

Individual item-level analyses of myasthenia gravis-specific outcomes during zilucoplan treatment in RAISE and RAISE-XT

Joseph Post¹, Miriam Freimer², Channa Hewamadduma^{3,4}, M. Isabel Leite⁵, Angelina Maniaol⁶, Kimiaki Utsugisawa⁷, Michael D. Weiss⁸, Jos Bloemers⁹, Babak Boroojerdi¹⁰, Paul Mahoney¹¹, Natasa Savic¹², James F. Howard Jr.¹³ on behalf of the RAISE and RAISE-XT study teams

¹UCB, Charlotte, NC, USA; ²Department of Neurology, The Ohio State University Wexner Medical Center, Columbus, OH, USA; ³NIHR BRC Neuroscience Centre, Academic Neuromuscular Unit, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; ⁴Sheffield Institute for Translational Neuroscience (SITraN), School of Medicine and Population Health, University of Sheffield, Sheffield, UK; ⁵Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK; ⁶Department of Neurology, Oslo University Hospital, Oslo, Norway; ⁷Department of Neurology, Hanamaki General Hospital, Hanamaki, Japan; ⁸Department of Neurology, University of Washington Medical Center, Seattle, WA, USA; ⁹UCB, Breda, The Netherlands; ¹⁰UCB, Monheim, Germany; ¹¹UCB, Slough, UK; ¹²UCB, Bulle, Switzerland; ¹³Department of Neurology, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

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Introduction

- Patients with gMG experience fluctuating, fatigable muscle weakness that may affect ocular, bulbar, respiratory and proximal muscles, leading to a diverse range of symptoms that can impact health-related quality of life^{1,2}
- Zilucoplan is a small (15-amino acid) potent macrocyclic peptide complement C5 inhibitor approved for the treatment of adults with anti-AChR Ab+ gMG^{3,4}
- In the Phase 3 RAISE study (NCT04115293), zilucoplan showed statistically significant and clinically meaningful improvements in MG-specific outcomes in patients with anti-AChR Ab+ gMG⁴
 - These improvements were sustained over 120 weeks in the Phase 3 OLE study, RAISE-XT (NCT04225871)⁵
- This *post hoc* analysis assessed change in individual item scores for MG-ADL, QMG and MG-QoL15r**

Methods

- In RAISE, adults with MGFA Clinical Class II–IV anti-AChR Ab+ gMG were randomized to self-administer once-daily subcutaneous zilucoplan 0.3 mg/kg or placebo⁴
- Adults who completed RAISE could enter RAISE-XT to receive once-daily zilucoplan 0.3 mg/kg⁵
 - The primary outcome of RAISE-XT was incidence of TEAEs
- Analyses of MG-ADL, QMG and MG-QoL15r from the RAISE and RAISE-XT (interim data cutoff: November 11, 2023) studies included:

Table 1 Across all MG-ADL and QMG items assessed, zilucoplan treatment resulted in a greater proportion of patients showing improvement or no symptoms versus placebo at Week 12 (RAISE)

Percentage of patients showing improvement or no symptoms

0 to <20%	20 to <40%	40 to <60%	60 to <80%	80 to 100%
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(a) MG-ADL

	Placebo N=88	Zilucoplan 0.3 mg/kg N=86
MG-ADL item, % (n/N)		
Chewing	49.4 (42/85)	71.4 (60/84)
Swallowing	55.3 (47/85)	71.4 (60/84)
Talking	57.6 (49/85)	73.8 (62/84)
Breathing	38.8 (33/85)	52.4 (44/84)
Double vision	50.6 (43/85)	66.7 (56/84)
Eyelid droop	48.2 (41/85)	65.5 (55/84)
Brush hair/teeth	52.9 (45/85)	58.3 (49/84)
Rise from chair	43.5 (37/85)	63.1 (53/84)

(b) QMG

	Placebo N=88	Zilucoplan 0.3 mg/kg N=86
QMG item, % (n/N)		
Double vision	35.7 (30/84)	51.8 (43/83)
Ptosis	50.0 (42/84)	65.1 (54/83)
Facial muscles	58.3 (49/84)	66.3 (55/83)
Swallowing 4 oz. water	76.2 (64/84)	83.1 (69/83)
Speech following counting	72.6 (61/84)	79.5 (66/83)
Forced vital capacity	63.1 (53/84)	74.7 (62/83)
R arm outstretched	26.2 (22/84)	43.4 (36/83)
L arm outstretched	25.0 (21/84)	41.0 (34/83)
R hand grip (male)	19.0 (8/42)	27.3 (9/33)
R hand grip (female)	19.0 (8/42)	26.0 (13/50)
L hand grip (male)	40.5 (17/42)	54.5 (18/33)
L hand grip (female)	31.0 (13/42)	46.0 (23/50)
R leg outstretched	22.6 (19/84)	45.8 (38/83)
L leg outstretched	22.6 (19/84)	47.0 (39/83)
Head lifted	34.5 (29/84)	54.2 (45/83)

Abbreviations: anti-AChR Ab+, anti-acetylcholine receptor antibody-positive; C5, component 5; CFB, change from baseline; gMG, generalized myasthenia gravis; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MG-QoL15r, Myasthenia Gravis Quality of Life 15-item revised; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; TEAE, treatment-emergent adverse event.

