Edgewise THERAPEUTICS

Becker Muscular Dystrophy Natural History and ARCH, an Open Label Study in Becker: Putting the Data into Context

Symposium at the 28th International Annual Congress of the World Muscle Society

Charleston, SC

October 3, 2023

Forward-Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties of Edgewise Therapeutics, Inc. ("Edgewise" or the "Company"). All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial condition, results of operations, business strategy and plans, and objectives of management for future operations, as well as statements regarding industry trends, are forward-looking statements. Such forward-looking statements include, among other things, statements regarding the potential of, and expectations regarding, Edgewise's drug discovery platform; Edgewise's product candidates and programs, including EDG-5506; the expected milestones and timing of such milestones for EDG-5506 including the expected timing of reporting of data for EDG-5506 and clinical trials; statements regarding the market opportunity for Edgewise's product candidates; statements regarding Edgewise's pipeline of product candidates and programs; and statements regarding Edgewise's financial position including its liquidity. In some cases, you can identify forward-looking statements by terminology such as "estimate," "intend," "may," "plan," "potentially" "will" or the negative of these terms or other similar expressions.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: negative impacts of the COVID-19 pandemic on Edgewise's operations, including clinical trials; risks associated with the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics and operating as an early clinical stage company; Edgewise's ability to develop, initiate or complete preclinical studies and clinical trials for, obtain approvals for and commercialize any of its product candidates; changes in Edgewise's plans to develop and commercialize EDG-5506 or any other product candidates; the potential for clinical trials of EDG-5506 or any other product candidates to differ from preclinical, interim, preliminary, topline or expected results; Edgewise's ability to enroll patients in its ongoing and future clinical trials; operating results and business generally; Edgewise's ability to raise funding it will need to continue to pursue its business and product development plans; regulatory developments in the United States and foreign countries; Edgewise's reliance on third parties, contract manufacturers and contract research organizations; Edgewise's ability to obtain and maintain intellectual property protection for its product candidates; risks associated with access to capital and credit markets; the loss of key scientific or management personnel; competition in the industry in which Edgewise operates; Edgewise's ability to develop a proprietary drug discovery platform to build a pipeline of product candidates; general economic and market conditions; and other risks. Information regarding the foregoing and additional risks may be found in the section entitled "Risk Factors" in documents that Edgewise files from time to time with the Securities and Exchange Commission. These risks are not exhaustive. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

This presentation concerns product candidates that are under clinical investigation, and which have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). It is currently limited by federal law to investigational use, and no representation is made as to its safety or effectiveness for the purposes for which it is being investigated.

EDG-5506 is an investigational agent and is not approved in any territory

Program Overview

- **Joanne M Donovan,** MD, PhD, Chair, Chief Medical Officer, Edgewise
  Introduction
- **Erik Niks**, MD, PhD, Pediatric and adult Neurologist, Leiden University Medical Center
  The Natural History of Becker Muscular Dystrophy
- **Sam Collins**, MD, PhD, Vice President, Clinical Development, Edgewise
  Twelve-month Data from ARCH, an Open Label Study in Becker Muscular Dystrophy
- **Barry Byrne**, MD, PhD, Director, Powell Gene Therapy Center, University of Florida
  Putting the Data into Context

Panel discussion to follow

Key Takeaways

- Becker muscular dystrophy is a serious dystrophinopathy. Once function begins to decline, individuals continue to irreversibly lose muscle and their disease progresses.

- Stabilizing function or even reducing the slope of decline is an important goal in Becker muscular dystrophy.

Edgewise THERAPEUTICS

The Natural History of Becker Muscular Dystrophy

Erik Niks, MD, PhD

Pediatric and Adult Neurologist

Leiden University Medical Center

Leiden University Medical Center

duchenne centre netherlands

Becker Muscular Dystrophy

Natural History

Erik Niks – pediatric & adult neurologist

Disclosures

Participant in advisory boards for Edgewise, Italfarmaco, Sarepta, Epirium, Regenxbio and Janssen

Principal investigator at LUMC for clinical trials from Edgewise, Italfarmaco, Sarepta, Fibrogen, NS Pharma, Reveragen, Santhera, BioMarin, ML Bio, Janssen, ArgenX and Alexion

Grants from Pfizer, EU, DPP, PBS, AFM, NWO, SvS

No personal financial interests. Reimbursement received by LUMC.

Becker Muscular Dystrophy

14 male patients

Onset 12-25 years

Slowly progressive

Hypertrophic calves

Waisting of quadriceps

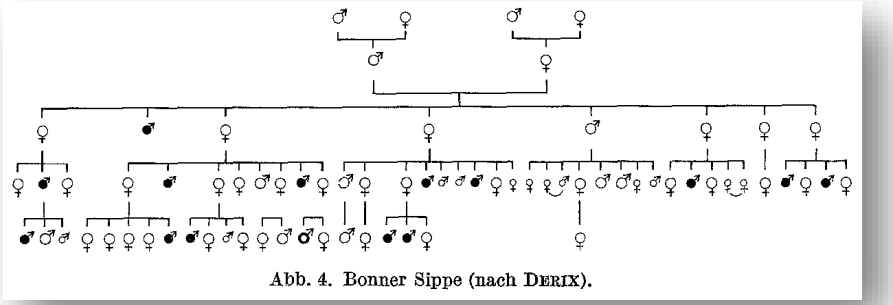


Abb. 4. Bonner Sippe (nach DERIX).

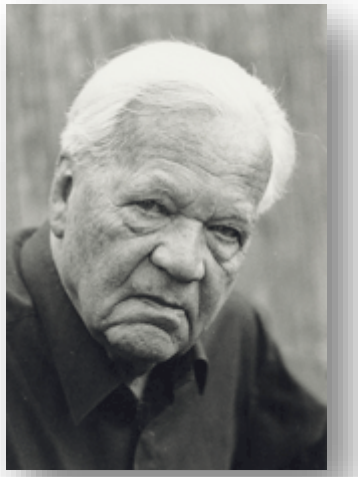
Eine neue x-chromosomale Muskeldystrophie.

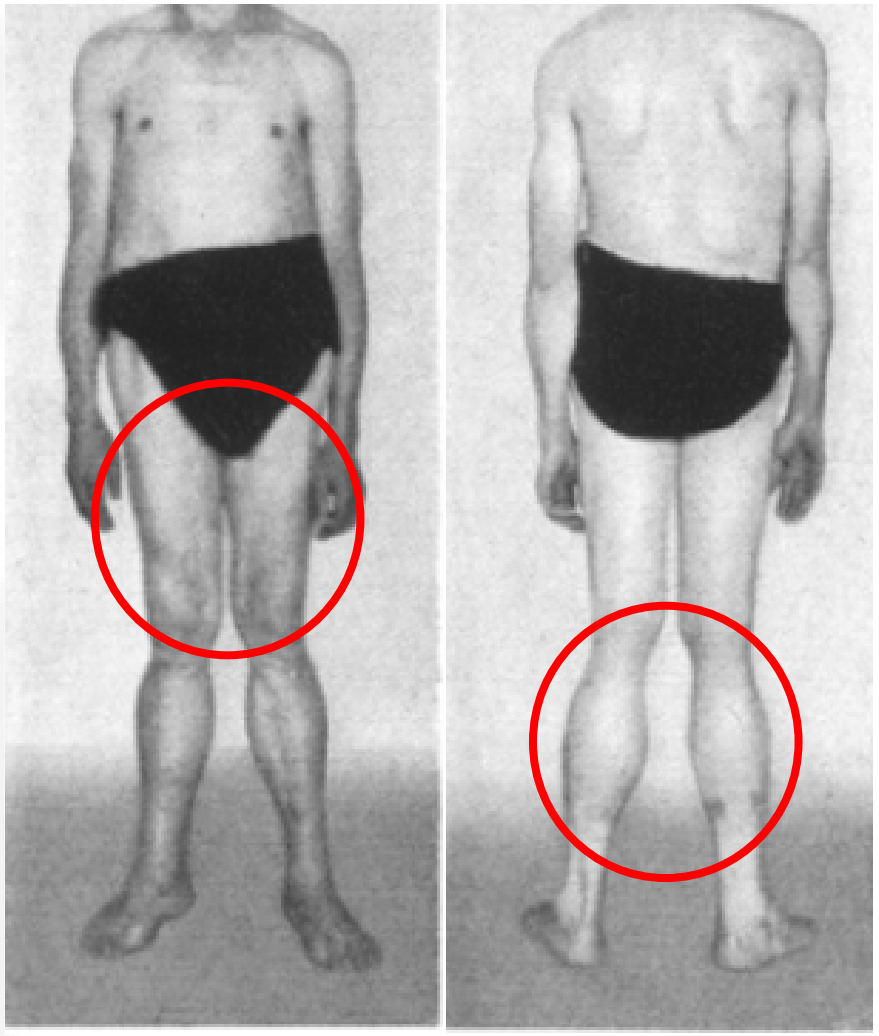
Von

P. E. BECKER und F. KIENER.

Mit 8 Textabbildungen.

(Eingegangen am 22. März 1955.)





Becker et al. Archiv für Psychiatrie und Zeitschrift Neurologie 1955

Becker Muscular Dystrophy

14 male patients

Onset 12-25 years

Slowly progressive

Hypertrophic calves

Waisting of quadriceps

Clinical variation

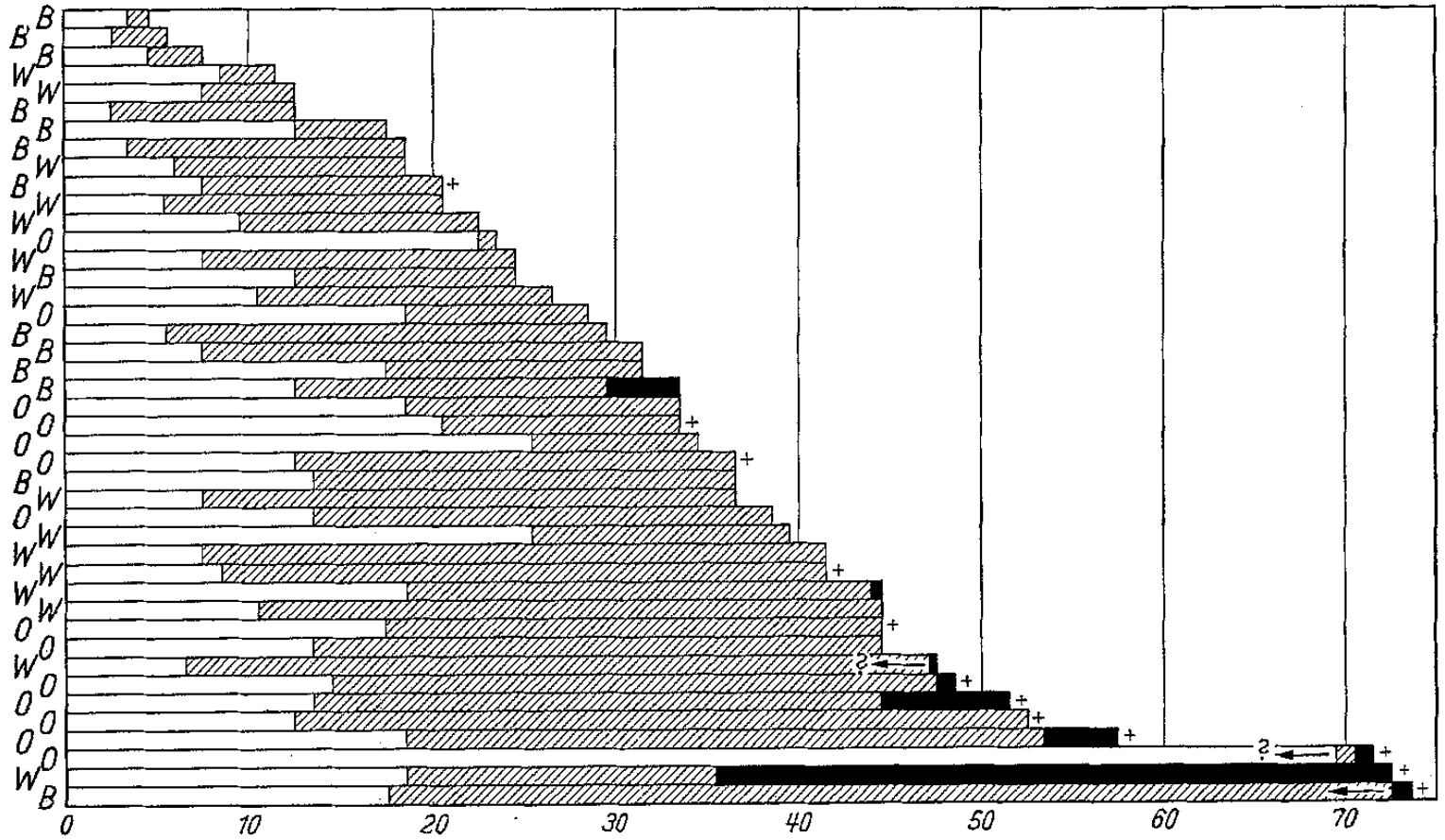
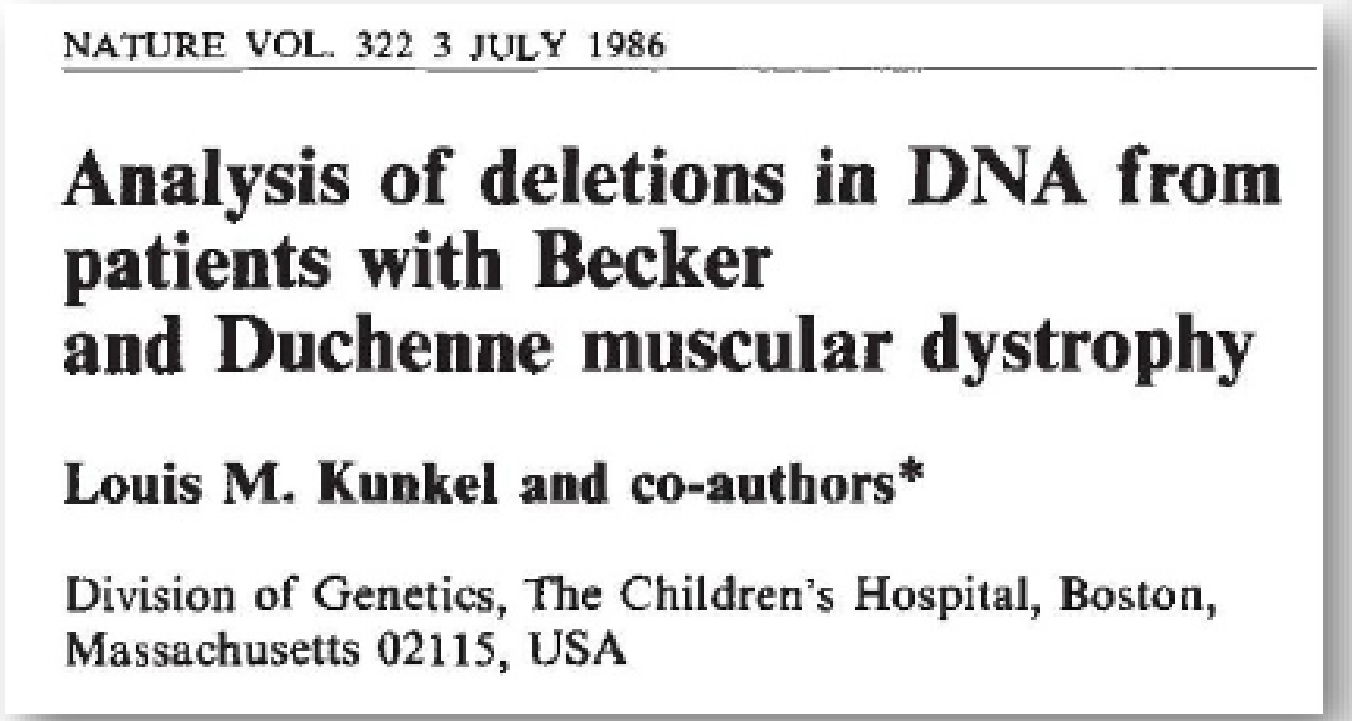


Abb. 6. Neue x-chromosomale Muskeldystrophie. Altersaufbau der Kranken. ▨ krank, ■ gehunfähig krank, ← ungenaue Angaben über die Zeit der Erkrankung. (Die Grenze, an der der Pfeil ansetzt, bezeichnet das Alter, in dem die Muskeldystrophie mit Sicherheit vorhanden war.) + verstorben.

Becker et al. Archiv für Psychiatrie und Zeitschrift Neurologie 1955

Becker and Duchenne share the gene and protein

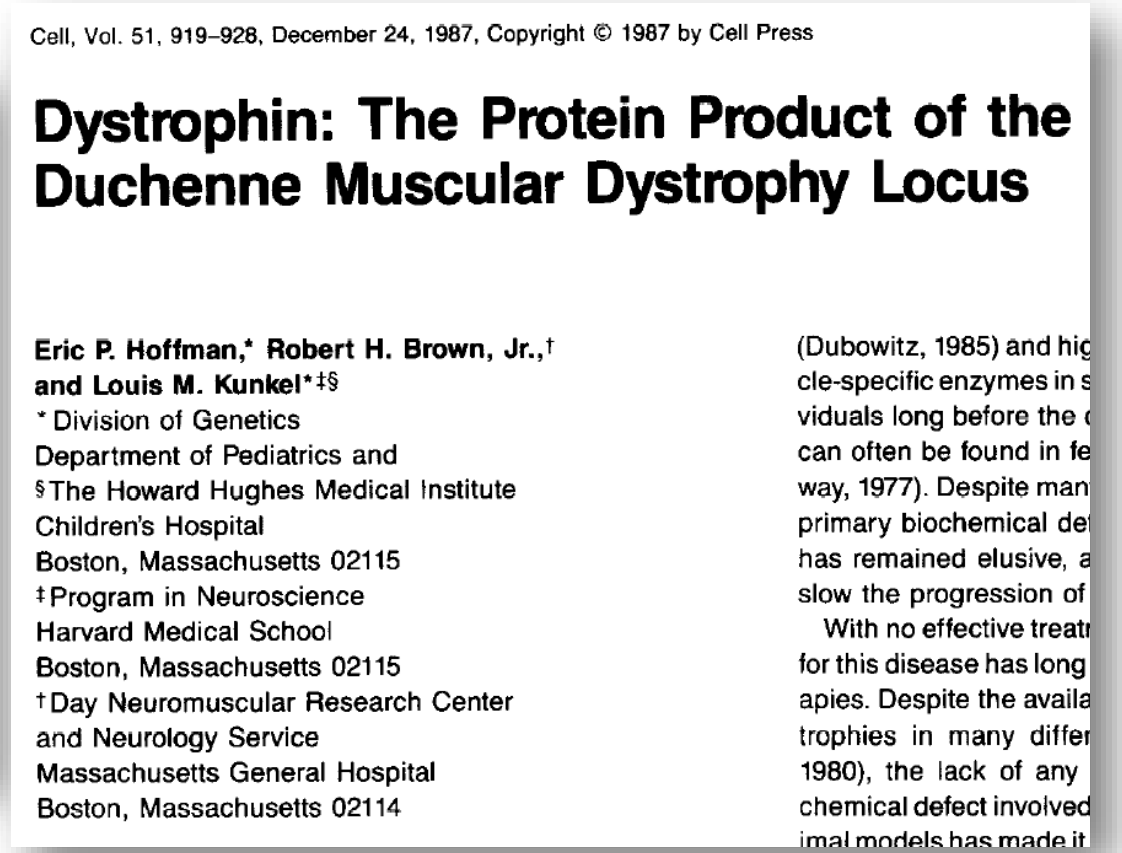


NATURE VOL. 322 3 JULY 1986

Analysis of deletions in DNA from patients with Becker and Duchenne muscular dystrophy

