Spotlight on Becker Muscular Dystrophy: Understanding the Lived Experience of Becker and Clinical Advancements with a Novel Agent

Symposium at the Muscular Dystrophy Association (MDA) Clinical & Scientific Conference

Dallas, Texas

Tuesday March 18, 2025

Edgewise THERAPEUTICS

This presentation is intended for healthcare providers only

Program Overview

Introduction
Joanne Donovan, MD, PhD

Shedding light on the lived experience of Becker muscular dystrophy
Michael Voto Jr. and Abby Bronson (moderator)

Natural history of Becker muscular dystrophy
Craig McDonald, MD

Clinical advancements with a novel agent: Sevasemten clinical program update
Craig McDonald, MD

Panel Discussion
Joanne Donovan, MD, PhD (moderator)

Craig McDonald, MD
Professor and Chair, PM&R
U of California Davis, CA

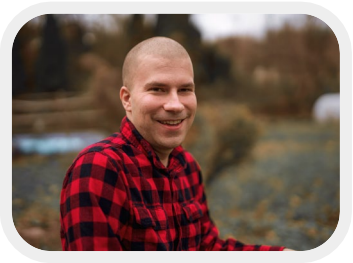
Michael Voto Jr.
Patient Advocate

Joanne Donovan, MD, PhD
CMO, Edgewise Therapeutics

Abby Bronson
VP, Patient Advocacy,
Edgewise Therapeutics

Sevasemten is an investigational agent that is not approved for use by any regulatory authority in any territory.

Our Goal Is to Positively Impact the Course of Becker Muscular Dystrophy



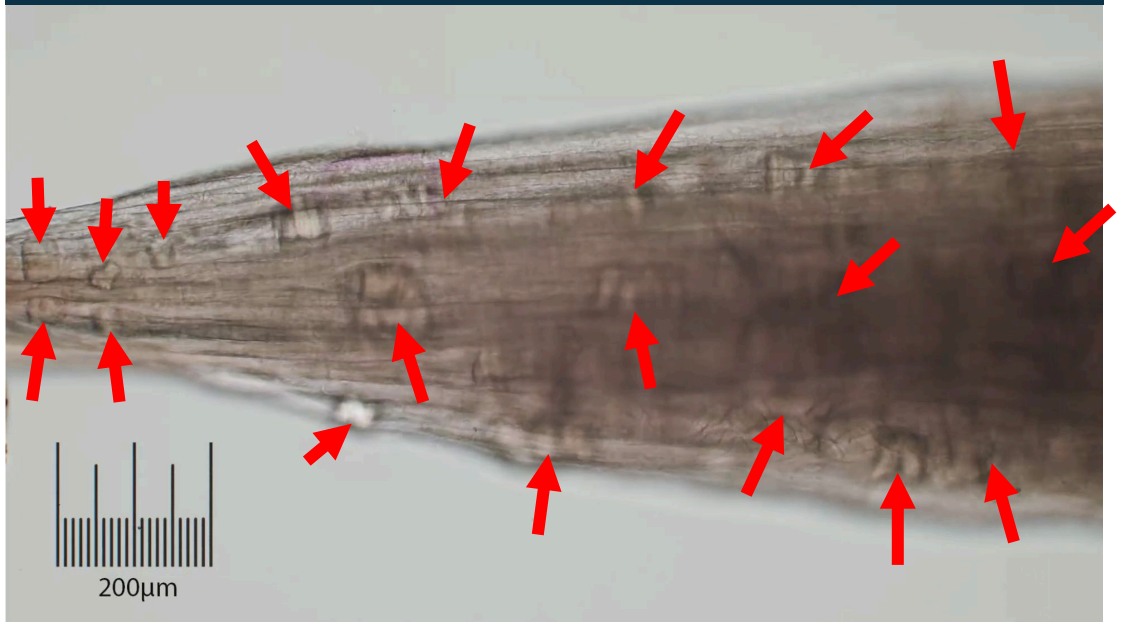
- Becker muscular dystrophy (Becker) is a rare, genetic, life-shortening, debilitating and degenerative neuromuscular disorder
- The disease predominately affects males and imposes significant physical, emotional, financial and social impacts on the individuals and their caregivers
- Individuals with Becker lose mobility, function and independence in the prime of their lives
- There is currently no treatment for Becker

> ***"I was told, 'You're lucky you don't have Duchenne.' It's frustrating that you live longer, but you are constantly going downhill"***
>
> – Individual living with Becker

NIH Genetics Home Reference - Duchenne and Becker muscular dystrophy; Romitti PA et. al., Pediatrics, 2015; Bushby KM, et. al., Lancet, 1991; Salari N, et. al., J Orthop Surg Res, 2022; : J Med Genet 2016;53:145–151; Lancet, 337 (8748), 1022–1024; J Orthop Surg Res 17, 96 (2022)

Sevasemten Targets Fast Myosin to Protect Dystrophic Muscle Against Contraction-Induced Injury in *mdx* Mice

Contracting at 100% without sevasemten



In *mdx* mouse muscle, even a few contractions cause visible injury

Contracting at 85% with sevasemten

By minimally decreasing contraction, while preserving function, contraction-induced injury is prevented

Both videos have been sped up 3x

Russell AJ, et al. J Clin Invest. 2023;133(10):e153837. doi:10.1172/JCI153837

Sevasemten Clinical Program: Completed and Ongoing Clinical Trials

Becker

ARCH	**Phase 1 Becker** N=12	*Open-label, safety, PK, function* → *OLE*	***Completed***
DUNE	**Phase 2 Becker, LGMD2i, & McArdle** N=21	*Exercise challenge study* → *OLE*	***Completed***
CANYON	**Phase 2 Becker** N=69	*Biomarkers, safety, function* → *OLE*	***Completed***
GRAND CANYON	**Pivotal Cohort Becker** N=175	*Function, biomarkers , safety* → *OLE*	***Active, not recruiting***
MESA	**Becker Open Label Extension Study**	*Open-label long-term safety, biomarkers, function*	***Enrolling by invitation***

Duchenne

LYNX	**Ph 2 Duchenne Dose-Ranging** N=76	*PK, biomarkers, safety* → *OLE*	***Active, not recruiting***
FOX	**Ph 2 Duchenne Boys on Gene Tx** N=48	*PK, biomarkers, safety* → *OLE*	***Active, not recruiting***

Shedding Light on the Lived Experience of Becker Muscular Dystrophy

Michael Voto Jr.
Patient advocate who lives with Becker muscular dystrophy

Abby Bronson (Moderator)
VP, Patient Advocacy, Edgewise Therapeutics, US

Disclosures

Michael Voto was reimbursed for all expenses related to his participation as a speaker in this session.