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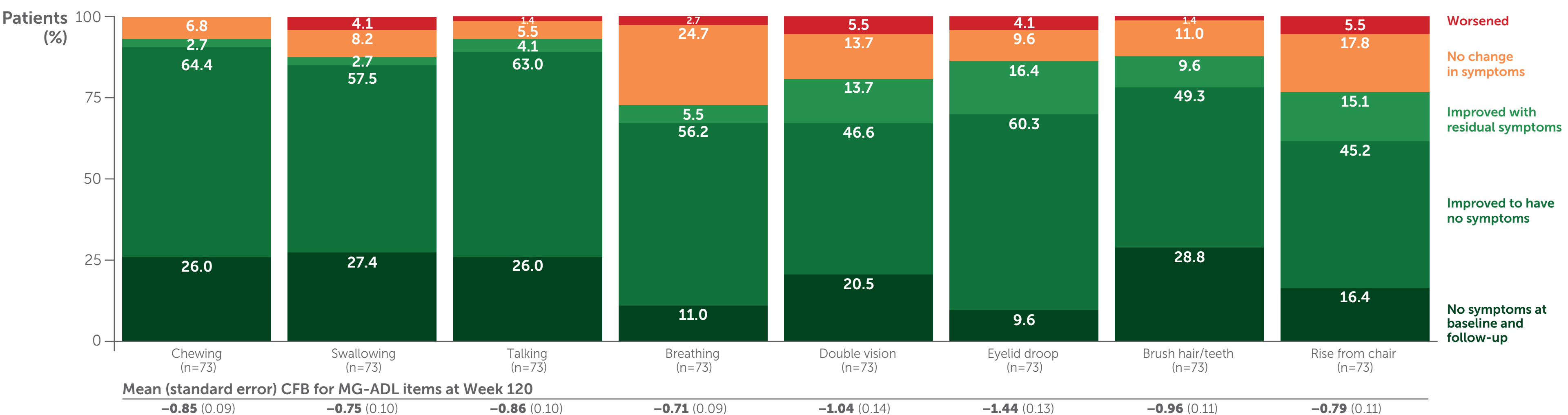
- The proportion of patients showing no symptoms, improvement, and no change from baseline to Week 12 (RAISE), and from double-blind baseline to Week 120 (RAISE-XT)
- Change from double-blind baseline (CFB) to Week 120

