Humoral immune response against BNT162b2 mRNA COVID-19 vaccine in patients with rheumatic disease undergoing immunosuppressive therapy
A Japanese monocentric study

Koichi Sugihara, MDa,*, Risa Wakiya, MD, PhDa, Tomohiro Kameda, MD, PhDa, Hiromi Shimada, MD, PhDa, Shusaku Nakashima, MDa, Mikiya Kato, MDa, Taichi Miyagi, MDa, Yusuke Ushio, MDa, Mao Mizusaki, MDa, Rina Mino, MDa, Kanako Chuo, MDa, Yumi Nomura, MDa, Masayuki Inoo, MD, PhDa, Norimitsu Kadowaki, MD, PhDa, Hiroaki Dobashi, MD, PhDa

Abstract
We investigated serum total antibody titers against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein receptor-binding domain after BNT162b2 mRNA vaccination against coronavirus disease 2019 (COVID-19) in Japanese patients taking various immunosuppressive medications for rheumatic disease. In 212 outpatients with rheumatic diseases at Kagawa University Hospital and 43 healthy volunteers (controls), all of whom had received 2 doses of BNT162b2 vaccine, serum antibody titers of SARS-CoV-2 spike protein were analyzed at least 14 days after the second dose. Many of the patients were taking immunosuppressive agents to manage their rheumatic disease. The antibody titers against SARS-CoV-2 spike protein in these patients were significantly lower than those in controls. The analysis of therapeutic agents revealed that the antibody titers in patients treated with rituximab were much lower than those in controls. In patients treated with tacrolimus, baricitinib, azathioprine, mycophenolate mofetil, abatacept, tumor necrosis factor inhibitors, cyclosporine, interleukin-6 inhibitors, methotrexate, or glucocorticoids, antibody titers were moderately lower than those of controls. Interleukin-17 and interleukin-23 inhibitors did not impair the humoral response. In addition, the combination of methotrexate with various immunosuppressive agents reduced titers, although not significantly. In Japanese patients with rheumatic disease, many immunosuppressants impaired the immune response to the BNT162b2 vaccine. The degree of decline in antibody titers differed according to immunosuppressant. When used concomitantly with other immunosuppressants, methotrexate may impair the immune response to the BNT162b2 vaccine. However, immunomodulatory treatments such as interleukin-17 and -23 inhibitors may not attenuate this response in patients with rheumatic disease.

Abbreviations: CI = confidence interval, COVID-19 = coronavirus disease 2019, IQR = interquartile range, JAK = Janus kinase, RMD = rheumatic and musculoskeletal diseases, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Keywords: antibody formation, COVID-19, immunosuppression therapy, mRNA vaccine, rheumatic diseases

1. Introduction
In comparison with the general population, patients with autoimmune and inflammatory rheumatic disease are generally at a higher risk for viral and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections that necessitate hospitalization. Outcomes of coronavirus disease 2019 (COVID-19) are also worse in these patients than in the general population. Therefore, patients with rheumatic and musculoskeletal diseases (RMDs) are strongly encouraged to receive COVID-19 vaccination. In patients with systemic rheumatic diseases, outcomes of COVID-19 are reportedly better in vaccinated patients than in unvaccinated patients. When used concomitantly with other immunosuppressants, methotrexate may impair the immune response to the BNT162b2 vaccine. However, immunomodulatory treatments such as interleukin-17 and -23 inhibitors may not attenuate this response in patients with rheumatic disease.
At the time that this article was written, 3 COVID-19 vaccines (BNT162b2, mRNA-1273, and ChAdOx1 nCoV-19) had been approved in Japan. Of these, BNT162b2 is the COVID-19 vaccine most frequently administered in Japan. Although the safety and efficacy of the BNT162b2 vaccine were proved in the general population in 1 study,[13] patients receiving immunosuppressive therapy were excluded from that trial. So far, various levels of immune responses to mRNA COVID-19 vaccines have been reported in patients taking immunosuppressive medication for rheumatic disease. Although the results of past studies were not always consistent, some immunosuppressants – rituximab, mycophenolate mofetil, abatacept, methotrexate, and glucocorticoids – may reduce the immune response to the BNT162b2 vaccine.[4–17] In contrast, the effects of other immunosuppressants – such as tumor necrosis factor inhibitors, interleukin-6 inhibitors, interleukin-23 inhibitors, interleukin-17 inhibitors, Janus kinase (JAK) inhibitors, azathioprine, cyclosporine, and tacrolimus – on immune responses to mRNA COVID-19 vaccines are unclear, and more data are needed.

