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Multiple Sclerosis (MS) patients may be exposed to disease modifying therapies (DMTs) during the first trimester in unplanned pregnancies. We aimed to evaluate pregnancy outcomes in MS patients exposed accidentally to DMTs.

Data of MS pregnant women were extracted from the national MS registry. Details of drug exposure and pregnancy outcomes were collected. Pregnancy outcomes in women who were exposed to DMTs were compared to women who discontinued DMTs prior to conception.

Outcomes of 142 pregnancies (120 women) were assessed; 80 (56.3%) of which were exposed to DMTs. There were no significant differences between DMT-exposed pregnancies and the non-exposed in terms of mean age ($p = 0.95$), age at onset ($p = 0.84$), age at pregnancy confirmation ($p = 0.37$) or disease duration ($p = 0.35$). In the exposed group, the most used DMTs were beta interferons (n=50; 35.2%), natalizumab (n=28; 19.7%), fingolimod (n=24; 16.9%), and dimethyl fumarate (n=5; 3.5%). In the non-exposed group, 53.2% (n=33) of patients were not on DMTs, while 21% (n=13) were on fingolimod, 19.4% (n=12) were on beta interferons and 4.8% (n=3) were on dimethylfumarate. Most pregnancies (~85%) resulted in full term births. There were no significant differences between the exposed and non-exposed in the rate of premature birth (5% versus 3.2%) and abortions (10% versus 11.3%) [$p = 0.47$]. No major fetal malformations were reported.

Most of the pregnancies in our cohort were exposed to disease modifying therapies. The pregnancy outcomes in patients exposed to DMTs is comparable to those were not exposed.

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1-Year Follow Up Efficacy of Fingolimod in the Treatment of Relapsing-Remitting Multiple Sclerosis (RR-MS) Among Saudi Patients

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Fingolimod is a sphingosine 1-phosphate (S1P) receptor modulator and was the first oral therapy to be approved for multiple sclerosis (MS), receiving a broad first-line indication for relapsing-remitting forms of MS (RR-MS) in the United States of America (USA) in 2010. Fingolimod has shown a significant effect on clinical and magnetic resonance imaging outcome. The aim of this study is to assess the clinical and radiological efficacy of 1 year of Fingolimoid in patients with RR-MS.

A retrospective study of Saudi patients diagnosed with relapsing RR-MS and managed with Fingolimod at Prince Sultan Military Medical City (PSMMC), Riyadh, Saudi Arabia, between 2014 and 2016. MS diagnosis was confirmed based on clinical relapses and T1 and T2 magnetic resonance imaging (MRI) findings consistent with Mcdonald criteria. Clinical characteristics including total number of relapses, Expanded Disability Status Scale (EDDS), along MRI findings outcomes were retrieved from medical records of compliant patients who has at least a 1- year follow up.

Between January 2014 and December 2016, 20 patients (15 women) were prescribed fingolimod 0.5 mg daily, either as first-line or escalation therapy. All patients were complaint to the treatment for at-least 1 year follow up. Mean age was 32.25+/-11.02. Furthermore, 19 patients had relapsing-remitting multiple sclerosis. The annual relapse rate (ARR) was 0 in 18 patients along with n EDSS of 0 in 15 patients. Moreover, there was significant reduction of gadolinium enhancement lesion on MRI in 17 patients and no new lesions in all. 85% of the fingolimod-treated petients achieved no evidence of disease activity (NEDA-3).

Fingolimod showed high efficacy in the stabilization of relapsing-remitting multiple sclerosis among Saudi patients following 1 year of treatment. This was reflected in terms of clinical and radiological findings. Fingolimod robust effect on NEDA-3 was quite clear.

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Rituximab is a Safe and Efficient Treatment in Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder: Real World Observational Study

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Rituximab is a safe, efficient and off-label drug in treatment of multiple sclerosis (MS) but is also approved in NMOSD.

100 patients entered the 2-year rituximab cohort study in our center, of whom 20 were males and 80 females. The mean age was 36. Out of the 100 patients, 58 were diagnosed with relapsing-remitting MS (RRMS), 33 with secondary progressive MS (SPMS), 4 with primary progressive MS (PPMS), 3 with neuromyelitis optica spectrum disorder (NMOSD), 1 with recurrent isolated optic neuritis (RION) and 1 with chronic relapsing inflammatory optic neuropathy (CRION). Rituximab 500-1000mg was prescribed every 6 months. 16 patients were treatment-naïve. Rituximab was discontinued in 9 patients for pregnancy planning or other reason. Five continued to receive their infusions in other centers.

80% of our patients were relapse-free during these 2 years. Annual relapse rate was reduced by 85% in multiple sclerosis patients. 47% had a stable Expanded Disability Status Scale (EDSS), 34% had improved EDSS and 17% had progression of their disability. Patients with other disorders (NMOSD, RION and CRION) were stable with no evidence of relapse or progression. 88% experienced infusion-reactions as acute advere events and 51% had delayed adverse events. All adverse events were not serious.

Rituximab is a safe and efficient drug in multiple sclerosis and neuromyelitis optica spectrum disorder.

