Clinical features and outcomes of COVID-19 in patients with rheumatic diseases treated with biological and synthetic targeted therapies

From the beginning of the COVID-19 pandemic, more than 4.7 million cases have been detected in the world, Spain being one of the countries hardest hit by the SARS-CoV-2.[1] The role of the immune system and immunomodulatory therapies in the evolution of this infection is still controversial.[2] The study of patients with rheumatic and musculoskeletal diseases (RMDs) such as rheumatoid arthritis (RA), spondyloarthropathies (SpA) or systemic lupus erythematosus, treated with immunomodulatory therapies is essential to understand the prognosis of COVID-19 in this specific population and to the management of these patients.

BIOBADASER is a multicentre prospective observational registry promoted by the Spanish Society of Rheumatology (SER) and supported by the Spanish Agency of Drugs and Medical Devices. It is aimed at assessing safety in patients with RMDs starting treatment with any biological (bDMARD) or targeted synthetic disease-modifying antirheumatic drug (tsDMARD). More than 6600 patients are prospectively followed up in BIOBADASER 3.0.

This report describes the clinical characteristics and outcomes of patients with COVID-19 in BIOBADASER. We have identified 41 patients with RMDs treated with bDMARD and tsDMARD diagnosed of COVID-19 at 15 hospitals in the registry. Thirty-one patients were diagnosed because positive PCR test for SARS-CoV-2, and 10 patients because a highly compatible clinical picture and close contact with confirmed positive cases. Table 1 shows baseline characteristics of the patients. Twenty-five (61.0%) patients were female and 16 (39,0%) male, with a mean age of 59.4 years. They had long-standing (12.8 years) refractory (three previous bDMARD/tsDMARDs) diseases with 5.7 years of bDMARD/tsDMARD therapy duration. Twenty-one patients (51.2%) had RA. Comorbidities included hypertension (36.6%), past or current smoker (36.8%), diabetes (9.8%) and high body mass index (BMI) (27.7 (5.6) kg/m^2—mean (SD)). Eighteen patients (43.9%) were using TNF inhibitors, seven JAK inhibitors (17.1%, 9.8% baricitinib and 7.3% tofacitinib) and five (12.2%) IL-6 inhibitors. Seventeen (41.5%) patients were using methotrexate and four (9,8%) hydroxychloroquine.

Three patients died (7.3%); a 63-year-old RA male on anakinra—plus prednisone 5 mg/day—(comorbidities: smoker, BMI 34.6); a 56-year-old SpA female on secukinumab—no glucocorticoids—(past smoker, BMI 28.4) and a 91-year-old vasculitis female on rituximab—plus prednisone 5 mg/day—(hypertension). Hospitalisation was required in 28 patients (68.3%) and intensive care unit (ICU) admission in 6. Thirty-five (85.4%) patients are fully recovered at the moment of this analysis, and three patients are still hospitalised, none in ICU.

Data on COVID-19 in patients with RMDs is still scarce.[3–6] Because of the rapid evolution of the pandemic, it is important to accrue information on the clinical course of rheumatic patients on bDMARD/tsDMARDs developing COVID-19. The reduced number of patients in our study limits the possibility of drawing solid conclusions. However, these findings point in the direction that COVID-19 course and mortality in patients

Table 1 Clinical features and treatments in patients with rheumatic diseases on targeted therapies with the diagnosis of COVID-19

