touchEXPERT BRIEFING

Multiple sclerosis today: Disease monitoring, biomarkers and family planning

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This resource has been downloaded from a touchEXPERT BRIEFING, hosted on touchSITE. The full activity, which includes video resources, can be accessed at:

www.touchneurologytmc.com/multiple-sclerosis/learning-zone/ms-today-diagnosis-prognosis-risk-factors/

This content is for healthcare professionals based in Austria, Germany, Norway, Portugal, Sweden, Switzerland and United Arab Emirates only.

Learning objectives

After watching the touchEXPERT BRIEFING activity, you should be able to:

- ✓ Describe the importance of biomarkers in the diagnosis, prognosis and management of multiple sclerosis (MS)
- ✓ Understand how biomarkers may be used to optimize treatment decisions and improve patient outcomes
- ✓ Discuss key considerations for the management of MS in women of childbearing potential

Expert faculty

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The role of biomarkers in the diagnosis, prognosis and management of MS

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Early treatment and diagnosis

- Achieving an early diagnosis and identifying optimal personalized treatment is essential to improving long term outcomes in MS[1]
- Currently, MRI (Gd and T2 lesions) and clinical characteristics, e.g., relapse and disability (EDSS), play the most important role in diagnosis and monitoring[1,2]
- However, MRI does not provide the whole picture and non-specific MRI findings can lead to misdiagnosis[3]
- Molecular biomarkers can complement MRI and clinical characteristics to identify patients in need of treatment and select the best treatment options for the individual[2]

CNS, central nervous system; DIS, dissemination in space; DIT, dissemination in time; EDSS, expanded disability status scale; Gd, gadolinium-enhancing; MRI, magnetic resonance imaging; MS, multiple sclerosis; T2, T2-hyperintense.

1. Smith AL, *et al. Neurotherapeutics* 2017;14:952–960; 2. Paul A, *et al. Cold Spring Harb Perspect Med* 2019;9:a029058; 3. Thompson AJ, *et al. Lancet Neurol* 2018;17:162–1734.

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Types of MS biomarkers

- ***Diagnostic***: those that distinguish patients with MS from healthy individuals
- ***Disease activity/prognosis***: those measured in patients with relapsing/remitting or progressive MS to evaluate disease course – e.g., disability, brain atrophy, or MS-associated pathophysiological processes
- ***Treatment–response***: those measured in patients receiving MS treatments to determine efficacy and safety

