One-year motor function outcomes following treatment with delandistrogene moxeparvovec-rokl in young boys with Duchenne Muscular Dystrophy: A single center experience

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Background

In June 2023, delandistrogene moxeparvovec-rokl received accelerated FDA approval for the treatment of boys with DMD aged 4 to 5 years old. This was based on increased expression of micro-dystrophin as well as improvement in functional outcomes measures at 52 weeks, including the NorthStar Ambulatory Assessment (NSAA), Time to Rise (TTR), and 10-meter walk run (TMWR), when compared to external natural history controls (ENDEAVOR)[1] However, data from the post marketing confirmatory placebo-controlled trial EMBARK failed to meet its primary endpoint, although secondary endpoints trended toward improvement and led to FDA approval for ambulatory individuals[2]. To understand the impact of this therapy, real-world data is needed.

Methods

This is a retrospective chart review analyzing the records of 13 boys with genetically confirmed DMD who received delandistrogene moxeparvovec-rokl between October 2023 and November 2024 at Children's Health in Dallas, TX.

Results

The records of 13 boys treated with delandistrogene moxeparvovec-rokl were reviewed. Age ranged from 4 years, 0 months to 9 years, 10 months old. Many younger boys were steroid naïve at the time of infusion, others received varied steroid regimens (Table 1).

Pt	Date of infusion	Age at infusion	Steroid regimen at dosing	Steroid regimen Post infusion	Genetic variant
1	1/31/24	4 yr, 11 mo	Steroid naïve	Weekend prednisone	c.8038C>T (p.Arg2680*)
2	10/3/23	4 yr, 7 mo	Steroid naïve	Weekend deflazacort	Exon 44 deletion
3	12/29/23	5 yr, 0 mo	Steroid naïve	Weekend deflazacort	Exon 42 and 43 duplication
4	11/8/23	4 yr, 11 mo	Steroid naïve	Vamorolone	Exon 43 deletion
5	2/6/24	5 yr, 2 mo	Daily prednisone	Weekend prednisone	Exon 49-50 deletion
6	1/22/24	5 yr, 6 mo	Daily prednisone	Weekend prednisone	Exon 46-50 deletion
7	1/2/24	5 yr, 8 mo	Daily prednisone	Weekend prednisone	Exon 51 deletion
8	1/24/24	5 yr, 10 mo	Daily prednisone	Daily prednisone	c.10108C>T (p.Arg3370*)
9	3/5/24	4 yr, 0 mo	Steroid naïve	Daily prednisone	c.2950-2AA>T (intron 22)
10	9/16/24	4 yr, 5 mo	Steroid naïve	Weekend prednisone	c.3645dup p.Leu1216Thrfs*4
11	10/1/24	9 yr, 10 mo	Vamorolone	Vamorolone	Exon 8-41 duplication
12	10/15/24	9 yr, 6 mo	Daily prednisone	Weekend prednisone	c.286del (p.Ser96Valfs*5)
13	10/22/24	8 yr, 10 mo	Weekend deflazacort	Weekend prednisone	Exon 45 deletion

Table 1. Demographic information and steroid treatment regimens.

Functional outcome measures were analyzed, including NSAA (Fig 1), TTR (Fig 2), and 10MWR (Fig 3). Several younger boys did not have reliable scores prior to dosing, related to cooperation or behavior. For those with pre-dosing assessments, mean score difference at last follow up was an improvement of 3.29 points (-4, +14) on the NSAA, an increase of 1.78 sec (0, +7) on TTR, and a decline of 0.35 seconds (-8, 2.2) on the 10MWR.

Patients 6, 8 and 12 showed significant decline despite treatment, with patient 8 skewing the mean scores listed. The remainder displayed relative stability throughout the year following infusion.

