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Overview of the Safety Profile From Efgartigimod Clinical Trials in Participants With Diverse IgG-Mediated Autoimmune Diseases

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BACKGROUND

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 (EFG) is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered for increased affinity for FcRn[2]
- EFG 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 other immunoglobulins
  - No reduction in albumin or increase in cholesterol levels

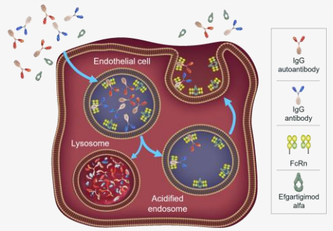
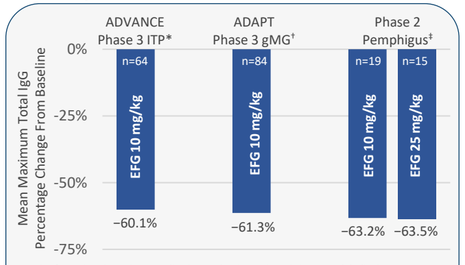


Image adapted from Kang TH, Jung ST. Boosting therapeutic potency of antibodies by taming Fc domain functions. Exp Mol Med. 2019;51:1–9 and distributed under the terms of the Creative Commons CC-BY license (https://creativecommons.org/licenses/by/4.0/).

- FcRn blockade with EFG does not lead to complete IgG removal[2,5]
- Patients treated with EFG in various IgG-mediated autoimmune disorders showed a mean maximum reduction of 60.1–63.5% in total IgG levels[4,6–8]
- EFG treatment did not lead to any abnormal infection patterns compared with placebo, and most infections were mild to moderate in severity[4,6–8]

Mean Maximum Reduction in Total IgG Levels From Baseline Upon Treatment With EFG



EFG, efgartigimod; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; ITP, immune thrombocytopenia.
*Measured in Week 4. †Measured 1 week after 4th infusion in cycle 1. ‡Measured on Day 29.

RESULTS

Generalized Myasthenia Gravis

Phase 3 ADAPT

EFG: n=84
Placebo: n=83

EFG 10 mg/kg IV

Study duration: up to 26 weeks
- Initiation – cycles of 4 weekly infusions
- Subsequent cycles administered according to individual clinical response using the MG-ADL score at least 8 weeks from initiation of previous cycle

Concomitant therapy:
- Acetylcholinesterase inhibitors (EFG: 85%; PBO: 81%)
- Corticosteroids (EFG: 71%; PBO: 81%)
- NSISTs (EFG: 61%; PBO: 61%)

Generalized Myasthenia Gravis OLE

Phase 3 open-label extension (OLE)
3-year maximum

EFG: N=151 rolled over from ADAPT; 145 received ≥1 dose

EFG 10 mg/kg IV

Study duration and dosing:
- Maximum 19 cycles
- Subsequent cycles administered according to individual clinical response using the MG-ADL score at least 7 weeks from initiation of previous cycle

Concomitant therapy:
- Acetylcholinesterase inhibitors (86%)
- Corticosteroids (77%)
- NSISTs (61%)

