Efficacy of the BNT162b2 mRNA COVID-19 vaccine in patients with chronic lymphocytic leukemia

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Patients with chronic lymphocytic leukemia (CLL) have an increased risk for severe COVID-19 disease and mortality. The goal of this study was to determine the efficacy of COVID-19 vaccine in patients with CLL. We evaluated humoral immune responses to the BNT162b2 messenger RNA (mRNA) COVID-19 vaccine in patients with CLL and compared responses with those obtained in age-matched healthy control subjects. Patients received 2 vaccine doses, 21 days apart, and antibody titers were measured by using the Elecsys Anti-SARS-CoV-2 S assay after administration of the second dose. In a total of 167 patients with CLL, the antibody response rate was 39.5%. A comparison between 52 patients with CLL and 52 sex- and aged-matched healthy control subjects revealed a significantly reduced response rate among patients (52% vs 100%, respectively; adjusted odds ratio, 0.010; 95% confidence interval, 0.001-0.162; \( P < .001 \)). The response rate was highest in patients who obtained clinical remission after treatment (79.2%), followed by 55.2% in treatment-naive patients and 16.0% in patients under treatment at the time of vaccination. In patients treated with either Bruton’s tyrosine kinase inhibitors or venetoclax ± anti-CD20 antibody, response rates were considerably low (16.0% and 13.6%). None of the patients exposed to anti-CD20 antibodies <12 months before vaccination responded. In a multivariate analysis, the independent predictors of response were younger age, female sex, lack of currently active treatment, immunoglobulin G levels \( \geq 550 \text{ mg/dL} \), and immunoglobulin M levels \( \geq 40 \text{ mg/dL} \). In conclusion, antibody-mediated response to the BNT162b2 mRNA COVID-19 vaccine in patients with CLL is markedly impaired and affected by disease activity and treatment. This trial was registered at www.clinicaltrials.gov as #NCT04746092.
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a single-stranded RNA virus that causes COVID-19, a disease with variable presentations ranging from a mild cold to severe respiratory failure. An increased risk for severe disease and death has been noted among elderly patients and persons with preexisting medical conditions. The coronavirus genome encodes 4 main structural proteins, designated spike (S), envelope, membrane, and nucleocapsid. The virus penetrates the host through binding of the viral S protein to angiotensin-converting enzyme 2 on oral mucosa epithelial cells and the lung alveolar type II cells. In general, patients with chronic lymphocytic leukemia (CLL) are predisposed to develop infections, both bacterial and viral, due to inherent immune defects related to their primary disease and as a result of therapy. The mechanisms underlining the immunodeficiency in CLL includes abnormal humoral and cellular immune responses due to quantitative and qualitative defects in immune effector cells, which may also reduce response to vaccines. During the previous months of the COVID-19 pandemic, 2 large multicenter retrospective studies reported high rates of severe COVID-19 disease and mortality in both untreated (“watch and wait”) as well as treated patients with CLL.

Recently, 2 vaccines (BNT162b2 and mRNA-1273) were approved and recommended by the US Food and Drug Administration and the European Medicines Agency to prevent COVID-19 disease. BNT162b2 and mRNA-1273 are lipid nanoparticle-encapsulated messenger RNA (mRNA)-based vaccines that encode the full-length S protein of SARS-CoV-2. In phase 3 trials, these vaccines showed 94% to 95% efficacy in preventing symptomatic SARS-CoV-2 infection independent of age. However, until now, hemato-oncology patients were excluded from clinical trials with COVID-19 vaccines. In the current study, we evaluated antibody-mediated response to the BNT162b2 mRNA COVID-19 vaccine in patients with CLL.
Table 1. Patient baseline demographic and disease characteristics