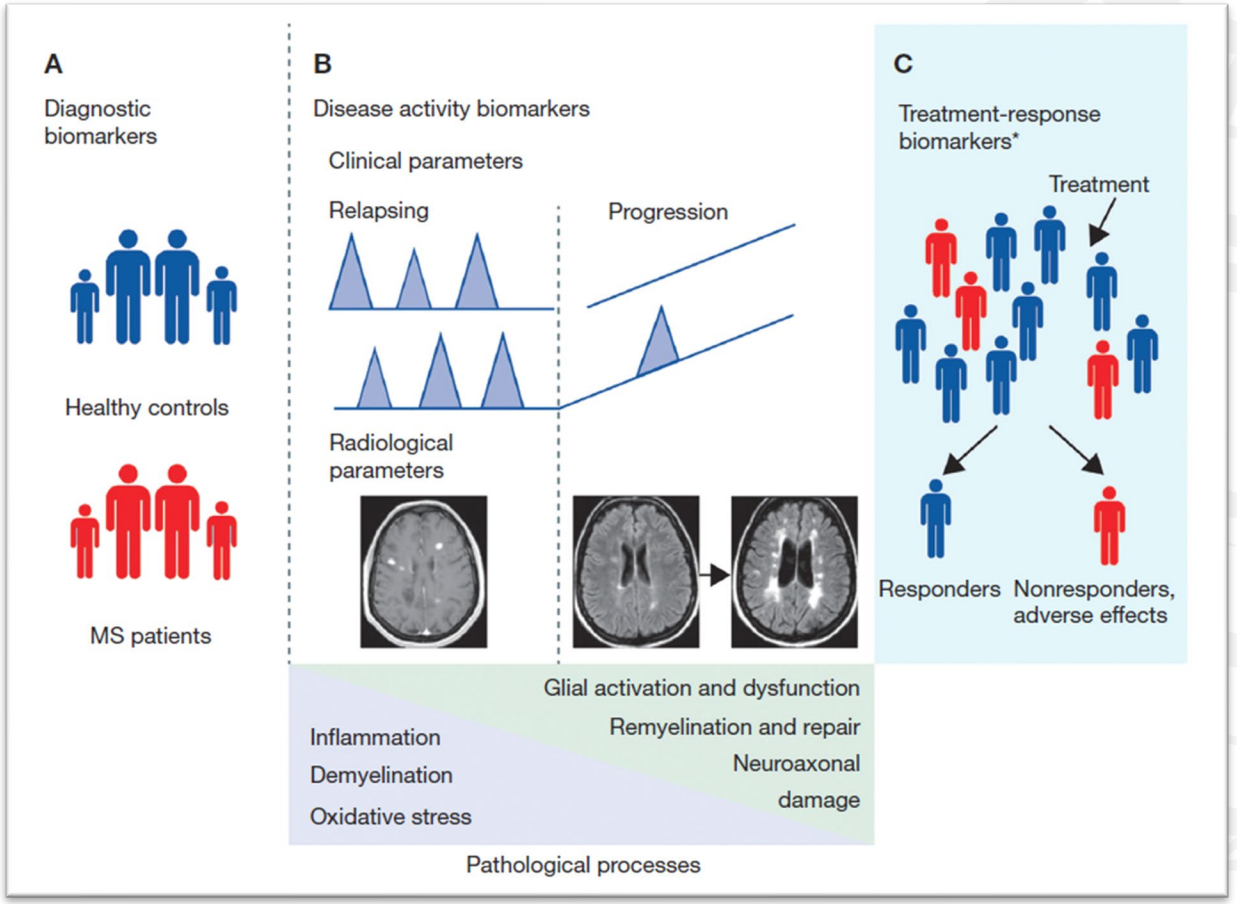

Figure adapted from Paul A, *et al. Cold Spring Harb Perspect Med* 2019;9:a029058.

Putative MS Biomarkers Beyond MRI

Diagnostic[1]

- **Oligoclonal bands**
  Present in the CSF (but not serum) of almost all patients with MS
- **IgG index**
  A CSF/serum ratio >0.7 is indicative of MS (occurs in ~70% of cases)
- **Antinuclear antibodies**
  Tissue non-specific autoantibodies against components of the cell nucleus. Recommended by the German Neurological Society for differential diagnosis[2]

Prognosis/activity[1]

- **Neurofilaments**
  Release is related to axonal or neuronal damage; can be detected in serum by single molecule arrays (SIMOA). Higher levels correlate with many clinical and tomographic characteristics of MS
- **Chitinase-3-like-1**
  Detected in the CSF; higher levels associated with conversion from CIS to MS and faster disability progression. Also a potential marker for treatment-response

Treatment–response[1,3]

- **Neurofilament light chain**
  Release is related to axon damage; also correlates with disease activity
- **Glial fibrillary acidic protein (GFAP)**
  Increased levels associated with astrocyte damage, astrogliosis and more severe disability
- **CXC motif chemokine-13**
  Involved in the recruitment of B cells into the CNS in MS; increases associated with disease activity and reductions associated with MS treatments

CIS, clinically isolated syndromes; CSF, cerebrospinal fluid; IgG, immunoglobulin G.

1. Ziemssen T, *et al. J Neuroinflammation* 2019;16:272; 2. DGN / KKNMS Leitlinie zur Diagnose und Therapie der MS (2014). Available at http://www.kompetenznetz-multiplesklerose.de/wp-content/uploads/2016/02/dgn-kknms_ms-ll_20140813.pdf (accessed 13 Oct 2022); 3. Paul A, *et al. Cold Spring Harb Perspect Med* 2019;9:a029058.

