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

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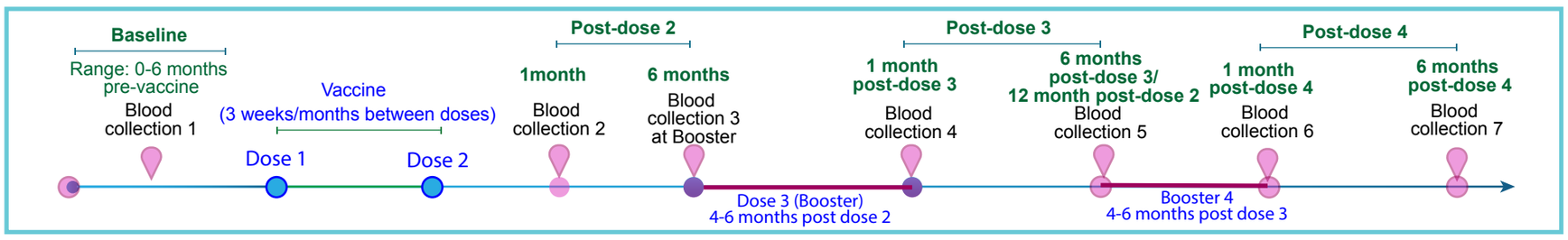
Introduction

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.brilot@sydney.edu.au. Funding: Novartis, MS Australia

Study timeline



Method: Live flow cytometry assay to detect spike antibodies

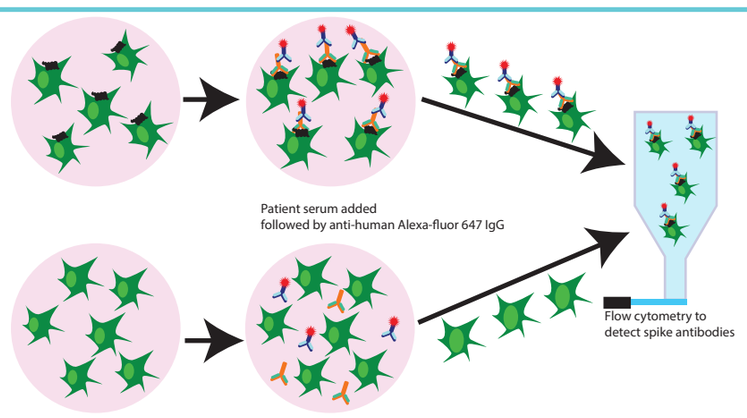


Figure 1. Spike antibodies bind with high affinity to Early Clade (D614G) Spike in comparison to Spike from VoCs

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 expressspike 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

