Long-Term Outcomes of Gene Therapy in Duchenne Muscular Dystrophy

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Disclosures

- Royalties for consulting services in the field of scientific and pedagogical activities (educational services,participation in expert councils, participation in research, etc.) from the following companies: Roche, PTC Therapeutics, Novartis, FARMAMONDO-BIOMEDICA

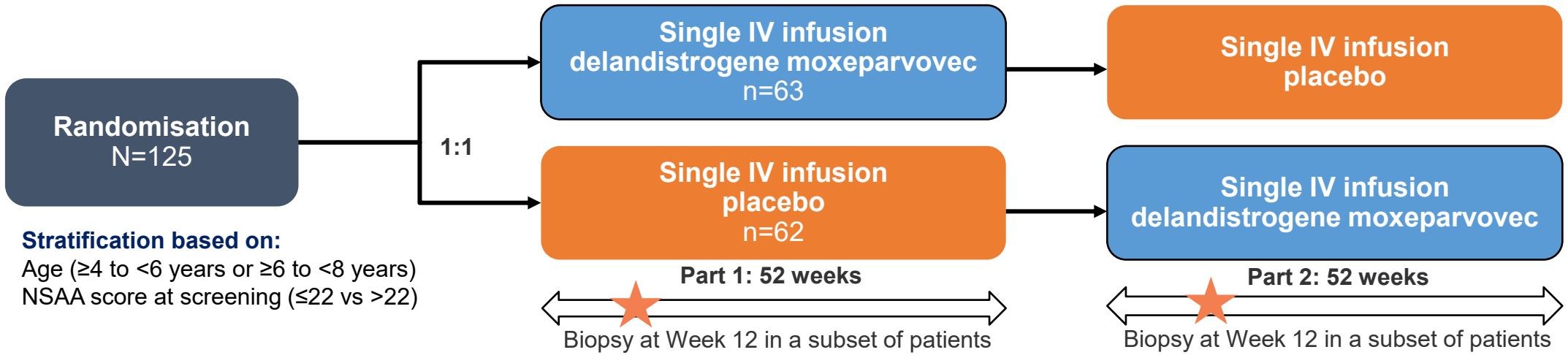
- Necessary permissions have been obtained for the use of photo and / or video materials from patients and/or their legal representatives in the form prescribed by law.

Plan of the report

- Gene Therapy: clinical trials data
- Experience of the National Medical Research Center for Children’s Health in DMD Gene Therapy
- Clinical Cases
- Conclusion and Key Learnings

EMBARK study design[1,2]

A Phase 3, multinational, double-blind, randomised, placebo-controlled study evaluating the safety and efficacy of delandistrogene moxeparvovec in patients with DMD aged ≥4 to <8 years old



Stratification based on:
Age (≥4 to <6 years or ≥6 to <8 years)
NSAA score at screening (≤22 vs >22)

Key inclusion criteria:

- Ambulatory boys aged ≥4 to <8 years
- **NSAA score >16 and <29 at screening**
- **TTR <5 seconds at screening**
- Total rAAVrh74 antibody titre <1:400
- Stable daily dose of oral corticosteroids for at least 12 weeks prior to screening
- *DMD* mutation within exons 18–79 (mutations between or including exons 1–17, in-frame deletions, in-frame duplications, variants of uncertain significance, and mutations fully contained within exon 45 [inclusive] were not eligible)

DMD, Duchenne muscular dystrophy; IV, intravenous; NSAA, North Star Ambulatory Assessment; rAAVrh74, recombinant adeno-associated virus rhesus isolate serotype 74; TTR, Time to Rise.

1. ClinicalTrials.gov. NCT05096221 (Accessed October 2024); 2. Mendell JR, et al. Presented at MDA 2024.

Demographics[1,2]

Characteristic	Statistics	Delandistrogene moxeparvovec (n=63)	Placebo (n=62)
Age, years	Mean (SD) Min, max	5.98 (1.06) 4.07, 7.87	6.08 (1.05) 4.03, 7.99
4–5 years	n (%)	30 (47.6)	29 (46.8)
6–7 years	n (%)	33 (52.4)	33 (53.2)
Race, white	n (%)	49 (77.8)	46 (74.2)
Ethnicity, Hispanic or Latino	n (%)	15 (23.8)	8 (12.9)
Height, cm	Mean (SD) Min, max	108.64 (6.74) 93.5, 127.0	110.68 (7.44) 95.2, 127.5
Dosing weight, kg	Mean (SD) Min, max	21.29 (4.62) 13.5, 38.5	22.37 (6.42) 14.4, 41.6
BMI, kg/m^2	Mean (SD) Min, max	17.85 (2.20) 13.69, 24.92	17.89 (3.20) 13.45, 26.86
Years since diagnosis of DMD	Mean (SD) Min, max	2.62 (1.73) 0.00, 6.71	2.60 (1.78) 0.24, 7.55
Years since corticosteroid treatment started	Mean (SD) Min, max	1.07 (0.92) 0.23, 6.17	0.97 (0.83) 0.24, 4.01
Genetic mutation	n (%)		
Large deletion		45 (71.4)	41 (66.1)
Large duplication		3 (4.8)	3 (4.8)
Small mutation		15 (23.8)	18 (29.0)

BMI, body mass index; DMD, Duchenne muscular dystrophy; SD, standard deviation.

1. Mendell JR, et al. Presented at MDA 2024; 2. Roche/Sarepta data on file 2023.

Baseline functional assessments

Characteristic	Statistics	Delandistrogene moxeparvovec (n=63)	Placebo (n=62)
NSAA total score	Mean (SD) Min, max	23.10 (3.75) 14.00, 32.00	22.82 (3.78) 15.50, 30.00
TTR, seconds	Mean (SD) Min, max	3.52 (0.81) 1.85, 5.75	3.60 (0.68) 2.25, 5.00
10MWR, seconds	Mean (SD) Min, max	4.82 (0.79) 3.20, 6.85	4.92 (0.73) 3.65, 7.00
SV95C, metres/second	Mean (SD) Min, max	1.82 (0.30) 1.06, 2.50	1.77 (0.29) 1.10, 2.35
100MWR, seconds	Mean (SD) Min, max	60.67 (15.55) 38.00, 129.20	63.01 (17.01) 38.70, 118.10
Ascend four steps, seconds	Mean (SD) Min, max	3.17 (1.01) 1.60, 7.10	3.37 (1.09) 1.50, 7.10

10MWR, 10-metre Walk/Run; 100MWR, 100-metre Walk/Run; NSAA, North Star Ambulatory Assessment; SD, standard deviation, TTR, Time to Rise; SV95C, Stride Velocity 95th Centile.
Mendell JR, et al. Presented at MDA 2024.

EMBARK: 2yr + 3yr EC methodology

In the absence of a placebo arm, EMBARK 2- + 3-year data were compared with an EC cohort of ambulatory patients with DMD who received SoC

Patients from the following studies were included:

- ✓ FOR-DMD (clinical trial)
- ✓ PRO-DMD-01 (natural history)
- ✓ CINRG DNHS (natural history)
- Eli Lilly (clinical trial)*
- DEMAND-III (clinical trial)*

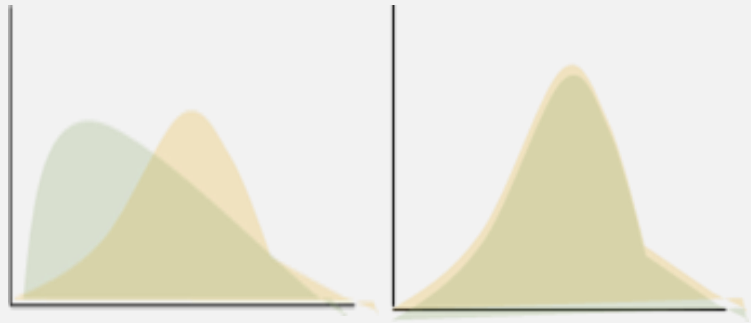
Pre-specified EC entry criteria:

- ✓ Aged ≥4 and <8 years
- ✓ NSAA total score ≥14 and ≤32
- ✓ TTR ≤5.75 seconds
- ✓ 10MWR time ≤6.85 seconds
- ✓ Stable dose of oral corticosteroids for ≥12 weeks

Propensity-score weighting based on baseline:

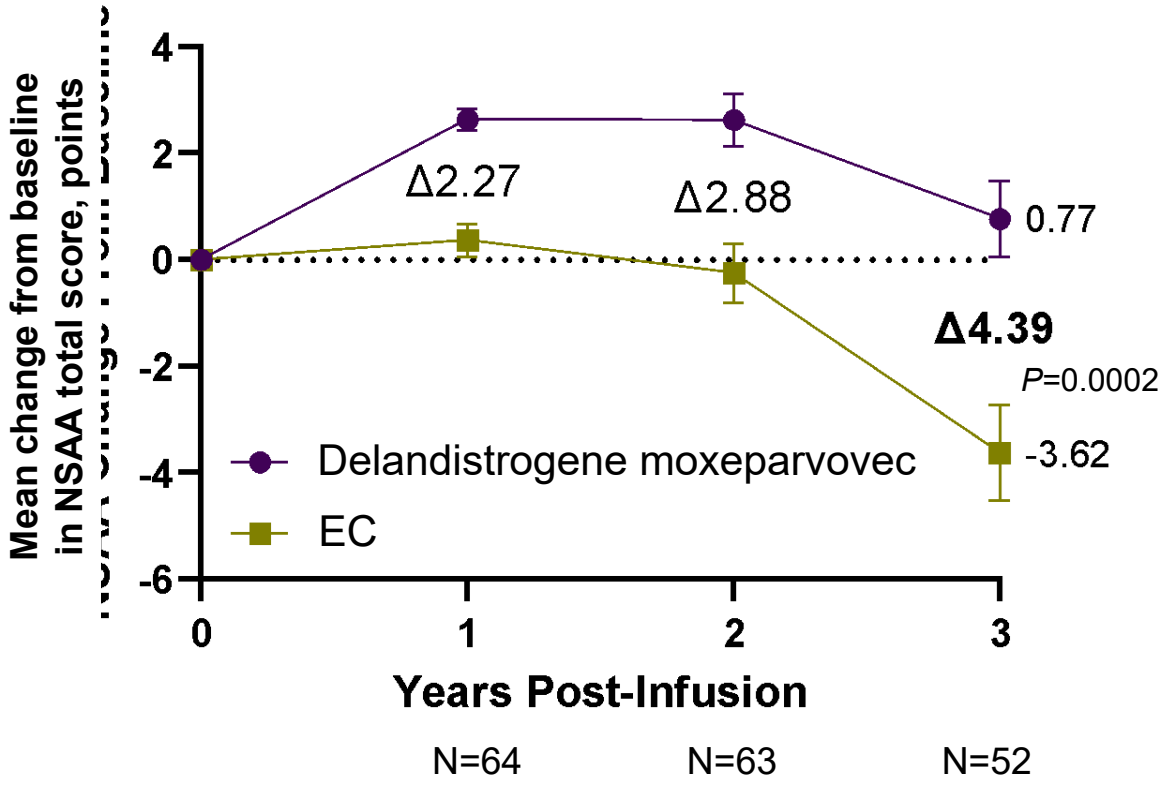
Age	NSAA total score
TTR	10MWR

Example ECs before and after propensity weighting*



*Propensity weighting involves taking an EC group with similar age and function, but unequal distribution, and ensuring overlap after propensity weighting.
10MWR, 10-metre Walk/Run; DMD, Duchenne muscular dystrophy; EC, external control; NSAA, North Star Ambulatory Assessment; SoC, standard of care; TTR, Time to Rise.
* not included for 3 year results
Roche/Sarepta data on file 2026.

