Response to rozanolixizumab across treatment cycles in patients with generalized myasthenia gravis: A *post hoc* analysis

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Robert M. Pascuzzi[1], Julian Grosskreutz[2], Ali A. Habib[3], Zabeen K. Mahuwala[4], Renato Mantegazza[5], Sabrina Sacconi[6], John Vissing[7], Tuan Vu[8], Raphaëlle Beau Lejdstrom[9], Bernhard Greve[10], Fiona Grimson[11], Thaïs Tarancón[12], Vera Bril[13]

[1]Neurology Department, Indiana University School of Medicine, Indiana University Health, Indianapolis, IN, USA; [2]Precision Neurology of Neuromuscular Diseases, Department of Neurology, University of Lübeck, Lübeck, Germany; [3]MDA ALS and Neuromuscular Center, University of California, Irvine, Irvine, CA, USA; [4]Department of Neuromuscular Medicine, Epilepsy and Clinical Neurophysiology, University of Kentucky, Lexington, KY, USA; [5]Department of Neuroimmunology and Neuromuscular Diseases, Fondazione IRCCS, Istituto Nazionale Neurologico Carlo Besta, Milan, Italy; [6]Université Côte d'Azur, Peripheral Nervous System & Muscle Department, Pasteur 2 Hospital, Centre Hospitalier Universitaire de Nice, Nice, France; [7]Department of Neurology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [8]Department of Neurology, University of South Florida Morsani College of Medicine, Tampa, FL, USA; [9]UCB Pharma, Bulle, Switzerland; [10]UCB Pharma, Monheim, Germany; [11]UCB Pharma, Slough, UK; [12]UCB Pharma, Madrid, Spain; [13]University Health Network, Toronto, ON, Canada

Introduction

- Rozanolixizumab is a humanized IgG4 mAb FcRn inhibitor for the treatment of adults with AChR Ab+ or MuSK Ab+ gMG[1,2]
- In the Phase 3 MycarinG study (MG0003/NCT03971422), one 6-week cycle of SC rozanolixizumab 7 mg/kg or 10 mg/kg once weekly significantly improved MG-specific outcomes compared with placebo in patients with gMG[1]
- Following MycarinG, patients could enroll in OLE studies MG0004 (NCT04124965) or MG0007 (NCT04650854)
- This *post hoc* analysis evaluated:
  - The consistency of response to rozanolixizumab over multiple cycles in the OLEs in patients who responded at Cycle 1 (in MycarinG)
  - Response at Cycles 2 and 3 among patients who were non-responders at Cycle 1

Methods

- Patients enrolled in MycarinG were aged ≥18 years with AChR Ab+ or MuSK Ab+ gMG and were being considered by the investigator for additional treatments such as IVIg and PLEX[1]
  - Patients could receive conventional MG therapy at baseline and throughout the study[1]
- Patients who completed MycarinG or whose disease severity worsened during the observation period could enroll in MG0004 and then MG0007, or in MG0007 directly (**Figure 1**)
  - Patients received chronic weekly rozanolixizumab 7 mg/kg or 10 mg/kg in MG0004 or rozanolixizumab 7 mg/kg or 10 mg/kg in symptom-driven cycles in MG0007
- Data were pooled across MycarinG, MG0004 (first 6 weeks) and MG0007 (interim analysis; data cut-off: July 8, 2022) for patients with ≥2 symptom-driven cycles ('efficacy pool')
- Response to rozanolixizumab was defined as an improvement from baseline of ≥2.0 points in MG-ADL score and ≥3.0 points in MGC and QMG scores at the end of each cycle (Day 43)
  - For Cycle 1 responders, proportions of patients who achieved a response at Cycles 2 to 6 were assessed
  - For Cycle 1 non-responders, proportions of patients who achieved a response at Cycle 2 and Cycle 3 were assessed

Results

Patients

- Efficacy pool comprised: 127 patients treated with either rozanolixizumab 7 mg/kg or 10 mg/kg who had ≥2 symptom-driven cycles (**Table 1**)
- Safety pool comprised: 188 patients with ≥1 cycle and ≤8-week follow-up period across MycarinG and MG0007; baseline demographics and characteristics were similar to those in the efficacy pool[3]

