Efficacy and Safety of Golodirsen and Casimersen Compared With Placebo in Duchenne Muscular Dystrophy (ESSENCE): Phase 3 Topline Results

Francesco Muntoni,[1,2] Emma Ciafaloni,[3] Fernando Chloca,[4] Nicolas Deconinck,[5] Ameneh Masud,[6] Ihor Sehinovych,[6] Kerri Drummond,[6] Weijian Liu,[6] Pamela Magistrado-Coxen,[6] Andrés Nascimento Osorio,[7] Sheffali Gulati,[8] Maria Judit Molnar,[9] Maria Mazurkiewicz-Beldzinska,[10] Eugenio Mercuri,[11] Craig M. McDonald[12]

[1]Dubowitz Neuromuscular Centre, University College London, Great Ormond Street Institute of Child Health, London, UK; [2]National Institute for Health Research Great Ormond Street Hospital Biomedical Research Centre, London, UK; [3]University of Rochester Medicine, Rochester, NY, USA; [4]Favaloro Foundation - Neurosciences Institute, Buenos Aires, Argentina; [5]Centre de Référence Neuromusculaire and Paediatric Neurology Department, Hôpital Universitaire des Enfants Reine Fabiola, Université Libre de Bruxelles, Brussels, Belgium; [6]Sarepta Therapeutics, Inc., Cambridge, MA, USA; [7]Neuromuscular Unit, Neuropaediatrics Department, Hospital Sant Joan de Déu, Fundacion Sant Joan de Déu, CIBERER - ISC III, Barcelona, Spain; [8]All India Institute of Medical Sciences, New Delhi, India; [9]Institute of Genomic Medicine and Rare Disorders, Semmelweis University, Budapest, Hungary; [10]Department of Developmental Neurology, Chair of Neurology, Medical University of Gdańsk, Gdańsk, Poland; [11]Pediatric Neurology Unit, Università Cattolica del Sacro Cuore Roma, Rome, Italy; Nemo Clinical Centre, Fondazione Policlinico Universitario A Gemelli IRCCS, Rome, Italy; [12]UC Davis Health, Sacramento, CA, USA

Background

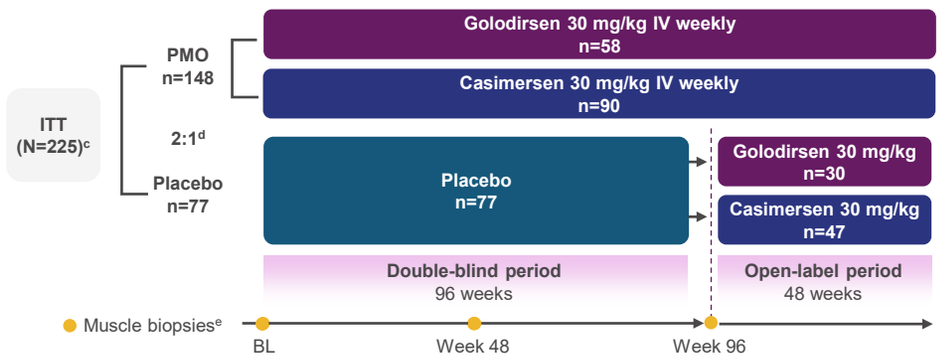
- Golodirsen and casimersen are phosphorodiamidate morpholino oligomers (PMOs) used for the treatment of Duchenne muscular dystrophy (DMD) in patients with pathogenic variants amenable to exon 53 and 45 skipping, respectively[1,2]
- Golodirsen and casimersen have demonstrated long-term tolerability and safety in treated clinical trial patients (up to 6 years) and in real-world patients since approvals in 2019 and 2021, respectively[1-4]
- This study evaluated the efficacy and safety of golodirsen and casimersen compared with placebo (PBO) in a phase 3, double-blind, multicenter study with an open-label extension (ESSENCE; NCT02500381)[5]
- To further contextualize these results, an expanded set of analyses developed through a principled, hypothesis-driven approach was performed
  - Two key factors were identified and evaluated in post hoc analyses: heterogeneity challenges related to DMD progression and the impact of COVID-19 on ESSENCE

Methods

Study design

- This study consisted of a double-blind, PBO-controlled treatment period for weeks 1 to 96, followed by an open-label treatment period for up to 48 additional weeks (**Figure 1**)

Figure 1 *Study design*



[a]Patients must have had intact right and left biceps brachii muscles or 2 alternative upper arm muscle groups to perform biopsies. [b]The dose of corticosteroid was expected to remain constant throughout the study (except for modifications to accommodate changes in weight). [c]Of the 228 patients enrolled, 2 patients were misrandomized and 1 patient withdrew before the first dose. [d]Within each genotype, randomization was further stratified by age (6-8.5 years vs >8.5-13 years). [e]Muscle biopsies were performed at baseline and one at either week 48 or week 96 of the double-blind, placebo-controlled treatment period.
6MWT, 6-minute walk test; BL, baseline; FVC, forced vital capacity; ITT, intent-to-treat; IV, intravenous; PMO, phosphorodiamidate morpholino oligomer.