Part 1-treated vs EC at Year 3: Treated patients showed statistically significant and clinically meaningful efficacy in NSAA

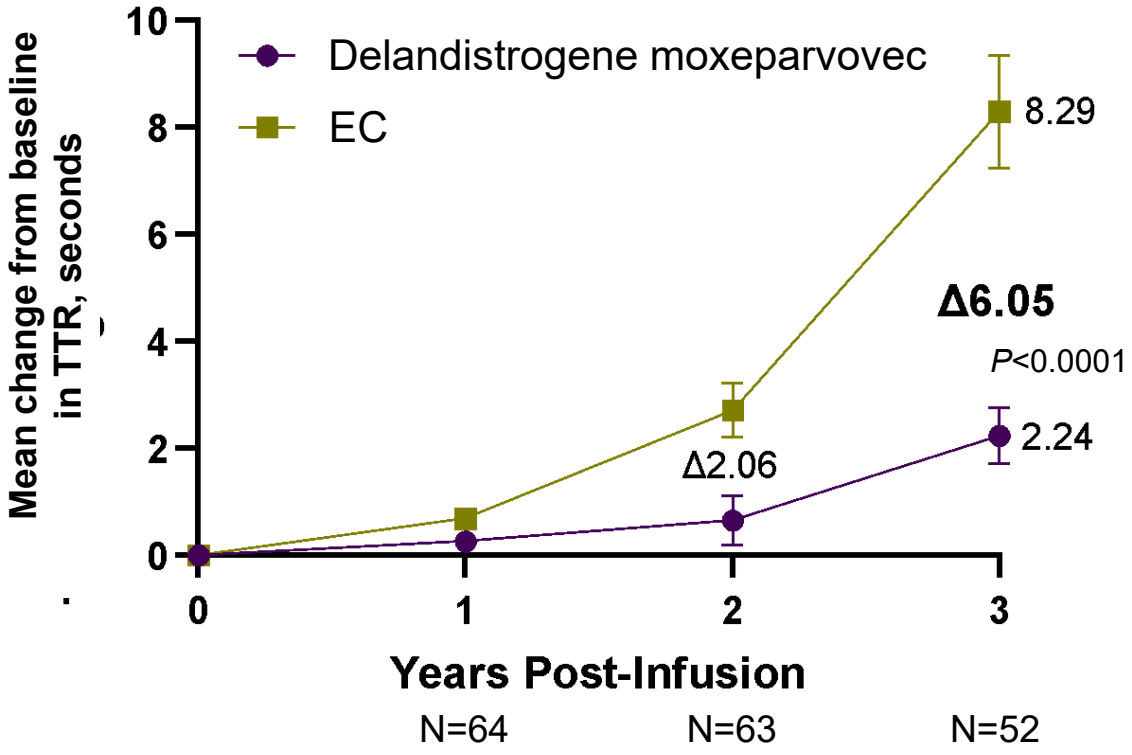


Key observations:

- NSAA is significantly higher in the delandistrogene moxeparvovec group at Year 3 compared with the EC group (*P*=0.0002)
- Year over year, the difference between the delandistrogene moxeparvovec and EC groups continues to grow larger
- Delandistrogene moxeparvovec-treated patients remain above baseline at Year 3

N numbers show number of patients in the delandistrogene moxeparvovec group.
EC, external control; NSAA, North Star Ambulatory Assessment.

Part 1-treated vs EC at Year 3: Treated patients showed statistically significant and clinically meaningful efficacy in TTR

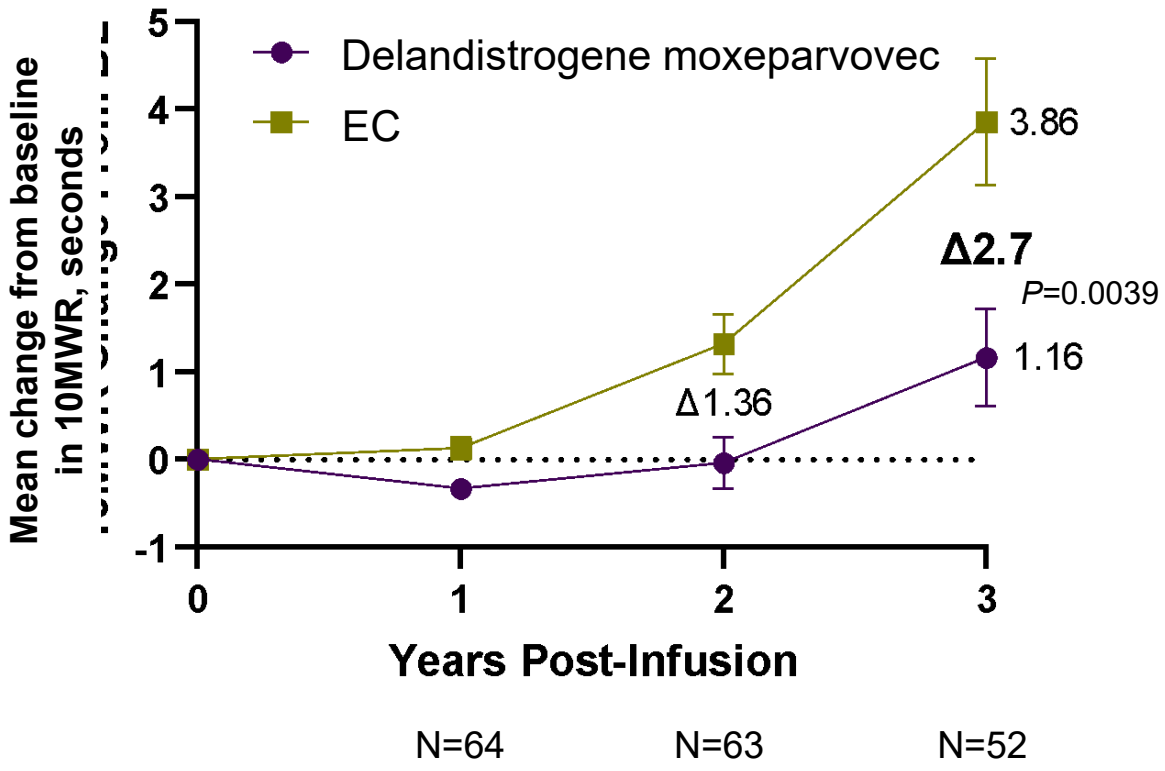


Key observations:

- TTR is significantly lower in the delandistrogene moxeparvovec group at Year 3 compared with the EC group (P<0.0001)
- Year over year, the difference between delandistrogene moxeparvovec and EC groups continues to grow larger

N numbers show number of patients in the delandistrogene moxeparvovec group.
EC, external control; TTR, Time to Rise.

Part 1-treated vs EC at Year 3: Treated patients showed statistically significant and clinically meaningful efficacy in 10MWR

