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

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Conflicts of Interest

Anthony Behin	Consultant: Alexion Pharmaceuticals, argenx BVBA, Sanofi-Aventis, Ultragenyx Pharmaceuticals; Honoraria: Alexion Pharmaceuticals, argenx BVBA, Sanofi-Aventis, UCB
Kelly Gwathmey	Consultant: Alexion Pharmaceuticals, argenx BVBA, Strongbridge, UCB; Honoraria: Alexion Pharmaceuticals
Catherine M. Broome	Honoraria: Alexion Pharmaceuticals, Apellis, argenx BVBA, Sanofi
Matthias Goebeler	Consultant: argenx BVBA, Almirall; Honoraria: Biotest, GSK, Janssen, Leo Pharma, Lilly, Novartis, UCB
Hiroyuki Murai	Consultant: Alexion Pharmaceuticals, argenx BVBA, Roche, UCB; Honoraria: Japan Blood Products Organization, Chugai; Research funding: Ministry of Health, Labour and Welfare, Japan
Zsuzsanna Bata-Csörgo	Consultant: Sanofi-Genzyme Hungary; Honoraria: Orvostovábbképzo Szemle; Research funding: NKFI Hungary
Adrian Newland	Consultant: Amgen, Angle, argenx BVBA, Dova, Novartis, Ono, Rigel, Shionogi; Honoraria: Amgen, Angle, argenx BVBA, Dova, Novartis, Ono, Rigel, Shionogi; Research funding: Amgen, Novartis, Rigel; Paid expert testimony: argenx BVBA, Rigel
Peter Ulrichts Rene Kerstens Jeffrey T. Guptill Sofiane Agha Ming Jiang	Employees of argenx BVBA and may own stock/options in the company
James F. Howard Jr	Honoraria: Alexion Pharmaceuticals, argenx BVBA, F. Hoffman-LaRoche Ltd., Immunovant Inc., NMD Pharma, Novartis Pharmaceuticals, Ra Pharmaceuticals, Regeneron Pharmaceuticals, Sanofi US, Viela Bio Inc.; Research funding: Alexion Pharmaceuticals, argenx BVBA, Cartesian Therapeutics, Ra Pharmaceuticals, Takeda Pharmaceuticals

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Efgartigimod Reduces IgG Recycling and Promotes Lysosomal Degradation of IgG by Blocking FcRn

