after vaccination.

Parameters	Before vaccination			After vaccination		
	Patient-1	Patient-2	Patient-3	Patient-1	Patient-2	Patient-3
Age	72	36	64			
Gender (F/M)	F	F	F			
Years Disease	15	6	8			
prednisone mg/day	2,5			2,5		
mycophenolate mg/day	360	360	360	360	360	360
Disease Activity[a]	3	2	2	3	2	2
CD3+ cells/mcl	1134	1543	2780	1142	1610	2930
CD3 + CD4+ cells/mcl	543	987	2212	402	1007	2348
CD3 + CD8+ cells/mcl	496	467	432	758	598	551
CD3-CD56 + CD16+ cells/mcl	534	467	546	652	532	691
CD19+ cells/mcl	138	176	21	140	167	18
CD20+ cells/mcl	56	61	15	88	89	16
CD27-naive cells/mcl	15	29	13	26	35	12
CD27 + memory cells/mcl	10	27	11	35	33	16
CD38+ cells/mcl	6	8	7	9	9	8
IgG SARS-CoV-2 RBD BAU/WHO mL				12	25	28

[a] SELENIA/SLEDAI and PDAI (Pemhigus Disease Area Index).

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with rituximab 500 mg in two doses for Pemphigus a year earlier. The value of neutralizing anti-SARS-CoV-2 RBD IgG antibodies (IgG antibodies against S1-protein quantified by FEIA Thermofisher, Uppsala Sweden) determined in the three patients was respectively 12, 25, 28 BAU / WHO mL (negative <28, borderline 28–42, positive>42 BAU / WHO ml). Data from previous vaccinations (influenza, pneumococcus, papillomavirus HPV, hepatitis B HBV, Haemophilus influenzae type B) in patients with SLE are reassuring in terms of efficacy and safety [5]. Two recent studies show that patients with RMD have neutralizing IgG antibody production after vaccination for SARS-CoV-2 with RNA vaccines. In the first report on 26 patients the antibody titer is lower than in the general population, but in the cohort evaluated there are no patients treated with mycophenolate [6]. In the second study on 123 patients, of which eleven in treatment with mycophenolate neutralizing antibodies were present in three patients, while in eight were absent [7]. The authors underline the attention to the treatment with mycophenolate as well as with RTX, in the response to vaccination. In our study only one out the three patients was taking prednisone 2.5 mg/day and was on stable treatment with mycophenolate and in clinical remission. We do not yet know the withdrawal times of this therapy as it has been proposed for other DMARDs and b-DMARDs during the vaccination for SARS-CoV-2 [3]. However, it is reasonable to think that due to its half-life of 8–16 hours, even mycophenolate can be discontinued in the week of the first vaccination and booster. Our three cases described in the current paper focus on the problem being a starting point for future research.

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Declaration of Competing Interest

M.B, M. I, M.M, F.LG, P.S.P., M.C, declare the absence of conflict of interest for this research and in the writing of the manuscript.

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Maurizio Benucci[a,*], Maria Infantino[b], Mariangela Manfredi[b], Francesca Li Gobbi[a], Piercarlo Sarzi-Puttini[c], Marzia Caproni[d]

[a] *Rheumatology Unit, S. Giovanni di Dio Hospital, Azienda USL-Toscana Centro, Florence, Italy*

[b] *Immunology and Allergology Laboratory, S.Giovanni di Dio Hospital, Azienda USL-Toscana Centro, Florence, Italy*

[c] *Rheumatology Unit, ASST-Fatebenefratelli L. Sacco University Hospital, University of Milan, Italy*

[d] *Department of Health Sciences, Section of Dermatology, USL Toscana Centro, Rare Diseases Unit, European Reference Network-Skin Member, University of Florence, Florence, Italy*

[*] Corresponding author at: Rheumatology Unit, Azienda Sanitaria USL-Toscana Centro, Hospital S. Giovanni di Dio, Via Torregalli 3, 50143 Florence, Italy.
E-mail address: maurizio.benucci@uslcentro.toscana.it (M. Benucci).