

Efficacy and Safety of Early Intervention With Delandistrogene Moxeparvovec in DMD^{MDX} Mice

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Background

- In DMD, the absence of dystrophin drives progressive muscle loss¹
- Delandistrogene moxeparvovec is an rAAVrh74 vector-based gene therapy designed to enable micro-dystrophin expression and has been associated with slowing of DMD disease progression^{1–4}
- Delandistrogene moxeparvovec is approved in the USA and select countries^{5,6}

Objective

- Evaluate the efficacy and safety of delandistrogene moxeparvovec treatment during different stages of development in DMD^{MDX} mice to better understand disease pathology from infancy to early adolescence

Methods

- Wild-type and DMD^{MDX} mice (n=8 per group) received intravenous saline or delandistrogene moxeparvovec (**Figure 1**)
- Dosing cohorts were PND2, 2 weeks, and 6 weeks, modeling pre-, peri-, and post-pathology onset, respectively
- Assessments included body weight, tibialis anterior muscle physiology, serum chemistry, biodistribution and micro-dystrophin expression, PDPF, central nucleation, fibrosis, and histopathology

Results

Figure 2 Earlier delandistrogene moxeparvovec intervention (PND2/2 weeks) reduced body weight (A) and skeletal muscle weight (B) in the DMD^{MDX} models

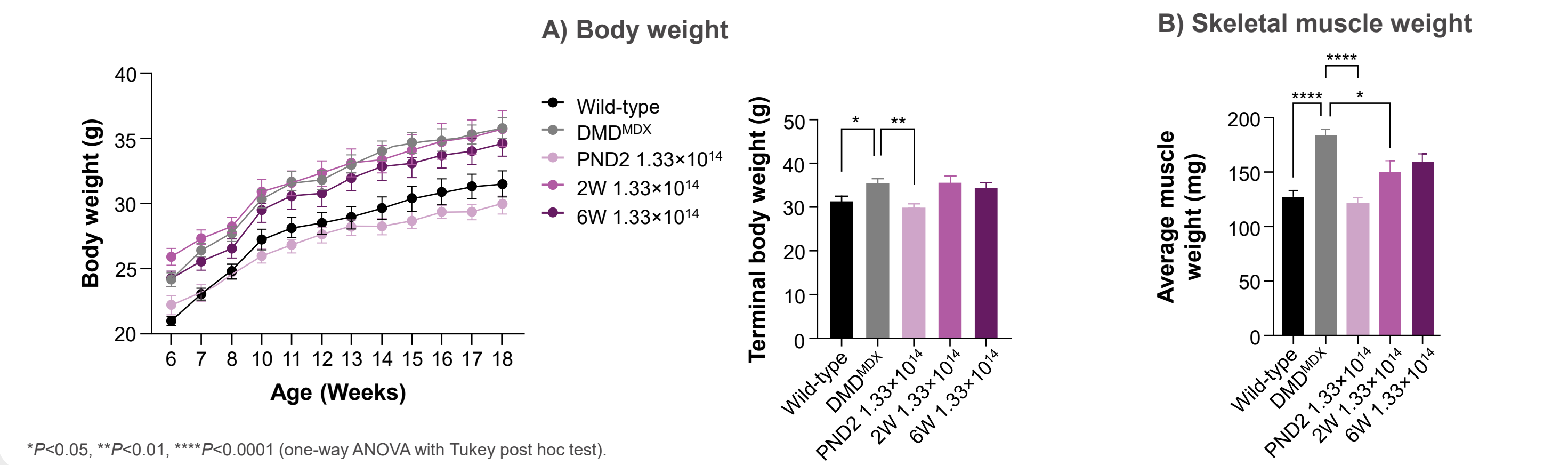


Figure 3 Earlier delandistrogene moxeparvovec intervention improved skeletal muscle force generation (A) and increased resistance to eccentric contraction-induced injury (B)

