Effectiveness and Safety of ANTI SARS-CoV-2 Vaccination in Transplant Patients Treated with Immunosuppressants: A Real-World Pilot Study with a 1-Year Follow-Up

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Abstract: SARS-CoV-2 is a betacoronavirus, which induced a severe pandemic infectious disease around the world. Even if several drugs have been suggested for its treatment, to date, the only strategy to reduce the severity of disease is represented by the use of vaccine. However, the lack of pre-marketing evidence in frail patients suggests the necessity of the real-world study of a vaccine benefit–risk profile. In this study, we evaluated the efficacy and the safety of SARS-CoV-2 vaccination in a cohort of 33 patients treated with an immunosuppressant after solid organ transplant. Both CLIA and LS/MS analysis were used to evaluate the levels of immunoglobulin (Ig)G anti SARS-CoV-2 and the therapeutic drug monitoring of immunosuppressant drugs. We documented that SARS-CoV-2 vaccination induced a dose- and gender-related serological response. In particular, in 63.6% of the enrolled patients, we documented a significant serological response at T2, and after a time related decrease, the booster dose induced a serological response in 72.7% of enrolled patients. In conclusion, the vaccine anti SARS-CoV-2 is immunogenic in patients under immunosuppression, and is not related to the development of ADRs. We also suggest that the booster dose could be used to increase the efficacy of the vaccination, particularly in women.

Keywords: SARS-CoV-2; vaccine; IgG; gender; safety

1. Introduction

SARS-CoV-2 is a betacoronavirus, an enveloped virus containing a large nucleoprotein (N)-encapsidated positive sense RNA genome. The viral lipid envelope incorporates three transmembrane proteins: the spike protein (S), membrane protein (M), and envelope protein (E). Streamers of SARS-CoV-2 bind to the receptor, ACE2, on the surface of the target cells and mediate subsequent viral uptake and fusion [1].
Some specific drugs have been approved for the treatment and prevention of SARS-CoV-2 infection:

- **Antivirals:** Nirmatrelvir/Ritonavir, Remdesivir, Molnupiravir;
- **Monoclonal antibodies:** Bamlanivimab/Etesevimab, Casirivimab/Imdevimab, Sotrovimab, Tixagevimab/Cilgavimab;
- **Vaccines:** mRNA vaccines, BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna) and viral vector vaccine Ad26.COV2.S (Johnson & Johnson/Janssen) [2], ChAdOx1-S (Astrazeneca).

According to the guidelines, COVID-19 vaccination is recommended, as soon as possible, for everyone who is eligible according to the CDC’s Advisory Committee on Immunization Practices Vaccination [2].

Since the beginning of the vaccination campaign, particular attention has been paid to frail patients because they are more prone to developing a serious and unfortunate clinical status. Patients with specific immunological conditions due to autoimmune diseases or those receiving immunosuppressive drugs or anti-cancer therapies have been considered as the priorities for immunization, particularly in Western countries, where, to date, they are almost fully vaccinated.

Even if there are no available data about these populations, because they had not been enrolled in the vaccine approval trials, vaccines in patients with cancer, hematopoietic stem cell transplantation, solid organ transplantation, multiple sclerosis (MS), inflammatory bowel disease (IBD), and rheumatologic and dermatologic autoimmune disorders were administered first [3].

Patients with organ transplantation are chronically treated with immunosuppressants that prevent the rejection of the transplanted organ but reduce immunocompetence, exposing the patient to severe forms of infections.

Peled et al. [4] documented a reduced immune response after two doses of COVID-19 vaccine in transplanted patients.

Moreover, Rincon-Arevalo et al. [5], when evaluating the effectiveness of the second dose of Comirnaty in 40 kidney transplant patients vs. the healthy controls, failed to report a comparable IgG titers, suggesting that immunosuppression resulted in impaired protective immunity after mRNA vaccination.