| Parameter                                      | Patients with CLL (N = 167) |
|------------------------------------------------|-----------------------------|
| Age, median (IQR), y                           | 71.0 (63.0-76.0)            |
| Age ≤65 y, N (%)                               | 50 (29.9)                   |
| Male sex, N (%)                                | 112 (67.1)                  |
| Disease/treatment status, N (%)                |                             |
| Treatment-naive                                | 58 (34.7)                   |
| On-therapy                                     | 75 (44.9)                   |
| Off-therapy in remission                       | 24 (14.4)                   |
| Off-therapy in relapse                         | 10 (6.0)                    |
| Binet stage, a N (%)                           |                             |
| A                                              | 43 (64.1)                   |
| B                                              | 14 (20.9)                   |
| C                                              | 10 (14.9)                   |
| IGHV mutational status, N (%)                  |                             |
| Mutated                                        | 61 (50.0)                   |
| Unmutated                                      | 61 (50.0)                   |
| FISH, N (%)                                    |                             |
| Normal                                         | 20 (12.0)                   |
| del(13q)                                       | 39 (23.4)                   |
| Trisomy 12                                     | 16 (9.6)                    |
| del(11q)                                       | 31 (18.6)                   |
| del(17p)                                       | 19 (11.4)                   |
| β2-microglobulin, N (%)                        |                             |
| ≤3.5 mg/L                                      | 90 (78.3)                   |
| >3.5 mg/L                                      | 25 (21.7)                   |
| Protocols of currently treated, N (%)          |                             |
| BTKis                                          | 50 (66.7)                   |
| Venetoclax ± anti-CD20 antibody                 | 22 (29.3)                   |
| Others                                         | 3 (4.0)                     |
| Time from last anti-CD20 antibody to vaccination, N (%) |                   |
| <12 mo                                         | 22 (28.6)                   |
| ≥12 mo                                         | 55 (71.4)                   |
| Laboratory parameters, median (IQR)            |                             |
| Absolute lymphocyte count, (10^9/L)             | 5.0 (2.0-18.5)              |
| β2-microglobulin, mg/L                         | 2.5 (2.0-3.5)               |
| IgG, mg/dL                                     | 723.5 (515.8-1000.3)        |
| IgM, mg/dL                                     | 32.0 (0.0-57.5)             |
| IgA, mg/dL                                     | 94.0 (49.0-146.8)           |

FISH, fluorescence in situ hybridization.

Results

Patient characteristics

From December 2020 through February 2021, a total of 167 patients with CLL/SLL and 52 age- and sex-matched control subjects were included in this study. Patient baseline demographic and disease characteristics are summarized in Table 1. The median age of the patients with CLL was 71 years (IQR, 63.0-76.0 years), and 112 (67.1%) were male. Fifty-eight patients (34.7%) were treatment naive, 75 (44.9%) were on active therapy, 24 (14.4%) were previously treated, in clinical complete remission (CR) or partial remission (PR), and 10 (6.0%) were currently experiencing disease relapse after being previously treated. The median time from CLL diagnosis to vaccination was 83.1 months (IQR, 48.5-139.5 months), and the median time from the second vaccine dose to serology testing was 15 days (IQR, 14-17 days).

Serologic response

Antibody-mediated response to the vaccine was evident in only 66 (39.5%) of the 167 patients with CLL. An sex- and aged-matched analysis, comparing the response rates in 52 patients with CLL (median age, 69 years; IQR, 63.0-73.7 years) and 52 age- and sex-matched healthy control subjects (median age, 68.0 years; IQR, 64.0-74.0 years), revealed a significantly reduced response rate (52% vs 100%, respectively; adjusted OR, 0.010; 95% CI, 0.001-0.162; P < .001) (Figure 1A-C) and lower antibody titers in patients with CLL (median of 0.824 U/mL [IQR, 0.4-167.3 U/mL], including 0.162; P < .001) (Figure 1A-C) and lower antibody titers in patients with CLL (median of 0.824 U/mL [IQR, 0.4-167.3 U/mL], including

Statistical analysis

SPSS version 27 (IBM SPSS Statistics, IBM Corporation) was used to perform the following: median with interquartile range (IQR), and mean for quantitative variables, and distributions. The Mann-Whitney U test and Kruskal-Wallis H test were used for comparing medians. Pearson’s χ² test, Fisher’s exact test, and the Fisher-Free-}

GraphPad Prism version 8.0.0 for Windows was used for creating figures.

In a univariate analysis (Table 2), the variables found to be significantly associated with response included: younger age (<65 years), female sex, early disease stage (Binet stage A), mutated IGHV, β2-microglobulin (≥3.5 mg/L), untreated/off-therapy ≥12 months from the last anti-CD20 therapy, IgG levels ≥550 mg/dL, IgM levels ≥40 mg/dL, and IgA levels ≥80 mg/dL. Treatment-naive patients...
had a higher response rate (55.2% [23 of 58]) and higher antibody levels (median, 1.7 U/mL; IQR, 0.4-136.0 U/mL) (Figure 2A-B; supplemental Table 1) compared with actively treated patients (16.0% [12 of 75]; OR, 0.16; 95% CI, 0.07-0.35; \( P \), .001); median antibody levels were 0.4 U/mL (IQR, 0.4-0.4 U/mL; \( P \), .001).

