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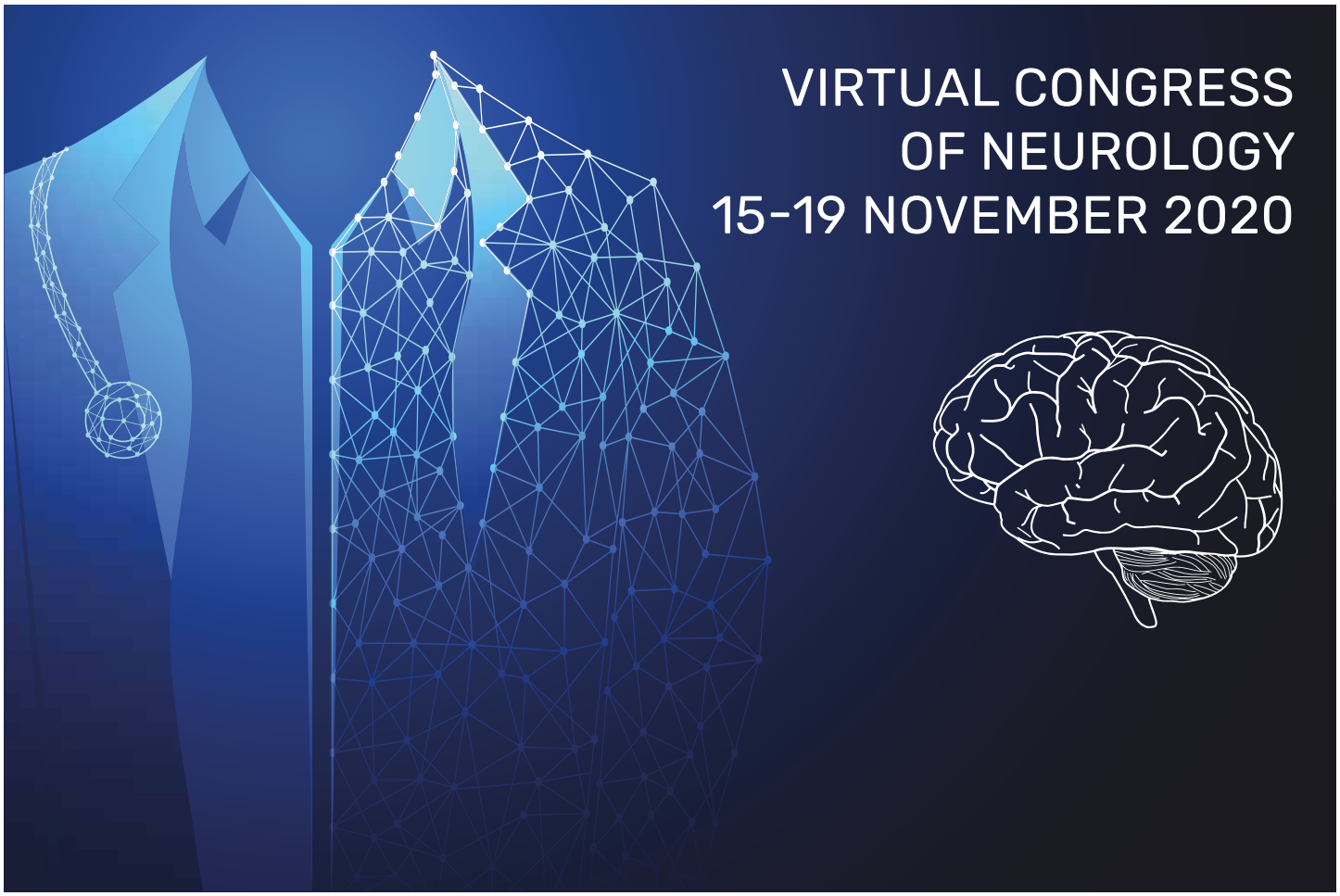

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PO Box 90
3740 AB Baarn
The Netherlands

Telephone +31 85 4012 560
E-mail publishers@medicom-publishers.com
www.medicom-publishers.com

COLOPHON
Editor Dr Rachel Giles
Medical writer Daniel Dresden
Publishing Director Paul Willers
Editorial Manager Lisa Colson
Editorial Coordinator Dr Joery Goossens
Graphic Design MOOZ grafisch ontwerp

Editor Conflict of Interest: no conflicts

1. No association between Ig levels and infection in ofatumumab-treated patients with relapsing MS

Multiple sclerosis (MS) patients are at an increased risk of infections compared with the general population. A recent analysis of the phase 3 ASCLEPIOS I/ ASCLEPIOS II trials showed no association between a decrease in serum immunoglobulin (Ig) levels and the incidence of infections in ofatumumab-treated patients with relapsing MS.