Similarly, in a real-world study, Havlin et al. [6] reported that none of the vaccinated lung transplant patients developed anti-SARS-CoV-2 IgG, suggesting that immunosuppressant therapy inhibits the humoral response to the COVID-19 vaccine. Furthermore, real-world data concerning vaccinated dialysis patients suggest that in these patients, the post-vaccination humoral response may be delayed and/or reduced by several factors related to the uremic condition [7].

However, there are no definitive data regarding the efficacy of vaccine in these patients. Moreover, the lack of pre-marketing evidence in these patients signals the need for the real-world study of a vaccine benefit-risk profile in immunocompromised patients.

Therefore, in the present study, we evaluated the response to anti SARS-CoV-2 vaccination in a cohort of patients undergoing solid organ transplantation through the serological immunoglobulin assay and the evaluation of the immunosuppressant drug blood concentration.

2. Materials and Methods

2.1. Study Design

We conducted a single center open label clinical study between 1 February 2021 and January 2022 in patients with solid organ transplant patients in treatment with immunosuppressive therapy referred to the University “Magna Graecia” of Catanzaro (Calabria, Italy) and vaccinated with the Comirnaty (BNT162b2) Pfizer-BioNTech vaccine. The study was approved by the Ethics Committee of Calabria Centro and carried out according to the Good Clinical Practice guidelines with the ethical principles of the Declaration of Helsinki. Before the start of the study, all participants signed their written informed consent.
2.2. Experimental Protocol

At the time of admission (T0) and before the administration of the first dose of anti-SARS-CoV-2 vaccine, the enrolled patients underwent two venous blood samples: One (plasma) for the evaluation of SARS-CoV-2 and the second (blood) for the therapeutic drug monitoring (TDM) of immunosuppressive drugs. Each patient sample was analyzed separately. The plasma sample was processed using SARS-CoV-2 IgG II Quant Assay Kit (Abbot Diagnostic, Irving, TX, USA) through the Architect i1000 instrument (Abbot Diagnostic, Irving, TX, USA). This assay is an automated two-step chemiluminescent microparticle immunoassay in which patient samples are incubated with the SARS-CoV-2 antigen coated paramagnetic microparticles, followed by the anti-human IgG acridinium labelled conjugate to generate a chemiluminescent reaction. The index (sample/control) was calculated by comparing the relative light units in the sample to the calibrator relative light units. Samples were interpreted as positive or negative according to the manufacturer’s instructions, with a cut-off index value of 1.0. The assay sensitivity was >99%. The samples were stored at 4–8 °C for up to one week, then frozen at −20 °C and thawed only once.

Blood samples, collected to evaluate immunosuppressant blood concentrations, were processed using liquid mass spectrometry (Shimadzu, Milan, Italy LCMS 8060/NX/50/45/40).

Follow-up was performed at several times: T1, II dose of vaccine: 3 weeks after T0; T2: 2 months after T1; T3: 3 months after T2; T4: 6 months after T1, in this time, the patients underwent the III dose of the vaccine; T5: 3 weeks after T4, end of the study. During the follow-ups, two blood samples (serum and blood) were taken from each patient for pharmacological studies. Moreover, during these times, each patient was evaluated for the development of adverse drug reactions using the Naranjo questionnaire, in agreement with our previous studies [8,9].

2.3. Inclusion and Exclusion Criteria

In this study, we enrolled patients of both sexes >18 years, with a history of renal transplant and in treatment with immunosuppressants, who underwent the vaccine anti-SARS-CoV-2 and signed the informed consent. On the other hand, patients with an history of allergy to one of the immunosuppressants were excluded.

2.4. End Points

The primary clinical end point was the statistically significant positivity to IgG anti-SARS-CoV-2 at each follow-up time compared to T0.

Finally, the primary safety end point was considered as the absence of ADRs, or drug–drug interactions (DDIs) related to the administration of vaccine. Consistent with our previous article, we used the Naranjo scale and the Drug Interaction Probability Scale to evaluate the development of ADRs or DDIs, respectively [10–13]. The development of ADRs that could lead to the discontinuation of treatment were defined as clinical failure.

