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# PB1872 ANTIBODY RESPONSES AFTER COVID-19 VACCINATION IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKAEMIA, EITHER TREATED OR NAÏVE. A MONOCENTRIC EXPERIENCE.

**Topic:** 06. Chronic lymphocytic leukemia and related disorders - Clinical

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**Background:** The efficacy of spike messenger RNA vaccines against SARS-COV2 in immunocompetent population is about of 94-95%, while in immunocompromised patients no precise value has been established. Most of patients with Chronic Lymphocytic Leukaemia (CLL) present a consistent immunological defect, which increases the risk of mortality and morbidity from infections, including SARS-COV2. Moreover, they have shown a highly heterogeneous response to vaccination, depending on many factors including baseline features, disease and treatment status, types of therapy, vaccine administered, and immunoglobulin level at time of vaccination.

**Aims:** We tried to evaluate the efficacy of vaccine, stratifying them according to treatment status (naïve, on treatment, off therapy) and of type of treatment, including chemo-immunotherapy (CIT), BTK or anti-Bcl2 inhibitors, monoclonal antibodies (MoAb).

**Methods:** This monocentric study included 100 CLL patients who received two/three dose of mRNA vaccine (BNT162b2 or mRNA-1273) between January 2021 and January 2022. Median age at time of vaccination was 69 years and 51% were males. 44% patiets presented unmutated IgHv, 7% del17p, 13% del11q. 61% patients suffered significant comorbidities as hypertension, diabetes, BPCO. 71% pts received at last one prior CLL therapy, including CIT or inhibitors; 44% were actively treated at the time of vaccination. CLL treatment was not held or modified at the time of vaccination. All patents were vaccinated: BNT162b2 was administered to 80%, mRNA-1273 to 14%, two BNT162b2 and mRNA-1273 booster to 6%. Baseline demographics, treatment history and laboratory parameters including lymphocyte count and IgG levels prior to first dose of COVID-19 vaccine were collected and patients were tested for SARS-COV2 anti-spike Ig at different times from vaccination (Table 1).

**Results:** No CLL patient experienced SARS-COV2 infection. Median IgG level at baseline was 733 mg/dL, 78% of patients had IgG levels above 500 mg/dL. At first serologic testing, at a median of 131 days after the 2$^{nd}$ dose, 53% patients tested negative and 47% positive. Among patients who did not develop immunity, 58% were on treatment with CIT (26%) or inhibitors, alone (62%) or in association with MoAb (12%). Among patients who developed immunity, 38% were naïve while 30% were off therapy. All patients who received MoAb in the previous six months failed to develop immunity; among patients who received MoAb from more than 6 months, 55% did not develop immunity, while 45% did. At second serologic testing, at a median of 44 days after the booster, 80% patients tested positive, with a 67% rate of seroconversion, and 20% patients tested negative (Table 1).

**Image:**

Patient's features: Clinical and Biological characteristics
100 pts (January 2021-January 2022)

| | |
|---|---|
| Sex M/F, % | 51/49 |
| Median age, years (range) | 69 (40-86) |
| ages ≤ 65 years, n, % | 74 (74%) |
| Age> 65 years, n, % | 26 (26%) |
| Median IgG at baseline, mg/dl ( normal range 700-1600) | 733 (257 – 2185) |
| IgG ≤ 500 mg/dl, % | 22 |
| IgG > 500 mg/dl, % | 78 |
| **Treatment status at time of vaccination** | |
| Therapy status at baseline | 29% treatment naive<br>27% off therapy<br>44% ongoing therapy |
| Ongoing therapy at baseline | 30% chemoimmunotherapy<br>54% inhibitors BTK<br>5% inhibitors Bcl-2<br>11% inhibitors plus MoAb |
| Timing of vaccination with respect to MoAb | 46% never MoAb<br>44% MoAb > 6 months<br>10% MoAb <6 months |
| **Vaccination features** | |
| Serologic result after two doses | **53% negative**<br>➢ 18% pts naïve<br>➢ 24% off therapy<br>➢ 58% on treatment<br>- 26 % CIT<br>- 53% inhibitors BTK<br>- 9% inhibitors Bcl-2<br>- 12% inhibitors plus MoAb |
| | **47% positive**<br>➢ 38% pts naïve<br>➢ 30% off therapy<br>➢ 32% on treatment<br>- 32% CIT<br>- 58% inhibitors BTK<br>- 10% inhibitors plus MoAb |
| Serologic result after booster, % (24/100 pts) | **80% positive**<br>- 67% rate of seroconversion |
| | **20% negative**<br>-33% persistently negative |

**Table 1.** Patients' characteristics at baseline and results after serology for SARS-COV2 following mRNA vaccination.

**Summary/Conclusion:** Our monocentric experience confirms a low humoral response in CLL, due to both disease and therapy related factors. Patients who, at the time of vaccination, were either naïve or off therapy yielded better results, probably due to a lower disease burden. The timing of MoAb administration strongly influences the response rate. Drugs that block the BTK receptors impair the humoral response of vaccination to any pathogen and behave accordingly for SARS-COV2. Data show that, in these patients, the third dose confers higher rates of response and a wider protective effect. In conclusion, vaccination is strongly recommended to all CLL patients. Due to the higher infectious risk, caused by immune dysregulation typical of CLL, it is important to evaluate the timing of vaccination and maintain safety measures at any time.