Efgartigimod: A Novel FcRn Antagonist in the Treatment of Autoimmune Diseases

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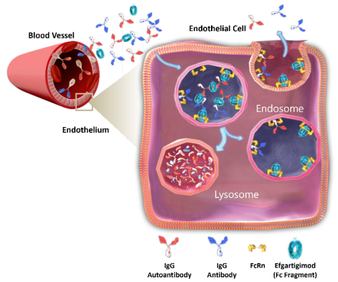
EFGARTIGIMOD: Engineered IgG1 Fc Fragment[1-5]



- The neonatal Fc receptor, FcRn, recycles immunoglobulin G (IgG), extending its half-life and serum concentration[1]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered for increased affinity for FcRn[2]
- Efgartigimod was designed to outcompete endogenous IgG, preventing recycling, and promoting lysosomal degradation of IgG, without impacting its production[2-5]
  - Targeted reduction of all IgG subtypes
  - No impact on IgM or IgA
  - No reduction in albumin levels
  - No increase in cholesterol

EFGARTIGIMOD IS CLINICALLY EFFECTIVE AND WELL TOLERATED IN PHASE 2 AND 3 TRIALS IN IGG-MEDIATED DISORDERS[4-8]

- Consistent depletion of total IgG levels of roughly 60% from baseline with efgartigimod intravenous (IV) treatment was observed across studies and populations
- In an open-label, phase 2 trial with efgartigimod IV in participants with **pemphigus** [pemphigus vulgaris (PV) and pemphigus foliaceus (PF)], disease control was achieved in **90%** of participants (median time: **17 days**)
- Topline results (TLR) of a phase 3, randomized, placebo-controlled study (ADVANCE IV) with efgartigimod IV in participants with **primary immune thrombocytopenia (ITP)** have also reported efficacy and safety in this patient population - the primary endpoint, platelet-related key secondary endpoints, and International Working Group (IWG) response criteria were met; no new safety signals were observed
- In a phase 3 trial in participants with **generalized myasthenia gravis (gMG)**, **68%** of participants responded to efgartigimod IV (MG-ADL responders*) compared with 30% of those in the placebo group
  - In a study comparing efgartigimod administered intravenously or subcutaneously in participants with gMG, consistent clinical efficacy and safety was observed in both groups (MG-ADL responders: 69.1% IV vs 69.1% SC; n=110)
- Efgartigimod treatment was **generally well tolerated** in phase 2 and 3 trials in participants with pemphigus (open-label study), primary ITP, and gMG
  - Most common adverse events in treatment and placebo groups across studies to date include headache, nausea, nasopharyngitis, diarrhea, abdominal pain, upper respiratory tract infection, and urinary tract infection

***MG-ADL responders** = ≥2-point Myasthenia Gravis Activities of Daily Living score improvement sustained for ≥4 weeks. IV, intravenous; SC, subcutaneous.

Pemphigus and Bullous Pemphigoid: IgG-Mediated Autoimmune Diseases[9-11]

- Pemphigus vulgaris (PV) and pemphigus foliaceus (PF) belong to a heterogenous group of autoimmune blistering diseases and are clinically characterized by mucosal erosions (PV) and cutaneous blisters (PV and PF)
- PV is characterized by the presence of pathogenic IgG autoantibodies targeting desmoglein 3 (Dsg-3) and, 50% of the cases, also against desmoglein 1 (Dsg-1)
- PF is attributed to the presence of IgG autoantibodies solely directed against Dsg-1
- Pemphigus is potentially life-threatening, primarily due to secondary infections
- Bullous pemphigoid (BP) is the most prevalent autoimmune blistering disease; it is characterized by subepidermal blisters and mediated by IgG autoantibodies directed against BP230 and BP180 antigens

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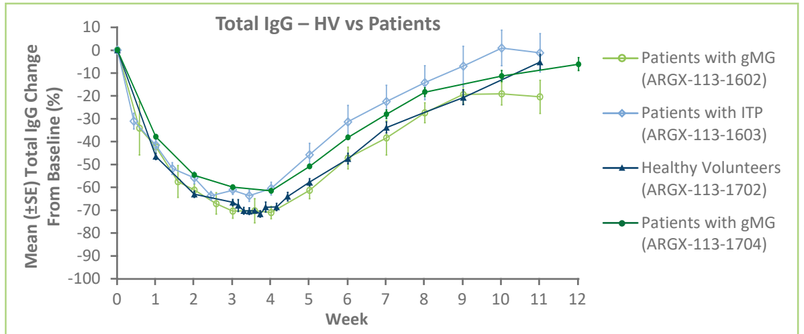
Efgartigimod Reduces Total IgG Including Pathogenic IgG Autoantibody Levels[4-7]



