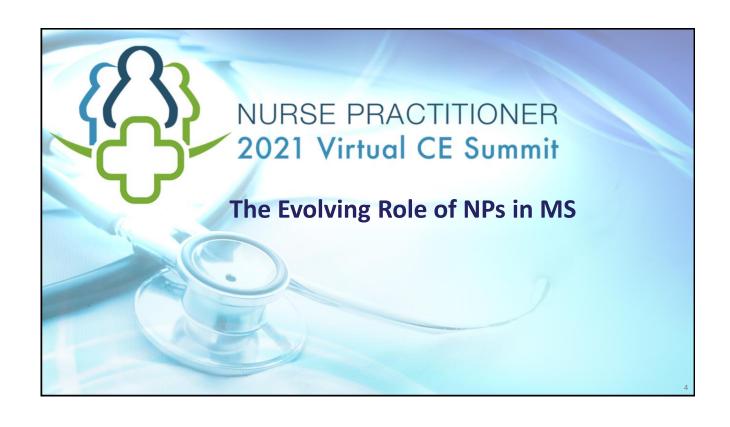


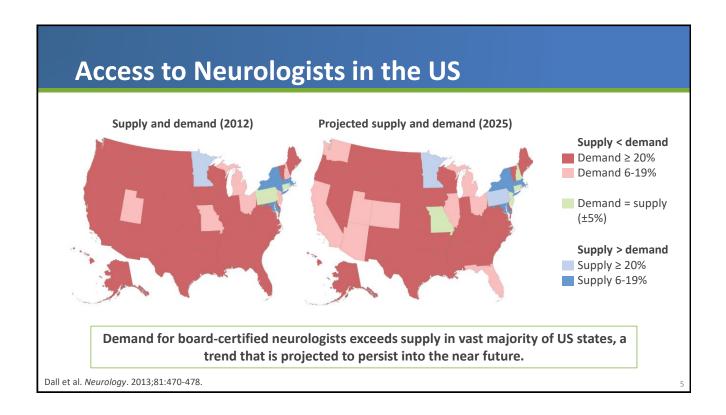
Supporter Acknowledgement

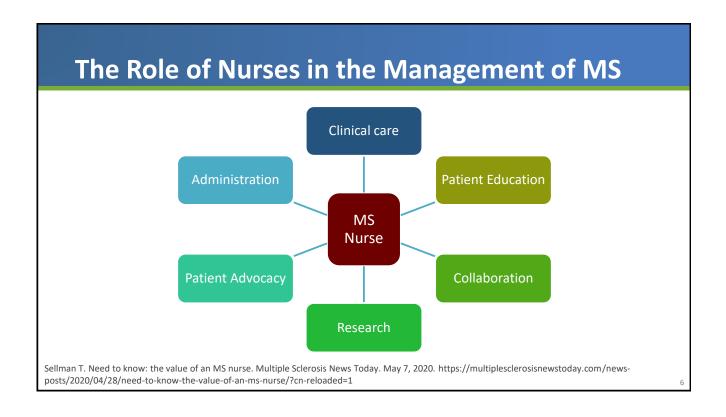
 This activity is supported by an educational grant from Biogen, Inc.

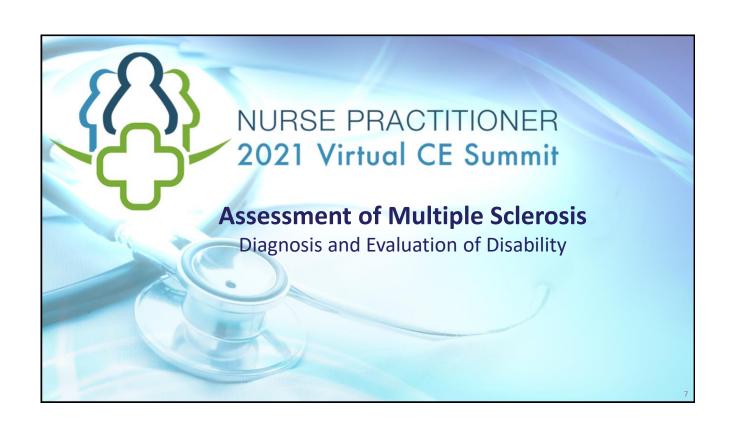
Learning Objectives

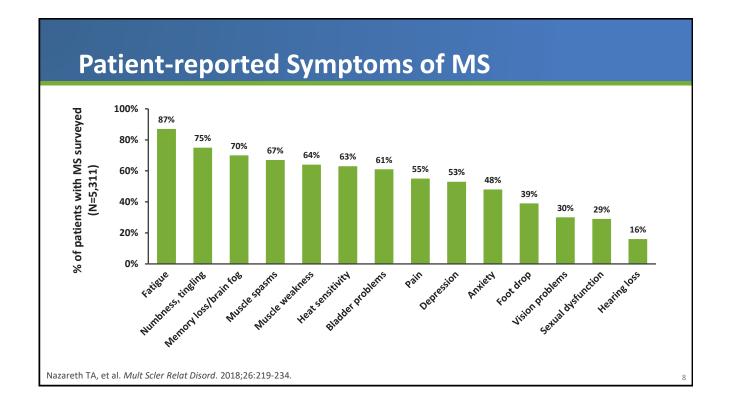
- Define the role of the NP in the healthcare setting, and their role in the diagnosis and treatment of multiple sclerosis (MS)
- Describe how to evaluate patients for signs and symptoms of early
 MS or relapse, to facilitate prompt referral to specialist care
- Identify available therapies for treatment of MS, and factors to consider in their use in individual patients
- Characterize strategies to address patient education and adherence challenges, and the long-term monitoring of overall wellness in patients with MS

