Long-Term Functional Improvement With Zeleciment Basivarsen in the Phase 1/2 ACHIEVE Trial

Karlien Mul, MD, PhD[1], Guillaume Bassez[2], Jordi Diaz-Manera[3], James Lilleker[4], Marika Pane[5], Richard Roxburgh[6], Benedikt Schoser[7], Christopher Turner[8], Allison Kreuzer[9], Alexandra Lovett[9], Soma Ray[9], Huaihou Chen[9], Shauna Andersson[9], Douglas Kerr[9], Valeria Sansone[10]

[1]Radboud University Medical Center, Nijmegen, the Netherlands; [2]Institut de Myologie, Paris, France; [3]John Walton Muscular Dystrophy Research Centre, Newcastle University, Newcastle-Upon-Tyne, UK; [4]Muscle Disease Unit, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK; [5]Fondazione Policlinico Universitario A. Gemelli, Rome, Italy; [6]Neurogenetics Clinic Centre for Brain Research, University of Auckland, Auckland, NZ; [7]Friedrich-Baur-Institute, Dep. of Neurology LMU Clinics, Ludwig-Maximilians University, Munich, Germany; [8]University College London Hospitals, London, UK; [9]Dyne Therapeutics, Inc., Waltham, MA, USA; [10]Centro Clinico NeMO, University of Milan, Milan, Italy

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Presentation

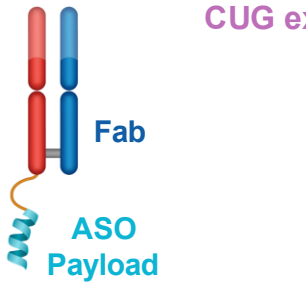
Appendix

Disclosure

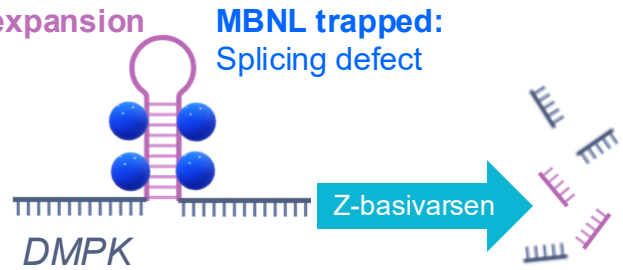
- Dr. Mul has served as a paid consultant for Dyne Therapeutics, Avidity Biosciences, and Sarepta Therapeutics. She received research funding from Vertex Pharmaceuticals and PepGen Inc.
- Zeleciment basivarsen (z-basivarsen, also known as DYNE-101) is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

Z-Basivarsen Addresses the Central Pathobiology of DM1 to Enable Broad Functional Improvement[1]

Robust and widespread delivery → ***DMPK* degradation in the nucleus** → **MBNL release and splicing correction** → **Early clinical effect** → **Functional outcomes**

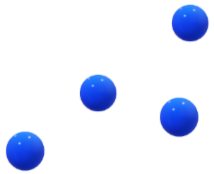


Z-basivarsen
Relevant tissue distribution

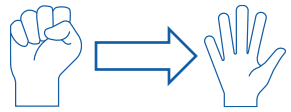


Differentiated MOA





MBNL released:
Splicing corrected



Myotonia:
Video Hand Opening Time (vHOT)

Muscle Strength:
Quantitative Muscle Testing

Timed-Function Tests:
5 Times Sit to Stand;
10-Meter Walk / Run

Patient-Reported Outcomes:
Myotonic Dystrophy Health Index (MDHI)

ACHIEVE

[1]Image depicts the intended z-basivarsen mechanism of action.
ASO, antisense oligonucleotide; CUG, cytosine, uracil, and guanine; DM1, myotonic dystrophy type 1; DMPK, dystrophia myotonica protein kinase; Fab, antigen-binding fragment. MBNL, muscleblind-like; MDHI, Myotonic Dystrophy Health Index; MOA, mechanism of action; vHOT, video hand opening time; z-basivarsen, zelecIment basivarsen

ACHIEVE Multiple Ascending Dose Study

6-Month Placebo-Controlled Period (MAD Cohorts)

- **6.8 mg/kg** N=8 (3:1) Q8W, Placebo
- **5.4 mg/kg** N=8 (3:1) Q8W, Placebo
- **3.4 mg/kg** N=16 (3:3:2) Q4W, Recovery, Placebo
- **3.4 mg/kg** N=8 (3:1) Q8W, Placebo
- **1.8 mg/kg** N=16 (3:3:2) Q4W, Recovery, Placebo

Muscle biopsies at baseline, 12 weeks, and 24 weeks

Transition to 6.8 mg/kg[1]

Open-label extension (OLE)

Long-term extension (LTE)

Population

- Ages 18–49 years

Primary endpoints

- Safety and tolerability

Additional endpoints

- Pharmacokinetics
- Change from baseline of:
  - Splicing
  - *DMPK* RNA expression
  - Multiple assessments of muscle strength and function
  - Patient-reported outcomes, including MDHI

Data from the MAD portion of the ACHIEVE study was used to select the registrational dose of 6.8 mg/kg Q8W that is being evaluated in the Registrational Expansion Cohort of the study[2,3]

