and corresponding 95% confidence intervals, will be estimated. Quality assurance, focusing on registry processes and practices as well as data quality will be tracked using pre-specified metrics and analysis plans.

CLARION will provide safety evidence for neurologists and patients to assist the treatment decision process for patients with highly active relapsing MS.

doi: 10.1016/j.msard.2019.11.076

Multiple Sclerosis and Related Disorders 37 (2020) 101602

Reduction of Risk of Secondary Progressive Multiple Sclerosis Within Two Years of Treatment with Cladribine Tablets: An Analysis of the CLARITY Study

Patrick Vermersch [1], Gavin Giovannoni [2], Per Soelberg Sørensen [3], Kottil Rammohan [4], Stuart Cook [5], Birgit Keller [6], Sanjeev Roy [7]

[1] *Univ. Lille, INSERM U995, CHU Lille, FHU Imminent, Lille, France*
[2] *Queen Mary University of London, Blizard Institute, Barts and The London School of Medicine and Dentistry, London, United Kingdom*
[3] *Danish MS Center, Department of Neurology, University of Copenhagen, Rigshospitalet, Copenhagen, Denmark*
[4] *University of Miami School of Medicine, MS Research Center, Miami, United States*
[5] *Rutgers, The State University of New Jersey, New Jersey Medical School, Newark, United States*
[6] *Merck KGaA, Darmstadt, Germany*
[7] *Merck, Aubonne, Switzerland*

Cladribine tablets 10mg (cumulative dose 3.5mg/kg [CT3.5];N=433) over 2 years showed efficacy vs placebo (PBO;N=437) in patients with relapsing multiple sclerosis (CLARITY). This post hoc analysis explored the relationship between baseline expanded disability status scale (EDSS) and risk of progression to secondary progressive multiple sclerosis (SPMS) or to EDSS ≥6.0, in CLARITY.

Progression to SPMS was not recorded during the trial, a proxy composite definition was used: confirmed disability progression (CDP), CDP within the leading functional score (FS), EDSS post-baseline ≥4.0, pyramidal FS ≥2, all conditions met for ≥3 months in the absence of a relapse. Progression to EDSS≥6.0 was defined by having ≥1 post-baseline EDSS≥6.0 with 3- or 6-month CDP. Odds ratios (OR) and corresponding confidence intervals (CI) were estimated by a logistic regression model with treatment and baseline EDSS (≤3.0 or ≥3.5) as fixed effects.

Proxy SPMS progression occurred in 6.7% CT3.5 patients vs 13.5% PBO (OR 0.46[95%CI:0.28,0.76]; p=0.0024). For baseline EDSS≤3.0 patients, proxy SPMS progression was 3.5%(CT3.5,n=257) vs 7.7%(PBO,n=235); OR 0.44(95%CI:0.19,0.99); p=0.0471. Baseline EDSS≥3.5, proxy SPMS progression was 12.2%(CT3.5,n=148) vs 22.4%(PBO,n=157); OR 0.48(95%CI:0.26,0.9); p=0.0212. Proportions of patients with ≥1 EDSS value ≥6.0 post-baseline were 6.4%(CT3.5) vs 14.5%(PBO); OR 0.4(95%CI:0.24,0.66); p=0.0004. Patients with 3-month CDP with EDSS≥6.0 were 3.5%(CT3.5) vs 8.0%(PBO); OR 0.42(95%CI:0.22,0.82); p=0.0114, patients with 6-month CDP with EDSS≥6.0, were 2.8%(CT3.5) vs 5.8%(PBO); OR 0.48(95%CI:0.22,1.02); p=0.0566. Patients with baseline EDSS≤3.0 that had ≥1 EDSS≥6.0, 0.8%(CT3.5) vs 4.3%(PBO); OR 0.18(95%CI:0.04,0.81); p=0.0262. Baseline EDSS≥3.5, 16.2%(CT3.5) vs 29.9%(PBO); OR 0.45(95%CI:0.26,0.79); p=0.0051.

The risks of progressing to SPMS (proxy) within 2 years of treatment, or experiencing EDSS≥6.0, were significantly reduced with CT3.5 vs PBO, regardless of baseline EDSS (≤3.0 or ≥3.5).

doi: 10.1016/j.msard.2019.11.077

Multiple Sclerosis and Related Disorders 37 (2020) 101603

Efficacy and Safety of the Bruton's Tyrosine Kinase Inhibitor Evobrutinib in Patients with Relapsing Multiple Sclerosis Over 48 Weeks: A Randomized, Placebo-Controlled, Phase 2 Study

Xavier Montalban [1], Douglas L Arnold [3], Martin S Weber [5], Ivan Staikov [7], Karolina Piasecka-Stryczynska [7], Emily C Martin [9], Sana Syed [9], Fernando Dangond [9], Jerry S Wolinsky [2,4,6,8,10]