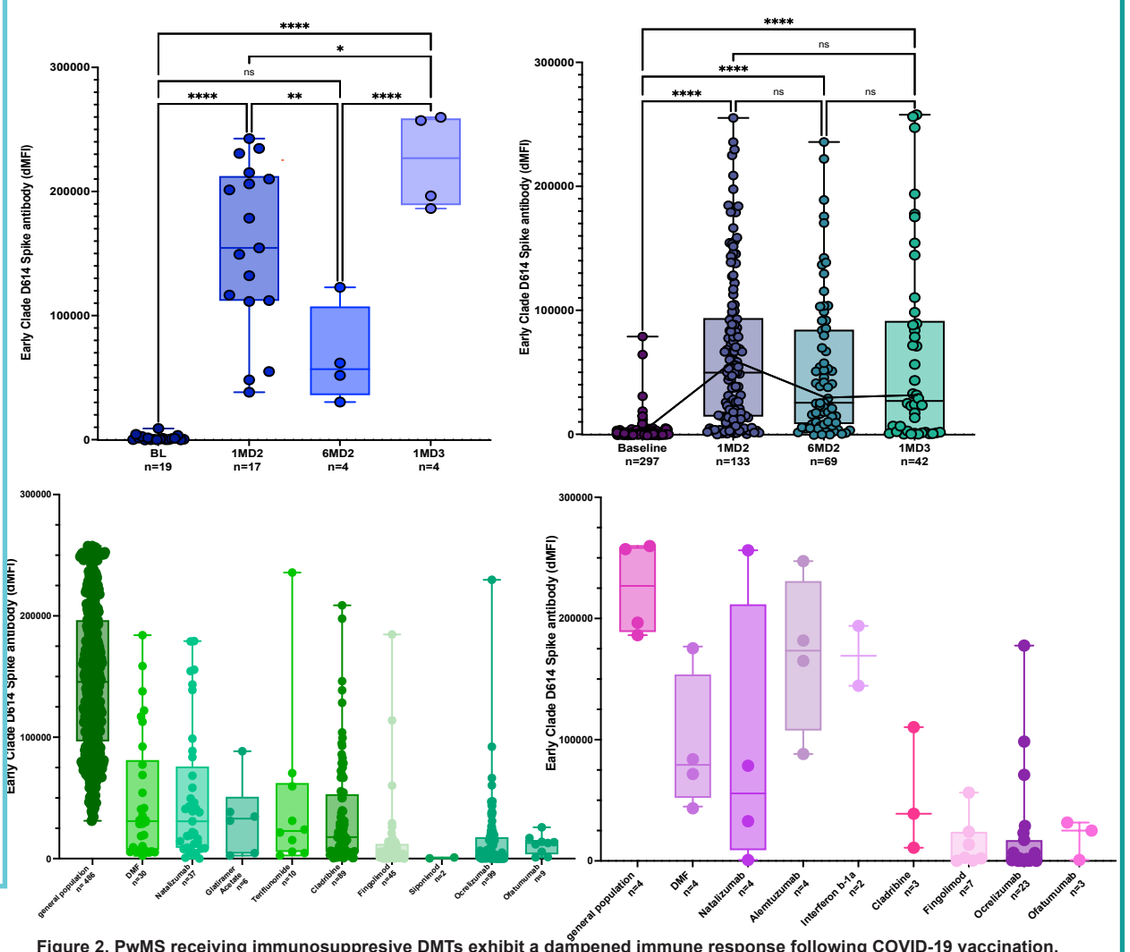


Figure 2. PwMS receiving immunosuppresive DMTs exhibit a dampened immune response following COVID-19 vaccination.

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), ofatumimab, (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

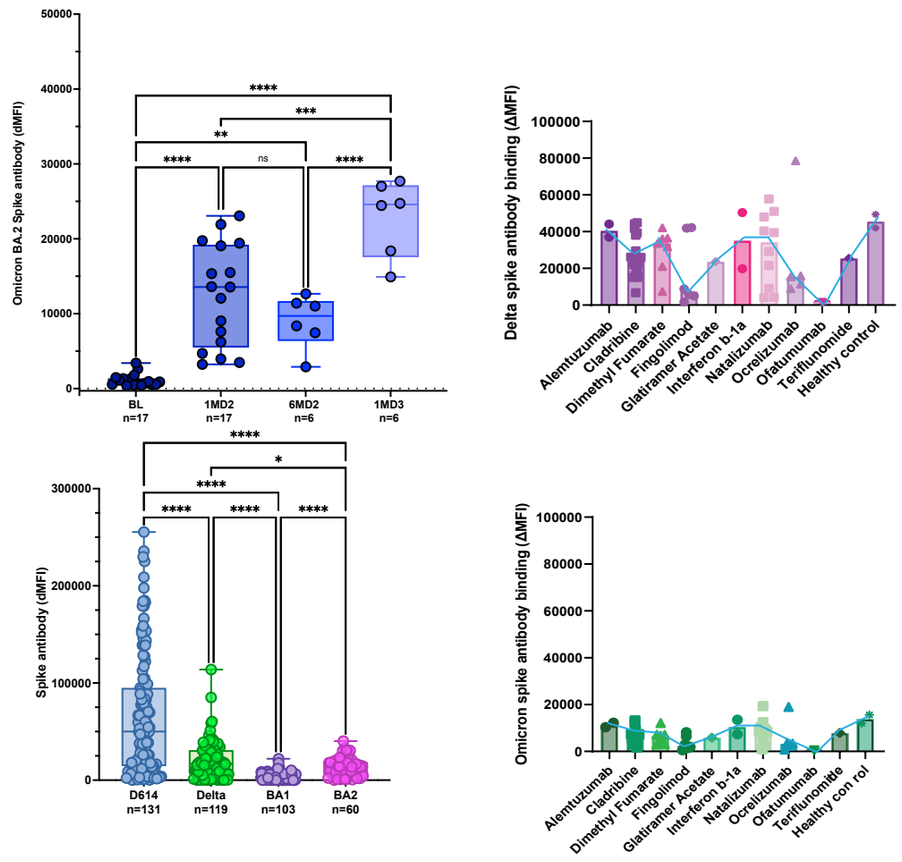


Figure 3. Dampened immune response towards emerging variants following vaccination