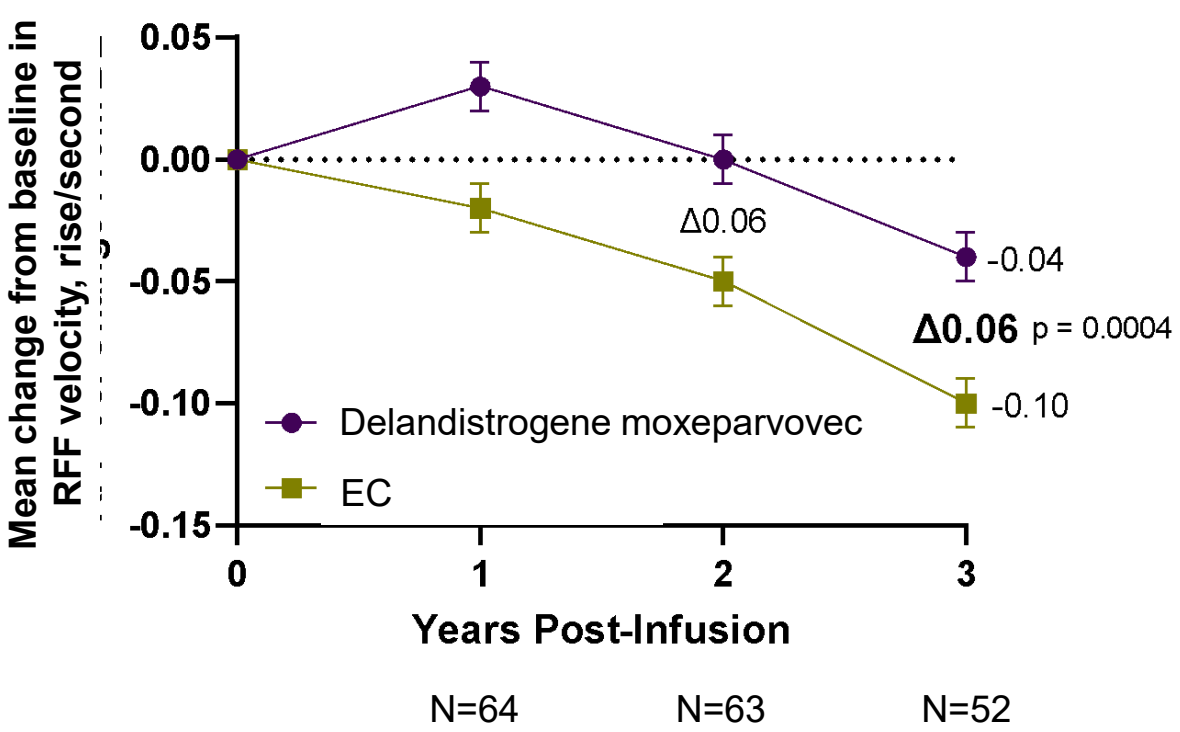


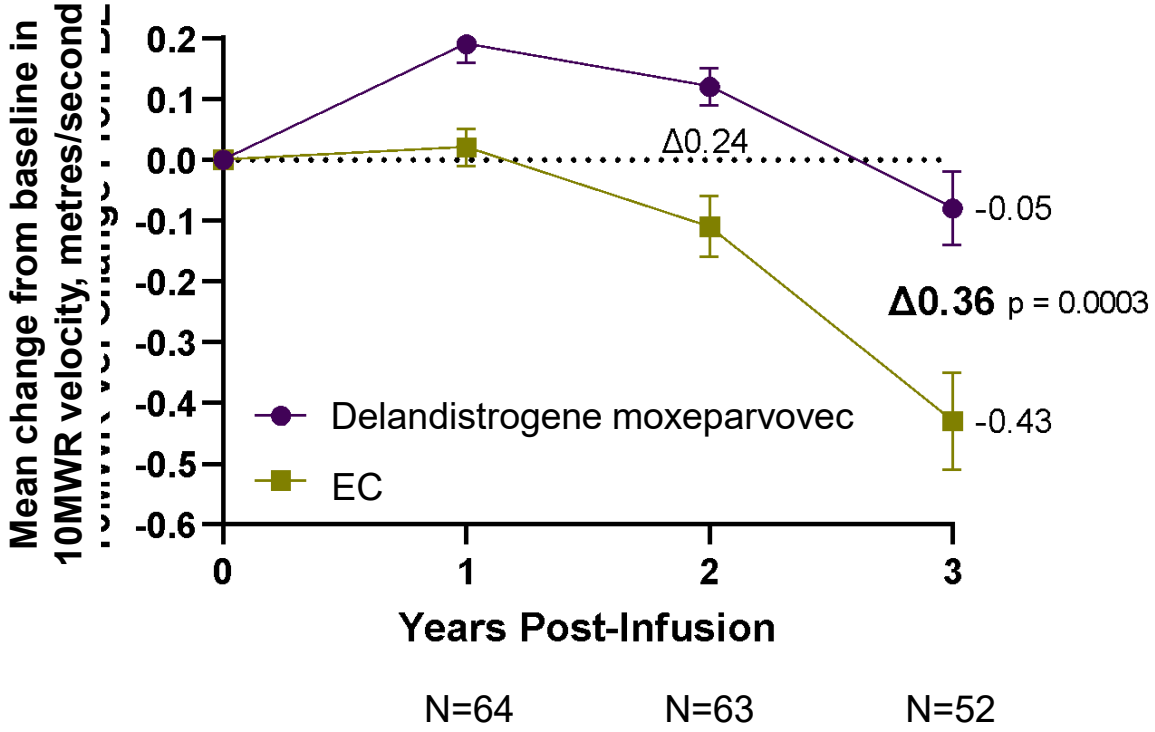
Key observations:

- 10MWR time is significantly lower in the delandistrogene moxeparvovec group at Year 3 compared with the EC group (*P*=0.0039)
- Year over year, the difference between delandistrogene moxeparvovec-treated and EC groups continues to grow larger

N numbers show number of patients in the delandistrogene moxeparvovec group.
10MWR, 10-metre Walk/Run; EC, external control.

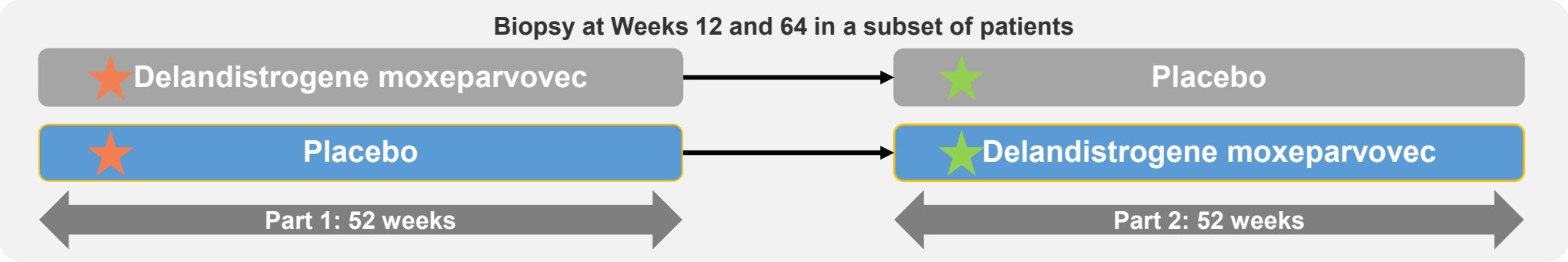
Part 1-treated vs EC at Year 3: Treated patients showed statistically significant and clinically meaningful efficacy in RRF velocity and 10MWR velocity





N numbers show number of patients in the delandistrogene moxeparvovec group.
10MWR, 10-metr Walk/Run; EC, external control; RFF, Rise from Floor.

EMBARK Part 1 and 2: Biological efficacy up to Week 64[1,2]



Mean (SD)	Part 1 delandistrogene moxeparvovec treated		Part 2 delandistrogene moxeparvovec treated	
	Week 12 n=17	Week 64 n=16	Week 12 (placebo) n=14	Week 64 n=15
Vector genome copies, n	2.26 (1.55)	0.88 (0.53)	0.00 (0.00)	3.22 (1.44)
Western blot, % control	34.29 (41.04)	45.68 (39.75)	0.00 (0.00)	27.88 (25.22)
PDPF, %	28.13 (26.10)	38.60 (26.93)	0.61 (1.27)	29.29 (22.95)
Fibre intensity, % control	54.70 (13.14)	82.82 (25.04)	31.92 (9.43)	59.40 (14.03)

PDPF, percent dystrophin-positive fibre; SD, standard deviation.

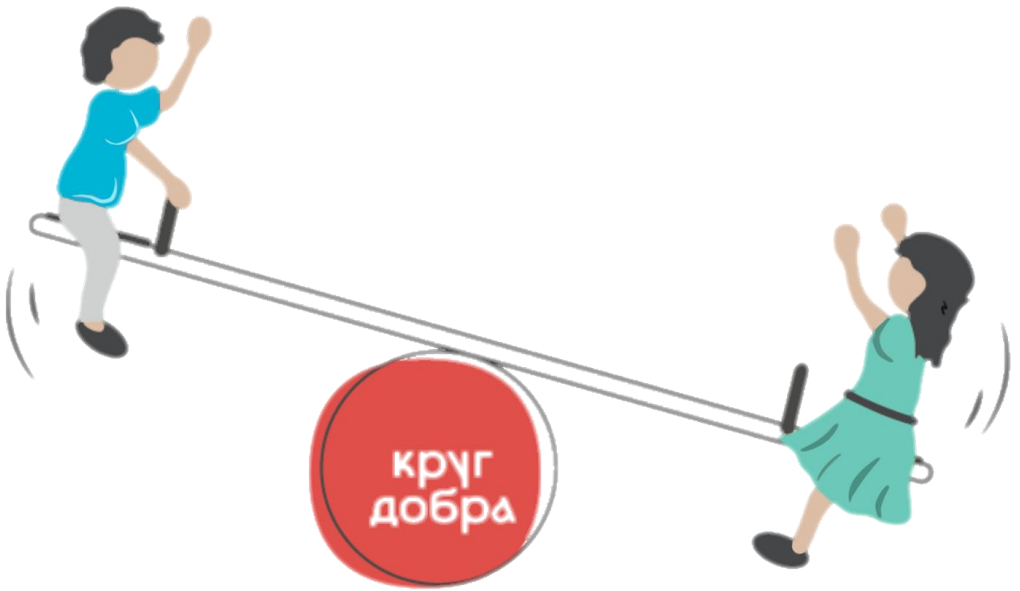
1. Roche/Sarepta data on file 2025; 2. Mendell JR, et al. *Nat Med*. 2025; 31:332–341.

Conclusion and Key Learnings

- EMBARK functional results up to 3-years build on the totality of evidence for delandistrogene moxeparvovec
- EMBARK Part 1 3-year results demonstrate statistically significant, clinically meaningful and durable efficacy versus ECs
- Delandistrogene moxeparvovec transduction efficiency, micro-dystrophin expression and sarcolemma localization was sustained from Weeks 12 to 64 in patients treated in Part 1

Pathogenic/gene therapy could be prescribed only by experts from Federal Centers

- The Circle of Kindness is a key funding source for rare disease treatment procurement for children
- Delandistrogene moxeparvovec*, Ataluren, Eteplirsen*, Viltolarsen and Golodirsen* are available for DMD patients according to CoK criteria
- 3 federal centers have been designated by the The Circle of Kindness as gene therapy centers for DMD



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* - off-label therapy, is not approved in Russia

Gene therapy for DMD in the National Medical Research Center for Children's Health

Inclusion of delandistrogene moxeparvovec* in the list of the Circle of Kindness Foundation for patients 4-5 years old

Administration to First Patients July 11, 2024

Expansion of the Circle of Kindness Foundation criteria - the use of therapy in patients 4-9 years

111 DMD patients treated with delandistrogene moxeparvovec*

* - off-label therapy, not registered in the Russian Federation

Data of the report author, S.G. Popovich, 2026

Delandistrogene moxeparvovec* therapy at National Medical Research Center for Children's Health as of April 2026.

- Delandistrogene moxeparvovec* received 111 patients
  - in 2024: 22 pts
  - in 2025: 68 pts
  - In 2026: 21 pts

  - **27** pts reached the 1-year treatment follow-up period
  - **69** pts reached the 6-month follow-up period
  - **96** pts reached the 3-month follow-up period

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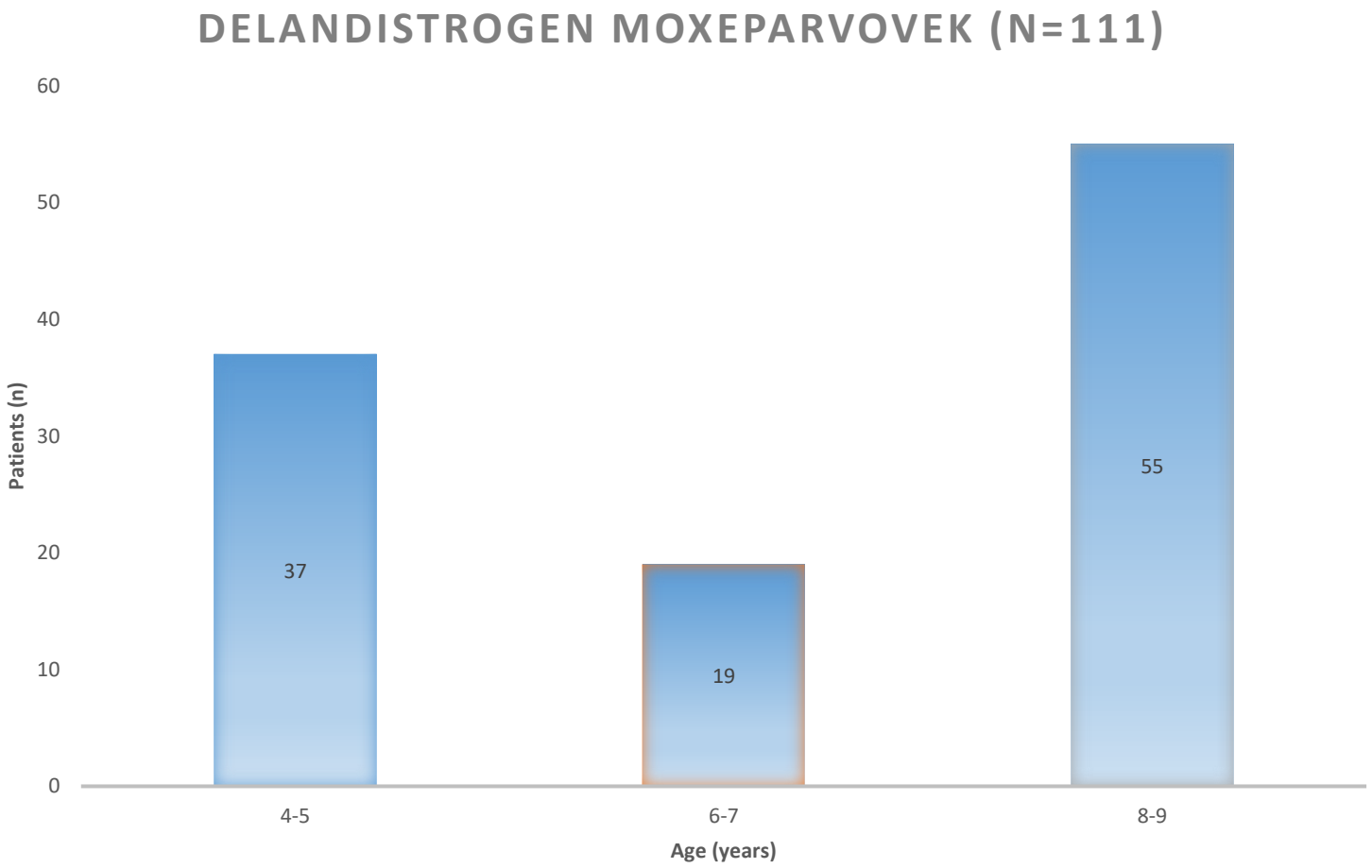
Data of the report author, S.G. Popovich, 2025