Louis M. Kunkel and co-authors*

Division of Genetics, The Children's Hospital, Boston, Massachusetts 02115, USA



Cell, Vol. 51, 919–928, December 24, 1987, Copyright © 1987 by Cell Press

Dystrophin: The Protein Product of the Duchenne Muscular Dystrophy Locus

Eric P. Hoffman,* Robert H. Brown, Jr.,† and Louis M. Kunkel*‡§
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Massachusetts General Hospital
Boston, Massachusetts 02114

(Dubowitz, 1985) and hig
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can often be found in fe
way, 1977). Despite man
primary biochemical de
has remained elusive, a
slow the progression of

With no effective treatr
for this disease has long
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trophies in many differ
1980), the lack of any
chemical defect involved
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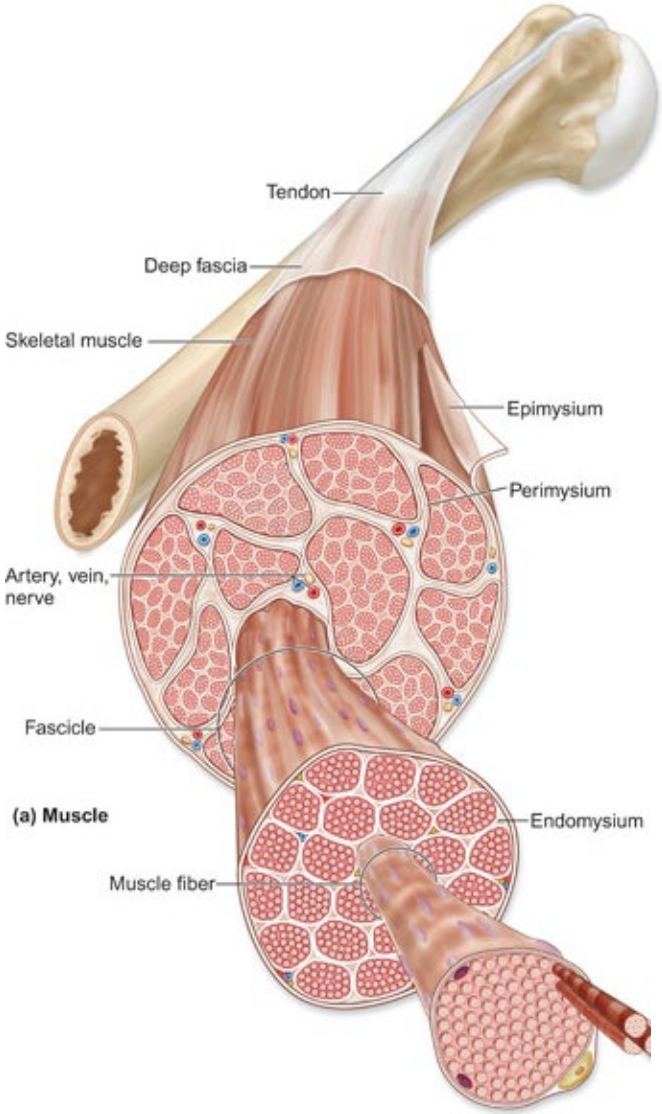
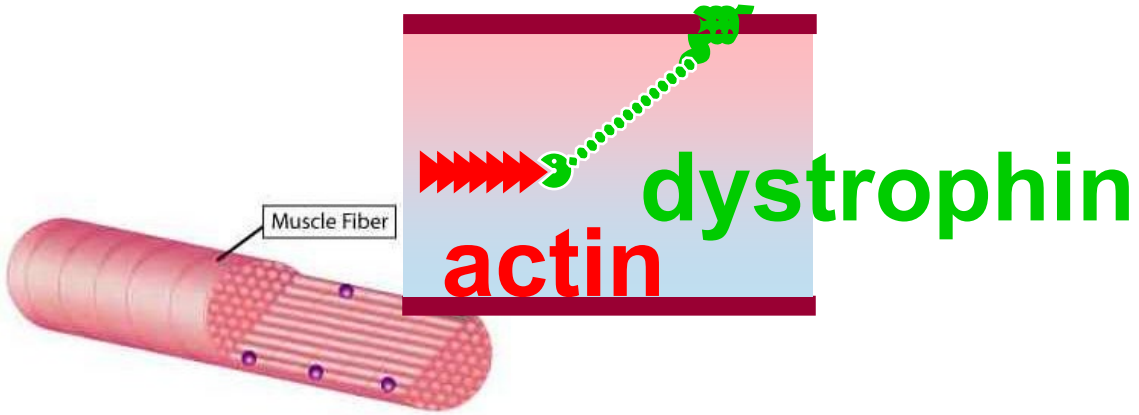
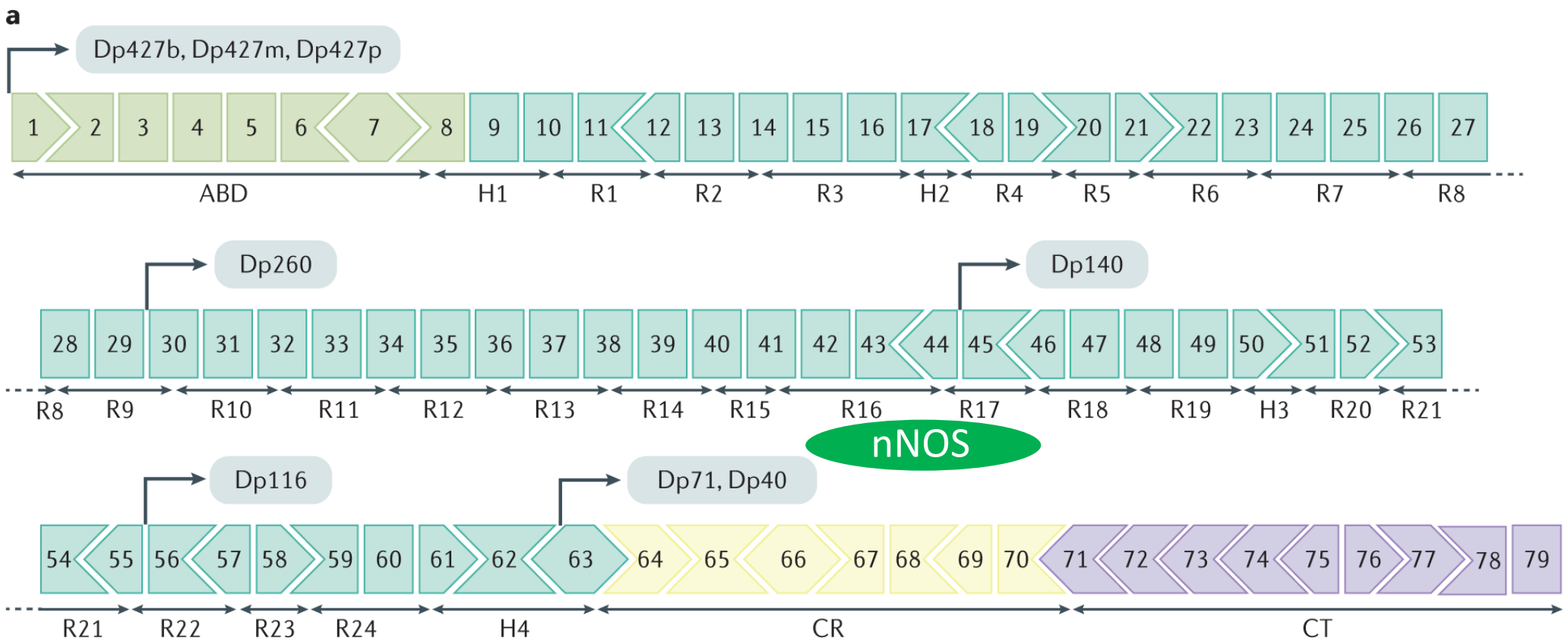
Dystrophin links sarcolemma and cytoskeleton



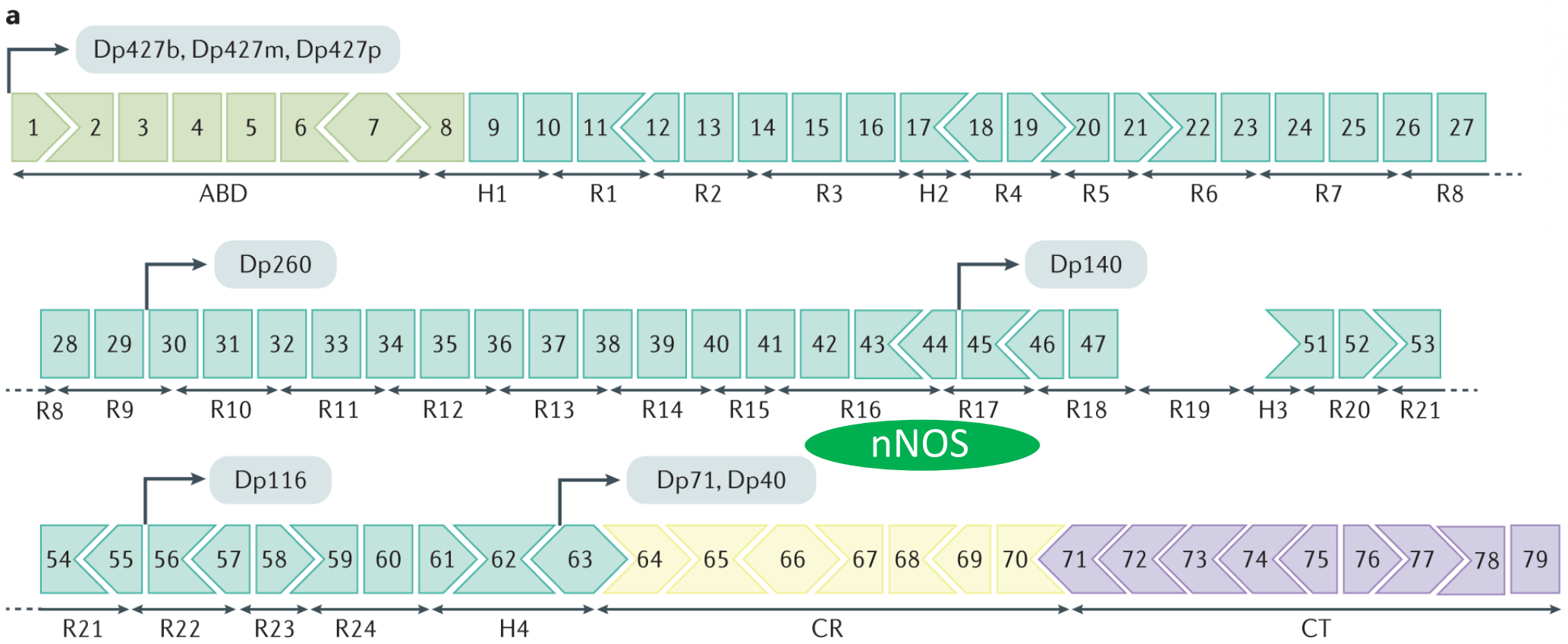


79 exons of the DMD gene



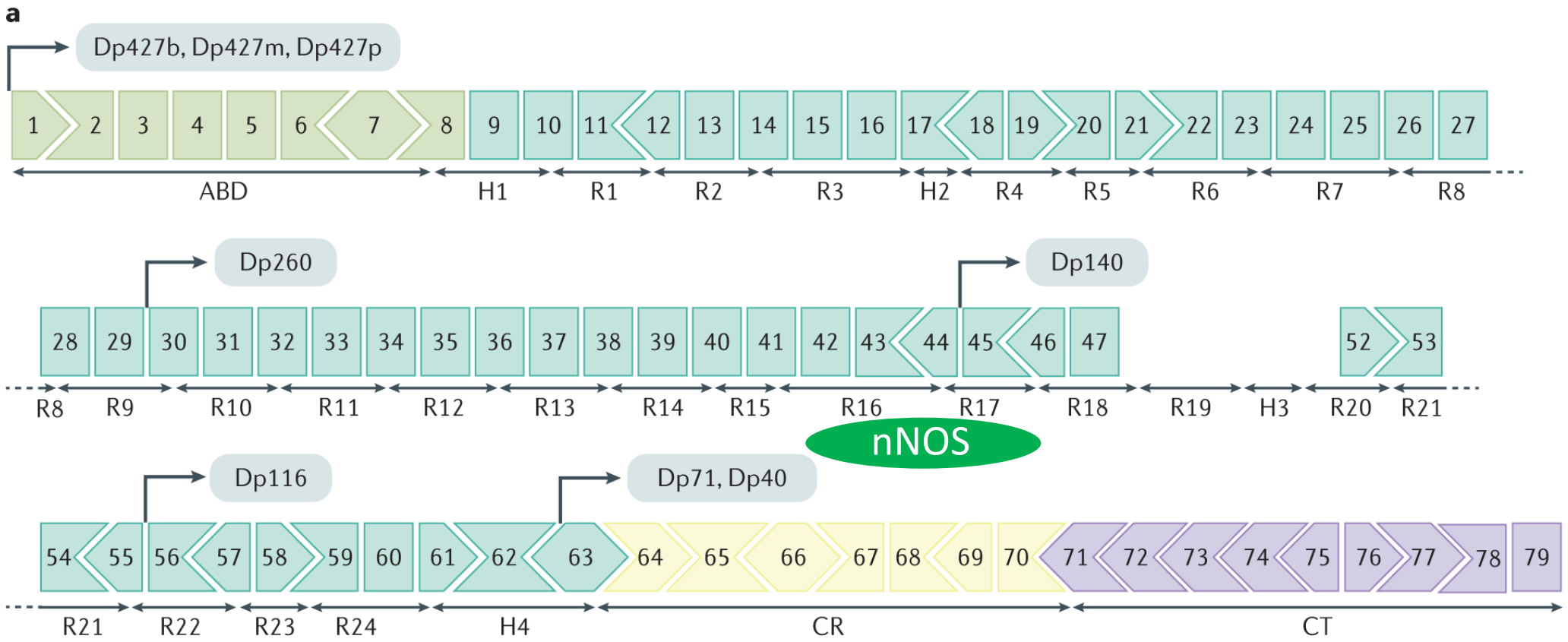
Adapted from Duan et al. Nat Rev Dis Primers 2021

Duchenne - out of frame deletions



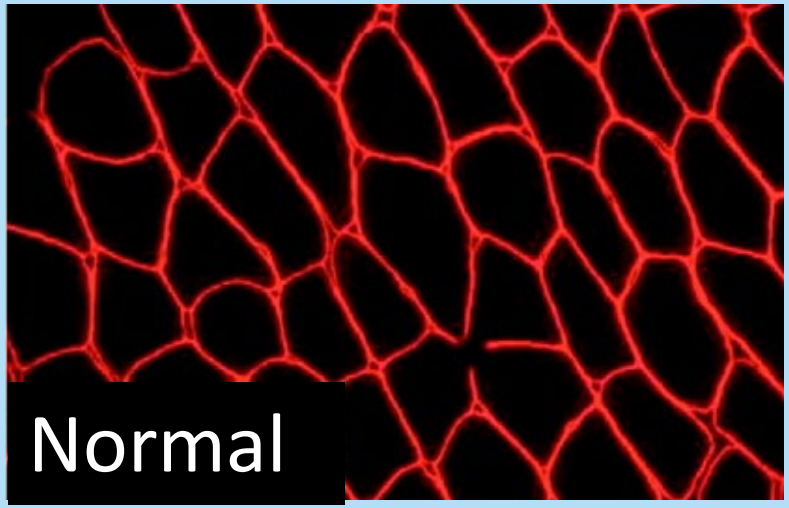
Adapted from Duan et al. Nat Rev Dis Primers 2021

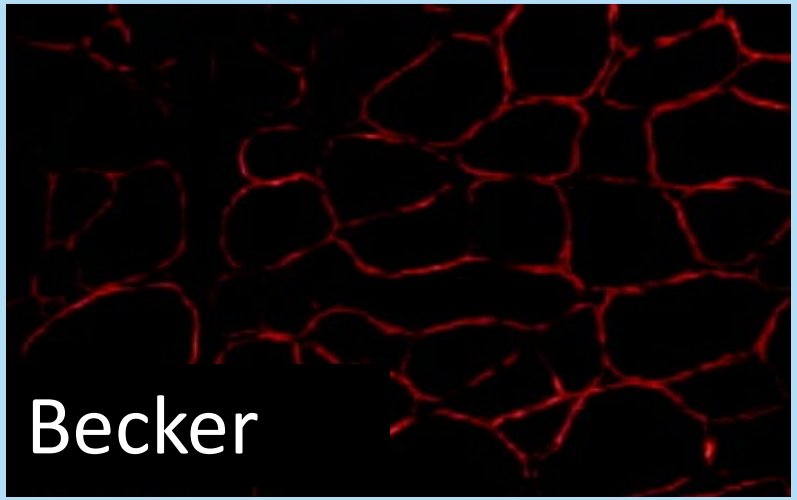
Becker – in frame deletions

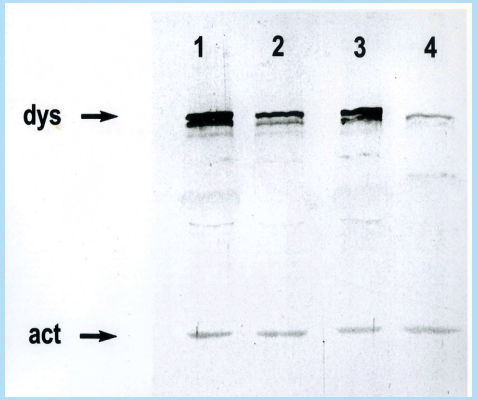


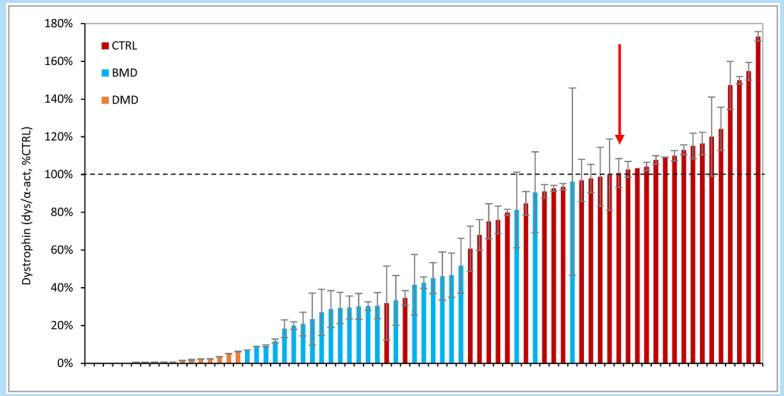
Adapted from Duan et al. Nat Rev Dis Primers 2021