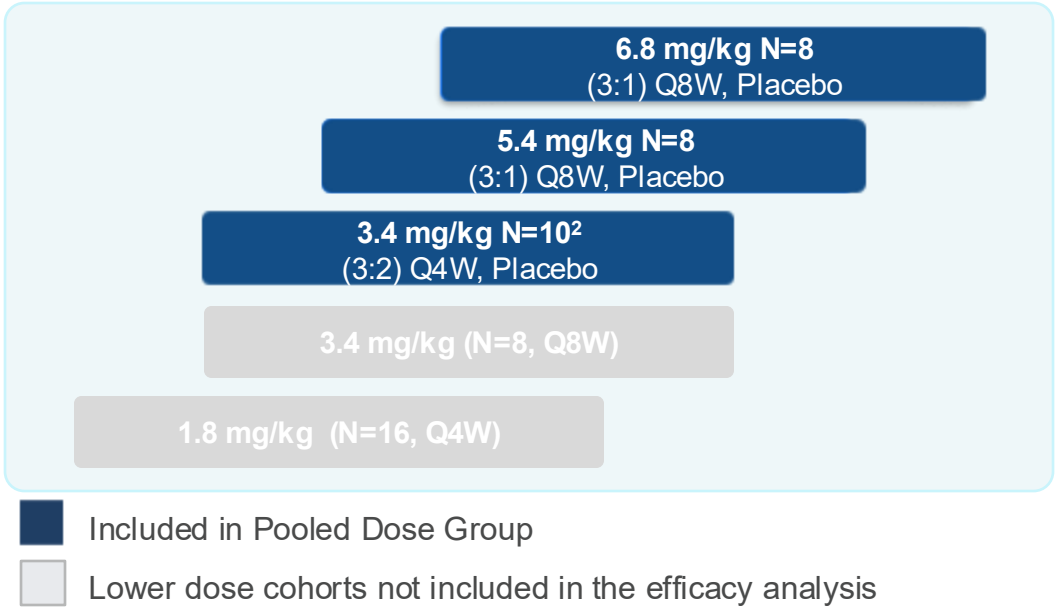
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Doses provided refer to approximate antisense oligonucleotide component of DYNE-101. Recovery cohort Q4W x 2 doses then placebo for the remainder of the 24-week placebo-controlled period. Q8W, every 8 weeks with a loading dose given 4 weeks after first dose of active drug. Additional endpoints include select secondary and exploratory endpoints. [1]Transition to 6.8 mg/kg dose occurs at non-uniform times during OLE or LTE. [2]Lilleker J. 2025 Annual MDA Clinical and Scientific Conference. March 16-19, Dallas, TX. [3]Sansone V, et al. Poster presentation at the Annual International Congress of the WMS, Vienna, Austria, October 7–11, 2025. Poster 380P.
DMPK, dystrophia myotonica protein kinase; MAD, multiple ascending dose; MDHI Myotonic Dystrophy Health Index; LTE, long-term extension; OLE, open-label extension; Q4W, every 4 weeks; Q8W, every 8 weeks; RNA, ribonucleic acid.

ACHIEVE MAD Study: Efficacy Analysis of Pooled Dose Group

- Previous long-term analysis included N=6 assigned to 6.8 mg/kg (registrational dose) at baseline[1]
- To determine if similar trends hold in a larger sample, we analyzed 12mo efficacy of a pooled dose group (N = 26)
- The pooled dose group includes a mixture of dose exposures and does not reflect the effect of maintaining 6.8 mg/kg for the entire treatment duration
- Only 8/26 participants in the pooled dose group received the registrational dose for the full 12 months analyzed, and most did not receive the registrational dose during this timeframe

Pooled Dose Group 1-Year Efficacy Analysis (N=26)



ACHIEVE

Pooled Dose Group includes participants from the 6.8 mg/kg Q8W, 5.4 mg/kg Q8W, and 3.4 mg/kg Q4W cohorts, including participants who initially received placebo within those cohorts and subsequently received active treatment. The participants who originally received placebo were re-baselined to the visit prior to their first active dose. 6.8 mg/kg and 5.4 mg/kg dose cohorts were treated with Q8W, every 8 weeks with a loading dose given 4 weeks after first dose of active drug. [1]Sansone V, et al. Poster presentation at the Annual International Congress of the WMS, Vienna, Austria, October 7–11, 2025. Poster 380P. [2]Patients assigned to recovery were not included in this analysis.
MAD, multiple ascending dose; Q4W, every 4 weeks; Q8W, every 8 weeks; z-bas, zeleciment basivarsen.

Z-Basivarsen ACHIEVE MAD Clinical Update

Safety

Data from ACHIEVE MAD as of **April 20, 2026**

Efficacy

Data from 6.8 mg/kg cohort and analysis of Pooled Dose Group:

- **vHOT**
- Clinical outcome measures of **muscle strength** and **function**
- **Patient-reported outcomes**

Divergence From Natural History[1]

Analysis of **ACHIEVE** versus **END-DM1 natural history**

ACHIEVE

[1]END-DM1 data transfer as of July 2026. Analysis presented with permission from the Myotonic Dystrophy Clinical Research Network (DMCRN). END-DM1 remains ongoing.
DM1, myotonic dystrophy type 1; MAD, multiple ascending dose; vHOT, video hand opening time; z-basivarsen, zeleciment basivarsen.

ACHIEVE MAD Baseline Characteristics

Mean (SD)	Placebo (N=14)	6.8 mg/kg Q8W (N=6)	Pooled dose group (N=26)
Age (years)	32.6 (9.6)	37.2 (9.7)	35.6 (8.0)
BMI (kg/m^2)	24.4 (4.7)	23.4 (5.6)	22.7 (3.9)
CASI-22	0.68 (0.20)	0.74 (0.25)	0.73 (0.19)
CTG repeats	597 (246)	542 (191)	527 (243)
vHOT (middle finger) (sec)	7.5 (3.0)	7.8 (3.8)	8.2 (4.4)
QMT total (% predicted)	51.5 (14.3)	51.3 (10.4)	48.0 (14.3)
Hand grip (% predicted)	44.8 (16.9)	49.0 (12.9)	41.5 (16.3)
10-meter walk/run (sec)	3.34 (0.48)	3.94 (1.56)	3.99 (1.49)
5 Times sit-to-stand (sec)	9.24 (2.03)	9.98 (3.33)	10.20 (3.94)
MDHI total[1]	18.7 (13.8)	26.5 (13.7)	24.4 (19.8)

Pooled Dose Group includes participants from the 6.8 mg/kg Q8W, 5.4 mg/kg Q8W, and 3.4 mg/kg Q4W cohorts, including participants who initially received placebo within those cohorts and subsequently received active treatment. The participants who originally received placebo were re-baselined to the visit prior to their first active dose. Only 8/26 participants in the pooled dose group received the registrational dose for the full 12 months analyzed, and most did not receive the registrational dose during this timeframe.

ACHIEVE

[1]Scored from 0–100, with 0 representing no disease burden, 100 maximal disease burden.
BMI, body mass index; CASI, composite alternative splicing index; CTG, cytosine, thymine, and guanine; MAD, multiple ascending dose; MDHI, Myotonic Dystrophy Health Index; Q8W, every 8 weeks; QMT, quantitative muscle testing; SD, standard deviation; sec, seconds; vHOT, video hand opening time.

