for patients diagnosed with psoriasis. The observed prevalence of psoriasis in MS patients was 12.19% however, the true prevalence is likely to be much higher as various symptoms of psoriasis were reported by a much larger proportion of MS patients. Of the 72 cases without psoriasis, various skin symptoms that were reported were intermittent irritation (for at least 6 months) or erythematous rash (35.4%), seasonal skin changes (39.0%) and thickened scaly skin behind ears and scalps (18.3%). Moreover, 18.3% had flaky, peeling or scaly skin while 24.4% experienced dandruff; 17.1% reported nail changes, and 13.4% reported a family history of psoriasis. The study also showed that combined psoriasis and eczema was relatively common at 3.7%.

Conclusions In this pilot study there is a high prevalence of psoriasis in patients with MS suggesting an immunopathological association between the two diseases and indicates that further studies should be done to elucidate common mechanisms, and the nature of this phenotype.

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006

COMPARISON OF MULTIPLE DISEASE MODIFYING THERAPIES IN MULTIPLE SCLEROSIS WITH MARGINAL STRUCTURAL MODELS

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10.1136/bmjno-2021-ANZAN.6

Background Because of methodological challenges comparisons of multiple treatments in multiple sclerosis cohorts have been limited to pairwise and triple comparisons.

Objectives Extend marginal structural models (MSM) to allow simultaneous comparisons of multiple MS treatments.

Methods We selected patients from the MSBase registry with Clinically Isolated Syndrome and Relapsing-Remitting MS followed for ≥ 1 year, with ≥ 3 visits, ≥ 1 visit per year and exposed to a MS therapy. MSMs were used to compare cumulative hazards of 6-month confirmed worsening and improvement of disability, and the incidence of relapses between treatments. MSMs were continuously re-adjusted for patient age, sex, pregnancy, date from first symptom, prior relapse history and MRI activity. We used MSMs to compare the Average Treatment Effect (ATE), the effect a treatment would have had if the entire study population had been

treated with this treatment vs. another treatment. We also estimated the Average Treatment Effect Among the Treated (ATT): comparison an observed effect of a treatment with a counterfactual (not observed) effect of another treatment in the same study population.

Results Among 23687 patients, we compared ATE of glatiramer acetate (reference), interferon b, natalizumab, fingolimod, dimethyl fumarate, and teriflunomide. In ATE, a reduction of relapse frequency was more prominent on natalizumab, followed by fingolimod (47% and 24% respectively, reference: glatiramer acetate) when compared with the other treatments. The ATT models confirmed these observations.

Conclusions Compared to other DMTs natalizumab and fingolimod were associated with superior reduction in relapse frequency than glatiramer acetate, interferon beta, teriflunomide and dimethyl fumarate.

007

IMMUNOTHERAPY RESPONSIVE NEUROPATHIC PAIN ASSOCIATED WITH LGI1 AND CASPR2 ANTIBODIES

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10.1136/bmjno-2021-ANZAN.7

Objective We evaluated pain in leucine-rich glioma inactivated1(LGI1) and contactin-associated protein2(CASPR2)-antibody positive(Ab+) patients, to evaluate clinical associations and pathophysiology of treatable pain syndromes.

Methods 108 LGI1-Ab+, 33 CASPR2-Ab+, and 6 LGI1/CASPR2-Ab+patients were phenotyped. Pain questionnaires were undertaken to identify neuropathic pain using the Douleur Neuropathique(DN4), patient reported outcome measurement information system(PROMIS), and quality of life(EQ5D). Skin biopsies, and serum binding to cell-based assays, sensory neuronal cocultures, and dorsal root ganglion(DRG) cultures were undertaken.

Results 39/147 patients described pain, including 17/33 CASPR2-Ab+(52%), 20/108 LGI1-Ab+(19%), and 2 LGI1/CASPR2-Ab+patients. Questionnaires completed in 23/39 (59%) revealed comparable DN4 scores($p=0.319$) with 58% of LGI1-Ab+ and 67% of CASPR2-Ab+patients having neuropathic pain. Patients rated $>50\%$ response in 8/30(27%) analgesia trials, versus 20/40(55%) immunotherapy trials ($p=0.045$). PROMIS ratings were similar between LGI1-Ab+ and CASPR2-Ab+patients at nadir($p=0.662$), but showed more improvement following immunotherapy in LGI1-Ab+ ($p=0.008$) than CASPR2-Ab+patients($p=0.125$). At follow-up(median 57 months) CASPR2-Ab+patients showed more impairment in mobility($p=0.014$), daily activities ($p=0.019$), and anxiety/depression($p=0.043$); and lower overall health($p=0.019$) on the EQ5D compared to LGI1-Ab+patients. Intraepidermal nerve fibre density was reduced in 2 LGI1-Ab+ and 1 CASPR2-Ab+patients. Serum immunoglobulin G(IgG) from 6/16 CASPR2-Ab+patients bound to sensory neuronal cocultures compared to 0/14 LGI1-Ab+patients($p=0.019$) and 0/12 healthy controls. Serum IgG from 10/16 CASPR2-Ab+patients bound to DRG cultures

compared to 1/14 LGI1-Ab+patients($p=0.0024$) and 1/12 healthy controls.

