# Concurrent Session Abstracts

## 6 SPIKE ANTIBODY SEROCONVERSION AND EMERGING VARIANT CROSS-REACTIVITY FOLLOWING COVID-19 THIRD VACCINATION DOSE IN AUSTRALIAN PEOPLE WITH MULTIPLE SCLEROSIS

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**Background** COVID-19 vaccination-induced Spike antibodies are attenuated in people living with multiple sclerosis (pwMS) on high-efficacy disease-modifying therapies (DMTs). It is currently unknown whether vaccine boosters will elicit a greater protective antibody cross-reactivity against emerging variants of concern, such as XBB.1 and BQ.1.1.

**Objective** We aimed to determine the breadth of Spike antibody immunoreactivity in pwMS after COVID-19 vaccination.

**Methods** Spike antibodies to Wuhan, XBB.1, and BQ1.1 SARS-CoV-2 were assessed in paired sera from pwMS (1-month post-second and -third doses, n=37) and general community controls (n=10). Demographic and treatment information was available in all patients.

**Results** At 1-month post-third dose, pwMS who did not seroconvert (n=12) were treated with ocrelizumab (11/21) and fingolimod (1/3). Natalizumab, fingolimod, ocrelizumab, dimethyl fumarate, and ofatumumab were associated with decreased titers of Spike antibody compared to controls, whereas alemtuzumab, cladribine, and IFNs were associated to titers comparable to controls. When serial Wuhan Spike antibody titers were compared at 1-month post-second and -third doses, most DMTs (alemtuzumab, fingolimod, cladribine, dimethyl fumarate, interferon-beta, natalizumab, ocrelizumab, and ofatumumab) were able to increase or maintain their Spike antibody titers. Spike antibody titers against XBB.1 and BQ1.1 was reduced by 80% compared to the Wuhan titers in all groups. The third dose increased median titres compared to the second dose in most DMTs including the CD20-depleting DMTs but to a much lesser extent (ocrelizumab n=10; ofatumumab n=2).

**Conclusion** Some SARS-CoV-2 variants and some DMTs reduce Spike antibody titres or prevent seroconversion even after a third dose of vaccine.

## 7 CLADIN: CLADRIBINE AND INNATE IMMUNE RESPONSES IN MULTIPLE SCLEROSIS

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**Introduction** Cladribine (Mavenclad®) is an oral treatment for relapsing remitting MS (RRMS). P2X7R is a purinergic receptor implicated in neuroinflammatory processes.

**Objective** To investigate the mechanism of action of Cladribine on peripheral monocytes.

**Methods** This is a Phase IV, open-label, multi-centre, 3-year, translational trial. 40 RRMS patients commencing Cladribine were prospectively recruited into this study. Peripheral monocytes were isolated from whole blood using negative selection, and stained with the following markers for flow cytometric analysis (CD14, CD16, HLADR, CD11b, P2X7R, DAPI). P2X7R Pore activity was assessed using YOPRO dye uptake experiments and confocal microscopy.

**Results** There was evidence of reduction in monocyte count at week 1 post-cladribine commencement compared to baseline (0.55 ±0.04 vs 0.08 ± 0.0187; p=10^-6). However, unlike lymphocytes, the cytotoxic effects of cladribine on monocytes was not sustained, and the cells repopulated at 2 months. CD14loCD16+ monocytes were the sub-population most reduced at week 1 compared to baseline, 2, and 6 months (P<0.001). *In vitro*, Cladrabine induced a reduction in P2X7R pore activity (p<0.001). MS relapse activity decreased in the 12 months after commencement of Cladribine (p<0.001). Relapse in the last 12 months, MRI disease activity and age did not predict changes in EDSS in the 12 months subsequent to Cladribine commencement.

**Conclusion** This study demonstrates a novel mechanism of action for Cladribine, highlighting that it exerts its effects acutely on peripheral monocytes, and possibly via P2X7R. The laboratory data will be linked to clinical data to decipher what innate immune parameters translate to better patient outcome.