Favorable Safety Profile With No Serious Related TEAEs[1]

Summary of treatment-emergent adverse events (TEAEs)[1]

TEAE category	Participants with ≥1 TEAE, n (%)					
	1.8 mg/kg Q4W+Rec. N=16	3.4 mg/kg Q4W+Rec. N=16	3.4 mg/kg Q8W N=8	5.4 mg/kg Q8W N=8	6.8 mg/kg Q8W N=8	Overall (N=56)
Any TEAE	16 (100)	16 (100)	8 (100)	8 (100)	8 (100)	56 (100)
Any related TEAE	10 (62.5)	10 (62.5)	4 (50)	6 (75)	7 (87.5)	37 (66.1)
Any serious TEAE	5 (31.3)	0	2 (25)	1 (12.5)	0	8 (14.3)
Any serious related TEAE	0	0	0	0	0	0
Any TEAE leading to withdrawal from study	0	0	0	2 (25)	0	2[2] (3.6)
Any TEAE leading to death	0	0	0	0	0	0

Most TEAEs were mild or moderate in intensity[1]

- **10 serious TEAEs unrelated to study drug**
  - Atrioventricular block first degree (1)[3]
  - Pneumonia (2 events in same participant)
  - Pulmonary embolism (1)[4]
  - Hyponatraemia (1)
  - Influenza B virus test positive (1)
  - Fall (1)
  - Gastroenteritis (1)
  - Meningioma (1)
  - Uterine leiomyoma (1)
- **Most common TEAEs (≥30% participant incidence)[5]**
  - Infusion-related reaction (50%)[6]
  - Nasopharyngitis (46.4%)
  - Diarrhoea (35.7%)
  - Headache (33.9%)
  - Procedural pain (33.9%)
  - Influenza (32.1%)
  - Back pain (30.4%)

Additional safety data

- **Liver enzyme elevations have been observed in a minority of participants**
  - No impact on liver function (bilirubin or coagulation)
  - Interpretation is complicated by underlying disease and elevated baseline values up to ~2.5x greater than the upper limit of normal
- **No participants have demonstrated persistent related anemia or thrombocytopenia**

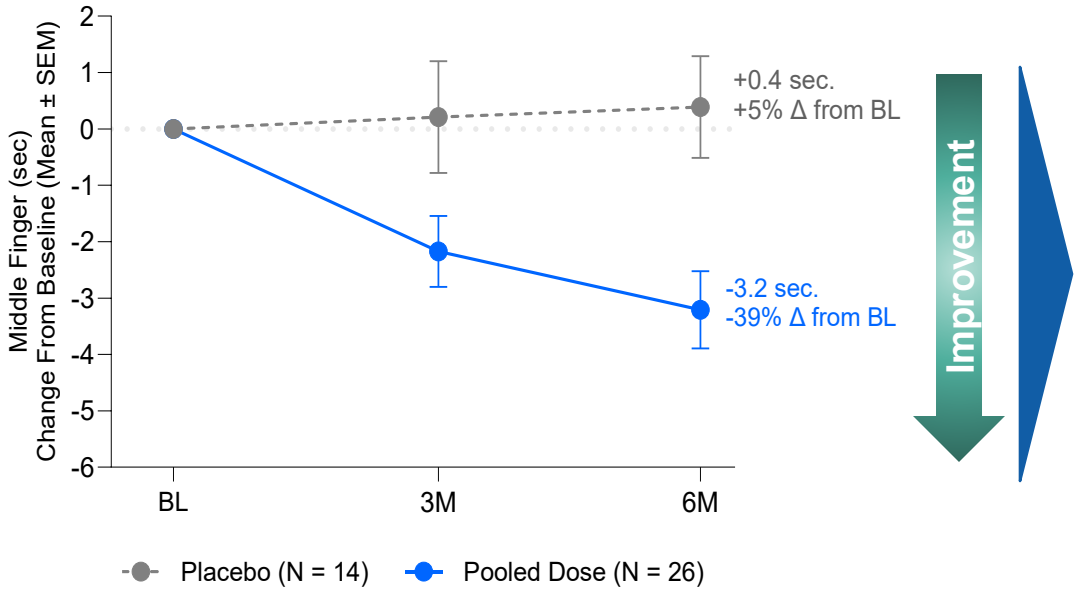
~1300 doses of study drug administered to date representing over 143 patient-years of follow-up[1]

ACHIEVE

[1]Data as of April 20, 2026. [2]TEAEs leading to study withdrawal were IRRs that resolved within 2-3 days in 2 participants who had received z-basivarsen for over 12 months. [3]Transient worsening of atrioventricular (AV) block in a participant with ongoing medical history of first-degree AV block. [4]Attributed to risk factors for pulmonary embolism. [5]All cohorts combined. [6]Most IRRs were mild or moderate in severity.
IRR, infusion-related reactions; Q4W, every 4 weeks; Q8W, every 8 weeks; Rec, Recovery Arm; TEAE, treatment-emergent adverse event; z-basivarsen, zeleciment basivarsen.

