

Introduction

- Facioscapulohumeral muscular dystrophy (FSHD) is a relentlessly progressive disease that leads to significant disability and severely impacts patients' quality of life.
- 82% of people with FSHD have moderate to severe difficulty with upper extremities.¹
- Reachable workspace (RWS) is a 3-dimensional assessment of upper limb function; the Microsoft Kinect system is used to track arm motion and measure relative surface area (RSA), a continuous variable normalized to an individual's arm length.
- In Phase 2 studies of losmapimod, a p38 α / β MAPK inhibitor under development for FSHD, efficacy endpoints included RWS, in dominant and non-dominant arms (arm dominance identified by patient report).
- This Phase 2 post-hoc analysis explores averaging RWS measurements across both arms.

Methods

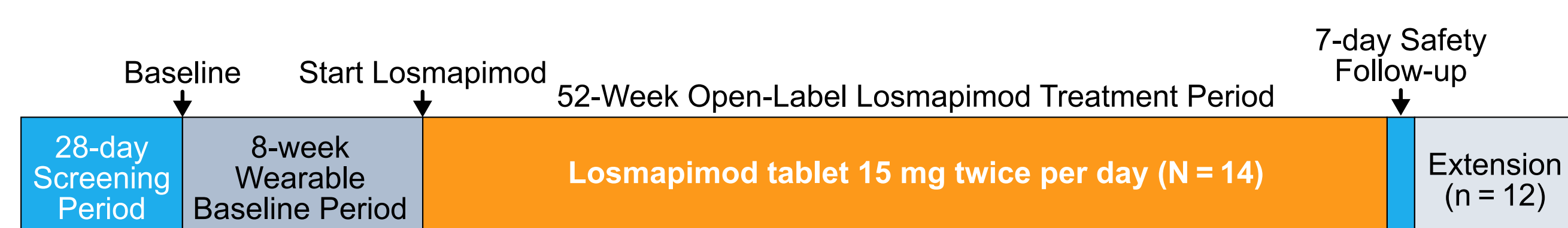
Main Inclusion / Exclusion Criteria

- **Inclusion Criteria:** age 18-65 years; genetically confirmed diagnosis of FSHD1; Ricci score 2-4; Presence on whole-body muscle magnetic resonance imaging (MRI) of STIR+ muscle safely accessible by biopsy needle
- **Exclusion Criteria:** medical conditions that can confound results of the study; contraindications to MRI; contraindications to muscle biopsy

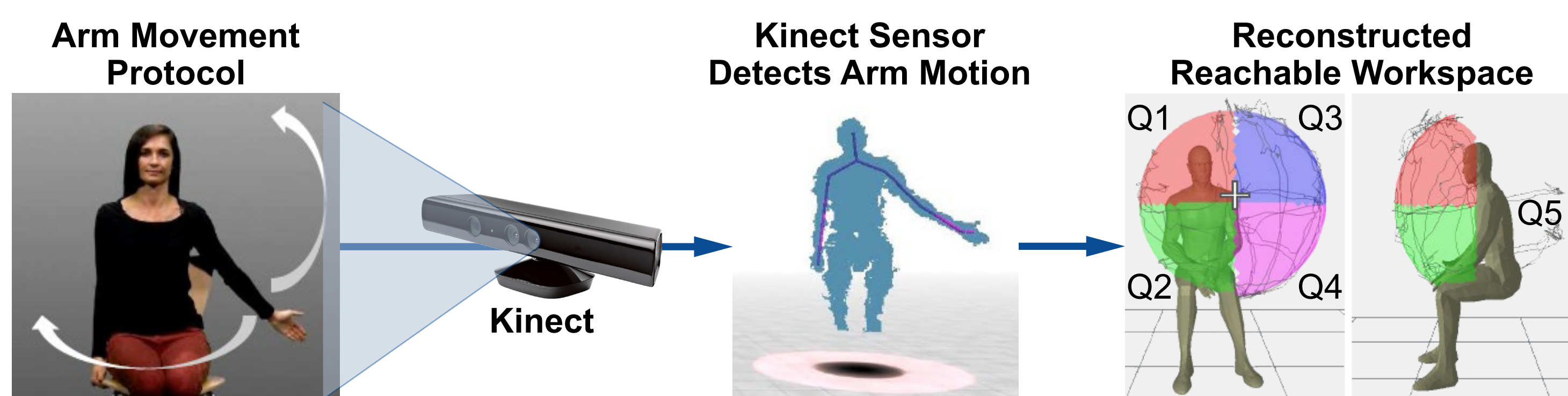
ReDUX4: 48-Week, Phase 2, Randomized Placebo-Controlled Study