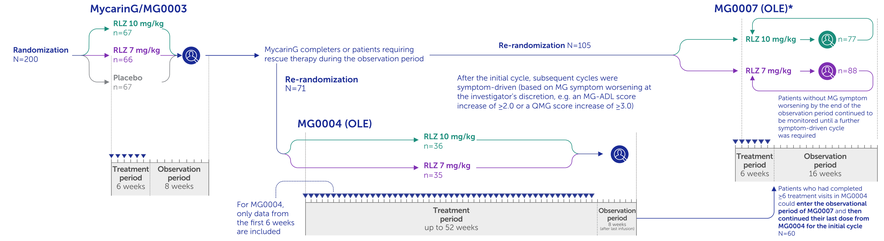
Efficacy

- At the end of Cycle 1, 74.0% (94/127), 73.2% (93/127) and 68.5% (87/127) of patients were MG-ADL, MGC and QMG responders, respectively (**Figure 2a**)
- Among responders at Cycle 1, MG-ADL, MGC and QMG response rates remained high over subsequent cycles (**Figure 2b**)
- Among non-responders at Cycle 1 (**Figure 2a**) who had ≥3 cycles, 57.1% (16/28), 57.1% (16/28) and 51.5% (17/33) achieved a response at Cycle 2 across the MG-ADL, MGC and QMG scales, respectively, and response rates were 61.8–75.0% by Cycle 3 (**Figure 2c**)

Safety

- Across all cycles, 89.9% (169/188) of patients in the safety pool experienced a TEAE
- Overall, the most frequently reported TEAEs were headache (46.3%), diarrhea (28.7%), pyrexia (18.1%), nausea (14.9%), COVID-19 infection (13.8%) and arthralgia (11.2%)
- In general, the incidence of TEAEs did not increase with repeated cycles of treatment compared with Cycle 1[4]

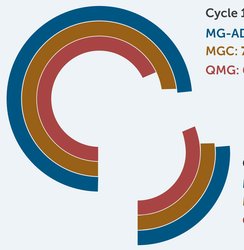
Figure 1 MycarinG and OLE study design



*After the initial cycle, dose modifications from 10 mg/kg to 7 mg/kg and *vice versa* were permitted at the beginning of each treatment cycle provided the benefit–risk ratio remained favorable for the patient.

Figure 2 Cycle 1 responders and non-responders to RLZ treatment and subsequent response rates

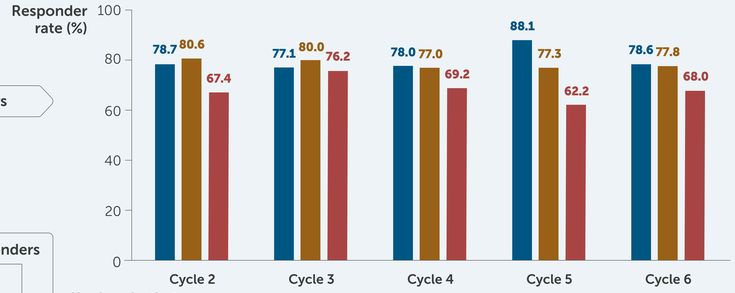
(a) Proportions of MG-ADL, MGC and QMG responders and non-responders to RLZ treatment at Cycle 1



Responders

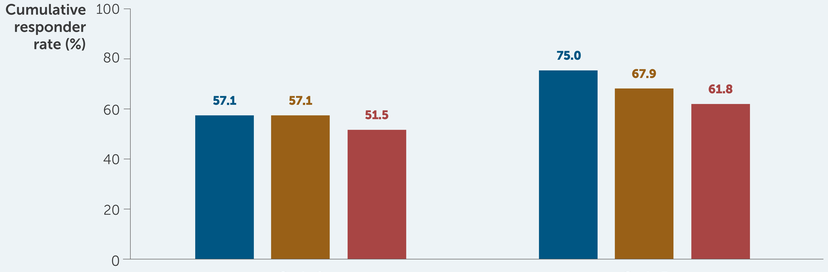
Non-responders

(b) Subsequent response rates were high among RLZ responders at Cycle 1



Number of patients	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6
MG-ADL	94	70	59	42	28
MGC	93	70	61	44	27
QMG	86	63	52	37	25

(c) High response rates at Cycle 2 and Cycle 3 were observed among patients who did not respond at Cycle 1



Number of patients with ≥3 cycles	Cycle 2	Cycle 3
MG-ADL	28	28
MGC	28	28
QMG	33	34

Summary and conclusions

This pooled analysis assessed the consistency of response across repeated cycles of rozanolixizumab treatment among Cycle 1 responders and the subsequent outcomes of Cycle 1 non-responders

