Humoral response to COVID-19 vaccine: a challenge in CLL

Antonella Capasso[1,2], Elisa Albi[1], Luana Schiattone[1,3], Francesca Martini[1], Emanuela Sant'Antonio[1], Lydia Scarfò[1,4,5], Pamela Ranghetti[4], Michela Frenquelli[4], AlessandroCampanella[4], Eleonora Perotta[4], Silvia Heltai[4], Maria Colia[1], Paolo Ghia[1,4,5]

[1]Strategic Research Program on CLL, IRCCS Ospedale San Raffaele, Milano, Italy
[2]Current affiliation: Università degli Studi di Milano Statale, Milano, Italy
[3]Current affiliation: UOSD Centro Diagnosi e Terapia dei Linfomi, PO Santo Spirito, Pescara, Italy
[4]Laboratory of B-cell Neoplasia, IRCCS Ospedale San Raffaele, Milano, Italy
[5]Università Vita Salute San Raffaele, Milano, Italy

Abstract

Patients with **CLL** have **high rates** of either **severe disease** or **death** from COVID-19 and a **low response** rate after COVID-19 **vaccination**.

We conducted a **single center study** to evaluate the **efficacy** of **COVID-19 vaccination** after the **second**, **third** and **fourth dose**. **166** patients with **CLL** were enrolled: **26%** treatment-naïve **(TN), 15%** previously **treated**, **57%** on **active therapy** and **2%** off-therapy in **relapse**.

Most patients received **BNT162b2 (87%)** followed by **mRNA-1273 (4%)** and **ChAdOx1-S (3%)**; data is missing in 6%.

The **response rate** and **antibody titers** post **second dose** were **higher** in treatment naïve (**TN**) patients and those **in clinical remission** after treatment.

The **benefit** of COVID-19 **vaccination** was **limited** in **actively treated** patients. **Serological response** was **absent** after recent exposure **(<12 months)** to **anti-CD20** antibodies **combination therapy** post **second** and **third dose.**

A **quarter** of **seronegative** actively treated patients **responded** to **third dose**. Almost all patients who **failed** to achieved an antibody response **after all four doses** of vaccine received **BTKi therapy.**

In summary, in **CLL** patients **vaccine immunization** was **impaired** and correlated to **disease activity** and **treatment status**.

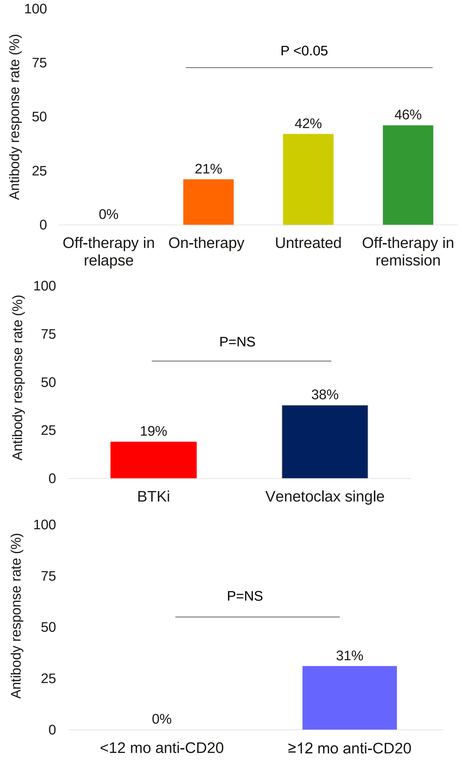
Background

- Chronic lymphocytic leukaemia (**CLL**) is associated with some degree of **immune dysfunction** as a result of the **disease itself** and/or **treatment**.[1]
- Consequently, patients with CLL may present a **higher incidence** of **recurrent severe infections** and **reduced efficacy of vaccines** [2,3].
- **COVID-19** has a major impact in **patients with CLL** who are at **increased risk** for **severe disease** and **death**. [4,5,6]

Objective

To understanding **the efficacy of anti-SARS-CoV-2 vaccines** in **patients with CLL**.

Figure 1. Response rate post-dose 2



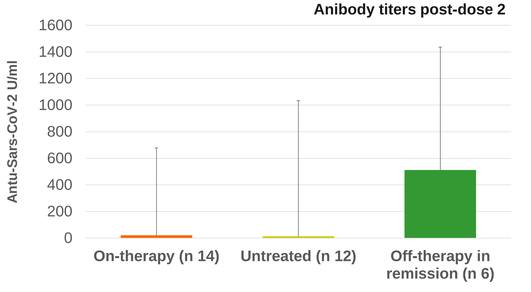
Materials & Methods

Study population: 166 vaccinated patients with CLL followed at our site (samples from January 2021); vaccine response was evaluated **post-dose 2** in **120** patients, **post-dose 3** in **77** patients and **post 4 dose** in **22** patients

Serology testing: SARS-CoV-2 S1/S2 IgG assay (Elecsys ® Anti-SARS-CoV-2), negative for antibody titers below 0.4 U/ml

Timepoints: baseline, 2 to 3 weeks after second, third and fourth vaccine doses

Statistical analysis: Pearson'Chi Square test, p-value < 0,05 were considered significant.



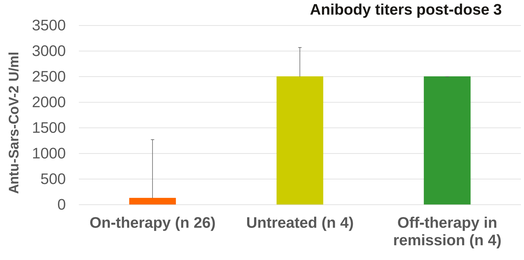


Figure 2. Antibody titers according to the disease status

Summary

Humoral immune response to the **COVID-19 vaccine** is **impaired** in most **patients with CLL** and correlates with treatment status.

Discussion

Post second dose:

- **Higher seroconversion** rate in **TN patients (42%)** and those with **sustained clinical response** after therapy discontinuation (**46%**) compared with **actively treated patients** (**21%;**[p=0,024; p=0,048, respectively]).
- Antibody response rate in **patients on BTKi** was considerably **lower 20%** (12/61); **3/8** (**38%**) patients **on venetoclax monotherapy** seroconverted.
- **None** of **8** patients **exposed to anti-CD20 antibodies** (3 with targeted therapy, 2 with chemotherapy, 3 as single agent) **<12 months** before vaccination responded.

Post third dose:

- **26%** of patients actively treated who **failed** to achieve a humoral response **after two-doses responded** to the **third dose**, although with a **weak antibody level** (median 8,64 U/ml, range 0,55-175).
- **None** of patients treated **with anti-CD20 anitbodies combination** therapy **< 12 months** before vaccination responded
- **Higher median** (IQR) **antibody titer** (127,9 U/mL; 0,55-2500) compared to the one post second dose (19 U/ml; 0,86-2500) in patients on therapy.
- **All patients in clinical remission** after treatment present titers **>2500 U/mL** post third dose → **reconstitution of humoral immunity** as the **result of disease control.**

Post fourth dose:

- **58%** of seronegative actively treated patients **failed** to respond **to fourth dose, mostly receiving BTKi** and only one receiving venetoclax

References

1.Tadmor T, Expert Rev Hematol. 2018
2.Mauro FR, Leukemia. 2021
3.Pleyer C, Blood. 2021
4.Scarfò L, Leukemia 2020
5.Chatzikonstantinou T, Leukemia 2021
6.Herishanu Y, Blood 2022