2020 CONSORTIUM OF MS CENTERS LATE BREAKING ABSTRACTS

Real World Evidence Assessment of Betaseron®(interferon beta-1b) Adherence Following the Introduction of the Betaconnect™ Auto-Injector

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Background:

- Maintaining adherence to DMTs is challenging for chronic conditions such as MS and poor adherence in MS has been associated with increased risk of disease activity and higher resource utilization.
- For DMTs requiring parenteral self-administration, such as Interferons, autoinjector devices may help patients overcome injection-related factors interfering with treatment adherence.
- The BETACONNECT device is an electronic autoinjector for the injection of Interferon beta-1b (Betaseron), a disease modifying therapy utilized in relapsing remitting multiple sclerosis (RRMS).

Objectives:

This retrospective analysis of a US claims database evaluated adherence, as indexed by medication possession ratio (MPR) and persistence, to two subcutaneous disease-modifying therapies (DMTs); Rebif® (interferon beta-1a) and Betaseron®(interferon beta-1b) during the period prior to and following the introduction of the BETACONNECT™ Auto-Injector for Betaseron in patients with multiple sclerosis (MS).

Methods:

Data from MarketScan, a US claims database, for patients with a medical claim for Rebif or Betaseron either prior to the introduction of BETACONNECT (Oct 2013–Sep 2015) or post approval and uptake of BETACONNECT (Oct 2016–Sep 2018), were evaluated. Patients aged ≥18 years with ≥1 confirmed MS diagnosis in the 12-month period prior to the first relevant DMT prescription within the defined time periods were included in this analysis. Four cohorts were defined: incident Rebif or Betaseron users over the 24-month period prior to the introduction of BETACONNECT or over the 24-month period following the introduction and

uptake of BETACONNECT. Within each time period, patient populations were propensity-score matched on demographic and clinical characteristics. MPR and persistence to both DMTs are described for the period prior to and following the introduction of BETACONNECT.

Results:

MPR: In the pre-BETACONNECT period,Rebif users met an 80% threshold, while Betaseron users did not. In the post-BETACONNECT periodboth Rebif and Betaseron users met an 80% threshold.

In the pre-BETACONNECT period, >80% of Rebif users met an 80% threshold, while almost 30% of Betaseron users did not. In the post-BETACONNECT period, >80% of both Rebif and Betaseron users met an 80% threshold.

Persistence: In the pre-BETACONNECT period, median persistence in days was higher for Rebif (199, 95%CI 167 – 235) than for Betaseron (152, 95%CI 105 – 231) while in post-BETACONNECT period, persistence was higher for Betaseron (327, 95%CI 244 – 440) than for Rebif (229, 95% CI 184 – 304).

Conclusions:

Following the introduction of BETACONNECT, Betaseron users were more adherent, with improved persistence and with >80% of users meeting 80% MPR, a threshold commonly used to define good adherence.

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Keywords: Disease-modifying treatments in MS, Equipment in MS, Patient empowerment in MS treatment

A Unique Case of a Patient with Tuberous Sclerosis and Recent Diagnosis of Neuromyelitis Optica

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Background:

Tuberous sclerosis complex (TSC) is an inherited neurocutaneous disorder that is characterized by pleomorphic features involving many organ systems, including multiple benign hamartomas of the brain, eyes, heart, lung, liver, kidney, and skin. Neuromyelitis optica (NMO, previously known as Devic disease) and neuromyelitis optica spectrum disorders (NMOSD) are inflammatory disorders of the central nervous system characterized by severe, immune-mediated demyelination and axonal damage predominantly targeting optic nerves and spinal cord. Traditionally considered a variant of multiple sclerosis, NMO is now recognized as a distinct clinical entity based on unique immunologic features.

