Expert perspective on improving patient outcomes in relapsing MS: From current oral disease-modifying therapies to emerging therapeutic options

Prof. Patricia K Coyle
Professor of Neurology,
MS Comprehensive Care Center,
Stony Brook University Hospital,
Stony Brook, NY, USA

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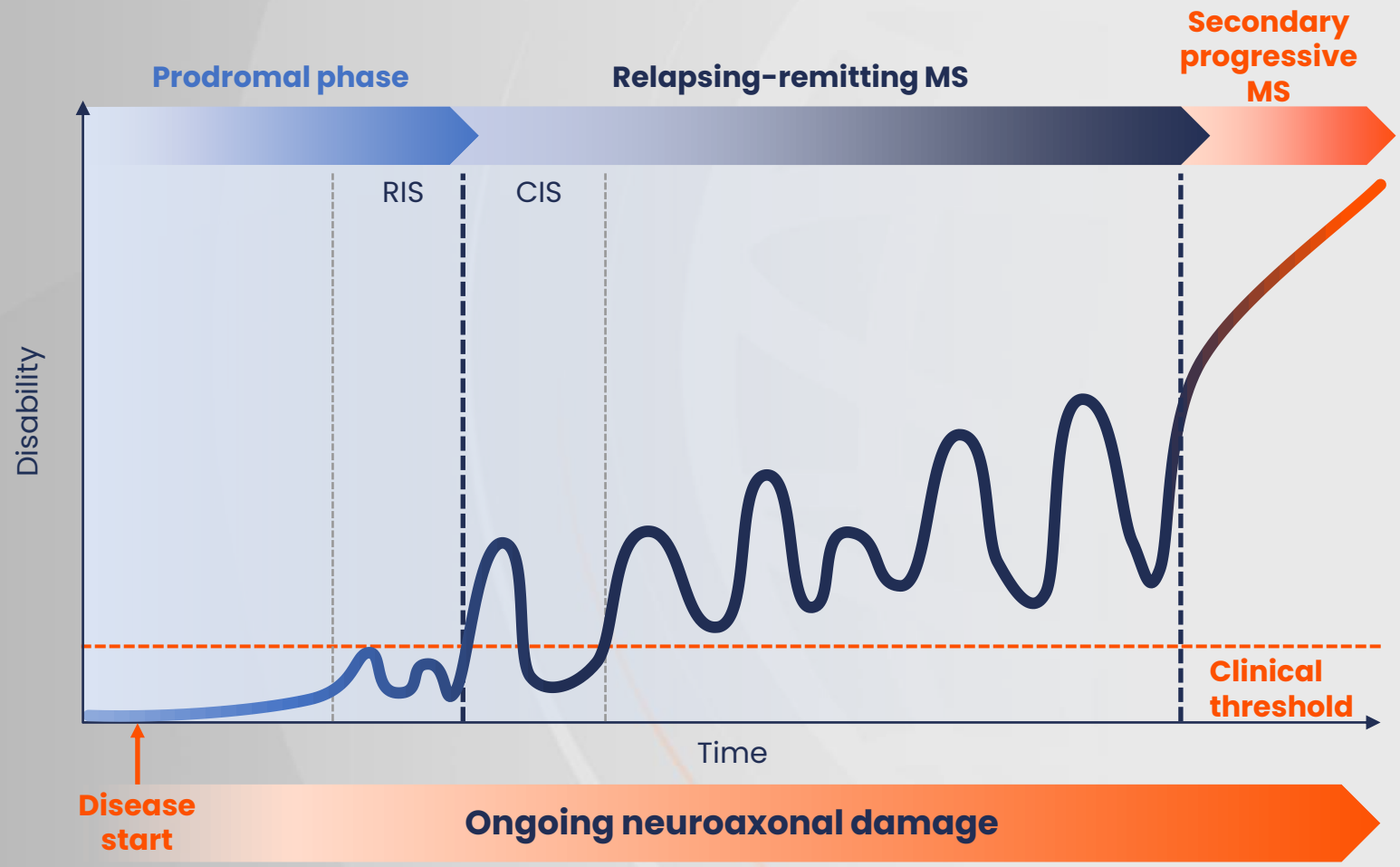
Optimal management of relapsing MS: How are DMTs used in clinical practice?

Relapsing MS: Patient journey

From preclinical to progressive disease[1,2]



CIS, clinically isolated syndrome; MRI, magnetic resonance imaging; MS, multiple sclerosis; NfL, neurofilament light chain; RIS, radiologically isolated syndrome.

1. Baecher-Allan C, et al. *Neuron*. 2018;97:742–68; 2. Tremlett H, et al. *Front Neurol*. 2022;12:761408.

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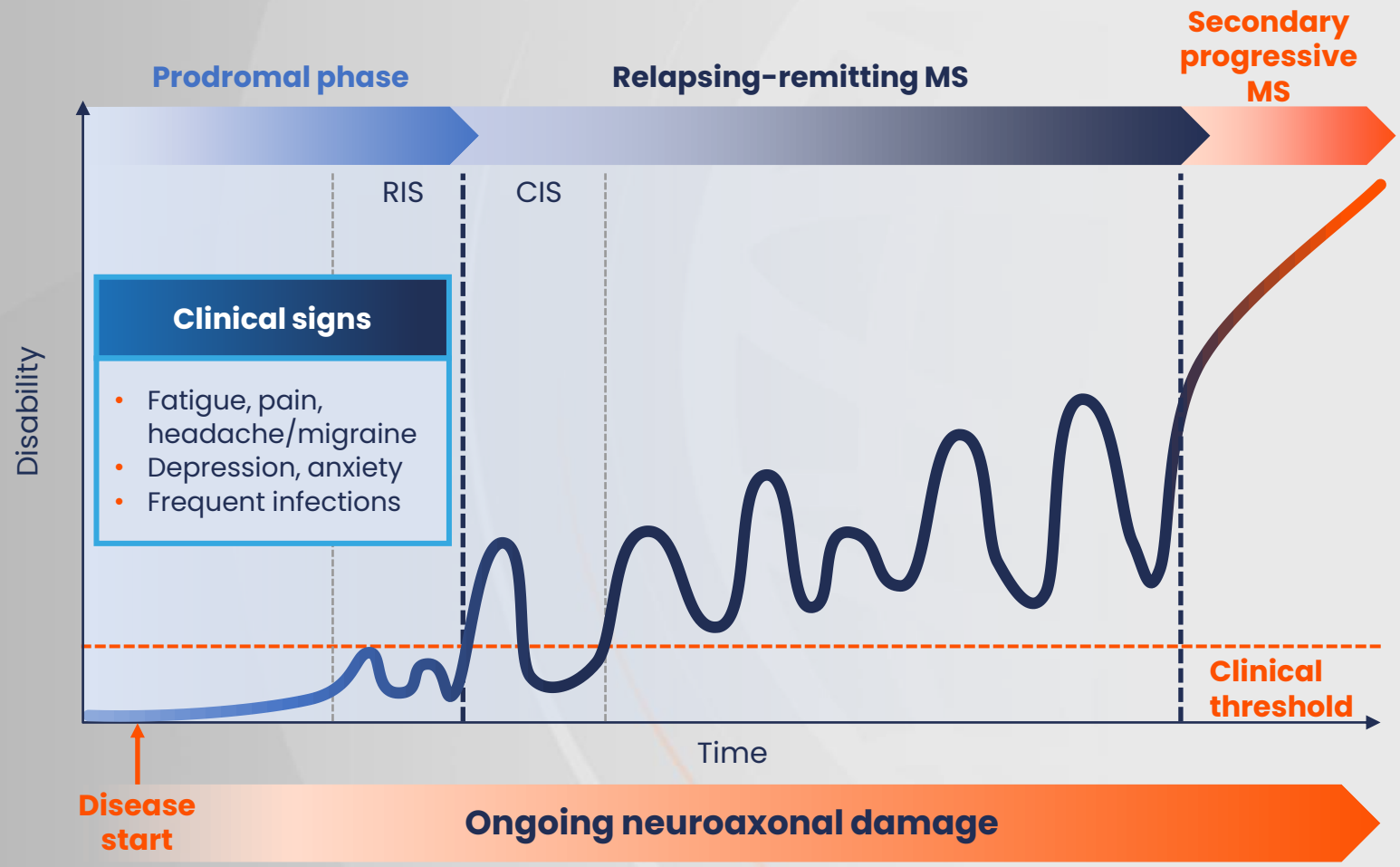
Relapsing MS: Patient journey

From preclinical to progressive disease[1,2]



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Relapsing MS: Patient journey

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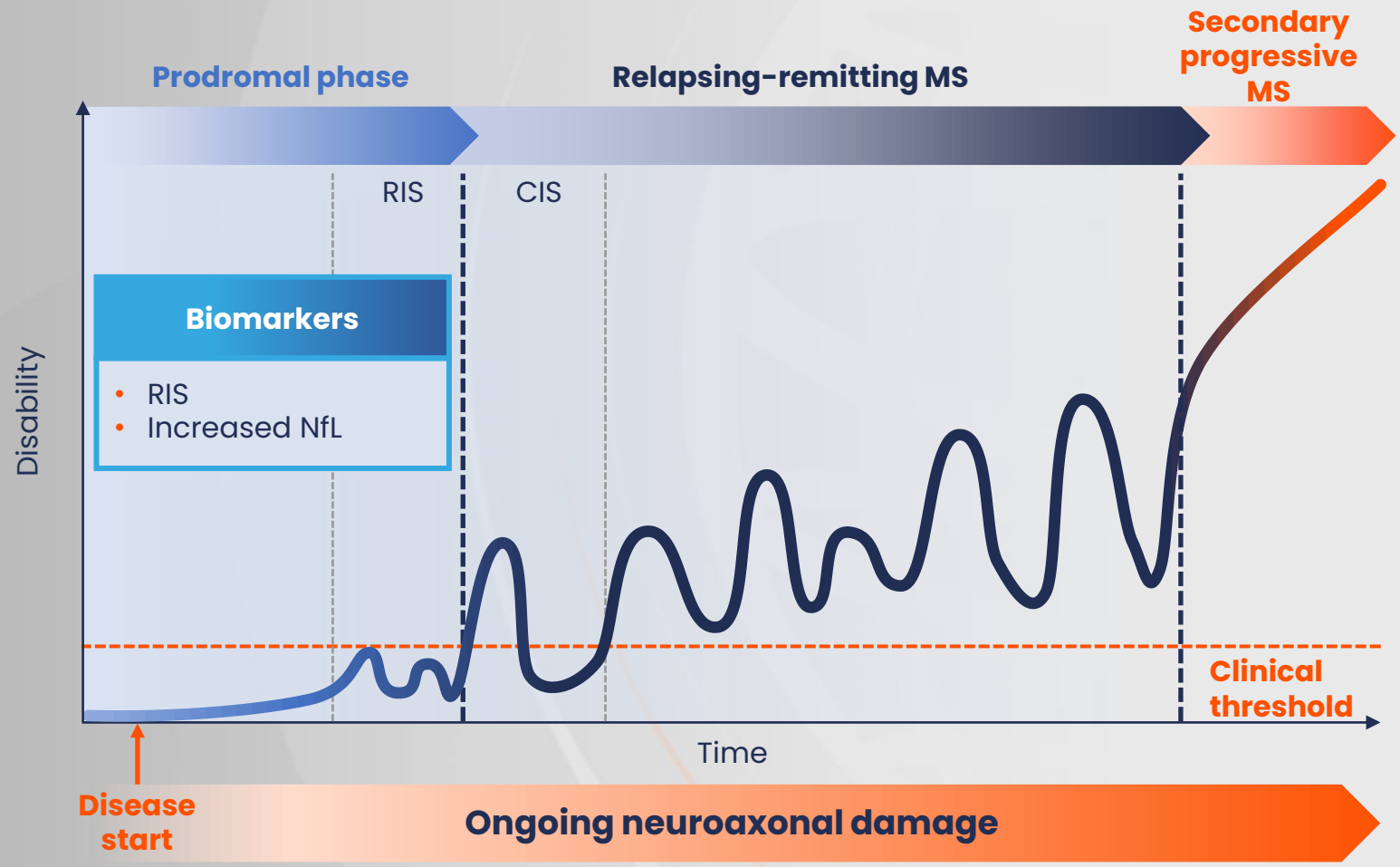

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Relapsing MS: Patient journey

