[CI]) of the following birth outcomes was described for IFNβ-exposed and unexposed women: low birth weight for live births (<2500g), low head circumference for infants with full-term live birth (≥37 gestational weeks) and small or large for gestational age (SGA and LGA respectively). For SGA, LGA, and head circumference, national gestational age and sex-specific national references were used. No adjustments for potential confounding factors were performed.

Among 666 IFNβ-exposed and 1330 unexposed live births, the prevalence of birth outcomes was similar between IFNβ-exposed vs unexposed. Prevalence of low birth weight (95%CI) was 3.9%(2.6-5.7) among IFNβ-exposed and 4.8%(3.7-6.1) among unexposed live births. Among 619 IFNβ-exposed and 1219 unexposed full-term live births, prevalence of low head circumference (95%CI) was 1.9%(1.0-3.4) vs 1.1%(0.6-1.8) respectively. Comparing the IFNβ-exposed vs unexposed, SGA (95%CI) was 2.1%(1.2-3.5) vs 2.0%(1.3-2.9), and LGA (95%CI) was 0.8%(0.2-1.7) vs 0.8%(0.4-1.5).

Data from Finnish and Swedish health registers showed no evidence that IFNβ exposure before and during pregnancy affected infant birth weight and head circumference.

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Efficacy and Safety of Satralizumab for Relapse Prevention in Neuromyelitis Optica Spectrum Disorder: A Pooled Analysis from Two Phase 3 Clinical Trials

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Satralizumab is a humanised recycling monoclonal antibody that binds to the interleukin-6 (IL-6) receptor; IL-6 has been implicated in the pathophysiology of neuromyelitis optica spectrum disorder (NMOSD). Satralizumab significantly reduced the risk of NMOSD relapse in two Phase 3 studies: SAkuraSky (SA-307JG; NCT02028884) and SAkuraStar (SA-309JG; NCT02073279). Hazard ratios (HR) for the risk reduction were 0.38 (95% confidence interval [CI] 0.16–0.88) in SA-307JG and 0.45 (95% CI 0.23–0.89) in SA-309JG (both p=0.018). Satralizumab was particularly effective in AQP4-IgG-seropositive patients (HR 0.21 [95% CI 0.06–0.75] in SA-307JG and HR 0.26 [95% CI 0.11–0.63] in SA-309JG).

Patients were randomized 1:1 (SA-307JG) or 2:1 (SA-309JG) to satralizumab (120 mg) or placebo, with treatment at Weeks 0, 2, 4, and Q4W thereafter. Satralizumab or placebo were administered as monotherapy (SA-309JG) or add-on to baseline immunosuppressants (SA-307JG). The primary endpoint of both studies and the pooled analysis was time to first protocol-defined relapse (PDR). Efficacy analyses were performed on the pooled intention-to-treat population. Between-group HRs for time to PDR were calculated based on Cox proportional hazards models, stratified by study. To assess the validity of pooling data across the two studies, individual study treatment effects within the pooled analysis and study by treatment interaction effect were calculated.

The pooled analysis included 104 patients who received satralizumab and 74 who received placebo. HR for time to first PDR was 0.42 (95% CI 0.25–0.71; 58% risk reduction vs placebo). For AQP4-IgG seropositive patients, the HR was 0.25 (95% CI 0.12–0.50; 75% risk reduction); in the seronegative group, the HR was 0.97 (95% CI 0.41–2.23). The validity of pooling the data was confirmed, as no interaction between study and treatment effect was observed. Incidence of adverse events was similar in satralizumab and placebo groups; there were no deaths or anaphylactic reactions.

This pooled analysis of data from two Phase 3 studies demonstrated the efficacy of satralizumab in reducing relapse risk in patients with NMOSD. Satralizumab had a favourable safety profile as monotherapy or alongside immunosuppressants.