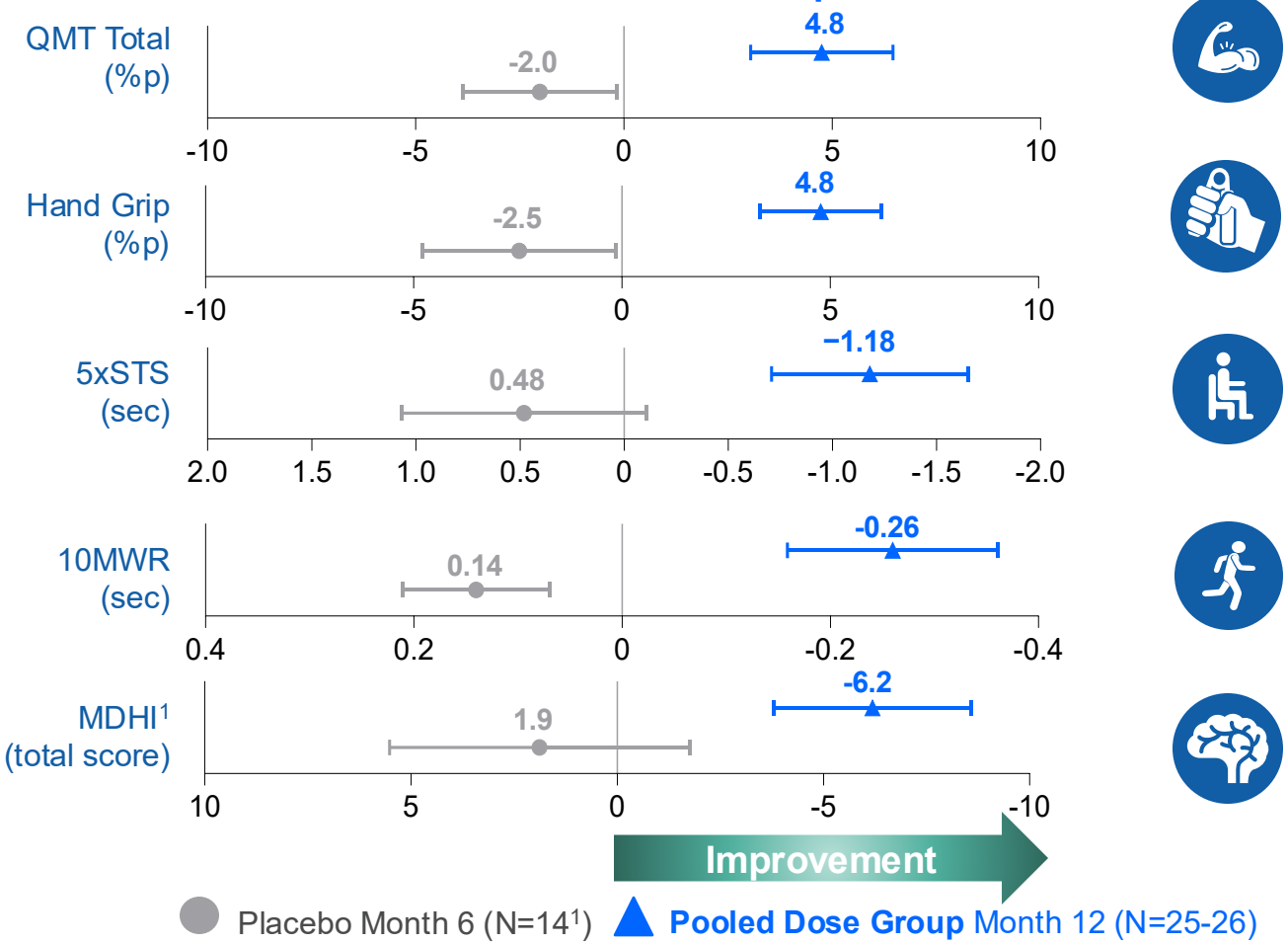
Pooled Efficacy Data Continue to Support vHOT as an Early Indicator of Functional Improvement

vHOT Middle Finger:
Pooled Dose Group



Baseline (sec), mean (SEM)	**7.5 (0.8)**	**8.2 (0.9)**

Mean Change From Baseline (SEM)
Pooled Dose Group



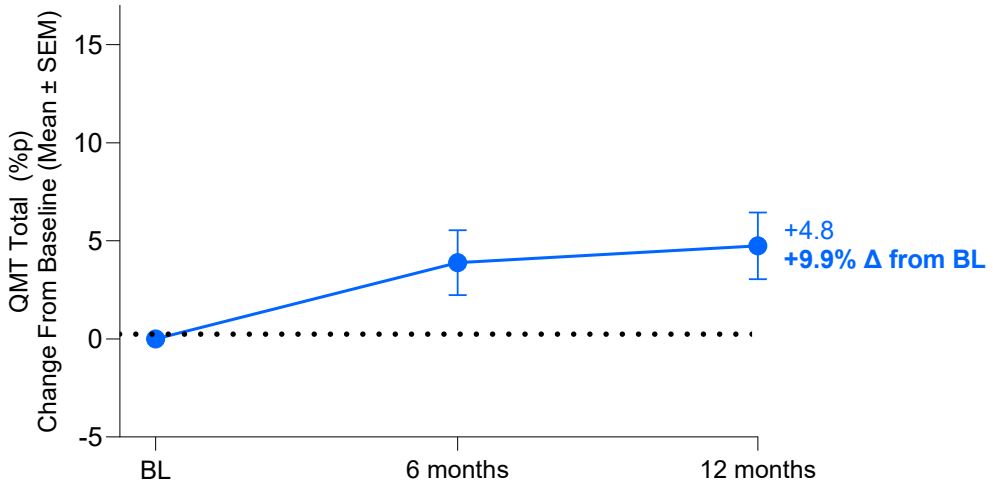
ACHIEVE

[1]MDHI, N=13. Percent mean change from baseline = (mean change from baseline/baseline mean) x 100. 6 months = 169 days; 12 months = 337 days.
For information on the Pooled Dose Group, see footnotes on slide 7
%p, percent predicted; 10MWR, 10-Meter Walk/Run; 5xSTS, 5 Times Sit to Stand; BL, baseline; M, months; MDHI, myotonic dystrophy health index; Q4W, every 4 weeks; Q8W, every 8 weeks; QMT, quantitative muscle testing; sec, seconds; SEM, standard error of the mean; vHOT, video hand opening time.

Improvement in Strength Is Sustained at 12 Months, as Measured by QMT (%p)

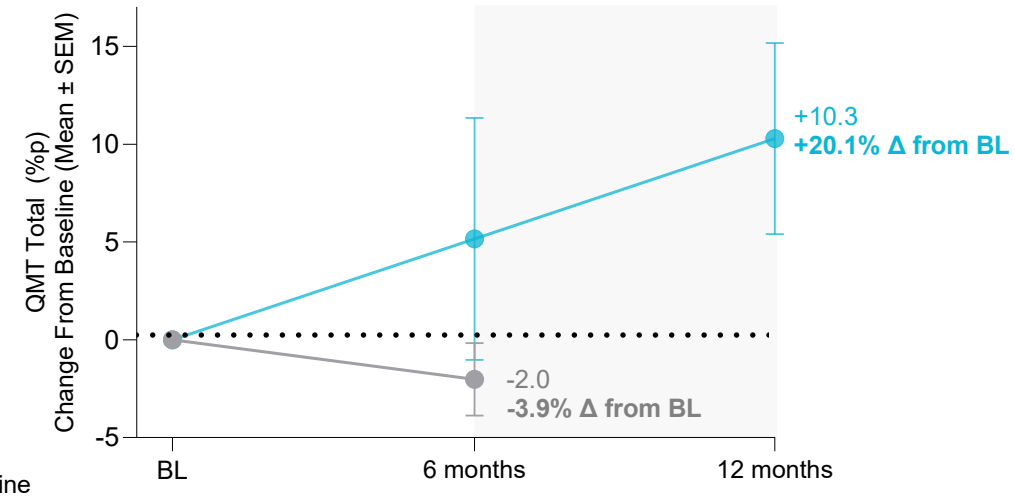
Quantitative Muscle Testing (QMT) Total Score