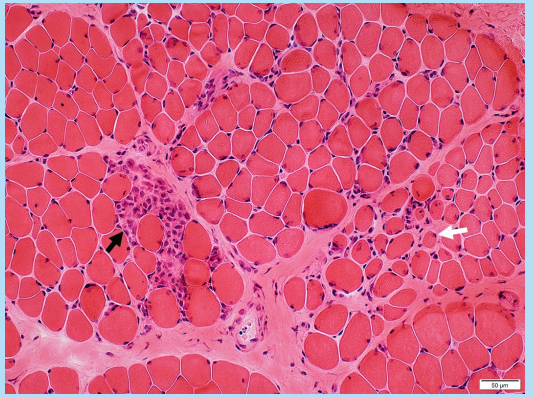
Muscle biopsy

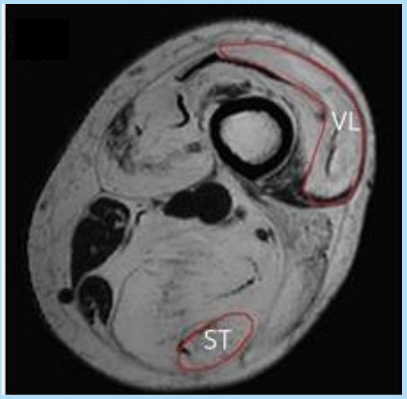












Beekman et al. PLoS One. 2018

Clinical symptoms

Proximal and paraspinal weakness

Acquire jumping and hopping

Ambulant beyond 16 yrs (no steroids)

Muscle pain and cramps

Muscle hypertrophy -> atrophy

Cardiomyopathy

North Star Ambulatory Assessment

17 items

Score of 0-2 per item

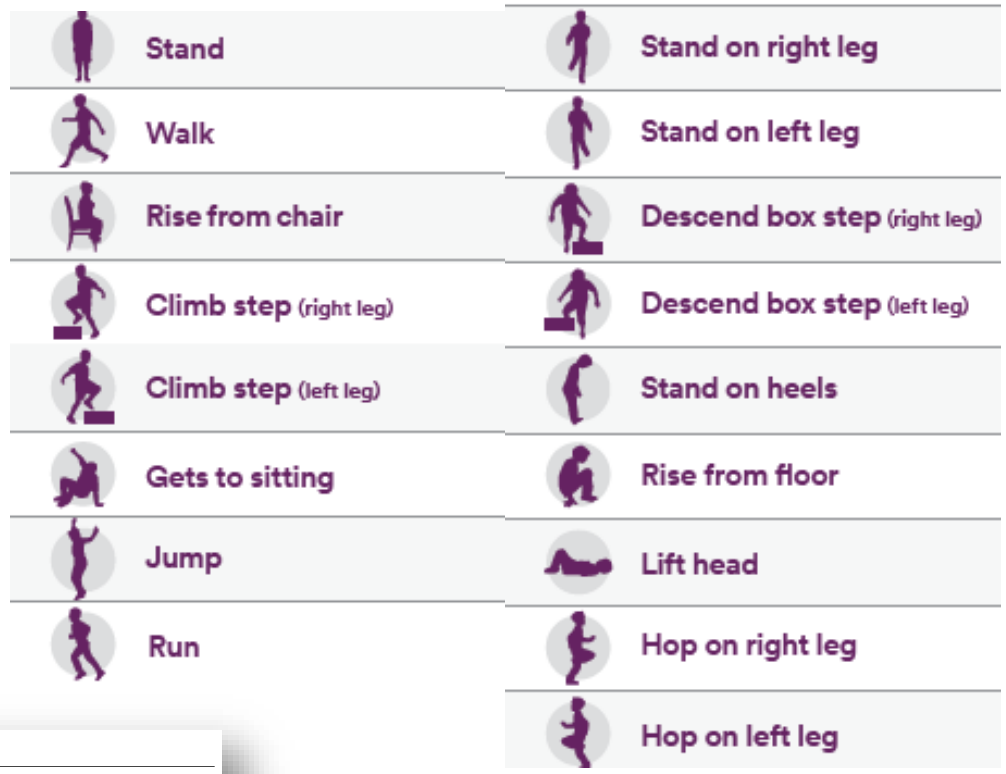
Unable - With assistance - Independent

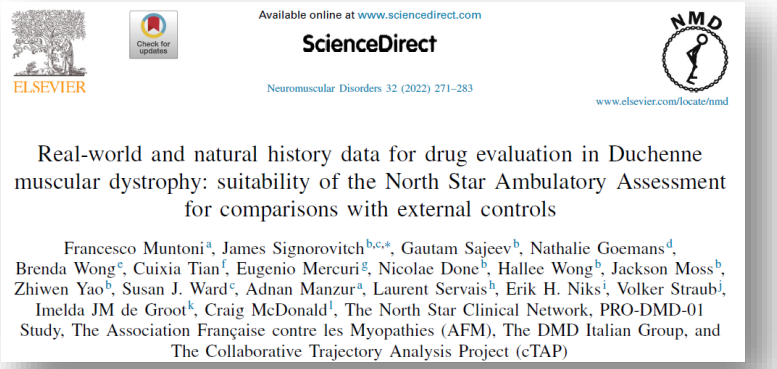
Maximum of 34 points

10-meter walk/run test

Primary endpoint in DMD and BMD trials

MCID and use for external controls in DMD





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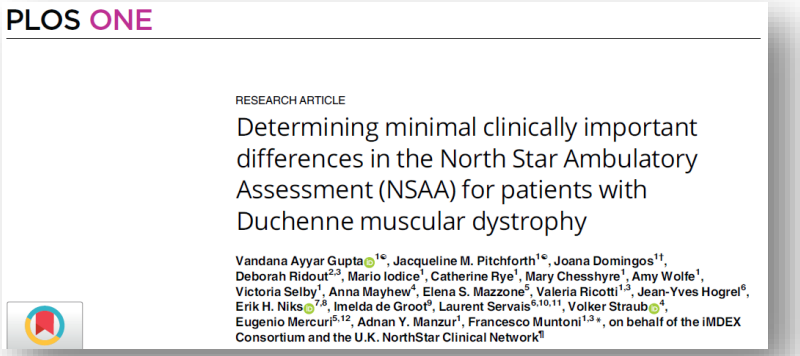
Neuromuscular Disorders 32 (2022) 271–283

www.elsevier.com/locate/nmd

Real-world and natural history data for drug evaluation in Duchenne muscular dystrophy: suitability of the North Star Ambulatory Assessment for comparisons with external controls

Francesco Muntoni[a], James Signorovitch[b,c,*], Gautam Sajeev[b], Nathalie Goemans[d], Brenda Wong[e], Cuixia Tian[f], Eugenio Mercuri[g], Nicolae Done[b], Hallee Wong[b], Jackson Moss[b], Zhiwen Yao[b], Susan J. Ward[c], Adnan Manzur[a], Laurent Servais[h], Erik H. Niks[i], Volker Straub[j], Imelda JM de Groot[k], Craig McDonald[l], The North Star Clinical Network, PRO-DMD-01 Study, The Association Française contre les Myopathies (AFM), The DMD Italian Group, and The Collaborative Trajectory Analysis Project (cTAP)



PLOS ONE

RESEARCH ARTICLE

Determining minimal clinically important differences in the North Star Ambulatory Assessment (NSAA) for patients with Duchenne muscular dystrophy

Vandana Ayyar Gupta[1☯], Jacqueline M. Pitchforth[1☯], Joana Domingos[1†], Deborah Ridout[2,3], Mario Iodice[1], Catherine Rye[1], Mary Chesshyre[1], Amy Wolfe[1], Victoria Selby[1], Anna Mayhew[4], Elena S. Mazzone[5], Valeria Ricotti[1,3], Jean-Yves Hogrel[6], Erik H. Niks[7,8], Imelda de Groot[9], Laurent Servais[6,10,11], Volker Straub[4], Eugenio Mercuri[5,12], Adnan Y. Manzur[1], Francesco Muntoni[1,3]*, on behalf of the iMDEX Consortium and the U.K. NorthStar Clinical Network[‡]

BMD Natural History study - Italy

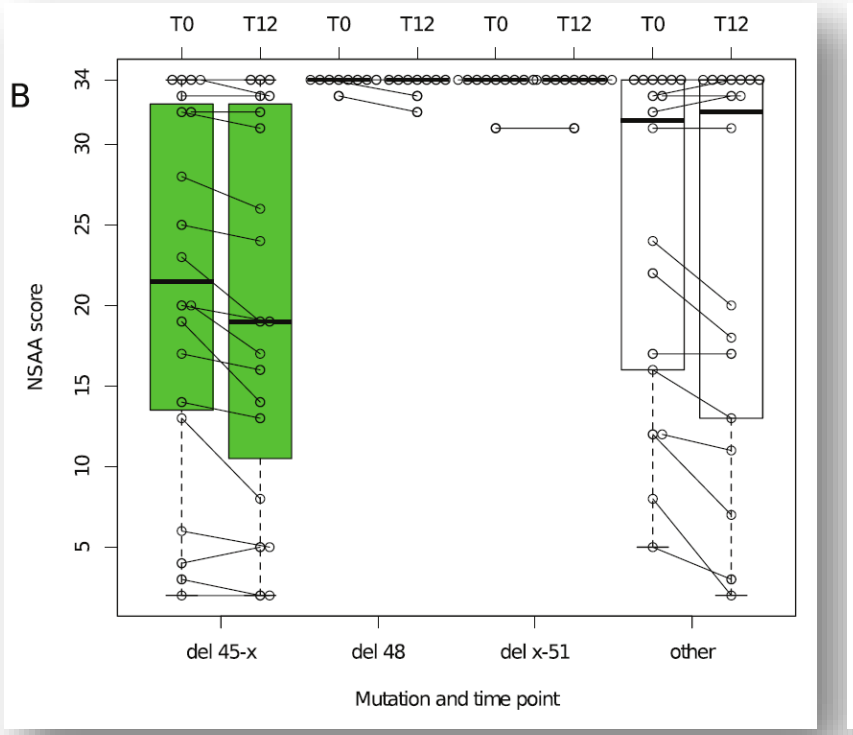
N = 69

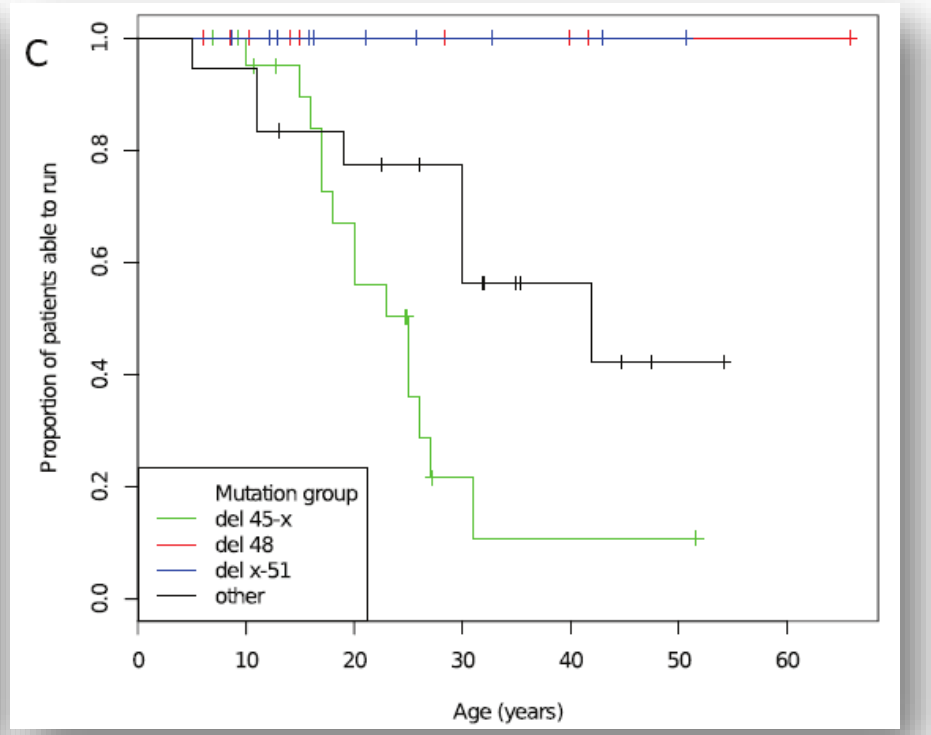
Age 6-69

Follow-up 12 months

Mutations

- Del 45-x (28)
- Del 48 (10)
- Del x-51 (10)
- Other (21)





NSAA at baseline 25.3 ± 10.8

Mean change at 12m -0.9 ± 1.6 (p<0.001)

Bello et al. Sci Rep 2016

BMD Natural History study - Netherlands

N = 36

Age 18-67

Annual FU - 3 years

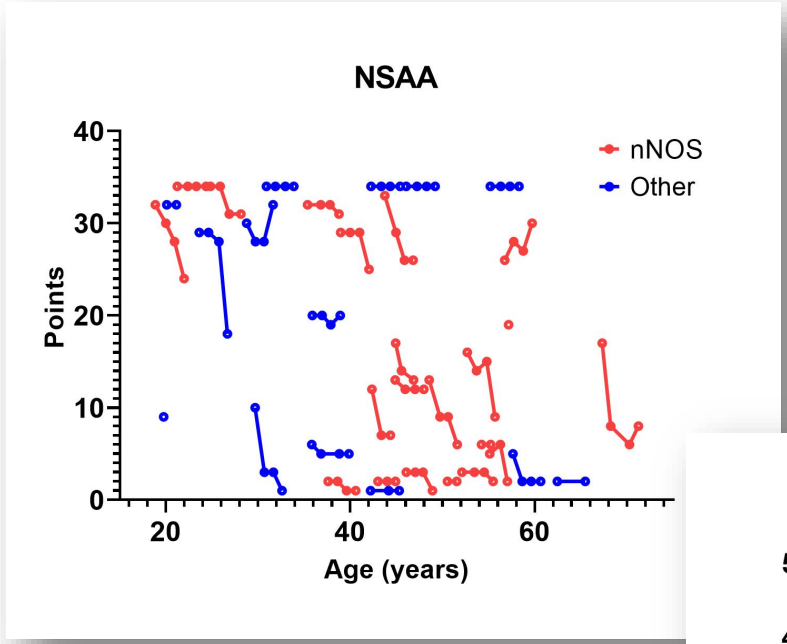
Yearly functional assessments

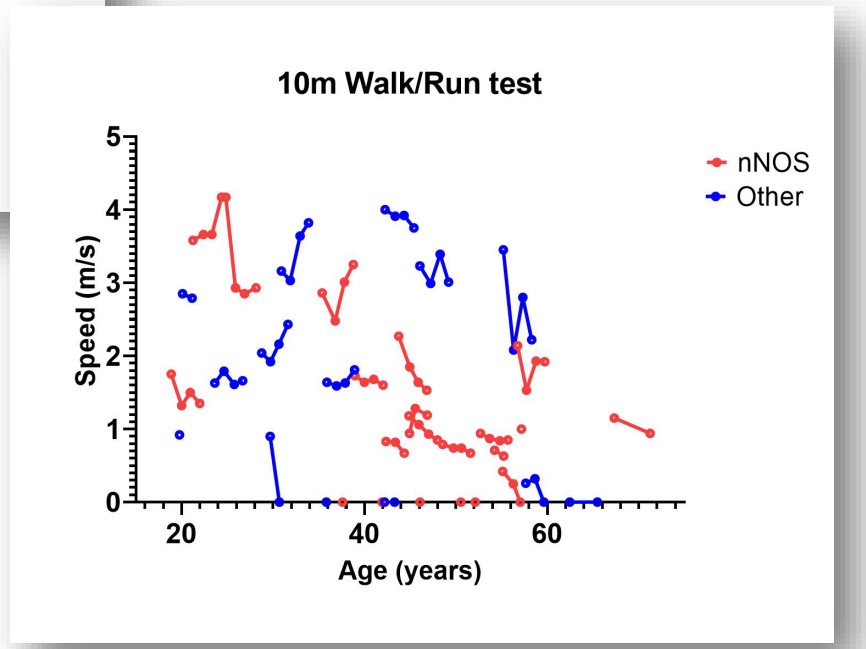
MRI optional (1st and 3rd visit)

Mutations

- Del 45-47 (11)
- Involving nNOS (21)

NSAA main decline in 10-32





Schrama and Koeks et al. In preparation

Responsiveness of functional tests at 1 and 3-year FU

Standardized Response Mean (SRM)

Sample size (SS) calculation based on 50% treatment effect in 1:1 randomisation

	N at baseline	Mean (SD) at baseline	Mean change at 1- year follow-up (SD)	SRM 1 year follow-up	SS 1 year follow-up	Mean change at 3-year follow-up (SD)	SRM 3 year follow-up	SS 3 year follow-up
NSAA	32	18.9 (12.7)	-1.36 (2.45)	-0.55	209	-2.65 (3.87)	-0.69	136
10MWRv (m/s)	25	1.97 (1.15)	-0.28 (0.41)	-0.68	137	-0.21 (0.52)	-0.39	412

