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Immune response after SARS-CoV-2 vaccination in patients with inflammatory immune-mediated diseases receiving immunosuppressive treatment

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BACKGROUND

- Although there is increasing evidence on how the response to the SC2 vaccine may be impaired in patients with rheumatic diseases, many areas remain to be clarified. There is an urgent need for real-world data on the immune response to the SC2 vaccine in patients with IMIDs treated with immunosuppressants and on the incidence and severity of SC2 infection in adequately vaccinated patients.

OBJECTIVE

- Our main aim was to study antibody-mediated protection and cellular-mediated response after SC2 vaccination in patients with IMIDs treated with different types of immunosuppressive drugs.
- Our secondary objectives were as follows: to describe the frequency and severity of SC2 infections after vaccination in patients with IMIDs.

METHODS

- Ambispective observational study of patients with various IMIDs, namely, rheumatoid arthritis (RA), spondyloarthritis (SpA), psoriatic arthritis (PsA), and connective tissue disease (CTD).
- Patients were receiving b/tsDMARDs, as follows: TNF inhibitors (TNFi), rituximab, anti-interleukin 6 receptor (anti-IL6R) agents, and JAKi.
- Patients were recruited consecutively over 3 months, during which time they were invited to participate at their visits to the clinic (the month before and after the second and third doses of vaccine).
- The **inclusion criteria** were as follows: i) IMIDs treated with b/tsDMARDs; and ii) availability of laboratory tests 4-6 weeks after the second and/or third dose of the SC2 vaccine.
- Serum samples were obtained 4-6 weeks after the second or third dose to evaluate the humoral, cell-mediated, and functional response to the vaccine.
- The **humoral response** was assessed using fluoroenzyme immunoassay (EliA SARS-CoV-2-Sp1 IgG Test, Thermo Fisher Scientific) with serum samples.
- The **cellular response** using a QuantiFERON SARS-CoV-2 (QTF-SC2) Starter Pack (Quiagen), was evaluated only in patients with a poor humoral response, which was defined as IgG antibody levels against SARS-Cov2 <100 IU/ml.
- The frequency data were compared using the Pearson chi-squared or Fisher exact test. Unpaired continuous data were compared using the unpaired t test or Mann–Whitney test, depending on the data distribution. For multiple comparisons, one-way ANOVA or the Kruskal–Wallis test was used. Associations between the humoral immune response to SC2 vaccine, clinical variables, and treatments were evaluated using univariate and multivariate logistic regression models.

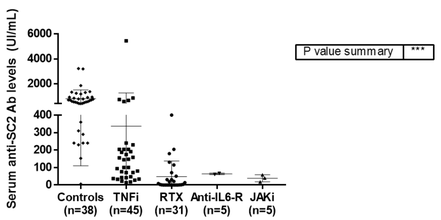
RESULTS

- **Patient characteristics**. Data for sex, comorbidities, diagnosis, serological findings, and use of methotrexate and corticosteroids are expressed as n (%). Data on age, BMI, and methotrexate and corticosteroid doses are expressed as mean±SD.

