

## Multiple sclerosis 1

## P1368

**The Kv1.3 channel: a potential biomarker for multiple sclerosis**

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**Introduction:** Recent evidence indicates that Kv1.3 channels, which are important regulators of T-lymphocyte function, could play an important role in the pathogenesis of multiple sclerosis (MS). Herein, we used patch-clamp, RT-PCR and immunofluorescence assays, to study Kv1.3 expression in peripheral blood T-lymphocytes of MS patients.

**Methods:** Two independent MS cohorts, from Greece and North America, were studied, compared to healthy individuals, patients with other neurological disorders, and patients with systemic lupus erythematosus. Kv1.3 currents were recorded from freshly isolated T-lymphocytes, in the whole-cell configuration of the patch-clamp technique. Semi-quantitative RT-PCR was used for assessing Kv1.3 mRNA expression in MS and control T-lymphocytes. A fluoresceinated channel ligand (ShK-F6CA) was also used to detect levels of Kv1.3 expression by flow cytometry.

**Results:** Kv1.3 channel densities were significantly increased in T-lymphocytes of MS patients ( $p < 0.001$ ), compared to healthy subjects and controls. Sub-grouping of MS patients showed significantly higher Kv1.3 channel densities in secondary progressive compared to relapsing remitting disease ( $p < 0.001$ ). A statistically significant ( $p < 0.001$ ) increase was also observed in MS patients, for both Kv1.3 mRNA as well as for flow-cytometric channel expression.

**Conclusions:** Our data demonstrate a significant and global increase of Kv1.3 expression that could probably enhance the responsiveness of MS T-lymphocytes to immune stimuli, promoting the activation, expansion and destructive potential of disease-associated autoreactive T-cells. They also suggest that Kv1.3 channels may be useful as a biomarker to distinguish MS from other CNS disorders, and support the importance of Kv1.3 channels as potential therapeutic targets for immunomodulation.

## P1369

**Analysis of clinical and radiological disease activity-free status in patients with relapsing-remitting multiple sclerosis treated with cladribine tablets, in the double-blind, 96-week CLARITY study**

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**Introduction:** Attaining complete remission of disease activity may become increasingly important as a measure of success in multiple sclerosis (MS) clinical trials.

**Objective:** To determine the effect of short-course treatment with cladribine tablets on composite measures of clinical and radiological disease activity in patients with relapsing-remitting MS in the CLARITY study.

**Methods:** Clinical (proportion of patients relapse-free and disability progression-free) and radiological (proportion of patients T1 Gd<sup>+</sup> and active T2 lesion-free) outcomes and combinations of these outcomes were assessed at 24, 48 and 96 weeks (pre-specified and post-hoc assessments) in the CLARITY study in patients (n=1326) randomized to cladribine tablets (cumulative doses of 3.5 and 5.25mg/kg) and placebo.

**Results:** In the cladribine tablets 3.5 and 5.25mg/kg vs. placebo groups, respectively, 71.8% and 70.4% vs. 52.6% of patients were relapse- and progression-free; 51.3% and 51.8% vs. 21.7% were progression- and magnetic resonance imaging (MRI) activity-free; and 48.0% and 49.6% vs. 17.8% were relapse- and MRI activity-free over 96 weeks (all  $p < 0.001$ ). For the most stringent composite outcome of disease activity-free (DAF) incorporating relapses, progression and MRI activity, 43.0% and 44.3% vs. 16.0% of patients were DAF over the entire 96-week study (both  $p < 0.001$ ). Statistically significant findings were reported as early as 24 weeks after initiating treatment.

**Conclusions:** Treatment with cladribine tablets statistically significantly increased the proportion of patients who were DAF compared with placebo as early as 24 weeks and up to 96 weeks after starting treatment, suggesting that cladribine tablets could be a promising new MS therapy.

## P1370

### Do atypical symptoms predict a non-demyelinating disease in patients with “query MS”?

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**Introduction:** Certain ‘red flags’ in the clinical picture may indicate an alternative diagnosis to MS. Using atypical symptoms at presentation as an adjunct to other diagnostic tools may improve diagnostic accuracy. We assessed the utility of defining ‘typical’ and ‘atypical’ symptoms in the diagnosis of patients referred as “query MS”.

**Methods:** We reviewed patients referred as “query MS” over a 3-year period. Patients were classified, on the basis of their first clinical assessment, as having ‘typical’ symptoms of MS or ‘atypical’ symptoms suggesting an alternative diagnosis. The initial clinical opinion was correlated with the eventual diagnosis. External raters, blinded to the diagnosis, were asked to assign ‘typical’ or ‘atypical’ status.

**Results:** A total of 233 patients were referred with suspected MS of whom 50% actually had MS. 107 (46%) patients had ‘atypical’ symptoms and 88 (82%) did not have MS and 19 (18%) had MS. 101 patients had ‘typical symptoms’ and of these 12 (12%) did not have MS. Sensitivity was 88% and specificity 82% for ‘atypical’ symptoms. Inter-rater agreement was 0.78.

**Conclusion:** ‘Atypical’ features as red flags to refute a diagnosis of ‘query MS’ have high sensitivity and specificity and may be a useful adjunct to diagnostic principles already in use.

## P1371

### Clinical and radiological characteristics of multiple sclerosis in Iran: a cohort study

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**Objective:** To determine the clinical and radiological patterns of Iranian multiple sclerosis patients and compare it to well documented studies from western countries.

**Methods:** An observational cohort study of 399 patients with retrospective data before 2009 and prospective follow-up to present. Participants were patients referred to our tertiary care centre (Sina hospital, Tehran, Iran) and the diagnosis was based on McDonald revised criteria.

**Results:** Our study demonstrates MS as an evolving disease in Iranian patients with an increasing rate in the last decade (75% of patients have a disease duration of  $\leq 9$  years) with a female to male ratio of 3.69. Mean age at onset was 26.1 years (95% CI, 25.2-27 years). Mean EDSS was 2.35 (95% CI, 2.12-2.58) of whom 79% had relapsing remitting course, 13% had secondary progressive form and 7% showed primary progressive course. The most common symptoms at the onset were sensory disturbances (46%), optic neuritis (32%), motor (27%), oculomotor impairment (23%) and cerebellar (15%). Of 204 patients with available magnetic resonance study, 96% showed supratentorial lesions, 47% showed infratentorial lesions and only 32% showed demyelinating cervical spine lesions. 95% of the patients had positive Barkhof’s criteria for dissemination in space.

**Conclusion:** Our study demonstrates that MS in Iran is more or less like in western countries and brain MRI is similar to European patients. Opticospinal MS is much less prevalent than typical MS.

## P1372

**Altered miRNA expression in T-regulatory-cells in the course of multiple sclerosis**

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**Objectives:** Multiple Sclerosis (MS) is a chronic inflammatory response against constituents of the central nervous system. It is known that regulatory T-cells (Tregs) play a key role in autoimmune balance and their improper function may facilitate the expansion of autoaggressive T-cell clones. Recently, microRNAs (miRNAs) have been involved in autoimmune disorders and their loss-of-function in immune cells was shown to facilitate systemic autoimmune disorders. Here, we analyzed the miRNA expression profile in Tregs from MS-RR.

**Methods:** We assessed miRNA genome-wide expression profile by microarray analysis on CD4+CD25+high Tregs from 12 MS Relapsing-Remitting patients in stable condition and 14 healthy controls. Furthermore, we validated these results by quantitative RT-PCR on CD4+CD25+high CD127dim/- cells.

**Results:** We found 23 human miRNAs differentially expressed between Treg CD4+CD25+high cells from MS patients versus healthy donors. Among the deregulated miRNAs, members of the miR-106b-25 cluster were found up-regulated in MS patients when compared to healthy donors.

**Conclusion:** miR-106b and miR-25 were previously shown to modulate the TGF- $\beta$  signalling pathway through their action on CDKN1A/p21 and BCL2L1/Bim. TGF- $\beta$  is involved in Tregs differentiation and maturation. Therefore, the up-regulation of this miRNA cluster may alter Treg cells activity in the course of MS, by blocking the TGF- $\beta$  biological functions.

## P1373

**Is there IRIS syndrome without PML in a patient who discontinued prolonged treatment with natalizumab?**

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**Introduction:** Immune Reconstitution Inflammatory Syndrome (IRIS) is a collection of inflammatory disorders associated with paradoxical worsening of pre-existing infectious processes mainly in HAART-treated HIV patients, and, lately, it has also been described in natalizumab-treated MS patients who developed PML.

**Case report:** A 32-year-old woman with a known history of RRMS for 6 years, previously treated with interferon-b1 $\alpha$ , was treated with natalizumab. Natalizumab was discontinued after 30 cycles because of concern for PML development due to clinical deterioration. She remained stable, treatment-free, for 3 months and then presented a relapse with left pyramidal syndrome for which she received intravenous methylprednisolone, and the symptoms subsided. One month later she presented with right pyramidal syndrome, cognitive impairment and seizures which progressed to a full-blown status epilepticus, for which she had to be intubated. MRI imaging showed the presence of multiple gadolinium-enhancing new demyelinating cortical and subcortical, supra- and sub-tentorial lesions. Repeated testing for JC virus in CSF and urine was negative. CNS malignancy and other possible infections were ruled out. Until conclusive diagnostic results were available, she received treatment with IVIG, plasmapheresis and IV prezozone but brain MRI showed continuous deterioration. Natalizumab was then reinitiated and the patient showed clinical improvement which coincided with lesions mildly subsiding in brain MRI. The patient is recovering.