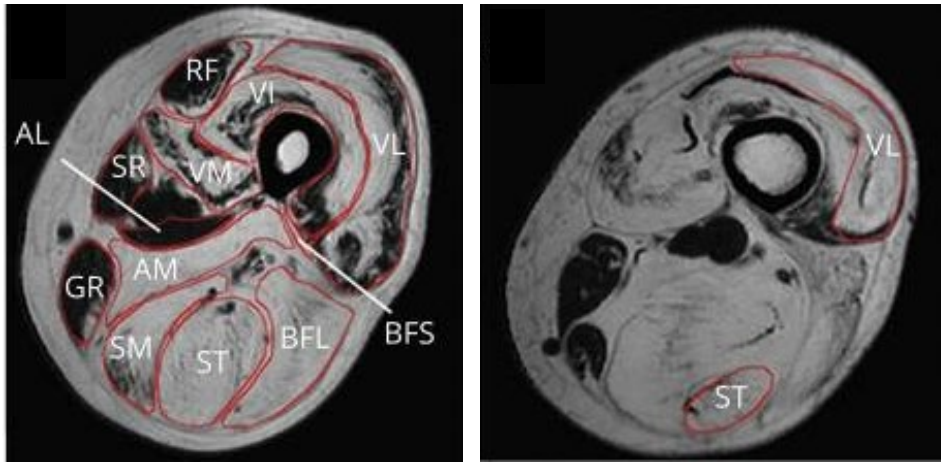
MRI as biomarker in BMD

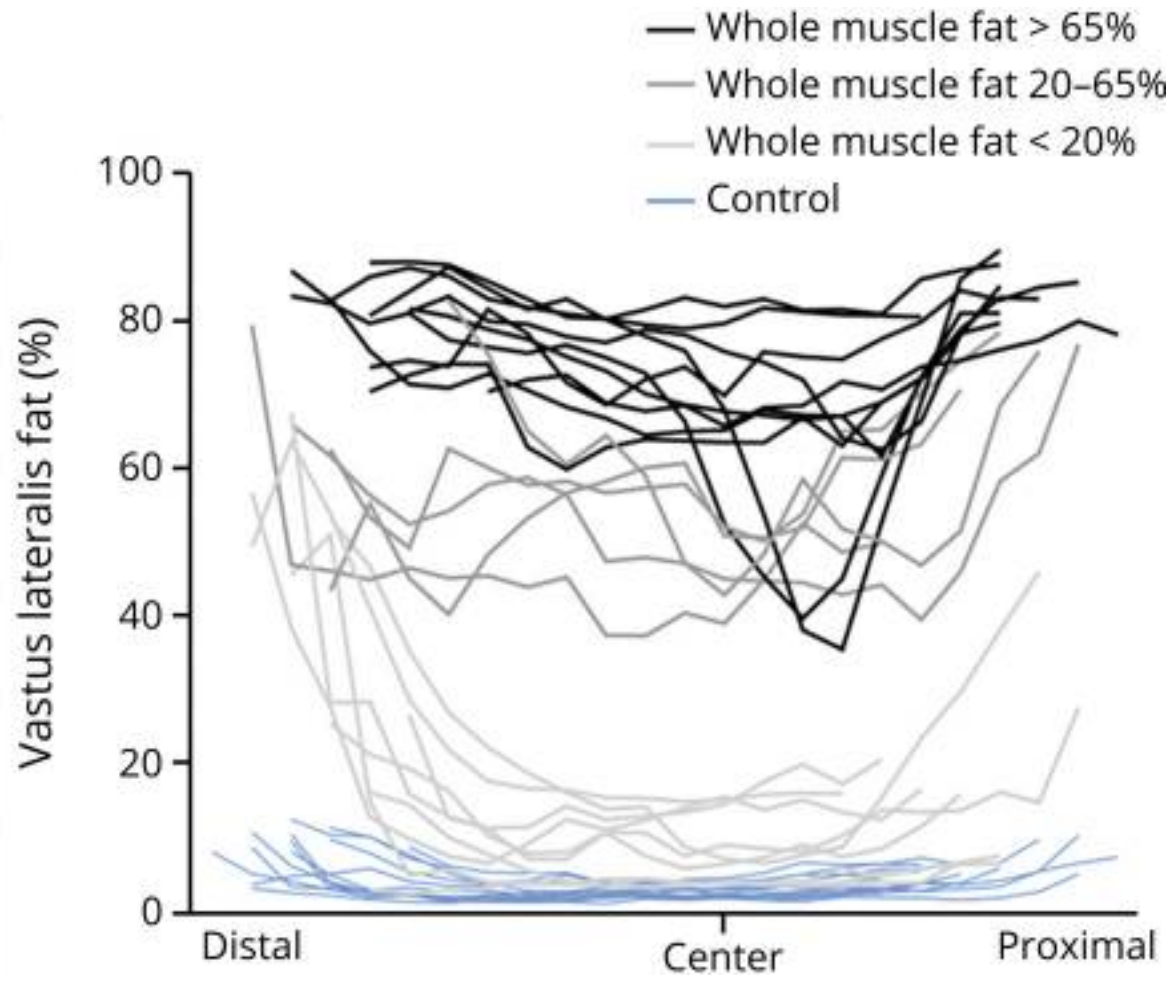
Increased fat fraction

Differs between muscles

Differs within muscles

Axial and longitudinal plane





Hooijmans et al. NMR in Biomed 2020 & van de Velde et al. Neurology 2021

MRI as biomarker in BMD

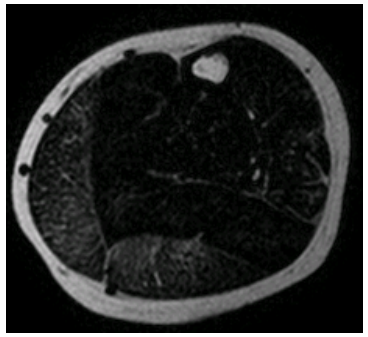
Fat fraction using Dixon

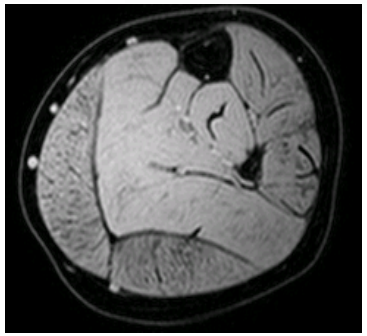
N = 24 at baseline, N = 20 after 2 years

Manual delineation of 19 muscles:

- 23 slices of 10 mm with 5 mm gap
- Middle slice based on anatomical landmarks
- Values for 3 center slices and whole muscle
- Values per muscle and for 6 groups

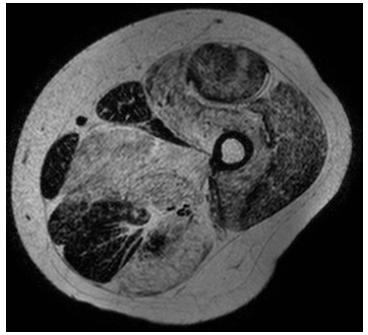
- Functional tests: NSAA, 6MWT, TMRv

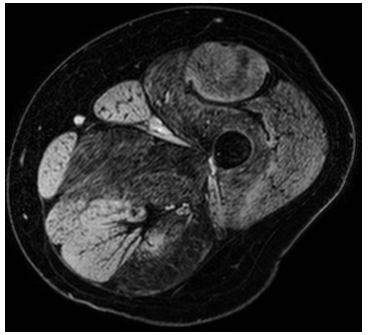




Fat

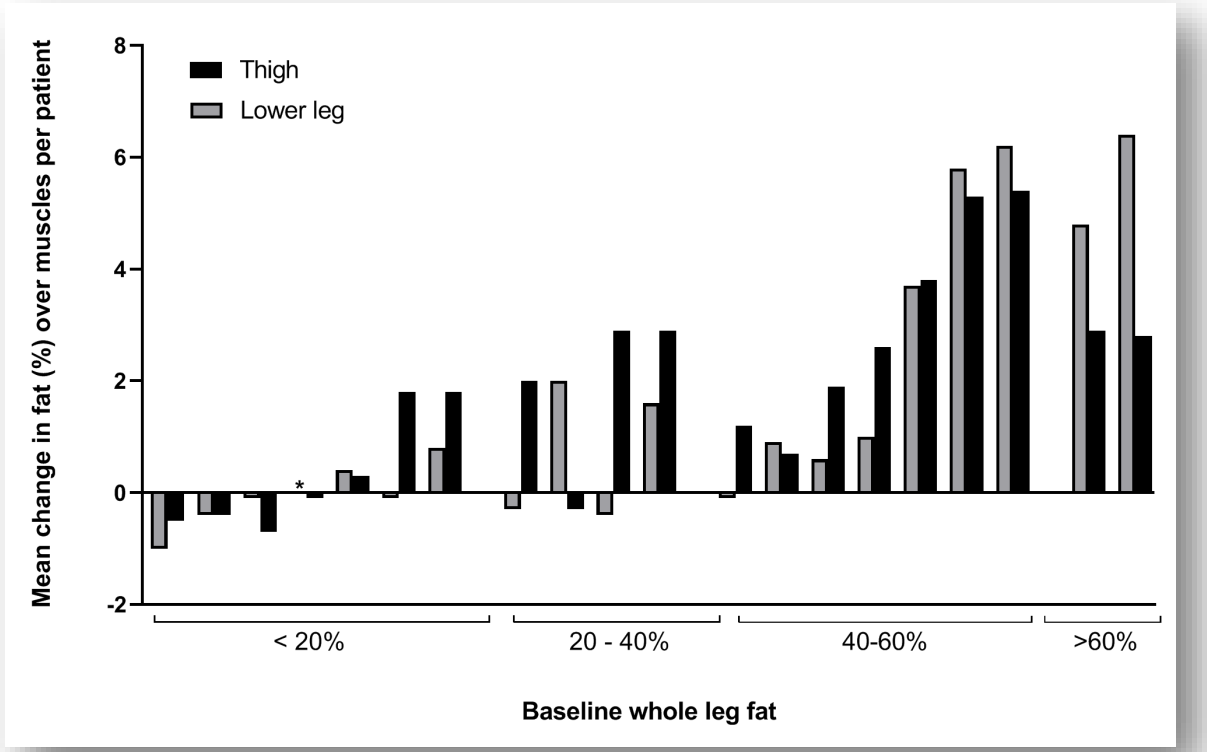
Water

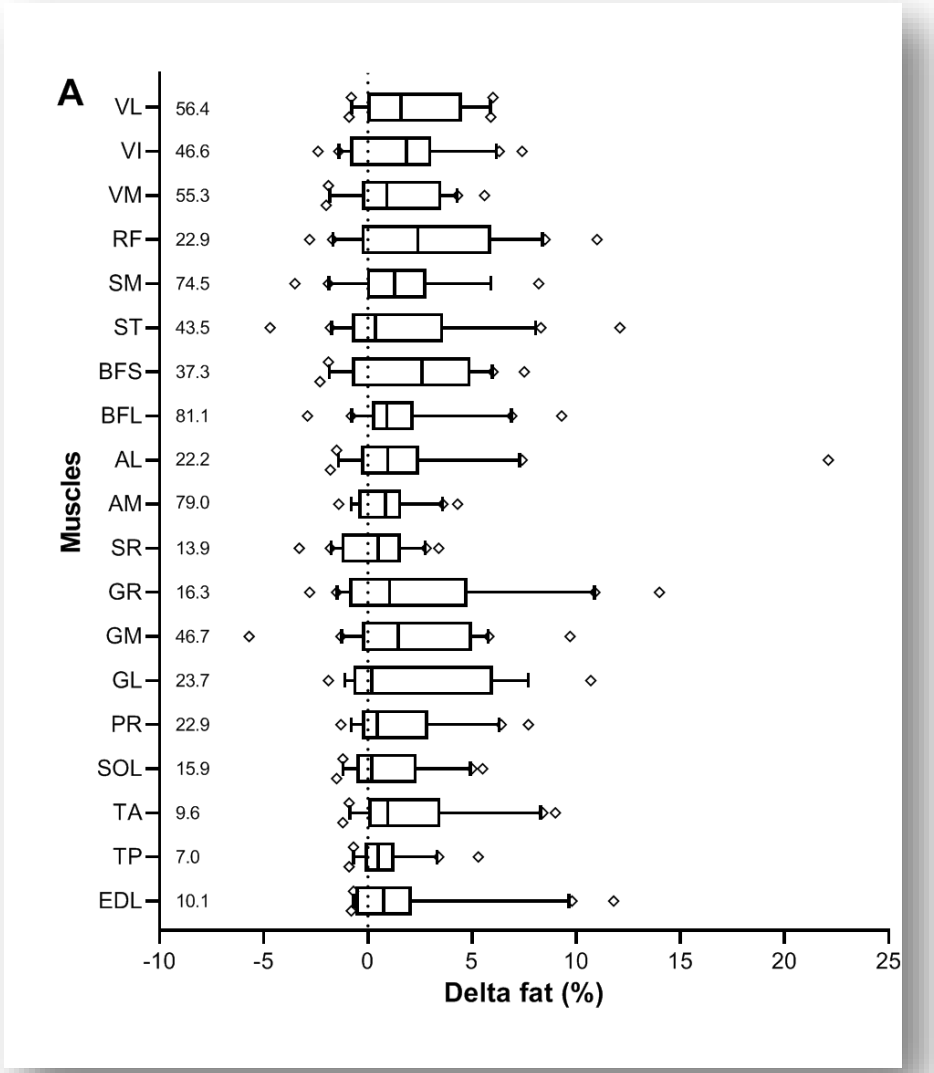




Increase in FF over 24 months

Median whole muscle FF increased between 0.2% and 2.6%





Functional change over 24 months

duchenne centre netherlands

Table 1 Change in Functional Assessments Between Baseline and After 24 months

Test	Median at baseline	Median change follow-up vs baseline (range)	*p* Value	SRM	SS
NSAA, points	18 (5 to 34)	−2.5 (−12.0 to 1.0)	0.002	−0.81	98
TMRv, m/s	1.45 (0.26 to 4.17)	−0.22 (−1.4 to 0.25)	0.014	−0.68	138
6MWT, m	385 (0 to 650)	−12.6 (−151.9 to 33.0)	0.063	−0.46	310
KE, kg	8.56 (2.9 to 54.5)	−1.3 (−11.1 to 3.8)	0.114	−0.49	264
KF, kg	8.19 (2.4 to 29.7)	−1.4 (−7.1 to 2.8)	0.040	−0.71	126

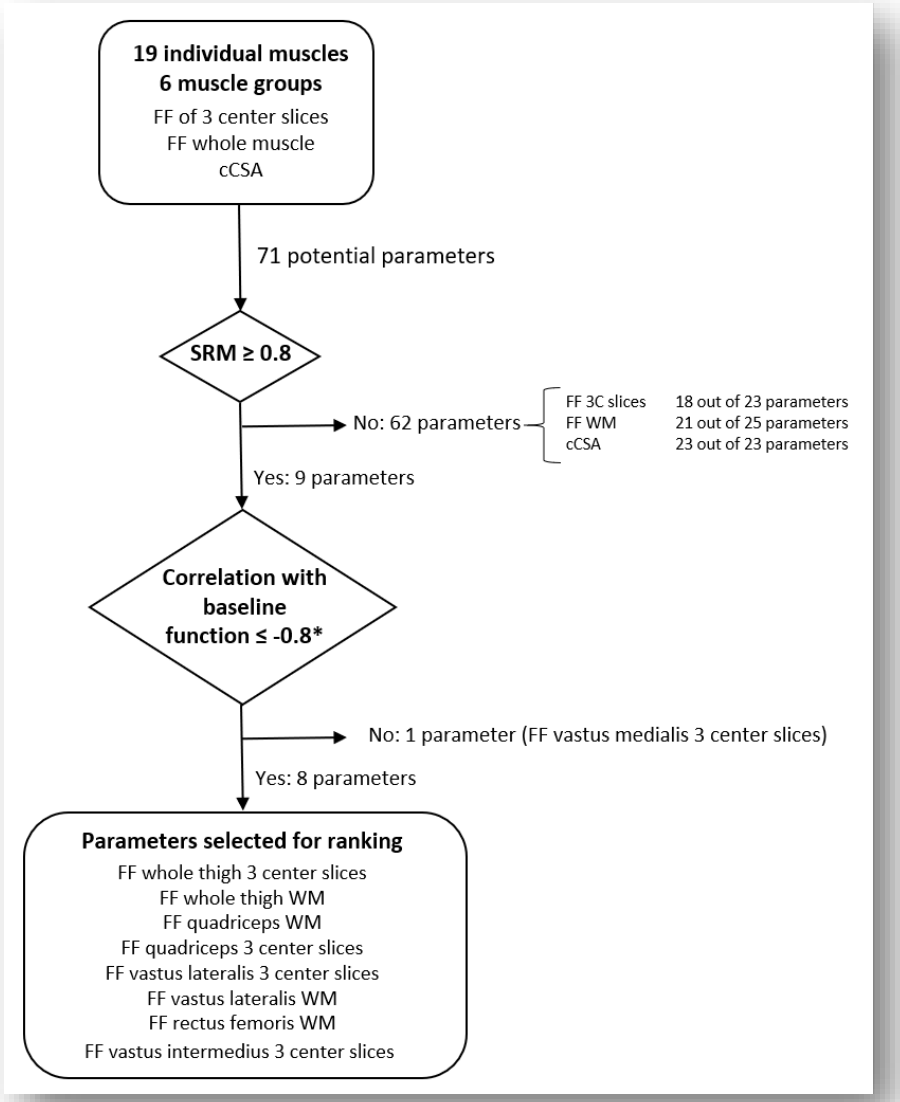
Abbreviations: 6MWT = 6-minute walk test; KE = knee extension; KF = knee flexion; NSAA = North Star Ambulatory Assessment; SRM = standardized response mean; SS = sample size; TMRv = 10-meter run velocity.

Stepwise analysis

Sensitivity to detect change (standardized response mean)

Correlation with baseline function (NSAA, 6MWT, TMRv)

Reproducibility



RESEARCH ARTICLE OPEN ACCESS

Selection Approach to Identify the Optimal Biomarker Using Quantitative Muscle MRI and Functional Assessments in Becker Muscular Dystrophy

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Whole thigh FF most sensitive and reproducible

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Table 2 Quantitative MRI Measures in Final Step of the Flowchart

Measure	SRM	SS	Correlation to baseline function			Reproducibility
			NSAA	TMRv	6MWT	
Whole thigh 3CS	1.04	59	−0.888	−0.865	−0.832	ICC: 1.000, SD of the difference 0.23%
Whole thigh WM	1.01	64	−0.924	−0.891	−0.872	ICC: 1.000, SD of the difference 0.24%
Quadriceps WM	0.99	65	−0.878	−0.842	−0.825	ICC: 1.000, SD of the difference 0.35%
Quadriceps 3CS	1.04	59	−0.878	−0.842	−0.807	ICC: 1.000, SD of the difference 0.47%
Vastus lateralis 3CS	0.83	94	−0.866	−0.832	−0.840	ICC: 1.000, SD of the difference 0.47%
Vastus lateralis WM	0.92	76	−0.858	−0.818	−0.828	ICC: 1.000, SD of the difference 0.69%
Rectus femoris WM	0.84	92	−0.896	−0.877	−0.846	ICC: 1.000, SD of the difference 0.83%
Vastus intermedius 3CS	0.85	90	−0.874	−0.849	−0.811	ICC: 0.999, SD of the difference 1.55%

Abbreviations: 3CS = 3 center slices; 6MWT = 6-minute walk test; ICC = intraclass correlation coefficient; KE = knee extension; KF = knee flexion; NSAA = North Star Ambulatory Assessment; SRM = standardized response mean; SS = sample size; TMRv = 10-meter run velocity; WM = whole muscle.

Cognition in BMD

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Original Article

Cognitive and Psychological Profile of Males With Becker Muscular Dystrophy

Helen K. Young, FRACP, MMed, Belinda A. Barton, PhD, Susan Waisbren, PhD, Lourdes Portales Dale, PhD, Monique M. Ryan, FRACP, MMed, Richard I. Webster, FRACP, MMed, and Kathryn N. North, MD

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CLINICAL RESEARCH ARTICLE

MUSCLE&NERVE WILEY

See editorial on pages 127–128 in this issue.