Endpoints

- Primary endpoint: change from baseline (CFB) in 4-step ascend velocity (step/s) at week 96 vs PBO
- Secondary endpoints: CFB in 4-step ascend velocity at week 144; CFB in 6-minute walk test (6MWT) distance, 10-meter walk/run (10MWR) velocity, rise from floor (RFF) velocity, and North Star Ambulatory Assessment (NSAA) at week 96; safety through week 144; and CFB in dystrophin protein levels measured by western blot and immunohistochemistry at week 48 or week 96
- Mixed model with repeated measures (MMRM) analysis was used to compare PMO treatment with PBO

Post hoc analyses

- Time to event
  - Time to event (TTE) measures the time from baseline to the first meaningful decline in 4-step ascend velocity (>0.3 steps/s)[6]
  - TTE analysis is less susceptible to potential ceiling effects in this heterogeneous trial population, offering a direct and sensitive way to assess meaningful decline
  - Cox proportional hazards regression analysis of TTE was stratified by genotype and age group and was adjusted for effects of baseline 4-step ascend velocity
- Predicted decline subgroup (prognostically relevant subpopulation)
  - The intent-to-treat (ITT) population was stratified based on a recent independently published prognostic model that ranked patients using a composite prognostic score incorporating baseline characteristics (age, 4-step ascend velocity, RFF velocity, 10MWR velocity, corticosteroid duration and type) to predict risk of future decline in 4-step ascend velocity[7]
  - The analysis included all patients expected to decline over the next year (baseline prognostic score <0.0)
  - A subset of patients that excluded floor and ceiling effects was also analyzed
- COVID-19 impact period
  - Patients whose baseline 4-step ascend velocity assessments occurred during the COVID-19 impact period (March 2020-July 2021)[8,9] were excluded from the ITT population to assess the impact of variability in baseline assessments during this period
    - Here, July 2021 was considered the end of the COVID-19 impact period based on evidence that the COVID-19 vaccination rates peaked in the middle of 2021, followed by a progressive resumption of normal daily activities
  - To minimize the potential variability related to COVID-19 operational disruptions, an analysis of covariance model was conducted with treatment, genotype, treatment-by-genotype interaction, and baseline age as continuous covariates

Results

Patients

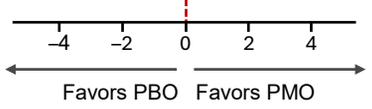
- Of the 228 patients enrolled from 2016 to 2022, including through the COVID-19 pandemic and across 24 countries, 225 were included in the ITT population (**Figure 1**)
- Baseline characteristics and functional assessments are included in the Supplement (**Supplemental Table 1**)

Primary analysis

- The primary endpoint, CFB at week 96 in 4-step ascend velocity, showed a numerical mean (standard deviation [SD]) change of −0.27 (0.39) steps/s in the PMO group (n=138) vs PBO (n=74; −0.34 [0.37]), with a least squares mean (LSM) difference of 0.06 (95% CI, −0.05 to 0.16; *P*=0.309) (**Figure 2**)
  - Although not statistically significant, 10MWR velocity, 6MWT distance, and NSAA total score trended to favor PMO; RFF trended to favor PBO

Figure 2 *Primary and secondary functional endpoints change from baseline*

Endpoint[a]	Standardized LS mean difference (PMO-PBO)[b]	LS mean difference (95% CI)	*P* value
4-step ascend velocity week 96		0.055 (-0.051 to 0.161)	0.309
4-step ascend velocity week 144		-0.004 (-0.123 to 0.115)	0.943
10MWR velocity week 96		0.020 (-0.097 to 0.137)	0.732
6MWT distance week 96		5.339 (-23.319 to 33.997)	0.714
RFF velocity week 96		-0.003 (-0.020 to 0.014)	0.728
NSAA total score week 96		0.61 (-0.90 to 2.12)	0.429



[a]Full ITT population was included in the analyses; MMRM methods account for missing data in these analyses. [b]LS mean difference and CI are standardized by dividing by the SE.
6MWT, 6-minute walk test; 10MWR, 10-meter walk/run; CI, confidence interval; **ITT, intent-to-treat;** LS, least squares; MMRM, mixed-effects model for repeated measures; NSAA, North Star Ambulatory Assessment; PBO, placebo; PMO, phosphorodiamidate morpholino oligomer; SE, standard error.

Dystrophin expression

- Significant treatment differences were observed at weeks 48 and 96 between PMO and PBO in CFB in the quantity of dystrophin expression (**Supplemental Table 2**)
  - Dystrophin expression by western blot: Compared with PBO, the PMO-treated groups demonstrated a greater increase from baseline, with a mean CFB difference (95% CI) of 0.69 (0.28-1.10; *P*<0.001; unadjusted) and 1.25 (0.20-2.31; *P*=0.020; muscle-content adjusted) percentage of normal
  - Dystrophin expression by fiber intensity immunohistochemistry: Compared with PBO, the PMO-treated group demonstrated a greater increase from baseline, with a mean CFB difference (95% CI) of 0.023 (0.015-0.031; *P*<0.001)

