Rozanolixizumab for treating antibody-positive generalised myasthenia gravis ID5092

Part 1 for projector – contains redacted CON information

Appraisal committee meeting 3

Technology appraisal committee B, 12 February 2026

Chair: Charles Crawley

External assessment group: Southampton Health Technology Assessments Centre (SHTAC)

Technical team: Chris Shah, Mary Hughes, Emily Crowe

Company: UCB

Rozanolixizumab for treating antibody-positive generalised myasthenia gravis

- ✓ **Recap**
- ❑ Key issues
- ❑ Other considerations
- ❑ Summary

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Background: generalised myasthenia gravis (gMG)

Causes of myasthenia gravis:

- An autoimmune disorder caused by antibody-mediated destruction of the neuromuscular junction which impairs neuromuscular transmission and causes muscle weakness and fatigue
  - ↳ When muscle groups other than eye muscles affected, the condition is known as generalised MG (gMG)

Epidemiology

- MG affects about 15 in every 100,000 people in the UK → Around 80% progress to gMG
- About 80 to 90% of people with gMG have detectable antibodies against AChR; estimated 3% have antibodies against MuSK
- More common in women; in women incidence peaks between 30 and 50 and in men increases with age
- Around 15% people with gMG are refractory to standard therapy

Symptoms and prognosis of gMG

- Symptoms: difficulties with swallowing, vision, speech, breathing, mobility, and persistent fatigue, may relapse and remit over time
- Up to 20% of people with gMG experience a myasthenic crisis at least once, where muscles that control breathing affected, which requires intensive care support and is main cause of MG-related deaths

Abbreviations: AChR, acetylcholine receptor; CT, computerised tomography; gMG, generalised myasthenia gravis; IgG, immunoglobulin G; MG, myasthenia gravis; MRI, magnetic resonance imaging; NMJ, neuromuscular junction

Rozanolixizumab (RYSTIGGO®, UCB)

Marketing authorisation	• Rozanolixizumab is indicated as an add-on to standard therapy for the treatment of generalised myasthenia gravis (gMG) in adult patients who are anti-AChR or anti-MuSK antibody positive • Licensed dose: ~7mg/kg • Date of MHRA approval: 7 March 2024
Administration	• Subcutaneous infusion once-weekly for 6 weeks (1 treatment cycle*), based on weight
Price	• List price: £31.93 per mg • Average cost of £107,285 for a 6-week treatment cycle • There is a confidential patient access scheme for rozanolixizumab

*1 dose per week for 6 weeks, further treatment cycles dependent on clinical evaluation and vary by patient

Note: In this appraisal, rozanolixizumab is being considered for treating *refractory* gMG in adult patients who are anti-AChR or anti-MuSK antibody positive

Link to Treatment pathway

Abbreviations: AChR, acetylcholine receptor; gMG, generalised myasthenia gravis; MuSK, muscle specific tyrosine kinase; MHRA, Medicines & Healthcare products Regulatory Agency

History of this appraisal

Note: Today's presentation shows some of the committee's conclusions and preferred modelling assumptions from the ACM2 discussion. If rozanolixizumab is not recommended following this ACM, stakeholders will have the opportunity to comment on the committee conclusions during the draft guidance consultation.

Abbreviations: ACM, appraisal committee meeting, gMG, generalised myasthenia gravis

Summary of committee conclusions after ACM2 (1/2)

Key issue	Committee preferences/conclusions on key issues discussed at ACM2	Further discussion needed?
Treatment response rates. (After ACM1 company included MSE to represent continued response state)	• Committee considered MSE to be clinically relevant but could not conclude on the appropriateness of the modelling of MSE • Committee noted uncertainty around using expert elicitation rather than empirical evidence to inform: ▪ MSE for IVIg, PLEX and the standard care basket ▪ the loss of response substate for all patients	Yes
Long-term treatment effect	Final results from MG0007 provided useful evidence of rozanolixizumab's long-term effectiveness, although this is uncertain because of the lack of a comparator arm and uncertainty around how MSE was reported.	Yes
Subsequent treatments (not included in ACM1 model)	Committee noted there was uncertainty about the most appropriate approach to model subsequent treatments. Committee noted that assumptions related to subsequent treatments had a large impact on the ICER.	Yes

Abbreviations: ACM, appraisal committee meeting; EAMS, early access to medicines scheme; gMG, generalised myasthenia gravis; IVIg, intravenous immunoglobulin; MSE, minimal symptom expression; PLEX, plasma exchange

Summary of committee conclusions after ACM2 (2/2)

Key issue	Committee conclusion	Further discussion needed?
Relevant comparator (see link for recap on EAMS)	Basket of standard care (excluding rituximab because used earlier in treatment pathway) with proportions informed by full EAMS cohort (n=48) rather than company's revised EAMS cohort (n=37).	No
Response assessment timepoint	A response assessment timepoint of 3 weeks reflected NHS practice for IVIg and PLEX, but an assessment timepoint of 6 weeks was appropriate for rozanolixizumab.	No
Improved ITCs requested at ACM1	Bivariate NMA results acceptable for decision making, but not adjusting for placebo response added considerable uncertainty to the estimates.	No
Utility values	Take account of any corticosteroid-sparing benefit qualitatively in its decision making rather than applying a utility decrement for corticosteroids.	No
Corticosteroid management	Corticosteroid costs informed by Lee et al. and applied equally for rozanolixizumab, IVIg and PLEX in the economic model was appropriate.	No
Treatment costs for IVIg and PLEX	It was appropriate to apply IVIg and PLEX costs every 4 weeks and to include administration costs for PLEX and IVIg.	No

Abbreviations: ACM, appraisal committee meeting; EAMS, early access to medicines scheme; gMG, generalised myasthenia gravis; ITC, indirect treatment comparison; IVIg, intravenous immunoglobulin; MSE, minimal symptom expression; NMA, network meta-analysis; PLEX, plasma exchange

Clarification sought from company after ACM2

Following ACM2, committee sought clarification from the company on the following issues:

- The transparency and executability of the model
- Detail and scenario analyses about the distribution of MSE events among patients and cycles
- Effect of exacerbation on time on treatment
- Modelling exacerbations and myasthenic crisis

Abbreviations: ACM, appraisal committee meeting; MSE, minimal symptom expression

Remaining issues for discussion

Issue	ICER impact
Modelling treatment responder substates	Unknown
Modelling subsequent treatments	Large
Exacerbation and myasthenic crisis	Large
Plausibility of time on treatment estimates	Unknown