Neurodevelopmental, behavioral, and emotional symptoms in Becker muscular dystrophy

Joshua T. Lambert MA[1] | Andrew J. Darmahkasih MD[2] | Paul S. Horn PhD[3] | Irina Rybalsky MD, PhD[1] | Karen C. Shellenbarger APRN, CPNP[4] | Cuixia Tian MD[3] | Brenda L. Wong MD[4]

JID: NMD [m5+;November 7, 2019;22:15]
Available online at www.sciencedirect.com
ScienceDirect
Neuromuscular Disorders xxx (xxxx) xxx
www.elsevier.com/locate/nmd

Psychiatric and neurodevelopmental aspects of Becker muscular dystrophy

Madoka Mori-Yoshimura[a,*], Yukio Mizuno[a], Sumiko Yoshida[b,c], Naoko Ishihara[c], Narihiro Minami[c,d,e], Emiko Morimoto[f], Kazushi Maruo[g,h], Ikuya Nonaka[i], Hirofumi Komaki[i], Ichizo Nishino[d,e], Masayuki Sekiguchi[j], Noriko Sato[f], Shin'ichi Takeda[k], Yuji Takahashi[a]

Journal of Neuromuscular Diseases 9 (2022) 543–553
DOI 10.3233/JND-210770
IOS Press

Original Study

The neurocognitive profile of adults with Becker muscular dystrophy in the Netherlands

Zaïda Koeks[a,1], Danique M.J. Hellebrekers[b,c,1], Nienke M. van de Velde[a,g], Iris Alleman[d], Pietro Spitali[e], Hermine A. van Duyvenvoorde[f], Jan J.G.M. Verschuuren[a,g], Jos G.M. Hendriksen[b,c,g,1] and Erik H. Niks[a,g,1,*]

Natural history - ongoing studies

CINRG

US, Canada, UK, Italy

GRASP - Defining Endpoints in BMD

US, Europe

NorthStar Assessment for LGMD (NSAD)

MRI

ImagingNMD

US

BIND (Brain Involvement iN Dystrophinopathies)

UK, Italy, Spain, Denmark, France, Netherlands

Summary

BMD and DMD are both part of a spectrum

High clinical variability and slow progression

Complex genotype-phenotype correlations

Changes in motor function > 12 months

Decline in baseline NSAA 10-32

MRI is a promising biomarker

Bridging the gap in NH data

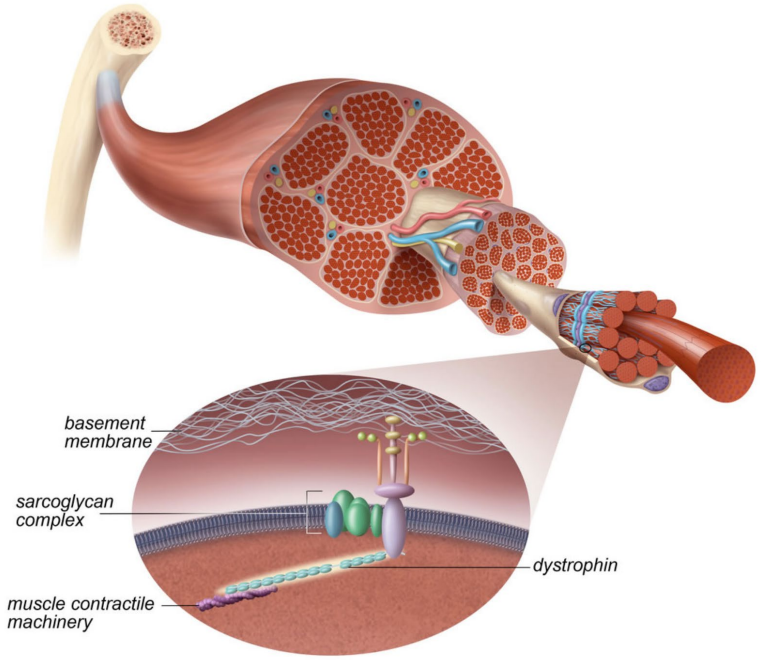
Edgewise THERAPEUTICS

Targeting Fast Myosin in Becker and Duchenne Muscular Dystrophy

Sam Collins, MD, PhD

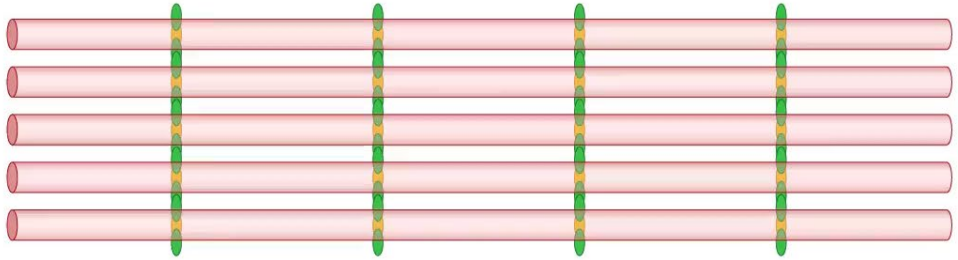
Vice President, Clinical Development

The Dystroglycan Complex Helps Prevent Injury in Contracting Fibers



Dystrophin connects contractile proteins to the membrane and surrounding matrix of fibers

Muscle fibers from different motor units contract independently

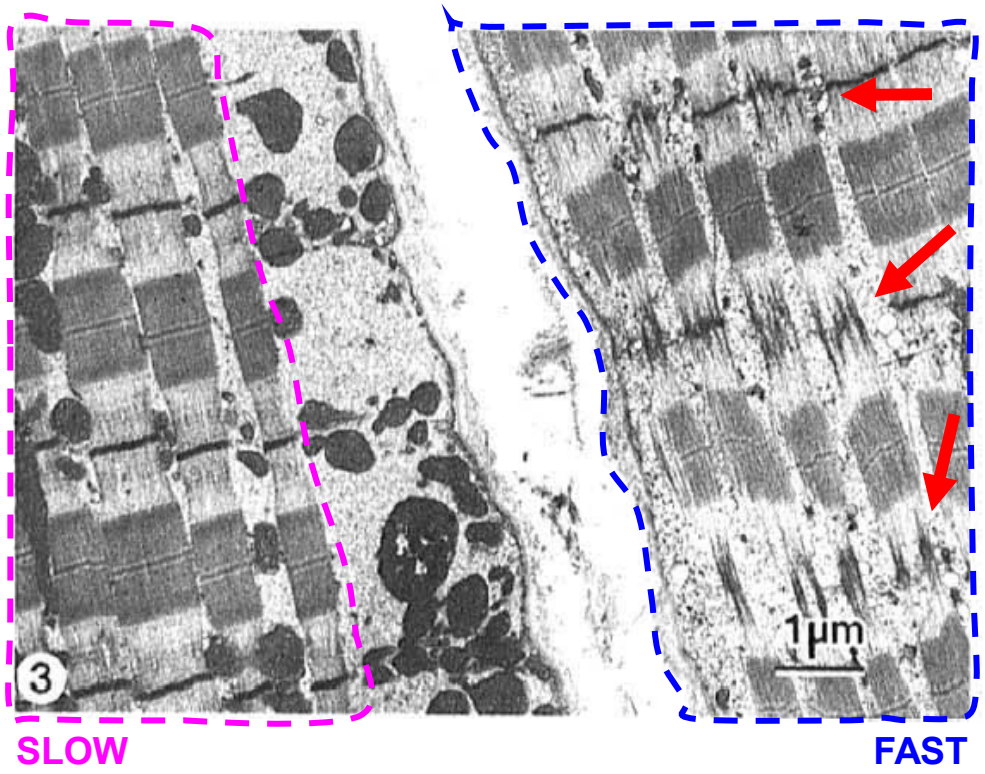


Resting skeletal muscle

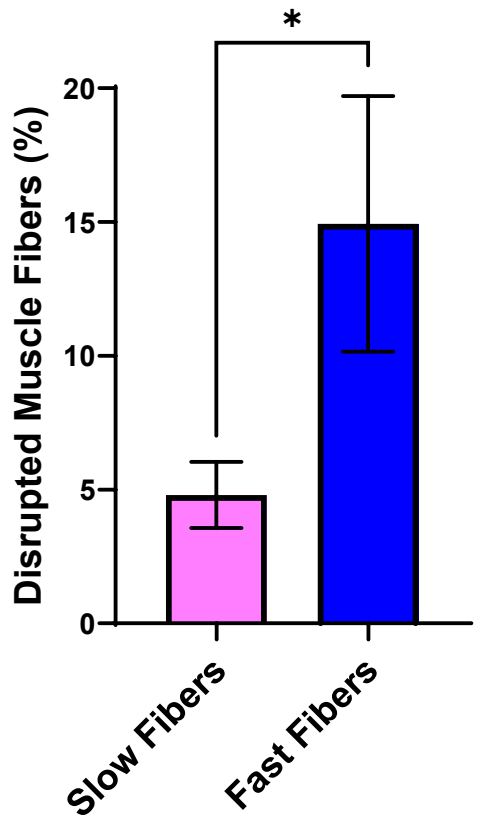
Long muscle fibers are more dependent upon dystrophin to help support fibers

Fast Muscle Fibers Are More Susceptible to Damage in Response to Eccentric Exercise in Unaffected Individuals

More Damage in Fast Muscle Fibers vs. Slow Muscle Fibers



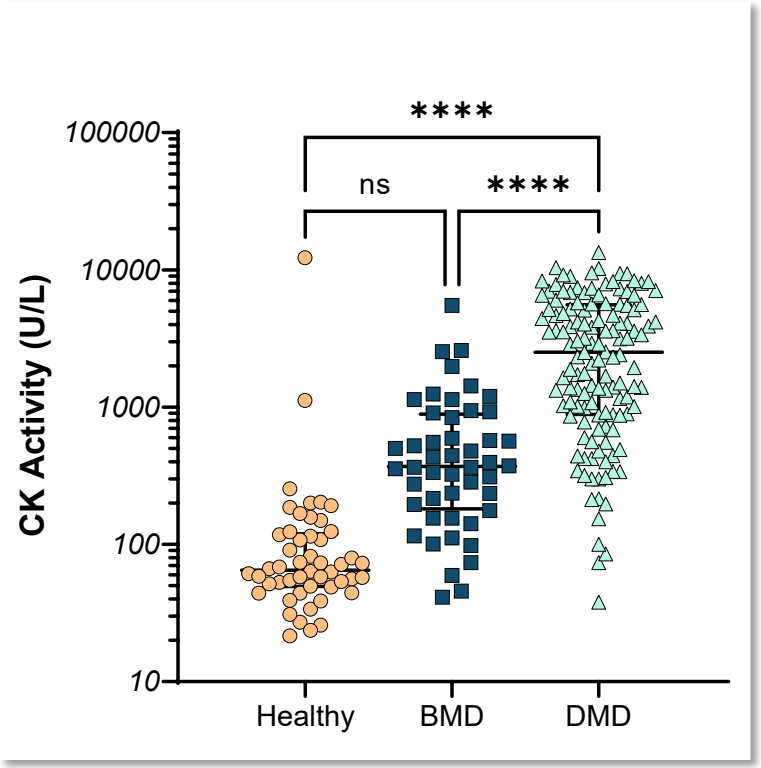
- 30 mins controlled eccentric exercise
- Muscle biopsy taken immediately after exercise



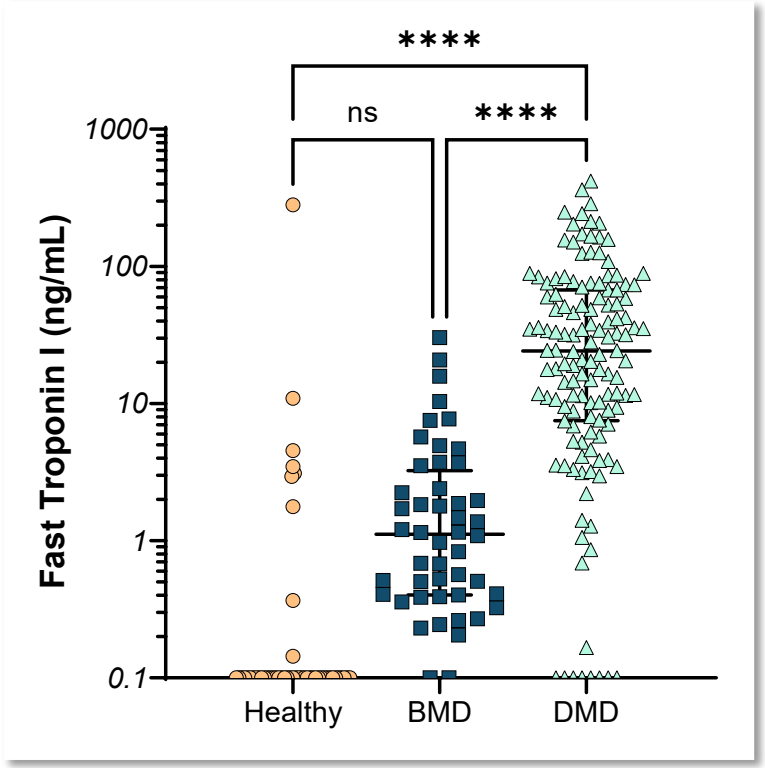
Reference: Fridén J, *et. al., Int. J. Sports Med.,* 1983

Injury Biomarkers Tell the Same Story: Fast but not Slow Fiber Biomarkers are Elevated in Becker and Duchenne

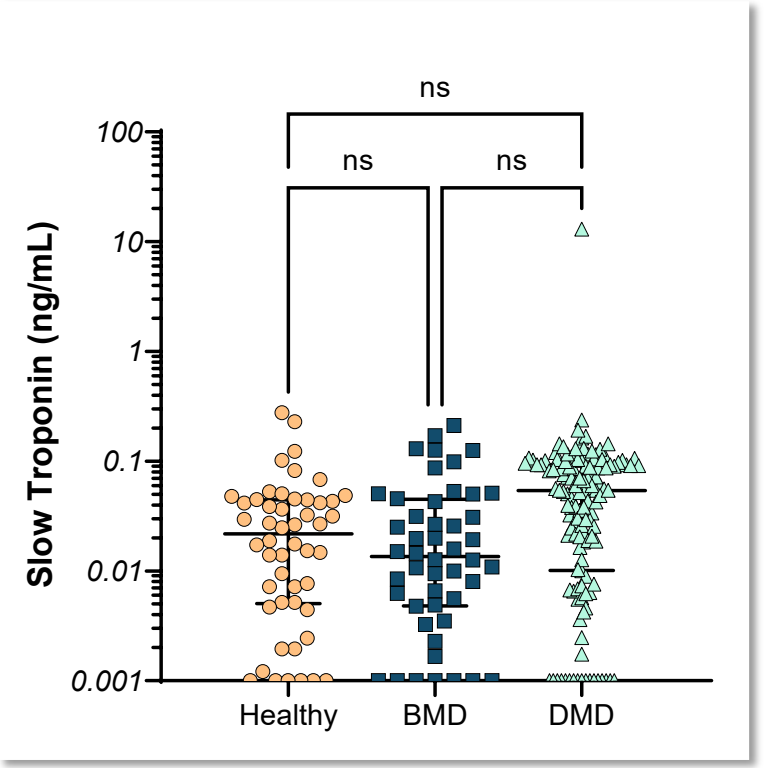
Creatine Kinase



Fast Skeletal Muscle Troponin I (TNNI2) †



Slow Skeletal Muscle Troponin I (TNNI1)

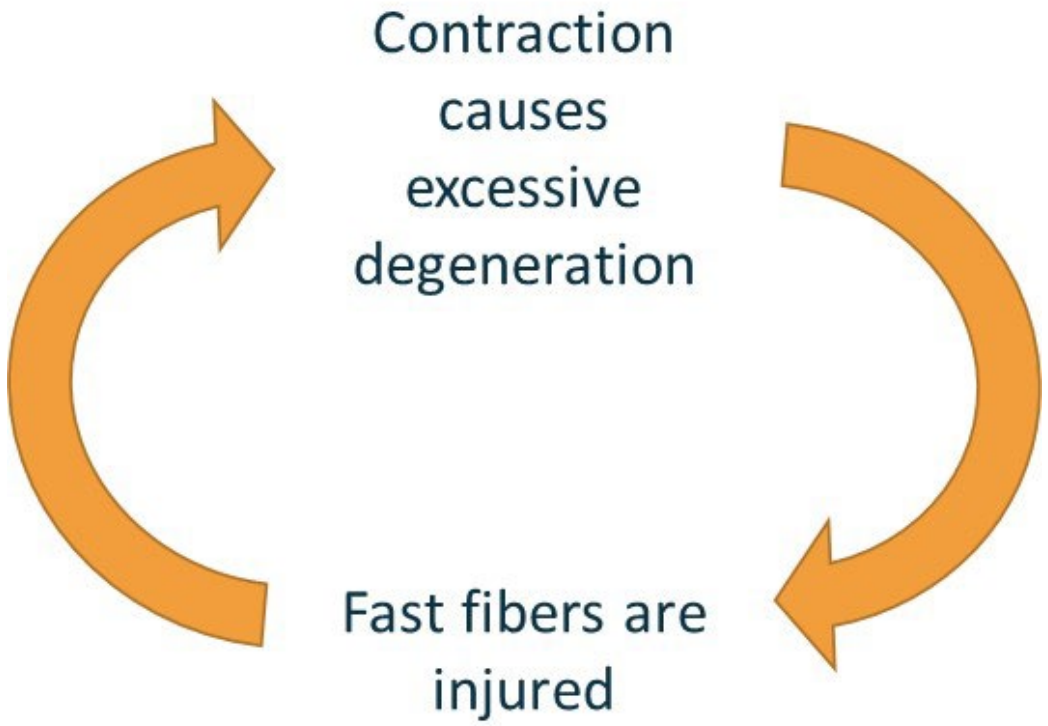


- Age ranges: Control 6-73 years, Becker 6-68 years, Duchenne 2-33 years

***** p < 0.0001*

132 Duchenne samples from Newcastle University Biobank, 52 Becker samples from the CINRG consortium and 52 healthy volunteers from Chen collaboration
~83% of volunteers had fast troponin levels below the LLQ of the ELISA, while only 4% of Becker and 6% of Duchenne patients had non-measurable levels of fast troponin
Reference: Barthel *et. al., Muscle and Nerve*, 2021

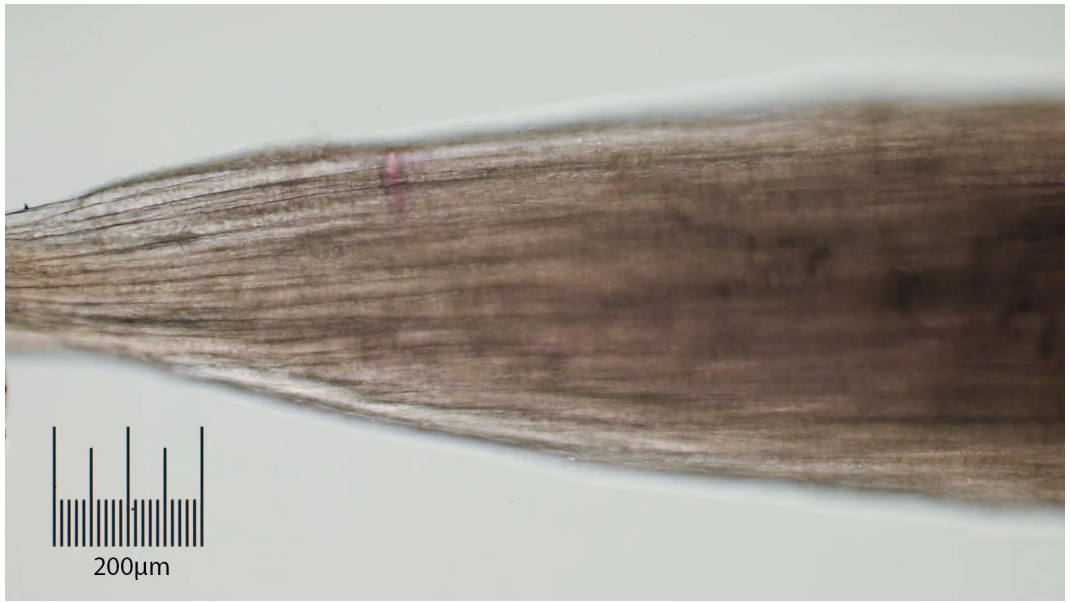
A New Strategy to Rebalance Dystrophic Muscle



Protecting muscle is predicted to preserve function

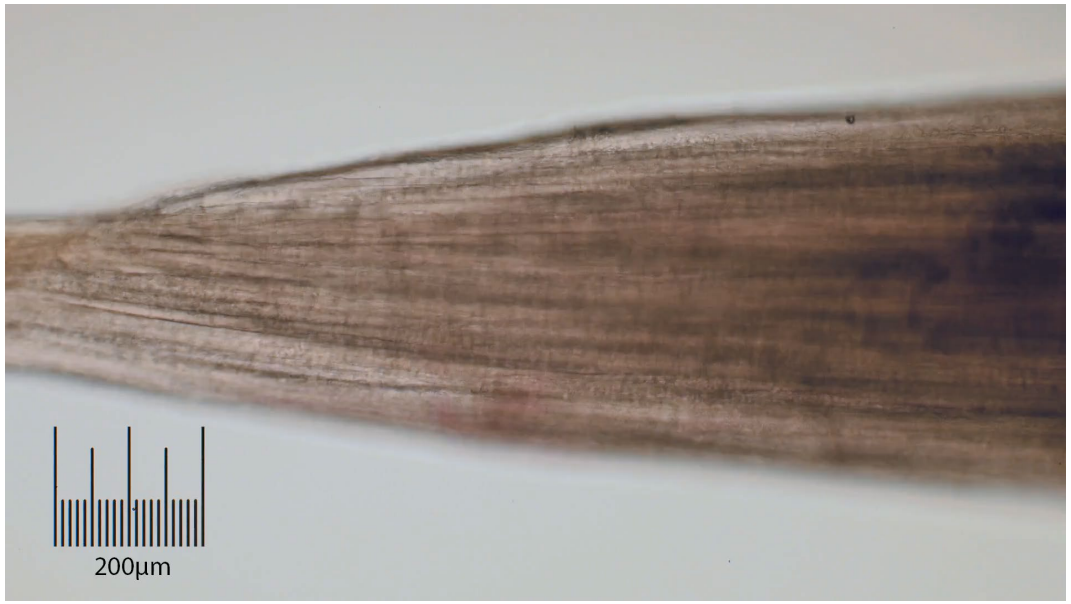
EDG-5506 Stops Fast Fiber Breakdown in Contracting *mdx* Muscles