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Long-Term Reduction of Relapse Rate and Confirmed Disability Progression After 6 Years of Ocrelizumab Treatment in Patients with Relapsing Multiple Sclerosis

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The efficacy and safety of ocrelizumab (OCR) in relapsing multiple sclerosis (RMS) were demonstrated in the 96-week controlled double-blind period (DBP) of the Phase III trials OPERA I and OPERA II (NCT01247324; NCT01412333). Results for the 3-year follow-up of the pooled OPERA open-label extension (OLE) period have previously been reported (Hauser SL, et al. ECTRIMS 2018;Abstract P590).

At the start of the OLE period, patients who completed the DBP either continued OCR (OCR-OCR) or were switched from interferon (IFN) β-1a to OCR (IFN-OCR). Adjusted annualised relapse rate (ARR), time to onset of 24-week confirmed disability progression (CDP24) and change in adjusted mean Expanded Disability Status Scale (EDSS) score from the DBP baseline were analysed.

Overall, 82.3% of patients who entered the OLE completed OLE study Year 4. Among IFN-OCR patients, ARR decreased from 0.20 in the year pre-switch to 0.10, 0.08, 0.07 and 0.04 at Years 1, 2, 3 and 4 post-switch (Year 1 vs pre-switch, p<0.001; Year 1 vs Year 2, p=0.31; Year 2 vs Year 3, p=0.56; Year 3 vs Year 4, p=0.05). OCR-OCR continuers maintained the low ARR through the year pre-OLE and the 4 years of the OLE period (0.13, 0.10, 0.08, 0.07 and 0.05). OCR-OCR continuers vs IFN-OCR switchers had lower proportions of patients with CDP24 in the year pre-switch (7.7% vs 12.0%), and at OLE Year 1 (10.1% vs 15.6%), OLE Year 2 (13.9% vs 18.1%), OLE Year 3 (16.2% vs 21.3%), and OLE Year 4 (19.2% vs 23.7%); p<0.05, all difference comparisons. The safety profile observed in the OLE was generally consistent with that observed during the DBP.

After 6 years of follow-up, the proportion of patients with CDP24 remained lower in patients who initiated ocrelizumab treatment earlier (OCR-OCR), compared with patients who received initial IFN treatment (IFN-OCR), demonstrating that the benefits of earlier initiation of ocrelizumab were maintained compared with patients switching from IFN. Switching from IFN to ocrelizumab after 2 years at the start of the OLE period was associated with a reduction in ARR. Both OCR-OCR

and IFN-OCR patients maintained their reduction in ARR through the 4-year follow-up of the OLE period.

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Long Term Effectiveness of Cladribine in Patients Enrolled in the CLARITY Trial: Real World Experience from the Lebanese Cohort

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Cladribine has been recently approved for treatment of relapsing remitting and active secondary multiple sclerosis (MS). However, long term data regarding its effectiveness beyond the trial period is still lacking.

Objective: To assess retrospectively long term effectiveness of cladribine tablets in patients with relapsing remitting MS (RRMS) enrolled in the pivotal CLARITY/CLARITY Extension trial, at the American University of Beirut MS Center-Lebanon.

Patients receiving at least one dose of cladribine were included in the final analysis. Baseline characteristics were extracted including age, gender,disease duration, EDSS, number of relapses in the previous 2 years and MRI lesions. The following outcome events were collected from the time of enrollment till the last follow-up visit at our MS center: EDSS, relapses conversion to secondary progressive MS (SPMS), new or Gd+ lesions on MRI and initiation of new DMTs.

24 patients were enrolled in the Clarity study, 2 of whom received placebo during Clarity and did not go into the extension. The average study duration was 3.6 (SD=1) years and the average follow up duration after study end was 6.2 years (SD=2.9). Overall the whole follow up was 9.8 years (SD=2). Out of 22 patients 13 started a new DMT during follow up. The annualized relapse rate (ARR) was 0.20 (95%CI=0.12-0.33) during the study and 0.20 (95%CI=0.14-0.29) during the post-study follow up. Out of 22 patients only 3 had an EDSS increase (+1.5, +1.5, +3.5) over the whole follow up period, 13 had a decrease and 6 were stable. Out of 22 patient, 2 converted to SPMS during follow up. MRI data will be reported.

