NEW TREATMENTS OF MS

Su-Hyun Kim

National Cancer Center, Korea

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Learning Objectives

- ✓Understand the clinical rationale for initiating early high-efficacy therapy in MS and its potential to delay long-term disability progression.
- ✓Critically evaluate the efficacy and safety profiles of novel targeted disease-modifying therapies in the treatment of MS
- ✓Recognize the importance of a personalized, patient-centered approach in optimizing therapeutic strategies for MS management.

Key messages

Key message 1: Effectiveness and Safety of Novel Targeted Therapies

- **Ocrelizumab** is a well-established B-cell–depleting therapy with robust efficacy in both relapsing and primary progressive MS. Monitoring is needed for infusion reactions and infection risk.
- **Ofatumumab** is a fully human anti-CD20 monoclonal antibody administered subcutaneously. It depletes B cells and has shown high efficacy in reducing relapses and MRI activity in relapsing MS. Compared to intravenous anti-CD20 therapies, it offers the convenience of at-home administration. Key safety considerations include injection-related reactions and infection risk due to B-cell depletion
- **Cladribine** offers high efficacy and long-term benefits with good adherence, though infection risk necessitates close monitoring due to its immunosuppressive action.
- **Four S1PR modulators (fingolimod, siponimod, ozanimod, ponesimod)** prevent lymphocyte egress by functionally antagonizing S1P1 receptors, reducing CNS inflammation. While all effectively control relapses, they differ in receptor selectivity, pharmacokinetics, safety, and indications (RRMS vs active SPMS). Shared adverse effects include bradycardia, macular edema, elevated liver enzymes, and infection risk.
- **Tolebrutinib**, an oral Bruton's tyrosine kinase (BTK) inhibitor that modulates B-cell and myeloid cell signaling, demonstrates delayed disability progression in non-relapsing SPMS with generally manageable side effects.

Key messages

Key message 2: Importance of Early High-Efficacy Therapy

- Initiating high-efficacy disease-modifying therapy (DMT) early in the disease course offers the greatest long-term benefit for patients with relapsing MS, especially those who are young, have high disease activity, and retain functional reserve.
- Early use of potent DMTs may not only prevent relapse-associated worsening but also delay the onset of progression independent of relapse activity (PIRA), a key contributor to long-term disability.

Key message 3: Need for a personalized treatment approach

- The importance of personalizing MS treatments based on individual patient factors, such as disease activity, treatment response, and lifestyle factors (e.g., pregnancy planning and age-related considerations).
- Given MS's heterogeneous nature, personalized treatment strategies can optimize therapeutic outcomes.

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