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Deramiocel and Duchenne Muscular Dystrophy

July 29, 2026

Cellular, Tissue, and Gene Therapies Advisory Committee

Sponsor: Capricor, Inc.

Introduction

Linda Marbán, PhD

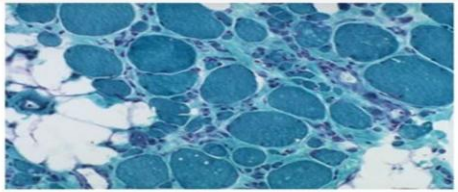
Chief Executive Officer and Director

Capricor, Inc.

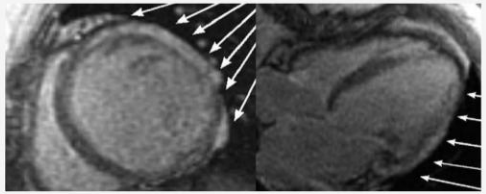
Duchenne Muscular Dystrophy

Fatal, X-Linked Muscle-Wasting Disease with No Cure

SKELETAL MYOPATHY



CARDIOMYOPATHY



These are the patients we studied, primarily later-stage, non-ambulatory young men for whom the consequences of DMD are most severe – they are facing loss of independence and loss of life

Deramiocel Has Been Evaluated in 3 Independent Clinical Trials in DMD Over ~5 Years in 200+ Patients

HOPE-DUCHENNE

Phase 1

N=25

- Statistically significant benefit vs placebo on cardiac scarring
- No serious safety issues

Victor, et al. *Neurology.* 2019

HOPE-2

Phase 2

N=20

- RCT
- **PUL** mid-level: 2.6 absolute treatment difference
- **LVEF**: 4% LVEF treatment difference
- Generally well-tolerated

McDonald, et al. *The Lancet*, 2022

HOPE-2 OLE

Phase 2

N=13

- 5-year extension study
- **PUL** total: less mean decline vs matched EC
- **LVEF:** Stable over 5 years vs 3.2%/year modeled decline
- Favorable long-term safety profile

HOPE-3

Phase 3

N=106

- RCT
- **PUL** total: 4.55% (1.1 absolute) treatment difference
- **LVEF:** 1.8% treatment difference
- Generally well-tolerated

McDonald, et al. 2026

IC infusion

IV infusion

Phase 1, 2, and 3 results independently reviewed and published

HOPE-3 Regulatory History

Protocol and SAP revisions driven by ongoing FDA feedback on Development Program (2022-2025)

PROTOCOLS

~2022
V1–V4.1
Phase 3 trial protocol (clinical drug supply)

AUG 2023
V5
Addition of commercial supply (Cohort B)

NOV 2024
V6
Analysis for Cohort A & B combined

FEB 2025
V7
Never implemented; study repositioning for OUS authorization

JUL 2025
V8
Never implemented; reverted to U.S. only enrollment, PUL→LVEF

SEP 2025
V9
PUL 2.0 retained as primary; LVEF → key secondary **(SAP 2.0)**
✓ Revised per FDA request

KEY INTERACTIONS

AUG 2024
Pre-BLA Meeting
FDA recommended cardiac-focused BLA filing; combine Cohorts A&B
✓ Agreement reached

JUL 2025
Complete Response Letter
FDA issues CRL

AUG 2025
Type A Meeting
Held to address CRL & primary endpoint

SEP 2025
Type A Meeting Minutes
FDA retained PUL 2.0 primary; LVEF key secondary
✓ FDA feedback incorporated

25 NOV 2025
DB Lock & Unblinding
HOPE-3 Phase 3 clinical milestone

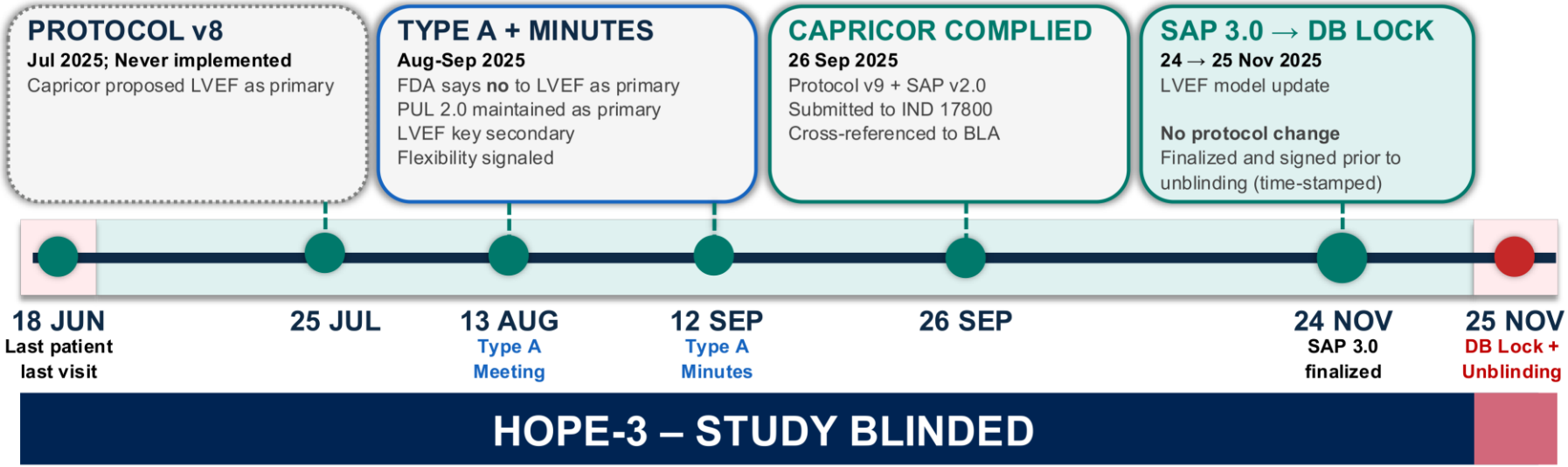
SAPs

DEC 2023
SAP 1.7
In place at the time of futility analysis
✓ Revised per FDA request

SEP 2025
SAP 2.0
Absolute → % change analysis; LVEF key secondary
✓ No FDA revisions requested

24 NOV 2025
SAP 3.0
Finalized pre-DB lock; **no protocol change v2→v3**

Capricor Remained Blinded Until Database Lock



- Capricor proposed LVEF primary ----- FDA said NO ----- Capricor complied
- Protocol v9, SAP v2.0 submitted September 2025
- SAP v3.0 was finalized before unblinding
- Blinding maintained as verified by audit trail

Voting and Discussion Questions

"FDA remains committed in collaborating with the applicant and will exercise further regulatory flexibility by reviewing the data from the HOPE-3 study to assess its primary endpoint as PUL and see the contribution of LVEF in the overall disease progression of the enrolled subjects."

FDA Type A Meeting Summary
September 12, 2025

Agenda

Deramiocel MoA	**Eduardo Marbán, MD, PhD** Distinguished Professor and Director Smidt Heart Institute, Cedars-Sinai Medical Center
Deramiocel Assay and Potency	**Kristi Elliott, PhD** Chief Scientific and Operating Officer, Capricor
Statistical Overview	**Adam Sullivan, PhD** Senior Director of Biostatistics, Capricor
Skeletal Efficacy	**Craig McDonald, MD** Distinguished Professor of Pediatrics and PM&R, Director MDA Clinics and Neuromuscular Research Laboratory, UC Davis Health, Chair CINRG Duchenne Natural History Study
Cardiac Efficacy	**Jonathan Soslow, MD, MSCI** Professor of Pediatrics and Director of Clinical Research, Pediatric Cardiology; Co-Director, Duchenne Multispecialty Clinic, Vanderbilt University Medical Center
Safety Overview	**Michael Binks, MD** Chief Medical Officer, Capricor
Meaningfulness of Results	**Mindy Leffler** Patient Advocacy, Capricor
Benefit / Risk	**Linda Marbán, PhD** Chief Executive Officer, Capricor

Deramiocel: Mechanism of Action and Preclinical Evidence of Efficacy

Eduardo Marbán, MD, PhD

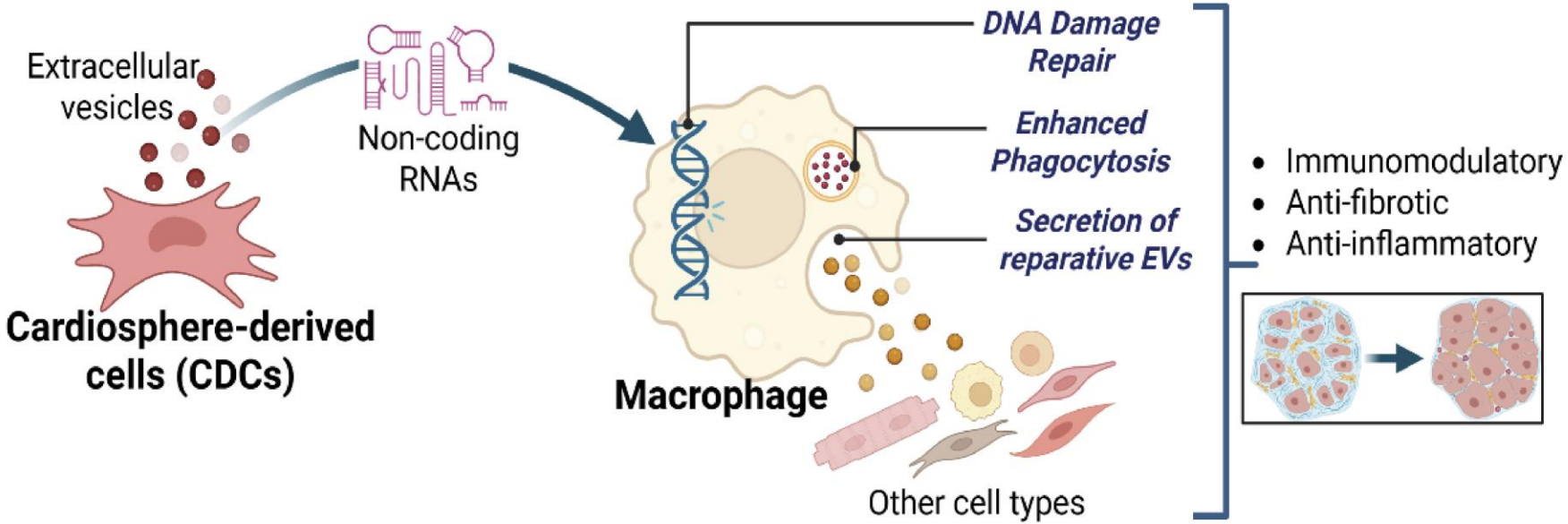
Distinguished Professor and Executive Director, Smidt Heart Institute,
Cedars-Sinai Health Sciences University, Los Angeles, California

Cardiosphere-Derived Cells – Active Ingredient of Deramiocel

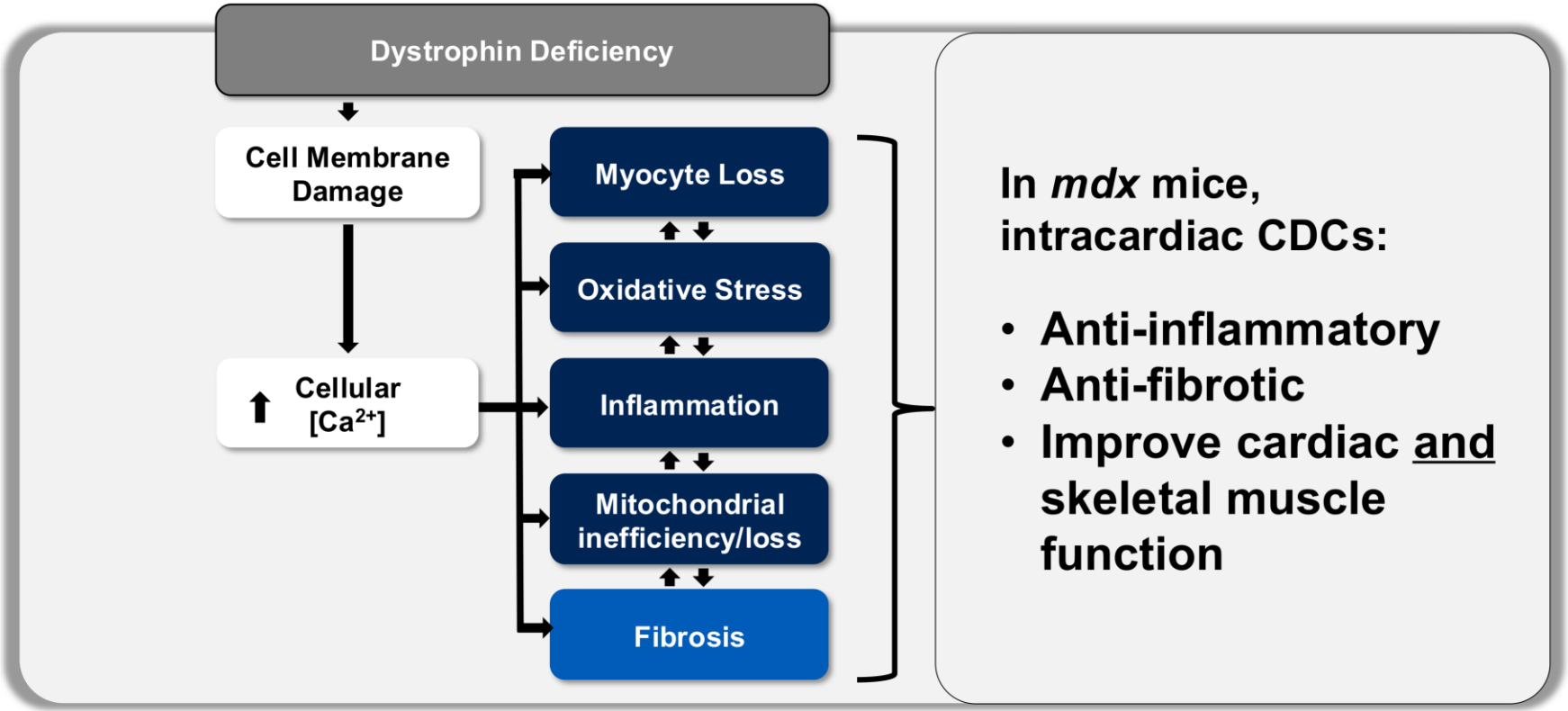
- CDCs
  - Stromal cells of endogenous cardiac origin; work indirectly
  - Remarkable broad-ranging disease-modifying activity
- Short-term engraftment, long lasting benefits
- Extracellular vesicles (EVs) mediate CDC effects
- 14 years of clinical experience with deramiocel
  - 11 clinical trials
  - Emergent mechanistic insights drove systematic clinical development pivots

CDCs Secrete ncRNA-Laden EVs that Reprogram Macrophages

MoA summary based on 22 years of investigation reported in > 50 papers



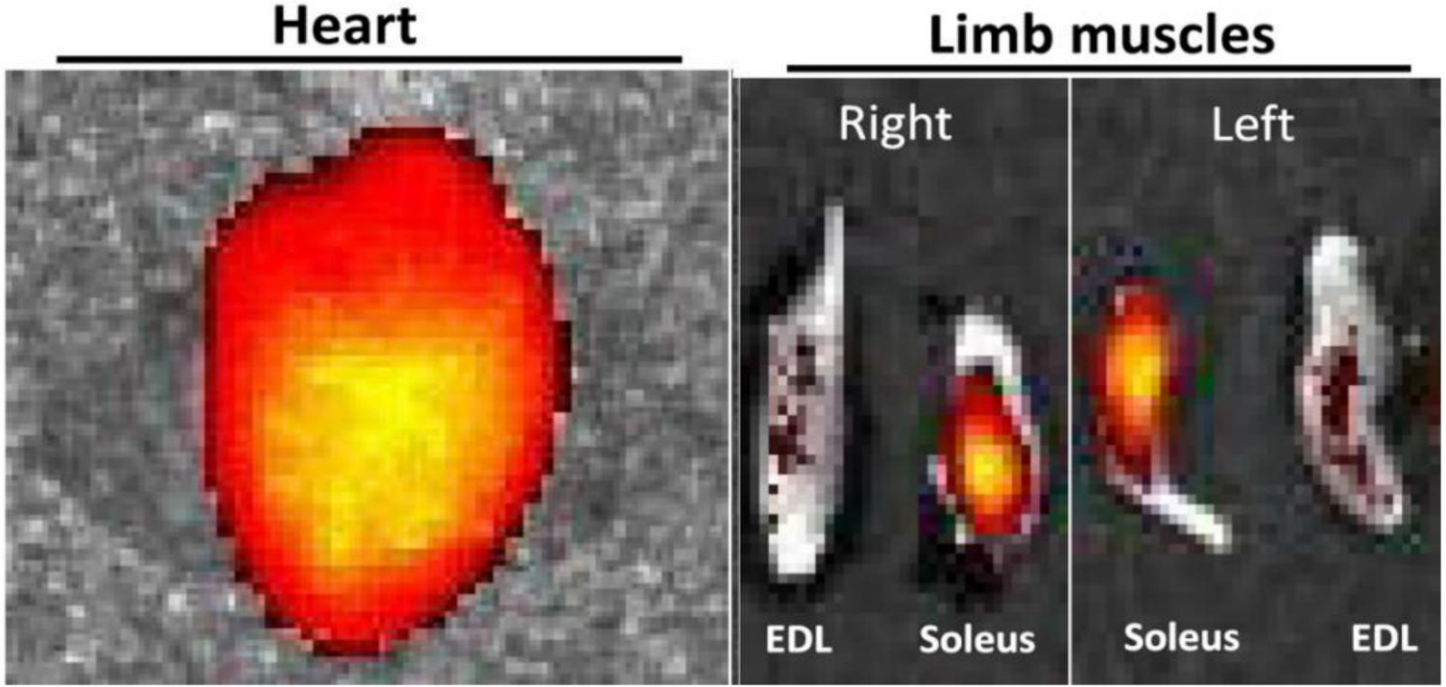
Mechanism Underlying Both Skeletal and Cardiac Myopathy Is Loss of Functional Dystrophin