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

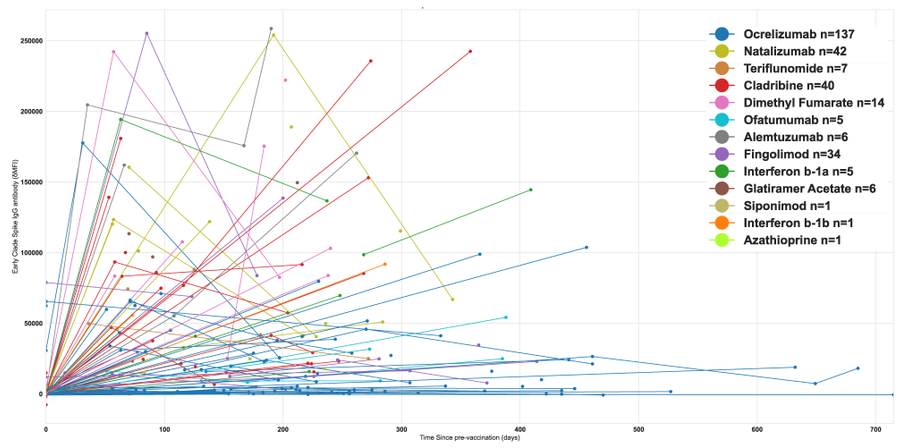


Figure 4. pwMS with DMT-associated low responses to the initial two vaccine doses can increase their responses after booster

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 immunomodulatroy 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.

Disclosures: AP, AY, SH, L L-K, VM, FXZL, KMR, SW, MVR, MT, OR, SS, AC: nothing to disclose. MJF-P has received research funding from MS Australia and travel compensation from Merck.VGK received conference travel support from Merck and Roche and speaker's honoraria from Biogen and Roche outside of the submitted work. She receives research support from the Australian NHMRC and MS Australia. VEM: has received research funding from Merck KGgA. TK served on scientific advisory boards for BMS, Roche, Janssen, Sanofi Genzyme, Novartis, Merck and Biogen, steering committee for Brain Atrophy Initiative by Sanofi Genzyme, received conference travel support and/or speaker honoraria from WebMD Global, Eisai, Novartis, Biogen, Sanofi-Genzyme, Teva, BioCSL and Merck and received research or educational event support from Biogen, Novartis, Genzyme, Roche, Celgene and Merck. MHB reports research grants from Genzyme-Sanofi, Novartis, Biogen, Merck and BMS; and is a Research Consultant for RxMx and Research Director for the Sydney Neuroimaging Analysis Centre. HB has received institutional (Monash University) funding from Biogen, F. Hoffmann-La Roche Ltd, Merck, Alexion, CSL, and Novartis; has carried out contracted research for Novartis, Merck, F. Hoffmann-La Roche Ltd and Biogen; has taken part in speakers' bureaus for Biogen,Genzyme, UCB, Novartis, F. Hoffmann-La Roche Ltd and Merck; has received personal compensation from Oxford Health Policy Forum for the Brain Health Steering Committee. SR has received research funding from the NHMRC and RACP. She serves as a consultant on an advisory board for UCB and Limbic Neurology, and has been an invited speaker for Biogen, Excemed, and Limbic Neurology. SAB has received honoraria for attendance at advisory boards and travel sponsorship from Bayer-Schering, Biogen-Idec, Merck-Serono, Novartis, and Sanofi-Genzyme, has received speakers honoraria from Biogen-Idec and Genzyme, is an investigator in clinical trials sponsored by Biogen, Novartis and Genzyme, and received was a research grant from Biogen. SWR has received travel support, honoraria, trial payments, research and clinical support from NHMRC, NBA, MAA, Lambert Initiative, Beeren foundation, Alexion, Biogen, CSL, Genzyme, Grifols, Merck, Novartis, Roche, Sanofi. JLS received travel compensation from Biogen, Merck and Novartis; has been involved in clinical trials with Biogen, Merck, Novartis and Roche; her institution has received honoraria for talks and advisory board service from Biogen, Merck, Novartis and Roche. AVDW has received institutional (Monash University) funding from Biogen, F. Hoffmann-La Roche Ltd, Merck, Alexion, CSL, and Novartis; has carried out contracted research for Novartis, Merck, F. Hoffmann-La Roche Ltd and Biogen; has taken part in speakers' bureaus for Biogen, Genzyme, UCB, Novartis, F. Hoffmann-La Roche Ltd and Merck. FB has received research funding from NSW Health, MS Australia, NHMRC, MRFF, and investigator-initiated grant from Novartis for this study. She was on an advisory board for Novartis and Merck, and has been an invited speaker for Biogen, Novartis, and Limbic Neurology.