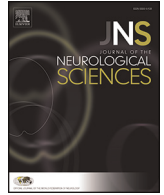




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## MS &amp; Demyelinating Diseases

974

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## MS &amp; Demyelinating Diseases

## Relationship between HLA-DRB1 genotype and clinical response to interferon-beta among Iranian multiple sclerosis patients

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**Objective:** To evaluate the relationship between HLA-DRB1 genotype, which has been proved to be more common in Iranian MS patients, and clinical response to interferon-beta, which is the most common immunotherapy for RRMS.

**Design and setting:** 68 Iranian patients with confirmed diagnosis of RRMS were selected from “December 2010 until May 2011” and patients were followed prospectively for 2 years and clinical data, including EDSS scores were recorded every 3 months. At the end of the following period each patient was to be classified as responder or non-responder. Since there is not any common and international criteria to define response to IFN $\beta$ , in this study we used Rio et al (2006) that is a stringent criteria in which patient is considered as non-responder when there is at least 1 point increase in his/her EDSS confirmed for 6-months of follow-up or when at least 1 relapse occurs during the follow-up period which must be two years.

**Methods:** The HLA-DRB1 genetic polymorphism was determined by DNA amplification with PCR and hybridized by specific sequence oligonucleotide primers using R.O.S.E.

**Results:** Total Number of individuals was 68 Iranian MS patients with 53 (77.9%) female and 15 (22.1%) male, mean aged of onset in years 20.1 ( $\pm 5$ ), mean disease duration in years 6.8 ( $\pm 5$ ). EDSS at entry was 1.9 ( $\pm 0.8$ ) and relapse no. 2 years before starting IFN $\beta$  was 1.7 ( $\pm 0.7$ ). There were 47 (69.1%) responders and 21 (30.9%) non-responders. Fisher's exact test did not show any difference between HLA-DRB1 allele frequencies in responders and non-responders.

**Conclusions:** We concluded that currently available data do not support a role for HLA class II genes as modifiers of response to immunotherapy.

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975

WFN15-0301

## MS &amp; Demyelinating Diseases

## The association between plasma chitotriosidase concentration and the disease activity in patients with MS

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**Introduction:** Multiple sclerosis is the most common autoimmune demyelinating disorder of central nervous system. The role of macrophage in myelin destruction in this disabling disease is undeniable. Chitotriosidase (Chit) is one of the mammalian enzymes synthesized and secreted by specifically activated macrophages. Recent studies indicate that Chit may have a role in the pathogenesis of MS disease.

**Methods:** We analyzed serum obtained from 40 relapsing remitting multiple sclerosis patients and 23 healthy individuals in Iranian population. Case and control group were sex and age matched, mean age were 31.92 and 33.54, respectively. In case group, sampling was done during attack before receiving steroid pulse or immunomodulatory drugs. EDSS of patients was 1.6 ( $\pm 0.86$ ). The concentration of Chit was measured by Enzyme linked Immunosorbent Assay (ELISA).

**Results:** Our results showed that there is no correlation between Chit concentration and MS disease ( $p = 0.87$ ). Also, we did not find any association between Chit concentration and the disease activity in patients with MS. In addition no differences have been detected between relapsing and progressive clinical forms.

**Conclusion:** It seems Chit does not play a key role in the pathogenesis of MS and other inflammatory mediators might be involved in this scenario. However, it should be considered that chit expression is dependent to ethnic background. In our study, negative correlation between multiple sclerosis activity and chit activity compared to control group, may be due to high expression of chit even in normal Iranian population.

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976

WFN15-1422

## MS &amp; Demyelinating Diseases

## Rate of sero-conversion of anti-JC virus antibody among multiple sclerosis patients in Kuwait

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**Background:** Anti-JC virus (JCV) antibody testing plays an important role in risk stratification of multiple sclerosis (MS) treatments given the associated risk of progressive multifocal leukoencephalopathy with natalizumab therapy.

**Objectives:** To assess the rate of seroconversion of anti-JCV antibody among MS patients in Kuwait.

**Methods:** A cross-sectional study examined the data of MS patients who were tested for anti-JCV antibody. Several demographic and disease variable along with anti-JCV titers were collected. Chi-square and independent-t tests were used to determine significance

**Results:** Data of 338 MS patients were assessed; of which 61% were females. Mean age and mean disease duration were 34.7 and 8.9 years respectively. The prevalence of JC seropositivity was 44.1%. There was no statistically significant association between risk of seropositivity and gender ( $p = 0.80$ ), age ( $p = 0.06$ ), disease duration ( $p = 0.39$ ), or prior exposure to disease modifying therapies ( $p = 0.06$ ). It was observed that 25.6% of seropositive patients had received > 24 natalizumab infusions. A subset of the cohort ( $n = 163$ ) was followed longitudinally for  $14.8 \pm 6.56$  months. The sero-conversion rate was 14.7%. The number of natalizumab infusion was associated with higher rate of sero-conversion ( $p = 0.03$ ). Few patients ( $n = 4$ ; 2.4%) reverted to seronegative status and their JC titers were persistently below 0.9.

**Conclusion:** The prevalence of anti-JC virus antibody in Kuwait is lower than international figures. However, the rate of JC sero-conversion appeared to be higher than what was previously reported and this was associated the higher number of natalizumab infusions.

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977

WFN15-1423

#### MS & Demyelinating Diseases

##### Puberty does not affect clinical presentation of multiple sclerosis in children

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**Background:** Multiple sclerosis (MS) is rare before puberty and the data on pre-pubertal patients is scarce.

**Objective:** To compare the demographic and clinical characteristics between children of pre-pubertal and post-pubertal onset of MS.

**Methods:** Utilizing the national MS registry in Kuwait, a cross-sectional study was conducted to identify children with MS who had their disease onset  $\leq 12$  or  $> 12$  years of age (pre-pubertal and post-pubertal cohorts). Chi Square and student *t* test were used to compare the demographics and clinical variables between the two cohorts.

**Results:** A total of 111 children with MS were identified; of whom 19 (17.12%) had disease onset  $\leq 12$  years of age. Post-pubertal cohort had higher female to male ratio (2.8:1 versus 1.4:1). Mean disease duration was comparable between both cohorts ( $p = 0.64$ ). Symptoms at onset did not differ between the two cohorts (supratentorial " $p = 0.41$ "; optic neuritis " $p = 0.39$ " brainstem/ cerebellum " $p = 0.55$ " and spinal " $p = 0.29$ "). There was no statistical difference in mean number of relapses ( $p = 0.89$ ) and mean EDSS score (2.02 versus 2.45;  $p = 0.33$ ) between both cohorts. Although the time to develop SPMS was longer in patients with pre-pubertal onset, the difference was non statistically significant (17.70 versus 14.58 years;  $p = 0.39$ ).

**Conclusions:** There was an increase in the proportion of female MS children in the post pubertal age. However, puberty did not affect clinical presentation at the onset, number of relapses or disease progression over the observation period.

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978

WFN15-0511

#### MS & Demyelinating Diseases

##### Neuromyelitis optica (NMO) antibody positive disorder: a case series from Saudi Arabia

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**Background:** NMO is a B-cell mediated, autoimmune disease of central nervous system (CNS) associated with aquaporin-4 antibodies. Case reports, but no case series, of NMO have been published from Saudi Arabia.

**Objective:** To report a case series of seropositive NMO patients from Saudi Arabia

**Methods:** A retrospective chart review was performed from 2012 to 2014. All patients with NMO antibodies were included. Demographic, clinical, laboratory and neuroimaging data were collected and analyzed. The study was approved by the Institutional Review Board.

**Results:** Ten patients, 9 female and 1 male, aged 18 to 78 years were identified. Referring diagnosis included relapsing remitting MS(6), NMO(2), transverse myelitis(1) and spinal cord infarction(1). Symptom onset prior to diagnosis ranged from 2 months to 9 years. MRI of the brain and spine was interpreted as typical MS with cord involvement (5) atypical MS with cord involvement (2), transverse myelitis(2) and spinal cord infarction (1). Cerebrospinal fluid analysis (CSF, 5/10) revealed mildly elevated protein (2/5) oligoclonal bands (1/5) and was otherwise normal. Anti-nuclear (4) and Sjogrens antibodies (2) were elevated.

**Conclusions:** NMO antibody positive patients exist and pose diagnostic challenges in the Saudi population. There is variability in age of onset and presenting symptomatology. MRI of the brain may demonstrate typical features of MS however spinal cord involvement was present in all. CSF analysis was nonspecific. Additional autoantibodies especially ANA, SSA and SSB are expressed in some perhaps indicating diffuse B-cell activation. A high index of suspicion must be maintained to identify these patients.

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979

WFN15-1108

#### MS & Demyelinating Diseases

##### Neuromyelitis optica and neuromyelitis optica spectrum disorders: the evaluation of 86 patients followed by Istanbul Bilim University, Department of Neurology

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**Background and objectives:** Neuromyelitis optica (NMO) and its spectrum disorders (NMOSD) are relatively rare disorders. We aimed to evaluate clinical characteristics and disease course of the NMOSD patients followed at our department.

**Patients and methods:** All the patients with the diagnosis of NMO/NMOSD followed since the establishment of our multiple sclerosis clinic in April 2011, were evaluated.

**Results:** There were 86 patients (66 female, 20 male) with NMO/NMOSD followed at our MS unit; 24 had NMO, 42 had recurrent optic neuritis (RON); and 20 had longitudinally extensive transverse myelitis (LETM). The disease course was relapsing in 70 patients

(81%). The first attack was bilateral ON (BON) and TM in 3 patients, ON and TM in 1 patient, ON in 50 patients (bilateral in 6) and TM in 26 patients. NMO IgG was positive in 12 patients with NMO (55%), 4 patients with LETM (25%), and 8 patients with RON (25%). Oligoclonal band was positive in 15 out of 44 patients (34%). In NMO/NMOSD patients, cranial magnetic resonance imaging (MRI) showed no abnormality in 48; nonspecific lesions in 37; and 1 patient had hypothalamic lesion. In spinal MRIs, 41 patients had LETM; six had suspected hyperintense T2 lesion in C5.

**Conclusion:** This is one of the largest single center series collected over 4 years. NMO/NMOSD seems to be over-represented in our center since it is one of the few where NMO IgG testing is available. In NMO/NMOSD, early diagnosis and treatment is important to prevent the patient from the permanent disability.

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980

WFN15-1113

MS & Demyelinating Diseases

**Intravenous immunoglobulin treatment for neuromyelitis optica and its spectrum disorders**

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**Background and objective:** There are very few reports on the effects of intravenous immunoglobulin (IVIg) treatment for NMO and NMOSD. We aimed to evaluate our patients with NMO/NMOSD who were treated with IVIg.

**Methods:** Data from all our patients with the diagnosis of NMO/NMOSD, who received IVIg treatment were retrospectively evaluated.

**Results:** Nine patients had received IVIg, three of these patients had NMO, 5 had recurrent optic neuritis [RION], and one had recurrent longitudinally extensive transverse myelitis [R-LETM]. These patients were aged 20-63, and started receiving monthly IVIg from 1 to 20 years after onset of disease. Two out of three NMO patients and one RION patient and the R-LETM patient were NMO-Ig G positive.

Under current treatments the patients had continued to have attacks therefore IVIg was given in addition to the existing drug. The follow up of was between 12 to 27 months except one patient who received IVIg for acute relapse. Two of the patients with NMO had attacks under IVIg at month 10 and month 13, and month 1, month 6, and month 12, respectively, and were switched to rituximab; the patient with R-LETM also had attacks at month 2 and month 19 when the treatment was interrupted. Only one patient with RION had an attack at month 3.

**Conclusion:** Monthly IVIg is well-tolerated and safe and it seems to be more effective in RION. It may also be an option for NMO when current therapies are contraindicated or could not be tolerated.

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981

WFN15-1454

MS & Demyelinating Diseases

**Disease re-activation during pregnancy after natalizumab suspension in patients with multiple sclerosis**

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**Background:** While the risk of disease re-activation after natalizumab suspension is widely acknowledged, little is known on disease activity during pregnancy occurring after suspension of natalizumab in multiple sclerosis (MS) patients.

**Objective:** To assess MS disease activity during pregnancy after natalizumab exposure (NE) and the impact of NE on pregnancy outcomes.

**Patients and Methods:** we recruited NE pregnancies in MS patients prospectively followed-up in 16 Italian MS Centres, in the period 2010-2014. NE was defined as suspension < ten weeks prior to conception. Clinical relapses and pregnancy outcomes were compared with data from the Italian dataset on interferon-beta exposure (IFNBE) (Amato et al., 2010). All the patients were administered a structured interview which gathered detailed information on pregnancy course and outcomes, as well as on possible confounders. Group comparisons were assessed through the chi<sup>2</sup> test, the analysis of variance and mixed factorial design.

**Results:** so far 50 pregnancies were recruited. Pregnancies resulted in 38 live-births, nine spontaneous abortions and three voluntary abortions. The occurrence of relapses during pregnancy in 14/38 (36.8%) patients was higher than that observed in IFNBE patients (10/75, 13.3%; mixed factorial design F = 4.162, p < 0.001). Proportion of spontaneous abortion in NE pregnancies (19%) was within the limits expected in the general population. Main pregnancy outcomes were also comparable to those of IFNBE pregnancies (p > 0.3).

**Conclusions:** in our study pregnancy did not protect from disease re-activation after natalizumab suspension. The risk of relapses during pregnancy should be taken into account in the counselling of natalizumab-treated MS patients contemplating pregnancy.

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982

WFN15-1124

MS & Demyelinating Diseases

**Prognostic factors associated with long-term disability and secondary progression in patients with multiple sclerosis**

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In Multiple Sclerosis, determining prognostic factors in early stages of disease is important, though controversial. Most studies were performed in North American and European cohorts, with different results. The objective of this study is to evaluate in a

Brazilian mixed cohort the occurrence of prognostic factors associated with long-term disability and progression.

**Methods:** 303 patients attended at the reference center of demyelinating diseases in Rio de Janeiro, Brazil, with at least 2 years of disease had records analyzed prospective and retrospectively. Endpoints were: time to reach EDSS 3, 6 and progression. Clinical, demographic, evolving and treatment variables were analyzed.

**Results:** Caucasian patients, with interval longer than two years between first and second relapses and with one relapse in the first year of disease were more frequent among benign forms (35.6%). More than one relapse in the first year, without recovery from the first relapse and no initiated treatment before reaching EDSS 3 were overrepresented among malignant forms (4.6%). Influenced the time to reach the endpoints: African ancestry, non-recovery from the first relapse, two or more relapses in the first year of disease, motor and cerebellar presentation, polysymptomatic presentation and no treatment before reaching EDSS 3. After multivariate analysis the mentioned factors remained significant, except polysymptomatic presentation.

**Conclusions:** Factors found in our results were in their majority comparable to other studies. African ancestry and reaching EDSS 3 before starting treatment are factors poorly explored. Our results reinforce the need to consider ancestry in therapeutic decisions along with the clinical and demographic factors.

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983

WFN15-0363

MS & Demyelinating Diseases

Multiple sclerosis: varied symptoms, one disease

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**Background:** A demyelinating disease is any disease of the nervous system in which the myelin sheath of neurons is damaged. Demyelinating diseases are caused by genetics, some by infectious agents, some by autoimmune reactions, some by exposure to chemical agents, and some by unknown factors

**Material and methods:** We present the case of a 57 year old patient who in the summer of 2012 was shown to have an episode with fever, sweating, lumbalgia and a purpuric rash on left leg.

**Results:** A biopsy was performed and she was diagnosed with Castleman's disease. After discharge the patient showed sudden appearance of abnormalities in walking and speaking (that disappeared in about 1 month). She started chemotherapy and radiation, which lasted for about 1 year. The walking and speaking disorders reappeared, with the persistence of abnormal walking. The cortical CT exams showed no new lesions, which is why the investigations continued. The cerebral MRI suggested hypersignal T2 and FLAIR lesions and hyposignal T1 with diffusion restriction situated periventricular and juxtacortical, some with confluent characteristics (plaque aspect). An electroneurographic exam showed chronic inflammatory demyelinating polyneuropathy.

**Conclusion:** Given the varied symptoms, the certainty of a diagnosis is difficult to establish and requires continued vigilance.

**Keywords:** Demyelinating disease, cronicinflammatory demyelinating polyneuropathy, demyelinating lesions

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984

WFN15-0628

MS & Demyelinating Diseases

Inhibition of kynurenine aminotransferase I, II and III activities due to human serum and cerebrospinal fluid

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**Background:** Kynurenic acid (KYNA) is a metabolite of tryptophan degradation and an endogenous antagonist of ionotropic glutamate receptors and the alpha-7 nicotinic acetylcholine receptor. Alterations of KYNA levels were observed in various inflammatory and degenerative diseases. Drugs able to modulate KYNA synthesis are proposed as promising pharmacological approaches. Exogenous compounds affecting KYNA synthesis are of special interest and we were interested to find if serum or cerebrospinal fluid (CSF) has the ability to influence kynurenine aminotransferase activities I, II, III (KAT I, II, III), respectively KYNA levels.

**Patients and methods:** Serum and CSF from 30 patients (Neurological Department of the General Hospital Amstetten and Neuropsychiatric Hospital Mauer, Austria) with different neurological disorders were investigated. Eight different amounts of serum or CSF (between 2 and 75 µl) were applied to the incubation medium of the assay and KAT I, II, III activities were determined. Synthesized KYNA was analysed by HPLC method. The statistical analysis was carried out by one-way-ANOVA and Student's-T-Test. The study was performed according to the ethical regulations of the government of Lower Austria.

**Results:** Serum and CSF have the ability to block significantly and dose dependently KAT I, KAT II and KAT III activities. Revealed inhibition curves of serum and CSF show differences in respect to different diseases.

**Conclusion:** Serum and CSF exert a variable ability to inhibit KAT activities and respectively to modulate KYNA synthesis and probably could act as therapeutic compounds. Value of ratio from KAT activities might be used as diagnostic parameter for neuro-inflammatory diseases.

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985

WFN15-0013

MS & Demyelinating Diseases

An option for the treatment of primary progressive multiple sclerosis

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**Background:** At the present time, there are no medications approved for the treatment of primary progressive multiple sclerosis (PPMS). Because all of the approved disease-modifying therapies work primarily by reducing inflammation in the central nervous system, they do not work as well in a disease course that is characterized by nerve degeneration rather than inflammation. We studied whether long-term pulse intravenous methylprednisone (IVMP) therapy may delay the progression or disability in patients with PPMS.

**Methods:** A study of 24 patients (14 female, 10 male) with PPMS had received monthly pulses of IVMP at a dose of 1 g/mo for 1 year. The EDSS score was assessed at baseline and after 6 months and 12 months of treatment.

