P001

MS-like presentations of HTLV-1 infection: Case-series and review of literature

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Iran

Introduction: Human T-lymphotropic virus type 1 (HTLV-1), was the first human retrovirus to be discovered in 1980. The majority of HTLV-1 infected individuals (95%) will remain asymptomatic for their lifelong; whereas 5% of these patients will be symptomatic, mainly hematologic and neurologic.

Case report: We present four patients with HTLV-1 infection (from Mashhad and Neyshabur cities in Khorasan province in the northeast of Iran as an endemic region) who were referred with MS-like clinical picture associated with some hyperintense lesions in brain MRI.

Discussion: Multiple disorders including HTLV-associated myelopathy/tropical spastic paraparesis (HAM/TSP) and other infrequent neurological complications such as polyneuropathy, amyotrophic lateral sclerosis (ALS) like syndrome, cerebellar ataxia, cranial neuropathy, dementia, myositis and MS-like presentation have been related to this virus. The latter is reported rarely.

One of the probable etiologic factors in MS is HTLV1. However, this neurotropic virus produces a chronic inflammatory myelopathy similar to primary progressive MS (PPMS). In addition, a degenerative phase quite reminiscent of MS comes after inflammatory phase of HAM/TSP. Therefore, it is sometimes misdiagnosed as MS.

Magnetic resonance imaging (MRI) of the brain and spinal cord is usually normal, but may occasionally show hyperintense signal abnormalities on T2-weighted images and atrophy of the spinal cord in late disease. The patterns of signal enhancement in HAM/TSP tend to be diffuse, in contrast to discrete or multifocal abnormalities seen in MS. Like our patients, periventricular white matter lesions may also be seen. In patients with suspected MS, one should always keep in mind the other conditions that may have similar clinical and radiological presentations; hence, it is better to call it “MS syndrome” rather than “MS disease”.

Conclusion: This article argues about similar presentations between HTLV-1 infection and MS, not mentioned before. Occasionally, HTLV-1 infection is misdiagnosed as MS and it should be considered in the differential diagnosis of patients supposed to have MS, especially in endemic areas. In other words, as MS is a diagnosis of exclusion, it is quite reasonable to do a routine HTLV-1 serological study (ELISA) for all suspected MS patients in endemic areas.

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P002

Clinical predictors of disease progression in multiple sclerosis patients with relapsing onset in a Nationwide Cohort


Kuwait

Background: Prognosis of multiple sclerosis (MS) is variable. Predicting the progression of disability over time is challengeable despite the florid clinical and paraclinical data provided.

Objective: We aimed to assess whether baseline clinical variables of MS patients would predict the conversion to progressive phase of the disease.
Method: Utilizing the national MS registry, patients who had relapsing onsets and had confirmed EDSS score at baseline and follow-up visits were included. Primary progressive MS and CIS patients were excluded. Clinical variables (gender, age at onset, disease duration, number of relapses, and EDSS score) were collected. The end point was conversion to secondary progressive MS or reaching the stage of sustained irreversible neurological disability (EDSS 4). Chi square and multivariable logistic regression were used to determine the influence of clinical variables on disease progression.

Results: Data of 803 MS patients with relapsing onset were analyzed. Mean age at onset and mean disease duration were 26.62 and 8.12 years respectively. Eighty five (10.6%) patients reached the end point at last follow-up visit; 43.5% of whom were men. The risk of disease progression was significantly higher in men (adjusted odds ratio \( \text{aOR} = 2.02 \); 95% confidence interval (CI): 1.16-4.16; \( P = 0.015 \)), in patients who developed MS 40 years of age (aOR=4.36; 95% CI: 1.35-14.09; \( P = 0.041 \) ) and who had? 3 relapses during their disease course ( \( P < 0.001 \)). Spinal cord presentation at onset was predictive of progression (aOR=2.01; 95% CI: 0.97-4.36; \( P = 0.06 \)) while optic neuritis at onset was associated with lower risk of progression (aOR=0.30, 95% CI: 0.10-0.87; \( P = 0.03 \)).

Conclusion: Men and patients who presented at age 40 years or beyond had increased risk of MS progression. Spinal cord symptoms at onset and 3 or more relapses were predictive of progression.

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P003
Demographics and clinical characteristics of pediatric onset multiple sclerosis

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Kuwait

Background: Although several studies indicated that the prevalence of pediatric multiple sclerosis (MS) is approximately 5% of the adult MS cohort, reports on clinical features of pediatric MS is scarce in our region.

Objective: To study the demographics and clinical characteristics of MS patients whose disease started before the age of 17 years.

Methods: Utilizing the national MS registry, we conducted a cross-sectional study to identify MS patients who had their disease onset before 17 years of age. Demographics and clinical characteristics (age, age at onset, symptoms presentation at onset, disease duration, disease course, relapses, expanded disability status scale (EDSS), and use of disease modifying therapies (DMTs)) were collected.

Results: Records of 111 pediatric MS patients were analyzed; of whom 71.2% were females. Mean age at onset and mean disease duration were 14.85 and 9.49 years respectively. Family history was reported in 12.6%. Supratentorial, optic pathway, cerebellar/brainstem, and spinal symptoms were the presenting symptoms in 28.8%, 23.4%, 35.1%, and 27% of patients respectively. 14.4% of patients presented with multifocal symptoms at onset. Most of the patients (82%) had relapsing remitting course, while clinically isolated syndrome group constituted 8.1%. The mean number of relapses was 3.36 and the mean EDSS at last visit was 2.51. Most of the patients (75%) had EDSS less than 4. The mean time to secondary progressive MS in 9.9% of the patients was 14.63 years. Of 79.08% patients who were exposed to DMTs, 13.51% had aggressive course necessitating the use of Natalizumab as a first line therapy while 37.36% escalated to second line therapies during their disease course.

Conclusions: MS patients with pediatric-onset had comparable clinical characteristics to adult onset MS. Most patients had low EDSS scores despite the relatively higher percentage of patients with initial aggressive course and breakthrough disease during their disease course.

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P004
Cognitive impairment in patients with clinically isolated syndrome

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Iran

Background: Cognitive impairment is a known topic in multiple sclerosis but it is not well known in patients with clinically isolated syndrome (CIS).

Methods: Patients with CIS (N=35) and healthy control participants (N=35), were assessed by the Brief International Cognitive Assessment for MS (BICAMS). The maximum time between first demyelinating event and cognitive evaluation was 1 year. Symbol Digit Modality Test (SDMT) to test of information processing speed, California Verbal Learning Test (CVLT) to test verbal memory, and Brief Visuospatial Memory Test-Revised (BVMT-R) to test of visual memory, were used. The normal range for each test was obtained from the matched healthy control group and the test was considered failed if the score was out side of the normal range.

Results: Nineteen patients (54.3%) obtained scores lesser than the normal range in at least one test. Eight patients (22.4%) failed in two tests. Impairment on all three tests, was not observed. Patients had impairment in SDMT (42.9%), CVLT (40%), and BVMT-R (17.1%) in decreasing order of frequency. Regarding to CIS presenting symptoms, optic neuritis (N=20), spinal cord involvement (N=8), and brain stem involvement (N=7), there was no significant difference in cognitive performance.
Conclusion: Our findings indicate that there is a significant cognitive dysfunction from the very earliest stage of the disease.

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P005

Progression from radiologically isolated syndrome to multiple sclerosis

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Iran

Background: The aim of this study was to estimate the progression rate from radiologically isolated syndrome (RIS) to clinically definite multiple sclerosis (MS).

Methods: During the mean (SD) follow-up period of 17.4 (5.4) (range 8–29) months, 25 subjects with RIS and without neurological symptom aged 22–45 years have been examined for the occurrence of clinically definite MS. The mean (SD) age of participants was 35.1 (6.2) years at first brain MRI. The criteria for definite MS were based on the revised McDonald’s criteria (2010).

Results: Six among 25 patients developed clinical symptom consistent with criteria for definite MS. The progression rate from RIS to definite MS was 1.5 (95% confidence interval CI) 0.54, 3.17) per 100 person-months based on 480 person-months of follow-up. Multivariate analysis revealed that the presence of contrast-enhancing lesions on the initial MRI was marginally significantly associated with MS (hazard ratio 1.83, 95% CI 0.98, 3.45, p = 0.060).

Conclusions: This is the first estimate of progression rate from RIS to definite MS in Iran. The progression rates from RIS to definite MS in these participants are high and intensive follow-up and intervention strategies are recommended for these high risk individuals. A larger study is warranted to assess this risk in greater detail.

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P006

Association between trigeminal neuralgia and multiple sclerosis: A population-based study

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Iran

Background: Multiple sclerosis (MS) is a chronic neuro-inflammatory disease of central nervous system (CNS) which is characterized by variable evolution and different clinical manifestations. Although pain is one of the most common problems of MS patients, the presence of trigeminal neuralgia (TN) in a patient’s life-span is rare.

Methods: In a retrospective study, we investigated the presence of TN amongst MS patients inspecting total Isfahan multiple sclerosis (TIMs) records which were registered in Isfahan Multiple Sclerosis Society (IMMS) from April 2003 until July 2014.

Results: We could find 20 cases with diagnosis of both TN and MS, suggesting a significant higher prevalence of TN among MS patients (0.4%) in comparison with general population (0.04%) (P<0.05).

Conclusions: Our results showed a significant association between these two disorders supporting previous hypothesis based on the role of MS in etiology of TN.

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P007

A case of acute disseminated encephalomyelitis mimicking multiple sclerosis attack treated by plasmapheresis

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Turkey

Acute disseminated encephalomyelitis (ADEM) is an acute multifocal demyelinating disease of the central nervous system. Its clinical course in most cases is monophasic; however, relapsing ADEM is rarely seen, which poses a diagnostic challenge for distinguishing this disease from multiple sclerosis (MS). The common treatment approach in ADEM consists of high daily doses of intravenous methylprednisolone for 3–5 days, followed by an oral corticosteroid taper. However, some patients with ADEM are refractory to steroid therapy. In case of insufficient response to corticosteroids, intravenous immunoglobulin G is a therapeutic option. Plasmapheresis might be an effective treatment and life-saving in cases of fulminant ADEM.

We report a case of a 22-year-old man admitted to our clinic as a MS attack but lately suffering from fulminant ADEM. The patient did not respond to corticosteroid therapy but exhibited a dramatic recovery with plasmapheresis. Effectiveness of plasmapheresis has been demonstrated by previous case reports. For severe or life-threatening cases of ADEM, plasmapheresis should be considered early in the disease course.

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P008

A prospective study on the prognosis of multiple sclerosis in Tunisia: Do we really have a distinct disease course in North Africa?

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Sleep quality among patients with multiple sclerosis in West Azerbaijan
**Introduction:** Few epidemiological data on multiple sclerosis (MS) patients are available in North Africa (NA). Studies of immigrants from NA showed a more aggressive course of MS in NA than in European patients.

**Objective:** To describe clinical, long term course characteristics and prognostic factors of MS in a Tunisian population.

**Methods:** We performed a prospective multicentric study of 437 MS patients in Tunisia between 2010 and 2012. We considered as endpoints the time to reach non-reversible disability levels corresponding to EDSS scores of 3.0, 4.0 and 6.0, and the beginning of a secondary progressive phase. We used Kaplan-Meier analyses and Cox regression models to determine the influence of the clinical variables on the time to disability onset.

**Results:** Sex ratio was 2.34. Mean age of onset was $30.3 \pm 9.5$ years and the duration of illness was $8.4 \pm 6.7$ years. The course was relapsing-remitting (RR) in 77% of patients, secondary progressive (SP) in 15.5% and primary progressive (PP) in 8.5%. Median time to secondary progressive onset was 19.1 years. Median times from onset of multiple sclerosis to assignment of a score of 3, 4 and 6 were 8, 10.7 and 15 years respectively. A greater number of functional systems involved at onset, progressive from as well as late age, motor, cerebellar and sphincter symptoms at onset were factors predictive of a poor outcome. A longer first inter-attack interval was associated with a better prognosis. Once EDSS 4 was reached, the time course of progressive disability was similar in patients with progressive onset and those with RR MS.

**Conclusion:** This is the first multicentric study in our country. The present study showed a similar course of MS in a North African population compared to European cohorts. Similar long term prognosis factors were found.

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**P010**

**Neuromyelitis optica: Case reports from Oman**

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**Oman**

Neuromyelitis optica (NMO), a multiple sclerosis mimic, is a rare disorder with a combination of optic neuritis and transverse myelitis. Only few cases were reported in Oman and were considered a diagnostic challenge. Most of them had an unusual presentation and were confused with multiple sclerosis. The neuromyelitis optica IgG test helped confirming the diagnosis. We present 4 cases of neuromyelitis optica from a tertiary referral hospital, Royal Hospital, Oman. The criterion of Wingerchuk et al. was used for the diagnosis. All patients had MRI brain and spine and neuromyelitis optica IgG test.