Furthermore, most of the data on immune responses against mRNA COVID-19 vaccines in patients receiving immunosuppressive therapy for their rheumatic disease come from Western countries, and such data from Japanese patients, whose genetic backgrounds differ from those of Western populations, are limited. Recently, we demonstrated and reported that immunogenicity to BNT162b2 is decreased in Japanese patients with RMDs under methotrexate treatment, similar to Western reports.[18] However, the differential effects of various rheumatic disease drugs, including methotrexate, on the immunogenicity of this vaccine have not yet been fully elucidated. Therefore, we compared the immunogenicity of the BNT162b2 vaccine in Japanese patients receiving various immunosuppressive drugs for RMDs with healthy controls.

2. Methods

2.1. Participants

For this study, we recruited 212 outpatients (aged ≥ 20 years) with RMDs at Kagawa University Hospital, Kagawa, Japan, who had received 2 doses of the BNT162b2 vaccine. All patients included in the study had rheumatologist-confirmed definitive diagnoses of RMDs. Clinical information, such as age, sex, type of RMD, and treatment, came from medical records. Forty-three healthy volunteers vaccinated with 2 doses of BNT162b2 served as the control group. No patient or healthy volunteer had a history of COVID-19.

Participants received the second vaccine dose between March 13, 2021 and September 18, 2021, and their serum was collected at least 14 days afterward. The date of vaccination was confirmed and recorded with the vaccination certificate at an outpatient visit. The participants continued to receive immunosuppressive therapy before and after COVID-19 vaccination without temporary suspension.

This study was approved by the ethical committee of Kagawa University (2021-078) and was carried out according to the principles of the Declaration of Helsinki. Informed consent to participate was obtained from each participant.

2.2. Endpoints of the study

This study’s endpoint was the effect of immunosuppressive treatment on immunogenicity induced by the BNT162b2 vaccine in patients with RMDs and controls, measured at least 2 weeks after the second vaccine dose. We defined biologics, JAK inhibitors, methotrexate, azathioprine, mycophenolate mofetil, tacrolimus, cyclosporine, and glucocorticoids as immunosuppressive agents. Patients who had received rituximab at any time were considered treated with rituximab.

2.3. Measurement of antibody response

Titers of serum total antibody (immunoglobulins M and G) to the SARS-CoV-2 spike protein receptor-binding domain were tested by enzyme-linked immunosorbent assay (Elecsys Anti-SARS-CoV-2 S RUO; Roche, Basel, Switzerland) according to the manufacturer’s instructions.

2.4. Statistical analysis

All values reported are medians with interquartile ranges (IQRs) unless otherwise noted. We used the Mann–Whitney U, Kruskal–Wallis, and Steel tests to compare antibody levels. All P values were 2-sided, and a P value of <.05 was considered significant. We used JMP® Pro 14 software (SAS Institute, Cary, NC) to analyze the data.

3. Results

3.1. Study population

Table 1 lists the clinical features of healthy controls and patients with RMDs. The average ages were 63.1 ± 14.7 years for the patients with RMD and 50.4 ± 12.6 years for the healthy controls; the difference was significant (P < .001). The association between age and antibody titer was insignificant for the controls (correlation coefficient: -.6, 95% confidence interval [CI]: -.35 to +.25) but weakly negative for the patients (correlation coefficient: -.20, 95% CI: -.33 to -.07). The median time between the second immunization and blood sampling was significantly shorter for the patients (32 days; IQR 22–49 days) than for the healthy controls (57 days; IQR 55–58 days; P < .001). The association of median time between second immunization and blood sampling with antibody titer was also insignificant for healthy controls (correlation coefficient +.03, 95% CI: -.27 to +.33) but weakly negative for the patients (correlation coefficient: -.16, 95% CI: -.29 to -.02).

Among the 212 patients with RMDs, rheumatoid arthritis was the most common disease, followed by Sjögren’s syndrome and systemic lupus erythematosus (Table 2).

The medications most commonly taken by patients were glucocorticoids, followed by methotrexate and tacrolimus (Table 3). The median time between the last treatment with rituximab and the first vaccine dose was 325 days (IQR 124–872).