Among the 75 patients on treatment at the time of vaccination, 72 (96%) were treated with novel agents, including Bruton’s tyrosine kinase inhibitor (BTKi) monotherapy (ibrutinib or acalabrutinib, \( n = 50 \)) or venetoclax and anti-CD20 antibodies (22; 5 patients treated with venetoclax alone, and 17 patients treated with venetoclax plus rituximab or obinutuzumab). Antibody response rate in patients receiving BTKi was 16.0% (8 of 50) compared with 13.6% (3 of 22) in patients treated with venetoclax and anti-CD20 antibodies (\( P \) = not significant) (Figure 2C). Two (40%) of the 5 patients who received venetoclax monotherapy achieved a positive serologic response, with relatively low antibody titers (range, 2.19-4.5 U/mL). Demographic, disease-related, and treatment-associated factors (including the number of prior lines) had no statistically significant impact on response rate in actively treated patients.

A total of 77 patients with CLL had been previously exposed to anti-CD20 therapy: 22 within the last 12 months before vaccination (median, 5.3 months; IQR, 0.75-8.0 months) and 55 patients \( \geq 12 \) months before vaccination (median, 53.1 months; IQR, 25.5-76.8 months). Most patients (18 of 22 [81.8%]) exposed to anti-CD20 antibodies \( < 12 \) months before vaccination received it in combination with venetoclax. The majority of patients (43 of 55 [78.1%]) treated with anti-CD20 therapy \( \geq 12 \) months before vaccination received chemoimmunotherapy. None of the patients treated with anti-CD20 antibodies (\( n = 22 \)) within the last 12 months has responded vs 45.5% (25 of 55) of those who were exposed to anti-CD20 therapy \( \geq 12 \) months before vaccination (adjusted OR, 37.6; 95% CI, 2.2-651.3; \( P <= .001 \)). In the subgroup of patients treated with anti-CD20 antibody \( \geq 12 \) months before vaccination, there was no association between the time that elapsed from the end of the anti-CD20 therapy and the patients’ serologic response.

A particularly high response rate (79.2%) and antibody levels (median, 297.6 U/mL; IQR, 1.2-1149.8 U/mL) were observed among the 24 patients who completed treatment (mostly chemoimmunotherapy or targeted therapies) and maintained their response (CR/PR) at the time of vaccination (Figure 2A-B; supplemental Tables 2-3). Serologic response rate was remarkably high in those who completed treatment beyond 12 months before vaccination compared with those who completed therapy within \( < 12 \) months (94.1% vs 50.0%; \( P = .04 \)) (supplemental Table 2).

In a multivariate analysis (Table 3), the independent predictors of response were age (\( \geq 65 \) years; OR, 3.17; 95% CI, 1.16-8.67; \( P = .025 \), sex (female; OR, 3.66; 95% CI, 1.46-9.18; \( P = .006 \)), lack of active therapy (including treatment-naive and previously treated patients; OR, 6.59; 95% CI, 2.30-18.86; \( P < .001 \)), IgG levels
Table 2. Univariate analysis for serologic response rate in patients with CLL