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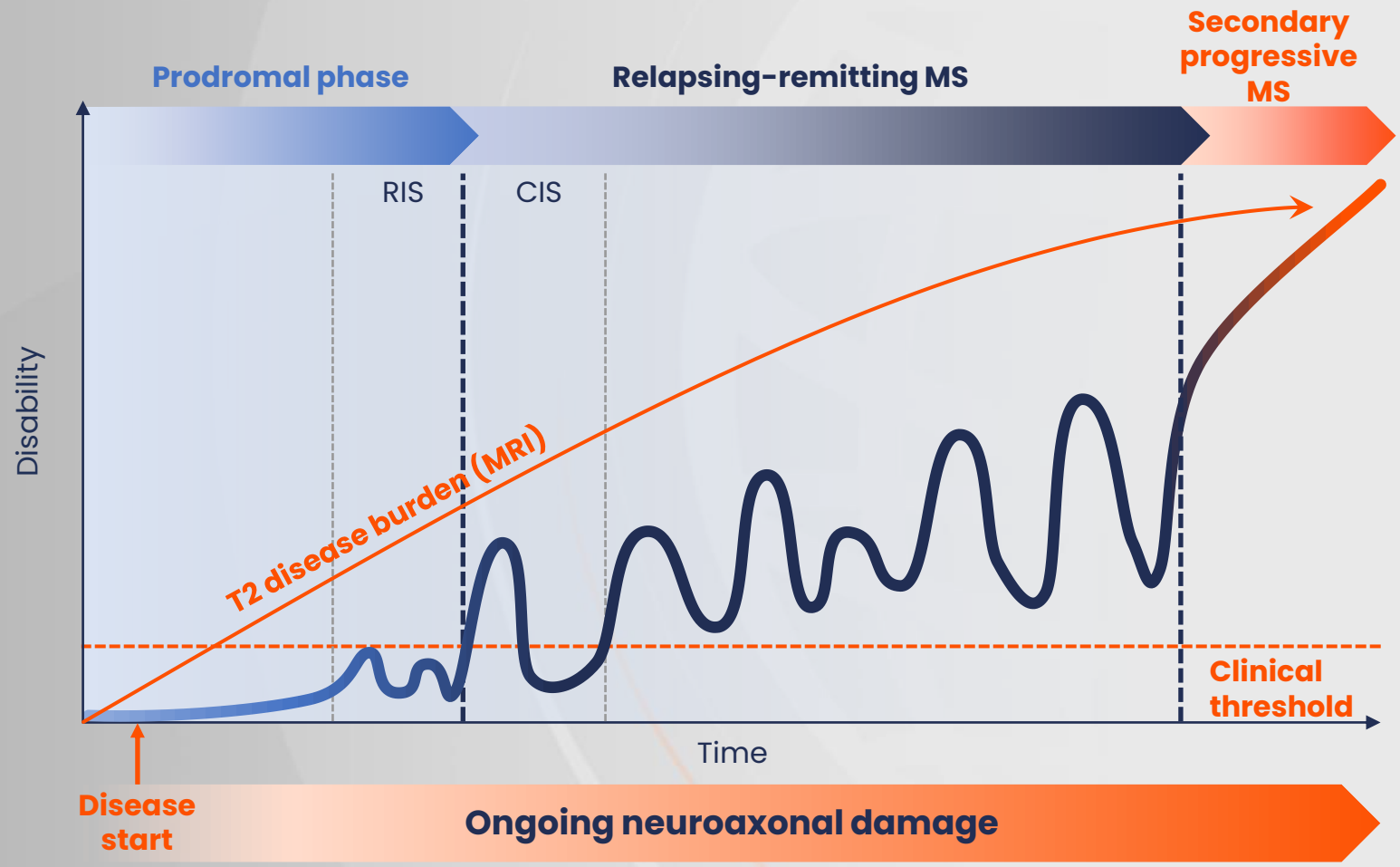

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Relapsing MS: Patient journey

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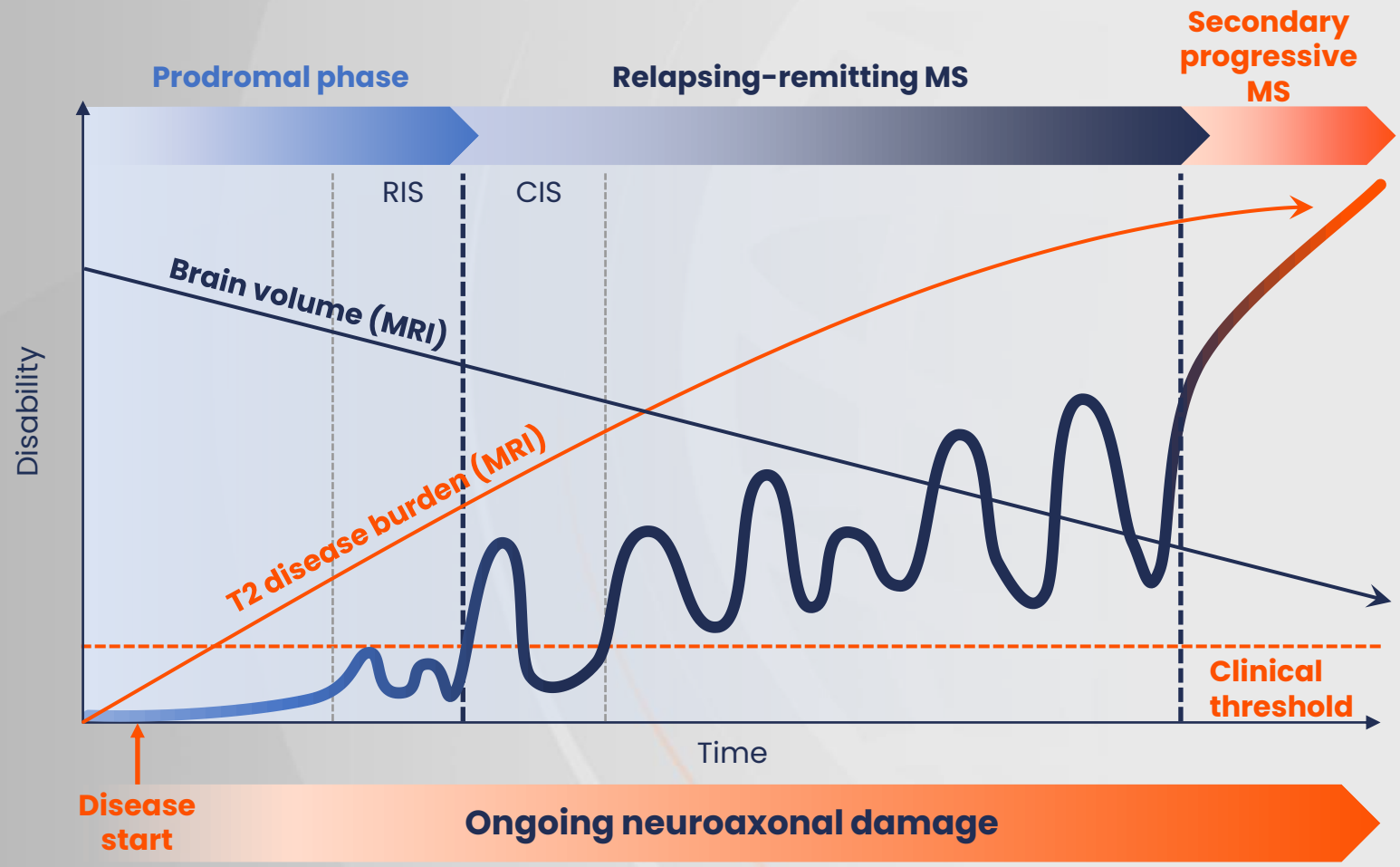

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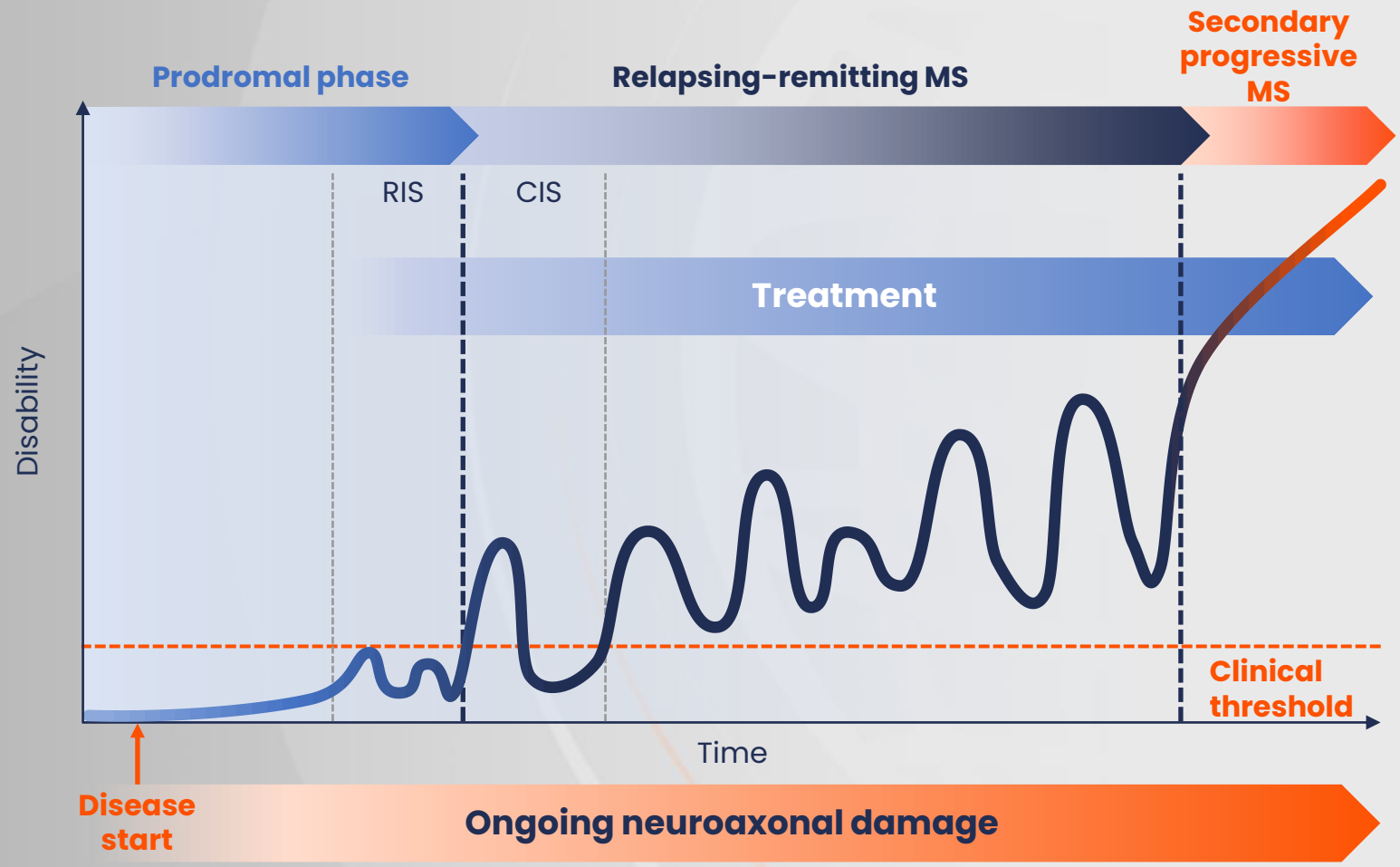
Relapsing MS: Patient journey

From preclinical to progressive disease[1,2]



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Approved DMTs for relapsing MS

A summary of the available therapeutic classes and targets

Injectable immunomodulators[1]

- Beta interferons
- Glatiramer acetate

Monoclonal antibody infusions[1]

- **Anti-CD20:** ocrelizumab, ofatumumab and rituximab
- **Anti-CD52:** alemtuzumab
- **Anti-α4β1 -integrin**: natalizumab

Oral therapies[1,2]

- **S1PR modulators:**
  - **1st generation:** fingolimod[2]
  - **2nd generation:** ozanimod, siponimod and ponesimod[2]
- **Fumarates:** dimethyl fumarate, diroximel fumarate, monomethyl fumarate
- **Dihydroorotate dehydrogenase inhibitor:** teriflunomide
- **Purine analogue:** cladribine

DMT, disease-modifying therapies; MS, multiple sclerosis; S1PR, sphingosine-1-phosphate receptor.

1. Hauser SL, Cree BAC. *Am J Med.* 2020;133:1380–90; 2. Chun J, et al. *Drugs.* 2021;81:207–31.

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Management of relapsing MS

Risk stratification and treatment goals

MRI, magnetic resonance imaging; MS, multiple sclerosis.
Freedman MS, et al. *Can J Neurol Sci.* 2020;47:437–55.