Listening to the Needs of the Becker Community is Important

Some common reasons cited by patients for their lack of motivation to seek care:

- Do not “know they need help until they do”
- Feel that Becker muscular dystrophy is often ignored by the community
- Do not accept inevitable severity of disease
- Do not realize that they are declining; lack of awareness that cardiac and other health complications can occur before muscular decline

Becker, Becker muscular dystrophy
Reference: Patient stories from Becker Education and Engagement Day (BEED) events

A Recent Survey was Conducted with Becker Patients

Primary research survey conducted with 50 persons in the US impacted by Becker

- Included persons diagnosed with Becker who were 18 years of age or older (34, or 68%) or their parent/legal guardian (11, or 22%)
- Persons diagnosed with Becker who were between 14 and 17 years old were allowed to participate along with their parent/legal guardian (5, or 10%)

Participants were recruited using a variety of methods

- Social media platforms
- Becker educational events
- Individual promotion and outreach

Becker, Becker muscular dystrophy

1. Bronson A, et al. Poster presented at WMS 2024. 2. Patient Survey Conducted by Engage Health 2023.

Results: The Road to a Becker Diagnosis is Often Long and Frustrating for Patients

Major themes were expressed by patients about the challenges of diagnosing Becker:

- **Waiting for a diagnosis:** many in the Becker community are living with symptoms for years before receiving a diagnosis.
- **Can be misdiagnosed:** over one third of patient respondents were originally misdiagnosed.
- **Increased familiarity is needed:** overall awareness of Becker is needed.

> "*… I could have been diagnosed sooner.*"
>
> – patient survey response

> "*This diagnosis was presented as "mild," but it feels SO BIG.*"
>
> – patient survey response

An accurate diagnosis of Becker can mean appropriate care can start earlier.

Becker, Becker muscular dystrophy

1. Bronson A, et al. Poster presented at WMS 2024. 2. Patient Survey Conducted by Engage Health 2023.

Results: Living with Becker has Many Unseen Challenges

Pain, fatigue, and isolation felt on a daily basis by patients living with Becker are often unseen

- **Pain and fatigue:** very prevalent and often impact day-to-day life while not being visible to others
- **Emotional strain:** significant mental strain associated with having to carefully consider every activity and the way it affects pain, fatigue, and muscle weakness
- **Education and employment:** navigating school systems and advocating for accommodations are taxing for parents and children living with Becker
- **Finding community:** those in the Becker community desire opportunities to connect with others impacted by Becker

Patient Responses to "Where Do You Receive Support?"

Family

Friends

Others impacted by Becker

Healthcare professionals

Patient advocacy groups

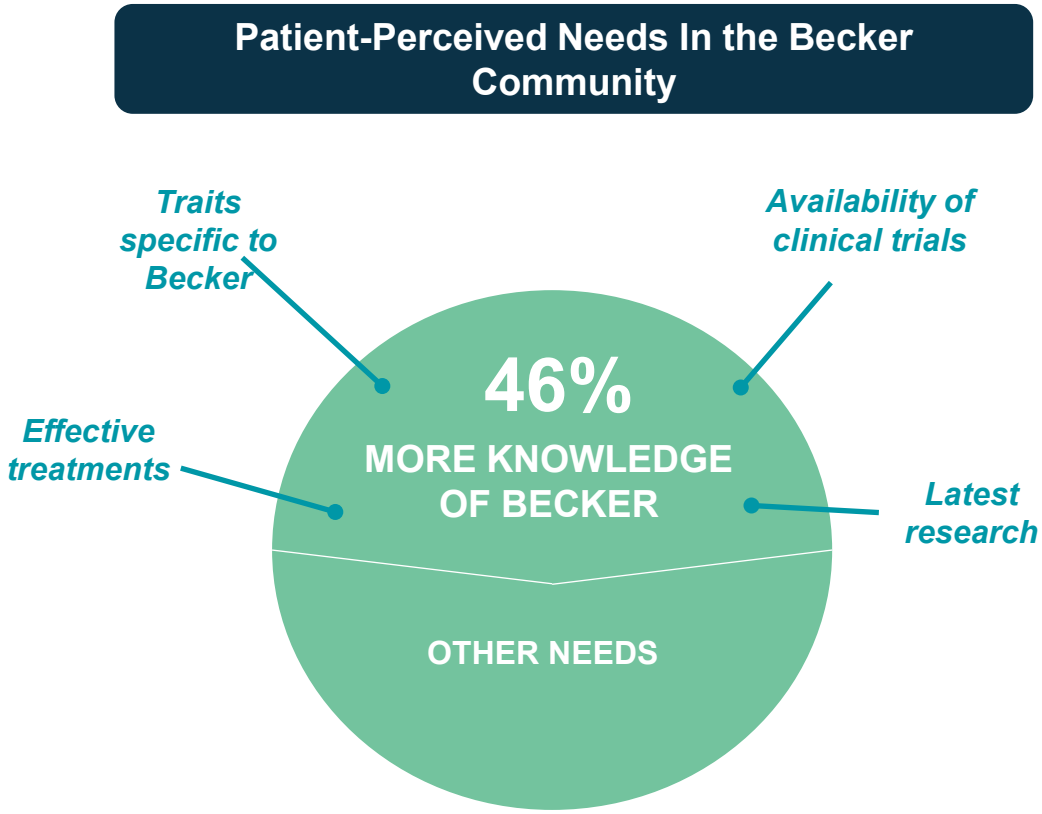
Becker significantly impacts quality of life. Disease specific assessments and considerations are needed.

Becker, Becker muscular dystrophy

1. Bronson A, et al. Poster presented at WMS 2024. 2. Patient Survey Conducted by Engage Health 2023.

Results: Gaps in Care and Support Lead to Uncertainty and Frustration

- **Specialty care declines in adulthood:** Specialized care becomes less consistent around the same age that symptoms often escalate
- **Cardiac care is important:** Cardiac issues are the most pressing health concern for patients
- **Pain management:** a majority of those in the Becker community experience pain and patients would benefit from increased discussions about proper management
- **Research & Clinical Trial Education:** Dedicated research and education is desired by the Becker community



Consistent care and increased knowledge about Becker continue to be needs expressed by patients.

Becker, Becker muscular dystrophy

1. Bronson A, et al. Poster presented at WMS 2024. 2. Patient Survey Conducted by Engage Health 2023.

Incorporating the Becker Community Voice Into Activities and Clinical Programs Is Impactful and Important

Key Takeaways:

- Care and access to care is variable for patients living with Becker
- Continued need for Becker specific information overall
- Need for a standard of care and care guidelines
- Desire for the healthcare community to incorporate the patient voice in clinical program and activities to increase awareness of the disease burden

  Examples:
  - Becker Education & Engagement Day
  - TREAT-NMD Expert Becker Muscular Dystrophy
  - Incorporating patient input into shaping the sevasemten clinical program

Becker, Becker muscular dystrophy

Natural History of Becker Muscular Dystrophy

Craig McDonald, MD
Professor and Chair
Department of Physical Medicine & Rehabilitation
Professor of Pediatrics
Director of MDA Neuromuscular Disease Clinics
University of California Davis Health

Disclosures

Sevasemten is an investigational agent that is not approved for use by any regulatory authority in any territory.