Safety

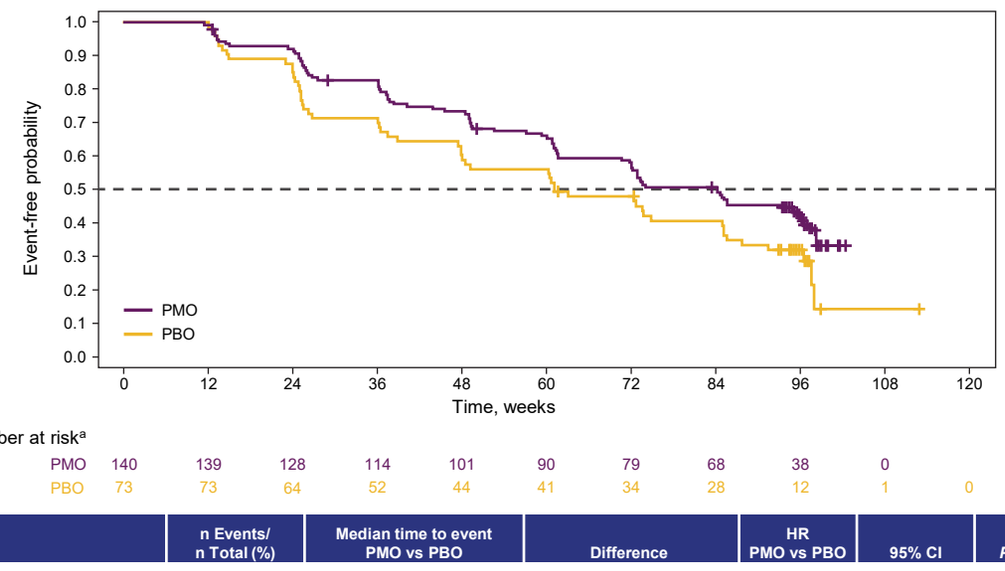
- Most treatment-emergent adverse events (TEAEs) were mild or moderate and resolved without treatment through 96 weeks (**Table 1**)
  - The most common TEAEs (≥20% of treated patients) were vomiting (36.4%), nasopharyngitis (35.1%), pyrexia (34.7%), headache (33.8%), cough (29.3%), fall (27.1%), upper respiratory infection (23.6%), diarrhea (23.1%), and procedural pain (20.9%)
  - There were 8 (3.6%) adjudicated rhabdomyolysis TEAEs of special interest observed in the 225 treated patients, of which 3 (37.5%) were deemed possibly related to treatment
  - There were no treatment-related TEAEs leading to discontinuation
- Through week 144, no new safety signals were reported

Table 1 *Overall summary of treatment-emergent adverse events through 96 weeks*

Parameter, n (%)	PMO n=148	PBO n=77	Overall N=225
TEAEs	2,533	1,034	3,567
Mild	2,230 (88.0)	922 (89.2)	3,152 (88.4)
Moderate	276 (10.9)	100 (9.7)	376 (10.5)
Severe	27 (1.1)	12 (1.2)	39 (1.1)
Non-serious TEAEs	2,487 (98.2)	1,012 (97.9)	3,499 (98.1)
Serious TEAEs	46 (1.8)	22 (2.1)	68 (1.9)
Patients with ≥1 TEAE	144 (97.3)	76 (98.7)	220 (97.8)
Mild	69 (46.6)	39 (50.6)	108 (48.0)
Moderate	57 (38.5)	28 (36.4)	85 (37.8)
Severe	18 (12.2)	9 (11.7)	27 (12.0)
Treatment-related TEAEs	56 (37.8)	16 (20.8)	72 (32.0)
Treatment-emergent SAEs	30 (20.3)	17 (22.1)	47 (20.9)
Treatment-related, treatment-emergent SAEs[a]	5 (3.4)	0	5 (2.2)
Rhabdomyolysis	3 (2.0)	0	3 (1.3)
Blood creatine phosphokinase increased	1 (0.7)	0	1 (0.4)
Urine protein/creatinine ratio increased	1 (0.7)	0	1 (0.4)
Hypoesthesia	1 (0.7)	0	1 (0.4)
Myoglobinuria	1 (0.7)	0	1 (0.4)
Hyperhidrosis	1 (0.7)	0	1 (0.4)
TEAEs leading to discontinuation	2 (1.4)[b]	0	2 (0.9)
TEAEs leading to death	1 (0.7)[c]	0	1 (0.4)

[a]Of the 5 patients who experienced SAEs, 2 patients experienced rhabdomyolysis only; 1 patient experienced rhabdomyolysis, myoglobinuria, and blood creatine phosphokinase increase; 1 patient experienced hypoesthesia and hyperhidrosis; and 1 patient experienced urine protein/creatinine ratio increase. [b]One patient discontinued due to cardiac arrest, hyperkalemia, and rhabdomyolysis, and the other patient discontinued due to acute myocarditis. [c]Death was due to rhabdomyolysis, reported as a treatment-emergent SAE unrelated to treatment; the patient discontinued treatment at the time of the SAE report. PBO, placebo; PMO, phosphorodiamidate morpholino oligomer; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Figure 3 *Time to first decline in 4-step ascend velocity through week 96*



Parameter	n Events/ n Total (%)	Median time to event PMO vs PBO	Difference	HR PMO vs PBO	95% CI	Cox *P* value
Time to decline of 4-step ascend velocity >0.3 steps/s	135/213 (63.4)	84 vs 61 weeks	~23 weeks	0.685	(0.483-0.972)	0.0339

[a]Time to event was measured from date of randomization. One patient's week 96 visit was at 108 weeks due to a delay following randomization.
CI, confidence interval; HR, hazard ratio; PBO, placebo; PMO, phosphorodiamidate morpholino oligomer.