**First patient,** a 29 years old female, was referred to outpatient clinic with a history of an attack of left optic neuritis. Subsequently had 3 recurrent attacks in Rt eye. After each attack she received IV methylprednisolone followed by a tapering dose of oral prednisolone. She had a partial recovery after each attack. Initial CSF oligoclonal bands and NMO IgG were --ve. MRI brain showed non-specific white matter changes. After the 4th attack of optic neuritis she was started on a monthly dose of cyclophosphamide. After the 7th dose she was changed to oral mycophenolate. After 9 months she had a new attack of optic neuritis and same treatment was continued. After 2 years free of relapses mycophenolate was stopped. After 4 months she developed acute paraplegia. MRI spine showed focal T2 hyperintensities from T3 to T5. Repeat NMO IgG was +ve. At this point a diagnosis of

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**P009**

**Inflammatory cytokines in relapsing-remitting multiple sclerosis (RRMS) patients**

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**Iran**

**Background/objectives:** Multiple sclerosis (MS) is a chronic neurodegenerative disease with unknown etiology and variable clinical evolution. Interleukin-33 (IL-33), the most recently discovered member of the Interleukin-1 superfamily, is a dual functional cytokine that has involved in various autoimmune diseases pathogenesis.

Interleukin-27 (IL-27) possesses pro- and anti-inflammatory properties and so participates in pathogenesis of various autoimmune diseases. The objective of the project is to measure some cytokines levels in plasma of multiple sclerosis (RRMS) patients in comparison with healthy control subjects.

**Design and methods:** In a case-control study, plasma was collected from healthy subjects as control group ($n=45$) and relapsing-remitting multiple sclerosis patients ($n=45$). The plasma levels were assessed by ELISA method. Statistical analysis was performed with SPSS (Ver. 16).

**Results:** Plasma levels of IL-27 and IL-33 in MS patients were significantly increased compared to the control subjects (296.60 ± 22.50 vs. 258.71 ± 24.73, P-value = 0.027 and 74.25 ± 21.15 vs. 24.05 ± 3.02, P-value = 0.005 respectively).

**Conclusions:** Our findings revealed the increased IL-27 and IL-33 levels in patients’ group. In conclusion, the inhibition of IL-27 and IL-33 might be a novel and promising therapeutic strategy, especially in the therapy of autoimmune inflammatory diseases. IL-27 and IL-33 play pivotal roles in development of MS and might be a specific marker and therapeutic target for MS inhibition. As important of cytokines in pathogenesis of neurodegenerative diseases, future therapeutic approach for molecular inhibitors should be designed for regulation of disorders progression.

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neuromyelitis optica was made and patient was planned for Rituximab therapy.

Second patient is a 35 years old female, presented to neurology clinic with history of recurrent optic neuritis for which she was followed up by ophthalmologist. After 16 months she was admitted with acute transverse myelitis and optic neuritis. Initial NMO IgG was –ve. MRI brain showed nonspecific T2 hyperintensities. MRI spine showed diffuse T2 hyperintensities from C5 through T10. She was treated with IV methyl prednisolone, and because the response was not favorable, IV immunoglobulins was given, and maintained on prednisolone (tapering dose) and mycophenolate. On out patient follow up she continued to have mild residual weakness. After a year she developed another attack of paraplegia and optic neuritis; and was started on interferon. A repeat NMO IgG was +ve. After 2 months she developed another attack of paraplegia. And after 4 months it also recurred. She was offered treatment with Mitoxantrone but refused.

Third patient is a 24 years old female, transferred to our hospital with 2 months H/O acute transverse myelitis and optic neuritis for which she was admitted to a local hospital and received IV methyl prednisolone. MRI brain showed multiple white matter T2 hyperintensities. MRI spine showed diffuse T2 hyperintensities C2 to T1 and T7-T12. Patient refused lumbar puncture. She was seen in neurology clinic after 2 months with 3 weeks H/O Lt optic neuritis and received IV methyl prednisolone. NMO IgG was +ve and was started on interferon. A repeat MRI brain showed good clinical outcomes once treated with antihelminthic treatment. Patient lost to follow up. She subsequently deteriorated and was started on Rituximab.

Fourth patient is a 46 years old female, admitted with urinary retention, generalized weakness, and altered sensorium. MRI brain: non-specific T2 white matter changes. MRI spine: extensive T2 hyperintensities from C2 to T1 and from T8 to T10 with contrast enhancement. Treated with methyl prednisolone. Had gradual progressive recovery. After 4 months she was admitted with optic neuritis. MRI spine: T2 hyperintensities from lower medulla to T10. Received IV methyl prednisolone. CSF oligoclonal bands was +ve. NMO IgG was +ve. ANCA-PR3 A6 was +ve. Cyclophosphamide treatment was attempted but was not tolerated by patient and was stopped.

Neuromyelitis optica should be suspected in any patient presenting with optic neuritis, transverse myelitis or both with an MRI brain not suggestive of multiple sclerosis. Neither a positive oligo clonal band in CSF, nor an initial negative NMO IgG test can exclude the diagnosis of NMO, as the former may be present in 35% of patients with NOM and the latter can turn positive later on in the disease course. The diagnosis of NMO warrants early initiation of a disease specific therapy to prevent relapses.

Lebanon

Background/objectives: The etiology of isolated myelitis is often difficult to find. Helminthic infections of the spinal cord are thought to be very rare. The diagnosis is usually suspected in patients with myelitis and CSF and/or blood eosinophilia. In the current case-series study, we report 20 cases of isolated Toxocara myelitis recruited at the American University of Beirut, with full description of the clinical presentation, laboratory data, MRI findings, and response to antihelminthic treatment.

Design and methods: Clinical and laboratory data were collected for 20 patients who presented with evidence of spinal cord disease. The clinical presentation included sensory, motor, and autonomic dysfunction, predominantly in the lower extremities.

Results: Patients exhibited a subacute or chronic course; this was either slowly progressive or remitting-relapsing with mild to moderate disability. The patients underwent extensive blood and CSF studies as well as MRI of the spinal cord and brain. Eosinophilia was not a universal finding; only 2 patients had a high eosinophil count in the CSF, although blood eosinophilia was seen in 6 patients. All patients tested positive for Toxocara canis antibodies in the blood and CSF. MRI of the spinal cord revealed a single characteristic lesion with fusiform enlargement that was isointense on T1-weighted images and hyperintense on T2-weighted images. Nodular enhancement was seen after gadolinium injection. MRI of brain was normal in all the cases. Treatment with albendazole, with or without steroids, resulted in marked neurologic improvement and normalization of the MRI in all patients.

Conclusions: The finding of a single inflammatory MRI lesion in the spinal cord with positive Toxocara canis serology in the blood and CSF in cases of subacute or chronic myelitis suggests the diagnosis of Toxocara myelitis, irrespective of the presence of eosinophilia. All these cases showed good clinical outcomes once treated with antihelminthic agents.

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Kuwait

Pediatric onset multiple sclerosis patients tend to have slower disease progression

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Background: Data on the difference between pediatric and adult onset multiple sclerosis (MS) in terms of disease course and progression is scare in our region.

Objective: To compare the demographic and clinical characteristics between pediatric-onset and adulthood-onset MS.

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Methods: Utilizing the national MS registry, we conducted a cross-sectional study to dichotomize MS patients based on age of disease onset (under 17 years or above). Demographics and clinical characteristics (age, symptoms presentation at onset, disease duration, disease course, relapses, EDSS score, and use of disease modifying therapies) were collected. Simple descriptive statistical tests were used to describe numerical and non-numerical values. Variables of both groups were compared using chi-square and Student t-tests.

Results: A total of 984 records of MS patients were assessed; of whom 111 (11.3%) had the disease onset before 17 years of age. Pediatric onset MS patients were more likely to be female (female:male ratio 2.5 vs. 1.85; \( p < 0.05 \)), higher brain-stem/cerebellum (36% versus 26%, \( p < 0.03 \)) and multifocal (15.3% versus 8.1%, \( p < 0.01 \)) manifestations at onset. There was no significant difference in the mean EDSS score between the two cohorts (2.51 versus 2.69; \( p > 0.38 \)) or mean number of relapses (3.38 versus 3.05; \( p < 0.14 \)). The time to reach secondary progression MS was longer in the pediatric-onset MS (14.63 versus 11.03 years; \( p < 0.0001 \)). A higher proportion of the pediatric cohort was treated with aggressive therapy (14.4% versus 8.8%; \( p < 0.05 \)) and required earlier escalation therapy (33.3% versus 27.7%; \( p < 0.04 \)).

Conclusions: MS patients, who had their disease onset before age 17, tend to be female and have brainstem/cerebellar and multifocal symptoms at disease onset. Despite the comparable relapse rate and disability measures between the two cohorts, patients with pediatric onset had slower disease progression.

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P014
Genetics of MS in Saudi Arabia
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Saudi Arabia

Pathogenesis of multiple sclerosis (MS) is poorly understood, evidence suggests that genetic and environmental factors may play substantial roles in disease development. The role of genetics is evident by many reports showing familial aggregation of the disease, high concordance rate among twins, association with MHC and the increased risk among relatives of MS patients. Genome-wide association studies (GWAS) showed an association between subset of single-nucleotide polymorphism (SNPs) and multiple sclerosis.

The Saudi community is a very young population where 54% are below the age of 18 years. It is characterized by large family size and prevalent consanguineous marriages. The incidence and prevalence of multiple sclerosis have been increasing in the last few years regionally in Saudi Arabia and it is expected from demographics point view to further increase. In our local registry we have found that 21% of our patients reported having at least one relative affected. It is not clear if parental consanguinity has any role in non-genetic diseases, especially those with an expected genetic predisposition such as MS.

We have reported that parental consanguinity might be a risk factor for familial multiple sclerosis. WE have studied and reported the common association of single-nucleotide polymorphism (SNPs) and multiple sclerosis by Genome-wide association studies (GWAS). We found that SNPs rs498169 and 10984447 are the two most significant multiple sclerosis linked SNP in our Saudi MS population outside the MHC region. Our results suggest that it is possible to use a more homogenous genetic pool to identify the most significant MS-linked SNPs in the Saudi population, even with a very small sample size. Our finding is in agreement with many other studies that used much larger sample sizes and were performed in many ethnic groups. These data has encouraged us to further study the genetic
basis of MS in the Saudi MS patients. Our ongoing investigations included using whole genome, high-resolution array comparative genomic hybridization (array CGH) of variations in genomic dosage compared to the normal reference dosage within FMS cases as well as Hall exon sequencing and studying the MHC region by junior sequencing of the HAL region. We will present the initial data from two large families.

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P015
Epidemiology of multiple sclerosis in the Middle East: A systematic review and meta analysis
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Iran

Background: The epidemiology of multiple sclerosis (MS) in Middle East has been a major topic of concern during the recent years. A sharp increase in the prevalence and incidence of MS in this region is observed during the recent years. In this study, for the first time, we aimed to provide a comprehensive review regarding the incidence and prevalence of MS across the Middle East.

Objective and methods: A comprehensive literature search was performed using Pubmed, Embase, and, Web of Science. We also did manual search of reference lists from primary articles and relevant reviews.

Results: A total of 29 articles met the inclusion criteria and were reviewed in this study. Incidence data were found in 10 studies and ranged from 0.09 per 100,000 per year in Sistan and Balouchestan, Iran to 26.3 in Isfahan, Iran followed by 6.8 in Kuwait and Dubai. Prevalence was reported in all studies and ranged from 5.1 per 100,000 in Afro-Asian origin patients in Israel to 240 in Liopetri village of Cyprus.

Conclusions: Epidemiologic studies in Middle East area represented a significant increase in the incidence and prevalence of MS over time. There were no prevalence study identified in several Middle East countries such as Saudi Arabia, Iraq, Bahrain, Oman and Yemen. Accordingly our knowledge about epidemiology of MS in the Middle East is extremely limited. Nationwide studies should be conducted to report the epidemiology of the disease in different countries of the region. Such an effort along with further research towards improvement of data on previously studied areas can enable a field to be opened up to identify the patterns of MS in varied genetic backgrounds, and environments of Middle East.

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P016
Evaluation of SNP rs763361 on Gly307Ser gene in multiple sclerosis patients compared to healthy subjects
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Iraq

Introduction: The prevalence of MS 20-60/100,000 in Iran and 73/100,000 in Isfahan. Isfahan is considered as an area with high risk of MS. The patients affected MS interface with physical, psychological, family, occupation, societal, and family problems. MS is a multifaceted gene-environment interactions. Recently, there has been increasing evidence that an non-synonymous exchange (Gly307Ser/rs763361) of the CD226 gene on chromosome 18q22 is linked to some autoimmune diseases such as multiple sclerosis (MS). On the other hand MS has an increasing rate in our area and we know that the genetical model of the disease would be varied in different ethnic and geographic areas, we decided to study the polymorphism of the Gly307Ser gene in Relapsing Remitting Multiple Sclerosis (RRMS) patients in order to identify some disease susceptibility gene variants

Materials and methods: After written consent, blood samples from 200 patients with RRMS (180 females and 20 male; mean age = 31.65 ± 8.3) with clinically and MRI defined RRMS who had recruited to MS research center (Isfahan, Iran), and 200 age and sex matched healthy subjects of blood donors (160 females and 40 male; mean age = 31.74 ± 7.75) with no history of neurological disorders were included in the study. DNA was extracted from whole blood using a commercially available kit (Qiagene) and stored at -20 °C until used for genotyping. SNP analysis was performed using Highy Resolution Melt (HRM) Real Time PCR (Corbett). Differences in allele and genotype frequencies among the respective groups were evaluated by chi square calculation.