Professor McDonald has served on Advisory Boards, done consulting work on Becker and Duchenne muscular dystrophy clinical trials, and has received research funding for the conduct of clinical trials from Edgewise Therapeutics.

Natural History is Important to Our Understanding of Disease Progression, Patient Care, and Clinical Trial Development

Disease Progression

Provides the communities with an increased understanding of the disease progression

Prognostic Purposes

- Clinical and genetic counseling
- Identification of prognostic markers (inclusion criteria)
- Insights about pathology (therapeutic targets)

Functional Change Measures

- Insightful for powering and designing clinical trials

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

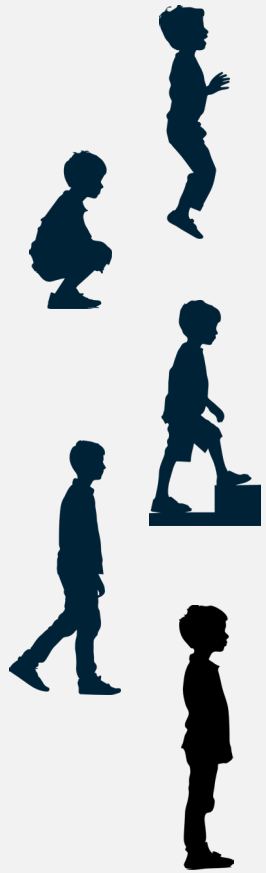
Composite evaluation of motor function across 17 tests with increasing difficulty

- Hop left leg
- Hop right leg
- Stand on heels
- Rise from floor
- Run
- Jump
- Lift head
- Descend box step (L)
- Descend box step (R)
- Climb box step (L)
- Climb box step (R)
- Stand one leg (L)
- Stand one leg (R)
- Get to sitting
- Rise from chair
- Walk
- Stand

Hardest → Easiest

Each activity is scored on whether it can be completed

+2 pts	Perform normally
+1 pts	Perform with compensation due to weakness
0 pts	Cannot perform



Real-world implications for Becker individuals

Measure	Activity
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
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
Gets to sitting	Sitting up in bed, adjust to falls
Rise 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

How a 1-Point NSAA Change in Becker Could Be Interpreted

For individuals living with Becker, **this decline could look like:**

From using stairs or steps…

…to requiring assistance from another person or mobility device.

From using the toilet independently…

…to asking for help to get up from the toilet.

From being able to get up from a fall…

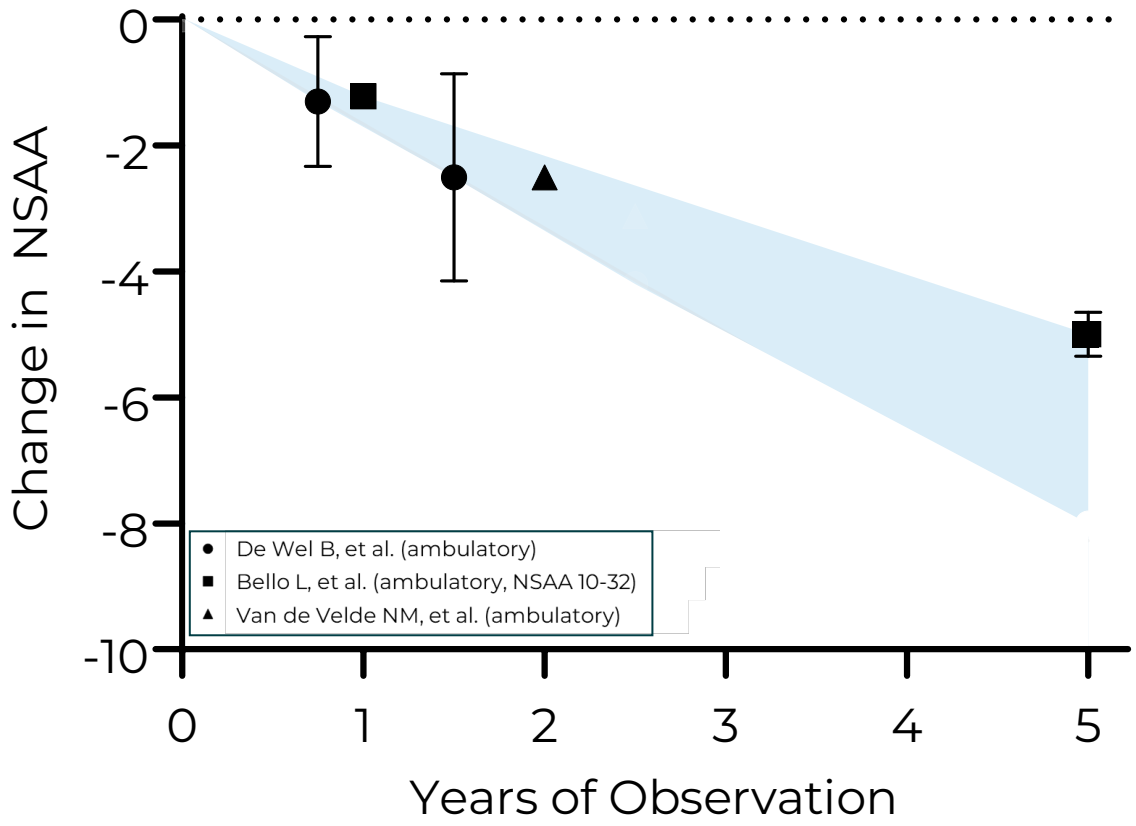
…to requiring someone else's help to get back up.

