Multi-modal benefits of deramiocel (CAP-1002) in late-stage patients with DMD:

A new treatment approach to target skeletal and cardiac muscle pathogenesis

(HOPE-2-OLE Trial - 36 Month data)

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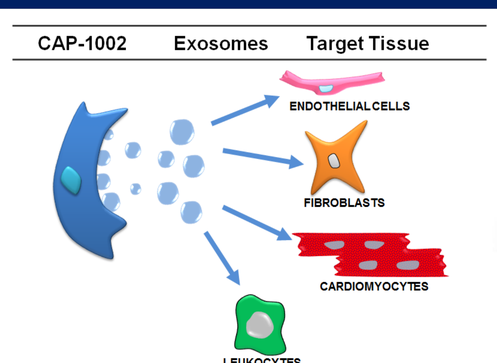
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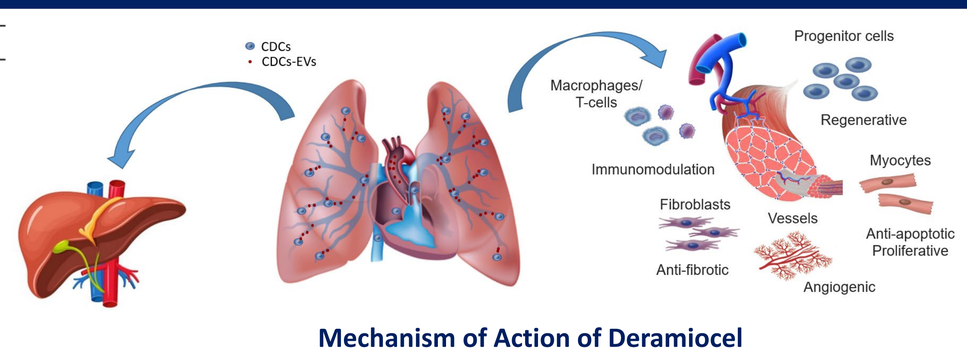
WMS World Muscle Society

BACKGROUND AND MECHANISM OF ACTIONS

Deramiocel (CAP-1002) is an investigational cell-based product that has been evaluated in more than 200 volunteers, showing promising clinical outcomes for the treatment of DMD and cardiac disease secondary to DMD in multiple clinical trials, including the HOPE-2 study and its open-label extension study (HOPE-2-OLE).

Deramiocel promotes release of exosomes, and growth factors to address inflammation and fibrosis associated with DMD. The mechanism of action of deramiocel is its composite ability to be immunomodulatory, anti-inflammatory, anti-fibrotic, and pro-regenerative.