Pooled Dose Group (N=26)



Baseline Mean (SEM)	Patients, N		
	BL	6 months	12 months
48.0 (2.8)	26	26	25

6.8 mg/kg Cohort



	Baseline Mean (SEM)	Patients, N		
		BL	6 months	12 months
Placebo	51.5 (3.8)	14	14	-
6.8 mg/kg	51.3 (4.2)	6	6	6

Improvement

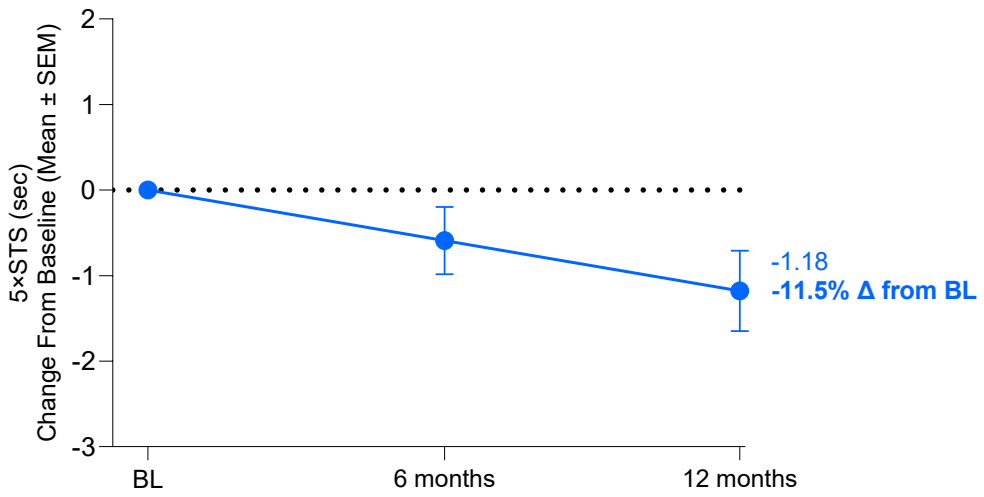
ACHIEVE

For information on the Pooled Dose Group, see footnotes on slide 7.
Percent mean change from baseline = (mean change from baseline/baseline mean) x 100. 6 months = 169 days; 12 months = 337 days.
%p, percent predicted; BL, baseline; Q4W, every 4 weeks; Q8W, every 8 weeks; QMT, quantitative muscle testing; SEM, standard error of the mean.

Improvement in Motor Function Is Sustained at 12 Months, as Measured by 5xSTS Timed Function Test

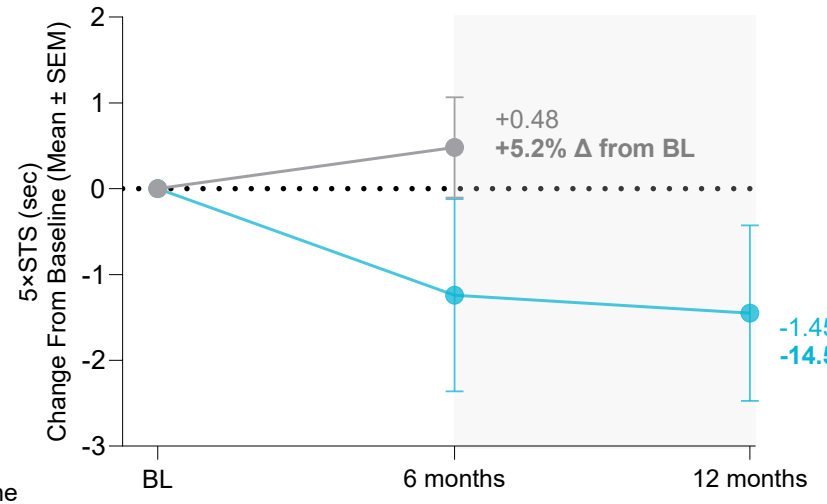
5 Times Sit to Stand

Pooled Dose Group (N=26)



Baseline Mean (SEM)	Patients, N		
	BL	6 months	12 months
10.2 (0.8)	26	26	26

6.8 mg/kg Cohort



	Baseline Mean (SEM)	Patients, N		
		BL	6 months	12 months
Placebo	9.2 (0.5)	14	14	-
6.8 mg/kg	10.0 (1.4)	6	6	6



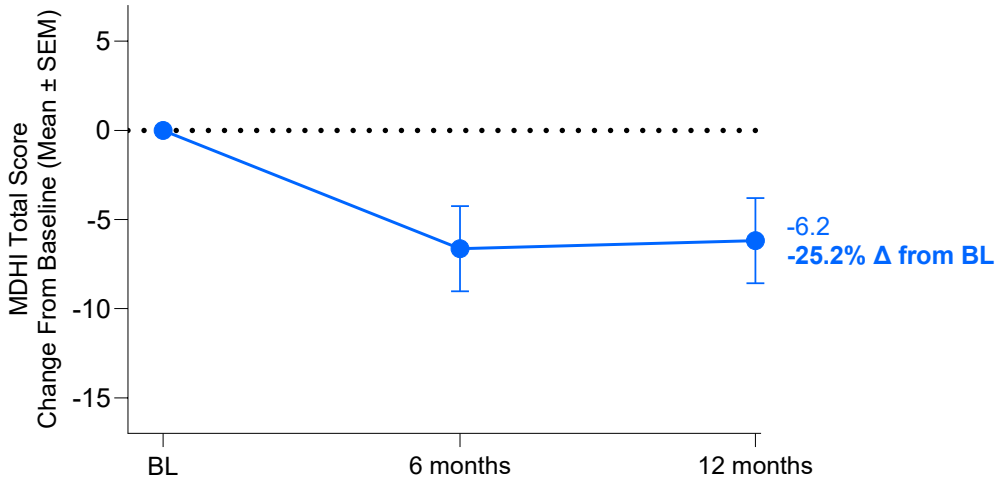
ACHIEVE

For information on the Pooled Dose Group, see footnotes on slide 7.
Percent mean change from baseline = (mean change from baseline/baseline mean) x 100. 6 months = 169 days; 12 months = 337 days.
5xSTS, 5 Times Sit to Stand; BL, baseline; Q4W, every 4 weeks; Q8W, every 8 weeks; sec, seconds; SEM, standard error of the mean.