Igs play a major role in immunoprotection. In MS patients receiving disease-modifying therapies, particularly B-cell-depleting therapies, serum IgM and IgG levels below the lower limit of normal (LLN) have been associated with an increased risk of infections. Igs have also been considered as a biomarker for assessment of infection risk in MS patients.

In the phase 3 ASCLEPIOS I/II trials, ofatumumab, a fully human anti-CD20 monoclonal antibody with a monthly 20 mg subcutaneous dosing regimen, demonstrated superior efficacy versus teriflunomide 14 mg oral once daily, and a manageable safety profile in patients with relapsing MS [1]. Now, in a study presented by Prof. Heinz Wiendl (University of Muenster, Germany), it was shown that average serum IgG and IgM levels remained well within the reference ranges over time in both treatment groups [2]. In a few patients, a reduction in the mean serum IgM levels from baseline was observed over time, but these levels remained well above the LLN. There was no decrease in mean IgG levels from baseline over time.

In addition, the current analysis showed no association between a decrease in Ig levels and the incidence of infections in both ofatumumab- and teriflunomide-treated patients. A total of 31.1% and 29.0% of patients, respectively, experienced at least 1 infection within 1 month prior and until 1 month after the reduction in Ig levels below the LLN. Most infections reported were non-serious in nature and were mild to moderate in severity. Most cases resolved while patients were continuing treatment.

The authors concluded that assessing Ig levels prior to and during initiation of anti-CD20 therapy is important, but additional long-term studies are needed to elucidate the frequency and implications of low Ig levels at baseline and during treatment.

1. Hauser SL, et al. N Engl J Med. 2020;383:546–57.
2. Wiendl H, et al. Serum Immunoglobulin Levels and Infections in Relapsing Multiple Sclerosis. ECF 28th Annual Meeting. Abstract 33.

2. Defining phenotypes of MS-related cognitive impairment

In a large and heterogeneous cohort of multiple sclerosis (MS) patients from Italy, 5 homogenous and clinically meaningful phenotypes of MS-related cognitive impairment were defined. These results can pave the way to future research on neuroanatomical substrates and help define tailored management strategies.

Cognitive impairment is a common and disabling feature of MS, affecting 40-70% of patients. Altering the behaviour and quality of life of MS patients, it can lead to social and personal difficulties, sometimes despite minimal concurrent physical disability. Information processing speed and episodic memory are the cognitive functions most frequently affected in MS, but additional difficulties in executive function, verbal fluency, and visuospatial abilities have been reported. MRI has proven to represent a powerful tool in investigating the neuroanatomy of cognitive impairment in MS patients, but a precise characterisation of cognitive phenotypes is still lacking.

In a study presented by Dr Ermelinda De Meo (Vita-Salute San Raffaele University, Italy), 1,212 clinically stable MS patients were compared with 196 healthy controls on a clinical, neuropsychological, and neuroanatomical level [1]. Based on the results, 5 cognitive phenotypes of MS were identified:

- preserved cognition in 19% of patients;
- mild verbal memory/semantic fluency in 30%;
- mild multi-domain involvement in 19%;
- severe attention/executive involvement in 14%; and
- severe multi-domain involvement in 18%.

Patients with a preserved cognition and/or mild-verbal memory/semantic fluency were on average younger and had shorter disease duration compared with individuals manifesting other phenotypes. Physical disability was lowest in patients with a preserved cognition and highest in patients with a severe multi-domain involvement. Severe cognitive phenotypes prevailed in progressive patients.

At MRI evaluation, reduced hippocampal volume was associated with mild verbal memory/semantic fluency, reduced cortical grey matter volume was associated with mild multi-domain involvement, higher T2-hyperintense lesion volume was associated with severe attention/executive involvement, and extensive brain damage was associated with severe multi-domain involvement.

1. De Meo E, et al. Identifying distinct cognitive phenotypes in multiple sclerosis. ECF 28th Annual Meeting. Abstract 50.