**Results:** The mean age of the patients sample was 49.2 years and the mean duration of disease was 25.4 years. The medium EDSS before treatment was 6.9, and after 1 year of treatment, the EDSS was 4.3. Patients with an improved EDSS at 12 months had a shorter mean

progressive time course (4.3 years) than patients who stabilized or worsened (9.1 years) ( $p < 0.05$ ). IVMP treatment was also associated with improvement in fatigue, spasticity and motor strength. None of the patients presented noticeable drug side effects or intolerance.

**Conclusion:** This study showed that IVMP treatment was well tolerated and suggested that a better response occurred in cases with a short progressive time course. It has also been shown to prevent sustained disability. We therefore propose the use of IVMP treatment early in the course of the disease in PPMS patients.

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986

WFN15-0014

MS & Demyelinating Diseases

Dysphagia limit in multiple sclerosis

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**Objective.** Swallowing mechanism and neurogenic dysphagia in MS have been rarely studied by electromyographical methods. This study aims to evaluate the presence of subclinical dysphagia in patients with mild multiple sclerosis (MS) using electrophysiological methods.

**Methods:** A prospective study of 51 patients with relapsing remitting multiple sclerosis (RRMS) and 18 age-matched healthy adults were investigated. We used electromyography to measure the activity of the submental muscles during swallowing, as well as respiration, electrocardiographic and electrodermal activity during the procedures of dysphagia limits and sequential water swallowing. Electrophysiological recordings of patients were obtained during relapse, after relapse and at any time in remission period.

**Results:** Clinical dysphagia was found in 12 % of MS patients while electrophysiological swallowing abnormalities were encountered in 33% of patients. Subclinical dysphagia was determined in 35% of patients during an MS relapse and 20 % of patients after a relapse based on EMG findings. Duration of swallowing signal of submental muscles in all MS patients was found to be longer than in normal subjects ( $p = 0.001$ ). During swallowing of 50 ml of sequential water, the compensatory respiratory cycles occurred more often in MS patients than normal subjects, especially during a relapse ( $p = 0.005$ ).

**Conclusion:** This is the first study investigating swallowing abnormalities and subclinical dysphagia from the electrophysiological aspect in MS patients with mild disability. The electrophysiological tests described in this study are useful to uncover subclinical dysphagia since they have the advantage of being rapid, easy to apply, non-invasive and without risk for the patients.

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987

WFN15-0667

MS & Demyelinating Diseases

Rare coexistence of multiple sclerosis, insulin-dependent diabetes mellitus and Graves-Basedov thyroiditis - case report with literature overview

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Autoimmune diseases are caused by defect of human immune system to recognize their own antigens and pathological response against these antigens. Multiple sclerosis (MS), insulin-dependent diabetes mellitus (DM-1) and Graves-Basedov thyroiditis are

polygenic organ-specific autoimmune disorders of unknown etiology affecting young adults. They share a number of characteristics, thereby suggesting common underlying pathways or mechanisms.

We conducted a clinical observation of 36-year-old white man who presented with coexisting MS, DM-1 and Graves-Basedov thyroiditis.

**Case Report:** A 30-year-old male with DM-1 from age of 8 and newly diagnosed Graves-Basedov thyroiditis was referred to our Neurological Department due to vertigo and balance disturbances progressing for 6 months. In the age of 15 he had left side retrobulbar neuritis, and left side hemiparesis. Neurological examination revealed left side hemiparesis, mild ataxia in upper and lower limbs, gait ataxia. Brain MRI showed typical demyelinating changes fulfilling MRI criteria for MS. He underwent a complete differential diagnosis for MS. CSF analysis was positive. Finally multiple sclerosis was diagnosed. There were some therapeutic difficulties - due to contra-indication to Interferon Beta treatment, patient was treated with mitoxantrone without definite effect - patient has EDSS 7.0 now.

**Conclusion:** The coexistence of these 3 organ-specific autoimmune diseases in our patient supports the concept of an immune-mediated damage in these diseases, an important aspect for an effective therapeutic choice by neurologists. However, the immunopathogenetic association between MS and other autoimmune remains speculative, thereby warranting further clarification. Coexistence of DM-1 and thyroiditis may present difficulties in effectively treating MS.

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988

WFN15-0785

MS & Demyelinating Diseases

Longterm immunomodulatory therapy in 4.938 outpatients with relapsing-remitting multiple sclerosis (RRMS) under special consideration of switching to oral DMD

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**Background:** NeuroTransData, a German neurologists network of 75 offices is using an MS database to gather "real world" data for 8 years ( $n = 18.608$  patients).

**Objectives:** Analysis of the clinical course of patients with DMD during the observation period and the reasons for switching therapy.

**Methods:** Inclusion criteria ( $>7$  y of patient history; treatment for more than 2 y with injectable DMD on average (Avonex<sup>R</sup>, Rebif<sup>R</sup>, Betaferon/Extavia<sup>R</sup>, Copaxone<sup>R</sup>) led to the identification of 4.938 patients (female 3.675; 74.4%; male 1.263; 25.6%) with RRMS.

Those patients, who switched to oral DMD during the observation period were analyzed with respect to reasons for switching.

**Results:** 1.520 (30.8%) of these 4.938 patients were switched to oral DMD (Dimethylfumarate  $n = 580$ , Fingolimod  $n = 717$ , Teriflunamide  $n = 223$ ). The main reasons for switching were insufficient therapeutic effect ( $n = 502$ ; 34.9%), followed by side effects and patient's wish. Within another 3 months (median) 177 of these already switched patients were switched once again to another DMD, whereas 1.274 patients (84%) remained on their current therapy. The main reasons for switch this time were sideeffects (62.1%) followed by insufficient therapeutic effect. 38 (21.5%) patients were switched to the DMD before switching the first time.

**Conclusions:** The main reason for switching from injectable to oral DMD was the therapeutic effect (optimizing of therapy), followed by side effects and patient's wish. In those patients who switched a second time, the exact opposite was true. Most patients ( $n = 1.274$ ; 84%) who switched to oral DMDs remained on that therapy during the observation period.

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989

WFN15-0103

MS &amp; Demyelinating Diseases

**25-OH vitamin D levels in relapsing remitting multiple sclerosis and clinically isolated syndrome**A. Küçük<sup>a</sup>, L.S. Bir<sup>a</sup>, S. Demir<sup>b</sup>. <sup>a</sup>Neurology, Pamukkale University Medical School, Denizli, Turkey; <sup>b</sup>Biochemistry, Pamukkale University Medical School, Denizli, Turkey

Vitamin D is an important regulator of the immune system and it has been shown that deficiency of Vitamin D is significant environmental factor in some immune-mediated diseases such as multiple sclerosis (MS). In this study we aimed to detect 25-OH Vitamin D levels in patients with relapsing remitting multiple sclerosis and also in patients with clinically isolated syndrome (CIS).

Patients who have been following in our multiple sclerosis unit, between 18-45 years, were included to the study. Serum 25-OH Vitamin D, calcium, phosphorus, alkaline phosphatase, parathyroid hormone, insulin and glucose levels were detected in 40 MS patients, 40 CIS patients and 60 healthy volunteers and were compared among the groups. Disease duration, number of relapses, T2 hyperintense lesion load in cranial magnetic resonance imaging (MRI), existence of lesion in cervical MRI, and CIS attack type were also recorded.

25-OH Vitamin D levels were significantly lower in RRMS and CIS groups than controls. No significant difference was found among the patient groups. No statistically significant correlations were detected between the levels of vitamin D and other biochemical, clinical and radiological parameters.

As far as we know, this is the first Vitamin D study in CIS. It appears that Vitamin D levels are low at the early stages of the demyelinating process. Replacement vitamin D therapy might be important for prevention of MS.

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990

WFN15-0243

MS &amp; Demyelinating Diseases

**Retrospective analysis of the effect of pregnancy on the course of multiple sclerosis in Russia**

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The most frequent debut of MS is noted in ages from 18 to 45 years- the active childbearing period. Data on the effect of pregnancy on the course of MS are contradictory. Retrospective analyses of data from the Russian MS register of 279 women with MS having from 1 to 4 children at the start of the study. We assessed the number of exacerbations during pregnancy, the risks of exacerbations after abortion, during pregnancy and in the postpartum period, as well as the effects of disease modifying treatment (DMT). The average age of onset of MS was  $24.24 \pm 6.47$ , frequency of exacerbations (AFE) in the two years before the pregnancy was  $1.02 \pm 0.63$ , the average score of EDSS scale before the pregnancy-  $1.94 \pm 0.63$ . Before pregnancy 183 patients (65,6%) treated by DMT, which was stopped by the fact of pregnancy. During pregnancy the AFE significantly decreased ( $p < 0.05$ ): 1-st trimester-  $0.13 \pm 0.4$ , 2-nd trimester-  $0.08 \pm 0.31$ , 3-rd trimester-  $0.03 \pm 0.19$ . We noted lower AFE in the period up to 3 month after delivery compared with the data before the pregnancy-  $0.24 \pm 0.51$ . The EDSS increased after delivery to  $2.13 \pm 0.68$  ( $p < 0.05$ ) which was due to

increase disease activity in the period up to the 3-rd month after the delivery (Spearman  $R = 0.146, p = 0.015$ ). Causes of lower AFE after delivery than before pregnancy: early beginning therapy by DMT (about  $3,19 \pm 3,52$  month)-Spearman  $R = -0,32, (p = 0.02)$ ; positive patient's DMT anamnesis before the pregnancy ( $\chi^2 = 38.44, p < 0.05$ ). Type of delivery didn't influence the rate of development and severity of exacerbation. The course of the pregnancy and delivery in patients with MS is the same as in healthy women. Delivery method should be chosen based on obstetric indications.

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991

WFN15-0426

MS &amp; Demyelinating Diseases

**The role of dopamine in regulating interactions of the immune and nervous system in multiple sclerosis**M.V. Melnikov<sup>a</sup>, M.A. Hasaeva<sup>a</sup>, O.O. Belousova<sup>a</sup>, V.V. Murugin<sup>b</sup>, M.V. Pashenkov<sup>b</sup>, A.N. Boyko<sup>a</sup>. <sup>a</sup>Department of Neurology, Pirogov Russian National Research Medical University, Moscow, Russia; <sup>b</sup>Division of Clinical Immunology, Institute of Immunology, Moscow, Russia

**Introduction:** Multiple sclerosis (MS) is a chronic autoimmune neurodegenerative disease. Dopamine is one of the possible modulators of neuro-immune network important in MS pathogenesis.

**Objective:** to study the interaction in MS course, dopamine status characteristics and several characteristics of the Th17-system and other parameters of immune regulation in MS.

**Materials and methods:** data of clinical and neuropsychological status of 53 relapsing-remitting MS patients and 20 healthy controls were included. Flow cytometry parameters and levels of cytokines in supernatants of peripheral blood mononuclear cells (PBMC), stimulated with anti-CD3/anti-CD28 antibodies with or without dopamine, were studied.

**Results:** Dopamine levels in serum were comparable in all groups. The number of Th17-cells in blood and production of IL17 by PBMC in MS during relapse was higher than in remission or control group ( $p < 0,05$ ), and in MS patients with depression - higher than in control group and in MS patients without depression ( $p < 0,05$ ). Only in MS patients at remission, independently on demographic characteristics, disease duration or EDSS level, dopamine at a concentration of  $10^{-5}$  M was able to suppress IL-17 production by PBMC ( $p < 0,05$ ).

**Conclusion:** Effects of dopamine on IL-17 production could be proposed as an additional factor of immunoregulation in MS.

I have obtained patient and Institutional Review Board (IRB) approval.

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992

WFN15-1052

MS &amp; Demyelinating Diseases

**Daclizumab HYP reduces total disability burden of patients with multiple sclerosis: results from an exploratory area under the curve analysis**A. Boyko<sup>a</sup>, L. Kappos<sup>b</sup>, J. Rose<sup>c</sup>, K. Selmaj<sup>d</sup>, D.L. Arnold<sup>e</sup>, E. Havrdova<sup>f</sup>, M. Kaufman<sup>g</sup>, H. Wiendl<sup>h</sup>, S. Greenberg<sup>i</sup>, S. Shang<sup>j</sup>, P. Wang<sup>j</sup>, L. Barbato<sup>j</sup>. <sup>a</sup>Department of Neurology and Neurosurgery, Russian National Research Medical University Named after N. I. Pirogov and the Moscow Multiple Sclerosis Center, Moscow, Russia; <sup>b</sup>Neurology Departments of Medicine Clinical Research and Biomedicine, University Hospital Basel, Basel, Switzerland; <sup>c</sup>Department of Neurology and the Neurovirology Research

Laboratory, University of Utah VASLCHCS, Salt Lake City UT, USA; <sup>d</sup>Department of Neurology, Medical University of Lodz, Lodz, Poland; <sup>e</sup>Montreal Neurological Institute, McGill University and NeuroRx Research, Montreal, Canada; <sup>f</sup>First Faculty of Medicine, Charles University in Prague, Prague, Czech Republic; <sup>g</sup>Cole Neurological Institute, University of Tennessee, Knoxville TN, USA; <sup>h</sup>Department of Neurology, University of Münster, Münster, Germany; <sup>i</sup>Clinical Development, AbbVie Biotherapeutics Inc., Redwood City CA, USA; <sup>j</sup>World Wide Medical, Biogen, Cambridge MA, USA

**Background:** Daclizumab high-yield process (DAC HYP) 150 mg subcutaneous every 4 weeks significantly reduced 12-week confirmed disability progression by 57% ( $P = 0.0211$ ) versus placebo over 52 weeks in SELECT. In DECIDE, 16% ( $P = 0.1575$ ) and 27% ( $P = 0.0332$ ) reductions in 12-week and 24-week confirmed disability progression, respectively, were observed for DAC HYP 150 mg versus intramuscular interferon beta-1a over 144 weeks.

**Objective:** To determine the effect of DAC HYP on total longitudinal disability burden measured by area under the curve (AUC) integrating all measured Expanded Disability Status Scale (EDSS) worsening and improvement experienced by patients over 52 and 96 weeks in SELECT and DECIDE, respectively.

**Methods:** AUC for EDSS change from baseline was calculated post hoc using the trapezoidal rule with missing data imputed using last observation carried forward method (units of EDSS years). Positive value in AUC denotes net worsening in EDSS from baseline and negative value net improvement. Least squares mean AUC was obtained using ANCOVA; between-treatment group comparison used ANCOVA on rank of AUC. Patient and/or IRB approval was obtained.

**Results:** In SELECT, DAC HYP patients ( $n = 199$ ) had net improvement in disability ( $-0.042$  EDSS years) while placebo patients ( $n = 196$ ) had net worsening ( $+0.074$  EDSS years; between-treatment difference  $P = 0.0089$ ). In DECIDE, DAC HYP patients ( $n = 912$ ) had net improvement in disability ( $-0.062$  EDSS years) while interferon beta-1a patients ( $n = 900$ ) had net worsening ( $+0.027$  EDSS years; between-treatment difference  $P = 0.0267$ ).

**Conclusions:** These findings from SELECT and DECIDE suggest positive effects of DAC HYP on total longitudinal disability burden.

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993

WFN15-0710

MS & Demyelinating Diseases

Prevalence of multiple sclerosis in the city of Volta Redonda – Rio de Janeiro, Brazil- using the capture-recapture method

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**Background:** Multiple Sclerosis prevalence in Latin America was estimated in some regions ranging from 0.75 to 30/100000. The reasons for variation in rates of prevalence around the world still are not clear, but there are environmental and genetic explanations for this fact.

**Objective:** This study was to estimate MS prevalence in Volta Redonda, Brazil.

**Material and Method:** Three sources of cases ascertainment were used and the method of capture-recapture was applied for assessing corrected prevalence in the city of Volta Redonda in November, 2012. Capture-Recapture method uses data from incomplete lists and allows to calculate the number of unregistered cases. Data were analyzed using a log-linear model.

**Results:** It was found a total of 40 MS cases by withdrawing overlaps of sources and it was estimated a number of 40 cases (95% CI 13.5–118.8) not detected by the sources. The prevalence was, then, 30.7/100,000.

**Conclusion:** Our study was the first in Brazil using the capture-recapture method to assess the prevalence of MS, demonstrating the highest prevalence rate so far in Brazil. It is necessary to perform other similar studies and in other regions of the country using the same method for a better evaluation of the true prevalence of MS our country.

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994

WFN15-1295

MS & Demyelinating Diseases

The real-life experience with fingolimod in Mexico: a multicenter post-marketing study

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**Background:** Fingolimod is a disease modifying therapy (DMT) approved for the treatment of relapsing multiple sclerosis (MS). Latin American patients were scarcely represented in pivotal studies that lead to fingolimod approval; therefore, it is desirable to have information derived from the real-life experience in Latin America.

**Objective:** To describe the post-marketing experience with the use of fingolimod in Mexican patients.

**Patients and methods:** We registered consecutive MS patients treated with fingolimod in a multicenter registry. Records were collected in a standardized research format by the treating neurologists.

**Results:** A total of 127 patients (76% women, median age 34 years) were registered; 62% initiated fingolimod due to previous DMT failure, 16% due to injectables intolerance, 13% were naïve patients and 9% due to adverse effects to previous DMTs. Adverse reactions other than first-dose phenomena were recorded in 9.4% of patients (only 2 requiring drug interruption). Within a median follow-up of 12 months with fingolimod, mean EDSS changed from 2.57 to 2.01 ( $P < 0.001$ ). Consequently, the progression index (EDSS divided by disease duration) decreased from 0.89 to 0.48 ( $P < 0.001$ ). In all, 45% patients experienced EDSS improvement (4% experienced worsening). Actuarial Kaplan-Meier analyses showed that, compare to DMT-experienced patients, naïve subjects had a shorter time to attain EDSS  $\geq 2.5$  before the use of fingolimod ( $P = 0.001$ ), but this difference disappeared after fingolimod treatment ( $P = 0.56$ ).

**Conclusion:** This post-marketing data show that fingolimod is safe and effective, with results comparable to those of pivotal studies. Fingolimod was mainly indicated to young patients with a high disability prospect.

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995

WFN15-0414

**MS & Demyelinating Diseases****Spatial attention in multiple sclerosis**

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**Background:** Cognitive impairment is recognized as a core feature of multiple sclerosis (MS). Mostly memory, attention, information processing speed and executive functions are affected.

**Objective:** To evaluate whether spatial distribution of attention differs between MS patients and controls in an institutional review board approved study.