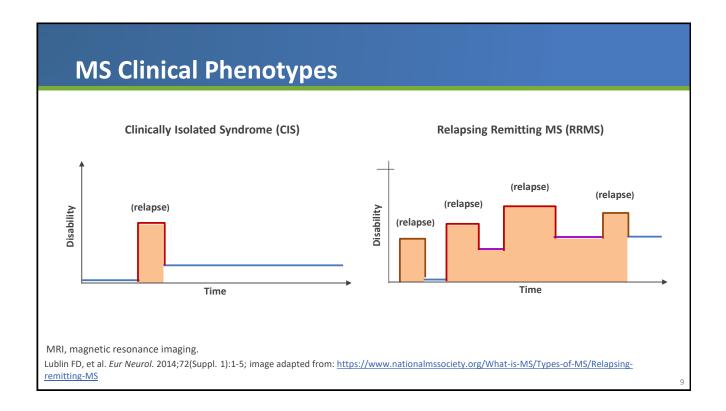


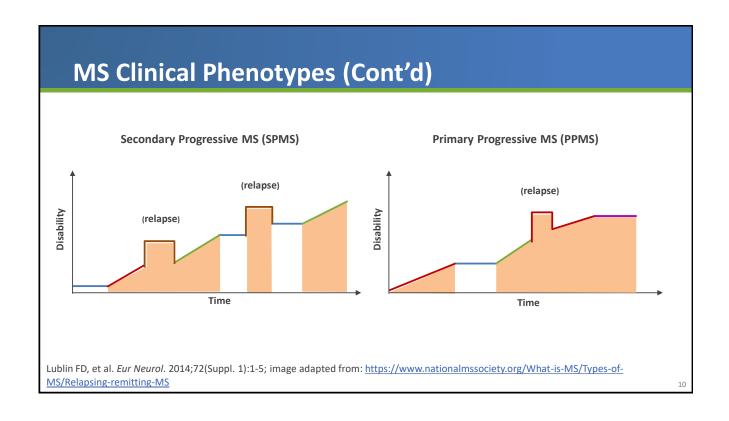












MS Disease Activity

Active vs not active

- Applicable to all phenotypes
- Has there been the following in the *prior year*?
- A clinical relapse OR
- A new or enlarging T2 lesion or contrast lesion

Progressing vs not progressing

- Applicable to PPMS and SPMS
- Has the patient gradually worsened neurologically independent of acute attacks in the prior year?

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Diagnosis of Patients With an Attack at Onset

2017 Revised McDonald Criteria

Clinical attack(s)	Lesions with objective clinical evidence	Additional data needed for diagnosis
≥2	≥2	• None
≥2	1 (& clear evidence of previous attack involving a lesion in a distinct anatomical location)	• None
≥2	1	 Dissemination in space demonstrated by an additional clinical attack implicating a different CNS site or by MRI
1	≥2	 Dissemination in time demonstrated by an additional clinical attack or by MRIs OR demonstration of CSF-specific oligoclonal bands
1	1	 Dissemination in space demonstrated by an additional clinical attack implicating a different CNS site or by MRI AND dissemination in time demonstrated by an additional clinical attack or by MRIs OR demonstration of CSF-specific oligoclonal bands

CNS, central nervous system; CSF, cerebral spinal fluid. Thompson AJ, et al. *Lancet Neurol*. 2018;17:162-173.

Diagnosis of Patients With Primary Progressive MS

2017 Revised McDonald Criteria

Criteria

One year of disability progression (retrospectively or prospectively determined) independent of clinical relapse

AND

Two of the following:

- ≥1 T2-hyperintense lesions* characteristic of multiple sclerosis in ≥1 of the following brain regions: periventricular, cortical or juxtacortical, or infratentorial
- ≥2 T2-hyperintense lesions* in the spinal cord
- Presence of CSF-specific oligoclonal bands

Thompson et al. Lancet Neurol. 2018;17:162-173.

1

Definition of MS Relapse



 New symptoms of neurological dysfunction OR worsening of existing symptoms in a patient stable for ≥30d



Acute or subacute onset



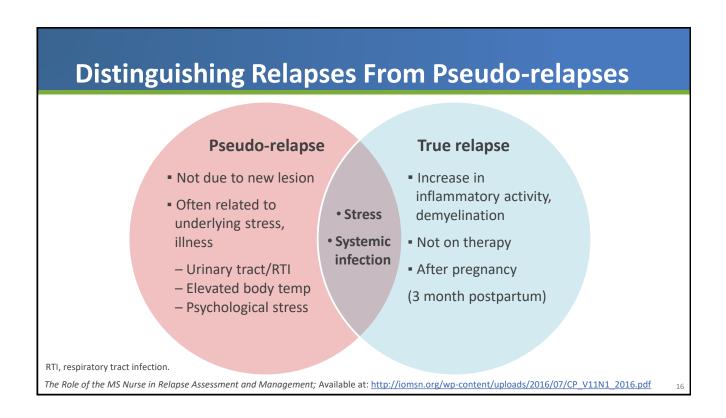
• Lasting >24 hours



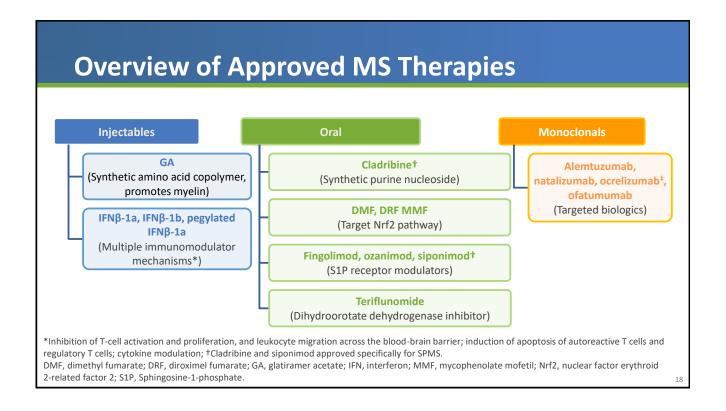
Not attributable to another cause such as infection (not a pseudo-relapse)

