

Cardiosphere-derived cells for the treatment of Duchenne Cardiomyopathy: Six-Month Results of the Halt cardiomyopathy ProgrESSION [HOPE]-Duchenne Trial

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Introduction

- HOPE-Duchenne (Halt cardiomyopathy ProgrESSION in Duchenne, NCT02485938) is a randomized, open-label trial to test safety and explore efficacy of a single dose of intracoronary CAP-1002 in DMD cardiomyopathy.
- CAP-1002 is a cell-based therapeutic comprised of allogeneic cardiosphere-derived cells (CDCs) with immunomodulatory, anti-fibrotic, and regenerative properties.
- In the *mdx* mouse DMD model, intramyocardial CDCs improve cardiac function, but also act systemically via secretion of exosomes to increase exercise capacity, and ultimately improve long-term survival.

Methods

- Cardiac magnetic resonance imaging (MRI) and Performance of the Upper Limb (PUL) tests were used to assess efficacy in this population with advanced myopathy.

Patient Enrollment

- Twenty-five males who met all eligibility criteria (age ≥12; myocardial scar in ≥4 left ventricular segments by MRI and EF > 35%; systemic corticosteroid regimen ≥6 months) were randomized 1:1 to either CAP-1002 (n=13) or control (n=12).

- Both groups received standard medical care.

- Mean age of enrolled subjects was 18 years, and 68% were wheelchair-dependent.