3. First long-term efficacy data of a BTK inhibitor

In the open-label extension of a phase 2 trial, the improvement in annualised relapse rate (ARR) with the Bruton's tyrosine kinase (BTK) inhibitor evobrutinib 75 mg twice daily (BID) at week 48 was maintained at week 108. These long-term efficacy data in patients with relapsing multiple sclerosis (MS) are the first to be reported for the class of agents that inhibits BTK.

Evobrutinib targets both B cells and myeloid cells, which are known to play a key role in the pathogenesis of autoimmune diseases, such as MS. A previous phase 2, randomised controlled trial showed clinical efficacy of evobrutinib in relapsing MS, with a significant reduction of T1 Gd-enhancing lesions compared with placebo at week 24 and a continued efficacy through week 48 [1]. Of 213 patients randomised in the double-blind phase of the trial, 164 patients (77%) entered the open-label extension phase. Of them, 148 patients (90%) completed ≥108 weeks of treatment overall. At the ECF 28th Annual Meeting, results of long-term efficacy of evobrutinib in the ongoing open-label extension were presented by Prof. Xavier Montalban (Hospital University Vall d'Hebron, Spain) [2].

Efficacy was assessed by ARR as well as cumulative probability of and time to first qualified relapse in patients completing ≥60 weeks of open-label extension treatment. Compared with those initiated in other double-blind period arms, patients initiated on evobrutinib 75 mg BID had lower ARR (0.11 at week 48, and 0.12 at week 108) and lower cumulative probability of first qualified relapse (0.08 at week 48, and 0.20 at week 96).

The estimated time by which 20% of patients had a qualified relapse was almost 3 times longer for those initiated on 75 mg BID versus placebo.

Both outcome measures of probability and time to first qualified relapse highlighted that patients initiated on 75 mg BID achieved greater treatment efficacy than those initiated on evobrutinib 25 mg once daily, 75 mg once daily, or placebo.

1. Montalban X, et al. N Engl J Med. 2019;380:2406-2417.
2. Montalban X, et al. Evobrutinib efficacy is maintained over two years in patients with relapsing MS Clinical relapse rates in relapsing multiple sclerosis patients treated with the BTK inhibitor evobrutinib: results of an open-label extension to a Phase II study. ECF 28th Annual Meeting. Abstract 31.

4. Novel disease-specific scale confirms huge impact of fatigue

A real-world study in US adults with relapsing multiple sclerosis (MS) confirmed that fatigue has a huge impact on day-to-day functioning in most patients with relapsing MS. Fatigue increases with symptom exacerbation, depression, sleep disorders, and pain. The Fatigue Symptoms and Impacts Questionnaire-Relapsing Multiple Sclerosis (FSIQ-RMS) is a novel MS-specific assessment that can advance the understanding and management of fatigue.

Fatigue is defined by subjective experience and measured via patient-reported outcome (PRO) instruments. PRO tools that are MS-specific can improve understanding of MS fatigue and its impact, improving its clinical management. However, currently available PROs that assess MS-related fatigue do not meet instrument development and psychometric property requirements based on current guidelines.

The FSIQ-RMS is a novel MS-specific PRO instrument, which was developed to assess both fatigue in patients with relapsing MS and its impact on physical activity, cognitive and emotional functioning, and coping mechanisms [1]. An ongoing non-interventional prospective, longitudinal study, presented by Marion Azoulai (Carenity, France), aimed at measuring MS-related fatigue symptoms and its impact on daily life in a real-world population using a self-administered online questionnaire, including the FSIQ-RMS [2].

A total of 200 relapsing MS patients completed the 7-day assessment. The most impactful symptoms on daily functioning were fatigue and walking difficulties. Patients with lower disability rated fatigue as the most impactful symptom on daily life. A majority of patients (55%) experienced fatigue before MS diagnosis. Most patients (76%) were not currently relapsing, and these had a mean fatigue symptom domain score of 55.6, compared with 67.3 in relapsing patients. A majority of patients were not depressed (54%) and did not report a sleep disorder (71%). Heat exposure was the most common triggering factor for fatigue (82%).

In conclusion, this survey showed that fatigue occurred in most MS patients and influenced their daily functioning. The FSIQ-RMS measures fatigue symptoms and impact, which is relevant and meaningful to patients.

1. Hudgens S. Value Health. 2019;22(4):453-466.
2. Azoulai M, et al. A real-world study characterizing symptoms and impacts of fatigue in US adults with relapsing multiple sclerosis using a novel disease specific scale. ECF 28th Annual Meeting. Abstract 38.

