Correspondence on 'EULAR December 2020 viewpoints on SARS-CoV-2 vaccination in patients with RMDs'

In light of their increased risk of worst outcomes following COVID-19 infection, patients with rheumatic and musculoskeletal diseases (RMDs) on immunosuppressive therapy, including systemic glucocorticoids, biological (b) and targeted synthetic (ts) disease-modifying antirheumatic drugs (DMARDs), represent a vulnerable population which should be prioritised to receive vaccination. Controlled data on the effectiveness and safety of different COVID-19 vaccines on patients with RMD are not available yet. However, rheumatology providers and health professionals should be ready to offer timely guidance for the optimal use of vaccines for patients on immunomodulatory drugs. Based on the long-time experience with other non-live vaccines, the COVID-19 Task Force of the European League Against Rheumatisms (EULAR) first delivered a preliminary set of information in December 2020.[1] Overall, it is expected that the safety and immunogenicity of COVID-19 vaccines for most of the DMARDs will be comparable with that registered for the general population,[2–4] so that postponing vaccination pending more information appears unjustified. A number of independent surveys have however alarmingly reported that, among patients with RMD, potential acceptance of COVID-19 vaccines may not exceed 60%, without apparent differences in relation to specific diseases, comorbidities and type of medication.[5–8] Strategies to effectively engage high-risk patients with RMD into vaccination programmes are therefore urgently needed.

Starting from 19 March 2021, rheumatologists of the IRCCS Policlinico San Matteo University Hospital of Pavia, Italy, have been actively involved in the vaccination campaign by personally contacting, booking and administering COVID-19 vaccines to patients with RMD on b/tsDMARDs followed at our institution. In course of phone contacts, rheumatologists identify themselves and offer a vaccination date. In agreement with the most recent determination of the Italian Ministry of Health (https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2021&codLeg=79076&parte=1&serie=null), patients are informed that they will receive alternatives to Oxford–AstraZeneca; the vaccine currently available at our hospital is the Pfizer/BioNTech. On the day of vaccination, patients are asked on their potential acceptance of other COVID-19 vaccines (Oxford–AstraZeneca, Moderna, Johnson & Johnson). Demographic and clinical characteristics are retrieved from electronic records and are detailed in online supplemental table 1. All patients provide their informed consent for the use of their anonymous data.