**Patients and methods:** A case-control study was conducted in 30 MS (with EDSS lower than 3) patients, and age- gender- and education-matched 30 healthy individuals. Working memory, attention and executive functions were evaluated with PASAT and Trail Making Test part-A/B. Judgment of Line Orientation Test and Target Cancellation task were used to evaluate visual spatial perception and spatial distribution of attention, respectively. All subjects were also administered Beck Depression Inventory and Mini-Mental State Examination.

**Results:** Patient and control groups did not differ in means of gender, age and education. BDI scores were similar in both groups and general cognitive functioning of patients were much the same. MS subjects performed more poorly on the TMT part A/B and PASAT tests than the control group. Although MS patients' performance on visual spatial perception were much the same as control group (MS:22.6 ± 4.2, control:22.0 ± 3.9, p = 0.612), they performed poor on cancellation task (MS:122.2 ± 52.9 sec, control:92.7 ± 34.5 sec, p = 0.014). However, omission and commission errors were much the same. In MS group, cancellation time showed positive correlation with TMT-A (r:0.720, p = 0.000) and TMT-B (r:0.415, p = 0.023), and a negative correlation with PASAT scores (r:0.588, p = 0.001). As the disease duration and EDSS score increased cancellation task performance slowed down (r:0.440, p = 0.015; r:0.629, p = 0.000, respectively).

**Conclusion:** Our results suggest that visual spatial attention of MS patients is compromised.

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996

WFN15-0384

**MS & Demyelinating Diseases****Interferon-beta 1A and disability progression in relapsing-remitting multiple sclerosis: 9-year follow-up study**

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**Background:** Well-designed observational studies are currently recognized as a design which could provide significant information on the long-term impact of therapy.

**Objective:** To assess the impact of interferon (IFN)-beta treatment on the progression of unremitting disability in IFN-beta treated and untreated relapsing-remitting (RR) patients with multiple sclerosis (MS) using prospective cohort study.

**Patients and methods:** A cohort of 264 RRMS (133 IFN-beta-1a sc-treated and 131 untreated) patients was followed for up to 9 years. Cox proportional hazards regression models adjusted for the number of relapses in the last year before first visit was used to assess the

differences between the two groups for the three end points: secondary progression (SP), and sustained Expanded Disability Status Scale (EDSS) score 4 and 6. Time from disease onset was used as survival time variable.

**Results:** There were no significant differences between the IFN-beta-treated and untreated MS patients for all baseline clinical variables except for number of relapses in the last year before the visit. The IFN-beta-treated group showed a highly significant reduction (hazard ratio [HR], 0.21, 95% confidence interval [CI] 0.11-0.40, p < 0.001) in the risk of SP when compared with untreated patients. There were significant differences in favor of the IFN-beta-treated group for the end point EDSS score of 4 (HR = 0.40, 95%CI 0.23-0.65, p < 0.001) and EDSS score of 6 (HR = 0.20, 95%CI 0.09-0.45, p < 0.001).

**Conclusion:** This observational study further supports the notion that IFN-beta could have potential beneficial effect on disease progression in RRMS.

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997

WFN15-0872

**MS & Demyelinating Diseases****Gray matter involvement in multiple sclerosis; correlation of clinical and cognitive disability with DTI magnetic resonance imaging findings**

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**Introduction:** The relevance of grey matter (GM) pathology in MS relate better to cognitive and clinical disability than white matter (WM) lesions. Neocortex is typically affected but gray matter demyelination may also be found in non-cortical areas such as the hippocampus, thalamus, basal ganglia, cerebellar cortex and the spinal cord gray matter.

**Objectives:** Our aim was to investigate whether a particular pattern of cortical and deep GM atrophy is associated with cognitive impairment in patients RRMS.

**Methods:** Expanded Disability Status Scale (EDSS), MS functional composite (MSFC) scores and MRI data from 40 people with RRMS and 20 d healthy controls were included in this study. Neuropsychological testing contributed measures of using the PASAT, SDMT and verbal fluency test (VFT) respectively. 3 T-DTI and tractography were performed.

**Results:** In DTI-FT measurements, FA values of cortical GM areas were lower in all MS patients and MD values of GM areas were higher in MS patients (p = 0,0001). GM volume values were lower in MS (p = 0,0001). MD was significantly decreased in the right/left thalamus of patients with MS compared with controls (p = 0.0001), There was significant differences of caudate nucleus FA and MD patients with MS compared controls (p = 0,005, p = 0,001). A negative correlation between GM volume values of patients group and VFT was determined (r = -0,340 There was significant correlation of PASAT scores and left thalamus and caudate nucleus FA and MD in MS patient compared to controls.

**Conclusions:** Our study confirms that focal grey matter pathology contributes to physical disability and cognitive deficits in MS patients. Our results suggest that significant role of thalamus and caudate nucleus involvement in MS-associated cognitive deficits.

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998

WFN15-1144

**MS & Demyelinating Diseases****Effects of switching from placebo to peginterferon beta-1A in the advance study in patients with relapsing multiple sclerosis**S. Shang, V. Evilevitch, X. You. *Worldwide Medical, Biogen, Cambridge, USA*

**Background:** ADVANCE investigated the efficacy and safety of peginterferon beta-1a in patients with relapsing multiple sclerosis (RMS) over 2 years. To ensure all patients had the opportunity to benefit from active treatment, patients randomized to placebo at baseline were re-randomized to peginterferon beta-1a at Week 48.

**Objective:** To model actual outcomes in patients from the ADVANCE trial who switched from placebo to peginterferon beta-1a every 2 weeks, versus estimated outcomes if patients had continued on placebo through Year 2.

**Methods:** For patients receiving placebo in Year 1 (n = 500), a Weibull regression model was used to estimate time to first relapse and time to onset of 24-week confirmed disability progression (CDP) during Year 2 if patients had remained on placebo. A Branson and Whitehead switch model with iterative parameter estimation was used to calculate the ratio between these estimated times and times observed following switch to active treatment every 2 weeks.

**Results:** The time to first relapse after switching to peginterferon beta-1a was 2.27 fold longer (95% confidence interval [CI] 1.63, 3.12) than the estimated time should these patients have remained on placebo. The time to onset of CDP after switching to peginterferon beta-1a was 2.00 fold longer (95% confidence interval [CI] 1.26, 3.06) than the estimated time should these patients have remained on placebo.

**Conclusions:** In RMS patients initially randomized to placebo, switching to peginterferon beta-1a every 2 weeks significantly delayed time to first relapse and onset of 24-week CDP, by factors of 2.3 and 2.0, respectively, during Year 2.

**Study sponsored by:** Biogen (Cambridge, MA, USA).

I have obtained patient and/or Institutional Review Board (IRB) approval, as necessary.

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999

WFN15-1161

**MS & Demyelinating Diseases****Peginterferon beta-1A dosed every 2 weeks maintained efficacy over 3 years in patients with relapsing multiple sclerosis**V. Evilevitch<sup>a</sup>, B. Sperling<sup>a</sup>, S. Liu<sup>b</sup>, S. Shang<sup>a</sup>, S. Hung<sup>c</sup>. <sup>a</sup>*Worldwide Medical, Biogen, Cambridge, USA*; <sup>b</sup>*Biostatistics, Biogen, Cambridge, USA*; <sup>c</sup>*Clinical Development, Biogen, Cambridge, USA*

**Background:** ATAIN is a 2-year extension of the Phase 3, 2-year ADVANCE study, to evaluate long-term safety, tolerability, and efficacy outcomes of peginterferon beta-1a in patients with relapsing multiple sclerosis (RMS).

**Objective:** To investigate the efficacy of peginterferon beta-1a 125 mcg dosed every 2 weeks over 3 years (ADVANCE [Years 1, 2] and the first year of ATAIN [Year 3]).

**Methods:** Patients who received subcutaneous peginterferon beta-1a 125 mcg every 2 weeks were evaluated. Annualized relapse rate (ARR), mean number of gadolinium-enhanced lesions (Gd+), new/newly enlarging T2 lesions, and new T1 hypointense lesions were evaluated in each study year in ADVANCE and ATAIN, and

compared over time. The impact of baseline characteristics on efficacy over 3 years was also examined.

**Results:** In total, 512, 438, and 376 patients receiving peginterferon beta-1a every 2 weeks from the ADVANCE intent-to-treat population were included in the analysis for Years 1, 2, and 3, respectively. The adjusted ARR in Years 1, 2, and 3 was 0.282, 0.201, and 0.215 respectively. The mean number of Gd + lesions stayed constant at 0.2 in each year. In Years 1, 2, and 3, the mean number of new/newly enlarging T2 lesions was 4.1, 1.9, and 1.9, respectively, and the mean number of new T1 lesions was 1.8, 0.7, and 0.8, respectively. Efficacy by baseline demographics and disease characteristics subgroup will also be presented.

**Conclusion:** In patients with RMS, peginterferon beta-1a dosed every 2 weeks maintained efficacy on clinical and MRI outcomes over 3 years.

**Study sponsored by:** Biogen (Cambridge, MA, USA).

I have obtained patient and/or Institutional Review Board (IRB) approval, as necessary.

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1000

WFN15-0771

**MS & Demyelinating Diseases****A case-control study for establishing the outcome of pregnancy, delivery and newborn in multiple sclerosis**M. Gedizlioglu<sup>a</sup>, G. Gürbüz<sup>b</sup>, A. Köskderelioglu<sup>a</sup>, P. Ortan<sup>a</sup>. <sup>a</sup>*Neurology, Izmir Bozyaka Research and Training Hospital, Izmir, Turkey*; <sup>b</sup>*Child Neurology, Izmir Behcet UZ Children's Hospital, Izmir, Turkey*

**Background:** In multiple sclerosis, to inform patients about pregnancy carries utmost importance as most of the patients are females of reproductive age.

**Aim:** To evaluate obstetrical and pediatric outcomes related to the births during MS course by comparing with pre-MS pregnancies and features of childless MS patients.

**Method:** The data of 39 MS patients registered in MS clinic who experienced 51 pregnancies after the diagnosis of MS were retrospectively collected. The data of 45 patients with pre-MS pregnancies and MS patients without any history of pregnancy (n = 47) were collected as controls.

**Results:** The patients without children and with somewhat shorter disease duration was much younger, higher educated and slimmer (p = 0.0001 for each). No assisted delivery, stillbirth or congenital abnormality was reported. Obstetrical complications, low birth weight, and abortion rates were somewhat higher in MS group, though statistically not different. However, cesarean section and general anesthesia were remarkably more frequent in MS-associated pregnancies (p = 0.0001). Majority of women with both pre-MS and post-MS pregnancies had breastfed their babies exclusively. Pre- and post-delivery EDSS was not different in MS-associated pregnancies' group.

**Conclusion:** The noticeable finding in this study was high rate of cesarean delivery and general anesthesia in patients with pregnancies after MS diagnosis. To our opinion, this may reflect the attitude of obstetricians towards MS patients. The features of childless MS patients, younger, higher educated and slimmer, probably reflect their differential life choices. No remarkable obstetrical and pediatric problem was encountered. The course of MS was also not affected by pregnancies.

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1001

WFN15-0829

MS &amp; Demyelinating Diseases

Multiple sclerosis lesion heart X mitoxantrone

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**Case report:** Woman, 40, was diagnosed with relapsing-remitting multiple sclerosis (RRMS) in October 2005. After several relapses and poor response to immunomodulators and corticosteroid, mitoxantrone (MitX) 12 mg/m<sup>2</sup> (20 mg) was administered with no adverse effects. Patient had stable, normal general examination, and an echocardiogram showed an ejection fraction (EF) of 74% and the ECG was normal. After 103 days of the infusion, the patient was admitted to hospital with acute respiratory distress, chest pain, sweating and vomiting. In the initial cardiac evaluation, blood pressure was 200/ 100 mmHg and heart rate of 115 bpm. ECG showed sinus tachycardia with supra-inferolateral the ST segment. Echocardiography showed acute biventricular heart failure with reduced EF to 38%.

CK-MB and troponin were high. Patient did badly with a progressive worsening of cardiac function and cardiac transplantation was proposed. Conclusions: Mitoxantrone is an antineoplastic synthetic agent which has been used as second-line agent for the treatment of recurrent forms of severe multiple sclerosis. The MitX has a dose-dependent cardiotoxic effect.

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1002

WFN15-0839

MS &amp; Demyelinating Diseases

Injuries of neuroimaging optical neuritis and neuromyelitis optica

S. Gomes. Neurology, b.Portuguesa, Sao Paulo, Brazil

Injuries of neuroimaging optical neuritis and neuromyelitis optica  
**Introduction:** Neuromyelitis optica (NMO) is characterized by acute optic neuritis and myelitis. The presence of lesions in other locations diagnosis.

In 2004 NMO-IgG antibody was described. Its presence determines with high sensitivity and specificity in distinction between MS and NMO. It was integrated in the criteria for diagnosis of this entity in 2006. This antibody binds specifically the channel Aquaporin 4 (AQP4) having a specific distribution in the CNS, mainly optic nerve or spinal cord. This fact changed the diagnostic criteria and neuroimaging. Case report: Female patient, 28 years suffered in September/ 2007 by sudden decrease in visual acuity on the right. History of the sudden loss of vision right, four years before. The brain MRI was normal. Visual evoked potentials were suggestive of demyelinating disease, right. Additional other studies were normal. She had a partial response to corticosteroids using, methylprednisolone pulse therapy. In 2009 she began to have alteration of gait and positional alteration of sensation in the lower limbs. MRI T2 and FLAIR, showed abnormalities at thalamocapsular, hypothalamus, peri-ventricular white matter and aqueductal, optic chiasm and brainstem extending to C1. CSF - discrete leukocyte pleocytosis, and NMO-IgG. New positive pulses with corticosteroids and azathioprine started. In October / 2010 another MRI showed improvement of lesions. She remained clinically stable. Conclusions: The clinical case of a patient without formal clinical criteria for neuromyelitis optica with NMO-IgG positivity showed atypical lesions at sites of high expression of AQP4.

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1003

WFN15-0841

MS &amp; Demyelinating Diseases

Esclerosis multiple and depression

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Multiple sclerosis (MS) is often associated with depression. However, there are few clinical trials in the treatment of depression in MS and no agreement recommendations for the evaluation and monitoring. We present evidence-based recommendations for various aspects of MS depression, including screening for depression, recognition of other concomitant psychiatric conditions, the risk of suicide, disability, fatigue, cognition, adherence to treatment, effect of drugs used to treat depression in MS and possible pharmacological treatments for depression in MS.

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1004

WFN15-1032

MS &amp; Demyelinating Diseases

Neuromyelitis optica X spectrum manifestation

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Neuromyelitis Optica X Spectrum manifestation

**Introduction:** The neuromyelitis optica with a twenty years predominantly inflammatory pathology among the forty year old.

**Objective:** To report a case of late onset and with positive for aquaporin 04 and only unilateral optic neuritis.

**Result:** Patient's female, 70 years old, and translator writer with intellectual and physical loss of vision in total right eye. Computed tomography of brain was considered normal. There was no response after 15 days with therapeutic aspirin, and she had MRI brain. Neurological examination normal except the right amaurosis. Investigation continued with cervical and skull of angiogram, cardiologic evaluation, transesophageal echocardiogram – all normal. Labs for serology, metabolites, normal. Proposed three days corticosteroid pulse does little improvement of vision. CSF was normal. Aquaporin 4 antibody was positive 1/160. Cervical thoracic spine MRI were normal, visual evoked potentials amended and body normal. Pulse after begins to have peripheral vision and gradual improvement with confirmed for new trial and high return after 30 days with ophthalmology. Corticoids and azathioprine treatment helped.

**Conclusion:** This case shows that NMO should be considered in the differential diagnosis of optic neuritis.

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1005

WFN15-1033

MS &amp; Demyelinating Diseases

Injuries of neuroimaging optical neuritis and neuromyelitis optica

S. Gomes. Neurology, b.Portuguesa, Sao Paulo, Brazil

Injuries of neuroimaging optical neuritis and neuromyelitis optica

**Introduction:** Neuromyelitis optica (NMO) is characterized by acute optic neuritis and myelitis. The presence of lesions in other locations diagnosis.

In 2004 was described NMO-IgG antibody, with high sensitivity and specificity in distinction between MS and NMO, being integrated

in the criteria for diagnosis of this entity in 2006. This antibody binds specifically the channel Aquaporin 4 (AQP4) having a specific distribution in the CNS, nonexclusive Optic nerve or spinal cord. This fact changed the diagnostic criteria and neuroimaging. Case report: Female patient, 28 years Observed in September / 2007 by sudden decrease in visual acuity on the right. History of the sudden loss of vision right, four years before. The skull-brain MRI was normal evoked potentials visuals were suggestive of demyelinating disease, right. Additional other study was normal. Partial response to corticosteroids, methylprednisolone pulse therapy. In 2009 she began to experience alteration of gait and positional alteration of sensation in the lower limbs. MRI T2 and FLAIR, with images at thalamocapsular, hypothalamus, peri-ventricular white matter and aqueductal, optic chiasm and brainstem extending to C1. CSF - discrete leukocyte pleocytosis, and NMO-IgG . New positive pulses with corticosteroids and azathioprine started. In October / 2010 MRI demonstrated improvement of lesions, and she remained clinically stable. Conclusions: The clinical case of a patient without formal clinical criteria for neuromyelitis optica with NMO-IgG positive, showing atypical lesions at sites of high expression of AQP4.

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1006

WFN15-1359

MS & Demyelinating Diseases

**Mmunoglobulin treatment of relapse in multiple sclerosis pseudotumoral on pregnancy**

*S. Gomes. Neurology, b.Portuguesa, Sao Paulo, Brazil*

IMMUNOGLOBULIN TREATMENT OF RELAPSE IN MULTIPLE SCLEROSIS PSEUDOTUMORAL IN PREGNANCY

**Introduction:** The inflammatory-demyelinating pseudotumor disorders may be single or multiple with dimensions greater than 2 cm appearing as initial and expression of an idiopathic disease or a multiple sclerosis (MS). Objective: to report a case of pseudotumoral ms with initial attack in pregnancy, with good response to immunoglobulin.

**Case report:** TLL, 27, female, pregnancy, 14 weeks, G1POA0, presents in December 2013, right optic neuritis, with paresthesia in left and right legs, hemiparesis complete with brachial dominance. Investigative process was checked for the presence of an expansive process intracranial. Evaluation was performed by magnetic resonance of brain and showed hyperintense T2/Flair lesions in corpus callosum splenium and white matter parieto-occipital bilateral, with surrounding vasogenic edema and enhancement with gadolinium in right splenium. Biopsy of lesion was recommended, and pseudotumor inflammatory demyelinating brain disease was confirmed with immunohistochemical. Then started pulse therapy with steroids and human immunoglobulin soon after. She had improvement of visual, motor and sensory symptoms. Pregnancy outcomes by cesaren without complications. Interferon was started after wide investigation. Patient remained in good overall condition, with reversal of deficits initially presented.