Analysis of all patients treated with delandistrogene moxeparvovec* in 2024-2026: age distribution



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Data of the report author, S.G. Popovich, 2026

Safety control after discharge from the hospital

10 weeks

Test	Frequency of control	Wk 1	Wk 2	Wk 3	Wk 4	Wk 5	Wk 6	Wk 7	Wk 8	Wk 9	Wk 10	Wk 11	Wk 12
CBC	Weekly												
ALT, AST													
LDH													
GGT													
Total bilirubin													
Urea													
Creatinine													
CPK													
Troponin-I													

! Clarifying to caregivers the need to **immediately inform the Center of gene therapy** about any abnormality in the child's condition, entering this information in the discharge summary, mentioning the most common symptoms of possible SAEs

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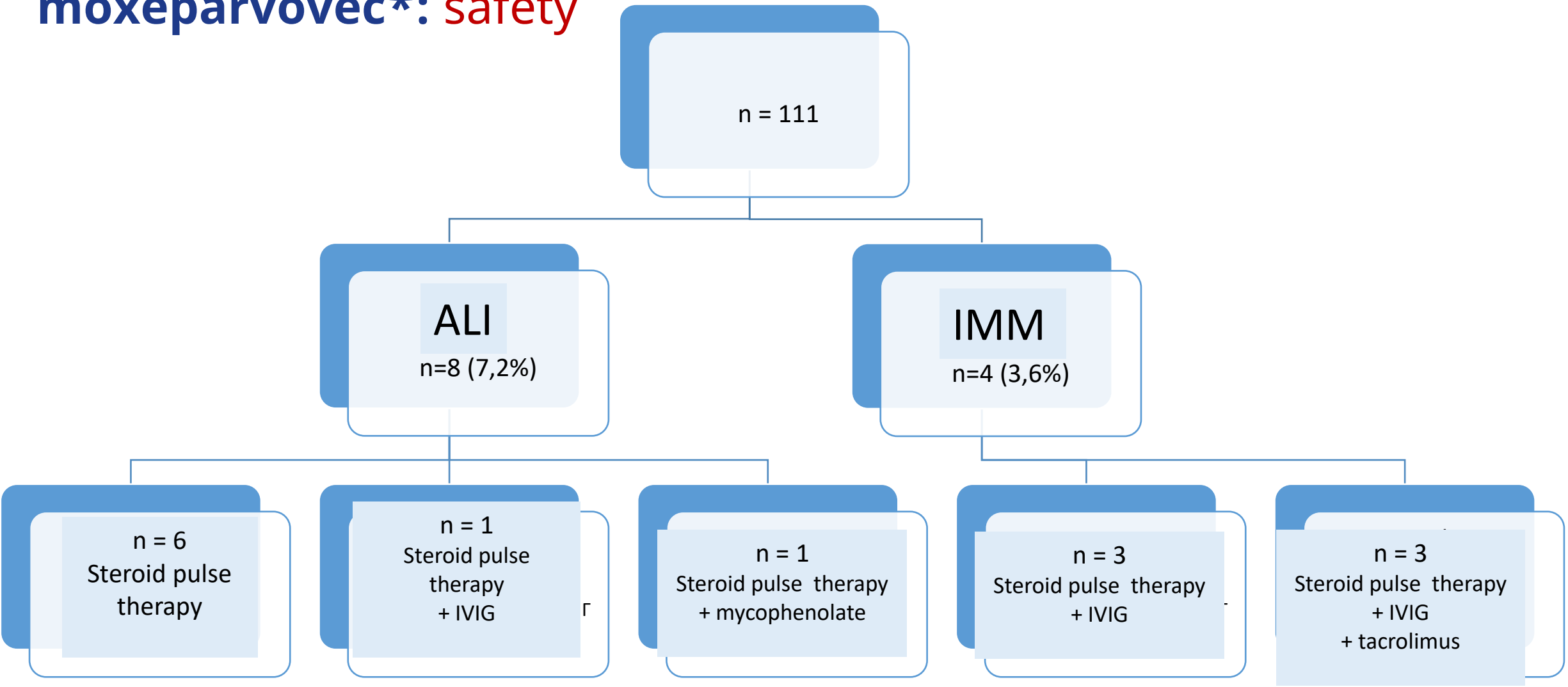
Data of the report author, S.G. Popovich, 2025

Analysis of all patients treated with delandistrogene moxeparvovec*: safety



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ALI - acute liver injury; IMM - immune mediated myositis; IVIG - immune globulins IV

Safety ID: RU241111 (associated RU24734, RU24735, RU24965 and RU241015, RU2557, RU2511)

Subgroup analysis of patients treated with delandistrogene moxeparvovec* more than 1 year as of April 2026: characteristics before initiation of therapy

	NSAA	6MWT, m	4TTR, s	4SC, s	10MWR
Numbers of patients	25	18	18	20	16
Mediana	21	339	4	3,5	6,3
Min	12	206,5	1,6	1,1	1
Max	34	521	10,4	11	11,6

NSAA – North Star Ambulatory Assessment
6MWT – 6-Minute Walk Test
TTR – Time to Rise from Floor
4SC – 4-Stair Climb (Ascend 4 Steps)
10MWR (or 10MWT) – 10-Meter Walk/Run Test

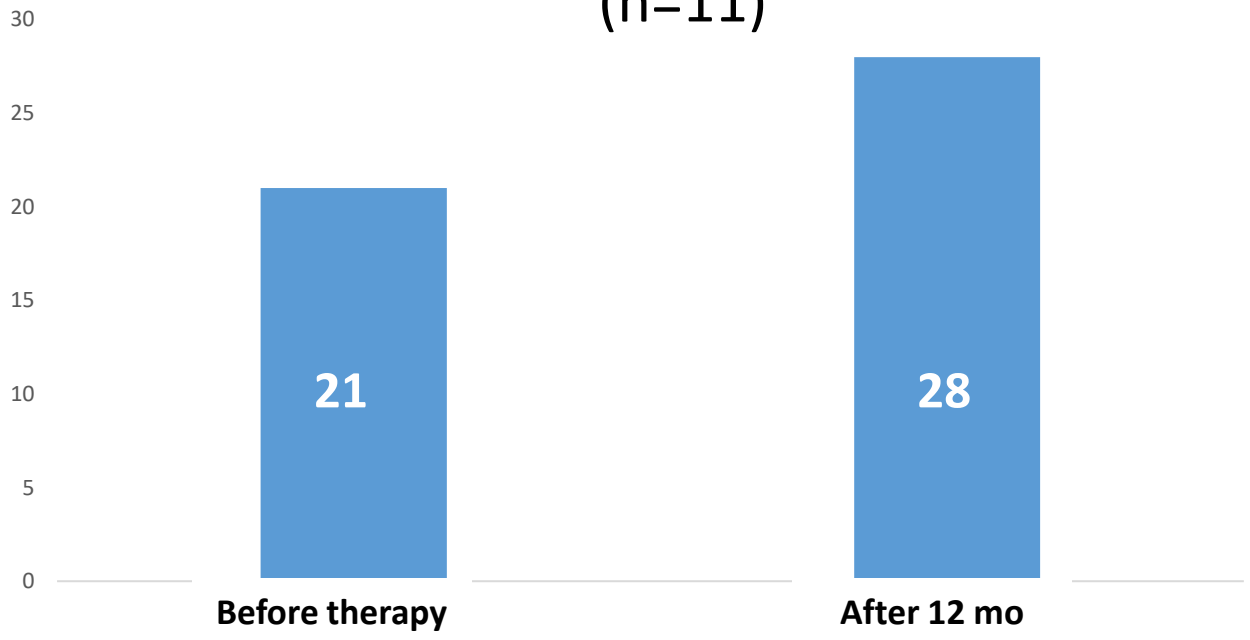
* - off-label therapy, not registered in the Russian Federation

Data of the report author, S.G. Popovich, 2026

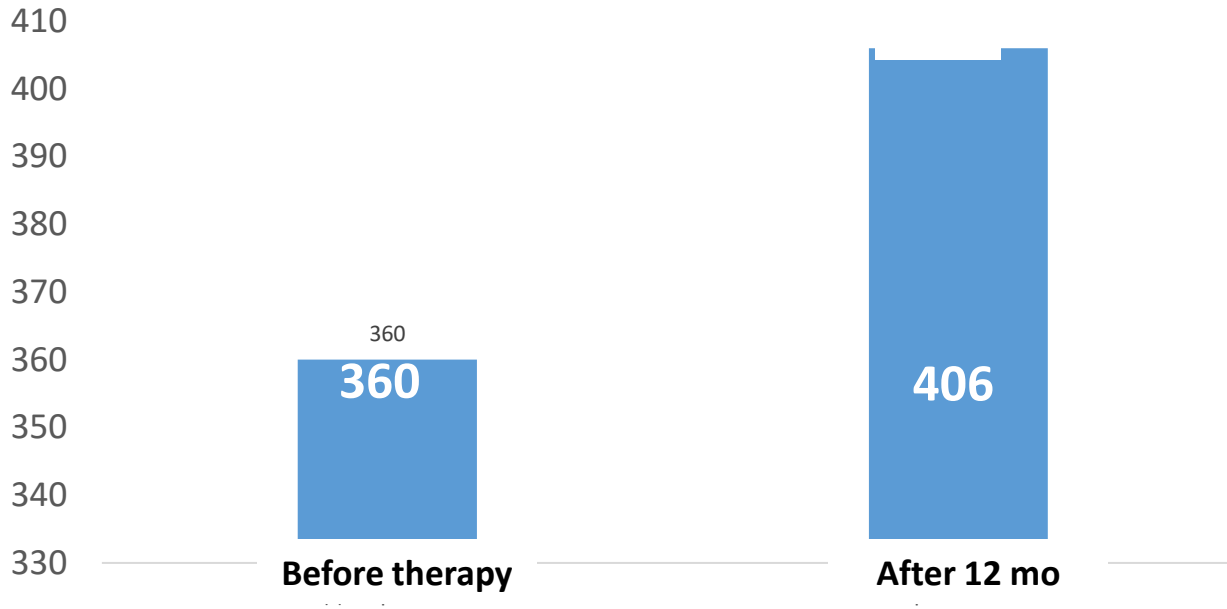
Subgroup analysis of patients treated with delandistrogene moxeparvovec* more than 1 year: effectiveness