Objectives: to report a unique case of TS and NMO

Methods: Case report

Results: A 30 year old woman who carries the diagnosis of TSC suddenly started to have tingling in the legs and vomiting. The vomiting was intractable and continued for a week. Her tingling progressed up to her waist and into her abdomen. She also started having episodic spasms in her arms and legs. A month later she started having difficulty walking and tingling in her hands. She underwent MRI of spine that showed longitudinally extensive spinal cord lesions in her upper cervical and lower thoracic cord. Deferential diagnosis at that time was included in neuromyelitis optica, transverse myelitis and astrocytoma in the setting of tuberous sclerosis but then NMO IGG antibody find to be positive both in serum and CSF.

The patient received 5 days of steroids and as she still had symptoms she was given Plasma Exchange for 5 sessions and then continue treatment plan with Rituximab.

Conclusions:

This is a unique case of a patient who diagnosed with TSC with clinical (seizures) and brain MRI features (cortical tubers) of TSC in her childhood and now diagnosed with NMO at the age of 30 with clinical features, Longitudinally extensive spinal cord lesions and positive NMO IGG antibody in serum and CSF.

Further studies needed to find out more information regarding the co-occurrence of an genetic disorder like TSC and an immune-mediated disease like NMO.

Disclosure: *Nothing to disclose.*

Keywords: Genetics and MS, NMO, TS

Shorter Infusion Time of Ocrelizumab: Primary Results from the Ensemble PLUS Study in Patients with Relapsing-Remitting Multiple Sclerosis

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Background:

Ocrelizumab is an intravenously administered anti-CD20 antibody approved for relapsing and primary progressive multiple sclerosis (MS). Shortening the infusion to 2hrs may reduce the total site stay from 5.5–6hrs (approved infusion duration including mandatory pre-medication/observation) to 4hrs, which may reduce patient and site staff burden.

Objectives:

To investigate the safety profile of ocrelizumab when administered over a shorter infusion period, using primary results from ENSEMBLE PLUS.

Methods:

ENSEMBLE PLUS is a randomized, double-blind substudy to the single-arm ENSEMBLE study (NCT03085810). In ENSEMBLE, patients with early-stage relapsing-remitting MS (18–55 years; treatment-naïve; disease duration ≤3 years; EDSS score 0–3.5) receive ocrelizumab 600mg infusions every 24 weeks for 192 weeks. In ENSEMBLE PLUS, ocrelizumab (600mg) administered over the approved infusion time (3.5hrs; conventional duration), is compared with a 2hr infusion (shorter duration); the initial infusion (2×300mg) duration remains unaffected. The ENSEMBLE PLUS primary endpoint is the proportion of patients with infusion-related reactions (IRRs) following the first randomized infusion (frequency/severity assessed during and 24hrs post-infusion).

Results:

As of September 2019, 291 and 289 patients were randomized to the conventional and shorter infusion groups, respectively. Following the first randomized infusion, 67 patients (23.1%) in the conventional and 71 patients (24.6%) in the shorter infusion group experienced IRRs, from which 17.9% versus 31.0% were throat irritation, and 25.4% versus 23.9% were fatigue,

respectively. The majority of IRRs were mild or moderate; >98% of all IRRs resolved without sequelae in both groups. No IRRs were life-threatening, serious or fatal; one severe IRR occurred in both the conventional (laryngeal inflammation [second randomized dose]) and shorter duration groups (fatigue [first randomized dose]). No IRR-related discontinuations occurred. During the first randomized dose, 14 (4.8%) and 25 (8.7%) patients in the conventional and shorter infusion groups had IRRs leading to infusion interruption/slowing, respectively.

Conclusions:

Primary analysis suggests that the frequency/severity of IRRs are comparable between conventional and shorter infusions. No new safety signals were detected.

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Keywords: Disease-modifying treatments in MS, ocrelizumab

Effect of Ofatumumab on Serum Immunoglobulin Levels and Infection Risk in Relapsing Multiple Sclerosis Patients from the Phase 3 Asclepios I and II Trials

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Background:

Ofatumumab, the first fully human anti-CD20 monoclonal antibody, demonstrated superior efficacy versus teriflunomide in relapsing multiple sclerosis (RMS) patients in the Phase 3 ASCLEPIOS I/II trials. A decline in serum immunoglobulin (Ig) levels was observed with other anti-CD20 therapies.