**Discussion:** we report a case of a patient with multiple sclerosis pseudotumoral form, with good response with use of immunoglobulin. This approach is based on data from the literature showing immunoglobulin as an alternative immunotherapy in pregnancy, with proven benefits.

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1007

WFN15-1442

MS & Demyelinating Diseases

**Tumefactive radiologic tumor as in multiple sclerosis and pregnancy**

*S. Gomes. Neurology, b.Portuguesa, Sao Paulo, Brazil*

Tumefactive radiologic tumor as in multiple sclerosis (MS) is not a common finding in MRI. This presentation creates an extra challenge to the already difficult diagnosis of MS. We report on a clinical MS case with this unusual radiological presentation and diagnostic difficulties in this patient the pregnancy. We also discussed our case, compared to the world literature.

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1008

WFN15-1594

MS & Demyelinating Diseases

**Neuromyelitis spectrum disorders and trigeminal neuralgia**

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Symptoms of brain stem are increasingly diagnosed in clinical picture as a participant in the neuromyelitis optica spectrum. Exact frequency and the start time yet to be determined. Common symptoms of brain stem in neuromyelitis optica are nausea, vomiting and frequent hiccups, Commitment, the result of the area postrema, located on the back of the bulb. A number of other symptoms of the brain stem have been described, but related to the core / dysfunction trigeminal nerve are sporadic. The patient in question had trigeminal neuralgia treatment with ha 02 years and carbamazepine and gabapentin use before the onset of bilateral optic neuritis and extensive transverse myelitis. Antibody to aquaporin 04 present. MRI of the brain shows lesions that are compatible as described in neuromyelitis optica.

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1009

WFN15-1041

MS & Demyelinating Diseases

**Training patients with multiple sclerosis for use interferon. paper to the principal nurse**

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**Introduction:** The nurses team to work with Multiple Sclerosis (MS) patients are very important factor in the multidisciplinary group to attend this disease. They have many functions like consultants and educators to the people to facilitate a better understanding and knowledge about MS, in the social and health fields. And these persons are very significant to the pharmacological treatment of this kind of patients.

**Objectives:** Training patients and parents to the use of auto injector interferon Rebif-44mcg (1 a).

**Methods:** To train 105 patients (75females, 29 males) with relapsing-remitting MS over a period of 1 to 10 years. We explain and make a practical demonstration about the basic procedure to

auto injector and the use of documents related with corporal mass and biotype patients.

**Results:** All the patients learned the techniques and performed the auto injection without problems. These patients showed clinical improvement confirmed by MRI.

**Conclusions:** Our results demonstrated that it is possible to educate patients how to perform injections at different sites. This guarantees adequate administration of the drug and contributes to the clinical improvement of the patients.

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1010  
WFN15-0080

### MS & Demyelinating Diseases

#### Morphological analysis of varicella zoster virus-like particles in fibroblast cultures inoculated with CSF from patients with relapsing-remitting multiple sclerosis

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**Introduction:** The involvement of herpesvirus in the pathogenesis of multiple sclerosis (MS) has been suspected considering epidemiological and molecular data. A history of infection with varicella zoster virus (VZV) in childhood has been one of the most important findings in clinical records of patients with MS. Previous studies have identified viral particles morphologically similar to VZV in CSF from patients in early days of relapsing.

**Objective:** To identify and morphologically analyze VZV in human fibroblasts cultures inoculated with CSF from patients with relapse of MS.

**Material and Methods:** CSF samples were analyzed in relapsing-remitting MS controls to determine the viral load of varicella-herpes virus by real-time PCR. Human fibroblasts were cultured and inoculated with CSF from patients with relapse of MS. Samples were processed to identify the presence of viral particles by transmission electron microscopy.

**Results:** The viral load VZV was increased in CSF from patients in the early days of relapsing. In human fibroblasts inoculated with CSF, the presence of VZV-like viral particles were observed in the cytoplasm of fibroblasts and the measurement of viral load of these cultures was increased.

**Conclusions:** There is evidence of the presence of VZV-like viral particles during relapse of patients with MS. We have also demonstrated that these particles multiply in cell culture inoculated with CSF.

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1011  
WFN15-0500

### MS & Demyelinating Diseases

#### Clinical efficacy of delayed-release dimethyl fumarate in Hispanic patients with relapsing-remitting multiple sclerosis: integrated analysis of define and confirm

L. Hernandez<sup>a</sup>, R.J. Fox<sup>b</sup>, R. Gold<sup>c</sup>, J.T. Phillips<sup>d</sup>, M. Okwuokeny<sup>a</sup>, A. Zhang<sup>a</sup>, J. Rana<sup>a</sup>. <sup>a</sup>Biogen, Cambridge, USA; <sup>b</sup>Cleveland Clinic, Mellen Center for Multiple Sclerosis Treatment and Research, Cleveland, USA; <sup>c</sup>St. Josef Hospital, Ruhr University, Bochum, Germany; <sup>d</sup>Multiple Sclerosis Program, Baylor Institute for Immunology Research, Dallas, USA

**Background:** In Phase 3 DEFINE and CONFIRM studies, delayed-release dimethyl fumarate (DMF; also known as gastro-resistant DMF) demonstrated robust efficacy in a broad range of relapsing-remitting multiple sclerosis (RRMS) subgroups.

**Objective:** To assess the clinical efficacy of DMF throughout 2 years in a post-hoc analysis of integrated data from the DEFINE and CONFIRM studies in Hispanic patients with RRMS.

**Design/methods:** Eligibility criteria included age 18-55 years, RRMS diagnosis, and Expanded Disability Status Scale score 0-5.0. Patients were randomized and received DMF 240 mg twice (BID) or thrice daily, placebo, or glatiramer acetate (CONFIRM only) for up to 2 years. Patient and/or IRB approval was obtained, as necessary. Bayesian (diffuse prior) statistical methods were applied due to the small sample size.

**Results:** Of 2301 intent-to-treat patients (1540 treated with DMF BID or placebo), 54 were of Hispanic descent; 31 treated with DMF BID and 23 treated with placebo. At Year 2, the annualized relapse rate (95% credible interval [CrI]) in patients treated with DMF BID vs placebo was 0.15 (0.04-0.56) vs 0.49 (0.14-1.68); posterior mean rate ratio (95%CrI) was 0.31 (0.10-0.95). Additionally, the proportion of patients with confirmed 12-week disability progression was lower with DMF BID compared with placebo, 8.2% vs 30.2% (posterior mean hazard ratio [95%CrI]: 0.17 [0.001-0.600]), respectively.

**Conclusion:** Consistent with relapse and disability outcomes in the overall intent-to-treat population, DMF demonstrated significant treatment effect in the Hispanic population. Due to the small sample size, these analyses are underpowered and should be considered exploratory.

**Study supported by:** Biogen

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1012  
WFN15-0492

### MS & Demyelinating Diseases

#### Clinical efficacy of delayed-release dimethyl fumarate in Asian patients with relapsing-remitting multiple sclerosis: integrated analysis of define and confirm

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**Background:** In the Phase 3 DEFINE and CONFIRM studies, delayed-release dimethyl fumarate (DMF; also known as gastro-resistant DMF) demonstrated robust efficacy in a broad range of relapsing-remitting multiple sclerosis (RRMS) subgroups.

**Objective:** To assess the clinical efficacy of DMF throughout 2 years in a post-hoc analysis of integrated data from the DEFINE and CONFIRM studies in Asian patients with RRMS.

**Design/methods:** Eligibility criteria included age 18-55 years, RRMS diagnosis, and Expanded Disability Status Scale score 0-5.0. Patients were randomized and received DMF 240 mg twice (BID) or thrice daily, placebo, or glatiramer acetate (CONFIRM only), for up to 2 years. Patient and/or IRB approval was obtained, as necessary.

**Results:** Of 2301 intent-to-treat patients (1540 treated with DMF BID or placebo), 136 were of Asian descent; 66 treated with DMF BID and 70 treated with placebo. At 2 years, the annualized relapse rate (95% confidence interval [CrI]) in patients treated with DMF BID vs placebo was 0.14 (0.03-0.66) vs 0.21 (0.05-0.93); rate ratio (95% CrI) was 0.64 (0.30-1.34). Additionally, the proportion of patients with confirmed 12-week disability progression was numerically lower with DMF BID compared with placebo, 19.6% vs 24.8% (hazard ratio [95% CrI]: 0.71 [0.32-1.58]), respectively.

**Conclusion:** There was a trend favoring DMF in the Asian population. Due to the small sample size, these analyses are underpowered and should be considered exploratory.

**Study supported by:** Biogen

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1013

WFN15-0099

**MS & Demyelinating Diseases**

**Olfactory functioning in early multiple sclerosis : Sniffin' sticks test study**

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**Introduction:** Previous studies have shown that olfactory functioning is affected by multiple sclerosis (MS). The aim of this study was to determine the level of the olfactory functioning of patients with MS by using the Sniffin' Sticks test.

**Methods:** This study included 30 patients with MS or clinically isolated syndrome and 30 healthy controls. The demographic and clinical data of participants were collected, and the Sniffin' Sticks test was applied.

**Results:** We found no differences in the odor discrimination (OD), odor identification (OI) and threshold-discrimination-identification (TDI) scores between the MS and control groups, but the odor threshold (OT) scores were higher in the control group than in the MS group ( $p = 0.49$ ). The odor scores obtained by patients with MS on olfactory tests were not associated with their scores on the Mini-Mental Status Examination (MMSE) or Expanded Disability Status Scale (EDSS), disease duration, optic neuritis, immune-modulatory therapy. Age of the patients was found to be associated with OI, OT, TDI scores.

**Discussion:** The higher scores of OT subtest of patients with MS seem to be associated with the duration and the course of the disease. The progression of the disease, and its acute inflammatory process can influence olfactory dysfunction.

**Conclusion:** Olfactory dysfunction appears to be a consequence of neurodegeneration, and it is suggested that this neurodegeneration is a time dependent process that is not obvious in the very early stages of MS.

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1014

WFN15-0271

**MS & Demyelinating Diseases**

**Predictive factors of rapid clinical disability progression in remittent recurrent forms of Tunisian multiple sclerosis**

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**Background:** Since 2006, our country became rated among regions of medium prevalence for multiple sclerosis (MS). A great interest is actually carried to MS. Little is known about long-standing and disabling MS.

**Objective:** We propose to study predictive factors of poor prognosis in short (1-5 years), medium (5-10 years) and long term (>10 years).

**Patients and methods:** We have conducted a retrospective study including remittent recurrent (RR) MS patients in whom the disease evolved since at least one year. Prognostic factors were evaluated using Progression index (EDSS/ disease duration), time to assess EDSS 4 and time to assess EDSS 6.

**Results:** 116 patients were included. Predictive factors of rapid clinical disability progression were: late onset, polysymptomatic onset, motor signs and high EDSS at onset, incomplete recovery after the first relapse, short time between first and second relapse, high IgG index, infra-

tentorial and medullar lesions on baseline MRI. We noted that whatever was the disease duration, initial clinical and paraclinical data no longer influenced clinical course of the disease once EDSS 4 was reached. Only two factors influenced this stage: high IgG index and presence of medullar lesions on baseline MRI.

**Conclusions:** These findings support the hypothesis of presence of two stages in MS: First stage would be inflammatory and its evolution is in relation with different factors cited. Second stage would be degenerative and begin once EDSS 4 was reached. Determination of predictive factors could be a first step for establishing a multifactor and consensual prognostic index for MS disease.

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1015

WFN15-0200

**MS & Demyelinating Diseases**

**Is there early axonal trans-section in radiologically isolated syndrome?**

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**Background & Objective:** Incidental detection of white matter lesions is named as radiologically isolated syndrome (RIS). Some of these patients develop multiple sclerosis (MS) in time. In MS brains, axonal injury was observed in normal appearing white matter and retinal nerve fiber layer (RNFL) of the unaffected eye. Retinal axonal loss begins early in the course of MS. In the absence of clinically evident optic neuritis, RNFL thinning was detected in patients with clinically isolated syndrome. There is no study of acknowledged axonal injury in RIS subjects. In this study, we investigated whether axonal trans-section occurred in retinal layer of the RIS subjects.

**Patients & Methods:** This is the preliminary data of an ongoing, prospective study. Spectral-domain optical coherence tomography (SD-OCT) is performed to measure RNFL thickness and macular volume (MV) in individuals fulfilling 2009 Okuda Criteria and healthy controls.

**Results:** SD-OCT has been done in both eyes of twelve RIS subjects (7 female, 5 male) and twelve controls. Overall RNFL thickness and MV were not statistically different between groups. When taken individually, atrophy of RNFL was detected in one subject and borderline RNFL thickness was detected in retina of six more subjects compared to general population, whereas in the control group the measurements were between normal limits.

**Conclusion:** These data suggest that axonal transection in retina might be elicited in RIS subjects. SD-OCT may reveal subclinical retinal axonal loss at the earliest stages of MS. Whether there might be an apparent consistency between brain MRI -DTI and retinal OCT will be the next analysis of this study.

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1016

WFN15-0923

**MS & Demyelinating Diseases**

**Is glatiramer acetate better for pregnancy in multiple sclerosis?**

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**Background:** Several studies have shown the negative impact of MS on pregnancy and fetal development. Using of disease-modifying drugs (DMD) in general, does not affect the outcome of pregnancy.

**Objective:** To evaluate the effects of DMD received in utero in early pregnancy on child first-year development.

**Material&Methods:** Structured interviews on pregnancies in MS patients which ended in live-births: all were divided into three groups GA, IFN or unexposure to DMD at time of conception. Development in the first year of life for all children, including the abnormalities in psychomotor (WHO six milestones), was evaluated. Statistical analysis - McNemar Chi-square, Median Test.

**Results:** Twenty pregnancies analyzed (8 IFN, 6 GA, 6 unexposed to DMD). No significant differences between the three groups were found in the mother's age ( $p = 0.47$ ), EDSS ( $p = 0.14$ ), relapse rate ( $p = 0.28$ ), gestation age ( $p = 0.39$ ). Birth weight was significantly higher ( $p = 0.036$ ) in GA than in IFN and unexposed. Similar results were obtained for the size of the head ( $p = 0.022$ ) and chest ( $p = 0.041$ ). No significant differences between the groups for sitting without support ( $p = 0.51$ ), hands-&-knees crawling ( $p = 0.84$ ), standing with assistance ( $p = 0.89$ ) and alone ( $p = 0.88$ ). Walking with assistance and alone was significantly later in IFN and unexposed group, then in GA ( $p = 0.039$  and  $p = 0.031$ ).

**Conclusion:** Thus, in women of childbearing age with MS it is preferable to use glatiramer acetate. This drug, apparently, has the property to reduce the negative impact of the disease on the fetus and the mother with multiple sclerosis, including first-life year development.

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1017

WFN15-0351

**MS & Demyelinating Diseases**

**Local reactions of multiple sclerosis disease modifying drug therapy in patients with multiple sclerosis and high titers of antithyroid antibodies**

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**Background:** Some studies have shown an increased co-occurrence of multiple sclerosis (MS) with autoimmune thyroid diseases as compared to the general population. So the influence of thyroid autoimmunity on the therapy of MS is an actual problem.

**Objective:** To explore of the local reactions to drugs of MS in patients with high titers of antibodies to thyroid antigens.

**Methods:** 83 patients (14 men, 69 women), RRMS (McDonald W.I., 2005), remission. The mean age was  $39,2 \pm 10,08$  years (19– 61 years).

Original scale of 4-point evaluation, Likert scale. Ultrasound study of the thyroid gland, analysis serum thyroid hormones and antithyroid antibodies. Statistical analysis - non-parametric statistic: U Mann-Whitney.

**Results:** We have formed two groups of patients: 21 MS patients with high titers of antibodies to the thyroid antigens without thyroid dysfunction, in the comparison group included 22 MS patients without thyroid disorders. These groups were comparable in age, gender composition, and therapy

Itching at the injection site was detected in 12 patients (57%) with a high titer of antithyroid antibodies, in the control group - 6 patients (27%). Swelling, redness, induration at the injection site is significantly larger in group with thyroid autoimmunity, than in comparison group ( $U = 2,19$ ,  $p = 0,02$ ,  $U = 2,8$ ,  $p = 0,005$ ,  $U = 2,78$ ,  $p = 0,005$ , respectively).

**Conclusion:** Thus, the MS patients with high titers of antithyroid antibodies had more local reactions to drugs for disease modifying of MS and may be included in the high risk group of side-effects of the drugs for their prevention.

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1018

WFN15-0819

**MS & Demyelinating Diseases**

**A genome-wide association study (GWAS) in the Japanese population reveals novel genetic risk factors for multiple sclerosis and neuromyelitis optica**

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**Background:** While genetic risk variants for multiple sclerosis (MS) have been identified among Europeans by GWAS, the variants have not been clarified in Asians.

**Objective:** To clarify genetic risk factors associated with MS and neuromyelitis optica (NMO) in Japanese.

**Methods:** Genome-wide 600,000 SNPs were genotyped in 533 MS cases and 1789 controls, and 200 NMO cases and 1752 controls. MS genetic burden (MSGB) scores were calculated based on the established risk SNPs for European descent MS outside the major histocompatibility complex (MHC) region. We tested genome-wide SNP association with various clinical characteristics in MS patients by using linear/logistic regression analyses.

**Results:** Twenty-six loci (FDR corrected  $p < 0.05$ ) associated with MS and 33 suggestive loci ( $p < 1.0 \times 10^{-4}$ ) associated with NMO were identified outside the MHC. There was no common risk region between MS and NMO. Thirteen SNPs out of the 97 risk variants for European MS were replicated ( $p < 0.05$ ) in the Japanese population. MSGB score was significantly higher in MS cases than in controls ( $p < 2.2e-16$ ). MSGB scores were correlated with MS Severity Score ( $\rho = 0.086$ ,  $p = 0.049$ ) and higher in patients with oligoclonal IgG bands (OCB) or brain lesions fulfilling Barkhof's criteria than in those without such phenotypes ( $p = 0.048$  and  $0.00049$ , respectively). Neurotrophic tyrosine kinase receptor type 2 rs2808707 was associated with age of onset ( $2.37 \times 10^{-7}$ ).

**Conclusion:** GWAS in the Japanese population identified novel genetic risks for MS and NMO. MSGB indicated common genetic effects for MS between European and Japanese, and had a correlation with OCB positivity and MS-like brain lesions.