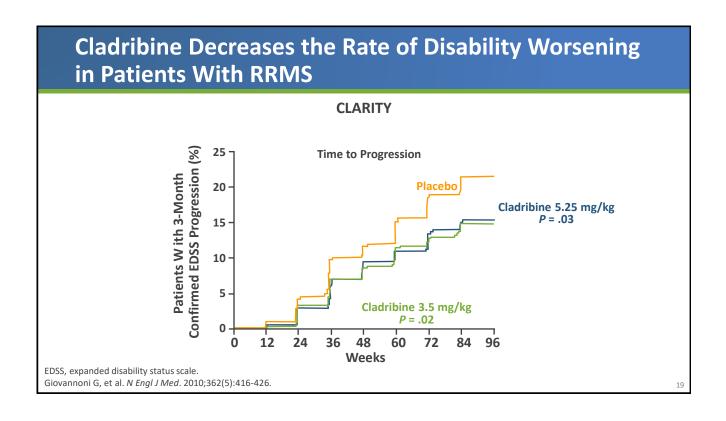
The Role of the MS Nurse in Relapse Assessment and Management; Available at: http://iomsn.org/wp-content/uploads/2016/07/CP_V11N1_2016.pdf

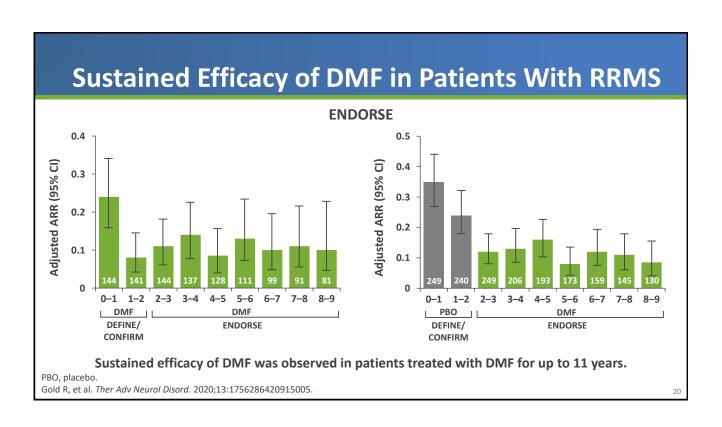
Evaluation and Management of Acute Relapse of MS: IOMSN Algorithm Is presentation consistent with a relapse? New signs/symptoms OR worsening of existing Onset acute or subacute (hours/days) • Symptoms present at least 24 hours? Yes Could this be a pseudo-relapse? • Is there underlying infection (UTI or URI)? • Do symptoms fluctuate based on setting? (Hot vs cold environment, home vs work, change in stress level) Does the relapse require treatment? • Are symptoms failing to improve? Are symptoms severe enough to warrant corticosteroids? • Do symptoms impair functional ability? Inpatient treatment or **Outpatient treatment:** contraindication to oral steroids: IOMSN, International Organization of 1,250 mg prednisone Multiple Sclerosis Nurses; URI, upper 1,000 mg IV methylprednisolone 3-5 days respiratory infection; UTI, urinary tract 3-5 days infection. The Role of the MS Nurse in Relapse Assessment and Management; Available at: http://iomsn.org/wp-content/uploads/2016/07/CP V11N1 2016.pdf