NSAA, The North Star Ambulatory Assessment

Natural History Data in Becker Supports That Functional Decline, Measured by NSAA, is Consistent and Predictable

Natural history of Becker muscular dystrophy

- The North Star Ambulatory Assessment NSAA) is utilized in muscular dystrophy natural history studies to longitudinally assess function.
- Multiple natural history studies in individuals with Becker demonstrate a **NSAA average score decline of 1.0 to 1.7 points annually**.[1,2,3,4]
- Becker Natural history studies support that NSAA decline is consistent in Becker patients who are already progressing



1. Bello L, et al. 2016. 2. De Wel B, et al. Eur J Neurol. 2024. 3. Van de Velde NM, et al. Neurology. 2021.;4. Bello L et al 2024 WMS; 95% CI shown

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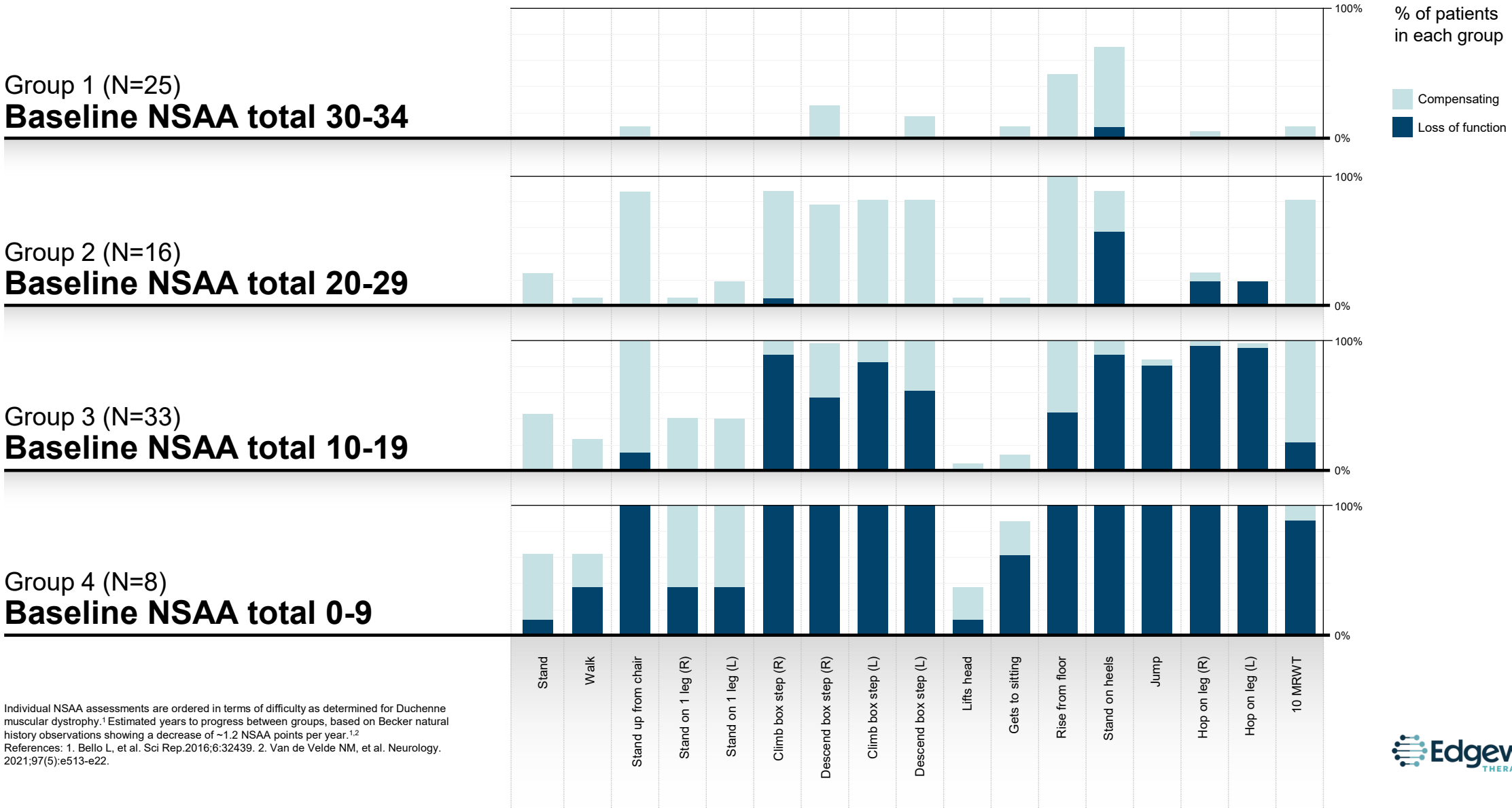
Padova Cohort: Longitudinal NSAA by Mutation Group

5-Year NSAA Changes

Group	n (pts)	n (evals)	Estimate of annual change	SE	p-value
All	89	504	-0.63	0.04	< 0.0001
del 45-48	15	94	-0.74	0.08	< 0.0001
del 45-47	14	80	-1.00	0.08	< 0.0001
del x-51	11	50	-0.03	0.01	0.0007
del 48	12	63	-0.08	0.04	n.s.
del 45-55	5	12	-0.47	0.16	n.s.
del 48-49	3	14	-1.35	0.16	< 0.0001
nonsense	2	24	-0.38	0.10	0.002

Bello L, et al. Poster presented at WMS. 2024

Individuals with Becker Experience Muscle Decline Compensation and Rapid Loss of Function as NSAA Scores Decline



Individual NSAA assessments are ordered in terms of difficulty as determined for Duchenne muscular dystrophy.[1] Estimated years to progress between groups, based on Becker natural history observations showing a decrease of ~1.2 NSAA points per year.[1,2]

References: 1. Bello L, et al. Sci Rep.2016;6:32439. 2. Van de Velde NM, et al. Neurology. 2021;97(5):e513-e22.

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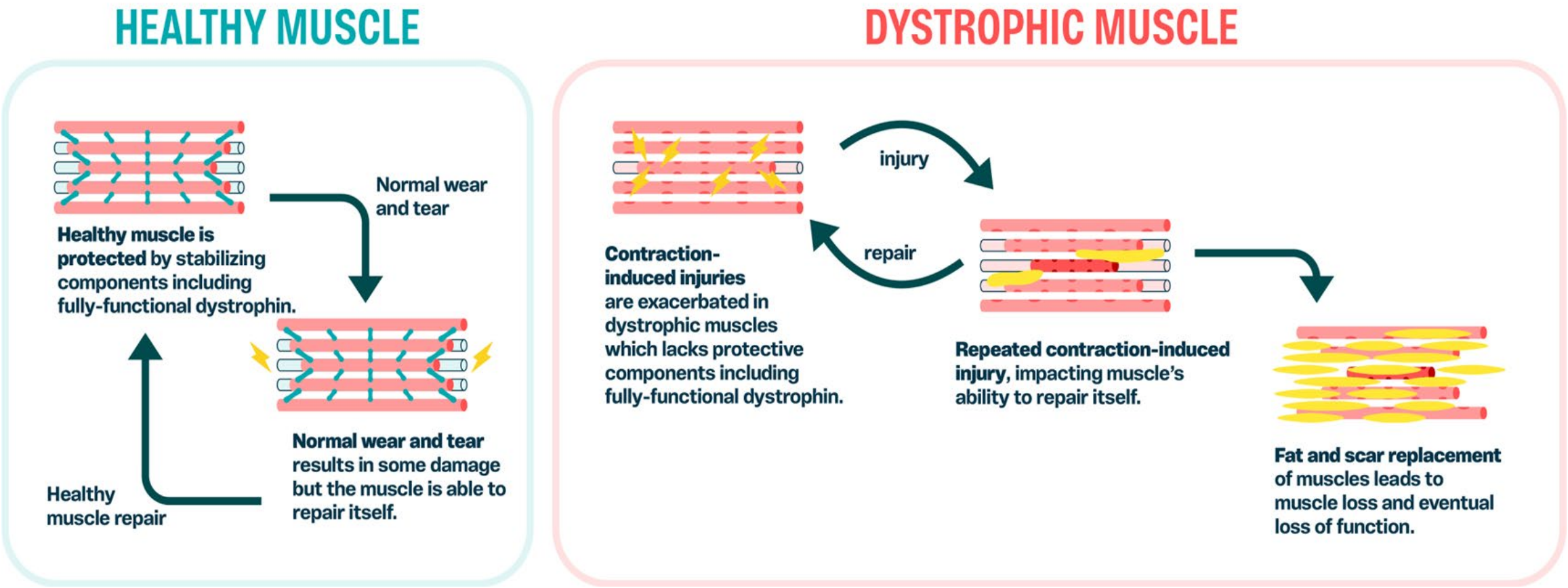
Becker Natural History: Key Takeaways