Results

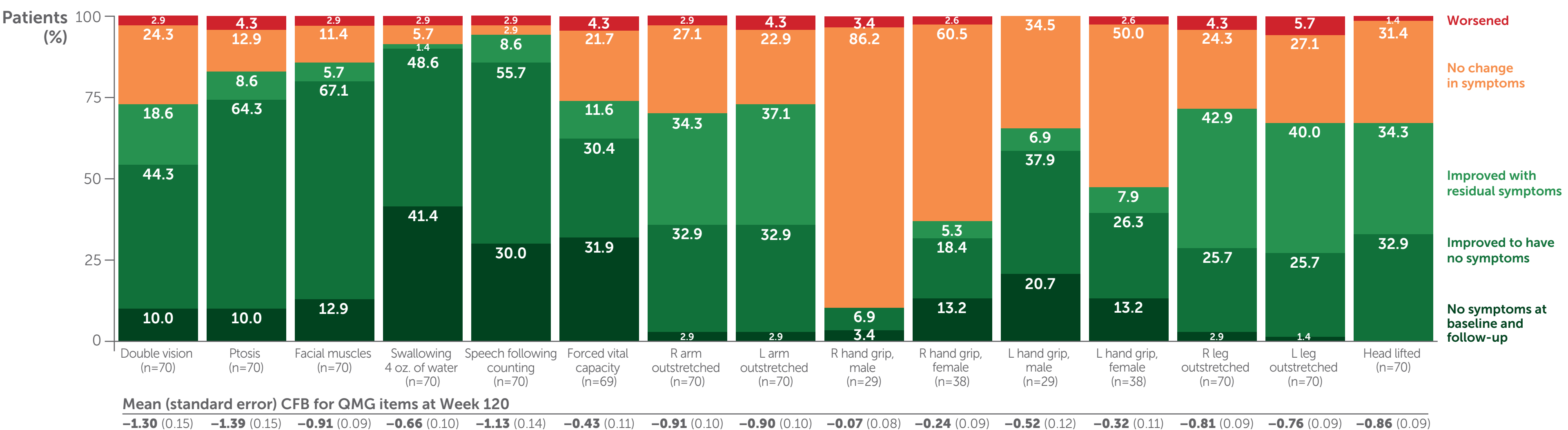
- Overall, 200 patients enrolled in RAISE-XT; 183 received either zilucoplan 0.3 mg/kg or placebo in the double-blind studies⁵
- In RAISE, treatment with zilucoplan resulted in a greater proportion of patients showing improvement or no symptoms versus placebo at Week 12 across all MG-ADL and QMG items assessed (**Table 1**)
 - Similar results were observed for MG-QoL15r
- In RAISE-XT, the proportion of patients demonstrating improvements or no symptoms further increased and was sustained through to Week 120
- The items with the highest proportion of patients showing improvement or no symptoms at Week 120 were (**Figure 1**):
 - MG-ADL items: chewing and talking (both 93.2%); swallowing and brush hair/teeth (both 87.7%)
 - QMG items: swallowing 4 oz. water (91.4%), facial muscles (85.7%) and speech following counting from 1 to 50 (94.3%)
 - MG-QoL15r items: Trouble grooming and loss of personal independence (both 76.5%); trouble eating (88.2%) and difficulty speaking (86.8%)
- TEAEs occurred in 97.0% (n=194/200, RAISE-XT) of patients
 - The two most frequently occurring TEAEs were COVID-19 (35.5% [71/200]) and MG worsening (29.5% [59/200])

Figure 1 Most patients had improved MG-ADL, QMG and MG-QoL15r item scores at Week 120 (RAISE-XT)

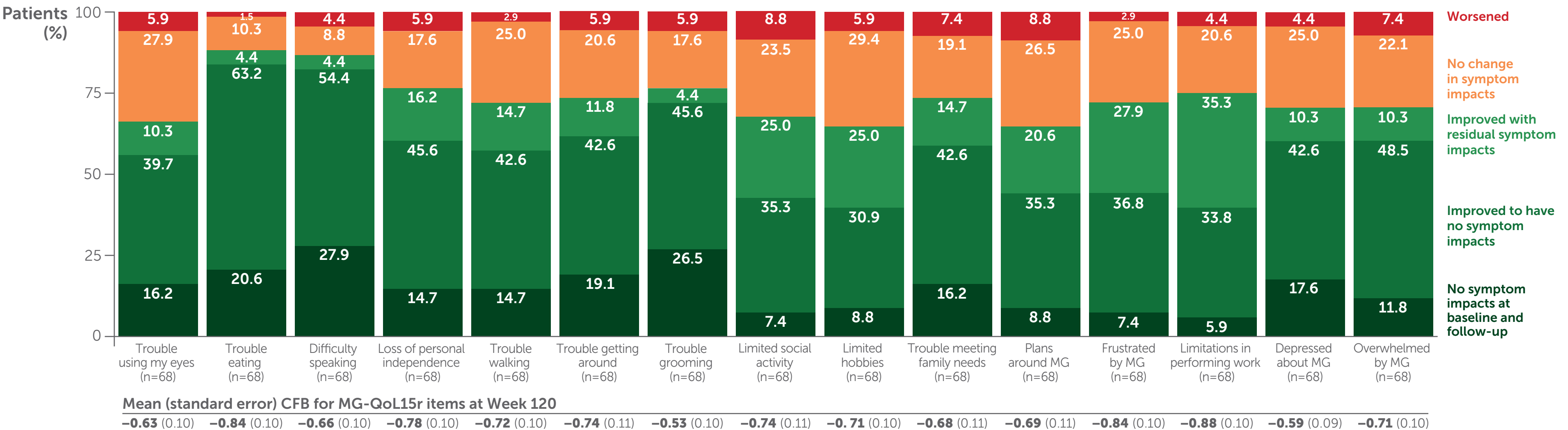
(a) MG-ADL



(b) QMG



(c) MG-QoL15r



No patients had worsened scores for chewing (MG-ADL) and L hand grip (male; QMG). MG-ADL and QMG item severity scores range from 0 to 3 and MG-QoL15r items range from 0 to 2. Higher scores correspond to more severe impairment. A decrease from baseline indicates improvement.

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