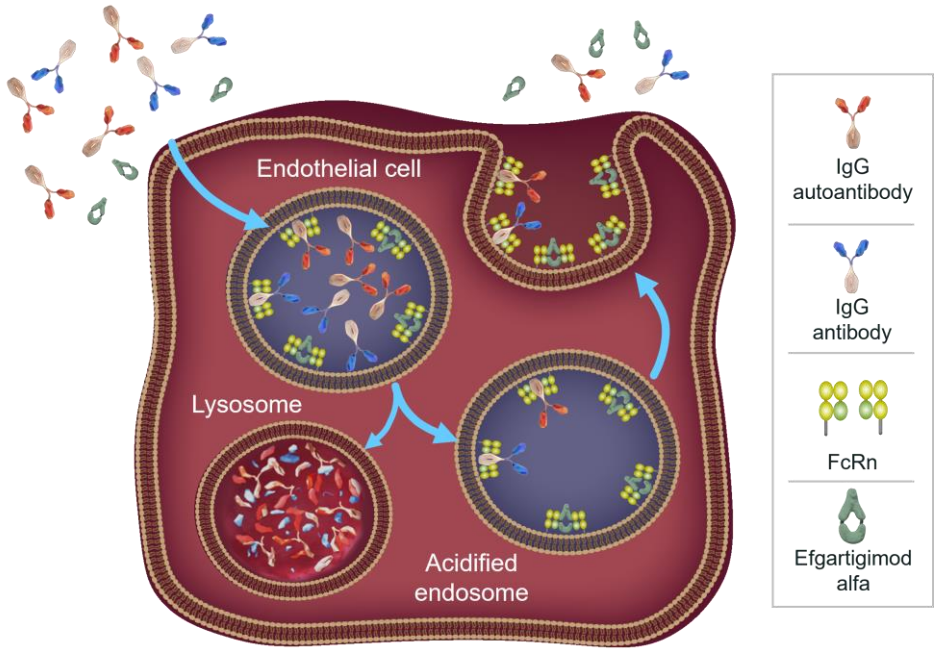


Image adapted from Kang TH, Jung ST. Boosting therapeutic potency of antibodies by taming Fc domain functions. *Exp Mol Med*. 2019;51:1–9 and distributed under the terms of the Creative Commons CC-BY license (https://creativecommons.org/licenses/by/4.0/).

FcRn **extends the half-life** and serum concentration of **IgG antibodies** by recycling[1]

- This includes **pathogenic IgG autoantibodies**

Efgartigimod is a **first-in-class 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 IgA, IgD, IgE, and IgM
- No reduction in albumin levels or increase in cholesterol levels

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

AChR, acetylcholine receptor; EMEA, Europe, the Middle East, and Africa; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; Ig, immunoglobulin; US, United States.

1. Sesarman A, et al. *Cell Mol Life Sci.* 2010;67:2533–50. **2.** Ulrichts P, et al. *J Clin Invest.* 2018;128:4372–86. **3.** Vaccaro C, et al. *Nat Biotech.* 2005;23:1283–8. **4.** Howard JF Jr, et al. *Lancet Neurol*. 2021;20:526–36. **5.** Nixon AE, et al. *Front Immunol.* 2015;6:176.

Efgartigimod Safety Was Assessed in IgG-Mediated Autoimmune Disorders

adapt myasthenia gravis study

Phase 3 ADAPT[1] N=167 Up to 26 weeks

Efgartigimod 10 mg/kg IV + stable dose of concurrent therapy

Initiation – 4 weekly cycles

Subsequent cycles, according to individual clinical response, ≥8 weeks from initiation of previous cycle

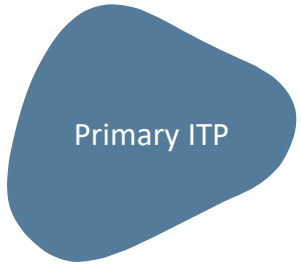
adapt+ myasthenia gravis study

Phase 3 ADAPT+ OLE[2] N=145 3 years

Efgartigimod 10 mg/kg IV + stable dose of concurrent therapy

Maximum 19 cycles

Cyclical dosing

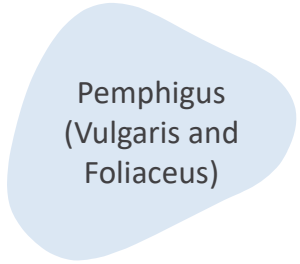


advance immune thrombocytopenia study

Phase 3 ADVANCE[3] N=131 24 weeks

Efgartigimod 10 mg/kg IV + concurrent ITP therapy

- Weeks 1–4: weekly dosing
- Weeks 4–15: weekly or biweekly based on individual's platelet response
- Weeks 16–24: fixed based on Week 15 dosing



Phase 2 Open-label[4] N=34 Up to 38 weeks

Efgartigimod 10 mg/kg IV ± stable dose of corticosteroids

Efgartigimod 25 mg/kg IV + stable dose of corticosteroids

Continuous dosing

ITP, immune thrombocytopenia; IV, intravenous; OLE, open-label extension.

1. Howard JF Jr, et al. *Lancet Neurol.* 2021;20:526–36. **2.** Howard JF, et al. Presented at the AANEM Annual Meeting; September 21–24, 2022; Nashville, TN. **3.** Broome CM, et al. 64th ASH Annual Meeting and Exposition; December 10–13, 2022; New Orleans, LA. **4.** Goebeler M, et al. *Br J Dermatol.* 2022;186:429–39.