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1019

WFN15-0360

**MS & Demyelinating Diseases**

**Cloud based multicentre multiple sclerosis registry in Lithuania: on line approach for continuous patient care and national data collection**

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**Introduction:** Large-scale multiple sclerosis (MS) registries exist. There is an increasing interest in studying MS characteristics in large populations and monitoring the long-term outcome. Prevalence of MS in Lithuania (LT) 78 cases to 100 thousands inhabitants. Number

of MS patients in LT, registered in 2007 was 2621 (male 875, female 1746). MS data collection till 2012 was based on individual records in iMed PC –based software. There was no electronic possibility to follow MS patient medical history. A need for the development of real-time MS registries made an obligation to create a new national MS data registry, based on electronic data documentation using new cloud based patient electronic data collection, compatible with international data exporting.

**Methods:** Multicentre Lithuanian MS registry was created in 2013, data collection was started in three MS Centres, University hospitals: Vilnius, Kaunas and Klaipeda. Protocol was approved by the Lithuanian Bioethics Committee.

**Results:** Each neurologist was identified by individual credentials. Data collecting forms were constructed to match MS Base and iMed data sets containing general and epidemiological information: disease onset time, symptoms, time of diagnosis, diagnosis accuracy, course of MS, disability, disease activity, immunomodulatory and symptomatic therapies, and socioeconomics aspects. Additional forms concerning pregnancy, MRI, laboratory investigations were introduced. Real-time data about patient's MS and concomitant medical history, collected in different MS centres, accessible for authorized neurologists will be demonstrated on line as well. Centralized MS patient data base prevents duplication of MS patients.

**Conclusions:** Lithuanian MS registry has proven to be a new and effective tool for studying MS epidemiology and monitoring every MS patient. With its cloud and specific data access solution this national MS registry is an innovative example for National patient registries across the world.

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## 1020

### WFN15-0397

#### MS & Demyelinating Diseases

##### Genetic basis of individual treatment response to disease modifying drugs in multiple sclerosis patients

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**Background:** 30-50% of multiple sclerosis (MS) patients do not respond to specific disease modifying drugs (DMD) therapy of first line – interferon beta (IFN-beta) or glatiramer acetate (GA).

**Objective:** to evaluate the influence of polymorphic variants of genes of the immune system on the effectiveness of MS therapies.

**Materials and Methods:** 100 patients with relapsing-remitting MS according to McDonald criteria (2010) were included. 46 patients were treated with GA, 54 –IFN-beta1a i/m. The lack of efficacy means saving of previous annual relapse rate (at least 12 months) with negative dynamics on brain MRI or progression of disease (confirmed after 6 months). The molecular-genetic study of polymorphic loci: rs1800629 (*TNFA*), rs4149584 (*TNFRSF1A*), rs6074022, rs1883832, rs1535045 and rs11086998 (*CD40*) was performed. IRB approval has been granted and all patients consented informed consent forms.

**Results:** The baseline clinical and MRI characteristics of the patients before DMD were not significantly different between responders and non-responders. The association of individual *CD40* gene polymorphisms with treatment response was revealed. The risk of developing of resistance to GA therapy is higher in MS patients carrying TT, TC rs1883832 *CD40* variants (OR 4.29,  $p = 0.018$ ), to IFN-beta1a IM –carriers of TC, CC genotypes in rs6074022 *CD40* (OR 5.00,  $p = 0.009$ ).

**Conclusion:** This study found an explanation why some patients became good responders after switching to another first line DMD

and provides a basis for further development of pharmacogenomic approach in MS. The data need to be clarified on a large sample and confirmed in an independent population.

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## 1021

### WFN15-0295

#### MS & Demyelinating Diseases

##### Interferon- $\beta$ therapy and risk of thrombocytopenia in multiple sclerosis patients

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**Background/Aims:** Thrombocytopenia is a well-described adverse event of several disease-modifying therapies (DMT) in multiple sclerosis (MS). On the other hand, an increased prevalence of MS has been reported in patients with immune thrombocytopenia. In this retrospective, cross-sectional, case-control study we evaluated in a heterogeneous MS cohort: 1) the prevalence of thrombocytopenia in comparison with sex- and age-matched controls; 2) the relationship between thrombocytopenia and patients' demographic, clinical characteristics; 3) the risk for thrombocytopenia in relation to DMT.

**Methods:** 187 consecutive MS patients [51 males, mean age ( $\pm$ SD) 44.5  $\pm$  10.7 years] and 200 controls (56 males, mean age 45.5  $\pm$  12 years) were included. Thrombocytopenia was defined as platelet count lower than normal laboratory values (130-400 $\times$ 10<sup>9</sup>/L).

**Results:** The prevalence of thrombocytopenia was significantly higher in MS patients than in controls (7% vs 2.5%,  $p = 0.04$ ). Thrombocytopenia was present only in relapsing-remitting MS cases, and significantly associated with lower EDSS ( $p = 0.002$ ) and with a trend for shorter disease duration ( $p = 0.06$ ). It was more frequent in patients on high-dose interferon- $\beta$  therapy compared with those on low-dose interferon- $\beta$  therapy, other therapies or untreated patients ( $p = 0.02$ ). High-dose interferon- $\beta$  therapy was associated with more than 8-fold increase in the risk for thrombocytopenia (Odds ratio 8.60, 95% Confidence Interval: 1.01-74.48 adjusted for EDSS, disease duration and type of disease).

**Conclusion:** The prevalence of thrombocytopenia was increased in MS patients treated with DMT. High-dose interferon- $\beta$  therapy is the variable most strongly associated with thrombocytopenia likely through the activation of innate immunity.

I have obtained patient approval.

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## 1022

### WFN15-0479

#### MS & Demyelinating Diseases

##### Clinical characteristics of multiple sclerosis patients undergoing immunomodulatory treatment in Poland

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In Poland, only patients meeting the National Health Fund (NFZ) criteria can apply for NFZ funded treatment as part of the Multiple

Sclerosis Drug Prescription Treatment Programme (PLSM). Difficulties faced by multiple sclerosis (MS) patients in meeting the strict selection criteria for the Programme result in a delayed commencement of the treatment.

The aim of the multi-centre study was to determine the period of time from disease diagnosis to the commencement of treatment including the assessment of disease stage and response to therapy.

Clinical and demographic parameters such as gender, age, smoking, date of MS diagnosis, commencement of treatment, disability according to EDSS were analyzed. The disease activity was determined by the annualized relapse rate (ARR) and by MRI.

The group studied comprised 312 patients: 215 women and 97 men; 224 non-smokers and 88 smokers. Average time from disease diagnosis to commencement of treatment was  $4.0 \pm 3.9$  years. Average patient age was  $37.8 \pm 9.8$  years, EDSS was  $2.1 \pm 1.1$  and ARR 1.2. After 2 years of treatment, ARR was 0.08. Average EDSS after one and two years of treatment was  $2.14 \pm 1.1$  and  $2.11 \pm 1.0$ , respectively. New lesions were detected with MRI in 25.3% and 17.4% of patients after one and two years of treatment, respectively. Positive correlation between smoking and occurrence of new lesions in MRI was observed ( $r = 0.29$ ,  $p < 0.01$ ).

With the current patient selection criteria for PLSM in place, the immunomodulatory treatment in MS continues to start too late with regard to the internationally accepted standards. Smoking seems to worsen course of MS.

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1023

WFN15-0391

MS & Demyelinating Diseases

**Atopic myelitis, a common form of myelitis with good long-term prognosis: a hospital-based experience**

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Atopic myelitis (AM) has been claimed to be a distinct form of myelitis with predominantly sensory and autonomic presentation. Because the lesions are commonly longitudinally extensive, it is crucial to differentiate AM from neuromyelitis optica (NMO).

All patients presented with myelitis at Eulji Hospital from January 2004 to March 2014 were included. Patients had myelopathic presentation with either CSF pleocytosis or enhancing cord lesion. Among myelitis, diagnosis of AM was made if hyperIgEemia or atopic diathesis is present after clinicolaboratory exclusion of other relevant disorders like NMO, MS and related disorders. Patients were interviewed about relapses and current disability with Functional Independence Measure & Functional Assessment Measure (FIM-FAM) and Spinal Cord Independence Measure-III (SCIM-III). The IRB approved the study.

Forty-six myelitis patients were included (M:F, 25:21; onset,  $44.3 \pm 14.1$  years). Among them, 18 had AM (42% of all myelitis, M:F, 14:4; onset,  $43.4 \pm 14.0$  years). Five AM patients have reported relapses (27.8%, M:F, 5:0) and there were no significant differences in regards to sex, age of onset, serum IgE, or sensitization to house dust mite, except for status of atopic diathesis (3/5 vs. 1/13,  $p < .05$ ) and duration from onset to nadir ( $156.4 \pm 80.6$  vs.  $70.4 \pm 67.5$ ,  $p < .05$ ). Functional status of AM patients was well preserved regardless of relapses (9 patients; FIM-FAM,  $201 \pm 18.7$ ; SCIM-III,  $95.6 \pm 9.5$ ) with disease duration of  $6.2 \pm 3.2$  years.

Most AM patients presented with subacute/chronic progressive manifestation over months. Almost all reported relapses in some AM patients were separated by a few months from the inaugural events,

and then there were no further relapses. This suggests that reported relapses be mere symptomatic aggravations during its protracted course. The clinical characteristics and prognosis according to presence of relapses were not different.

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1024

WFN15-0550

MS & Demyelinating Diseases

**Literature update on intramuscular interferon beta-1a outcomes from four recent phase 3 trials**

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**Background:** Intramuscular (IM) interferon (IFN) beta-1a was one of the first disease-modifying therapies (DMTs) approved for relapsing-remitting multiple sclerosis (RRMS) treatment. However, in the ~20 years since its initial approval, MS knowledge and management have evolved, and IM IFN beta-1a is now being evaluated as a reference/comparator in trials of new DMTs.

**Objective:** To examine the apparent consistent and/or increased effectiveness of IM IFN beta-1a in recent clinical trials versus its registration trial.

**Materials/Methods:** MEDLINE and congress abstracts (1/2010-5/2015) were searched using MeSH terms that included “multiple sclerosis relapsing-remitting,” “interferon-beta,” “phase 3,” and “randomized controlled trial.” Four trials of IM IFN beta-1a at 30 mcg/week versus other DMTs were identified (BRAVO, CombiRx, DECIDE, and TRANSFORMS). Key outcomes from each study (annualized relapse rate and 3- or 6-month confirmed Expanded Disability Status Scale [EDSS] progression) were compared with those from the IM IFN beta-1a RRMS registration trial (MSCRG).

**Results:** Baseline characteristics were generally similar among all studies (age, 36-39 years; relapses in previous year, 1.0-1.7; EDSS score, 2.0-2.5). Fewer relapses/patient-year were observed with IM IFN beta-1a in all 4 recent studies (BRAVO, 0.26; CombiRx, 0.16; DECIDE, 0.39; TRANSFORMS, 0.33) than in MSCRG (0.61). Percentages of patients with confirmed EDSS progression in each study was as follows: BRAVO, 8%-11%; CombiRx, 22%; DECIDE, 18%-20%; TRANSFORMS, 8%; MSCRG, 21%).

**Conclusions:** The apparent increased effectiveness of IM IFN beta-1a in recent studies may stem from improvements in MS management relative to ~20 years ago and may reset expectations for treatment outcomes going forward.

**Support:** Biogen.

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1025

WFN15-1095

MS & Demyelinating Diseases

**Use of administrative database to describe physician services utilization and care patterns in multiple sclerosis in France**

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**Background:** As multiple sclerosis (MS) is a chronic disease which starts at young adulthood, overall care consumption is known to be high in patients. This has never been precisely described in France although the number of prevalent cases is estimated to be 100,000. French health insurance database is now open to researchers through a random sample of 1/97th of national health system beneficiaries.



**Objective:** Describe physician services utilization and care patterns in multiple sclerosis in France using a sample of the national health insurance system.

**Materials and methods:** Study population was defined according to specific MS codes in hospital admissions (International Classification of Diseases 9/10) codes and prescription claims. The study period was 2007–2012. Physician service utilization (treating physician, neurologists and others) and hospitalizations rates (all-cause and MS-related) were measured in people affected with MS. Differences according to gender, year of birth, year of MS onset, and region of residence were assessed.

**Results:** Pilot study was conducted for the year 2007 only and is the only available up to now. A total of 621 MS cases (453 women and 168 men) were identified. Women and young patients had a higher number of medical visits than men and older patients respectively. The number of medical at-home visits increased with age. Moreover physician service utilization differed according to administrative regions and seemed to be linked to the medical density.

**Discussion:** The present study will be the first one investigating the care patterns in MS in France using administrative database.

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1026

WFN15-0307

#### MS & Demyelinating Diseases

##### Unenhanced CT may be more effective in distinguishing tumefactive demyelinating lesions from glioma and primary central nervous system lymphoma

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**Objective:** To evaluate the role of brain CT scanning for distinguishing tumefactive demyelinating lesions (TDLs) from glioma or primary central nervous system lymphoma (PCNSL).

**Methods:** 60 TDLs and 65 gliomas and 30 PCNSLs were pathologically diagnosed, whose brain CT imaging were retrospectively reviewed and compared between brain tumors and TDLs.

**Results:** (1) On unenhanced CT imaging, there were 64 of 95 brain tumor cases (67.4%, including 39 gliomas and 25 PCNSLs), in whose brain lesions hyperdense were observed, and isodense lesions were found in 11 of 95 cases (11.6%, 7 gliomas and 4 PCNSLs), and hypodense lesions in 20 of 95 cases (21.1%, 19 gliomas and 1 PCNSLs). In contrast, all the lesions of 58 TDLs (n = 60, 96.7%) showed hypodense, and only 2 TDLs had isodense lesions. (2) The hyperdense lesions of WHO grade II, III and IV were respectively observed in 10, 19, and 10 cases, and accordingly respectively in 3, 3, and 1 cases for isodense lesions, so there were no difference between different grade ( $\chi^2 = 3.138, P = 0.534$ ). (3) According to the shape of hyperdense lesions of the 95 primary brain tumors, 23 cases (11 gliomas, 12 PCNSLs) manifested with symmetric hyperdense mass, 18 cases (8 gliomas, 10 PCNSLs) with diffused hyperdense lesions, and 19 cases (16 gliomas, 3 PCNSLs) with ring-shaped hyperdense lesions, only 4 gliomas with asymmetric hyperdense patches.

**Conclusions:** CT scan as a simple, economical and practical examination could make significant role of differentiating TDLs from glioma or PCNSL and could be used as a meaningful adjuvant method for MRI. The hyperdense or isodense lesions on unenhanced CT may suggest glioma or PCNSL more than TDLs.

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1027

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#### MS & Demyelinating Diseases

##### Overview of multiple sclerosis in the medical services of “Petroleos Mexicanos” from April 2009 to April 2015

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MS has been considered as a rare disease in Mexico. The Mexican Oil Company “Petroleos Mexicanos”(PEMEX), has its own medical system which provides healthcare to a closed population of about 800000 people.

**Methods:** We identify the electronic records of the patients with diagnosis of MS, coded G35, by the ICD10, from April 1, 2009 to April 1, 2015.

**Results:** 4716 consultations coded as G: 35 were done: 229 patients. 59 wrong diagnosis Being eligible 170 patients: 126 women and 44 men. Highest peak: women between 25 and 44 years. 125 patients had remitting relapsing EM; 33 had progressive forms; 4 had remained with clinical isolated syndrome, and 3 with radiological isolated syndrome. 2 had breast cancer; 1 had a meningioma, and a couple of twins showed MS. 10 patients failed to return. 5 remain in diagnostic doubt. 6 died directly because of MS, 1 suicide, all of them with progressive forms with more than 5 years of evolution. All disease-modifying drugs available were used. More detail results in poster or presentation.

**Conclusion:** MS was not a rare disease within PEMEX's medical system; early diagnosis and treatment were directly associated to better outcomes. Since this is a closed population, it is relatively easy to follow. We intend to study the MS behaviour as a model of the disease in Mexico, aiming to improve MS patients care through the comparison of data from other epidemiological sources in Mexico and Latin America, with the data generated through this and subsequent studies. With IRB approval.

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1028

WFN15-1482

#### MS & Demyelinating Diseases

##### Sera from CIDP patients disrupt blood-nerve barrier via activation of rho-kinase pathway

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**Objective:** In our recent *in vitro* study, sera from chronic inflammatory demyelinating polyneuropathy (CIDP) patients were shown to possess effects to disrupt blood-nerve barrier (BNB). We studied the molecular background of BNB damage in CIDP using patients' sera and cultured microvascular endothelial cells derived from human peripheral nerve (PnMECs).

**Methods:** We have obtained patient and Institutional Review Board (IRB) approval, as necessary. We evaluated the effects of sera obtained from patients with CIDP on the expression levels of tight junction proteins, intercellular cell adhesion molecule-1 (ICAM-1), actin stress fiber formation and transendothelial electrical resistance (TEER) value in the PnMECs. We then investigated the influence of the CIDP sera on PnMECs in the presence of specific rho-kinase inhibitor (Y-27632) in order to determine whether rho-kinase pathway is involved in BNB alterations induced by patients' sera.

**Results:** The sera obtained from the patients with CIDP significantly decreased the amount of claudin-5 and ZO-1 protein levels and TEER values in the PnMECs as compared with normal controls. CIDP sera also increased ICAM-1 protein amount and actin stress fiber formation. Treatment with Y-27632 attenuated reduction of TEER values and claudin-5 expression levels induced by CIDP sera. Y-27632 treatment also prevented the increase of ICAM-1 protein amount and excessive actin stress fiber formation.

**Conclusion:** Humoral factors in the sera of CIDP patients may disrupt BNB via activation of rho-kinase pathway.

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1029

WFN15-1121

**MS & Demyelinating Diseases**

**Biological markers of neurodegenerative and inflammatory processes in multiple sclerosis**

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**Background:** Currently, the biomarkers of neurodegenerative processes are studied, such as tau protein, beta amyloid and also the biomarkers of immune response, such as alpha-1 antitrypsin, a protease inhibitor, beta-2-microglobulin, a protein associated with class 1 antigens of the major histocompatibility complex.

**Objective:** The aim of the study was to compare markers of inflammatory and neurodegenerative processes in cerebrospinal fluid (CSF) in patients with clinically isolated syndrome (CIS), relapsing-remitting multiple sclerosis (RR) and primary progressive multiple sclerosis (PP).

**Patients and Methods:** The authors examined the group of 158 patients, 119 female and 39 male. 94 patients were diagnosed with RR, 39 patients with CIS and 25 patients with PP. Groups of RR and CIS patients were therapeutic native. OCB was assessed by isoelectric focusing and immunofixation. The statistical analysis was provided on the SPSS software, version 15 (Chicago, USA).