Table 1 Factors associated with adhesion to COVID-19 vaccination

	Acceptance of COVID-19 vaccine (Pfizer/BioNTech)				Acceptance of COVID-19 vaccine (any)			
	Univariable analysis		Multivariable analysis		Univariable analysis		Multivariable analysis	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age	0.99 (0.97 to 1.03)	0.81			1.01 (0.99 to 1.03)	0.49		
Age ≥70	0.51 (0.17 to 1.45)	0.19	0.42 (0.13 to 1.30)	0.13	0.56 (0.25 to 1.28)	0.17	—	—
Age <50	0.74 (0.30 to 1.85)	0.52			0.59 (0.31 to 1.12)	0.10	0.26 (0.08 to 0.83)	**0.02**
Male gender	2.22 (0.73 to 6.79)	0.16	2.57 (0.82 to 8.08)	0.11	1.56 (0.79 to 3.09)	0.19	4.13 (0.89 to 19.13)	0.06
Smoking	0.97 (0.20 to 4.71)	0.97			1.35 (0.42 to 4.34)	0.62		
BMI	1.06 (0.91 to 1.24)	0.45			0.95 (0.85 to 1.05)	0.30		
BMI >30	1.58 (0.18 to 13.86)	0.68			0.35 (0.09 to 1.32)	0.12	0.29 (0.06 to 1.40)	0.12
Hypertension	0.96 (0.30 to 3.08)	0.95			1.62 (0.67 to 3.89)	0.28		
Diabetes	0.36 (0.07 to 1.99)	0.24			0.35 (0.08 to 1.49)	0.15	—	—
Rheumatic diagnosis								
RA	Reference		—	—	Reference			
PsA	3.17 (0.70 to 14.46)	0.14			1.12 (0.51 to 2.47)	0.78		
SpA	1.41 (0.44 to 4.50)	0.57			0.81 (0.38 to 1.75)	0.60		
Vasculitis	1.01 (0.21 to 4.89)	0.99			1.06 (0.32 to 3.52)	0.93		
Disease duration	0.99 (0.99 to 1.00)	0.71			0.99 (0.99 to 1.00)	0.37		
Use of PDN	0.88 (0.37 to 2.10)	0.77			0.79 (0.43 to 1.45)	0.45		
PDN dose	1.01 (0.90 to 1.29)	0.41			1.03 (0.93 to 1.14)	0.55		
PDN dose ≥5 mg/day	2.28 (0.65 to 8.01)	0.19	3.36 (0.86 to 13.21)	0.08	1.14 (0.56 to 2.34)	0.71		
Use of csDMARDs	2.20 (0.83 to 5.82)	0.11	2.19 (1.03 to 5.60)	**0.04**	1.75 (0.93 to 3.28)	0.08	3.90 (0.92 to 16.56)	0.07
Type of b/tsDMARD								
Cytokine inhibitor	Reference		0.22 (0.04 to 1.15)	0.07	Reference			
CTLA4-Ig	0.95 (0.30 to 3.05)	0.93			1.19 (0.37 to 3.87)	0.77		
Anti-CD20	0.26 (0.06 to 1.12)	0.07			1.18 (0.52 to 2.71)	0.69		
JAK inhibitor	1.79 (0.22 to 14.47)	0.58			0.86 (0.21 to 3.47)	0.83		
PDE4 inhibitor	—	—			0.73 (0.18 to 3.07)	0.67		
Influenza vaccination	0.67 (0.22 to 2.41)	0.59			0.59 (0.17 to 1.35)	0.25		

The associations between demographic and clinical variables and acceptance of COVID-19 vaccine were investigated by means of univariable and multivariable logistic models including non-collinear variables with p<0.2 at the univariable analysis. Results are presented as ORs and 95% CIs. All analyses were conducted using MedCalc V.12.7.0.0, and the level of significance was set at 0.05.

BMI, body mass index; b/ts, biological/targeted synthetic; cs, conventional synthetic; CTLA4, cytotoxic T-lymphocyte antigen 4; DMARD, disease-modifying antirheumatic drug; JAK, Janus kinase; PDE4, phosphodiesterase 4; PDN, prednisone; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SpA, spondyloarthritis.

The general restrictions in vaccine supply are impacting on the rate of recruitment, with 224 patients out of a total cohort of ~900 having been contacted in the first 15 days of the campaign. Twenty-three patients (10.3%) opposed to vaccination despite extensive counselling; 23 (10.3%) had already been vaccinated (91.3% with Pfizer/BioNTech); 8 (3.5%) had recovered from COVID-19 for <3 months and, in agreement with the rheumatologist, postponed vaccination of 3 months; 35 (15.6%) expressed initial hesitancy but accepted vaccination following rheumatologists' recommendations; 135 (60.3%) immediately endorsed the vaccination proposal. Collectively, adhesion to vaccination was thus spontaneous in 70.5% of the cases (23 already vaccinated+135 agreeing to vaccinate irrespective of the rheumatologist), a proportion that increased to 89.7% (n=201) following rheumatologists' recommendations in recent COVID-19 and hesitant patients. Of the 201 patients who received at least the first dose or were willing to do so, 154 (76.6%) would have accepted any vaccine, 24 (11.9%) any apart from Oxford–AstraZeneca, 12 (6%) Pfizer/BioNTech only, and 11 (5.5%) were uncertain but ready to follow rheumatologists' advice. As a result, despite active involvement of rheumatologists, potential adherence to vaccines alternative to Pfizer/BioNTech was significantly lower (73.7% vs 89.7%, p<0.001). As shown in table 1, factors associated with acceptance of Pfizer/BioNTech were mostly related to the intensity of immunosuppression, with a significant impact of combination therapy with conventional synthetic DMARDs, a trend for higher odds for prednisone doses ≥5 mg/day and lower odds for rituximab. In contrast, factors conditioning individual preferences among vaccines were predominantly demographic, with women of younger age (<50 years) and higher body mass index (>30) more frequently expressing scepticism towards alternatives to Pfizer/BioNTech.