2.5. Statistical Analysis

At the baseline, the independent sample 2-tailed t-test was used to compare the variables. For the categorical parameters, the chi-square test was applied. Changes from the baseline to the end of the study were analyzed using a ranked one-way analysis of variance (ANOVA) with a term for the treatment group. All data were expressed as the mean ± standard deviation (SD). The statistical significance was established at p < 0.05. All reported p-values are two-sided. All statistical analyses were performed by using SPSS 21.0 (IBM Corporation, Armonk, NY, USA).

3. Results

During the study period, 33 patients of both sexes were enrolled (mean age 55.4 ± 12.8) and completed the study. Of these, 19 were men (mean age 54.7 ± 12.7) and 14 women (mean age 55.9 ± 14.2) (p > 0.05) (Table 1). The most common transplant was from cadavers.
(30 patients, 88.2%), while three patients (three men) received an organ from a living donor (Table 1). The most common therapy was a triple treatment (61.7%) and the most common drug used was mycofenolate (26 patients, 78.8%) and then tacrolimus (25 patients; 75.8%) (Table 1).

Table 1. The demographics of the patients enrolled in the study. T0: admission; T1: II dose of vaccine: 3 weeks after T0; T2: 2 months after T1; T3: 3 months after T2; T4: 6 months after T1, in this time, the patients underwent the III dose of vaccine; T5: 3 weeks after T4, end of the study.

| Characteristics                  | Data        |
|----------------------------------|-------------|
| Patients (number)                | 33          |
| Men (number)                     | 19          |
| Women (number)                   | 14          |
| Age (mean ± standard deviation)  | 55.4 ± 12.8 |
| Tacrolimus (number)              | 25          |
| Everolimus (number)              | 1           |
| Cyclosporine (number)            | 7           |
| Mycofenolate (number)            | 26          |
| Sirolimus (number)               | 1           |
| Prednisone (number)              | 24          |
| Dexamethasone (number)           | 1           |
| Azathioprine (number)            | 1           |
| Transplant from                  |             |
| Cadaver (number)                 | 30          |
| Living (number)                  | 3           |

IgG-SARS-CoV-2 (AU/mL; mean ± standard deviation)

| T0       | 0     |
| T1       | 23.83 ± 52.14 |
| T2       | 1606.32 ± 3476.97 |
| T3       | 599.18 ± 1025.64 |
| T4       | 325.46 ± 568.15  |
| T5       | 9646.33 ± 14,176.99 |

3.1. Therapeutic Drug Monitoring (TDM)

Using the LC/MS instrument, we documented that the blood immunosuppressant levels were in the normal range during the follow-ups. The retrospective evaluation of TDM recorded in the same patients in the pre-pandemic period showed similar values (Table 2).

Table 2. The therapeutic drug monitoring of the immunosuppressants before and after I dose of vaccine and during the follow-ups. P-p: pre-pandemic. T0: admission; T1: II dose of vaccine: 3 weeks after T0; T2: 2 months after T1; T3: 3 months after T2; T4: 6 months after T1, in this time, the patients underwent the III dose of vaccine; T5: 3 weeks after T4, end of the study. Data are expressed as the mean ± standard deviation.