Aminzadeh, et al. *Stem Cell Reports,* 2018

IV CDC Exosomes Accumulate in Heart and Skeletal Muscles

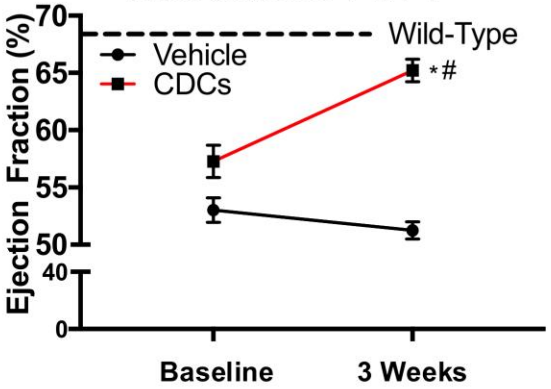
CDC-EV Biodistribution



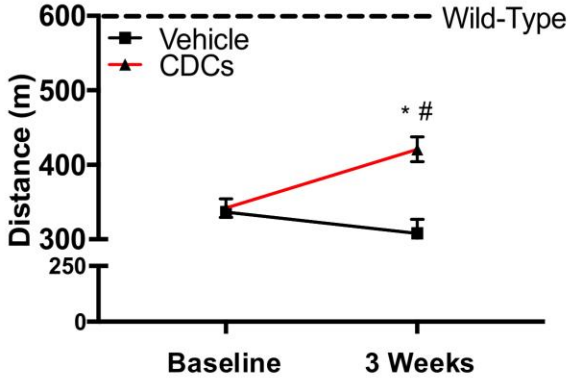
Aminzadeh, et al. *Stem Cell Reports,* 2018

Preclinical Foundation of HOPE-3 – IV CDCs Work in *mdx* Mouse Model of DMD

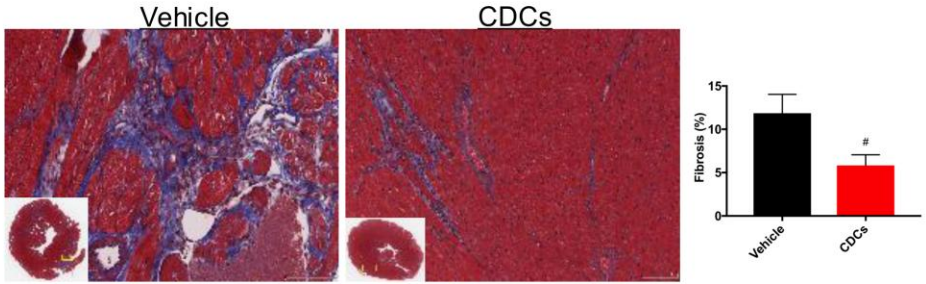
Increased LVEF



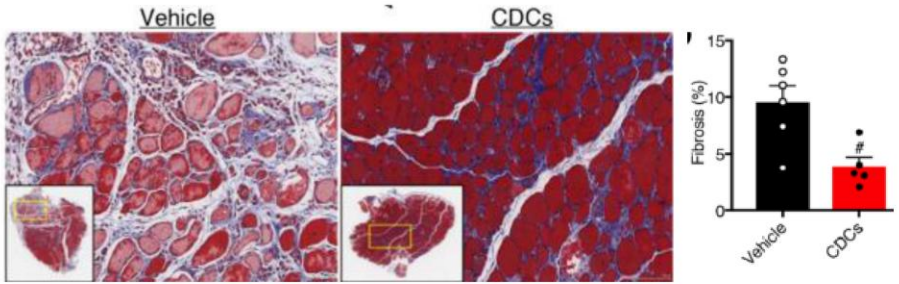
Increased Exercise Capacity



Decreased Heart Fibrosis



Decreased Skeletal Muscle Fibrosis



R. Rogers, et al. *JCI Insight*, 2019

Deramiocel: Well Established Mechanism of Action

- Mechanism of Action better established than for any other cell therapy for heart disease
- Extensive preclinical studies faithfully predicted the positive clinical findings in HOPE, HOPE-2, HOPE-2 OLE, and HOPE-3

FDA's critiques regarding "biological plausibility of deramiocel's mechanism of action" are scientifically unwarranted

Deramiocel Potency

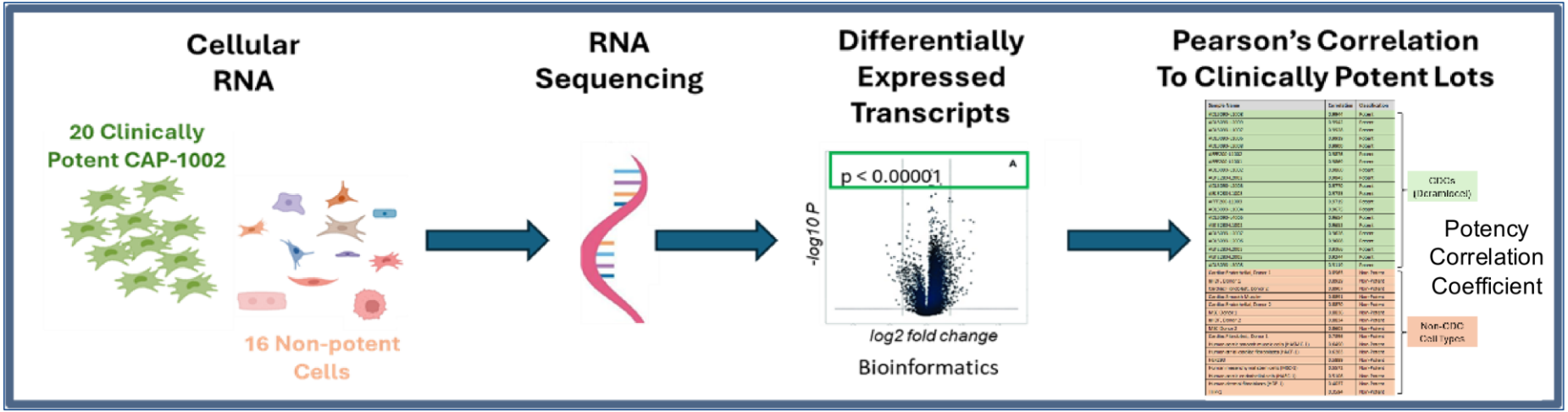
Kristi Elliott, PhD

Chief Scientific and Operating Officer

Capricor, Inc.

Confirmatory Potency Assays Ensure Deramiocel Is Anti-Fibrotic and Correlates to Clinical Efficacy

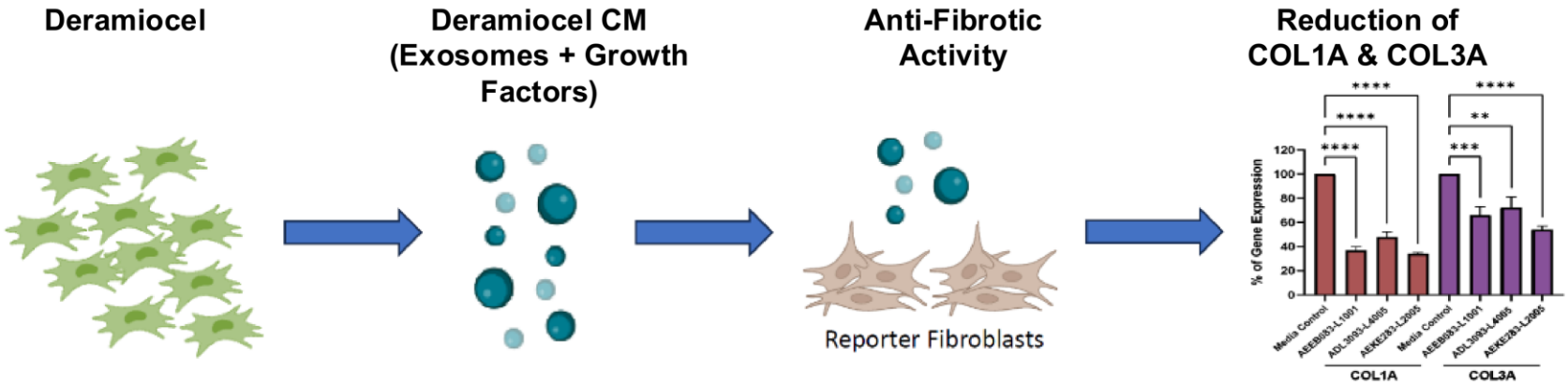
Clinical Correlation Potency Assay



- mRNA sequencing to create a cell profile or unique "**fingerprint**" of CDCs
  - Stringent, statistically significant ($p < 0.00001$) analysis of profile
- **Different from other cells:** using profile of non-CDC cells
- **Correlates to clinical potency** using profile of clinically efficacious CDCs (HOPE-2 studies)

Potency Assay Ensures Deramiocel Is Anti-Fibrotic

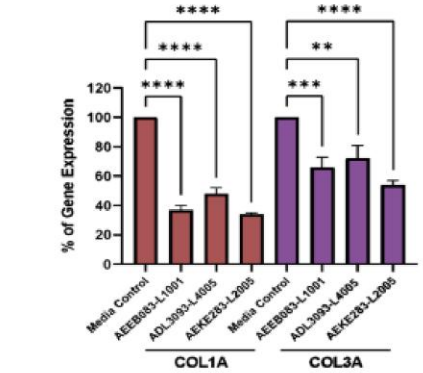
Anti-Fibrosis Potency Assay



- **Key mechanism of action** of CDCs
- Cell-based assay shows anti-fibrotic activity of released exosomes and factors from Deramiocel
  - Significant reduction in COL1, COL3
- **Potency demonstrated using an anti-fibrosis assay, indicative of mechanism of action**

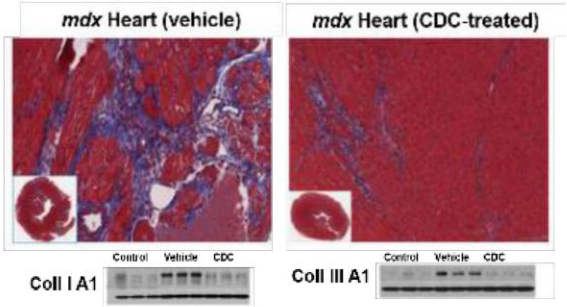
Deramiocel is Immunomodulatory, Anti-Fibrotic, and Improves Muscle Function

Potency Assay



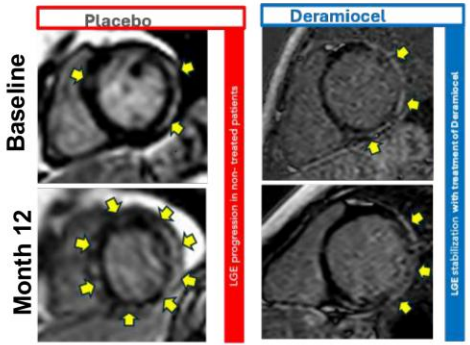
- Fibrosis
- Immunomodulation
- Correlates to clinical efficacy

Preclinical Studies



- Inflammation & Fibrosis
- Muscle function
- Cardiac function

Clinical Studies



- Fibrosis by LGE
- Muscle function
- Cardiac structure & function

In vitro potency, pre-clinical and HOPE-3 LGE consistently demonstrate MoA

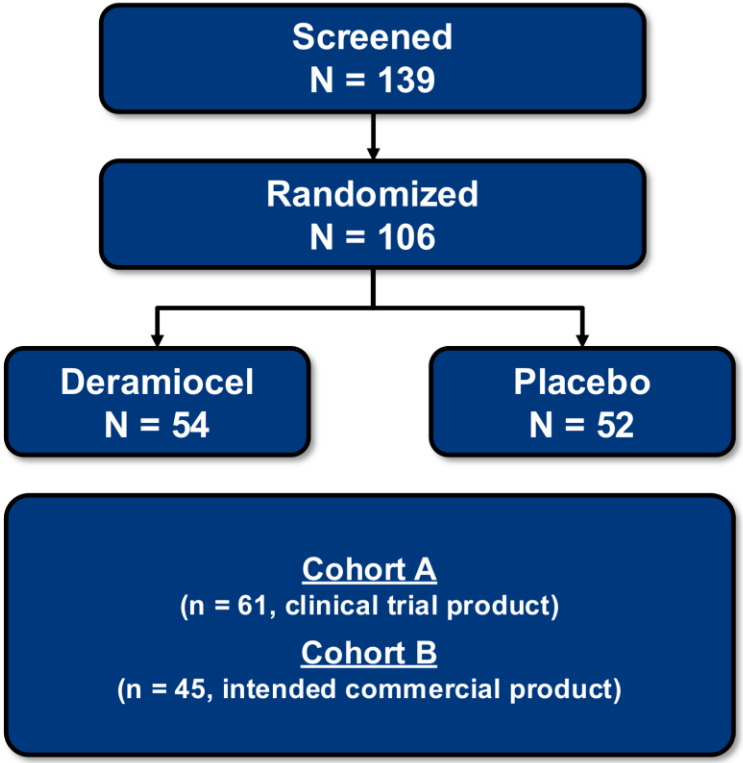
Statistical Overview and Methods

Adam Sullivan, PhD

Senior Director of Biostatistics

Capricor, Inc.

