Zilucoplan in pediatric patients with acetylcholine receptor autoantibody-positive generalized myasthenia gravis: ziMyG (MG0014) and ziMyG+ (MG0015) clinical study designs

Presented by Sigrid Nilius on behalf of:

Anna Kostera-Pruszczyk[1], Ibironke Addy[2], Ann Cleverly[3], Caroline Legendre[4], Elke Muehlegger-Leers[2], Sigrid Nilius[2], Anna Nordmark[5], Frank Tennigkeit[2], John Brandsema[6]

[1]Department of Neurology, Medical University of Warsaw, Warsaw, Poland; [2]UCB Pharma, Monheim, Germany; [3]UCB Pharma, Slough, UK; [4]UCB Pharma, Bulle, Switzerland; [5]UCB Pharma, Stockholm, Sweden; [6]Children's Hospital of Philadelphia, Philadelphia, PA, USA

MGFA Scientific Session 2023
Phoenix, AZ, USA; November 01, 2023

Conflicts of interest

Anna Kostera-Pruszczyk has received honoraria for advisory boards and speaking at educational events for CSL Behring, Kedrion, Baxter/Shire/Takeda, argenx, Medison Pharma, UCB Pharma and AstraZeneca.

Ibironke Addy, Ann Cleverly, Caroline Legendre, Elke Muehlegger-Leers, Sigrid Nilius and **Frank Tennigkeit** are employees and shareholders of UCB Pharma.

Anna Nordmark is a contractor for UCB Pharma.

John Brandsema is a consultant for Alexion, Audentes, AveXis/Novartis, Biogen, Cytokinetics, Dyne, Edgewise, Fibrogen, Genentech/Roche, Janssen Pharmaceuticals, Marathon, Momenta (now Johnson and Johnson), NS Pharma, PTC Therapeutics, Sarepta, Scholar Rock, Takeda, UCB Pharma and WaVe, a Speaker for AveXis and Biogen, a Medical Advisory Council member for Cure SMA, and a Site Investigator for clinical trials with Alexion, Astellas, AveXis/Novartis, Biogen, Catabasis, CSL Behring, Cytokinetics, Fibrogen, Genentech/Roche, Ionis, Pfizer, PTC Therapeutics, Sarepta, Scholar Rock, Summit, UCB Pharma and WaVe.

These studies are funded by UCB Pharma.

Zilucoplan: Pediatric-centric drug development to address pediatric therapeutic needs

High and specific therapeutic needs in pediatric MG:

Approved drugs with appropriate dosing and safety information needed **as fast as possible**

How are we addressing these needs?

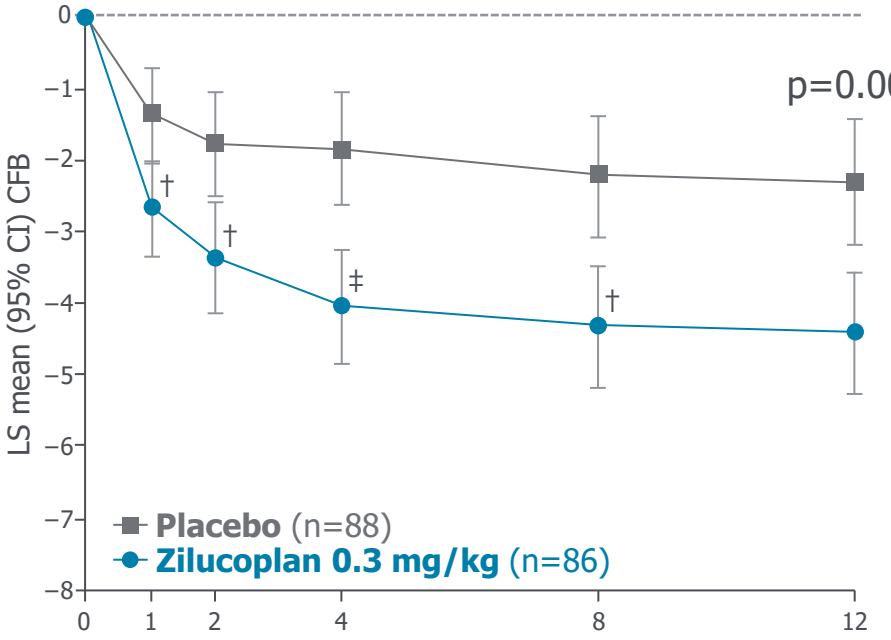
Pediatric-centric drug development, including **customized**, **integrated** and **innovative** study designs

MG, myasthenia gravis.

