(10%) opted for 'non-applicable'. In total, 258/332 (78%) pwMS indicated family planning was not considered when selecting treatment.

Overall, 56% of pwMS reported that the disease affected, with different degrees of impact, their family planning decision-making. HCPs were the main source of information.

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Efficacy of Subcutaneous Interferon B-1a in Patients with a First Clinical Demyelinating Event in REFLEX is Maintained After Application of the 2017 McDonald Criteria

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In REFLEX, subcutaneous interferon β-1a (scIFNβ-1a) reduced conversion to McDonald (2005 criteria) and clinically definite (CD) multiple sclerosis (MS) versus placebo in patients with a first clinical demyelinating event. Retrospective analysis demonstrated overall results were unchanged after application of McDonald-2010 MS criteria. Revised McDonald-2017 MS criteria included presence of cerebrospinal fluid specific oligoclonal bands, symptomatic lesions, and cortical lesions. Effect of scIFNβ-1a on time to McDonald-2005 MS and CDMS, and annualised relapse rate (ARR) during REFLEX was assessed, stratified by retrospective diagnosis of patients at baseline that did/did not meet McDonald-2017 MS criteria.

During REFLEX, patients were randomised to scIFNβ-1a three times (tiw) or once weekly (qw), or placebo for 2-years. Patients in the intention-to-treat population were retrospectively stratified into McDonald-2017-positive (retrospectively met the McDonald-2010 MS criteria at baseline or had positive oligoclonal bands) and -negative subgroups. Kaplan-Meier curves estimated time to McDonald-2005 MS or CDMS by treatment group for each McDonald-2017 subgroup.

Oligoclonal band detection was optional during REFLEX and only a small number of patients were added from the McDonald-2010 analysis. Overall, 235/517 patients were McDonald-2017-positive at baseline (40 were McDonald-2010-negative but had positive oligoclonal bands). In the McDonald 2017-positive subgroup, scIFNβ-1a tiw or qw versus placebo significantly delayed time to McDonald-2005 MS (hazard ratio [HR] versus placebo: tiw,0.47;p<0.001; qw,0.58;p=0.002) and CDMS (HR versus placebo: tiw:0.46;p=0.010; qw:0.42;p=0.003). scIFNβ-1a qw and tiw significantly reduced mean ARR versus placebo in McDonald-2017-positive patients (69.1% and 59.3%;p<0.001).

Effect of scIFNβ-1a observed in McDonald-2010 patients on time to McDonald-2005 MS and CDMS was maintained in McDonald-2017-positive patients, although only a small number of patients were added after applying the 2017 criteria.

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Subcutaneous Interferon Beta-1a 22/44 mg Demonstrates Comparable Effectiveness Versus Teriflunomide in Newly Treated Patients with Multiple Sclerosis. a Study in a French Nationwide Cohort of Multiple Sclerosis: Observatoire Francais De La Sclérose En Pla

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Subcutaneous interferon beta-1a (scIFNβ-1a) is a well-established multiple sclerosis therapy with approximately 1.69 million patient-years of exposure. Comparing real-world outcomes for scIFNβ-1a 22/44μg and teriflunomide (TFN) can provide insights into the benefits of both therapies. Effectiveness of IFNβ-1a versus TFN was compared by assessing relapse incidence (Year-2), proportion of patients with disability progression confirmed over 6-months with the expanded disability status scale (EDSS; Year-2), and proportion of patients achieving no evidence of disease activity (NEDA-3; Year-1).

Patients with relapsing-remitting multiple sclerosis (RRMS) onset date, initiating IFNβ-1a or TFN between Jan-2014–Jun-2018 were included. Patients, pregnant, or with RRMS duration ≥10 years were excluded. Patients were categorised by drug initiated and followed regardless of drug discontinuation. Risk of first relapse was compared by proportional hazard Cox model with hazard ratio (HR; 95% confidence intervals [CI]) and EDSS and NEDA-3 status by logistic regression with odds ratio (OR; 95%CI). To account for baseline differences, results were weighted on propensity score via Inverse Probability of Treatment Weighting (IPTW) method.

Respectively, 244 and 688 patients were included in IFNβ-1a and TFN cohorts for relapse risk. Year-2: 39.4%(95%CI,34.7-51.4) IFNβ-1a versus 49.2%(42.7-54.7)TNF patients had ≥1 relapse (HR, 0.79[0.59-1.06]); 8.5%(95%CI,2.2-22.3) IFNβ-1a versus 11.4%(6.4-22) TNF patients presented disability progression (OR, 0.72[0.24-2.13]). Year-1: 73.1%(95%CI,40.0-79.6) IFNβ-1a versus 55.1%(43.7-68.5) TFN patients achieved NEDA-3 (OR, 2.22[0.90-5.56]).

Considering baseline confounders, no differences in relapse incidence (Year-2), disability progression (Year-2), or achievement of NEDA-3 (Year-1) were observed with IFNβ-1a versus TFN. However, since the IPTW method did not balance some baseline differences between groups, remaining confounders may have biased the conclusions. The small sample size limited power of analyses.