HOPE-3: Randomized, Double-Blind, Placebo-Controlled 12 Month Study Across 106 Patients



Analysis Sets

ITT N = 106	LVEF ITT N = 83
Cardiomyopathy N = 64	LGE (Cohort B) N = 22

HOPE-3: Prespecified Endpoints and Stat Methods

Primary Endpoint	PUL 2.0 total score, % change from baseline to Month 12 (MMRM)
Key Secondary	LVEF by cardiac MRI, change from baseline to Month 12 (ranked ANCOVA; central read)
Type 1 Error Controlled Secondary	PUL 2.0 Mid-level score, change from baseline to Month 12 (MMRM)
Type 1 Error Controlled Secondary	Total GST: combination of PUL 2.0, LVEF and PGI-S (ANCOVA)
Type 1 Error Controlled Secondary	LGE Segments, Cohort B (ranked ANCOVA)

HOPE-3: PUL 2.0 Primary Endpoint and Analysis

Model

- MMRM, ARH(1); response is percent change from baseline in PUL 2.0; adjusted for treatment, cohort, pooled site, visit, treatment-by-visit, and baseline PUL 2.0

Percent Change

- Blinded absolute change data violated model assumptions with an increasing variance
- Modeling percent change stabilizes the variance

Patient A

- PUL 2.0 Score:
  - **16** at Baseline
  - **12** at Month 12

25% Change

Patient B

- PUL 2.0 Score:
  - **40** at Baseline
  - **36** at Month 12

10% Change

HOPE-3: LVEF Key Secondary Endpoint and Analysis

1 Prespecified for non-normality

Rank-based analysis was pre-planned in SAP v1.1 (2022) as the confirmatory fallback

2 Raised to key secondary

LVEF was elevated to key secondary at the FDA Type A meeting while blinded

3 Refined to ranked ANCOVA

Nonparametric analysis method (not a data transformation), robust to outliers and reader variability in a small (~83) cMRI sample; finalized before unblinding (SAP v3.0)

Rank ANCOVA is the significance test: treatment effect is reported on the absolute LVEF scale (percentage points), exactly as a clinician reads it

HOPE-3 Efficacy Results: Modeled and Observed

Model estimate

SAP v3.0, specified before unblinding

Presented for every endpoint in results that follow

=

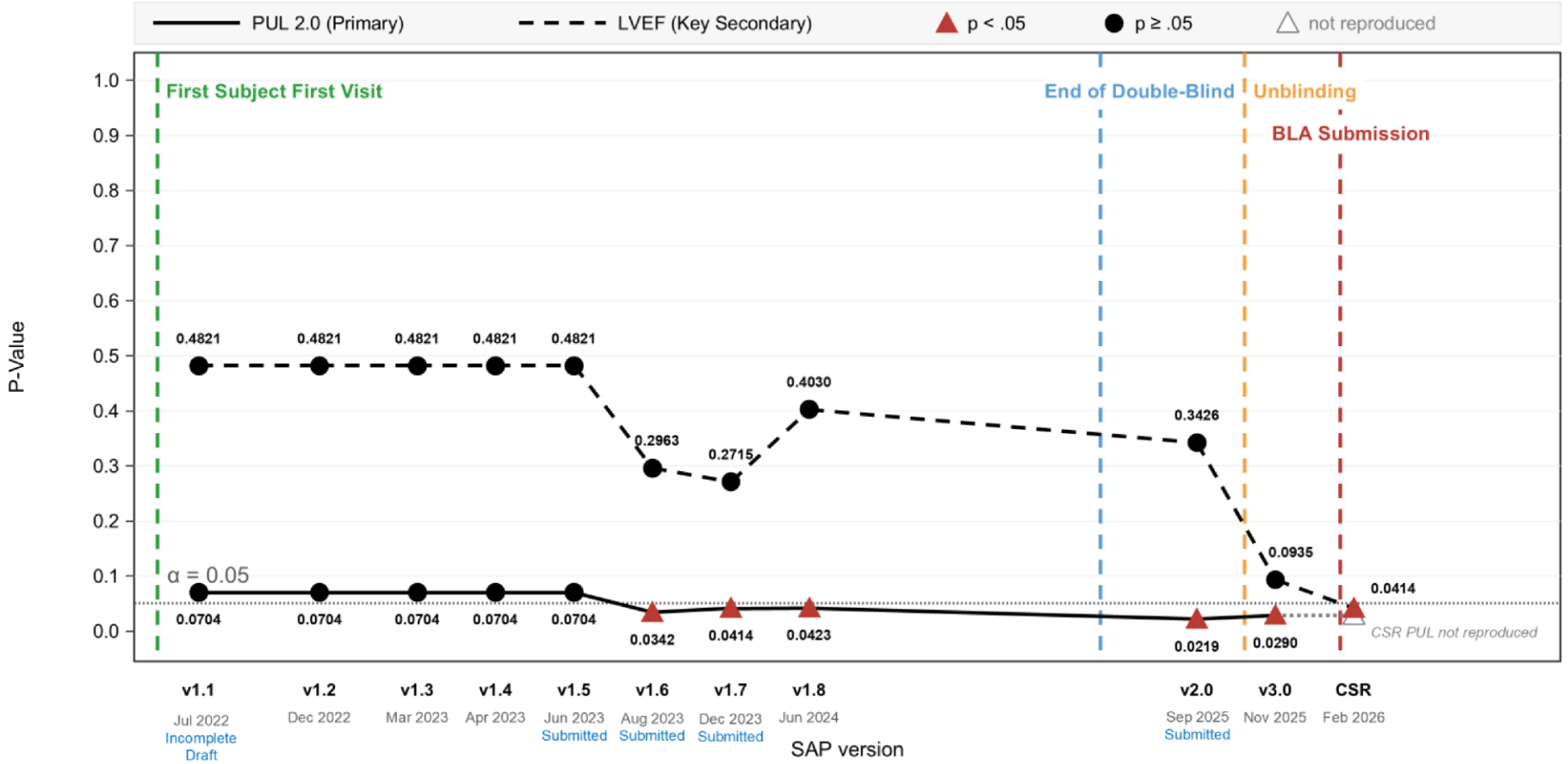
Observed data

Actual patient outcomes, no model

Agreement means shift is real, not a modeling choice

Agreement means the treatment effect is real and not an artifact of the model

Statistical Significance (p-values) Across SAP Versions – Retrospective Reanalysis



Re-analysis on locked ADaM 20260129_Final_DB; ITT; ANL01FL=Y; APHASE=BLINDED TREATMENT. PUL is each SAP's own designated primary metric (v1.1–v1.8 change from baseline; v2.0 and v3.0 percent change). LVEF v1.1–v2.0 are MMRM across visits; v3.0 is the prespecified ranked ANCOVA at Month 12. The CSR model is post-hoc and is not reproduced here.

Skeletal Efficacy – Phase 2 and Phase 3 Placebo-Controlled Randomized Trials

Craig McDonald, MD

Distinguished Professor of Pediatrics and PM&R

Director MDA Clinics and Neuromuscular Research Laboratory

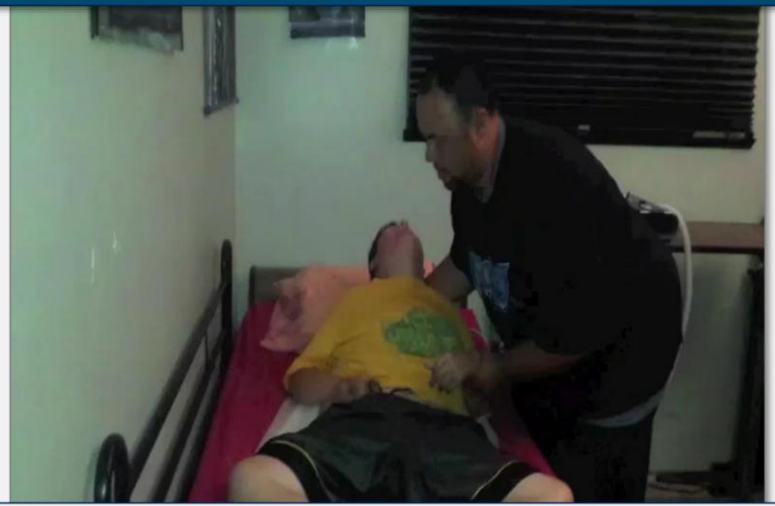
UC Davis Health

Chair CINRG Duchenne Natural History Study

Significant Unmet Need in Non-Ambulatory DMD

DMD Patient, Age 17

- Stable steroids (Emflaza)
- Lost upper limb function, head and trunk control
- Lisinopril, carvedilol, spironolactone
- Non-invasive mechanical ventilation



Cardiac LVEF% progressed to 38% – rate of decline of 3% per year from age 10 and LVEF predictive of 5x increased mortality

- **Two critical unmet needs in DMD**
  - Upper limb functional impairment and cardiomyopathy
  - Both need to be assessed separately; do not progress at same time

HOPE-3: Key Inclusion Criteria

INCLUSION CRITERIA

- DMD diagnosis (confirmed molecular genetics)
- Age > 10
- PUL 2.0 entry item score 2–6; total PUL 2.0 ≤ 40/42; if ambulatory, 10 M walk/run velocity < 1 m/s
- Loss of ambulation between 10th–18th birthday
- Standard of care at experienced DMD center
- Glucocorticoid > 12 months (stable dose > 6 mo)

PUL Entry Item

0	1	2	3	4	5	6
No useful function of hands	Can use hands to hold pen or pick up coin or drive powered chair	Can raise one or two hands to mouth, cannot raise a cup with a 200 g weight to mouth	Can raise standardized plastic cup with 200 g weight to mouth using both hands if necessary	Can raise both hands to shoulder height simultaneously with or without compensation	Can raise both hands simultaneously above head only by flexing the elbow	Full overhead reach without compensation

PUL 2.0: Recognized Standard for Evaluating Upper-Limb Function in DMD and Impact on Daily Living

PUL 2.0 assesses motor performance across 3 key dimensions:

Proximal (shoulder) domain
Evaluates high-level movements, such as lifting arms above head

Middle (elbow) domain
Measures functional actions using the elbow, such as bringing items to mouth and moving objects across tabletop

Distal (wrist) domain
Assesses fine motor functions, such as finger pinch/grip strength

PUL 2.0 scores decline

indicating progressive weakness and loss of upper-limb function with increasing age

PUL Scoring: 2 = Normal; 1 = with difficulty / compensation; 0 = lost function / can't perform

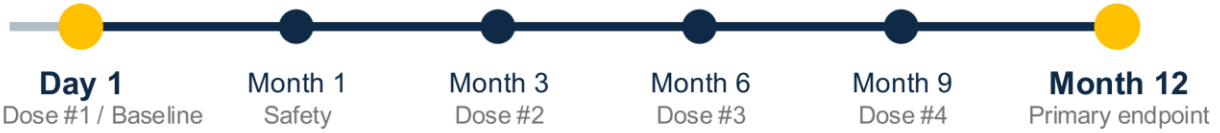
HOPE-3: Phase 3 Study Design

Deramiocel 150 M cells IV

1:1

Placebo

Screening
≤ 23 days before randomization



12-Month Double-blind Period

Prespecified Endpoints

Primary: Percent change in PUL 2.0 Total Score

Key Secondary: Change in LVEF by cardiac MRI

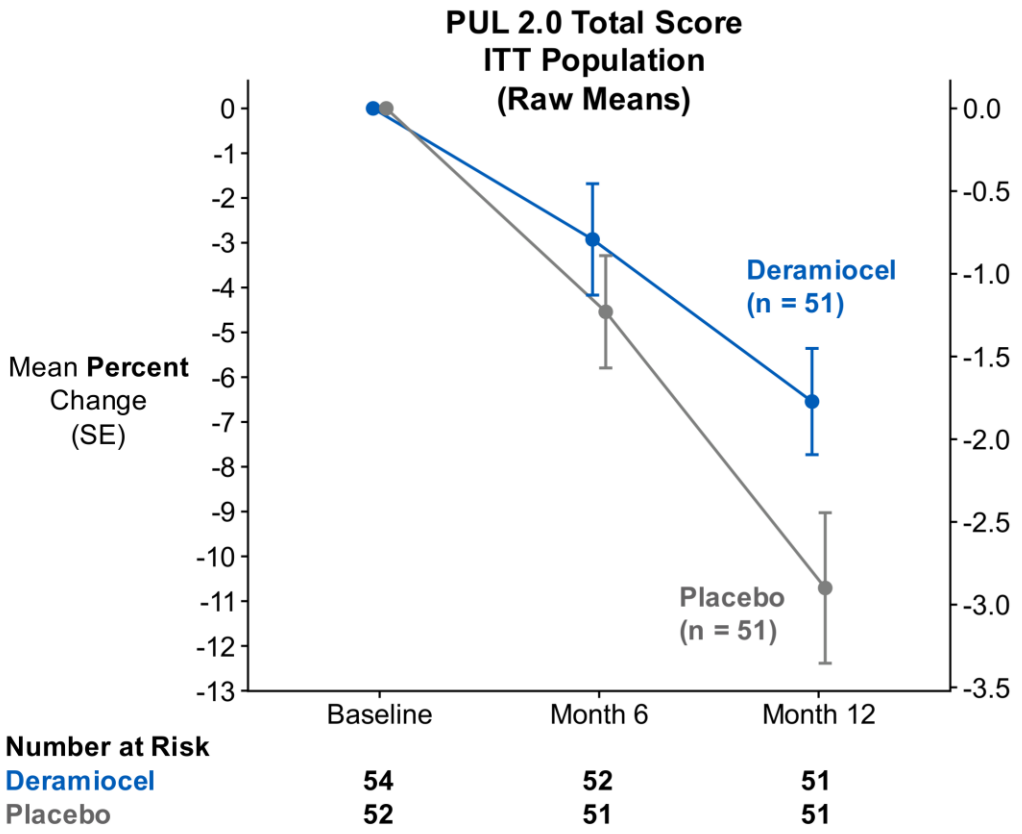
Type I Error: Mid-level PUL, LGE, GST

HOPE-3: Demographic and Baseline Disease Characteristics by Treatment Arm

Characteristic, n (%)	Deramiocel n = 54	Placebo n = 52
Age, years, mean (SD)	**15.4** (3.10)	**14.6** (2.95)
Male	**54** (100%)	**52** (100%)
White	**43** (80%)	**38** (73%)
Not Hispanic or Latino	**49** (91%)	**46** (89%)
BMI, kg/m^2, mean (SD)	**27.1** (6.99)	**26.9** (6.50)
Dystrophin gene deletion	**34** (63%)	**33** (64%)
Documented cardiomyopathy	**41** (76%)	**38** (73%)
Entry stratum II (PUL item 4 to 6)	**29** (54%)	**29** (56%)
Slow progressors (prespecified)	**1** (2%)	**5** (10%)
Baseline PUL 2.0 Total, mean (SD)	**27.6** (7.36)	**26.5** (6.70)
Baseline LVEF, %, mean (SD)	**55.3** (7.74)	**59.3** (6.11)
Systemic corticosteroids	**53** (100%)	**51** (98%)
Exon-skipping drugs	**14** (26%)	**12** (23%)

Intent-to-treat population (ADSL). Age range 10 to 22 years in both arms; all patients male; non-ambulatory at baseline 84.9% overall. Deramiocel arm entered with lower mean baseline LVEF and smaller proportion of prespecified slow progressors. Eligibility required PUL 2.0 Total Score of 40 or less (observed range 13 to 40).

HOPE-3: Primary Endpoint Met Regardless of Analysis

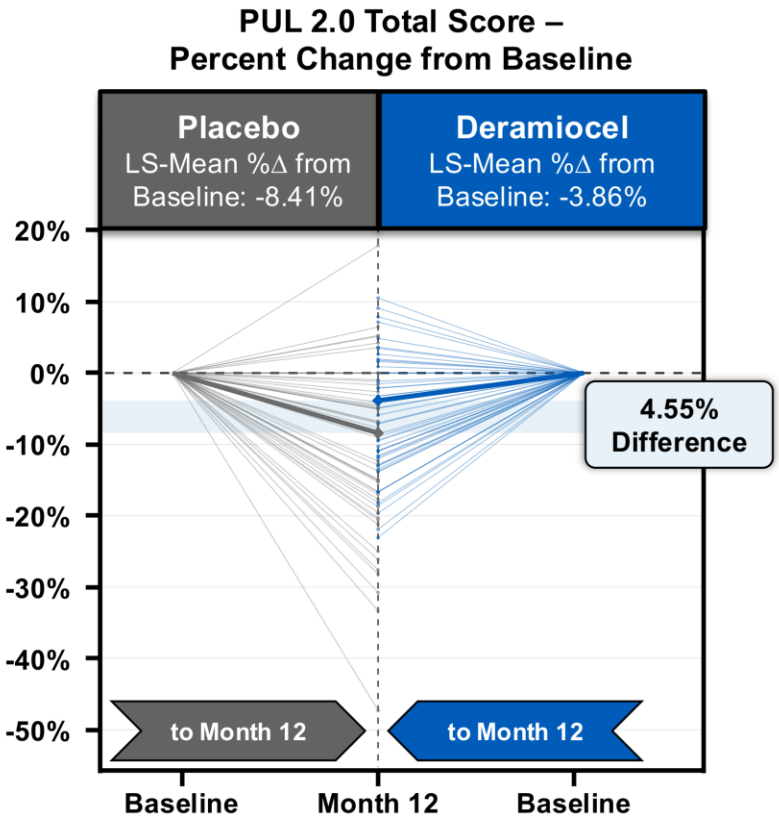


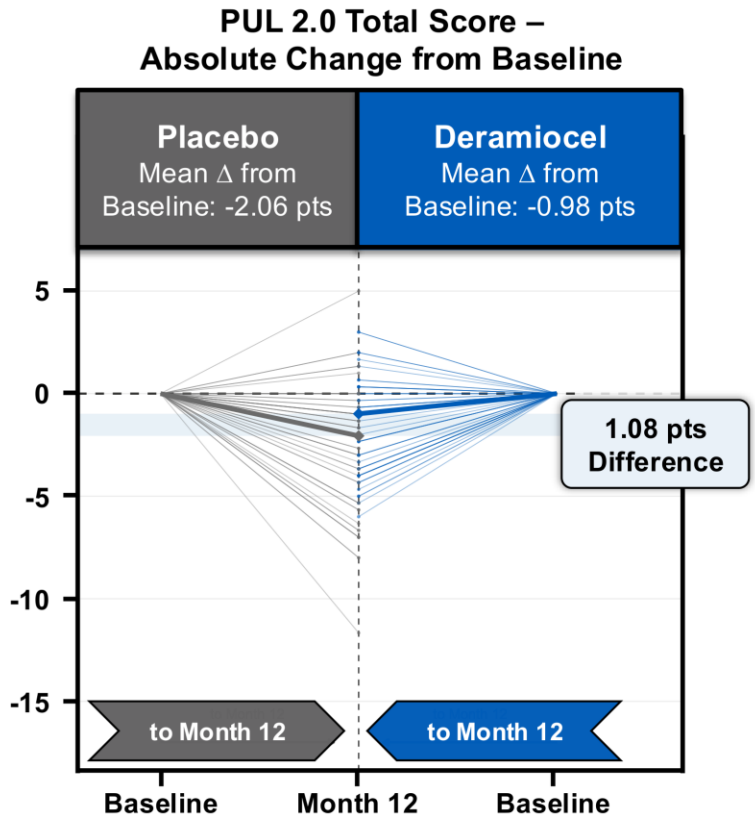
Percent Δ = 4.55% *primary endpoint* **p = 0.029 (MMRM)**