Median age 5 [4; 5] **y**

Median NSAA score
(n=11)



Median 6 MWT, m
(n=18)



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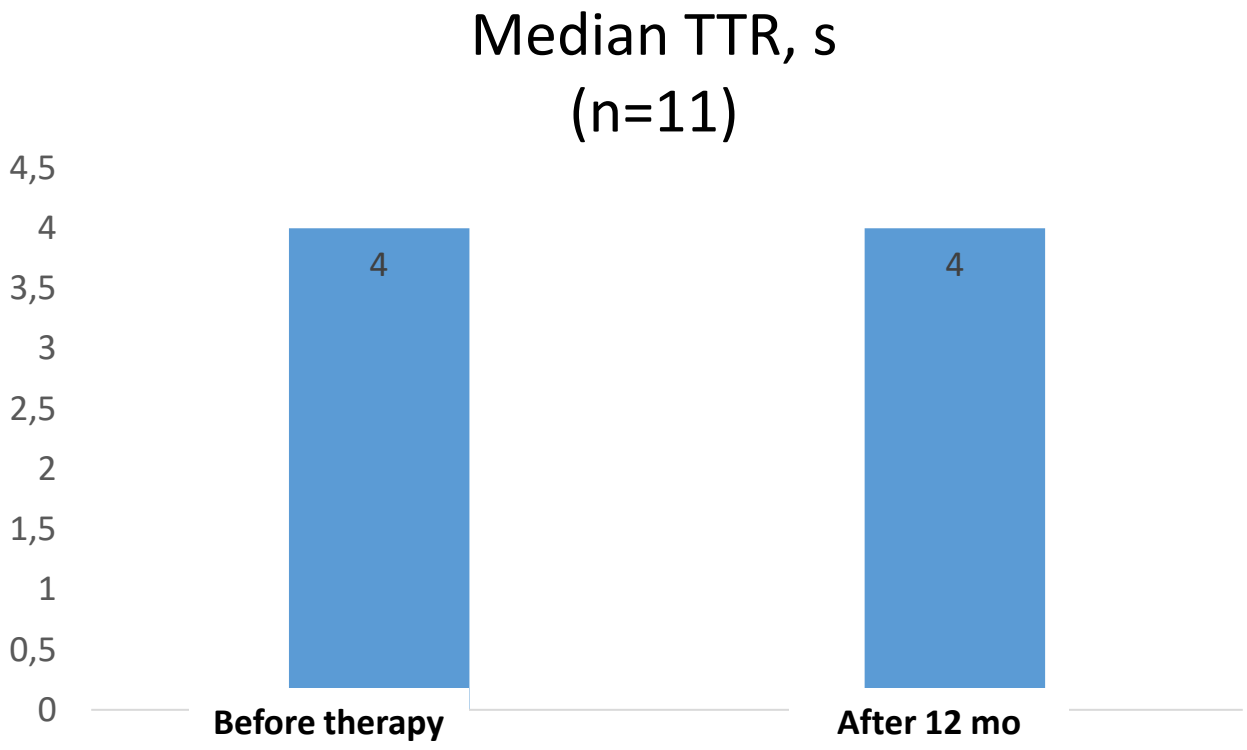
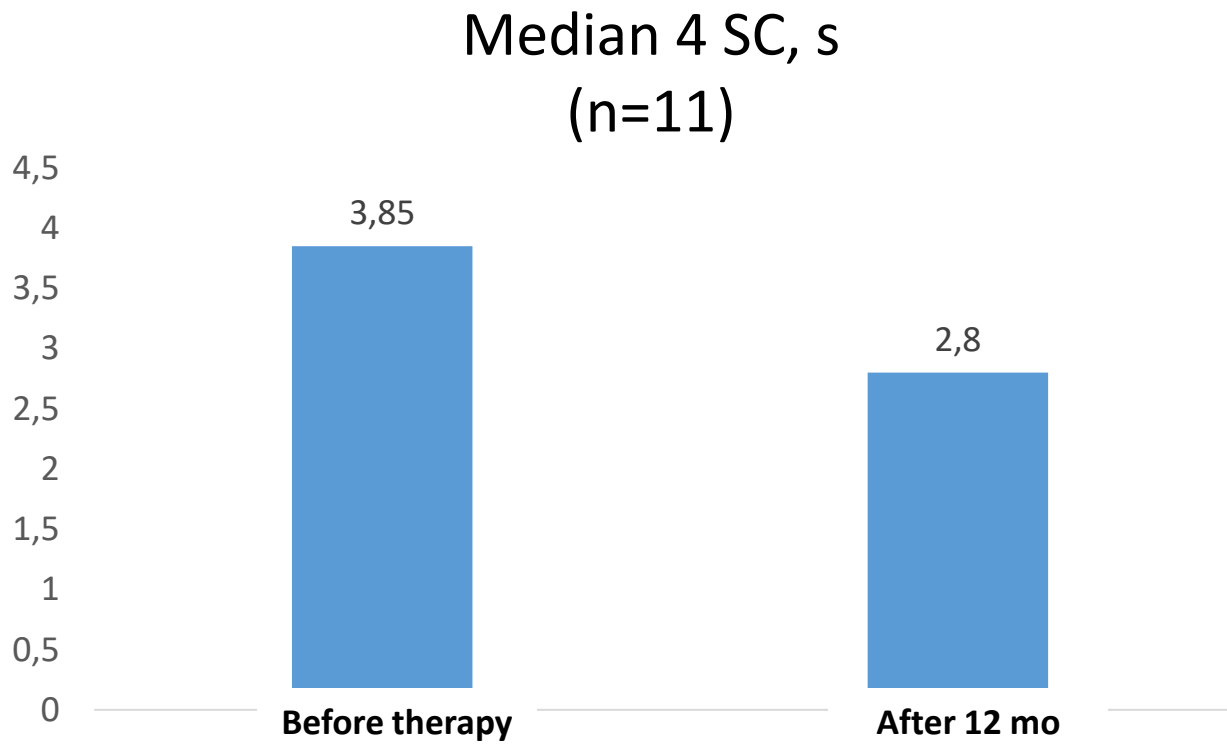
NSAA – North Star Ambulatory Assessment; 6MWT – 6-Minute Walk Test

Data of the report author, S.G. Popovich, 2026

Subgroup analysis of patients treated with delandistrogene moxeparvovec* more than 1 year: effectiveness

Median age 5 [4; 5] **y**





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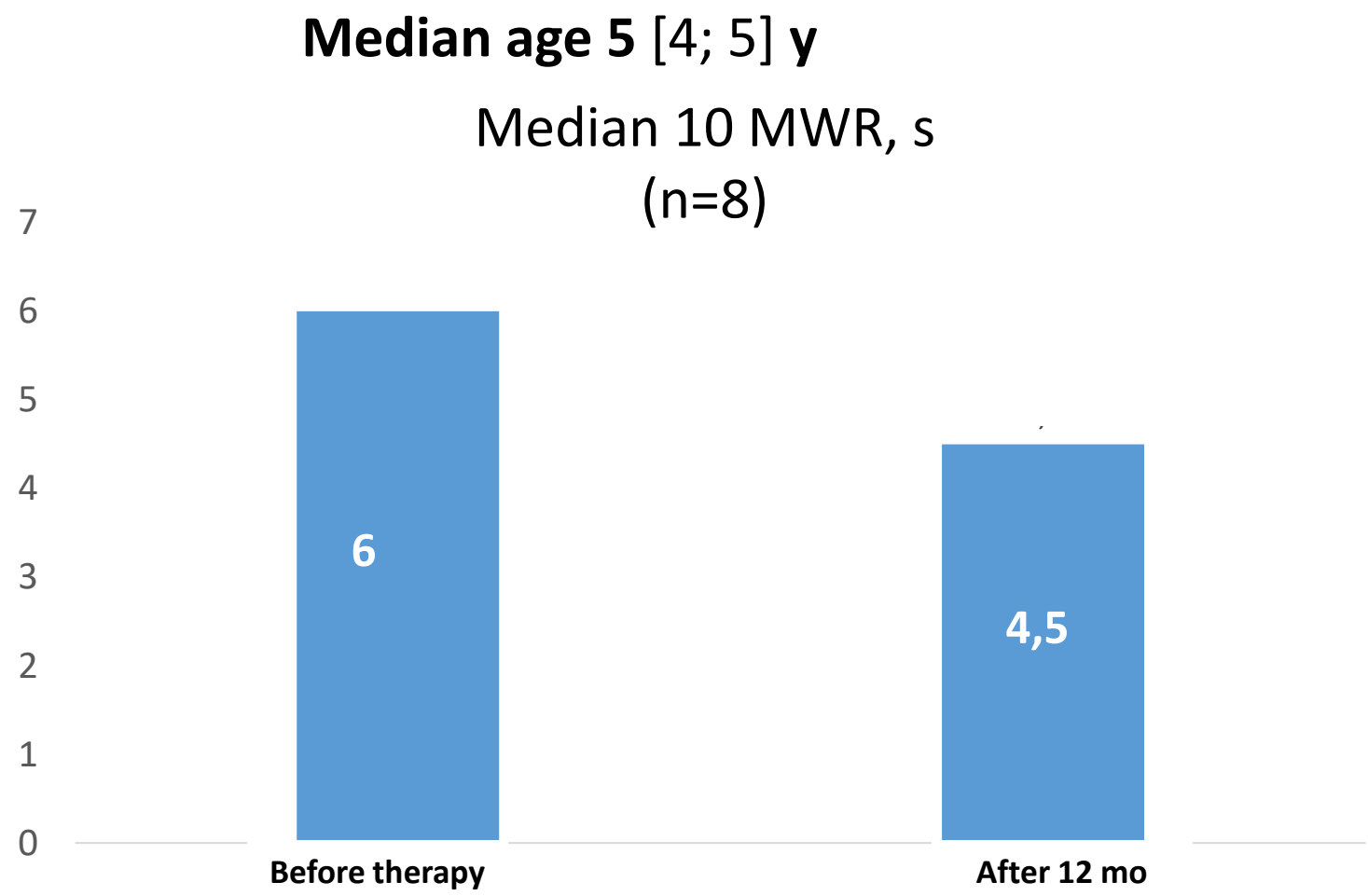
TTR – Time to Rise from Floor; 4SC – 4-Stair Climb (Ascend 4 Steps)