Primary Immune Thrombocytopenia

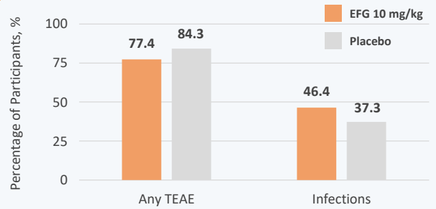
Phase 3 ADVANCE IV

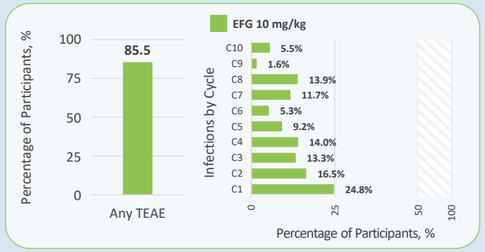
EFG: n=86
Placebo: n=45

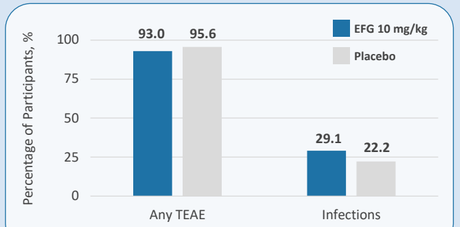
EFG 10 mg/kg IV

Study duration: 24 weeks
- Weeks 1–4: weekly dosing
- Weeks 4–15: weekly or every other week* dosing
- Weeks 16–24: continued based on Week 15 dosing

Concomitant therapy at baseline:
- Corticosteroids (EFG: 26%; PBO: 27%)
- TPO-RA (EFG: 23%; PBO: 20%)
- NSISTs (EFG: 9%; PBO: 13%)
- Danazol (EFG: 2%; PBO: 2%)







	Phase 3 ADAPT for gMG		Phase 3 ADAPT+ OLE for gMG	Phase 3 ADVANCE IV Primary ITP	
Incidence rate†	**EFG 10 mg/kg IV (n=84) [34.9 PY]**	**Placebo IV (n=83) [34.5 PY]**	**EFG 10 mg/kg IV [229.0 PY]**	**EFG 10 mg/kg IV (n=86) [38.0 PY]**	**Placebo IV (n=45) [19.2 PY]**
≥1 TEAE	7.2	7.8	3.5	13.6	17.9
≥1 serious TEAE	0.1	0.3	0.2	0.3	0.4
Discontinued due to AEs	0.2	0.1	0.1	0.1	0.0
Infection	1.6	1.2	0.7	1.0	0.6

Phase 2 Pemphigus Open-label Study

≥1 TEAE was experienced by 84% of participants receiving EFG 10 mg/kg (n=19) and 87% receiving EFG 25 mg/kg (n=15)

- Of 32 AEs of special interest (infections and infestations), 7 events in 5 participants (15.6%) were considered related to study treatment; none led to study discontinuation, and all were mild to moderate in severity, except 1 case of pneumonia and 1 tooth infection, which were both grade 3
- No abnormal infection patterns were observed; 2 serious AEs were reported, which were assessed as unrelated to EFG (pneumonia and tibia fracture)

In all studies, EFG treatment did not lead to reductions in albumin or increase in cholesterol levels

AE, adverse event; C, cycle number; EFG, efgartigimod; gMG, generalized myasthenia gravis; NSIST, nonsteroid immunosuppressive therapy; OLE, open-label extension; PBO, placebo; PY, patient years; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TPO-RA, thrombopoietin receptor agonist.
*The dosing schedule could change to every other week from Weeks 4–15 in participants who achieved platelet counts of ≥100×10⁹/L for 3 out of 4 consecutive weeks, including the last of these weeks. Treatment could change from every other week to weekly in participants whose platelet counts decreased to <100×10⁹/L for 2 consecutive weeks or <30×10⁹/L for 1 week or in participants who received rescue therapy. †Incidence rate calculated as number of events per patient year of follow-up.

KEY TAKEAWAYS

- EFG reduces IgG levels via FcRn blockade and does not lead to complete removal of IgG nor does it impact IgG production
- Patients with various IgG-mediated autoimmune disorders demonstrated 60.1–63.5% reduction in total IgG levels when treated with EFG
- EFG was well tolerated with comparable TEAE rates to placebo across multiple IgG-mediated autoimmune disorders
- Most TEAEs, including infections, were mild to moderate in severity and incidence rate did not increase with longer exposure
- EFG was well tolerated and demonstrated a consistent safety profile across varying dosing regimens and exposure times
- EFG treatment did not decrease albumin or increase cholesterol levels

EFG is approved for the treatment of generalized myasthenia gravis (gMG) in adult patients positive for anti-acetylcholine receptor (AChR) antibodies in the US and Europe, and in Japan for patients regardless of antibody status

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