| Variable                              | Serologic response, N (%) |         |       |       |       |       |
|---------------------------------------|---------------------------|---------|-------|-------|-------|-------|
|                                       | Positive | Negative | Total |       |       |       |
|                                       |          |          |       |       |       |       |
| **Age in time of vaccination**        |          |          |       |       |       |       |
| ≤65 y                                 | 26 (52.0)| 24 (48.0)| 50    | .031  | 2.09  | 1.01-4.32 |
| >65 y                                 | 40 (34.2)| 77 (65.8)| 117   |       |       |       |
| **Sex**                               |          |          |       |       |       |       |
| Female                                | 30 (54.5)| 25 (45.5)| 55    | .005  | 2.53  | 1.24-5.18 |
| Male                                  | 36 (32.1)| 76 (67.9)| 112   |       |       |       |
| **Treatment status (detailed)**      |          |          |       |       |       |       |
| Treatment-naive                       | 32 (55.2)| 26 (44.8)| 58    | <.001 | 1     |       |
| On-therapy                            | 12 (16.0)| 63 (84.0)| 75    | .16   | 0.07-0.35 |       |
| Off-therapy in remission (CR or PR)  | 19 (79.2)| 5 (20.8) | 24    | 3.01  | 1.02-9.40 |       |
| Off-therapy in relapse                | 3 (30.0)| 7 (70.0) | 10    | 0.35  | 0.08-1.48 |       |
| **Binet stage**                       |          |          |       |       |       |       |
| A                                     | 29 (67.4)| 14 (32.6)| 43    | .001  | 6.21  | 1.80-22.96 |
| B or C                                | 6 (24.0)| 18 (75.0)| 24    |       |       |       |
| **IGHV**                              |          |          |       |       |       |       |
| Mutated                               | 29 (47.5)| 32 (52.5)| 61    | .005  | 3.04  | 1.31-7.21 |
| Unmutated                             | 14 (23.0)| 47 (77.0)| 61    |       |       |       |
| **FISH test**                         |          |          |       |       |       |       |
| Normal                                | 9 (45.0)| 11 (55.0)| 20    | .061  | 1     |       |
| del(13q)                              | 16 (41.0)| 23 (59.0)| 39    | 0.85  | 0.28-2.52 |       |
| Trisomy 12                            | 6 (37.5)| 10 (62.5)| 16    | 0.73  | 0.19-2.80 |       |
| del(11q)                              | 11 (35.5)| 20 (64.5)| 31    | 0.67  | 0.21-2.12 |       |
| del(17p)                              | 1 (53.0)| 18 (94.7)| 19    | 0.07  | 0.01-0.61 |       |
| **β₂-microglobulin**                  |          |          |       |       |       |       |
| ≤3.5 mg/L                             | 43 (47.8)| 47 (52.2)| 90    | .004  | 4.80  | 1.44-20.54 |
| >3.5 mg/L                             | 4 (16.0)| 21 (84.0)| 25    |       |       |       |
| **Current treatment status**          |          |          |       |       |       |       |
| Untreated                             | 54 (58.7)| 38 (41.3)| 92    | <.001 | 7.46  | 3.38-17.14 |
| Treated                               | 12 (16.0)| 63 (84.0)| 75    |       |       |       |
| **Treatment protocol**                |          |          |       |       |       |       |
| BTKi                                  | 8 (16.0)| 42 (84.0)| 50    | .601  | 1     |       |
| Venetoclax ± anti-CD20 antibody       | 3 (13.6)| 19 (86.4)| 22    | 0.82  | 0.20-3.48 |       |
| Others                                | 1 (33.3)| 2 (66.7)| 3     |       |       |       |
| **Anti-CD20 (last treatment)**       |          |          |       |       |       |       |
| At least 12 mo later                  | 25 (45.5)| 30 (54.6)| 55    | <.001 | 37.6  | 2.2-651.3 |
| Within <12 mo                         | 0 (0.0)| 22 (100.0)| 22    |       |       |       |
| **Serum IgG level**                   |          |          |       |       |       |       |
| ≥550 mg/dL                           | 53 (49.1)| 55 (50.1)| 108   | <.001 | 5.37  | 2.11-15.34 |
| <550 mg/dL                           | 7 (14.6)| 39 (85.4)| 46    |       |       |       |
| **Serum IgM level**                   |          |          |       |       |       |       |
| ≥40 mg/dL                            | 39 (59.1)| 27 (40.9)| 66    | <.001 | 4.84  | 2.27-10.37 |
| <40 mg/dL                            | 20 (23.0)| 67 (77.0)| 87    |       |       |       |
| **Serum IgA level**                   |          |          |       |       |       |       |
| ≥80 mg/dL                            | 42 (34.5)| 47 (54.5)| 89    | .012  | 2.42  | 1.15-5.19 |
| <80 mg/dL                            | 17 (24.5)| 46 (38.5)| 63    |       |       |       |
550 mg/dL (OR, 3.70; 95% CI, 1.08-12.66; \( P = .037 \)), and IgM levels \( \leq 40 \) mg/dL (OR, 2.92; 95% CI, 1.21-7.02; \( P = .017 \)).

Within a median follow-up period of 75 days (IQR, 72-87 days) since the first vaccine dose, none of the patients developed COVID-19 infection.

### Adverse events

Fifty-two (31.1%) and 56 (33.5%) patients reported mild local reactions after the first and second dose of the vaccine, respectively (Figure 3; supplemental Table 4). These reactions included pain at the injection site and, less commonly, local erythema or swelling. There was no statistical difference in the rates of local reactions between the first and second dose of the vaccine (\( P = .629 \)) (supplemental Table 5).