5. No increased risk with IFN-β use during pregnancy

Data from the Middle East shows that exposure to subcutaneous interferon-beta (IFN-β) before and/or during pregnancy, especially in the first trimester, does not adversely affect pregnancy or infant outcomes. These findings are consistent with data collected from other registries and from the global safety database of the drug company.

Women with multiple sclerosis (MS) are often diagnosed and treated at childbearing age. Therefore, family planning is an important consideration for female patients undergoing treatment. IFN-β has been recently approved for use during pregnancy and lactation. Data from different registries has shown that exposure to IFN-β before and/or during pregnancy, especially during the first trimester, did not adversely affect pregnancy or infant outcomes [1].

The objective of the presented study was to carry out a descriptive analysis of data from the safety database of the drug company in the Gulf Cooperation Council region (GCC: United Arab Emirates, Saudi Arabia, Oman, Qatar, Kuwait, Bahrain, Yemen), regarding pregnancy outcomes in MS patients receiving subcutaneous IFN-β [2].

During the period between 2015 to 2019, a total of 224 adverse events (AEs) related to pregnancy and/or childbirth were identified in 114 cases. The majority (83.9%) of these AEs were not serious. Most common serious AEs were premature baby (n=5), premature delivery (n=5), low birth weight (n=5), and spontaneous abortion (n=4). Normal newborn outcome was identified with the highest frequency. In comparison with the global analysis of all pregnancy cases, no abnormal AE trend was identified for the GCC regions.

1. Hellwig K, et al. J Neurol. 2020;267:1715–1723.
2. Boshra A, et al. Pregnancy safety outcomes in subcutaneous interferon-beta-exposed patients with multiple sclerosis: Results from GCC region. ECF 28th Annual Meeting. Abstract 13.

6. Reliable and convenient method to assess cognitive function in MS patients

In a Japanese study, the Processing Speed Test (PST) score correlated with physical disability, brain volume, depression, fatigue, and quality of life in multiple sclerosis (MS) patients.

Cognitive dysfunction in MS patients is known to be associated with physical disability and impaired quality of life, but is often overlooked in clinical practice. To assess cognitive function in MS patients, several tests have been developed. However, performing these tests is challenging in routine clinical settings because of time constraints and unavailability of trained technicians.
The PST is a tablet/computer application designed to evaluate cognitive function in patients with MS. It is a modified form of the Symbol Digit Modality Test (SDMT) and its close performance correlates with the original SDMT.

One advantage of the PST is that it can be performed by patients themselves in a relatively short period. Therefore, the test is a reliable and convenient method for assessing cognitive function in MS patients in clinical settings.

Dr Yusei Miyazaki (NHO Hokkaido Medical Center, Japan) and colleagues evaluated the usefulness of the PST by assessing the relationship between performance and physiological disability domains of this test and brain volume, depression, fatigue, and quality of life in MS patients. Included were 47 patients with a mean age of 40.7; 68% were female; mean disease duration was 10.1 years; and median Expended Disability Status Scale (EDSS) score 2.0.

The mean PST score was 53.6, and this correlated negatively with EDSS, Beck Depression Inventory (BDI)-II, and Fatigue Severity Scale (FSS); while correlating positively with total brain volume, cortical grey matter volume, and Functional Assessment of MS (FAMS) score. The authors suggested that the PST is a reliable and convenient tool to evaluate cognitive function in MS patients.

1. Miyazaki Y, et al. Clinical utility of the Processing Speed Test in patients with multiple sclerosis. ECF 28th Annual Meeting. Abstract 76.

7. Tackling unmet MS-related cognitive challenges

Controlled studies comparing therapies with respect to their effects on rate of cognitive decline in multiple sclerosis (MS) are lacking. In addition, current open-label studies or clinical trials on cognitive functioning have not selected patients on criteria for cognitive dysfunction. So, the question remains if a cognitive-based early initiation of highly effective treatment should be considered.

Researchers from Spain initiated the CogEval project, comparing high efficacy versus usual first-line treatment in patients with cognitive dysfunction, evaluated via Processing Speed Test (PST) [1]. The PST is a self-administered iPad®-based tool to

measure MS-related deficits in processing speed and its use has shown an advantage over pen-and-paper cognitive batteries because of its ease of administration and a standardised scoring system.