Management of relapsing MS

Risk stratification and treatment goals

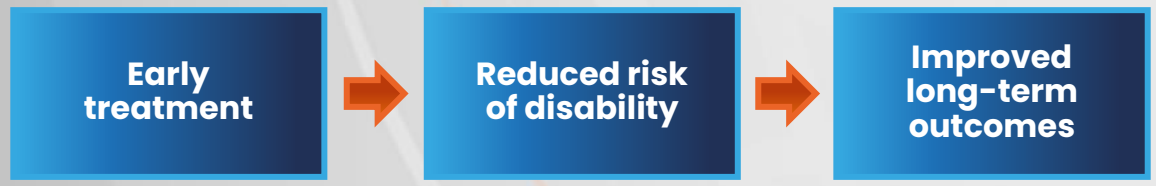
Prognostic risk factors

Demographic

- Age >40 years
- Male
- Non-white ethnicity
- Comorbidities

Clinical/radiological

- Relapse frequency
- Relapse severity
- Relapse recovery
- MRI findings

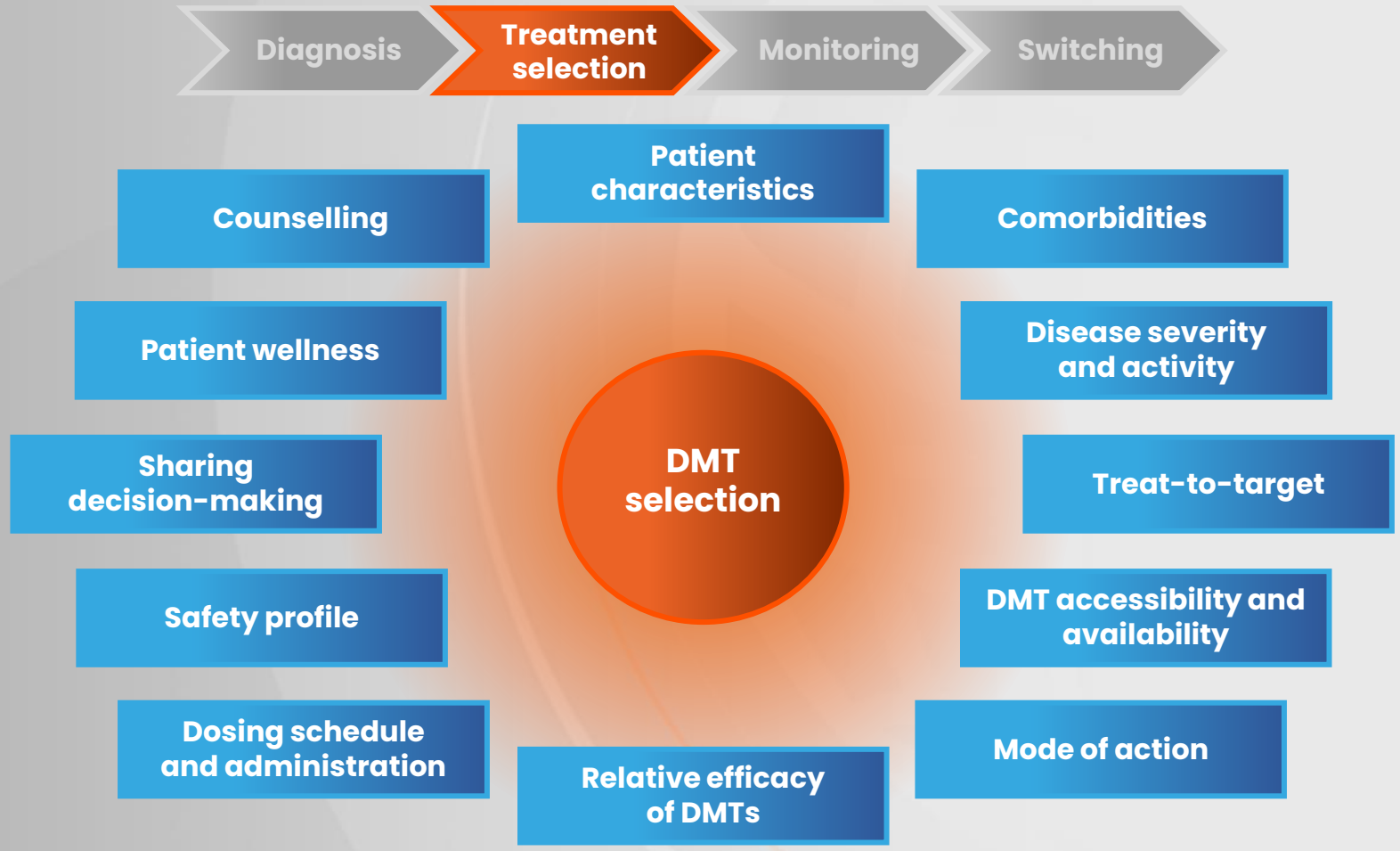


MRI, magnetic resonance imaging; MS, multiple sclerosis.

Freedman MS, et al. *Can J Neurol Sci.* 2020;47:437–55.

Management of relapsing MS

Considerations for selecting DMTs



DMT, disease-modifying therapies; MS, multiple sclerosis.
D'Amico, et al. *Neural Regen Res*. 2022;17:567–8.

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Management of relapsing MS

Escalation vs induction high-efficacy treatment approaches

Escalation

- Moderate-efficacy DMT with lower risk safety profile

VS

Induction high-efficacy

- High-efficacy DMT with higher risk safety profile

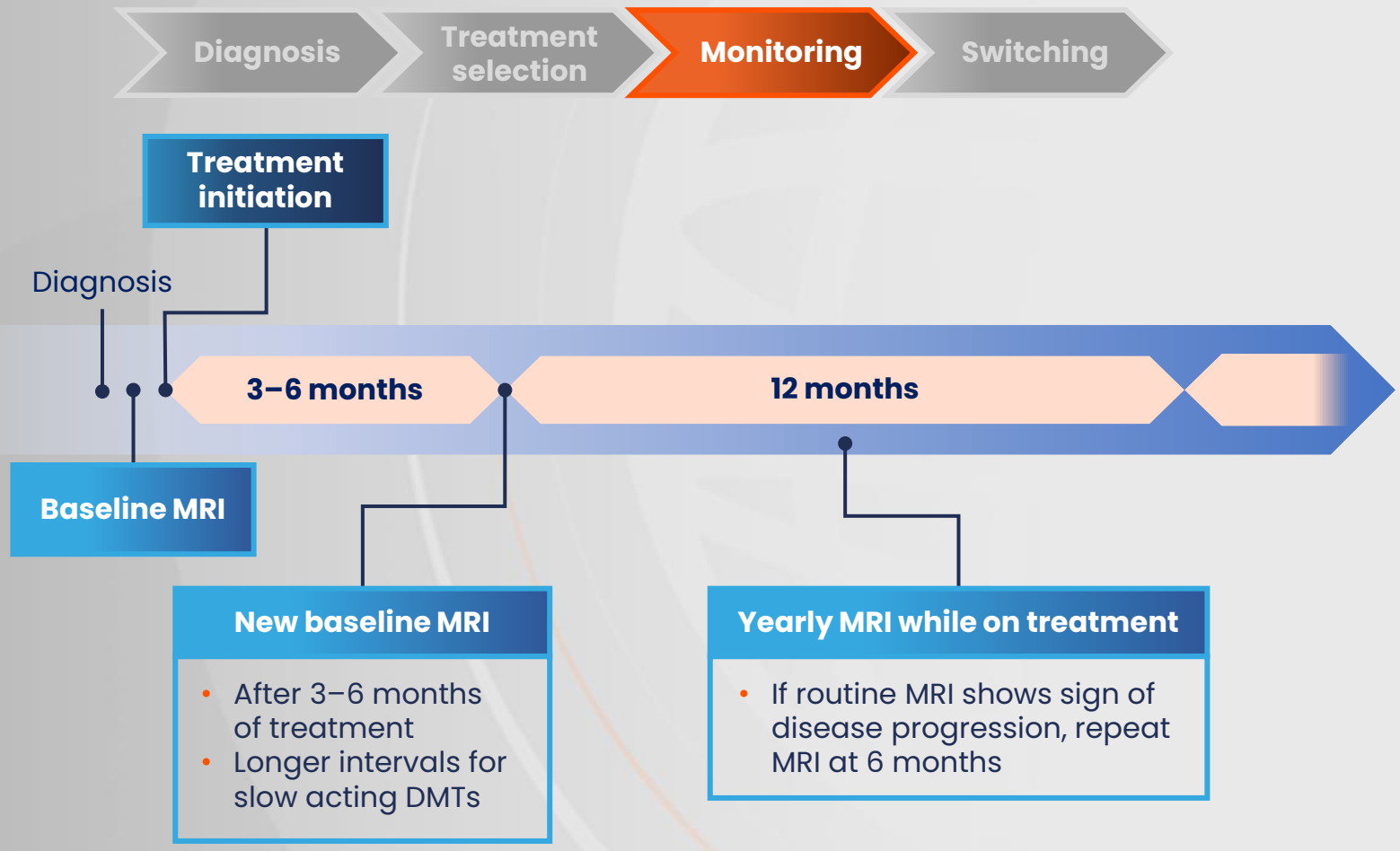
Evidence is accumulating for a therapeutic window of opportunity early in the disease course to maximize long-term outcomes

DMT, disease-modifying therapies; MS, multiple sclerosis.

Coyle PK. *Neurotherapeutics*. 2020;17:971–2.

Management of relapsing MS

Monitoring disease activity after DMT initiation



DMT, disease-modifying therapy; MRI, magnetic resonance imaging; MS, multiple sclerosis.

Wattjes MP, et al. *Lancet Neurol*. 2021;20:653–70.

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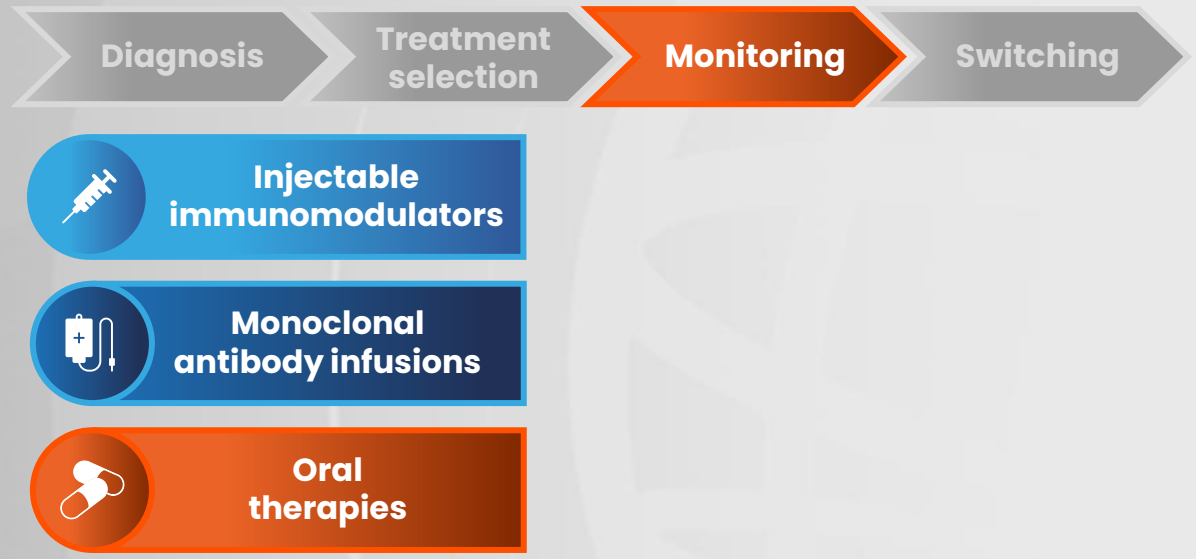
Management of relapsing MS

Adverse events



MS, multiple sclerosis.
Callegari I, et al. *Presse Med*. 2021;50:104068.

Management of relapsing MS

Adverse events

Injectable immunomodulators

- **Beta interferon**[1,2]
  - Injection-site reactions
  - Flu-symptoms
  - Asymptomatic liver dysfunction[1,2]
- **Glatiramer acetate**[3]
  - Injection-site reactions
  - Chest pain
  - Flushing
  - Dyspnoea
  - Palpitations
  - Anxiety

Monoclonal antibody infusions

Oral therapies

EMA, European Medicines Agency; FDA, US Food and Drug Administration; MS, multiple sclerosis; PI, prescribing information; SmPC, summary of product characteristics.

1. FDA. Interferon beta-1b. PI. 2021; 2. EMA. Interferon beta-1b. SmPC. 2021; 3. FDA. Glatiramer acetate. PI. 2022.
PI available at: www.accessdata.fda.gov/scripts/cder/daf/index.cfm. SmPC available at: www.ema.europa.eu/en/medicines (all accessed 8 March 2022).

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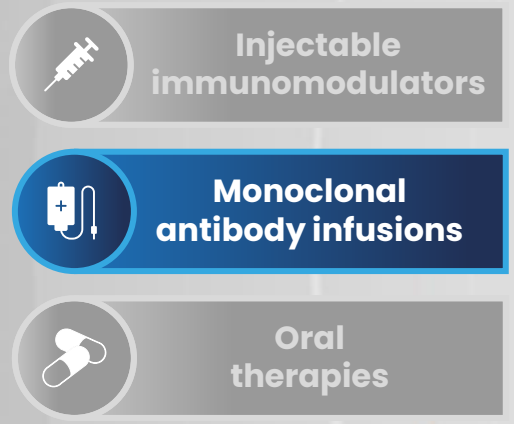
Management of relapsing MS

Adverse events



- **Anti-α4-integrin**
  Natalizumab[1,2]
  - Infusion-site reactions
  - Headache
  - Progressive multifocal leukoencephalopathy
- **Anti-CD52**
  Alemtuzumab[3,4]
  - Infusion-site reactions
  - Infections
  - Autoimmune disorders
- **Anti-CD20**
  Ocrelizumab[5,6]
  - Infusion-site reactions
  - Infections
  - Neutropenia

  Ofatumumab[7,8]
  - Injection-site reactions
  - Infections

EMA, European Medicines Agency; FDA, US Food and Drug Administration; MS, multiple sclerosis; PI, prescribing information; SmPC, summary of product characteristics.

1. FDA. Natalizumab. PI. 2021; 2. EMA. Natalizumab. SmPC. 2021; 3. FDA. Alemtuzumab. PI. 2022; 4. EMA. Alemtuzumab. SmPC. 2022; 5. FDA. Ocrelizumab. PI. 2020;
6. EMA. Ocrelizumab. SmPC. 2022; 7. FDA. Ofatumumab. PI. 2020; 8. EMA. Ofatumumab. SmPC. 2021;
PI available at: www.accessdata.fda.gov/scripts/cder/daf/index.cfm. SmPC available at: www.ema.europa.eu/en/medicines (all accessed 8 March 2022).

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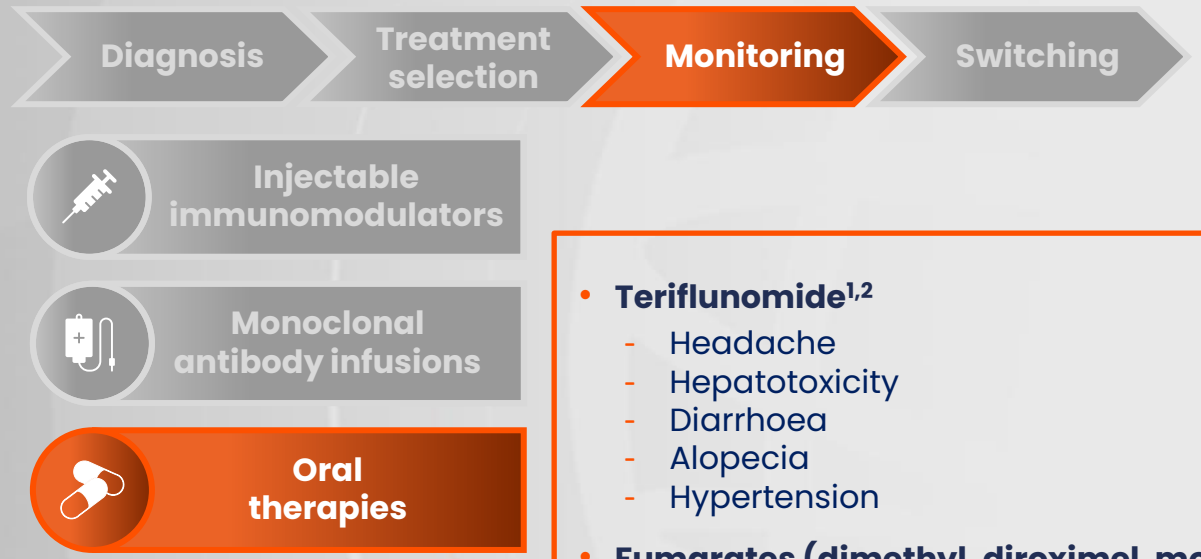
Management of relapsing MS

Adverse events



- **Teriflunomide**[1,2]
  - Headache
  - Hepatotoxicity
  - Diarrhoea
  - Alopecia
  - Hypertension
- **Fumarates (dimethyl, diroximel, monomethyl)**[3–7]
  - Gastrointestinal symptoms
  - Flushing
  - Skin reactions

EMA, European Medicines Agency; FDA, US Food and Drug Administration; MS, multiple sclerosis; PI, prescribing information; SmPC, summary of product characteristics.