Open-Label Study (OLS): 52-week, Phase 2 Study



Reachable Workspace (RWS)



- Individuals sit in front of the Microsoft Kinect sensor and undergo a standardized arm movement protocol under supervision of a clinical evaluator.
- Data from the movement protocol are centrally analyzed and expressed as RSA for five different quadrants (Q1-Q5) for each arm, with the shoulder joint serving as the origin.
- A longitudinal study in an FSHD patient population exhibited annual declines in RWS of approximately 3% (measured Q1-Q4) compared to baseline.³

Post-hoc Analyses

- RWS total RSA for each quadrant and across the five quadrants (scale for each quadrant: 0-0.25, scale for total score: 0-1.25) with and without 500 g wrist weights:
 - » Averaged across the dominant and non-dominant arms
 - » Compared with previously reported (ReDUX4 and OLS exploratory efficacy assessments) dominant-arm and non-dominant arm results^{4,5}
- ReDUX4 efficacy correlations by Spearman's rank correlation:
 - » RSA vs dynamometry assessments of shoulder abduction strength (ReDUX4 assessment at various timepoints including Week 48)
 - » RSA vs whole-body muscle MRI composite scores (ReDUX4 assessments at various timepoints including Week 48): lean muscle volume (LMV), muscle fat fraction (MFF), and muscle fat infiltration (MFI)

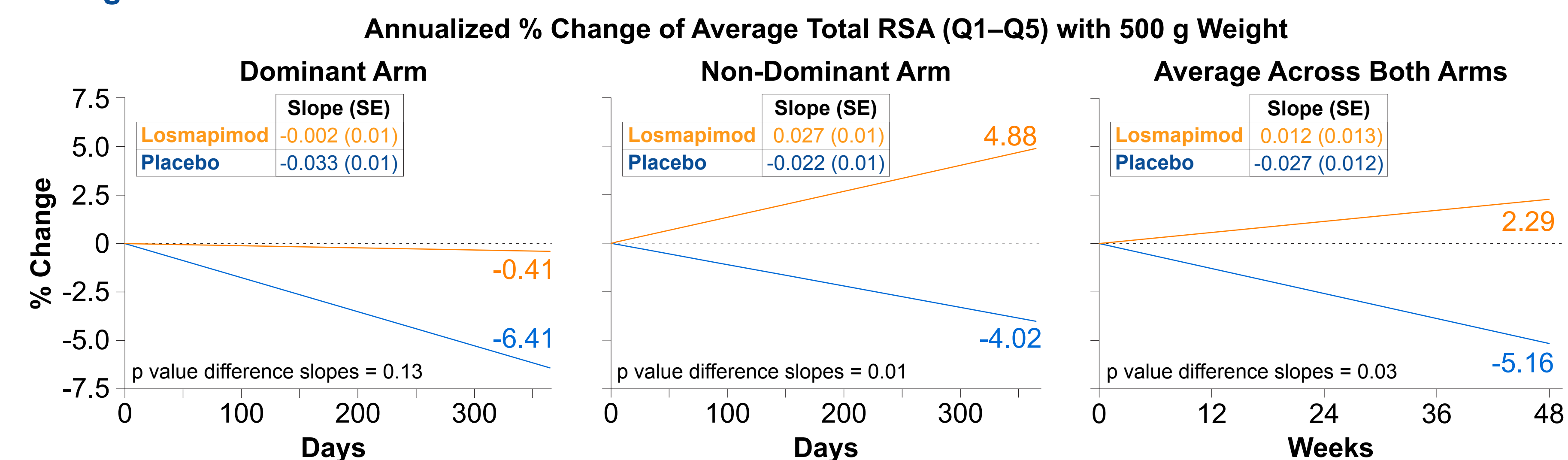
Study Demographics and Baseline Characteristics