3.2. Serum antibody titers against SARS-CoV-2 spike protein after BNT162b2 vaccine

Table 4 lists serum antibody titers against the SARS-CoV-2 spike protein according to the use of immunosuppressive treatments compared to control titers. Overall, the antibody titers were significantly lower in the patients than in the controls. The antibody titers of 27 patients who did not take immunosuppressive therapy were not significantly different from those of the healthy controls.

---

Table 1

**Characteristics of study participants.**

| Characteristic | Healthy controls | Patients with RMDs | P value |
|---------------|------------------|-------------------|--------|
| N             | 43               | 212               |        |
| Mean age, yrs (standard deviation) | 50.4 ± 12.6 | 63.1 ± 14.7 | <.001 |
| Gender        |                  |                   |        |
| Male (n)      | 14 (32.6%)       | 39 (18.4%)        |       |
| Female (n)    | 29 (67.4%)       | 173 (81.6%)       | .062  |
| Median number of d between second immunization and blood sampling (IQR) | 57 (65–58) | 32 (22–49) | <.001 |

IQR = interquartile range, RMD = rheumatic and musculoskeletal disease.
The titers of antibody to SARS-CoV-2 spike protein receptor-binding domain in the entire population of Japanese patients with RMDs in this study were lower than those in the healthy controls, as expected from past reports from Western countries.\[4,19\] Data in previous studies have suggested that interleukin-17 and interleukin-23 inhibitors do not impair the immunogenicity of mRNA COVID-19 vaccines. Mahil et al reported that in patients with psoriasis who were taking interleukin-17 or interleukin-23 inhibitors, the humoral immunogenicity was not impaired compared to healthy controls.\[6–12,14–17\] The effect of rituximab on the immunogenicity of mRNA COVID-19 vaccines has not been studied widely, although tacrolimus is frequently administered for RMDs in Japan. The reason may be that tacrolimus is not used much for RMDs in Western countries. In our study, 32 patients with RMDs were taking tacrolimus. To the best of our knowledge, this is the largest cohort of patients taking tacrolimus for RMDs. Our findings suggest that, compared with other immunosuppressants, tacrolimus might have a lesser effect on the immunological effects of the BNT162b2 vaccine.

The effect of tacrolimus on the immunogenicity of mRNA COVID-19 vaccines has not been studied widely, although tacrolimus is frequently administered for RMDs in Japan. The reason may be that tacrolimus is not used much for RMDs in Western countries. In our study, 32 patients with RMDs were taking tacrolimus. To the best of our knowledge, this is the largest cohort of patients taking tacrolimus for RMDs. Our findings suggest that, compared with other immunosuppressants, tacrolimus might have a lesser effect on the immunogenicity of the mRNA COVID-19 vaccines.

Many past reports indicated that rituximab severely impaired the immunogenicity of mRNA COVID-19 vaccines, as in this study.\[14–12,4–17\] The effect of rituximab on the immunogenicity of these vaccines is hypothesized to weaken with time.\[10\] The European League Against Rheumatism recommends that in patients receiving B cell–depleting therapy, including rituximab, vaccines should be administered 1 month before or 6 months after such therapy.\[21\] Our study found no distinct correlation between the time since the last rituximab treatment and the antibody titer. This suggests that rituximab continues to reduce the immunogenicity of mRNA COVID-19 vaccines for a long time.

### Table 2

| Diagnosis                        | N (%) |
|----------------------------------|-------|
| Rheumatoid arthritis             | 93 (43.9%) |
| Systemic lupus erythematosus     | 27 (12.7%) |
| Antiphospholipid syndrome        | 6 (2.8%) |
| Sjögren’s syndrome               | 35 (16.5%) |
| Systemic lupus erythematosus     | 9 (4.2%) |
| Polymyalgia rheumatica           | 1 (0.5%) |
| Polyarteritis nodosorum          | 15 (7.1%) |
| Anti–neutrophil cytoplasmic antibody–associated vasculitis | 12 (5.7%) |
| IgG4-related disease             | 5 (2.4%) |
| Spondyloarthrits                 | 17 (8.0%) |
| Behçet’s disease                 | 5 (2.4%) |
| Takayasu’s arteritis             | 5 (2.4%) |
| MCTD                             | 5 (2.4%) |
| Others*                          | 7 (3.3%) |

IgG4: immunoglobulin G4; MCTD: mixed connective tissue disease; RMD: rheumatic and musculoskeletal disease.