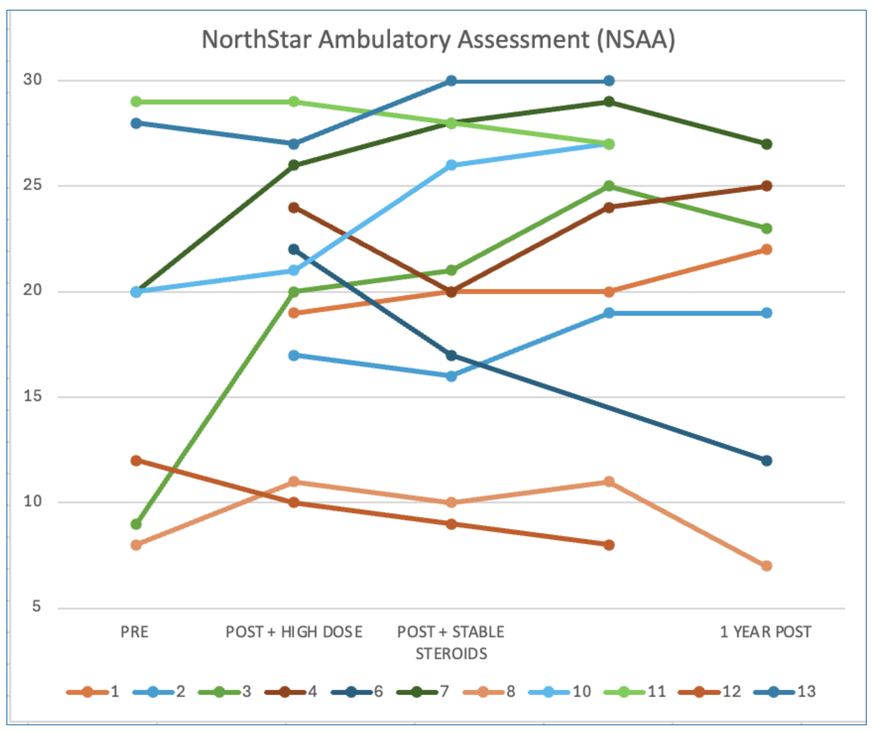

Figure 1. NorthStar Ambulatory Assessment scores.

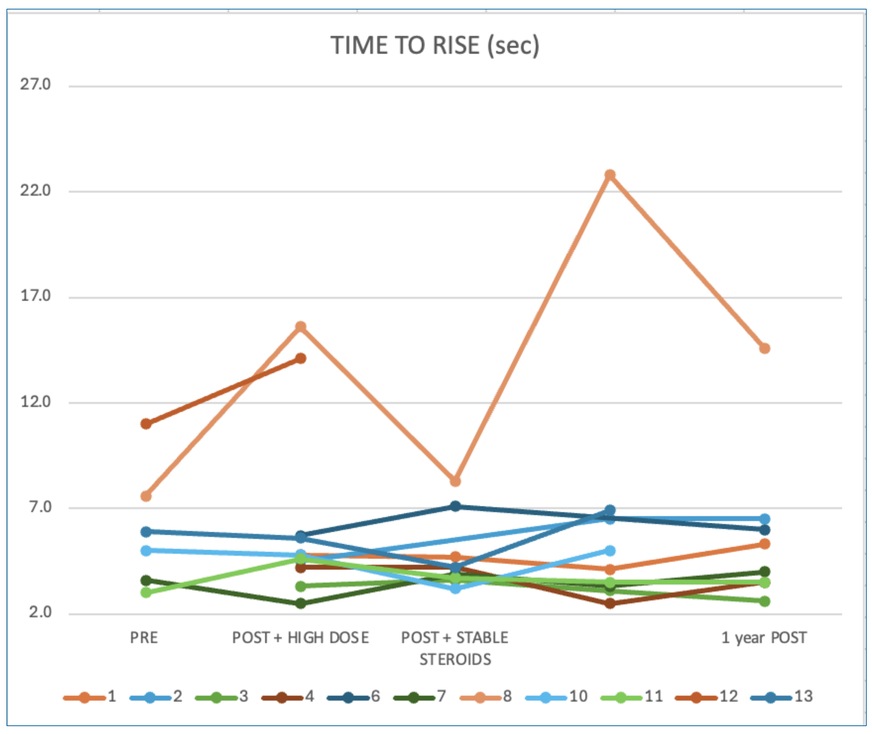

Figure 2. Time to Rise in seconds.

