**Table e-2: International Consensus Guidance Recommendations for treatment of Myasthenia Gravis: Symptomatic and Immunosuppressive Treatment**

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| A.      Pyridostigmine should be part of the initial treatment in most MG patients. Pyridostigmine dose should be adjusted as needed based on symptoms. The ability to discontinue pyridostigmine can be an indicator that the patient has met treatment goals and may guide the tapering of other therapies. Corticosteroids and/or immunosupressive (IS) therapy should be used in all MG patients who have not met treatment goals after an adequate trial of pyridostigmine.  |
| B     A non-steroidal IS agent should be used alone when corticosteroids are contraindicated or refused. A non-steroidal IS agent should be used initially in conjunction with corticosteroids when the risk of steroid side-effects is high based on medical co-morbidities. A non-steroidal IS agent should be added to corticosteroids when: i. Steroid side-effects, deemed significant by the patient or the treating physician, develop ii. Response to an adequate trial of corticosteroids is inadequate or iii. The corticosteroid dose cannot be reduced due to symptom relapse. |
| C.      Non-steroidal IS agents that can be used in MG include azathioprine, cyclosporine, mycophenolate mofetil, and tacrolimus. The following factors should be considered in selecting among these agents:i. There is widespread variation in practice with respect to choice of IS agent since there is little literature comparing them. ii. Expert consensus and some evidence from randomized controlled trials (RCT) support the use of azathioprine as a first line IS agent in MG. iii. Evidence from RCTs supports the use of cyclosporine in MG, but potential serious adverse effects and drug interactions limit its use. iv: Although available RCT evidence does not support the use of mycophenolate and tacrolimus in MG, both are widely used, and one or both are recommended in several national MG treatment guidelines |
| D.      Patients with refractory MG should be referred to a physician or a center with expertise in management of MG. In addition to the previously mentioned IS agents, the following therapies may also be used in refractory MG: i.   Chronic intravenous immunoglobulin (IVIg) and chronic plasma exchange (PLEX) ii. Cyclophosphamide iii. Rituximab should be considered as an early therapeutic option in patients with MuSK-Ab+ MG who have an unsatisfactory response to initial immunotherapy. iv. The efficacy of rituximab in refractory acetylcholine receptor antibody positive (AChR-Ab+) MG is uncertain. It is an option if patients fail or do not tolerate other IS agents. v. While evidence from RCTs is lacking, oral methotrexate may be considered as a steroid-sparing agent in patients with generalized MG who have not tolerated or responded to steroid-sparing agents that are better supported by RCT data. vi. Eculizumab should be considered in the treatment of severe, refractory, AChR-Ab+ generalized MG. vii. The role of eculizumab in the treatment of MG is likely to evolve over time. Until further data become available to allow comparisons of cost and efficacy with other treatments, eculizumab should be considered after trials of other immunotherapies have been unsuccessful in meeting treatment goalsviii. Recommendations of the Advisory Committee on Immunization Practice (ACIP) or other local guidelines regarding immunization against meningococcal meningitis should be followed prior to treatment with eculizumab.ix. Future research should include assessment of the duration of eculizumab therapy necessary to achieve and maintain treatment goals, its efficacy in other MG populations (MG with thymoma, seronegative MG), and in other stages of disease (MG crises, exacerbations, early therapy in non-refractory AChR-Ab+ MG) |
| E.      IS agent dosage and duration of treatment: i. Once patients achieve treatment goals, the corticosteroid dose should be gradually tapered. In many patients, continuing a low dose of corticosteroids long-term can help to maintain the treatment goal. ii. For non-steroidal IS agents, once treatment goals have been achieved and maintained for 6 months to 2 years, the IS dose should be tapered slowly to the minimal effective amount. Dosage adjustments should be made no more frequently than every 3-6 months iii. Tapering of IS drugs is associated with risk of relapse, which may necessitate upward adjustments in dose. The risk of relapse is higher in patients who are symptomatic, or after rapid taper. iv. It is usually necessary to maintain some immunosuppression for many years, sometimes for life.  |
| F.      Patients must be monitored for potential adverse effects and complications from IS drugs. Changing to an alternative IS agent should be considered if adverse effects and complications are medically significant or create undue hardship for the patient. |