**Results:** In the group of PP patients were found a statistically significant ( $p = 0,011$ ) increased values of Qalb comparing to the group of RR patients: In the group of PP patients were found a statistically significant increased ( $p = 0,006$ ) values of beta-2-microglobulin comparing to the group of RR patients.

**Conclusions:** Elevated values of tau protein can demonstrate the neurodegenerative processes followed by axonal loss in all forms and stages of MS. While tau protein can be considered as a general marker of neurodegeneration, elevated values of beta-2-microglobulin and alpha 1-antitrypsin only in the group of PP patients may be interpreted as the special marker for distinguishing the degree of axonal loss and immune response in MS patients.

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1030

WFN15-0423

**MS & Demyelinating Diseases**

**Pulmonary arterial hypertension in patients with multiple sclerosis treated with interferon beta. Case report**

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Pulmonary arterial hypertension in patients with multiple sclerosis treated with interferon beta. Case report.

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**Summary:** Pulmonary arterial hypertension (PAH) is characterized by elevated mean arterial blood pressure in the pulmonary artery, which may be approaching the values in the systemic circulation. This is associated with poor prognosis. PAH arises on the basis of a variety of causes, some of which are related to pharmacotherapy.

We report a 39-year-old female patient with relapsing-remitting multiple sclerosis treated with immunomodulatory therapy, who developed severe primary pulmonary arterial hypertension. We assume a causal relationship between PAH and interferon beta treatment. Therapy with interferon beta was terminated and specific pharmacotherapy of pulmonary arterial hypertension with sildenafil was initiated. In scientific literature there were described several cases of pulmonary arterial hypertension in patients treated with interferon beta, some of which were assessed to be possibly related to the treatment, including one published case report of patients with multiple sclerosis.

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1031

WFN15-0886

**MS & Demyelinating Diseases**

**Highly increased prevalence of multiple sclerosis on the island of Icaria, Greece**

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**Background:** We have recently reported increased multiple sclerosis (MS) prevalence ( $108/10^5$ ) on the island of Crete, Greece (Kotzamani et al, 2009) compared to what was previously thought for Greece. Furthermore, personal observations suggested frequent occurrence of MS in several islands of the Eastern Aegean Sea, including Icaria.

**Objective:** We aimed to assess MS prevalence on the island of Icaria.

**Patients and Methods:** Case ascertainment was accomplished via contacting local physicians and media advertisement. MS diagnosis was established using the International MS Panel criteria (McDonald et al, 2001). Additional information on family history was obtained by the patients, their relatives and local physicians. Patient approval was obtained, as necessary. Prevalence was defined as the number of MS patients per 100,000 inhabitants living in the study area on December 31, 2014 and had the clinical onset while living there (onset-adjusted prevalence rate).

**Results:** On Icaria (8,423 total population, 2011 census), we identified 13 patients, which accounts for a prevalence rate of  $154/10^5$ , greatly exceeding prevalence estimates for other Greek provinces. We identified 11 more patients that were currently residing in other areas of Greece or abroad, but who were former residents of Icaria. Interestingly, most of these patients came from families with multiple affected members.

**Conclusions:** A highly increased MS prevalence on Icaria, both on current residents and on immigrants currently living in other areas of Greece and abroad, was found. Further studies are warranted to identify the genetic or/and environmental factors underlying this frequent occurrence.

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1032

WFN15-0738

**MS & Demyelinating Diseases****CSF and serum levels of inflammatory markers at the time of first clinical symptoms in MS patients**

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**Background:** We hypothesized that the levels of some markers could be changed in MS in comparison with controls. We studied five inflammatory markers (interleukin-6, interleukin-8, interleukin-10, beta-2-microglobulin, orosomucoid).

**Methods:** The study was based on CSF and serum examination in patients with MS and control group (patients with non-inflammatory disease). In the MS patients, the lumbar puncture was indicated and performed at the time of the first clinical symptoms compatible with MS. None of our patients had been treated by corticosteroids before lumbar puncture. The aim of the study was to assess CSF and serum levels of inflammatory markers and compare these levels between MS group and control group. We tried to find inflammatory changes in early stage of MS.

**Results:** CSF and serum examination was performed in 102 patients with newly diagnosed MS meeting McDonald's revised diagnostic criteria (70 females; median 40 years) and 102 control group patients (79 females; median 37,5 years). No statistically significant differences in demographic data between MS patients and control group were found. Significantly higher CSF levels of IL-8 (median 59,1;  $p < 0.0001$ , Mann-Whitney U test) and beta-2-microglobulin (median 1,27;  $p < 0.0001$ , Mann-Whitney U test) in MS patients group were found. Significantly lower serum levels of IL-8 (median 8,00,  $p = 0,018$ , Mann-Whitney U test) were found.

**Conclusion:** The levels of two studied inflammatory markers were found to be increased at the time of first clinical symptoms of MS. As the etiology of MS is still unknown, research on inflammatory and neurodegenerative markers in MS should continue.

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1033

WFN15-1529

**MS & Demyelinating Diseases****Transorbital echography for optical nerve atrophy assessment in multiple sclerosis patients**

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**Background:** Multiple sclerosis (MS) is a disease in which myelin loss is involved. Optical nerve (ON) is usually impaired. A previous study developed in our centre has assessed its usefulness to determine ON atrophy.

**Material and methods:** Prospective observational case (MS patients)-control (healthy controls) by means of ON echography.

**Results:** 40 cases, 25 controls. Mean age: cases 44.35 ± 10.9 years old, controls 48.52 ± 9.7 years old. Significant statistical differences in ON diameter between cases and controls were found (RON: 3.71 ± 0.80 mm controls vs 2.80 ± 0.48 mm cases,  $p < 0.0001$ ; LON: 3.95 ± 0.84 mm controls vs 2.77 ± 0.51 mm cases,  $p < 0.0001$ ). The differences between ON diameter between controls and cases were consistent, even comparing controls with the subgroup of cases without previous clinical optical neuritis ( $p < 0.0001$ ). Similar diameter of ON were found in all cases subgroups, even comparing those with normal and impaired visual evoked potentials (VEP).

**Conclusions:** According with previous data, ON assessment by means of echography is a useful, non-invasive and simple method for ON atrophy assessment, and most of the time the nerve is echographically impaired even though there were no clinical damage recorded.

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1034

WFN15-1466

**MS & Demyelinating Diseases****Cladribine does not affect the 8-iso PGF<sub>2α</sub> serum level in primary-progressive MS patients**

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**Introduction:** Cladribine (2CDA) is an immunomodulatory agent that can be considered for multiple sclerosis (MS) treatment. Instead of known cladribine effect on lymphocytes' function, data relating to oxidative status are scant.

**Objective:** Evaluation of cladribine effect on one of lipids' peroxidation product (8-iso PGF<sub>2α</sub>) in MS patients serum.

**Material and methods:** Forty primary-progressive MS patients were enrolled. Cladribine was administrated subcutaneously (dose 20 mg for 2 days hospitalization). MS patients received cladribine treatment every 5 weeks, for 6 times. Serum samples were collected before 1st, 3rd and 6th course of treatment. Results were compared to healthy, sex and age-matched controls. Control serum was collected once. Neurological disability of MS patients was assessed with EDSS (Expanded Disability Status Scale). Determination of 8-iso PGF<sub>2α</sub> levels in serum was performed with ELISA test. Patient's and Institutional Review Board approvals were obtained.

**Results:** Statistically significant increase of 8-iso PGF<sub>2α</sub> serum level was noticed in MS patients in comparison to controls at each evaluated time-point (609.56; 617.80; 589.16 vs. 140.48 pg/ml for the 1st, 3rd, 6th course vs. controls respectively,  $p < 0.001$ ). Level of disability did not change significantly during cladribine treatment (EDSS before 1st dose 4.9; before 3rd 4.9 and 6th dose 5.0,  $p = 0.16$ ). Significant positive correlation between serum concentration of 8-iso PGF<sub>2α</sub> before the start of cladribine treatment vs. EDSS score was observed (Spearman,  $r = 0.92$ ;  $p < 0.0001$ ).

**Conclusions:** Cladribine administration does not affect 8-iso PGF<sub>2α</sub> serum level. Higher concentration of 8-iso PGF<sub>2α</sub> in the serum of MS patients compared to controls may suggest a significant effect of oxidative stress in MS pathogenesis. The concentration of 8-iso PGF<sub>2α</sub> and thus increased free-radical processes of lipid peroxidation were positively correlated with disability degrees in MS patients.

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1035

WFN15-1170

**MS & Demyelinating Diseases****Epidemiological, clinical, evolutionary and therapeutic profile of 142 patients registered in the reference center for multiple sclerosis of Paraiba, Brazil**

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**Introduction:** Multiple sclerosis (MS) is a chronic neurological disease, inflammatory, demyelinating and immune-mediated of the Central Nervous System, affecting, in the form of plaque lesions, white matter of the brain and spinal cord.

**Objective:** Evaluate epidemiological, clinical, evolutionary and therapeutic aspects of patients treated at the Reference Center for Multiple Sclerosis of Paraíba (CREMPB).

**Method:** Observational, cross-sectional and descriptive study with qualitative-quantitative approach, based on a review of medical records of patients treated between November 2012 to April 2015. Seven variables were assessed: gender, skin color, age of the first outbreak, time diagnostic in years, family history, clinical presentation and use of disease-modifying drugs.

**Results:** Prevalence of the disease in females at a ratio of 3.3:1, in white (52.1%), with age of the first outbreak between the 3rd and 5th decade of life (50.7%) and diagnostic time equal or more than five years (52.8%). Negative family history (88.7%), prevalence of clinical form relapsing-remitting (66.2%), followed by secondary progressive form (31.7%). Among the disease-modifying drugs, predominated the beta-interferons (subcutaneous  $\beta$ 1A: 37.3%, intramuscular  $\beta$ 1A: 16.2% and  $\beta$ 1B: 16.2%).

**Conclusion:** This study will contribute to the understanding of MS at the state of Paraíba, and help to guide the care and coordinate with other medical centers of Brazil and the world.

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1036

WFN15-1172

MS & Demyelinating Diseases

**Perception, knowledge and quality of life in 64 patients with multiple sclerosis treated at a Brazilian reference center**

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**Introduction:** Multiple sclerosis (MS) is a chronic neurological disease that can cause significant impact on patients' lives. Consideration of these effects is critical in the clinical management and monitoring of the disease evolution.

**Objective:** Evaluate the perception, knowledge and quality of life in patients from the Reference Center for Multiple Sclerosis of Paraíba (CREMPB), Brazil.

**Methods:** 64 MS patients were studied, based on review of records and interviews of patients treated between November 2012 to April 2015. The cases were analyzed by seven variables: patient's reaction at the time of diagnosis, prior knowledge about the disease, limitation to the activities of daily living (ADL), physical activity, memory impairment, need of support to walk and presence of voiding symptoms.

**Results:** 62.5% of patients had difficulty accepting the diagnosis, but understanding the disease helped the acceptance process. 92.1% of patients were unaware about the disease when they were diagnosed. On the other hand, 54.6% of patients reported some kind of limitation

to the ADL and 51.5% said they didn't perform any physical activity. The memory changes were predominant in 64.0% of the patients and 72.5% didn't use support to walk. 56.2% did not present voiding dysfunction, but when affected (43.8%), there was a predominance of urgency and urinary retention.

**Conclusion:** MS has a variable impact on quality of life of patients. Recognizing this impact is important on the clinical management, therapeutic and multidisciplinary approach of the disease.

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1037

WFN15-0444

MS & Demyelinating Diseases

**Monthly pulse methylprednisolone as an add-on therapy is effective in long-term treatment of relapsing remitting multiple sclerosis**

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**Background:** Although some conflicting results, there are some evidences for beneficial treatment effects of long-term pulsed intravenous methylprednisolone (IVMP) and combination of interferon beta (IFNB) and pulsed methylprednisolone in multiple sclerosis (MS), but more evidence are needed to establish clinical practice for such a treatment strategy.

**Objectives:** To evaluate the efficacy of monthly pulse methylprednisolone treatment added to IFNBs or Glatiramer acetate (GA) in breakthrough MS.

**Methods:** MS patients receiving ongoing IFNBs treatment were eligible if they had Expanded Disability Status Scale (EDSS) scores of 5.5 or less. Patients with at least two relapses or at least one relapse and new T2 or gadolinium enhanced lesion within the previous year. Patients received 1 g pulse IVMP once a month at least one year.

**Results:** A total of 89 (58 female) patients finished the one year study period. Relapse rate was decreased from 1.6/ year to 0.3/year ( $p = 0.000$ ). 64 patients (65.3%) became relapse free. Mean EDSS score was decreased significantly from  $3.01 \pm 2.3$  to  $2.89 \pm 1.82$  ( $p = 0.012$ ). Female patients responded better than male patients based on both relapse and disability. Health related quality of life (HRQoL) measured by MUSIQoL was significantly improved in the study population ( $p = 0.005$ ).

**Conclusions:** Our data suggested that methylprednisolone given in pulses every 4 weeks as an add-on therapy to subcutaneous interferon beta-1b, interferon beta 1a and glatiramer acetate in patients with relapsing-remitting multiple sclerosis leads to a significant reduction in relapse rate and disease progression. Significant improvement in HRQoL was also found in the study group. However, these findings need to be corroborated in larger cohorts.

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1038

WFN15-0446

MS & Demyelinating Diseases

**Utilization of the brief international cognitive assessment for multiple sclerosis during treatment of relapses in patients with multiple sclerosis**

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**Background:** As would be expected, a substantial number of multiple sclerosis (MS) patients are compromised neuropsychologically. The Expanded Disability Status Scale (EDSS) has been the most widely used clinical outcome measure in therapeutic trials of MS.

**Objectives:** We examined the changes in measurement of cognitive functions during pulse methylprednisolone (MP) treatment of MS exacerbations using the Brief International Cognitive Assessment for MS (BICAMS). We aimed to determine the availability and usefulness of BICAMS in the attack period.

**Methods:** Forty-nine (30 female) MS patients in an attack period were included in this study. Mean age was  $36,41 \pm 8,36$ . All patients received 1000-mg intravenous MP for 5 days, followed by tapering dose of oral prednisolone for 20 days. BICAMS battery, which includes Symbol Digit Modalities Test (SDMT), California Verbal Learning Test (CVLT2) and the revised Brief Visuospatial Memory Test (BVMTR), EDSS, MUSIQoL, Multiple Sclerosis Neuropsychology Questionnaire patents form (MSNQ-P) and Fatigue Impact Scale (FIS) were administered.

**Results:** Mean CVLT2 score was significantly improved on day 6 ( $p = 0.000$ ) and on day 30 ( $p = 0.000$ ). Mean SDMT score was also improved both on day 6 ( $p = 0.003$ ) and day 30 ( $p = 0.000$ ). M BVMTR score was improved on day 6 ( $p = 0.000$ ) and on day 30 ( $p = 0.000$ ). There was a strong correlation between CVLT2 and SDMT ( $r = 0.551$ ). Correlations between CVLT2 and BVMTR ( $r = 0,624$ ), and BVMTR and SDMT ( $r = 0,494$ ) were also found strong.

**Conclusions:** The present study is the first one regarding utilization of BICAMS battery in attack period. Our results indicated that BICAMS battery is well accepted by MS patients and may be used for rapid evaluation of cognition in an attack period. However, these preliminary findings need to be corroborated in larger cohorts.

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1039

WFN15-1047

MS & Demyelinating Diseases

**Baseline cognitive function is predictive of clinical disability progression in relapsing-remitting multiple sclerosis: a statistical approach**

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**Background:** We previously reported on identification of baseline cognitive function as a predictor of clinical disability progression in RRMS patients as measured by a novel composite outcome, using regression tree modeling in an integrated clinical trial database (IDB). One limitation of our approach was the presence of missing values for candidate baseline prognostic factors.

**Objective:** To assess baseline factors predictive of time to 24-week confirmed evidence of clinical disability progression in placebo-treated patients using a complete baseline dataset by employing Markov Chain Monte Carlo (MCMC) imputation.

**Patients and methods:** Patient and/or IRB approval was obtained, as necessary. The IDB comprises data from six Phase 3 RRMS clinical trials with a complex pattern of missing baseline values. An MCMC imputation approach preserving the structure of the original baseline data was implemented. A Cox proportional hazards regression tree was constructed for time to clinical disability progression.

**Results:** Baseline values were imputed for 2079 of 6574 (32%) patients using 45 groups defined by missing value pattern. Imputed baseline data deviated by <1% from original data based on mean and SD, except for 3 factors known to be highly skewed. Patients who

scored 39 or less correct items on baseline PASAT-3 were identified to be at significantly higher risk of progression.

**Conclusions:** Cognitive function measured by PASAT-3 is the most predictive baseline risk factor for clinical disability progression, consistent with our previous findings. Use of MCMC imputation appropriately addresses the presence of missing baseline data and allows for more accurate estimation of risk cutoff.

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1040

WFN15-1062

MS & Demyelinating Diseases

**Evaluation of interferon beta therapy for multiple sclerosis funded by the national resources fund in Uruguay in the period 2009-2014**

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**Introduction:** The National Resources Found (NRF) is the organization financing in Uruguay the high costs treatments. In 2009 NRF incorporated coverage first line treatments for Multiple Sclerosis (MS) in Uruguay, this involved the development of national legislation with internationally accepted criteria for the indication of this treatment this disease.

**Objectives:** a) To evaluate the authorized treatments by NRF with interferon beta in Uruguay for MS in the period from February 1, 2009 and January 30, 2014 b) Estimate the incidence of MS in Uruguay

**Material and methods:** We evaluated retrospectively the patient cohort of the NRF diagnosed with MS in that period, which was authorized treatment, the cut-off date for the follow-up was the January 31, 2015. It was estimated the national incidence rate for the disease fitting the data by clinical form and type of coverage health system (public-private)

**Results:** 388 treatments were authorized in the period considered, 73% were female with an average age of 38.6 years. The estimated annual incidence rate was 1.2 / 100,000 / year (IC95% 0,9 – 1,6) The flu-like syndrome was the most common adverse event observed, 22.3% discontinued treatment. 15 patients (3.9%) died (25% of tumors)

**Conclusions:** The first national data on the treatment of MS in Uruguay are reported. The application of national legislation implied the consequent equitable assistance immune-modulatory MS treatment in Uruguay. The estimated incidence is comparable to other Latin American studies.