**Conclusion:** The presented case suggests that the discontinuation of a prolonged treatment with natalizumab, without substitution by another treatment, may be associated with a detrimental immunological exacerbation not related to PML infection.

## P1374

**Down-regulation of Th2- and Th17-related cytokines by intravenous methylprednisolone in acute CIS and relapsing MS**

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**Introduction:** A key event in MS pathogenesis consists in CNS invasion by activated circulating T-cells. Much attention has been recently focused on T-cells producing IL-17 (Th17). Both IL-17 and IL-23 are expressed in active MS lesions. High dose intravenous methylprednisolone (ivMP) is commonly used to treat acute demyelinating events but it is not known whether it affects the expression of Th17-related cytokines.

**Methods:** We analysed the effects of ivMP on mRNA levels of TH1, Th2 and Th17 related cytokines in PBMC from 23 patients at onset of CIS, and from 10 relapsing, untreated, CDMS.

**Results:** IL-17, IL-23p19 and IL-6 expression was significantly down-regulated by ivMP, but the strongest inhibition involved IL-4 and IL-13 transcription, which are both Th2 related cytokines. This down-regulation was already observed after 4 infusions of ivMP, but was no longer present 30 days after treatment termination.

**Conclusions:** Systemic corticosteroid treatment has a broad but transient inhibitory effect on cytokines expression. An attractive hypothesis is that down-regulation of IL-4 favours the expansion of Treg cells as suggested by experimental animal models.

## P1375

**Oxidative stress and glutamate uptake in multiple sclerosis**

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**Background:** An impaired handling of extracellular glutamate is widely reported to be associated with excitotoxic neuronal damage in Multiple Sclerosis (MS). Platelet glutamate transporters may be easily used as peripheral markers to investigate the role of glutamate in patients with neurodegenerative disorders. Moreover, a growing body of evidences indicates that oxidative stress is involved in MS pathogenesis. The aim of our study was to investigate how, i.e. signal-transduction pathways, the oxidant-antioxidant imbalance can influence glutamate uptake.

**Methods:** 17 patients affected by MS (age: 33-64 years) and 16 controls (HC) (age: 33-56 years) were studied for serum levels of coenzyme-Q10, malondialdehyde, total, oxidized and reduced forms of glutathione, anti-oxidized-low-density lipoproteins antibodies (Anti-oxLDL), reactive-oxygen-species, and anti-oxidant-power. Platelet-glutamate uptake was also studied.

**Results:** By t-test, significant differences for increased Anti-oxLDL (MS:34.06±5.2 U/ml±S.E; HC:18.24±1.6; p≤0.03) and for reduced glutamate uptake (MS:Vmax 21.91±2.1pmol/mgprotein/30min, Km 44.5; HC:Vmax 30.47±2.6, Km 42; Vmax p≤0.02), together with a trend for decreased coenzyme-Q10 (MS:417.71±48.3µg/L; HC 523.79±60.8 p=0.09) were found in MS patients.

**Conclusions:** As in oligodendrocytes, in platelets from MS patients a decreased uptake activity was observed, without differences in Km values. At this stage, caution should be taken in interpreting these preliminary results in terms of causal relationship or fortuitous association between impaired glutamate uptake and oxidative imbalance. In the next months possible correlation between clinical features and biological markers will be assessed in a larger cohort of MS patients and HC. Linear regression models and neural artificial networks will be used together for statistical analyses.

## P1376

**Tumefactive multiple sclerosis**

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**Background:** Tumefactive Multiple Sclerosis (MS) represents a distinct form of disease presentation defined by atypical imaging features which often pose considerable diagnostic difficulty and may require brain biopsy.

**Objective:** To characterize the clinical, radiographic and CSF features associated with tumefactive MS forms, therapeutic options and clinical outcomes.

**Methods:** Retrospective analysis of clinical data of MS patients whose presentation was a tumefactive form. Inclusion criteria were atypical imaging features on MRI including size lesions >2cm, mass effect, oedema, and/or atypical enhancement patterns, with exclusion of other diseases.

**Results:** A total of 22 patients were included, median age at onset 30.8 years. Clinical presentation was mainly polysymptomatic (78.9%), with motor (58.8%) and cognitive/behavioural (47.1%) symptoms predominating. The frequency of CSF oligoclonal bands was 54.5%. Diagnosis was performed by brain biopsy in 3 patients and medullar biopsy in 1 patient. After an initial relapse, 8 patients presented a total recovery on steroid therapy. Those unresponsive to steroids experienced a significant response to plasmapheresis (6 patients) or immunoglobulin (5 patients). In 10 patients the immunomodulator therapy was preceded by an induction scheme with cyclophosphamide, with a favourable outcome. Follow-up median time was 6.3 years, median time to the second attack 2.1 years and median EDSS 2.5.

**Conclusion:** The clinic presentation of tumefactive MS is pleomorphic and frequently atypical, with cognitive/behavioural disorders representing a frequent symptom in this series. The clinical outcome was in general favourable but if there is no improvement on steroids, plasmapheresis or immunoglobulin, an induction scheme with cyclophosphamide seems to be a reasonable option.

## P1377

**Breastfeeding, post-partum and pre-pregnancy disease activity in multiple sclerosis revisited**

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**Objective:** To determine the breastfeeding prevalence among Finnish MS-patients, and the relationship between breastfeeding, post-partum and pre-pregnancy relapse frequency.

**Background:** It is well known that the risk of multiple sclerosis (MS) relapse is starkly diminished during late pregnancy and increases in the post-partum period. As disease modifying drugs (DMDs) are not recommended during pregnancy or lactation, mothers need to decide whether to resume early treatment to minimize risk of postpartum relapses or to breastfeed.

**Methods:** MS patients becoming pregnant during the years 2003-2005 in Finland were enrolled in this prospective study (n=61). MS relapses, information on DMDs and breastfeeding history were recorded.

**Results:** The majority of the mothers (55/61; 90.2%) breastfed their babies. Mothers with active pre-pregnancy disease chose to breastfeed less frequently but instead chose medication. The mean relapse rate during the pre-pregnancy year was significantly higher among mothers who did not breastfeed or only breastfed for a short time [ $<2$  months; n=12,  $1.42 \pm 1.24$  (SD)] when compared to mothers who breastfed for over two months [n=49,  $0.67 \pm 0.85$  (SD), p=0.040, Mann-Whitney U-test]. After the delivery the disease activity patterns continued similarly in the respective groups.

**Conclusions:** Breastfeeding is strongly promoted in Northern Europe, and there is reason to encourage breastfeeding also among MS mothers. However, for mothers with high pre-pregnancy disease activity early post-partum medication may be needed to keep the disease under control and will thus be more advisable than breastfeeding, and this should be taken into account in counselling.

## P1378

### The combination of interferon- $\beta$ and atorvastatin lowers high-sensitivity C-reactive protein in multiple sclerosis

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**Background and aims:** Statins exert pleiotropic effects on the immune system which attracted significant interest for the treatment of multiple sclerosis (MS), particularly as add-on therapy to interferon- $\beta$  (IFN $\beta$ ). Here, we evaluated whether statins continue to exert anti-inflammatory effects as evidenced by lowering of C-reactive protein (CRP) when applied in combination with IFN $\beta$  in relapsing-remitting MS (RRMS).

**Patients and methods:** 28 serum samples of patients with RRMS enrolled in the SWABIMS (SWiss Atorvastatin and IFN $\beta$ -1b Trial In MS) trial and healthy controls (n=8) were evaluated. High-sensitivity (hs-) CRP was measured with a conventional ELISA assay at baseline, after a 3-month monotherapy with IFN $\beta$  e.o.d, and at months 6 and 9 following a randomization either to continue on IFN $\beta$  (n=12) or with additional 40mg atorvastatin p.o. (n=16).

**Results:** Hs-CRP levels were similar in MS patients at baseline and in controls. Treatment with IFN $\beta$  over a period of 3 months was associated with a 37% increase of hs-CRP compared to baseline (p<0.01) and remained elevated over a period of 9 months. In contrast, atorvastatin as add-on therapy significantly decreased hs-CRP levels when evaluated at month 6 (-44.0%) and 9 (-50.6%, both p<0.05).

**Conclusions:** We provide evidence that statins as add-on treatment to IFN $\beta$  exert anti-inflammatory action in RRMS. Since increased levels of hs-CRP in RRMS were previously shown to be associated with relapses and risk for disease progression, lowering of hs-CRP by statins may impact a critical component of MS pathogenesis and disease progression.

