Comment on 'Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 global rheumatology alliance physician-reported registry' by Gianfrancesco M *et al*

We read with interest the publication on COVID-19 outcomes related to hospitalisation of people with chronic inflammatory rheumatic diseases (CIRD) by Gianfrancesco *et al*.[1] In our centre, we have taken a different approach by contacting 1495 patients with CIRD by telephone to ask for COVID-19 tests and symptoms. A total of 917 patients who agreed to participate (61%) was interviewed between 15 April and 15 June 2020: about 60% women, mean age 54, mean disease duration 12 years. Most had spondyloarthritis (SpA) including psoriatic arthritis (51%), 41% rheumatoid arthritis (RA) and 7% connective tissue diseases (CTD), mainly lupus. In RA, rheumatoid factor was found in 88%, anti-citrullinated protein antibodies (ACPA) in 77% and human leukocyte antigen (HLA) B27 in 73% of patients with axSpA, while 92% with CTD had antinuclear antibodies. Less than half of patients were vaccinated against *pneumococci* (43%) and *influenca* (47%).

The German government started a national shutdown on 22 March 2020. To give some guidance to rheumatologists, the German Society of Rheumatology (DGRh) released recommendations on 29 April 2020.[2] Our survey started about 2 weeks earlier.

The care of our patients with CIRD is largely based on the 'treat to target' approach. Most patients with RA were on cDMARDs with methotrexate (50%), while 47% took glucocorticoids (GC). Patients with CTD were mostly on GC (48%) and hydroxychloroquine (77%). In addition, 63% of patients were on bDMARDs, mostly on antitumour necrosis factor agents (60%), 12% on anti-interleukin 17 agents and on antibodies targeting B-cells. Of interest, about 30% of patients had recently changed medication in a shared decision process, about half due to the pandemic with significantly more patients changing bDMARDs versus cDMARDs.

Only 62 patients from our cohort (6.8%) told to have been tested against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with only 3 (4.8%) being PCR+ (all with mild disease), and 1.4% (out of 352 tested) had anti-SARS-CoV-2 IgG antibodies. The region our hospital is mainly serving is North Rhine-Westphalia with 17.9 million inhabitants. On 19 June 2020, 40 153 reports of confirmed SARS-CoV-2 tests had been registered corresponding to 0.22% of the population.[3] The median age of infected subjects was 49 years with 50% women, 15% were hospitalised and 9% had severe disease. Thus, the infection rates in our region were not as high as in other countries.[4] In our cohort, the cumulative prevalence of SARS-CoV-2 infections corresponds well with the SARS-CoV-2 IgG antibody seroprevalence of 1.42%, which is similar to the reported seroprevalence of 1.6% among healthcare workers in a hospital nearby[5] and consistent with the low rate of infections in our federal state. This seroprevalence indicates a dark figure factor of about 5 that seems to be considerably higher in other regions.[6]

