

Spike antibody seroconversion and breadth following SARS-CoV-2 vaccination in Australian people with Multiple Sclerosis

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Introduction

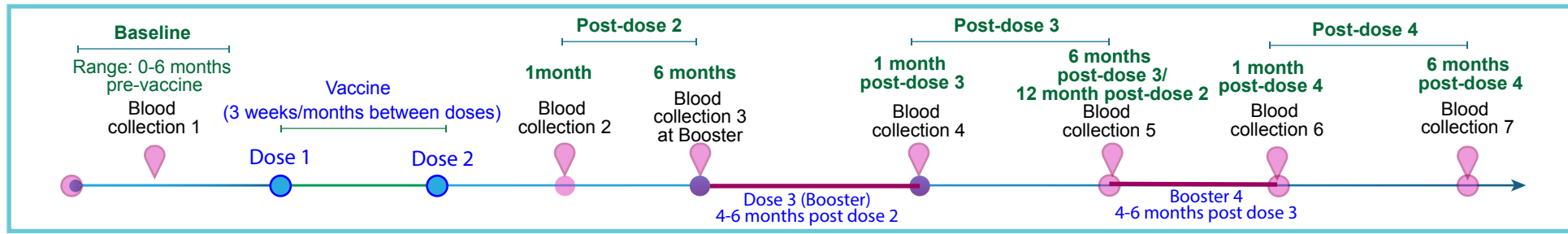
COVID-19 vaccination induces protective Spike antibodies. Some responses are attenuated in people with multiple sclerosis (MS) on high efficacy disease-modifying therapies (DMT). Whether antibodies afford immunity against emerging SARS-CoV-2 Variants of Concern (VoC) such as Delta and Omicron is unknown.

Objective: To assess the longevity and breadth of Spike antibody in MS patients after COVID-19 vaccination.