## P1379

### Fourteen MS cases with MRI findings of Baló concentric sclerosis type lesions

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**Introduction:** Baló concentric sclerosis (BCS) is an inflammatory-demyelinating disease of the central nervous system characterized by rings of demyelination alternating with preserved myelin. BCS is usually considered to be a rare but rapidly evolving variant of multiple sclerosis (MS) which was initially described at pathologic level. Recently magnetic resonance imaging (MRI) allows to diagnose BCS type lesions ante mortem.

**Methods:** BCS cases were diagnosed on the basis of the presence of typical alternating concentric lesions retrospectively observed in MRI. In all patients FLAIR, T1-weighted, PDT2-weighted and T1-weighted with contrast sequences were assessed. Clinical signs, course of the disease, cerebrospinal fluid findings and visual evoked potentials were correlated with the presence of BCS lesions. In addition BCS lesions were assessed with respect to lesions evolution and time of appearance. Coexistence of typical MS with BCS lesions was also evaluated.

**Results:** 14 cases of BCS lesions were identified. Most of patients (9/14) showed a remitting-relapsing course of the disease and the other patients had a monophasic (4/14) and secondary progressive (1/14) course. Only 4 of 12 patients had oligoclonal bands and 3 of 12 had elevated IgG index. High coexistence of BCS and MS lesions (13/14) and evolution of BCS towards MS lesions were also found (8/9).

**Conclusions:** Our results suggest that BCS lesions can occur during MS course and not necessarily define an independent fulminant type of disease.

## P1380

**Early MRI activity on IM IFN $\beta$ -1a predicts disease activity at 10 years**

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**Background:** CHAMPIONS, the open-label extension study of CHAMPS, showed that new T2 or Gd+ lesions on MRI scan 6 months after initiating IM IFN $\beta$ -1a predict conversion to CDMS, EDSS status, and disease activity at 5 years.

**Objective:** To determine whether MRI activity 6 months after starting IM IFN $\beta$ -1a predicts disease activity at 10 years.

**Methods:** CHAMPS was a randomized, double-blind, placebo-controlled study in which patients with a first demyelinating event and MRI evidence of subclinical demyelination were treated with IM IFN $\beta$ -1a 30mcg (n=193) or placebo (n=190) once weekly for up to 36 months. Patients not experiencing a relapse consistent with CDMS underwent MRI scans at 6, 12, and 18 months. 40% of patients from CHAMPS (155/383) enrolled in the CHAMPIONS 10 follow-up study

**Results:** Of 73 patients receiving immediate treatment with IM IFN $\beta$ -1a, undergoing MRI scan at 6 months, and enrolling in CHAMPIONS 10, 30.1% had lesion activity ( $\geq 2$  new T2 or  $\geq 2$  Gd+ lesions) suggesting suboptimal treatment response. In these patients, the risk of developing CDMS by year 10 was significantly higher compared with patients with  $< 2$  new T2 and  $< 2$  Gd+ lesions at month 6 (HR 3.83;  $p < 0.0001$ ). There was a trend for more suboptimal responders reaching an EDSS score  $\geq 3.0$  over 10 years with 31.8% vs. only 15.7% in the responder group ( $p = 0.1292$ ).

**Conclusion:** MRI activity 6 months after initiating IM IFN $\beta$ -1a is a significant predictor of conversion to CDMS at 10 years, with a trend towards prediction of EDSS status.

## P1381

**Trend of association to the Glypican 5 gene region to multiple sclerosis**

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**Introduction:** In multiple sclerosis (MS) both environmental and genetic factors contribute to disease development. During the last couple of years, genetic associations to genes outside the HLA complex have been found in MS by using genome-wide association studies, among these a region at chromosome 13q31, but there is uncertainty as to the exact origin of the signal. In other disease phenotypes, associations seem to localize in either the glypican 5 or 6 gene regions.

**Material and methods:** We investigated 34 SNPs in the glypican 5 and 6 gene regions in 1355 Norwegian MS patients and 1446 healthy Norwegian controls to verify the presence and localization of an association in MS.

**Results:** Four SNPs (rs7333912, rs9523787, rs17267815 and rs12876985) achieved nominal significance ( $p < 0.05$ ) while only the association to rs9523787 (18.4% in cases vs. 14.6% in controls, OR=1.32 (1.14-1.52),  $p_{\text{uncorr}} = 0.0002$ ,  $p_{\text{corr}} = 0.006$ ) in the glypican 5 gene was robust to correction for multiple comparisons.

**Conclusion:** The present finding gives further support to the glypican 5 gene suggesting that this locus may define MS susceptibility at chromosome 13q31.

## P1382

**How important is personality in neurological patients' quality of life perception?**

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In the last decades, the value of research on neurological patients' quality of life (QOL) has become unquestionable. In this context, most studies focus on the relationship between patients' QOL and their sociodemographic and/or clinical and/or modifiable psychosocial characteristics. They give us information regarding the sociodemographic and clinical profile most prone to low QOL reports and also on ways to improve patients' QOL (e.g., targeting their self-esteem). Nevertheless, little is known about the role non-modifiable psychosocial variables can have on patients' QOL perception. Consequently, the aim of the present study is to explore the relationship between QOL and personality in neurological patients. Two questionnaires (SF-36 and NEO-FFI) were completed by 179 outpatients: 100 with multiple sclerosis, 79 with epilepsy, mostly women (n=112), between 17 and 65 years of age (M=35.88, SD=8.83), with diagnoses from 1 to 49 years old (M=13.01, SD=10.14). There were no statistically significant differences between the two groups of patients regarding personality. Patients' QOL predictors were: Mental Health – Neuroticism (Ra2=0.399); Social Function – Neuroticism (Ra2=0.260); Vitality – Neuroticism and Extraversion (Ra2=0.208); Role Emotional – Neuroticism (Ra2=0.183); Bodily Pain – Neuroticism (Ra2=0.188); Role Physical – Neuroticism (Ra2=0.087); General Health – Neuroticism and Extraversion (Ra2=0.110); Physical Function - Neuroticism (Ra2=0.021). These preliminary results suggest that non-modifiable psychosocial variables, namely personality, can limit patients' QOL and that personality dimensions do not have similar associations with different QOL dimensions. They also indicate that secure, hardy, and generally relaxed and/or extroverted patients perceive better QOL.

## P1383

**Abstract cancelled**

## P1384

**Toll-like receptors and dendritic cells in MS patients**

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Toll-like receptors (TLRs) are a family of receptors important in pathogen recognition and host defence. TLRs are expressed by a variety of peripheral immune cells as well as resident cells of the CNS. Studies indicate that TLRs play a significant role in modulating Multiple Sclerosis (MS), as well as experimental autoimmune encephalomyelitis (EAE), an animal model of MS. The role of these receptors' response to complete Freund's adjuvant during initiation of CD4 T-cell responses in EAE, the animal model for multiple sclerosis, is broadly discussed. The aim of our research was to detect microbial products by Toll-like receptors (TLRs) leading to activation of DCs and subsequent orchestration of an adaptive immune response. We surveyed TLR4 sequence variation in the complete coding region (2.4 kb) in 65 MS patients and 52 healthy donors. In addition, both MS groups were surveyed at 1.1kb of intronic sequence. More than 85% of the chromosomes examined encoded the same structural isoform of TLR4, while the rest harboured 24 rare amino acid variants. The variants at silent sites (intronic and synonymous positions) occur at both low and high frequencies and are consistent with a neutral model of mutation and random drift. The spectrum of allele frequencies for amino acid variants shows a trend toward lower frequencies relative to both the neutral model and the pattern observed at linked silent sites. These obtained data showed a significant participation of TLR4 molecules in MS pathogenesis. Experimental model of EAE will demonstrate possible treatment modalities.

## P1385

**Initial manifestation(s) of multiple sclerosis in Oman: a clinical study from a university teaching hospital**

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**Introduction:** No comprehensive account of the initial manifestation(s) of Multiple sclerosis (MS) is available from Oman.

**Objective:** To document the clinical and demographic profiles of initial manifestation(s) of MS patients from Oman.

**Design/method:** Patients who attended Sultan Qaboos University Hospital, Oman and satisfied the revised McDonald criteria for MS diagnosis were retrospectively studied from 1991 to October 2009. Gender, nationality, age at disease onset, initial presentation and expanded disability status scale (EDSS) score, clinical course and annual relapse rate were ascertained.

**Results:** During the study period, 46 MS patients [21 females and 25 males; 40 (87%) Omani nationals and 6 (13%) expatriates were identified. Mean age at disease onset was  $26.7 \pm 7.4$  years. Initial manifestations were monofocal [n=38 (83%)], with the presentations being myelopathy [n=16 (35%)], optic neuritis [n=12 (26%)], brainstem/cerebellar involvement [n=7 (15%)] and supratentorial sensori-motor affliction [n=3 (7%)]. Brainstem/ cerebellar findings predominated in the multifocal onset group [n=8 (17%)]. CSF oligoclonal band was detected in 16% of cases who underwent lumbar puncture. 96% (n=44) of cases were placed on interferon treatment. Mean EDSS score before treatment was  $1.5 \pm 1.6$ . 98% (n=44) had a relapsing remitting course while primary progressive MS was distinctly uncommon [n=1(2%)]. The annual relapse rate was  $0.8 \pm 0.7$ .