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Expert Opinion on the Use of Cladribine Tablets in Clinical Practice for the Treatment of Relapsing Multiple Sclerosis

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Cladribine tablets are approved in Europe for the treatment of adults with highly active relapsing multiple sclerosis (MS). In general, in the EU, product labels may be too broad to provide recommendations on individual treatment options, leaving clinicians with many unanswered practical questions. Here we describe a consensus-based programme led by international MS experts with the aim of providing practical recommendations to support physicians in the use of cladribine tablets in real-life clinical practice.

Clinical recommendations were developed using a modified-Delphi consensus methodology by a steering committee (SC) of 9 international MS experts. The SC identified practical clinical questions concerning the use of cladribine tablets and a prioritisation exercise selected the 11 most important questions to answer. Statements to address each question were drafted using evidence obtained from a comprehensive literature search, a review of available evidence, and practical experiences and expert perspectives from SC members. An additional 33 faculty were invited to answer the questions via an online platform. Consolidated answers were reviewed and incorporated into clinical recommendations by the SC. Consensus on recommendations was achieved when ≥75% of respondents expressed an agreement score of 7–9, on a 9-point scale.

Consensus was achieved on 46 out of 47 clinical recommendations (n=34). Consensus in the range of 90–100% was achieved on 34/46 recommendations, 10 recommendations achieved 80–90% consensus and 2 recommendations achieved 75–80% consensus. The strength of recommendations ranged from 7–9. The one statement failing to achieve consensus scored 60.6%. Expert-agreed practical recommendations are provided on topics including: the definition of highly active disease; the patterns of treatment response and suboptimal response with cladribine tablets; and switching to and from cladribine tablets.

These expert recommendations provide up-to-date relevant guidance on the use of cladribine tablets in clinical practice.

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Efficacy of a Fourth Alemtuzumab Course in RRMS Patients from CARE-MS II Who Experienced Disease Activity After Three Prior Courses

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In RRMS patients with inadequate response to prior therapy, 2 alemtuzumab courses (12 mg/day; baseline: 5 days; 12 months later: 3 days) significantly improved outcomes versus SC IFNB-1a over 2 years (CARE-MS II [NCT00548405]). Efficacy remained durable in a 4-year extension study (NCT00930553); patients could receive as-needed alemtuzumab retreatment (≥12 months apart) for disease activity, or another disease-modifying therapy (DMT). Through Year 6, 88% remained on study; 50% received neither alemtuzumab retreatment nor another DMT; 16% received ≥4 courses; 3% received ≥5 courses. The objective was to evaluate Course 4 (C4) efficacy in RRMS patients receiving ≥4 courses of alemtuzumab.

Annualized relapse rate (ARR); improved/stable Expanded Disability Status Scale (EDSS) score (versus baseline); 6-month confirmed disability improvement (CDI). 11% of patients met inclusion criteria: ≥4 courses within 60 months of baseline; no DMT. Those receiving C5 were censored at that time.

ARR decreased after C4 (12 months pre-C4 [-12M]: 0.75; 12 months post-C4 [+12M]: 0.19; P<0.0001), remaining low (0.23) at Year 3 post-C4. More patients had stable/improved EDSS scores +12M (67.5%) versus at C4 administration (53.5%). Percentage of patients with CDI increased post-C4 (-12M: 10.0%; +12M: 26.7%).

C4 reduced relapses and stabilized/improved disability in patients with disease activity after initial treatment (C1, C2) plus one additional course (C3).

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Second-Line Therapy in Multiple Sclerosis

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Multiple sclerosis (MS) patients with breakthrough disease on immunomodulatory drugs are frequently offered to switch to second-line treatment (SLT). No head-to-head study has been performed yet to assess whether SLT is more effective than classical immunomodulators. We aim to retrospectively assess the moment of introduction, efficacity and tolerance of SLT.

We retrospectively enrolled the patients in our department with relapsing-remitting MS (RRMS) who received first-line treatment (FLT) for more than 12 months than switched to SLT for 5 consecutive years. Outcome measures were Rio Score (RS) and modified Rio Score (MRS), annualized relapse rate (ARR) and changes in expanded disability status scale (EDSS) score. We also reported the side effects developed under SLT.

We enrolled 20 patients, 6 males and 13 females. They all received interferon before switch. Twelve were switched to Natalizumab (NAT) and eight to Fingolimod (FIN). When switch was decided, 16 patients (80%) had high RS (2 or 3) and 19 (95%) had high MRS (2 or 3). Mean ARR was at 2.4 at the switch to SLT, it decreased significantly to 0.73 (70%) after 12 months and 0.4 (84%) after 5 years (p< 0.001). Nine patients were relapse-free after 12 months (75%) and 5 after 5 years (25%). Mean EDSS was at 3.36 at the switch to SLT, it significally decreased to 3 after 12 months and 1.5 after 5 years (p< 0.001). Side effects reported in 6 cases (30%); 3 cases of lymphopenia under FIN, 2 cases of lymphocytosis and on case of BK virus urinary infection under TYS.

MRS was better to predict suboptimal interferon responders than RS in our study. SLT was more effective than interferon on disease progress and activity during the first 5 years of treatment. However, prospective head to head studies are needed to get higher evidence level.

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