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1041

WFN15-1420

MS & Demyelinating Diseases

**Effect of fingolimod versus interferon-beta1a on neda-4 (no evidence of disease activity or worsening) in the transforms study**

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**Background:** Brain volume loss (BVL), accelerated in MS, is associated with focal and diffuse CNS damage, and independently predicts long-term disability. NEDA, used to capture MS treatment effects, has usually included 3 measures, addressing mainly focal damage: MRI-lesions, relapses, and disability-progression. Analyses of placebo-controlled FREEDOMS/FREEDOMS II data showed adding BVL to NEDA results in a more demanding but also more comprehensive, balanced measure of disease related activity, worsening and damage.

**Objective:** To compare oral fingolimod vs. i.m. IFN $\beta$ -1a, in achieving no evidence of disease activity or worsening status (NEDA-4) in patients with RRMS in TRANSFORMS.

**Patients/methods:** This post-hoc analysis of the one-year, phase-III TRANSFORMS study, utilized data from fingolimod 0.5 mg daily (n = 431) and IFN 30  $\mu$ g weekly (n = 435) groups. NEDA-4 was defined as: no confirmed relapses, no new/enlarging T2-lesions, no 6-month confirmed disability progression (CDP) and less than 0.4% mean annual BVL. 3-month CDP and additional percent brain volume change (PBVC) cut-offs representing mean BVL rates in healthy adults (0.2%) and in MS-patients (0.6% and 1.2%) were also tested. Odds-ratios (OR) were calculated for differences between fingolimod- and IFN-treated groups.

**Results:** Data were available for 425 fingolimod- and 418 IFN-treated patients. Significantly more fingolimod- than IFN-treated patients achieved NEDA-4 status: 27.9% vs. 16.7% (OR: 1.93; 95%CI: 1.36–2.73; p = 0.0002). Results were similar for other PBVC cut-offs: (>-0.2%): 20.2% vs 11.5%; 1.94; 1.30-2.90, p = 0.0011; (>-0.6%): 34.6% vs 20.4%; 2.06; 1.49-2.86, p < 0.0001; (>-1.2%): 40.8% vs 26.4%; 1.92; 1.42-2.60; p < 0.0001.

**Conclusion:** Fingolimod-treated patients had twice the odds of achieving NEDA-4 status over one-year than IFN-treated patients.

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## 1042

### WFN15-1137

#### MS & Demyelinating Diseases

##### Role preferences in treatment decisions of MS patients in Italy

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**Background:** The Control Preference Scale (CPS) is the most frequently used measure of patients' preferred roles in treatment decisions. Recently, an image-revised, computerized, patient self-administered version (eCPS) was produced.

**Objective:** We assessed role preferences, and their determinants, in 270 Italian relapsing-remitting multiple sclerosis (RRMS) patients who started electronic, self-injecting interferon beta-1a treatment. The eCPS was administered via tablet.

**Methods:** I have obtained patient and Institutional Review Board (IRB) approval. Vantage is a prospective, 2 year study on health-related quality of life in RRMS patients in Italy. Baseline data are considered in the present analysis. Variables associated with choice of an active/collaborative eCPS role at baseline were assessed.

**Results:** Mean age of the patients was 36.8 years (SD 9.7); 179 (66%) were women; median time from MS diagnosis was 13 months (interquartile range, IQR 2-83); median EDSS was 1.5 (IQR 1.0-2.0). Full eCPS scores were therefore available for 238 (88%). Of these, 137 (58%) preferred a collaborative, 69 (29%) a passive, and 32 (13%) an active role. Age, gender, education, area of Italy, and EDSS score were not associated with role preference. None of the independent variables had any significant effect in a multivariate model.

**Conclusions:** Valid scores obtained with tablet eCPS were similar to face-to-face and PC administration. Our data indicate that around 60% of Italian RR MS patients prefer a collaborative role. Role preferences did not differ across Italian areas and education. The use of an electronic device might create a selection bias towards active-collaborative patients.

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## 1043

### WFN15-0699

#### MS & Demyelinating Diseases

##### Factors associated with dimethyl fumarate use and treatment patterns among patients with multiple sclerosis in a real-world setting

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**Background:** The availability of multiple oral disease-modifying therapies (DMTs) provides an impetus to understand real-world treatment patterns among patients with multiple sclerosis (MS).

**Objective:** To assess factors associated with delayed-release dimethyl fumarate (DMF; also known as gastro-resistant DMF) use among MS patients.

**Materials and methods:** Using a large administrative US claims database, adult MS patients with first-observed prescription for DMT on or after 4/1/2013 (index date), continuously eligible for 12 months pre-index were identified. A logistic regression was used to identify baseline determinants of receiving DMF as the index DMT. **Results:** 31,359 patients met study criteria (age: 47 years; 76% female). 6,820 (22%) received an oral DMT and 3,419 (11%) were prescribed DMF. 66% of patients initiated on DMF were naïve to other DMTs. In logistic regression analyses, patients with a relapse in the 90-day pre-index period (OR: 1.63; 95% CI 1.46-1.82), younger patients (ages 18-34 {OR: 1.30; 95% CI 1.14-1.48}, ages 35-45 {OR: 1.29; 95% CI 1.16-1.44}, ages 46-54 {OR: 1.14; 95% CI 1.03-1.27}; all vs. patients aged 55-64), presence of bladder dysfunction (OR: 1.16; 95% CI 1.00-1.34), presence of fatigue (OR: 1.12; 95% CI 1.03-1.22), presence of MRI (OR: 2.03; 95% CI 1.86-2.22), and presence of a spinal tap (OR: 1.27; 95% CI 1.11-1.44) were significantly more likely to receive DMF as their index therapy.

**Conclusion:** In real-world settings, the majority of DMF patients newly initiated therapy. Given the relative recent launch of DMF, continuous monitoring of patterns of use with oral DMTs is warranted.

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1042

WFN15-0590

**MS & Demyelinating Diseases****Anosognosia and self awareness in multiple sclerosis**

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**Background:** Recognition of deficits in MS is frequently dissociated from the clinical picture. Anosognosia (impaired ability to recognize the presence or severity of disease) is well known in cortical processes, but poorly studied in MS.

**Objective:** To assess the ability of deficit recognition and the prevalence of anosognosia in Multiple Sclerosis (MS) patients.

**Methods:** 43 patients with definite MS were studied. Mean age was 36.2 and clinical picture was RR in 28 cases. Patients were evaluated with clinical and neuropsychological standards. Specific scales to evaluate anosognosia were the Visual-Analogue Test assessing anosognosia (VATA-m) and the Mayo-Portland Adaptability Inventory (MPAI). Severity was measured with the Bisiach Scale. Coincidences and discrepancies between caregivers and patients in IADL were studied. Correlation between MRI number, size, severity and localization of cerebral lesions was made.

**Results:** We observed a high prevalence of anosognosia (58 %), with strong dissociation when scales were administered to patients and caregivers. The grade of anosognosia was 1 or 2 and the awareness of impairment was mainly observed in neurocognitive tasks and fine motility skills. Problems in IADL were underestimated. Our findings correlated with EDSS, evolution time and the presence of a large number of lesions located in the right temporo-parietal subcortical areas. No relationship with other variables was observed.

**Conclusions:** Anosognosia is a highly prevalent disorder in MS, suggesting a dysfunction in the mechanisms of self awareness, with implications in the ADL and with predictive value on poor functional outcome. MRI studies revealed more often localization of lesions in right parieto-temporal hemispheric topography.

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1043

WFN15-1262

**MS & Demyelinating Diseases****Susac's syndrome as a differential diagnosis of demyelinating diseases. Report of two cases and literature review**

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**Background:** Susac's syndrome is a disease described in the 1970s by presenting two patients with retinal and brain microangiopathy not attributable to common vasculopathies, both responding to steroid therapy. It has similarities to MS and ADEM, therefore often misdiagnosed and mistreated. An autoimmune process remains the initial pathogenic hypothesis. It often presents with the triad of encephalopathy, branch retinal artery occlusions, and hearing loss, with corpus callosum involvement on imaging.

**Objective:** To report two patients who presented to our Clinics with impaired consciousness, agitation and headache who were initially misdiagnosed, due to neuroimaging and LP suggestive of common demyelinating diseases.

**Patients and methods:** We present two white male 29 and 52 y/o patients (A and B respectively), both presenting with progressive headache. Patient A also had agitation, subconjunctival hemorrhage and impaired consciousness, whereas patient B presented with progressive hearing loss, transitory hypoesthesia and hemiparesis, with an abnormal retinal angiography. Both patients presented corpus callosum lesions on imaging and CSF protein count was elevated, leading to misdiagnosis on initial approach. They improved gradually after steroid and azathioprine therapy.

**Results:** Both patients presented with similar clinical and imaging findings, some of them attributable to known demyelinating diseases, and others, such as preference corpus callosum and ophthalmic involvement are suggestive of Susac's Syndrome.

**Conclusions:** Susac's Syndrome is a rare disease that can be confused with common demyelinating diseases leading to undesired outcomes. Proper recognition will allow better understanding of the underlying mechanism and therefore aim in the development of better treatment options.

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1044

WFN15-0191

**MS & Demyelinating Diseases****Changes of olfactory and gustatory function in the course of disease in patients with multiple sclerosis**

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**Background:** Olfactory dysfunction in patients with multiple sclerosis (MS) was reported in several studies.

**Objective:** The aim was to investigate changes of the olfactory and gustatory function in MS patients in the course of disease and correlate it to the disease activity.

**Materials and methods:** 20 MS patients (4 with chronic progressive MS and 16 with relapsing remitting MS) were included, after excluding olfactory dysfunction with other reasons than MS. The Smell Discrimination Identification test (TDI) was used to evaluate the olfactory function. The Taste Strip Test (TST) was used to test gustatory function.

Ethical approval and trial registration was obtained by the medical ethics committee of Charité, University of Berlin. All patients gave written consent to participate at the study.

**Results:** 20 MS patients were tested longitudinally 4 years after initial testing.

The number of relapses in this period of time correlated with the changes of the olfactory test score ( $r = -0.5$ ,  $p = 0.06$ ).

The changes of the gustatory test score correlated with the disease progression, expressed in the changes of the EDSS score ( $r = -0.8$ ,  $p = 0.04$ ).

The olfactory test scores correlated with the subjective olfactory capacity of the patients, expressed on a Visual Analogue Scale (ranging from 1 – 10).

**Conclusions:** Olfactory and gustatory testing of MS patients could be useful to estimate disease activity. The patients were aware of their olfactory deficits.

The results suggest that olfactory and gustatory dysfunction in MS patients occur due to CNS damage rather than to peripheral damage of the olfactory nerve.

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1045

WFN15-0051

**MS & Demyelinating Diseases****Are gadolinium enhanced T1 MR sequences mandatory in the follow up of RRMS patients treated with natalizumab**

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**Background:** Gadolinium is known to produce side effects and has recently been shown to accumulate in the brain parenchyma especially in the basal ganglia. Since RRMS patients do undergo several MR examinations, these potential risks have to be considered in this group of patients.

Although guidelines advocate the use of gadolinium enhanced imaging in the follow-up of RRMS patients, the benefit of the use of gadolinium enhancement in the subgroup treated with natalizumab could be questionable.

**Methods and materials:** After IRB approval 201 brain scans and 24 spine exams were reviewed in consensus by 3 readers in a series of 27 patients treated with natalizumab (PS, EC, PwdG). These 27 patients were followed during a time span of 6 to 84 months (mean 49 months). Evolution of lesion load and contrast enhancement were scored. Particular interest was given to the diagnosis of PML. The results were compared with the clinical status and the treatment as reported in the patient charts.

**Results:** Clinical evaluation resulted in 12 episodes of clinical relapse in patients treated with natalizumab, 5 patients demonstrated respectively 1, 2 or 3 relapses.

None of the MR scans in the asymptomatic patients nor in the symptomatic patient group demonstrated contrast enhancement. No sign of PML were detected.

**Conclusion:** The benefit of T1 MR sequences post contrast as put forward in many guidelines could be questionable in the subgroup of RRMS patients treated with natalizumab.

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1046

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**MS & Demyelinating Diseases****Multiple sclerosis: epidemiological profile**

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**Introduction:** MS is the most common autoimmune, demyelinating CNS disease in young adults. Demyelination foci lead to multiform clinical manifestations, which vary in progression, severity and associated symptoms. It presents low prevalence in the state of Mato Grosso (4.41 / 100,000 inhabitants), which is compatible with what is observed in South America, being more common in the female gender and in the white race.

**Objective:** To describe the clinical profile of individuals with MS in Hospital Geral Universitário (HGU) of Cuiabá-MT, Brazil.

**Methods:** This is a descriptive study about the clinical profile of 15 patients identified with MS that were monitored in the Neurology

Clinic of HGU, from January to April 2015. The following surveys were applied: EDSS for disability, SF-36 for quality of life, Beck Anxiety Questionnaire, and Hamilton Questionnaire for Depression.

**Results:** The sample consists of 15 patients with a mean age of 29.8 years (12 to 59 years), F:M ratio of 0.25: 1, average time of 3.23 years since diagnostic (2 months to 12 years), average treatment time of 3.1 years (1 month to 12 years) and 80% clinically classified as relapsing-remitting. In relation to EDSS, there was a disability average of 3,26 (0-8) and, referring to QoL, SF-36 showed a mean of 54,9 (16-100).

**Conclusion:** The sample demonstrates a clinical profile that is similar to other regions of Brazil and the world. A small degree of disability was shown, but with significant impairment in QoL, despite the considerably short disease duration.

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1047

WFN15-0443

**MS & Demyelinating Diseases****Possible prognostic factors of MS progression in children**

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The aim of this study was to clarify the role of clinical, laboratory and radiological factors of progression of MS in children observed during 2009-2014.

**Materials and methods:** We have analyzed the course of MS in 40 children aged 9 to 18 years. All children were divided into two groups compared by number of patients (n = 20), sex and age. Children on the first group had EDSS <3.0 points. The second group had EDSS ≥ 3.0 points. We examined peripheral blood (PB) and cerebrospinal fluid (CSF) of all 40 children in the onset of the disease by PCR for EBV, HV 6, CMV. We analyzed the annual relapse rate (ARR) in both groups. During the first 2 years of the onset of MS we observed appearance of new T1, T2 lesions, gadolinium-enhanced (GD+) lesions on MRI brain (1.5Tesla).

**Results:** Patients of the first group had a slower rate of progression of ARR (0.05 ± 0.25) and in PB we detected EBV in 25%, HV6 - 10%, CMV - 10% cases, the CSF: EBV 5%, HV6 - 5%, CMV - 10%. The increase of T2 and T1-lesions was observed in 5 children, the appearance of Gd+ in 2 patients. ARR of the second group was 1.5 ± 0.5. We detected EBV in PB in 60% patients, HV6-50%, CMV - 45% cases, the CSF: EBV 45%, HV6-45%, CMV - 60%. New T2 and T1 lesions on MRI were observed in 7 patients (35%) and appearance of Gd+ lesions in 4 people (20%).

**Conclusion:** Thus possible prognostic factors of MS onset in children are: high ARR, the presence of herpes viruses (EBV, HV6, CMV) in the PB and CSF in the MS onset, and new T1, T2, GD+ lesions.

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1048

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**MS & Demyelinating Diseases****Development of a shortened version of the MSQOL-54 using factor analysis and item response theory**

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**Background:** The Multiple Sclerosis Quality Of Life-54 (MSQOL-54, 52 items distributed into 12 sub-scales, and two single items) is the most used multiple sclerosis (MS) specific health-related quality of life (HRQOL) inventory.

**Objective:** To develop a shortened MSQOL-54 version.

**Patients and Methods:** I have obtained patient and Institutional Review Board (IRB) approval. MSQOL-54 dimensionality and metric properties were investigated by confirmatory factor analysis (CFA) and Rasch model (partial credit) on a dataset of 473 MS patients. Differential item functioning (DIF) was evaluated for gender, age and Expanded Disability Status Scale (EDSS) score. Shortened inventory's sub-scales were assessed with exploratory factor analysis (EFA) and CFA, and cognitively debriefed by 12 MS patients.

**Results:** Mean patients' age was 41 years; 65% were women; median EDSS was 2.0 (range 0–9.5). CFA of MSQOL-54 sub-scales showed that the overall model fitted well the data. Two sub-scales (role limitation physical/emotional) did not fit Rasch model, and were removed; two sub-scales (health perception, social function) were retained as single items. Sexual satisfaction (single-item sub-scale) was also removed. The resulting MSQOL-29 consists of 29 items grouped in seven multi-item and four single-items. Fit statistics were within the acceptability range for all items except item 26 (DIF by age). MSQOL-29 EFA and CFA indicated adequate fit to the original two-factor (physical/mental composite) hypothesis. Debriefing interviews confirmed the suitability and relevance of the MSQOL-29 inventory.

**Conclusion:** The proposed MSQOL-29 is 50% shorter than the MSQOL-54, preserving key HRQOL dimensions. Prospective validation on an independent MS patient sample is ongoing.

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1049

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MS & Demyelinating Diseases

Medication utilization among pediatric-onset multiple sclerosis patients in the United States

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**Background:** Pediatric-onset multiple sclerosis (POMS) is well-recognized but relatively uncommon. A paucity of information exist examining medication utilization in this population.

**Objective:** To describe the demographic and medication utilization among POMS patients in a real-world sample of the insured US population.

**Patients and methods:** POMS patients were selected from a large US insurance-claims database from January 1, 2004 to June 31, 2011. Controls were matched on year of birth, gender, time in the database, and pharmacy benefit eligibility. IRB approval was not required due to the de-identified nature of this secondary data source.

Comorbidities and medications were classified using a system that groups International Classification of Disease 9th Revision (ICD-9) codes and National Drug Codes (NDC) into meaningful categories.

**Results:** Among the 110,349 MS patients in the database, 916 (0.8%) were less than 18 and 154 (0.14%) were less than 10 years of age. The mean age of POMS diagnosis was 14 years and 59% were females. The most common medications prescribed were: corticosteroids (20%), interferons (17%), macrolides (15%), penicillins (13%), analgesics (12%), and antiepileptics (11%). The majority of patients (~90%) were not prescribed any MS DMT.

**Conclusion:** There is scarce information on medication utilization among POMS patients in a real-world setting. Our data suggest that DMT use is infrequent, which may be due to lack of evidence supporting the use of DMTs in children apart from case-series or observational studies. Elucidating medications used to treat MS disease, symptoms and/or the comorbid conditions prevalent among POMS patients merits further investigation.

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1050

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MS & Demyelinating Diseases

Variability in the brain lesion in a patient with neuromyelitis optica spectrum disorder

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**Background:** Since the discovery of the antibody Aquaporin water channel 4 (anti AQP4) the definition Neuromyelitis Optica changed to Neuromyelitis Optica Spectrum Disorder. Brain lesions are often described on BMRI with configuration and location characteristics in this pathology.