Overall, 21 (12.5%) and 39 (23.4%) patients reported systemic adverse events after the first and second vaccine dose, respectively (Figure 3); they were more frequent after the second dose (\( P = .005 \)) (supplemental Table 5), and all were mild. The most frequently reported systemic reaction after the first dose included weakness (\( n = 11 \) [6.6%]), headache (\( n = 9 \) [5.4%]), fever (\( n = 4 \) [2.4%]), and muscle pain (\( n = 3 \) [1.8%]) (supplemental Table 4). The systemic side effects most commonly reported after the second dose were weakness (\( n = 14 \) [8.6%]), fever (\( n = 11 \) [6.6%]), chills (\( n = 10 \) [6.0%]), headache (\( n = 10 \) [5.4%]), and muscle pain (\( n = 8 \) [4.8%]). No statistically significant correlation was found between local or systemic reactions and a positive serologic response to the vaccine. In addition, there were no statistically significant differences in the rate of adverse events between patients who were actively treated at the time of vaccination vs those who were not.

### Discussion

This study evaluated the serologic response to SARS-CoV-2 vaccination after a 2-dose regimen of BNT162b2 mRNA COVID-19 vaccine, given 21 days apart, in patients with CLL. The anti–SARS-CoV-2 antibody response rate in patients with CLL was considerably low. This low response rate, approaching 40%, is consistent with response rates of 20% to 40% to pneumococcal conjugated vaccine (PCV13), pneumococcal polysaccharide vaccine (PPSV23), and the HepB-CpG vaccine\(^{16-19}\); it is also consistent with the reduced efficacy of influenza A and B vaccination reported in patients with CLL.\(^{20}\)

The underlying causes for poor humoral response to vaccination in patients with CLL are multifactorial and attributed to disease-related immune dysregulation and therapy-related immunosuppression.\(^{21}\) In our study, younger patients (aged \( \leq 65 \) years), female subjects, favorable disease-related factors (mutated IGHV, \( \beta_2 \)-microglobulin \( \leq 3.5 \) mg/L, and early

### Table 3. Multivariate analysis for serologic response in patients with CLL

| Variable                                      | OR     | 95% CI       | \( P \)  |
|-----------------------------------------------|--------|--------------|---------|
| Age \( \leq 65 \) y                           | 3.17   | 1.16-8.67    | .025    |
| Female sex                                    | 3.66   | 1.46-9.18    | .004    |
| Mutated IGHV                                  | 1.39   | 0.47-4.10    | .543    |
| \( \beta_2 \)-microglobulin \( \leq 3.5 \) mg/L | 1.36   | 0.36-5.19    | .645    |
| Lack of active therapy                        | 6.59   | 2.30-18.86   | < .001  |
| Serum IgG level \( \geq 550 \) mg/dL          | 3.70   | 1.08-12.66   | .037    |
| Serum IgM level \( \geq 40 \) mg/dL           | 2.92   | 1.21-7.02    | .017    |
| Serum IgA level \( \geq 80 \) mg/dL           | 1.09   | 0.41-2.94    | .862    |

Figure 2. Anti-SARS-CoV-2 antibody responses in patients with CLL according to disease status and treatment. (A-B) Response rate and anti-SARS-CoV-2 antibody levels in patients with CLL according to disease status: Treatment naive (\( n = 58 \)), on-therapy (\( n = 73 \)), off-therapy in remission (\( n = 24 \)), and off-therapy in relapse (\( n = 10 \)). (C) Response rate in patients with CLL treated with BTKi (\( n = 50 \)) and venetoclax (Ven = anti-CD20 antibody (\( n = 22 \)). NS, not significant.

\( \geq 550 \) mg/dL (OR, 3.70; 95% CI, 1.08-12.66; \( P = .037 \)), and IgM levels \( \geq 40 \) mg/dL (OR, 2.92; 95% CI, 1.21-7.02; \( P = .017 \)).

Within a median follow-up period of 75 days (IQR, 72-87 days) since the first vaccine dose, none of the patients developed COVID-19 infection.
These findings are consistent with previous studies showing that recent exposure to B cell–deleting agents (within the last 6-12 months) reduces response to influenza vaccine, pneumococcal polysaccharide vaccine, and other vaccines, and they have relevant bearings on the definition of the right timing for vaccination after an anti-CD20-based treatment. In addition, given that most patients today are treated with venetoclax in combination with an anti-CD20 antibody, we cannot draw firm conclusions about the effect of venetoclax monotherapy on response to the anti–COVID-19 vaccine, given the fact that only 5 patients have been treated with venetoclax alone.