[1] *Vall d'Hebron University Hospital, Barcelona, Spain*
[2] *University of Toronto, Toronto, Canada*
[3] *Montreal Neurological Institute and Hospital, Montreal, Canada*
[4] *NeuroRx Research, Montreal, Canada*
[5] *Institute of Neuropathology, Universitätsmedizin Göttingen, Göttingen, Germany*
[6] *Department of Neurology, Universitätsmedizin Göttingen, Göttingen, Germany*
[7] *Department of Neurology, Acibadem City Clinic Tokuda Hospital, Sofia, Bulgaria*
[8] *Outpatient Neurology Clinic, Hanka Hertmanowska MS Care Center, Plewiska, Poland*
[9] *Global Clinical Development Center, EMD Serono Research & Development Institute, Inc., Billerica, United States*
[10] *McGovern Medical School, University of Texas Health Science Center at Houston (UTHealth), Houston, United States*

Evobrutinib (M2951) is a highly selective oral inhibitor of Bruton's tyrosine kinase, a key regulator of B cell and myeloid cell functions implicated in multiple sclerosis (MS). This was a Phase 2 study to compare evobrutinib with placebo in relapsing MS (RMS).

In this double-blind study (NCT02975349), adults with RMS were randomized to evobrutinib 25 mg once-daily (QD), 75 mg QD, 75 mg twice-daily (BID), open-label dimethyl fumarate (240 mg BID; reference), or placebo for 48 weeks. Placebo-treated patients were switched to evobrutinib 25 mg QD after 24 weeks. Primary endpoint: total number of T1 gadolinium enhancing (T1 Gd+) lesions over Weeks 12–24. Secondary endpoints included annualized relapse rate (ARR), magnetic resonance imaging measures, and safety. The study received full patient and Institutional Review Board approval.

Of 267 randomized patients, 227 (85.0%) completed 48 weeks. Evobrutinib 75 mg QD and BID significantly reduced the total number of T1 Gd+ lesions over Weeks 12–24 versus placebo (primary endpoint; Table). There was no evidence of change in effect on T1 Gd+ lesions (mean±SD; Wilcoxon signed-rank test) between Weeks 24 and 48 with evobrutinib 75 mg BID (0.24±0.88 to 0.49±1.22; p=0.23) or evobrutinib 75 mg QD (0.28±0.91 to 0.85±2.87; p=0.57). ARR (unadjusted [95% confidence interval]) over 48 weeks was 0.25 (0.12–0.44) for evobrutinib 75 mg QD, 0.11 (0.04–0.25) for 75 mg BID, and 0.37 (0.21–0.59) for placebo (Table). All evobrutinib doses appeared well-tolerated. Transaminase elevations were predominantly mild; some Grade 3–4 events were observed; all had their onset within the first 24 weeks; transaminase elevations were asymptomatic and reversible on evobrutinib withdrawal.

To our knowledge, evobrutinib is the first BTK inhibitor to demonstrate disease activity reduction in MS. The observed benefit-risk profile of evobrutinib in this Phase 2 study supports further clinical development in RMS.

doi: 10.1016/j.msard.2019.11.078

Multiple Sclerosis and Related Disorders 37 (2020) 101604

Osteoporosis in Multiple Sclerosis: The Bystander Effect

Ruqqia Mir, Safana Alfardan

Sheikh Khalifa Medical City, Abu Dhabi, United Arab Emirates

Osteoporosis is a frequently encountered medical issue in practice. Several studies in patients with multiple sclerosis (MS) have shown a lower Bone Mineral Density (BMD) when compared to their age matched healthy controls; nonetheless, it has been found to be prevalent in patients with MS and contributes to both morbidity and mortality in this population. We aimed to determine if MS patients are screened and managed for osteoporosis at our facility.

A retrospective chart review of 28 patients between the ages of 45-70 years was conducted. Data collected included gender, MS type, mobility status, falls risk, history of glucocorticoid, smoking and alcohol use and lastly supporting radio graphic evidence; such as x-rays or BMD scan. Other data gathered included Vitamin D level, calcium supplementation and agents used for osteoporosis treatment.

Our cohort was comprised of 26 patients with either primary or secondary progressive MS; 24 of which were Emiratis and the remaining 2 were Arab non-nationals. Falls risk was significant in 19 patients. Wheel chair dependency was found in 10 patients and 7 had limited overall mobility.

All patients were supplemented with Vitamin D. However, only 8 had at least one course of IV Glucocorticoids. BMD scan was performed on 8 patients. Eight patients were diagnosed with Osteopenia/Osteoporosis, out of which 3 were treated with bisphosphonates. Two patients had X-Ray evidence of fractures.

Our findings show limited active participation by neurologists and physicians in general regarding the bone health of this cohort of MS patients. One major limitation of our study is that many of our patients are seen at multiple facilities, which may skew our findings towards the null. In conclusion, we propose that all MS patients should undergo a yearly structured and thorough bone health risk factor evaluation and be treated accordingly.

doi: 10.1016/j.msard.2019.11.079

Multiple Sclerosis and Related Disorders 37 (2020) 101605

Ultraviolet B Radiation Therapy Versus Vitamin D3 Supplementation: Effects on Cognitive Functions and Fatigue in Egyptian Relapsing Remitting Multiple Sclerosis Patients

Alaa Elmazny [1], Asmaa Ibrahim [1], Hatem Shehata [1], Nevin Shalaby [1], Eman Magdy [2], Hadeel Mohamed [1], Shimaa Essa [3], Maged Abdel-Nasser [1]

[1] *Cairo University, Cairo, Egypt*
[2] *Agouza Oolice hospital, Cairo, Egypt*
[3] *Health Insurance Organisation, Cairo, Egypt*

Vitamin D independent benefits of ultraviolet B radiation therapy has been previously outlined. The current work aimed to compare the impact of Broadband ultraviolet B radiation (BB-UVB) therapy to vitamin D3 supplementation on cognitive functions and fatigue in relapsing remitting multiple sclerosis (RRMS) patients.