Data of the report author, S.G. Popovich, 2026

Subgroup analysis of patients treated with delandistrogene moxeparvovec* more than 1 year: effectiveness



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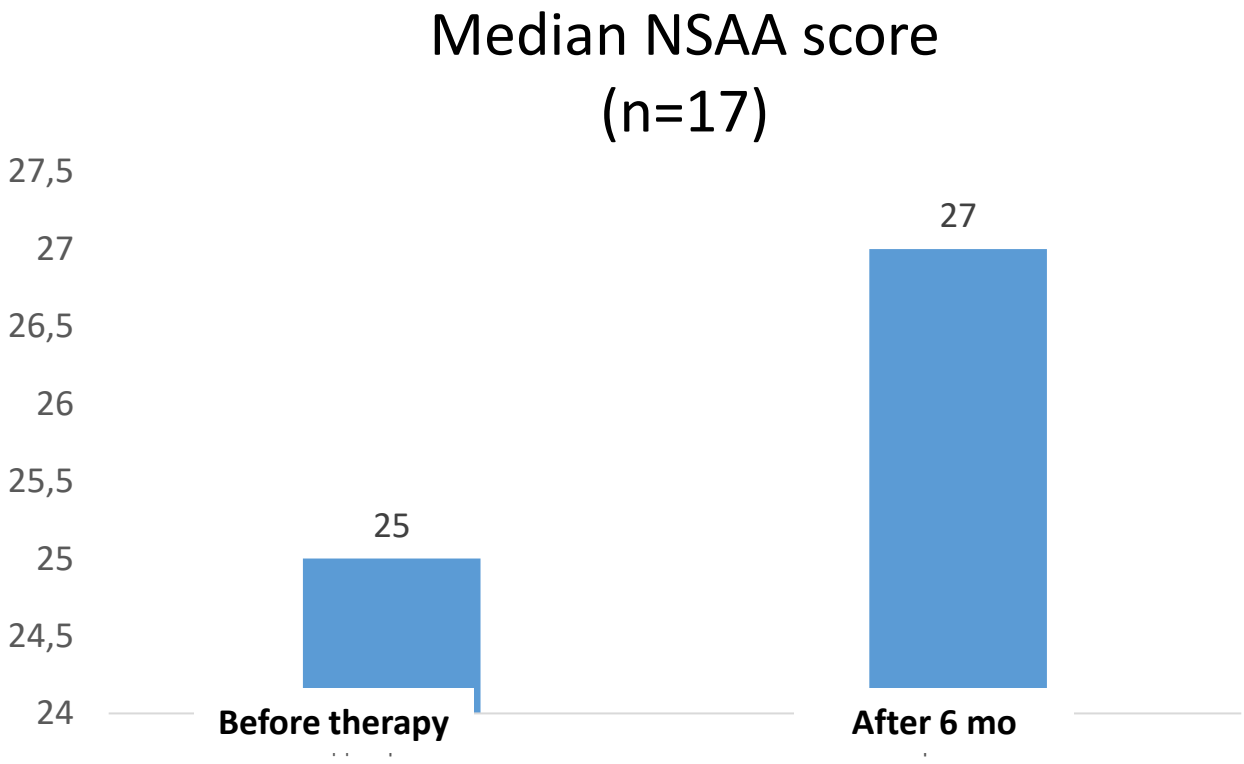
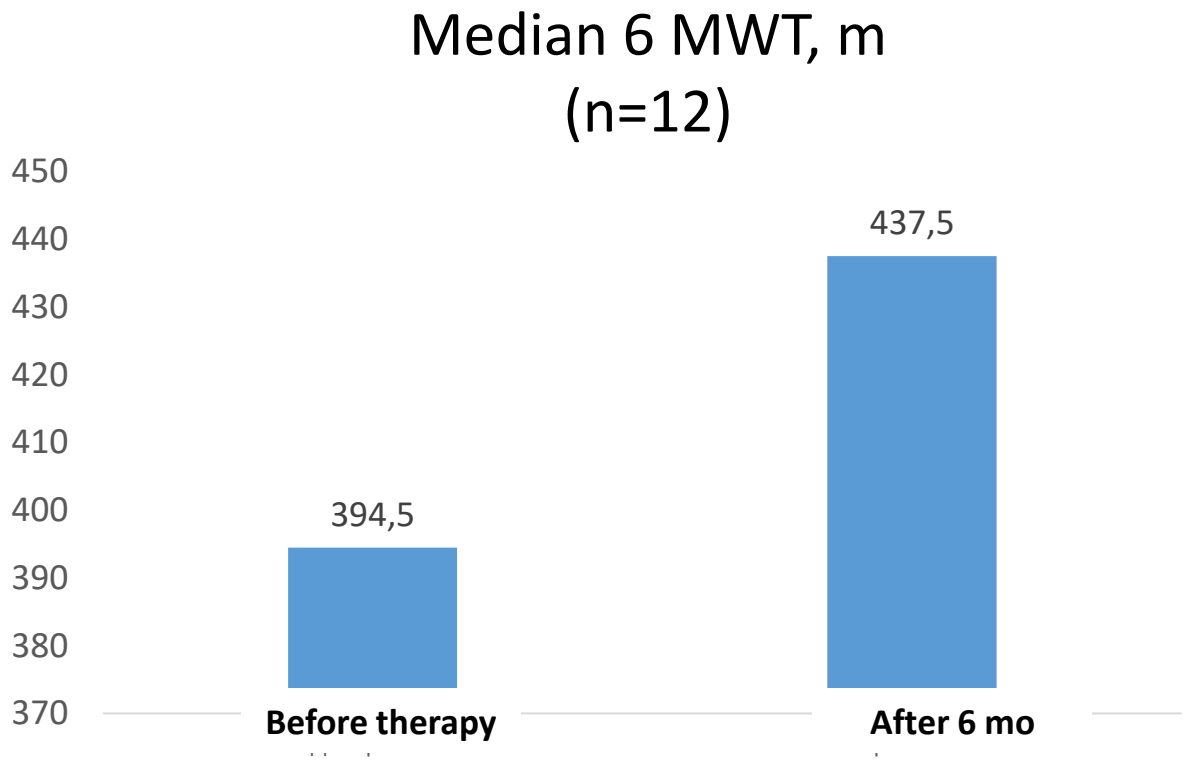
10MWR (or 10MWT) – 10-Meter Walk/Run Test

Data of the report author, S.G. Popovich, 2026

Subgroup analysis of patients aged 8-9 treated with delandistrogene moxeparvovec* after 6 months: effectiveness





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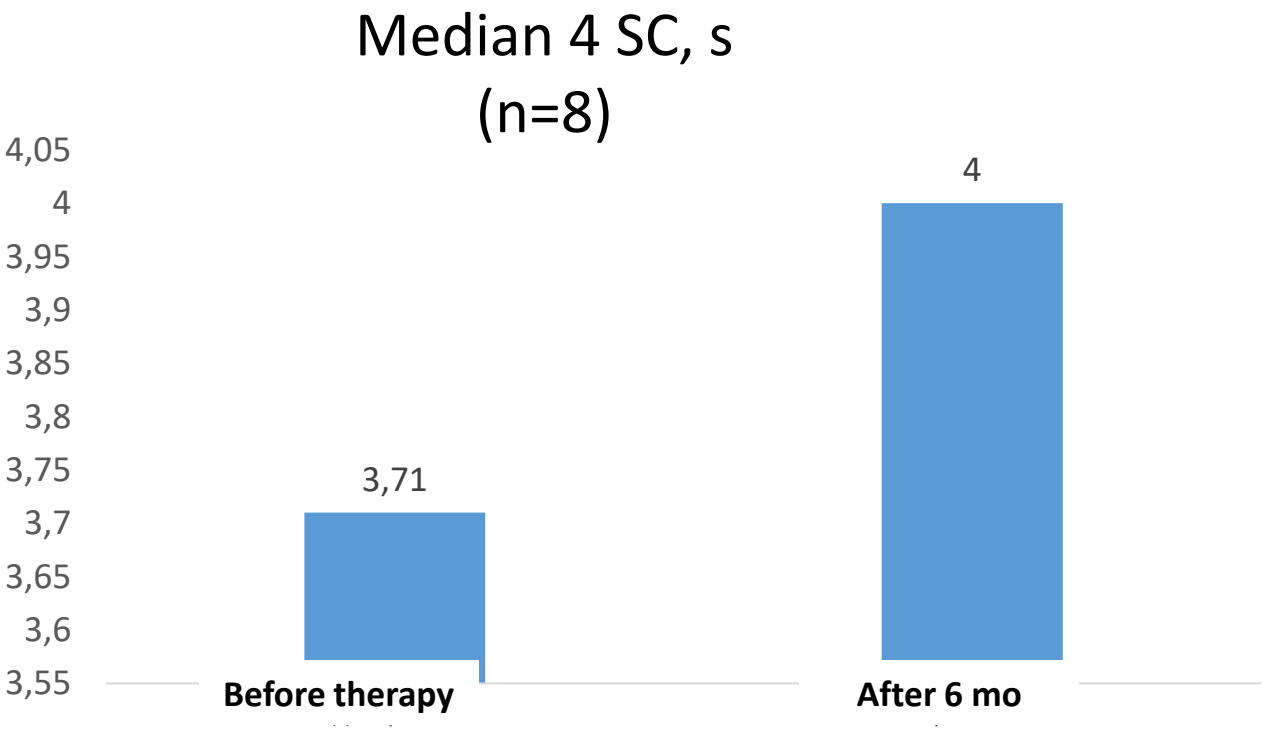
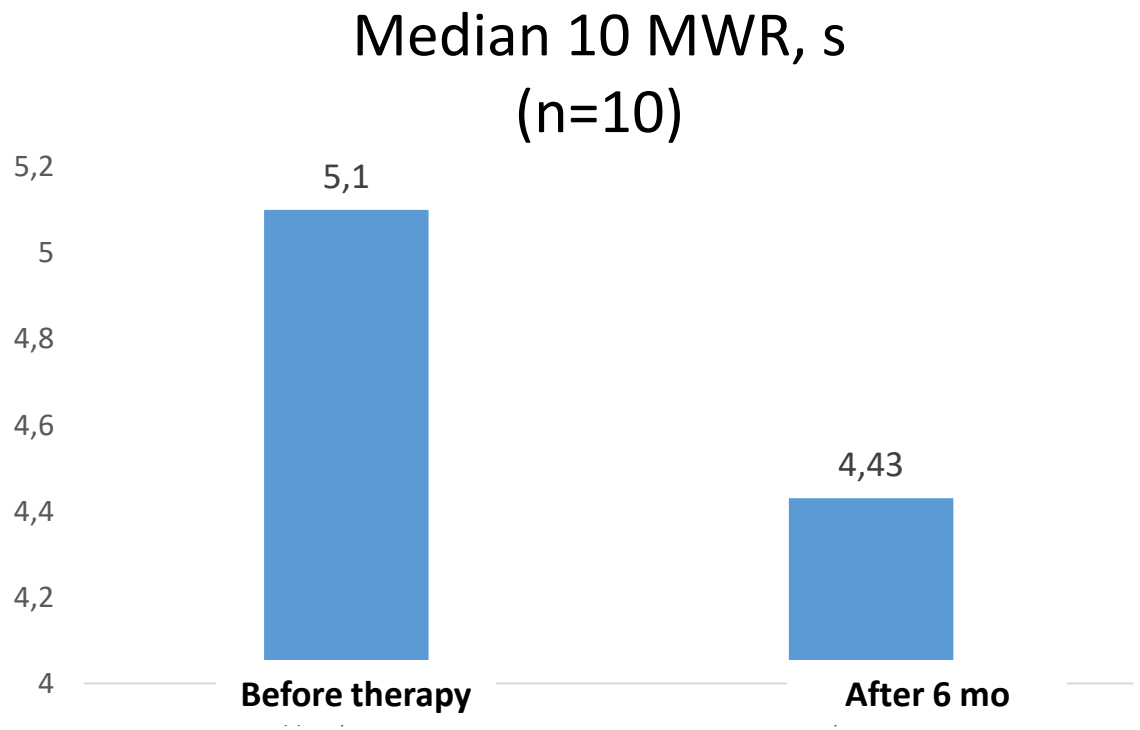
NSAA – North Star Ambulatory Assessment; 6MWT – 6-Minute Walk Test