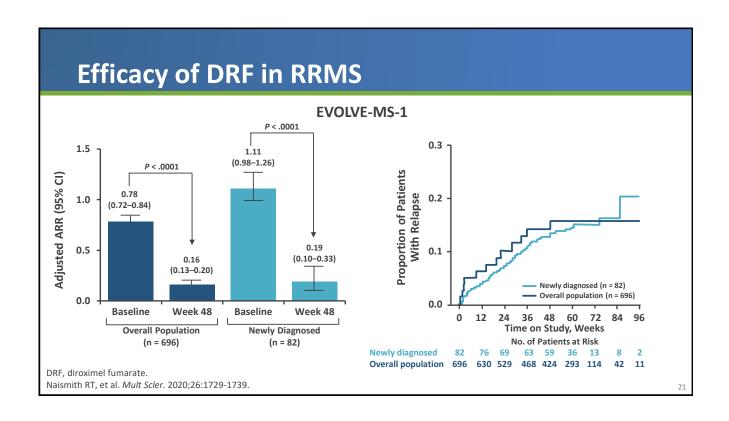


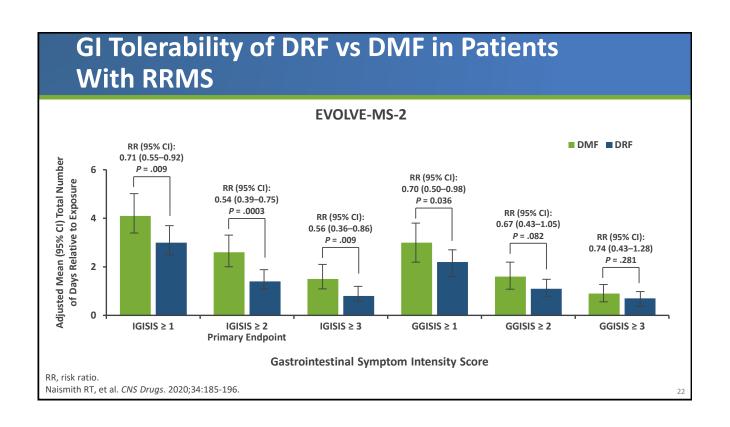


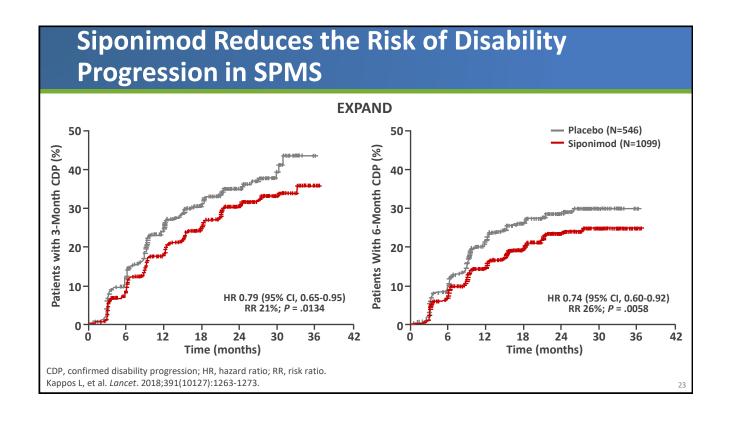


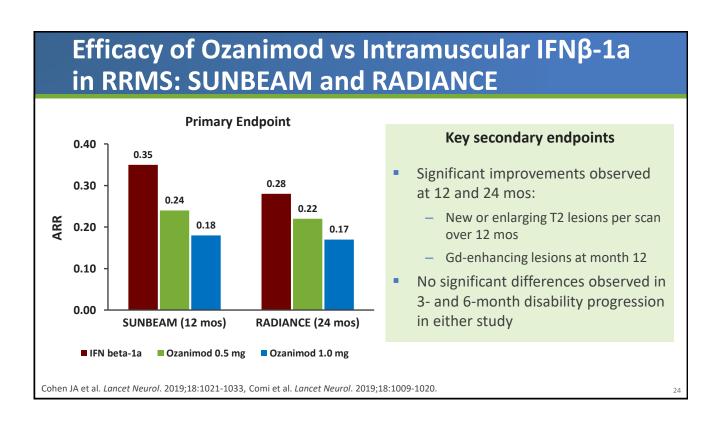


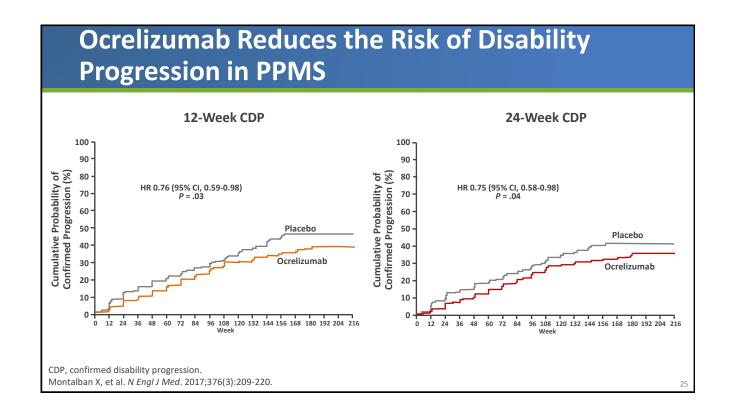


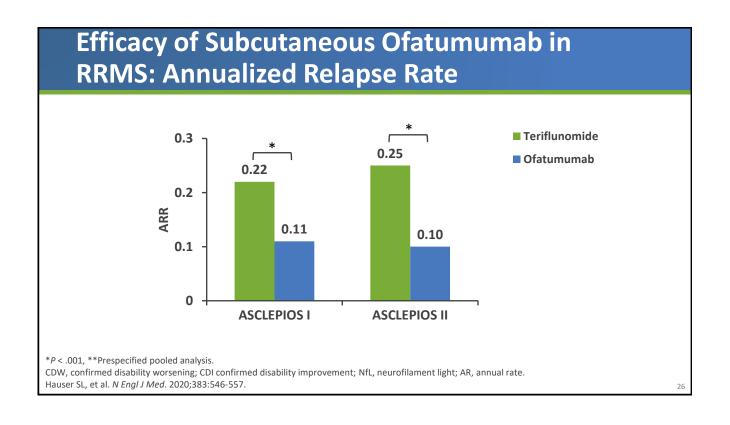












Efficacy of Subcutaneous Ofatumumab in RRMS: Key Secondary Endpoints

Outcome	ASCLEPIOS I	ASCLEPIOS II	<i>P</i> -value
CDW (HR)**	0.66 (0.50-0.86) 0.68 (0.50-0.92)		0.002 0.01
CDI (HR)	1.35 (0.95-1.92)		NS
Gd+ T1 lesions (RR)	0.03 (0.01-0.05)	0.06 (0.04-0.10)	<.001
New/enlarging T2 lesions (RR)	0.18 (0.15 to 0.22)	0.15 (0.13-0.19)	<.001
Serum NfL at 3m (Geometric mean)	8.8 (8.5-9.1) vs 9.4 (9.1-9.8)	8.9 (8.6 to 9.2) vs 10.0 (9.7-10.4)	0.01
Brain volume (AR of change)	0.07 (-0.02-0.15)	0.07 (-0.02-0.15)	NS

^{*}P < .001 vs teriflunomide, **Prespecified pooled analysis. Hauser SL, et al. N Engl J Med. 2020;383:546-557.