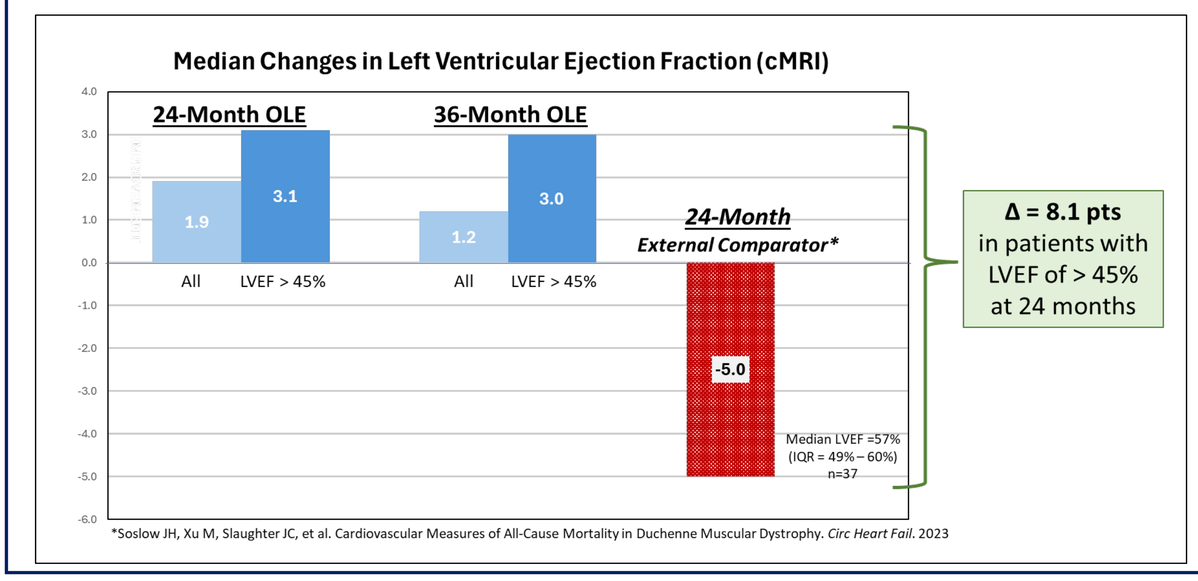




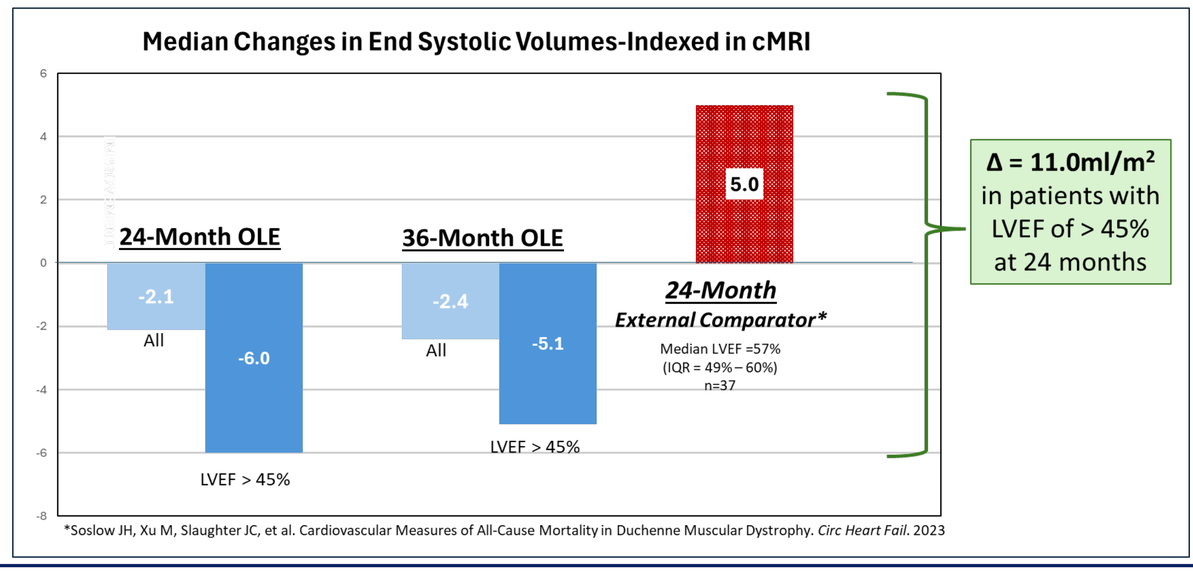
Mechanism of Action of Deramiocel

CARDIAC RESULTS FROM THE 36-MONTH HOPE-2-OLE STUDY FURTHER STRENGTHENED THE PREVIOUSLY REPORTED RESULTS FROM HOPE-2 AND COMPARED TO AN EXTERNAL COMPARATOR

