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OAB-045

COVID-19 vaccine responsiveness in patients with Multiple Myeloma and Waldenström Macroglobulinemia

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Background: Multiple myeloma (MM) and Waldenström macroglobulinemia (WM) are associated with significant immunoparesis. Based on the ongoing COVID-19 pandemic, there is an urgent need to understand whether patients are able to mount a sufficient response to COVID-19 vaccines. **Methods:** Patients were vaccinated with BNT162b2 mRNA (Pfizer/BioNTech), mRNA-1273 (Moderna), or JNJ-78436735 (Johnson & Johnson). SARS-CoV-2 spike protein (S) antibodies were detected with the Elecsys assay (Roche Diagnostics). Primary endpoint is S antibody detection 28 days after final vaccination. Secondary endpoints include functional serologic assessments and T-cell responses at 28 days, 6 months, 9 months, and 12 months. **Results:** 141 patients have been enrolled to date, 136 (91 MM and 45 WM) of whom had initial S antibody assessment. Median antibody titer was 178.0 (IQR, 16.10-1166.0) for MM and 3.96 (IQR, 0-282.8) for WM. S antibody response rate was 91% (83/91) in MM and 60% (27/45) in WM. However, response rates for achieving S antibody >100 U/mL were 56% (51/91) in MM and 33% (15/45) in WM. Vaccine-specific S antibody responses following mRNA-1273, BNT162b2, and JNJ-78436735 were 74% (25/34; p<0.05), 51% (24/47; p=NS), and 20% (2/10; p<0.05) in MM and 67% (10/15; p<0.005), 19% (5/27; p<0.05), and 0% (0/3; p=NS) in WM. Among MM patients with progressive disease, S antibody response >100 u/mL occurred in 45% (9/20) as opposed to 65% (35/54) for VGPR+ (p100 U/mL occurred in 53% (19/36) and 56% (31/55), respectively (p=NS). Among WM patients, S antibody responses >100 U/mL occurred in 73% (8/11) (p<0.05) previously untreated; 0% (0/8) (p<0.05) received rituximab within 12 months; 15% (3/20) (p<0.05) on an active Bruton Tyrosine Kinase (BTK) inhibitor; and 29% (4/14) (p=NS) received other therapies. **Conclusions:** These preliminary data suggest impaired serologic responses following COVID-19 vaccines in patients with both MM and WM. Overall, WM patients showed more severe impairment of COVID-19 S antibody responses. Most previously untreated WM patients achieved S antibody responses, however suboptimal antibody responses were seen in WM patients who received rituximab within 12 months or on active BTK inhibitors. In MM patients, being in disease remission associated with improved S antibody response. Vaccination among MM and WM patients with MRNA-1273 elicited significantly higher S antibody response rates comparison to other vaccines. Complete serologic responses including neutralization and T-cell studies are pending and will be updated. Further understanding of the immunological response to COVID19 vaccination is needed to clarify patients risks, and necessity for booster or alternative protective measures against COVID-19.

OAB-046

COVID-19 infection in multiple myeloma patients – retrospective analysis of 371 Czech patients

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Background: COVID-19 disease caused by SARS-CoV-2 coronavirus has affected millions of people worldwide. The mortality of this infection varies with age and comorbidities up to more than 10% in very elderly population. The aim of our study was to determine the disease pattern and mortality rate among multiple myeloma patients. **Methods:** We retrospectively analyzed entries in the Czech Registry of Monoclonal Gammopathies from patients who were infected with SARS-CoV-2 from March 2020 until May 2021. Demographic data, treatment patterns, comorbidities, symptoms of COVID-19, treatment modalities and healthcare utilization was compared in survivors and non-survivors. **Results:** Overall,