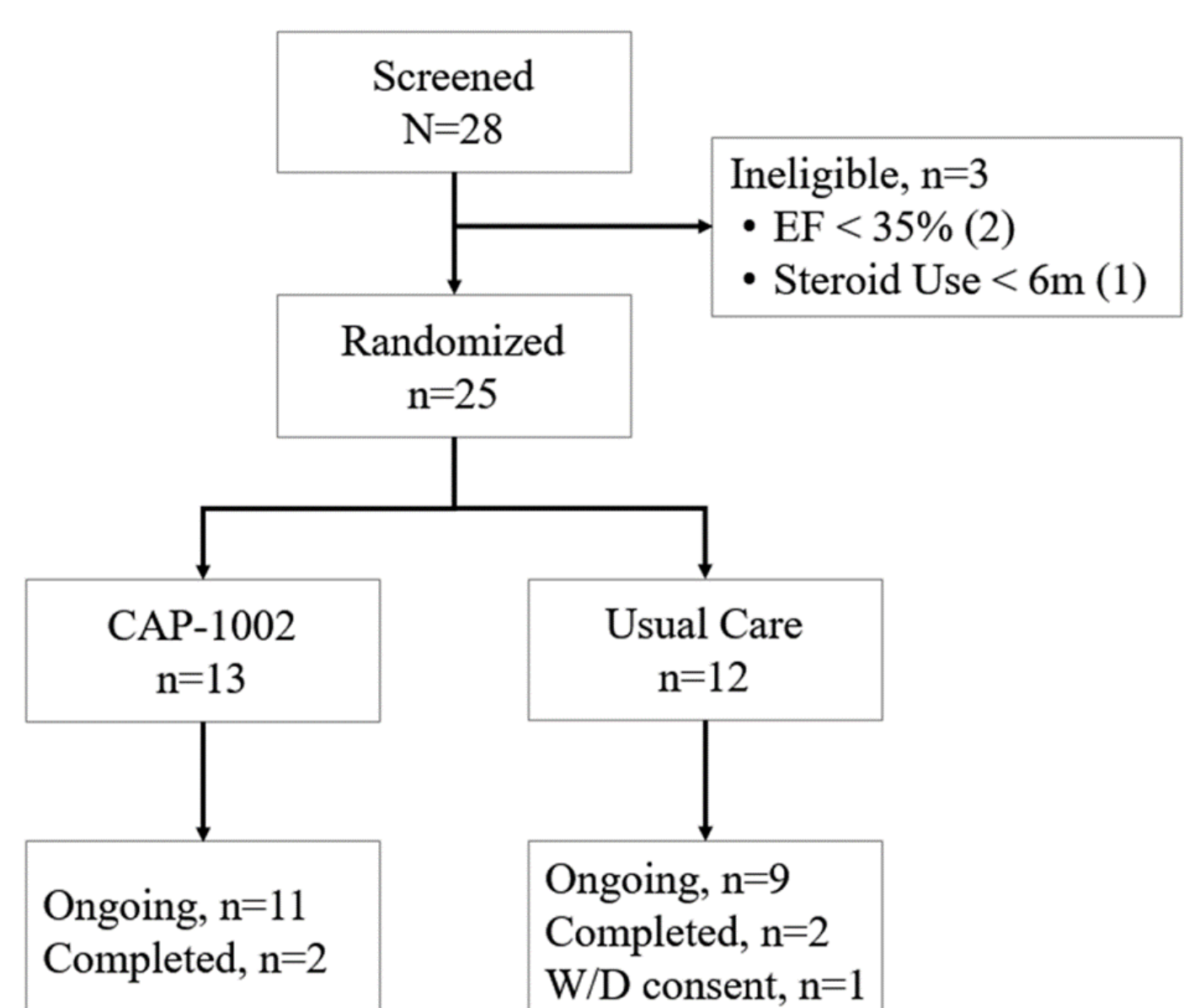


Fig. 1 Trial profile. Summary of patient disposition in the 6-month interim analysis

Demographics, Baseline Characteristics, and Safety

Table 1. Demographics and baseline characteristics

Parameter	Usual Care (N=12)	CAP-1002 (N=13)	All Patients (N=25)
Age (years)	16.9 (2.7)	18.7 (3.5)	17.8 (3.2)
Race [n (%)]			
White	10 (83.3)	11 (84.6)	21 (84.0)
Black or African American	1 (8.3)	1 (7.7)	2 (8.0)
Asian	0 (0.0)	1 (7.7)	1 (4.0)
Other (White, Asian, Filipino)	1 (8.3)	0 (0.0)	1 (4.0)
Ethnicity [n (%)]			
Not Hispanic or Latino	11 (91.7)	11 (84.6)	22 (88.0)
Hispanic or Latino	1 (8.3)	2 (15.4)	3 (12.0)
DMD Genetic Analysis [n (%)]			
Exon Deletion	5 (41.7)	12 (92.3)	17 (68.0)
Point Mutation	3 (25.0)	1 (7.7)	4 (15.4)
Other Exome Shift	1 (8.3)	0 (0.0)	1 (4.0)
Wheelchair Use [n (%)]			
Never	1 (8.3)	1 (7.7)	2 (8.0)
Rarely	2 (16.7)	1 (7.7)	3 (12.0)
Occasionally	8 (66.7%)	10 (76.9%)	18 (72.0)
Frequently	0 (0.0)	1 (7.7)	1 (4.0)
Always	1 (8.3)	0 (0.0)	1 (4.0)
Scar Size (%)			
Mean (SD)	21.39 (10.75)	17.55 (6.79)	19.39 (8.93)
CV (coefficient of variation)	50.28	38.98	47.92
ACE Inhibitor	48.39 (7.489)	49.58 (6.687)	49.01 (6.959)
Angiotensin II Antagonist	3 (25.0%)	2 (15.4%)	5 (20.0%)
Beta Blocker	7 (58.3%)	6 (46.2%)	13 (52.0%)
Diastolic antagonist	10 (83.3%)	9 (69.2%)	19 (76.0%)
Systemic Corticosteroid	12 (100.0%)	13 (100.0%)	25 (100.0%)
Deflazacort	11 (91.7%)	9 (69.2%)	20 (80.0%)
Prednisone/Prednisolone	1 (8.3%)	4 (30.8%)	5 (20.0%)
Hydrocortisone	0 (0.0%)	2 (15.4%)	2 (8.0%)
Exon 51-Skipping Therapy	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 2. Safety Outcome Measures

Parameter	Usual Care (N=12)	CAP-1002 (N=13)
Safety Endpoints		
Prior procedural TMI grade flow D-2	0	0
Prior procedural unexpected death	0	0
Prior procedural MACE	0	0
Sudden unexpected death	0	0
MACE	0	0
CV Hospitalization	0	0
Ventricular Tachycardia > 30 seconds	0	0
Cardiac Biomarker elevation*	2	13
DSA, MRI ≥ 1000	0	1
DSA, MRI ≥ 5000	0	0
Deaths	0	0
Any Treatment-Emergent Adverse Event (TEAE)	10 (83%)	11 (85%)
Severe TEAE	2 (17%)	1 (8%)
Serious Adverse Events (SAE)	1 (8%)	3 (23%)
Any drug-related TEAE	n/a	8 (62%)
Any procedure-related TEAE	n/a	7 (54%)
Discontinuation due to TEAE	0 (0%)	0 (0%)
Deaths	0 (0%)	0 (0%)

Table 3. Safety & Tolerability

Parameter	Usual Care (N=12)	CAP-1002 (N=13)
Related to treatment?		
Related to procedure?		
Related to product?		
Febrile reaction	No	Uncertain
Urinary tract infection	No	No
Fever and confusion	Uncertain	Uncertain
Ventricular fibrillation	Yes	No