As real-world experience accumulates, it is not surprising that the spontaneous acceptance of COVID-19 vaccination found here is higher compared with previous studies.[5–8] However, active involvement of rheumatologists may further engage hesitant patients, allowing coverage of nearly 90% of those receiving several immunomodulatory drugs in combination. In this perspective, the constitution of dedicated task forces, such as those promoted by EULAR[1] as well as by other national and international societies,[9 10] is fundamental to assist rheumatology providers with updated guidelines on the optimal use of COVID-19 vaccines for patients with RMD. The treating rheumatologists should then be at the fore of outreach strategies aimed at engaging as many patients with RMD as possible among those followed at their centres. Still, misinformation about individual characteristics potentially affecting the efficacy and adverse reactions of different vaccines may introduce delays in a proportion of immunosuppressed patients[11] for whom efforts of the treating rheumatologists are unlikely to produce significant effects in the absence of forceful public campaigns.

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Correspondence on "EULAR December 2020 View points on SARS-CoV-2 vaccination in patients with RMDs" by Bijlsma. Active involvement of the treating rheumatologists increases acceptance of COVID-19 vaccines.

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Supplementary Material

Supplementary Table S1. Characteristics of the study population and acceptance of COVID-19 vaccination

	Patients n=224
Age, mean (SD), years	56.1 (14.3)
Female gender, n. (%)	156 (69.6%)
Current smokers, n. (%)	31 (13.8)
BMI, mean (SD)	25.8 (5.5)
Obesity, n. (%)	32 (14.3)
Hypertension, n. (%)	78 (34.8)
Diabetes, n. (%)	15 (6.7)
Rheumatic diagnosis, n. (%)	
Rheumatoid arthritis	119 (53.1)
Psoriatic arthritis	46 (20.5)
Spondyloarthritis	43 (19.2)
Vasculitis	16 (7.1)
Disease duration, median (IQR), years	11 (7-17)
Use of oral PDN/equivalents, n. (%)	91 (40.6)
PDN dose, mean (SD), mg/day	4.7 (3.6)
Use of csDMARDs, n. (%)	119 (53.1)
methotrexate	94 (42)
sulphasalazyne	17 (7.6)
leflunomide	7 (3.1)
others	1 (0.4)
Type of b/tsDMARD, n. (%)	
TNF inhibitor	97 (43.3)
IL6-R inhibitor	26 (11.6)
IL17 or IL23 inhibitor	27 (12.1)
CTLA4-Ig	38 (17)
Anti-CD20	10 (4.5)
JAK inhibitor	17 (7.5)
PDE4 inhibitor	9 (4)
Influenza vaccination, n. (%)	148 (66.1)
Acceptance of COVID-19 vaccination with Pfizer/BioNTech	
already vaccinated	23 (10.3)
recent COVID19 willing to be vaccinated	8 (3.5)
hesitants accepting upon rheumatologists' advice	35 (15.6)
immediately endorsing vaccination proposal	135 (60.3)
total number accepting vaccination	**201 (89.7%)**
Preferences on COVID-19 vaccine	
any	154 (68.8)
uncertain but potentially accepting any upon rheumatologists' advice	11 (4.9)
total number accepting any vaccine	**165 (73.7)**

BMI = body mass index; PDN = prednisone; DMARD = disease modifying anti-rheumatic drug; cs = conventional synthetic; b/ts = biological/targeted synthetic; TNF = tumor necrosis factor; IL = interleukin; CTLA4 = cytotoxic T-lymphocyte antigen 4; JAK = janus kinase; PDE4 = phosphodiesterase 4.