	ReDUX4		OLS
	Placebo BID (N=40)	Losmapimod 15 mg BID (N=40)	Losmapimod 15 mg BID (N=14)
Completed, n (%)	38 (95.0%)	39 (97.5%)	14 (100%)
Discontinued, n (%)	2 (5.0%)	1 (2.5%)	0
Age (years)	Mean (SD)	45.7 (12.7)	45.7 (11.1)
D4Z4 Repeat Category, n (%)	1-3 Repeats	6 (15.0%)	3 (21.4%)
	4-9 Repeats	34 (85.0%)	11 (78.6%)
	2	0	0
	2.5	7 (17.5%)	5 (12.5%)
	3	18 (45.0%)	5 (35.7%)
	3.5	7 (17.5%)	2 (14.3%)
	4	8 (20.0%)	6 (42.9%)

Abbreviations: FSHD = Facioscapulohumeral muscular dystrophy; LMV = lean muscle volume; MFF = muscle fat fraction; MFI = muscle fat infiltration; MRI = magnetic resonance imaging; Q = quintant; RSA = relative surface area; RWS = reachable workspace. **References:** 1) Arjomand JB, et al. Facioscapulohumeral muscular dystrophy (FSHD) voice of the patient report. FSHD Society; November 5, 2020. 2) Tawil A. *Neurology*. 2023;100(17_supplement_2):3913. 3) Hatch MN, et al. *Neuromuscul Disord*. 2019;29(7):503-13. 4) Kools J, et al. *Neurology*. 2022;98(18_supplement):2826. 5) Tawil R, et al. *Neurology*. 2022;98(18_supplement):2824.

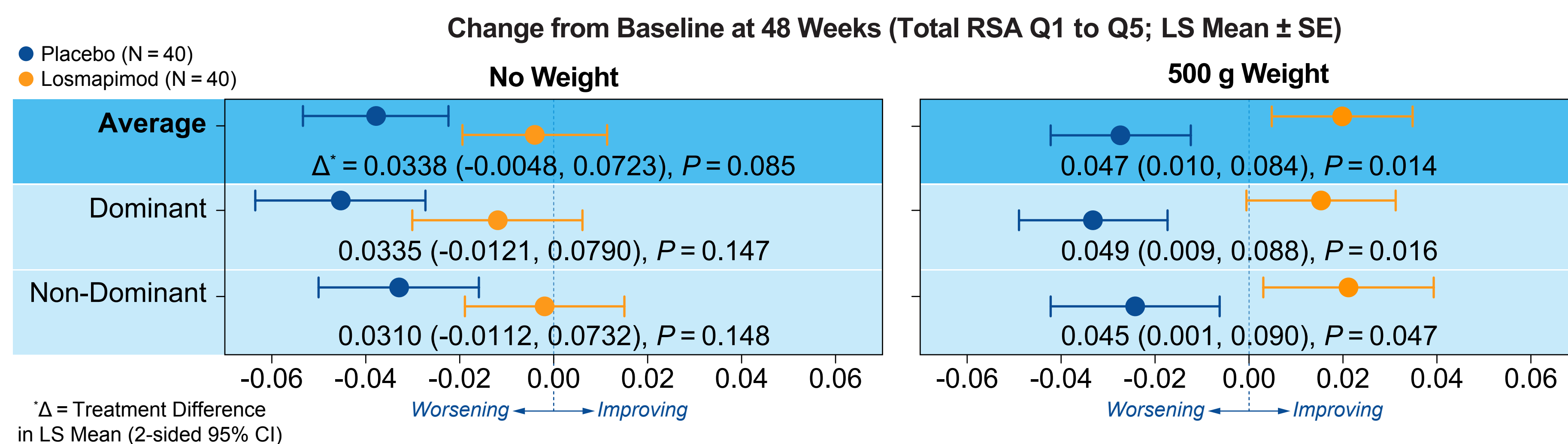
Results

ReDUX4: Losmapimod Showed Treatment Benefits in RWS Annualized Rates of Change Averaged Across Both Arms