Post hoc analysis: trajectory-based assessments

- Although mean baseline values were comparable across treatment groups, ESSENCE enrolled a broad population, with participants aged 6 to 13 years at various stages of disease progression. The use of trajectory-based assessments reduced variability and enhanced endpoint sensitivity within the trial duration

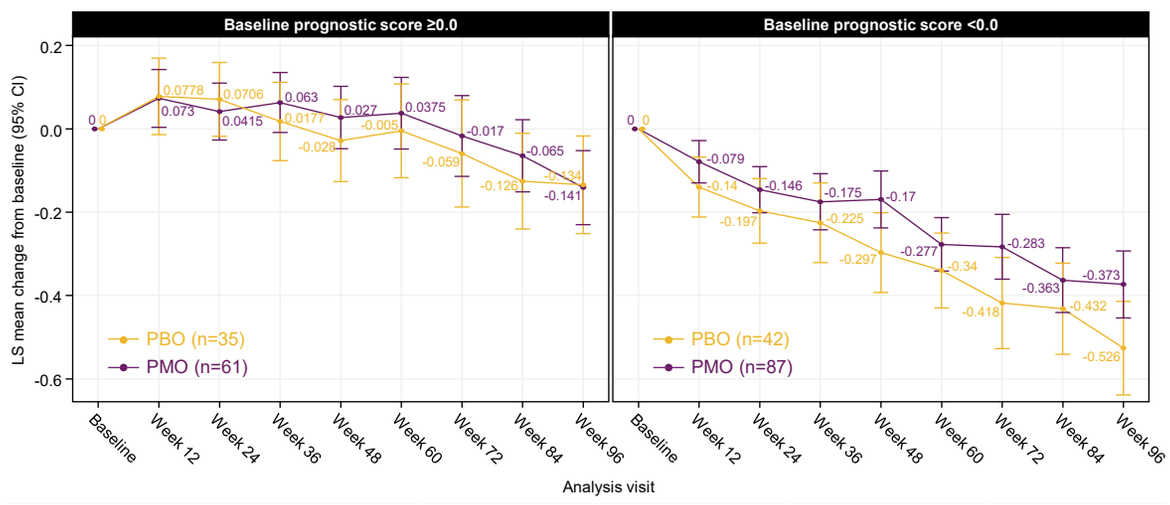
Time to event

- Patients in the PMO group had an ~31% reduction in the hazard of time to first decline of 4-step ascend velocity >0.3 steps/s compared with PBO (hazard ratio [95% CI], 0.685 [0.48-0.97]; *P*=0.034) (**Figure 3**)
  - Over 96 weeks, including the COVID-19 impact period, patients in the PMO group experienced an approximately 23-week (>5-month) delay in the median time to first decline compared with PBO

Predicted decline subgroup

- Among all patients expected to decline over the next year (prognostic score <0.0), treatment with PMO significantly reduced the decline in 4-step ascend velocity at week 96 by 0.153 steps/s (95% CI, 0.018-0.288; *P*=0.026) (**Figure 4; Supplemental Table 3**)
- In the analysis that excluded patients prone to floor and ceiling effects, treatment with PMO significantly reduced the decline in 4-step ascend velocity by 0.186 steps/s (95% CI, 0.045-0.327; *P*=0.010)

Figure 4 *4-step ascend velocity based on prognostic score through week 96*



Parameter	LS mean difference	95% CI	*P* value
Change in 4-step ascend velocity at week 96 (predicted decline subgroup <0.0)	0.153 steps/s	0.018-0.288	0.026

CI, confidence interval; LS, least squares; PBO, placebo; PMO, phosphorodiamidate morpholino oligomer.

Post hoc analysis: COVID-19 impact period

- A total of 23 patients (~10% of the ITT population) had baseline 4-step ascend velocity assessments during the COVID-19 impact period
- In the ITT set excluding the 23 COVID-19–impacted patients (refined ITT population), the LS mean difference (95% CI) CFB of 4-step ascend velocity at week 96 was 0.12 steps/s (0.0001-0.2348; *P*=0.050) (**Supplemental Figure**)
- During the 96-week double-blind period, ≥2 consecutive missed doses occurred in 43% of the patients in the PMO group within the COVID-19–impact period (n=37), vs 23% outside the COVID-19–impact period (n=111), with an average of 8 consecutive missed doses, including some up to 26 doses

Conclusions

- While the primary endpoint was not met in ESSENCE, principled, hypothesis-driven post hoc analyses were performed to evaluate heterogeneity challenges related to DMD progression and the COVID-19 impact
- Dystrophin expression was increased in the PMO group vs PBO at week 96
- No new safety signals were observed in ESSENCE. Golodirsen and casimersen were well tolerated over 144 weeks, consistent with previous clinical and real-world experience
- Across all 3 post hoc analyses—time to event, predicted decline subgroup, COVID-19–impact period—the PMO group showed a consistent reduction in 4-step ascend decline at week 96 vs PBO
- The totality of PMO evidence including the ESSENCE post hoc analyses suggest the clinical benefits of golodirsen and casimersen

Acknowledgments and Disclosures

Acknowledgments: This study was funded by Sarepta Therapeutics, Inc., Cambridge, MA, USA. Editorial support was provided by Kimberly Fischer, PhD, of Envision 90TEN, an Envision Medical Communications agency, a part of Envision Pharma Group, in accordance with Good Publication Practice (GPP) 2022 guidelines (https://www.ismpp.org/gpp-2022) and was funded by Sarepta Therapeutics, Inc., Cambridge, MA, USA.

