Dear Editor,

Question

Considering safety and future disability, which approach (high-efficacy disease-modifying therapy OR escalation) is preferable in multiple sclerosis (MS) patients?

Search strategy

The search was performed in PubMed and Cochrane databases using the keywords “multiple sclerosis” AND “escalation” OR “early intense therapy” OR “high efficacy therapy” OR “high efficacy disease-modifying therapy”.

Cochrane Results: not matched

Search outcome

Forty articles were found. Title and abstracts of all articles were evaluated. 14 relevant studies were found: 3 cohorts, 6 reviews, 3 cross-sectional retrospectives, 1 clinical trial, and 1 editorial. Three recent and most relevant articles were selected.

Comments

The treatment strategy for MS is a highly controversial debate. Disease-modifying therapies for MS are divided into escalation therapies and high-efficacy therapies. Escalating treatment means starting with the safest disease-modifying therapies with moderate effect. High-efficacy therapies mean starting with a strong immune intervention.

The majority of studies agree on this issue that the advantage of the escalation scheme is to allow many patients to have satisfying control of the disease while receiving relatively safe drugs and never escalating to more aggressive therapy (Table 1). But the disadvantage is exposing some patients to the risk of losing precious years spent receiving a treatment that was not potent enough and potentially leading to sustained accumulation of disability. The advantage of high-efficacy disease-modifying therapies is to facilitate an earlier achievement of “no evidence of disease activity”, and the disadvantage is the risk to expose some patients needlessly to serious side effects.

Clinical bottom line

The current challenge in therapeutic strategy is to identify the most effective drug and strategy during a specific phase of the disease of every single patient. Sex, age, and presenting symptoms might predict increased disease severity in MS patients. With present markers, such as volumetric MRI and emerging markets such as serum neurofilament light chain, early and accurate prognostication in individual patients will become possible. New MRI techniques (brain and spinal cord imaging) should help us to identify those MS patients, especially individuals without any real disability, who are more at risk of developing destructive CNS lesions with or without first-line therapy and who are therefore more eligible for an early and more aggressive treatment strategy (6).

The higher costs of high-efficacy therapies can present challenges, particularly for patients without comprehensive insurance coverage or those residing in regions with limited access to healthcare resources. Escalation therapies, on the other hand, may be more cost-effective initially, but they might not provide the same level of disease control as high-
High-efficacy disease-modifying therapies (DMTs) in the context of MS can provide potent control over the disease, but they are also accompanied by potential adverse effects (7). These may encompass immunosuppression, reactions during infusion or injection, potential harm to the liver, cardiac complications, an elevated risk of developing certain cancers, blood-related disorders, headaches, flu-like symptoms, gastrointestinal disturbances, and alterations in mood. Patients considering the use of high-efficacy DMTs should be well-informed about these potential side effects and engage in...
comprehensive discussions with their healthcare providers to carefully assess the risks and benefits of these treatment options tailored to their individual MS management plan (8). Regular monitoring and open communication with healthcare providers are fundamental to effectively manage any possible side effects and maximize the benefits of these therapies (1).

Considering lifestyle modifications, especially exercise and diet, alongside disease-modifying therapies is crucial in managing MS. Lifestyle factors can significantly impact the disease's progression and should be a part of the overall treatment strategy. Regular exercise offers numerous benefits for individuals with MS, including improved muscle strength, balance, mobility, reduced fatigue, and enhanced mood and well-being (9). A well-balanced diet, rich in nutrients, antioxidants, and omega-3 fatty acids, can help reduce inflammation and support brain health in MS patients. Including information about lifestyle modifications in treatment discussions would lead to a more comprehensive approach to MS management, empowering patients to actively participate in their care and enhance their overall health and quality of life (10).

**Keywords:** Escalation, high-efficacy, Multiple Sclerosis

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**Conflict of interest**

The authors declare no conflict of interest regarding the publication of this paper.

**Ethical approval**

No need

**Consent for publication**

This manuscript has been approved for publication by all authors.

**References**