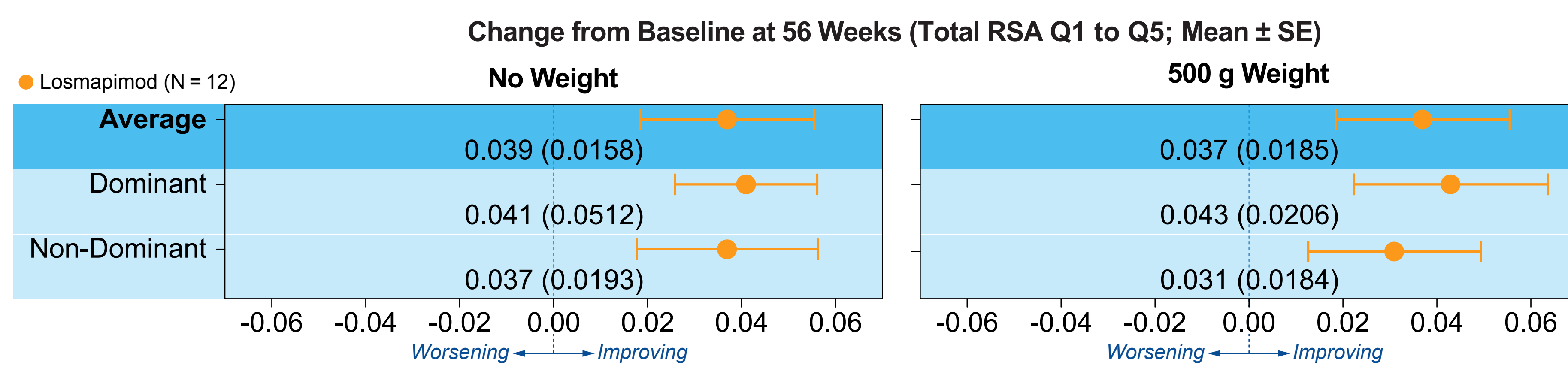


Note: Annualized rate of change (%) was calculated using a linear mixed-effects model to estimate percent change per year (y-axis). Dominant-arm and non-dominant-arm figures adapted and updated from previously reported results.² Excluded two data points due to software anomaly on dominant total RSA (Q1 to Q5) with 500 g weight at Weeks 12 and 48.

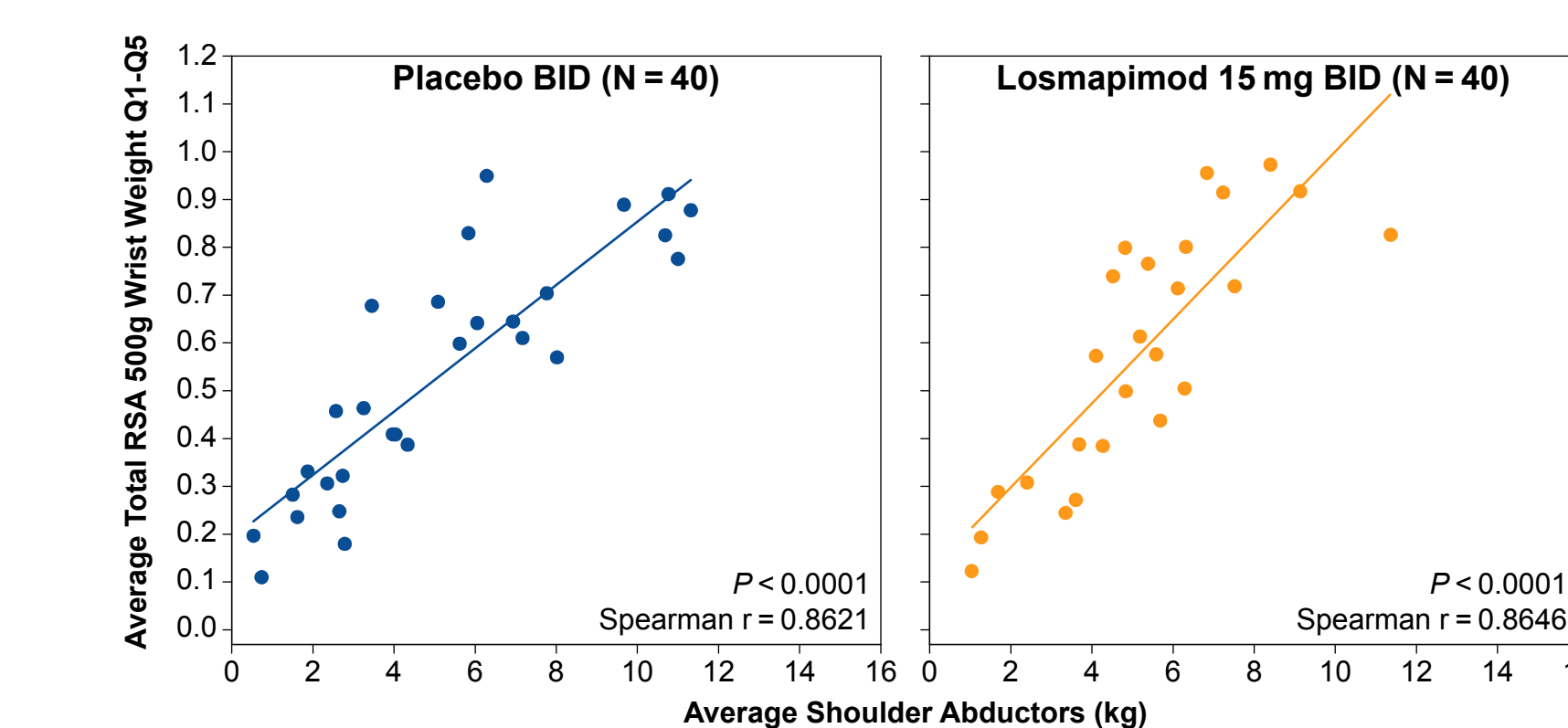
ReDUX4: Losmapimod Treatment Benefit Shown by RSA Averaged Across Both Arms Appears Consistent with Individual Arm Assessments



