Booster and BTKi Interruption Improve Response to SARS-CoV-2 Vaccine in Patients with CLL

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Background

- Patients with chronic lymphocytic leukemia (CLL) have dysregulated immune function
- Vaccination response in patients with CLL on Bruton's tyrosine kinase inhibitors (BTKi) is sub-optimal[1]
- We investigated the effect of SARS-CoV-2 booster vaccination and BTKi interruption on antibody (Ab) and cellular response

Methods

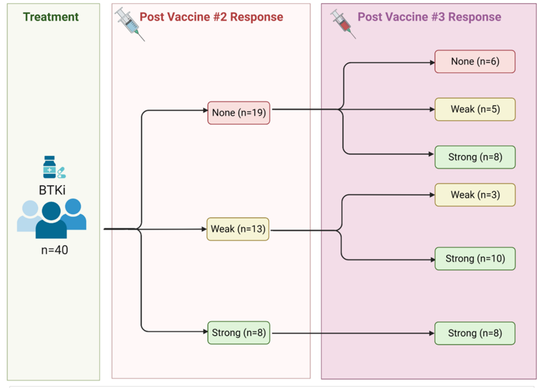
- Single-institution cohort study at NIH from 2020-2022
- **Patients with CLL on ibrutinib and acalabrutinib**
- Measured **anti-spike Ab titers** (Roche Elecys assay) after both:
  1) **The SARS-CoV-2 primary vaccination series**
     - *(defined as 2 doses of Pfizer-BioNTech/Moderna vaccines or 1 dose of Janssen vaccine)*
  2) **The first SARS-CoV-2 booster**
- Exclusions for humoral response assessment: receipt of IVIG, convalescent plasma, or mAb for SARS-CoV-2 within 3 months
- Seroconversion was defined by an anti-spike IgG level ≥0.8 u/mL after vaccination
- **T-cell response after primary series** was measured using ultra-deep TCRß sequencing (Adaptive Biotechnologies)
- Exclusions for cellular response assessment: receipt of convalescent plasma or COVID-19 infection within 3 months
- A positive cellular response to vaccination was defined as significant expansion of ≥1 spike-specific clonotype

Results

Antibody response

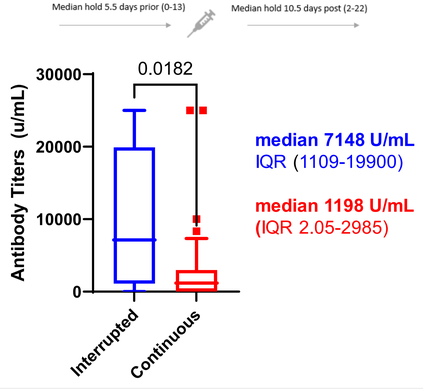
Booster vaccination improves strength of SARS-CoV-2 Ab response in patients on BTKi

Only patients with Ab data available post primary series and post boost were included in this analysis. Response to vaccine was categorized by anti-spike ab as negative (< 0.8 u/mL), weak (0.8-50 u/mL), or strong (>50u/mL).



BTKi interruption improves response to SARS-CoV-2 after booster vaccination

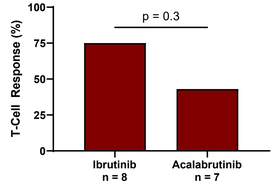
12/54 patients interrupted BTKi peri-booster (median of 21 days). Box and whiskers show median anti-spike Ab titer with IQR and 1.5x IQR. P-value was calculated with Mann Whitney test.



T- Cell response

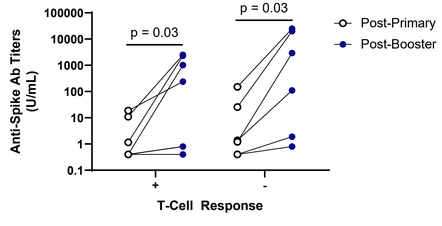
BTKi type does not affect T-cell response to primary SARS-CoV-2 vaccination

T-cell response data was available for 15 patients on BTKi after primary series SARS-CoV-2 vaccination. Of the 15 patients on BTKi, 9 (60%) had a T-cell response. There was no difference between T-cell response rates between ibrutinib and acalabrutinib.



Booster SARS-CoV-2 vaccination improves ab response independent of T-cell response

Anti-spike Ab titers significantly increased post-booster in patients with and without a T-cell response post-primary series.



Discussion

- SARS-CoV-2 booster improved the rate of seroconversion in patients with CLL on BTKi
- More than half of patients who were seronegative post primary series responded to the booster, emphasizing the importance of repeated antigenic exposure to cross the threshold of humoral response in patients with CLL
- BTKi interruption peri-booster improved seroconversion compared with continuous BTKi therapy, underlining the role of BTK in antibody formation
- BTKi type does not affect T-cell response to primary series
- SARS-CoV-2 booster improves Ab response independent of T-cell response

Summary

1. Among patients with CLL on BTKi, increasing anti-spike antibodies with subsequent vaccinations support additional boosters in this population
2. BTKi interruption at the time of SARS-CoV-2 booster results in a more robust antibody response and should be considered in select patients with CLL

References

1. Pleyer, C., et al., *Effect of Bruton tyrosine kinase inhibitor on efficacy of adjuvanted recombinant hepatitis B and zoster vaccines.* Blood, 2021. 137(2): p. 185-189.

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