Abbreviations: ICER, incremental cost-effectiveness ratio

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Overview of company's model

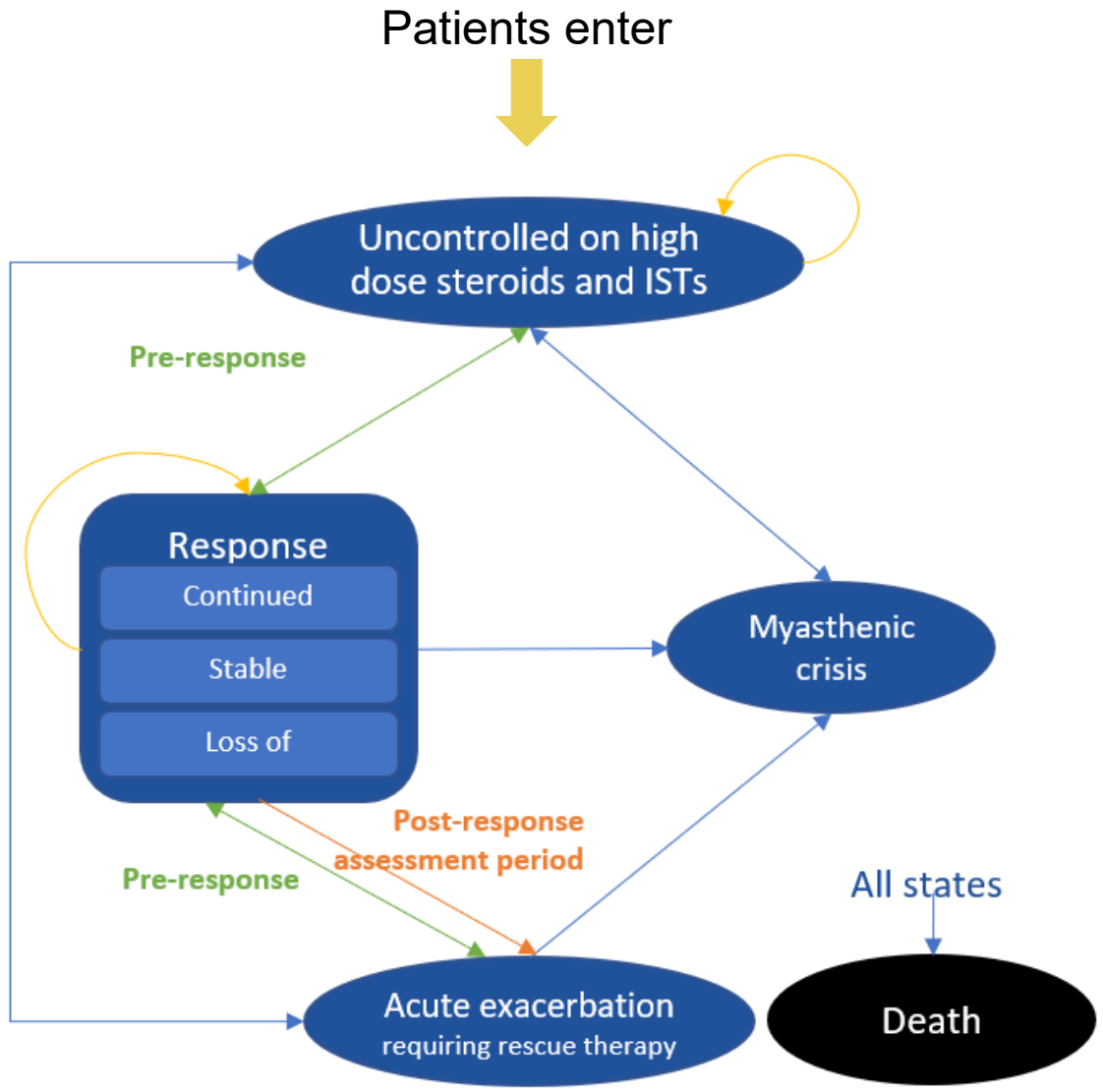
Link to use of MSE in model

- Response rate informed by bivariate NMA
- Responders separate into 1 of 3 response subgroups at response assessment timepoint but cannot move between response substates
- Company changed its definition of continued response to MSE (MG-ADL 0 or 1) after ACM1

Continued response
Model at ACM1: drop of ≥2 points in MG-ADL from baseline, **and ongoing improvement** (≥2 points)
Model at ACM2: patients have reached MSE (MG-ADL score of 0 or 1 – free/nearly free of symptoms)

Stable response
Model at ACM1: drop of ≥2 points in MG-ADL from baseline, **no ongoing improvement** (≥2 points)
Model at ACM2: proportion = 1 minus the other 2 states

Loss of response
Model at ACM1: drop of ≥2 in MG-ADL from baseline, **and a worsening in score until it returns to baseline**
Model at ACM2: no change (5% in all treatment arms based on expert opinion)



Abbreviations: ACM, appraisal committee meeting; IST, immunosuppressant; MG-ADL, myasthenia gravis activities of daily living; MSE, minimum symptom expression; NMA, network meta-analysis

Unknown effect on ICER

Key issue: Modelling treatment responder substates (1/3)

Background:

- Using MSE to inform continued response utilises data from MycarinG (MG003) and MG0007 for rozanolixizumab and SoC only (NSISTs and CSs) but requires expert elicitation for IVIg and PLEX

Company base case response distributions

Treatment	Continued response	Loss of response	Stable response	Source for proportion in continued response
Rozanolixizumab	[redacted]	[redacted]	[redacted]	MSE rate for rozanolixizumab from MycarinG and MG0007
IVIg	[redacted]	[redacted]	[redacted]	MSE rate estimated by expert elicitation
PLEX	[redacted]	[redacted]	[redacted]	MSE rate estimated by expert elicitation
Standard care basket (revised EAMS proportions)	[redacted]	[redacted]	[redacted]	Weighted average of placebo MSE data from MycarinG and IVIg and PLEX from expert elicitation

Committee discussion at ACM2:

- Agreed that MSE is clinically relevant but could not conclude on appropriateness of MSE to inform continued response health state (due to lack of clarity of the data submitted by company)
- Model assumes that people stay in continued response unless they experience an exacerbation, but this is not based on empirical evidence
- Noted uncertainty around using expert elicitation, rather than empirical evidence, to inform MSE for IVIg, PLEX and the standard care basket, and to inform loss of response rate for all treatments

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Abbreviations: ACM, appraisal committee meeting; CSs, corticosteroids; EAMS, early access to medicines scheme; IVIg, intravenous immunoglobulin; MG-ADL, myasthenia gravis activities of daily living; MSE, minimum symptom expression; NSISTs, non-steroidal immunosuppressants; PLEX, plasma exchange

Unknown effect on ICER

Key issue: Modelling treatment responder substates (2/3)

Committee requests for clarification following ACM2:

- Requested further analyses from company including:
  a) Details about the distribution of MSE events among people having rozanolixizumab and treatment cycles
  b) Evidence to justify the assumption that, of the people who respond, the proportion of MSE responders is greater in the rozanolixizumab arm than other treatment arms
  c) Scenario analyses varying the proportion of responders reaching MSE and assuming the same proportion of responders in each treatment arm will have this quality of response

Company response to request for clarification:

- Provided distribution of MSE rates for cycle 1 responders and for all participants up to cycle 13 from MG0007
- Provided requested scenario analyses
- Considers proportion of MSE responders greater in rozanolixizumab arm than SoC basket arm based on:
  a) Structured clinical expert elicitation exercise where MSE estimates provided for IVIg, PLEX and SoC (CSs and NSISTs) were lower compared with observed rozanolixizumab MSE rates
  b) Change from baseline in MG-ADL scores statistically significant for rozanolixizumab versus placebo (proxy for SoC only), and NMA results numerically higher for rozanolixizumab than IVIg or PLEX
  c) In MycarinG, the response rate for rozanolixizumab arm was statistically significantly higher than placebo arm (25% vs 3%)

Abbreviations: ACM, appraisal committee meeting; CS, corticosteroid; IVIg, intravenous immunoglobulin; NSIST, non-steroidal immunosuppressant; MG-ADL, myasthenia gravis activities of daily living; MSE, minimum symptom expression; PLEX, plasma exchange; SoC, standard of care

Link to complete tables provided by company

Distribution of MSE rates across cycles

Proportion of responders having MSE is consistent across cycles but sample size reduced in later cycles

MSE (MG-ADL 0-1) rates in rozanolixizumab ~7mg/kg arm: Cycle 1 MG-ADL responders* vs all participants

Symptom-driven cycle number	MSE among responders at Day 43 of Cycle 1 (Safety set) n/ Nsub (%)	MSE among all participants (Safety Set) n/ Nsub (%)
Cycle 1	N/A	[redacted]
Cycle 2	[redacted]	[redacted]
Cycle 3	[redacted]	[redacted]
Cycle 4	[redacted]	[redacted]
Cycle 5	[redacted]	[redacted]
Cycle 6	[redacted]	[redacted]
Cycle 7	[redacted]	[redacted]
Cycle 8	[redacted]	[redacted]
Cycle 9	[redacted]	[redacted]
Cycle 10	[redacted]	[redacted]
Cycle 11	[redacted]	[redacted]
Cycle 12	[redacted]	[redacted]
Cycle 13	[redacted]	[redacted]

*MG-ADL responder is defined as a participant with a 2.0-point improvement in MG-ADL Score from Baseline at Day 43 of Cycle 1

Why did some people who were not MG-ADL responders in cycle 1 appear to have MSE in subsequent cycles?