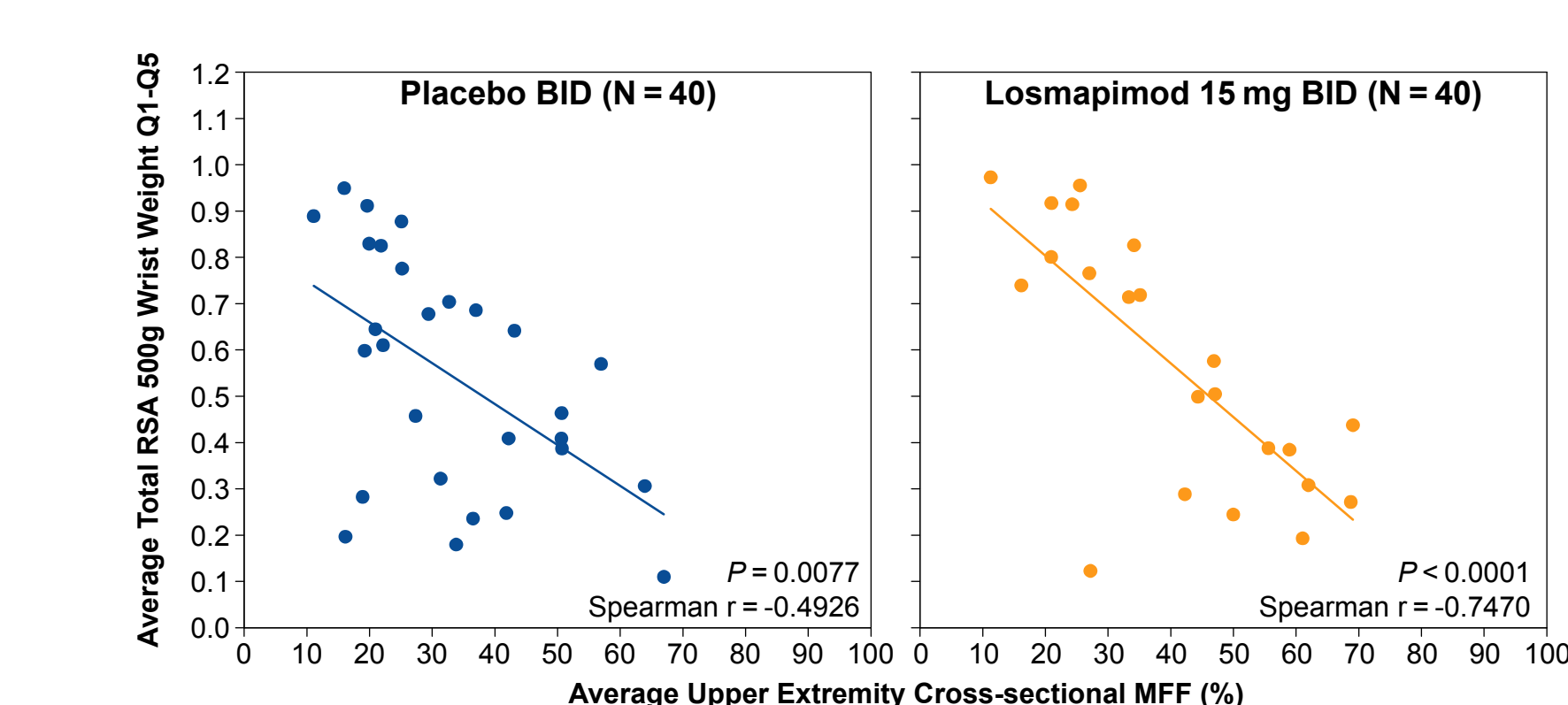
Open-Label Study: Change from Baseline in RSA Averaged Across Both Arms Is Similar to Dominant-Arm Improvement



