P1439 IMMUNE RESPONSE TO ANTI-SARS-COV-2 MRNA VACCINES IN MULTIPLE MYELOMA AND CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS

**Topic:** 24. Gene therapy, cellular immunotherapy and vaccination - Biology & Translational Research

**Background:**
Multiple myeloma (MM) and chronic lymphocytic leukemia (CLL) patients have increased morbidity and mortality rates of COVID-19 due to immunosuppression associated with the disease and ongoing therapy. The same immune impairment accompanying CLL and MM also affects suboptimal vaccine response. The analyses of the effectiveness of the post-vaccination response may lead to the optimization of vaccination.

**Aims:**
The study assessed the effectiveness of the humoral and T cell-mediated immunity as well as characterized immune system populations following mRNA COVID-19 vaccination using either BNT162b2 or mRNA-1273 in the short-term (2-5 weeks after 2nd dose) and long-term follow-up (12 weeks after vaccination).

**Methods:**
Blood samples were obtained from 62 CLL and 60 MM patients from eight hematology departments in Poland and were assessed at pre and post-vaccination in three time points. Anti-SARS-CoV-2 antibodies (IgM, IgG, and IgA) were evaluated in qualitative and quantitative (IgG) ELISA. Flow cytometry was used to characterize changes in the immune system of patients after anti-SARS-CoV-2 mRNA vaccination. Evaluation of specific cytotoxic T cell response after vaccination was performed in HLA-A*0201 positive CLL and MM patients with the most common and the highest binding score SARS-CoV-2 specific epitope - HLA-A*0201/YLQPRTFLL269-277.

**Results:**
Total neutralizing antibodies were detected in 37% MM patients before vaccination, increased to 91% and 94% in short- and long-term follow-up, respectively. In CLL, serological responses were detectable in 21% of patients before vaccination and increased to 45% in the short-term and 71% in long-term observation.
We detected a tendency to higher frequencies of specific CD8+ T cells against SARS-CoV-2 after vaccination compared to samples before vaccination in MM patients (median: 0.18% vs 0.11%, P<.06), and no changes in frequencies of specific T cells in CLL patients.

Comparison between MM and CLL serological response showed a significant increase in OD values in MM samples in the short-term (median: 1.71 vs 0.12, P<.0001) and long-term (median: 3.57 vs 0.90, P<.005) follow-up. COVID-19 naïve patients treated for CLL demonstrated significantly lower serological response early after the 2nd dose (median 0.08 vs 2.2, P<.001) as well as in long-term follow-up (median: 0.21 vs 2.86, P<.05) than untreated COVID-19 naïve patients.

Flow cytometry characteristics of immune system subpopulations showed a moderate positive correlation between IgG antibodies levels and percentage of iNKT cells (P<.04, r=0.59) in short-term follow-up in CLL patients. Interestingly, we found a significant decrease in levels of iNKT PD-1+ cells after mRNA vaccination in CLL patients in short-term (median: 50% vs 65.22%, P<.05) as well as in long-term response (median: 46.67% vs 66.67%, P<.03, compared to baseline in paired samples. Analysis of the impact of frequent infections in patients with CLL showed higher levels of NKT (median: 6.37% vs 1.36%, P<.02) in short-term follow-up and levels of NKT (median: 7.4% vs 1.93%, P<.02), iNKT (median: 0.021% vs 0.007%, P<.02) and CD8PD-1+ (median: 34.2% vs 20.14%, P<.02) cells in long-term follow-up in patients without infections.

Summary/Conclusion:

This study provides novel insights into mRNA vaccination efficacy in immunocompromised MM and CLL patients. Our findings highlight that specific CD8+ T cells against SARS-CoV-2 might be induced by vaccination but do not correlate positively with serological responses.

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