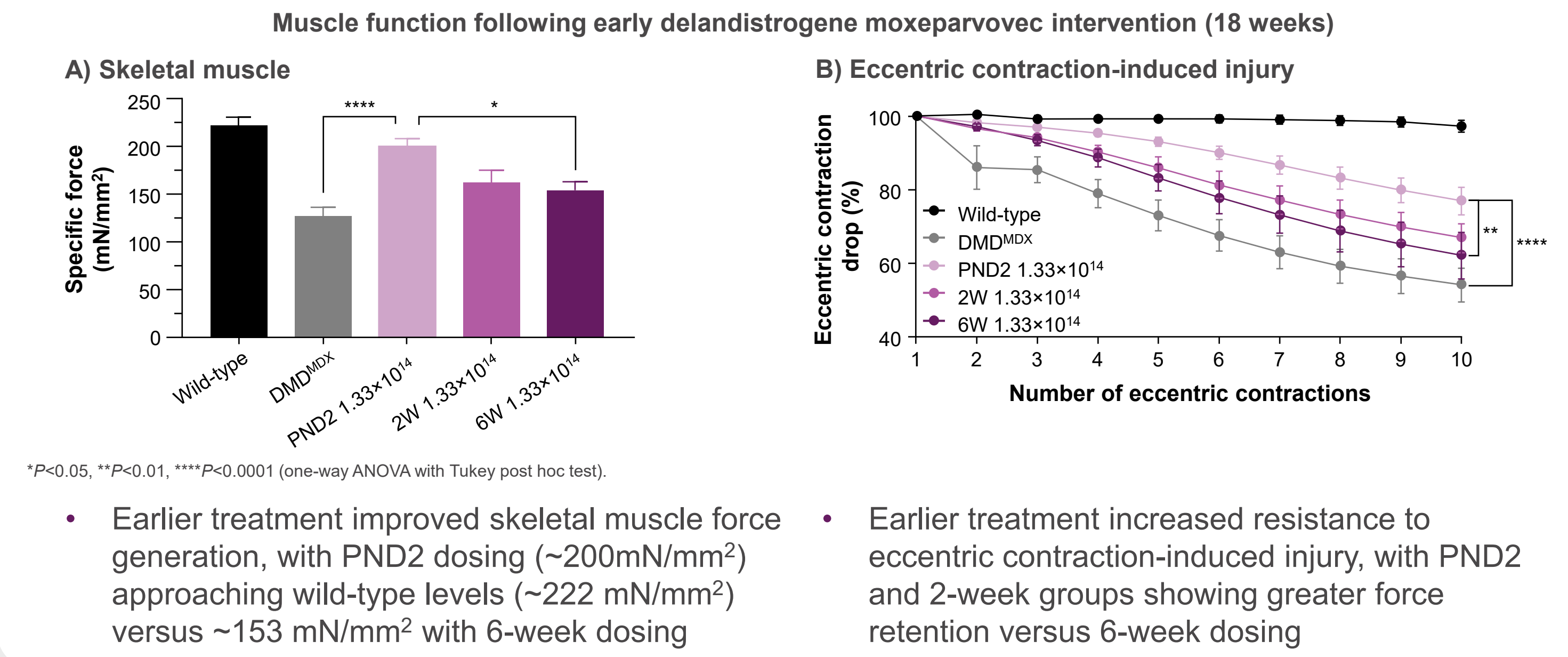


Figure 4 Earlier delandistrogene moxeparvovec intervention enabled efficient target tissue transduction (A–C) while reducing off-target liver exposure (D) by 14-fold (*P*<0.0001) versus 6-week dosing

