# KEEPING UP WITH ADVANCES IN MS:
## CASES IN DIAGNOSIS AND TREATMENT, A CASE-BASED ROADMAP FOR IMPROVED PATIENT OUTCOMES IN MULTIPLE SCLEROSIS

## Clinical Insight

### INTRODUCTION

Multiple sclerosis (MS) is a chronic, progressive, and disabling inflammatory neurologic condition that may cause irreversible damage to the central nervous system (CNS).[1] The clinical presentation of MS is heterogeneous, with a wide range of symptoms, potentially impacting cognitive and motor function, activities of daily living, and patient quality of life. It is prevalent among young adults and is a common cause of nontraumatic neurologic disability in individuals between 10 and 65 years old.[2] Early diagnosis, treatment, and monitoring are fundamental to optimizing management in patients with MS.

### DIAGNOSIS

The diagnosis of MS remains a clinical diagnosis that requires a comprehensive assessment of the patient, during which clinical symptoms are evaluated by history and physical examination, testing is ordered, and conditions on the differential diagnosis for MS are excluded. The McDonald criteria, revised most recently in 2017, can be used to integrate clinical and paraclinical findings in making the diagnosis. Specifically, clinical evaluation, magnetic resonance imaging (MRI) findings, and cerebrospinal fluid (CSF) testing are used to assess a patient for MS.[3]

As part of the diagnosis of MS, determining whether a patient evidences progression at onset is an important step toward defining clinical subtypes and determining treatment planning.[3] **Table 1** describes the 2017 McDonald criteria for MS in patients with an attack at onset, that is, relapsing-remitting MS, and **Table 2** describes the McDonald criteria for diagnosing MS in patients whose disease course is characterized by progression from onset, that is, PPMS.[4]

**Table 1**: 2017 McDonald Criteria – Attack Onset[4]

| Clinical Presentation | Additional Data Needed for MS Diagnosis |
|---|---|
| ≥2 clinical attacks and objective clinical evidence of ≥2 lesions | None |
| ≥2 clinical attacks and objective clinical evidence of 1 lesion | **DIS** demonstrated by an additional clinical attack implicating a different CNS site **OR** by MRI |
| 1 clinical attack and objective clinical evidence of ≥2 lesions | **DIT** demonstrated by an additional clinical attack **OR** by MRI **OR** CSF-specific oligoclonal bands |
| 1 clinical attack and objective evidence of 1 lesion | **DIS** demonstrated by an additional clinical attack implicating a different CNS site **OR** by MRI<br>**DIT** demonstrated by an additional clinical attack **OR** by MRI **OR** CSF-specific oligoclonal bands |

*DIS: Dissemination in Space; DIT: Dissemination in Time

**Table 2**: 2017 McDonald Criteria – Progression from Onset (PPMS)[4]

| Clinical Presentation | Additional Data Needed for MS Diagnosis |
|---|---|
| 1 year of disability progression independent of clinical relapse | **Two** of the following criteria:<br>• One or more T2-hyperintense lesions in the periventricular, cortical or juxtacortical, or infratentorial brain regions<br>• Two or more hyperintense lesions in the spinal cord<br>• Presence of CSF-specific oligoclonal bands |

**PROGNOSTICATION**

Multiple risk factors have been identified that suggest a patient may be at an increased risk of an aggressive disease course of MS or a poor prognosis **(Table 3).**[5-7]

**Table 3**: Examples of Potential Risk Factors for Aggressive Multiple Sclerosis or Cases With a Poor Prognosis[5-7]

| |
|---|
| Male sex |
| Older age |
| Nonwhite race |
| • African American |
| Smoking |
| Low vitamin D levels |
| Frequent relapses |
| Shorter interattack time |
| Incomplete recovery between attacks |
| Cerebellar, pyramidal, or sphincter involvement |
| Multisymptom presentation |
| Increased disability from onset |
| Progression from onset |
| Increased T2 lesion burden |
| Gadolinium-enhancing lesions |
| Whole brain atrophy |
| Grey matter atrophy |
| Infratentorial lesions |
| Spinal cord lesions |
| Presence of oligoclonal bands |
| High levels of neurofilament light chains |

**TREATMENT**

*Relapsing MS*

The treatment of relapsing MS has changed dramatically over the years with the development of new medications being approved by the US Food and Drug Administration on an almost yearly basis. **Tables 4** summarizes available disease-modifying therapies by mechanism of action.[8]

**Table 4: Summary of MS Therapies by Mechanism of Action[8]**

| |
|---|
| Immunomodulation<br>• Fumarates<br>• Glatiramer acetate<br>• Interferon-beta<br>• Teriflunomide |
| Cell Migration Inhibition/Lymphocyte-Sequestering<br>• Natalizumab<br>• Sphingosine-1-phosphate agonists |
| Lymphocyte Depleting<br>• Alemtuzumab<br>• Cladribine<br>• Ocrelizumab<br>• Ofatumumab |

When initiating treatment with a disease-modifying therapy, multiple real-world considerations may factor into the decision toward treatment selection, including those related to the disease, patient, and treatment, as well as access issues. Examples of disease-related factors include frequency and severity of relapses, duration since disease onset, lesion burden and location, and residual deficits. Patient-related factors include preferences regarding potency/safety, risk tolerability, monitoring requirements, route of administration, and family planning. Treatment-related factors include therapeutic risks vs benefits. Access issues may include formulary restrictions or out-of-pocket costs. Selecting the best treatment for a patient requires careful consideration and analyses of these various factors.[9-12]

*Progressive MS*

Ocrelizumab has been approved for primary progressive MS, and siponimod has been approved for secondary progressive MS.[13-14] There are also multiple ongoing clinical trials for these MS subtypes.