Result: According to our findings frequency of the T allele for rs763361 in case group comparing with control group showed different (P=0.035) and genotype frequency was CC (25%), CT (43%), TT (32%) in patient group.

Conclusion: This Case-Control study provided evidence that rs763361 SNP is not correlated to RRMS susceptibility in studied population.

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P017
Role of microchimeric cells in pathogenesis of multiple sclerosis
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Iran

Background: Multiple sclerosis (MS) is a chronic neuroinflammatory disease of central nervous system (CNS). Although the exact etiology of MS in not fully known, it has been shown that an interaction of environmental and genetic factors are
involved. During pregnancy maternal and fetal cells commute back and forth leading to fetal microchimerism in the mother and maternal microchimerism in the child that can persist for years and contribute in pathogenesis of autoimmune diseases. Thus, in this study we aimed to measure levels of microchimeric cells in blood of MS patients.

Methods: In a case control study, blood was collected from women with diagnosis of definite MS (n=40) and healthy women as control group (n=40). DNA was extracted and microchimeric cell level measurement was performed using quantitative Real-Time PCR.

Results: Microchimeric cell level in MS patients was significantly higher than control subjects (p<0.05).

Conclusions: Our results suggested that microchimeric cells have a role in pathogenesis of MS although, further evidence will be required to establish this cells as a modifier in the risk of MS.

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P018
Brain MRI findings in Iranian patients with optic neuritis

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Iran

Background and purpose: Optic neuritis is one of the common causes of unilateral or bilateral visual loss. The most common cause of this disorder is demyelinating disease of the central nervous system (CNS) and most of the patients with optic neuritis will present other signs of multiple sclerosis (MS). The diagnosis depends on the clinical findings, however, magnetic resonance imaging (MRI) is the choice of imaging method for detecting demyelinating lesions. The aim of this study was to investigate the MRI findings in patients with optic neuritis.

Materials and methods: This descriptive-cross sectional study consisted all patients with optic neuritis (n=70) referring to neurology department of Ghaem Hospital in Mashhad, Iran, 2008. The diagnosis was made based on clinical signs and symptoms. Information including demographic details and visual findings was collected through questionnaires. Conventional brain MRI was performed for all patients and evaluated for abnormal findings. We used chi square test for qualitative variables and T-test for quantitative variables.

Results: Thirty-nine (55.7%) patients with optic neuritis were seen with abnormalities in MRI. In this group, 31 (79.4%) cases had plaques in the supratentorial and 22 patients (54.6%) in the infratentorial areas. In 24 cases (61.5%) periventricular region was the most common site with plaques. We observed optic nerve lesions in two (5.1%) patients.

Conclusion: Standard MRI of the brain is useful for detecting CNS lesion, however, it is ineffective in revealing optic nerve lesions. So, appropriate imaging techniques must be used in such patients to find abnormalities in the affected optic nerve.

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P019
Intracranial Germinoma: Very rare mimicker of multiple sclerosis

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United Arab Emirates

Background: Multiple sclerosis (MS) mimickers are neurological conditions that may share clinical, biologic and radiologic features similar to MS. Standard MS treatments often fail.

Objectives: To report a very rare case of intracranial Germinoma with clinical, biological and radiological features similar to MS.

Methods: We report 26 year old Emirati male patient who presented with history of recurrent attacks of neurological dysfunction and recurrent brain stem lesions since 2010.

Results: MRIs of the brain revealed recurrent brain stem T2 hyperintense lesions changing in size and location but remained localized in the brain stem. Initially CSF was positive for OCB so he was diagnosed as clinically isolated syndrome and was started on Rebif injections.

In 2011 he developed another relapse and new lesion appeared in the left side of the brain stem like mirror image of the old right side lesion which has disappeared. The symptoms included episodic diplopia, facial paresthesias with subsequent brainstem symptoms that improve with a high dose of corticosteroids. He developed oral ulceration in 2011. Diagnostic work up excluded all other possibilities and Neuro Behcet’s disease (NBD) was considered, he responded well to Azathioprine and steroid. He remained well but in 2013 he developed relapse and MRI revealed that left sided midbrain has expanded. CSF revealed lymphocytic pleocytosis without OCB. Patient refused brain biopsy. He received three cycles of Infliximab but he deteriorated clinically and radiologically. The behavior of the disease and the lesion was suggestive of MS in the first year and suggestive of NBD in the second and third year, but in the fourth year it was not typical of MS or NBD. Brain biopsy was performed at John Hopkins hospital in USA in April 2014 and the lesion was reported Germinoma responsive to radiotherapy. The tumor disappeared after radiotherapy.

Conclusion: Intracranial Germinoma is very rare intracranial tumor that occurs at 0.7 per million, it is even more rare to be a mimicker for MS. This patient was treated successfully with radiotherapy.

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P020
Comparative investigation of different sequences of Magnetic Resonance Imaging such as FLAIR, T2WI and PDWI in detection of Multiple Sclerosis patients referred to Magnetic Resonance Imaging Department of Imam Khomeini Hospital, Urmia, Iran

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Introduction: Multiple Sclerosis is the most common neurologic disorder that affects the CNS with an inflammatory demyelinating process and the most frequent cause of disability in young people. Diagnosis of multiple sclerosis disease is based on observation, neurologic examination and para clinical assays. Obviously Magnetic Resonance Imaging imaging changes the approach to the disease and it is the selective modality for diagnosis, monitoring and prognosis assessment. These years Multiple Sclerosis is diagnosed and treated with the use of Magnetic Resonance Imaging technique. We have several studies about Multiple Sclerosis and its correlation with Magnetic Resonance Imaging. Since the Multiple Sclerosis plaques have different importance in various era (such as peri-ventricular, centrum semi-ovale, corpus callosum, ventricles and spine). Thus one Multiple Sclerosis plaque in infra tentorium and 9 peri-ventricular have the same value and in various era. T1, T2, FLAIR, PD and STIR have different sensitivities in diagnosis of Multiple Sclerosis; for example normal spine Magnetic Resonance Imaging in T2 and FLAIR sequences may show heterogeneous lesion by STIR sequence. We were encouraged to evaluate the relation of Multiple Sclerosis plaques and difference of their detectivity with different sequences.

Methods: We compared 50 Multiple Sclerosis patients Magnetic Resonance Imaging images in FLAIR, T2WI, PDWI sequences with radiologist guidance and evaluated the correlation of the Magnetic Resonance Imaging findings with sex and age of those patients.

Results: We found a significant difference between sex and PDWI Magnetic Resonance Imaging sequences (P value=0.001). There were no significant difference between other Magnetic Resonance Imaging sequences (FLAIR and T2WI) and age or sex.

Conclusion: Based on our study, PDWI Magnetic Resonance Imaging sequences is superior than FLAIR or T2WI sequences in detection of Multiple Sclerosis specific plaque in cerebellum.

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P021
Role of histamine and diamine oxidase enzyme in Multiple Sclerosis

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Iran

Background/objectives: Multiple Sclerosis (MS) is a chronic inflammatory disease of the Central Nervous System (CNS) which is characterized by demyelination and axonal loss. It has been shown that Diamine Oxidase (DAO) enzyme degrades histamine. Histamine has a role in increasing permeability of Blood-Brain Barrier (BBB) that leads to immune cells infiltration of CNS and has a proinflammatory effect via H1R receptor. The objective of the project is to measure serum levels of histamine and DAO enzyme of patients with Relapsing Remitting Multiple Sclerosis (RRMS) in comparison with healthy control subjects.

Design and methods: In a case-control study, venous blood was collected from RRMS patients (n=60) and healthy subjects (n=60) as control group. The serum levels of histamine and DAO enzyme were measured using ELISA method.

Results: Decreased serum level of DAO enzyme and elevated level of histamine has been observed in patients with RRMS in comparison with control group (P value<0.05).

Conclusions: It should be considered that although defect of DAO enzyme can cause elevated serum levels of histamine in MS patients, low level of this enzyme can also elevate serum levels of histamine which can contribute in pathogenesis of MS.

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P022
Role of adiponectin in multiple sclerosis

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Iran

Background/objectives: Multiple sclerosis (MS) is an autoimmune disease of human central nervous system in which chronic inflammation play a pivotal role. On the other hand, production of anti-inflammatory factors by some parts of body including adipose tissue may have protective effects in MS patients. So, in this study we tested the hypothesis that adiponectin has a protective role in MS.

Design and methods: In a case-control study, venous blood was collected from MS patients (n=50), and healthy subjects (n=40) as control group. Plasma levels of adiponectin were measured using ELISA method.

Results: In this study, significantly decreased serum levels of adiponectin were found in MS patients compared with control group (P-value<0.05).

Conclusions: Our data suggested a protective role of adiponectin in MS patients which can be considered as a therapeutic strategy; however further studies are needed to demonstrate adiponectin as a treatment of MS.

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P023
Investigation of Oncostatin M protein expression in Iranian relapsing remitting multiple sclerosis patients
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Iran

Background: Oncostatin M (OSM) is an interleukin-6 (IL-6) cytokine secreted by diverse immune cells in order to moderate cell proliferation, survival, differentiation, and inflammation by effecting gp-130 cell surface receptors. Relapsing remitting multiple sclerosis (RRMS) is the common type of MS influencing 85% of MS patients. It seems that up-regulation of cytokines has an undeniable role in arising autoimmune mechanisms and symptoms. Isfahan province, Iran, is an area with an alarming increase in incidence and prevalence of MS in recent years. Thus, we focused on the investigation of OSM as an immune-dependent risk factor in disease patho-physiology in Isfahan RRMS patients.

Objectives: To measure the association between OSM plasma level in MS patients and the healthy subjects. To evaluate the correlation between the demographic info such as age, sex, EDSS, drugs, and OSM concentration in cases.

Methods: Blood sample from 60 RRMS patients and 30 healthy subjects between 15 and 40 years was gathered on EDTA and the evaluation on OSM in their plasma was accomplished utilizing EASTBIOPHARMA enzyme-linked immunosorbent assay (ELISA) kit. The statistical analysis was performed utilizing SPSS software.

Results: Data showed a significant higher OSM plasma level in the cases than the healthy donors (P value = 0.05).

Conclusions: As the first step of studying IL-6 cytokine family in autoimmune diseases in Iranian population, we accomplished to approve the OSM active role in RRMS patients of Isfahan province. Further future investigation of IL-6 family such as “studying IL-6 in central nervous system (CNS) plaques”, “genetic polymorphisms in association with MS”, and “revealing newer aspects of their implications in cellular pathways” might result in development of immunotherapy and diagnosis in chronic autoimmune diseases of the CNS.

P025
A study of general health status and depression in multiple sclerosis patients and its relation with some of their individual characteristics in the Urmia City, Islamic Republic of Iran
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Iran

Introduction: Mental health is a branch of general health that mostly discusses about decreasing psychological disorders in community. Somatic illness is known as a prominent risk factor affecting psychological health. Multiple sclerosis is classified in central nervous system disorders that destroys different segments of brain and spinal cord, by immune system attacks.

Depression is associated with most of multiple sclerosis patients and unfortunately suicidal thoughts is obvious in these patients. This problem effects cognitive abilities and quality of life of patients.

Materials and method: In this analytic/descriptive study, 142 multiple sclerosis sufferers admitted in Imam Khomeini Hospital, Neurology Department of Urmia University of Medical Science, were evaluated after randomized selection. Then the patients were educated about questionnaire. Data collection was carried out using 2 questionnaires, one General Health Questionnaire GHQ-28 and other Beck Depression

P024
Effects of recurrent fasting on fatigue and quality of life in patients with multiple sclerosis
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Iran

Background: Fasting is one of the recommended worships of several great religions in the world. During the Ramadan, circadian rhythm and pattern of eating changes results in physiological, biochemical and hormonal changes in the body. Many of Muslims with medical considerations ask their physicians about the feasibility and safety of fasting during Ramadan. We proposed this study to assess the effect of Ramadan fasting on the quality of life and fatigue in multiple sclerosis (MS) patients.

Patients and methods: Patients with definite diagnosis of relapsing-remitting MS according to McDonald’s criteria and with mild disability (expanded disability status scale (EDSS) score = 1-5.5) were included in this study. Fatigue and quality of life were assessed using the validated Persian versions of Modified Fatigue Impact Scale (MFIS) and Multiple Sclerosis Quality of Life-54 (MSQOL-54) questionnaires, respectively.