Disclosures: FM: Received consultant fees and speaker honoraria from Sarepta Therapeutics, Inc. **EC:** No conflicts in relation to this poster. **FC:** Participated in advisory board for Sarepta Therapeutics, Inc. **ND:** Participated in advisory boards for Sarepta Therapeutics, Inc. **AM, IS, KD, WL,** and **PMC:** Employees of Sarepta Therapeutics, Inc. and may own stock/options in the company. **ANO:** Received consultant fees and speaker honoraria from Sarepta Therapeutics, Inc. **SG:** Nothing to disclose. **MJM:** Member of the COMP of EMA. **MMB:** Serves as a consultant for Biogen, Novartis, Roche, and UCB. **EM:** Received consultant fees from Sarepta Therapeutics, Inc. **CMM:** Reports grants from Avidity, Capricor Therapeutics, Catabasis, Edgewise Therapeutics, Epirium Bio, Italfarmaco, Pfizer, PTC Therapeutics, Santhera Pharmaceuticals, Sarepta Therapeutics, Inc., and Solid Biosciences and has a consultancy/advisory role with BioMarin, Capricor Therapeutics, Catalyst, Edgewise Therapeutics, F. Hoffmann-La Roche Ltd., Italfarmaco, NS Pharma, PTC Therapeutics, Santhera Pharmaceuticals, Sarepta Therapeutics, Inc., and Solid Biosciences. He has received honoraria from Edgewise Therapeutics, PTC Therapeutics, and Sarepta Therapeutics, Inc.

References

1. Golodirsen. Prescribing information. Sarepta Therapeutics, Inc.; 2024. **2.** Casimersen. Prescribing information. Sarepta Therapeutics, Inc.; 2026. **3.** Shieh P, et al. Poster presented at: NMSG 2025; September 26-28, 2025; Stresa, Italy. Poster 1210. **4.** Muntoni F, et al. Poster presented at: WMS 2023; October 3-7, 2023; Charleston, SC. Poster P147. **5.** ClinicalTrials.gov identifier: NCT02500381. Updated November 18, 2025. Accessed February 16, 2025. https://clinicaltrials.gov/study/NCT02500381. **6.** Muntoni F, et al. *PLoS One*. 2024;19(7):e0304984. **7.** Goemans N, et al. *PLoS One*. 2020;15(6):e0232870. **8.** World Health Organization. Accessed February 20, 2026. https://www.who.int/europe/emergencies/situations/covid-19. **9.** National Center for Immunization and Respiratory Diseases (US). Division of Viral Diseases. Accessed January 28, 2026. https://stacks.cdc.gov/view/cdc/108355.

Efficacy and Safety of Golodirsen and Casimersen Compared With Placebo in Duchenne Muscular Dystrophy (ESSENCE): Phase 3 Topline Results

Francesco Muntoni,[1,2] Emma Ciafaloni,[3] Fernando Chloca,[4] Nicolas Deconinck,[5] Ameneh Masud,[6] Ihor Sehinovych,[6] Kerri Drummond,[6] Weijian Liu,[6] Pamela Magistrado-Coxen,[6] Andrés Nascimento Osorio,[7] Sheffali Gulati,[8] Maria Judit Molnar,[9] Maria Mazurkiewicz-Beldzinska,[10] Eugenio Mercuri,[11] Craig M. McDonald[12]

[1]Dubowitz Neuromuscular Centre, University College London, Great Ormond Street Institute of Child Health, London, UK; [2]National Institute for Health Research Great Ormond Street Hospital Biomedical Research Centre, London, UK; [3]University of Rochester Medicine, Rochester, NY, USA; [4]Favaloro Foundation - Neurosciences Institute, Buenos Aires, Argentina; [5]Centre de Référence Neuromusculaire and Paediatric Neurology Department, Hôpital Universitaire des Enfants Reine Fabiola, Université Libre de Bruxelles, Brussels, Belgium; [6]Sarepta Therapeutics, Inc., Cambridge, MA, USA; [7]Neuromuscular Unit, Neuropaediatrics Department, Hospital Sant Joan de Déu, Fundacion Sant Joan de Déu, CIBERER - ISC III, Barcelona, Spain; [8]All India Institute of Medical Sciences, New Delhi, India; [9]Institute of Genomic Medicine and Rare Disorders, Semmelweis University, Budapest, Hungary; [10]Department of Developmental Neurology, Chair of Neurology, Medical University of Gdańsk, Gdańsk, Poland; [11]Pediatric Neurology Unit, Università Cattolica del Sacro Cuore Roma, Rome, Italy; Nemo Clinical Centre, Fondazione Policlinico Universitario A Gemelli IRCCS, Rome, Italy; [12]UC Davis Health, Sacramento, CA, USA

ITT and Predicted Decline Subgroup Analyses

- Baseline characteristics and functional assessments for patients included in the ITT population (**Supplemental Table 1**) and the predicted decline subgroup analysis (**Supplemental Table 3**)

Supplemental Table 1 *Baseline characteristics and functional assessments in the ITT population*