Among Cycle 1 responders, MG-ADL, MGC and QMG response rates remained high over Cycles 2–6

Among Cycle 1 non-responders, >50% responded to a second cycle of treatment across the MG-ADL, MGC and QMG scales, and response rates remained high among patients who had a third cycle

Patients receiving rozanolixizumab who responded in the first treatment cycle demonstrated a consistent response rate over multiple cycles, while initial non-responders may benefit from additional rozanolixizumab treatment cycles

Table 1 Baseline demographic and patient characteristics (efficacy pool)

	RLZ total N=127
Age, years, mean (SD)*	**50.6** (16.2)
Sex, female, n (%)	**76** (59.8)
Thymectomy at baseline, yes, n (%)[†]	**55** (43.3)
AChR Ab+, n (%)[†,‡]	**115** (90.6)
MuSK Ab+, n (%)[†,‡]	**12** (9.4)
MG-ADL score at baseline, mean (SD)	**8.8** (3.4)
QMG score at baseline, mean (SD)	**16.0** (3.8)
Duration of disease, years, mean (SD)	**8.2** (8.6)

*Missing age was calculated as year of informed signed consent minus year of birth.
[†]Captured from historical data case report form.
[‡]One patient was both anti-AChR Ab+ and anti-MuSK Ab+.

Abbreviations: Ab+, autoantibody positive; AChR, acetylcholine receptor; COVID-19, coronavirus disease 2019; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IVIg, intravenous immunoglobulin; mAb, monoclonal antibody; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGC, Myasthenia Gravis Composite; MuSK, muscle-specific tyrosine kinase; OLE, open-label extension; PLEX, plasma exchange; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SC, subcutaneous; SD, standard deviation; TEAE, treatment-emergent adverse event.

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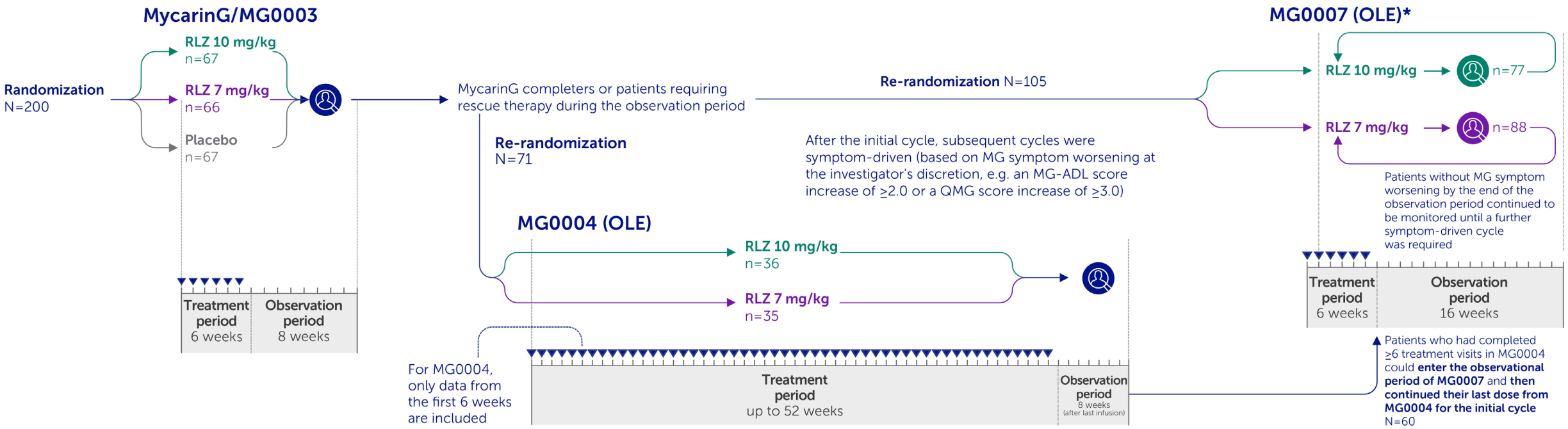
Figure 1 MycarinG and OLE study design



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MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab.