Randomized controlled trial conducted on 40 RRMS patients attending the Kasr Al Ainy hospital multiple sclerosis clinic. Patients were assigned into two equal groups receiving either BB-UVB radiation (3 sessions/week for 4 weeks) or oral vitamin D3 (weekly 50,000 IU for 3 months). Comprehensive cognitive battery [Montreal Cognitive Assessment (MoCA), Symbol Digit Modalities Test (SDMT) and Brief Visuospatial Memory Test-Revised (BVMT-R)], Fatigue Severity Scale (FSS) and serum vitamin D3 levels were done at baseline and 3 months following either treatments.

Baseline vitamin D3 levels and scores of fatigue and cognitive scales were comparable in both groups. Median scores of MoCA, SDMT, BVMT-R and FSS pre and post BB-UVB treatment were [27 (3.0)) vs 28.5 (2.0), 33.5 (9.8) vs 37 (10.5), 24 (11.7) vs 32 (6) and 4.4 (1.6) vs 3.2 (2.5)], p-value (<0.001, <0.001 <0.001 and <0.001) respectively, and the median scores pre and post vitamin D3 were [26.0 (2.8) vs 28.0 (2.0), 29.5 (8.3) vs 35.0 (5.0), 27.0 (9.0) vs 31.0 (5.0) and 4.1 (1.0) vs 3.2 (1.2), p-values (<0.001, <0.001 <0.001 and <0.001) respectively. No statistically significant difference was found when comparing both groups post therapies vitamin D3 levels, MoCA, SDMT, BVM-R and FSS scores ($p= 0.512$, $p = 0.355$, $p = 0.779$, $p = 0.620$ and $p=0.758$).

Both BB-UVB therapy and oral vitamin D3 supplementation are equally effective in improving cognition and fatigue in RRMS patients.

doi: 10.1016/j.msard.2019.11.080

Multiple Sclerosis and Related Disorders 37 (2020) 101606

Patterns of Complementary and Alternative Medicine Use Among Adult Patients with Multiple Sclerosis: A Cross-Sectional Study

Muhannad Abdulaziz Alnahdi, Abdullah Alsulayhim, Ahmed Bin Selim, Dr. Emad Masuadi, Dr. Yaser Almalik

College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia

Multiple sclerosis (MS) is a chronic autoimmune disease that causes demyelination of the central nervous system. No treatment has shown to be completely effective, thus, the tendency for patients with MS to use non-conventional therapies like Complementary and Alternative Medicine (CAM) might increase. The study aims to explore the pattern of CAM use among patients with MS at a tertiary health care center in Saudi Arabia.

This is a questionnaire-based observational cross-sectional study that targeted adult patients diagnosed with MS at a tertiary care center, Riyadh, Saudi Arabia. The study sample size was 176 patients, and consecutive non-probability sampling technique was used to approach them during their appointments. An Arabic validated questionnaire was used to evaluate patients' use of CAM.

The mean age was 34.6 ± 10.9 years, and the majority of patients were females. Eighty-nine percent of the participants reported using CAM at least once. Praying was the most frequent modality (60%), followed by supplication (59%), Ruqia (52%), and vitamins (44%). Symptomatic improvement was reported by 49 (27.8%) of complementary medicine users and 81 (46%) of alternative medicine users.

The study found a high prevalence of CAM utilization among Saudi adult patients with MS exceeding internationally reported rates. Although some patients described some improvement in their symptoms, further research is needed to evaluate the effectiveness of CAM.

doi: 10.1016/j.msard.2019.11.081

Multiple Sclerosis and Related Disorders 37 (2020) 101607

B Cell Over Population Following Alemtuzumab Therapy in a Multiple Sclerosis Patient

Shaima Nasser Al Mashgari, Ahmed Shatila, Sudhir Kumar Palat Chirakkara

Mafraq Hospital, Abu Dhabi, United Arab Emirates

Alemtuzumab is an anti-CD52 monoclonal antibody therapy for relapsing remitting multiple sclerosis (RRMS), which depletes T and B-lymphocytes resulting in their reduction and subsequent repopulation.It decreased relapses compared to interferon beta-1a in clinical trials.However incidence in causing B-cell autoimmunity and hyper-proliferation has not extensively described for CNS involvement.

We report on a 24-year-old female diagnosed with RRMS since 2011 following multiple episodes of optic neuritis and hand tremors. She was started on Natalizumab from an outside facility but developed a relapse. Hence Alemtuzumab was recommended due to fact that