Results

Cardiac Assessment

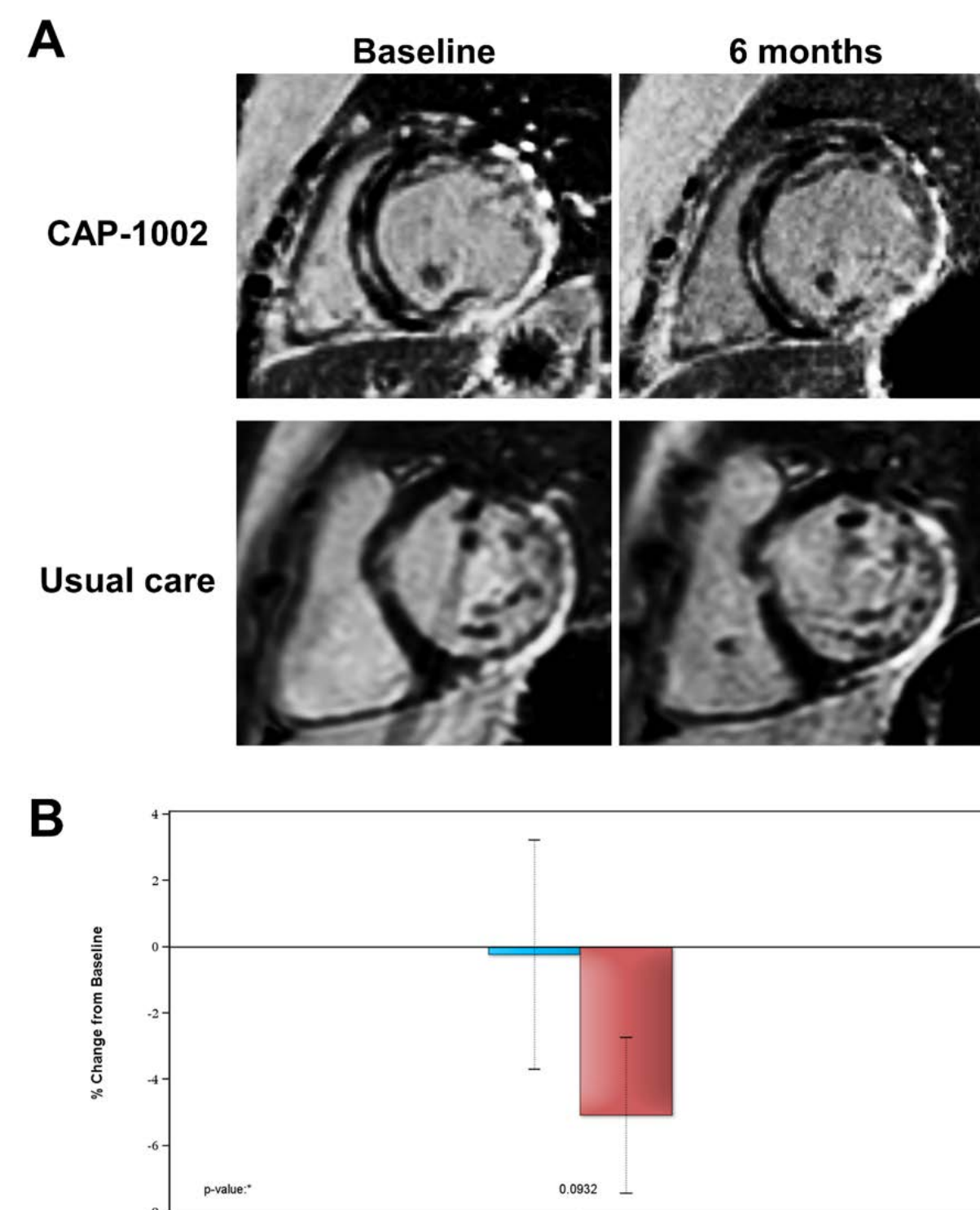


Fig. 2 Change in myocardial scar by LGE MRI. **A)** Short-axis images at end-diastole at baseline (left) and 6 months (right) from a patient treated with CAP-1002 (top row) and from a patient receiving usual care (bottom row). **B)** Relative change in myocardial scar (expressed as a percent of LV mass) from baseline to 6 months is shown for usual care (blue) and CAP-1002 treated (red) patients.