Improvement in Patient-Reported Disease Burden Is Sustained at 12 Months, as Measured by MDHI Total Score

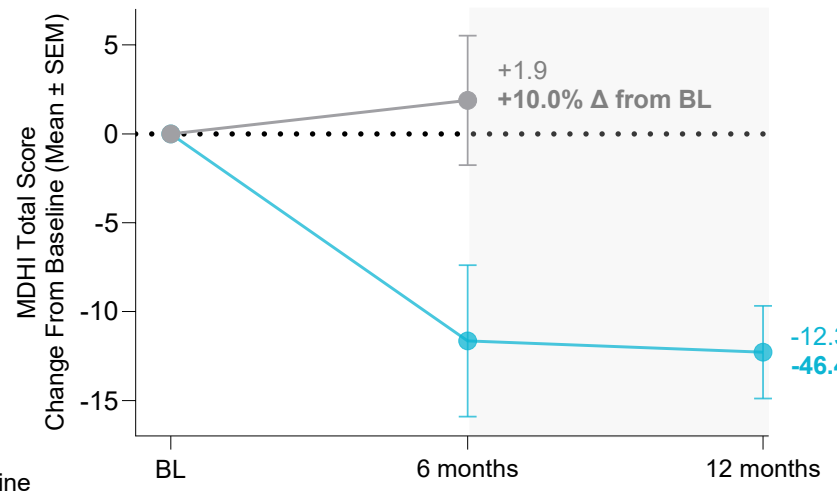
Myotonic Dystrophy Health Index (MDHI) Total Score

Pooled Dose Group (N=26)



Baseline Mean (SEM)	Patients, N		
	BL	6 months	12 months
24.4 (3.9)	26	26	25

6.8 mg/kg Cohort



	Baseline Mean (SEM)	Pateints, N		
		BL	6 months	12 months
Placebo	18.7 (3.8)	13	13	-
6.8 mg/kg	26.5 (5.6)	6	6	6

Improvement

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For information on the Pooled Dose Group, see footnotes on slide 7.
Percent mean change from baseline = (mean change from baseline/baseline mean) x 100. 6 months = 169 days; 12 months = 337 days.
BL, baseline; MDHI, Myotonic Dystrophy Health Index; Q4W, every 4 weeks; Q8W, every 8 weeks; SEM, standard error of the mean.

END-DM1[1] Assesses Natural DM1 Progression

END-DM1 is an ongoing, international, prospective DM1 natural history study designed to expand understanding of DM1 disease progression and to establish biomarkers and endpoints appropriate for interventional studies[1,2]

Propensity-Matched Baseline Characteristics

	END-DM1 Matched Cohort[3] Mean (SD)	ACHIEVE Pooled Dose Group Mean (SD)
N	49	26
Age at diagnosis (years)	27.5 (11.9)	23.7 (8.3)
Male (%)	19 (38.8)	14 (53.8)
Age at baseline (years)	36.1 (10.7)	35.6 (8.0)
BMI (kg/m^2)	23.3 (4.8)	22.7 (3.9)
vHOT (sec)	7.7 (4.6)	8.2 (4.4)
QMT Total (%p)	53.9 (17.6)	48.0 (14.3)
QMT hand grip (%p)	43.2 (22.8)	41.5 (16.3)
10MWR (sec)	4.19 (1.91)	3.99 (1.49)

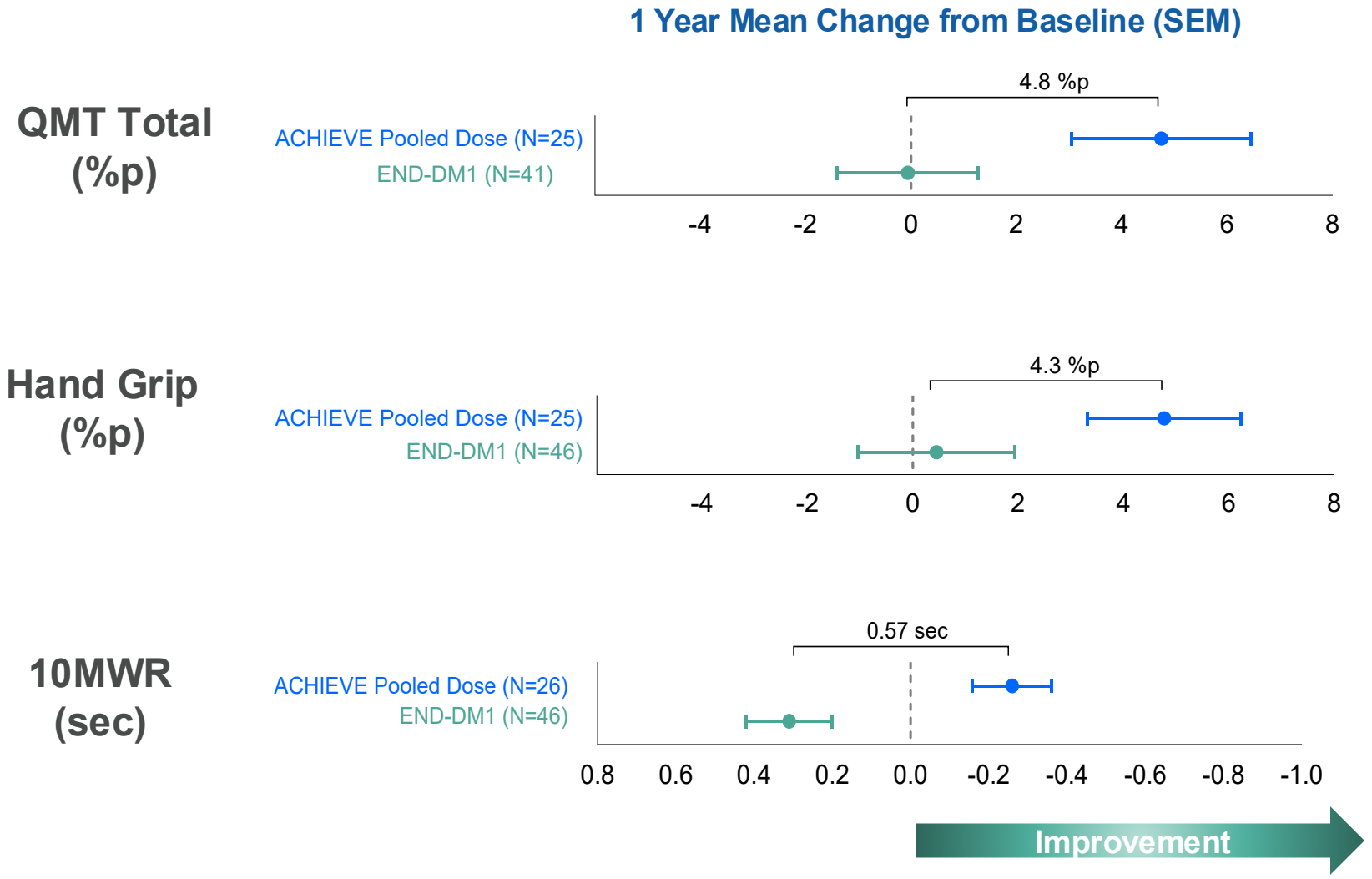
Parameters for propensity matching included age, sex, and measures of strength and function.