Objectives:

To determine serum IgG and IgM levels and investigate associations between IgG/IgM levels and risk of infections in ofatumumab-treated patients.

Methods:

In the ASCLEPIOS trials, patients received subcutaneous ofatumumab 20 mg on Days 1, 7, and 14, Week 4, and every 4 weeks thereafter or once-daily oral teriflunomide 14 mg for up to 30 months (average follow-up duration: 18 months). Serum IgG/IgM levels were monitored at baseline, Weeks 4 and 12, and every 12 weeks thereafter (ofatumumab, n=946; teriflunomide, n=936). A notable decline in IgG/IgM levels was defined as 50% of the lower limit of normal (LLN) at any time (IgG, 3.5 g/L; IgM, 0.2 g/L). Outcomes included the proportion of patients with IgG/IgM levels <50% LLN, and association between low IgG/IgM levels and incidence of infections.

Results:

At Week 120, no patients reached IgG levels <50% LLN with ofatumumab (median IgG [g/L]: ASCLEPIOS I and II, 10.57 and 9.57, respectively) or teriflunomide (10.01 and 9.65). The proportion of patients who reached IgM levels <50% LLN was 2.1% (n=20/944) with ofatumumab (median IgM [g/L]: 0.91 and 0.59) and 0.6% (n=6/933) with teriflunomide (0.84 and 0.92) at Week 120. Of these patients, five experienced infections with ofatumumab, mostly non-serious (Grade 1/2 in severity), except one Grade 3 recurrent urinary tract infection, but all

infections were resolved. One patient on teriflunomide who experienced nasopharyngitis had not recovered at the time of last follow-up.

Conclusions:

A reduction in serum IgG levels <50% LLN was not observed with either treatment. IgM levels showed reductions with both ofatumumab and teriflunomide treatments; there was no apparent association with increased rate of serious/non-serious infections in RMS patients.

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Keywords: Disease-modifying treatments in MS, Immunology and MS, Safety of DMTs in MS

Ofatumumab Vs Teriflunomide in Relapsing Multiple Sclerosis: Analysis of No Evidence of Disease Activity (NEDA-3) from the Asclepios I and II Trials

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Background:

Ofatumumab, the first fully human anti-CD20 monoclonal antibody, demonstrated superior efficacy versus teriflunomide in the Phase 3 ASCLEPIOS I/II relapsing multiple sclerosis (RMS) trials. No evidence of disease activity (NEDA-3) , a comprehensive composite measure, is commonly used to determine the treatment outcome in RMS.

Objectives:

To investigate the effect of subcutaneous ofatumumab 20 mg (monthly) versus oral teriflunomide 14 mg (once daily) in achieving NEDA-3, and to separately assess the annualized relapse rate (ARR) and gadolinium-enhancing (Gd+) T1 lesions activity in the pooled ASCLEPIOS I/II trials.

Methods:

We pooled data from the ASCLEPIOS I (n=927) and II (n=955) trials. Outcomes included NEDA-3 (defined as a composite of no 6-month confirmed disability worsening [6mCDW], no confirmed multiple sclerosis relapse, no new/enlarging T2 lesions, and no Gd+ T1 lesions) and its individual components in a modified full analysis set (modified FAS; logistic regression model). ARR by time intervals and Gd+ T1 lesions in the FAS (negative binomial model for both) were also analyzed.

