BNT162b2 COVID-19 VACCINE RESPONSE IN IMMUNOCOMPROMISED POPULATIONS (FOLLICULAR LYMPHOMA AND WALDENSTROM'S MACROGLOBULINEMIA):

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Background: Patients with haematological malignancies are at high risk of severe SARS-CoV-2 infection. We assessed the BNT162b2 vaccine responses in Follicular lymphoma (FL) and Waldenstrom's Macroglobulinemia (WM) at baseline, 21 days after 1st and 2nd dose, prior to and ~14 days after 3rd dose in: 24 FL patients on rituximab-chemotherapy (FLT); 11 FL patients' treatment-naïve (FLN); 15 WM patients on rituximab-chemotherapy (WMT); 13 WM patients on Bruton's Tyrosine Kinase inhibitors (WMB); 9 WM patients' treatment-naïve (WMN); 13 Healthy controls (HC).

Methods: Immune response was measured by flow cytometric detection of anti-SARS-CoV-2 spike antibodies (ASAb), using our established live cell assay and live virus neutralisation to variants of concern. *Ex vivo* T cell responses were measured by the flow cytometric OX40 assay. Differences between groups were determined by the Mann-Whitney test.

Results: No participants had prior SARS-CoV-2 exposure. In FL post 2nd dose, median fluorescence intensity (MFI) of HC (228255) and FLN (245898) was statistically higher than FLT (p=0.001). In WM, rise in ASAb was observed post 2nd dose in WMN (220645), WMT (147197) but not in WMB (39093). All patients demonstrated reactive CD4+ and CD8+ T cells with no difference in SARS-CoV-2 spike-specific CD4+CD25+CD134+ and CD8+CD69+CD137+ T cells across groups.

Post 3rd dose, a 7.5-fold increase in ASAb MFI was observed which correlated with neutralisation to delta and early-clade but not omicron variant. A subset of WMB underwent patient-initiated BTKi interruption for 1-3 weeks. These patients had 4X increase in ASAb MFI compared to patients on continuous BTKi.

Conclusion: FLN and WMN have comparable COVID-19 vaccine induced humoral immunity, unlike WMB. The subgroup that received 3rd dose showed additional seroconversion, with increased IgG titre and neutralization, though the majority had lower neutralization to omicron variant. SARS CoV-2-specific T cell responses in B cell-depleted patients may indicate broader benefits of vaccination.

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