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Multiple sclerosis (MS) is a neurological disorder, characterised by inflammation and neurodegeneration. Though originally viewed as an illness of white matter of the central nervous system, advanced imaging methods have shown early and ongoing grey matter damage. Patients diagnosed with MS usually have several fluctuating and disabling symptoms (impaired mobility, fatigue, mood and cognitive alterations, pain, visual disturbances, etc.) with a significant influence on quality of life. Most MS patients have relapses and remission of the symptoms, particularly in the early stages of the disease. However, gradual progression independent of acute inflammatory attacks, known as progressive or degenerative changes, may take place early on and increase in incidence over time.

Table 1: 2014 RADS committee guidelines for multiple sclerosis (MS) treatment strategies.

			Drug choice				
Disease type	**Disease activity**		**1st**	**2nd**	**3rd**	**4th**	**5th**
Clinically isolated syndrome	Mild		Interferon beta 1-alpha*	Glatiramer acetate	Interferon beta 1b	-	
	Active		Interferon beta 1-alpha†	Glatiramer acetate	Interferon beta 1b	-	
RRMS	Mild-to-moderate		Teriflunomide	Interferon beta 1-alpha*	Glatiramer acetate	Interferon beta 1-alpha†	Interferon beta 1b
	Active	JC -ve	Natalizumab	Fingolimod	-		
		JC +ve	Fingolimod	No previous immunosuppressive treatment: Natalizumab for 12 (max. 24) months	-		
				Previous immunosuppressive treatment: Alemtuzumab	-		
	Breakthrough	JC -ve	Natalizumab	Fingolimod	-		
		JC +ve	Fingolimod	No previous immunosuppressive treatment: Natalizumab for 12 (max. 24) months	-		
				Previous immunosuppressive treatment: Alemtuzumab	-		
	With significant side effects on IFN-β or glatiramer acetate		Teriflunomide	-			
	With significant side effects on teriflunomide		Interferon beta 1-alpha*	Glatiramer acetate: Interferon beta 1-alpha†	Interferon beta 1b	-	
Secondary progressive MS	With superimposed relapses		Interferon beta 1-alpha†	Interferon beta 1b	-		
	With rapid disease progression but without superimposed relapses		Interferon beta 1b	-			

*Avonex, †Rebif.
RRMS: relapsing remitting multiple sclerosis; JC: John Cunningham virus antibody.

Table 2: 2015 RADS committee guidelines for multiple sclerosis (MS) treatment strategies.

			Drug choice				
Disease type	**Disease activity**		**1st**	**2nd**	**3rd**	**4th**	**5th**
Clinically isolated syndrome	All		Teriflunomide	Interferon beta 1-alpha*	Interferon beta 1-alpha†	Glatiramer acetate	Interferon beta 1b
RRMS	Mild-to-moderate		Teriflunomide	Dimethyl fumarate	Peginterferon beta-1a	Interferon beta 1-alpha*	Glatiramer acetate‡
	Active	JC -ve	Natalizumab	Fingolimod	-		
		JC +ve	Fingolimod	No previous immunosuppressive treatment: Natalizumab for 12 (max. 24) months	-		
				Previous immunosuppressive treatment: Alemtuzumab	-		
	Breakthrough	JC -ve	Natalizumab	Fingolimod	-		
		JC +ve	Fingolimod	No previous immunosuppressive treatment: Natalizumab	-		
				Previous immunosuppressive treatment: Alemtuzumab	-		
	With significant side effects on IFN-β or glatiramer acetate		Teriflunomide	-			
	With significant side effects on teriflunomide		Dimethyl fumarate	-			
	With significant side effects on teriflunomide and dimethyl fumarate		Peginterferon beta-1a	Interferon beta 1-alpha*	Glatiramer acetate	Interferon beta 1-alpha	Interferon beta 1b
Secondary progressive MS	With superimposed relapses		Interferon beta 1-alpha†	Interferon beta 1b	-		
	With rapid disease progression but without superimposed relapses		Interferon beta 1b	-			

Treatment of patients with clinically isolated syndrome should be offered if the following four criteria are met:
1) Other diagnoses are ruled out after relevant examinations
2) The severity of the relapse is such as to interfere with daily living
3) The requirement for dissemination in space according to the McDonald criteria are met
4) Oligoclonal band in cerebrospinal fluid
*Avonex; †Rebif.
‡ 6th and 7th line options are Interferon beta 1-alpha (Rebif) and Interferon beta 1b, respectively.
RRMS: relapsing remitting multiple sclerosis; JC: John Cunningham virus antibody.

There are several considerations related to the therapy of MS:

1. Early treatment is essential, since inflammation and degeneration occur early on in the disease (treatment should occur as soon as possible following the diagnosis of relapsing MS)
2. Patients showing early clinical symptoms together with magnetic resonance imaging results consistent with MS who are not treated have a high probability of further disease activity
3. Depression, fatigue, and cognitive impairment occur in the early stages of the disease

4. Treatment with the medication should be continued indefinitely with the following exceptions: sub-optimal treatment response, serious side effects, inadequate adherence to the treatment regimen, and availability of a more appropriate drug

To date, the following disease-modifying agents have been approved (and result in a relative decrease in annualised relapse rate compared with placebo):

- Self-injected agents: glatiramer acetate (29%), interferon beta 1-alpha (Avonex, 32%; Rebif, 18%), interferon beta 1b (34%)
- Oral agents: dimethyl fumarate (44–53%), fingolimod (54%), teriflunomide (31%)
- Intravenous agents: mitoxantrone (67%), natalizumab (68%), alemtuzumab (55%)

Concerning the treatment strategies of MS patients, the RADS Committee suggested the following guidelines in 2014 (Table 1) and an update in 2015 (Table 2), which we prefer to follow in our everyday clinical practice.

Factors affecting the choice of treatment at any point in the disease course are complex and most appropriately analysed collaboratively by the patient and his or her treating neurologist.

In the future, however, an interesting approach may be the combination of immunmodulatory agents with neuroprotective agents like LINGO-1. Further research is required for profiling patients; for example, research into T or B cell targeted approaches or susceptibility for specific infectious side effects.

FURTHER READING

1. Ingwersen J et al. Advances in and algorhitms for the treatment of relapsing-remitting multiple sclerosis. Neurotherapeutics. [Epub ahead of print].

2. MS Coalition. The Use of the Disease-Modifying Therapies in Multiple Sclerosis: Principles and Current Evidence. Available at: http://www.nationalmssociety.org/getmedia/5ca284d3-fc7c-4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color. Last accessed: 13 January 2016.

3. RADS Committee for the Disease Modifying Treatment of Multiple Sclerosis. Treatment guidelines, including product recommendations for the diseases modifying treatment of multiple sclerosis. 2014.