Results:

The odds of achieving NEDA-3 with ofatumumab versus teriflunomide were >3-fold higher at Month (M) 0–12 (47.0% vs 24.5% of patients; odds ratio [95% confidence interval (CI)]: 3.36

[2.67; 4.21], p<0.001) and >8-fold higher at M12–24 (87.8% vs 48.2% of patients; 8.09 [6.26; 10.45], p<0.001). Over 2 years, a higher proportion of ofatumumab-treated patients were free from 6mCDW (91.9% vs 88.9%), relapses (82.3% vs 69.2%) and lesion activity (54.1% vs 27.5%) compared with teriflunomide. Ofatumumab significantly reduced ARR compared with teriflunomide at all cumulative time intervals: M0–3 (p=0.011), and all subsequent time intervals from M0–27 (p<0.001). Ofatumumab significantly reduced the mean number of Gd+ T1 lesions per scan by 95.9% compared with teriflunomide (mean [95% CI]: 0.02 [0.01; 0.03] vs 0.50 [0.42; 0.59]; p<0.001).

Conclusions:

Ofatumumab increased the probability of achieving NEDA-3 and demonstrated superior efficacy versus teriflunomide in patients with RMS.

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Keywords: Comprehensive care and MS, Disease-modifying treatments in MS, Immunology and MS

Real-World Findings of Usability and Usefulness of MS Progression Discussion Tool– a Physician-Completed Digital Tool to Evaluate Early Signs of Disease Progression

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Background:

MSProDiscuss™ is a validated physician-completed tool based on a set of weighted questions that include information on multiple sclerosis (MS) relapses, symptoms and impacts experienced by the patient within the past 6 months. The tool's traffic light system-linked output is meant as an aid for discussing the signs of MS disease progression. The tool is available online at www.msprodiscuss.com.

Objectives:

To report physician findings on usability and usefulness testing of the MSProDiscuss tool while discussing disease progression with patients in the real-world setting.

Methods:

An online qualitative survey was undertaken in 34 countries. Healthcare practitioners (HCPs), who completed individual questionnaires (*i*) after using MSProDiscuss during face-to-face patient consultations and a final questionnaire (*f*) to capture the overall experience on the tool. The HCPs also provided general feedback and recommendations for improving the tool.

Results:

In total, 301 HCPs (including 23 MS Nurses and 6 Neurology nurse practitioners) tested the tool in 6974 MS patients. The time taken to complete MSProDiscuss during a regular consultation was 1–4 minutes in 97% (*i*) to 98% (*f*) of the time. In 94% (*i*) to 97% (*f*) cases, HCPs agreed that patients were able to comprehend the questions from the tool. HCPs were willing to use the tool again in the same patient 91% (*i*) of the time. MSProDiscuss was useful in discussing MS symptoms and its impact on daily activities (88% *i* / 92% *f*) and cognitive function (79% both *i* and *f*) and in discussing progression in general (88% *i* / 90% *f*). While completing the final questionnaire, 95% of HCPs agreed that the questions were similar to those asked in regular consultation. MSProDiscuss was also found helpful for *understanding* the impact of MS symptoms on daily activities (91%) and cognitive function (80%). Overall, 92% of the HCPs would recommend MSProDiscuss to a colleague. Regarding integration of MSProDiscuss into their clinical practice, 92% of HCP think that it is feasible and 86% are willing to integrate. Key recommendations were to allow for longitudinal follow-up, expand on cognitive assessments, and provide a patient-completed version; these are considered in the updated version of MSProDiscuss.

Conclusions:

The findings from this real-world study suggest that MSProDiscuss is a usable and useful tool to facilitate physician-patient discussion on disease progression in daily clinical practice by capturing structured disease history.

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Keywords: Comprehensive care and MS, Symptoms of disease progression

Efficacy and Safety of the Bruton's Tyrosine Kinase Inhibitor (BTKI) Evobrutinib in Relapsing Multiple Sclerosis over 108 Weeks: Open-Label Extension to a Phase 2 Study

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Background: In a Phase 2 randomized, controlled trial (RCT; NCT02975349) in patients with relapsing multiple sclerosis (MS), evobrutinib 75 mg twice daily (BID) reduced total T1 gadolinium-enhancing lesions (primary endpoint) and annualized relapse rate (ARR) over 24 weeks versus placebo, with efficacy maintained through Week 48.