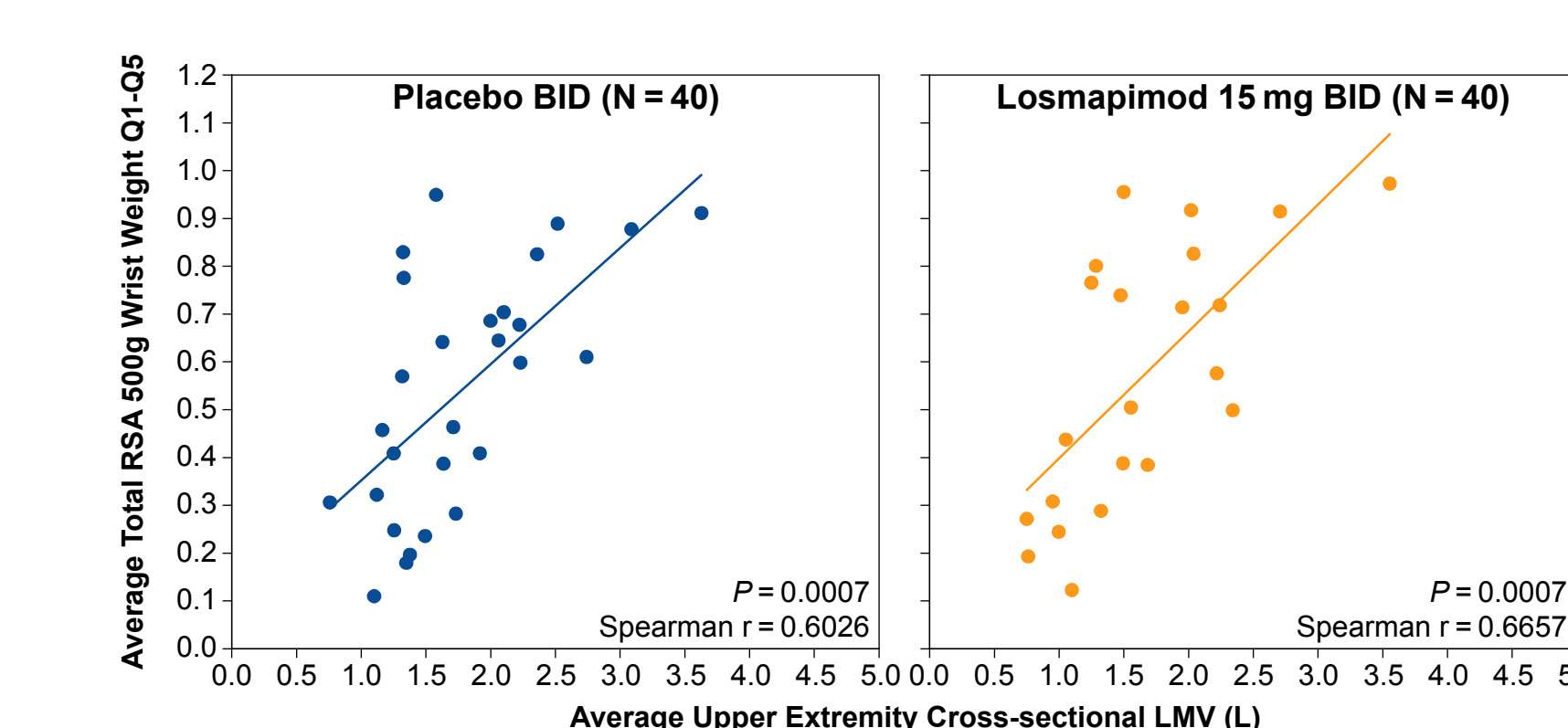
ReDUX4: RSA Averaged Across Both Arms Correlates Strongly with Shoulder Strength