**Conclusion:** Clinical profile of MS in Oman closely resembles that of other Asian countries. The most common initial presentation was characterized by monofocal onset with either optic neuritis or myelopathy. Further immunological and genetic studies might provide more information on the aetio-pathogenesis and the differentiation from neuromyelitis optica.

## P1386

**Prevalence of depression in MS patients**

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**Aim of study:** To determinate prevalence of depression, like a significant, disabling symptom in MS patients.

**Methods:** The prevalence of major depression has been analyzed, as well as general demographic and clinical parameters in MS patients. In this study were included 87 patients with definite diagnosis of MS according to McDonald Criteria, age 17 to 60 years, with EDSS score up to 8.0 and without acute relapse. Exclusion criteria were: exacerbation of MS in the last month, severe chronic diseases, pre-existing psychiatric and psychological disorders, corticosteroid therapy in the last month. In this study we used the following scales: Expanded Disability Status Scale (EDSS), Hamilton Depression Rating Scale (HDRS) and Hamilton Anxiety Rating Scale (HARS). Statistical analysis of collected data included, among others,  $\chi^2$  test, Student's t-test and analysis of variance (ANOVA).

**Results:** The study included 30 men and 57 women having MS. Patients' average age at time of examination was  $37.7 \pm 10.2$  years. At disease onset patients' average age was  $30.1 \pm 9.3$  years. Relapse-remittent forms of MS represented majority of cases (77%) if compared to secondary progressive (17.2%) and primary-progressive (5.7%) forms. EDSS score medium value amounted to  $3.1 \pm 1.4$ . Average duration of the disease was  $7.2 \pm 6.1$  years. Prevalence of major depression in the population of patients with MS examined was 48.3%.

**Conclusions:** In order to overlook the complete psychophysical state of MS patients, patients' self estimation of symptoms and signs should be considered.

## P1387

**Serum uric acid level in Iranian patients with multiple sclerosis**

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**Background:** Multiple sclerosis (MS) is an immune-mediated disease, with inflammation and neurodegeneration contributing to neuronal demyelination and axonal injury leading to disability in young adults. Several findings suggest low level of antioxidants in the pathomechanism of the disease.

**Purpose:** We conducted this study to evaluate the serum level of uric acid, a putative endogenous antioxidant, in patients with multiple sclerosis.

**Method:** The study group consisted of a total of 55 relapsing-remitting MS patients and 55 age-sex-matched controls who were referred to the MS clinic from January 2008 to February 2009. The diagnosis of MS was based on Mc Donald Criteria. Patients who received interferons or cytotoxic medication were excluded.

**Result:** MS patients were found to have significantly lower serum uric acid (Mean [SD]: 4.161±1.30mg/dl) in comparison with the controls (Mean [SD] 5.069±1.37mg/dl) (p=0.001).

**Conclusion:** These results suggest that uric acid, a strong peroxynitrite scavenger, may play a role in the pathomechanism of MS and the low level of uric acid is a primary and constitutive loss of protection against the oxidative agents.

## P1388

**Comprehensive symptom profile (CSP-MS) for symptom assessment in patients with multiple sclerosis (MS): applicability and characteristics**

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Comprehensive symptom assessment and monitoring before and during MS treatment as well as at follow-up is worthwhile. We aimed to develop a new symptom assessment tool CSP-MS for patients with MS and test its applicability. CSP-MS Complete Form is developed to assess the severity of 42 symptoms specific for MS patients. There have been identified 8 clusters of symptoms, which were clinically relevant and increased the practicability of the tool. 63 patients with different types of MS: secondary progressive - 18, primary progressive - 7, progressive-relapsing - 1, relapsing-remitting - 37 were included in the study to test applicability of CSP-MS and provide initial validation. Mean age - 34.0 years; male/female distribution - 23/40; mean EDSS - 3.4. The utility of CSP-MS was demonstrated. Reliability of CSP-MS was satisfactory (Chronbach's alpha coefficient varied from 0.83 to 0.96). The construct validity was proved by the "known-groups" method: the severity of the majority of symptoms in the group with low disability (EDSS≤3) was lower than in the group with high disability (EDSS≥3.5); the difference was statistically significant for more than 50% of symptoms (p<0.05). High sensitivity to changes in symptom status was demonstrated by a statistically significant difference (p<0.05) in symptom severity before and after treatment. CSP-MS is an appropriate and practical tool to assess symptom profile and severity in MS patients. The utility of the questionnaire was shown; initial validation demonstrated satisfactory psychometric properties. Final validation study is needed before the use of CSP-MS in clinical practice and clinical trials.

## P1389

**Diagnostic significance of optical coherent tomography (OCT) and multimodal evoked potentials (MEPs) in patients with optical neuritis affected by multiple sclerosis**

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**Purpose:** The evaluation of the capacity of MEPs and OCT in the diagnosis of optic nerve affections in patients with MS.

**Materials and methods:** There were 40 patients with unilateral ON and diagnosed MS examined. The examination consisted of detection of visual acuity, computer perimetry, visual (VEPs), acoustic (AEPs) and somatosensory evoked potentials (SEPs).

**Results:** Visual acuity in the patients with ON varied from 0.01 to 1.0 and of the coupled eye it was 1.0 in all patients. The VEPs analyses showed latent prolongation from 112 to 147 ms in 27 (30 eyes) patients and amplitude reduction up to 2mkV in 9 (11 eyes) patients. While analyzing AEP in 11 patients with ON, we observed some increase of latent period of pic5 and increase of inter-pics intervals I-III up to 3.7ms and I-V up to 6.2ms. While analyzing SEPs of middle nerve in 22 patients with MS we observed increase of pic P8 latent period. We detected decrease of pics N20 and N13 amplitude in 7 cases in comparison with norm. We observed decrease of RNFL thickness in the affected eyes of 36 patients with MS between 72-85 mkn. Coupled eyes showed decrease of RNFL thickness from 103 to 109 in 17 cases.

**Conclusion:** The methods of MEPs and OCT, implemented in the patients with ON against a background of MS are very useful for the determination of the diagnosis of ON in the affected eye and let us detect even very minor, undetectable clinical changes of the optic nerve.

## P1390

**MS – from first clinical presentation to confirmed diagnosis. How does an Irish clinic measure up?**

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**Introduction:** The NICE guidelines recommend a timeline of 12 weeks from a patient's first clinical presentation to a diagnosis of multiple sclerosis (MS).

**Objective:** We audited our clinical management of people referred with possible MS in the outpatient setting.

**Methods:** All referrals with possible MS between January 2007 and January 2010 were reviewed. We analysed patient demographics, time taken to obtain an MRI, time from MRI to clinical review, time from review to LP (if performed) and the overall interval from first presentation to diagnosis.

**Results:** There were 116 new diagnoses of 'demyelinating disease', of whom 31 (27%) had a Clinically Isolated Syndrome, 74 had relapsing remitting MS and 11 (9%) had primary progressive MS. Almost 60% had an MRI prior to review. Of those who had an MRI after the first consultation, 31% were done within 12 weeks. LP was performed in 77% of the total cohort and 56% of these were done within 4 weeks. In total, 66% received their final diagnosis within 12 weeks of their first review.

**Conclusions:** Whilst our practice is producing a timely diagnosis in the majority of patients with MS, a number of problems remain. The main rate-limiting steps are the availability of imaging and CSF processing time.

## P1391

**Comparison of neurological scales used for disability assessment in multiple sclerosis**

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**Introduction:** Guy's Neurological Disability Scale (GNDS) is a subjective Multiple Sclerosis scale.

**Aim:** To compare the GNDS to Expanded Disability Status Scale (EDSS) and Hospital Anxiety and Depression Scale (HADS).

**Methods:** In Vilnius University Hospital Santariskiu clinics 56 patients with confirmed MS diagnosis were examined. EDSS and GNDS sum scores (ss), separate functions, HADS anxiety and depression scores (HADSa and HADSd) were estimated.

**Results:** 55 pt were included into final analysis: 14 (25.5%) men, 41 (74.5%) women, median age 40.31±10.98 years (y), a median disease duration 9.92±7.73 y, a median EDSS(ss) 3.98±1.68; a median GNDS(ss) 16.74±8.94; a median HADSa 7.71±4.07, a median HADSd 6.13±3.75. MS courses: 44 (80%) relapsing remitting; 8 (14.5%) – secondary progressive, 3 (5.5%) – progressive relapsing. EDSS (ss) correlated moderately with GNDS (ss) ( $r=0.574$ ;  $p<0.001$ ), GNDS limbs and fatigue sum score ( $r=0.596$ ;  $p<0.001$ ). GNDS(ss) correlated with HADSa ( $r=0.500$ ;  $p<0.001$ ) and HADSd ( $r=0.500$ ;  $p<0.001$ ). There were no correlations between EDSS (ss) and GNDS cognitive function (cf) score, HADSa and HADSd, between EDSS(cf) and GNDS(cf). HADSd correlated moderately with GNDS cognitive function and fatigue (cf+fat) sum score ( $r=0.509$ ;  $p<0.001$ ), weakly with GNDS (cf) ( $r=0.418$ ;  $p=0.003$ ). HADSa correlated moderately with GNDS (cf+fat) ( $r=0.574$ ;  $p<0.001$ ) and GNDS (cf) ( $r=0.492$ ;  $p<0.001$ ).