Parameter	ITT population PMO n=148	ITT population PBO n=77	ITT population Overall N=225
Age, years			
Mean (SD)	9.4 (2.0)	9.4 (1.9)	9.4 (2.0)
Min, max[a]	6, 14	7, 14	6, 14
6-8.5 years, n (%)	62 (41.9)	30 (39.0)	92 (40.9)
>8.5-13 years, n (%)	86 (58.1)	47 (61.0)	133 (59.1)
Genotype			
Exon-45 skippable, n (%)	90 (60.8)	47 (61.0)	137 (60.9)
Exon-53 skippable, n (%)	58 (39.2)	30 (39.0)	88 (39.1)
Race			
White, n (%)	125 (84.5)	65 (84.4)	190 (84.4)
Ethnicity			
Not Hispanic or Latino, n (%)	130 (87.8)	63 (81.8)	193 (85.8)
Height, cm			
Mean (SD)	123.5 (8.7)	124.2 (8.9)	123.8 (8.8)
Min, max	105.9, 146.0	107.1, 149.5	105.9, 149.5
Weight, kg			
Mean (SD)	30.0 (8.7)	29.9 (8.4)	30.0 (8.6)
Min, max	17.6, 62.1	16.8, 53.1	16.8, 62.1
BMI, kg/m²			
Mean (SD)	18.5 (3.9)[b]	18.5 (3.8)[c]	18.5 (3.8)[d]
Min, max	11.6, 32.5	12.4, 28.3	11.6, 32.5
Time since DMD diagnosis, months			
Mean (SD)	64.0 (33.4)	58.1 (30.5)	62.0 (32.5)
Min, max	2.2, 154.6	5.8, 141.8	2.2, 154.6
Duration of prior corticosteroid use, months			
Mean (SD)	43.0 (28.2)	37.8 (22.5)	41.2 (26.5)
Min, max	6.4, 127.0	5.7, 103.8	5.7, 127.0
4-step ascend velocity, steps/s			
Mean (SD)	1.0 (0.5)[e]	1.1 (0.6)[f]	1.1 (0.5)[g]
Min, max	0.0, 2.9	0.0, 2.9	0.0, 2.9
10MWR velocity, m/s			
Mean (SD)	1.8 (0.5)[e]	1.8 (0.5)	1.8 (0.5)[h]
Min, max	0.9, 3.1	1.0, 3.3	0.9, 3.3
6MWT distance, m			
Mean (SD)	378.2 (38.0)	379.6 (42.4)	378.7 (39.5)
Min, max	300.5, 450.5	301.5, 449.5	300.5, 450.5
RFF velocity, rise/s			
Mean (SD)	0.2 (0.1)[b]	0.2 (0.1)[f]	0.2 (0.1)[i]
Min, max	0.0, 0.4	0.0, 0.4	0.0, 0.4
NSAA total score			
Mean (SD)	22.0 (6.5)	22.4 (6.2)	22.2 (6.4)
Min, max	7.5, 34.0	9.0, 32.5	7.5, 34.0

[a]Some patients were 13 years old at the time of screening. [b]n=145. [c]n=75. [d]n=220. [e]n=147. [f]n=76. [g]n=223. [h]n=224. [i]n=221.
6MWT, 6-minute walk test; 10MWR, 10-meter walk/run; BMI, body mass index; DMD, Duchenne muscular dystrophy; ITT, intent-to-treat; max, maximum; min, minimum; NSAA, North Star Ambulatory Assessment; PBO, placebo; PMO, phosphorodiamidate morpholino oligomer; RFF, rise from floor; SD, standard deviation.

Supplemental Table 3 *Baseline characteristics and functional assessments in the predicted decline subgroup analysis with a prognostic score <0.0*