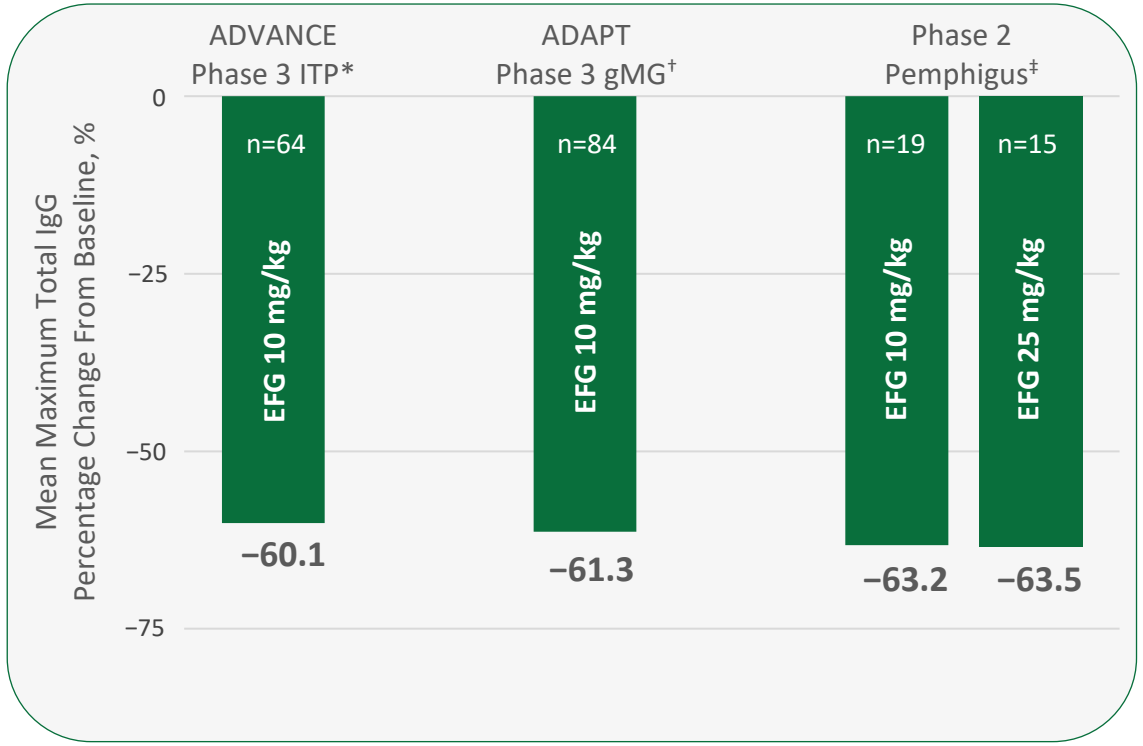
Reducing IgG Levels With Efgartigimod Did Not Lead to a Meaningful Increase in Infections

Patients treated with efgartigimod in various IgG-mediated autoimmune disorders showed a mean maximum reduction of 60.1–63.5% in total IgG levels[1–4]

Efgartigimod treatment did not lead to any abnormal infection patterns compared with placebo[1–4]

Most infections were mild to moderate in severity[1–4]

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

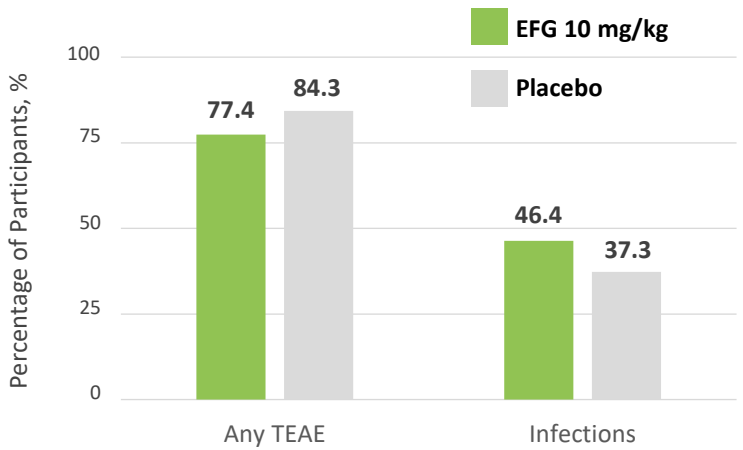


EFG, efgartigimod; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; ITP, immune thrombocytopenia.
*Measured in Week 4. †Measured 1 week after 4th infusion in cycle 1. ‡Measured on Day 29.