The aim of CogEval is to determine whether early initiation of highly effective disease-modifying therapy (DMT) in patients with relapsing-remitting MS is associated with a decreased rate of longitudinal cognitive decline. Dr Andrés Labiano-Fontcuberta (University Hospital "12 de Octubre", Spain) presented the methods and objectives of this randomised open-label pilot study. Patients who are not under consideration for initiation of high-efficacy DMT but whose results on PST are below normal limits will be enrolled.

Participants will randomly be allocated into 2 groups:

- experimental or intervention group, initiating highly-effective DMT (natalizumab, ocrelizumab, or alemtuzumab); and
- control group without intervention, which will continue with the conventional first-line treatment.

After a treatment period of 24 weeks, change from baseline PST and proportion of cognitive decline-free patients will be assessed. Recruitment is still ongoing.

1. Labiano-Fontcuberta A. CogEval project: tackling unmet multiple sclerosis-related cognitive challenges. ECF 28th Annual Meeting. Abstract 41.

8. Progressive aerobic exercise improves fatigue

In a representative sample of multiple sclerosis (MS) patients, 24 weeks of progressive aerobic exercise induced a clinically relevant and long-lasting reduction in fatigue impact and seemed to positively influence walking ability and capacity. These findings from Denmark suggest that long-term progressive aerobic exercise could be recommended for MS patients.

In MS patients, fatigue and difficulty with walking are 2 of the most common and disabling symptoms. Fatigue is a multidimensional and complex symptom, affecting 70-90% of MS patients. The prevalence of walking impairment increases from 32% to 100% across the adult life span. In the last few decades, exercise has proven to be a promising approach to alleviate fatigue and to improve walking impairment.

Researchers from Denmark investigated the effects of a 24-week high-intensity progressive aerobic exercise intervention, followed by 24 weeks of follow-up, on self-reported fatigue impact and severity, objectively measured walking capacity, self-reported walking ability, and quality of life [1]. A total of 86 mildly to severely impaired MS patients were randomised to exercise or habitual lifestyle, with a 24-week crossover follow-up.

The nominal differences between group were as follows:

- Fatigue impact, measured by the Modified Fatigue Impact Scale (MFIS) total score: Δ -5.3;
- MFIS physical subscore: Δ -2.8;
- MFIS psychosocial subscore: Δ -0.9;
- Walking ability, measured by the 12-item MS Walking Scale (MSWS-12): Δ -5.9;
- Walking capacity, measured by the 6-Minute Walk Test (6MWT): Δ +14 meters; and
- Cardiorespiratory fitness, measured by VO_{2max}: Δ +3.5 mL O_2/min/kg.

These improvements were maintained at follow-up after 48 weeks.

No changes were observed in Fatigue Severity Scale (FSS), Six Spot Step Test (SSST), nor in the physical and mental subscores of the Short Form health survey (SF-36).

1. Langeskov-Christensen M, et al. Efficacy of aerobic exercise on fatigue, walking, and quality of life in MS. ECF 28th Annual Meeting. Abstract 26.

9. Characteristics of a population-based MS cohort treated with DMDs

A Canadian population study identified that almost 1 in 5 multiple sclerosis (MS) patients were ≥50 years old at the time of their first disease-modifying drug (DMD). Additionally, about the same percentage has at least some comorbidity. As these individuals are typically excluded from clinical trials, the study illustrates there is a need to understand the harms and benefits of DMD use in understudied groups.

The efficacy of DMDs is typically established via short clinical trials with a follow-up of 2-3 years, in highly select and motivated groups of MS patients. In clinical practice, DMDs are used for many years in a much more diverse patient population. Relatively little is known about the use of DMDs for MS in the population-based universal healthcare setting. The current study from Canada described the characteristics of a cohort of 10,418 MS patients exposed to their first DMD in the real-world setting; 74% were women [1].

At study entry, 17% of patients had some comorbidity (Charlson Comorbidity Index score ≥1). Mean age at first DMD was 39.6 years. Nearly 20% was aged ≥50 years when filling their first DMD and 3% was ≥60 years old. The mean age at first DMD prescription ranged from 35.9 years for alemtuzumab (n=37) to 43.6 years for teriflunomide (n=338).

Pattern of treatment changed over time, reflecting increased availability of DMDs. From 1996-2012, the most common first

DMD prescriptions filled were for beta-interferon (72%) or glatiramer acetate (27%). From 2013-2018, the most common first DMD prescriptions filled were for glatiramer acetate (33%), dimethyl fumarate (27%), or beta-interferon (22%).