- Becker muscular dystrophy is a serious muscular dystrophy.
- NSAA is a clinically meaningful functional measure utilized in muscular dystrophy natural history studies to longitudinally assess function.
- Once function begins to decline, individuals continue on an irreversible path to losing muscle and consequently, function.
- Stabilizing function or even reducing the slope of decline is an important and urgent goal in Becker muscular dystrophy.

Clinical Advancements with a Novel Agent: Overview of the Sevasemten Clinical Program

Sevasemten is an investigational therapy that is not currently approved in any territory.

Contraction-Induced Muscle Injury is the Root Driver of Disease Progression in Muscular Dystrophy



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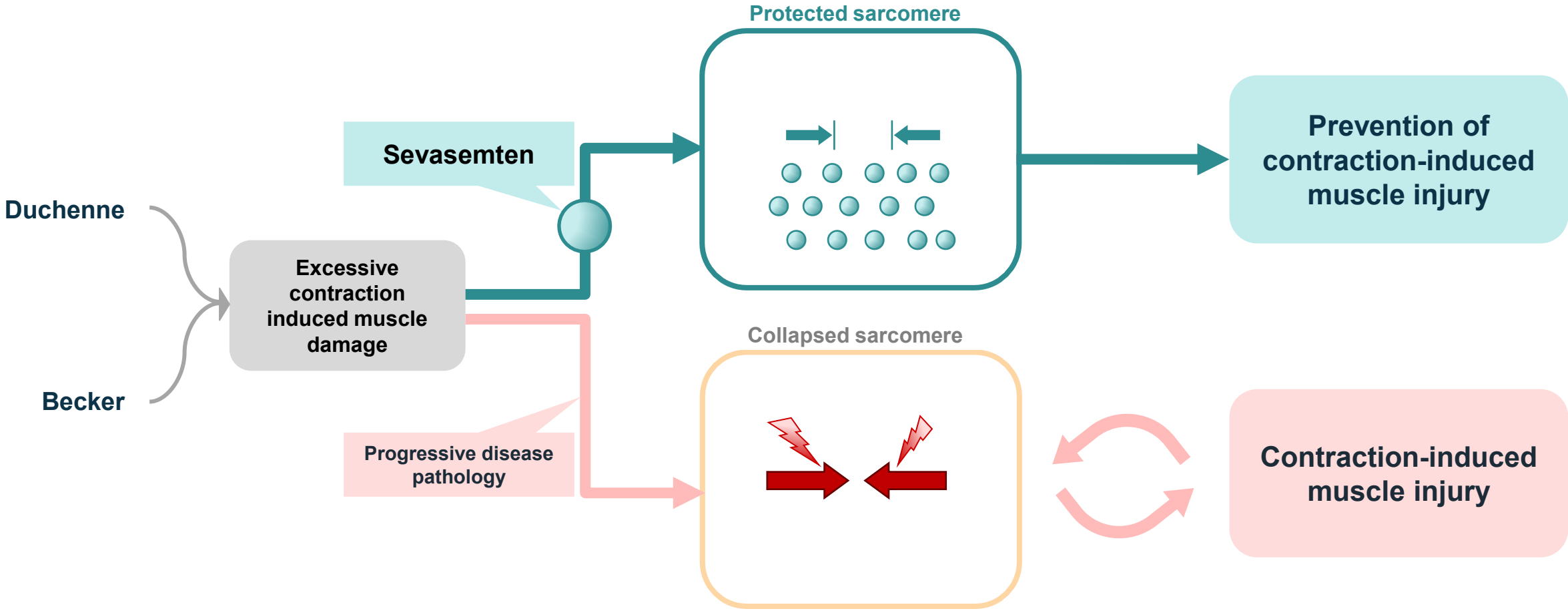
Sevasemten: A First-in-Class Fast Myofiber (type II) Myosin Inhibitor Designed to Protect Against Contraction-Induced Muscle Injury

Sevasemten Therapeutic Hypothesis



Sevasemten is an investigational therapy that is not currently approved in any territory.

The Sevasemten Clinical Program in Becker

Becker, Becker Muscular Dystrophy; LGMD, Limb-Girdle Muscular Dystrophy; NSAA, North Star Ambulatory Assessment; PK, pharmacokinetics

ARCH

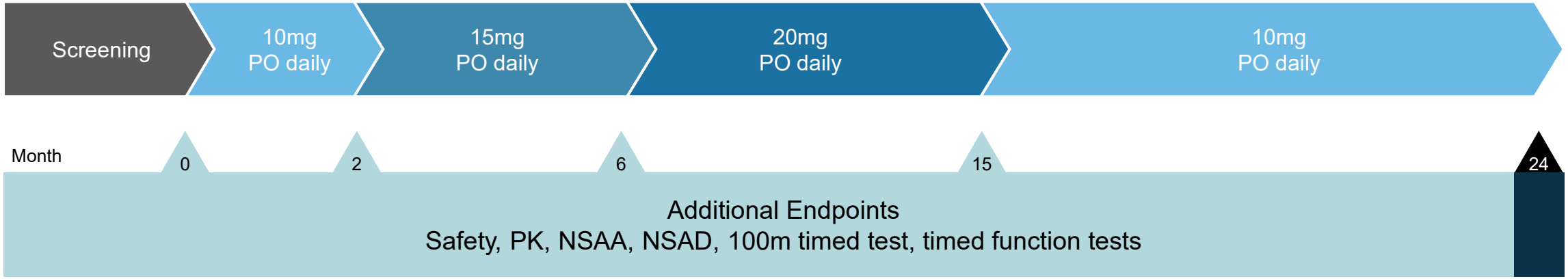
An open-label, single-center study to assess sevasemten safety and pharmacokinetics in adults with Becker

NCT05160415

ARCH An Open-Label, Single-Center Study to Assess Sevasemten Safety and Pharmacokinetics in Adults with Becker

- **Primary objective:** Safety and tolerability at 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
- **Patients enrolled:** 12

Study design - 24 months



Phan H, et al. Oral presentation presented at: American Academy of Neurology; April 13-18, 2024; Denver, CO.