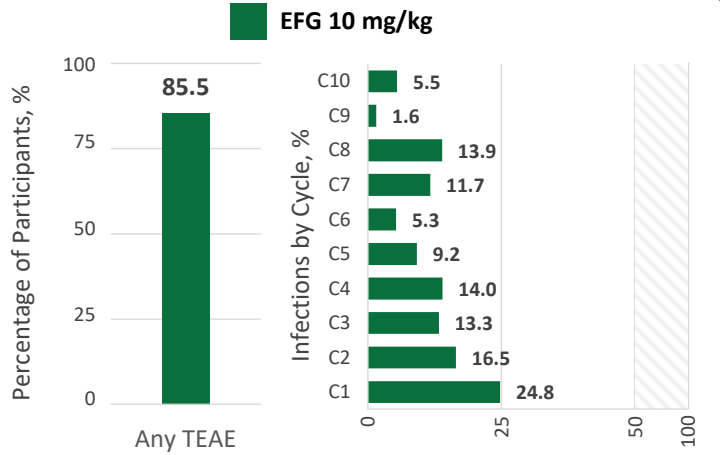
1. Howard JF Jr, et al. *Lancet Neurol.* 2021;20:526–36. **2.** Goebeler M, et al. *Br J Dermatol.* 2022;186:429–39. **3.** Newland AC, et al. *Am J Hematol.* 2020;95:178–87.
4. Broome CM, et al. 64th ASH Annual Meeting and Exposition; December 10–13, 2022; New Orleans, LA.

Efgartigimod Showed a Consistent Safety Profile Across Varying Dosing Regimens and Treatment Periods

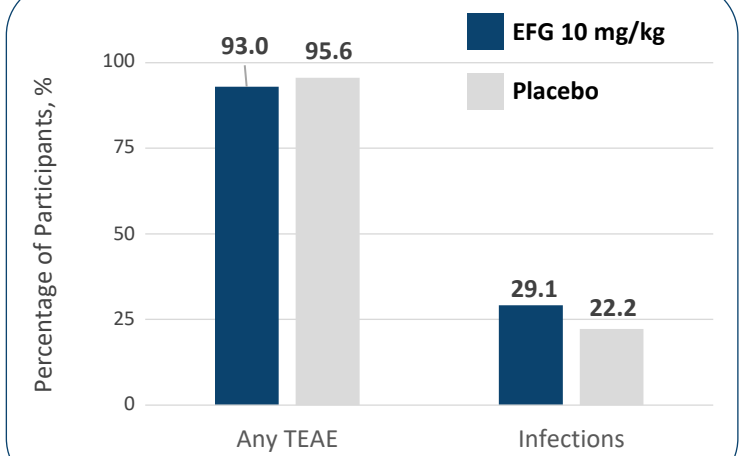
Phase 3 ADAPT for gMG



Phase 3 ADAPT+ OLE for gMG



Phase 3 ADVANCE IV for Primary ITP



	Phase 3 ADAPT for gMG		Phase 3 ADAPT+ OLE for gMG	Phase 3 ADVANCE IV for 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
Severe TEAEs (grade ≥3)	0.3	0.4	0.3	0.6	0.7
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 reported 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 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; EFG, efgartigimod; gMG, generalized myasthenia gravis; ITP, immune thrombocytopenia; OLE, open-label extension; PY, patient-year; TEAE, treatment-emergent adverse event.
*Incidence rate calculated as number of events per patient-years of follow-up.

Conclusions

- Efgartigimod **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 efgartigimod
- Efgartigimod 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
- Efgartigimod was well tolerated and demonstrated a **consistent safety profile across varying dosing regimens and exposure times**
- Efgartigimod treatment did not decrease albumin or increase cholesterol levels

FcRn, neonatal Fc receptor; IgG, immunoglobulin G; TEAE, treatment-emergent adverse event.