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Updated Safety of Cladribine Tablets in the Treatment of Patients with Multiple Sclerosis: Integrated Safety Analysis and Post-Approval Data

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Integrated analysis of pooled clinical safety data allows comprehensive characterisation of the safety profile of cladribine tablets (CT) 10mg (3.5mg/kg cumulative dose over 2 years [CT3.5]) in patients with relapsing multiple sclerosis. This analysis aimed to update the previously reported serious treatment emergent adverse event (TEAE) profile of CT3.5 following integration of final data from the PREMIERE registry, and report post-approval safety data from worldwide sources.

The monotherapy oral cohort (CT3.5, N=923, patient-years [PY]=3936.69; placebo [PBO], N=641, PY=2421.47) was derived from the CLARITY, CLARITY Extension, and ORACLE-MS trials, and the PREMIERE registry. Adjusted incidences per 100PY were calculated for AEs, cumulative to the end of PREMIERE (October 2018). Serious and non-serious AEs from post-approval sources are also summarised.

Patient characteristics were balanced between treatment groups (mean age [37.8 years,CT3.5; 37.2 years,PBO], proportion of females [66.3%,CT3.5; 66.1%,PBO] and proportion of patients with prior disease modifying drug experience [19.9%,CT3.5; 20.4%,PBO]). Incidences per 100PY for ≥1 serious TEAE were 3.80 (CT3.5), and 3.05 (PBO). Incidences per 100PY for serious lymphopenia (preferred term [PT]) was 0.10 (CT3.5), 0 (PBO). For serious infections and infestations (system organ class), incidences per 100PY were 0.60 (CT3.5), 0.42 (PBO); for serious herpes zoster (PT): 0.05 (CT3.5), 0 (PBO). Incidences per 100PY for malignant tumours were 0.26 (CT 3.5), 0.12 (PBO). Post-approval sources reported 1622 AEs in the Periodic Benefit-Risk Evaluation Report, of which 275 were serious; none represented a new safety signal.

No new major safety findings were identified in this finalised integrated dataset which includes final data from PREMIERE. This profile is consistent with the previously published integrated safety analysis profile. No new safety signals were identified in the real world post-approval data of cladribine tablets.

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Long-Term Disease Stability Assessed by the Expanded Disability Status Scale in Patients Treated with Cladribine Tablets in the CLARITY and CLARITY Extension Studies

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Treatment with cladribine tablets 10mg (cumulative dose 3.5mg/kg [CT3.5] over 2 years) in CLARITY and CLARITY Extension reduced relapse rate and slowed disability progression versus placebo in patients with relapsing remitting multiple sclerosis (RRMS). This post hoc analysis evaluated long-term disease stability assessed by the Expanded Disability Status Scale (EDSS) after treatment with CT3.5 in patients with RRMS in CLARITY and CLARITY Extension.

Patients randomised to CT3.5 in CLARITY and placebo in CLARITY Extension, with ≥1 post-baseline EDSS measurement, were included (CP3.5; n=98). EDSS score over-time (from CLARITY randomisation to end of follow-up in CLARITY Extension, including the bridging interval between studies) was assessed at 6-monthly intervals, and separately time to 3- and 6-month confirmed EDSS score progression from CLARITY baseline. EDSS score worsening/improvement in each year was defined as any increase/decrease in minimum EDSS score at 6-monthly intervals; all other cases were classified as stable. Increase or decrease was defined as an EDSS score change of 1, 1.5 or 0.5 points at baseline EDSS ≤4.5, 0, ≥5.0 respectively.

Five years post-CLARITY baseline, median EDSS remained stable versus baseline. Median EDSS score (95% confidence interval [CI]) for CP3.5 patients was 2.5(2.0-3.5) versus 3.0(2.5-3.5) at baseline. In each 12-month period, percentage of patients with EDSS score stability was >50%; improvement, 21-30%; worsening, 0-25%. During Year 5, percentage of patients with EDSS stability was 53.9%; improvement, 21.3%; worsening, 24.7%. Less than 30% of patients reached 3- or 6-month confirmed EDSS progression by Year 5.

EDSS score was stable up to 5 years post-CLARITY baseline for the CP3.5 group. Between 20-30% of patients demonstrated improvement in EDSS score versus baseline each year.

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Long Term, Registry-Based, Prospective, Post-Authorization Safety Study Evaluating Adverse Events of Special Interest in Patients with Highly Active Relapsing Multiple Sclerosis Newly Started on Cladribine Tablets – CLARION

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To generate high quality safety data, multiple Sclerosis (MS) registries have begun to collect safety data more systematically, and use MedDRA coding of serious adverse events (SAE) to harmonise data collection across registries. Major MS registries and seven pharmaceutical companies all agreed on a common safety protocol, which is informing a standardised approach to the use of MS registries for SAE collection. CLARION is a prospective, multi-country, observational cohort study involving nine MS registries covering 14 countries. CLARION will evaluate the safety profile, in terms of adverse events of special interest (AESI), of patients initiating cladribine tablets (CT, n=4,000) versus those initiating fingolimod (n=4,000).

CLARION combines primary (Germany) and secondary data (other countries) and is projected to last up to 15 years with 10 years of follow-up for each included patient. Enrolled patients are those newly initiating CT or fingolimod according to the local label for MS after the date of CT launch in the relevant country or, in countries with primary data collection, after providing signed informed consent (<24 weeks after initiation of CT or fingolimod treatment). Patients are excluded if they received fingolimod prior to CT or if they received CT prior to fingolimod. Analysis of merged data from the different registries will be performed. Adjusted incidence rate and adjusted incidence rate ratios of each AESI