Table 4. Change in global myocardial scar by LGE MRI

Scar % of Myocardial Mass	n	Usual Care (N=11)	Median (min, max)	n	CAP-1002 (N=13)	Median (min, max)	p-value
Observed							
Baseline	11	21.58 (8.45)	22.30 (10.13, 34.32)	13	18.62 (9.72)	15.25 (7.73, 33.42)	0.4386
Month 6	11	21.90 (7.30)	21.39 (10.38, 31.09)	13	17.52 (8.84)	14.13 (6.38, 29.27)	
Δ from Baseline							
Month 6	11	-0.53 (2.86)	0.25 (-6.71, 2.88)	13	-1.11 (1.63)	-1.150 (-4.53, 1.22)	0.0911
% Change from Baseline							
Month 6	11	-0.23 (11.48)	1.82 (-23.9, 34.2)	13	-5.09 (8.48)	-4.78 (-34.5, 14.0)	0.0932

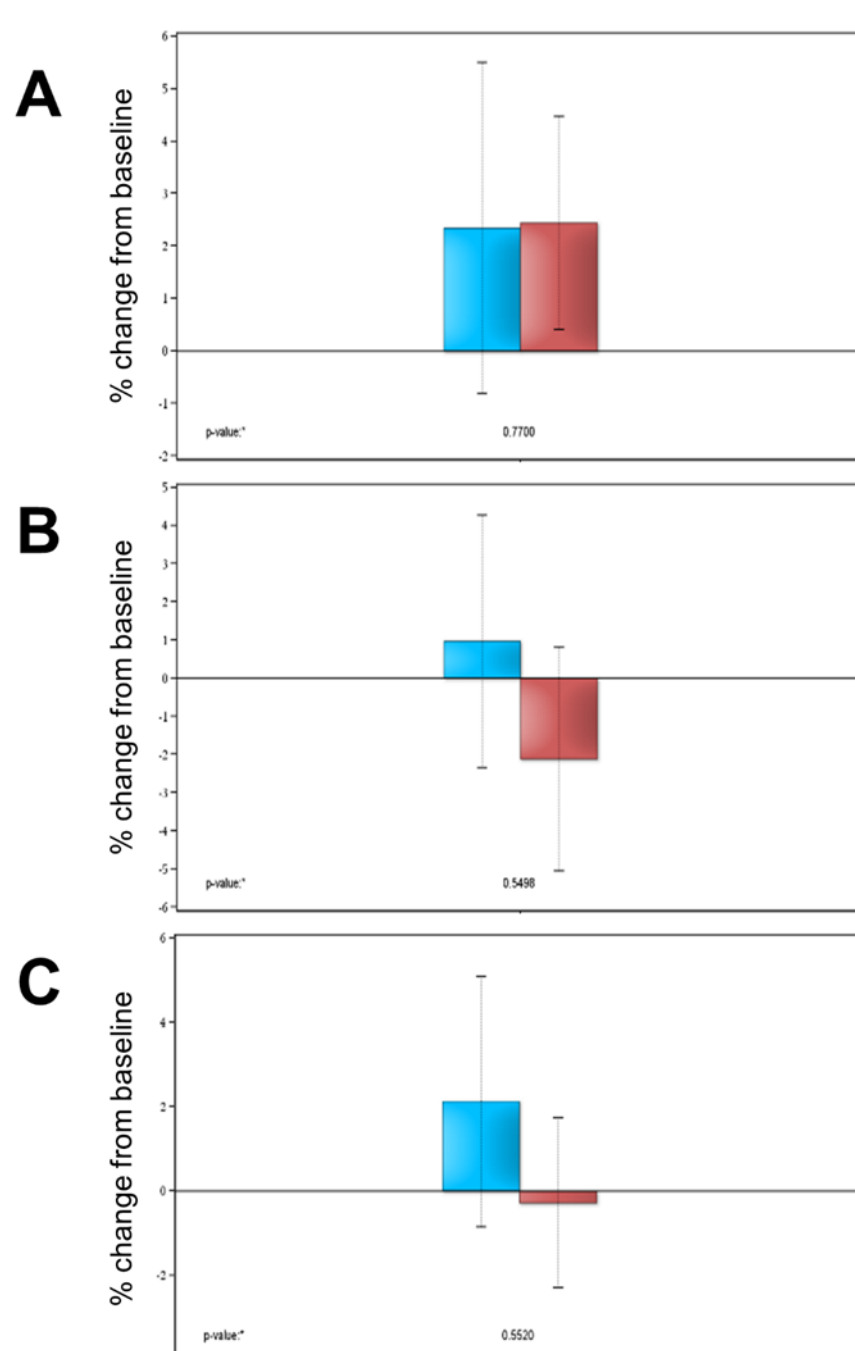


Fig. 3 Changes in LVEF and cardiac volumes by MRI. Relative change from baseline in **A)** LVEF, **B)** LVESV, and **C)** LVEDV is displayed for usual care (blue) and CAP-1002-treated (red) subjects.