Abbreviations: MG-ADL, myasthenia gravis activities of daily living; MSE, minimum symptom expression; NMA, network meta-analysis; PLEX, plasma exchange

Unknown effect on ICER

Key issue: Modelling treatment responder substates (3/3)

EAG:

- MSE data provided by the company indicates that MSE rates were similar whether response was achieved during the first cycle or not
- The range of response rates across cycles appears broad but this is likely due to small sample sizes (N[redacted] sample sizes appear from Cycle 8 onwards). Response rates increase consistently across the incremental MG-ADL response thresholds.
- Company's rationale for the proportion of MSE responders being greater in patients receiving rozanolixizumab relies on expert elicitation and assumptions around clinical plausibility. The EAG cannot identify stronger evidence, but further expert opinion may help validate clinical plausibility of company's assumptions
- It is unclear why some people who did not have a response in cycle 1 had MSE in subsequent cycles

- Is it appropriate to use MSE to inform continued response?
- Is it appropriate to assume that the proportion of responders who have MSE is greater for rozanolixizumab than IVIg or PLEX?
- If so, is it appropriate to use company's expert elicitation to inform MSE for IVIg and PLEX?
- Is it appropriate to assume that people who have a response remain in their response substate (continued, stable or loss of response) unless they experience an exacerbation or myasthenic crisis?
- Is it appropriate to use company's expert elicitation to inform loss of response for all treatments?

Abbreviations: ACM, appraisal committee meeting; CS, corticosteroid; ICER, incremental cost-effectiveness ratio; IVIg, intravenous immunoglobulin; MG-ADL, myasthenia gravis activities of daily living; MSE, minimum symptom expression; NSIST, non-steroidal immunosuppressant; PLEX, plasma exchange; SoC, standard of care

Key issue: Modelling subsequent treatments (1/2)

Large impact on ICER

Company applies same approach to treatment arms, whereas EAG prefers different approach for each arm

	Company preference	EAG preference
Standard care basket arm: subsequent treatments	Apply subsequent treatment proportions from Delphi panel for IVIg and PLEX to revised EAMS proportions (included re-treatment) • IVIg: 14.05% • PLEX: 35.73% • SoC (CS/NSISTs): 50.22%	Apply treatment proportions from Delphi panel for IVIg and PLEX to unrevised EAMS proportions (excluded retreatment): • IVIg: 8.2% • PLEX: 27.16% • SoC (CS/NSISTs): 64.64%
Rozanolixizumab arm: subsequent treatment proportions	Same proportions as standard care basket: Over time the mix of subsequent treatments will be the same across treatment arms • IVIg: 14.05% • PLEX: 35.73% • SoC (CS/NSISTs): 50.22%	Use unrevised EAMS proportions: company estimates do not align with expert assumptions after Roza • IVIg: 43.8% • PLEX: 14.6% • SoC (CS/NSISTs): 41.6%

Are the mean subsequent treatment proportions from the Delphi panel plausible?

Link to supplementary material

Mean of subsequent treatment proportions from Delphi panel:

Subs Tx after IVIg	Mean
IVIg + SoC retreatment	6%
PLEX + SoC	62%
SoC only	32%
Subs Tx after PLEX	
IVIg + SoC	56%
PLEX + SoC retreatment	4%
SoC only	40%
Subs Tx after Roza*	
IVIg + SoC	44%
PLEX+ SoC	29%
SoC only	24%

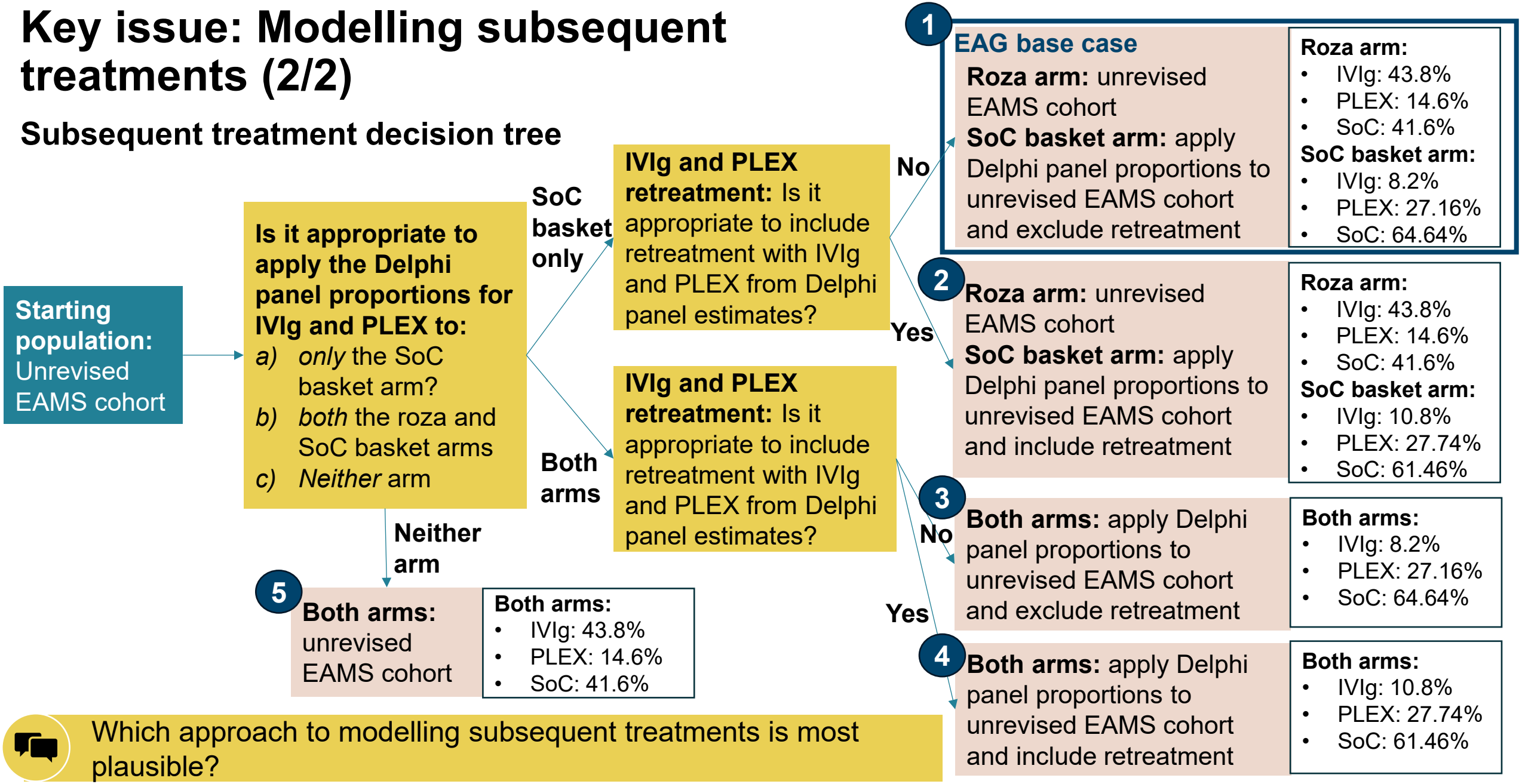
*Based on subsequent treatment proportions for zilucoplan but used by EAG to validate proportions for rozanolixizumab