1. FDA. Teriflunomide. PI. 2021; 2. EMA. Teriflunomide. SmPC. 2022; 3. FDA. Dimethyl fumarate. PI. 2022; 4. EMA. Dimethyl fumarate. SmPC. 2022; 5. FDA. Diroximel fumarate. PI. 2021; 6. EMA. Diroximel fumarate. SmPC. 2021; 7. FDA. Monomethyl fumarate. PI. 2020.

PI available at: www.accessdata.fda.gov/scripts/cder/daf/index.cfm. SmPC available at: www.ema.europa.eu/en/medicines (all accessed 8 March 2022).

Management of relapsing MS

Adverse events

Diagnosis → Treatment selection → **Monitoring** → Switching

- Injectable immunomodulators
- Monoclonal antibody infusions
- **Oral therapies**

- **First-generation S1PR modulators**
  Fingolimod[1,2]
  - Influenza
  - Sinusitis
  - Bronchitis
- **Second-generation S1PR modulators**
  Ozanimod[3,4]
  - Upper respiratory tract infection
  - Urinary tract infection
  - Hepatic transaminase elevation
  - Orthostatic hypotension

  Siponimod[5,6]
  - Headache
  - Hypertension
  - Hepatic transaminase elevation

  Ponesimod[7,8]
  - Upper respiratory tract infection
  - Hepatic transaminase elevation
  - Hypertension

EMA, European Medicines Agency; FDA, US Food and Drug Administration; MS, multiple sclerosis; PI, prescribing information; SmPC, summary of product characteristics.

1. FDA. Fingolimod. PI. 2019; 2. EMA. Fingolimod. SmPC. 2021; 3. FDA. Ozanimod. PI. 2020; 4. EMA. Ozanimod. SmPC. 2021; 5. FDA. Siponimod. PI. 2021; 6. EMA. Siponimod. SmPC. 2022; 7. FDA. Ponesimod. PI. 2021; 8. EMA. Ponesimod. SmPC. 2022.

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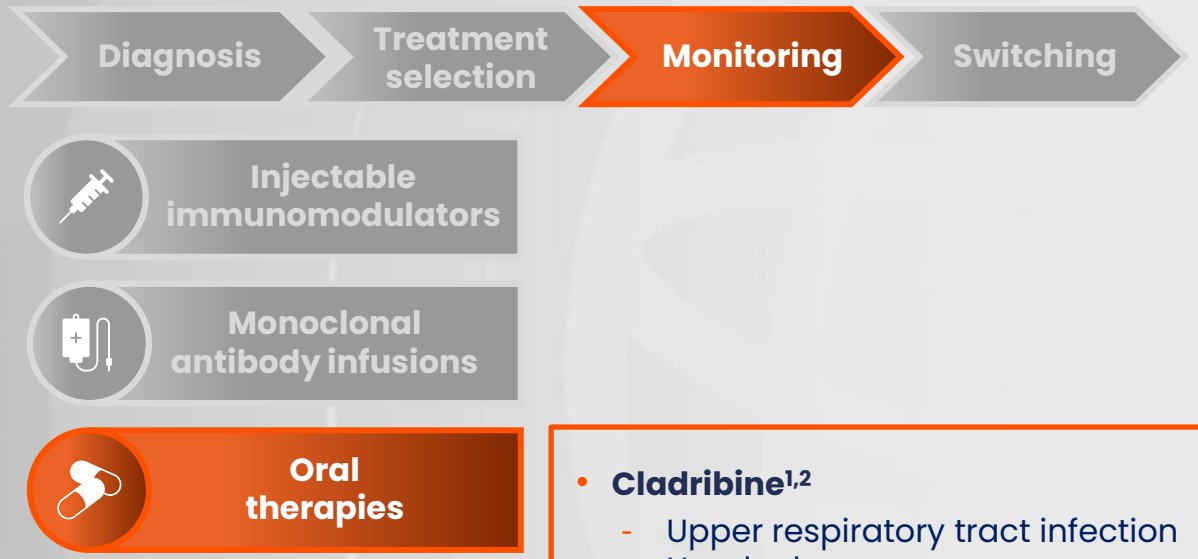
Management of relapsing MS

Adverse events



EMA, European Medicines Agency; FDA, US Food and Drug Administration; MS, multiple sclerosis; PI, prescribing information; SmPC, summary of product characteristics.
1. FDA. Cladribine. PI. 2019; 2. EMA. Cladribine. SmPC. 2022.
PI available at: www.accessdata.fda.gov/scripts/cder/daf/index.cfm. SmPC available at: www.ema.europa.eu/en/medicines (all accessed 8 March 2022).

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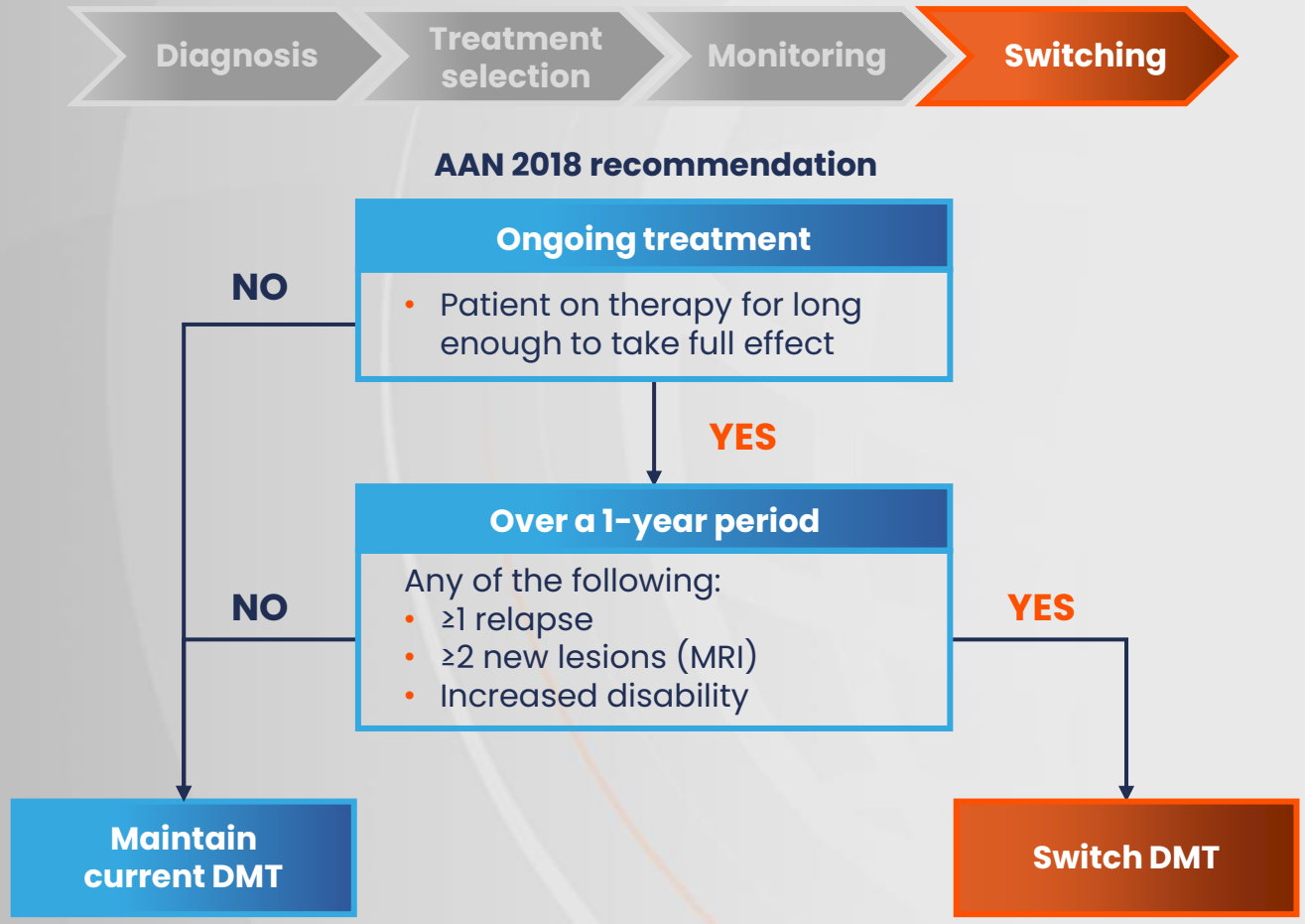
Management of relapsing MS

Switching therapy at treatment failure



AAN, American Academy of Neurology; DMT, disease-modifying therapy; MRI, magnetic resonance imaging; MS, multiple sclerosis.
Rae-Grant A, et al. *Neurology*. 2018;90:777–88.

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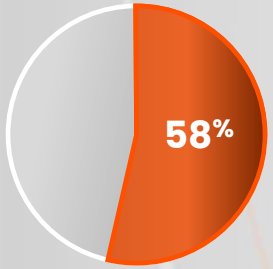
Management of relapsing MS

Clinical and patient determinants of switching

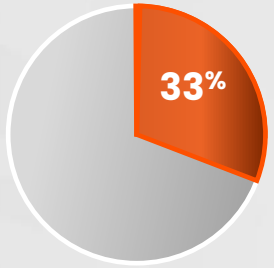
Diagnosis → Treatment selection → Monitoring → **Switching**

SWITCH study in relapsing-remitting MS:

- Lack of efficacy and safety/tolerability were identified as the main reasons for switching therapy



Lack of efficacy



Safety/tolerability

MS, multiple sclerosis.

Patti F, et al. *Mult Scler Relat Disord*. 2020;42:102124.

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Management of relapsing MS

Clinical and patient determinants of switching

SWITCH study in relapsing-remitting MS:

- Other reasons for switching or modifying therapy included:

- Inconvenience
- Patient request
- Compliance
- Pregnancy
- Mode of administration
- Surgery
- Injection fatigue
- Abnormal lab test

MS, multiple sclerosis.

Patti F, et al. *Mult Scler Relat Disord*. 2020;42:102124.

Conclusions

DMTs have demonstrated efficacy in reducing relapse frequency and controlling the symptoms of MS

There is debate on whether an escalation or a high-efficacy approach should be used when starting a patient on a DMT

When choosing from a broad range of DMTs, clinicians must consider individual patient characteristics, comorbidities, disease activity, drug's safety profile and accessibility

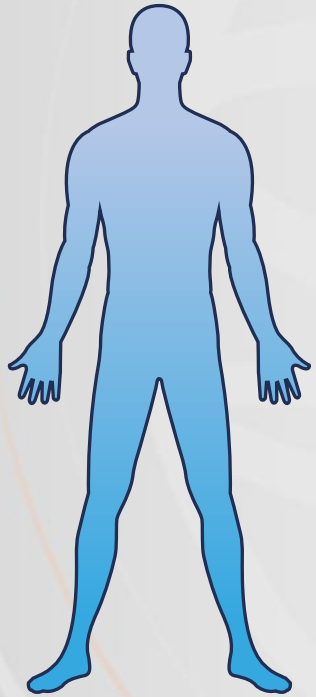
DMT, disease-modifying therapies; MS, multiple sclerosis.

Improving the QoL of patients with relapsing MS: How to reduce the burden of symptoms with DMTs

Burden of MS on QoL

MS has a wide variety of common symptoms[1–3]

- Emotional impairment:
  - Depression
  - Anxiety
- Vision problems:
  - Diplopia
  - Blurred vision
  - Pain
- Bowel dysfunction
- Bladder dysfunction
- Less common:
  - Dysphagia
  - Dysarthria
  - Breathing problems
  - Hearing loss
  - Seizures
  - Headache
- Cognitive impairment



- Sexual problems
- Dizziness and vertigo
- Sensory disturbance
  - Tingling
  - Itching
  - Burning
  - Pain
- ‘MS hug’
- Fatigue
- Spasticity
- Walking difficulties:
  - Fatigue
  - Weakness
  - Spasticity
  - Loss of balance
  - Tremor

MS, multiple sclerosis; QoL, quality of life.

1. Ghasemi N, et al. *Cell J*. 2017;19:1–10; 2. Hanna M, et al. *Mult Scler Relat Disord*. 2020;44:102261; 3. Ford H. *Clin Med*. 2020;20:380–3.