**Objective:** To show BMRI lesions at different times of disease evolution with different configuration and location for its evolution of 10 years.

**Clinical case:** 55 year old woman diagnosed with Multiple Sclerosis. Treated with Interferon Beta 1b then changed to Natalizumab. After 24 months she suffered a relapse with aphasia, unconsciousness, dysarthria, left hemiparesis. JC Virus PCR Negative. Anti AQP4 positive. NMOSD diagnostic and treatment began with plasmapheresis and Azathioprine. A year later she presented a new relapse and started taking Mycophenolate mofetil. BRMI showed at the beginning (2004) focal lesions hyperintense on T2 FLAIR sequences, partially irregular periventricular and juxtacortical margins. November 2011 T2 FLAIR hyperintense wide lesions in the bilateral parietal and occipital region. New deep white matter, bilateral, frontoparietal, juxtacortical lesions. March 2012 resembled significant improvement in January 2014. T2 FLAIR hyperintense pseudotumoral lesions in thalamus, internal capsule and cerebral peduncles. Diffuse recurrence of lesions located in deep white matter in December 2014 FLAIR hyperintense T2 lesions, pseudotumorals and irregular edges in bilateral frontal and parietal region, one in the right cerebellar hemisphere.

**Conclusion:** In this patient diagnosed with NMOSD, we observe change in the configuration and location in BRMI lesions, which changed drastically in the course of the disease.

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1051

WFN15-0953

**MS & Demyelinating Diseases****Developing multiple sclerosis in an ankylosing spondylitis patient**

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**Background:** Although ankylosing spondylitis (AS) is primarily a disease of the spine and the large joints, it may also have extra-articular involvement. There are limited cases of AS patients developing multiple sclerosis (MS).

**Objective:** In this report, we present an AS patient who developed MS during the follow up period.

**Patient and methods:** A 36-year-old male complained of back stiffness and back pain for about 4–5 years. He had physiotherapy for about a year. His complaints did not decline. In January of 2014, sacroiliitis was detected on the patient's sacroiliac MRI. HLA-B27 was positive. The patient was diagnosed with ankylosing spondylitis. In February of 2014, he was unable to walk. After 3 doses of 20 mg IM methylprednisolone treatment, his complaints partially resolved. A thoracic MRI was taken to determine the etiology of the walking impairment. Demyelinating lesions were detected in multiple levels. The patient was referred to our clinic. Neurological examination revealed bilateral Achilles clonus, spastic gait, and brisk deep tendon reflexes on the left lower extremity.

**Results:** A brain and cervical MRI were taken on suspicion of demyelinating disease. Multiple demyelinating lesions were detected in the brain and at multiple levels on the cervical MRI.

**Conclusion:** Although MS can be associated with many autoimmune diseases, coexistence with AS is very rare. Although the individual pathogenesis of both diseases is unknown, when they develop together, the most likely mechanism is T-cell-mediated autoimmunity. Due to the absence of demyelinating lesions in the previous cervical MRI, another cervical MRI was not taken after clinical deterioration. Demyelinating lesions were incidentally detected in the thoracic MRI. Clinicians should consider the possibility of MS in patients with AS, especially those who are worsening.

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1052

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**MS & Demyelinating Diseases****Neuromyelitis optica with hydrocephalus responsive to plasma exchange: a case report**

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**Background:** Neuromyelitis optica (NMO) is a demyelinating disease of the central nervous system (CNS) that is sometimes difficult to diagnose and treat. Some researchers suggest that it is a severe variant of multiple sclerosis (MS). Hydrocephalus is very rare in NMO patients.

**Objective:** We present a case of NMO with hydrocephalus that responded to plasma exchange (PLEX) therapy.

**Patient-Methods:** A 16-year-old female presented to a neurology clinic complaining of double vision and loss of balance. MRI of the brain and cervical region showed demyelinating lesions. 1000 mg/day methylprednisolone was given for five days. The patient's complaints declined. Control imaging of the brain revealed that hydrocephalus emerged. The patient had no complaints for a while, but diplopia reoccurred. The patient's level of consciousness changed to lethargy. She was admitted to our clinic to take PLEX. Her neurological examination revealed the following: lethargic, no cooperation, and strength of 2/5 in the upper extremities, 1/5 in the lower extremities according to the Medical Research Council scale. There was extensor posturing in the legs, but plantar responses were bilaterally silent.

**Results:** The patient was considered NMO because of episodes of optic neuritis and contiguous spinal cord MRI lesion extending over 3 vertebral segments. NMO-IgG was negative. 7 sessions of PLEX were executed. After treatment, the patient's neurological examination revealed the following: clear state of consciousness, full cooperation, strength of 3/5 in the upper extremities, 2/5 in the lower extremities

**Conclusion:** The available data presents a limited number of cases of NMO complicated with hydrocephalus. Management of NMO associated hydrocephalus is difficult. Successful treatment of NMO with PLEX is critical. Clinicians should consider PLEX in NMO in early stages to prevent complications such as hydrocephalus

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1053

WFN15-0712

**MS & Demyelinating Diseases****Depression correlates with sexual dysfunction and fatigue in multiple sclerosis patients**

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**Introduction:** Depression is often unrecognized and untreated disorder in patients with multiple sclerosis.

The aim of our study was to determine the existence of depression in patients with multiple sclerosis and correlation with fatigue, sexual dysfunction and disorders in the fields of physical and emotional health.

**Material and methods:** We used Multiple Sclerosis Quality of Life-54 (MSQoL-54) which is translated and adapted for patients in Serbia, Fatigue Severity Scale, and Hamilton Rating Scale for Depression. For statistical data processing, we used the Pearson correlation test and Student's t test.

**Results:** In this study we enrolled 120 patients with multiple sclerosis, 68 females and 52 males.

The average age of respondents was 47.36 years, and average duration of illness 17 years. The mean value for the Hamilton Rating Scale for Depression was 19.86. We found depression in 100 multiple sclerosis patients (83.34%) while 20 patients (16.66%) had normal values for the Hamilton Rating Scale for Depression. Statistically significant, negative correlation was observed between depression and domains of Emotional Well-Being ( $r = -0.612$ ,  $p = 0.0001$ ), Energy ( $r = -0.612$ ,  $p = 0.0001$ ) and Physical Component Summary Score ( $r = -0.584$ ,  $p = 0.001$ ), and Mental Component Summary Score ( $r = -0.656$ ,  $p = 0.0001$ ). We found the positive, statistically significant correlation between depression and Fatigue Severity Scale score ( $r = 0.460$ ,  $p = 0.009$ ) and sexual dysfunction  $r = -0.394$ ,  $p = 0.035$ ).

**Conclusions:** We found depression in 83% of our multiple sclerosis patients. We also found a significant association of depression with

sexual dysfunction. Unlike other aspects of multiple sclerosis, depression is treatable.

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1054

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**MS & Demyelinating Diseases**

**Use of natalizumab in relapsing remitting multiple sclerosis: experience from a tertiary center in Turkey**

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Use of natalizumab (NTZ) was first started in 2007 and 2008 in our country and our MS center, respectively. In this study, we aimed to share our experience between the years 2008 and 2015 with NTZ in the treatment of RRMS patients in our MS center. The demographic features of our patients who used NTZ treatment, the treatments before the use of NTZ, attack frequencies, EDSS values and serum JCV antibody status both before and after the treatment were evaluated retrospectively.

Thirty-six RRMS patients underwent NTZ therapy during 2008 and 2015. Four patients with missing data in their follow up visits were excluded. The mean age of 32 patients (27 female; 5 male) was 37.6 years. The mean duration of disease was 9 years. The mean duration of NTZ use was 19 months (min-max: 3-50 months). Five patients with positive JCV virüs discontinued NTZ after 24 months of use. The mean number of attacks during the 2 years before and after the onset of NTZ therapy was 7.2 and 0.4 per year, respectively. Three patients experienced attacks because of interruption of NTZ. EDSSs were stable before and after treatment in 26 patients. Among 27 patients with baseline antibody status testing, 16 had JCV antibody positivity while 11 were negative. 12 patients became positive for JCV antibody after NTZ use. None of the patients developed PML. In line with the previous studies, there was a decrease in the frequency attacks in RRMS patients under NTZ.

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1055

WFN15-0343

**MS & Demyelinating Diseases**

**Comparison of magnetic resonance imaging and blink reflex in patients with multiple sclerosis**

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Despite many new developments and studies, multiple Sclerosis (MS) is still difficult to diagnose. Magnetic resonance imaging (MRI) is an important aid in the patients clinically diagnosed as MS. Functional assessment of the patient's symptoms increases the importance of neurophysiological methods, especially in cases with negative MRI findings. Impulse conduction in MS as a result of demyelination in the central nervous system fibers changes and delays. In this study, we compared blink reflex (BR), which is a neuropsychological methods with MRI examination. We aimed to determine the relationship between the BR abnormalities and lesion localization and their values in the diagnosis of MS. We studied 21 patients (mean age 33 ± 9 years; 7 men and 14 women) and 33 age-matched healthy subjects (mean age 34 years, 19 females and 14 males). MRI and BR were studied in all the subjects. BR showed abnormalities in 66.7% of patients and these abnormalities were apparent in the brainstem

lesion. We conclude that BR, which can be easily and rapidly performed in an EMG laboratory can provide useful and objective information about in particular the brainstem lesions.

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1056

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**MS & Demyelinating Diseases**

**Natural course of neuromyelitis optica (NMO) in patients with no long-term treatment**

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**Background:** Neuromyelitis optica (NMO) is a rare inflammatory disorder of central nervous system (CNS) and antibodies against aquaporin-4 water channel plays a major role. According to current guideline, early diagnosis and aggressive treatment is critical for preventing disability.

**Objective:** Some of our NMO cases rejected to receive long term treatment (LTT) and we compared non-treated NMO patients with the treated ones. The aim of our study was to explore the effect of LTT on the course of disease.

**Patients and methods:** Sixty one patients followed with a diagnosis of NMO/NMO Spectrum Disorders were included in this study. Clinic and demographic features were assessed. Long term treatment modalities consisted glatiramer acetate, interferons, oral steroid, azathioprine, cyclophosphamide and monthly high dose IV methylprednisolone. Indirect immunofluorescence method by using commercial kits (EURO-IMMUNE) were used for NMO-IgG detection.

**Results:** Twenty two of the patients were on LTT (19 male,3 male) and 39 patients were not receiving any LTT (32 female,7 male). The mean disease duration was 68.07 + 64.02 months in nontreated and 58.76 + 29.59 in treated group. Mean annual progression index (PI) was found to be higher in the nontreated group.

**Conclusion:** The absence of NMO IgG seems to be a positive predictive factor on the course of disease regardless of treatment modalities. The patients with negative NMO IgG have responded to immunosuppressive treatment better, and their PI was found to be lower significantly (p:0.003). Therefore, new treatment modalities are warranted which could be effective in NMO positive patients.

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1057

WFN15-0781

**MS & Demyelinating Diseases**

**Clinical and etiopathological evaluation of the patients with OCB IGG pattern IV and V positivity**

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**Background:** The relationship between oligoclonal band (OCB) pattern-II with multiple sclerosis (MS) and pattern-V with monoclonal diseases such as multiple myeloma (MM) are well-known, however, there is very limited data on diseases which are associated with OCB pattern-IV and V.

**Objective:** We aimed to determine the etiopathological and clinical profile of the patients with oligoclonal IgG band (OCB) pattern-IV or V positive.

**Patient and methods:** Serum and CSF samples of the pattern IV (n = 52) and V (n = 15) positive patients were collected at the time of an acute (<1 month) and/or ongoing progressive disease period between 2005–2013. OCB analyses were performed via isoelectric focusing (IEF). The routine serum and CSF characteristics, detailed demographic, clinic and radiologic data were obtained through a review of the medical records.

**Results:** Diagnostic spectrum of the 52 OCB pattern IV positive patients (mean age 46, f/m = 2/3) were classified as follows: 35% CNS inflammatory demyelinating diseases [CDMS(14), CIS(4)], 19% peripheral inflammatory demyelinating diseases, 31% inflammatory nondemyelinating diseases, 15% noninflammatory nondemyelinating diseases. Otherwise, 15 pattern V positive patients (mean age 48, f/m = 3/2) had shown diagnosis profile as follows: 13% CNS inflammatory demyelinating diseases [CDMS(2)], 33% peripheral inflammatory demyelinating diseases, 40% inflammatory non-demyelinating diseases and 13% noninflammatory nondemyelinating diseases.

**Conclusion:** In our study group, MS patients comprised the major part of OCB pattern IV positive patients. Although, pattern V was not found frequently as expected in monoclonal gammopathies, peripheral inflammatory polyneuropathies and vasculitis were in the first line.

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1058

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MS & Demyelinating Diseases

**Brain mri white matter hyperintensities meeting revised 2010 mcdonald and barkhof criteria for dissemination in space among headache patients**

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**Background:** Increased use of magnetic resonance imaging (MRI) in clinical practice resulted in an increased detection of incidental white matter hyperintensities (WMH) in the brain. Consequently migraine has become one of the most frequently overdiagnosed diseases with MS, due to similar presentation ages, and similar MRI findings of patients with migraine and MS. Thus, half of the patients with radiologic isolated syndrome (RIS) have their initial MRI because of headache. Therefore, more precisely defined radiological features along with clinical associations of WMH in migraine should be sought.

**Methods:** In this study we tried to find out the percentage of migraine patients with incidental MRI lesions that could be fulfilling the "Revised 2010 McDonald Criteria for MS". Consecutive patients undergoing MRI for headache over 24 month period (diagnosed as migraine according to the International Headache Disorder II criteria) were retrospectively identified. The mean age of the patients (n = 100) were 33.71 ± 7.02, females (n = 72) %72, males (n = 28) %28. Patients were classified as meeting 1) 2010 McDonald dissemination in space and 2) Barkhof criteria for MS based on: FLAIR/T2 scans for WMH.

**Results: One out of three "Revised 2010 McDonald DIS Criteria" were met in 35/100 patients (%35); while only 8/100 patients (8%) fulfilled 2/3 of the criteria. However none of the patients fulfilled Barkhof Criteria.**

**Conclusion:** We suggest utmost caution in interpreting asymptomatic MRI findings especially in migraine patients in order not to end with an overdiagnosis.

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1059

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MS & Demyelinating Diseases

**A more promising novel rock inhibitor-FSD-C10**

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**Background:** Although therapeutic potential of Fasudil in EAE is promising, there are some limitations. We have designed a novel ROCK inhibitor FSD-C10 that exhibits therapeutic potential in EAE.

**Objective:** To observe the therapeutic effect of Fasudil and FSD-C10 on EAE, explore its mechanisms and compare the cell cytotoxicity and vasodilation between Fasudil and FSD-C10.

**Material and methods:** Mouse EAE was induced by MOG<sub>35–55</sub> immunization and treated with Fasudil or FSD-C10 in vivo. The study was approved by the Ethics Committee of Shanxi Datong University. BV-2 microglial and primary neurons were cultured in vitro for different experiments.

**Results:** FSD-C10 via intranasal administration is able to delay EAE onset (p < 0.05) and declined maximum clinical score (p < 0.01) as compared with EAE control group. FSD-C10 induced neurite outgrowth of neurons and dendritic formation of BV-2 microglia and enhanced the production of neurotrophic factors BDNF, GDNF and NT3. The in vitro experiments showed cytotoxicity of FSD-C10 was lower than Fasudil. Both Fasudil and FSD-C10 exhibited the inhibitory efficiency of ROCK I and II. The inhibitory effect of ROCK I by FSD-C10 is relatively weak that may be related to insensitivity of vasodilation.

**Conclusion:** FSD-C10 can easily be delivered via nasal administration and effectively suppresses EAE by inhibiting efficiency of ROCK and also by promoting neuroprotection. What's more, the cell cytotoxicity and vasodilation of FSD-C10 are relatively smaller as compared with Fasudil. (Grant: National NSF of China, 81272163; Research Project Supported by Datong Municipal Science and Technology Bureau, 2014105-1; Shanxi Scholarship Council of China, 2014-00023).

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1060

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MS & Demyelinating Diseases

**Profiling of lymphocyte transcriptome changes in multiple sclerosis patients treated with fingolimod**

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**Background:** Fingolimod is a S1P receptor modulator inducing the homing of lymphocytes to lymphoid tissues. The reduction of circulating lymphocytes differs among cell subpopulations. The

molecular effects have so far not been investigated at the transcriptome level.

**Objective:** Transcriptome changes in response to fingolimod therapy may help to better understand the drug's molecular mechanisms and to identify biomarkers for therapy monitoring. Therefore, we compared the gene expression patterns of different cell types before and during fingolimod treatment in patients with relapsing-remitting MS.

**Methods:** With approval by the ethics committee and informed consent by the patients, blood samples were drawn before fingolimod therapy as well as after 24 hours and 3 months. CD4+, CD8+, CD19+ and CD56+ cells were separated, and the isolated RNA was analyzed with Affymetrix HTA 2.0 microarrays. Differentially expressed genes (DEG) were defined by fold-change > 2.0 and t-test p-value < 0.001.

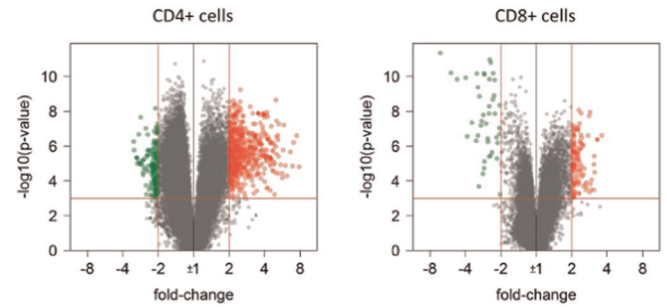
**Results:** No gene was expressed at higher or lower levels 24 hours after first dose of fingolimod. After 3 months, there were 890 and 169 DEG in CD4+ and CD8+ cells, respectively (table, figure). The levels of 35 genes were increased (e.g., FCGR3A and FCGR3B) or decreased (e.g., CCR7) in both cell types.

**Conclusion:** We present the first high-resolution gene expression microarray analysis on transcriptome shifts of lymphocytes during fingolimod therapy. Hundreds of DEG were observed after 3 months of treatment in CD4+ and CD8+ cells, including genes involved in T-cell activation.

Table:

Cell population	24 hours vs. baseline		3 months vs. baseline	
	Cell count	DEG	Cell count	DEG
CD4+	-21.1 %	0	-92.4 %	890
CD8+	+18.7 %	0	-59.5 %	169
CD19+	-14.2 %	0	-87.0 %	10
CD56+	+15.5 %	0	-15.7 %	0

Figure:



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