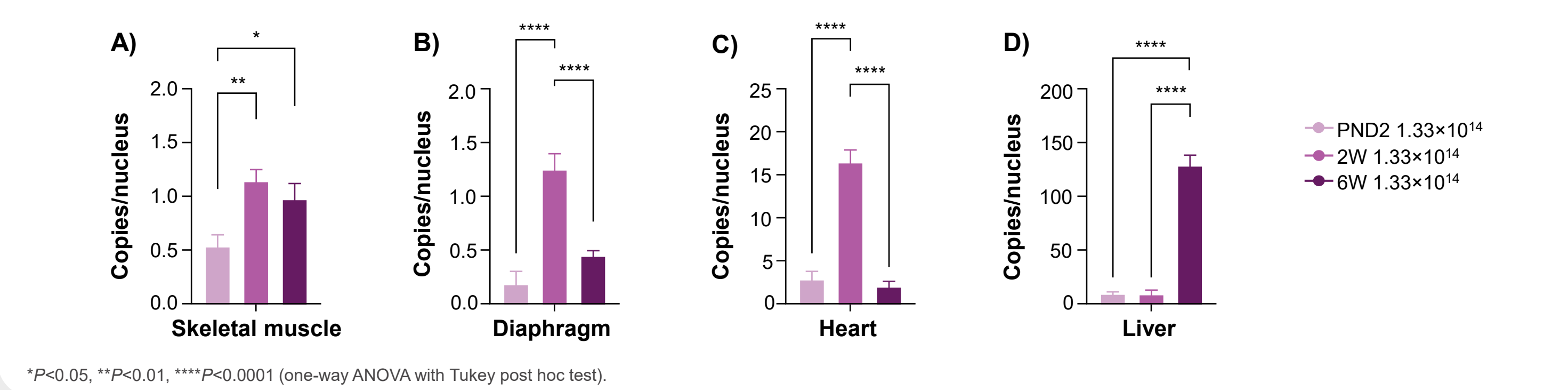


Figure 5 Earlier delandistrogene moxeparvovec intervention increased micro-dystrophin expression across skeletal muscle (A; ~2×), diaphragm (B; ~3×), and heart (C; ~1.5×) compared with 6-week dosing

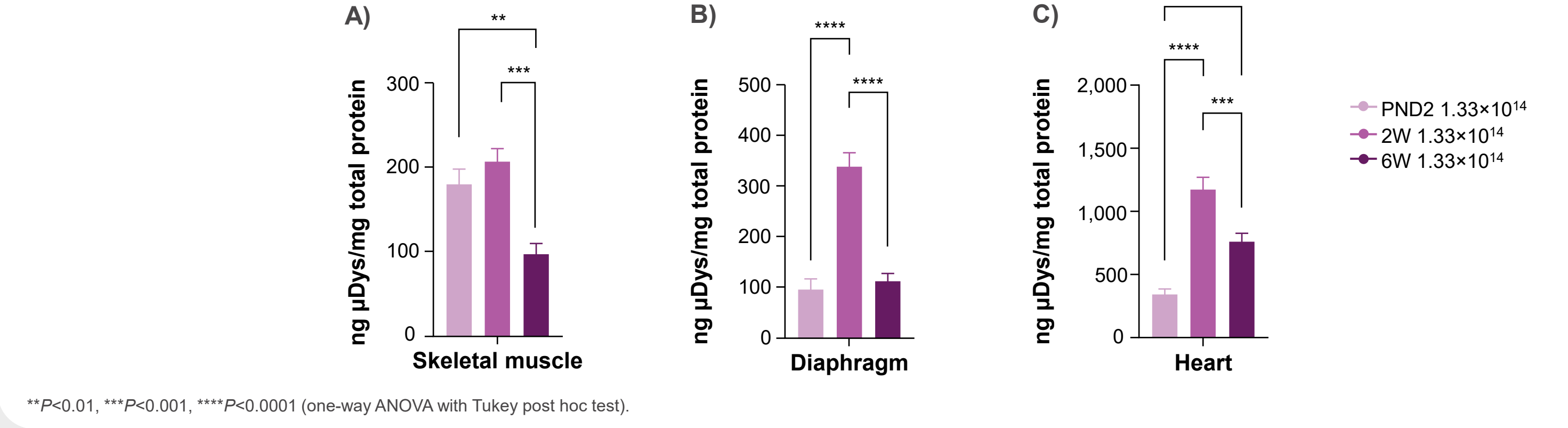


Figure 1 Study design and treatment schema



Strain	Age at dosing	Approximate human equivalent age	Test/control article	Terminal age (in-life)
Wild-type	6 weeks	6 years ⁷	Saline	18 weeks (12 weeks)
DMD ^{MDX}	6 weeks	6 years ⁷	Saline	18 weeks (12 weeks)
DMD ^{MDX}	PND2	Infant	Delandistrogene moxeparvovec	18 weeks (18 weeks)
DMD ^{MDX}	2 weeks	1–2 years ⁷	Delandistrogene moxeparvovec	18 weeks (16 weeks)
DMD ^{MDX}	6 weeks	6 years ^{7,8}	Delandistrogene moxeparvovec	18 weeks (12 weeks)

Figure 6 Earlier delandistrogene moxeparvovec intervention increased dystrophin-positive fibers expression (% PDPF; A) and dystrophin expression in the heart (B) versus 6-week dosing