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ARCH Participants Had Significant Functional Impairment & Decreased Muscle Mass at Baseline

CHARACTERISTIC	BECKER PARTICIPANTS (n=12)	AGE NORMATIVE VALUES
Age (SD)	33 (8) 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	55%	>75%

Adults with similar baseline NSAA scores expected to decrease by 1.2 points per year[2,3]

DXA, dual energy x-ray absorptiometry

1. Phan H, et al. Oral presentation presented at: American Academy of Neurology; April 13-18, 2024; Denver, CO.
2. Bello L, et al. Sci Rep. 2016. 3. Van de Velde NM, et al. Neurology. 2021.

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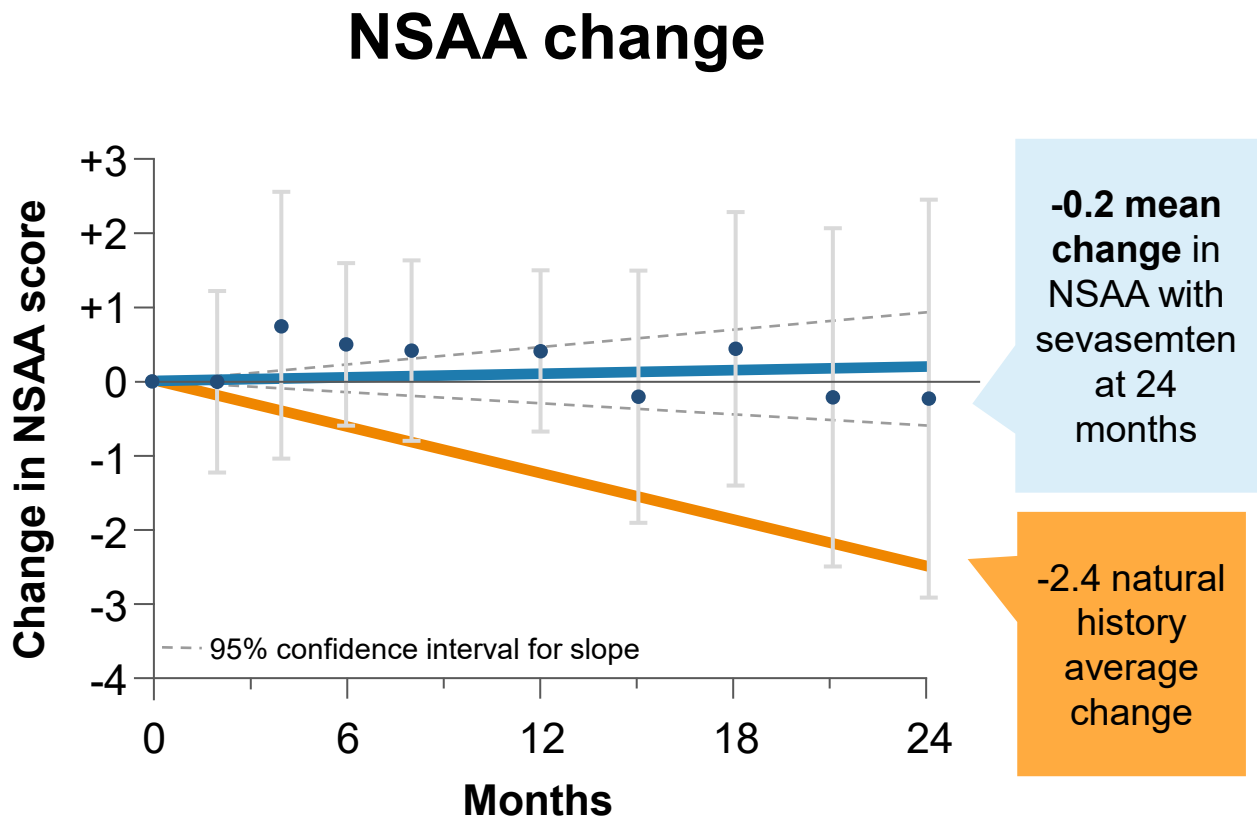
ARCH NSAA Stabilized, Diverging from Natural History at 24 Months

- Early and rapid reductions in CK and TNNI2, biomarkers of muscle damage, were sustained to 24 months.
- Stabilization of functional assessments was seen.
  - NSAA diverged from natural history.
  - No statistically significant change in 100-meter timed test velocity and max grip strength.



CK, creatine kinase; TNNI2, fast skeletal troponin I; NSAA, The North Star Ambulatory Assessment; PK, pharmacokinetics

Phan H, et al. Oral presentation presented at: American Academy of Neurology; April 13-18, 2024; Denver, CO.

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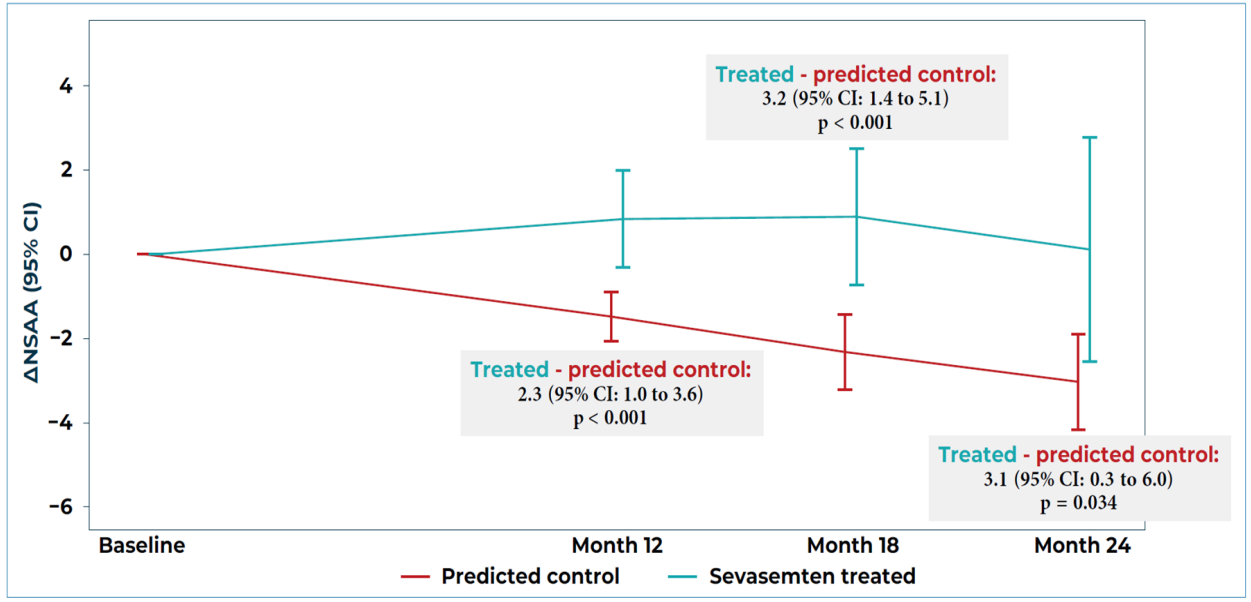
ARCH Predictive Modeling Analysis