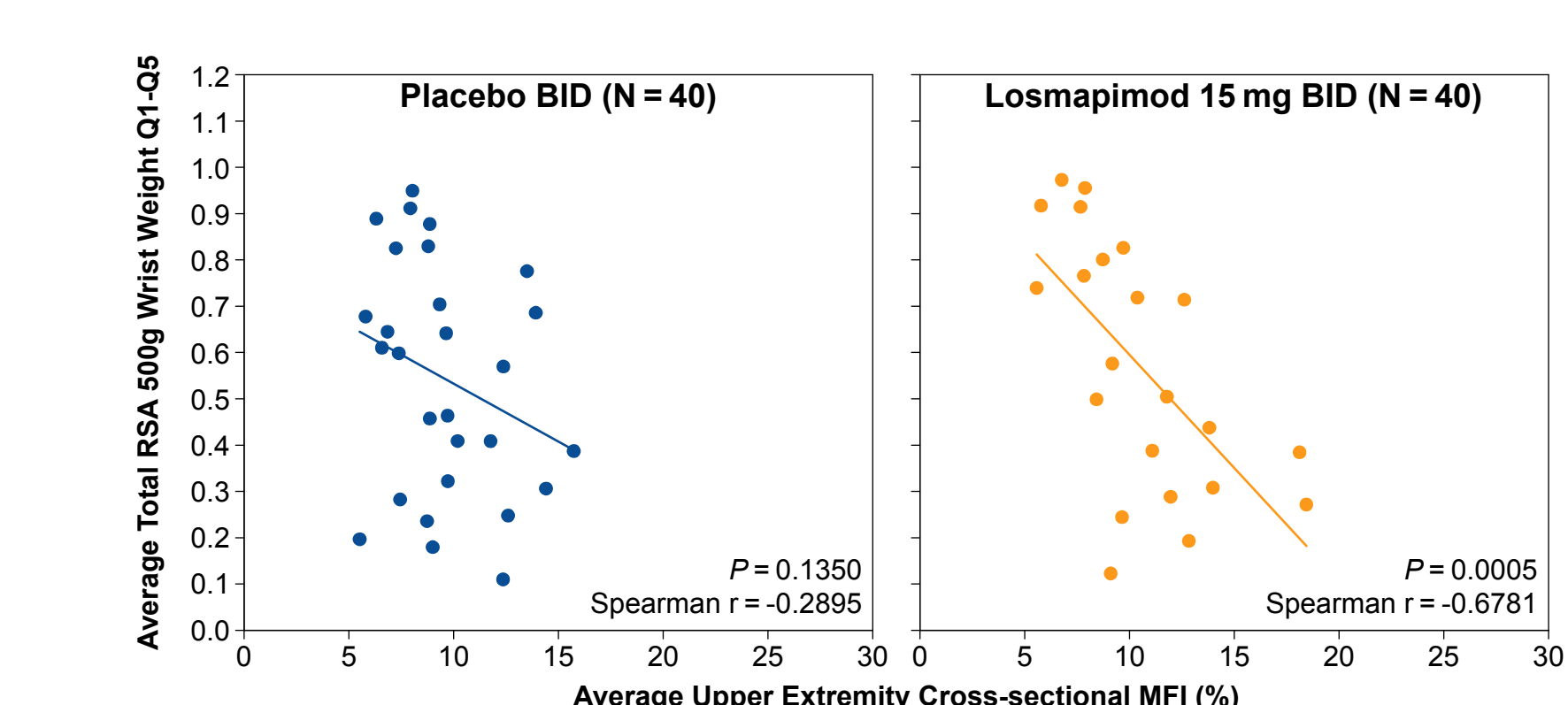
ReDUX4: RSA Averaged Across Both Arms Correlates Moderately-to-Strongly with MFF



ReDUX4: RSA Averaged Across Both Arms Correlates Moderately with LMV



ReDUX4: RSA Averaged Across Both Arms Correlates with MFI in Losmapimod-Treated Patients



Conclusions

- These results support the potential benefits of using total RSA with weight averaged over both arms as a clinical endpoint in FSHD.
 - » Averaging scores over both arms may provide a more complete assessment of patient function than individual arm assessments.
- This bilateral assessment of RSA provides a robust measure of FSHD functional impairment and disease progression, aligning with other objective measures of muscle strength and structure.

Acknowledgments

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