Absolute Δ = 1.1 *sensitivity analysis* **p = 0.050 (MMRM)**

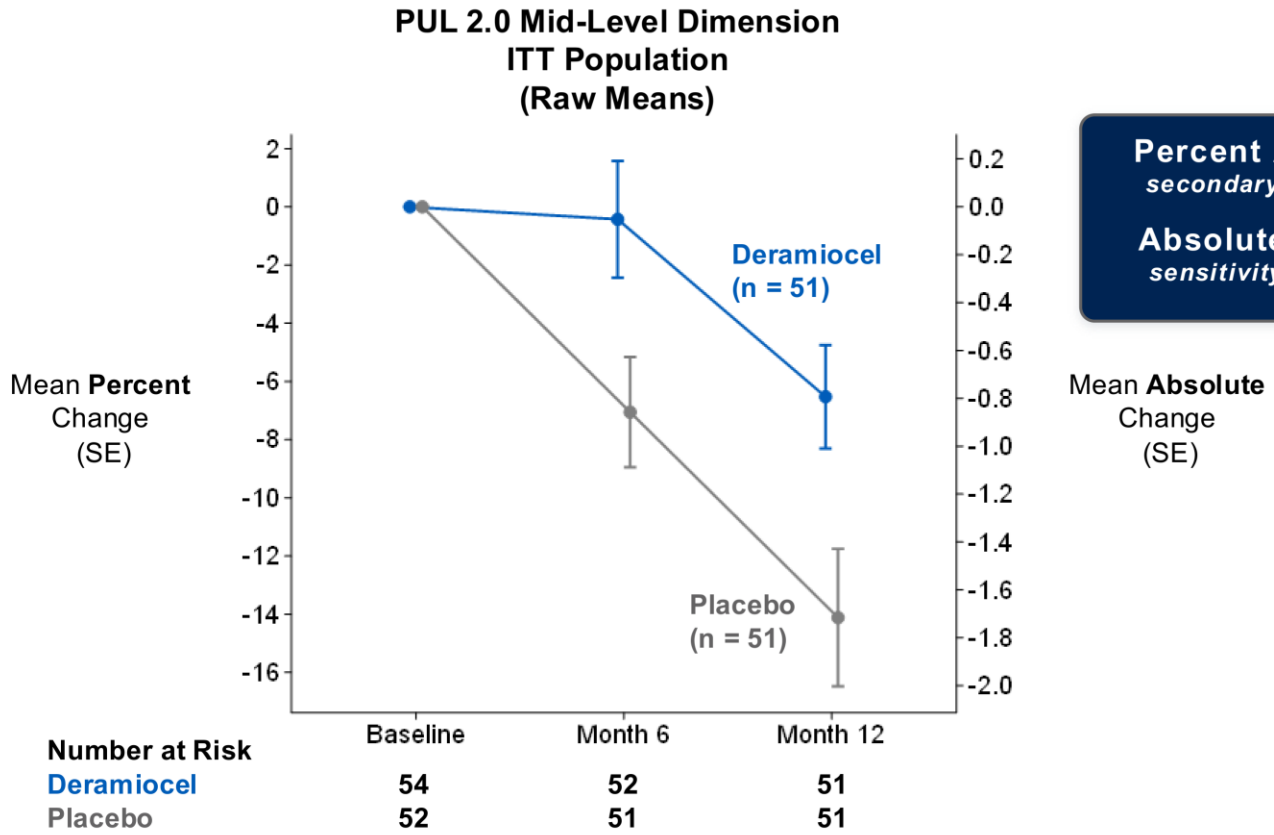
McDonald, et al. 2026

HOPE-3: Slowing of Disease Progression with Deramiocel Across Individual Patients





HOPE-3: Treatment Effect of Deramiocel Is Significant – PUL 2.0 Mid-Level Score

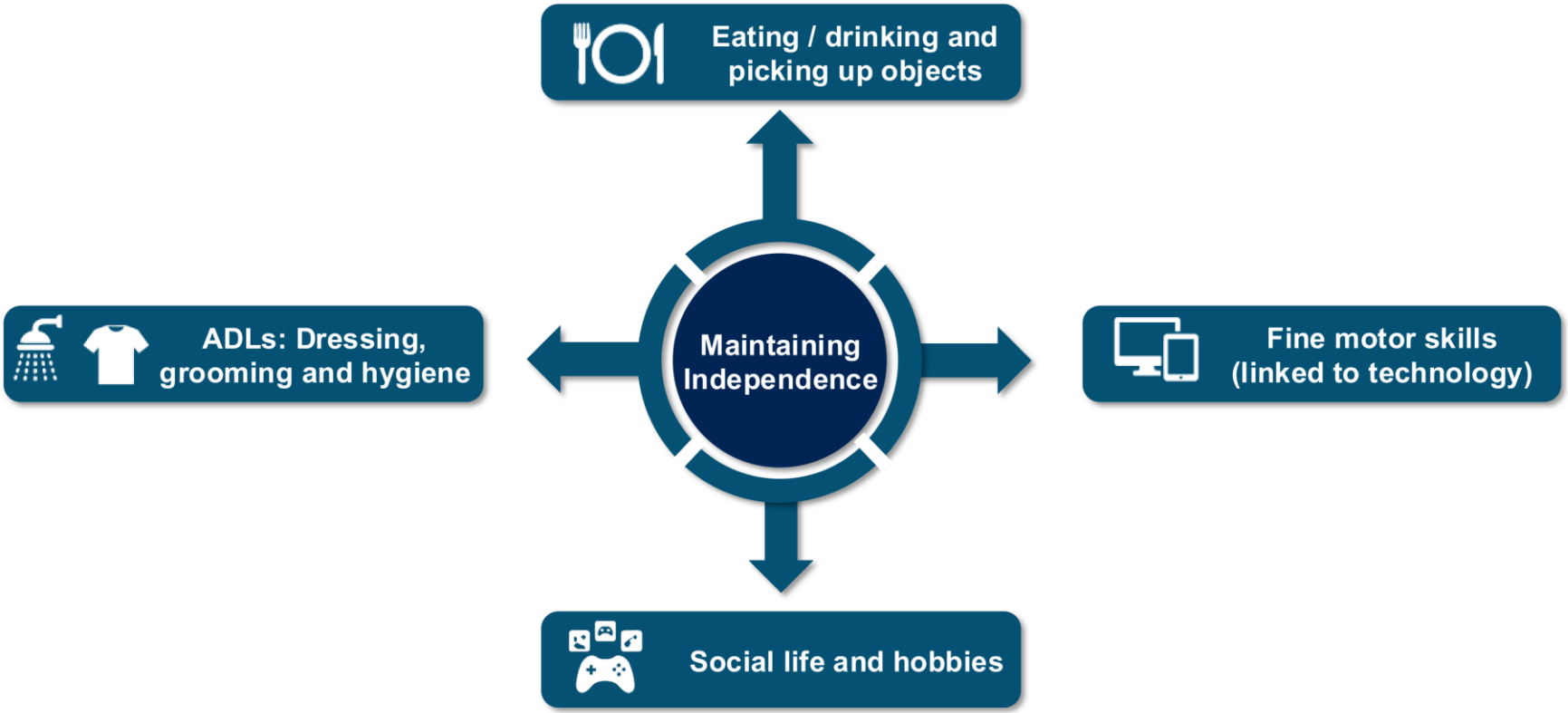


Percent Δ = 8.1% *secondary endpoint* **p = 0.008 (MMRM)**

Absolute Δ = 0.9 *sensitivity analysis* **p = 0.016 (MMRM)**

McDonald, et al., 2026

Clinical Meaningfulness of PUL 2.0 (1-Point Change)



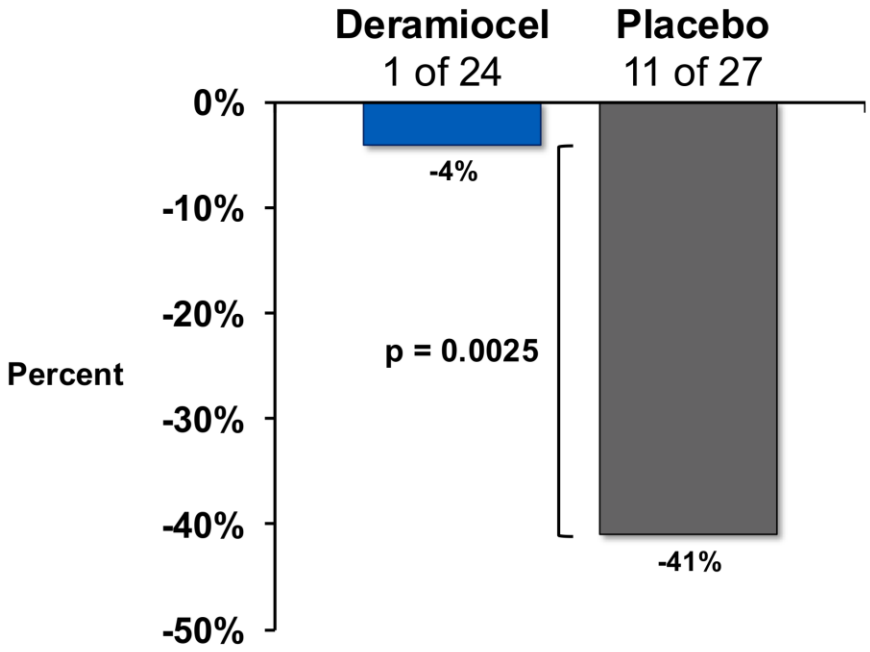
Gillman 2025

HOPE-3: Normal Hand to Mouth Ability Lost at 12 Months

PUL 2.0 Bringing Hand to Mouth = 2 ➡ 1

Disease Progression

PUL 2.0 Score	
2	Normal Ability
1	With difficulty / compensation
0	Unable to perform



1-Point Change in PUL 2.0 Is Clinically Meaningful

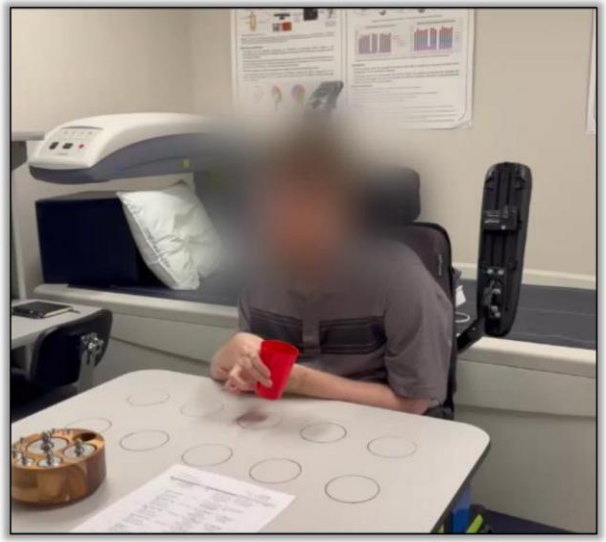
Disease Progression

PUL 2.0 Score	
2	Normal Ability
1	With difficulty / compensation
0	Unable to perform

Bringing Hand to Mouth
PUL 2.0 Score = 2
(Normal)

PUL 2.0 Bringing Hand to Mouth

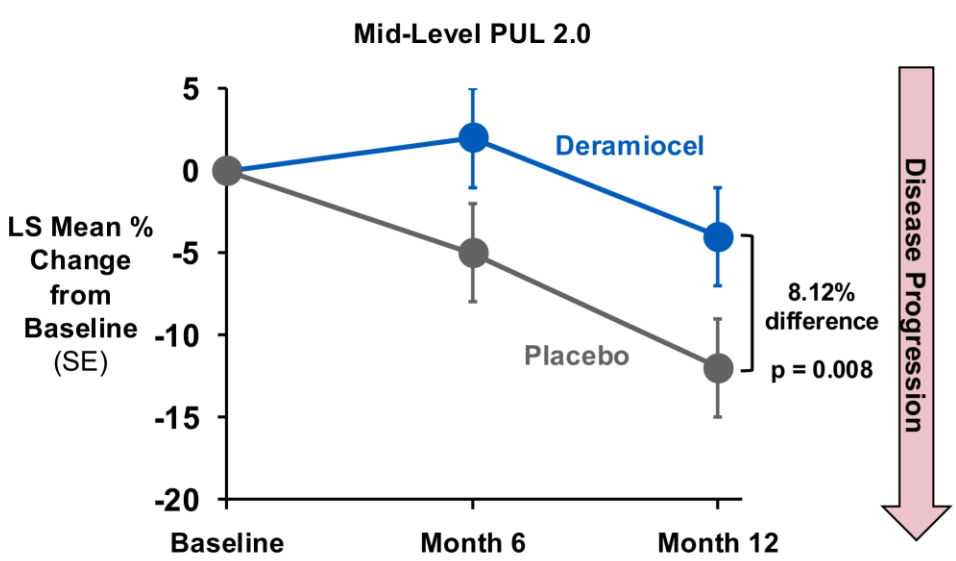
Bringing Hand to Mouth
PUL 2.0 Score = 1
(Difficulty/Compensation)



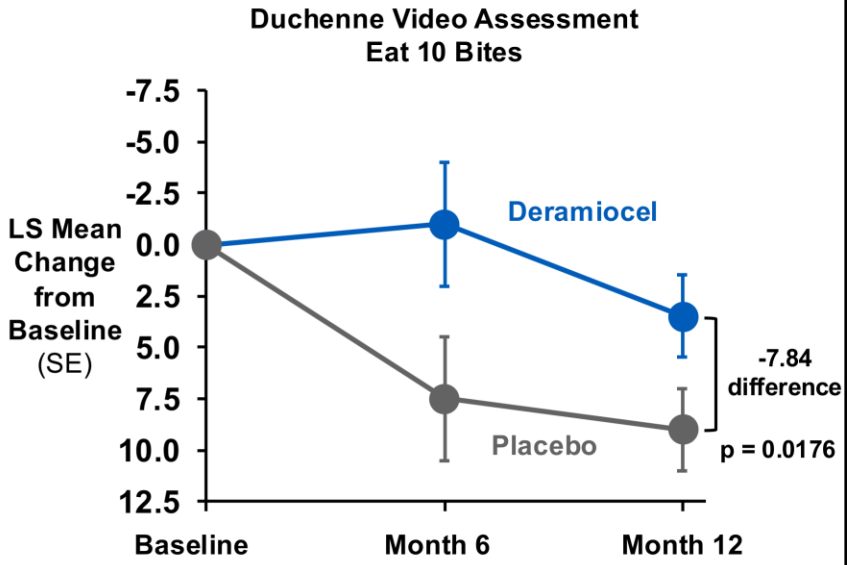
PUL 2.0 Bringing Hand to Mouth

Mid-Level PUL vs Duchenne Video Assessment (DVA) Eat 10 Bites

Eat 10 Bites Criteria	11 Points Total
A. Ability to perform task	0 or 11 points
B. Upper body movement	0 – 3 points
C. Use of table/other arm/hand for assistance	0 – 3 points
D. Use of fork	0 – 3 points
E. Strategy to get feeding hand closer to food	0 – 1 points