Dystrophic muscle (*mdx* mouse) no treatment



Contracting at 100%

Dystrophic muscle (*mdx* mouse) 0.3 uM EDG-5506



Contracting at 85%

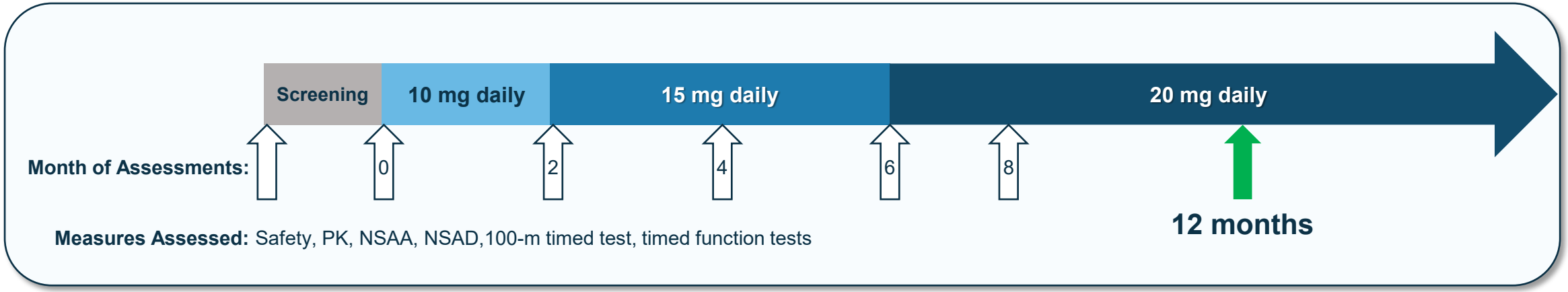
Claflin, Su and Brooks. U Michigan

mdx mouse lumbrical muscle – 20, 1 second maximal isometric contractions (video sped up)

Reference: Russell et al JCI, 2023

ARCH Open-Label Study Design in Becker Patients

- An open-label, single-center study of EDG-5506 to assess the safety and pharmacokinetics of EDG-5506 in adults with Becker
- Primary objective: Safety and tolerability at 12 months, now extended to 24 months
- Key inclusion criteria
  - Ambulatory males aged 18 to 55 years with a dystrophin mutation and a Becker phenotype, not on corticosteroids, who could complete 100-m timed test
- Enrollment: 12



Baseline Characteristics: Becker Participants Had Significant Functional Impairment and Decreased Muscle Mass

ARCH

Characteristic	Becker Participants (N=12)	Age Normative Values
Age (SD)	32.8 (8.1) years	
Functional Measures (median)		
10-meter walk/run	8.4 sec	< 4 sec
Rise from floor	6/12 could perform	< 3 sec
NSAA	15.5 (range 4-31)	
Serum Creatinine (mean, mg/dL)	0.44	0.92 - 1.16
Serum CK (mean, U/L)	1,390	<210
DXA % Lean Mass	54.9%	>75%

Unlike clinical trials for children with Duchenne, **the Becker patients in ARCH were in the functional decline phase of their disease course**

Source: Data on file

EDG-5506 Was Well Tolerated at All Doses; No Dose Reductions, No Treatment Discontinuations and No SAEs

Number of Participants Reporting an AE

Treatment Emergent AE	10 mg EDG-5506 2 months of dosing	15 mg EDG-5506 4 months of dosing	20 mg EDG-5506 6 months of dosing	Total 12 months
Dizziness	2 (17%)	3 (25%)	1 (8%)	4 (33%)
COVID-19	-	1 (8%)	3 (25%)	4 (33%)
Arthralgia	-	-	4 (33%)	4 (33%)
Somnolence	2 (17%)	1 (8%)	-	3 (25%)
Headache	1 (8%)	2 (17%)	2 (17%)	3 (25%)
Nasopharyngitis	1 (8%)	1 (8%)	1 (8%)	3 (25%)
Fall*	-	3 (25%)	3 (25%)	3 (25%)
Viral URI	1 (8%)	-	3 (25%)	3 (25%)
Influenza	-	-	2 (17%)	2 (17%)
Sinusitis	-	1 (8%)	1 (8%)	2 (17%)
GERD	-	-	2 (17%)	2 (17%)
Procedural pain	1 (8%)	-	1 (8%)	2 (17%)

* Unassociated with other AEs and typical of falls observed in Becker patients

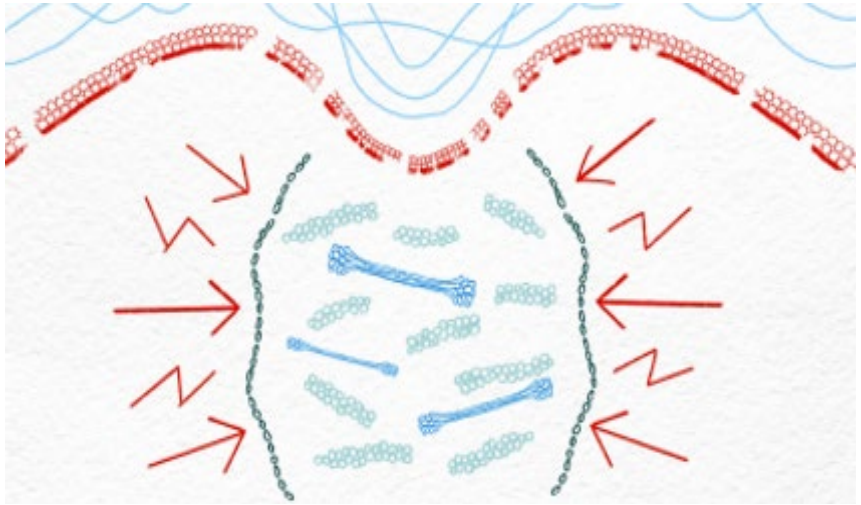
Source: Data on file

Muscle Damage in Muscular Dystrophies Leads to Leak of Injury Biomarkers, including CK, TNNI2 and Myoglobin

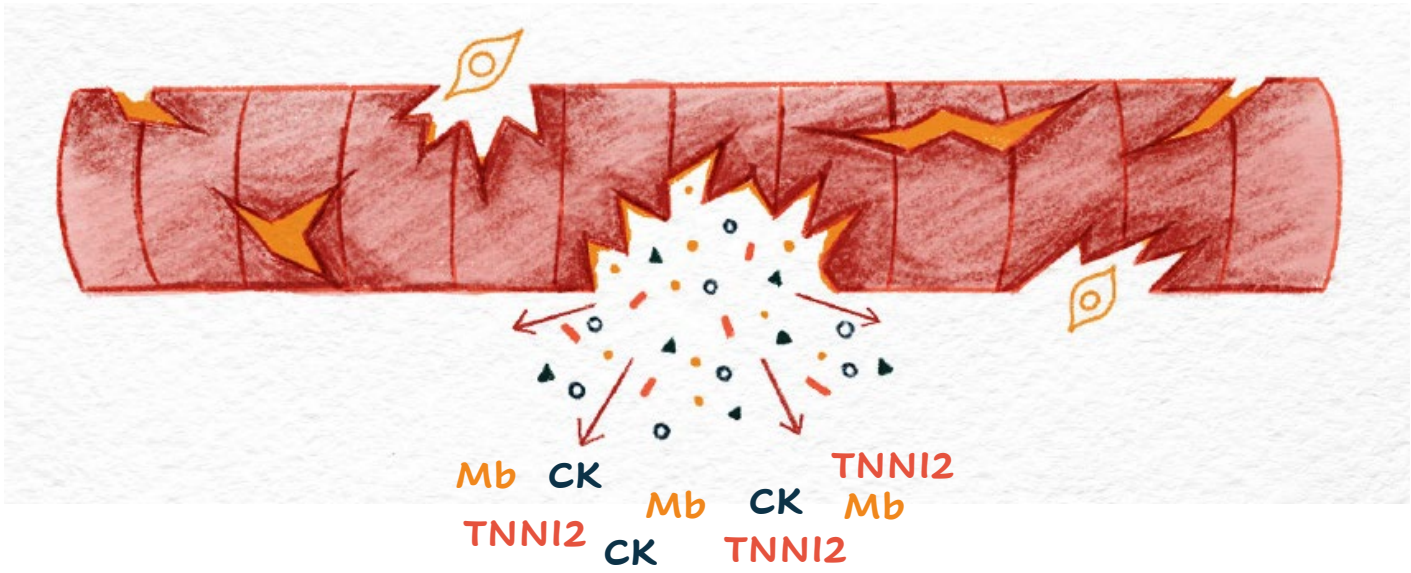
ARCH

Activity-Induced Muscle Injury in Muscular Dystrophies

Contraction induced muscle damage causes excessive degeneration



Fast fibers are subsequently injured leading to release of muscle injury biomarkers into the circulation



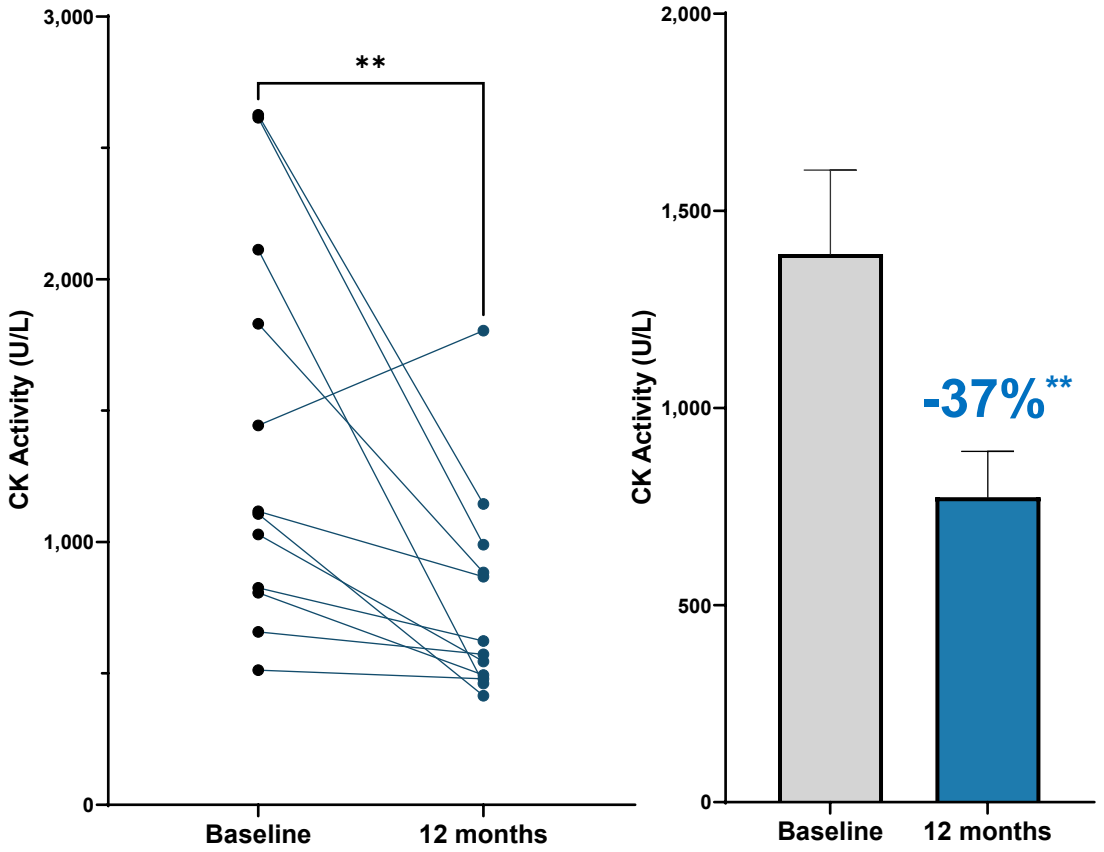
Legend: CK, Creatine Kinase; TNNI2, Fast Skeletal Muscle Troponin I; Mb, Myoglobin

Circulating Levels of Muscle Injury Biomarkers Can be Measured to Determine Ongoing Muscle Damage in Muscular Dystrophies

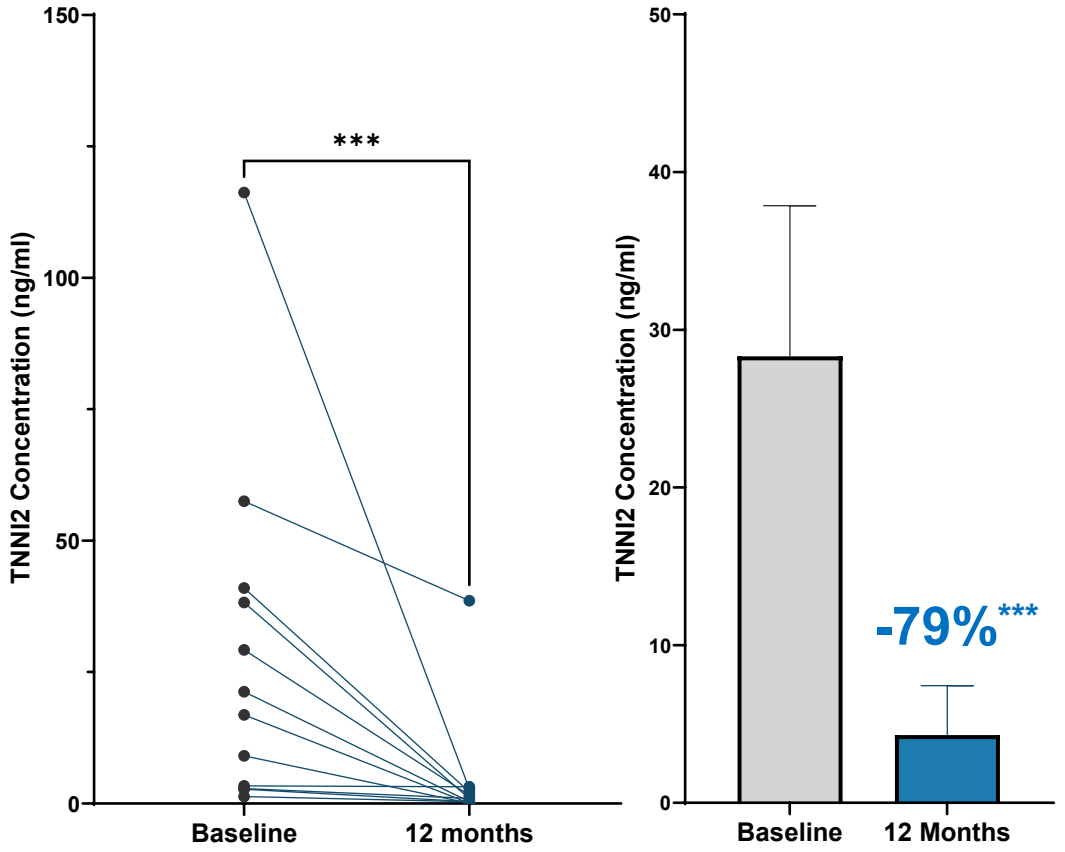
EDG-5506 Led to a Sustained Decrease in Biomarkers of Muscle Damage After 12 Months of Dosing

ARCH

Creatine Kinase



Fast Skeletal Muscle Troponin I (TNNI2)



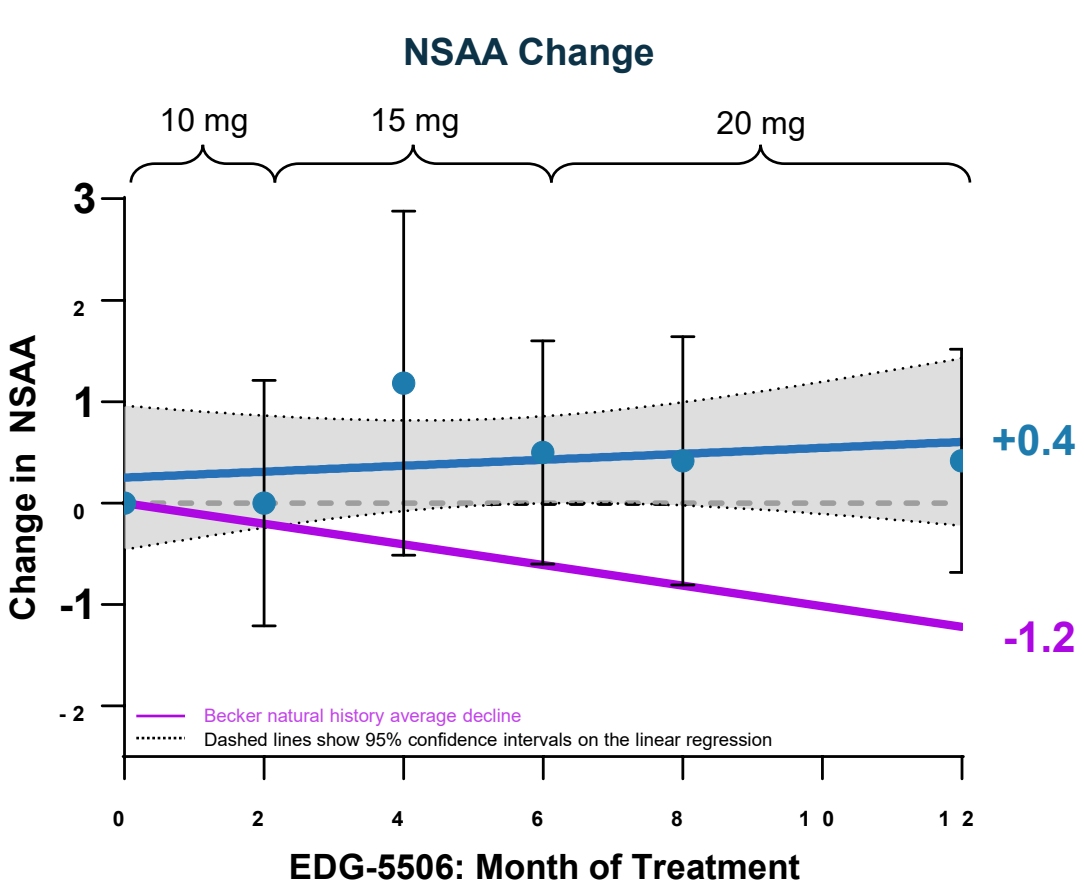
Individuals with the Highest Baseline Values Show Greatest Biomarker Effect, Suggesting Protection Against Activity-Induced Damage