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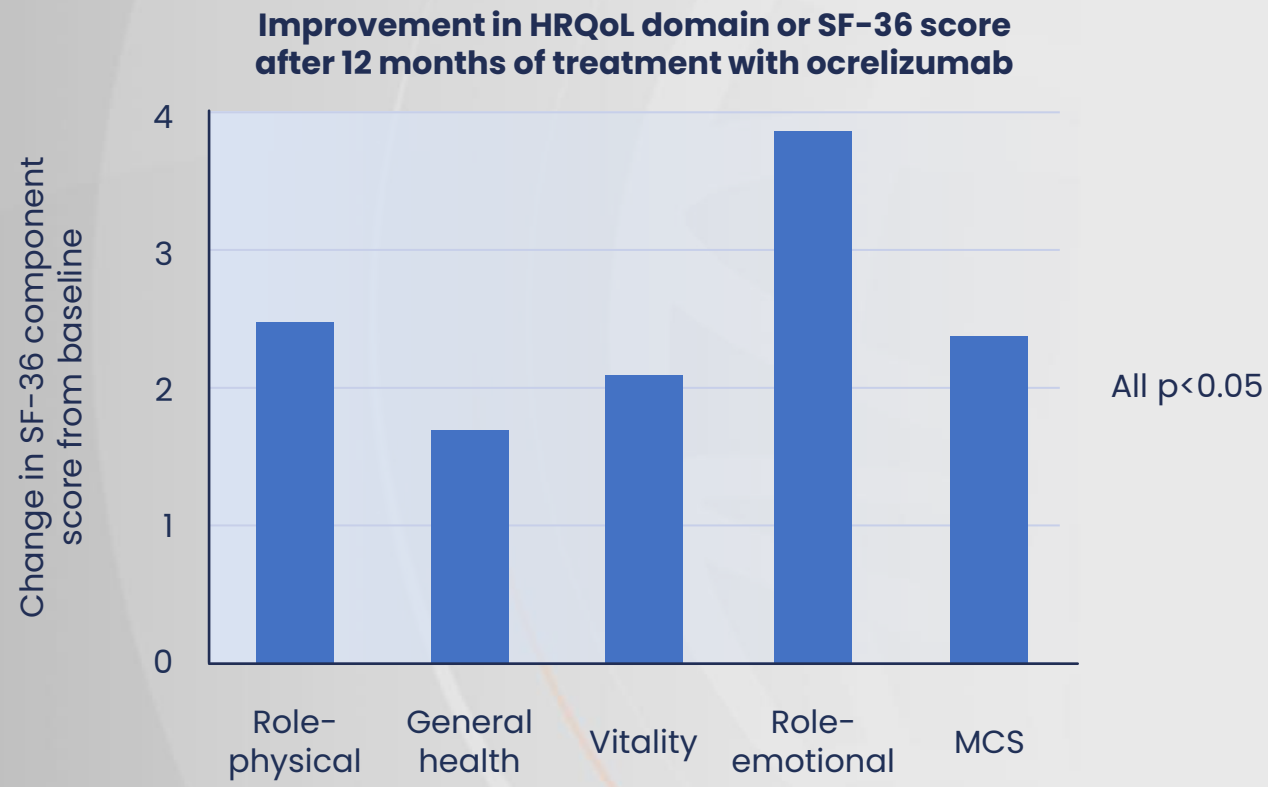
Impact of DMTs on patient-reported outcomes

Ocrelizumab: HRQoL



DMT, disease-modifying therapy; HRQoL, health-related quality of life; MCS, Mental Component Summary; SF-36, Short-Form 36.
Glanz BI, et al. *Mult Scler J Exp Transl Clin*. 2021;7:20552173211007523.

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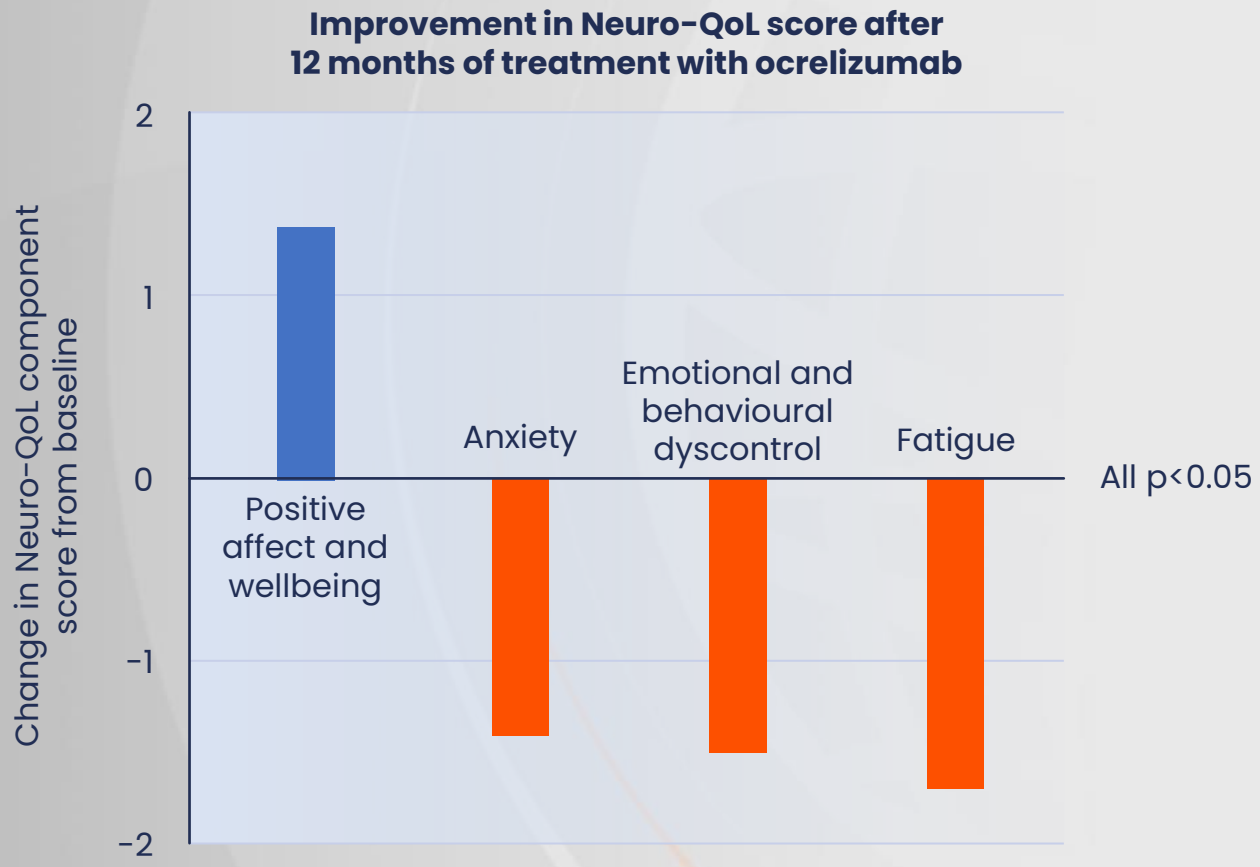
Impact of DMTs on patient-reported outcomes

Ocrelizumab: Neuro-QoL

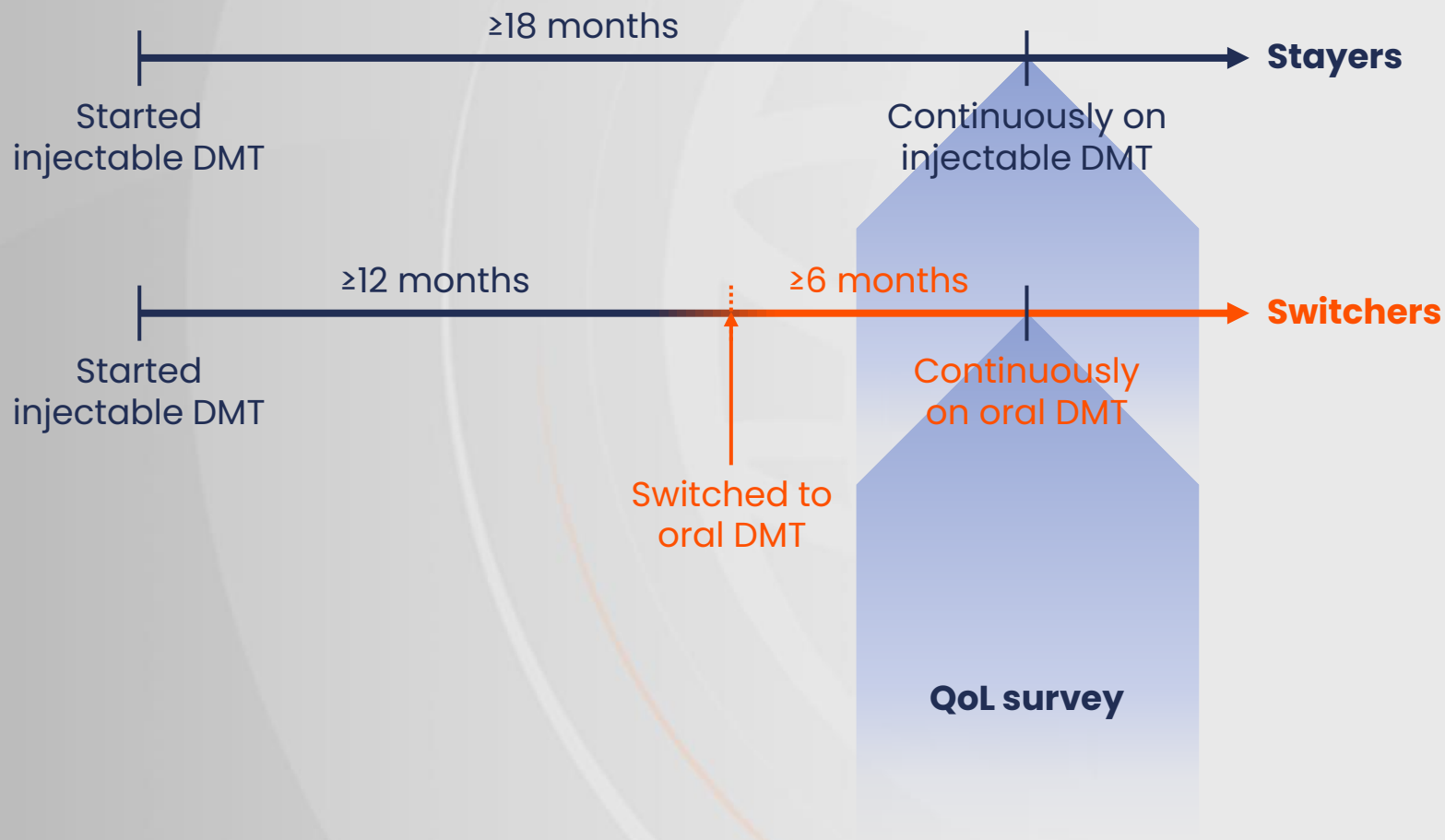


DMT, disease modifying therapy; QoL, quality of life.

Glanz BI, et al. *Mult Scler J Exp Transl Clin*. 2021;7:20552173211007523.

Switching from injectable to oral DMTs

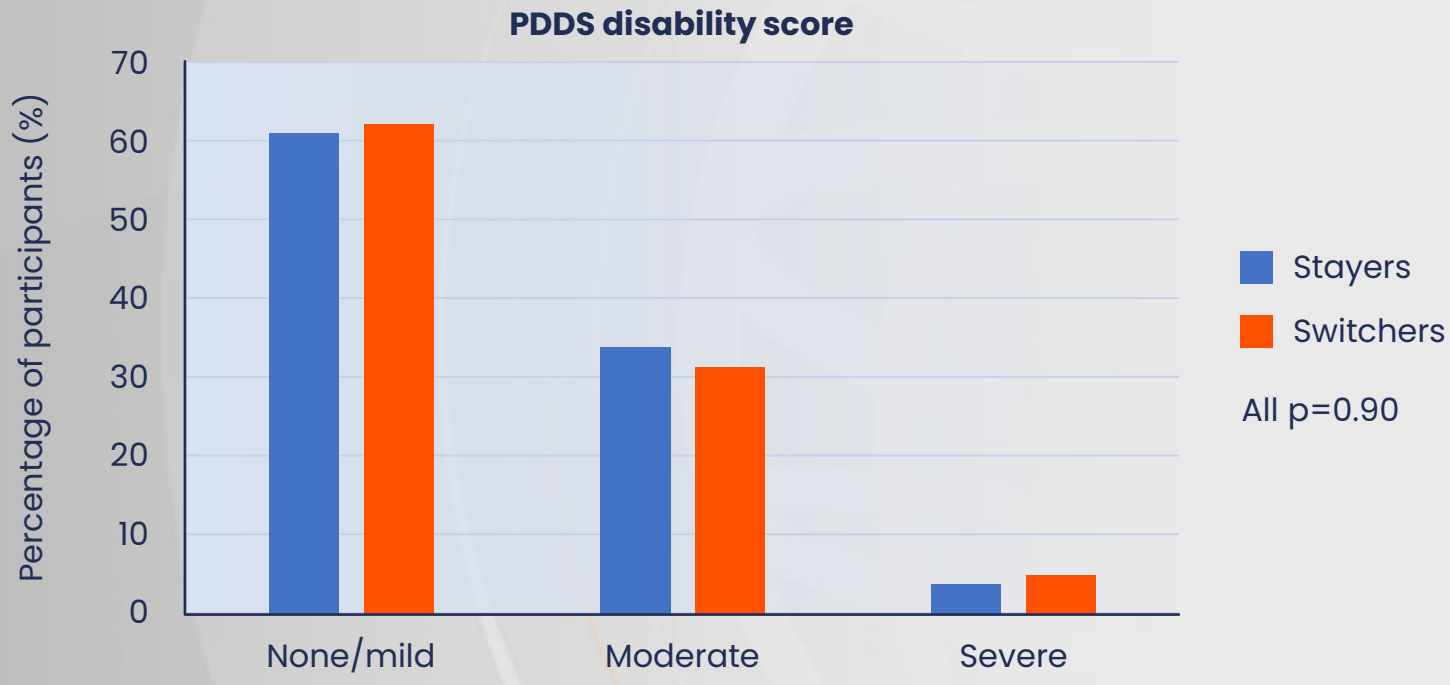
Patients with relapsing MS: Study design **Pacific Northwest MS Registry**



DMT, disease-modifying therapy; MS, multiple sclerosis; QoL, quality of life.
Stuchiner T, et al. *BMC Neurol*. 2020;20:439.