Note: wide range in clinical expert estimates

Abbreviations: CS, corticosteroids; EAMS, early access to medicines scheme; NSISTs, non-steroidal immunosuppressants; IVIg, intravenous immunoglobulin; PLEX, plasma exchange; SoC, standard of care; Subs Tx, subsequent treatments

Key issue: Modelling subsequent treatments (2/2)

Subsequent treatment decision tree



Which approach to modelling subsequent treatments is most plausible?

Abbreviations: EAMS, early access to medicines scheme; IVIg, intravenous immunoglobulin; PLEX, plasma exchange; SoC, standard of care

Large impact on ICER

Key issue: Exacerbation and myasthenic crisis (1/2)

Link to exacerbation and crisis costs

Background:

- Higher cost associated with treating an exacerbation for standard care basket than rozanolixizumab
- Lower cost associated with treating a crisis for standard care basket than rozanolixizumab
- Rates of exacerbation and myasthenic crisis applied equally across treatment arms and response substates
- After ACM2, committee requested clarification from company regarding exacerbation and crisis costs

Company response to request for further analyses

- Clarified that the LoS for exacerbation and myasthenic crisis is set at 28 days in all treatment arms (in line with committee preferred assumptions), and that any errors have been corrected
- Difference in cost of exacerbation or myasthenic crisis between treatment arms driven by differing use of IVIg and PLEX as acute rescue treatment based on clinical advice:

Exacerbation and myasthenic crisis acute treatment proportions by index treatment

	Index treatment		
	Rozanolixizumab or SoC only	IVIg	PLEX
Exacerbation acute treatment	73% IVIg; 27% PLEX	100% PLEX	100% IVIg
Crisis acute treatment	5% IVIg; 95% PLEX	100% PLEX	100% IVIg

Exacerbation and myasthenic crisis costs by treatment arm

	Rozanolixizumab	Standard care basket (company)	Standard care basket (EAG)
Cost per exacerbation	£14,540	£16,906	£16,368
Cost per crisis	£41,550	£40,560	£40,785

Abbreviations: ACM, appraisal committee meeting; IVIg, intravenous immunoglobulin; LoS, length of stay; PLEX, plasma exchange SoC, standard of care

Large impact on ICER

Key issue: Exacerbation and myasthenic crisis (2/2)

EAG:

- Unsure how company calculated proportions receiving IVIg and PLEX following rozanolixizumab or SoC only using Phillips et al. (2022) but these proportions have not changed since previous ACMs
- Considers company justifications and calculations appropriate.
- Clinical experts did not highlight concerns with proportions receiving IVIg or PLEX as rescue treatment for exacerbation or crisis.

Is it appropriate to assume a lower cost associated with an exacerbation for people in the rozanolixizumab arm than in the standard care basket arm and a higher cost associated with a myasthenic crisis?

Abbreviations: ACM, appraisal committee meeting; IVIg, intravenous immunoglobulin; LoS, length of stay; PLEX, plasma exchange SoC, standard of care

Key issue: Plausibility of time on treatment estimates

Unknown effect on ICER

Background:

- Model assumes that patients with continued response and stable response have same risk of exacerbation
- Committee requested scenario analyses exploring a higher probability of exacerbation for people in stable response than in the MSE/continued response state and an assessment of how this affected time on treatment

Scenario analyses submitted by company

Transition probability from stable response to exacerbation (% increase from base case)	Time on treatment (months)			
	Rozanolixizumab	IVIg	PLEX	SoC basket (revised EAMS proportions)
Base case: 0.009	[redacted]	[redacted]	[redacted]	[redacted]
0.01 (+10%)	[redacted]	[redacted]	[redacted]	[redacted]
0.011 (+20%)	[redacted]	[redacted]	[redacted]	[redacted]
0.012 (+30%)	[redacted]	[redacted]	[redacted]	[redacted]
0.013 (+40%)	[redacted]	[redacted]	[redacted]	[redacted]
0.014 (+50%)	[redacted]	[redacted]	[redacted]	[redacted]
0.015 (+60%)	[redacted]	[redacted]	[redacted]	[redacted]
0.016 (+70%)	[redacted]	[redacted]	[redacted]	[redacted]
0.017 (+80%)	[redacted]	[redacted]	[redacted]	[redacted]
0.018 (+90%)	[redacted]	[redacted]	[redacted]	[redacted]
0.019 (+100%)	[redacted]	[redacted]	[redacted]	[redacted]

EAG:

- Uncertain if scenarios reasonable range
- Clinical expert advice regarding increased risk of exacerbation for patients in stable response compared with MSE would be beneficial

- Is it reasonable to assume that people receiving rozanolixizumab spend ~50% longer on treatment than people receiving other treatments?
- Is the assumption of equal exacerbation risk for stable and continued response states appropriate?

Link for results shown by % increase in annual exacerbation rate of 0.244

Abbreviations: ACM, appraisal committee meeting; EAMS, early access to medicines scheme; IVIg, intravenous immunoglobulin; MSE, minimum symptom expression; PLEX, plasma exchange; SoC, standard of care

Rozanolixizumab for treating antibody-positive generalised myasthenia gravis

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Equality considerations

At ACM2, the committee:

- Considered that gMG may have a different burden on women than men (more prevalent and women may be younger at onset and have higher mortality)
- Noted the variation in access to IVIg and PLEX across the NHS
- Noted comments from patient and clinical experts that to have treatment with IVIg and PLEX people have to live near to a hospital or have the means to travel regularly
- Heard from the company that it has a home care service that helps people administer rozanolixizumab themselves at home
- Noted that pregnancy may contraindicate some types of treatment and heard from clinical experts that the improved disease control with rozanolixizumab may help people become healthy enough to be able to start a family

Are there any other equality or health inequality considerations for decision making?

Abbreviations: ACM, appraisal committee meeting; gMG, generalised myasthenia gravis; IVIg, intravenous immunoglobulin; PLEX, plasma exchange

Uncaptured benefits

At ACM2, the committee concluded that some benefits of rozanolixizumab may not have been captured in the QALY calculation, including:

- As rozanolixizumab is a short-duration subcutaneous infusion, it could be more convenient and could improve adherence compared with IVIg or PLEX, which are time-consuming and require regular hospital stay
- People who have rozanolixizumab may be able to reduce their corticosteroid use, which could lead to fewer corticosteroid-related adverse effects

Are there any other uncaptured benefits?