Table 1 Characteristics of patients related to change of medication

Item	Total cohort	RA	AxSpA	PsA	CTD	P value
N	917	378	292	179	68	
Changed medication	292 (31.8)	139 (36.8)	84 (28.8)	61 (34.1)	8 (11.8)	<0.001
Changed DMARDs	243 (83.2)	109 (78.4)	80 (95.2)	48 (78.7)	6 (75.0)	0.003
Stopped	41 (16.9)	18 (16.5)	9 (11.3)	13 (27.1)	1 (16.7)	
Net dose reduction	164 (67.5)	73 (67.0)	63 (78.8)	26 (54.2)	2 (33.3)	
Net dose increase/start of new therapy	26 (10.7)	13 (11.9)	5 (6.3)	6 (12.5)	2 (33.3)	
No net change or change of drug	12 (4.9)	5 (4.6)	3 (3.8)	3 (6.3)	1 (16.7)	
Additional GC change	31 (12.8)	22 (20.2)	2 (2.5)	3 (6.3)	4 (66.7)	<0.001
Changed GC medication	80 (27.4)	52 (37.4)	6 (7.1)	16 (26.2)	6 (75.0)	<0.001
Stopped	21 (26.2)	12 (23.1)	4 (66.7)	5 (31.3)	0	
Dose reduction	27 (33.8)	21 (40.4)	0	2 (12.5)	4 (66.7)	
Dose increase/start	32 (40.0)	19 (36.5)	2 (33.3)	9 (56.3)	2 (33.3)	
Time point of change	[71] (N=219)	[42] (N=97)	[8] (N=76)	[19] (N=42)	[4] (N=4)	
After 30 April 2020	4 (1.8)	3 (3.1)	1 (1.3)	0	0	0.608
After 15 March 2020 (cumulative)	144 (65.8)	71 (73.2)	47 (61.8)	25 (59.5)	1 (25.0)	0.087
Reason for change	[19] (N=273)	[17] (N=122)	[2] (N=82)	(N=61)	(N=8)	
Corona pandemic	138 (47.3)	56 (40.3)	52 (61.9)	28 (45.9)	2 (25.0)	0.009
Activity of rheumatic disease	63 (21.6)	31 (22.3)	10 (11.9)	17 (27.9)	5 (62.5)	0.003
Inactivity of rheumatic disease	77 (26.4)	38 (27.3)	22 (26.2)	16 (26.2)	1 (12.5)	0.835
Other	66 (22.6)	30 (21.6)	19 (22.6)	15 (24.6)	2 (25.0)	0.97
Responsible for change	[11] (N=281)	[8] (N=131)	[1] (N=83)	[2] (N=59)	(N=8)	
Patient alone	29 (10.3)	11 (8.4)	9 (10.8)	8 (13.6)	1 (12.5)	0.739
Physician alone	27 (9.6)	16 (12.2)	4 (4.8)	7 (11.9)	0	0.22
Shared decision patient/physician	225 (80.1)	104 (79.4)	70 (84.3)	44 (74.6)	7 (87.5)	0.498
Using b/ts DMARDs	182 (78.1) [10]	78 (74.3) [4]	69 (87.3) [1]	34 (73.9) [2]	1 (33.3) [3]	0.032
Not using b/ts DMARDs	36 (15.5) [10]	18 (17.1) [4]	7 (8.9) [1]	9 (19.6) [2]	2 (66.7) [3]	0.024

Numbers are N (%). Numbers in square brackets indicate the number of missing values and/or unknown state.
CTD, connective tissue diseases; GC, glucocorticoids; PsA, psoriatic arthritis; RA, rheumatoid arthritis.

The prevalence is similar to Veneto in Italy[7] but Spanish patients with CIRD had 1.32-fold higher prevalence of SARS-CoV-2 infections than the reference population.[8] In another study from Northern Italy, 10% of SARS-CoV-2 infected patients with CIRD died.[9] In contrast, from Wuhan where the pandemic started[10] and New York,[11] different outcomes were reported. However, two German patients treated with rituximab had normal IgG levels but a fatal course of COVID-19,[12] and two patients with lymphoma on rituximab developed SARS-CoV-2 viraemia and died.[13] We did not observe problems with rituximab to date. Thus, whether patients with CIRD on immunosuppressants are at risk for SARS-CoV-2 infections is not clear to date.

How did our patients handle the pandemic? Asked about their behaviour, patients told to have been rather careful and more than 90% of patients with CIRD announced to follow the advice not to change therapy because of the pandemic.[14] However, our results tell a different story (table 1).

In the early days of the pandemic, before 30 April 2020, about 30% of our patients had already changed their medication with about 80% reducing DMARDs and about 30% changing GC, and significantly more changed bDMARDs and tsDMARDs as compared with cDMARDs. The majority reduced the dose or even discontinued but some active patients also increased the dose. Importantly, about 80% of patients declared that this was a shared decision-making with their rheumatologist. Currently, we do not know about the outcome of these decisions but follow-ups are planned. The recommendations of DGRh released early[2] may have guided to stop the tendency of reducing medication.