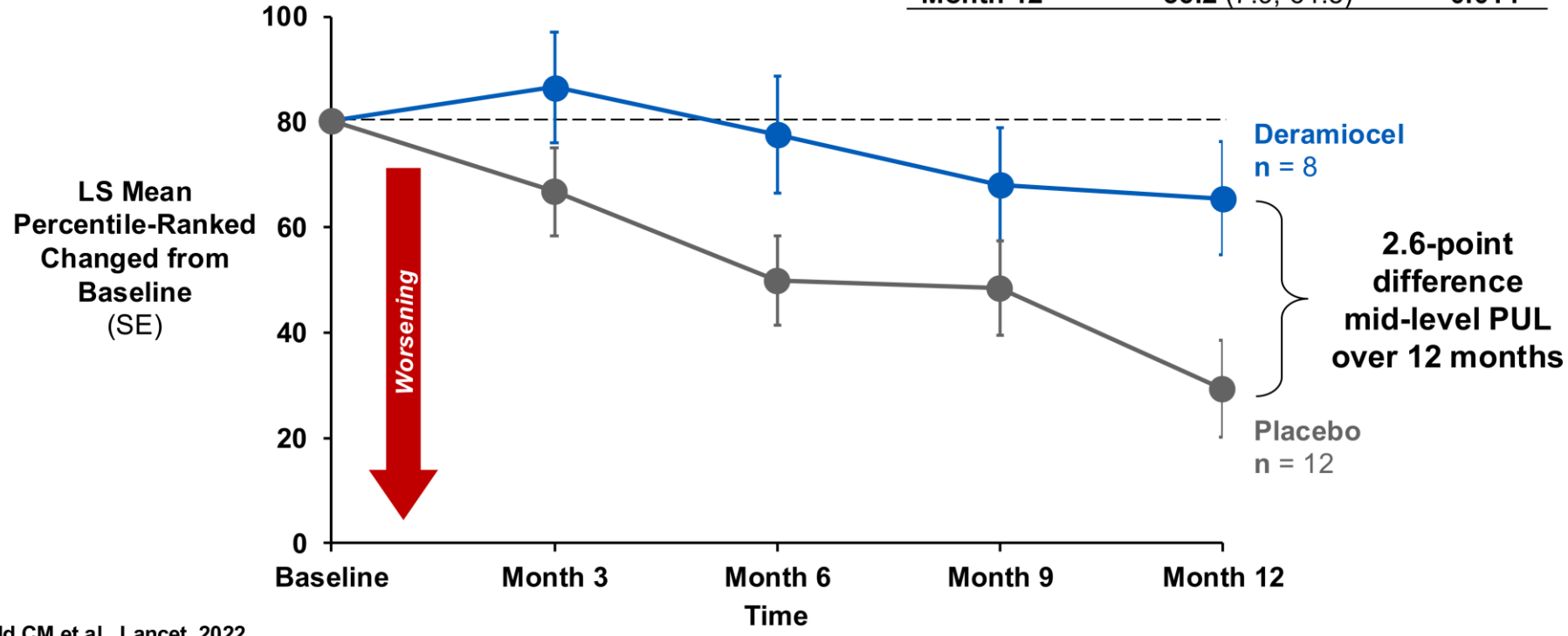


Disease Progression



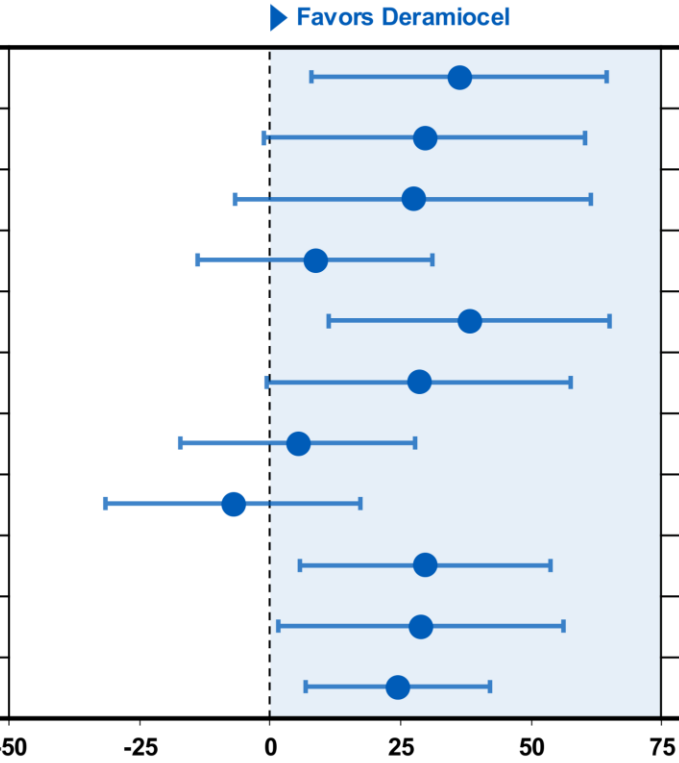
HOPE-2: Deramiocel Met Primary Endpoint with 71% Slowing of Decline (Mid-Level PUL 1.2)

Difference (95% CI)	Deramiocel n = 8	Placebo n = 12	p-value
Month 12	**36.2** (7.9, 64.5)		**0.014**



McDonald CM et al., Lancet. 2022

HOPE-2: Primary Analysis Supported by Multiple Sensitivity Analyses

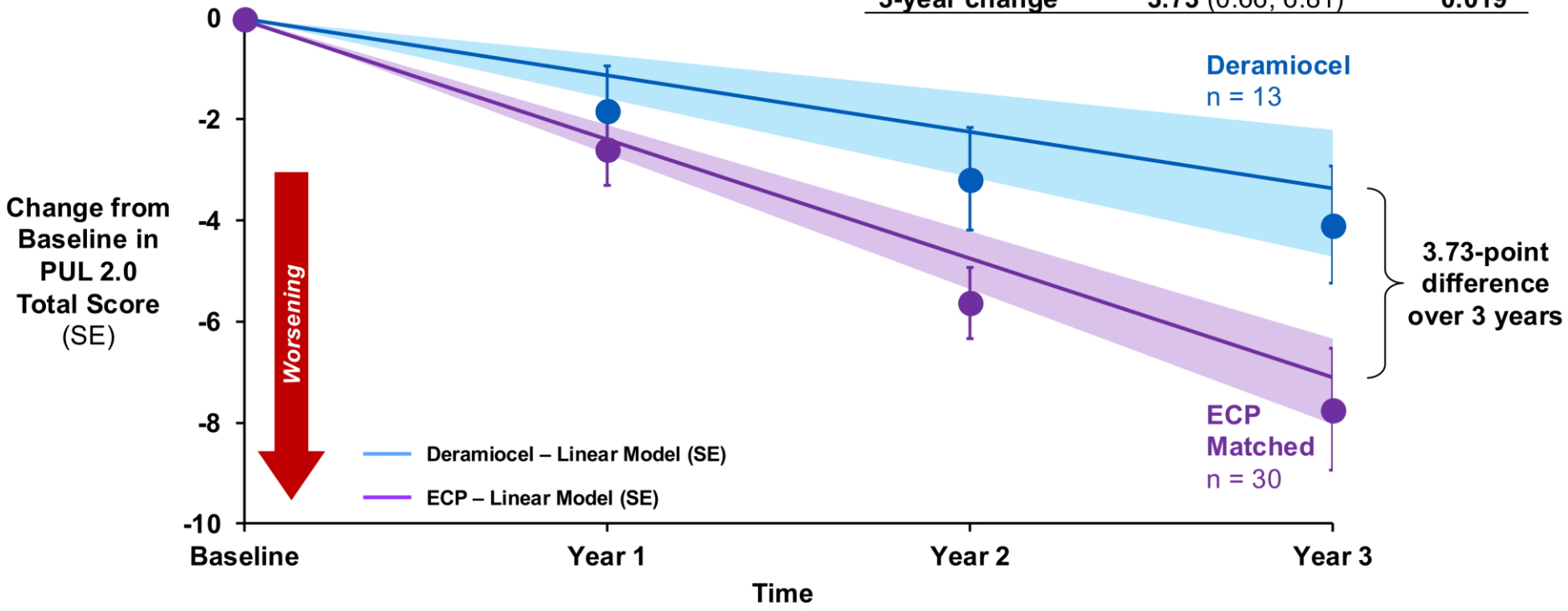


	LS Mean (95% CI)	p-value
Mid-level PUL 1.2	**36.2** (7.9, 64.5)	**0.0140**
Mid-level PUL 2.0	**29.6** (-1.1, 60.4)	**0.0586**
High-level PUL 1.2	**27.4** (-6.8, 61.6)	**0.1112**
High-level PUL 2.0	**8.6** (-14.0, 31.2)	**0.4413**
Combined mid-level and distal-level PUL 1.2	**38.1** (11.1, 65.1)	**0.0076**
Combined mid-level and distal-level PUL 2.0	**28.4** (-0.7, 57.6)	**0.0555**
Distal-level PUL 1.2	**5.2** (-17.2, 27.7)	**0.6402**
Distal-level PUL 2.0	**-7.1** (-31.5, 17.4)	**0.5609**
Total PUL 1.2	**29.7** (5.7, 53.7)	**0.0171**
Total PUL 2.0	**28.8** (1.5, 56.1)	**0.0399**
GST of PUL Measures	**24.4** (6.8, 42.1)	**0.0067**

McDonald CM et al. Lancet. 2022

HOPE-2-OLE: Statistically Significant Decline Over 3 Years with Deramiocel Treatment

Difference (95% CI)	Deramiocel n = 13	ECP Matched n = 30	p-value
3-year change	**3.73** (0.66, 6.81)		**0.019**



Deramiocel PUL 2.0 Treatment Effects Consistent Across HOPE-3 and HOPE-2

Endpoint	Metric	HOPE-3 Deramiocel n = 53 Placebo n = 52	HOPE-2 Deramiocel n = 8 Placebo n = 12
Total PUL 2.0	**PCHG**	**4.6%** (2.1), **p = 0.03**	**7.2%** (3.8), **p = 0.07**
Total PUL 2.0	**CHG**	**1.1** (0.6), **p = 0.05**	**1.8** (0.9), **p = 0.05**[a]
Mid-level PUL 2.0	**PCHG**	**8.1%** (3.0), **p < 0.01**	**7.7%** (4.5), **p = 0.10**
Mid-level PUL 2.0	**CHG**	**0.9** (0.4), **p = 0.02**	**0.9** (0.5), **p = 0.11**

Values are effect (SE); MMRM. CHG = absolute change; PCHG = percent change.
a. Sensitivity analysis only; CHG is the prespecified primary for HOPE-2, PCHG for HOPE-3.

Cardiac Efficacy

Jonathan Soslow, MD, MSCI

Professor of Pediatrics

Director of Clinical Research, Pediatric Cardiology

Co-Director, Duchenne Muscular Dystrophy Multispecialty Clinic

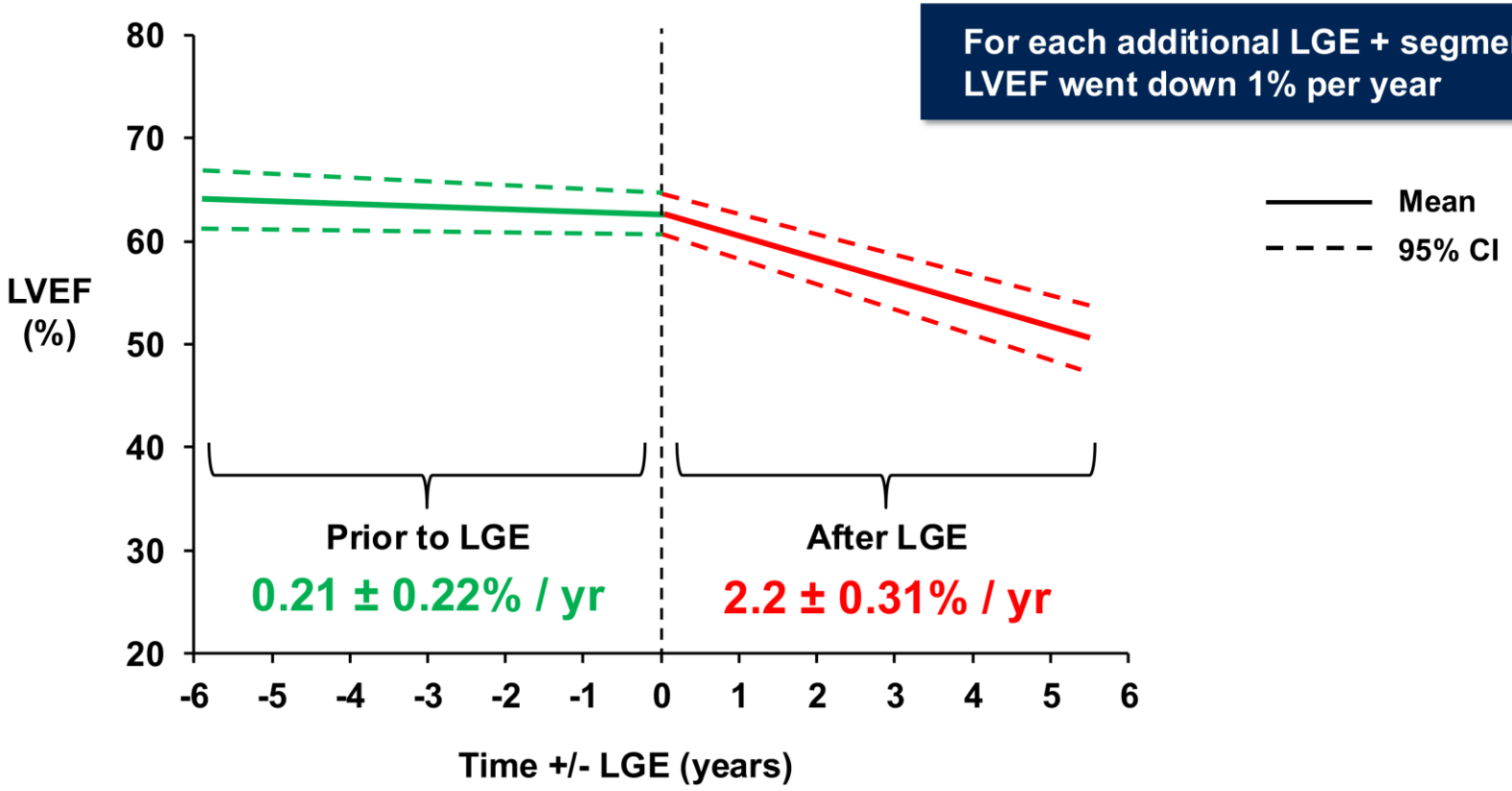
Director of the Duchenne Muscular Dystrophy Cardiovascular Care Consortium (DMDCCC)

Vanderbilt University Medical Center

Overview of Cardiomyopathy in DMD

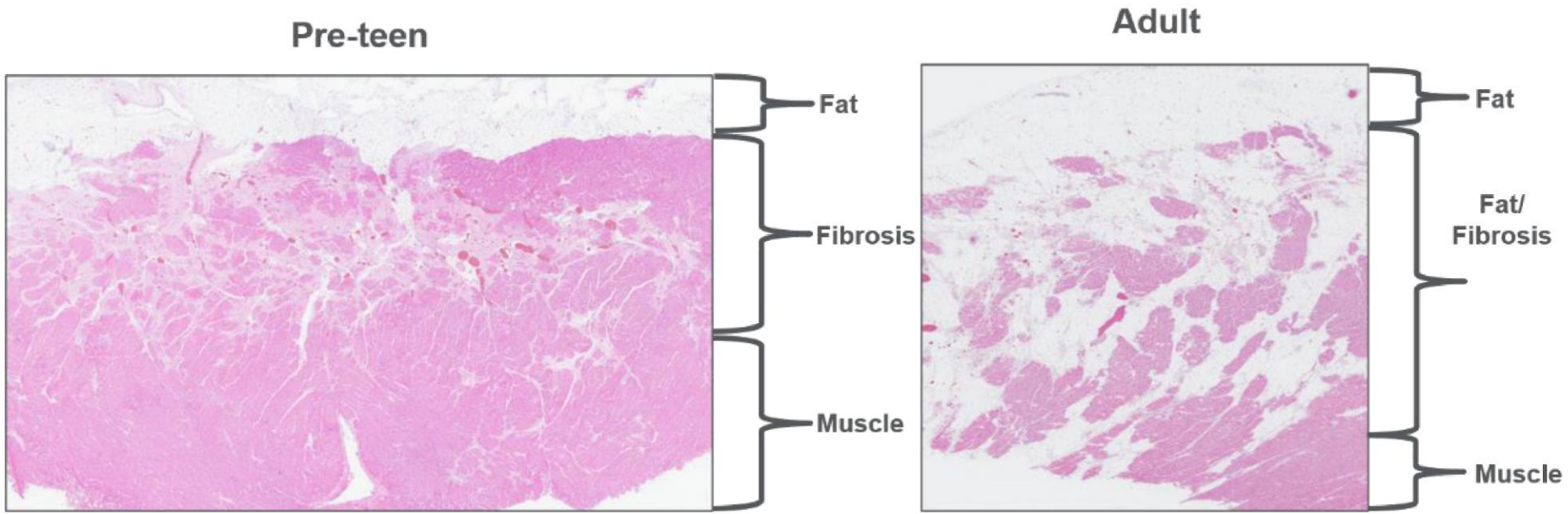
- DMD cardiomyopathy is different from idiopathic dilated cardiomyopathy
  - Once cardiomyopathy begins, there is a progressive inexorable decline in function
  - Decline is due to loss of cardiomyocytes and resultant fibrofatty replacement
- Standard metrics of feels, function, and survives cannot be used for DMD cardiomyopathy
- LVEF associates strongly with mortality

