DMD Therapy for Multiple Sclerosis Based on Disease Activity

Selection of disease-modifying drugs (DMDs) for multiple sclerosis (MS) based on disease activity: Consensus from the Arabian Gulf

Guidance for healthcare professionals addressing the treatment of multiple sclerosis in the Arabian Gulf countries

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INTRODUCTION

Multiple sclerosis (MS) is a lifelong, neurodegenerative disease with a potential for long-term disability.

The prevalence of MS in the Gulf countries has increased recently and it poses a challenge to the healthcare systems in these countries.

The treatment landscape for MS has changed in recent years. New treatments have become available and access to these treatments has improved.

There is also an improved knowledge of the safety profiles of DMDs, leading to a greater understanding of their risks and mitigation strategies.

It is important that appropriate guidance is available to physicians to use these medicines effectively. Currently, guidance specifically for the Gulf countries is lacking.

Here we present the consensus recommendations on MS management in the Gulf.

- The objective of this consensus was to establish recommendations that would support the treating physicians in the Gulf region in the management of MS.
- The recommendations were based on the level of disease activity, taking into account several other factors such as efficacy, safety, monitoring burden, lifestyle, and pregnancy.

CONSENSUS RECOMMENDATIONS FOR THE MANAGEMENT OF RRMS

CLASSIFYING DISEASE AT FIRST PRESENTATION

Patients with active MS without indicators of poor prognosis

- One relapse in the last 1 year, or two relapses in the last 2 years
- No poor prognostic indicators
- This category replaces the 'low' or 'mild' disease group usually used in disease activity classifications

Patients with highly active disease

- Patients with at least two relapses in the previous year
- And more than nine T2 lesions, or ≥1 Gd+ lesion without an impact on EDSS (i.e. no residual disabilities after steroid treatment)

Patients with rapidly evolving severe RRMS

- At least one disabling relapse (defined in Box 1) with impact on EDSS score (i.e. residual disabilities) or with MRI lesions in strategic prognostic areas (spinal cord, cerebellum, brain stem) or poor prognostic factors

Box 1. NHS England definition of a disabling MS relapse

Affects the patient's social life or occupation, or is otherwise considered disabling by the patient.

Affects the patient's activities of daily living as assessed by an appropriate method.

Affects motor or sensory function sufficiently to impair the capacity or reserve to care for themselves or others.

Needs treatment/hospital admission.

TREATMENT RECOMMENDATIONS

Table 1. Consensus recommendations on the use of DMDs in people with RRMS according to disease activity and previous treatment status.

Disease activity at first presentation	Treatment recommendation		
	No prior DMD (1st-line)	1 prior DMD (2nd-line)	2 prior DMD (3rd-line)
Active MS without indicators of poor prognosis	Beta Interferon Glatiramer acetate Teriflunomide Dimethyl fumarate	Cladribine tablets Dimethyl fumarate* Fingolimod Natalizumab[b]	Cladribine tablets Natalizumab Fingolimod Ocrelizumab Alemtuzumab[b]
Highly active MS	Cladribine tablets Natalizumab Fingolimod Ocrelizumab Dimethyl fumarate[a]	Cladribine tablets Natalizumab Ocrelizumab Alemtuzumab[a] Fingolimod[a]	Cladribine tablets Natalizumab Ocrelizumab Alemtuzumab
Rapidly evolving severe MS	Cladribine tablets Natalizumab Ocrelizumab Fingolimod[a]	Natalizumab Ocrelizumab Alemtuzumab[a] Cladribine tablets[a]	Natalizumab Alemtuzumab Ocrelizumab

All recommendations were achieved via a high level of expert consensus (at least seven out of 10 experts agreed), except where indicated as a moderate consensus (between four and six experts agreed) or [b]low consensus (three experts or fewer agreed). DMD: disease-modifying drug.

*DMF may be considered as second-line therapy in patients without poor prognostic indicators as there is some evidence for greater efficacy compared with other platform therapies.

The choice of third-line treatment is not evidence based due to the lack of well designed clinical trials based on patients who have received two DMDs previously. These recommendations are therefore based on the experience and judgement of the authors.

IDENTIFYING AND MANAGING SUBOPTIMAL RESPONSE IN RRMS

There is no evidence base from randomized clinical trials for defining suboptimal response and subsequent decision of switching/escalation from second-line therapies.

The consensus definitions of suboptimal response and actions recommended are shown in Table 2.

Table 2. Actions recommended for specific manifestations of suboptimal treatment response.

Suboptimal response after 1 year of 1st line treatment	Action recommended
A single MRI lesion in a strategic location (spinal cord, cerebellum, brain stem) or ≥3 MRI lesions in non-strategic locations. or Single relapse (non-disabling), without EDSS progression[a] or MRI activity.	This may prompt scheduling further follow-up MRI at 6 months or lateral switching to other DMD (with different mechanism of action) but this depends on the overall presentation (consider a higher efficacy DMD)
MRI progression + relapse or EDSS progression + relapse	Switching DMD treatment

[a]Usually defined as progression by 1 point for EDSS <5, or 0.5 points if EDSS ≥5.

SWITCHING OF THERAPY

A switch of DMD due to a tolerability or patient preference issue may be achieved via a new DMD of similar efficacy, but a different mechanism (a 'lateral switch').

The mechanisms of action, pharmacokinetics, and pharmacodynamics of a DMD may provide important information relating to the need or otherwise to switch a treatment.

For alemtuzumab and cladribine tablets, it is recommended to finish the 2-year course even if a relapse occurs during the first year of treatment before judging the efficacy of such immune reconstitution DMDs.

Other factors such as long-term safety, monitoring burden, lifestyle/compliance, and pregnancy are important to consider when initiating/escalating DMDs.

REFERENCE:

Alroughani R, Inshasi J, Al-Asmi A, et al. Expert consensus from the Arabian Gulf on selecting disease-modifying treatment for people with multiple sclerosis according to disease activity. Postgraduate Medicine, DOI: 10.1080/00325481.2020.1734394

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