- Left Ventricular Ejection Fraction (LVEF), End Systolic Volume-Indexed (ESVI), and End Diastolic Volume-Indexed (EDVI) are associated with mortality and serve as the best outcome measures for cardiovascular therapeutic trials as reported by Soslow et al, 2023.
- Median changes in LVEF in all patients with cMRI (n=10) show improvement of 1.9 percentage points after 24 months of treatment with deramiocel. Benefits are sustained after 36 months of treatment with a median improvement of 1.2 percentage points. [light blue]
- A subgroup analysis of patients with a starting LVEF > 45% (n=8) demonstrated a median improvement of 3.1 points at 24 months and further sustained at 36 months with a 3.0 percentage point improvement. [dark blue]
- An external comparator (EC) from Soslow et al 2023 reports a median decline in LVEF of 5.0 percentage points over 24 months. [red]
- **The Subgroup of deramiocel treated patients with a starting LVEF >45% (Median baseline LVEF = 54.2%) compared to the External Comparator (Median baseline LVEF = 57%) demonstrates a robust benefit of deramiocel after 24 months of treatment with a difference of 8.1 difference in LVEF.**
- Median changes in ESVI in all patients (n=10) show improvement in cardiac function with a decrease of 2.1 ml/m^2 of after 24 months of treatment with deramiocel. Improvement sustained after 3 years of treatment with a median decrease of 2.4 ml/m^2. [light blue]
- A subgroup analysis of patients with a starting LVEF > 45% (n=8) demonstrated a median improvement of 6.0 ml/m^2 at 24 months and further sustained at 36 months with a 5.1 ml/m^2 decrease in ESVI. [dark blue]
- An external comparator from Soslow et al 2023 observed a decline in cardiac function with a 5.0 ml/m^2 median increase in ESVI over 24 months. [red]
- **The Subgroup of deramiocel treated patients with a starting LVEF >45% (Median baseline LVEF = 54.2% compared to the External Comparator (Median baseline LVEF = 57%) demonstrates a robust benefit of deramiocel after 24 months of treatment with a difference of 11.1 ml/m^2 in ESVI.**
- **Similar findings in EDVI were observed with a difference of 15.7 ml/m^2 in the subgroup analysis of deramiocel treated patients at 24 months compared to the external comparator. [not shown]**



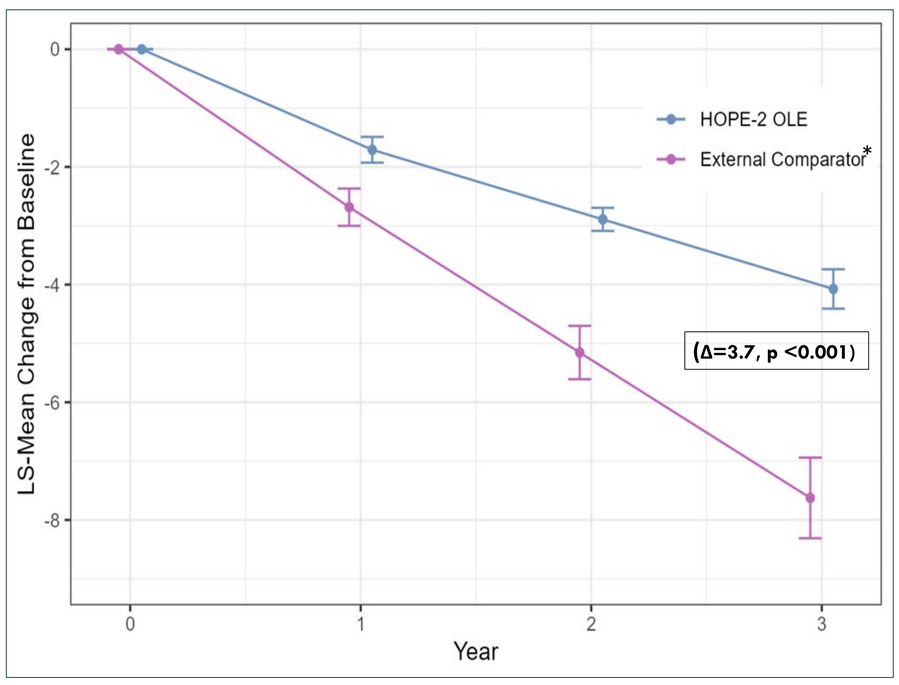
*Soslow JH, Xu M, Slaughter JC, et al. Cardiovascular Measures of All-Cause Mortality in Duchenne Muscular Dystrophy. *Circ Heart Fail*. 2023