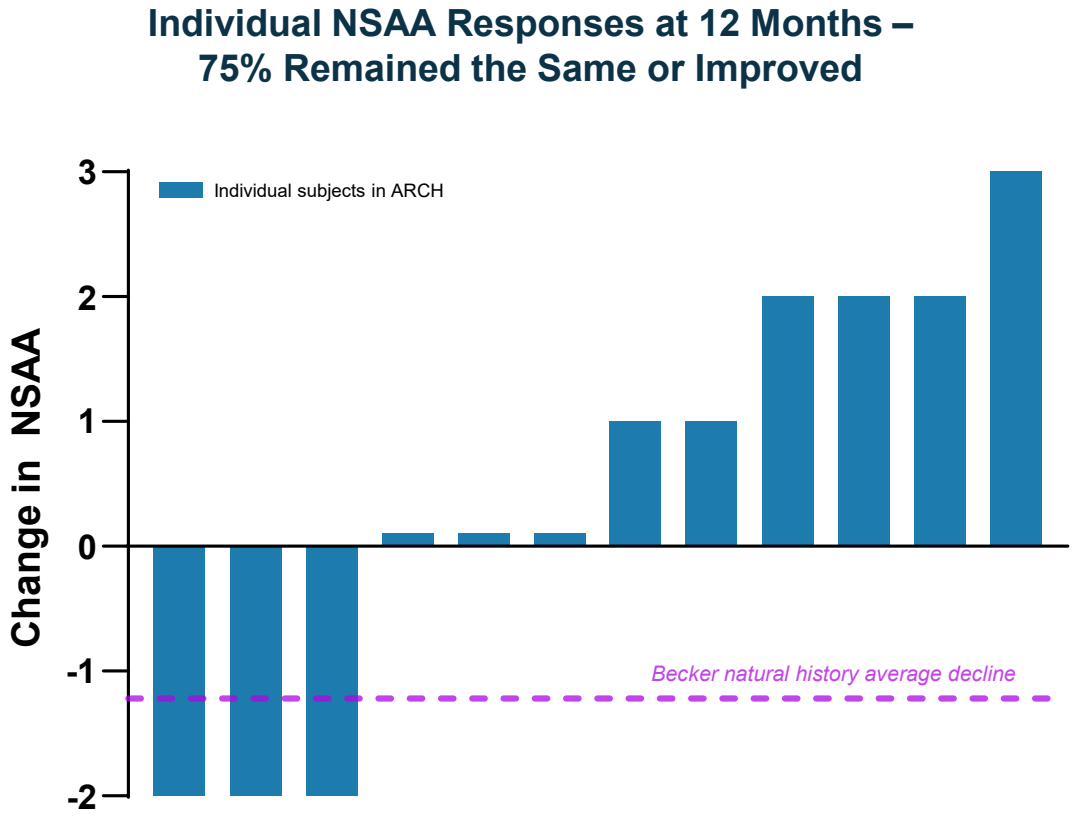
Edgewise THERAPEUTICS

Source: Data on file, TNNI2 data projected from SOMAscan
% difference from mean baseline shown; Means ± SEM (**p=0.001 and ***p<0.0001)

NSAA Shows Stabilization and Trend Toward Improvement – Mean **+0.4** Improvement Relative to Predicted -1.2 Point Decline from NHx

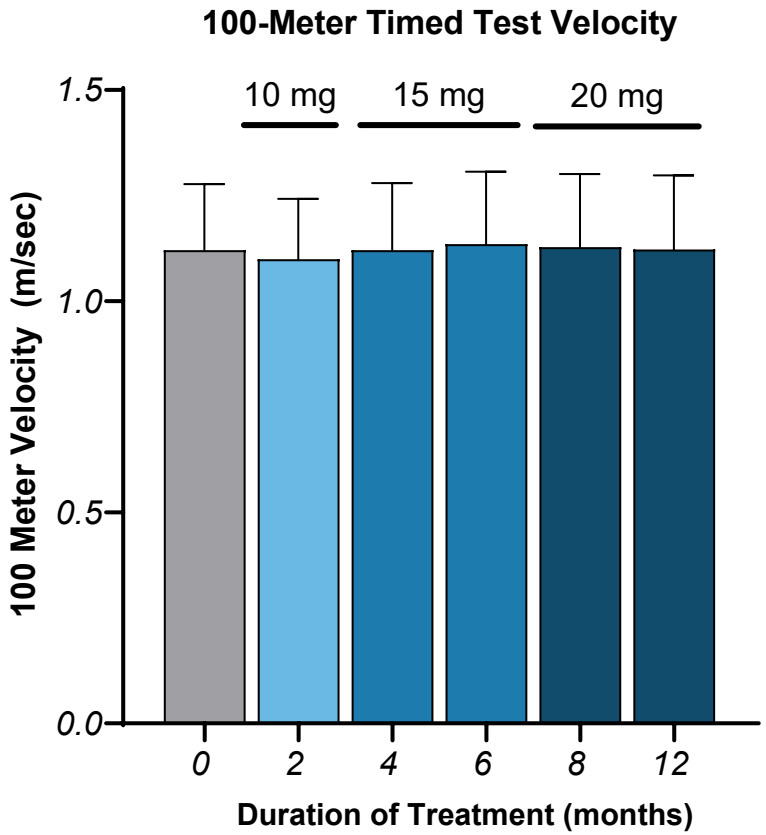
ARCH



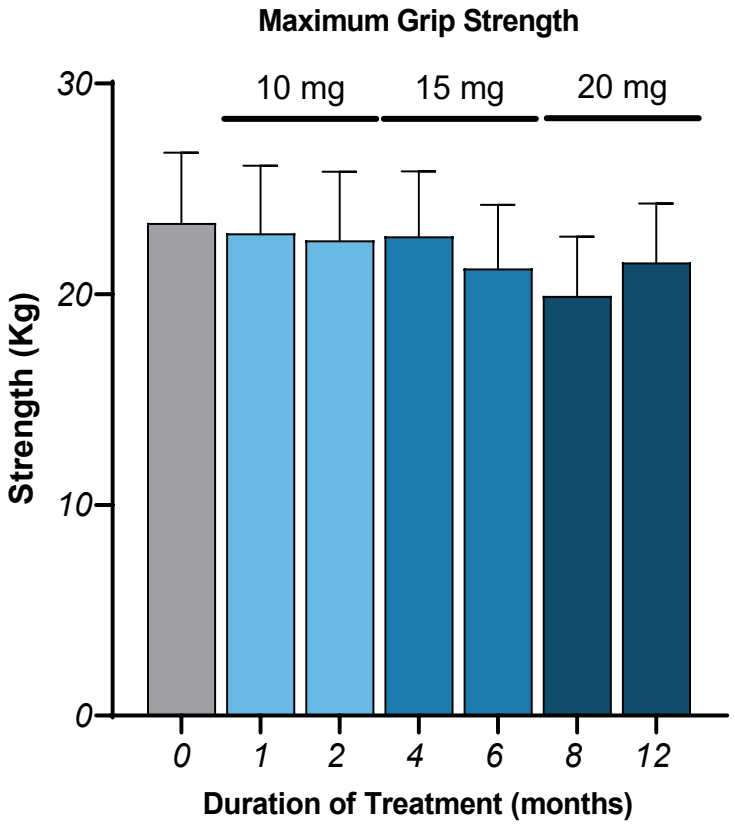


Means ± 95% CI; Source: data on file
Natural history based on data presented by Luca Bello at MDA (2022) and van de Velde NM *et. al., Neurology*, 2021

No Decline from Baseline On 100 Meter Time Test Velocity; No Significant Impact on Grip Strength



No statistically significant change at 12 months



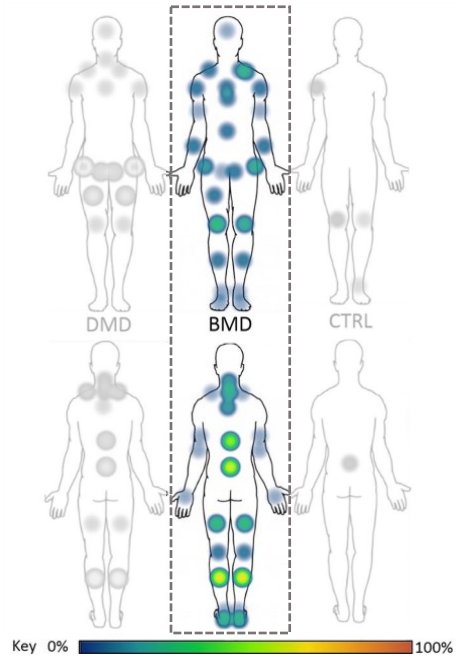
No statistically significant change at 12 months

*last observation carried forward (all N=12, except for 2 missing values, month 4 and 8)
Source: data on file

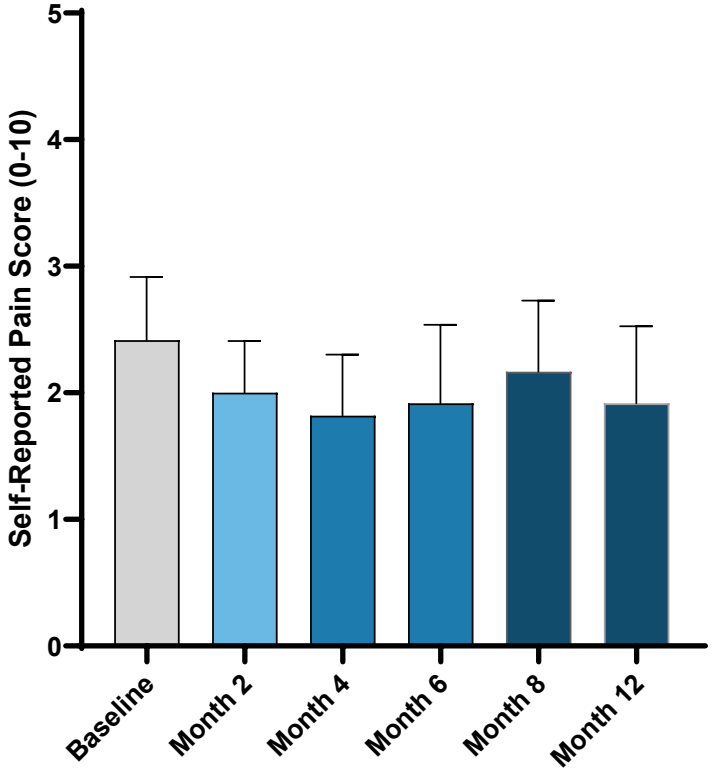
Pain is a Significant Hallmark of Becker and Self-Reported Pain Scores Trended Better after 12 Months with EDG-5506

ARCH

Becker Individuals Report Diffuse Pain, Focus on Spine And Calves



References: Jacques MF, *et. al.*, 2019, *PLOS ONE*



- While the ARCH study is not placebo controlled, a positive trend in self-reported pain scores was observed after 12 months of EDG-5506 dosing

Means ± SEM; Source: Data on file

Outcomes of the ARCH Study

✓ Safety	✓ Biomarkers	✓ Function	✓ Pivotal Dose Identified
Well-tolerated at all doses	Demonstration of rapid, sustained and significant decreases in multiple biomarkers of disease progression	Stabilization of functional assessments with trends toward improvement	Maximal biomarker response even at 10 mg dose PK/PD supportive of 10 mg dose for pivotal cohort

Overall, the ARCH trial identified key factors for the design of a potentially registrational trial

Edgewise THERAPEUTICS

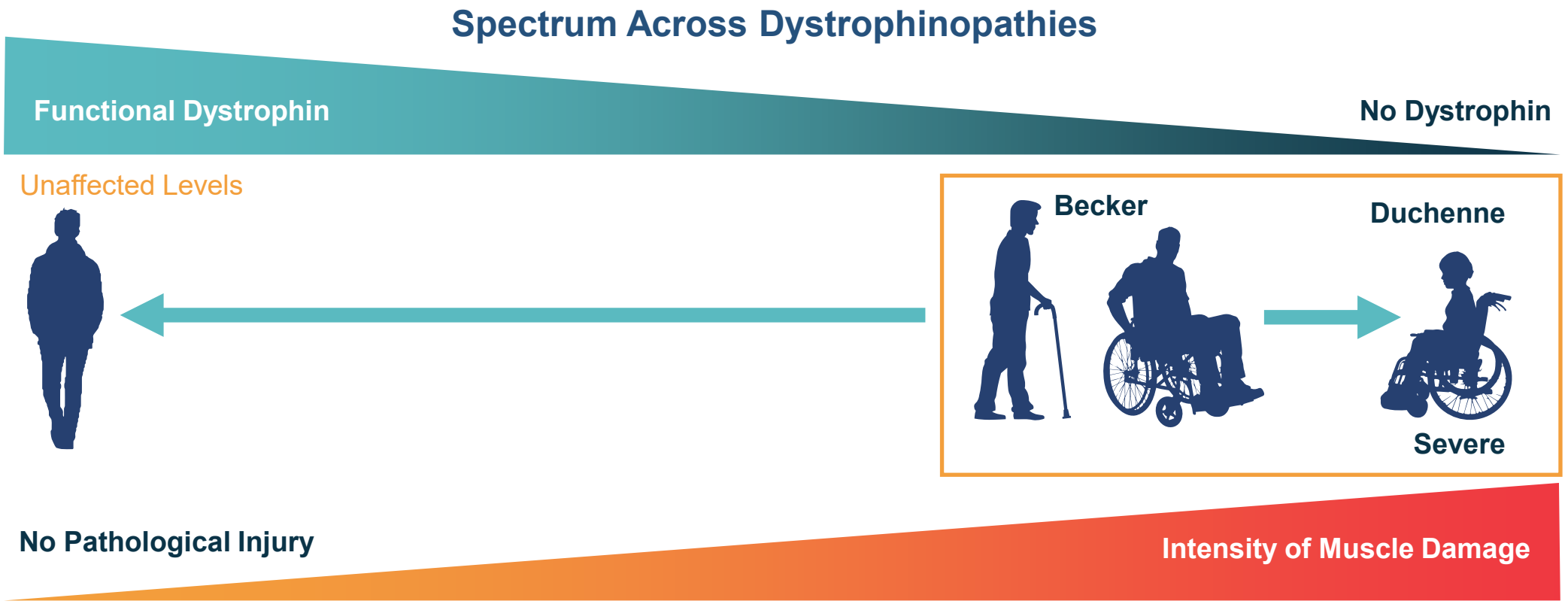
Putting the Data into Context

Barry Byrne, MD, PhD

Director, UF Health Center for Advanced Therapeutics and Powell Gene Therapy Center

University of Florida

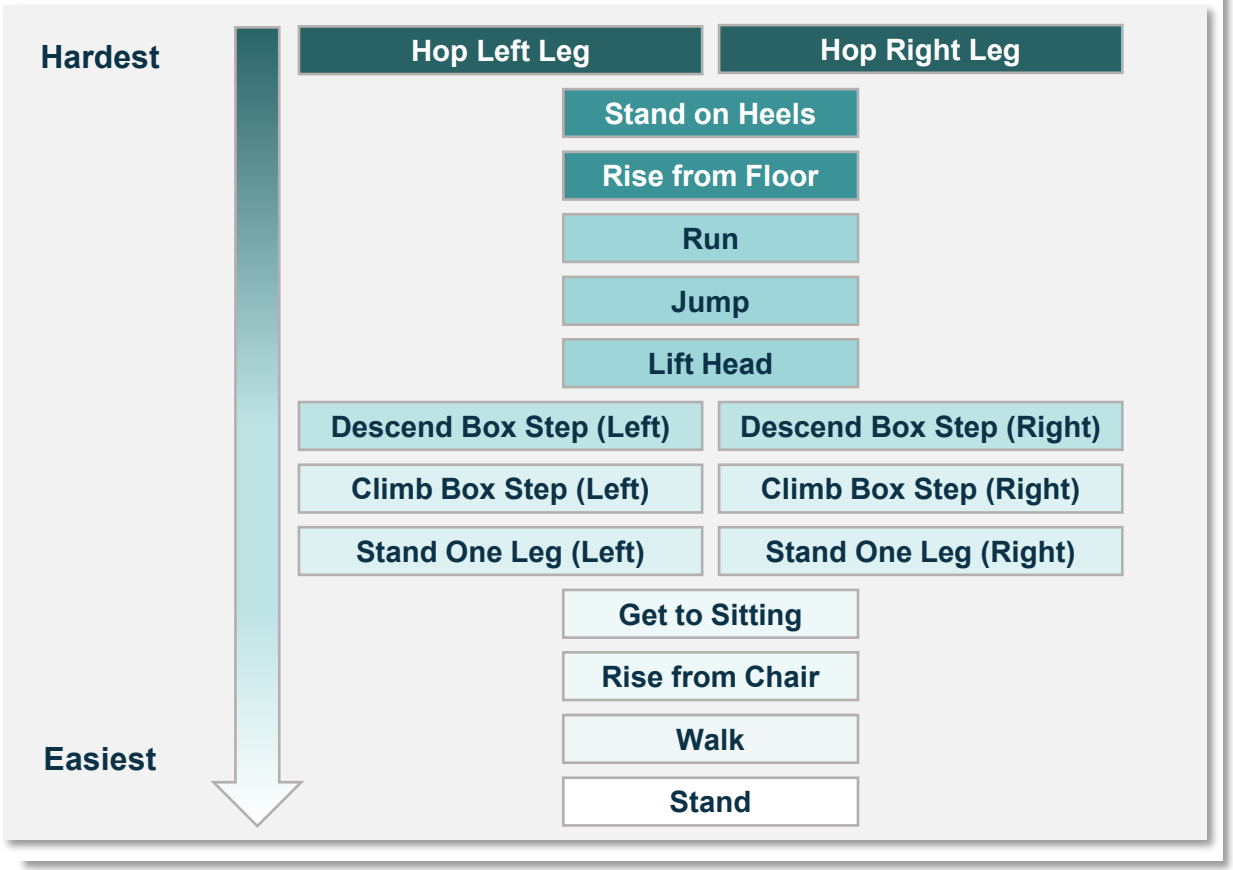
Becker and Duchenne Muscular Dystrophy are Related Dystrophinopathies



The combination of dystrophin functionality and background genetics place Becker individuals on a spectrum with Duchenne muscular dystrophy

NSAA: A Well-Established and Validated Measure of Global Function that is Clinically Meaningful in a Real-World Context

- Composite evaluation of motor function across 17 test items with increasing difficulty



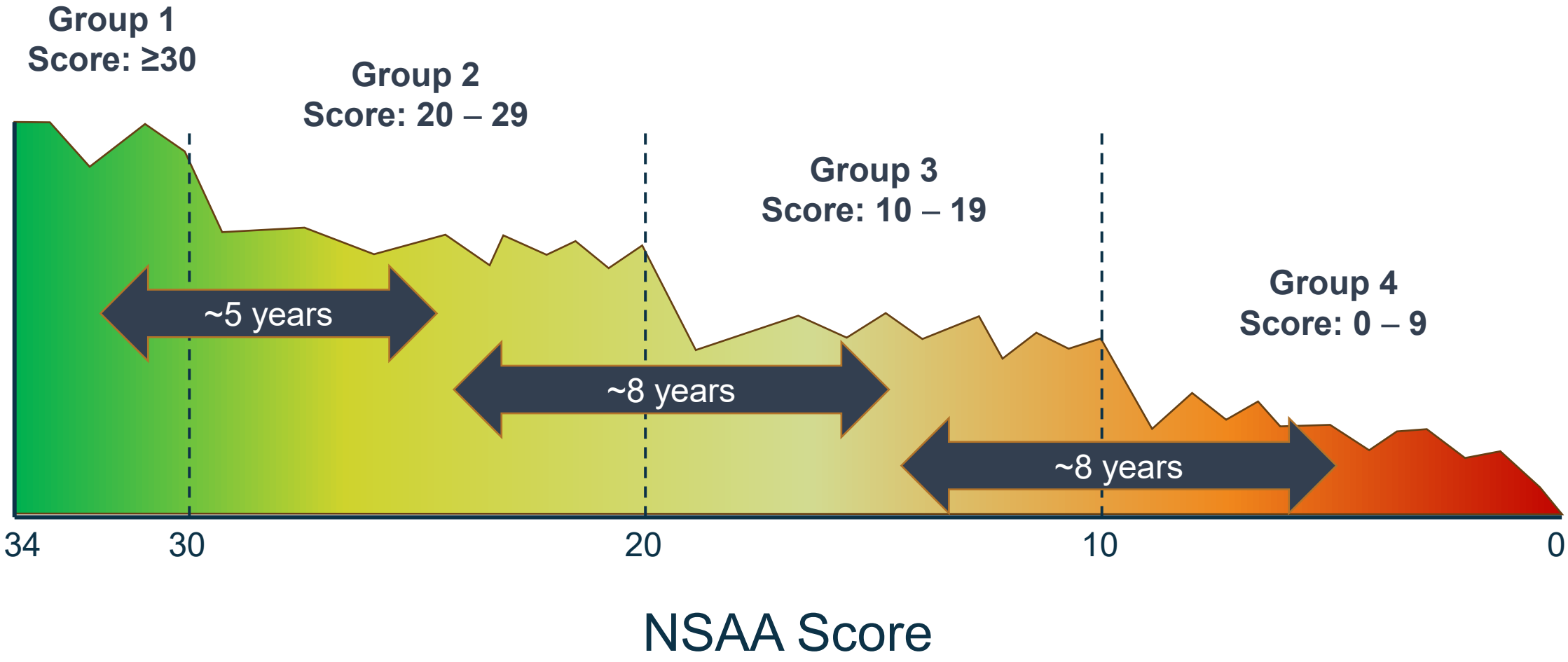
- Each activity scored on whether it can be completed:
  - Normally (**2 points**)
  - With an adjustment due to weakness (**1 point**)
  - Not at all (**0 points**)

Measure	Real-World Implication for Individual w/Becker
Jump, Hop, Run	*Playing sports*
Stand on Heels	*Walking on uneven ground, cycling, difficulty getting out of a chair, striding, cycling*
Rise from Floor	*Getting up after falling, playing on the floor with children*
Gets to Sitting	*Sitting up in bed, adjust to falls*
Climb Box Steps	*Independent outdoor mobility particularly easy tasks like stairs and sidewalk curbs*
Stand on one Leg	*Dressing oneself, putting on shoes/socks while standing, reaching high shelves*
Stand from Chair	*Using a toilet independently, getting out of bed, using public transportation to get around*
Walk	*Walking to mailbox to pick up mail, hiking, everyday mobility*
Stand	*Grooming, preparing meals, adapting to mobility device, transferring to chair*

What Does a Nominal NSAA Mean to an Individual with Becker?