Systolic Function Declines After Onset of Late Gadolinium Enhancement (LGE)



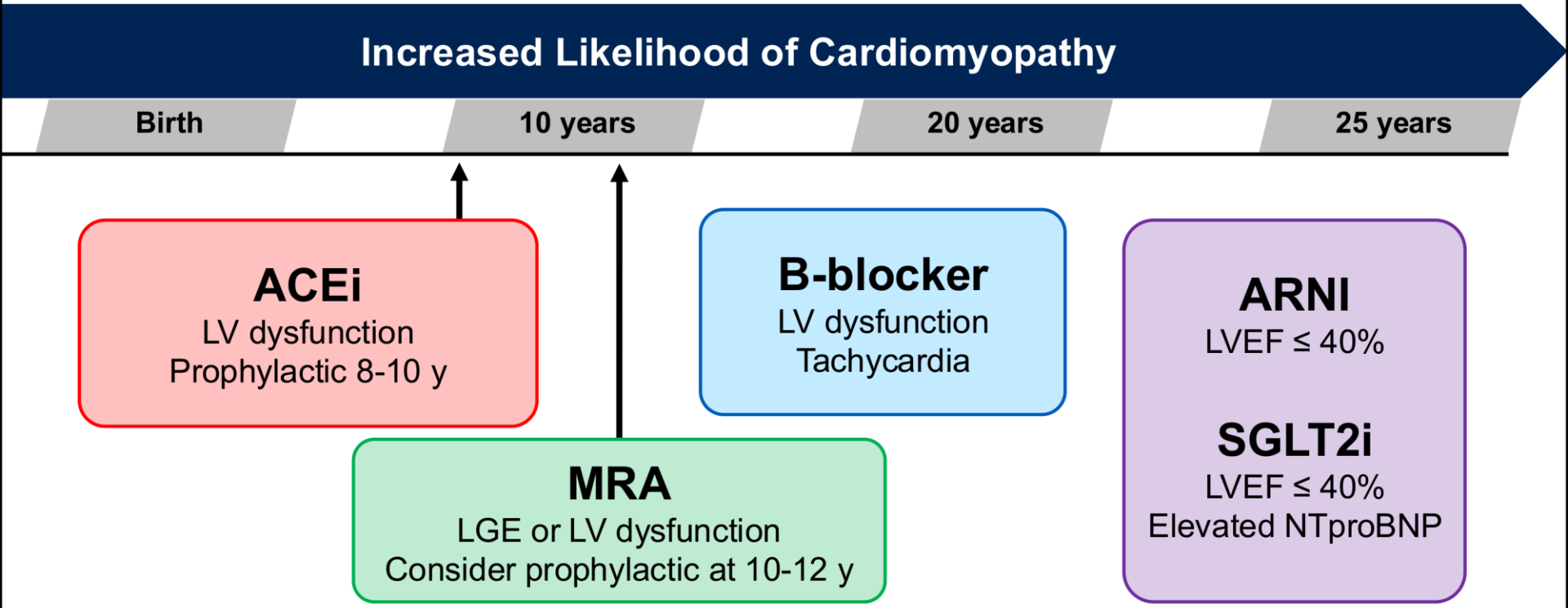
Tandon, et al. 2015

DMD Cardiomyopathy Is Different from Other Dilated Cardiomyopathies and Ischemic Cardiomyopathy



Breaux, et al. *JAHA*, 2024

ACTION Medication Recommendations



ACTION: Advanced Cardiac Therapies Improving Outcomes Network
Esteso, et al. 2024

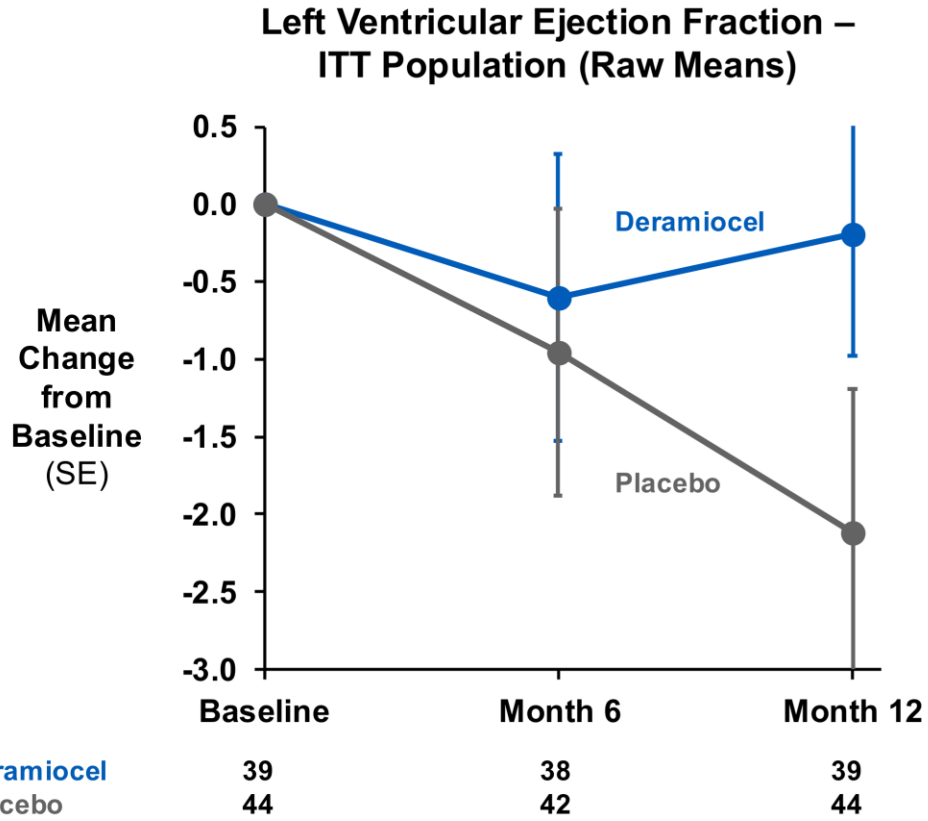
HOPE-3: Demographics of Cardiac Evaluable ITT

Overview, n (%)	Deramiocel n = 39	Placebo n = 44
Median Age, (range) (Years)	**16** (10-22)	**14** (10-22)
Median LVEF (%) at Baseline	**55.17**	**59.45**
Cardiomyopathy, n (%)	**32** (82%)	**32** (73%)
Baseline LVEF Group, n (%)		
< 45%	**5** (13%)	**0**
≥ 45%	**34** (87%)	**44** (100%)
Baseline Cardiac Medication Type, n (%)		
ACE/ARB/ARNI	**37** (95%)	**40** (91%)
Beta Blockers	**17** (44%)	**17** (39%)
SGLT2i	**3** (8%)	**2** (5%)
MRA	**21** (54%)	**29** (66%)
No Cardiac Medication	**2** (5%)	**3** (7%)

HOPE-3: Cardiac MRI Interpretation

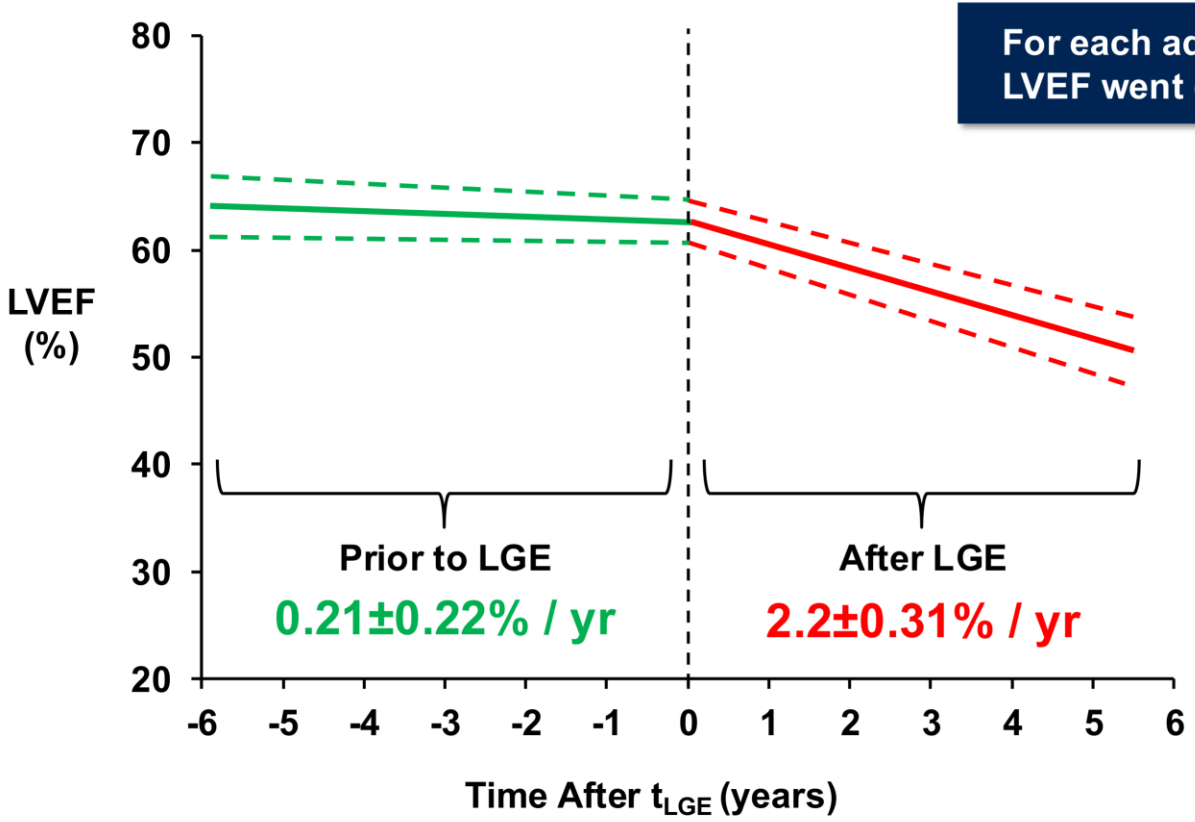
- Standard cardiac MRI protocol
- Single, blinded reader
- ~20% missing data, as expected in this patient population
  - Difficulty with breath-holds
  - Significant discomfort
  - Unable to fit in scanner due to contractures or obesity
- LGE missing data higher, due to above issues plus
  - Difficulty with IV access
  - Higher technical difficulties performing LGE

HOPE-3: Key Secondary Analysis of LVEF



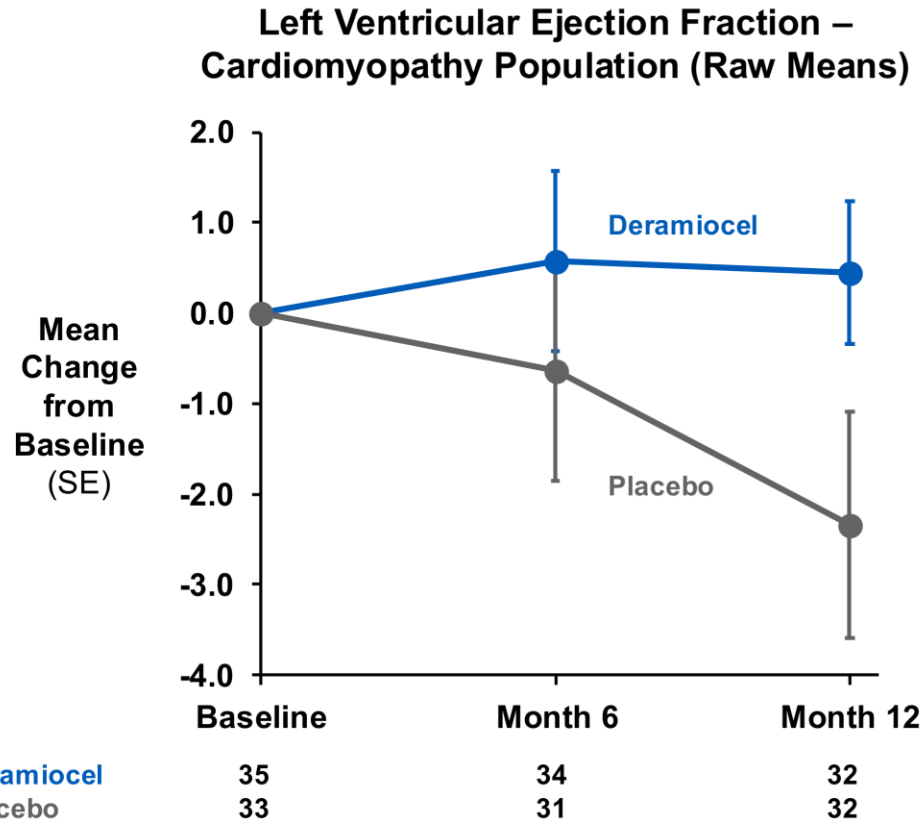
Δ = 1.8% p = 0.0935 (Ranked ANCOVA)
p = 0.0525 (Wilcoxon Rank Sum)

Systolic Function Declines After Onset of Late Gadolinium Enhancement (LGE)