Zilucoplan in adults with AChR Ab+ gMG: Phase 3, double-blind, placebo-controlled trial (RAISE)*[1]

Zilucoplan showed rapid, statistically significant and clinically meaningful improvements in MG-specific efficacy outcomes, had a favorable safety profile, and was well tolerated, with no major safety findings[1]

MG-ADL score (primary endpoint)



Difference in LS mean (95% CI) CFB between **placebo** and **zilucoplan** at Week 12: **−2.09 (−3.24 to −0.95)[1]**

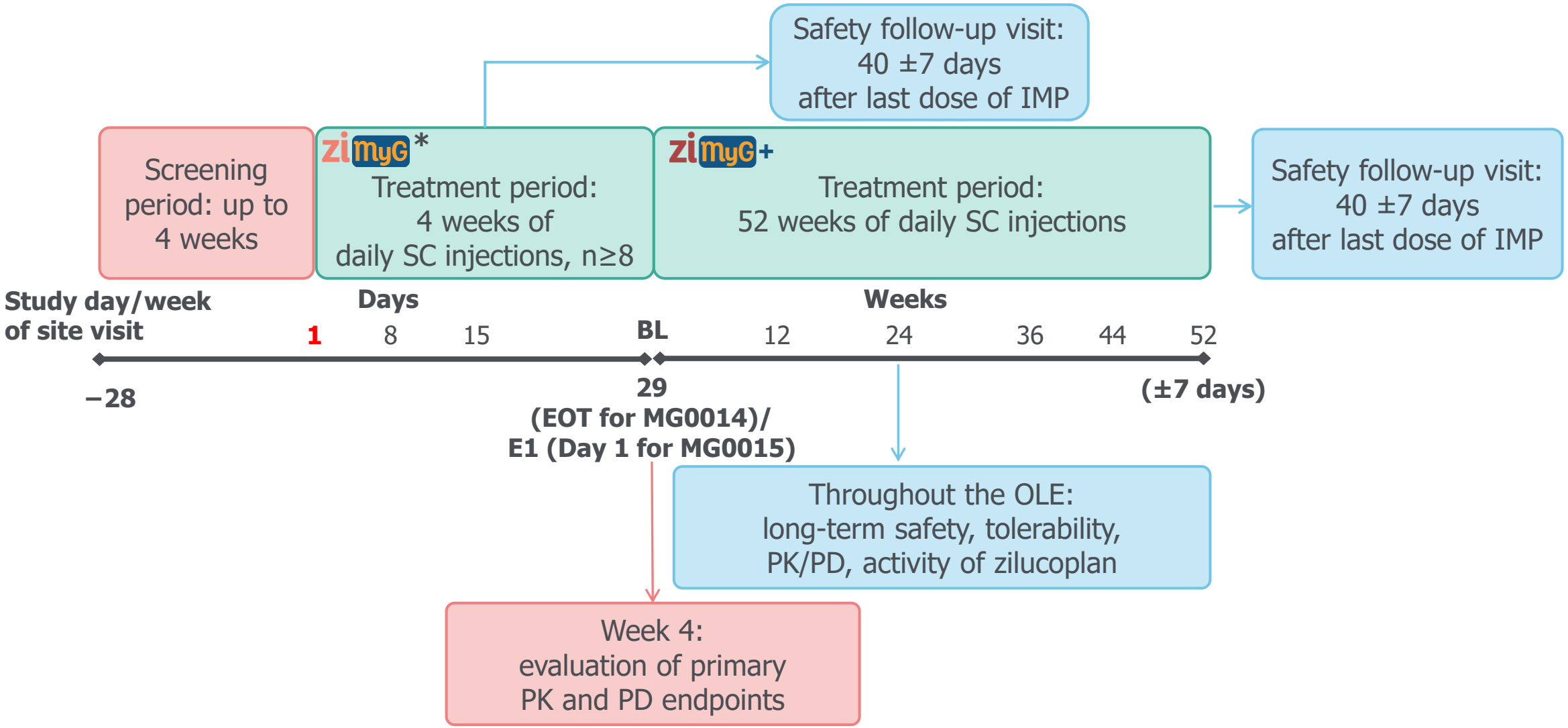
Self-administration by daily SC injection

Rapid onset of action (Week 1)

Can be used **concomitantly** with **IVIg** and **PLEX** without the need for supplemental dosing

Adapted from Howard JF Jr., et al. Lancet Neurol. 2023;22:395–406.
*NCT04115293; †p<0.01 vs placebo (*post-hoc*, not multiplicity-controlled); ‡p<0.001 vs placebo (*post-hoc*, not multiplicity-controlled).
AChR Ab+, positive for autoantibodies against the acetylcholine receptor; CFB, change from baseline; CI, confidence interval; (g)MG, (generalized) myasthenia gravis; IVIg, intravenous immunoglobulin; LS, least squares; MG-ADL, Myasthenia Gravis Activities of Daily Living; PLEX, plasma exchange; SC, subcutaneous.
1. Howard JF Jr., et al. Lancet Neurol. 2023;22:395–406.

zimyG* and zimyG+ studies



*NCT06055959.
BL, baseline; E1, extension study day 1; EOT, end of treatment; IMP, investigational medicinal product; OLE, open-label extension; PD, pharmacodynamics; PK, pharmacokinetics; SC, subcutaneous.