2

Efficacy of Ponesimod vs Teriflunomide in RRMS

OPTIMUM

Outcome	Ponesimod	Teriflunomide	<i>P</i> -value
ARR (primary endpoint)	0.202	0.290	0.0003
FSIQ-RMS	-0.01	3.57	0.0019
CUALs per year on MRI	1.405	3.164	<0.0001
CDA risk estimates 12-week 24-week	10.1% 8.1%	12. 4% 9.9%	NS NS
Brain volume loss at Week 108	-0.91%	-1.25%	<0.0001
% of patients achieving NEDA-3	25.0%	16.4%	0.0004

CDA, confirmed disability accumulation; CUALS, combined unique active lesions per year; FSIQ-RMS, fatigue symptom and impact questionnaire-RMS; NEDA, no evidence of disease activity
Fox et al. *Neurology*. 2020;94:3972.

Masitinib Treatment for PPMS and Non-active SPMS

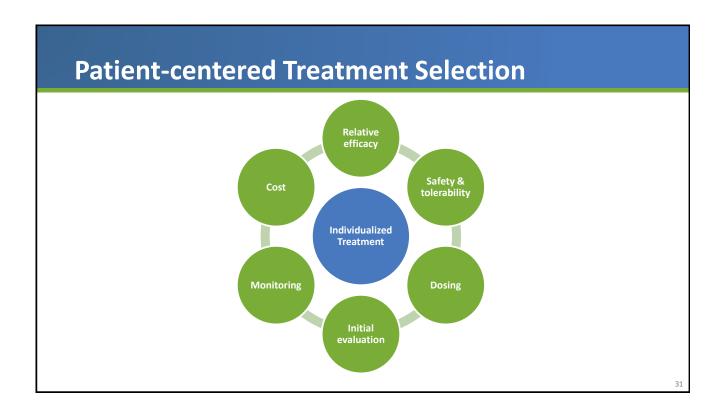
Outcome	Masitinib (4.5 mg/kg) vs PBO	95% CI	<i>P</i> -value
Change in EDSS (primary)	ΔLSM = -0.097 (effect maintained for nSPMS and PPMS subgroups)	-0.192, -0.002	0.0256
Risk for EDSS progression	HR = 0.610	0.376, 0.988	0.0446
Risk for first progression	HR = 0.58	0.35, 0.96	0.034
Risk for 12-week confirmed disease worsening	HR = 0.63	0.33, 1.20	NS

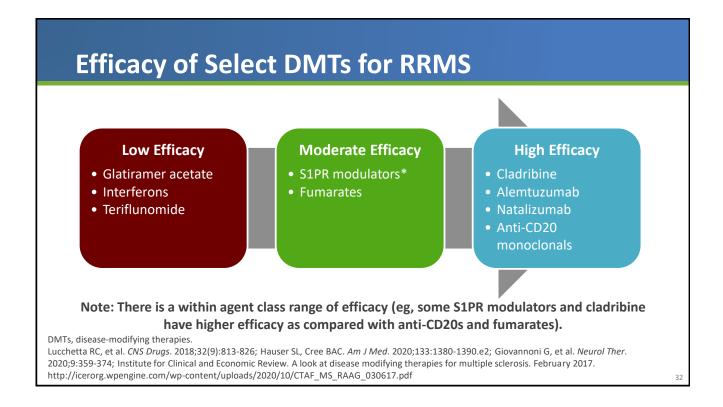
- Treatment with a higher dose (6.0 mg/kg) of masitinib did NOT result in significant beneficial effects over PBO
- Common treatment-emergent AEs being diarrhea, nausea, rash, and hematological assessments
- % of patients presenting ≥1 AE was 94.5% for MAS vs 87.1% for PBO

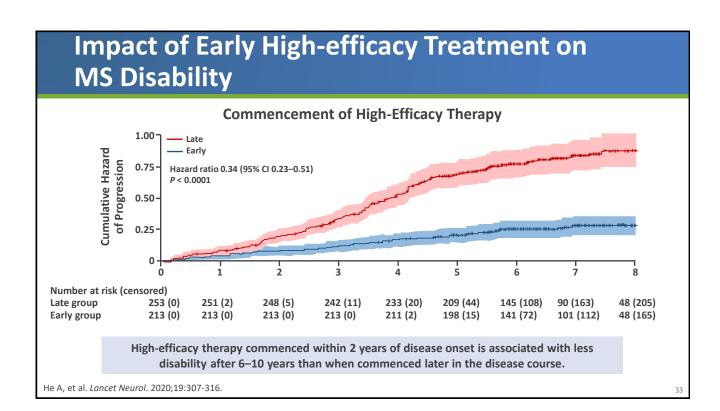
AE, adverse event; MAS, masitinib.

Vermersch P, et al. ACTRIMS/ECTRIMS MSVirtual 2020. Multiple Sclerosis Journal 2020; 26: (S3) 9–42.