More than 10 million cases of SARS-CoV-2 infections and over 500 000 deaths have been globally reported until 10 July 2020. Our data are—as several others—also not consistent with an increased risk of COVID-19 in patients with CIRD. However, patients may have protected themselves well. A high number of patients changed their medication due to the pandemic, mostly those on biologics. Most patients reduced but some also increased the dose due to disease activity. Although the data are reassuring, caution is still mandatory. The low vaccination rate in patients with CIRD is not acceptable. Timely expert recommendations are important in such a situation.

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REFERENCES

1 Gianfrancesco M, Hyrich KL, Al-Adely S, *et al*. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 global rheumatology alliance physician-reported registry. *Ann Rheum Dis* 2020;79:859–66.
2 Schulze-Koops H, Specker C, Iking-Konert C, *et al*. Preliminary recommendations of the German Society of rheumatology (DGRh eV) for the management of patients with inflammatory rheumatic diseases during the SARS-CoV-2/COVID-19 pandemic. *Ann Rheum Dis* 2020;79:840–2.
3 Corona-Meldelage, 2020. Available: http://www.lzg.nrw.de/inf_schutz/komp_zentr_inf_schutz/corona_meldelage/index.html
4 Coronavirus disease 2019 (COVID-19) situation report – 75. Available: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200404-sitrep-75-covid-19.pdf?sfvrsn=99251b2b_4
5 Korth J, Wilde B, Dolff S, *et al*. SARS-CoV-2-specific antibody detection in healthcare workers in Germany with direct contact to COVID-19 patients. *J Clin Virol* 2020;128:104437.
6 Lavezzo E, Franchin E, Ciavarella C, *et al*. Suppression of a SARS-CoV-2 outbreak in the Italian municipality of VO'. *Nature* 2020. doi:10.1038/s41586-020-2488-1. [Epub ahead of print: 30 Jun 2020].
7 Favalli EG, Monti S, Ingegnoli F, *et al*. Incidence of COVID-19 in patients with rheumatic diseases treated with targeted immunosuppressive drugs: what can we learn from observational data? *Arthritis Rheumatol* 2020. doi:10.1002/art.41388. [Epub ahead of print: 07 Jun 2020].
8 Pablos JL, Abasolo L, Alvaro-Gracia JM, *et al*. Prevalence of hospital PCR-confirmed COVID-19 cases in patients with chronic inflammatory and autoimmune rheumatic diseases. *Ann Rheum Dis* 2020;79:1170–3.
9 Fredi M, Cavazzana I, Moschetti L, *et al*. COVID-19 in patients with rheumatic diseases in northern Italy: a single-centre observational and case–control study. *Lancet Rheumatol* 2020.
10 Ye C, Cai S, Shen G, *et al*. Clinical features of rheumatic patients infected with COVID-19 in Wuhan, China. *Ann Rheum Dis* 2020;79:1007–13.
11 Haberman R, Axelrad J, Chen A, *et al*. Covid-19 in Immune-Mediated Inflammatory Diseases - Case Series from New York. *N Engl J Med* 2020;383:85–8.
12 Schulze-Koops H, Krueger K, Vallbracht I, *et al*. Increased risk for severe COVID-19 in patients with inflammatory rheumatic diseases treated with rituximab. *Ann Rheum Dis* 2021;80:e67.
13 Tepasse P-R, Hafezi W, Lutz M, *et al*. Persisting SARS-CoV-2 viraemia after rituximab therapy: two cases with fatal outcome and a review of the literature. *Br J Haematol* 2020;190:185–8.
14 Schmeiser T, Broll M, Dormann A, *et al*. [A cross sectional study on patients with inflammatory rheumatic diseases in terms of their compliance to their immunsuppressive medication during COVID-19 pandemic]. *Z Rheumatol* 2020;79:379–84.