Switching from injectable to oral DMTs

Data from patients with relapsing MS: Study design
Pacific Northwest MS Registry



! No significant difference in **self-reported disability** between participants who switched to an oral DMT and those who stayed on an injectable

DMT, disease-modifying therapy; MS, multiple sclerosis; PDDS, Patient Determined Disease Steps.
Stuchiner T, et al. *BMC Neurol*. 2020;20:439.

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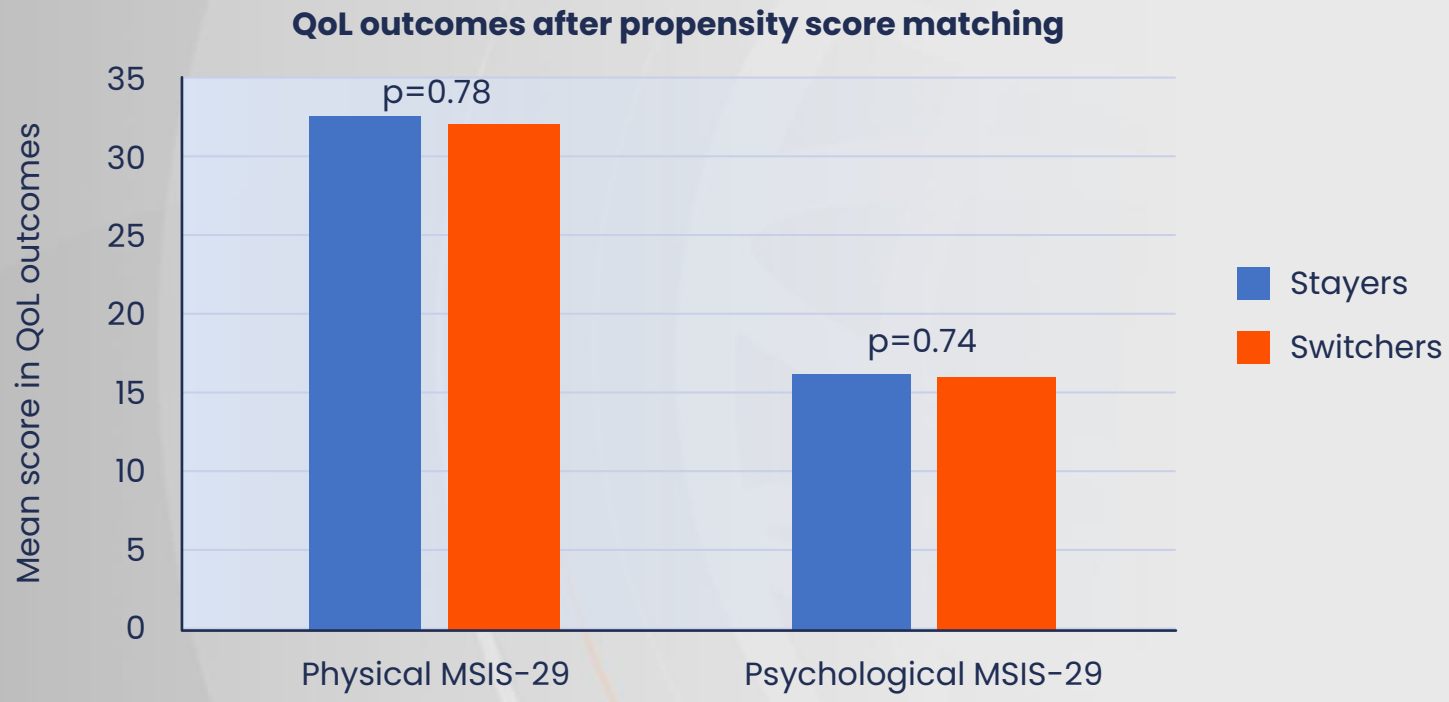
Switching from injectable to oral DMTs

Data from patients with relapsing MS: Study design
Pacific Northwest MS Registry



No significant difference in **physical and psychological QoL measures** between participants who switched to an oral DMT and those who stayed on an injectable

DMT, disease-modifying therapy; MS, multiple sclerosis; MSIS, Multiple Sclerosis Impact Scale; QoL, quality of life.
Stuchiner T, et al. *BMC Neurol*. 2020;20:439.

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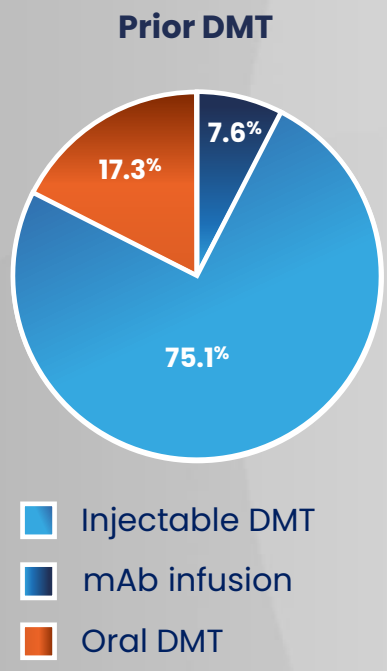
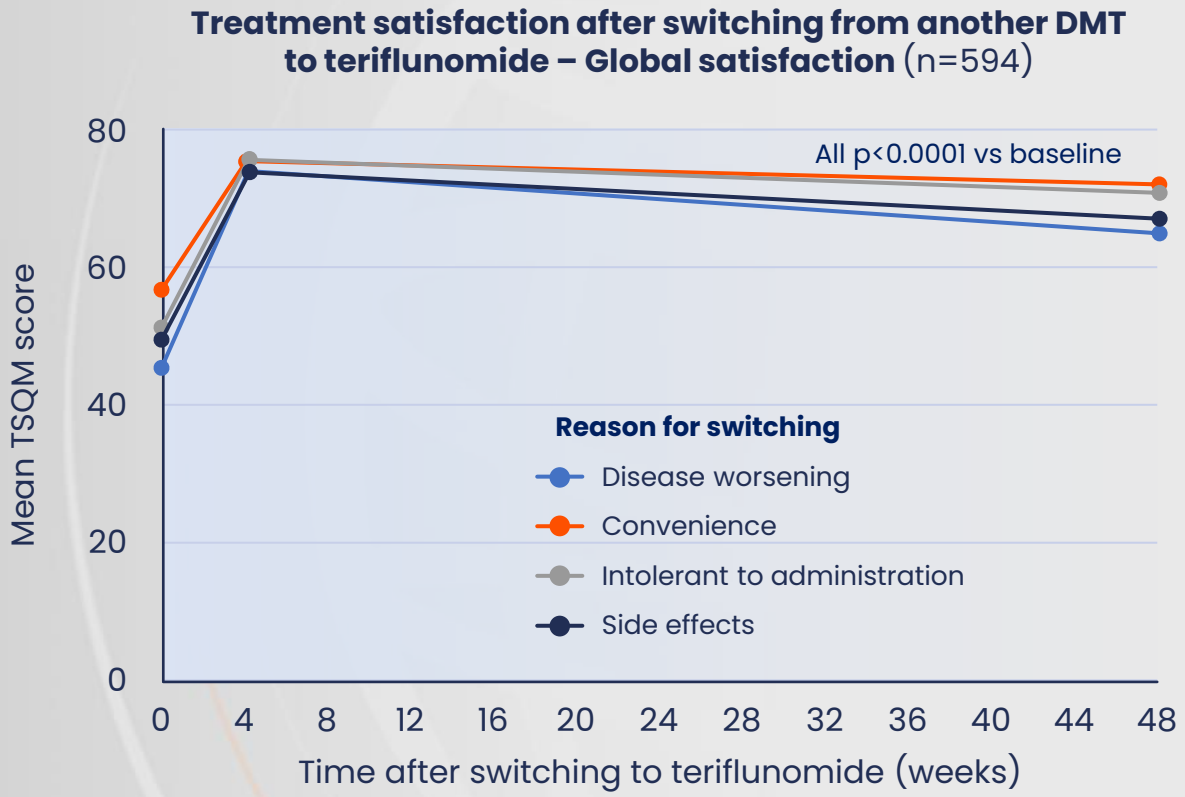
Treatment satisfaction with oral DMTs

Teri-PRO study (phase IV)





! Significant **improvements in treatment satisfaction** scores following the switch to teriflunomide, regardless of the reason for switching

DMT, disease-modifying therapy; mAb, monoclonal antibody; TSQM, Treatment Satisfaction Questionnaire for Medication.

Coyle PK, et al. *Mult Scler Relat Disord*. 2018;26:211–8.

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Burden of fatigue in MS

Fatigue has a substantial impact on patients' lives

37–78% Prevalence of fatigue in patients with MS

- **Increased unemployment and under-employment**
- **Increased work absences**
- **Increased physical limitations**

MS, multiple sclerosis.

Oliva Ramirez A, et al. *BMC Neurol*. 2021;21:468.

Causes of fatigue in MS

Primary fatigue	Secondary fatigue
• No apparent cause • Specific to MS	• Consequence of another condition, even if related to MS

Secondary cause	Clinical red flags
Depression	Sleeping/eating disorders, low mood, sadness
Sleep disorders	Excessive sleepiness, clinical features of anxiety, sleep apnoea, obesity
Medication side effects	Recent start of new drug/increased dose of existing drug
Pain, muscle spasms	Pain or increased muscular tone during examination
Bladder dysfunction	Nocturia

MS, multiple sclerosis.

Tur C. *Curr Treat Options Neurol*. 2016;18:26.

Monitoring fatigue in MS

Validated self-reported measures of fatigue

- Fatigue Severity Scale (FSS)[1]
- MS-Specific Fatigue Severity Scale (MS-FSS)[1]
- Modified Fatigue Impact Scale (MFIS)[1]
- Visual Analogue Scale (VAS)[1]
- Neuro-QoL[2]
- Fatigue Symptom and Impact Questionnaire – Relapsing Remitting MS (FSIQ-RMS)[3]

MS, multiple sclerosis.

1. Flachenecker P, et al. *Mult Scler*. 2002;8:523–6; 2. Cella D, et al. *Neurology*. 2012;78:1860–7; 3. Hudgens S, et al. *Value Health*. 2019;22:453–66.

Management of fatigue in MS

Non-pharmacological therapies[1]

- Fatigue management programme
- Programmed rest periods
- Aquatic exercise training
- Cooling techniques
- Work accommodations
- Assistive devices
- Pulsed electro-magnetic devices
- Energy conservation interventions
- Psychological interventions

Pharmacological therapies[2,3]

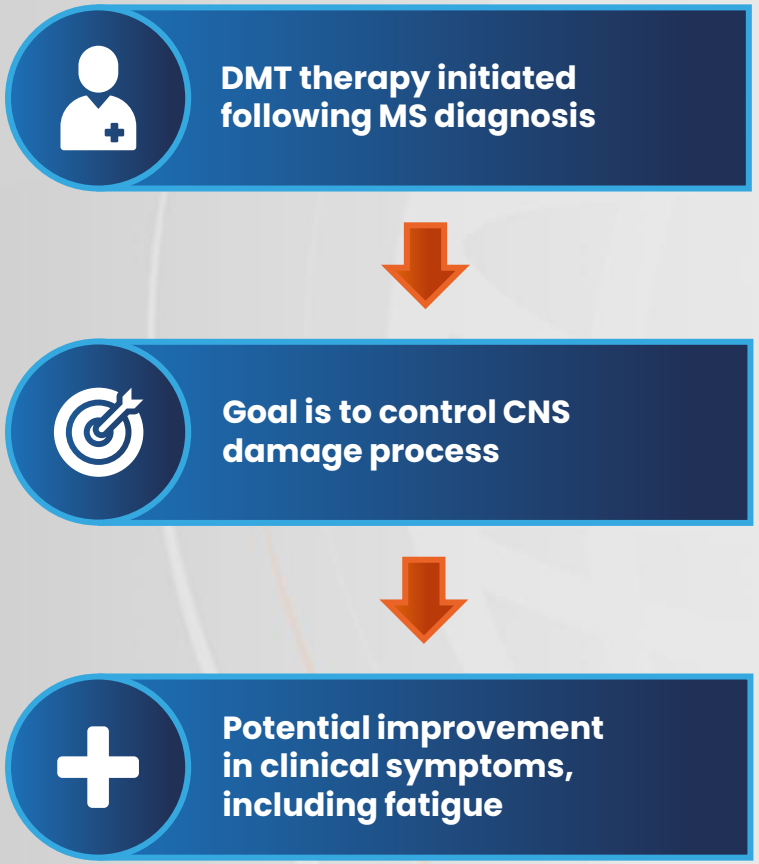
Often in combination with anti-depressants:

- Amantadine
- Modafinil
- Armodafinil
- Amphetamine
- Methylphenidate

MS, multiple sclerosis.

1. Khan F, et al. *Front Neurol*. 2014;5:177; 2. Zielińska-Nowak E, et al. *J Clin Med*. 2020;9:3592; 3. Palotai M, et al. *Sci Rep*. 2019;9:14781.

Management of fatigue in MS



CNS, central nervous system; DMT, disease-modifying therapy; MS, multiple sclerosis.

Wiendl H, et al. *Ther Adv Neurol Disord.* 2021;14:17562864211039648.

Management of fatigue in MS

Impact of DMTs on fatigue: Ocrelizumab

- n=98 patients with relapsing MS
- n=32 patients with progressive MS
- Ocrelizumab for 12 months
- Patient-reported outcomes (Neuro-QoL)

Significant decrease in self-reported fatigue score from baseline to 12 months

DMT, disease-modifying therapy; MS, multiple sclerosis; QoL, quality of life.

Glanz BI, et al. *Mult Scler J Exp Transl Clin*. 2021;7:20552173211007523.