Contact Details: fabienne.briolot@sydney.edu.au. Funding: Novartis, MS Australia



Study timeline



Method: Live flow cytometry assay to detect spike antibodies

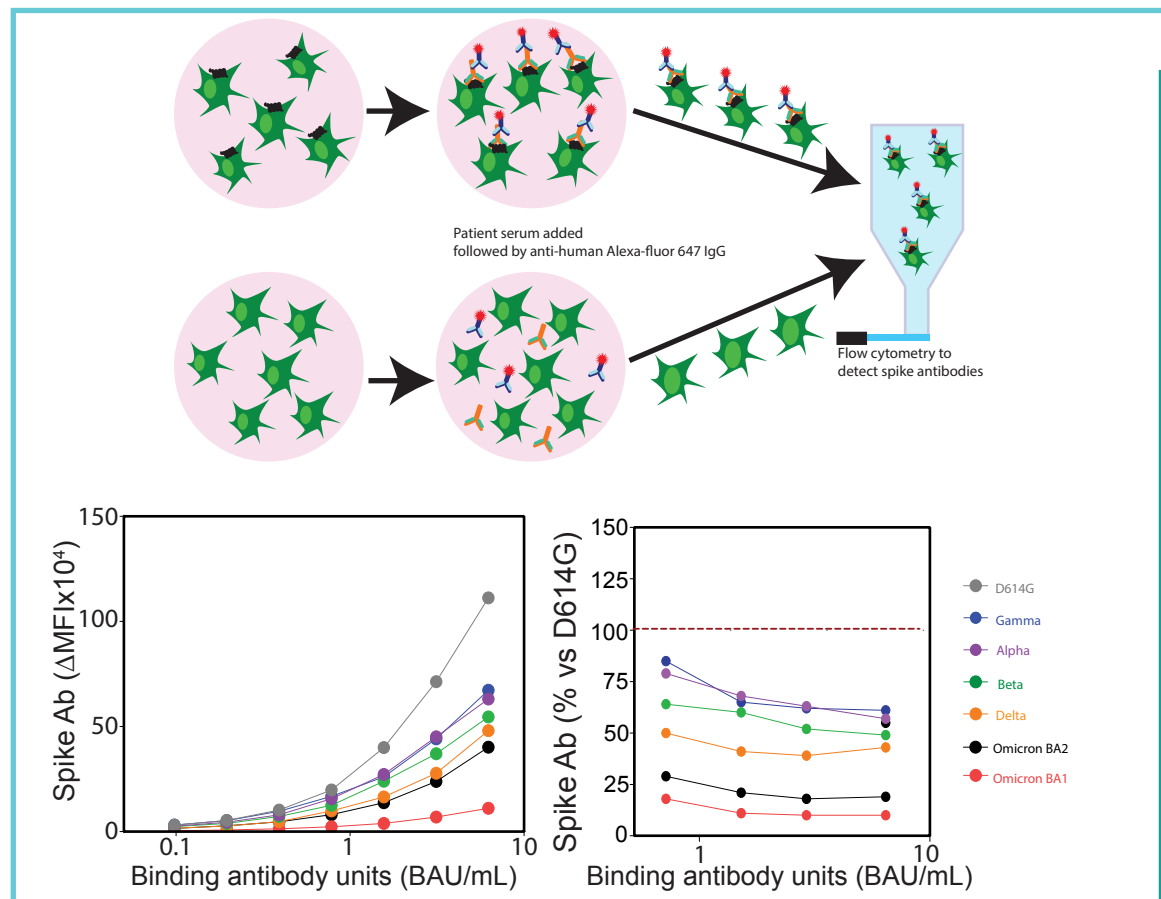


Figure 1. Spike antibodies bind with high affinity to Early Clade (D614G) Spike in comparison to Spike from VoCs
A live flow cytometry cell-based assay was performed to detect the presence of spike antibodies in patient serum. HEK-293 cells were transfected to express spike proteins on the cell surface. Cells were incubated with patient serum, followed by anti-human Alexa-fluor 647-conjugated anti-human IgG antibody. Standard curves generated using WHO NIBSC 21/134 standard. There is high antibody binding to D614G (early clade) spike, in comparison to VoCs, such as Delta and Omicron spike.

Seroprevalence of Spike antibody in the general community and in pwMS treated by DMTs after COVID-19 vaccination