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LONG-TERM IMPROVEMENT OF SKELETAL MUSCLE FUNCTION IN PUL

- The year-over-year skeletal muscle function using the Performance of the Upper Limb v2.0 (PUL v2.0) shows evidence of disease attenuation in deramiocel treated patients
- Patients treated with deramiocel had a mean decline of the PUL 2.0 of 1.74 points during Year 1 of treatment, 1.20-point decline during Year 2 and 1.08-decline during Year 3. [blue]
- EC group (n=30) from a database from CCHMC* matched by age, range of PUL 2.0 total score and entry item score, standard of care steroid treatment and had multi year follow-up observations. [purple]
- Deramiocel treated patients had a 4.0-pt mean decline in the PUL v2.0 over 36 months of treatment compared to the EC which showed a mean decline of 7.7 points (Δ=3.7, p <0.001).
- **Translates to 47% slowing of disease progression.**



* Cincinnati Children's Hospital Medical Center

OVERVIEW OF ADVERSE EVENTS/SAFETY IN OLE

AE Categories	Deramiocel (N=13) n (%)
Any TEAE[1]	13 (100.0%)
TEAE by maximum severity[2]	
Mild or Moderate (≤ Grade 2)	13 (100.0%)
Severe or life-threatening or disabling (Grade 3 or 4)	5 (38.5%)
Death	0
TEAE related to IP or administration procedure[3]	9 (69.2%)
TEAE related to IP[3]	9 (69.2%)
TEAE related to administration procedure	9 (69.2%)
Any SAE related to IP or administration procedure	0

AE: adverse event; IP: investigational product; IV: intravenous; SAE: serious adverse event; TEAE: treatment-emergent adverse event defined as an AE occurring after the initiation of the IV catheter placement for the initial dose of IP.

1. A total of 143 TEAEs occurred by Month 36 in HOPE-2-OLE.
2. Each Subject is counted once by the worst severity. AEs with missing severity are counted as "severe".
3. Each Subject is counted once by the greatest relationship to IP or administration procedure, ie, "probable or possible". AEs with missing relatedness to the IP or IP administration will be considered to have "possible" relatedness. A total of 34 events were considered as related to IP, and 30 related to administration procedure.
4. AEs with missing seriousness are counted as "serious".

CONCLUSIONS

- Deramiocel is novel, first-in-class, allogeneic cellular therapy that demonstrates safe and effective long-term treatment benefits for patients with DMD.
- Compared to an external comparator, long-term treatment with deramiocel provides clinically meaningful benefits observed by cMRI, by stabilizing or improving left ventricular ejection fraction, end systolic and end diastolic indexed volumes.
- Statistically significant disease attenuation in skeletal muscle function as measured by the PUL 2.0 compared to a long-term external comparator database.
- Deramiocel was well-tolerated without new safety signals identified and continues to maintain a favorable risk/benefit profile in HOPE-2-OLE.
- Ongoing long-term open-label extension studies continue to confirm the unprecedented therapeutic durability and established safety of deramiocel beyond 36 months for the treatment of both skeletal and cardiac muscle function in DMD.

REFERENCES

- McDonald, CM, et al. Repeated intravenous cardiosphere-derived cell therapy in late-stage Duchenne Muscular Dystrophy (HOPE-2): A multicentre, randomised, double-blind, placebo-controlled, phase 2 trial. The Lancet, 2022; 399(10329), 1049–1058.
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The Lancet (McDonald et al, 2022)

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