Dyne Therapeutics is one of multiple companies funding the END-DM1 study, along with the US Food and Drug Administration (FDA) and the Myotonic Dystrophy Foundation (MDF). The Myotonic Dystrophy Clinical Research Network (DMCRN), consisting of END-DM1–participating centers, has extended permission to present these analyses. END-DM1 data transfer July 2026. Note: END-DM1 is an ongoing natural history study, and data comparisons are subject to change. For information on the Pooled Dose Group, see footnotes on slide 7.

[1]ClinicalTrials.gov NCT03981575. https://clinicaltrials.gov/study/NCT03981575. Accessed September 14, 2026. [2]Mul K, et al. *PLoS One*. 2025;20(12):e0331163.[3]The 5xSTS assessment was not included in the original END-DM1 protocol.

%p, percent predicted; 10MWR, 10-Meter Walk/Run; BMI, body mass index; DM1, myotonic dystrophy type 1; QMT, quantitative muscle testing; SD, standard deviation; sec, seconds; vHOT, video hand opening time.

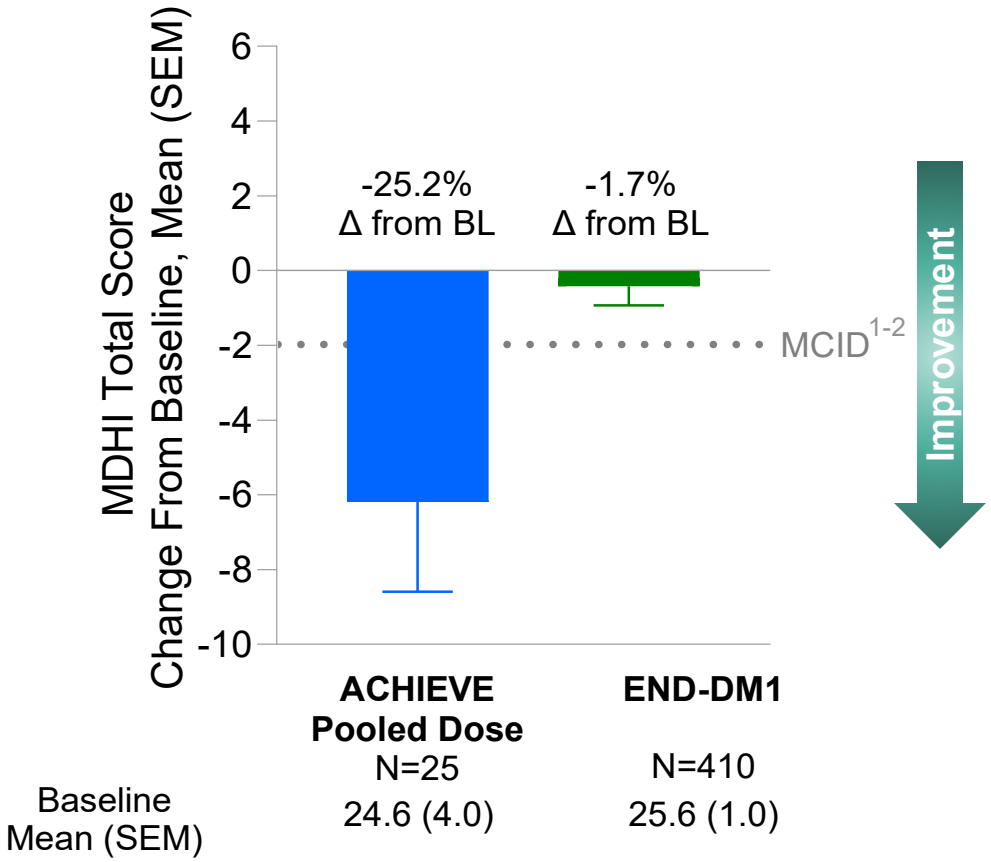
ACHIEVE Pooled Dose Group Improves From Baseline and Diverges From Natural History in Strength and Ambulation