Results: Eighteen patients were enrolled in our study. The mean total score of MSIF after fasting was 26.94 ± 16.65 versus 25.50 ± 13.81 before fasting (P = 0.58). The mean physical health composite and mental health composite of quality of life increased significantly after fasting (P = 0.008 and P = 0.003 respectively).

Conclusion: Our results have shown that fasting during Ramadan can improve the quality of life in MS patients. Furthermore, no unfavorable effect was observed between fatigue before and after fasting. However, larger prospective clinical studies are needed to shed more light on our results.

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P026
Real world use of fingolimod in patients with relapsing remitting multiple sclerosis: A retrospective study utilising the national multiple sclerosis registry in Kuwait

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Kuwait

Background: Fingolimod is an oral sphingosine-1-phosphate-receptor modulator, which has demonstrated efficacy in clinical trials and recently been approved for multiple sclerosis (MS) treatment in Kuwait. Post-marketing studies are important to demonstrate real-life efficacy and safety.

Objective: To examine the efficacy and safety of fingolimod treatment in a clinical setting.

Methods: Using the national Kuwait MS registry, relapsing remitting MS (RRMS) patients who had been prescribed fingolimod for ≥6 months were retrospectively identified. Three monthly clinical evaluations and 6 monthly MRIs were performed. Patient status pre- and post-treatment was compared using chi-square and Student t-tests.

Results: A total of 175 patients were included: 75.4% female (n=132); mean age 33.3±9.2 years; mean disease duration 7.2±5.2 years; mean fingolimod use 21.7±9.1 months. Most had used previous disease-modifying therapy (78.9%; n=138), mainly interferons (66.9%; n=117). Twenty three patients (11.4%) discontinued/withdrew fingolimod; of whom 8 had relapses. The proportion of relapse-free patients improved significantly (86.3% vs. 32.6%; p<0.001), while the proportion of patients with MRI activity decreased (18.3% vs. 77.7%; p<0.001). Mean Expanded Disability Status Scale (EDSS) score at last visit improved when compared to pre-treatment (2.26±1.49 vs. 2.60±1.44; p=0.03). Forty three (24.6%) patients experienced adverse events; headaches and lymphopenia were the most common reported adverse events. Conclusion: Fingolimod treatment was associated with reduced relapse and MRI activity, and improved EDSS score. Discontinuation/withdrawal rates and adverse events were low. Fingolimod presents a promising treatment for MS in Kuwait.

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P027
Severe reactivation of multiple sclerosis after discontinuation of fingolimod: An IRIS-associated phenomenon

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Kuwait

Background: Data on the mechanism of rebound activity post-withdrawal of fingolimod in multiple sclerosis (MS) patients is scarce.

Objectives: To describe a patient with multiple sclerosis (MS) who developed severe reactivation after discontinuation of fingolimod.

Method: Case report and review of literature.

Results: A 36-year old woman with aggressive MS since 1998 was switched to fingolimod due to JC virus seropositivity after receiving 24 infusions of natalizumab. The 8-week natalizumab washout period was unremarkable. While on fingolimod, she developed severe lymphopenia (0.2 × 109/L) necessitating withdrawal of fingolimod. Seven weeks later, she presented with dysarthria and right-sided pyramidal weakness, which rapidly progressed to drowsiness and coma within few days. The clinical presentation and radiological features were suspicious for progressive multifocal leukoencephalopathy (PML). CSF JCV DNA was negative. She received plasmapheresis and maintenance corticosteroids afterwards. A clinical improvement was observed within 14 days but she sustained significant hemiparesis requiring extensive rehabilitation. The final diagnosis of severe reactivation of MS post-withdrawal of fingolimod was established. It is postulated that the significant reactivation of MS was due to its association with an Immune Reconstitution Inflammatory Syndrome (IRIS) given the abrupt rise in lymphocyte count after fingolimod withdrawal.

Conclusion: Our case highlighted the diagnostic dilemma in JC virus seropositive patients who developed relapses after discontinuing potent immunomodulators. Patients who discontinued fingolimod might be at risk of developing IRIS resulting in disease reactivation in the washout period.

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P028
The risk of short-term relapse in patients switching from natalizumab to fingolimod

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Objectives: To examine the efficacy and safety of fingolimod in clinical trials and recently been approved for multiple sclerosis (MS) treatment in Kuwait. Post-marketing studies are important to demonstrate real-life efficacy and safety.

Methods: Using the national Kuwait MS registry, relapsing remitting MS (RRMS) patients who had been prescribed fingolimod for ≥6 months were retrospectively identified. Three monthly clinical evaluations and 6 monthly MRIs were performed. Patient status pre- and post-treatment was compared using chi-square and Student t-tests.

Results: A total of 175 patients were included: 75.4% female (n=132); mean age 33.3±9.2 years; mean disease duration 7.2±5.2 years; mean fingolimod use 21.7±9.1 months. Most had used previous disease-modifying therapy (78.9%; n=138), mainly interferons (66.9%; n=117). Twenty three patients (11.4%) discontinued/withdrew fingolimod; of whom 8 had relapses. The proportion of relapse-free patients improved significantly (86.3% vs. 32.6%; p<0.001), while the proportion of patients with MRI activity decreased (18.3% vs. 77.7%; p<0.001). Mean Expanded Disability Status Scale (EDSS) score at last visit improved when compared to pre-treatment (2.26±1.49 vs. 2.60±1.44; p=0.03). Forty three (24.6%) patients experienced adverse events; headaches and lymphopenia were the most common reported adverse events. Conclusion: Fingolimod treatment was associated with reduced relapse and MRI activity, and improved EDSS score. Discontinuation/withdrawal rates and adverse events were low. Fingolimod presents a promising treatment for MS in Kuwait.

http://dx.doi.org/10.1016/j.msard.2014.09.176
Kuwait

Background: Risk stratification is an important pillar in treating high-risk multiple sclerosis (MS) patients. In JC virus seropositive patients, switching natalizumab to fingolimod is often considered after analyzing the risk versus benefit ratio.

Objectives: To determine the short-term risk of relapse after switching natalizumab to fingolimod in MS patients, and to assess its association with demographic and clinical parameters.

Methods: Data of MS patients who were prescribed fingolimod and natalizumab were extracted from the national MS registry. Demographics, clinical characteristics and duration of disease modifying therapies were collected. The risk of relapse of patients who were switched from natalizumab to fingolimod was compared to non-switchers. A multivariate analysis of specific demographics and clinical characteristics was conducted.

Results: Twenty nine patients were switched from natalizumab to fingolimod due to JC virus seropositivity. The mean duration of fingolimod exposure was 8.8 months. Men were more likely to continue on natalizumab (20.7% versus 41.7%; \( P = 0.04 \)). The mean disease duration was significantly higher in the switcher group (10.9 versus 6.29; \( P < 0.0001 \)). The proportion of patients with relapses was higher in patients who switched to fingolimod compared to those who continued on natalizumab (13.8% versus 4.2%; \( P < 0.0001 \)). There was a significant negative association between the length of natalizumab exposure and relapse rate on fingolimod (\( r = -0.415; \) \( P = 0.025 \)). Longer washout duration was significantly associated with higher risk of relapses (\( r = 0.416; \) \( P = 0.025 \)).

Conclusions: The short-term risk of relapse in patients switched to fingolimod was higher than those who continued natalizumab.Switchers were more likely to be women and had longer disease duration. Patients, who stayed longer on natalizumab before switching to fingolimod and had short washout periods, had lower rates of relapses. Further studies are needed to assess the long-term risk of relapses in patients who switched from natalizumab to fingolimod.

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P029

Efficacy and safety of fingolimod treatment in multiple sclerosis: The clinical experience of the AUBMC Multiple Sclerosis Center in Lebanon

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Lebanon

Background: Fingolimod is the first oral disease-modifying therapy (DMT) approved by the US Food and Drug Administration (FDA) in September 2010 and by the European Medicines Agency (EMA) in March 2011 for the treatment of relapsing-remitting multiple sclerosis (RRMS). The available efficacy and safety data of fingolimod derives from the two completed Phase III clinical trials, FREEDOMS and TRANSFORMS which demonstrated a reduction in the relapse-rate, disability progression and gadolinium-enhancing lesions compared to placebo and intramuscular interferon beta 1a. However, there are still no or few data about the real-world efficacy and safety of fingolimod, at least after one year of treatment in the Middle East region.

Objective: To describe our clinical experience with fingolimod looking at different outcomes including efficacy, tolerability and safety in multiple sclerosis (MS) patients presenting to our MS Center.

Methods: MS patients who were treated with fingolimod and visited our AUBMC-MS Center from October 2011 to December 2013 were identified. Demographics, MS disease related variables, first-dose and follow up recorded adverse events and efficacy outcomes were extracted from our medical charts. Main efficacy outcomes were the annualized relapse rate (ARR), the disability progression (EDSS) and the magnetic resonance imaging (MRI) activity.

Results: Eighty seven RRMS patients who were prescribed fingolimod were included in the analysis. Fifty eight were women and 29 men. Mean disease duration was 6.8 ± 6.1 years and mean EDSS at fingolimod initiation was 2.33 ± 1.4. Eight patients received fingolimod between 3 and 5 months, 26 patients received treatment between 6 and 11 months, 32 patients between 12 and 23 months, and 21 patients >24 months. First dose observation was uneventful in all patients. Within a period of 14.9 ± 8 months, treatment was discontinued in 21 patients (24.4%) due to progression of the disease to secondary progressive MS (n=6), lack of efficacy (n=10), pregnancy (n=1), recurrent infections (n=1), varicella zoster virus (VZV) radiculitis (n=1), and patients’ personal decision (n=2). ARR in the year previous to fingolimod treatment was 1.31 and decreased to 0.26 during the overall treatment period. In patients treated with fingolimod for <12 months (n=53), 60.4% were free from EDSS progression and 62.3% were free from MRI activity.

Conclusion: In our study patients, fingolimod was safe, well tolerated and effective in reducing disease activity and progression of disability.

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P030

Fingolimod (Gilenya) may improve the chances of conception in women with multiple sclerosis (MS) associated with secondary infertility

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United Arab Emirates

Background: Fingolimod is sphingosine-1-phosphate (SIP) receptor modulator which is indicated in patients with relapsing remitting multiple sclerosis (RRMS) and it is
contraindicated in pregnancy. Many RRMS patients have infertility due to many pathological factors at hormonal and immunological levels as well as hypthalamic dysfunction.

Objectives: We report five women with RRMS and secondary infertility who lost hope of conceiving so they took Fingolimod without any contraceptive measures. They conceived and three gave birth to normal babies and two expected to deliver in few months.

Methods: Between 2010 and 2014, 148 patients with RRMS received Fingolimod, 112 were females. Five of them conceived after 3-7 years history of infertility and none of them used any assected measures for conception or contraception assuming that they are infertile and each of them has 2-5 children in the past. Local gynecological causes were excluded. Three of them have autoimmune thyroid disease. They were aged 25-40 years with 2-12 years duration of RRMS. Their EDSS ranged from 1.0 to 4.0. They received fingolimod 0.5 mg daily for 5 months to 2 years prior to becoming pregnant. Fingolimod was discontinued 3-8 weeks after conception. Three patients gave birth to normal babies and the other two expected to deliver in few months.

Results: We identified five women with RRMS and secondary infertility who conceived after taking Fingolimod. They were infertile for 3-7 years. We suggest that Fingolimod may improve chances of conception in some infertile women at hormonal and immunological levels. They may have antibodies affecting the fertilization process, and Fingolimod may modulate and prevent this process. Also it may work at hypothalamic level.

Conclusion: Fingolimod may improve conception in women with RRMS and secondary infertility. It may work at hormonal and immunological levels. The exact mechanism is unknown. SIP receptors exist in the CNS but it is not known if they have any role in the fertilization process. Further studies are recommended.

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P032

Consistent reduction in the annualized rate of brain volume loss across phase 3 core and extension trials of fingolimod in relapsing multiple sclerosis

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Background/objective: In phase 3 trials, fingolimod 0.5 mg or 1.25 mg daily reduced brain atrophy versus placebo over 2 years (FREEDOMS and FREEDOMS II), and versus interferon beta-1a IM (IFNβ-1a) over 1 year (TRANSFORMS). Rates of brain atrophy on continuous fingolimod treatment were sustained in extension studies, but diminished number of completers might limit interpretability. We estimated the continuous effect of fingolimod treatment on brain volume (BV) loss, using all data from phase 3 and extension trials.

