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COMMENTARY

European and American Guidelines for Multiple Sclerosis Treatment

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THE COMPLEX SCENARIO OF MULTIPLE SCLEROSIS THERAPY

- The management and treatment of multiple sclerosis (MS) is becoming more and more complex: many medications are now available for the treatment of MS, with different routes of administration (oral, intramuscular, subcutaneous, intravenous), different mechanisms of action, different effectiveness and safety profiles;
- this impressive development of knowledge has dramatically changed the management of MS;
- physicians now dispose of a wide spectrum of medications, with the possibility, in discussion with the patient, of selecting the right medication for the individual;
- physicians are asked to be more and more expert in the management of MS, to properly evaluate the efficacy/lack of clinical response to medications, and to manage adverse events appropriately, some of which are rare and severe;
- physicians, patients, patient associations and other stakeholders are solicited to design and develop new models of care to properly manage the complexity of MS.

HOW TO CHOOSE THE RIGHT DRUG FOR INDIVIDUAL PATIENTS

- The decision-making process for choosing the right medication is a complex task requiring:
  - a careful evaluation of the results of clinical trials
  - up-to-date information on post-marketing data
  - the capability to critically translate data from studies (that include carefully selected patients) for application in the cases of patients in everyday clinical practice (patients who are not carefully selected)
- The lack of head to head trials (with few exceptions) makes it difficult to compare the effectiveness of medications;
- Systematic reviews and experts' papers also offer a valuable source of learning and facilitate clinical updates, critically summarizing the results produced from many studies;
- Guidelines produced by scientific societies provide valuable and irreplaceable help.

The ECTRIMS and EAN societies have recently delivered guidelines for MS treatment:

- Montalban X., Gold R., Thompson A.J. et al. ECTRIMS/EAN Guideline on the pharmacological treatment of people with multiple sclerosis. Mult Scler. 2018;24(2):96-120
- Rae-Grant A., Day G.S., Ann Marrie R. et al. Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology Neurology 2018;90(17):777-788
- Rae-Grant A., Day G.S., Ann Marrie R. et al. Comprehensive systematic review summary: Disease-modifying therapies for adults with multiple sclerosis. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology Neurology 2018;90(17):789-800

The two guidelines provide recommendations on the following topics

- the treatment of Clinically Isolated Syndrome, Relapse Remitting MS, Primary Progressive MS, and Secondary Progressive MS
- MS monitoring
- Switching of therapies

Some aspects are specifically addressed by the two guidelines:

- by the AAN Guidelines:
  - the issues of adherence, the need for dialogue between doctors and people with MS, the need to address patient preferences and to carefully evaluate risks and benefits of disease modifying therapies
  - the issues of switching, as well as some specific questions about the use of natalizumab, and the occurrence of serious adverse events (infections, neoplasms etc.)
- by the ECTRIMS/EAN Guidelines:
  - the need to establish MS center, for appropriate monitoring of patients and for detection and management of adverse events
  - the use of MRI for MS monitoring

The topic of pregnancy is approached differently by the two guidelines:

- ECTRIMS/EAN guidelines don't avoid the use of glatiramer acetate, consider continuing interferon beta-1b and glatiramer acetate until pregnancy is confirmed, and consider continuing the treatment during pregnancy, if there is risk of MS reactivation.
- ECTRIMS/EAN guidelines consider natalizumab as an option for women with highly active MS who decide to plan for pregnancy after discussion of the possible risks; alemtuzumab is also an option for women with active MS who are planning pregnancy, with the recommendation of an interval of 4 months from the last infusion.
- AAN guidelines suggest considering the possible risks of teriflunomide and cyclophosphamide for men in relation to their reproductive plans.

Possible explanations for discrepancies between the two guidelines:

- differences in research questions that have been delineated, elaborated and adopted differently ;
- differences in the assessment of the level of evidence;
- differences in the process of quality appraisal.

A future objective could be to better identify and unify clinical questions, starting from the current guidelines, to develop a list of common questions: in this way we could expect to have more homogeneous answers.

Guidelines are not only the end of a process, but also the starting point for their implementation in clinical practice.

The validation in clinical practice will provide meaningful feedback on their applicability and usefulness.

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Compliance with Ethics Guidelines.

This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

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