1. Ng HS, et al. Characteristics of a population-based MS cohort treated with disease-modifying drugs. ECF 28th Annual Meeting. Abstract 06.

10. Real-world efficacy of ocrelizumab in MS patients

An interim analysis of the non-interventional phase 4 CONFIDENCE study showed the efficacy of ocrelizumab in multiple sclerosis (MS) patients in a real-world setting. The majority of patients in this analysis experienced treatment success, with Expanded Disability Status Scale (EDSS) and MSIS-29 remaining constant over the first year of ocrelizumab treatment.

The safety and efficacy of ocrelizumab in MS patients have been characterised in phase 2 and phase 3 clinical trials. As of July 2020, over 170,000 patients were treated with ocrelizumab. CONFIDENCE is a non-interventional post-authorisation phase 4 safety study evaluating the safety and effectiveness of ocrelizumab in patients with relapsing MS and primary progressive MS (PPMS) in a real-world setting. This study aims to collect data for 3,000 ocrelizumab-treated patients and 1,500 patients treated with other DMTs in Germany for up to 10 years.

The 1-year interim analysis presented by young investigator Julius Eggebrecht (Roche Pharma, Germany) included data from 559 patients newly treated with ocrelizumab [1]. Of these patients, approximately 82% had relapsing MS and 18% had PPMS; 64% of patients were female (66% of relapsing MS and 55% of PPMS patients). Mean baseline EDSS was 3.3 for patients with relapsing MS and 4.5 for patients with PPMS. At baseline, patients with relapsing MS and PPMS were on average 7 and 8 years older, respectively, than those in the pivotal clinical trials. Patients with relapsing MS had a higher mean baseline EDSS score, while patients with PPMS had a slightly lower mean baseline EDSS score than patients in the pivotal trials.

Over a 1-year period, 83.6% of patients with relapsing MS and 93.2% of PPMS patients experienced treatment success. About 85.3% of patients with relapsing MS experienced no relapses. The mean change in EDSS from baseline after 1 year of treatment was 0.0 for patients with relapsing MS and 0.1 for patients with PPMS.

1. Buttmann M, et al. Assessing the real-world effectiveness of ocrelizumab in patients with MS. ECF 28th Annual Meeting. Abstract 20.

11. Long-term safety and efficacy of ozanimod in relapsing MS

In the open-label extension DAYBREAK study, ozanimod was associated with low annualised relapse rate (ARR) and low new and enlarging T2 and gadolinium-enhancing (Gd+) multiple sclerosis (MS) lesion counts over time. Most participants were relapse-free and did not experience disability progression. Ozanimod was generally well tolerated and no new safety concerns emerged with long-term use.

Ozanimod, an oral selective sphingosine 1-phosphate (S1P) receptor modulator, has recently been approved for treatment of adults with relapsing forms of MS (FDA) or relapsing-remitting MS (EMA). In controlled phase 3 trials of relapsing MS, ozanimod significantly reduced annualised relapse rate (ARR), new and enlarging T2 and Gd+ lesion count, and brain volume loss compared with interferon-β-1a and was well tolerated. Participants with relapsing MS who completed a phase 1–3 ozanimod trial were eligible for the ongoing open-label extension DAYBREAK study. The objective is to characterise the long-term safety and efficacy of ozanimod in participants with relapsing MS.

The current interim analysis included almost 2,500 participants with mean ozanimod exposure of 35.4 months during the open-label extension [1]. At DAYBREAK entry, mean age was 37.7 years and 66.9% were female. Adjusted ARR was 0.112 for the total DAYBREAK population. At month 24 and month 36, 79% and 75% of patients were relapse-free, respectively. By data cut-off, 3-month confirmed disability progression was observed in 10.8% of open-label extension participants, 6-month confirmed disability progression in 8.6%. Mean number of new and enlarging T2 and Gd+ lesion was low.

In the open-label extension study, 81.8% of participants had treatment-emergent adverse events, most common being nasopharyngitis, headache, and upper respiratory tract infection. Observed rates were similar to those reported in parent trials, and did not differ across parent trial treatment groups. No new safety concerns emerged with long-term use.

1. Selmaj K, et al. Long-term safety and efficacy of ozanimod in relapsing multiple sclerosis in DAYBREAK: an open-label extension study of ozanimod phase 1–3 trials. ECF 28th Annual Meeting. Abstract 18.