Design/methods: We determined annualized percentage BV change (PBVC) for all patients individually, to account for variable treatment-time exposures. During phase 3 studies and extensions, annualized PBVC was calculated for each patient from fingolimod treatment initiation until last available scan. Descriptive analyses included cohorts of patients receiving fingolimod 0.5 mg continuously, and all patients receiving fingolimod (combined-dose group).
continuous for up to 60 months from phase 3 baseline. Further analyses, using these dose-group definitions, were also conducted for up to 24 months from extension baseline to compare annualized PBVC among patients after switching to fingolimod from placebo or IFNβ-1a, with that determined on long-term fingolimod treatment.

Results: Respectively, mean annualized PBVC in the long-term continuous fingolimod 0.5 mg and combined-dose groups was FREEDOMS, 0.45% (n = 372), 0.42% (n = 718); FREEDOMS II, 0.41% (n = 279), 0.38% (n = 553); TRANSFORMS, 0.31% (n = 379), 0.31% (n = 728); and after switching was FREEDOMS, 0.49% (n = 135), 0.44% (n = 259); FREEDOMS II, 0.47% (n = 47), 0.43% (n = 103); TRANSFORMS, 0.25% (n = 130), 0.19% (n = 267).

Conclusion: Annualized PBVC during fingolimod phase 3 and extension studies demonstrate a consistent low rate of brain atrophy, supporting previous observations from individual studies. After switching to fingolimod from the comparator, patients exhibited similar atrophy rates to those initially randomized to fingolimod. Annualized PBVC calculation incorporates all available PBVC data, despite varying treatment-time exposures, and partly addresses discontinuation bias that may occur in long-term analyses.

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P034

Four-year Expanded Disability Status Scale (EDSS) outcomes in patients treated with fingolimod in the Phase 3 and extension trial program

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Background/objective: Assessment of long-term disability status is important for characterizing the benefit-risk profile of disease modifying MS therapies, although a lack of control group and selective drop-outs may produce bias. Here we explored longitudinal Expanded Disability Status Scale (EDSS) outcomes in fingolimod treated patients in the FREEDOMS, FREEDOMS 2 and TRANSFORMS Phase 3 and extension trials.

Design/methods: EDSS data from patients initiating fingolimod in Phase 3 or extension were pooled for post-hoc analysis. Kaplan-Meier (KM) estimates of proportions not reaching EDSS 4, 6 and 7 were calculated from start of fingolimod 0.5 mg or any dose (all-FTY). Proportions with EDSS score less than or equal to EDSS 4, 6 and 7 were calculated from start of fingolimod 0.5 mg or any dose (all-FTY). Proportions with EDSS score less than or equal to the baseline score at start of fingolimod (FTY-BL), and decreased compared to FTY-BL, after 24, 36, and 48 months were analyzed descriptively.

Results: The pooled 0.5 mg/all-FTY (N = 1641/3283) cohorts had median (25th, 75th percentile) treatment exposures of 967/918 (556/1343, 482/1325) days. KM estimates of proportions not reaching EDSS 4, 6 and 7 were 71.3%, 87.8% and 96.7% for 0.5 mg and 69.5%, 87.0% and 96.3% for all-FTY. At months 24 (N = 1324/2580), 36 (N = 909/1727) and 48 (N = 587/1110), the proportions with EDSS score less than or equal to FTY-BL were 67.9%, 64.7% and 66.8% for 0.5 mg and 69.0%, 66.4% and 66.2% for all-FTY. Of these, EDSS was improved at months 24, 36 and 48 compared to FTY-BL in 15.7%, 17.4% and 17.4% for 0.5 mg and 17.5%, 18.7% and 18.5% for all-FTY.

Conclusion: Most Phase 3 and extension trial patients treated with fingolimod in either dose for up to 4.9 years remained free of the need for walking assistance.
Approximately two-thirds of fingolimod patients continuing on treatment had the same or better EDSS score after 2, 3 and 4 years of treatment, while 16-18% had improved scores. Absence of a control group and selective drop-outs may bias these results.

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P035

Long-term safety of fingolimod: Interim evaluation of data from the longterms trial
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Background/objective: Multiple sclerosis patients participating in the fingolimod phase 2/3 core and extension studies were eligible to transfer to LONGTERMS, an open-label, multicentre, single-arm, long-term safety and tolerability study. Here, we compared the long-term fingolimod (0.5 mg dose) safety data in the LONGTERMS study (up to data cut-off), with shorter-term (1-2 years) safety data pooled from the randomized controlled trials.

Design/methods: In this study, patients from two cohorts (Core Cohort, CC; LONGTERMS cohort, LC) were compared. Patients in CC [n=1212; median (range) exposure: 1.6 (0.01-2.4) years] were pooled from the fingolimod 0.5 mg arms of the core phase 2/3 trials. Patients in LC [n=1655; median (range) exposure: 3.7 (0.01-7.4)] included CC and phase 2/3 core comparator patients transitioned to fingolimod 0.5 mg in their extensions. Incidence rates (number of patients experiencing ≥1 event/100 patient-years) were determined for adverse events (AEs) of special interest.

Results: The incidence rates for AEs of special interest were similar or lower in LC compared with CC, for: infections (LC, 68.3; CC, 91.0), skin cancer and other malignant neoplasms (LC, 0.7 and 0.4; CC, 1.3 and 0.4), thromboembolic events (LC, 0.9; CC, 1.0), hypertension (LC, 3.6; CC, 5.5), respiratory conditions (LC, 1.2; CC, 1.5) and reactivation of viral infections (LC, 5.3; CC, 5.9).

Conclusion: With long-term use of fingolimod (median: 3.7 years), incidence rates for AEs of special interest were comparable with those in controlled studies. There were no new safety signals detected with the long-term use of fingolimod.

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P036

Siponimod (BAF312) for the treatment of secondary progressive multiple sclerosis: Design of the phase 3 EXPAND trial
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USA, UK, Germany, France, Switzerland

Background/objective: Siponimod (BAF312), a next generation selective sphingosine 1-phosphate (S1P)-1 and -5 receptor modulator administered once-daily orally reduces lymphocyte infiltration into the CNS and may have direct CNS effects. Experimental studies indicate that siponimod readily crosses the blood-brain-barrier and may modulate neurobiological processes via S1P1 and S1P5 receptors on astrocytes and oligodendrocytes. In relapsing MS, S1P receptor modulation reduces accumulation of neurological impairment and slows progression of brain atrophy. These clinical and radiographic effects suggest that S1P receptor modulation might be effective in secondary progressive MS (SPMS). We present here the design of a phase 3 study intended to demonstrate the efficacy, safety and tolerability of siponimod compared to placebo in individuals with SPMS.

Design/methods: EXPAND (Exploring the efficacy and safety of siponimod in patients with secondary progressive multiple sclerosis) is a multicenter, randomized, double-blind, parallel-group, placebo-controlled variable treatment duration study (anticipated range 23-42 months). Approximately 1530 individuals, aged 18-60 years with SPMS (EDSS score of 3.0–6.5) will be randomized. Treatment will start with a 6-day dose titration (0.25, 0.25, 0.5, 0.75, 1.25, 2 mg) and continue at a dose of 2 mg or placebo (2:1). The primary objective of the study is to demonstrate the efficacy of siponimod relative to placebo in delaying the time to 3-month confirmed disability progression as measured by EDSS. The study has 90% power to detect a 30% reduction in the risk of 3-month confirmed disability progression (hazard ratio 0.70). Study will be stopped when 374 events (patients with progression) are observed.

Results: Details of study design will be presented at the congress.

Conclusion: New therapies, that are effective in delaying disability progression in patients with SPMS, are an important unmet medical need. The EXPAND study will explore the potential of siponimod in SPMS and help advance the knowledge of SPMS pathophysiology.

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P037

Categorical change in T2 lesion volume and clinical outcomes in the Phase III FREEDOMS and its extension study, evaluating fingolimod in patients with relapsing-remitting multiple sclerosis
D. Jeffery, E.V.D. Cantogno, D.P. Meier, M. Meinel, P. Chin, A. Shamim
Libya 2011

Background/objective: Clinical evidence in relapsing-remitting multiple sclerosis (RRMS) suggests an association between changes in T2 lesion volume (LV) and confirmed disability progression (CDP). Here, we investigated the clinical outcomes in the FREEDOMS study and its extension, by categorical change in T2LV.

Design/methods: Post-hoc analyses were performed in the overall fingolimod 0.5 mg, and placebo groups in patients with baseline and M24 evaluations for T2LV (1057/1272 patients overall; 372/425 fingolimod 0.5 mg; 342/418 placebo). Categorical subgroups were defined based on change in T2LV from baseline to M24: decreased (500 mm³). Clinical outcomes included M3 and M6 CDP measured by mean change in Expanded Disability Status Scale (EDSS) score and Multiple Sclerosis Functional Composite (MSFC) z-scores. Additional analyses assessed the relationship between LV change in the first two years and disability through M48.

Results: At M24 the proportions with decreased, stable and increased T2LV were 15.5% (164/1057), 59.9% (633/1057), and 24.6% (260/1057), respectively. More and increased T2LV were 15.5% (164/1057), 59.9% (633/1057), and 24.6% (260/1057), respectively. More and increased T2LV were 15.5% (164/1057), 59.9% (633/1057), and 24.6% (260/1057), respectively. Compared to stable or decreased LV, increased LV was associated with worsening disability at M24 (LV [decreased/stable/increased], all patients): change in EDSS [−0.01/−0.01/0.14] and MSFC [0.08/0.01/−0.08] scores; proportion with M3 [16.4%/17.4%/21.7%] and M6 CDP [11.3%/14.0%/19.0%]. Results within fingolimod and placebo groups were consistent with this overall pattern, and LV in the first two years was similarly associated with disability by M48.

Conclusion: Two year categorical T2LV change was related to disability over 24 and 48 months in RRMS patients. Patients with increased T2LV exhibited higher mean changes in EDSS and MSFC and more 3- and 6-M CDP/shorter time to CDP. Fewer fingolimod treated patients had increased T2LV while higher proportions demonstrated stable or decreased LV than placebo.

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P038

Impact of stop β interferon on 20 cases of relapsing remitting multiple sclerosis in BMC Benghazi-Libya 2011

M. Agiela

Libya

Background: Multiple sclerosis is a common demyelinating and inflammatory disease of the CNS with a presumed autoimmune etiology. Interferon β have been used for relapsing remitting multiple sclerosis through its regulatory properties on T-cell activation and cytokines production.

Objectives: During the war Benghazi-Libya (17 February 2011 revolution) multiple sclerosis patients have got stopped β interferon because unavailability of drugs which allow to evaluate the efficacy of β interferon on relapsing remitting multiple sclerosis regarding frequency and severity of relapses during months of stopping it.

Methods: Twenty cases of relapsing remitting multiple sclerosis aged 18-55 years of disease duration 1-11 years were on β interferon none of them have a relapse studied in comparative retrospective prospective study disease relapse, none of the patients has relapse, no relapse, its severity, nature of relapse and respond to Rx in months of stoppage of β interferon and before stop it using frequency, percentage and P value.

Results: Fifteen cases of 20 got relapse (75% relapse rate) significant rate, 3 cases have more than 1 relapse, 12 got severe relapse, 11 cases admitted to hospital, all patients received Methylprednisolone 1 g (3-5 days), 13 got complete respond and 2 incomplete.

Conclusion: β Interferon is efficient in prevention of relapse and decreasing severity of relapse in relapsing remitting multiple sclerosis.

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P039

Natalizumab treatment for multiple sclerosis: Middle East and North Africa regional recommendations for patient selection and monitoring


Egypt, Saudi Arabia, Jordan, Tunisia, Lebanon, Iran, Kuwait

Background: Natalizumab improves clinical and magnetic resonance imaging (MRI) outcomes and reduces disability progression in relapsing-remitting multiple sclerosis (MS). It is recommended for patients who have highly active disease or those who fail first-line disease modifying therapies (DMTs). Progressive multifocal leukoencephalopathy (PML) is a rare, serious adverse event associated with natalizumab.

Objective: To develop regional recommendations for the selection and monitoring of MS patients to be treated with natalizumab in the Middle East and North Africa (MENA) region.

Methods: After a review of available literature, a group of neurologists with expertise in the management of MS met to discuss the evidence and develop regional recommendations to guide appropriate use of natalizumab in the region.

Results: Natalizumab is considered as a first-line therapy in highly-active naive MS patients with disabling relapses in association with MRI activity. In patients with breakthrough
disease, natalizumab is recommended as an escalation therapy based on its established efficacy in Phase III studies. Several factors including prior immunosuppressant therapy (IS), anti-JC virus (JCV) antibody status and patient choice may contribute to the selection of natalizumab. Sero-negative patients should continue natalizumab therapy along with anti-JCV antibody testing every 6 months and annual MRI. In sero-positive patients, the expected benefits of natalizumab treatment have to be weighed against the risks. Anti-JCV Ab index may further differentiate PML risk in sero-positive patients with no prior IS therapy. In sero-positive patients who received 24 natalizumab infusions, the risk-benefit ratio should be reassessed. Accordingly, more clinical vigilance and frequent MRI scans (every 4-6 months) is recommended.