Data of the report author, S.G. Popovich, 2026

Subgroup analysis of patients aged 8-9 treated with delandistrogene moxeparvovec* after 6 months: effectiveness



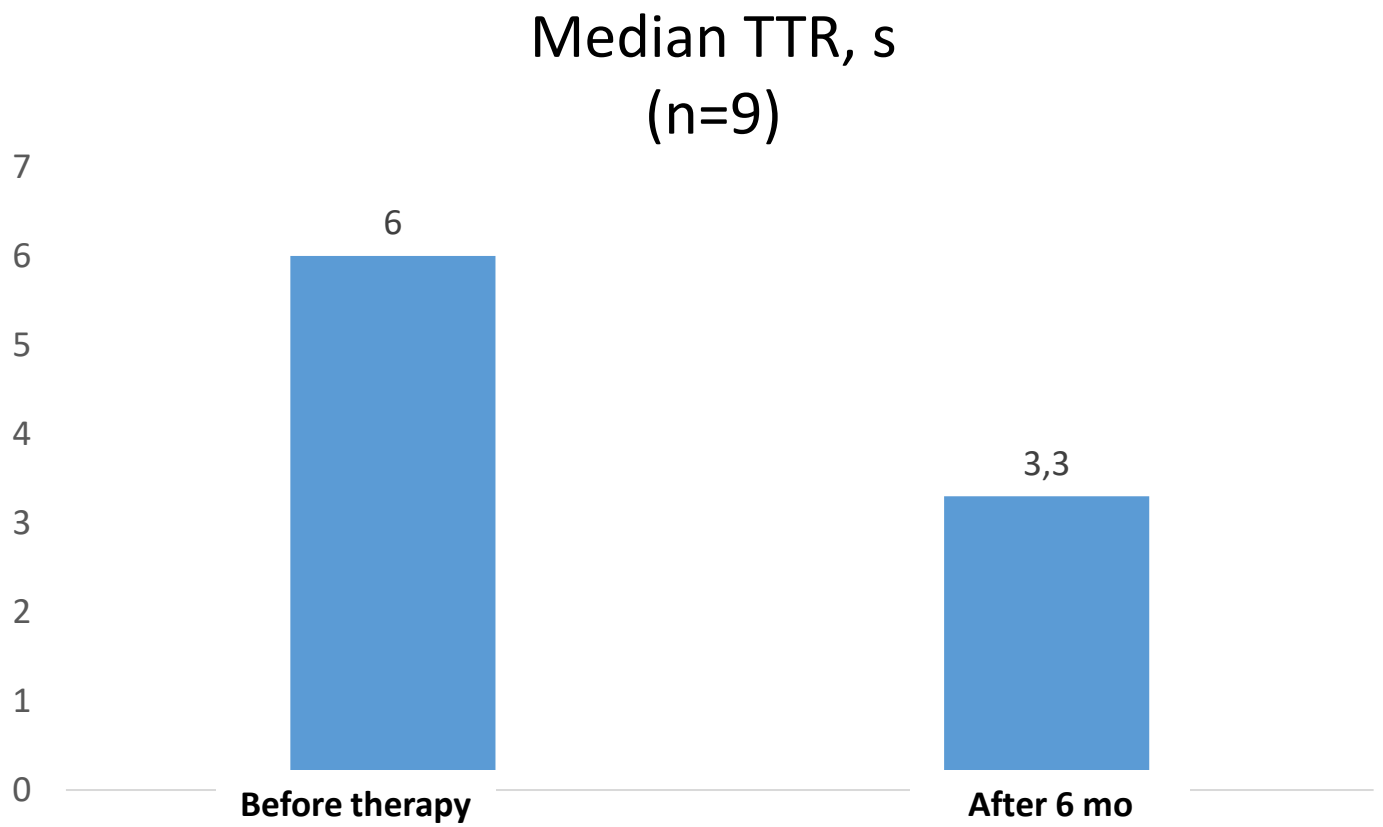


* - off-label therapy, not registered in the Russian Federation

4SC – 4-Stair Climb (Ascend 4 Steps); 10MWR (or 10MWT) – 10-Meter Walk/Run Test

Data of the report author, S.G. Popovich, 2026

Subgroup analysis of patients aged 8-9 treated with delandistrogene moxeparvovec* after 6 months: effectiveness



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TTR – Time to Rise from Floor

Data of the report author, S.G. Popovich, 2026

CLINICAL CASE 1

Case from the speaker's clinical experience and presented with permission from the patient and/or their caregiver.

The boy Zh., 5 y 9 mo

- 3rd pregnancy (1 pr. - girl, 2014, healthy, 2 pr. - girl, 2016, healthy)
- Birth at the 39 week of pregnancy, weight 3400 g, length 52 cm
- Previous illnesses: acute respiratory viral infections, measles
- Immunisation +
- Hereditary history: the mother's uncle has Duchenne muscular dystrophy

- First signs of muscular weekness since the age of 3

- Max CK level 11 518 U/l

- At the age of 5y 3 mo the diagnosis of Duchenne muscular dystrophy was confirmed (Variant C.5133 5135delinsCC (p.(Gln1711HisfsTer10))

Case from the speaker's clinical experience and presented with permission from the patient and/or their caregiver.

5 y 9 mo

Pre-delandistrogene moxeparvovec* administration period

- ✓Liver function, platelet counts and troponin-I - N.
- ✓Absence of acute infection and/or acute liver failure
- ✓ AAVrh74 antibody negative (The validity period of the result is 30 days.)
- ✓Apropriate doses of glucocorticosteroids (GCS): prednisone 0.75 mg/ kg/day (basic dose) + prednisone 1 mg/kg/day (added dose)

Post- delandistrogene moxeparvovec* administration period

- After 63d day we tapered the added peri-ELEVIDYS corticosteroids off during 4 weeks
- At the 5th week the patient has bronchitis** , amoxicillin with clavulanic acid were needed. Hospitalization was not required
- At the 10th week the patient has acute respiratory viral infection**. Hospitalization was not required

Case from the speaker's clinical experience and presented with permission from the patient and/or their caregiver.
* - Delandistrogene moxeparvovec is not approved in Russia

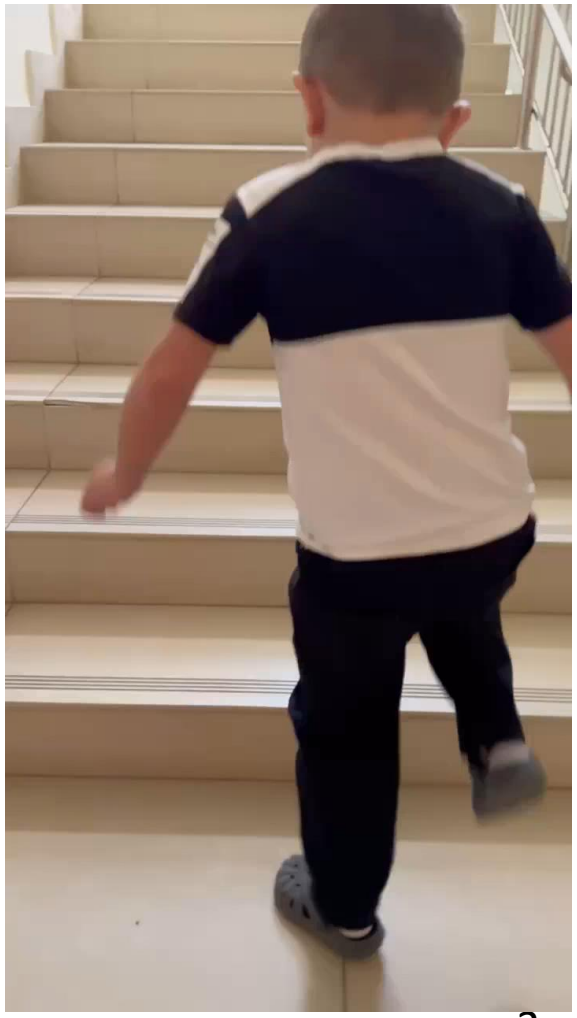
5 y 9 mo

Before therapy

Examination

Gower's signs ++.
Restriction of walking on the heels.
Pseudohypertrophy of the lower leg muscles.
"Duchenne jogging".
He ran, jumped, climbed the stairs, squated and stood up.

