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Insights Into MS

Evolving Therapeutic Targets

History of MS treatment



- The development of MS treatments started in the early 1990s with immunomodulators, such as glatiramer acetate and IFN-β; this first wave of drugs offered modest effects^{1,2}
- The second wave of MS therapies targeted inflammatory aspects of MS—specifically, lymphocytes^{1,2}—and provided some efficacy in slowing disease progression and reducing relapses¹



Adapted with permission from Melamed and Lee.³

Evolution of DMTs for RRMS treatment

The evolution of disease-modifying therapy over the past 30 years has led to more than 15 FDA-approved drugs for the treatment of relapsing-remitting $MS.^{3,4}$

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Current treatment targets



- The traditional view of T cell-mediated MS relapses has now been updated to include key interactions between several immune cells⁵
- The standard—currently first-line—therapies for MS target immunomodulation by inhibiting immune-cell trafficking, inhibiting cell replication, and influencing immune-cell function, which may alter cytokine production or effector-cell functions through multiple signaling pathways⁶
- Recent disease-modifying therapies can be categorized based on their presumed target or mechanism of action,⁶ with high-efficacy therapies targeting autoreactive B-cell activity⁶

Targets of current therapies



DMT; disease-modifying therapy; FDA, Food and Drug Administration; S1P, sphingosin-1-phosphate; IFN, interferon; MS, multiple sclerosis; NrF2, nuclear factor erythroid-derived 2-like 2; RRMS, relapsing-remitting MS.

Emerging targets



- Emerging targets may include⁷:
 - B- and T-lymphocyte inhibition
 - Mitochondria protection
 - Anti-inflammatory strategies
 - Remyelination
 - Hematopoietic stem cell or mesenchymal stem cell transplantation
- Determining which patients may benefit most from particular therapies will be essential for personalized approaches to MS treatment and management⁸



Adapted with permission from Baecher-Allan et al.9

The future of potential MS therapy



- Future MS treatments are focused on combining a reduction in neuroinflammation with neuroprotective and remyelination strategies^{7,10}
- Because not all patients respond equally to treatment, there is also considerable interest in identifying predictive biomarkers to help determine which patients might benefit from specific treatments and which patients might be prone to adverse drug reactions¹¹
- Neurofilament light chain is emerging as a potential biomarker of axonal damage in MS and can be quantified in the blood and cerebrospinal fluid⁵

Prognostic/Predictive Biomarkers



Treatment-Response Biomarkers



Adapted with permission from Ziemssen et al.11

MS, multiple sclerosis

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