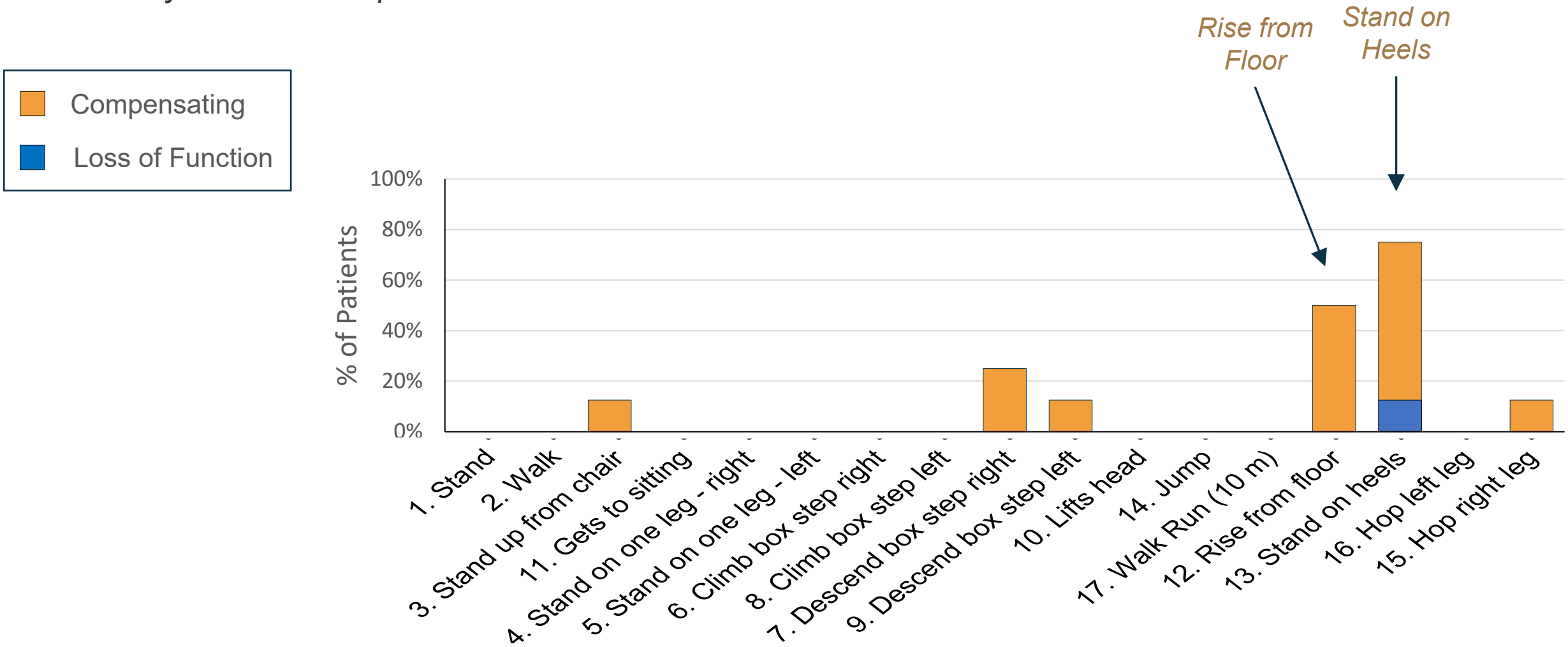
- Data: NSAA scores in 39 ambulatory adults enrolled in Edgewise studies
  - Grouped by baseline scores: ≥30, 20-29, 10-19, <10
- Methods:
  - At different NSAA scores, what functions are completely lost?
  - What functions require some degree of compensation because of weakness?
- Note this is a cross-sectional look at function, but from natural history studies, once decline begins, the decline in NSAA is about 1.2 points/ year

Natural History: Once Declining, Decrease of ~1.2 NSAA Points/Year



Group 1: Baseline NSAA 30 – 34
Can complete all functions

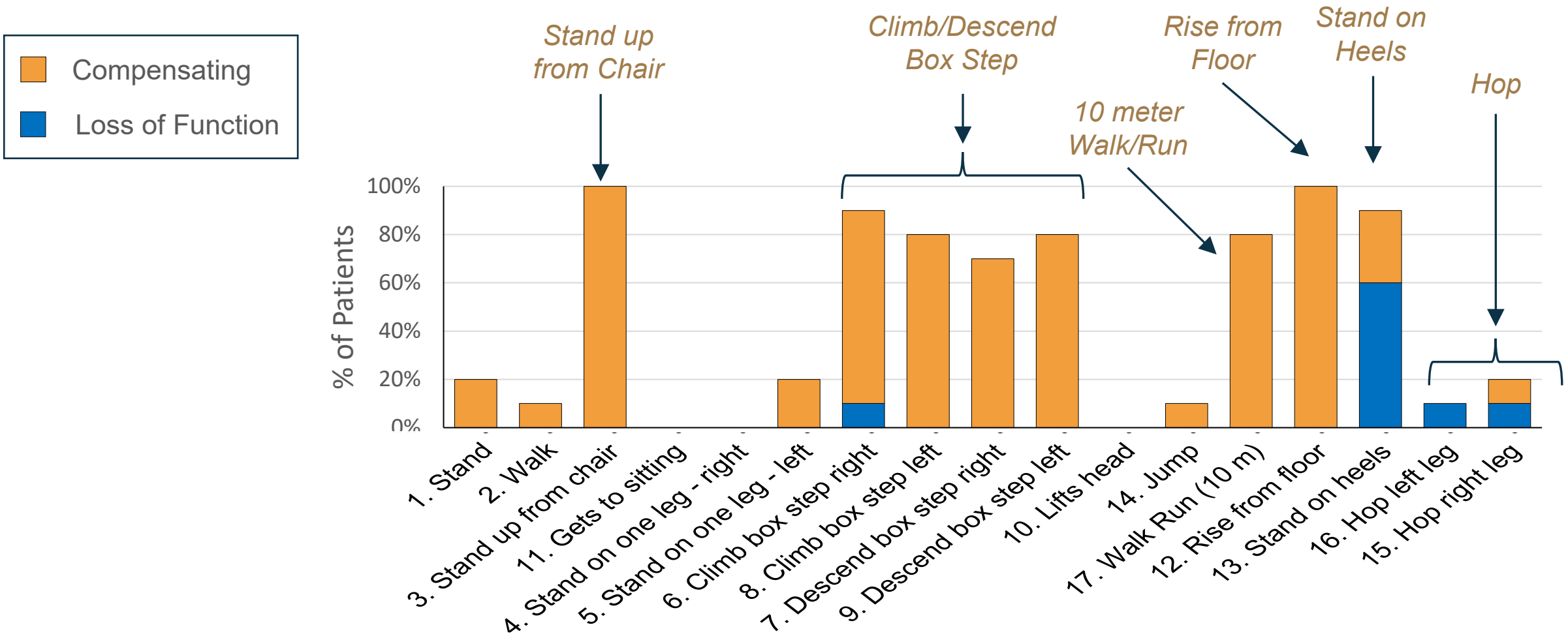
– *May need to compensate for certain functions because of weakness:*



Group 2: Baseline NSAA 20 – 29

Can complete most functions but need to compensate because of weakness

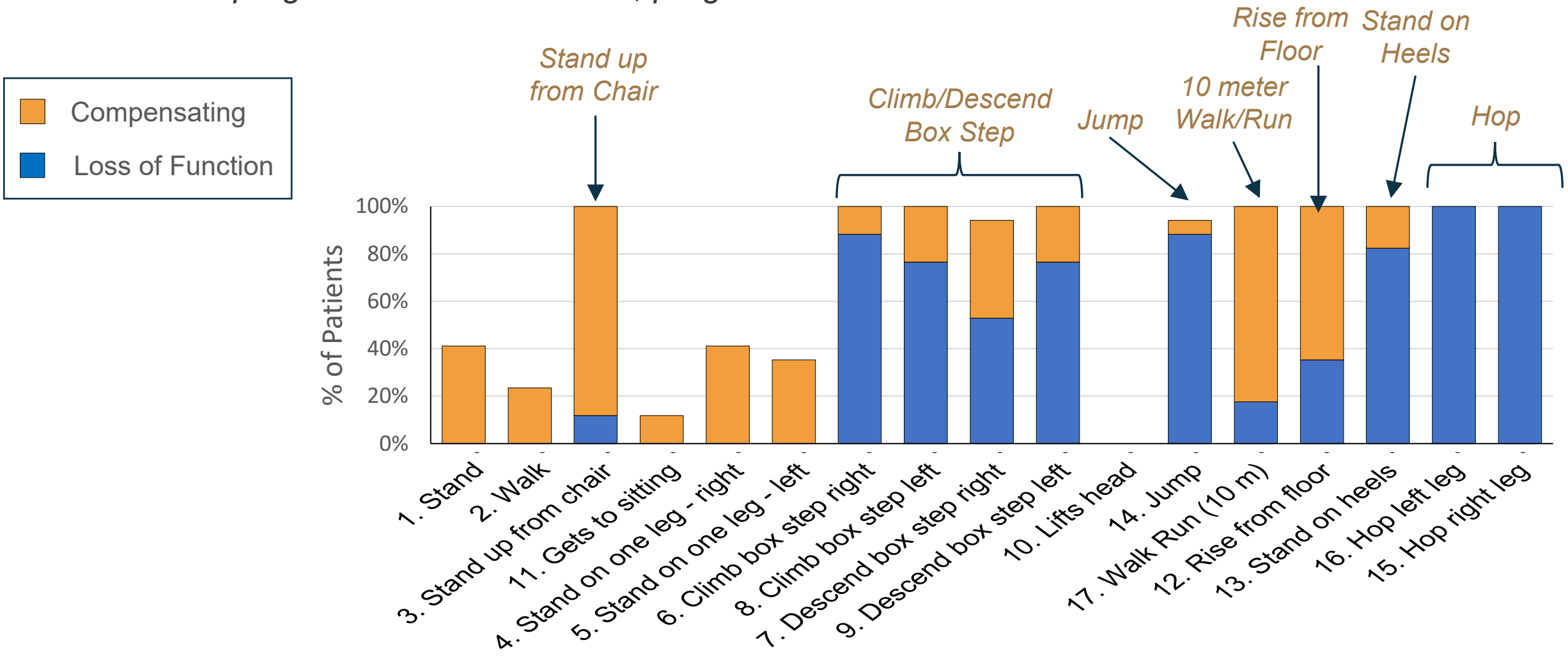
— *Reflects progressive loss of muscle, progressive weakness*



Group 3: Baseline NSAA 11 – 20

Unable to complete most functions and need to compensate for almost all functions

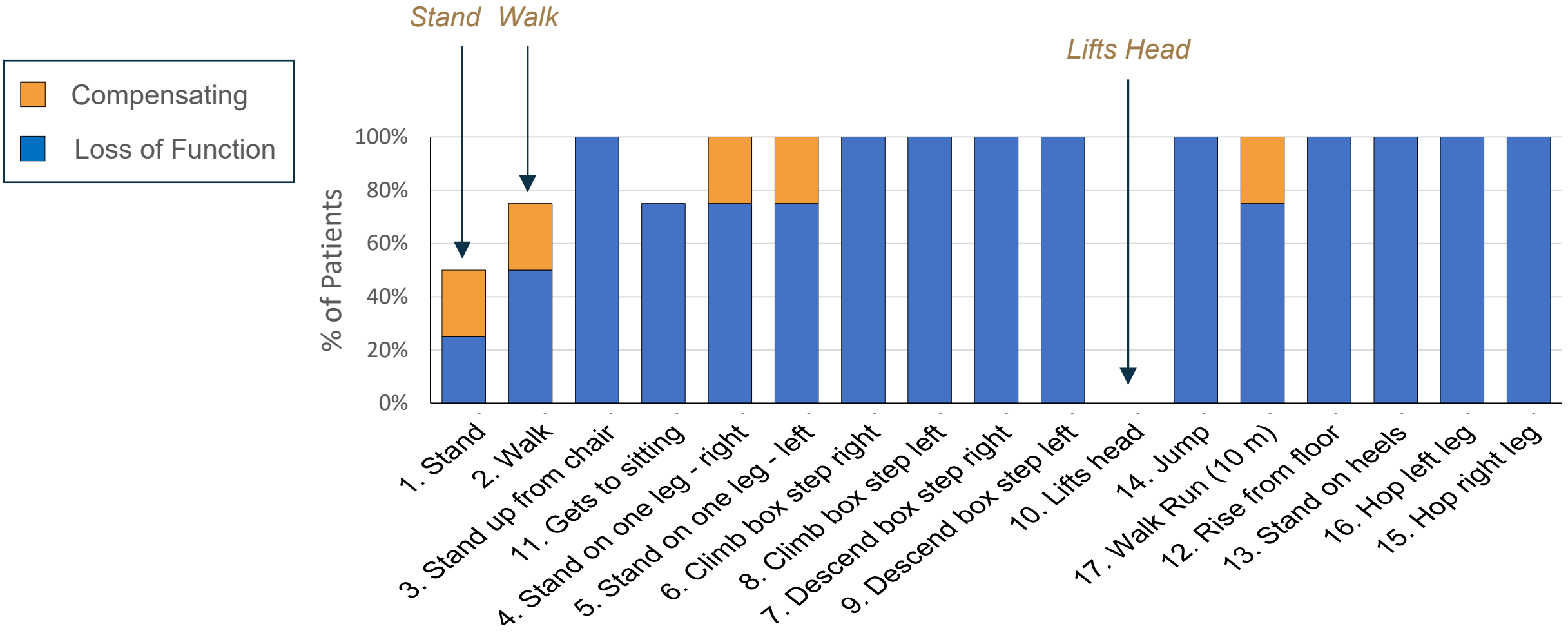
— *Reflects progressive loss of muscle, progressive weakness*



Group 4: Baseline NSAA 0 – 9

Minimal ability to complete typical ambulatory activities

— *Further loss of muscle, progressive weakness, near non-ambulatory*



Key Takeaways

- Becker muscular dystrophy is a serious dystrophinopathy. Once function begins to decline, individuals continue to irreversibly lose muscle and their disease progresses.

- Stabilizing function or even reducing the slope of decline is an important goal in Becker muscular dystrophy.

Next Steps

Joanne Donovan, MD, PhD
Chief Medical Officer
Edgewise Therapeutics

A Pivotal Study in Becker

A global 18-month trial to evaluate the safety and efficacy of EDG-5506 in individuals living with Becker

Population:

- ✓ Male, ages 18-50
- ✓ Genetic diagnosis of Becker
- ✓ Ambulatory with NSAA 5-32

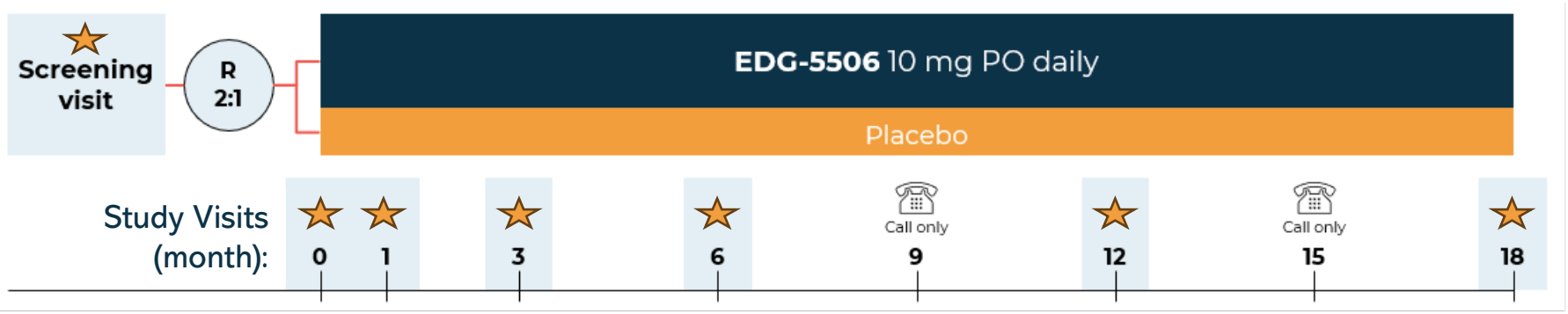
Primary endpoint:

- ✓ NSAA

Additional endpoints:

- ✓ TFT's, MRI, biomarkers, PROs

Visit Schedule



Edgewise THERAPEUTICS

Questions?

It's time to **get real** about **Becker muscular dystrophy**

BECKER EDUCATION & ENGAGEMENT DAY | SATURDAY DEC 2 2023

A day for individuals with Becker and their families

UF ReveraGen BioPharma · Edgewise Therapeutics · VCU · University of Pittsburgh · UC DAVIS HEALTH Department of Physical Medicine and Rehabilitation · Parent Project Muscular Dystrophy · IMAGING NMD · Children's Hospital Colorado · Department of Neurology School of Medicine University of Colorado Anschutz Medical Campus

MARK YOUR CALENDAR!

Registration Link and More Information Coming Soon

Acknowledgements:

Study Participants and their families

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