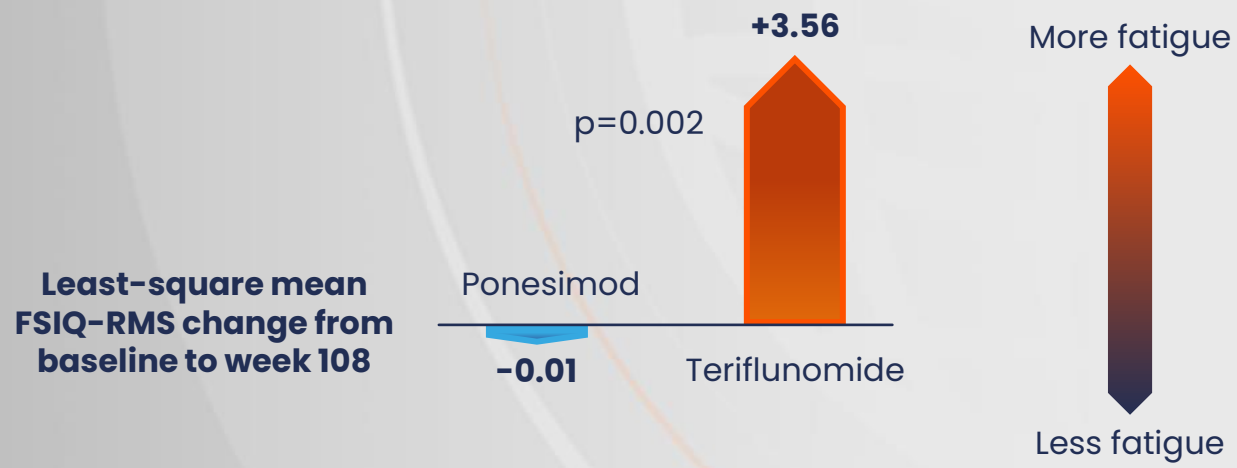
Management of fatigue in MS

Impact of DMTs on fatigue: Ponesimod

Active-comparator, superiority RCT comparing teriflunomide with ponesimod

- N=1,133 patients with relapsing MS
- Randomized 1:1 to ponesimod or teriflunomide
- FSIQ-RMS score at week 108

Significant improvement in MS-associated fatigue with ponesimod vs teriflunomide



DMT, disease-modifying therapy; FSIQ-RMS, Fatigue Symptom and Impact Questionnaire–Relapsing Multiple Sclerosis; MS, multiple sclerosis; RCT, randomized controlled trial.

Kappos L, et al. *JAMA Neurol*. 2021;78:558–67.

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Conclusions

QoL is an important consideration when choosing disease management strategies; the burden of MS on patients extends to less visible symptoms such as fatigue

It is essential to implement treatment strategies for reducing the impact of disease on patients' lives by decreasing fatigue and depression

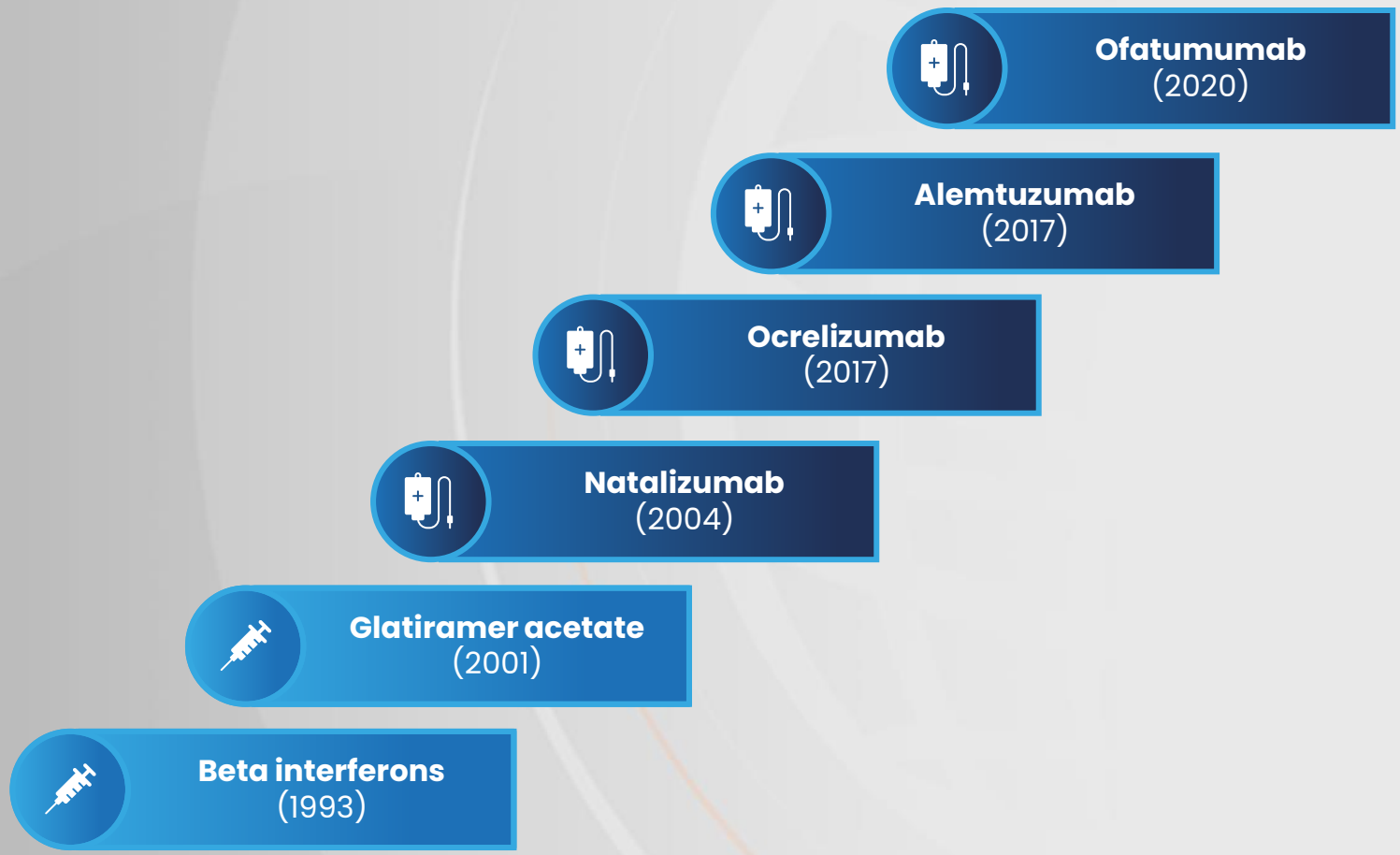
Switching from an injectable to an oral DMT alleviates symptoms with a more manageable regimen

DMT, disease-modifying therapy; MS, multiple sclerosis; QoL, quality of life.

How will practice change in the near future for patients with relapsing MS based on new clinical data?

Approved DMTs for relapsing MS

Injectables and monoclonal antibodies: Timeline of approvals



DMT, disease-modifying therapy; MS, multiple sclerosis.

US Food and Drug Administration. History of approval for all drugs. Available at: www.accessdata.fda.gov/scripts/cder/daf/index.cfm (accessed 17 March 2022).

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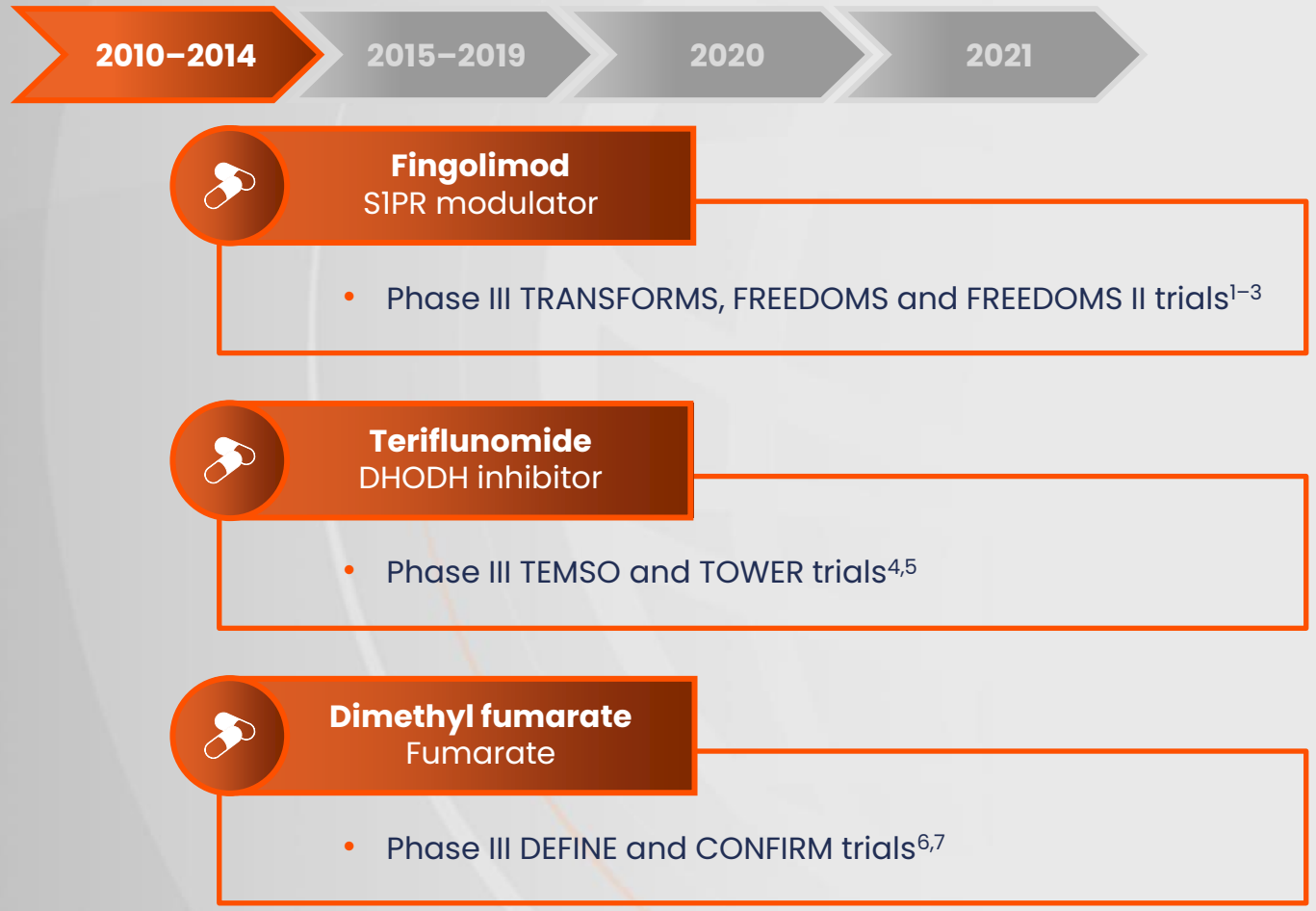
Approved DMTs for relapsing MS

Oral DMTs: Timeline of approvals and pivotal trials

Approved DMTs for relapsing MS

Oral DMTs: Timeline of approvals and pivotal trials

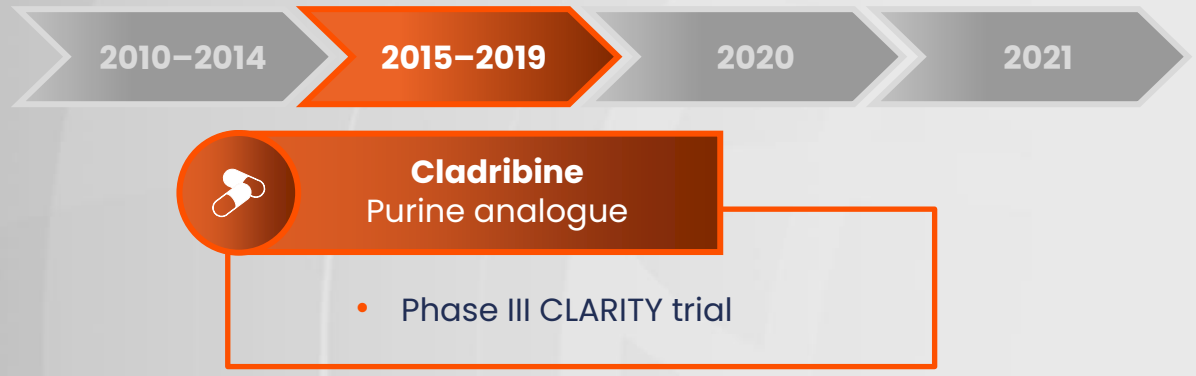


DHODH, dihydroorotate dehydrogenase; DMT, disease-modifying therapy; MS, multiple sclerosis; S1PR, sphingosine-1-phosphate receptor.

1. Cohen JA, et al. *N Engl J Med.* 2010;362:402–15; 2. Kappos L, et al. *N Engl J Med.* 2010;362:387–401; 3. Calabresi PA, et al. *Lancet Neurol.* 2014;13:545–56; 4. O'Connor P, et al. *N Engl J Med.* 2011;365:1293–303; 5. Confavreux C, et al. *Lancet Neurol.* 2014;13:247–56; 6. Gold R, et al. *N Engl J Med.* 2012;367:1098–107; 7. Fox RJ, et al. *N Engl J Med.* 2012;367:1087–97.

Approved DMTs for relapsing MS

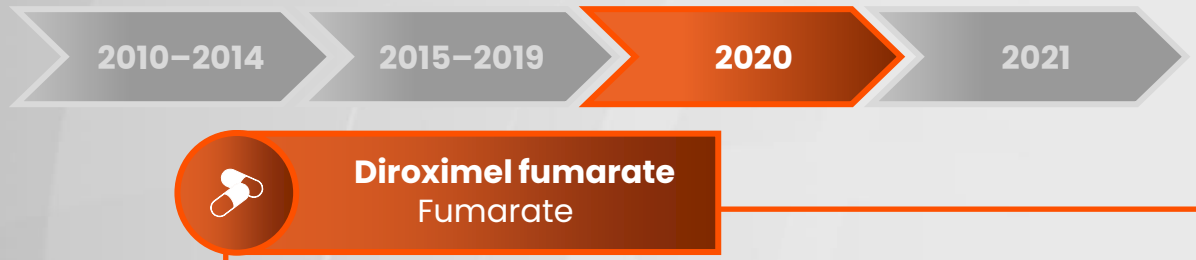
Oral DMTs: Timeline of approvals and pivotal trials



DMT, disease-modifying therapy; MS, multiple sclerosis.
Giovannoni G, et al. *N Engl J Med.* 2010;362:416–26.