Conclusion: These recommendations have been developed to guide MENA neurologists in selecting appropriate MS patients for natalizumab treatment and monitoring them to minimize the risk of PML.

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PO40

Good cardiac safety in patients with relapsing remitting multiple sclerosis upon first fingolimod dose

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Germany

Background/objective: Fingolimod, a sphingosine 1-phosphate receptor (S1PR) modulator, is approved for the treatment of relapsing-remitting multiple sclerosis (RRMS). Following treatment initiation, fingolimod activates S1PR at the surface of cardiac myocytes, resulting in transient pulse rate reduction, and in rare cases in atrioventricular conduction blocks. The START-study characterizes the cardiac safety profile of fingolimod treatment initiation in a RRMS patient population.

Design/methods: The START study is a prospective, 1-week, open-label study enrolling up to 7000 RRMS patients in >250 centers in Germany, according to the EU label criteria of fingolimod. The study consists of a screening period, a baseline visit, and a final visit after one week. The procedure at baseline is as follows: prior to the first intake of fingolimod, a 12-lead ECG is recorded. After the first dose, a continuous 6 h Holter ECG is carried out, while pulse and blood pressure are measured simultaneously, every hour. A final 12-lead ECG is performed afterwards. In 200 patients, diagnostics include a 24 h ECG during screening and at baseline. All ECG recordings are centrally evaluated by cardiologists.

Results: In a first, interim analysis based on 599 patients, there was no Mobitz type II 2nd degree AV-block. Only 1.4% and 0.3% of patients developed a Mobitz type I 2nd degree block and a 2:1 2nd degree AV block, respectively. Additionally, data regarding QT intervals after fingolimod treatment initiation will be available. The new data set will also be analyzed with regard to the potential impact of comedication on AV-conduction, relevant for sub-groups of RRMS patients, as symptomatic treatments upon occurrence of cardiac events.

Conclusion: This national study confirms the good cardiac safety profile of fingolimod, which has already been documented in the previous pivotal multicenter trials, leading to approval. Additionally, the possible impact of comedication on AV-conduction, relevant for sub-groups of RRMS patients, is addressed.

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PO41

Phase 2 BOLD extension study efficacy results for siponimod (BAF312) in patients with relapsing remitting multiple sclerosis

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USA, Germany, Switzerland, Spain

Background/objectives: In the adaptive dose-ranging, 6- or 3-month BOLD study in patients with relapsing-remitting multiple sclerosis, once-daily siponimod (BAF312) showed dose-dependent reduction of combined unique active lesion number and annualized relapse rate (ARR); near-maximal effects were observed at 2 mg. Here, we report the efficacy findings of first 12 months of the extension (representing >18 or 15 months of total treatment).

Design/methods: Patients either continued on siponimod doses assigned in the core phase or were re-randomized from placebo to siponimod 10, 2, 1.25, 0.5 and 0.25 mg: 33, 29, 43, 29 and 50 patients comprised each dose group, respectively. Patients had >7 days (washout time) study drug interruption between core and extension phases to enable siponimod dose titration from 0.25 mg over the first 10 days. Magnetic resonance imaging (MRI) was performed at extension baseline, month 6 and month 12.

Results: 263/297 (88.6%) patients completed the core study; 184 of these (62.0%) entered the extension. The following data pertain to patients taking 10, 2, 1.25, 0.5 and 0.25 mg: 33, 29, 43, 29 and 50 patients comprised each dose group, respectively. Patients had >7 days (washout time) study drug interruption between core and extension phases to enable siponimod dose titration from 0.25 mg over the first 10 days. Mean gadolinium-enhancing lesion numbers at extension month 12 were: 0.1, 0.5, 0.1, 0.6, 0.8 (compared with 1.7, 1.4, 1.8, 3.1, 1.3 at core study baseline, and 1.7 in placebo at month 6). Mean numbers of new/enlarged T2 lesions at extension month 12 were 0.4, 0.6, 0.2, 1.7 and 1.7, and ARRs were 0.27 (95% confidence interval, 0.14-0.52), 0.18 (0.08-0.42), 0.13 (0.06-0.28), 0.34 (0.18-0.64) and 0.33 (0.20-0.54). No new safety issues were observed.

Conclusion: Over the 12-month extension, MRI-assessed inflammatory lesion activity and ARRs remained low, particularly in the 1.25, 2 and 10 mg treatment groups, with no new safety concerns.
P042
Effect of natalizumab on clinical/radiological disease activity and EDSS of relapsing remitting multiple sclerosis patients
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Libya

Introduction: Natalizumab is a humanized monoclonal antibody that blocks T-cell transmigration through the blood-brain barrier into CNS.
Objective: AFFIRM showed monotherapy with Natalizumab for 2 year reduced the annualized relapse rate ARR by 68% and the disability progression rate by 42%. This is our first experience in use of Natalizumab in Benghaz-Libya. So we want to evaluate its efficacy.
Methods: Four patients of relapsing remitting multiple sclerosis on Natalizumab (JC virus negative and MRI prior to use drug done) followed in our clinical practice regarding frequency of relapse, EDSS and new T2-hyperintense lesion on MRI for 24 months for 3 patients and 1 patient for 12 months.
Results: All the patients have no relapse (frequency of relapse zero) during 24 months in 3 patients and 12 months in 1 patient, no new T2 hyperintense MRI lesion in 3 patients. there are decrease in EDSS in 3 patients. Table and graphs will show more details later on.
Conclusion: The efficacy of Natalizumab on disease activity i.e. relapse free is higher in my study which 100% in comparison with AFFIRM which was 68% (our study is small size) so our recommendation to have bigger size for right comparison and more evaluation of efficacy. No reaction to the drug (side effect) recorded during this follow up.

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P043
Pregnancy outcomes in female patients and partners of male patients in the teriflunomide clinical development program
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Kuwait

Background/objectives: Teriflunomide is a once-a-day oral immunomodulator approved for relapsing-remitting multiple sclerosis. Consistent efficacy and safety of teriflunomide were demonstrated in a large clinical trial program. Animal data suggest that teriflunomide may be associated with a risk of teratogenicity. Teriflunomide plasma concentrations <0.02 mg/L in the mother confer minimal risk of teratogenicity, and can be achieved with an accelerated elimination procedure in humans.
Design and methods: Despite the requirement for reliable contraception, pregnancies were reported across the teriflunomide clinical trial program. Upon discovery of pregnancy, patients were instructed to discontinue treatment and undergo an accelerated elimination procedure. Pregnancy outcomes were collected across phase 2 and 3 clinical studies in the teriflunomide clinical development program and available data through October 2013 are reported.
Results: Eighty-three pregnancies were reported in female patients and 22 in partners of male patients; 26 live births occurred in female patients and 16 in partners of male patients receiving teriflunomide. Twenty-nine pregnancies in female patients and two in partners of male patients were terminated electively. Newborns whose parents were exposed to teriflunomide were healthy and had no structural defects or functional deficits at birth. Spontaneous abortion rate (18.6%) was within the range for general population. Median birth weight for 18 newborns was 3.3 kg, and mean gestational age at birth among 23 cases was 39 weeks, all within typical ranges for general population.
Conclusions: Data from the clinical program have shown no teratogenic signals for teriflunomide in humans, consistent with findings of the Organization of Teratology Information Specialists registry and over 2.5 million patient-years of postmarketing data for leflunomide. Further prospective data in the postmarketing setting are being collected in global teriflunomide pregnancy registries.

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P044
Long-term clinical and magnetic resonance imaging outcomes from patients treated with teriflunomide: Results from a phase 2 extension study
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Saudi Arabia

Background/objectives: Teriflunomide is a once-daily oral immunomodulator for the treatment of relapsing-remitting multiple sclerosis. The clinical development program for teriflunomide demonstrated consistent efficacy and a well-characterized, manageable safety and tolerability profile. Here we report efficacy outcomes from patients treated long-term with teriflunomide in a phase 2 study (nct01487096) and its extension (nct00228163).
Design and methods: Patients with relapsing multiple sclerosis were randomized 1:1:1 to teriflunomide 14 mg or 7 mg, or placebo. Of 160 patients completing the 36-week core study, 147 entered the long-term extension.

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Terifilumide-treated patients continued on their original dose; placebo-treated patients were rerandomized 1:1 to terifilumide, 14 mg or 7 mg. Expanded disability status scale score was assessed every 24 weeks, magnetic resonance imaging was performed every 48 weeks until week 480, and clinical relapses were reported throughout the study.

Results: At June 28, 2013, cumulative duration of terifilumide exposure, including both dose groups, was >990 patient-years: 63 patients remained on study. Increases in mean expanded disability status scale score following up to 528 weeks of treatment were minimal. Annualized relapse rates were low: 0.190 (14-mg group) and 0.254 (7-mg group). In both dose groups, mean numbers of gadolinium-enhancing T1 lesions and newly active T2 lesions were lower at week 480 vs. core study end. Compared with the 7-mg group, the terifilumide 14-mg group had less of an increase from baseline in T2 lesion volume and less decline from baseline in cerebral volume at week 432. There were no new or unexpected safety signals with continued terifilumide exposure.

Conclusions: Clinical and radiological signs of disease remained low in patients receiving terifilumide for up to 12 years in a phase 2 study and its extension. These data are consistent with sustained efficacy of long-term terifilumide treatment in patients with multiple sclerosis.

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P045

Efficacy and safety of alemtuzumab in patients with relapsing-remitting multiple sclerosis who relapsed on prior therapy: Four-year follow-up of the Care-MS II study


USA

Background/objectives: Alemtuzumab is approved in over 30 countries for relapsing-remitting multiple sclerosis. In the 2-year, phase 3 CARE-MS II study (NCT00548405), alemtuzumab had superior efficacy over subcutaneous interferon beta-1a and manageable safety over 2 years; follow-up at Year 3 showed durable efficacy of alemtuzumab. Here we report results for years 3 and 4 after alemtuzumab initiation, and for years 1 and 2 after alemtuzumab initiation in patients initially treated with subcutaneous interferon beta-1a (crossover cohort).

Design and methods: In CARE-MS II, patients with active relapsing-remitting multiple sclerosis who relapsed on prior therapy received 2 courses of alemtuzumab (12 mg/day intravenously on 5 consecutive days and on 3 consecutive days 12 months later) or subcutaneous interferon beta-1a (44 µg 3 times/week). In the extension study (NCT00930553), alemtuzumab-treated patients could receive as-needed retreatment (12 mg/day intravenously on 3 consecutive days) ?1 year apart or other disease-modifying therapy. Crossover patients received 2 alemtuzumab courses (5 days then 3 days) 12 months apart.

Results: The extension enrolled 393 (93%) eligible patients from the core study alemtuzumab arm. Through 4 years, 68% received the first 2, but no additional courses; 24% and 7% received 1 or 2 additional courses, respectively; 5% received another disease-modifying therapy during the extension. Twenty-five patients (6%) discontinued study, none from adverse events. Among former interferon beta-1a patients, 146 (83%) entered the extension; 131 (90%) received 2 alemtuzumab courses. Seven extension withdrawals (5%) occurred in crossover patients, 1 from an adverse event. Efficacy and safety data will be reported.

Conclusions: Most patients receiving alemtuzumab in the core study required no re-treatment during the first 2 extension years; few received alternative therapies or withdrew from study. Among crossover patients, most received both treatment courses and remained in the study.

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P046

Cumulative review of thrombotic microangiopathy, thrombotic thrombocytopenic purpura and hemolytic uremic syndrome reports with SC interferon beta-1a

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Switzerland, USA

Background/objectives: Rare cases of thrombotic microangiopathy, manifested as thrombotic thrombocytopenic purpura or hemolytic uremic syndrome have been reported with interferon beta products. This was a cumulative review of thrombotic microangiopathy cases recorded in a Global Safety Database for subcutaneous interferon beta-1a.

Methods: Search criteria were all reported cases, serious and non-serious, from all sources (including non-healthcare professionals and clinical trial reports), regardless of event ranking and causality assessment by reporter or Company; data lock was 03 May 2014.

Results: Ninety one cases with 105 events were retrieved; 76.9% (70/91) patients were female, consistent with the underlying disease of multiple sclerosis. Time-to-onset varied from 2 months to 14 years; 31.9% events occurred within 2-years of treatment initiation. 7 patients had a fatal outcome (5 were secondary to other causes; 2 had insufficient information). 44 patients recovered, 32 had not recovered at the time of the report and in 8 cases the outcome was not reported/unknown. Treatment was discontinued in 84.6% (77/91). In 67.0% (61/91), a causal association between treatment and the occurrence of thrombotic microangiopathy, thrombotic thrombocytopenic purpura-hemolytic uremic syndrome was suspected. Risk factors and/or confounding factors were present in 41/91 cases (45.1%). Early prodromal syndrome or specific
patterns were not detected although 55.0% (50/91) contained insufficient information. The overall reporting rate of thrombotic microangiopathy, thrombotic thrombocytopenic purpura-hemolytic uremic syndrome was 7.2 per 100,000 patient-years. Reporting rates for human serum albumin-containing versus human serum albumin-free formulations were 5.72 and 7.68 per 100,000 patient-years, respectively. 