Conclusion Neuropathic pain may be present in both LGI-Ab + and CASPR2-Ab+patients, and is immunotherapy responsive. Serum IgG from CASPR2-Ab+patients more frequently bound sensory neurons and dorsal root ganglia, suggesting pathophysiological differences which may underlie the more severe pain in these patients.

008

DISEASE REACTIVATION AFTER CESSATION OF DISEASE-MODIFYING THERAPY IN RELAPSING-REMITTING MULTIPLE SCLEROSIS

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10.1136/bmjno-2021-ANZAN.8

Objectives To evaluate the rate of return of disease activity after cessation of multiple sclerosis (MS) disease-modifying therapy.

Methods This was a retrospective cohort study from two large observational MS registries: MSBase and OFSEP. Patients with relapsing-remitting MS who had ceased a disease-modifying therapy and were followed up for the subsequent 12-months were included in the analysis. The primary study outcome was annualised relapse rate in the 12 months after disease-modifying therapy discontinuation stratified by patients who did, and did not, commence a subsequent therapy. The secondary endpoint was the predictors of first relapse and disability accumulation after treatment discontinuation.

Results 18 029 eligible treatment discontinuation epochs were identified for seven therapies. Rates of relapse started to increase 2-months after natalizumab cessation. Commencement of a subsequent therapy within 2-4 months reduced the magnitude of disease reactivation. After discontinuation of fingolimod, rates of relapse increased overall, and stabilised faster in patients who started a new therapy within 1-2 months. Magnitude of disease reactivation for other therapies was low, but reduced further by commencement of another treatment 1-10 months after treatment discontinuation. Predictors of relapse were higher relapse rate in the year before cessation, female sex, younger age and higher EDSS. Commencement of a subsequent therapy reduced both the risk of relapse (HR 0.76, CI 0.72-0.81) and disability accumulation (0.73, 0.65-0.80).

Conclusion Understanding the rate of disease reactivation after discontinuing different MS immunotherapies will help guide optimal wash-out times for therapeutic agents during treatment sequencing.

009

PREDICTING INFECTION RISK IN MULTIPLE SCLEROSIS PATIENTS TREATED WITH OCRELIZUMAB: A RETROSPECTIVE COHORT STUDY

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10.1136/bmjno-2021-ANZAN.9

Objective To examine factors determining risk of self-reported infections and antimicrobial use in patients receiving Ocrelizumab for MS.

Methods Retrospective, observational cohort study conducted in Ocrelizumab-treated patients at the Royal Melbourne Hospital. The association of clinical and laboratory factors with self-reported infection rate and antimicrobial use were estimated using univariate and multivariable logistic regression models.

Results 185 patients were included in the study, and 176 infections were reported in 89 patients (46.1%), and in 47 patients (25.3%) antimicrobial use was identified. In univariate analyses, a higher serum IgA was associated with reduced odds of infection (OR 0.44, 95% CI 0.25 - 0.76). In multivariable analyses, older age (OR 0.94, 95% CI 0.88 - 0.99), higher serum IgA (OR 0.37, 95% CI 0.17 - 0.80) and higher serum IgG (OR 0.81, 95% CI 0.67 - 0.99) were associated with reduced odds of infection. Older age (OR 0.85, 95% CI 0.75 - 0.96) and higher serum IgA (OR 0.23, 95% CI 0.07 - 0.79) were associated with reduced odds of antimicrobial use, whilst longer MS disease duration (OR 1.22, 95% CI 1.06 - 1.41) and higher EDSS (OR 1.99, 95% CI 1.02 - 3.86) were associated with increased odds of antimicrobial use.

Conclusions Higher serum IgA, IgG and older age were associated with reduced odds of infection. Our findings highlight non-uniformity of infection risk in Ocrelizumab-treated MS patients, and substantiate the need to monitor immunoglobulin levels pre-treatment and whilst on therapy.

010

REAL-WORLD EXPERIENCE WITH OCRELIZUMAB IN THE MSBASE REGISTRY – AUSTRALIAN RRMS COHORT

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10.1136/bmjno-2021-ANZAN.10

Introduction Ocrelizumab (OCR) is a humanised anti-CD20⁺ monoclonal antibody for the treatment of Multiple Sclerosis.