12. Similar demographics, clinical characteristics, and treatment patterns in German claims study

Despite different administration methods and mechanisms of action, similar annualised relapse rates (ARR) and treatment persistence were observed in patients with relapsing multiple sclerosis (MS) on disease-modifying therapy (DMT). These were the results of a retrospective study using data from a German real-world insurance claims database.

Glatiramer acetate has been licensed as an injectable treatment for relapsing MS in Europe for over 20 years; follow-on glatiramer acetate received approval in 2016. Various oral DMTs have become available on the European market for the treatment of relapsing MS, including dimethyl fumarate and teriflunomide. However, overall real-world data on treatment patterns and associated health outcomes in patients with relapsing MS using these DMTs are limited.

The retrospective database analysis presented by Prof. Tjalf Ziemssen (University Hospital Carl Gustav Carus, Germany) evaluated patient demographics, clinical characteristics, and treatment patterns (switching and discontinuation) among relapsing MS patients on above-mentioned DMTs [1]. Of 16,283 patients with relapsing MS, 1,577 patients met all inclusion criteria. The group of patients using follow-on glatiramer acetate was too small for further analyses.

While interferons were the most frequently used DMTs in the pre-index period for all groups, patients in the glatiramer acetate cohort had the lowest proportion of interferon use during the pre-index period.

Patients who were prescribed glatiramer acetate and dimethyl fumarate were generally comparable in terms of demographics, overall relapse rate, and treatment persistence. Patients prescribed teriflunomide were numerically older and exhibited more comorbidities, as well as lower pre- and post-treatment overall relapse rate than the glatiramer acetate and DMF cohorts. Despite different administration methods and mechanisms of action, similar overall relapse rates and treatment persistence were observed across all 3 treatment groups.

1. Ziemssen T, et al. Real-world demographics, clinical characteristics and treatment patterns in relapsing multiple sclerosis patients on disease-modifying therapy (encore abstract from ACTRIMS/ECTRIMS). ECF 28th Annual Meeting. Abstract 24.

13. Superior effect of ponesimod versus teriflunomide on clinical disease activity and MRI-based outcomes

In the phase 3 OPTIMUM study, ponesimod showed benefit compared with teriflunomide on all MRI outcomes, including brain volume loss. A significantly higher proportion of patients achieved NEDA-3 and NEDA-4 status. These findings support the previously observed effect of ponesimod on clinical endpoints in patients with relapsing MS.

Ponesimod is an orally active, selective sphingosine-1-phosphate receptor modulator that causes dose-dependent sequestration of lymphocytes in lymphoid organs, thereby reducing the blood count. In the phase 3 OPTIMUM study (NCT02425644), ponesimod demonstrated superior efficacy compared to teriflunomide in reducing annualised relapse rate (ARR) in patients with relapsing-remitting MS. The current analysis of the OPTIMUM study evaluated prespecified MRI-based endpoints and 'no evidence of disease activity' (NEDA) status [1].

A total of 985 (86.9%) randomised patients completed the study. MRI findings for ponesimod versus teriflunomide, respectively, were:

- LS mean percent change in brain volume: −0.91% versus −1.25% (P<0.0001);
- LS mean difference for change in total T2-lesion load: −399.2 mm3 (P=0.002);
- mean number of new and enlarging T2-lesions per year: 1.40 versus 3.16 (rate ratio 0.44, P<0.0001; OR for absence of new/enlarging T2-lesions: 1.71, P=0.0001);
- mean number of new Gd+ T1-lesions per scan: 0.18 versus 0.43 (RR 0.42, P<0.0001; OR for absence of new Gd+ T1-lesions: 2.18, P<0.0001).

At week 108, 28.2% of ponesimod-treated patients and 18.3% of teriflunomide-treated patients achieved NEDA-3 (OR 1.70, P=0.0004) and 15.0% versus 8.5% achieved NEDA-4 (OR 1.85, P=0.0026), respectively. The most common reason for not achieving NEDA-3 or NEDA-4 status was presence of new and enlarging T2-lesions.

1. Kappos L, et al. Effect of oral ponesimod on clinical disease activity and MRI-based outcomes in patients with relapsing MS: Phase 3 OPTIMUM study. ECF 28th Annual Meeting. Abstract 34.