371 patients with MM and COVID-19 infection were identified. Median age at covid-19 diagnosis was 69 years (37-91 years), 53.4% (198/371) were males. There were 70.1% (260/371) survivors and 20.8% (77/371) deceased patients, outcome of 9.2% (34/371) of patients is unknown. PCR positivity was seen with median 20 days (1-84 days) in 79 evaluable patients. 6 patients were vaccinated prior to infection (5-68 days). Infection was acquired during actual treatment in 53.1% of patients (197/371). Median number of previous lines administered was 1 (0-7). Treatment preceding infection was most frequently composed of lenalidomide in 50.3%, bortezomib in 42.1% and daratumumab in 19.8%. Symptomatic infection was seen in 74.9% (278/371) of patients with fever being the leading symptom (49.6%) followed by cough (39.1%) and shortness of breath (35.0%). Inpatient treatment was needed in 45.0% (167/371) of patients, intensive care unit was required in 38.9% (65/167) of patients. Median length of in-hospital stay was 11 days (1-53 days). Artificial lung ventilation was necessary in 10.8% (18/167) patients, 24.6% (41/167) needed non-invasive ventilation or high flow oxygen and 35.3% (59/167) of patients needed low flow oxygen. Remdesivir was administered to 10.0% (37/371) and convalescent plasma to 4.9% (18/371) of patients. No difference was seen in mortality according to ISS stage (p=0.609), administered lines of therapy (p=0.119) or achieved treatment response (p=0.418). **Conclusions:** The mortality of MM patients with COVID-19 was very high (20.8%). Healthcare utilization was high with almost half of the infected myeloma patients needing inpatient treatment. No apparent risk factors in terms of disease status or previous treatment were identified. Supported by MH CZ - DRO (UHHK, 00169906) and by the program PROGRES Q40/8.

OAB-047

Plasma cell disorder patients are left vulnerable after one dose of the BNT162b2 mRNA or the ChAdOx-nCOV-19 COVID-19 vaccines

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Background: Concerns have been raised about the ability of patients with plasma cell disorders (PCD) to mount adequate immune responses to vaccination, particularly considering the initial extension to vaccination intervals in the United Kingdom to up to 12 weeks in December 2020, the start of the vaccination roll-out. Protecting this vulnerable patient group with anti-SARS-CoV-2 vaccination is critical. **Methods:** We measured the humoral responses in PCD patients after the first dose of the BNT162b2 and ChAdOx-1 nCOV-19 vaccines. Antibody levels were measured using Elecsys Anti-SARS-CoV-2S assay for quantitative detection of IgG Abs, specific for the SARS-CoV-2 spike-protein receptor binding domain. Positive cut-off of ≥0.80 U/mL defined serologic response. Testing was performed at (or closest to) 4 and 8 weeks post-dose. Baseline nucleocapsid Ab results were available from previous screening in a subset of patients. Clinical information was retrieved from medical records. **Results:** 198 PCD patients (178 multiple myeloma, 15 amyloid, 3 SMM/MGUS, other 2 PCD), median age 63 (range 35-84), had serologic assessment after one vaccine dose against SARS-CoV-2. 69% (138) were on chemo-immunotherapy treatment (CIT) within 4 weeks of first dose. Previous COVID-19 infection and exposure was defined as a positive COVID-19 PCR swab or positive N-antibody at baseline and were excluded from analysis. Patients were tested at median 42 days (range 11-90) after their first dose. After one dose, 68% (135/198) were seropositive, with median Ab titres 21 U/mL (IQR 3.92-133.5). In those with negative baseline Ab test, seroconversion to one dose was 67% (64/96). Forty-one patients were tested more than once after one dose, at median 33 days (12-62) and again at 67 days (38-91). 22 were seronegative at first testing, of these, 6 seroconverted on second testing, prior to second dose. Age ≥70, light chain (LC) disease, disease status less than VGPR, CIT within 4 weeks, low IgM and ASCT more than 12m were statistically significant seronegative predictors on univariate analyses. LC disease, less than VGPR and IgM less than 0.4g/L, retained statistical significance on multivariate analyses. On linear regression analysis in seropositive patients, more lines of treatment and CIT within 4 weeks were significantly associated with lower antibody titres. **Conclusion:** Serologic response to SARS-CoV-2 vaccination is lower in PCD patients than reported healthy controls at 68% after one dose. Further work in PCD is needed to understand how Ab levels correlate to neutralisation capability, cellular responses, protection from infection and how long seroconversion lasts to better define correlates of protection. Nearly a third do not respond to a single vaccine dose causing concerns that PCD patients are left vulnerable with a delayed vaccination strategy and should be prioritised to receiving the second dose at the recommended manufacturers time scale of 3 or 4 weeks.

OAB-048

Suboptimal humoral immune response to SARS-CoV-2 mRNA vaccination in myeloma patients is associated with anti-CD38 mAb and BCMA-targeted treatment

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