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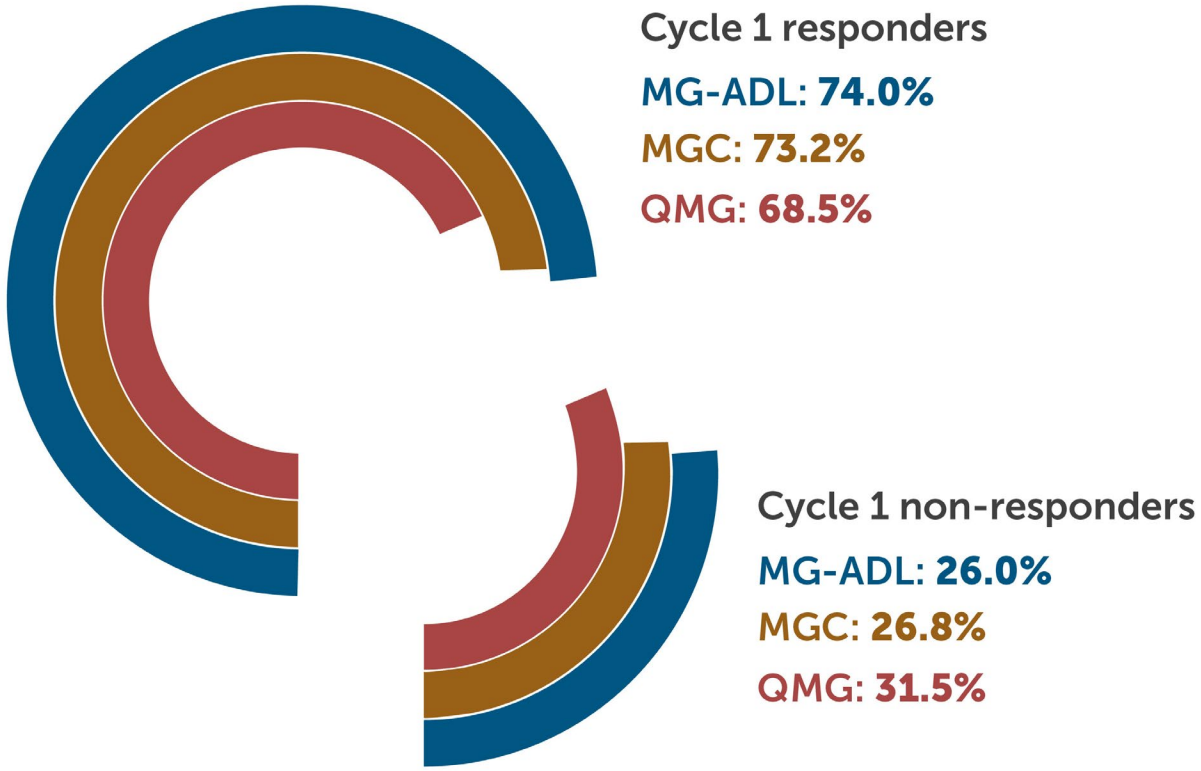

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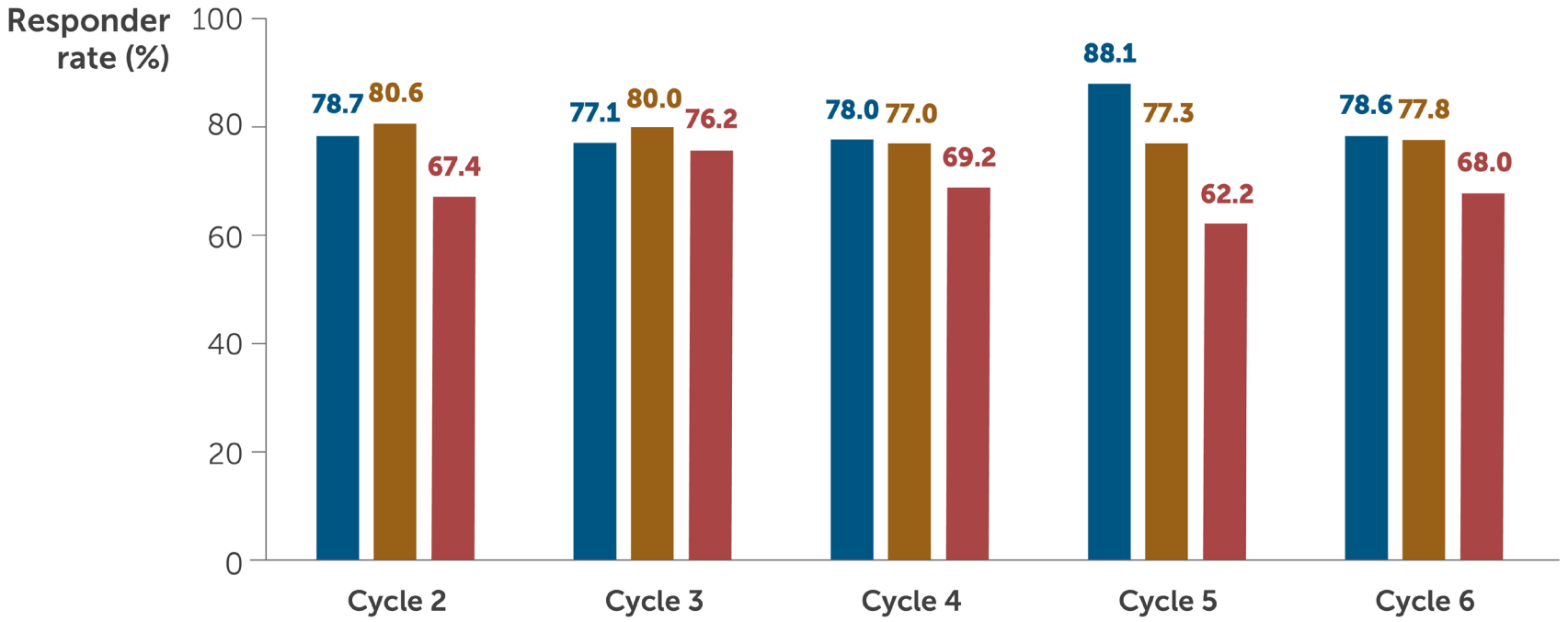