Conclusions: No new signal relating specifically to increased frequency of thrombotic microangiopathy, as thrombotic thrombocytopenic purpura and hemolytic uremic syndrome with the human serum albumin-free formulation was detected and no additional risk mitigation measures were required regarding the different formulations. The benefit-risk balance of subcutaneous interferon beta-1a remains positive and routine pharmacovigilance monitoring is appropriate.

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P047
Sustained benefit of natalizumab in pediatric multiple sclerosis with breakthrough activity: A case report
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Lebanon

Objective: Limited data are available on natalizumab in pediatric multiple sclerosis. This is to report the sustained therapeutic benefit of natalizumab over 32 months follow up in a 12-year old child with a breakthrough activity disease. 

Methods: In February 2009, the diagnosis of childhood onset relapsing remitting multiple sclerosis was confirmed at age 9, based on the “International Pediatric Multiple Sclerosis Study Group”. A disease breakthrough activity with suboptimal response was considered after 26 months of a well tolerated treatment with beta-interferon-1b; 6 relapses, rapid neurological deterioration and an increase by 4 new plaques on average per year with at least one showing enhancement after gadolinium injection were observed on MRI follow up. Monthly natalizumab 300 mg intravenous infusion was initiated on February 2012, after written consent. Negative JCV antibodies from serum samples were confirmed using the “STRATIFY JCV” test before treatment initiation and at 6 months intervals; clinical evaluation and biological tests were performed on routine base every 3 months.

Results: The patient’s neurological status improved dramatically with rapid recovery after the second natalizumab infusion. Presently, this 13-year-old patient has received a total of 32 infusions of natalizumab and is still asymptomatic with no occurrence of any clinical relapse or no new lesion. Treatment is still well tolerated.

Conclusion: This report highlights the tolerability and sustained therapeutic efficacy of natalizumab as second-line therapy in childhood multiple sclerosis with breakthrough disease activity when critical decision of shifting from first-line therapy has to be made in children with potential greater risk in reaching progressive neurological disability at younger age.

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P048
Seizures and epilepsy in multiple sclerosis patients: A Tunisian study of 9 cases
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Tunisia

Introduction: The prevalence of seizures and epilepsy in patients with multiple sclerosis (MS) is higher than in general population. We investigated the clinical, electrical and radiological findings for Tunisian patients with MS who had experienced seizures.

Methods: We retrospectively reviewed the medical records of patients who had epileptic seizures and MS, over a 22-year period, from February 1992 to May 2014, at the department of neurology in Hbib Bourguiba hospital. The diagnosis of MS was made according to McDonald revised criteria. The diagnosis of epilepsy was based on the criteria proposed by the International League against Epilepsy (ILAE) 1993 and seizures were classified according to the classification of ILAE, 1981. All patients with seizures or epilepsy were submitted to EEG recording and MRI imaging.

Results: We identified 9 patients (8 female). The mean age at the onset of MS was 47 years old. None had the history of seizure or epilepsy before clinical MS onset. 7 patients had relapsing remitting MS that became secondary progressive in 3 cases. The mean age at the onset of seizures was 40.6 years old. Epileptic seizures were recurrent in 3 cases and 2 patients had epilepsy. The seizures occurred essentially during the course of the disease (7 cases) and the delay between the onset of MS and seizures was 7.1 years. Seizures are related to a new relapse in 7 cases. The mean concomitant EDSS score was 2.9. 4 patients had partial seizures with secondary generalization in 1 case. Cognitive impairment was observed in 3 cases. Interictal EEG was normal in 4 patients, focal or generalized epileptic discharges were seen in 3 patients and generalized slowing was noted in 1 patient. All patients had lesions in juxtacortical areas and in the brain stem. Gadolinium-enhancing were visible in 3 cases and cortical atrophy in 4 cases. Anti-epileptic drugs were administered in all patients and six were on monotherapy. The Carbamazepine is the most prescribed. Seizures were controlled in 5 cases, but 1 patient presented a status epilepticus.

Conclusion: Seizures and epilepsy are more frequent in the MS patients. The causal link between MS and epileptic seizures is unclear. The presence of cortical and juxtacortical lesions and progressive brain atrophy can probably be the pathophysiological mechanism underlying this association. The higher frequency of partial seizures and the better response to antiepileptic drugs are noted.
**Introduction:** Multiple sclerosis (MS) is the most common autoimmune disease affecting the central nervous system (CNS) (1). It affects adults during their most productive years. The estimated prevalence of MS around the world is 30 per 100,000 (2). Prevalence of MS in Saudi Arabia has not been determined; however, researchers suggest an increase in incidence and prevalence in the Middle East (3 and 4). Clinically isolated syndrome (CIS) is the first neurologic symptom that results from a demyelinating process in the CNS. Recent trials using beta-interferon in patients with a CIS have demonstrated that early treatment may delay developing MS in about 50% (5). Early treatment has also been shown to slow the progression and reduce disability at 3 years by 40% (6,7). A lack of knowledge about the disease symptoms may cause patients to present late and miss the opportunity to reap the benefits of early intervention. This study examines the awareness, knowledge and the sources of knowledge on Multiple Sclerosis disease in Saudi population of Riyadh city. This information would help building more targeted public health awareness campaigns that may aid in early intervention of MS.

**Aim:** To evaluate the awareness, knowledge and sources of the information on MS among the Saudi population in Riyadh City.

**Methodology:** A community based cross sectional study that was conducted in different public areas (shopping malls, coffee-shops, social clubs, supermarkets, and mosques) of different regions of Riyadh, the capital city of Saudi Arabia. Adult Saudis age 18 years and above were included and all health professionals/students and subjects diagnosed with MS were excluded. A structured questionnaire including questions on awareness, knowledge and sources of knowledge on MS was administered by an interview using convenience stratified quota sampling using the size of age strata of Saudi population published from the 2010 census during June 2014. Based on prior research studies, expected knowledge was 20%. Assuming a significant level of 5% and precision of 0.15 a sample size of 246 was sought.

**Results:** Two hundred and forty six subjects were interviewed in 22 settings. The mean age (SD) was 38.4 (13.9) with equal numbers of males/females (M/F). The education levels of subjects were 14 (5.69%), 95 (38.62%) and 137 (55.69%) for subjects with no education, some education and all education respectively. Less than a third of respondents (30.3%) reported being aware of MS. Knowledge was assessed using 15 questions and a ‘knowledge score’ was calculated from 100%. Mean knowledge score was low (M = 24%, F - 32%) with no significant difference in knowledge between M/F, age groups or educational levels. Subjects who knew someone diagnosed with MS had significantly higher scores of 37.0% (p=0.001). The most frequent source of knowledge of subjects was ‘learning from people around them’ with a significantly higher mean knowledge score of 34.7% (p=0.009).

**Conclusion:** Multiple sclerosis awareness and knowledge is suboptimal in Saudi population. The only source of information, which showed significantly higher knowledge scores, was ‘learning from people around them’ and those who reported knowing a person diagnosed with MS. Our samples reliance on knowledge from people around them may indicate a lack of available information via the Internet or television on MS. We recommend the use of public awareness campaigns through various media to ensure reliable information reach the public in order for early detection and management of this serious disease.
P051
Vitamin D receptor polymorphisms and HLA-class II genotypes among Lebanese with multiple sclerosis - A pilot study

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Lebanon

Background: Multiple sclerosis (MS) is an autoimmune disease with multifactorial etiology. Previous studies showed that HLA-DRB1*15 allele is a major genetic risk factor for MS in other populations possibly through regulation of vitamin D receptor (VDR) complex. In this study, we investigated the HLA class II genotypes and VDR gene polymorphism among a group of Lebanese MS patients and controls.

Methods: Fifty MS patients (remitting/raselping, aged: 19-74years, male:female = 1:2.1) were selected for this study, based on the Expanded Disability Status Scale. The controls included: 49 healthy subjects (aged: 15-59years, male:female = 1:2) and 51 neurologic patients other than MS (Non-MS, aged 13-70 years, male:female = 1:1.12). After a thorough history, blood in EDTA tube was collected. Extracted genomic DNA was used for molecular analysis of VDR genotypes(ApaI, TaqI and BsmI) and HLA class II typing (low resolution HLA-DRB1/3/4/5) (Luminex, San Diego, CA). Differences between groups were evaluated using Mann Whitney-U test. Chi-square test was used for association between various categorical variables (p = 0.05); therefore both were combined into one control group for analysis.

Frequency of HLA-DRB1*15 was significantly higher in MS patients compared to controls. None of the VDR gene alleles differed between the two groups. Odds ratio (OR) for MS in the presence of DRB1*15 allele was 3.21 (p = 0.016; 95% CI = 1.20-8.59). Cosegregation of HLA-DRB1*15 and VDR genotypes showed no increase in risk for MS in the presence of A-allele (OR = 3.40; p = 0.022; 95% CI = 1.14-10.19). Similarly, combination of DRB1*15 with b-allele resulted in higher OR of 4.22 although not statistically significant (p = 0.08; 95% CI = 0.75-23.89).

Conclusion: Our results confirm that HLA-DRB1*15 is a strong predisposing factor for MS in Lebanese patients. Furthermore, the interaction between specific VDR alleles and HLA polymorphism does not significantly increase the susceptibility to MS.

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P052
Cortical venous sinus thrombosis after LP and high dose steroid in a case clinically isolated syndrome

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India

Role of lumbar puncture and high dose steroids have been implicated previously in causing cerebral venous sinus thrombosis in multiple sclerosis. We report a case of clinically isolated syndrome who developed cerebral venous sinus thrombosis after Lumbar puncture and high dose steroids.

Forty two years old gentleman presented with right hand numbness and weakness over 1 week. MRI brain and spine showed periventricular and cerebellar white matter lesions suggestive of multiple sclerosis. ANA, ANCA, APLA, B12 and NMO antibody were negative. VEP was normal. CSF showed oligoclonal bands. Post lumbar puncture he received pulse dose of 1 gm Methylprednisolone for 5 days. He developed occipital headache on the 6th day especially on sitting up which improves on lying down. On the 9th day the headache became frontal and continuous with no relief on lying down. He developed generalized tonic clonic seizures on the 12th day and MRI brain done revealed sagittal sinus thrombosis with bilateral sulcal subarachnoid hemorrhage. He was started on low molecular heparin followed by Warfarin. Headache resolved. His thrombophilia screen revealed Protein C and S deficiency with heterozygous MTHFR gene mutation whether Lumbar puncture which caused the low pressure headache along with high dose steroids provoked cerebral venous thrombosis in this predisposed patient who had Protein C and S deficiency can be debated. There have been many cases reported of similarly of CVT in MS after LP and steroids. It can be debated that LP and steroids are routinely given simultaneously in MS patients and questionably this can be avoided.

Conclusion: This is a case of CIS who developed cerebral venous sinus thrombosis post lumbar puncture and mega steroids pulse therapy, initially he presented with symptoms similar to headache of intracranial hypotension followed by seizure. High index of suspicion of CVT post LP and steroids therapy should be considered.

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P053
Osteopontin and Oncostatin M increase significantly in Iranian relapsing-remitting multiple sclerosis patients

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Iran

Background/objectives: Osteopontin is a multitasking secreted protein with a bold role in autoimmune processes. It is a pro-inflammatory cytokine implicating in cell-matrix and cell-cell interactions, inflammation, recruitment, survival. Thus, it is crucial for T helper-1 immunity. A therapeutic-based study demonstrated that Natalizumab binding to a4-subunit of a4-B1 integrin reduces cell adhesion
of invasive immune cells to the endothelium of the central nervous system. The a4-B1 is an osteopontin binding partner. Consequently, it seems that a reduction of osteopontin can ameliorate multiple sclerosis relapses. Oncostatin m is an interleukin-6 family member secreted by variety of immune and none immune cells suggesting roles for oncostatin m in physiological and pathological conditions such as regulation of prostaglandin expression in astrocytes, involvement in dendritic cell's activities, neutrophil recruitment, immunosuppression, inhibition of proliferation of neural precursor cells, and enhancement of oligodendrocytes progenitor cell activity in demyelinated sites. In this study, we assessed these markers in Iranian relapsing-remitting multiple sclerosis patient's plasma level according to the healthy controls.

**Design and methods:** One hundred and twenty relapsing-remitting multiple sclerosis patients and 60 healthy subjects with no neurodegenerative disease background were included. Blood samples were gathered and enzyme-linked immonosorbent assay was done using “Booster” and “Eastbiopharm” ELISA kits and micro-plate reader. Statistical analysis was performed by SPSS 16.

**Results:** There was a significant difference between the cases and the controls for both osteopontin and oncostatin m protein expression (P-value < 0.05).