Abbreviations: ACM, appraisal committee meeting; IVIg, intravenous immunoglobulin; PLEX, plasma exchange QALY, quality-adjusted life year

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Summary of remaining issues and questions for committee

Issue	Questions for committee	ICER impact
Modelling treatment responder substates	• Is it appropriate to use MSE to inform continued response? • Is it appropriate to assume that the proportion of responders who have MSE is greater for rozanolixizumab than IVIg or PLEX? • Is it appropriate to use expert elicitation to inform MSE for IVIg and PLEX? • Is it appropriate to assume that people who have a response remain in their response substate (continued, stable or loss of response) unless they experience an exacerbation or myasthenic crisis? • Is it appropriate to use expert elicitation to inform loss of response for all treatments?	Unknown
Subsequent treatments	• Are the mean subsequent treatment proportions from the Delphi panel plausible? • Which arms should the Delphi panel proportions be applied to? • Is it appropriate to include IVIg and PLEX retreatment from Delphi panel? • Which approach to modelling subsequent treatments is most plausible?	Large
Modelling exacerbations and myasthenic crisis	• Is it appropriate to assume a lower cost associated with an exacerbation for people in the rozanolixizumab arm than in the standard care basket arm and a higher cost associated with a myasthenic crisis?	Large
Plausibility of time on treatment estimates	• Is it reasonable to assume that people receiving rozanolixizumab spend ~50% longer on treatment than people receiving other treatments? • Is the assumption of equal exacerbation risk for stable and continued response states appropriate?	Unknown

Abbreviations: ICER, incremental cost-effectiveness ratio; IVIg, intravenous immunoglobulin; MSE, minimal symptom expression; PLEX, plasma exchange

Company, EAG and committee preferences after ACM2 (1/2)

Assumption	Company base case	EAG base case	Committee preference
Relevant comparator	IVIg and PLEX	Standard care basket informed by unrevised EAMS cohort	Standard care basket informed by unrevised EAMS cohort
Source of data for response	Bivariate NMA	Bivariate NMA	Bivariate NMA
Response assessment time points	6 weeks for roza; 12 weeks for SoC basket	6 weeks for roza; 3 weeks for SoC basket	6 weeks for roza; 3 weeks for SoC basket
IVIg and PLEX admin costs frequency	Both every 4 weeks PLEX cost set to £0 in model	Both every 4 weeks PLEX cost of £2,482.50 per model cycle included	Both every 4 weeks PLEX cost of £2,482.50 per model cycle included
MSE proportion used to inform 'uncontrolled off initial treatment' health state	Standard care basket	Use standard care only (CSs and NSISTs only) MSE proportion	Use standard care only (CSs and NSISTs only) MSE proportion
Corticosteroid disutility	Included	Excluded	Exclude
Corticosteroid resource use costs	Costs from Stirnadel-Farrant et al. (2023)	Costs from Lee et al. (2018)	Costs from Lee et al. (2018)

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Abbreviations: ACM, appraisal committee meeting, CS, corticosteroids EAG, external assessment group; IVIg, intravenous immunoglobulin; NMA, network meta-analysis; NSISTs, non-steroidal immunosuppressants; PLEX plasma exchange; SoC, standard of care

Company, EAG and committee preferences after ACM2 (2/2)

Assumption	Company base case	EAG base case	Committee preference after ACM2
Modelling treatment response	• MSE from MG0007 to inform continued response state for roza and SoC (CSs and NSISTs). • Expert elicitation to inform MSE for IVIg and PLEX	• Same as company	For discussion
Subsequent treatments	Both treatment arms: Delphi panel proportions applied to revised EAMS cohort (including IVIg and PLEX retreatment)	• Roza: Unrevised EAMS cohort proportions • SoC basket: Delphi panel proportions for IVIg and PLEX applied to unrevised EAMS cohort proportions (excluding IVIg and PLEX retreatment)	For discussion
Modelling exacerbation and myasthenic crisis	Use different proportions of IVIg or PLEX as acute treatment in each arm based on clinical advice	Same as company	For discussion

Abbreviations: ACM, appraisal committee meeting, CS, corticosteroids EAG, external assessment group; EAMS, early access to medicines scheme; IVIg, intravenous immunoglobulin; MSE, minimal symptom expression; NSISTs, non-steroidal immunosuppressants; PLEX plasma exchange; SoC, standard of care

Cost-effectiveness results

All ICERs are reported in PART 2 slides because they include confidential comparator PAS discounts

Supplementary appendix

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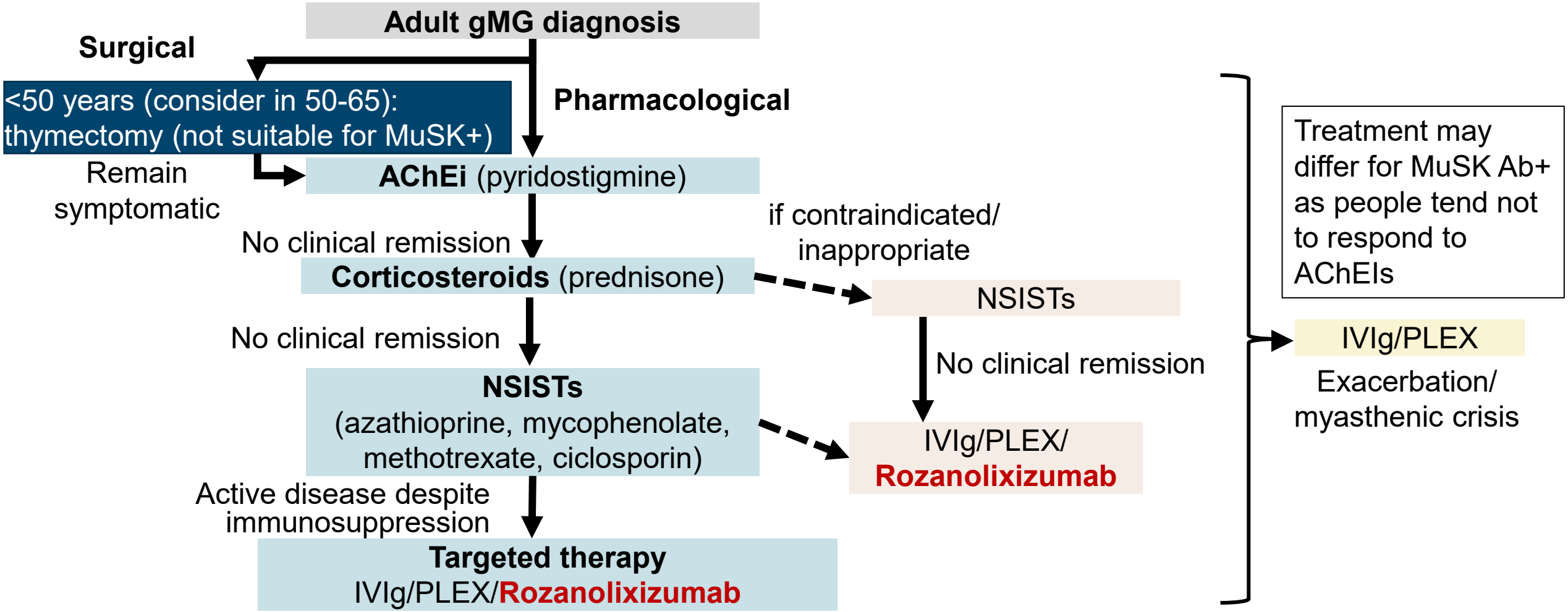
Treatment pathway for generalised myasthenia gravis



Company proposed positioning: Rozanolixizumab as an add-on to standard care (corticosteroids and NSISTs) for refractory AChR+ or MuSK+ gMG