Safety and Tolerability: Injectable Therapies

Agent	Adverse Events		
GA	Injection site reactions, systemic/immediate post-injection reaction		
IFNβ-1a	Headache, flu-like symptoms, injection site pain and inflammation		
• Flu-like symptoms, headache, injection site reactions, injection site breakdown, low white blood cell count			
Pegylated IFNβ-1a	Flu-like symptoms, headache, injection site reactions		

Available at: http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Brochure-The-MS-Disease-Modifying-Medications.pdf; Vumerity [package insert]. Cambridge, MA: Biogen, Inc.; 2019.

Safety and Tolerability: Oral Therapies

Agent	Adverse Events		
Cladribine	• URI, headache, lymphopenia; black box warning for potential malignancy and teratogenicity risks in treated patients		
MMF, DMF, DRF	• Flushing, GI-related (nausea, diarrhea, abdominal pain)		
• Headache, flu, diarrhea, back pain, liver enzyme elevations, sinusitis, abdominal pain, pain in extremities and cough			
• Back pain, BP changes, URI, frequent and painful urination			
• Headache, HTN, and liver enzyme elevations			
• Headache, hair thinning, diarrhea, nausea, abnormal liver tests; b warning for potential hepatoxicity and teratogenicity risks in treat			

Teriflunomide carries a black box warning for potential hepatoxicity and teratogenicity risks in treated patients; Cladribine carries a black box warning for potential malignancy and teratogenicity risks in treated patients. BP, blood pressure; HTN, hypertension; GI, gastrointestinal.

Available at: http://www.nationalmssociety.org/NationalMsSociety/media/MsNationalFiles/Brochures/Brochure-The-MS-Disease-Modifying-Medications.pdf; Vumerity [package insert]. Cambridge, MA: Biogen, Inc.; 2019.

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Safety and Tolerability: Monoclonals

Agent	Adverse Events		
Alemtuzumab	 Rash, headache, fever, nasal congestion, nausea, UTI, fatigue, insomnia, upper RTI, herpes viral infections, hives, itching, thyroid gland disorders, fungal infection, pain in joints, extremities and back, diarrhea, vomiting, flushing Infusion reactions (eg, nausea, hives, itching, insomnia, chills, flushing, fatigue, shortness of breath, changes in the sense of taste, indigestion, dizziness, pain) common during and for 24 hours or more after infusion PML has occurred (1 case). 		
Natalizumab	 Headache, fatigue, joint pain, chest discomfort, UTI, lower RTI, gastroenteritis, vaginitis, depression, pain in extremity, abdominal discomfort, diarrhea, rash PML (over 800 cases) 		
Ocrelizumab	• Infusion reactions (most commonly itchy skin, rash, throat irritation, flushed face or fever, headache), which in rare instances may be life-threatening; increased risk of infections, including RTI and herpes infections; possible increase in malignancies, including breast cancer		
Ofatumumab	 Upper RTIs, injection-related (systemic) and injection-site (local) reactions, headache, UTIs, back pain As expected with B-cell depletion, decreased immunoglobulin levels have been observed 		

NOTE: Monitoring for hypogammaglobulinemia recommended with anti-CD20s (based on rituximab data). PML, progressive multifocal leukoencephalopathy.

Recommended Monitoring During Treatment: Oral and Self-Injectable Therapies

DMT	CBC w/ diff	LFT	Thyroid Function Tests	ВР	Cardiac Exam*	Eye Exam	Skin Exam
GA							
IFNβ-1	✓	✓	✓		✓		
Teriflunomide	✓	ALT monthly for first 6 mos		✓			
Fingolimod, siponimod, ozanimod	✓	✓		✓	√ **	✓	✓
DMF, DRF	6 mos after initiation, then every 6–12 mos	As clinically indicated					
Cladribine	At 2 mos, then every 6 mos after initiation	As clinically indicated					

^{*}In patients with certain preexisting cardiac conditions; **For ozanimod.

Zeposia. Prescribing Information. Celgene Corp.

Recommended Monitoring During Treatment: Monoclonal Therapies

Alemtuzumab

- Skin exams & HPV screening annually
- CBC, serum creatinine, & urinalysis monthly until 48 mos after last infusion
- TFTs every 3 mos until 48 mos after last infusion

• HIV

Natalizumab

- JCV antibody testing every 3 months
- CBC & LFTs every 6 months

Ocrelizumab

- CBC
 Lymphocyte subsets every 6 months
- Immunoglobulins every 6–12 months
- Comprehensive metabolic profile
- HBV*

Ofatumumab

- Immunoglobulins (especially in patients with opportunistic or recurrent infections, & after discontinuation)
- discontinuationHBV*

• пв и

*If indicated.

HBV, hepatitis B virus; HPV, human papillomavirus; JCV, John Cunningham virus or human polyomavirus 2; TFT, thyroid function test. Gross RH, et al. *Continuum* (Minneap Minn). 2019;25(3):715-735.

ALT, alanine transaminase; CBC, complete blood count; LFT, liver function tests.

Gross RH, et al. Continuum (Minneap Minn). 2019;25(3):715-735; Vumerity. Prescribing Information. Biogen, Inc; 2019.

