Efgartigimod: Clinical Development of a Novel FcRn Antagonist in the Treatment of Autoimmune Diseases

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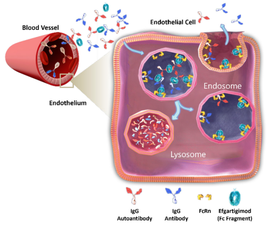
Efgartigimod: Engineered IgG1 Fc Fragment[1–5]



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- 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 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 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 were observed in both groups (MG-ADL responders: 69.1% IV vs 69.1% subcutaneous [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.

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

- PV and PF belong to a heterogeneous 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 BP-230 and BP-180 antigens

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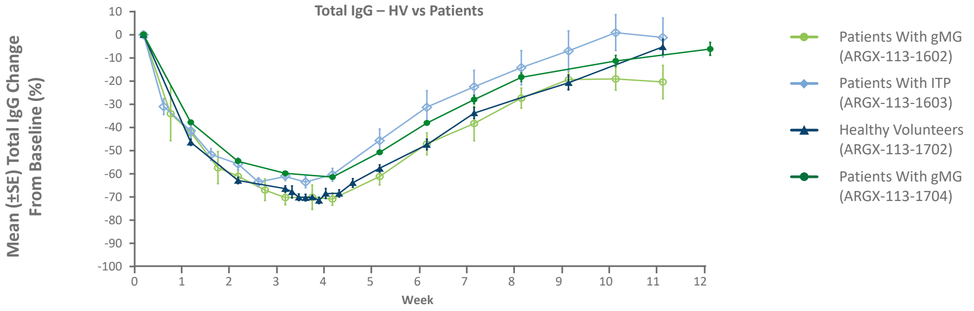
Efgartigimod Reduces Total IgG Including Pathogenic IgG Autoantibody Levels[4–7]



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]

gMG, generalized myasthenia gravis; HV, healthy volunteer; IgG, immunoglobulin G; ITP, immune thrombocytopenia; IV, intravenous; SE, standard error.

- In a phase 2 study of participants with **ITP**, treatment with efgartigimod IV 10 mg/kg induced a **reduction in serum levels of total IgG up to a mean change of 64% from baseline**[4]
  - In **70% of participants** treated with efgartigimod IV 10 mg/kg, **a reduction >40%** in at least 1 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 total IgG levels decreased by a median of **62%** with efgartigimod IV 10 mg/kg and by a median of **66%** with efgartigimod IV 25 mg/kg[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 total IgG by **61.3%** was observed in participants treated with efgartigimod IV 10 mg/kg[6]

Efgartigimod is approved for the treatment of gMG in patients positive for AChR antibodies in the US, as an 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 nonsteroid immunosuppressive therapies in Japan

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

Program	Indication	Preclinical	Phase 1	Phase 2	Phase 3
Efgartigimod	Generalized Myasthenia Gravis (SC)				
	Chronic Inflammatory Demyelinating Polyneuropathy (SC)				
	Idiopathic Inflammatory Myopathy/Myositis (SC)				
	Pemphigus Vulgaris and Foliaceus (SC)				
	Bullous Pemphigoid (SC)				
	Primary Immune Thrombocytopenia (IV)				
	Primary Immune Thrombocytopenia (SC)				
	Membranous Nephropathy				
	Lupus Nephritis				
	Sjogren Syndrome				
	COVID-19 Mediated Postural Orthostatic Tachycardia Syndrome				
ARGX-117	Multifocal Motor Neuropathy				
	Delayed Graft Function After Kidney Transplantation				
ARGX-119	Neuromuscular Indications				
ARGX-120	Undisclosed				
ARGX-118	Airway Inflammation (*Non-Autoimmune Program*)				

NEUROMUSCULAR HEMATOLOGY DERMATOLOGY NEPHROLOGY OTHER

IV, intravenous; 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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