| Drug       | Normal Range ng/mL | P-p | T0     | T1     | T2     | T3     | T4     | T5     |
|------------|---------------------|-----|--------|--------|--------|--------|--------|--------|
| Tacrolimus | 5–15                | 6.2 ± 1.4 | 6.5 ± 1.6 | 6.3 ± 1.5 | 6.6 ± 1.8 | 6.4 ± 1.5 | 6.2 ± 1.4 | 6.3 ± 1.6 |
| Everolimus | 3–8                 | 5.2  | 5.6    | 5.4    | 5.6    | 5.7    | 5.5    | 5.6    |
| Cyclosporine| 300–600             | 86 ± 21.5 | 92 ± 25.3 | 90 ± 23.8 | 88 ± 23.4 | 87 ± 24.6 | 89 ± 25.4 | 87 ± 23.8 |
| Sirolimus  | 8.4                 | 7.8  | 8.1    | 8.3    | 7.9    | 8.2    | 8.3    |        |
| Mycofenolate| 2.8 ± 0.7           | 2.6 ± 0.9 | 2.9 ± 1.2 | 2.8 ± 1.1 | 3.1 ± 1.2 | 3.2 ± 1.1 | 3.1 ± 1.1 |       |
3.2. IgG Anti SARS-CoV-2

The CLIA test revealed that at T0, the serum IgG levels were 0.02 ± 0.08 µg/mL, without a gender difference (p > 0.05) (Table 3).

Table 3. The serum IgG levels in the enrolled patients at different times of the study. T0: Admission, I dose of vaccine; T1: II dose of vaccine: 3 weeks after T0; T2: 2 months after T1; T3: 3 months after T2; T4: 6 months after T1, in this time, the patients underwent the III dose of vaccine; T5: 3 weeks after T4, end of the study). We defined unresponsive to vaccine as IgG values < 50 AU/mL. Data are expressed as mean values. *p < 0.01.

| Patients            | T0   | T1      | T2      | T3      | T4      | T5      |
|---------------------|------|---------|---------|---------|---------|---------|
| All patients        | 0.22 | 23.83   | 1606.32 | 599.18  | 316.60  | 9024.51 |
| Unresponsive to vaccine | 0.02 | 8.72       | 8.42     | 7.27    | 15.29   | 15.24   |
| Responsive to vaccine | 0.22 | 174.93 * | 2519.40 * | 895.13 * | 658.15 * | 12,710.12 * |

In T1, we recorded a statistically significant increase in the serum IgG values in three patients: 1: man 45-year treated with mycophenolate + tacrolimus; serum IgG value: 209.9 µg/mL; 2: man 33-year treated with mycophenolate + tacrolimus + methylprednisone; serum IgG value: 158.3 µg/mL; 3 woman 57-year, treated with cyclosporine alone; IgG value: serum 156.6 µg/mL).

In T2, in 21 patients (63.6%) (13 men and eight women; mean age 56.4 ± 13.5), we documented a significant increase (p < 0.01) in IgG values (mean serum concentration 2519.4 ± 4057.13 AU/mL; Figure 1). The evaluation performed at T3 revealed that in 20 patients (59.4%; 12 men, eight women, mean age 56.3 ± 14.1), there was a significant decrease (p < 0.01) in the IgG levels (mean serum concentration 895.13 ± 1135.9 AU/mL) (Table 2). In these patients, mycophenolate and prednisone had been the drugs most commonly used (n: 14; 70%), followed by tacrolimus (n: 13; 65%). About six months after the II dose (T4), we documented a further significant decrease in the IgG levels (p < 0.01) and only 15 patients (45.4%; mean age 51.5 ± 14.7) presented a protective value of IgG (mean serum concentration 658.15 ± 668.1 AU/mL; Table 2). Finally, the booster dosage (T5) induced in 24 patients (72.7% mean age 57.6 ± 13.1) a significant increase (p < 0.01) in the IgG values (mean serum concentration 127,10.12 ± 15,584.40 AU/mL) (Table 3).

Figure 1. The gender difference of patients with protective values of IgG anti SARS-CoV-2 (>50 arbitrary unit/mL) during the follow-ups (T1, II dose of vaccine: 3 weeks after admission; T2: 2 months after T1; T3: 3 months after T2; T4: 6 months after T1, in this time, the patients underwent the III dose of vaccine; T5: 3 weeks after T4, end of the study). *p < 0.01.
When we evaluated the IgG values with respect to gender, we found that men were significantly related to the expression of IgG ($p < 0.01$; Figure 1), even if women presented significantly higher levels of IgG with respect to men ($p < 0.01$; Figure 2).