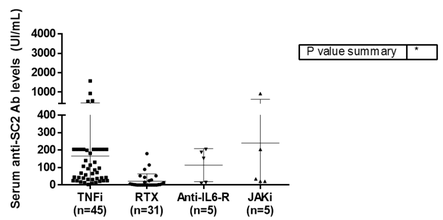
	Controls n=38	All patients N=86	TNFi n=45	RTX n=31	Anti-IL6R n=5	JAKi n=5
Demographic and clinical characteristics						
Sex (female)*	30 (79%)	55(64%)	19 (42%)	27 (87%)	4 (80%)	5 (100%)
Age	48±14	56±14*	53±13	61±12	52±22	56±10
BMI	24±2.4	27±6.1*	26±6.4	27±5.4	26±8.5	21±1.6
Comorbidities						
Diabetes	0 (0%)	1 (1.2%)	1 (2.2%)	0 (0%)	0 (0%)	0 (0%)
Arterial hypertension	7 (18%)	29(34%)	12 (27%)	15 (48%)	1 (20%)	1 (20%)
Current smokers	4 (12%)	12(14%)	5 (31%)	5 (31%)	1 (6.3%)	1 (6.3%)
Chronic lung disease	4 (12.5%)	2(2.3%)	0 (0%)	2 (6.5%)	0 (0%)	0 (0%)
Dyslipidemia	11 (29%)	26 (30%)	13 (29%)	13 (42%)	0 (0%)	0 (0%)
Diagnosis						
RA	---	50 (58%)	15 (33%)	27 (87%)	3 (60%)	5 (100%)
SpA	---	20 (23%)	20 (45%)	0 (0%)	0 (0%)	0 (0%)
PsA	---	10 (12%)	10 (22%)	0 (0%)	0 (0%)	0 (0%)
CTD	---	6 (7%)	0 (0%)	4 (13%)	2 (40%)	0 (0%)
Serology findings						
RF+	---	45 (47%)	13 (29%)	25 (83%)	2 (40%)	5 (100%)
ACPA+	---	47(55%)	14 (34%)	25 (86%)	3 (75%)	5 (100%)
HLA-B27+	---	14(16%)	14 (47%)	0 (0%)	0 (0%)	0 (0%)
ANA+	---	19 (22%)	5 (12%)	11 (38%)	3 (40%)	0 (0%)
Treatment						
Methotrexate use	---	63 (73%)	23 (51%)	16 (52%)	2 (40%)	4 (80%)
Methotrexate dose (mg/week)	---	16.5±6.1	16±6.5	17.5±5.5	17.5±3.5	13±8
Prednisone use	---	23 (27%)	6 (13%)	14 (45%)	2 (40%)	1 (20%)
Prednisone dose (mg/day)	---	3.14±2.1	1±1.1	3.6±1.6	6.3±1.7	2.5±3.5
Time under b/tsDMARD	---	12.1±14.7	10.3±7.4	17±9.2	17±13.2	16±3.8

- **Humoral immune response after the second and third vaccine doses.** A) Comparison of anti-SC2 Ab levels between controls and treatment groups after the second vaccine dose. B) Comparison of anti-SC2 Ab levels between treatment groups after the third vaccine dose.

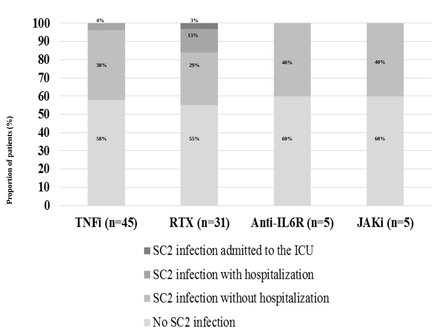
A)



B)

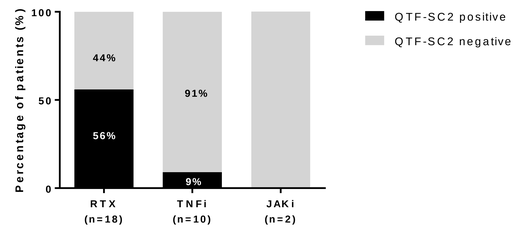


- **Proportion of patients with SC2 infections in each therapy group.**



- A **regression analysis** was performed to assess which factors were associated with undetectable levels of anti-SC2 antibody. In the multivariate analysis, **only receiving rituximab was associated with lack of humoral response (OR: 18.5, 95%IC: 2-172).**

- **Cellular immune response after the second and third vaccine doses.** Comparison of cellular response between treatment groups after the second vaccine dose



CONCLUSIONS

- **The humoral immune response to the SC2 vaccine is poorer in patients than in healthy controls, especially in those treated with rituximab.**
- **Cellular-mediated immune response can be detected despite having a poor humoral response, especially in patients under rituximab.**
- **A scheduled delay of the rituximab infusion to ensure a better humoral response to the vaccine would be recommended in patients with IMID.**
- **Severe infections in vaccinated patients with IMIDs are rare, mainly observed in patients treated with rituximab.**