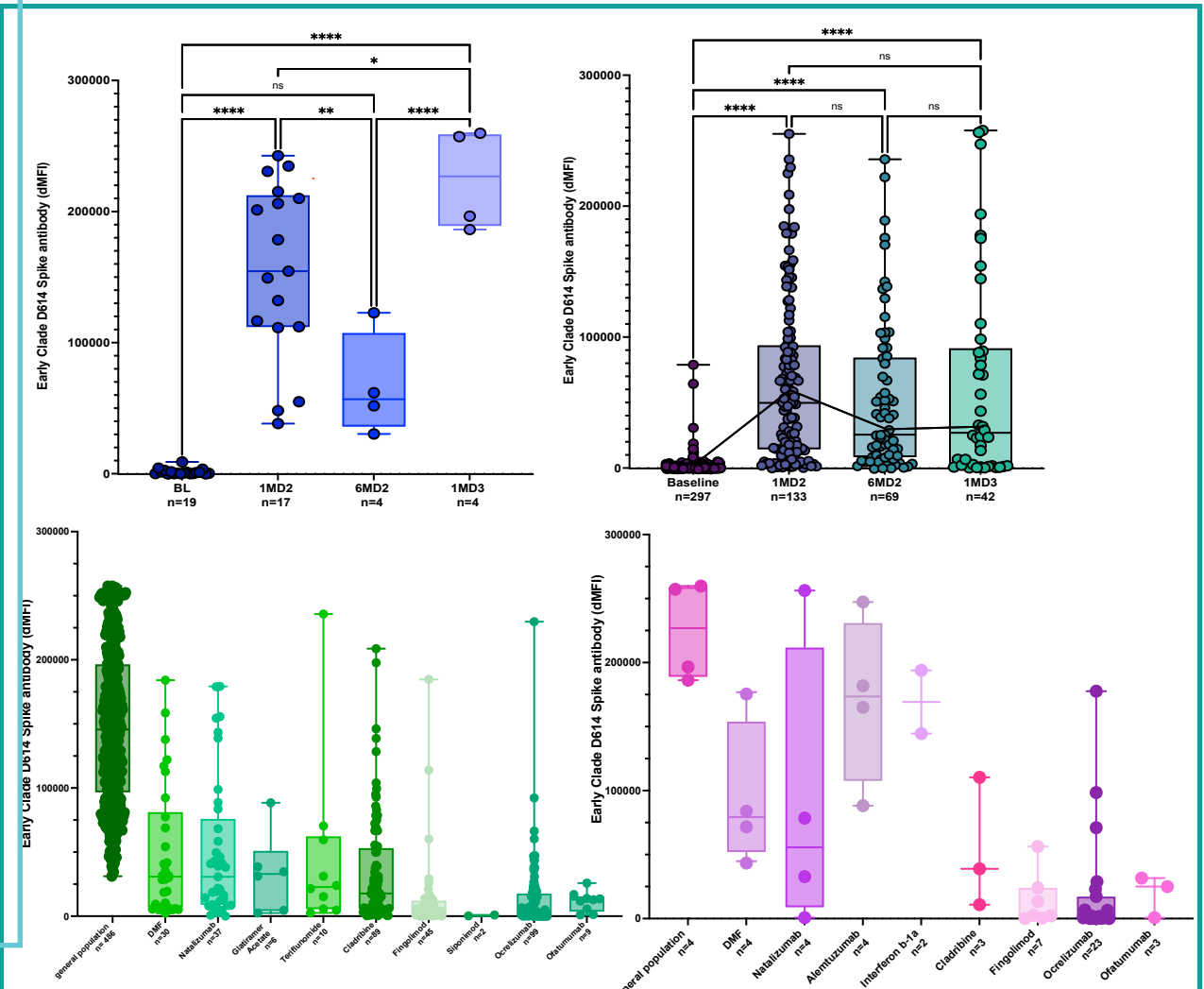


Figure 2. pwMS receiving immunosuppressive DMTs exhibit a dampened immune response following COVID-19 vaccination.
123/133 sera at 1 month post-second dose, 61/69 at 6 months post-second dose, and 29/42 at 1 month post-third dose were positive for Spike antibodies (top, right). All sera from general population controls seroconverted (top and bottom left). pwMS who did not seroconvert at 1 month post-second (bottom, left) and 1 month post-third dose (bottom, right) were treated with ocrelizumab (n=43, 18), ofatumumab (n=2, 1), cladribine (n=10), fingolimod (n=15, 3), and siponimod (n=2). At 1 month post-second dose, the median and IQR Spike antibody levels were 49,763± 78,259 in pwMS (n=133) compared to 149,340± 99,967 in controls (n=486).