**Figure 1.** The gender difference of patients with protective values of IgG anti SARS-CoV-2 (>50 arbitrary unit/mL) during the follow-ups (T1: II dose of vaccine: 3 weeks after admission; T2: 2 months after T1; T3: 3 months after T2; T4: 6 months after T1, in this time, the patients underwent the III dose of vaccine; T5: 3 weeks after T4, end of the study). *$p < 0.01$.

**Figure 2.** The serum IgG levels in the enrolled response to vaccine (IgG > 50 AU/mL) in men and women. Data are expressed as the mean ± standard deviation at different follow-up (T0: admission, I dose of vaccine; T1: II dose of vaccine: 3 weeks after T0; T2: 2 months after T1; T3: 3 months after T2; T4: 6 months after T1, in this time, the patients underwent the III dose of vaccine; T5: 3 weeks after T4, end of the study). *$p < 0.05$; **$p < 0.01$.

### 3.3. ADRs Related to Vaccine

During the study period, we did not record the development of ADRs or of DDIs (primary safety end point), while we recorded 100% adherence to the treatment and 100% compliance with the experimental protocol.

However, six patients of both sexes (four men and two women) developed COVID-19 infection after the end of the study, with mild flu-like symptoms, without a correlation with respect to drugs or age (Table 4). Only in one patient (woman) did we document the absence of immunological response to the vaccine.

**Table 4.** The demographics of the enrolled patients who developed COVID-19 after the end of the study. Cyc: cyclosporine; Myc: mycophenolate; Methyl: methylprednisolone; Tac: tacrolimus. IgG levels represent the last value recorded before the SARS-CoV-2 infection.

| Patient | 1 | 2 | 3 | 4 | 5 | 6 |
|---------|---|---|---|---|---|---|
| Sex     | Man | Man | Man | Man | Woman | Woman |
| Age     | 45 | 71 | 49 | 35 | 72 | 61 |
| IgG (AU/mL) | 5682.3 | 5248.2 | 3985.2 | 2773.8 | 184.4 | 0.8 |
| Immunosuppressant | Cyc + myc | Cyc + Myc + Methyl | Tac + Myc + Methyl | Tac + Myc + Methyl | Tac + Myc + Methyl | Tac + Myc + Methyl |
| Organ transplant | Cadaver | Cadaver | Cadaver | Living | Cadaver | Cadaver |


4. Discussion

In this study, we evaluated the efficacy and safety of the vaccine anti SARS-CoV-2 in transplant patients under immunosuppressant treatment.

Immunosuppressants, usually used to reduce the immune activity in patients after organ transplant, could both increase the risk of viral load and reduce the immunogenicity of vaccines.

In a recent study, Haddadin et al. [10] documented that in patients >65 years of age, the use of mycophenolate and the mammalian target of rapamycin inhibitors in the post-transplant period were associated with decreased serologic response to influenza vaccines. To reduce the risk of losing the effectiveness of vaccines, in transplanted patients, there is a widespread practice of reducing anti-rejection with the increased probability of inducing graft rejection [11]. Data recorded using other vaccines may not be translated to the novel vaccines deployed for SARS-CoV-2.

In our study, comparing the TDM values of the immunosuppressants during the study with those of the same patients before the COVID-19 pandemic period, we did not evaluate any difference. In fact, as reported in the clinical records of each patient, the daily definite dose of the immunosuppressants was not modified during the vaccination period. A reduced seroconversion rate after one vaccination in patients with kidney transplant [12] and in patients treated with immunosuppressants was also observed [13].

Pendecki et al. [14], in 140 patients treated with immunosuppressant drugs for autoimmune rheumatic and glomerular diseases and evaluated both the serological and T-cell response after the first and the second-dose of SARS-CoV-2 vaccine, documented the immunogenicity of SARS-CoV-2 vaccination.