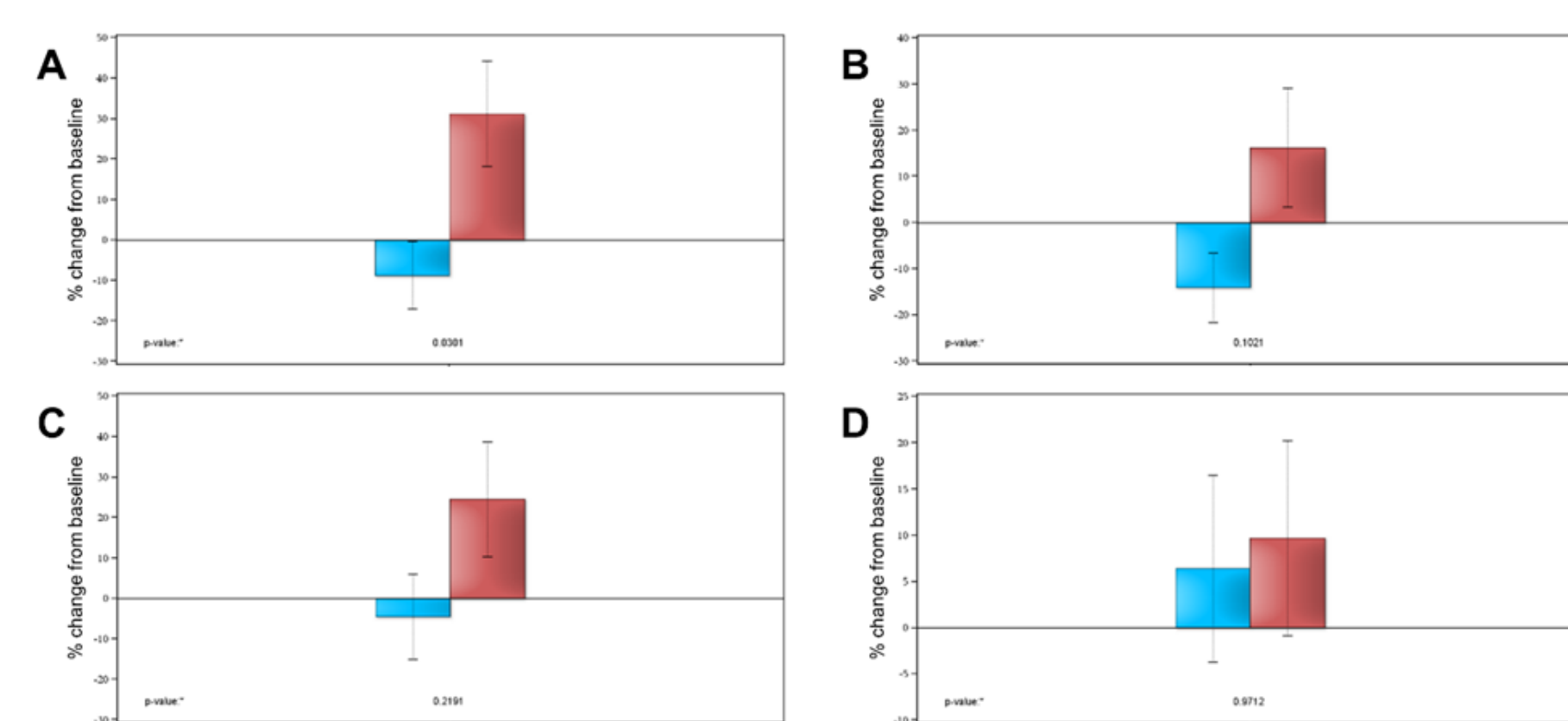


Fig. 4 Change in regional myocardial function by MRI. Relative change from baseline in LV systolic wall thickening in the **A)** inferior, **B)** anterior, **C)** lateral, and **D)** septal regions is displayed for usual care (blue) and CAP-1002-treated (red) subjects.

