Susceptibility and severity of COVID-19 in patients treated with bDMARDS and tsDMARDs: a population-based study

Patients with autoimmune conditions treated with biological agents have an increased risk of severe infections.[1 2] Very few studies have evaluated the susceptibility and severity of coronavirus disease 2019 (COVID-19) in patients treated with biological disease-modifying antirheumatic drugs (bDMARDs) or targeted synthetic DMARDs (tsDMARDs).[3 4] Some of these studies suggest a protective role of these drugs for COVID-19; however, they consist of small series, and the results are unclear.

Therefore, we decided to evaluate in a population-based study the risk of COVID-19 infection and its severity in the patients treated with bDMARDs or tsDMARDs in a geographic area (Emilia Romagna) at high diffusion of COVID-19.

We identified 1195 patients treated with the bDMARDs or tsDMARDs listed in table 1 in Reggio Emilia area on 31 December 2019. Biological agents were classified according to the mechanism of action. The patients were registered in the database of the Hospital Pharmaceutical Service of the Reggio Emilia area, which delivers the drug directly to the patients. The database is updated every 3 months. All residents of Reggio Emilia area who have had rhinopharyngeal swabs, positive swabs and were hospitalised or died from COVID-19 from the beginning of the outbreak (27 February 2020) are registered in a centralised index. Swabs were performed in symptomatic patients at risk of having COVID-19. The fiscal code was used to identify and match patients treated with biological agents and with COVID-19 infection. We used data updated at 24 April. Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Table 1 Residents of the Reggio Emilia area treated with bDMARDS or tsDMARDS versus all residents: comparison among residents tested and residents positive for COVID-19 stratified by gender and classes of age

Residents of the Reggio Emilia area treated with bDMARDs or tsDMARDs									
	Total, n			Tested, n			Positive, n		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
Overall	523	672	1195	8	17	25	3	6	9
Hospitalised									4
Death									1
Age									
≤45	143	167	310	2	4	6	0	0	0
45–65	267	302	569	3	7	10	3	3	6
>66	113	203	316	3	6	9	0	3	3
Drug mechanism of action									
Anti-TNF-alpha*	334	436	770	4	13	17	2	3	5
Anti-IL-1†	12	7	19	0	1	1	0	1	1
Anti-IL-6R‡	14	56	70	0	0	0	0	0	0
Anti-IL-12/IL-23 anti-IL-23§	41	29	70	1	0	1	0	0	0
Anti-IL-17°¶	103	85	188	2	2	4	0	2	2
Anti-JAK**	14	39	53	1	1	2	1	0	1
Abatacept	5	20	25	0	0	0	0	0	0

All residents of the Reggio Emilia area									
	Total, n			Tested, n			Positive, n		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
Overall	261 563	270 328	531 891	3405	4542	7947	1697	2049	3746
Hospitalised									1342
Death									383
Age									
≤45	133 037	126 701	259 738	835	1377	2212	294	453	747
45–65	81 057	82 183	163 240	1177	1514	2691	655	691	1346
>66	47 469	61 444	108 913	1393	1651	3044	748	905	1653

*Etanercept, infliximab, adalimumab and their biosimilars, certolizumab pegol and golimumab.
†Anakirna and canakinumab.
‡Tocilizumab and sarilumab.
§ustekinumab and guselkumab.
¶Secukinumab, brodalumab and ixekizumab.
**Tofacitinib and baricitinib.
bDMARDs, biological disease-modifying antirheumatic drugs; tsDMARDs, targeted synthetic disease-modifying antirheumatic drugs.

Table 1 compares the residents of the Reggio Emilia area treated with bDMARDs or tsDMARDs versus all residents. The difference regarding the frequencies of patients with swabs was significant (1.7% vs 1.4%, p=0.001), not that of positive swabs (36.0% vs 47.1%, p=0.318), nor that of hospitalised or dying patients (44.4% vs 35.8%, p=0.730; 11.1% vs 10.2%, p=1.000, respectively). table 1 also shows the different bDMARDs and tsDMARDs grouped by the mechanism of action. None of the 70 patients treated with IL-6 blockers and only 1 of the 70 patients treated with anti-IL-12/IL-23 and anti IL-23 were tested. The one tested resulted negative. At multivariate logistic and Cox proportional hazards analyses adjusted by sex and age, patients treated with bDMARDs or tsDMARDs had a tendency of being more frequently tested (OR 1.19, 95% CI 0.80 to 1.77) and hospitalised (HR 1.28, 95% CI 0.32 to 5.11) and to be less frequently positive when tested (OR 0.62, 95% CI 0.27 to 1.42); however, the differences were not significant.

In our study, which had an accurate case ascertainment from two reliable sources and a sufficiently long follow-up to observe deaths, we did not find any statistically significant difference regarding the probability of being tested, having a positive swab when tested, being hospitalised and dying in our patients treated with bDMARDs or tsDMARDs . The observed tendency towards a reduced probability of being positive at swabs is probably related to the higher proportion of patients tested compared with general population. Our data confirm some preliminary data from Lombardia, the Italian area with the highest incidence of COVID-19, which seem to indicate that patients treated with traditional immunosuppressive drugs or bDMARDs or tsDMARDs are not at increased risk of severe COVID-19, but we did not observe a protective role.[3 4] We cannot exclude that patients with immune-mediated disorders taking IL-6 inhibitors or compounds suppressing IL-12/IL-23 axis might be somewhat protected against COVID-19 infection. In conclusion, our study did not show a different susceptibility and severity of COVID-19 in patients treated with bDMARDs or tsDMARDs. The number of patients is too small to provide definitive conclusions; further larger prospective studies need to be done to confirm our results.

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