Boyarsky et al. [15], in an observational study, found that 301 transplanted patients (46%) had no antibody response following dose 1 or 2 of the SARS-CoV-2 mRNA vaccines. In our study, we documented that SARS-CoV-2 vaccination induced a dose- and gender-related serological response. In the present study, the vaccine caused a dose- and gender-related serological response. In fact, we documented an increased response 1 month after the second dose and after the booster dose. In 63.6% of the enrolled patients, we documented a significant serological response at T2, particularly in women.

In fact, in our study, we found that women presented significantly higher levels of IgG with respect to men, three and six months after the II dose of the vaccine (T3 and T4) and after the booster dose (T5). Even if we were not able to demonstrate the role of gender on immune response, this could represent a limitation of our study, so we can suppose that both sex hormones and the gene expression off the X chromosome could be involved in this difference. In particular, Libert et al. [16] documented that the X chromosome is involved in immune functions such as the Toll-like receptor 7, CD40 ligand, and forkhead box P3, which could explain this difference. However, we also cannot exclude that this difference may be related to the small sample size, and this represents another limitation of the present study.

Moreover, our data agreed with the clinical study of Palich et al. [17], which suggested to not delay the second dose beyond 21 days from the first vaccination dose. In our study, we also documented that the serological response decreased with a time-dependent pattern, particularly 6 months after the second dose. The booster induced an increase in immunological response in 24 patients (72.7%). Finally, in these patients, we did not record the development of ADRs related to the vaccine. At the end of the study, six patients developed COVID-19, but we failed to find a correlation with respect to the age or gender. Only in one patient did the vaccine not induce the stimulation of SARS-CoV-2 antibodies.

In conclusion, the vaccine anti SARS-CoV-2 is immunogenic in patients under immunosuppression, and is not related to the development of ADRs. Moreover, we suggest that the booster dose could be used to increase the efficacy of the vaccination, particularly in women.
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References

1. Ke, Z.; Oton, J.; Qu, K.; Cortese, M.; Zila, V.; McKeane, L.; Nakane, T.; Zivanov, I.; Neufeldt, C.J.; Cerikan, B.; et al. Structures and distributions of SARS-CoV-2 spike proteins on intact virions. Nature 2020, 588, 498–502. [CrossRef] [PubMed]

2. National Institutes of Health. Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19): NIH: Bethesda, MD, USA, 2022; Volume 2019, pp. 1–243.

3. Negahdaripour, M.; Shafiekhani, M.; Moezzi Iman, S.M.; Amiri, S.; Rasekh, S.; Bagheri, A.; Mosaddeghi, P.; Vazin, A. Ad... [CrossRef] [PubMed]

4. Peled, Y.; Ram, E.; Lavee, J.; Segev, A.; Wieder-Finesod, A.; Mandelboim, M.; Indenbaum, V.; Levy, I.; Raanani, E.; et al. Clinical experience and antibody response. J. Heart Lung Transpl. 2021, 40, 759–762. [CrossRef] [PubMed]

5. Rincon-Arevalo, H.; Choi, M.; Stefanski, A.-L.; Halleck, F.; Weber, U.; Szelinski, F.; Jahrsdörfer, B.; Schrezenmeier, H.; Ludwig, C.; Sattler, A.; et al. Impaired humoral immunity to SARS-CoV-2 BNT162b2 vaccine in kidney transplant recipients and dialysis patients. Sci. Immunol. 2021, 15, 60. [CrossRef] [PubMed]

6. Havlin, J.; Svorcova, M.; Dvorackova, E.; Lastovicka, J.; Lischke, R.; Kalina, T.; Hubacek, P. Immunogenicity of BNT162b2 mRNA COVID-19 vaccine and SARS-CoV-2 infection in lung transplant recipients. J. Heart Lung Transpl. 2021, 40, 754–758. [CrossRef] [PubMed]