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Expert opinion

"What are the most promising biomarker candidates beyond MRI?"

"What assessments would you use in your practice?"

*"In addition to standard MRI assessment, neurofilament light chains are the most promising as they are specific for neuroaxonal damage. Clinical assessments [e.g., EDSS] are just as important, however"**

*"In the future, technology such as smartphones may also provide digital biomarkers, for example, in the assessment of neuropsychological deficits"**

*Summary quotations based on discussions between Prof. Eva Kubala Havrdová and Prof. Ludwig Kappos.

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Summary

1. MRI remains the most important clinical tool for disease diagnosis, disease activity, and treatment response in MS, though it does not provide the full picture[1,2]
2. Biomarkers could complement MRI to provide a more accurate picture of disease activity/progression and treatment efficacy[1,2]
3. Neurofilament light chain is the most promising biomarker candidate for activity/treatment–response, as it measures neuroaxonal damage[1–3]

MRI, magnetic resonance imaging; MS, multiple sclerosis.

1. Paul A, *et al. Cold Spring Harb Perspect Med* 2019;9:a029058; 2. Expert opinion from Prof. Eva Kubala Havrdová and Prof. Ludwig Kappos; 3. Ziemssen T, *et al. J Neuroinflammation* 2019;16:272.

The impact of MS on women of childbearing potential

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Key topics to consider during pre-pregnancy counselling

- MS is most commonly diagnosed in young women, who may still wish to have children[1]
- As such, pre-pregnancy counselling should be conducted at, or soon after, diagnosis, to discuss any risks to the patient/baby and provide reassurance[1,2]
- One of the key questions is therefore: should we stop/change MS treatment if pregnancy is planned?

2019 'Association of British Neurologists' pre-pregnancy MS counselling guidelines[1]