Patients actively treated with BTKIs or with venetoclax + anti-CD20 were unlikely to respond to vaccination. Because BTKIs block the B-cell receptor signaling, in both malignant and normal B cells, it is not unexpected that these agents impair the humoral response to vaccination. Previous studies have described antibody-mediated response rates of 7% to 26% to influenza vaccine in patients with CLL treated with BTKIs; more recently, Pleyer et al showed that BTKIs are associated with a decreased de novo immune response to the anti–hepatitis B vaccine HepB-CpG. Given the lower IgG levels obtained in patients on BTKIs, one should also consider the possibility of postponing the start of treatment until safe for the patients and allow enough time to conclude the vaccination program. Furthermore, patients with CLL treated with anti-CD20 antibody (rituximab or obinutuzumab) within the last 12 months before vaccination failed to produce anti–SARS-CoV-2 antibodies, whereas better responses were observed in patients who completed anti-CD20 therapy at least 12 months before vaccination. These findings are consistent with previous studies showing that recent exposure to B cell–deleting agents (within the last 6-12 months) reduces response to influenza vaccine, pneumococcal polysaccharide vaccine, and other vaccines, and they have relevant bearings on the definition of the right timing for vaccination after an anti-CD20-based treatment. In addition, given that most patients today are treated with venetoclax in combination with an anti-CD20 antibody, we cannot draw firm conclusions about the effect of venetoclax monotherapy on response to the anti–COVID-19 vaccine, given the fact that only 5 patients have been treated with venetoclax alone.

![Figure 3. Local and systemic reactions reported after injection of BNT162b2 in patients with CLL (N = 167). Reactions reported after the first vaccine dose (A) and after the second vaccine dose (B).](image-url)
cellular immune systems. It is generally considered that humoral immunity plays an important role in the protection against SARS-CoV-2.\textsuperscript{30,31} It is supported by the relatively high levels of antibody responses to the S protein in patients who have recovered from COVID-19 infection\textsuperscript{32} and the therapeutic benefit of high-titer convalescent plasma and of the anti-spike neutralizing monoclonal antibody bamlanivimab together with etesevimab.\textsuperscript{33} The serologic response can also, indirectly, represent T helper (CD4) function, given their contribution to recruitment and activation of antibody-producing B cells, beyond their role in cellular immunity. Furthermore, CD4\textsuperscript{+} T-cell responses to the viral S protein were recently shown to correlate with the degree of the anti–SARS-CoV-2 IgG and IgA titers.\textsuperscript{34,35} Nevertheless, the effects of SARS-CoV-2 vaccine on cellular immunity should be further studied in patients with CLL, to better understand its protective role, particularly in patients who failed to achieve an optimal antibody-mediated response. Indeed, both humoral and cellular responses seem to be important in this setting. However, there are several reports,\textsuperscript{36,37} including in patients with non-Hodgkin lymphoma who were infected with COVID-19,\textsuperscript{37} suggesting that T-cell response is generally preserved in patients who have been recently treated with B cell-depleting therapy. Moreover, a robust humoral response seems to be important for the achievement of rapid clearance of COVID-19 infection. In addition, it remains to be established if and for how long the patients with CLL who exhibited an immune response to the vaccine will maintain these levels throughout time as well as if they will be able to maintain a B-cell memory response. Only longer follow-up will tell us.

In summary, the antibody-mediated response to SARS-CoV-2 vaccine in patients with CLL is considerably impaired and affected by disease activity and treatment. Thus, vaccinated patients with CLL should continue to adhere to masking and social distancing, and vaccination of their close contacts should be strongly recommended. Serologic test results after the second injection of the COVID-19 vaccine can provide valuable information to the individual patient and perhaps may be integrated into future clinical decisions. In the future, the efficacy of booster doses should be studied in patients who failed to achieve an optimal response, especially in patients who completed treatment attaining a deep and sustained response.

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### Authorship

**Contribution:** Y.H. and I.A. initiated the trial, designed the study, analyzed data, and wrote the paper; A.A., G.S., Y.S.A., and M.M. performed the serologic testing; Y.B. collected the data; S.L., T.Z., and E.J. analyzed the data; L.S. designed the study; C.P. wrote the paper; and P.G. designed the study and wrote the paper.

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### Footnotes

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For original data, please contact the corresponding author.

The online version of this article contains a data supplement.

There is a Blood Commentary on this article in this issue.

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