*Polyarteritis nodosorum (n = 1), relapsing polychondritis (n = 1), undifferentiated connective tissue disease (n = 1), adult-onset Still’s disease (n = 1), and syndrome of thrombocytopenia, anasarca, fever, reticulin fibrosis, and organomegaly (TAFD; n = 1).

### Table 3

| Immunosuppressant               | N (%) |
|----------------------------------|-------|
| Methotrexate (9.2 ± 2.8 mg/wk)   | 78 (36.8%) |
| Azathioprine                     | 13 (6.1%) |
| Mycophenolate mofetil            | 11 (5.2%) |
| Tacrolimus (2.2 ± 1.0 mg/d)      | 32 (15.1%) |
| Cyclosporine                     | 8 (3.8%) |
| Tumor necrosis factor inhibitors | 26 (12.3%) |
| Interleukin-6 inhibitors         | 10 (4.7%) |
| Rituximab                        | 6 (2.9%) |
| Abatacept                        | 10 (4.7%) |
| Interleukin-17 or interleukin-23 inhibitors | 7 (3.3%) |
| Baricitinib                      | 6 (2.8%) |
| Glucocorticoids (prednisolone, 3.5 ± 3.2 mg/d) | 103 (48.6%) |
| No immunosuppressant             | 27 (12.7%) |

RMD: rheumatic and musculoskeletal disease.

immunosuppressive medication and 7 patients treated with interleukin-17 or interleukin-23 inhibitors were similar to controls. The antibody titers in patients treated with rituximab were much lower than those in the controls. In patients treated with tacrolimus, baricitinib, azathioprine, mycophenolate mofetil, abatacept, tumor necrosis factor inhibitors, cyclosporine, interleukin-6 inhibitors, methotrexate, and glucocorticoids, antibody titers were moderately lower than those of the controls.

Table 5 lists serum antibody titers against SARS-CoV-2 spike protein according to immunosuppressive drugs received concomitantly with methotrexate. Interleukin-6, interleukin-17, and interleukin-23 inhibitors were taken with methotrexate, as were tacrolimus, glucocorticoids, cyclosporine, tumor necrosis factor inhibitors, abatacept, and baricitinib. The antibody titers were lower, although not significantly, in patients treated with a combination of methotrexate and any of these immunosuppressants, except abatacept, than in the controls.

### 4. Discussion

In this study, the patients with RMDs were significantly older than the healthy controls. The median time between the second immunization and blood sampling was significantly shorter for the patients than for the controls. Although these differences might have affected the results, we hypothesized that the antibody titers of patients with RMDs could be compared with those of healthy controls because the expected variations by age and trial between second immunization and blood sampling were smaller than the difference in antibody titers between the patients and the controls, and so they may have canceled each other out.

The titers of antibody to SARS-CoV-2 spike protein receptor-binding domain in the entire population of Japanese patients with RMDs in this study were lower than those in the healthy controls, as expected from past reports from Western countries.\[4,19\] Data in previous studies have suggested that interleukin-17 and interleukin-23 inhibitors do not impair the immunogenicity of mRNA COVID-19 vaccines. Mahil et al reported that in patients with psoriasis who were taking interleukin-17 or interleukin-23 inhibitors, the humoral immunogenicity in response to a second dose of the BNT162b2 vaccine was not impaired compared to healthy controls.\[20\] In a multicenter study in Israel, interleukin-17 inhibitors did not reduce the immunogenicity of the BNT162b2 vaccine.\[4\] These results and our findings indicate that interleukin-17 and interleukin-23 inhibitors do not counteract the immunological effects of the BNT162b2 vaccine.
Methotrexate is one of the immunosuppressive drugs most frequently used for RMD globally, and its effects on immune responses induced by mRNA COVID-19 vaccines have been reported by many researchers. Although Braun-Moscovici et al and Tani et al reported that methotrexate did not negatively affect the humoral response,[7,13] many other authors have found that methotrexate impaired the immunogenicity of the mRNA COVID-19 vaccines.[11,13,15–17,22,23] Methotrexate is often combined with other immunosuppressants, but little is known about the effect of such combinations on the immunogenicity of mRNA COVID-19 vaccines.[9] Our findings suggest that methotrexate potentially impairs the immunogenicity of these vaccines when it is taken concomitantly with other immunosuppressants.