VoCs are associated with a reduction in Spike antibodies post vaccination

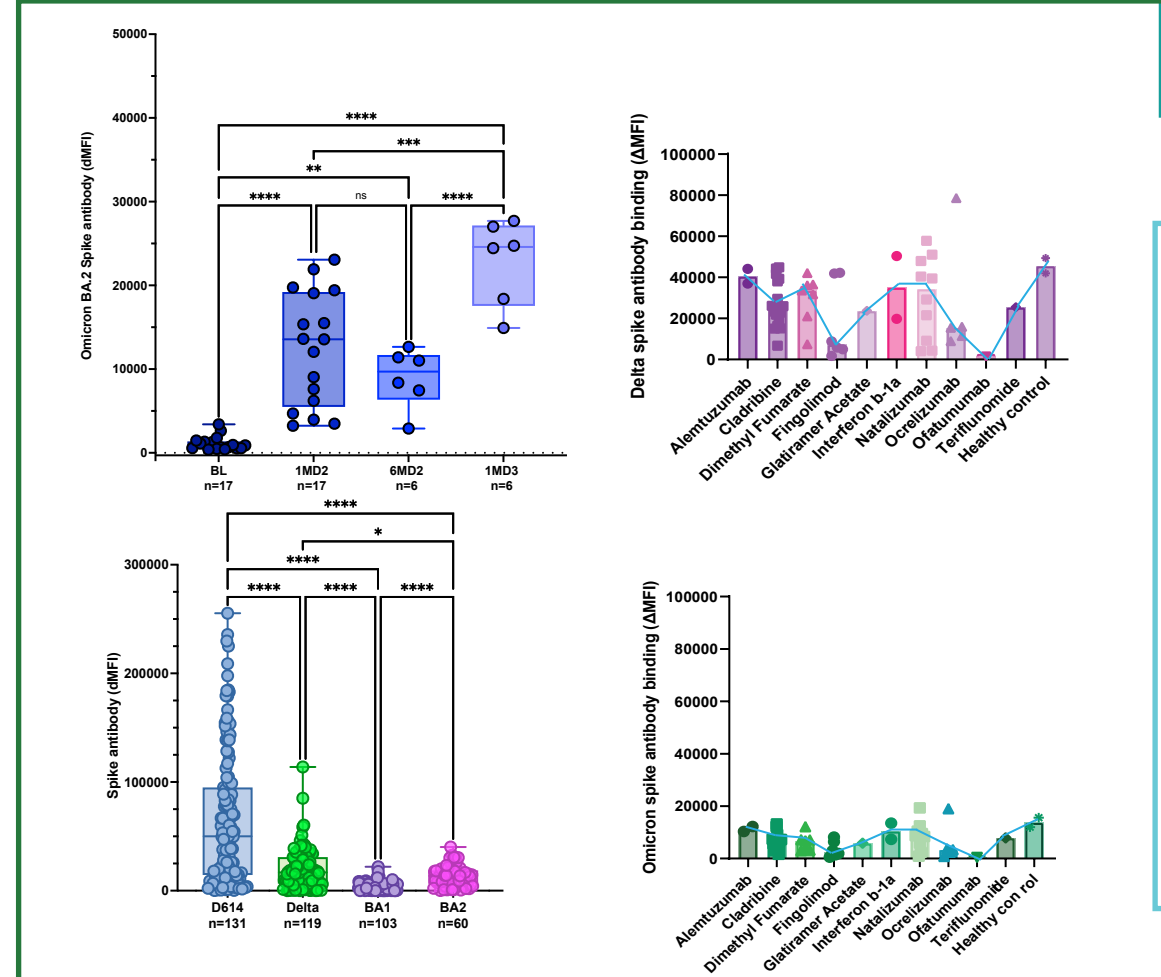


Figure 3. Dampened immune response towards emerging variants following vaccination
Spike antibody immunoreactivity was decreased in controls from the general community and pwMS by 70% against Delta Spike and 90% for Omicron BA1 Spike compared to the original Early clade Spike (1MD2). As observed for Early Spike antibody, DMTs, such as ocrelizumab, fingolimod, and ofatumumab, decreased the antibody binding to Delta and Omicron Spike. Still, the pattern of antibody recognition was similar between the three Spikes and all DMTs analysed, i.e. alemtuzumab, natalizumab,

Some DMTs are associated with increase in Spike antibody production post booster

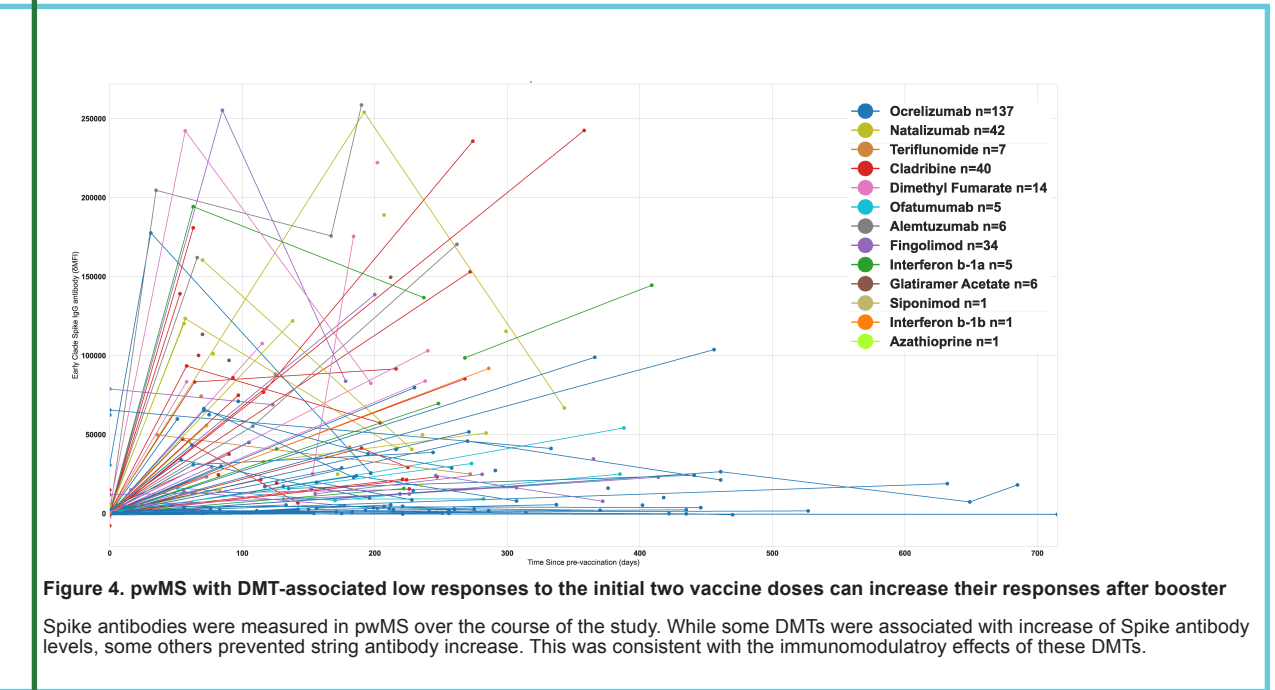


Figure 4. pwMS with DMT-associated low responses to the initial two vaccine doses can increase their responses after booster
Spike antibodies were measured in pwMS over the course of the study. While some DMTs were associated with increase of Spike antibody levels, some others prevented string antibody increase. This was consistent with the immunomodulatory effects of these DMTs.

Conclusions

Some DMTs reduce Spike antibody titres or prevent seroconversion. Our data suggest that, irrespectively of DMTs, antibodies generated after vaccination did not bind Spike from recent VoCs to the same extent as the original Spike used in COVID-19 vaccines. pwMS may benefit from the new generation of COVID-19 vaccines.

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