**Conclusion:** EDSS disability is related to GNDS subjective disability, mostly with limbs and fatigue sum score. GNDS disability is related to anxiety and depression. GNDS cognitive disability, a complex of cognitive disability and fatigue is related to depression and anxiety, mostly to anxiety. Fatigue increases cognitive disability relation to depression and anxiety.

## P1392

**Oligodendroglioma and multiple sclerosis**

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**Introduction:** Some observations describe a causal relationship between multiple sclerosis (MS) and glioma. Application of MRI proves that coincidence in the same patient.

**The aim:** To report the case of an MS patient treated for years with immuno modulating drug, developing a primary glial tumour.

**Case:** 49 y.o., female, started to complain of seizures (looking into one point and short freezing) three months ago. EEG registered paroxysmal activity. 10 years before she felt paraesthesia and weakness in legs and fatigue. Neurological examination revealed central lower paraparesis and ataxia. Brain MRI determined demyelinated lesions consistent with MS. Relapsing remitting MS course was diagnosed in 2008, confirmed by positive oligoclonal bands in CSF, elevation of IgG index, SSEP time prolongation and MRI C5 demyelinated Gd(-) lesion. Interferon (IFN) beta 1a, im was started in 2008. Brain MRI was repeated in Nov. 2009 and a mass in the right parasagittal frontal lobe with oedema, specific to glial brain tumour was determined. After biopsy applying neuronavigation, confirming the gliomaG2 tumour, neurosurgical operation was performed. Temporal left side weakness was observed, with the previous EDSS 3.5 in March 2010. IFN beta 1a, im was restarted.

**Conclusion:** With more than 2000 MS patients during the last ten years, this is our first observation of coincidental primary CNS tumour and MS. New atypical symptoms appearing on MS course require repetition of MRI. To diagnose low grade astrocytoma MRI, biopsy or radical removal are required. Beta IFN is unrelated to the development of glioma, although there is no current evidence of a therapeutic use in gliomas.

P1393

### Cognitive impairment in multiple sclerosis patients using a Spanish Brief Neuropsychological Battery (BNB)

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**Introduction:** Cognitive impairment is increasingly being recognized as a common and disabling symptom of multiple sclerosis (MS) that contributes to poor quality of life in patients. Therefore, brief cognitive tests to identify these are needed.

**Objectives:** To study cognitive alterations in MS patients with a new validated Spanish brief neuropsychological battery and to determine the relationship between age, disease duration, and disability and the presence of cognitive impairment.

**Methods:** It is a cross-sectional study. A new validated Spanish brief neuropsychological battery (BNB) was used by the neurologists as a quick screen to assess cognitive dysfunction in patients with relapsing-remitting MS (RRMS). The BNB can be administered and scored in about 20 minutes and includes a Spanish version of the Free and Cued Selective Recall Test, the Symbol Digit Modality Test, a test of verbal fluency and a modified version of PASAT.

**Results:** 80 RRMS patients were studied. Median EDSS score was 2.5 and mean disease duration was 132 months. 40% of our patients were affected by some degree of cognitive deficit, in particular 24% had mild, 11% moderate and 5% had severe impairment. Deficits in speed of information processing (39%) and verbal fluency (32%) were the commonest abnormalities. Significant correlations were found between cognitive alterations, disability and disease duration.

**Conclusion:** These results suggest the effectiveness of the BNB as a fast screen for cognitive impairment in MS in the daily clinical practice. The study confirms the sensibility of the SDMT to detect impairment of speed of information processing.

P1394

### A retrospective assessment of the clinical profile in patients with relapsing-remitting multiple sclerosis treated with disease modifying treatment – “PROFIL-SM”

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**Introduction:** PROFIL-SM retrospectively analyzed the clinical profile of patients treated with first line DMT.

**Objective:** To collect data on efficacy of DMT in patients with RRMS over 12 months.

**Design and methods:** Data of 317 patients from 4 different MS centres in Slovakia treated with DMT for at least 12 months has been analysed. Data on demographics, number of relapses, EDSS, MRI findings, treatment history and employment status were collected.

**Results:** 15% of patients had at least one relapse within the last year. 10% of patients worsened in EDSS within the last 12 months, mean EDSS increase was 0.7. MRI data were available for 301 patients. Data on gadolinium-enhancing lesions were available for 162 patients; 19% of them had at least one gadolinium-enhancing lesion. Data on T2 lesion number were available for 178 patients; 76% of them had at least 9 T2 lesions on the last MRI, 18% had an increase in T2 lesion number in comparison with previous MRI. 40% of patients had at least 1 DMT change in the course of the disease. 21% of patients terminated their employment due to a disease.

**Conclusion:** DMT represents the golden standard in treatment of patients with MS. However, approximately 15% of patients treated have experienced at least one relapse within the last 12 months. Additionally MRI findings indicate that the number of patients with disease activity and progression could be higher than was concluded from clinical parameters only.

## P1395

**Clinical and serological features of borrelial infection in multiple sclerosis patients**

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**Background:** The Yaroslavl region is an endemic area for Lyme disease (LD) with one of the highest levels of morbidity in Russia.

**Aim:** To investigate the frequency of positive *Borrelia burgdorferi* antibodies in serum of multiple sclerosis (MS) patients; to analyze the clinical features in antibody positive MS patients

**Methods:** 100 patients with definite MS were examined: 27 male and 73 female, 17-60 years old (37±11.28). Sera were examined for *Borrelia burgdorferi* antibodies by ELISA, indirect immunofluorescence test or western-blot.

**Results:** 38 MS patients were antibody positive. Among them 17 patients (44.7%) had false-positive serological results and significantly large duration of MS ( $p=0.044$ ) in comparison with antibody negative patients. The true-positive MS patients (MS+possible LD) as compared with 62 antibody negative MS patients had following features:  
1) more frequently had a tick bite (in 52% and 24% cases accordingly,  $p=0.033$ )

2) pyramidal dysfunction was the most frequent sign at onset of MS (57% and 25.8%,  $p=0.007$ )

3) arthralgia was observed in 33% ( $p=0.006$ )

4) sensory dysfunction was more often met in the antibody positive group (81% and 50%,  $p=0.026$ ).

15 MS patients with high level of *B. Burgdorferi* antibodies were treated with antibiotics. After treatment the antibody level decreased in all cases (100%) and clinical improvement was observed in 67% (10 patients).

**Conclusions:** In the endemic region there may be a combination of LD and definite MS in 21% cases. The false-positive serological results were determined in 44.7% cases. It is necessary to diagnose and treat borrelial infection in MS patients.

## P1396

**Diagnostic criteria for chronic herpes encephalitis**

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**Methods:** Clinical, virological, immunological, cerebrospinal fluid (CSF) assay (antigens to herpes simplex virus, cytomegalovirus, adenovirus, Kokoksi virus, Ekcho virus, Epstein-Barr virus); MRI of the brain and spinal cord. 69 chronic herpes encephalitis (CHE) patients were evaluated in the age range of 21-64 years.

**Results:** According to the clinical course of the disease, the following forms were registered: meningoencephalitic (16 patients (23.2%)), encephalitic (38 (55.1%)), encephalomyelitic (15 (21.7%)). MRI of the brain detected sites of reduced signal intensity in T-1W mode with concurrent increased signal intensity sites in T-2W mode in 24 (34.7%) patients. Demyelination of the white substance in the form of scattered foci was observed in 7 (10.1%) patients. CSF examination revealed four groups of patients. Group 1: 16 (23.2%) patients with very low protein content (0.02-0.09g/l); group 2: 34 (49.3%) with moderate reduction (0.1-0.19g/l); group 3: 12 (17.4%) with normal content (0.22-0.4g/l); group 4: 7 (10.1%) with high protein content (0.8-1.8g/l). Lymphocytic cytolysis in the Liquor ranged from 5/3 to 105/3, with additional isolated neutrophils. Antigens to herpes simplex virus were found in 47 (68.1%) patients, cytomegalovirus - in 28 (40.6%), adenovirus - 12 (17.4%), Kokoksi, Ekcho - in 8 (11.6%), Epstein-Barr - in 3 (4.3%). PCR diagnosed herpes virus in CSF only in 2 (2.9%) patients.

**Conclusion:** Etiologic diagnosis of CHE in clinical conditions is feasible, allowing for changes in the clinical pattern, findings of brain and spinal cord MRI, CSF assay detecting mainly antigens to viruses and only rarely viruses themselves.