Parameter	Predicted decline subgroup with a prognostic score <0.0 PMO n=87	PBO n=42	Overall N=129
Age, years			
Mean (SD)	10.2 (2.1)	10.1 (2.0)	10.2 (2.0)
Min, max[a]	6.7, 14.0	6.6, 14.0	6.6, 14.0
6-8.5 years, n (%)	24 (27.6)	10 (23.8)	34 (26.4)
>8.5-13 years, n (%)	63 (72.4)	32 (76.2)	95 (73.6)
Genotype			
Exon-45 skippable, n (%)	56 (64.4)	23 (54.8)	79 (61.2)
Exon-53 skippable, n (%)	31 (35.6)	19 (45.2)	50 (38.8)
Race			
White, n (%)	78 (89.7)	36 (85.7)	114 (88.4)
Ethnicity			
Not Hispanic or Latino, n (%)	76 (87.4)	36 (85.7)	112 (86.8)
Height, cm			
Mean (SD)	126.6 (8.2)	126.0 (8.7)	126.4 (8.4)
Min, max	107.6, 146.0	111.0, 149.5	107.6, 149.5
Weight, kg			
Mean (SD)	32.1 (9.0)	32.0 (9.2)	32.1 (9.0)
Min, max	19.5, 62.1	19.0, 53.1	19.0, 62.1
BMI, kg/m²			
Mean (SD)	18.6 (3.8)[b]	19.0 (4.3)	18.7 (3.9)[c]
Min, max	11.6, 29.8	12.6, 28.3	11.6, 29.8
Time since DMD diagnosis, months			
Mean (SD)	74.9 (34.6)	69.9 (32.5)	73.3 (33.8)
Min, max	2.2, 154.6	8.9, 141.8	2.2, 154.6
Duration of prior corticosteroid use, months			
Mean (SD)	54.7 (28.4)	46.5 (23.8)	52.0 (27.2)
Min, max	6.9, 127.1	8.9, 103.8	6.9, 127.1
4-step ascend velocity, steps/s			
Mean (SD)	1.1 (0.6)[b]	1.1 (0.6)[d]	1.1 (0.6)[e]
Min, max	0, 2.9	0, 2.9	0, 2.9
10MWR velocity, m/s			
Mean (SD)	1.8 (0.5)[b]	1.7 (0.5)	1.8 (0.5)[c]
Min, max	0.9, 3.1	1.0, 3.3	0.9, 3.3
6MWT distance, m			
Mean (SD)	379.3 (40.8)	378.2 (44.5)	378.9 (41.9)
Min, max	300.5, 450.5	301.5, 449.5	300.5, 450.5
RFF velocity, rise/s			
Mean (SD)	0.2 (0.1)[f]	0.2 (0.1)[d]	0.2 (0.10)[g]
Min, max	0, 0.4	0, 0.4	0, 0.4
NSAA total score			
Mean (SD)	21.6 (6.9)	21.6 (6.3)	21.6 (6.7)
Min, max	7.5, 34.0	9.0, 32.0	7.5, 34.0
Baseline prognostic score			
Mean (SD)	-0.3 (0.2)[h]	-0.3 (0.2)[i]	-0.3 (0.2)[j]
Min, max	-0.8, -0.1	-0.7, -0.1	-0.8, -0.1

[a]Some patients were 13 years old at the time of screening. [b]n=86. [c]n=128. [d]n=41. [e]n=127. [f]n=84. [g]n=125. [h]n=82. [i]n=40. [j]n=122.
6MWT, 6-minute walk test; 10MWR, 10-meter walk/run; BMI, body mass index; DMD, Duchenne muscular dystrophy; max, maximum; min, minimum; NSAA, North Star Ambulatory Assessment; PBO, placebo; PMO, phosphorodiamidate morpholino oligomer; RFF, rise from floor; SD, standard deviation.

Dystrophin Expression

- Significant treatment differences were observed at weeks 48 and 96 between PMO and PBO in CFB in the quantity of dystrophin expression (**Supplemental Table 2**)

Supplemental Table 2 *Dystrophin expression by western blot and immunohistochemistry*

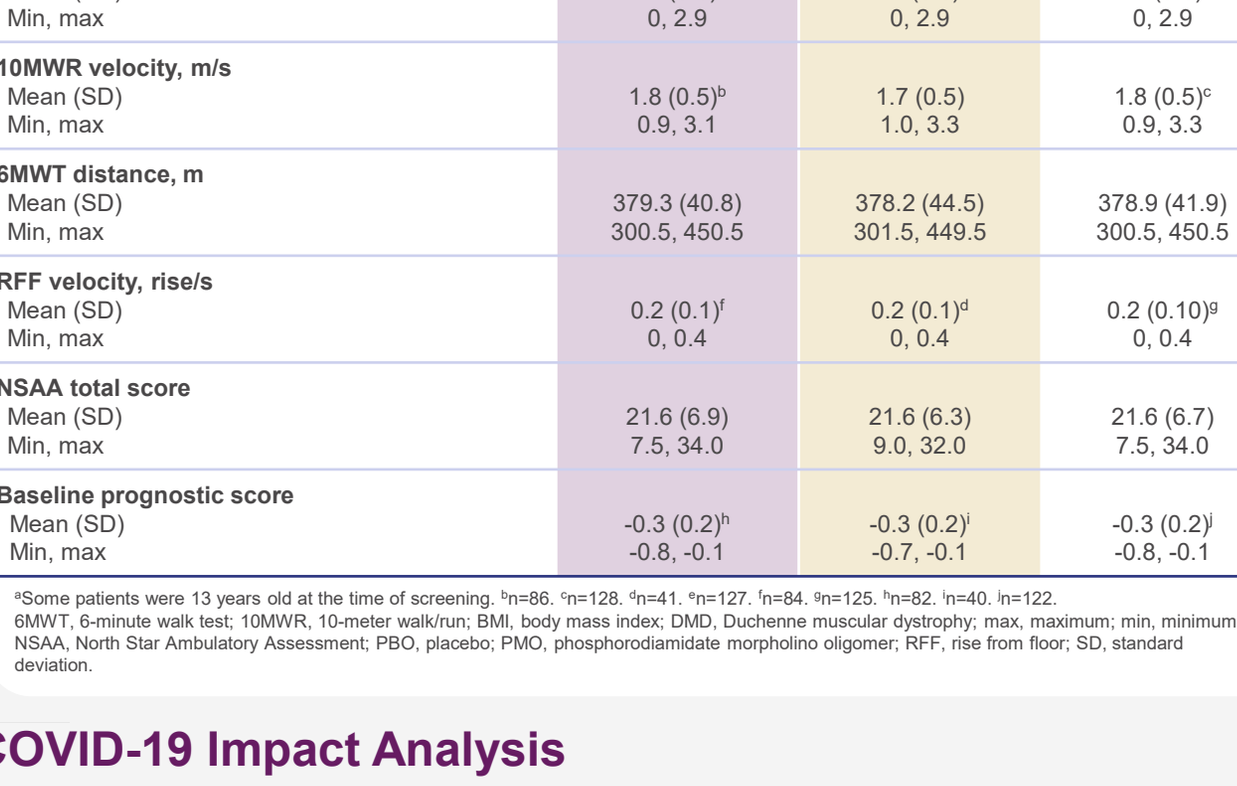
Parameter[a]	PMO (n=127)	PBO (n=66)	Mean difference of CFB compared with PBO (95% CI) *P* value
Dystrophin expression by western blot; muscle-content unadjusted, % of normal			
Baseline			
n	127	66	
Mean (SD)	0.773 (1.536)	0.562 (1.029)	
Week 48			
n	39	22	0.605
Mean (SD)	1.437 (1.707)	0.582 (1.019)	(0.311-0.899)
CFB mean (SD)	0.772 (0.719)	0.168 (0.427)	*P*<0.001
Week 96			
n	88	44	0.689
Mean (SD)	1.728 (2.336)	0.852 (1.796)	(0.277-1.101)
CFB mean (SD)	0.906 (1.252)	0.217 (1.057)	*P*<0.001
Dystrophin expression by western blot; muscle-content adjusted, % of normal			
Baseline			
n	100	50	
Mean (SD)	1.506 (3.149)	1.155 (2.730)	
Week 48			
n	12	6	2.048
Mean (SD)	2.474 (1.565)	0.380 (0.798)	(0.898-3.197)
CFB mean (SD)	2.343 (1.529)	0.295 (0.771)	*P*=0.008
Week 96			
n	88	44	1.254
Mean (SD)	3.692 (4.436)	2.046 (4.017)	(0.201-2.308)
CFB mean (SD)	1.999 (3.236)	0.745 (2.678)	*P*=0.020
Dystrophin fiber intensity by immunohistochemistry			
Baseline			
n	125	65	
Mean (SD)	0.096 (0.053)	0.088 (0.050)	
Week 48			
n	38	22	0.048
Mean (SD)	0.209 (0.082)	0.149 (0.058)	(0.025-0.071)
CFB mean (SD)	0.058 (0.057)	0.010 (0.030)[b]	*P*<0.001
Week 96			
n	87	43	0.023
Mean (SD)	0.101 (0.047)	0.071 (0.033)	(0.015-0.031)
CFB mean (SD)	0.030 (0.033)	0.007 (0.013)	*P*<0.001