- Prediction models for natural history trajectories can provide important benchmarks for the outcomes of patients receiving novel therapies.
- This is especially valuable over multi-year periods in Becker Muscular Dystrophy (BMD) for which placebo controls are not feasible.
- A prediction model for changes in the North Star Ambulatory Assessment (NSAA) total score in BMD patients was developed based on longitudinal natural history data.
- The model was then validated against published studies of independent BMD data.



For more information, please see MDA poster P10 and P11!

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DUNE

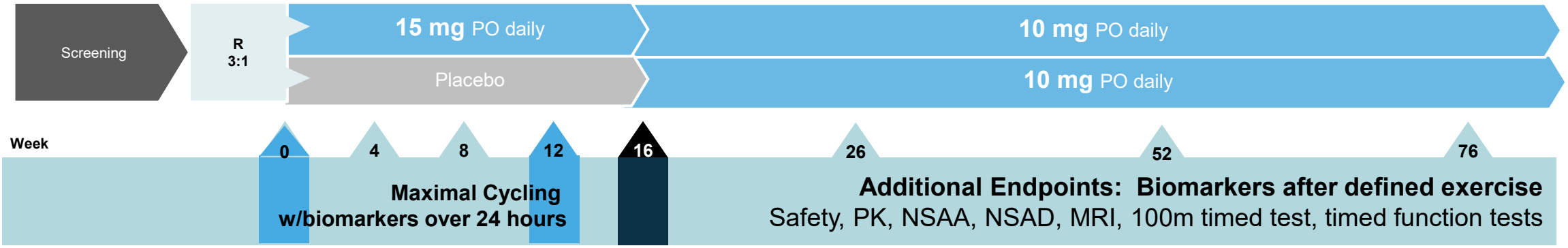
A Phase 2 study of the effect of sevasemten on biomarker response to exercise in adults with Becker muscular dystrophy, McArdle disease, or Limb-Girdle muscular dystrophy

DUNE

A 2-Part, Single-Center Phase 2 Study of Sevasemten in Adults with Becker, McArdle Disease, and Limb-Girdle MD 2I

- **Primary endpoint:** Change from baseline in biomarkers at 16 weeks (interim analysis)
- **Objective:** Does sevasemten reduce elevations in biomarkers of muscle damage after exercise?
- **Key inclusion criteria:** Ambulatory individuals aged ≥ 18 years with confirmation of genetic disease, not on corticosteroids
- **Patients enrolled:** 9 Becker, 9 LGMD 2I, 3 McArdle

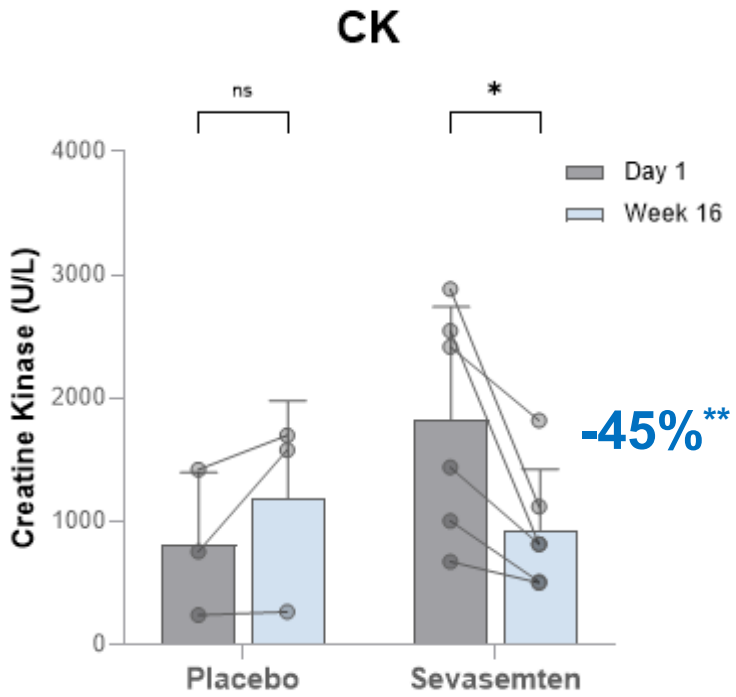
Study design

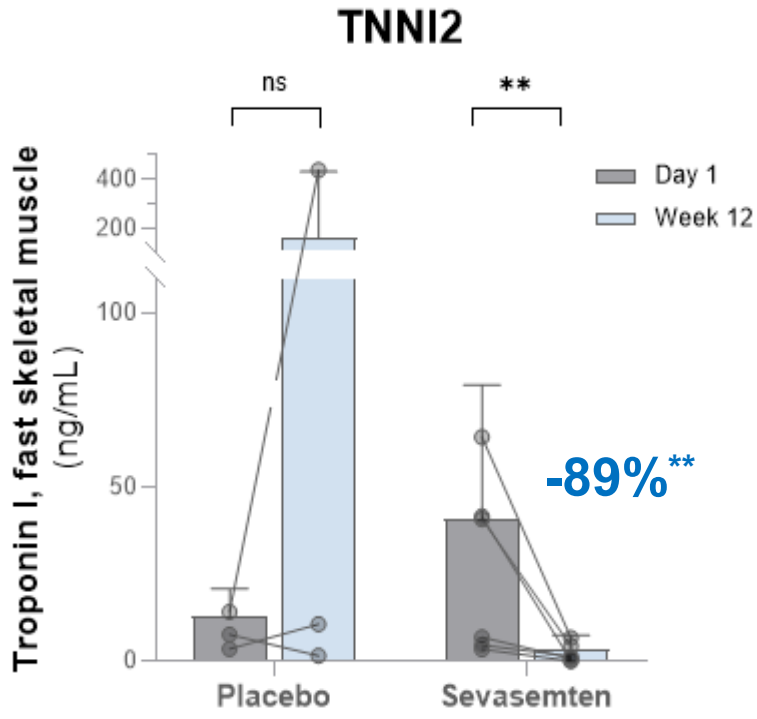


Becker, Becker muscular dystrophy; CK, creatine kinase; R, randomization; HR, heart rate; NSAA, North Star Ambulatory Assessment; LGMD2I, Limb Girdle Muscular Dystrophy; McArdle, McArdle Disease

