Efgartigimod: Potential Impact on IVIG Therapy

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Each month we present highlights from the Ask the Expert section of the American Academy of Allergy, Asthma & Immunology (AAAAI) website written by the Ask the Expert editors. For more questions and answers, visit www.aaaai.org/ask-the-expert.aspx.

Question:

I have a 70-year-old male patient with a history of myasthenia gravis diagnosed in 2011. He was treated with mycophenolate and prednisone from 2011 to 2020, and large B-cell lymphoma was diagnosed in early 2020 s/p rituximab, cyclophosphamide, hydroxydaunorubicin hydrochloride, vincristine (Oncovin) and prednisone from June 2020 to September 2020. He is currently in remission. Now being treated for myasthenia with rituximab q6 months, the last dose was given in December 2021. He was on chronic prednisone 10 mg daily from 2011 to 2020, which was eventually tapered to discontinuation from February 2021. He was diagnosed with common variable immunodeficiency and started intravenous immunoglobulin (IVIG) in October 2021 with improvement in recurrent sinopulmonary infections and severe chronic fatigue. He received Evusheld in March 2022.

His neurologist is considering discontinuing rituximab and starting Vyvgart/efgartigimod alfa, which antagonizes neonatal Fc receptor (FcRn), resulting in reduced circulating autoantibodies.

My question is: will efgartigimod reduce the efficacy of IVIG and/or Evusheld? Could IVIG reduce the efficacy of efgartigimod?

I expect we will see more patients being transitioned from rituximab to efgartigimod.

Answer:

Thank you for your question to Ask the Expert. Studies have shown that efgartigimod alpha can bind and block the FcRn, reducing IgG antibodies. Efgartigimod alpha, an IgG1 Fc fragment, is designed for increased affinity for FcRn. It competes with IgG to occupy FcRn and therefore reduce overall IgG recycling. FcRn has been shown to bind IgGs and rescue them from lysosomal degradation, extending IgG half-life (approximately 21 days). Targeting and inhibiting the FcRn results in increased IgG catabolism, resulting in reduced overall IgG in the peripheral circulation. Furthermore, studies have demonstrated that efgartigimod alpha reduces IgG levels rapidly and consistently without a similar impact on IgM, IgA, or albumin. On the basis of these data, I agree that efgartigimod alpha would be expected to lower IgG levels of IVIG. It is unlikely that IVIG would impact the efficacy of efgartigimod alfa.[1,2]

I reached out to Dr Francisco "Tony" Bonilla, an expert in this area. His response is as follows: I agree with what Dr Demain wrote. Furthermore, I am not sure I see a therapeutic benefit to adding efgartigimod to IVIG or subcutaneous immunoglobulin. Exogenous therapeutic IgG by itself acts as an "FcRn antagonist." In fact, this is one of the supposed modes by which IVIG exerts a beneficial effect for the treatment of autoantibody-mediated disease.[3]

It might be cheaper and just as effective to use high-dose IVIG. In any case, if the drug is used, IgG levels should be followed closely, and I would seriously consider transition to subcutaneous administration that gives steadier IgG levels, especially if immunoglobulin catabolism or other rate of loss is increased.

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