Objectives: To assess long-term efficacy and safety in the open-label extension (OLE) of the study.

Methods: In the 48-week double-blind period, patients received evobrutinib 25 mg or 75 mg once daily (QD), evobrutinib 75 mg BID, open-label dimethyl fumarate (240 mg BID), or placebo for the first 24 weeks; all arms continued with the original treatment assignment until 48 weeks, except placebo patients who were switched to evobrutinib 25 mg QD. At Week 48, all patients could enter the OLE, where treatment was initially evobrutinib 75 mg QD (for approximately 48 weeks, median) before switching to 75 mg BID. The OLE assessed long-term efficacy (0–108 weeks) and safety (60-week OLE) of evobrutinib.

Results: Of 267 randomized patients, 213 (79.8%) completed 108 weeks of treatment (48-week main study, 60-week OLE). For patients who received evobrutinib 75 mg BID in the double-blind period, the ARR (95% CI) was 0.11 (0.04–0.25) at Week 48 and 0.12 (0.06–0.22) for the 108-week period. Evobrutinib was generally well tolerated, with the safety profile maintained

during the 60-week OLE. Transient elevated liver aminotransferases, reported in the 48-week double-blind period, were not observed in the OLE.

Conclusions: Efficacy and safety were maintained long-term. Two Phase 3 RCTs evaluating the efficacy and safety of evobrutinib in relapsing MS patients commence in 2020.

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Keywords: Disease-modifying treatments in MS

Natalizumab-Treated Patients with RRMS Report Better "Feel-Good" Outcomes on Key Physical, Emotional and Cognitive Domains Compared to Other Dmts

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Background: Natalizumab is an efficacious therapy for patients with relapsing-remitting multiple sclerosis (RRMS). Some patients have reported a feel-good experience on natalizumab. Prior qualitative interviews of natalizumab-treated patients have suggested that the feel-good experience may be associated with increased energy and improved emotional and cognitive functioning.

Objectives: To describe survey results assessing patients self-reporting a "feel-good" experience while receiving natalizumab or other disease modifying therapies (DMTs).

Methods: Surveys were administered to adult patients with RRMS through MyMSTeam (part of the MyHealthTeam application). Patients were asked about their current DMT use and its "feel-good" effect assessed by self-reported improvements in physical, emotional, or cognitive domains. Natalizumab vs other-DMT patient responses were corrected for multiple measures and compared using t-test and Log Rank tests.

Results: Patients receiving natalizumab (n=95) or other-DMT (n=252) were included. Time since RRMS diagnosis was <6 years in 29% (natalizumab) and 35% (other-DMT) and >15 years in 29% (natalizumab) and 27% (other-DMT). Significantly higher percentages of natalizumab than other-DMT patients reported that they "feel good" on their DMT (63% vs 45%; *P*=0.001). Physical benefits were reported by 78% of natalizumab and 67% of other-DMT patients (*P*=0.017), with significantly higher rates of improved energy (23% vs 12%; *P*=0.011) and coordination (22% vs 12%; *P*=0.017) for natalizumab vs other-DMT. Comparison of patients on natalizumab vs other-DMT indicated significantly higher scores on emotional components involving improved motivation (25% vs 13%; *P*=0.007) and happiness (24% vs 11%; *P*=0.004); and improvement on cognitive component involving organizing one's thoughts (24% vs 14%; *P*=0.021). Among natalizumab patients, 59 out of 95 (61%) scored high (either 4 or 5 for "agree"/"strongly agree") on feel-good effect, and also reported significantly increased energy, balance, coordination, motivation, happiness and cognitive benefits (each *P*<0.001).

Conclusions: These real-world patient-centric survey results suggest that natalizumab is associated with a feel-good experience compared with other-DMTs. Increased physical, emotional and cognitive functioning were more common among natalizumab than other-DMT patients, consistent with qualitative interviews. These results are limited by the subjective nature of the survey responses.

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Keywords: Disease-modifying treatments in MS, Patient-reported outcomes