Abbreviations: AChEi, acetyl-cholinesterase inhibitor; gMG, generalised myasthenia gravis; IVIg, intravenous immunoglobulin; MuSK, muscle specific tyrosine kinase; NSIST, non-steroidal immunosuppressive therapy; PLEX, plasma exchange; SC, standard care

Revised vs unrevised EAMS basket

Back to main presentation

The standard care basket uses data on the proportion having treatments from the efgartigimod EAMS

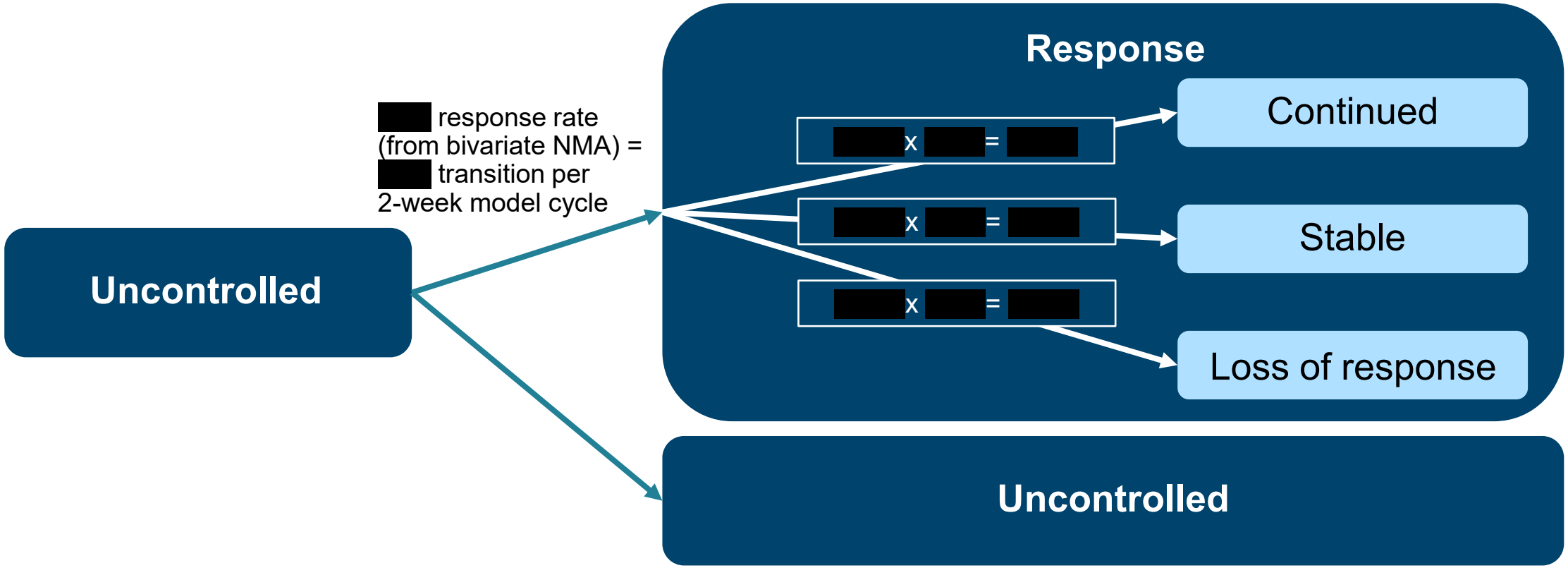
	Unrevised EAMS population	Revised EAMS population
N	48	37
Definition	All people with AChR antibody-positive gMG who were treated with efgartigimod in the EAMS	Removes people from the EAMS cohort whose condition was not considered refractory, who had no treatment, and who were on corticosteroids only. Added 2 people who were on corticosteroids only.
Proportion of treatments at the time of starting efgartigimod	• IVIg (and CS and NSISTs): 43.8% • PLEX (and CS and NSISTs): 14.6% • SoC (CS and NSISTs): 41.6%	• IVIg (and CS and NSISTs): 56.7% • PLEX (and CS and NSISTs): 18.9% • SoC (CS and NSISTs): 24.4%
Preference	EAG and committee preference	Company preference

Abbreviations: AChR, acetylcholine receptor; CS, corticosteroids; EAMS, early access to medicines scheme; gMG, generalised myasthenia gravis; IVIg, intravenous immunoglobulin; NSISTs, non-steroidal immunosuppressants; PLEX, plasma exchange; SoC, standard of care

Use of MSE in the model

Link to response rates used in company model
Link to main slides

Distribution of people whose myasthenia gravis responds to first-line treatment with rozanolixizumab, of responders, [redacted] had MSE (based on data from MycarinG and MG0007) and 5% were assumed would lose response, the remaining responders had a stable response.



 Abbreviations: ICER, incremental cost effectiveness ratio; IVIg, intravenous immunoglobulin; MG-ADL, myasthenia gravis activities of daily living; MSE, minimum symptom expression; NMA, network meta-analysis; PLEX, plasma exchange

Link to main slides

Company response: updated model efficacy assumptions and inputs

Bivariate NMA informed updated company model

Primary response rate and response assessment timepoint

Treatment	Response rate used in the model	Response assessment timepoint used in the model (weeks)	Source
Rozanolixizumab	[redacted]	6	Bivariate NMA
IVIg	[redacted]	3	Bivariate NMA
PLEX	[redacted]	3	Bivariate NMA
Standard care basket*	[redacted]	12	Bivariate NMA

Response distribution

Treatment	Continued response	Loss of response	Stable response	Source for proportion in continued response
Rozanolixizumab	[redacted]	[redacted]	[redacted]	MSE rate for rozanolixizumab from MycarinG and MG0007
IVIg	[redacted]	[redacted]	[redacted]	MSE rate estimated by expert elicitation
PLEX	[redacted]	[redacted]	[redacted]	MSE rate estimated by expert elicitation
Standard care basket*	[redacted]	[redacted]	[redacted]	Weighted average of placebo MSE data from MycarinG and IVIg and PLEX from expert elicitation

Treatment-specific MG-ADL score change from baseline (source: bivariate NMA)

Treatment	Continued response	Loss of response	Stable response
Rozanolixizumab	[redacted]	[redacted]	[redacted]
IVIg	[redacted]	[redacted]	[redacted]
PLEX	[redacted]	[redacted]	[redacted]
Standard care basket*	[redacted]	[redacted]	[redacted]

*Using revised EAMS population; abbreviations: IVIg, intravenous immunoglobulin; MG-ADL, myasthenia gravis activities of daily living; MSE, minimum symptom expression; NMA, network meta-analysis; PLEX, plasma exchange

Distribution of MSE rates (1/2)

Link to main slides

MG-ADL MSE Rate by Cycle - Subsequent MSE Rates Among Responders at Day 43 of Cycle 1 (Safety Set)

Symptom-driven cycle number	RLZ ~7mg/kg n/ Nsub (%) MG-ADL MSE (0-1)	RLZ ~7mg/kg n/ Nsub (%) MG-ADL (0-2)	RLZ ~7mg/kg n/ Nsub (%) MG-ADL (0-3)	RLZ ~7mg/kg n/ Nsub (%) MG-ADL (0-4)
Cycle 2	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 3	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 4	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 5	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 6	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 7	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 8	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 9	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 10	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 11	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 12	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 13	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: ICER, incremental cost effectiveness ratio; IVIg, intravenous immunoglobulin; MG-ADL, myasthenia gravis activities of daily living; MSE, minimum symptom expression; NMA, network meta-analysis; PLEX, plasma exchange