Real-world Differences in Disability and DMT Use Among Patients With RRMS by Race and Ethnicity

- NARCRMS registry December 2016–May 2020
- MS patients aged 18-50 years across 24 sites in the US and Canada (N = 722)

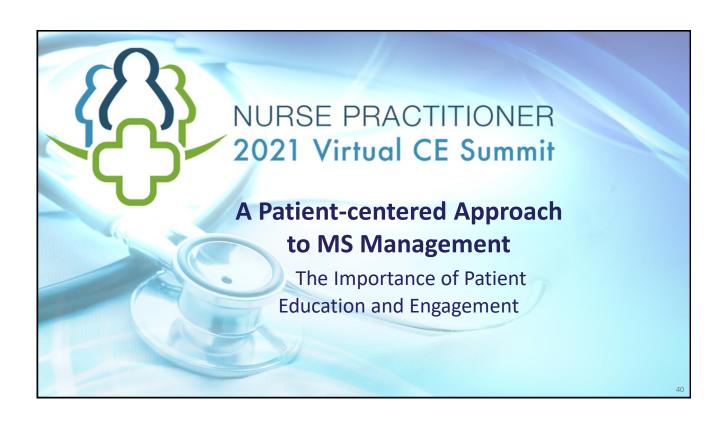
Disability

- Patients with EDSS ≥ 4.0
 - Blacks/AAs: 20%
 - Whites: **9.7%**

DMT Use

- 57% of patients treated with DMTs
 - 50% using injectables
 - 37% using oral DMTs
- Hispanic patients *less likely to use DMTs* vs non-Hispanics **(43% vs 62%)**
- Black/AA-Hispanics least likely to use DMTs among groups evaluated (26%)

NARCAMS North American Registry for Care and Research in Multiple Sclerosis; AA, African American. Rivera et al. ACTRIMS/ECTRIMS MSVirtual 2020. Abstract P0494.



Patient and Care Partner Education

Goals of Education

- Active patient participation (informed choices about health behaviors & competent, confident self-care)
- Maximal wellness (coping, adaptation, & empowerment toward better QoL & greater hope)
- Specific goals:
 - √ Understanding diagnosis & coping with life impact
 - √ Critical planning (eg, relationships, parenting, employment, and lifestyle)
 - √ Preventing disabling outcomes, with specific goals related to new symptoms

Role of the Nurse

- Assist with activities promoting health or recovery that patients can later perform unaided
- · Help individuals carry out prescribed therapy
- Contribute to behavior changes that provide knowledge & skills to maintain & improve health
- Repeatedly assess patient understanding & behavioral change
- Promote & encourage treatment adherence

QoL, quality of life. http://iomsn.org/clinical-practice-guidelines/

4

Real-world DMT Adherence and Persistence in Patients With MS

- Systematic review of 31 studies published between January 2010 and April 2018
- 31 studies of patients with MS treated with once- and twice-daily oral DMDs (N=16,398)

Outcome	No. of studies	Mean (%)	95% CI
Overall 1-year MPR	4	83.3	74.5–92.1
Overall 1-year PDC	4	76.5	72.0-81.1
Pooled 1-year MPR ≥80%	6	78.5	63.5–88.5
Pooled 1-year PDC ≥80%	5	71.8	59.1-81.9
Pooled 1-year discontinuation	20	25.4	21.6–29.7

At one year, approximately one in five patients with MS do not adhere to, and one in four discontinue, daily oral DMDs.

MPR, medication possession ratio; PDC, proportion of days covered . Nicholas et al. *BMC Neurol*. 2020;20:281.

Barriers to Adherence Among Patients With MS

DMT characteristics

- Injection-related reasons (anxiety, skin reaction, pain)
- Coping with adverse events

Ability to take DMTs as prescribed

- Disease symptoms (impaired vision, poor manual dexterity, spasticity)
- Forgetting to take medication
- Cognitive impairment, depression, anxiety

Patient perceptions

- Perceived lack of medication efficacy
- Complacency

HCP-patient relationship

- Lack of comfort in the context of the dynamic
- Ineffective communication

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Key Factors Associated With Successful Shared Decision-Making in MS

Patients well informed about MS & treatment rationale

Increased adherence

Active, dynamic communication

Reduced clinicianpatient gaps in expectation & goals Taking into account of patient preferences*

Optimal DMT selection & adherence

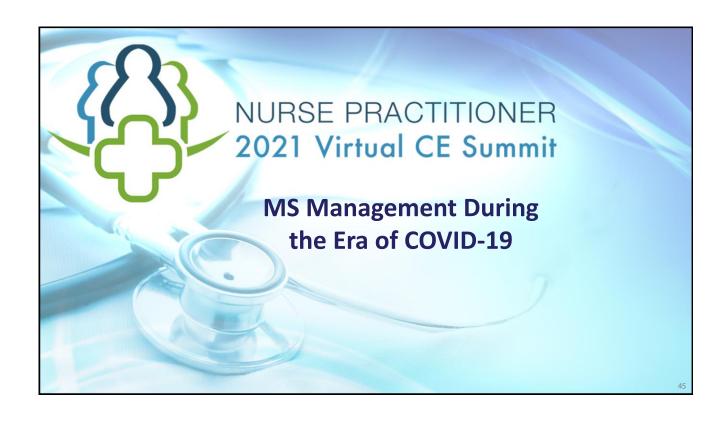
Sharing of patient preference & clinician experience

Effective evaluation of medication riskbenefit trade-offs Healthcare teamled education

Correction of patient misconceptions about disease & treatment

*This should include route of administration, tolerance, work environment, lifestyle.

Ben-Zacharia A, et al. Int J MS Care. 2018;20(6):287-297.