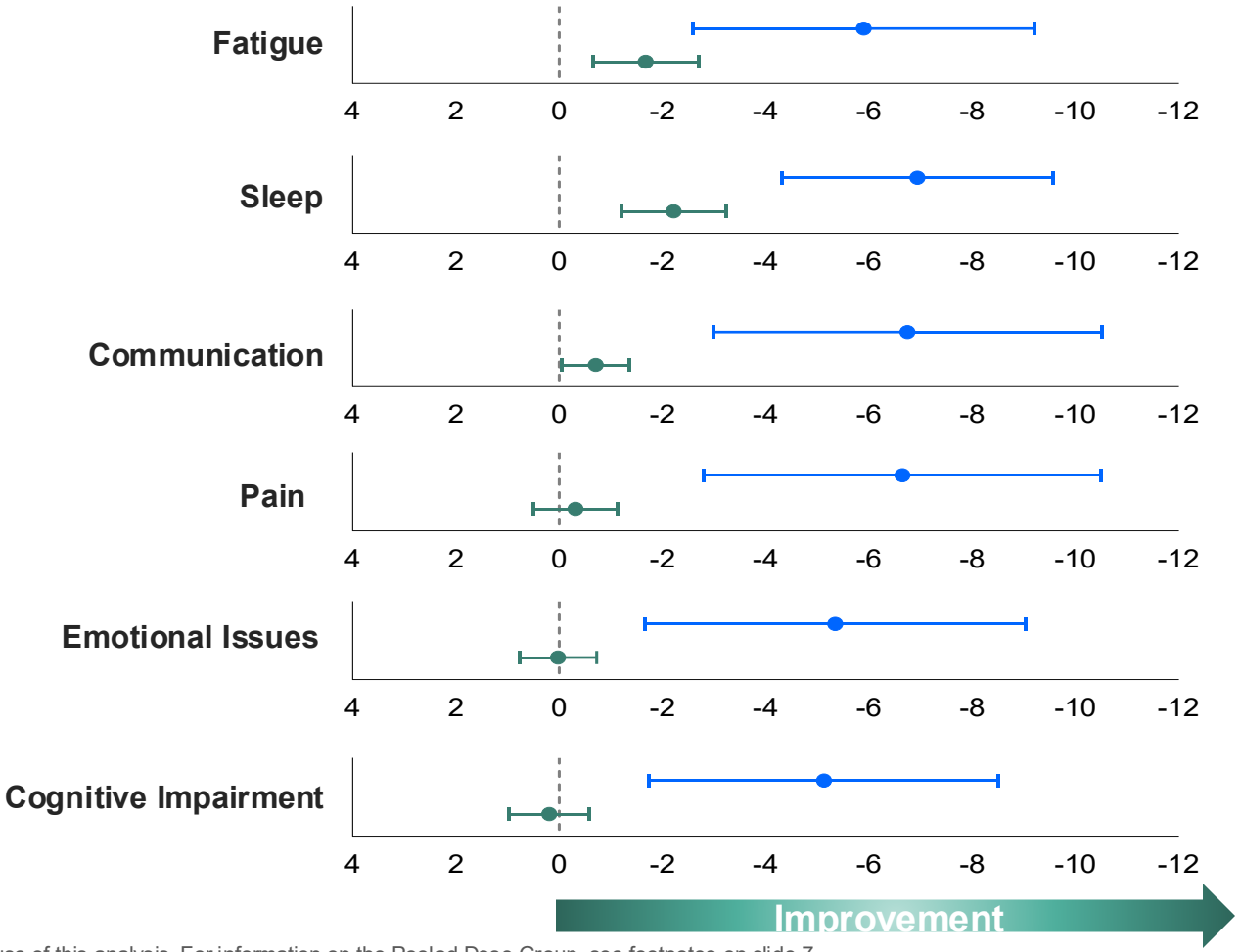
Thank you to END-DM1 Executive Committee for reviewing and approving use of this analysis.
N's reflect number of participants with assessments at baseline and Year 1. END-DM1 remains ongoing. 12 months = 337 days.
The 5xSTS assessment was not included in the original END-DM1 protocol. For information on the Pooled Dose Group, see footnotes on slide 7.
%p, percent predicted; 5xSTS, 5 Times Sit to Stand; 10MWR, 10-Meter Walk/Run; DM1, myotonic dystrophy type 1; Q4W, every 4 weeks; Q8W, every 8 weeks; QMT quantitative muscle testing; sec, second; SEM, standard error of the mean.

Improvement in MDHI in ACHIEVE Pooled Dose Group Exceeded MCID

MDHI Total Score Year 1
Pooled Dose Group (N=25) vs END-DM1 (N=410)



CNS-Related MDHI Subscales



Thank you to END-DM1 Executive Committee for reviewing and approving use of this analysis. For information on the Pooled Dose Group, see footnotes on slide 7.

[1]Sansone V, et al. *Muscle & Nerve.* 2026:1–11. [2]MDHI Total Score MCID values by Sansone, et al. 2026 were calculated utilizing an anchor-based approach with the domain delta questionnaire related to "overall health" at Year 2 upon study completion. MCID values ranged from 4.71 to -2.06. The mean change in MDHI Total Score for the ACHIEVE pooled dose group also exceeds MDC ESch-based proposed by Sansone et al. 2026. Mean change from baseline (SEM) is presented.

BL, baseline; DM1, myotonic dystrophy type 1; MCID, Minimal Clinically Important Difference; MDC, Minimal Detectable Change; MDHI, Myotonic Dystrophy Health Index; SEM, standard error of the mean; Y, year.

ACHIEVE

Summary: Z-Basivarsen ACHIEVE MAD Clinical Update

Safety

Safety findings through April 20, 2026, remain favorable

Efficacy

- **6.8 mg/kg cohort** demonstrated **durable functional improvement** in myotonia, motor function, and strength[1]
- Data continues to support **vHOT as an early indicator of functional improvement**
- **Pooled dose analysis** (N=26) showed functional improvement at 1 year, with **consistent efficacy** trends observed across endpoints
- **Participants reported improvements in disease burden**, including CNS-related impacts

Divergence From Natural History[2]

- Z-basivarsen–treated participants **showed divergence from natural history** across functional and strength outcomes
- **Functional improvements** in MDHI Total Score exceeded MCID and diverged from natural history control

ACHIEVE

[1]Sansone V, et al. Poster presentation at the Annual International Congress of the WMS, Vienna, Austria, October 7–11, 2025. Poster 380P. [2]END-DM1 data transfer as of July 2026. Analysis presented with permission from the Myotonic Dystrophy Clinical Research Network (DMCRN). For information on the Pooled Dose Group, see footnotes on slide 7.
CNS, central nervous system; DM1, myotonic dystrophy type 1; MAD, multiple ascending dose; MDHI, Myotonic Dystrophy Health Index; vHOT, video hand opening time; z-basivarsen, zeleciment basivarsen.

Acknowledgments

- ACHIEVE participants, families, investigators, and site staff
- Myotonic Dystrophy Clinical Research Network (DMCRN) and END-DM1 participants, families, and research personnel
- Members of the DM1 community who have provided feedback, insights, and questions

To view the presentation, related, or the HARMONIA study design poster, please scan the QR codes below:

Presentation

Appendix

HARMONIA study design poster
Enrollment ongoing