COVID-19 pneumonia in a large cohort of patients treated with biological and targeted synthetic antirheumatic drugs

We read with interest the article by Monti *et al*,[1] who evidenced, in a cohort of subjects affected by COVID-19, a low prevalence of patients treated with biological disease-modifying antirheumatic drugs (bDMARDs) and targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs).

Despite a notable heterogeneity in different countries and even in different regions of the same country, a high lethality is reported among elderly patients with several comorbidities.[2]

National and international registers have been created to collect patients affected by rheumatic diseases, as well as patients with interstitial lung disorders.[3]

Since 20 February to 7 April 2020, we collected clinical data of 859 patients affected by different rheumatic diseases and sarcoidosis, treated with stable and full dosage of bDMARDs or tsDMARDs at Siena Rheumatology Unit and Siena Regional Referral Centre for Sarcoidosis.

All patients underwent a telephone survey in order to establish their clinical status, the appearance of signs and symptoms of COVID-19 and the presence of nasal–pharyngeal swab positivity. Patients were predominantly from central and southern regions of Italy. During telephone assessment, the patient's health status and chronic disease therapy during the pandemic period were evaluated. Clinical and pharmacological data of our population are summarised in table 1.

Only two patients were diagnosed with COVID-19. The first one, a 50-year-old woman affected by rheumatoid arthritis and treated with rituximab since 2016, presented bilateral diffuse interstitial pneumonia at chest X-ray; she was hospitalised, treated with lopinavir–ritonavir and discharged after 3 days.

The second patient was an 87-year-old woman affected by diabetes mellitus and in treatment with tocilizumab for 9 months for giant cell arteritis. She lived in a retirement home where COVID-19 outbreak was reported, leading to several intensive care unit (ICU) hospitalisations among the other inmates. In this context, she underwent nasal–pharyngeal swab with a positive result; she remained fully asymptomatic, without interrupting biological therapy.

Our findings may suggest that a limited number of patients affected by immune–inflammatory diseases and treated with biological therapies were diagnosed with COVID-19 during the 45-day period of pandemic in Italy. None of our patients developed a severe COVID-19 infection. Notably, one of them was asymptomatic, despite living in a small cluster with a high incidence of COVID-19. This severe impaired patient was in treatment with tocilizumab, a drug recently proposed for COVID-19 in phase II and III clinical trials.

COVID-19 led to concerns for the increased risk of severe respiratory complications in patients treated with bDMARDs and tsDMARDs.

However, our preliminary survey shows that patients treated with bDMARDs or tsDMARDs did not develop life-threatening complications from COVID-19.

This apparently surprising finding can better be explained through the comprehension of the pathological mechanisms leading to acute respiratory distress syndrome, in which overexpression of inflammatory mediators plays a crucial role.[4]

An immune dysregulation is reported in patients affected by COVID-19 with an imbalance in T cells,[5] high serum levels of interleukin (IL)-6, IL-1 and tumour necrosis factor alpha, particularly in those subjects requiring hospitalisation and ICU admission,[6] suggesting an intriguing role of bDMARDs in the treatment of COVID-19.[7]

Since bDMARDs significantly modify and impair circulating inflammatory cytokines involved in both rheumatic diseases and acute respiratory distress syndrome, we may postulate that our patients lack the immune triggers responsible of the most severe clinical features.

In line with Monti *et al*,[1] our survey can support clinicians for the management of this kind of patients, not suggesting a preventive interruption of bDMARDs and tsDMARDs in relation to COVID-19 pandemic. Nevertheless, our findings should not lead to enthusiastic conclusion on a protective role of bDMARDs: our patients are fully aware of their increased invective risk and during the very first phases of the pandemic adopted all protective measures. Finally, we may hypothesise that some of our patients were misdiagnosed due to an oligoasymptomatic course of the disease.

Table 1 Patients features

Drug	Patients	Mean exposure to drug (years)	Mean age (years)	Disease (n)
Adalimumab	91	4.9	57.47	AS: 28 PsA: 42 RA: 15 Takayasu: 1 Sarcoidosis: 5
Etanercept	94	5.3	61.3	AS: 22 PsA: 27 RA: 45
Infliximab	90	4.5	57.97	AS: 47 PsA: 26 EA: 2 RA: 5 BD: 5 Takayasu: 1 SAPHO: 1 Sarcoidosis: 3
Certolizumab	41	1.5	52.41	AS: 6 PsA: 25 RA: 10
Golimumab	44	3.1	54.68	AS: 8 PsA: 31 RA: 4 EA: 1
Rituximab	225	2.9	61.96	RA: 158 SSc: 54 AAV: 8 IIM: 5 SLE: 6 SS: 3 Sweet: 1
Tocilizumab	38	3.5	62.9	RA: 27 GCA: 11
Sarilumab	12	1.1	61.25	RA: 12
Ustekinumab	7	2.1	59.71	PsA: 7
Secukinumab	75	2.1	55.16	AS: 20 PsA: 55
Ixekizumab	6	0.5	57.16	PsA: 6
Canakinumab	1	1.0	50.0	Still: 1
Abatacept	55	2.7	62.2	RA: 55
Baricitinib	68	1.9	60.46	RA: 68
Tofacitinib	12	1.2	61.18	RA: 12

AAV, ANCA-associated vasculitis; AS, ankylosing spondylitis; BD, Behçet disease; EA, enteropathic arthritis; GCA, giant cell arteritis; IIM, idiopathic inflammatory myopathies; PsA, psoriathic arthritis; RA, rheumatoid arthritis; SAPHO, synovitis, acne, pustulosis, hyperostosis, osteitis; SLE, systemic lupus erythematous; SS, Sjogren's syndrome; SSc, systemic sclerosis.

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