[a]All patients underwent a muscle biopsy at baseline. A second biopsy was at either week 48 or 96. [b]n=21.
CFB, change from baseline; CI, confidence interval; PBO, placebo; PMO, phosphorodiamidate morpholino oligomer; SD, standard deviation.

COVID-19 Impact Analysis

- In the ITT set excluding the 23 COVID-19–impacted patients, the LS mean difference (95% CI) CFB of 4-step ascend velocity at week 96 was 0.12 steps/s (0.0001-0.2348; *P*=0.050)

Supplemental Figure *4-step ascend velocity at week 96 in the refined ITT population*



CFB, change from baseline; CI, confidence interval; ITT, intent-to-treat; LS, least squares; PBO, placebo; PMO, phosphorodiamidate morpholino oligomer.

Acknowledgments and Disclosures

Acknowledgments: This study was funded by Sarepta Therapeutics, Inc., Cambridge, MA, USA. Editorial support was provided by Kimberly Fischer, PhD, of Envision 90TEN, an Envision Medical Communications agency, a part of Envision Pharma Group, in accordance with Good Publication Practice (GPP) 2022 guidelines (https://www.ismpp.org/gpp-2022) and was funded by Sarepta Therapeutics, Inc., Cambridge, MA, USA.

Disclosures: FM: Received consultant fees and speaker honoraria from Sarepta Therapeutics, Inc. **EC:** No conflicts in relation to this poster. **FC:** Participated in advisory board for Sarepta Therapeutics, Inc. **ND:** Participated in advisory boards for Sarepta Therapeutics, Inc. **AM, IS, KD, WL,** and **PMC:** Employees of Sarepta Therapeutics, Inc. and may own stock/options in the company. **ANO:** Received consultant fees and speaker honoraria from Sarepta Therapeutics, Inc. **SG:** Nothing to disclose. **MJM:** Member of the COMP of EMA. **MMB:** Serves as a consultant for Biogen, Novartis, Roche, and UCB. **EM:** Received consultant fees from Sarepta Therapeutics, Inc. **CMM:** Reports grants from Avidity, Capricor Therapeutics, Catabasis, Edgewise Therapeutics, Epirium Bio, Italfarmaco, Pfizer, PTC Therapeutics, Santhera Pharmaceuticals, Sarepta Therapeutics, Inc., and Solid Biosciences and has a consultancy/advisory role with BioMarin, Capricor Therapeutics, Catalyst, Edgewise Therapeutics, F. Hoffmann-La Roche Ltd., Italfarmaco, NS Pharma, PTC Therapeutics, Santhera Pharmaceuticals, Sarepta Therapeutics, Inc., and Solid Biosciences. He has received honoraria from Edgewise Therapeutics, PTC Therapeutics, and Sarepta Therapeutics, Inc.