According to several reports, mycophenolate mofetil and abatacept reduce the immunogenicity of mRNA COVID-19 vaccines.[4,7,8,12,15–17,24] In our study, too, these drugs reduced the antibody titers.

The effects of tumor necrosis factor inhibitors, interleukin-6 inhibitors, and JAK inhibitors on the immunogenicity of the mRNA COVID-19 vaccine are currently unclear because previously reported data have been inconsistent.[6,10,17,22,23] In our study, these drugs reduced the antibody titers moderately. More data are needed to clarify these drugs' effects.

Evidence that glucocorticoids impair responses to mRNA COVID-19 vaccines has been reported, as in this study; the mean glucocorticoid dosages in previous studies were 6.2 mg/day[4] and 3.8 mg/day.[13] No significant dose-dependent effect of glucocorticoids on vaccine response was observed in our study. However, expected variations in antibody titer according to immunosuppressive treatment on the immunogenicity of the COVID-19 vaccine. Still, the benefit of the suspension might not outweigh the risk of RMD flare.

This study was conducted with Japanese patients who had RMDs. Our previous reports have shown that methotrexate reduces the immunogenicity of the BNT162b2 in Japanese patients with RMDs.[9] This study newly showed the effects of various immunosuppressive drugs, including methotrexate, on the immunogenicity of the BNT162b2 in Japanese patients with RMDs but the results were little different from past reports about Western patients. There may be little racial difference in the effects of immunosuppressive drugs on the immunogenicity of this vaccine.

In this study, we investigated antibody titer as an indicator of humoral immunity. In order to gain a deeper understanding of the effects of individual immunosuppressants on the humoral immunity of mRNA COVID-19 vaccines, detailed functional analysis related to antibody production, including dendritic cells, T-lymphocytes and B-lymphocytes will be important.

This study had several limitations. First, the antibody titers might not reflect total vaccine efficacy. Both humoral and cellular immune responses are important in immunity to the virus. The BNT162b2 vaccine reportedly induced neutralizing antibodies and poly-specific T cells in humans.[31] Although a significant correlation between the humoral and the cellular responses to mRNA COVID-19 vaccines was reported,[24] the antibody titer might reflect only part of the overall response. Furthermore, the level of the antibody needed for immunity remains unclear. Further study is needed to clarify the relationship between the antibody titer and vaccine efficacy. Second, the significant differences in average age and the median time between the second immunization and blood sampling between the patients and the healthy controls might have affected the results. However, expected variations in antibody titer according to these factors were small. Third, although no participants in this study reported any history of COVID-19, the serum antibody level was not measured before vaccination; we, therefore, could not confirm whether any participants had been exposed previously to SARS-CoV-2.

In conclusion, many immunosuppressants taken for RMDs impaired the immunogenicity of the BNT162b2 vaccine in Japanese patients. The degree of decline of antibody titers differed according to immunosuppressant. Methotrexate potentially impairs the immunogenicity of mRNA COVID-19 vaccines when used concomitantly with other immunosuppressants. However, immunomodulatory treatments such as interleukin-17 and interleukin-23 inhibitors may not attenuate the effect of the BNT162b2 vaccine in patients with RMDs. Further study with larger numbers of participants is needed to clarify the effects of individual immunosuppressants and diseases on the efficacy of mRNA COVID-19 vaccines.

Table 5

| Table 5 | Serum antibody titer against SARS-CoV-2 spike protein according to the concomitant use of methotrexate. |
|--------|----------------------------------------------------------------------------------|
| Immunosuppressive medication | Median serum antibody titer (IQR), U/mL | Pvalue |
|        | With methotrexate | Without methotrexate |        |
| Interleukin-17 or interleukin-23 inhibitors (n = 7) | 255.4 (202.9–307.9) n = 2 | 1148 (755.6–4201.5) n = 5 | .081 |
| Tacrolimus (n = 32) | 366.8 (22.6–655.0) n = 11 | 397.1 (128.8–838.2) n = 21 | .341 |
| Glucocorticoids (n = 103) | 113.1 (32.3–266.3) n = 26 | 232.4 (43.2–406.1) n = 77 | .126 |
| Interleukin-6 inhibitors (n = 10) | 171.8 (130.3–183.3) n = 3 | 399.2 (241.9–501.3) n = 7 | .111 |
| Cyclop香港 | 168.2 (168.2–168.2) n = 1 | 248.7 (1.0–548.1) n = 7 | .663 |
| Tumor necrosis factor inhibitors (n = 26) | 48.5 (21.3–208.4) n = 20 | 248.2 (157.2–311.7) n = 6 | .083 |
| Abatacept (n = 10) | 117.7 (100.4–134.9) n = 2 | 51.3 (13.5–228.0) n = 8 | .695 |
| Baricitinib (n = 6) | 62.4 (40.6–161.3) n = 4 | 127.6 (4.9–250.2) n = 2 | 1 |

IQR = interquartile range.
Acknowledgments
The authors would like to thank Enago (www.enago.jp) for the English language review.