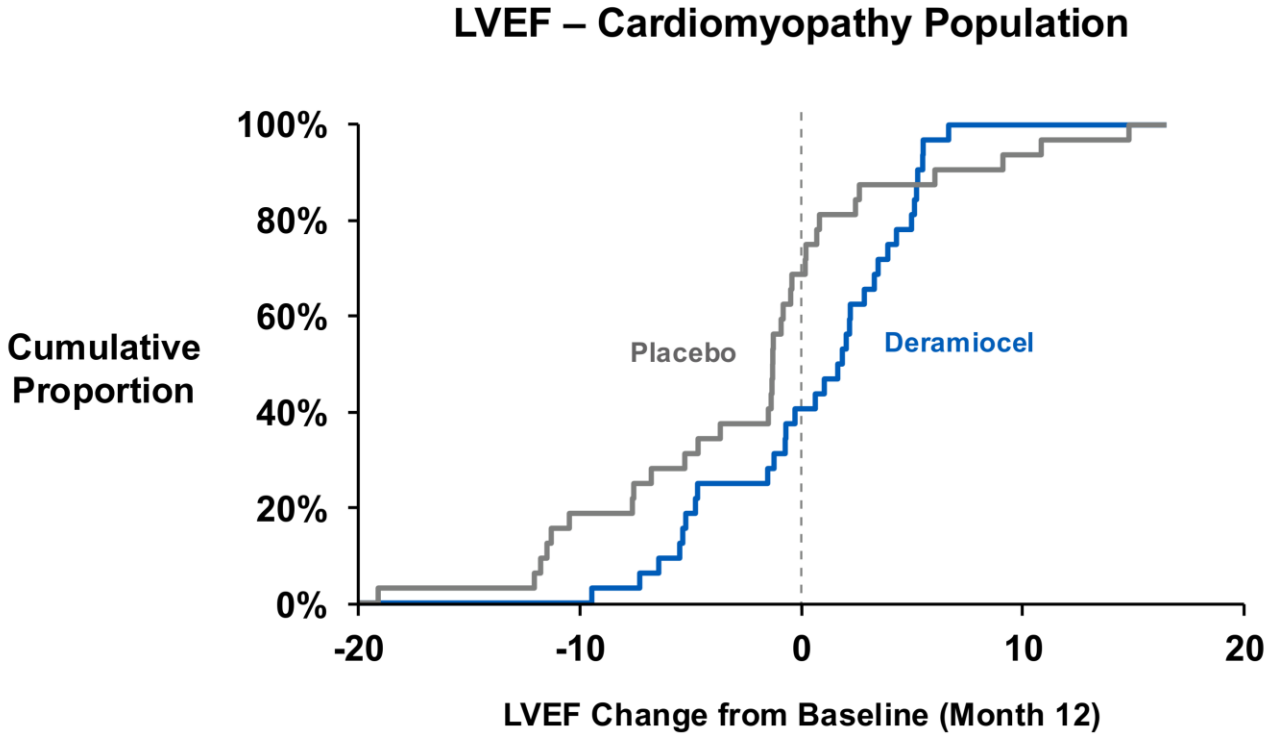
Tandon, et al. 2015

HOPE-3: LVEF Preserved in Patients with Cardiomyopathy

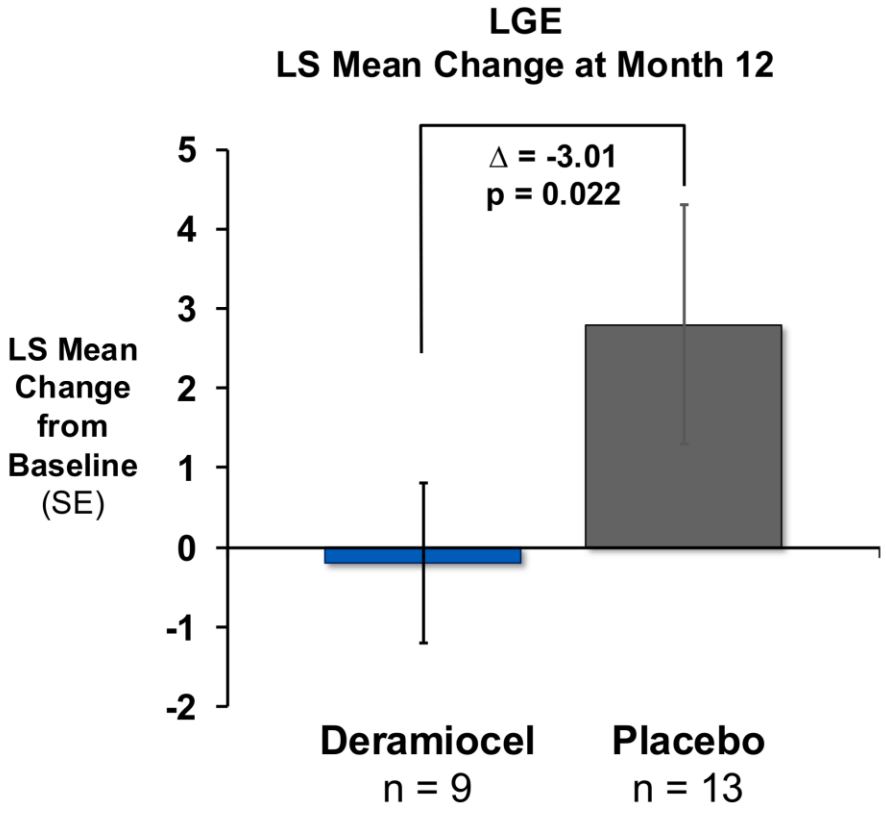


Δ = 2.9% p = 0.035 (Ranked ANCOVA)
p = 0.026 (Wilcoxon Rank Sum)

HOPE-3: Treatment Arms Separate Throughout Entire Distribution – LVEF in Cardiomyopathy Subgroup



HOPE-3: Late Gadolinium Enhancement (LGE) – Stabilization in Patients on Deramiocel

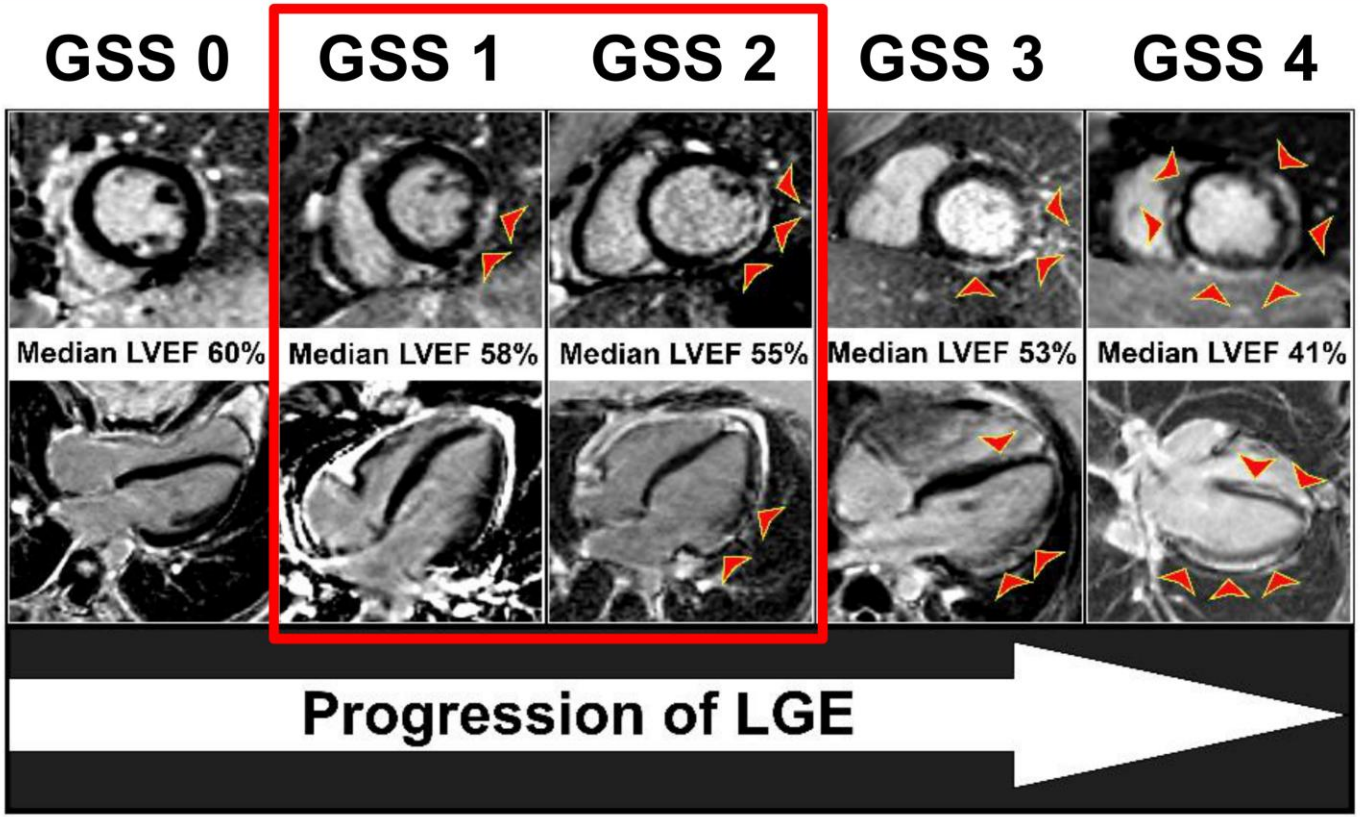


Cardiac Challenge – Silent Progression

- Functional testing, including 6-Minute Walk and Cardiopulmonary Exercise Tests are not feasible due to lack of ambulation
- Heart Failure patient and clinician reported outcomes (PROs, CROs) are not validated or feasible
  - KCCQ-12 and PROMIS including multiple questions directly related to ambulatory activities
  - CROs like the NYHA have similar limitations

PRO: Patient reported outcomes; CRO: Clinician reported outcomes; KCCQ: Kansas City Cardiomyopathy Questionnaire; PROMIS: Patient-reported outcomes measurement information system; NYHA: New York Heart Association

Fibrosis and Fibrofatty Replacement Is a Pathogenic Feature of DMD



Top row: short-axis views · Bottom row: long-axis views · Red arrowheads mark LGE (scar). Groups span median LVEF 60% → 41%.

Assessment of Mortality Would Require Many Years

- Mortality trials would require starting drugs at correct window of opportunity then following patients for 10-15 years
  - Drug trial of this duration is infeasible
  - Drug trial of this duration is unethical

Left Ventricular Dysfunction and Dilation on Cardiac MRI Associates with All-Cause Mortality

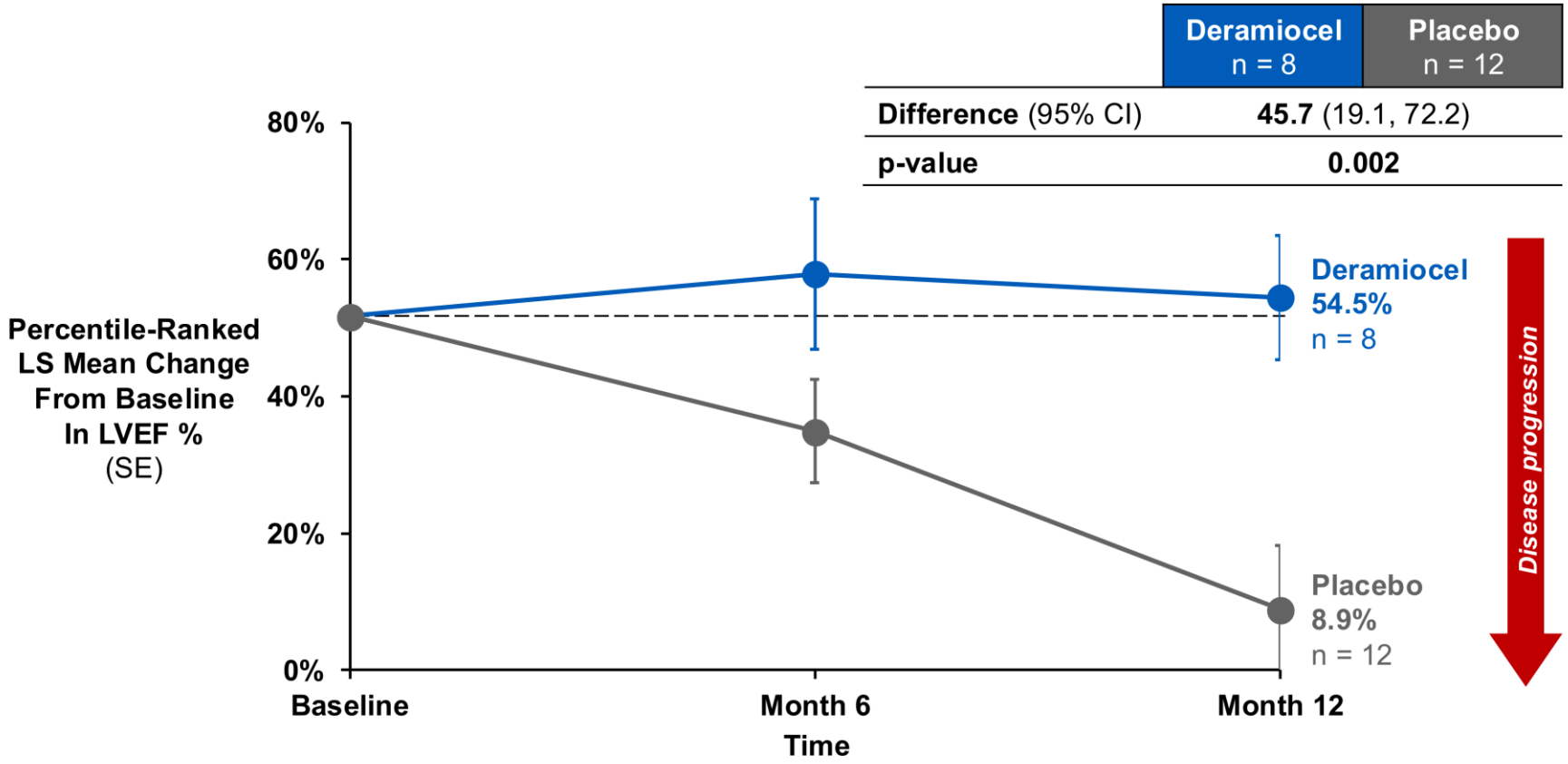
Measure	N	HR (95% CI)	p-value
LVEF per 3% decrease	**78**	**1.32** (1.12, 1.55)	**< 0.001**
LVEDV*i* per 4 mL/m^2 increase	**77**	**1.20** (1.09, 1.32)	**< 0.001**
LVESV*i* per 2 mL/m^2 increase	**77**	**1.12** (1.06, 1.19)	**< 0.001**
LGE full width half maximum per 5.9% increase	**15**	**1.24** (1.06, 1.46)	**0.008**

Menon, et al. 2014; Florian, et al. 2014; Soslow, et al. 2023

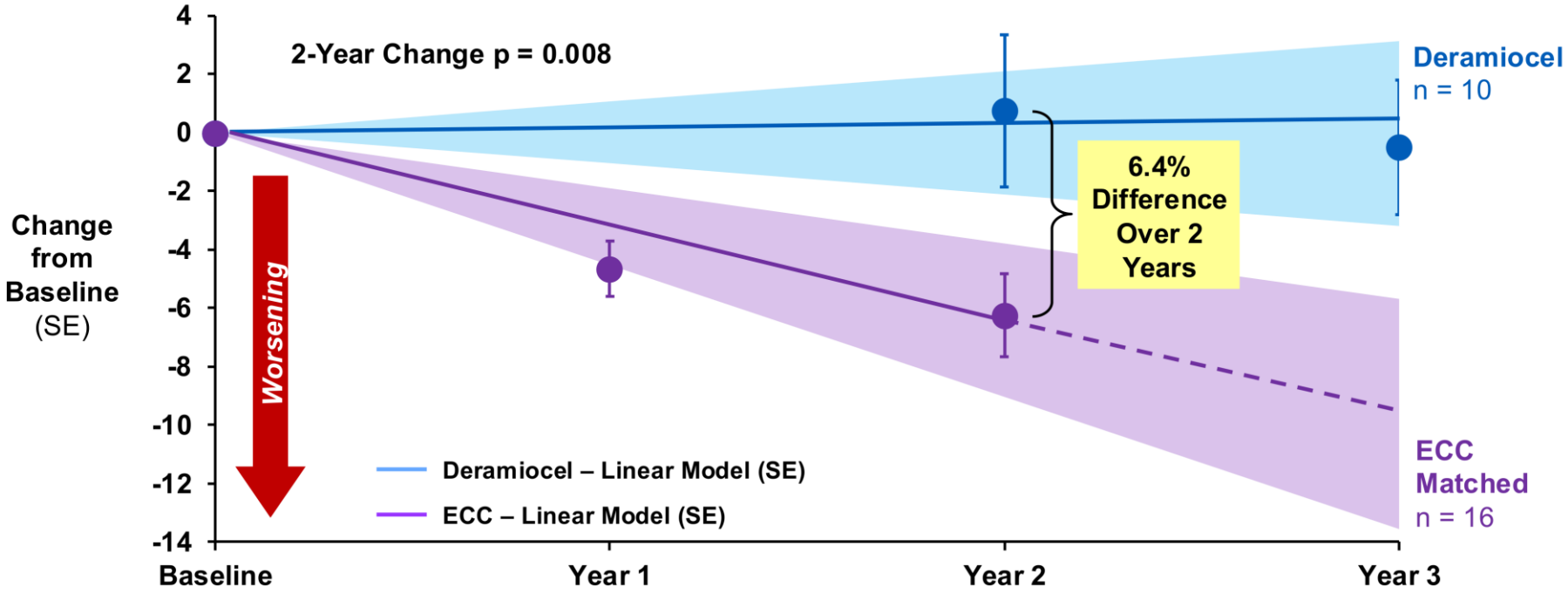
Studies Associating Echo or cMRI Findings with DMD Mortality

Associations Between Imaging Studies and Mortality				
Studies (N = 1448)	**Diagnosis**	**Measure**	**Outcome**	**Method**
1. Corrado, et al. *Am J Cardiol.* 2002	DMD	Fractional Shortening (FS)	Mortality	Echo
2. Schram, et al. *JACC*. 2013	DMD	LVEF	Mortality	Echo
3. Wang, et al. *Open Heart,* 2018	DMD	LV dysfunction < 18 y vs ≥ 18 y	Mortality	Echo
4. Wittlieb-Weber, et al. *Pediatr Cardiol*, 2020	DMD	LVEF, FS	Mortality	Echo
5. Segawa, et al. *Neuropsychiatr Dis Treat*, 2020	DMD	LV Dilation	Mortality	Echo
6. Cha, et al. *ESC Heart Failure*, 2022	DMD	LVEF < 40% vs LVEF ≥ 40%	Mortality	Echo
7. Lechner, et al. *ERJ Open*, 2023	DMD	LVEF	Mortality	Echo
8. Menon, et al. *Pediatr Cardiol,* 2014	DMD	LVEF, LVESVi	Mortality	CMR
9. Florian, et al. *JCMR,* 2014	DMD/BMD	LVEF	Mortality + MACE	CMR
10. Silva, et al. *JAMA Cardiology,* 2017	DMD/BMD	Myocardial fibrosis	Mortality	CMR
11. Florian, et al. *Circ: Cardiovasc Imaging,* 2020	DMD/BMD	LVEF > 45% vs LVEF ≤ 45%	Mortality + MACE	CMR
12. Starnes, et al. *Pediatr Cardiol*, 2022	DMD	LVEF, LGE	Mortality	CMR
13. Soslow, et al. *Circ: Heart Failure*, 2023	DMD	LVEF, LVEDVi, LVESVi	Mortality	CMR
14. Starnes, et al. *J Am Heart Assoc*, 2023	DMD	Progression of LVEF, LVEDVi, LVESVi	Mortality	CMR

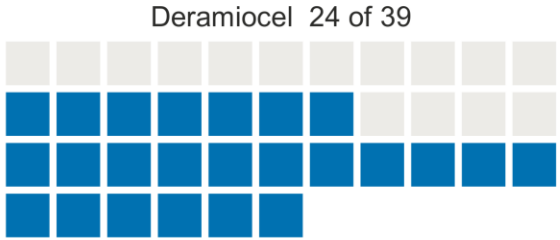
HOPE-2: Deramiocel Demonstrated Stable LVEF vs Placebo



HOPE-2-OLE: Deramiocel Demonstrated Stable LVEF vs External Comparator Cohort



Clinician's Responder Analysis: PUL and LVEF



Responders*
61.5% vs 4.5%

Deramiocel vs placebo

Nominal p-value
< 0.0001

Fisher exact test

Responder classified as a patient whose change was above the overall median change in PUL and LVEF

61.5% vs 4.5% (+57 pts)
Odds ratio: 33.6

*Model based analysis

Safety

Michael Binks, MD

Chief Medical Officer

Capricor, Inc.