This is first report assessing the long term effectiveness of cladribine tablets in a cohort of patients enrolled in the original pivotal CLARITY/CLARITY Extension trials and followed for up to 10 years. Cladribine was highly effective inpreventing long term disability progression, relapses and conversion to SPMS.

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Pregnancy Outcomes in Patients Treated with Ocrelizumab

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Ocrelizumab (OCR) is a humanised anti-CD20+ monoclonal antibody approved for the treatment of relapsing and primary progressive forms of multiple sclerosis (MS) and has also been studied in clinical trials for rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). As many patients with MS are women of reproductive age, pregnancy outcomes in OCR-exposed patients are important. B-cell levels in neonates exposed to OCR in utero have not been studied in trials, and the effect of OCR on the immune system of the newborn is unknown.

Analysis includes pregnancies in women treated with OCR in clinical trials/post-marketing sources up to 31/03/2019. In the EU, women of childbearing potential are recommended to use contraception while receiving and for 12 months after the last OCR infusion; use of two contraceptive methods until 48 weeks after the last OCR infusion/until B-cell repletion (whichever longer) was required in trials. A foetus was considered to have in utero OCR exposure if the last infusion occurred within 3 months of conception or during pregnancy or if the date was unknown.

As of 31/03/2019, a total of 362 pregnancies exposed to OCR (MS, N=267; RA or SLE, N=33; no reported indication, N=62) have been reported. Of these, 267 were MS patients (trials, N=78; post-marketing, N=189); 118 were considered to have foetal OCR exposure (N=47 with no foetal exposure; N=102 foetal exposure unknown). Preliminary outcomes of the 267 pregnancies in women with MS exposed to OCR at cut-off include 62 live births, 86 ongoing pregnancies, 25 elective abortions, 10 spontaneous abortions, 1 stillbirth, 3 ectopic pregnancies, 22 lost to follow-up and 58 unknown or not reported outcomes.

Reviewed cases to date do not suggest an increased risk of adverse pregnancy outcomes, including spontaneous abortions or malformations, with OCR treatment. The current update remains in line with previous reports. Data will continue to be collected and assessed as part of post-authorisation commitments.

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Family Planning Decision Making is Affected in People with Multiple Sclerosis

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Many people diagnosed with multiple sclerosis (MS) are of child bearing age, therefore family planning is an important concern. This survey aimed to understand family planning decision making in people with MS (pwMS).

In total, 332 pwMS were recruited from a specialist patient panel agency to participate in a smartphone-enabled standing panel, conducted across the United States (USA; n=76), United Kingdom (UK; n=51), France (n=53), Germany (n=50), Italy (n=51) and Spain (n=51). We submitted a survey consisting of 70-80 questions that focussed on decision-making and information sources in family planning, and behaviour during/after pregnancy. Male patients did not respond to specific questions on pregnancy.

Of 332 participants, 271/332 (82%) were female; 185/271 (56%; n=185) of these females were of child bearing age (18-45 years). In the 35-45 age subgroup, 77/271 (28%) were less likely to have children (40% USA, 50% UK, 45% France, 60% Germany, 30% Italy, 38% Spain) than females of the same age in the general population USA and United Nations censuses (16-19%). Overall, 116/332 (35%) participants stated that the disease altered (69/332, 21%) or made them decide against (47/332, 14%) having children; 22/332 (6%) indicated the disease delayed their plans for having children, 50/332 (15%) led to minimal impact and 144/332 (44%) indicated no impact on plans. Primary sources of information on family planning were: 1.Healthcare professionals (HCPs): neurologists (41%), obstetricians (16%), general practitioners and family physicians (15%), MS nurses (9%); 2.Search engines and online (4%); 3.Various (5%). The remaining participants