Variable	RA	SpA	Other rheumatic diseases	Total
N	21	12	8	41
Age at COVID-19 onset, years (SD)	61.3 (13.9)	57.1 (11.5)	57.1 (23.9)	59.4 (15.6)
Sex, female, n (%)	14 (66.6)	5 (41.7)	6 (75.0)	25 (61.0)
Disease duration (time since rheumatic diagnosis to COVID-19), years (SD)	12.0 (8.3)	15.0 (14.2)	11.4 (7.9)	12.8 (9.8)
Time with bDMARDs/tsDMARDs (time since beginning of treatment to COVID-19), years (SD)	5.8 (5.2)	5.3 (5.8)	5.7 (9.6)	5.7 (5.7)
Comorbidities and risk factors				
Charlson index, mean (SD)	2.5 (1.6)	2.3 (1.7)	3.4 (3.1)	2.6 (2.0)
BMI, mean (SD)	27.9 (5.1)	29.4 (4.7)	25.2 (7.5)	27.7 (5.6)
Hypertension, n (%)	6 (28.6)	5 (41.7)	4 (50.0)	15 (36.6)
Smoking status, n (%)				
Never smoker	14 (66.7)	8 (66.7)	5 (62.5)	27 (65.8)
Current smoker	2 (9.5)	0 (0.0)	2 (25.0)	4 (9.8)
Former smoker	5 (23.8)	4 (33.3)	1 (12.5)	10 (24.4)
COVID-19 diagnosis, evolution and outcome				
COVID-19 diagnosis, n (%)				
Confirmed cases (positive PCR test)	16 (76.2)	8 (66.7)	7 (87.5)	31 (75.6)
Suspicious cases (highly compatible clinical picture)	5 (23.8)	4 (33.3)	1 (12.5)	10 (24.4)
COVID-19 outcome				
Recovered without sequelae	18 (85.7)	11 (91.7)	6 (75.0)	35 (85.4)
Not yet recovered	2 (9.5)	0 (0.0)	1 (12.5)	3 (7.3)
Death	1 (4.8)	1 (8.3)	1 (12.5)	3 (7.3)
Hospitalisation, n (%)	16 (76.2)	8 (66.7)	4 (50.0)	28 (68.3)
Intensive care unit, n (%)	4 (19.0)	2 (16.7)	0 (0.0)	6 (14.6)
Rheumatic disease: treatment and clinical features				
Last DAS-28 available (previous to COVID-19), mean (SD)	3.9 (1.4)	3.3 (1.3)	–	3.6 (1.4)
bDMARD/tsDMARDs previous to COVID-19), n (%)				
TNF inhibitors	7 (33.3)	7 (58.3)	4 (50.0)	18 (43.9)
Anti-IL6 monoclonal antibodies	3 (14.3)	0 (0.0)	2 (25.0)	5 (12.2)
Anti-CD20 monoclonal antibodies	2 (9.5)	0 (0.0)	1 (12.5)	3 (7.3)
Anti-IL1 monoclonal antibodies	1 (4.8)	0 (0.0)	0 (0.0)	1 (2.4)
Anti-IL17A monoclonal antibodies	0 (0.0)	5 (41.7)	0 (0.0)	5 (12.2)
Abatacept	1 (4.8)	0 (0.0)	1 (12.5)	2 (4.9)
JAK inhibitors	7 (33.3)	0 (0.0)	0 (0.0)	7 (17.1)
Baricitinib	4 (9.0)	0 (0.0)	0 (0.0)	4 (9.8)
Tofacitinib	3 (14.3)	0 (0.0)	0 (0.0)	3 (7.3)
Number of previous bDMARD/tsDMARDs, mean (SD)	4.2 (2.9)	2.0 (1.0)	1.6 (0.7)	3.0 (2.4)
Use of concomitant csDMARDS				
Methotrexate	11 (52.4)	4 (33.3)	2 (25.0)	17 (41.5)
Hydroxychloroquine	2 (9.5)	0 (0.0)	2 (25.0)	4 (9.8)
Others	0 (0.0)	2 (16.7)	0 (0.0)	2 (4.9)
Monotherapy	12 (57.1)	6 (50.0)	4 (50.0)	22 (53.7)
Use of glucocorticoids, n (%)	13 (61.9)	2 (16.7)	5 (62.5)	20 (83.3)
Dose of glucocorticoids (before COVID-19), mg, mean (SD)	5.5 (3.3)	7.5 (2.1)	6 (2.2)	5.8 (2.9)
Concomitant use of NSAIDs, n (%)	7 (33.3)	3 (25.0)	0 (0.0)	10 (24.4)

bDMARDs, biological disease-modifying antirheumatic drugs; BMI, body mass index; n, number of patients; NSAIDs, non-steroidal anti-inflammatory drugs; RA, rheumatoid arthritis; SpA, spondyloarthropathies; tsDMARDs, targeted synthetic disease-modifying antirheumatic drugs.

with RMDs treated with b/tsDMARD do not differ from the general population (12.0% mortality rate and hospitalisation rate 53.6% by COVID-19 in Spain[1]). Of interest, these high mortality and hospitalisation rates are likely due to a diagnostic bias with PCR testing reserved for the most symptomatic patients, as suggested by a recent (unpublished) report by the Spanish Ministry of Health showing a prevalence of IgG seroconversion to SARS-Cov-2 of 5% in Spain. That is 10 times greater than the PCR confirmed cases (1). The present data, in addition to previous publications, is crucial to clarify the risks of patients with rheumatic diseases and their immunosuppressive medications. Doubtlessness, additional studies are still needed. To this end, the SER is prospectively collecting information on COVID-19 in three registries (BIOBADASER, RELESSER and CARMA) in more than 9000 patients with rheumatic diseases.

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