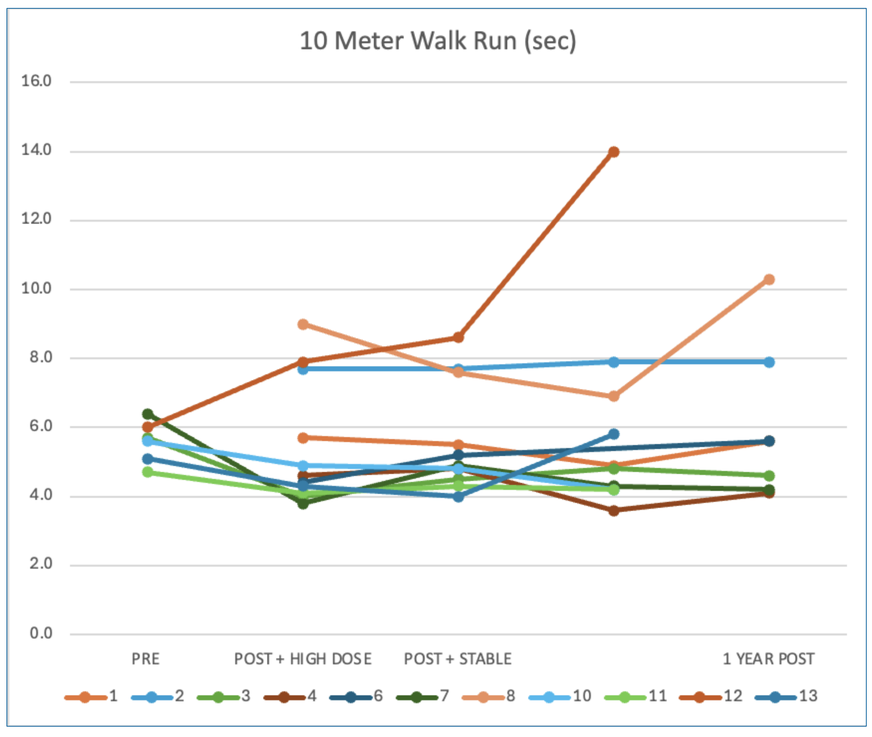

Figure 3. 10-meter walk run in seconds.

Discussion

To understand the impact of newly approved DMD therapies, long term outcomes in a real world setting are needed, especially in younger boys treated prior to onset of expected motor decline.

In our cohort of boys, many of those aged 4-5 experienced improvement in functional testing, similar to what was reported in EMBARK[2]. This may be related to combination of high dose steroid treatment as well as developmental maturation. However, two of our patients experienced decline despite treatment. Therefore, these two factors are insufficient to explain all gains universally. Of the three older boys, two showed improvement at last follow up while one declined, which is promising given the expected course of disease at 8-9 years old.

Assessment can be challenging in young boys and those with autism spectrum disorder or cognitive impairment, who have difficulty performing functional outcome measures. In these cases, parent reports and observational analysis are crucial. These individuals were unlikely to be involved in early trials, and so commercial availability has allowed us to expand the phenotype of those treated to improve equity.

Conclusion

Delandistrogene is a promising therapy for the treatment of DMD. However, additional information is needed to assess long term functional outcomes, durability, and impact on pulmonary function and cardiac health to guide re-evaluation of standard of care guidelines.

References

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2. Mendell JR, Muntoni F, McDonald CM, et al. AAV gene therapy for Duchenne muscular dystrophy: the EMBARK phase 3 randomized trial. *Nat Med*. 2025;31(1):332-341. doi:10.1038/s41591-024-03304-z

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