NSAA 28 points
TTR 10.4 s
10 MWR 4.5 s
6 MWT 350 m
4SC (4 stair climb)2 s



Case from the speaker's clinical experience and presented with permission from the patient and/or their caregiver.
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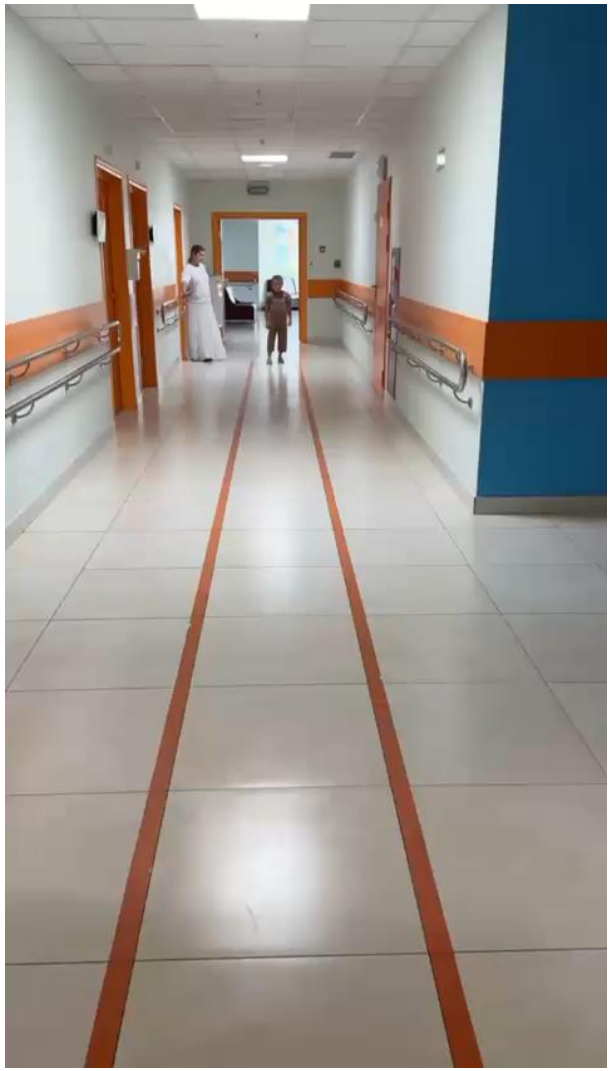
6 y 9 mo

12 months after gene therapy

NSAA 31 points (+3)
TTR 4,5 s (-6 s)
10 MWR - 4.5 sec
6 MWT 450 m (+100 m)
4SC (4 stair climb)1,75 s



Case from the speaker's clinical experience and presented with permission from the patient and/or their caregiver.
* - Delandistrogene moxeparvovec is not approved in Russia

CLINICAL CASE 2

Case from the speaker's clinical experience and presented with permission from the patient and/or their caregiver.

The boy V., 8 y 11 mo

- 2nd pregnancy (1 pr. – healthy girl)
- Birth at 39 week of pregnancy, weight 3200 g, length 56 cm
- Hereditary history: the mother's uncle has Duchenne muscular dystrophy
- No allergic history

- First signs of muscular weekness since the age of 5,5

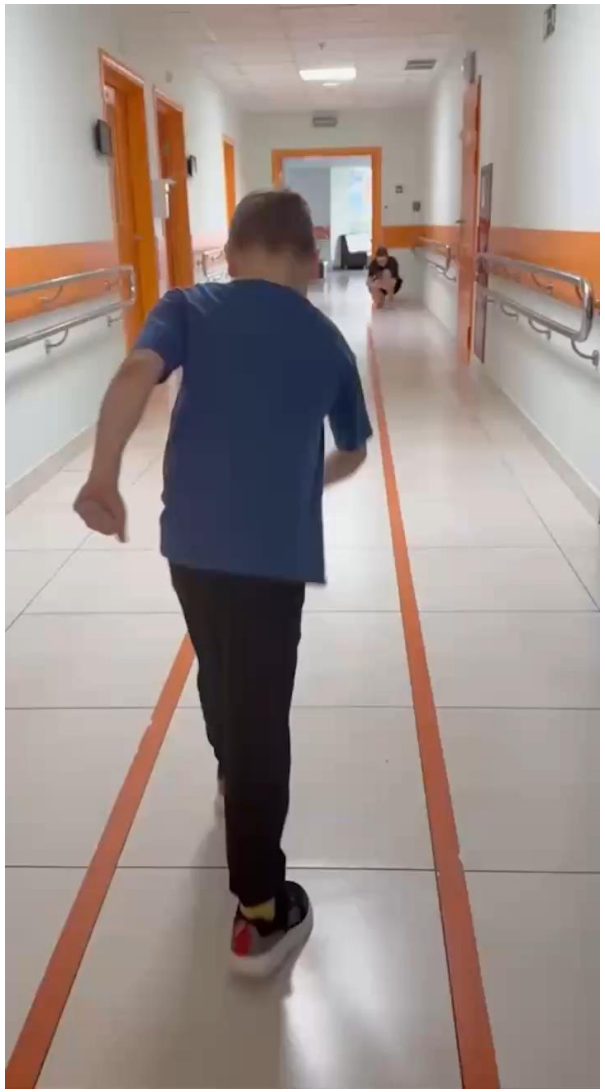
- Max CK level 12 129 U/l

- At the age of 6y 6 mo the diagnosis of Duchenne muscular dystrophy was confirmed
- (12-13 ex del in DMD gene)

Case from the speaker's clinical experience and presented with permission from the patient and/or their caregiver.

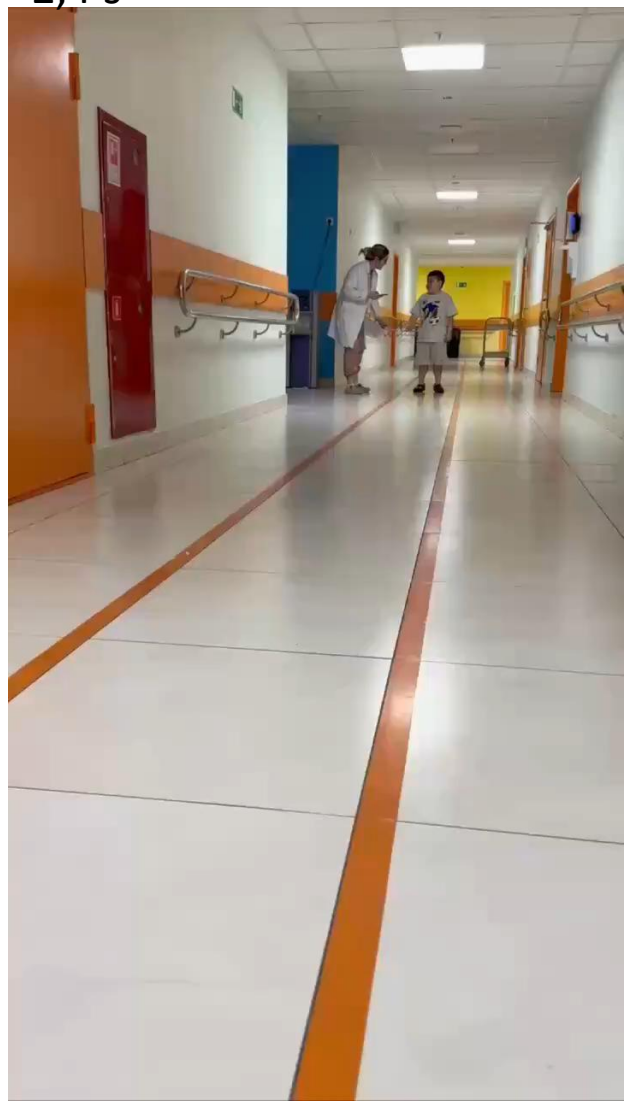
8 y 11 m0.

NSAA 28 points
TTR 3,7 s
10 MWR 5,2 s
6 MWT 500 m
4SC – 3,7 s



9 y 5 mo

NSAA 31 points
TTR 2,75 s
10 MWR 3,53 s
6 MWT 485 m
4SC – 2,4 s



Case from the speaker's clinical experience and presented with permission from the patient and/or their caregiver. * - Delandistrogene moxeparvovec is not approved in Russia

8 y 11 mo - 9 y 5 mo

Pre-delandistrogene moxeparvovec* administration period

✓Liver function, platelet counts and troponin-I - N.

✓Absence of acute infection and/or acute liver failure

✓ AAVrh74 antibody negative (The validity period of the result is 30 days.)

✓Apropriate doses of glucocorticosteroids (GCS): one day prior to infusion deflazacort 0.9 mg/ kg/day (basic dose) + prednisolone 1 mg/kg/day (added dose)

Post- delandistrogene moxeparvovec* administration period

- After 63d day we tapered the added peri-ELEVIDYS corticosteroids off during 4 weeks
- The basic dose of deflazacort 0.9 mg/ kg/day remained the same
- No advers evens registrated

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CLINICAL CASE 3

Case from the speaker's clinical experience and presented with permission from the patient and/or their caregiver.

The boy G., 5 y
del 61-79 ex DMD
Immune mediated myositis

- Pulse steroid therapy 30 mg/kg №5 >>>
  prednisolone 2 mg/kg, per os
  + IVIG 2 g/kg

prednisolone 1 mg/kg, per os

prednisolone 0.75 mg/kg from 25 W

		W0	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	W13	W14	W15	W16	W17	W18	W19	W20
Tr	W	333	223	309				362	413	369	344	335	300	376								
Neu		3,88	2,6	3,37				8,68	5,02	5,5	4,8	3,3	2,92	3,39								
Mon		0,56	0,66	0,96				1,49	1,48	1,33	1,28	1,01	0,88	1,32								
ALT (N < 40 U/l)		399	467	568	467	582	1110	828	499	443	263	212	243	470	311	331	270	342	312	327	297	357
ASTT (N < 42 U/l)		174	306	350	255,4	385,8	646,7	182	164	148	102	119	141	192	170,6	116	111	188	127	158	129	131
LDG (N < 295 U/l)		1050		1542	1280	1244	2237		973	974	662	492	616	1026	811	777	718	856	746	780	849	830
CK (N < 475 U/l)		4997		8327	3992	4903	6890	2585	1589	1792	793	547	1381	2542	2044	2051	2311	3410	2652	2917	2630	3054
GGT (N < 35 U/l)		9	9	10	9	24	29	29	33	32	29	25	24	18	18	16	15	14	14	13	11	13
Bilirubin (N < 20 mcmol/l)		5,1	2,5	3,3	1,7	1,8	4,3	2,9	2,6	2,1	4,4	4,2	4,5	5	4,3	2,3	2,2	4	2,2	4,8	2,5	2,3
creatinine (N 22 – 67 U/l)		14	14	14			7	12	13	12		15	14									
Urea(N <6,4 ммоль/л)		4					3,6	5,1	5,1	3,7	4,8	3,7	3,8									
Troponin I (N <0,16 ng/ml)		0,02	0,01	0,01	0,14	0,13		0,01	0,01	0,01	0,01	0,02	0,02	0,22	0,2	0,22		0,1	0,1	0,1	0,1	

Safety ID: RU241111 (associated cases RU24734, RU24735, RU24965 и RU241015, RU2557, RU2511)

Myositis clinical symptoms

12 mo after gene therapy

Case from the speaker's clinical experience and presented with permission from the patient and/or their caregiver. * - Delandistrogene moxeparvovec is not approved in Russia

Conclusion and Key Learnings

- Preliminary data from the treated cohort demonstrate encouraging functional changes
- Local experience has shown efficacy and safety outcomes comparable to those observed in clinical trials
- The requirement for an MDT assessment and a Federal Medical Board decision for initiating therapy underscores the high level of clinical governance involved in patient selection and risk mitigation
- Safety monitoring is critically important for the successful and safe administration of gene therapy in DMD patients.

Thank you very much for your attention

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