## P1397

**Pregnancy after high-dose immunosuppressive therapy followed by autologous haematopoietic stem-cell transplantation in a patient with multiple sclerosis**

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**Objective:** A number of pre-transplant conditioning regimens (CD) for autologous haematopoietic stem cell transplantation (AHSCT) include agents, which may cause germ cell injury, gonadal dysfunction and infertility. Although successful pregnancies after AHSCT have been reported previously, the evidence suggests that female survivors may be at an increased risk of spontaneous abortions and miscarriages, pre-term delivery and low-birth weight babies.

**Methods:** A female patient, 22 years old, with a 4-year history of primary-progressive MS and EDSS score of 6.0 underwent high-dose immunosuppressive therapy (HDIT) followed by AHSCT. Peripheral blood stem cells were mobilized with cyclophosphamide (CY) granulocyte colony-stimulating factor (filgrastim). The HDIT consisted of CY (120mg/kg in 2 days), rabbit antithymocyte globulin Fresenius (Germany) (30mg/kg for 3 days) and methyl-prednisolone.

**Results:** Her follow-up after AHSCT is now 53 months. After AHSCT her neurological status has been stable with slight deterioration in 0.5 points of EDSS score 24 months after AHSCT. MRI evaluations were obtained before mobilization, 6 months, and every year after AHSCT. There were no new enhancing lesions on gadolinium-enhanced brain MRI. 39.5 months after AHSCT she fell pregnant. Pregnancy was without complications. The development of the foetus was normal. At 38.5<sup>th</sup> week of gestation caesarean section was performed. Now the patient's neurological status is stable. The development of the baby is normal.

**Conclusion:** This case provides encouraging data for patients who underwent AHSCT, indicating that reduced intensity conditioning regimen, or non-myeloablative AHSCT could preserve fertility.

## P1398

**Increased neurofilament concentrations in cerebrospinal fluid in multiple sclerosis**

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**Background:** Axonal damage in multiple sclerosis (MS) is recently recognized as an early occurrence in the inflammatory lesions of MS and plays an important role in the accumulation of disability in patients with MS. This process may be accompanied by the release of cytoskeletal proteins such as neurofilaments into the cerebrospinal fluid (CSF).

**Objectives:** To evaluate CSF levels of the light subunit of neurofilaments (NFL) in MS patients and controls.

**Patients and methods:** The concentration of NFL in CSF was measured using ELISA in 21 patients with MS (mean age  $\pm$  standard deviation, 35 $\pm$ 10, 16 females) and in 43 age-matched control subjects (37 $\pm$ 10, 29 females).

**Results:** The NFL concentration was 1.97pg/ml (median, range 0.44-9.7) in MS patients and 0.76pg/ml (median, range 0.24-13.8) in controls. We found a significant difference ( $p=0.0002$ ) between NFL concentrations in MS patients and controls.

We found a significant correlation between the NFL concentrations and the age in controls ( $r=0.49$ ;  $p=0.0008$ ), but not in MS patients.

**Conclusions:** The significant increase in cerebrospinal NFL concentrations in MS patients may reflect axonal damage. This study was supported by the research projects KAN200520701, IGA MZCR 10369-3 and GACR30909H072.

## P1399

**Differential diagnosis of multiple sclerosis with other neurologic diseases in children**

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On the basis of the examination of 91 children (clinical, computer tomography, magnetic resonance imaging, visual evoked potentials) we determined the possibilities of diagnosis and differential diagnosis of multiple sclerosis (MS) in children, to establish a range of diseases that are necessary to differentiate MS. In 31 children (19 girls and 12 boys) clinically true MS was diagnosed. The age of debut was 4 to 15 years, the peak of age constituting 12 to 13 years. The first symptoms in 8 children (26%) appeared prior to the age of 10. The earliest start was noted in a 4-year-old girl. A monosymptomatic start prevailed in 21 children (68%), a polysymptomatic start in 10 (32%). The initial symptoms were retrobulbar neuritis of the optic nerve, ataxia, insulated disturbance of sensitivity, facial nerve neuropathy, dyskinesia. In 25 cases clinically probable MS was diagnosed. In 35 children MS was excluded and other neurological diseases were diagnosed: tumours of brain and spinal cord (10), inflammatory diseases of the central nervous system (7), subacute sclerosing panencephalitis (5), leukodystrophy (4), olivopontocerebellar degeneration (2), neurofibromatosis with spinal cord compression (1), Strumpel's disease (1), Hallervorden-Spatz disease (1), Schilder's disease (1), spinal stroke (1), Louis-Bar syndrome (1), MELAS (1). The significant meaning of the computer tomography and magnetic resonance imaging was noted in the differential diagnosis of MS.

## P1400

**Lack of strong correlation between vestibular symptoms and infratentorial lesions in magnetic resonance imaging in the early stage of relapsing remitting multiple sclerosis (preliminary report)**

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**Objective:** The aim of this study is to analyze the correlation between the vestibular symptoms and infratentorial lesions on MRI in the early stage of RRMS.

**Material and method:** 30 patients with RRMS were included to the study. Neurological examination and cranial MRI were performed after detailed history of vestibular symptoms. Correlation analyses were performed between clinical features (type and characteristics of vestibular symptoms, time of the vestibular symptoms, concomitant symptoms, concomitant examination findings) and existence of infratentorial MRI lesions.

**Results:** Mean age of patients was  $37.9 \pm 9.0$  years and mean EDSS score was  $1.77 \pm 1.35$ . The ratio of patients who had any vestibular symptom in their medical history was 86.7%. We did not find any statistically significant correlation between the clinical parameters and the existence of infratentorial MRI lesions but there are some results that can be important as clinical point of view: All of the patients who experienced true vertigo during attacks (10%) have cerebellar lesions; and all of the patients who experienced any vestibular symptom in their first attack (33.3%) have infratentorial lesions.

**Conclusion:** Our results suggest that vestibular symptoms and/or findings in RRMS can be seen without any visible infratentorial lesion on MRI. Conventional MRI might fail to show the micro-plaques or vestibular symptoms could be the result of other lesions or mechanisms effecting the vestibular pathways. Therefore it is strongly suggested to use other diagnostic procedures such as electrophysiological tests to understand the problem.

## P1401

### Dysarthria clumsy-hand as a manifestation of multiple sclerosis. Review of our experience

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**Introduction:** Dysarthria clumsy-hand has been classically identified as a lacunar syndrome in cerebrovascular disease. Responsible lesions have been found in internal capsule, thalamus, basal ganglia, pons, corona radiata and semioval centres. An alternative diagnosis to stroke may have therapeutic and prognostic implications.

**Objective:** To describe clinical and radiological findings of three cases with multiple sclerosis (MS) and dysarthria clumsy-hand syndrome as a manifestation of relapse, with compatible radiological findings.

**Patients and methods:**

Case 1: A 33-year-old woman with clinically isolated syndrome presenting as blurred speech and clumsiness in precision movements with her right hand. Magnetic Resonance Imaging (MRI) showed a large tumefactive lesion in the internal capsule.

Case 2: A 33-year-old woman with a history of 8 years of MS, presenting blurred speech and difficulties in writing due to impoverished left hand dexterity. MRI showed a new gadolinium-enhancing left periventricular lesion.

Case 3: A 43-year-old woman with a previously diagnosed relapsing-remitting MS. She was unable to write, dress herself, and had difficulties on speech. Physical examination showed dysarthria and slowness of movement of the right hand. MRI showed a new tumefactive lesion in the left semioval centre with gadolinium enhancement.

**Discussion:** Lesions in the pyramidal tracts have been largely described as causes for dysarthria-clumsy-hand syndrome. Though rare, these lesions may be demyelinating and an alternative diagnosis to stroke should be considered in young patients without cardiovascular risk or in patients with previously known demyelinating disease.

## P1402

### Mitoxantrone-related acute leukaemia in multiple sclerosis

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**Background:** Mitoxantrone is approved to treat worsening relapsing and secondary progressive Multiple Sclerosis (MS). Acute leukaemia is a well known serious adverse event, nevertheless the real incidence is not well established.

**Case report:** We report two cases of acute leukaemia observed among 87 MS patients treated with mitoxantrone since July 2001, not exceeding the maximum cumulative dose of 140mg/m<sup>2</sup>.

Patient1: A 47-year-old woman with secondary progressive MS, EDSS 6.0, initiated treatment with mitoxantrone in February 2003. The last cycle was in July 2004, with a total dose of 95mg/m<sup>2</sup>. One year after mitoxantrone discontinuation, the patient developed spontaneous diffuse haematoma and diagnosis of acute myeloblastic leukaemia was made. She was treated with chemotherapy followed by autologous bone marrow transplantation with stabilization of haematological and neurological disease.

Patient2: A 53-year-old man with secondary progressive MS, EDSS 4.0, initiated treatment with mitoxantrone in March 2004. The last infusion was in August 2004, with a total dose of 60mg/m<sup>2</sup>. 12 months after mitoxantrone discontinuation, the patient presented with pancytopenia and pneumonia, and the investigation led to diagnosis of acute myeloblastic leukaemia, dying a few days after. We retrospectively found that his father had died of leukaemia.

