Start Eculizumab, the newly FDA-approved drug for refractory MG

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Myasthenia gravis (MG) is an autoimmune disease treated with conventional immunosuppressive therapies, but 10-20% of patients may fail to respond adequately. Chronic immunosuppression is effective but the mechanism of action is aspecific. Complications, exacerbations and myasthenic crises can require hospital and intensive care unit admissions with prolonged stays and can be life-threatening. Anti AChR antibodies, diagnostic for MG, exert their pathogenic effects via distinct mechanisms: a. binding to AChR and complement-mediated postsynaptic focal destruction; b. inducing an accelerated internalization of the AChRs; c. inhibiting functional activity of AChR. Eculizumab is a complement inhibitor which blocks the terminal part of the complement cascade, already marketed for paroxysmal nocturnal hemoglobinuria and atypical hemolytic uremic syndrome. Eculizumab was used in a placebo-controlled phase III study (REGAIN) and data indicated that it was clinically effective in patients with anti-AChR+ refractory gMG and well tolerated[1]. Subsequently, analysis of the open-label extension phase evaluated Eculizumab's long-term safety and efficacy: safety was consistent with that observed in REGAIN; no meningococcal infections were reported and MG exacerbations were reduced by 75% from the year before REGAIN; improvements in activities of daily living, muscle strength, and quality of life were maintained through 3 years; overall 56% of patients achieved minimal manifestations or pharmacological remission. Patients who were in placebo during REGAIN and shifted to Eculizumab experienced rapid and sustained improvements during the open-label phase[2]. [1]Howard JF Jr et al. Lancet Neurol. 2017;16:976-986. [2]Muppidi S et al: Muscle & Nerve 2019 doi: 10.1002/mus.26447.