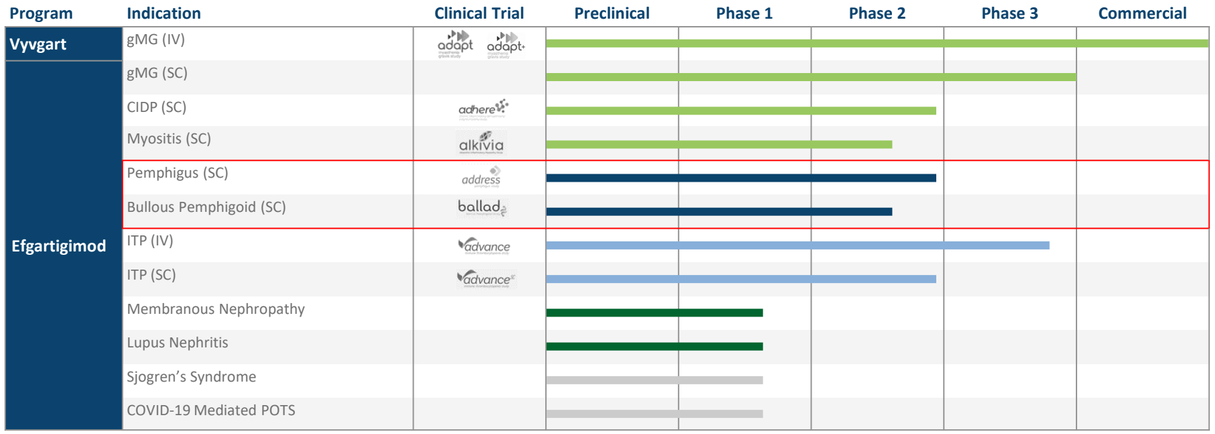
Mean percentage change from baseline in serum levels of total IgG in participants with gMG, primary ITP, and healthy volunteers treated with efgartigimod IV.[4,6]

EFG, efgartigimod; IgG, immunoglobulin G; IV, intravenous; SEM, standard error of the mean.

- In a phase 2 study of participants with **ITP**, treatment with 10 mg/kg efgartigimod IV induced a **reduction in serum levels of total IgG (tIgG) up to a mean change of 64% from baseline**[4]
  - In **70% of participants** treated with 10 mg/kg efgartigimod IV, **a reduction >40%** in at least one type of platelet-associated autoantibody (GPIIb/IIIa, GPIb/IX, GPIa/IIa) signal was observed at days 25/29 and/or day 78[4]
- In a phase 2 study of participants with **PV** or **PF**, serum tIgG levels decreased by a median of **62%** with 10 mg/kg efgartigimod IV and by a median of **66%** with 25 mg/kg efgartigimod IV[5]
  - At the end of induction, serum levels of anti-Dsg-1 and anti-Dsg-3 IgG reached a median 61% reduction from baseline for anti-Dsg-1 and 49% for anti-Dsg-3 antibodies[5]
- In a phase 3 study of participants with **gMG** positive for acetylcholine receptor (AChR) antibodies, a mean maximum reduction of tIgG **61.3%** was observed in participants treated with 10 mg/kg efgartigimod IV[6]

Efgartigimod is approved for the treatment of gMG in patients positive for AChR antibodies in the US, as add-on to standard therapy in patients positive for AChR antibodies in the EMEA, and in patients with and without AChR antibodies with insufficient response to steroids or non-steroid immunosuppressive therapies in Japan

Efgartigimod is also being evaluated in phase 3 trials in chronic inflammatory demyelinating polyneuropathy (CIDP), idiopathic inflammatory myositis, pemphigus (PV and PF), BP, and primary ITP



IV, intravenous; POTS, Post-Orthostatic Tachycardia Syndrome; SC, subcutaneous.
Efgartigimod is co-formulated with hyaluronidase PH20 for convenient SC administration in <2 min.
The investigational study drug, efgartigimod, has not been approved for use in PV/PF or BP by any regulatory agency as efficacy and safety have not been established.

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