Assessments of Upper Limb Performance

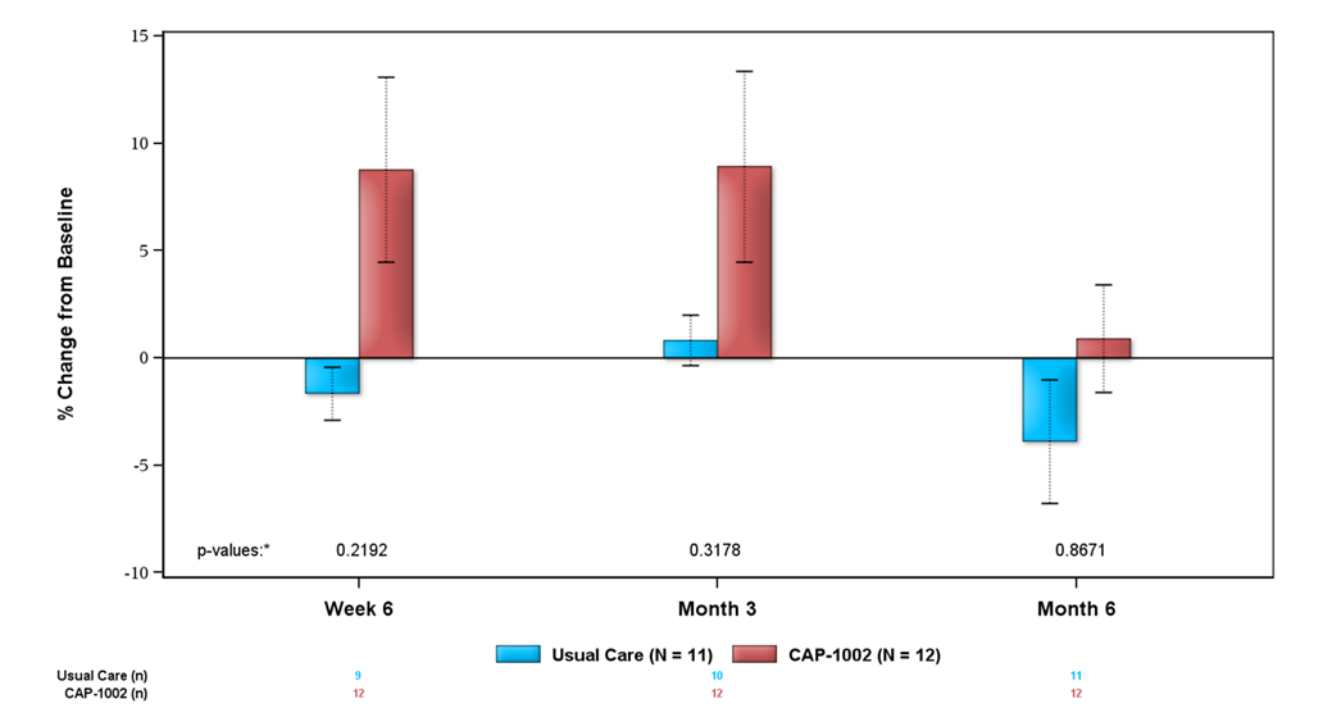


Fig. 5 Change in skeletal muscle function. Relative changes in PUL middle + distal dimensions from baseline to six weeks, three months, and six months is shown for usual care (blue) and CAP-1002-treated (red) patients in the mITT population.