7. Danthu, C.; Hantz, S.; Dahlem, A.; Duval, M.; Ba, B.; Guibbert, M.; Ouafii, Z.E.; Ponsard, S.; Berrahal, I.; Achard, J.-M.; et al. Humoral Response after SARS-CoV-2 mRNA Vaccination in a Cohort of Hemodialysis Patients and Kidney Transplant Recipients. J. Am. Soc. Nephrol. 2021, 32, 2153–2158. [CrossRef] [PubMed]

8. Serra, R.; Grande, R.; Buffone, G.; Gallelli, L.; De Francisiscis, S. The effects of minocycline on extracellular matrix in patients with chronic venous leg ulcers. Acta Phlebol. 2013, 14, 99–107.

9. Gareri, P.; Fazio, P.D.; Gallelli, L.; Fazio, S.D.; Davoli, A.; Seminara, G.; Cotroneo, A.; Sarr, G. De Venlafaxine—Propafenone Interaction Resulting in Hallucinations and Psychomotor Agitation. Ann. Pharmacother. 2008, 42, 434–438. [CrossRef] [PubMed]

10. Haddadin, Z.; Krueger, K.; Thomas, I.D.; Overt, E.T.; Isom, M.; Halasa, N. Alternative strategies of posttransplant influenza vaccination in adult solid organ transplant recipients. Am. J. Transpl. 2021, 21, 938–949. [CrossRef] [PubMed]

11. Vručišćak, M.; Grašalek, K.; Beliančinová, M.; Jesenák, M.; Macháleková, K.K.; Benko, J.; Samoš, M.; Dedinská, I. Acute kidney rejection after anti-SARS-CoV-2 virus-vectorized vaccine—Case report. NPJ Vaccines 2022, 7, 30. [CrossRef] [PubMed]

12. Negrea, L.; Rovin, B.H. Gross hematuria following vaccination for severe acute respiratory syndrome coronavirus 2 in 2 patients with IgA nephropathy. Weak anti—SARS-CoV-2 antibody response after the first injection of an mRNA COVID-19 vaccine in kidney transplant recipients. Kidney Int. 2021, 99, 1467. [CrossRef] [PubMed]

13. Boyarsky, B.J.; Ruddy, J.A.; Connolly, C.M.; Ou, M.T.; Werbel, W.A.; Garonzik-Wang, J.M.; Segev, D.L.; Paik, J.J. Antibody response to a single dose of SARS-CoV-2 mRNA vaccine in patients with rheumatic and musculoskeletal diseases. Ann. Rheum. Dis. 2021, 80, 1098–1099. [CrossRef] [PubMed]

14. Prendezki, M.; Clarke, C.; Edwards, H.; McIntyre, S.; Mortimer, P.; Gleeson, S.; Martin, P.; Thomson, T.; Randell, P.; Shah, A.; et al. Humoral and T-cell responses to SARS-vaccination in patients receiving immunosuppression. Ann. Rheum. Dis. 2021, 80, 1322–1329. [CrossRef] [PubMed]

15. Boyarsky, B.J.; Werbel, W.A.; Avery, R.K.; Tobian, A.A.R.; Massie, A.B.; Segev, D.L.; Garonzik-Wang, J.M. Antibody Response to 2-Dose SARS-CoV-2 mRNA Vaccine Series in Solid Organ Transplant Recipients. JAMA 2021, 325, 2204–2206. [CrossRef]

16. Libert, C.; Dejager, L.; Pinheiro, I. The X chromosome in immune functions: When a chromosome makes the difference. Nat. Rev. Immunol. 2010, 10, 594–604. [CrossRef] [PubMed]

17. Palich, R.; Veyri, M.; Marot, S.; Vozy, A.; Gligorov, J.; Maingon, P.; Marcelin, A.-G.; Spano, J.-P. Weak immunogenicity after a single dose of SARS-CoV-2 mRNA vaccine in treated cancer patients. Ann. Oncol. 2021, 32, 1051–1053. [CrossRef] [PubMed]