Study design: Endpoints and dose confirmation

Primary endpoints

- PK: Week 4 zilucoplan plasma concentrations
- PD: CFB in sRBC lysis and C5 levels at Week 4
- TEAEs*
- Treatment-emergent SAEs*
- TEAEs leading to permanent withdrawal of IMP*
- Treatment-emergent infections*

Key clinical outcome measures

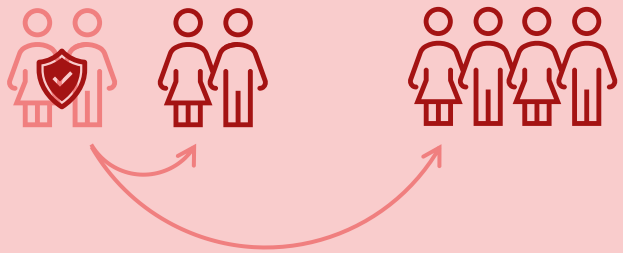
- MG-ADL
- QMG
- MGFA-PIS
- PedsQL™
- NeuroQoL™
- CGI-S

Dose confirmation

- PK/PD datasets from the first two adolescent participants will be analyzed before:
  - **Continuing** Cohort A recruitment
  - **Starting** Cohort B recruitment

Cohort A
(12 to <18 years)

Cohort B
(2 to <12 years)



*Collected during the course of the study.
C5, component 5; CFB, change from baseline; CGI-S, Clinical Global Impression-Severity; IMP, investigational medicinal product; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA-PIS, Myasthenia Gravis Foundation of America Post-intervention Status; NeuroQoL™, Quality of Life in Neurological Disorders; PD, pharmacodynamics; PedsQL™, Pediatric Quality of Life Inventory; PK, pharmacokinetics; QMG, Quantitative Myasthenia Gravis; SAE, serious adverse event; sRBC, sheep red blood cell; TEAE, treatment-emergent adverse event.

Study design: Eligibility criteria

Key inclusion criteria

- Aged ≥2 to <18 years
- AChR Ab+ gMG
- MGFA Disease Class II to IV
- At time of screening:
  - >12 years: MG-ADL total score of ≥6
  - <12 years: weakness in ≥1 limb, neck or bulbar muscle
- Received existing conventional treatment for gMG prior to screening
- Received meningococcal vaccine prior to first dose of zilucoplan

Key exclusion criteria

- MuSK Ab+ gMG
- Prior history of meningococcal disease
- Systemic infection or infection requiring IV antibiotics prior to baseline
- Thymectomy or rituximab therapy received in the last 6 months

AChR Ab+, positive for autoantibodies against the acetylcholine receptor; gMG, generalized myasthenia gravis; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MuSK Ab+, positive for autoantibodies against muscle-specific tyrosine kinase.

Summary: Zilucoplan zimyG and zimyG+ pediatric-centric studies to address pediatric needs

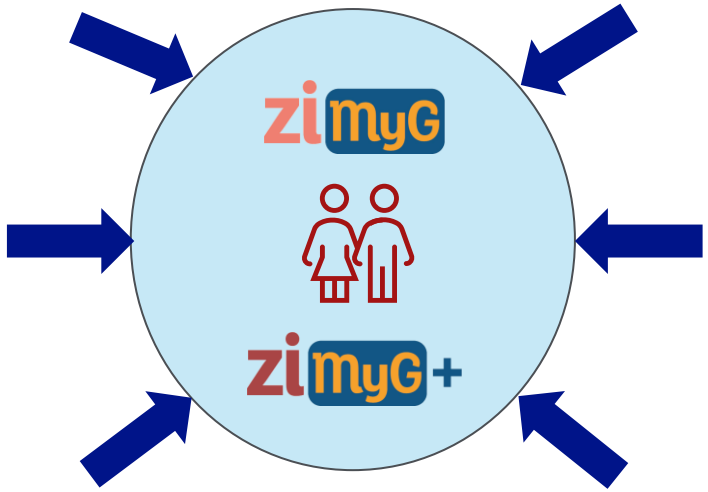
Adolescent patient council:

- Patient journey
- PRO selection
- Study design
- Drug administration

Input from pediatric MG experts

Pediatric MG RWE data to gain insights into:

- Epidemiology
- Population characteristics
- Treatment pathways



Optimized/reduced assessments and blood sampling

Family-friendly assistance with:

- Option for overnight stays
- Transportation
- Digital engagement app

Extrapolation of efficacy from adult studies →

- Small PK/PD and safety study supported by modeling and simulation for dose confirmation

Zilucoplan zimyG zimyG+ studies:
Clinicaltrials.gov NCT06055959

Rozanolixizumab romyG romyG+ studies:
AANEM Poster 204

MG, myasthenia gravis; PD, pharmacodynamics; PK, pharmacokinetics; PRO, patient-reported outcome; RWE, real-world evidence.