Recommendations for DMT During COVID-19

- 1 Patients should generally be advised to continue their current DMT
- 2 Discuss therapies with patients if COVID symptoms develop or a positive test result is obtained
- Before starting a new DMT, discuss optimal choice based on individual circumstances:
 - MS course and activity
 - Risks and benefits normally associated with treatment options
 - Individual COVID-19 risk:
 - Other risk factors for more severe COVID-19 (eg, age, medical comorbidities, current DMT)
 - Current and anticipated COVID-19 risk in the local area
 - Risk of exposure due to lifestyle
 - Emerging evidence on potential treatment interactions

 $\underline{https://www.nationalmssociety.org/coronavirus-covid-19-information/multiple-sclerosis-and-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-coronavirus/ms-treatment-guidelines-during-guidelines-during-guidelines-during-guidelines-during-guidelines-during-guidelines-during-guidelines-during-guidelines-during-guidelines-during-guidelines-during-guidelines-during-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guidelines-guideli$

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Impact of DMTs on COVID-19 Severity: Current Evidence

DMT	Impact on COVID-19 Severity	Additional Comments
Interferons and GA	• Unlikely to increase	Some evidence of reduced COVID-related hospitalization for GA
DMF, DRF, teriflunomide, fingolimod, natalizumab, ozanimod and siponimod	Not linked to increase	
Ocrelizumab and rituximab	Possible link to increase	 Advise patients taking these or ofatumumab to be especially vigilant about advice to reduce risk of COVID-19 infection
Alemtuzumab and cladribine	More data needed	 For patients being treated who live in close proximity to an outbreak, low lymphocyte counts should prompt isolation (as possible) to reduce risk

Note: Patients due for additional dosing **alemtuzumab**, **cladribine**, **ocrelizumab** or **rituximab** should consult their HCP about risks and benefits of postponing treatment.

Available at: https://www.nationalmssociety.org/coronavirus-covid-19-information/multiple-sclerosis-and-coronavirus/ms-treatment-guidelines-during-coronavirus

NURSE PRACTITIONER
2021 Virtual CE Summit

Case Evaluations

Case Study # 1: Patient Description

Kevin is 35-year-old high school teacher. He lives with his wife and twin 4-year-old sons. He is generally very active and participates in road races several times a year. He is in the office today for symptoms that include a noticeable increase in fatigue over the past several weeks, blurred vision in his left eye, and tingling in his hands and feet. He has no prior medical history that would appear to account for his symptoms.

Case Study # 1: Discussion Question

Which of the following should be included as part of Kevin's workup?

- A. MRI
- B. CSF analysis
- C. JCV antibody test
- D. CBC
- E. BMP

Case Study # 1: Discussion Question

Kevin's MRI and labs reveal a total of 3 T2 lesions (1 on his spine and 1 of which was Gd-enhancing). CSF analysis reveals the presence of oligoclonal bands and OCT confirms optic neuritis. His other labs are within normal limits. Based on these findings, he is diagnosed with RRMS. How would you characterize his risk for aggressive disease?

- A. Low
- B. Moderate
- C. High
- D. Not sure

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Case Study # 1: Discussion Question

During your conversation about his diagnosis, Kevin confides that he feels overwhelmed by the number of treatment options and has several questions about their effectiveness and safety. After assuring him that this is not at all unexpected, how do you address his concerns?

- A. Attempt to allay his anxiety by answering his questions in detail
- B. Provide him with a broad overview of the different therapies
- C. Schedule a dedicated follow-up appointment to discuss treatments

Case Study # 1: Discussion Question

Which of the following do you think is an appropriate DMT for Kevin?

- A. Glatiramer acetate
- B. An interferon-based therapy
- C. DRF or DMF
- D. A S1P receptor modulator
- E. A targeted biologic

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Case Study #2: Patient Description

Marisol is 45-year-old woman with a 12-year history of RRMS. She is currently being treated with GA. She is the manager of a local grocery store and lives with her adult niece. During her regular follow-up visit, she reports that over the last 6 months, she has experienced a gradual increase in difficulty with her endurance and balance. Exam reveals new proximal leg weakness, mild tandem unsteadiness.

Case Study #2: Discussion Question

After further evaluation, you diagnose Marisol with SPMS. Which of the following DMTs is an appropriate treatment in light of this new diagnosis?

- A. DMF
- B. Teriflunomide
- C. Cladribine
- D. Siponimod

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Case Study #2: Discussion Question

Given the current pandemic, would you elect to begin a new therapy immediately?

- A. Yes. Evidence indicates little additional COVID-related risk associated with treatments for SPMS.
- B. No. Evidence suggests that switching therapies would engender additional risk of infection.
- C. No. There is insufficient evidence to support the safety of switching therapies during the pandemic.

Case Study #2: Discussion Question

Once Marisol begins a new treatment regimen. How long would you wait before scheduling a follow-up visit to evaluate her treatment response?

- A. 1 month
- B. 2 months
- C. 3 months
- D. 6 months

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Program Summary

- Nurses involved in the care of patients with MS shoulder a broad range of responsibilities beyond clinical care, including patient advocacy, research, collaboration with the multidisciplinary healthcare team, and patient and care partner education
- Primary care nurses are often the first point of contact for patients with any type of motor, sensory, or cognitive deficit, and are thus well situated to facilitate early recognition of an MS attack
- This is especially important in light of growing recognition of the need for early effective treatment, and the recent expansion of DMTs with the potential to reduce disease progression as well as improve symptoms
- By providing patient-centered care that includes education and management guidance, nurses can help ensure that patients are equipped to participate in decision-making and achieve optimal therapeutic success