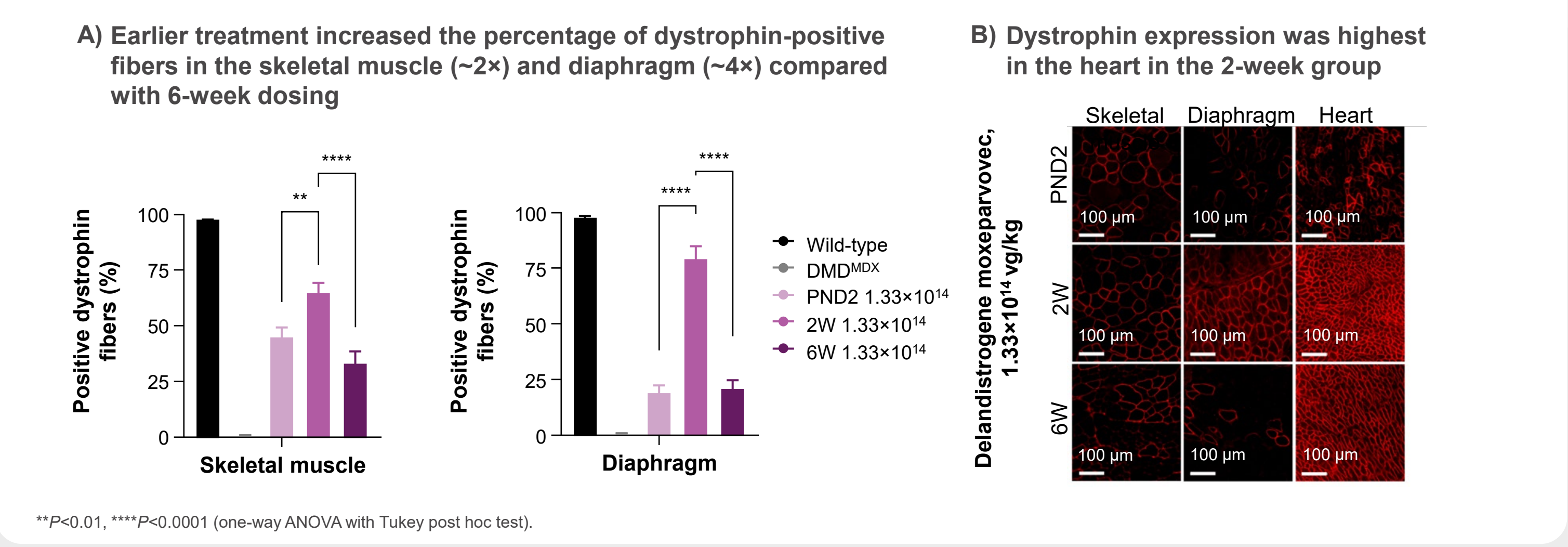


Figure 7 Earlier delandistrogene moxeparvovec treatment preserved skeletal muscle architecture (A), reduced muscle fibrosis (B), decreased central nucleation (C), and normalized fiber size (D)