**Conclusions:** Osteopontin and Oncostatin M are two inflammatory markers in multiple sclerosis with some anti-inflammatory features as well. As the primary study, we evaluated the protein level in plasma and compared to the healthy donors which was quite successful. For future studies, we suggest gene expression methods and also investigations on their variations in Iranian patients in order to gain more knowledge and finally suggest diagnosing and therapeutic paths for such mediators.

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**P054**

**MS and cancers**

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**USA, Iran**

Many studies have been performed throughout the universe suggested that there might be associations between multiple sclerosis and many tumors, such as Hodgkin lymphoma, brain tumors, nasopharyngeal carcinoma and particularly breast cancer. However, cancer occurrence in patients suffering from multiple sclerosis is a fact that still requires more studies.

In this study, we followed 1391 multiple sclerosis patients of Isfahan multiple sclerosis society from 2004 to 2013. The ratio of observed cases to the number of expected standardised incidence ratio (SIR) was applied as an indication of relative risk.

During this time 50 cases of cancers were occurred in 1391 multiple sclerosis patients with 8346 person-years follow up (SIR=0.97 [CI=0.95%]). Furthermore, adjusting for age and gender has yielded similar results. We also found that incidence of breast cancer among multiple sclerosis patients is significantly higher than general population.

This study suggested that it is not imperative that multiple sclerosis patients be at an increased risk of cancer, however women with multiple sclerosis might be at an increased risk of developing breast cancer a little more.

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**P055**

**Characteristics of a cohort of MS patients in Abu Dhabi**

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**UAE**

**Background/objective:** Evidence suggests the prevalence of multiple sclerosis (MS) in the Middle East is higher than expected. A study in Dubai demonstrated a surprisingly high crude prevalence rate in the Emirate population (medium to high risk) 1. This underscores the importance of looking at other Emirate cohorts. Thus a study of MS patients in Al Ain was conducted to examine disease characteristics among Emirate MS patients.

**Methods:** A retrospective chart review was conducted on MS patients at Tawam Hospital, Al Ain. Characteristics examined included gender, MS type, age at symptom onset, type of symptoms at onset, immunomodulatory therapy, vitamin D and B12 levels, concurrent ANA positivity, oligoclonal/IgG positivity, family history and presence of spinal cord lesions.

**Results:** One hundred and five MS patients were identified. Average age of onset was 26.6 years. Male:female ratio was 1:2.75. Emirate patients comprised 82% and 13% were of Middle Eastern descent. The majority (88.5%) had EDSS scores below 5.5% and 83% were RRMS. SPMS patients comprised 9.5% and CIS 6.6%. Sensory symptoms were the most common presenting symptom (39%) followed by visual (36%). Average vitamin D levels among patients tested was 28 nmol/L without supplementation. Average vitamin B12 levels were 262 pmol/L and 13% of patients had concurrent ANA positivity. 8.8% of patients had a relative affected with MS and 83% of patients had spinal cord lesions on MRI imaging. The most popular immunomodulatory treatments were interferons (35%), natalizumab (12%) and fingolimod (9.5%).

**Conclusions:** Findings were similar to the Dubai Emirate cohort patients in male/female ratio with almost identical mean age of onset. Results differed for symptoms at onset with sensory symptoms followed by visual, then motor. A low vitamin D level in our study is consistent with findings published from other cohorts of MS patients. Treatment choices were similar to western trends.

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Prevalence, demographics and clinical features of multiple sclerosis in Bahrain

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Bahrain

Background: In the Arab world the reported prevalence of MS varies widely from 3.4 to 42/100,000. Data from neighboring Arabian Gulf countries (Kuwait, Saudi Arabia, Dubai and Qatar) show increasing prevalence and incidence of MS. No studies are reported from Bahrain that share same ethnic background.

Objectives: This study aims to estimate incidence, prevalence, demographics and clinical characteristics, including EB Virus status and Vitamin D3 level estimation of MS patients in Bahrain.

Methods: Data for all MS Bahraini patients fulfilling McDonald criteria (2010) and seen in Salmaniya Medical Complex, Manama, Bahrain, from 1st July 2011 till 31st October 2013, were analyzed. We already established an MS registry in the hospital.

Results: Two hundred and eighty-seven MS Bahraini patients were identified. The female to male ratio was 2.49:1. The mean age of onset was 35 ± 10.2 years. The prevalence of MS in 2013 was 59.9/100,000 (95% C.I. 41.99–57.55) with an annual incidence rate of 5.8/100,000 (95% C.I. 2.8–8.87) during 2012–2013. The median and mean expanded disability status scale (EDSS) was 2.0 and 3.0 respectively on presentation. 36.6% presented with optic neuritis, 32.4% had sensory symptoms and 62.0% had motor presentation while 32% had brain stem and 9% had pure cerebellar ataxia. 64.7% of our patients are EBV Seropositive (EBNA positive).

Conclusion: Bahrain should be considered as one of the countries with high risk for MS. This high prevalence is consistent with what reported from neighboring Arabian gulf countries. Studies are in need to elaborate more in the role of genetic and environmental factors in this increasing risk of MS.

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Remarkable response of seropositive neuromyelitis optica to rituximab therapy - First report from kingdom of Bahrain

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Bahrain

Background: Neuromyelitis optica (NMO) is an inflammatory demyelinating disease of the central nervous system that causes severe optic neuritis and myelitis attacks. Humoral immunity seems to have a prominent role in the pathogenesis of the disease. Recently the nature and understanding of NMO have been revolutionized by two factors (1) the identification of both a NMO IgG as a sensitive and specific diagnostic marker and (2) the identification of both specific radiological and pathologic features of the disease. Also with the limited treatment options, recently positive results reported with the use of the anti-CD20 monoclonal antibody rituximab are promising.

Objectives: We present 2 cases, first to be reported in Kingdom of Bahrain, of NMO with positive NMO IgG and favorable response to Rituximab.

Methods and results: Case # 1: 56 year old female patient. She had on 2008 left optic neuritis with residual visual loss. On September 2011 she had right optic neuritis. For both she received Methylprednisolone plus therapy for 4 days with partial response and residual visual loss. On October 2011, she developed severe myelitis with severe spastic paraplegia (grade 0-1) and urinary retention. The patient became bed bound. Her initial MRI of brain showed few scattered lesions for which the patient was diagnosed as multiple sclerosis and maintained on Betaseron injection as a disease modifying therapy. The repeated MRI showed long segment lesion of the spinal cord and her blood test was positive to NMO IgG. The patient did not respond to steroid or IVig therapy. However, she responded remarkably well to Rituximab injection. In 3 months she is fully independent in her movements with almost normal power and continent.

Case # 2: 43 year old female patient. On 2009, she developed a right optic neuritis that responded well to steroid therapy. 2 years later she developed spastic Paraparesis due to myelitis, she responded partially to steroid therapy and was put on Avonex injection as her MRI brain showed changes was diagnosed as MS in private hospital. However, one year later, she developed another severe myelitis that made her wheelchair bound with bladder involvement. Her MRI showed fairly long segment lesion of the spinal cord and her blood test was positive to NMO IgG. I gave her Rituximab injection therapy on which she showed remarkable improvement. In 3 months she is able to walk by herself and she independent in her ADL and bladder continent.

Conclusion: The remarkable recovery of these 2 patients from their severe disability in this case report support other reports of the effectiveness of Rituximab in the treatment of NMO and the humoral immunity nature of the illness. These are the first cases of NMO with positive IgG to be reported from Bahrain. NMO is not often seen in Bahrain despite high prevalence of MS.

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Efficacy and safety of Alemtuzumab in treatment-naive patients with relapsing-remitting multiple sclerosis: Four-year follow-up of the Care-MS I study

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Background/objectives: Alumtzumab is approved in over 30 countries for relapsing-remitting multiple sclerosis. In the 2-year, phase 3 CARE-MS I study (NCT00530348), Alemtuzumab significantly reduced relapses compared with subcutaneous interferon beta-1a, with manageable safety in treatment-naive patients with active relapsing-remitting multiple sclerosis. Durable efficacy of Alemtuzumab was demonstrated at 3-year follow-up. Here we report results for years 3 and 4 after Alemtuzumab initiation, and for years 1 and 2 after Alemtuzumab initiation in patients initially treated with subcutaneous interferon beta-1a (crossover cohort).

Design and methods: In CARE-MS I, patients received Alemtuzumab (12 mg/day intravenously on 5 consecutive days and on 3 consecutive days 12 months later) or subcutaneous interferon beta-1a (44 μg 3 times/week). In the extension study (NCT00930553), patients could receive as-needed Alemtuzumab re-treatment (12 mg/day on 3 consecutive days) ≥ 1 year apart or other disease-modifying therapy. Crossover patients received 2 Alemtuzumab courses (5 days then 3 days) 12 months apart.

Results: The extension enrolled 349 (95%) eligible patients from the core study Alemtuzumab arm. Through 4 years, 73% of these patients received only 2 annual courses, while 21% and 5% received 1 or 2 additional courses, respectively; <5% of patients received another disease-modifying therapy during the extension. Nine patients (3%) discontinued from the study, none due to adverse events. Among patients who received subcutaneous interferon beta-1a in CARE-MS I, 144 (83%) entered the extension and 132 (92%) received 2 courses of Alemtuzumab. There were 8 withdrawals (6%) in the crossover group during the 2-year extension period, none due to adverse events. Efficacy and safety data will be reported.

Conclusions: Most patients receiving Alemtuzumab during the core study required no re-treatment during the 2-year extension period; few sought alternative therapies or withdrew from the study. Among crossover patients, most received both treatment courses and remained in the study.

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P060
Evaluation of circulating endothelial cell level in patients with optic neuritis attack

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Objective: Optic neuritis (ON) is inflammation of the optic nerve. In multiple sclerosis (MS) acute demyelization of optic nerve is a common cause of ON in some parts. Endothelial progenitor cells (EPCs) are present in circulation and contribute to vasculogenesis in adults. The aim of present study was to determine the number of circulating EPCs in MS patients with ON.

Material and methods: Blood samples were collected from 50 MS patients with ON and 40 healthy individuals (mean ages: 26 ± 5). Together with the collection of demographic data, a sample of venous blood was drawn to assess a complete blood count with differential; circulating,
VEGF2, CD31, CD144 and CD309 as ECs markers and CD34 as hematopoietic cell marker using flow cytometry. Data are expressed as mean ± SD. Results were analyzed statistically, using the Independent sample T test. Values of \( p < 0.001 \) were taken as significant.

**Results:** The median absolute percentage of circulating CD34\(^+\)HPCs in the overall population of ON patients was 18 ± 9.96. Against in the healthy was 26.31 ± 14.33\% (\( p < 0.001 \)). Patients with ON had EPCs which it was significantly higher than in healthy controls. In addition, the large number of EPCs but less number of circulating CD34 hematopoietic progenitor cells detected in patients.

**Conclusion:** Overall, data indicated EPCs circulate in peripheral blood of MS patients with an early phase of ON. It seems to increase of EPC relates to a good outcome. It may be that Heightened mobilization of EPCs represents an important role in prevention from BBB disruption or may be caused neoangiogenesis in MS patients with ON.

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**P061**

**Sleep quality among patients with multiple sclerosis in West Azerbaijan**

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**Background and objectives:** Life quality, being of utmost significance, has been studied for years through the investigations regarding chronic diseases such as Multiple Sclerosis (MS). Sleeping is one of the indices that seriously affect human life quality. Given that doctors pay less attention to the sleeping disorders in comparison with the other serious complications in MS patients, the later consequences remain untreated. This study is aimed at investigating sleeping disorder in MS patients in order to improve the patients' life quality owing to the little knowledge concerned with the treatment of the most chronic diseases.

**Design and methods:** The current research is a descriptive/analytic study being conducted periodically in 2013 in West Azerbaijan province, Iran. One hundred and fifty two patients were randomly selected using inclusion-exclusion criteria among the patients of West Azerbaijan center of MS. Patients filled the sleeping quality related questionnaire (PSQI) voluntarily after being served with sufficient information. This questionnaire was qualified for several times by retranslating into English from the regional language and subsequently comparing it with the original version. It was then evaluated and modified by sociologist/linguist, psychotherapist, and neurologist. Data analysis was performed using SPSS software applying the following tests: \( t \)-test, Fisher’s exact test and chi-square. For validity qualification of the questionnaire, \( \alpha \) Chronbach was employed.

**Results:** In this research, 105 patients (69.1\%) had PSQI \( \geq 5 \) (bad quality of sleeping) and 47 patients (30.9\%) had PSQI < 5 (good quality of sleeping) resulting in the average of 9.28 ± 1.12 for PSQI among them.

Table. Absolute and relative frequency distribution of useful life in patients with good and bad quality of life according to PSQI score will be presented.

**Conclusion:** The obtained results indicated that sleeping disorder in MS patients had a high percentage expressing that more than half of the patients had a bad quality of sleeping. This high prevalence can reinforce the role of MS in the development of sleeping disorders in patients.

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