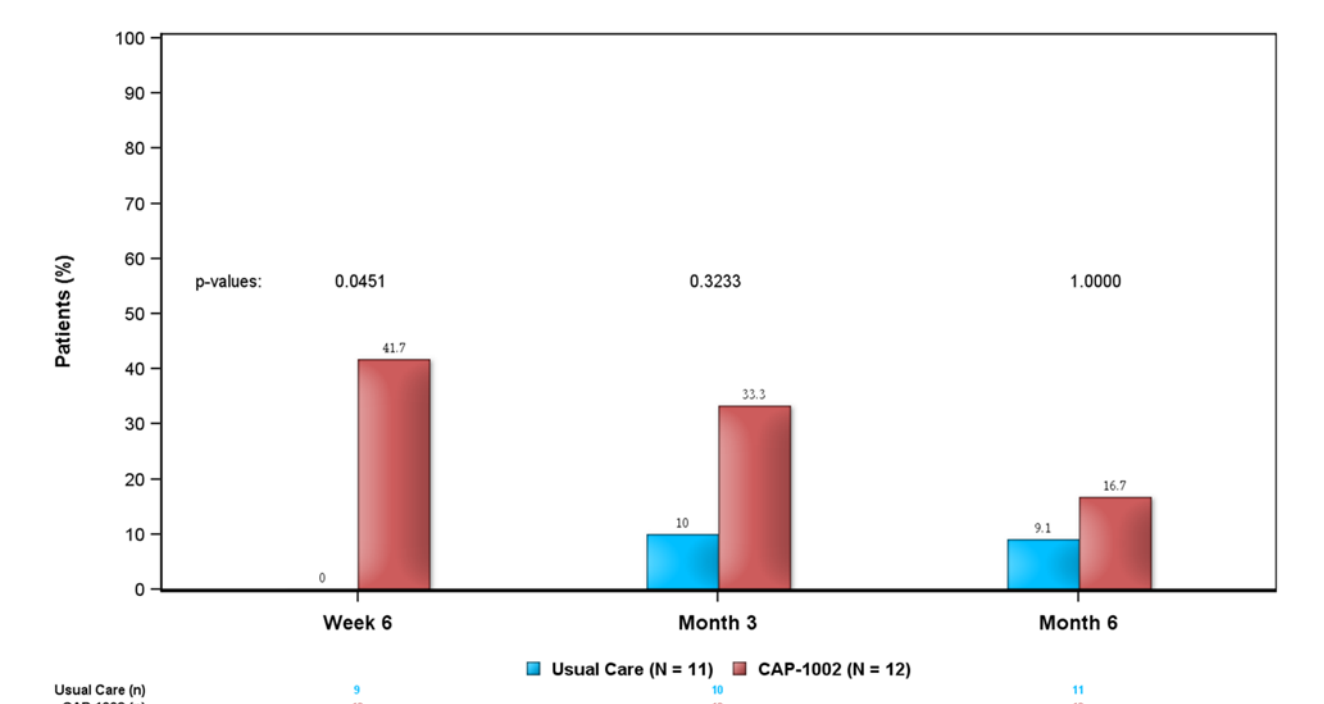


Fig. 6 Percent of subjects with improvements in skeletal muscle function. Percent responders (defined post hoc as patients with ≥10% or maximum possible improvement in middle-plus-distal PUL) from baseline to six weeks, three months, and six months for usual care (blue) and CAP-1002-treated (red) patients.

Table 5. Summary of PUL scores

Change from Baseline	n	Usual Care (N=11)	Median (min, max)	n	CAP-1002 (N=12)	Median (min, max)	p-value
Shoulder							
Week 6	5	2.57 (25.998)	0.00 (-30.0, 42.9)	3	0.93 (23.625)	0.00 (-25.0, 22.2)	0.9021
Month 3	6	3.69 (27.959)	0.00 (-25.0, 57.1)	3	-12.04 (12.526)	-11.11 (-25.0, 0.0)	0.5237
Month 6	6	8.45 (33.188)	0.00 (-43.3, 79.0)	3	-17.36 (16.710)	-18.75 (-33.3, 0.0)	0.2474
Wrist							
Week 6	9	-2.36 (5.045)	-2.94 (-8.7, 7.7)	12	22.74 (16.045)	2.94 (-6.7, 10.0)	0.3861
Month 3	10	2.64 (11.140)	0.00 (10.0, 20.0)	12	25.31 (18.172)	0.00 (-6.7, 14.4)	0.3406
Month 6	11	-6.60 (20.739)	-2.94 (-6.5, 28.4)	12	3.11 (12.763)	-4.12 (-7.7, 0.0)	0.0852
Distal							
Week 6	9	-0.22 (7.878)	0.00 (-13.0, 15.0)	13	2.77 (8.188)	0.00 (-12.5, 79.4)	0.5421
Month 3	10	2.10 (7.503)	0.00 (8.3, 20.0)	13	2.39 (9.563)	0.00 (-4.5, 29.4)	0.0807
Month 6	11	0.96 (4.533)	0.00 (-4.3, 10.0)	13	-3.19 (19.811)	0.00 (-66.7, 15.0)	0.3433
Elbow							
Week 6	5	-1.43 (6.303)	0.00 (-11.4, 8.4)	3	-0.79 (4.419)	0.00 (-5.6, 3.2)	0.8618
Month 3	6	0.73 (3.808)	0.00 (-3.6, 7.9)	3	-2.88 (2.862)	-3.59 (-5.0, 0.0)	0.3904
Month 6	6	0.65 (3.448)	0.00 (-2.1, 7.1)	3	-5.62 (4.472)	-4.12 (-7.7, 0.0)	0.0852
Middle + Distal							
Week 6	9	-1.65 (3.704)	0.00 (6.8, 2.2)	12	8.78 (14.956)	1.28 (-3.4, 34.5)	0.2192
Month 3	10	0.82 (3.672)	0.88 (-5.9, 6.7)	12	8.81 (15.363)	0.00 (-2.9, 40.9)	0.3178
Month 6	11	-3.90 (9.527)	-1.75 (-30.4, 3.2)	12	0.90 (8.698)	0.00 (-9.3, 18.2)	0.8671