**Conclusion:** The real incidence of mitoxantrone-related acute leukaemia is not yet known and recent data indicate that it might be higher than previously described. Although this report represents a narrow series, the observed frequency of cases was considerably high (2.3%). Considering dose/time limitation, long term adverse effects and the new MS therapeutics available, we restricted mitoxantrone utilization in our patients.

## P1403

### Assessment of adherence to subcutaneous interferon beta-1a treatment in clinical practice among patients with relapsing multiple sclerosis using an electronic self-injection device

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**Background:** Poor treatment adherence may impact efficacy outcomes. The ongoing SMART study will provide the first large-scale, accurate assessment of patient adherence to disease-modifying drug therapy in multiple sclerosis (MS).

**Objective:** To assess adherence to subcutaneous (sc) interferon (IFN) $\beta$ -1a among patients with relapsing MS (RMS) using an electronic self-injection device (RebiSmart<sup>TM</sup>).

**Methods:** This 12-month, observational study includes patients with RMS (McDonald criteria), a baseline Expanded Disability Status Scale score  $\leq 6$ , and who are naïve to treatment or currently self-injecting sc IFN beta-1a using the device but for  $< 6$  weeks. Patients will use the device to self-inject sc IFN $\beta$ -1a, 22 or 44mcg three times weekly. Treatment compliance and persistence will be calculated using data (date; time of injections) recorded by the device. Primary endpoint: proportion of expected injections completed during 12 months of treatment. Secondary endpoints include reasons for missed injections, relapse outcomes and patient/ physician assessment of the device.

**Results:** Enrolment commenced in October 2009 (target: 1,100 patients across 300 centres in 18 European countries), with 61 patients recruited (157 centres in 5 countries) as of March 2010.

**Conclusions:** The ongoing, multinational SMART study will accurately assess adherence to sc IFN $\beta$ -1a therapy in clinical practice in patients with RMS, via an innovative electronic self-injection device. Reasons for, and implications of, suboptimal adherence will also be evaluated. Accurate monitoring of patient compliance and persistence with self-injected therapies may help healthcare providers to improve overall treatment adherence.

Sponsor: Merck Serono S.A.-Geneva, Switzerland, an affiliate of Merck KGaA, Darmstadt, Germany.

## P1404

### Evaluation of an optimized nursing care programme for patients with relapsing-remitting multiple sclerosis in Germany

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**Background:** Patient support during initiation of multiple sclerosis (MS) therapy is critical to ensure continued treatment adherence and optimal benefit to patients.

**Objective:** To assess patient and physician satisfaction with an introductory care programme delivered by MS nurses in Germany during initiation of subcutaneous (sc) interferon (IFN) $\beta$ -1a treatment.

**Methods:** Eligible patients (clinically confirmed relapsing-remitting MS [RRMS]; beginning sc IFN $\beta$ -1a therapy) were enrolled in the introductory care programme and self-administered sc IFN $\beta$ -1a, 44 or 22mcg, three times weekly. Planned observation period following therapy initiation was 15 weeks. At the final visit, physicians reported missed doses and changes in patients' neurological status. A survey assessed physicians' perceptions of the support programme and their impression of overall patient satisfaction.

**Results:** A total of 1,426 patients were eligible (mean [SD] age: 37.4 [10.5] years; 72.7% women): 94.1% regularly injected treatment and 94.4% continued treatment throughout the study. At study end, 49.8% (681/1,368) of patients had improved neurological status; deterioration occurred in 5.3% (72/1,368). Physicians judged that the programme had improved treatment satisfaction in 92.7% (1,275/1376) of cases and continuation could be beneficial for compliance in 75.9% (1,040/1371) of cases. In total, 93.2% (1,298/1392) of patients gave positive feedback on the programme to the physician; 92.8% (1283/1383) were classified as 'motivated to continue treatment'.

**Conclusion(s):** This large, non-interventional study suggests that an introductory MS nurse care programme is beneficial to patients beginning sc IFN $\beta$ -1a therapy for RRMS, and may enhance motivation to continue treatment.

**Sponsor:** Merck Serono S.A.-Geneva, Switzerland, an affiliate of Merck KGaA, Darmstadt, Germany.

## P1405

**Sexual dysfunction in young men with relapsing remitting multiple sclerosis**

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**Objectives:** The purpose of this study was to examine the sexual complaints and severity of sexual dysfunction in young men with relapsing-remitting multiple sclerosis (RRMS).

**Material and methods:** Frequency and characteristics of sexual disturbances were reported by 18 patients with RRMS (mean age 30.8±4.3). They were asked about their sexual function using International Index of Erectile Function (IIEF) questionnaire and Multiple Sclerosis Intimacy and Sexuality Questionnaire (MSISQ-19). Neurological status was assessed by Expanded Disability Status Scale (EDSS). All patients underwent MRI. For statistical evaluation Spearman's criteria was used.

**Results:** 77.7% (14/18) of patients had erectile dysfunction (ED) of various severity: 7.1% severe ED, 14.2% moderate ED, 7.1% mild to moderate and 71.4% had mild ED. 38.8% (7/18) had disturbances in orgasmic function. Decrease in sexual desire was reported by 83.3% (15/18). None of the patients was completely satisfied with the intercourse. Decrease in overall satisfaction of intercourse mentioned by 61.1% (11/18). 77.7% (14/18) reported changes in their intimacy and sexuality. It was also found that ED correlates with bladder dysfunction ( $r=-0.61$   $p<0.05$ ). No significant correlation was shown for ED and duration of the disease ( $r=0.36$   $p>0.05$ ), ED and score on EDSS ( $r=-0.028$ ,  $p>0.05$ ).

**Conclusions:** Erectile dysfunction (77.7%) and decrease in sexual desire (83.3%) is common for young men with RRMS and does not depend on duration of the disease and disability status. Changes in sexuality and intimacy due to MS are also frequent (77.7%). The symptoms of SD should not be missed in young patients and may need further treatment.

## P1406

**Mesenchymal stem-cell transplantation reduces demyelination and inflammation and induces clinical recovery in experimental autoimmune encephalomyelitis**

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**Objective:** To investigate the therapeutic potential of mesenchymal stem-cells (MSCs) in the acute experimental autoimmune encephalomyelitis (EAE).

**Methods:** EAE in Wistar rats was induced with complete Freund's adjuvant. MSCs of the second passage at a dose of  $1 \times 10^6$  were injected intravenously at the peak of the disease. In some experiments prior to transplantation MSCs were stained with PKH26 (Sigma-Aldrich). Control rats with EAE received the injection of the same volume of medium. Rats were observed for 42 days after immunization. Section slides were stained according to standard methods. Brain and spinal cord frozen sections were analyzed by fluorescence microscopy for localization of PKH26-labeled cells. Before and after injection of MSCs, proliferative response of EAE rat lymphocytes derived from peripheral blood, spleen and lymph nodes to myelin antigens was studied using flow cytometry.

**Results:** MSCs transplantation strikingly reduced disease severity and prevented relapses. This clinical effect was associated with reduction of demyelination and infiltrates of T-cells and absence of macrophagic reaction both in brain and spinal cord of treated rats as compared with controls. Fluorescence microscopy showed PKH26-labeled MSCs to be present in many organs (spleen, liver, bone marrow, lymph nodes) with rare incidence in brain and spinal cord. MSCs injected in vivo had a strong inhibitory effect on myelin-induced proliferation of EAE rat lymphocytes in vitro and suppression indices varied from 59 to 67%.

**Conclusion:** Our results indicate that MSCs may provide a feasible and practical way for immunomodulation and possibly remyelination in multiple sclerosis.

## P1407

**Influence of pain and sphincter disorders on quality of life in multiple sclerosis patients**

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**Objective:** To investigate the impact of pain and sphincter disorders on quality of life in multiple sclerosis (MS) patients.

**Methodology:** 100 MS patients treated at the Neurology Clinic in Sarajevo were involved in this study. Each patient underwent a complete clinical assessment, including disability status (EDSS), cognitive function (MMSE) and measurement of quality of life (MSQOL-54). Internal consistency of Bosnian MSQOL version was evaluated. Linear regression analyses were performed to identify significant predictors from sociodemographic and clinical characteristics in predicting MSQOL-54 physical and mental composite scores.

**Results:** The mean age of 100 patients (69% female and 31% male) was 39.88±10.03. The mean EDSS score was 3.57±1.73. Cronbach's alpha coefficients were high (range 0.78-0.95). 64% of patients had presence of pain, 52% of patients had presence of sphincter disorders of different types. Patients with pain and sphincter disorders had significantly lower physical and mental health composite scores than patients without pain and sphincter disorders ( $p<0.001$ ). Linear multivariate regression analyses revealed that presence of pain was the most dominant in predicting both physical ( $R^2=0.287$ ,  $p<0.001$ ) and mental health composite scores ( $R^2=0.139$ ,  $p<0.001$ ), while presence of sphincter disorders was one of the dominant variables in predicting physical health ( $R^2=0.186$ ,  $p<0.001$ ), without significant role in predicting mental health composite score.