Link to main slides

Distribution of MSE rates (2/2)

MG-ADL MSE Rate by Cycle – All participants (Safety Set)

Symptom-driven cycle number	RLZ ~7mg/kg n/ Nsub (%) MG-ADL MSE (0-1)	RLZ ~7mg/kg n/ Nsub (%) MG-ADL (0-2)	RLZ ~7mg/kg n/ Nsub (%) MG-ADL (0-3)	RLZ ~7mg/kg n/ Nsub (%) MG-ADL (0-4)
Cycle 1	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 2	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 3	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 4	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 5	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 6	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 7	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 8	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 9	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 10	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 11	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 12	[redacted]	[redacted]	[redacted]	[redacted]
Cycle 13	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: ICER, incremental cost effectiveness ratio; IVIg, intravenous immunoglobulin; MG-ADL, myasthenia gravis activities of daily living; MSE, minimum symptom expression; NMA, network meta-analysis; PLEX, plasma exchange

Link to main slides

Subsequent treatment proportions from Delphi panel

Treatment	Expert 1	Expert 2	Expert 3	Expert 4	Expert 5	Expert 6	Expert 7	Expert 8	Expert 9	Mean
Following failure on IVIg + SoC (no option of zilucoplan)										
% IVIg + SoC retreatment	0%	0%	0%	33%	0%	21%	0%	0%	0%	6%
% PLEX +SoC	25%	0%	100%	33%	84%	43%	89%	80%	100%	62%
% SoC only	75%	100%	0%	33%	16%	36%	11%	20%	0%	32%
Total	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Following failure on PLEX + SoC (no option of zilucoplan)										
% PLEX + SoC retreatment	0%	0%	0%	33%	0%	5%	0%	0%	0%	4%
% IVIg +SoC	14%	50%	90%	33%	83%	74%	0%	60%	100%	56%
% SoC only	86%	50%	10%	33%	17%	21%	100%	40%	0%	40%
Total	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Following failure on zilucoplan										
% IVIg + SoC	13%	53%	80%	33%	44%	63%	11%	0%	100%	44%
% PLEX +SoC	13%	0%	10%	11%	44%	13%	89%	80%	0%	29%
% SoC only	75%	47%	10%	28%	11%	25%	0%	20%	0%	24%
% zilucoplan + SoC retreatment	0%	0%	0%	28%	0%	0%	0%	0%	0%	3%
Total	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%

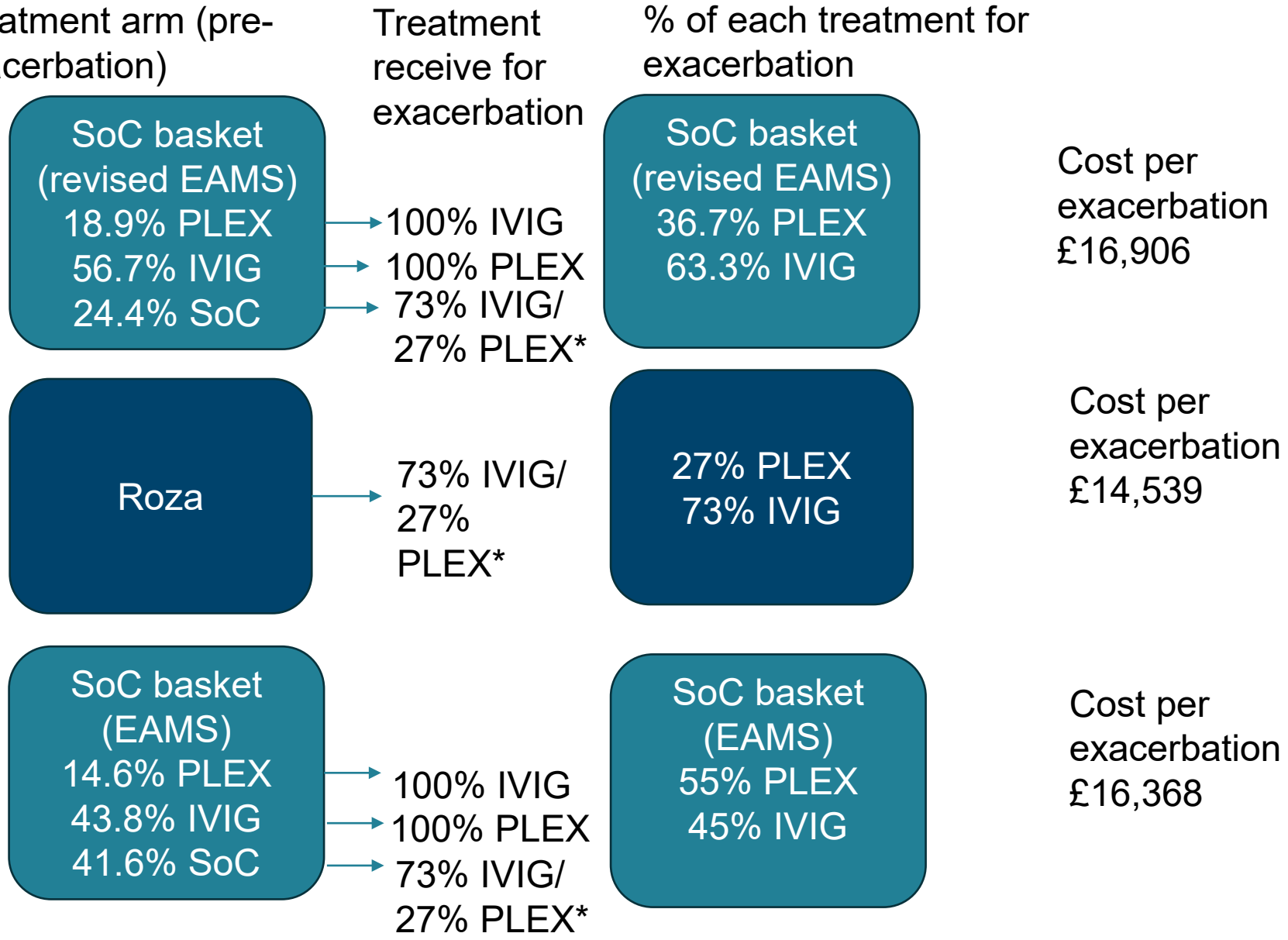
Committee preferred approach to modelling subsequent treatments in ID4008 zilucoplan

Subsequent treatments in zilucoplan arm	Subsequent treatments in standard basket arm
Use unrevised EAMS proportions: • IVIg: 43.8% • PLEX: 14.6% • SoC (CSs and NSISTs): 41.6%	Use unrevised EAMS proportions and apply equal switching from IVIg to PLEX ([redacted]) and vice versa: • IVIg: [redacted]% • PLEX: [redacted]% • SoC (CSs and NSISTs): [redacted]%

Abbreviations: CS, corticosteroid; EAMS, early access to medicines scheme; IVIg, intravenous immunoglobulin; NSISTs, non-steroidal immunosuppressants; PLEX, plasma exchange; SoC, standard of care