Quality of Life

Table 6. Change in patient-reported PODCI parameters

Change from Baseline	n	Usual Care (N=11)	Median (min, max)	n	CAP-1002 (N=11)	Median (min, max)	p-value
Upper Extremity and Physical Function							
Week 6	10	-3.2 (7.02)	0.0 (-16.9)	13	0.0 (14.69)	0.0 (-17.33)	0.7317
Month 3	10	-0.8 (19.56)	0.0 (-25.42)	13	1.2 (15.28)	0.0 (-24.25)	0.8847
Month 6	10	-7.4 (11.99)	0.0 (-33.0)	13	-6.4 (17.89)	-8.0 (-34.25)	0.9845
Transfer and Basic Mobility							
Week 6	10	7.5 (52.70)	0.0 (-49.150)	13	0.1 (16.04)	0.0 (-7.26)	0.4864
Month 3	10	-24.0 (23.28)	-24.0 (18.5, 33.3)	13	1.1 (13.34)	0.0 (-21.18)	0.7811
Month 6	10	-12.8 (18.55)	-10.8 (-59.7)	13	-9.3 (13.73)	-7.0 (-38.7)	0.3466
Sports/Physical Functioning							
Week 6	10	7.2 (30.10)	0.0 (-21.88)	13	-2.2 (7.53)	-3.0 (-13.9)	0.1496
Month 3	10	-9.4 (9.80)	-6.5 (-25.0)	13	-1.5 (4.88)	-3.0 (-8.9)	0.7322
Month 6	10	-9.1 (9.90)	-5.0 (-33.9)	13	-2.5 (7.53)	-4.0 (-11.1)	0.6079
Pain/Comfort							
Week 6	10	-1.5 (9.85)	0.0 (-9.15)	13	-1.2 (6.73)	0.0 (-1.1)	0.9051
Month 3	10	-4.7 (5.53)	-3.5 (-22.9)	13	0.1 (10.18)	0.0 (-2.1)	0.2058
Month 6	10	3.7 (9.74)	1.0 (-9.23)	13	0.5 (7.52)	0.0 (-1.2)	0.3423
Hop/Balance							
Week 6	10	6.1 (19.17)	3.5 (-20.47)	13	5.2 (99.65)	0.0 (-33.128)	0.6224
Month 3	10	3.4 (22.89)	0.0 (-27.54)	13	7.8 (38.29)	0.0 (-33.128)	0.5830
Month 6	10	21.0 (29.29)	3.0 (-26.47)	13	2.0 (16.81)	0.0 (-25.0)	0.8841
Global Function							
Week 6	10	2.8 (14.29)	-1.0 (-7.42)	13	-1.5 (7.25)	-3.0 (-13.14)	0.0090
Month 3	10	-10.0 (10.10)	-8.0 (-31.7)	13	-2.0 (16.32)	-2.0 (-11.1)	0.0041
Month 6	10	-4.3 (5.31)	-5.0 (-12.5)	13	-3.1 (5.82)	-4.0 (-14.6)	0.8559

Table 7. Change in patient-reported PedsQL parameters

% Change from Baseline	n	Usual Care (N=11)	Median (min, max)	n	CAP-1002 (N=11)	Median (min, max)	p-value
Daily Activities							
Week 6	10	-3.37 (15.477)	-6.70 (-33.3, 18.8)	13	18.80 (72.428)	0.0 (-69.2, 233.3)	0.8584
Month 3	10	1.10 (15.904)	0.0 (-23.3, 33.3)	13	22.59 (75.838)	6.25 (-69.2, 233.3)	0.7445
Month 6	10	-2.38 (11.988)	0.0 (-25.0, 16.7)	13	32.61 (90.732)	0.0 (-69.2, 233.3)	0.8140
Treatment Burdens							
Week 6	10	4.71 (13.739)	6.61 (-3.3, 33.3)	13	12.28 (72.405)	-7.75 (-26.2, 250.0)	0.1117
Month 3	10	-2.01 (10.041)	0.0 (-18.5, 33.3)	13	5.97 (49.711)	0.0 (-21.18)	0.0790
Month 6	10	-1.22 (12.690)	0.0 (-10.0, 33.3)	13	11.34 (62.357)	0.0 (-83.3, 200.0)	0.1342
Worry							
Week 6	10	-5.02 (13.082)	0.0 (-33.3, 6.7)	13	8.44 (46.203)	-4.20 (-17.5, 1	