Approved DMTs for relapsing MS

Oral DMTs: Timeline of approvals and pivotal trials



Diroximel fumarate
Fumarate

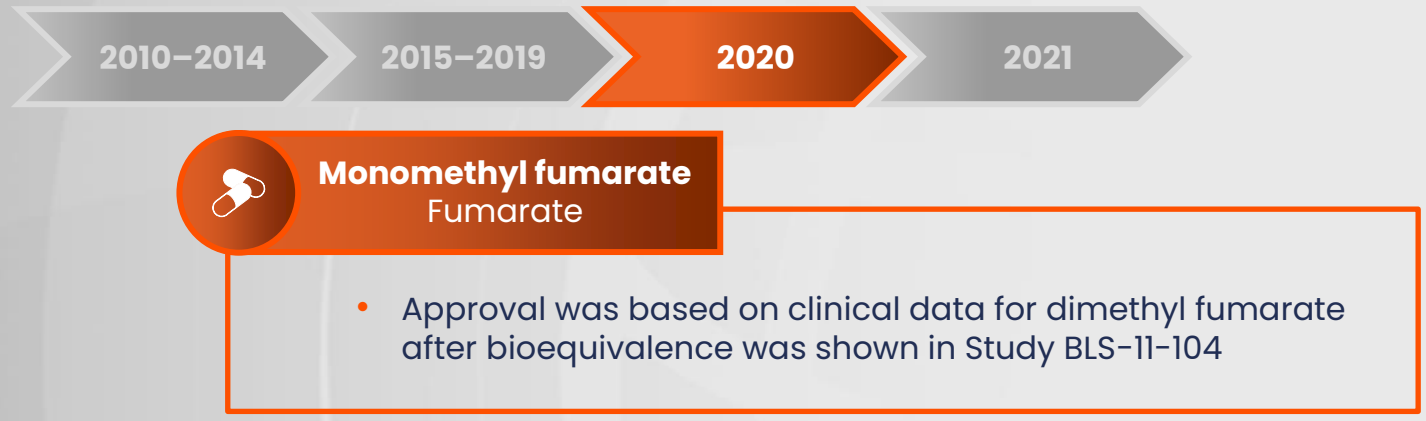
- Phase III EVOLVE-MS-1 trial interim results confirmed safety and efficacy in newly diagnosed relapsing-remitting MS and patients previously treated with IFN or GA[1]
- The phase III EVOLVE-MS-2 trial demonstrated an improved gastrointestinal tolerability profile of diroximel fumarate compared with DMF[2]
- Transition to diroximel fumarate from GA, IFN or DMF is a reasonable treatment strategy[3]

DMF, Diroximel fumarate; DMT, disease-modifying therapy; GA glatiramer acetate; IFN, interferon; MS, multiple sclerosis.

1. Naismith RT, et al. *Mult Scler*. 2020;26:1729–39; 2. Naismith RT, et al. *CNS Drugs*. 2020;34:185–96; 3. Wray S, et al. *Adv Ther*. 2022:1–22.

Approved DMTs for relapsing MS

Oral DMTs: Timeline of approvals and pivotal trials



DMT, disease-modifying therapy; FDA, US Food and Drug Administration; MS, multiple sclerosis.

FDA. Available at: www.accessdata.fda.gov/drugsatfda_docs/nda/2020/210296Orig1s000SumR.pdf (accessed 25 February 2022).

Approved DMTs for relapsing MS

Oral DMTs: Timeline of approvals and pivotal trials

2010–2014 | 2015–2019 | **2020** | 2021

Siponimod
S1PR modulator

- Phase III EXPAND trial in secondary progressive MS (N=1,651)
- Significantly fewer patients receiving siponimod had 3-month CDP vs placebo (HR 0.79, 95% CI 0.65–0.95; RRR 21%; p=0.013)

- Safety profile was similar to that of other S1PR modulators

CDP, confirmed disability progression; CI, confidence interval; DMT, disease-modifying therapy; HR, hazard ratio; MS, multiple sclerosis; RRR, relative risk reduction; S1PR, sphingosine-1-phosphate receptor.

Kappos L, et al. *Lancet*. 2018;391:1263–73.

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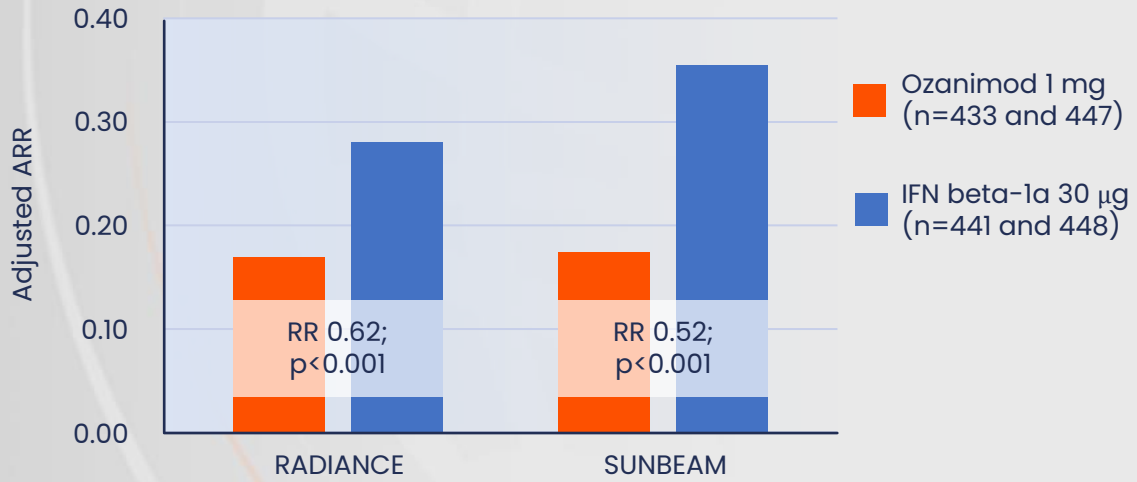
Approved DMTs for relapsing MS

Oral DMTs: Timeline of approvals and pivotal trials

2010–2014 | 2015–2019 | **2020** | 2021

Ozanimod
S1PR modulator

- Phase III RADIANCE and SUNBEAM trials[1,2]



- More participants in the IFN beta-1a groups vs the ozanimod groups had TEAEs leading to treatment discontinuation

ARR, annualized relapse rate; DMT, disease-modifying therapy; MS, multiple sclerosis; RR, relative risk; S1PR, sphingosine-1-phosphate receptor; TEAE, treatment-emergent adverse event.
1. Cohen JA, et al. *Lancet.* 2019;18:1021–33; 2. Comi G, et al. *Lancet Neurol.* 2019;18:1009–20.

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Approved DMTs for relapsing MS

Oral DMTs: Timeline of approvals and pivotal trials

2010–2014 | 2015–2019 | 2020 | **2021**

Ponesimod
S1PR modulator

- Phase III OPTIMUM superiority trial with teriflunomide

- Safety profile was similar to that of other S1PR modulators

ARR, annualized relapse rate; DMT, disease-modifying therapy; MS, multiple sclerosis; RRR, relative risk reduction; S1PR, sphingosine-1-phosphate receptor.
Kappos L, et al. *JAMA Neurol*. 2021;78:558–67.

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Novel treatment approaches in MS

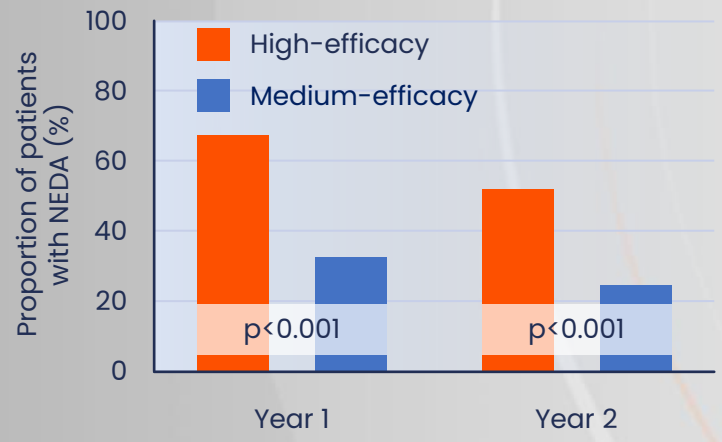
High- and medium-efficacy DMTs

High-efficacy DMTs[1,2]

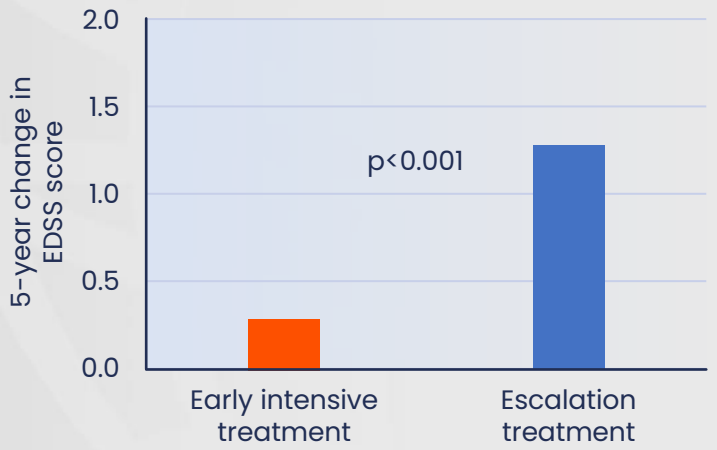
- Alemtuzumab
- Natalizumab
- Ocrelizumab
- Ofatumumab
- Rituximab
- Cladribine

Medium-efficacy DMTs[1]

- Dimethyl fumarate
- Glatiramer acetate
- Beta interferon
- Teriflunomide
- S1PR modulators



NEDA at year 1 and 2 was significantly more likely in patients on high-efficacy DMTs vs moderate-efficacy DMTs[3]



The 5-year change in EDSS score was significantly lower in the early intensive treatment group vs those receiving escalation therapy[4]

DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; NEDA, no evidence of disease activity; S1PR, sphingosine-1-phosphate receptor.

1. Wiendl H, et al. *Neurol Res Pract*. 2021;3:44; 2. Simpson A, et al. *Curr Treat Options Neurol*. 2021;23:19; 3. Simonsen CS, et al. *Front Neurol*. 2021;12:693017;
4. Harding K, et al. *JAMA Neurol*. 2019;76:536–41.

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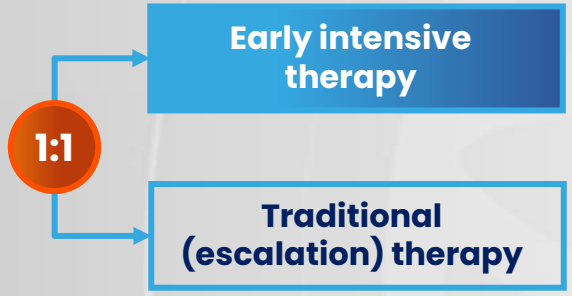
Novel treatment approaches in MS

Early intensive therapy vs escalation therapy: RCTs

TREAT-MS (NCT03500328)

N=900
Adults with RRMS



Primary endpoint

- Time to sustained disability progression (EDSS+)

Estimated primary completion: 2024

DELIVER-MS (NCT03535298)

N=800
Adults with RRMS

Primary endpoint

- Brain volume loss to month 36

Estimated primary completion: 2025

EDSS+, Expanded Disability Status Scale Plus; MS, multiple sclerosis; RCT, randomized controlled trial; RRMS, relapsing-remitting MS.
Clinical trials can be accessed at ClinicalTrials.gov using the study identifier.

Ongoing clinical trials with DMTs in relapsing MS

Novel DMTs: Ongoing clinical trials in comparison with teriflunomide

Agent	Trial	MoA
Ublituximab (anti-CD20)	• Phase III ULTIMATE 1 (NCT03277261) • Phase III ULTIMATE 2 (NCT03277248) • Study complete	• Depletion of B lymphocytes[1]
Tolebrutinib (BTK inhibitor)	• Phase III GEMINI 1 (NCT04410978) • Phase III GEMINI 2 (NCT04410991) • Estimated study completion: 2023	• Modulation of B lymphocytes, macrophages and microglia[2]
Evobrutinib (BTK inhibitor)	• Phase III evolutionRMS 1 (NCT04338022) • Phase III evolutionRMS 2 (NCT04338061) • Estimated study completion: 2023	
Fenebrutinib (BTK inhibitor)	• Phase III FENhance 1 (NCT04586023) • Phase III FENhance 2 (NCT04586010) • Estimated study completion: 2025	

BTK, Bruton's tyrosine kinase; DMT, disease-modifying therapy; MoA, mechanism of action; MS, multiple sclerosis.
Clinical trials can be accessed at ClinicalTrials.gov using the study identifier.
1. Roach CA, et al. *Front Neurol*. 2021;11:595547; 2. Dolgin E. *Nature Biotech*. 2021;39:3–5.

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Conclusions

The management of relapsing MS has become increasingly complex with the emergence of novel DMTs

Oral DMTs are becoming an increasingly important option for patients with relapsing MS

Novel treatment options for relapsing MS are needed, as the majority of patients will require more than one DMT during their lifetime

Novel drug classes in MS offer multiple treatment options to meet the needs of different patients

DMT, disease-modifying therapies; MS, multiple sclerosis.