Breakdown of exacerbation costs

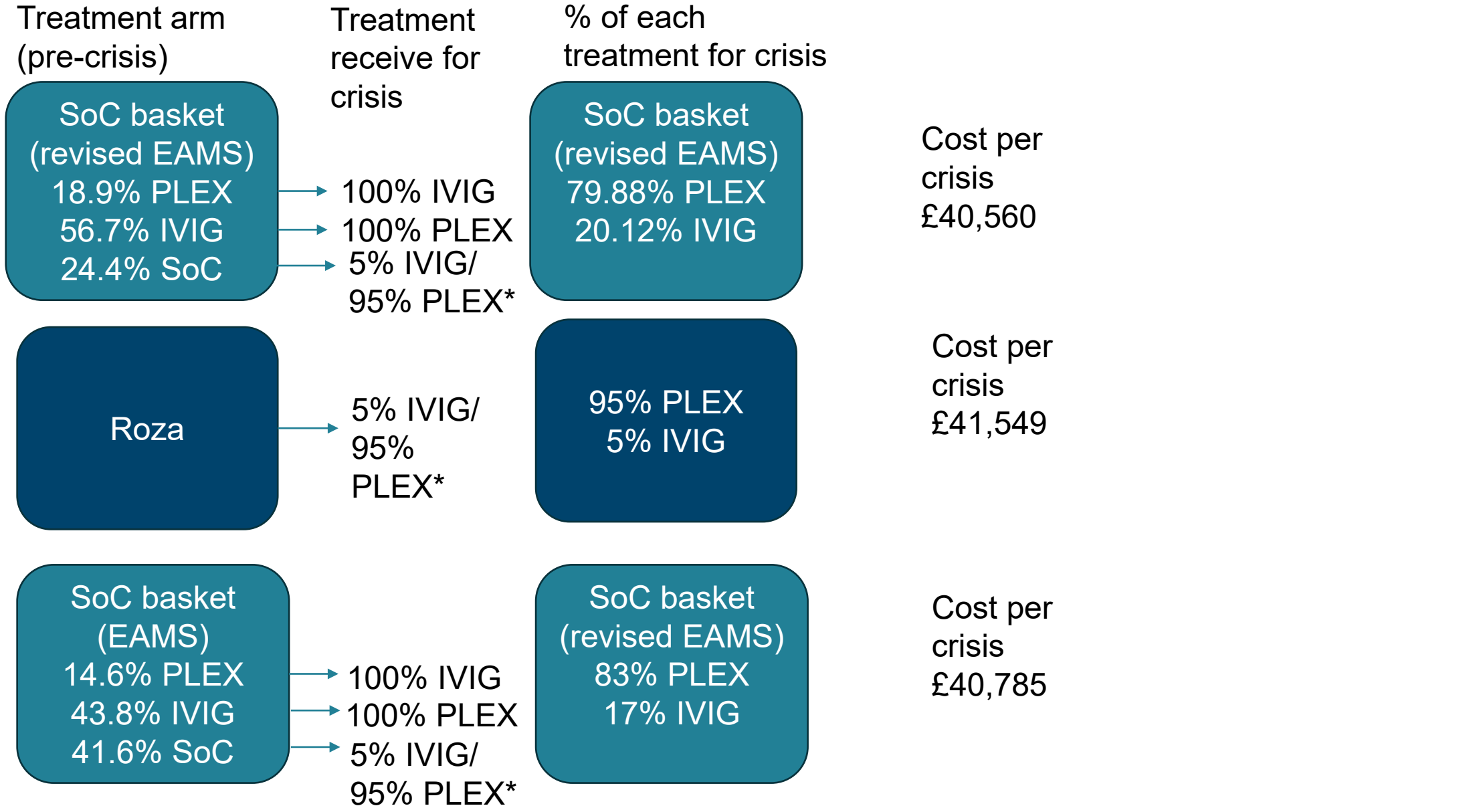
Link to main slides



* Informed by Phillips et al, 2022; next treatment for people who have IVIg or PLEX as their pre-exacerbation treatment : clinical opinion

Breakdown of myasthenic crisis costs

Link to main slides



* Informed by Phillips et al, 2022; next treatment for people who have IVIg or PLEX as their pre-crisis treatment : clinical opinion

Key issue: Plausibility of time on treatment estimates

Unknown effect on ICER

Background:

- Model assumes that patients with continued response and stable response have same risk of exacerbation
- Committee requested scenario analyses exploring a higher probability of exacerbation for people in stable response than in the MSE/continued response state and an assessment of how this affected time on treatment

Scenario analyses submitted by company

Stable response substate annual exacerbation risk (% increase from base case)	Time on treatment (months)			
	Rozanolixizumab	IVIg	PLEX	SoC basket (revised EAMS proportions)
Base case: 0.244	[redacted]	[redacted]	[redacted]	[redacted]
0.268 (+10%)	[redacted]	[redacted]	[redacted]	[redacted]
0.293 (+20%)	[redacted]	[redacted]	[redacted]	[redacted]
0.317 (+30%)	[redacted]	[redacted]	[redacted]	[redacted]
0.342 (+40%)	[redacted]	[redacted]	[redacted]	[redacted]
0.366 (+50%)	[redacted]	[redacted]	[redacted]	[redacted]
0.390 (+60%)	[redacted]	[redacted]	[redacted]	[redacted]
0.415 (+70%)	[redacted]	[redacted]	[redacted]	[redacted]
0.439 (+80%)	[redacted]	[redacted]	[redacted]	[redacted]
0.464 (+90%)	[redacted]	[redacted]	[redacted]	[redacted]
0.488 (+100%)	[redacted]	[redacted]	[redacted]	[redacted]

EAG:

- Uncertain if scenarios reasonable range
- Clinical expert advice regarding increased risk of exacerbation for patients in stable response compared with MSE would be beneficial

- Is it reasonable to assume that people receiving rozanolixizumab spend ~50% longer on treatment than people receiving other treatments?
- Is the assumption of equal exacerbation risk for stable and continued response states appropriate?

Abbreviations: ACM, appraisal committee meeting; EAMS, early access to medicines scheme; IVIg, intravenous immunoglobulin; MSE, minimum symptom expression; PLEX, plasma exchange; SoC, standard of care

Company response: long-term treatment effect

Company: final results from open-label extension study (MG0007) show consistent efficacy in AChR- and MuSK-positive generalised MG

ACM1 MG0007 ([redacted]; [redacted] ~7 mg/kg, [redacted] ~10 mg/kg [unlicensed]); committee conclusion: some supporting evidence for rozanolixizumab's effectiveness

Company draft guidance response

- Final results ([redacted]): meaningful improvements in each treatment cycle
- Responses (≥2-point reduction in MG-ADL score) from day [redacted] of each treatment cycle, with a median time to MG-ADL response of [redacted] in the first [redacted] 6-week treatment cycles; MG-ADL scores plateaued at around [redacted] compared with baseline after repeated cycles (MG0007 long-term results)

EAG comments

Data supports ongoing efficacy of rozanolixizumab; but limitations in study completion and discontinuation:

- [redacted] participants in the 7 mg arm completed the study
- by cycle [redacted], [redacted] participants remained in the 7 mg arm for MSE data
- [redacted] total participants completed the study
- [redacted] discontinued for reasons listed as 'other' - not clearly explained
- important to understand subsequent treatments - gMG is chronic, rozanolixizumab is not curative

Abbreviations: ACM, appraisal committee meeting; EAG, external assessment group; gMG, generalised myasthenia gravis; MG-ADL, myasthenia gravis activities of daily living; MSE, minimum symptom expression

MG0007 efficacy outcomes

Change from baseline to day 43 in MG-ADL score during each treatment cycle

Abbreviations: BL, baseline; MG-ADL, myasthenia gravis activities of daily living; RLZ, rozanolixizumab

MG0007 long-term results

MG-ADL score stabilised at around -3 compared with baseline

MG-ADL, myasthenia gravis activities of daily living; RLZ, rozanolixizumab; TRT, treatment