Author contributions
All authors were involved in drafting the article and revising it critically for important intellectual content. KS and RW wrote the manuscript. KS interpreted and analyzed the data together with RW, HS, MK, TK, SN, TM, YU, RM, MM, KC, YN, MI, NK, and HD. All authors read and approved the final manuscript.

Conceptualization: Koichi Sugihara, Hiroaki Dobashi.
Data curation: Koichi Sugihara.
Investigation: Koichi Sugihara.
Supervision: Hiroaki Dobashi.
Validation: Risa Wakiya, Tomohiro Kameda, Hiromi Shimada, Shusaku Nakashima, Mikiya Kato, Taichi Miyagi, Yusuke Ushio, Mao Mizusaki, Rina Mino, Kanako Chuo, Yumi Nomura, Masayuki Inoo, Norimitsu Kadowaki, Hiroaki Dobashi.
Writing – original draft: Koichi Sugihara, Risa Wakiya.
Writing – review & editing: Koichi Sugihara, Risa Wakiya.

References
[1] Curtis JR, Johnson SR, Anthony DD, et al. American college of rheumatology guidance for COVID-19 vaccination in patients with rheumatic and musculoskeletal diseases, version 3. Arthritis Rheumatol. 2021;73:e60–75.
[2] Papagoras C, Fragoulis GE, Zioga N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med. 2020;383:2603–15.
[3] Furer V, Eviatar T, Zisman D, et al. Antibody response to a single dose of the BNT162b2 mRNA COVID-19 vaccine in patients with rheumatic and musculoskeletal diseases. Ann Intern Med. 2021;174:1572–85.
[4] Boyarsky BJ, Ruddy JA, Connolly CM, et al. Antibody response to the BNT162b2 mRNA COVID-19 vaccine in people receiving methotrexate or targeted immunosuppression: a longitudinal cohort study. Lancet Rheumatol. 2022;4:e42–52.
[5] Kennedy NA, Lin S, Goodhand JR, et al. Effect of methotrexate and targeted immunosuppression on humoral and cellular immune responses following BNT162b2: a cohort study. Lancet Rheumatol. 2021;3:e627–37.
[6] Sugihara K, Wakiya R, Shimada H, et al. Immunogenicity against the BNT162b2 mRNA COVID-19 vaccine in rheumatic disease patients receiving immunosuppressive therapy: An observational cohort study. Intern Med. 2022;61:1951–8.
[7] Haberman RH, Herati R, Simon D, et al. Methotrexate hampers immunogenicity to BNT162b2 mRNA COVID-19 vaccine in immune-mediated inflammatory disease. Ann Rheum Dis. 2021;80:1330–8.
[8] Friedman MA, Curtis JR, Winthrop KL. Impact of disease-modifying antirheumatic drugs on vaccine immunogenicity in patients with inflammatory rheumatic and musculoskeletal diseases. Ann Rheum Dis. 2021;80:1255–65.
[9] Iancovici L, Khateeb D, Harel O, et al. 2021. Rheumatoid arthritis and COVID-19: a multicenter study assessing humoral immunogenicity and safety of the mRNA SARS-CoV-2 vaccines in Greek patients with systemic autoimmune and autoinflammatory rheumatic diseases. J Autoimmun. 2021;125:102743.
[10] Sieiro Santos C, Calleja Antolin S, Moriano Morales C, et al. Immune responses to mRNA vaccines against SARS-CoV-2 in patients with immune-mediated inflammatory rheumatic diseases. RMD Open. 2022;8:e001898.
[11] Tzionouas AG, Bakasis AD, Goules AV, et al. A prospective multi-center study assessing humoral immunogenicity and safety of the mRNA SARS-CoV-2 vaccines in Greek patients with systemic autoimmune and autoinflammatory rheumatic diseases. J Autoimmun. 2021;80:1306–11.