STUDENTS' CORNER
LETTER TO THE EDITOR

The tale and trials of Efgartigimod: A newly FDA approved drug for the treatment of Myasthenia gravis

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Dear Editor, The significant diminished muscle function is observed in Myasthenia gravis (MG), an autoimmune disease. The muscles of respiration, swallowing, speech, etc., are usually affected. As a result, functional deficits and poor quality of life are imminent.[1] The underlying pathophysiology of MG involves immunoglobulin G (IgG) autoantibodies which attack the nicotinic acetylcholine receptor (AChR) or other parts of the neuromuscular junction, which impairs the normal synaptic transmission in affected patients.[2]

Myasthenia gravis is typically treated with a highdose of corticosteroids and steroid-sparing agents as an adjunct. According to an estimate, 20,000 patients suffering from MG were intolerant or failed to respond to these conventional treatments.[3] Other effective treatment options include lowering the accumulation of autoantibodies from the periphery or B cell removal through plasmapheresis), administrations of intravenous immunoglobulin (IVIg), and immunoadsorption adjuvants. These therapies are expensive and come with prominent side effects emphasizing the need for alternative pathogenic IgG-reducing measures.[4]

Blockage of neonatal Fc receptor (FcRn) is an anticipated IgG-reducing strategy. In patients suffering from generalized MG, efgartigimod; Fc fragment of IgG1 antibody is altered to decrease levels of IgG autoantibody.[4]

The first-in-human, placebo-controlled, randomized and double blinded trial involving efgartigimod with 62 volunteers were given single and multiple gradually increasing doses of the drug. The trial revealed a 50% reduction in IgG levels with a single administration, and subsequent dosing further reduced IgGs by 75% of baseline.[4]

Phase 2 was a randomized and double-blinded trial that included placebo and patients on a fixed dose of their regular MG treatment. It assessed the safety, efficacy and pharmacokinetics of efgartigimod and was conducted at 15 centres in eight countries. The trial results observed an abrupt drop in the total IgG and anti-Ach receptor autoantibody levels, and four efficacy scales were used for its analysis showing 75% of the patients had quick and lasting effects after receiving the treatment.[2]

The phase 3 was a placebo-controlled, randomized and double-blinded trial that did not include any previous ongoing MG treatment, named ADAPT, was carried out at 56 neuromuscular community and academic institutes in Europe, Japan and North America including a large population of patients with generalized MG. The trial achieved up to 9-point reductions in MG-ADL, which stands for Myasthenia Gravis activities of daily living, and 10-point reductions in Quantitative Myasthenia Gravis (QMG) score with treatment cycles based on the clinical response of individuals to the drug.[1]

All these trials concluded that the novel mechanism of efgartigimod which lowers the IgG levels specifically through antagonization of FcRn is a safe, efficacious and well-tolerated treatment for generalized MG. In all three trials, side effects related to efgartigimod administration observed were nausea, vomiting, diarrhoea, headache, nasopharyngitis, and infections in the urinary tract and upper respiratory tract.[1] The process through which efgartigimod antagonizes FcRn results in effective and constant decreased IgG levels in serum.[4]

Efgartigimod was FDA approved for treating myasthenia gravis on 17th December 2021.[5]

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