**Conclusion:** Assessment of quality of life provides additional information especially considering psychological impact of the disease. Recognition and management of pain and sphincter disorders are highly important in treatment of MS patients.

## P1408

**Decide rationale/design: daclizumab high yield process monotherapy in relapsing remitting multiple sclerosis (RRMS)**

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**Background:** The phase 2 CHOICE trial demonstrated that daclizumab, when added to IFN $\beta$ -1a treatment of MS, reduced new/enlarged gadolinium-enhancing lesions by 72% compared to IFN $\beta$ -1a alone. Clinical efficacy was associated with a marked expansion of immunoregulatory CD56bright natural killer cells.

**Objectives:** To test the superiority of daclizumab high-yield process (DAC HYP) when compared to IFN $\beta$ -1a in preventing relapses and slowing disability in subjects with RRMS, and to identify predictive biomarkers of treatment response.

**Methods:** The DECIDE trial is a global, phase 3, double-blind active comparator study. Eligible subjects (N~1500) are randomized 1:1 to receive either 150mg of subcutaneous DAC HYP every 4 weeks, or 30mcg intramuscular IFN $\beta$ -1a once/week for a minimum of 96 weeks.

**Results:** Superiority of DAC HYP will be assessed via annualized relapse rate (primary efficacy endpoint), brain MRI (T2 hyperintense and T1 hypointense lesions, gadolinium-enhancing lesions, brain atrophy), sustained disability progression, multiple sclerosis functional composite scores, cognitive testing, and visual function. Safety and tolerability throughout the study and follow-up will be evaluated by a battery of physical, neurological, and psychological examinations. Pharmacodynamic and pharmacogenetic analyses will be performed to identify potential biomarkers of clinical responses to DAC HYP.

**Conclusions:** The DECIDE trial is designed to provide a definitive assessment of the efficacy and safety of DAC HYP in comparison to an established standard of MS care and a confirmatory assessment of CD56bright natural killer cell expansion as a marker of optimal response to DAC HYP.

## P1409

**Clinical outcome of relapsing remitting multiple sclerosis among Hong Kong Chinese**

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**Background:** A significant proportion of relapsing remitting multiple sclerosis (RRMS) patients develop irreversible deterioration, secondary progressive phase (SPMS) with accumulating neurological disability. Reported outcome and prognostic factors are inconsistent.

**Aim:** To study the clinical outcome of Chinese RRMS patients with duration  $\geq 10$  years.

**Method:** RRMS patients with MRI abnormalities fulfilling Barkhof's criteria for dissemination in time and space followed up at our hospital were studied retrospectively.

**Results:** 61 RRMS patients were studied. Their mean age at symptom onset was 26.5 years (range 12-50), mean duration after symptom onset was 20.3 years (range 10-33); 48 (79%) were female. At 10 years, 30% patients had EDSS score  $\leq 2$ , 34% EDSS 2.5-3.5, 20% EDSS 4.0-5.5 and 16% EDSS  $\geq 6$ , and 20% developed SPMS. At latest follow-up (mean duration 20.3 years), 15% patients had EDSS  $\leq 2$ , 20% EDSS 2.5-3.5, 19% EDSS 4.0-5.5 and 46% EDSS  $\geq 6.0$ , and 59% developed SPMS. The median time from symptom onset to EDSS 6 was 22 years. The mean duration from symptom onset to SPMS was 13.2 (range 7-20) years. No differences were detected in demographic characteristics, presenting neurological features, relapse frequency, neuroradiological findings and disease modifying therapies between patients with EDSS  $< 6$  and EDSS score  $\geq 6$  at ten years.

**Conclusion:** The median time from symptom onset to progress to EDSS score 6 was 22 years for Hong Kong Chinese RRMS patients.

## P1410

**Development and long-term safety evaluation of cladribine tablets as a short-course, oral therapy for relapsing and early forms of multiple sclerosis: ongoing clinical trials**

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**Introduction:** Cladribine tablets therapy is being developed for multiple sclerosis (MS), since it provides targeted, sustained reductions in specific lymphocyte subtypes in an annual short-course oral dosing regimen.

**Objective:** A clinical development plan (CDP) has been conceived to provide extensive efficacy and safety data in relapsing and early forms of MS.

**Methods:** The CDP includes clinical trials which will demonstrate the efficacy and safety of cladribine tablets in patients with relapsing forms of MS and patients with a clinically isolated syndrome (CIS) who are at risk of developing MS. All subjects who have participated in these clinical trials are eligible for PREMIERE, a PROspective observational long-term safEty registry of Ms patIEnts who have participated in clinical trials with cladRibinE tablets. In PREMIERE, subjects will be followed for up to 8 years or until registry completion (anticipated in 2018).

**Results:** Clinical trials with cladribine tablets are planned to enrol more than 2000 patients with relapsing MS (CLARITY, CLARITY Extension, ONWARD, ONWARD Extension) and early MS (ORACLE- MS). It is estimated that 75% of these subjects will participate in PREMIERE.

**Conclusion:** Clinical trials with cladribine tablets and the prospective safety registry are intended to establish the short-course regimen of cladribine tablets as an effective and safe therapy for relapsing and early MS.

Study supported by: Merck Serono S.A. – Geneva, Switzerland, an affiliate of Merck KGaA, Darmstadt, Germany.

## P1411

**Spirituality components and quality of life of neurological patients**

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Spirituality has been proved to be closely related with quality of life (QOL). Nevertheless, health care professionals often report difficulty in assessing and promoting spirituality. Consequently, the aim of the present study was to analyze the relationship between QOL and the scores derived from a very short spirituality scale in neurological patients. Two questionnaires (SF-36; Escala de Avaliação da Espiritualidade em Contextos de Saúde - EAECs) were completed by 176 outpatients: 99 with multiple sclerosis, 77 with epilepsy, mostly women (n=110), between 18 and 65 years of age (M=35.87, SD=8.69), with diagnoses from 1 to 49 years old (M=13.04, SD=10.20). There were no statistically significant differences between the two groups of patients regarding beliefs and hope/ optimism (spirituality dimensions). Spirituality predicted QOL as follows: Mental Health – Hope/Optimism and Beliefs (Ra2=0.101); Vitality – Hope/Optimism (Ra2=0.034); Role Emotional – Beliefs and Hope/Optimism (Ra2=0.082); Role Physical – Beliefs (Ra2=0.024); General Health – Hope/Optimism and Beliefs (Ra2=0.109). No spirituality score predicted social function, bodily pain or physical function. The results show that the scores derived from 2 (Beliefs) or three (Hope/Optimism) items of the EAECs, although easy and rapid to obtain, are not good predictors of the sample's QOL. Hence, their clinical utility should be reconsidered. The results also indicate that different spirituality components have associations of diverse magnitude with QOL indicators. Consequently, one could hypothesize that different approaches to spiritual care (more or less focused on religion/existentialism) could have a discrepant success on different QOL domains.

## P1412

**Depression in patients with multiple sclerosis**

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## P1413

**Combined therapy with methylprednisolone and swine brain hydrolyzed protein in multiple sclerosis**

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## P1414

**The influence of piracetamum on psychic disorders in patients with multiple sclerosis**

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## P1415

**Increase of IL-6 levels in the acute phase of multiple sclerosis is possibly related with the presence of depression**

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## P1416

**One-year data on the safety and efficacy of natalizumab in Cypriot patients with relapsing-remitting multiple sclerosis**

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P1417

**Clinically isolated syndrome and early multiple sclerosis: the value of visual evoked potentials**I. Sereike<sup>1,2</sup>, V. Budrys<sup>1,2</sup>, R. Kizlaitiene<sup>1,2</sup>*<sup>1</sup>Clinic of Neurology and Neurosurgery, Vilnius University, Faculty of Medicine, <sup>2</sup>Centre of Neurology, Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania*

P1418

**Reasons for interrupting the therapy of interferon beta in a group of patients with relapsing-remitting multiple sclerosis**

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P1419

**The role of emotional instability and stress in onset of multiple sclerosis**A. Karapetyan<sup>1</sup>, M. Hakobyan<sup>1</sup>, A. Nazaryan<sup>1</sup>,E. Gevorgyan<sup>2</sup>, H. Manvelyan<sup>1</sup>*<sup>1</sup>Neurology, Yerevan State Medical University, <sup>2</sup>Neurology, Clinical Hospital # 2, Yerevan, Armenia*

P1420

**Cases of doubtful diagnosis between multiple sclerosis and cerebrovascular disease**E.G. Shipova<sup>1,2</sup>, N.N. Spirin<sup>1,2</sup>, I.O. Stepanov<sup>2,3</sup>,N.S. Baranova<sup>1,2</sup>, V.A. Shadrichev<sup>1,2</sup>, O.A. Fadeeva<sup>1</sup>*<sup>1</sup>Neurology and Medical Genetics, Yaroslavl State Medical Academy, <sup>2</sup>Regional Multiple Sclerosis Centre, <sup>3</sup>Neurology #3, Municipal Clinical Hospital #8, Yaroslavl, Russia*

P1421

**Health-related quality of life in multiple sclerosis patients: the impact of depression and anxiety**

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