HOPE-3: Overall Safety Summary

Overview, n (%)	Deramiocel n = 53	Placebo n = 52
Any AE	**50** (94%)	**43** (83%)
AE related to IP or administration procedure	**44** (83%)	**19** (37%)
AE related to IP	**44** (83%)	**16** (31%)
AE related to administration procedure	**23** (43%)	**9** (17%)
AEs related to IP or administration procedure by maximum severity		
Mild	**19** (36%)	**15** (29%)
Moderate	**25** (47%)	**3** (6%)
Severe	**0**	**0**
Life-threatening	**0**	**1** (2%)
Fatal	**0**	**0**
AEs leading to death	**0**	**0**
Any SAE	**1** (2%)	**5** (10%)
SAE related to IP or administration procedure	**1** (2%)	**1** (2%)

AEs leading to study drug withdrawal occurred in 1 patient in each group
No deaths occurred and serious AEs occurred less frequently in deramiocel group vs placebo

HOPE-3: Hypersensitivity Responses Were Mild to Moderate with Rapid Resolution

Preferred Term, n (%)	Deramiocel n = 53	Placebo n = 52
Any hypersensitivity reactions	**22** (42%)	**8** (15%)
Pyrexia	**13** (25%)	**0**
Tachycardia	**6** (11%)	**3** (6%)
Throat irritation	**6** (11%)	**0**
Heart rate increased	**3** (6%)	**1** (2%)
Rash	**2** (4%)	**1** (2%)
Flushing	**1** (2%)	**2** (4%)
Tachypnoea	**1** (2%)	**1** (2%)
Hypersensitivity	**1** (2%)	**0**
Throat tightness	**1** (2%)	**0**
Anaphylactic reaction	**0**	**1** (2%)

Hypersensitivity reactions were mild to moderate in severity, resolved within 24-48 hours and managed with standard supportive measures

Summary of Safety from HOPE Program

- **Deramiocel intravenous infusion takes approximately 60 minutes**
  - Pre-medication with oral prednisone and anti-histamines
  - Observation for at least 2 hours post infusion
- **Infusions are well-tolerated**
  - AEs balanced, predominantly mild, transient and manageable
  - **Mild to moderate hypersensitivity responses are common**
- **Related SAE frequency similar to placebo**
  - SAE frequency remains low in long-term studies
- **No known long term safety concerns**

Meaningfulness of Results

Mindy Leffler

Patient Advocacy

Capricor, Inc.

DVA Tool and Process – Standardized Home-Based Data Collection

Supplies

Caregiver / participant

- Download study mobile application
- Receive study supplies

Training

Caregiver / participant

- Read Training Manual
- Watch training videos

Video Capture

Caregivers video record participants performing DVA movement tasks with study mobile application

Data Review

Data monitors review video quality and request video reshoots if videos do not meet quality standards

Scoring

DVA-certified physical therapists score approved videos using scorecards with prespecified compensatory movement criteria

Analysis

Statistical team derives DVA endpoints and analyzes data

DVA – Validated and Published

Quality of Life Research (2019) 28:2979–2988
https://doi.org/10.1007/s11136-019-02245-2

Adapting traditional content validation methods to fit purpose: an example with a novel video assessment and training materials in Duchenne muscular dystrophy (DMD)

Michelle K. White[1] · Mindy Leffler[2] · Kaitlin Rychlec[1] · Chris Jones[3] · Christine McSherry[2] · Linsey Walker[4] · Mark Kosinski[1]

Accepted: 3 July 2019 / Published online: 13 July 2019

Received: 15 March 2022 | Revised: 1 November 2022 | Accepted: 31 December 2022
DOI: 10.1002/pri.1993

RESEARCH ARTICLE

WILEY

Home-based video assessment of ease of movement for patients with Duchenne: Interviews with physical therapists to select movement tasks

Marielle G. Contesse[1] | Jason Hodges[1] | Hannah Staunton[2] | Linda P. Lowes[3] | Bassem Elmankabadi[4] | Sonya J. Elder[1] | Maitea Guridi Ormazabal[5] | Laura Dalle Pazze[6] | Mindy G. Leffler[1]

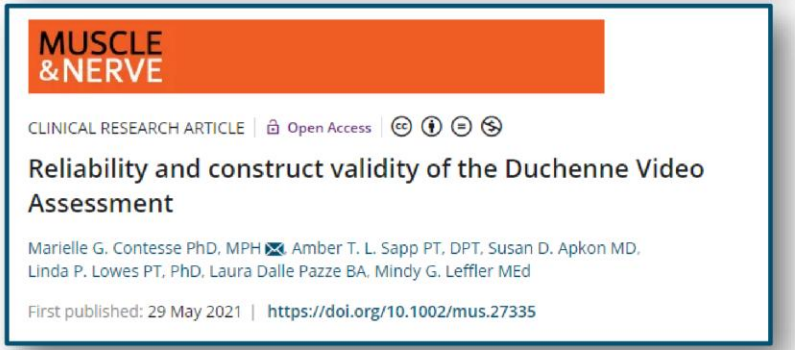
PLOS ONE

OPEN ACCESS PEER-REVIEWED
RESEARCH ARTICLE

Development of Duchenne Video Assessment scorecards to evaluate ease of movement among those with Duchenne muscular dystrophy

Marielle G. Contesse, Linda P. Lowes, Michelle K. White, Laura Dalle Pazze, Christine McSherry, Lindsay N. Alfano, Megan Iammarino, Natalie Reash, Kelly Bonarrigo, Michael Kiefer, Katie Laubscher, Melissa McIntyre, Shelley Mockler, [...], Mindy G. Leffler [view all]

Published: April 13, 2022 • https://doi.org/10.1371/journal.pone.0266845



MUSCLE &NERVE

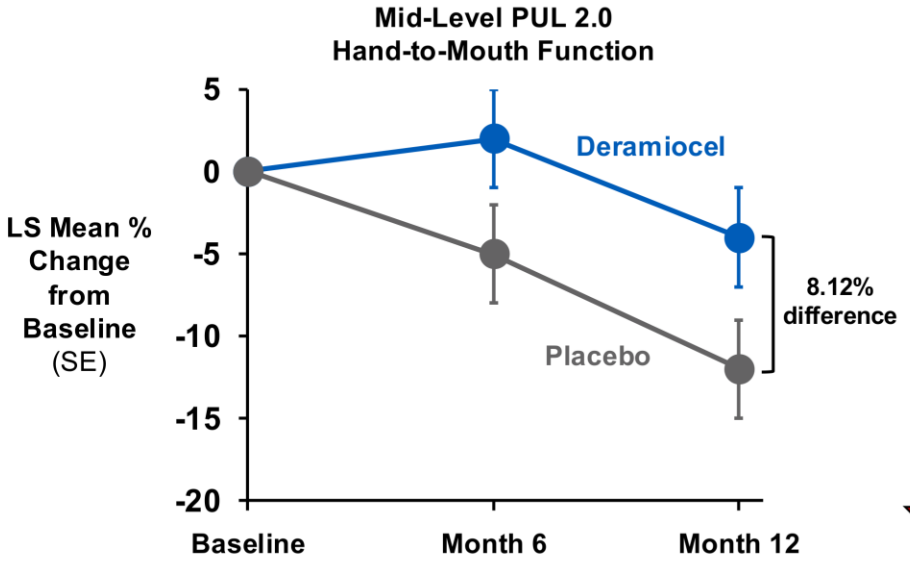
CLINICAL RESEARCH ARTICLE | Open Access

Reliability and construct validity of the Duchenne Video Assessment

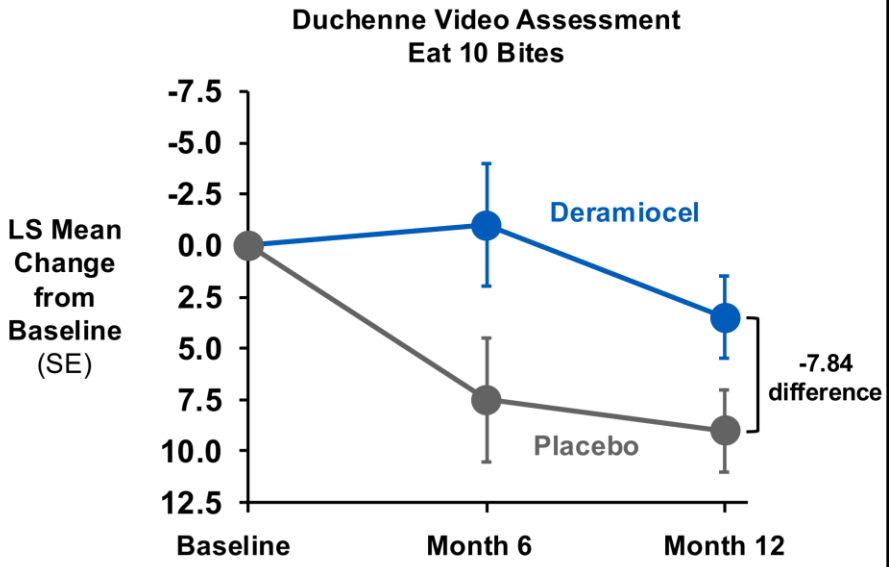
Marielle G. Contesse PhD, MPH, Amber T. L. Sapp PT, DPT, Susan D. Apkon MD, Linda P. Lowes PT, PhD, Laura Dalle Pazze BA, Mindy G. Leffler MEd

First published: 29 May 2021 | https://doi.org/10.1002/mus.27335

Ability to Feed Oneself Is Meaningful Outcome



Disease Progression



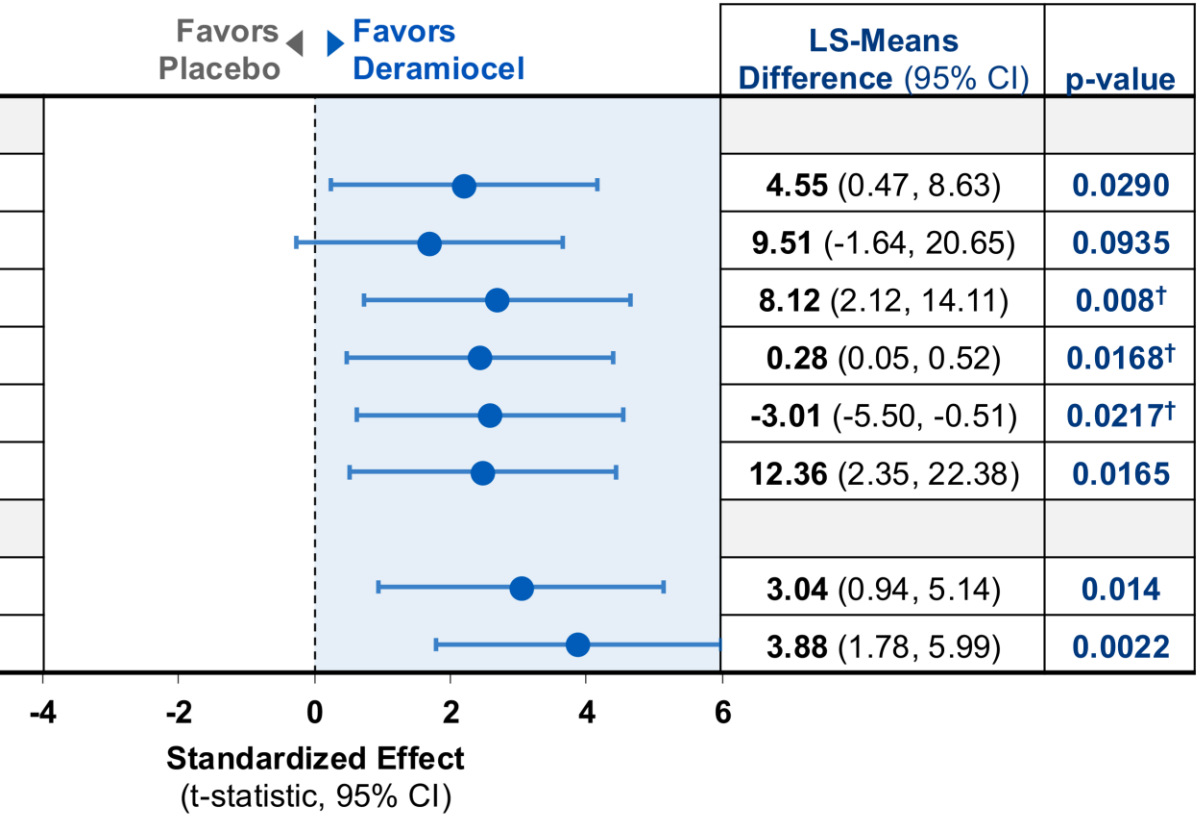
Conclusions

Linda Marbán, PhD

Chief Executive Officer and Director

Capricor, Inc.

Substantial Evidence of Efficacy Across Two RCTs



	LS-Means Difference (95% CI)	p-value
HOPE-3		
PUL 2.0 Total Score (Primary)	**4.55** (0.47, 8.63)	**0.0290**
LVEF (%) (Key secondary)	**9.51** (-1.64, 20.65)	**0.0935**
PUL 2.0 Mid-level Score*	**8.12** (2.12, 14.11)	**0.008†**
Total Global Statistical Test*	**0.28** (0.05, 0.52)	**0.0168†**
Late Gadolinium Enhancement (segments)*	**-3.01** (-5.50, -0.51)	**0.0217†**
LVEF (%) (Cardiomyopathy)	**12.36** (2.35, 22.38)	**0.0165**
HOPE-2		
PUL 1.2 Total Score (Primary)	**3.04** (0.94, 5.14)	**0.014**
LVEF**	**3.88** (1.78, 5.99)	**0.0022**

McDonald, et al. 2026

* Type 1 error-controlled secondary endpoints; ** exploratory; † p-values are nominal

Deramiocel Benefits Far Outweigh Risks

- **Clinically meaningful results CONSISTENT across 2 RCT trials and OLE**
  - HOPE-3 is the largest clinical trial in primarily non-ambulatory patients
  - Skeletal primary: **PUL**
  - Cardiac secondary: **LVEF**

- **All SAPs submitted prior to unblinding; verified by audit trail**
  - SAP 1.1 is an incomplete draft
  - Not submitted to FDA; provided as Information Request in 2026

- **Capricor requested indication expansion "for treatment of DMD"; FDA declined**
  - Submitted and amended BLA for cardiomyopathy in alignment with FDA
  - FDA committed to review of primary PUL endpoint

Deramiocel and Duchenne Muscular Dystrophy

July 29, 2026

Cellular, Tissue, and Gene Therapies Advisory Committee

Sponsor: Capricor, Inc.