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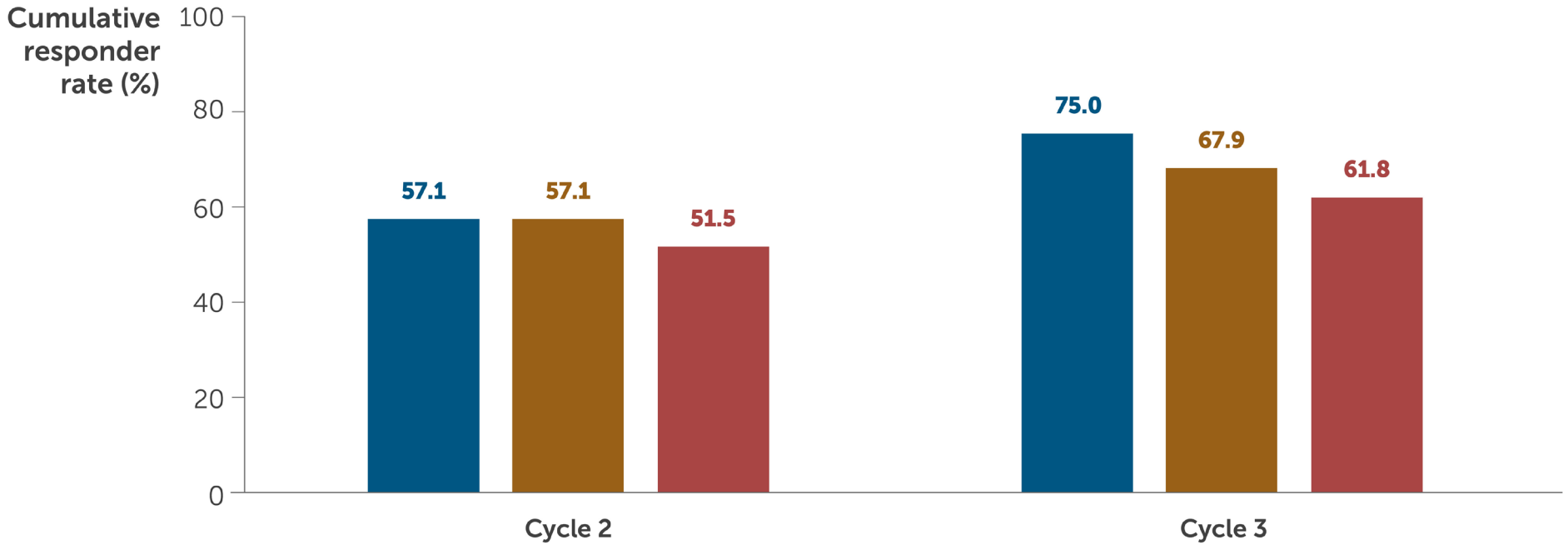

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