14. Decreased EDSS after plasma exchange in NMOSD

In a large cohort of patients with relapsing neuromyelitis optica spectrum disorders (NMOSD), treatment with steroids and plasma exchange was accompanied by a significant decrease in Expanded Disability Status Scale (EDSS). The benefit of plasma exchange correlated with the number of cycles received and was independent of the underlying clinical syndrome.

NMOSD are a group of inflammatory disorders of the CNS characterised by episodes of humoral-mediated inflammation. In concordance with the humoral pathogenesis, plasma exchange has proven to be a beneficial therapy in patients with severe NMOSD attacks [1]. The mechanism of action of plasma exchange involves the removal of different molecules that contribute to relapses of NMOSD, such as autoantibodies, complement proteins, and immune complexes.

In an observational, retrospective study presented by Dr Enrique Gómez-Figueroa (National Institute of Neurology and Neurosurgery, Mexico), all NMOSD patients who were treated with plasma exchange on top of standard methylprednisolone at the institute between 2010-2019 were included [2]. A total of 89 patients (78.7% female) were identified; mean age at onset was 38 years. Clinical syndrome was optic neuritis in 22.4%, longitudinally extensive myelitis in 28.1%, short transverse myelitis in 12.4%, and brainstem syndrome in 3.4% of patients.

The mean time from symptomatic onset to starting plasma exchange was 21 days. After a mean number of 5 plasma exchanges, a significant decrease was noted in median EDSS (6.5 to 6.0; P<0.001). The benefit of plasma exchange was irrespective of the clinical NMOSD disorder.

1. Srisupa-Olan T, et al. Mult Scler Relat Disord. 2018 Feb;20:115-121.
2. Enrique Gomez-Figueroa. Therapeutic Plasma Exchange Effect on Neuromyelitis Optica Spectrum Disorder. ECF 28th Annual Meeting. Abstract 58.

15. No support for IVIG as treatment of acute attacks in NMOSD

Results of a retrospective study from China did not support treatment with intravenous immunoglobulin (IVIG) alone as a first-line option for acute attacks of neuromyelitis optica spectrum disorders (NMOSD). However, the addition of IVIG therapy to high-dose intravenous steroids may be superior to steroids alone for NMOSD patients with high Expanded Disability Status Scale (EDSS) scores at onset.

Because NMOSD is an inflammatory autoimmune syndrome of the CNS with devastating clinical outcomes, adequate treatment of early attacks is decisive to prevent severe disability.

The first-line treatment for acute attacks is high-dose intravenous steroid therapy. Therapeutic plasma exchange and immunoadsorption serve to remove plasma components involved in the inflammation. IVIG has been used for the treatment of a number of autoimmune disorders with various efficacy, but has not produced consistent results for acute attacks in immune-mediated demyelinating diseases. Currently, IVIG is considered empirically as an alternative and/or additional treatment for acute attacks of NMOSD after steroids and plasma exchange fail to offset symptoms or are contraindicated.

This retrospective study by Dr De-Cai Tian (Capital Medical University, China) investigated the efficacy of IVIG for patients with NMOSD during acute attacks [1]. A total of 198 patients were included; 85% was female, mean age at onset was 38 years, median EDSS at onset was 5.0. In these patients, 243 attacks occurred, classified as isolated acute myelitis (50.6%), isolated optic neuritis (9.9%), simultaneous acute myelitis and optic neuritis (14.0%), or other (25.5%). The following treatments were given:

- high-dose intravenous steroids in 153 attacks;
- IVIG in 14 attacks;
- episodes of IVIG plus high-dose intravenous steroids in 69 attacks; and
- plasma exchange in 7 attacks.

Of those attacks treated with IVIG alone, 35.7% showed a moderate decrease of EDSS score 33%-65%, while the other attacks alleviated poorly (<33% decrease). Significantly fewer patients treated with IVIG alone had better outcomes compared with patients who received high-dose intravenous steroids alone (P=0.004). No significant difference was found between IVIG plus high-dose steroids compared with steroids alone (P=0.073). When stratified by EDSS score at onset (≤6.0 versus ≥6.5), sequential treatments of IVIG in addition to high-dose steroids increased the likelihood of clinical improvement in severe attacks for patients with higher EDSS score at onset, compared with steroids alone (P=0.040).

1. Li X, et al. Intravenous immunoglobulin for acute attacks in neuromyelitis optica spectrum disorders. ECF 28th Annual Meeting. Abstract 79.