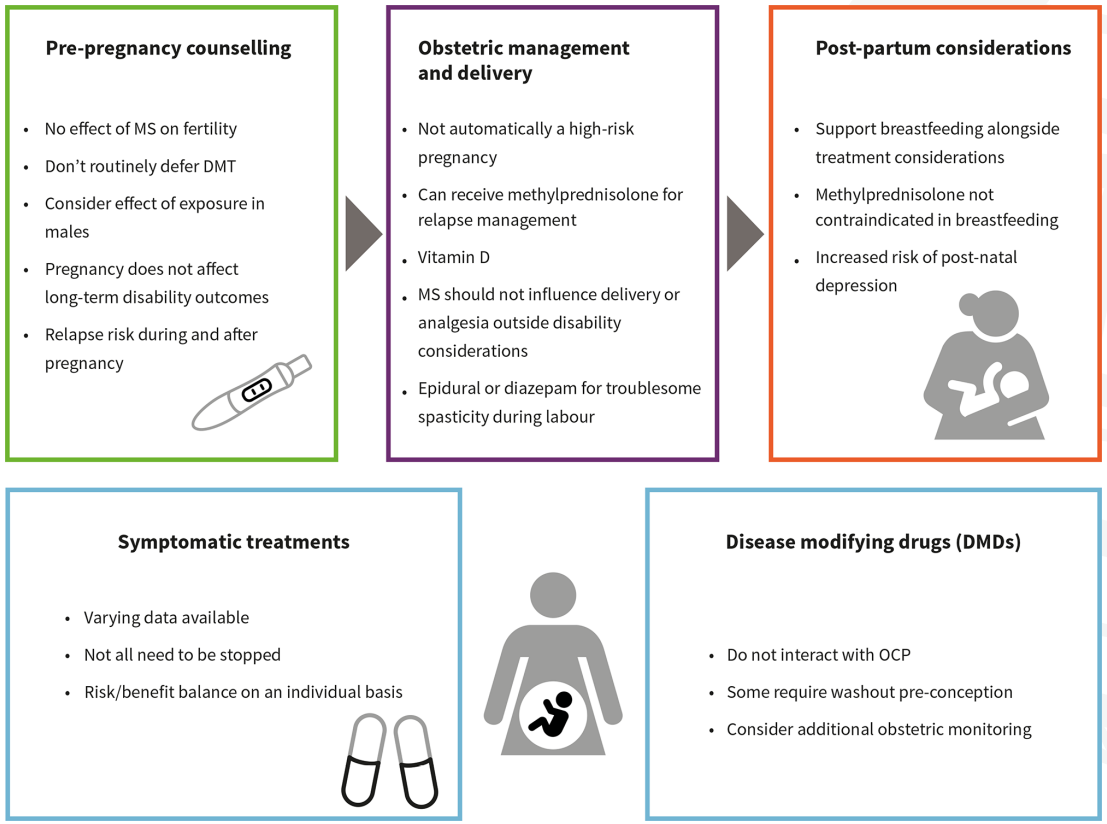

Figure adapted from Dobson R, *et al. Pract Neurol* 2019;19:106–114

DMT, disease modifying therapy; FDA, US Food and Drug Administration; MS, multiple sclerosis; OCP, oral contraceptive pill.

1. Dobson R, *et al. Pract Neurol* 2019;19:106–114; 2. Krysko KM, *et al. Curr Treat Options Neurol* 2021;23:11.

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Considerations for DMTs in women planning to have children

- While it may seem sensible to discontinue DMTs in women with MS planning to conceive, extended drug delays may lead to re-emergence of disease activity
- Any treatments plans should consider pregnancy planning (up to conception), pregnancy and the postpartum period – disease activity, impact of therapy, impact of therapy withdrawal, and plans for breastfeeding should all be considered
- Data indicate that some treatments are safe to continue to conception and throughout pregnancy, while others are contraindicated
- Similarly, research indicates that some MS treatments may be compatible with breastfeeding

DMT, disease modifying therapy; MS, multiple sclerosis;
Krysko KM, *et al. Curr Treat Options Neurol* 2021;23:11.

Example case

- 25 years of age, married and planning to have children
- Diagnosed with MS 4 years ago – what do you do?
- ***Recommendation***:*
  - Check that she is not receiving treatments for which pregnancy is contraindicated
  - Maintain treatment and/or suggest more appropriate treatments if necessary (personalized based on patient characteristics, lifestyle and patient preference)
  - Monitor condition to ensure stable disease prior to pregnancy
  - Recommend hormonal contraception until disease control is achieved

Image is illustrative of a patient but does not feature an actual patient.
*Based on discussions between Prof. Eva Kubala Havrdová and Prof. Ludwig Kappos.

Expert opinion

"What if the patient doesn't agree with this approach?"

"Can she participate in fertility programs?"

*"If alternative treatments are recommended but the patient does not want to switch, inform the patient of the risks and continue current treatment until delivery"**

*"IVF is successful in patients with MS and requires no additional restrictions, but ensure close monitoring of disease activity"**

IVF, *in vitro* fertilization.
*Summary quotations based on discussions between Prof. Eva Kubala Havrdová and Prof. Ludwig Kappos.

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Summary

1. For women with MS planning to conceive, pre-pregnancy planning is essential, and should be individualized based on current treatment, disease activity and preference[1,2]
2. MS treatment should be maintained through pregnancy if possible, switching to more appropriate medications if the current treatment is contraindicated[2]
3. The patient should be monitored to ensure that stable disease is achieved prior to pregnancy[2]
4. MS treatment can be delayed during breastfeeding, though some treatments have been shown to be compatible with breastfeeding[1,2]

1. Krysko KM, *et al. Curr Treat Options Neurol* 2021;23:11; 2. Expert opinion from Prof. Eva Kubala Havrdová and Prof. Ludwig Kappos.