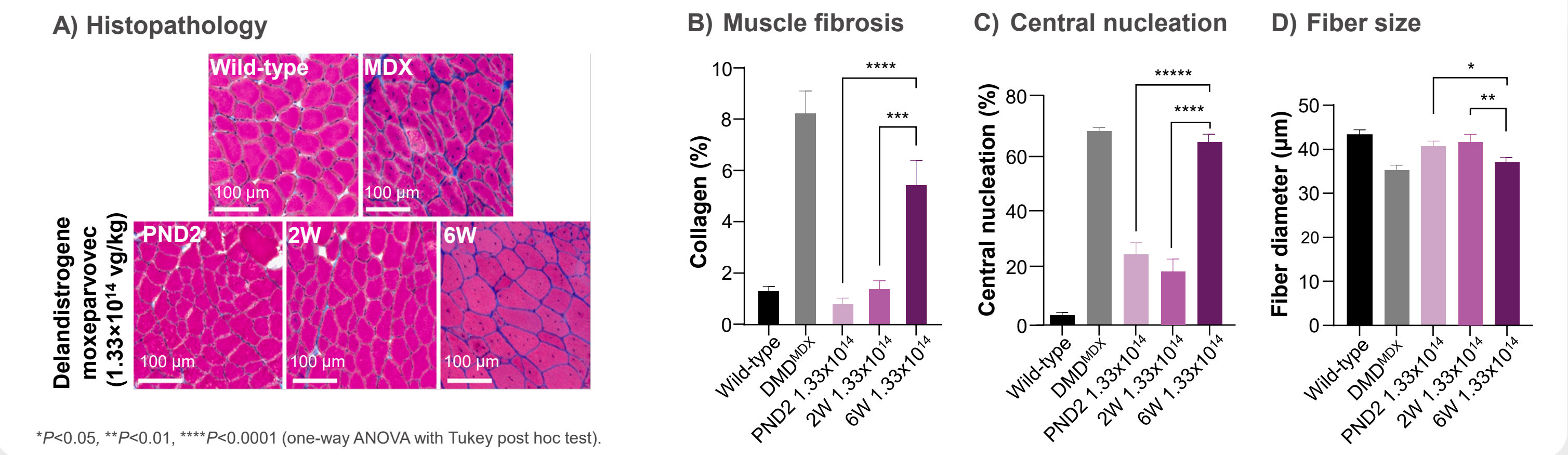
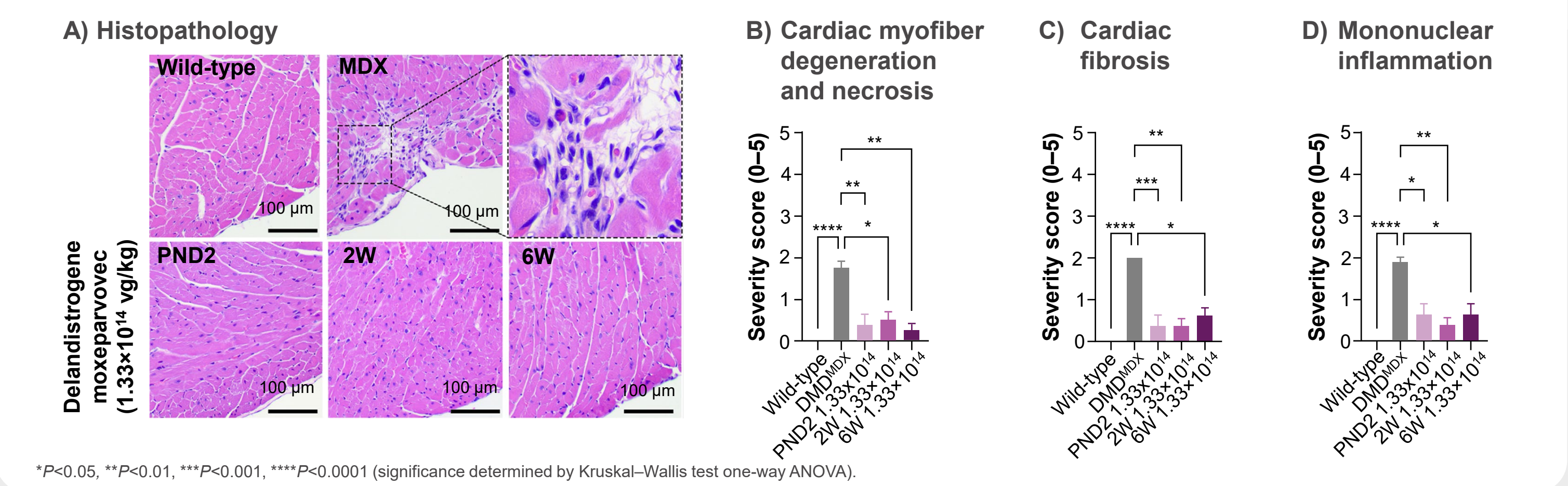


Figure 8 Delandistrogene moxeparvovec significantly reduced cardiac pathology observed in DMD^{MDX} mice (A), including cardiac muscle degeneration and necrosis (B), fibrosis (C), and inflammation (D)



Conclusions

- Early intervention with delandistrogene moxeparvovec was beneficial in DMD^{MDX} mice, with increased skeletal muscle function, increased vector transduction, increased micro-dystrophin expression, and improved pathology observed in the PND2 and 2-week cohorts (pre- and peri-pathology onset) compared with the 6-week cohort (post-pathology onset)
- Delandistrogene moxeparvovec was well tolerated with no mortalities
- These findings support earlier administration of delandistrogene moxeparvovec, prior to significant muscle degeneration and fibrosis

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Disclosures: Delandistrogene moxeparvovec is approved for the treatment of ambulatory patients with DMD in the USA, Japan, Israel, United Arab Emirates, Qatar, Kuwait, Bahrain, and Oman. NP, JS, BP, EN, and RP are employees of Sarepta Therapeutics, Inc. and may have stock options. Previously presented at the New Directions in Biology and Disease of Skeletal Muscle Conference, June 7–10, 2026; Ft. Lauderdale, FL, USA.

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Abbreviations

ANOVA, Analysis of Variance; DMD, Duchenne muscular dystrophy; Dys, dystrophin; DMD^{MDX}, dystrophin-deficient mouse model of Duchenne muscular dystrophy; PDPF, percent dystrophin-positive fibers; PND2, Postnatal Day 2; rAAVrh74, recombinant adeno-associated virus serotype rh74; TA, tibialis anterior; W, weeks.

References

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