HOW TO TREAT A HIGHLY ACTIVE RRMS PATIENT AFTER ONE DISEASE MODIFYING DRUG (DMD) HAS FAILED?
CLASSICAL IMMUNOSUPPRESSION

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For patients with relapsing remitting multiple sclerosis (RRMS), seven pharmacotherapies are currently approved. Three interferon beta (INFβ) preparations and glatiramer acetate (GA) are considered first line therapies. All of these medications have been shown to alter the natural course of RRMS. Natalizumab and mitoxantrone are considered second line therapies for patients who fail either IFNβ or GA.
While most patients with RRMS benefit from first line agents, aggressive forms of RRMS and progressive disease forms of MS still presents a great challenge to neurologists. In this scenario, intense immunosuppression has been a feasible therapeutic option for many decades. While natalizumab may be a feasible option in patients with aggressive RRMS, the situation is more complex once patients transition to secondary progressive MS (SPMS). In patients with progressive forms of MS, lymphoid tissues have been detected in the brain that may play a critical role in perpetuating local inflammation. Agents that are currently approved for patients with MS have no, or very limited bioavailability in central nervous system (CNS). This includes mitoxantrone, which is approved in some countries for patients with SPMS. In contrast, cyclophosphamide (CYC), an alkylating agent, penetrates the blood-brain barrier (BBB) and CNS parenchyma well. CYC has been used in clinical trials and off-label in clinical practice in patients with MS for over three decades. However, data on its efficacy is inconclusive due to diverse study populations. Relatively novel myeloablative treatment paradigms with CYC may provide a therapeutic option in patients with RRMS or SPMS who do not respond to other agents