Stemmerik MG, et al. Poster presented at WMS 2024. #732LBP

In Becker, Sevasemten Significantly Reduced Elevations in Biomarkers of Muscle Damage





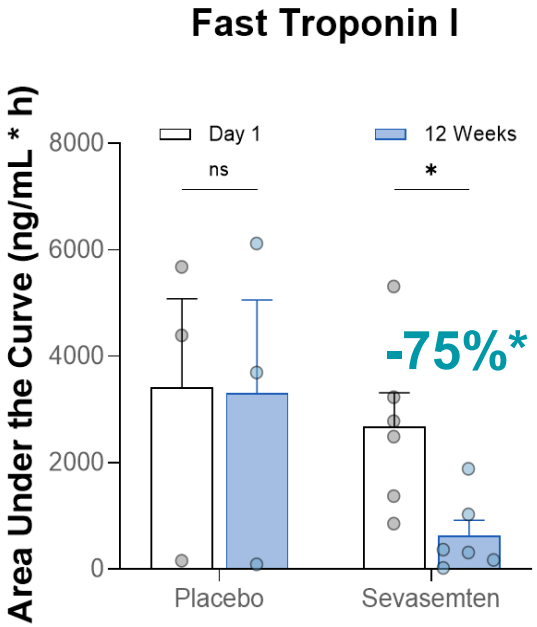
Primary endpoint: CK change from baseline after 16 weeks sevasemten vs. placebo in Becker

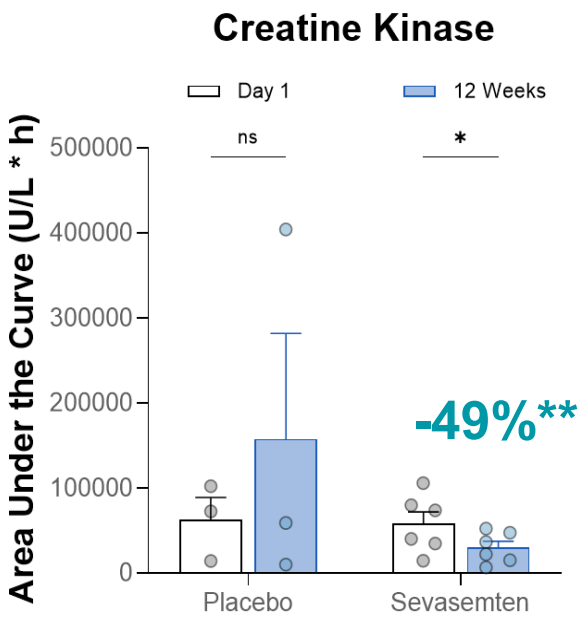
- With sevasemten, CK was significantly decreased compared to baseline(**p<0.01) and compared to placebo (*p<0.05) during a period of normal activity.
- At 12 weeks, with sevasemten, TNNI2 was significantly decreased by 89% compared to baseline (p<0.01) and compared to placebo (p<0.05) during a period of normal activity.

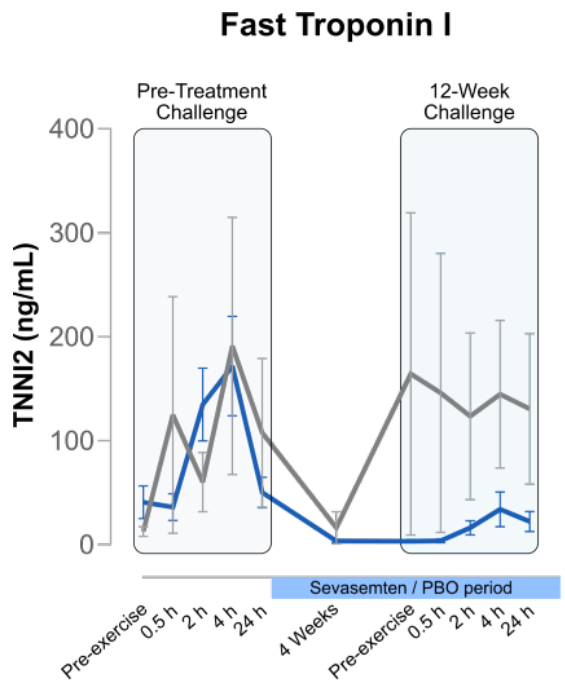
Becker, Becker muscular dystrophy; LGMD2I, Limb Girdle Muscular Dystrophy; McArdle, McArdle Disease; CK, creatine kinase; TNNI2, fast skeletal troponin I
Stemmerik MG, et al. Poster presented at WMS 2024. #732LBP

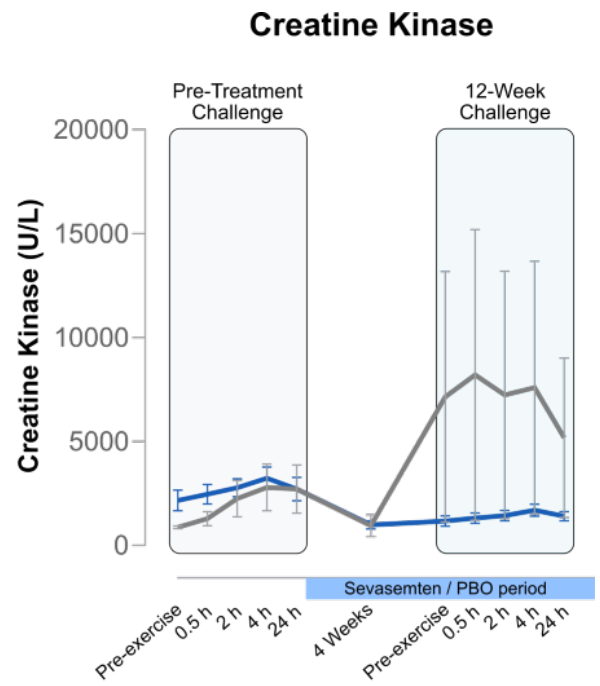
In Becker, Sevasemten Significantly Reduced Post-Exercise Increases in TNNI2 and CK

Area Under the Curve over 24 Hours









- With sevasemten, TNNI2 was decreased in the 24 hours after exercise compared to baseline (*p<0.05) and compared to placebo (p=0.07).
- With sevasemten, CK was significantly decreased in the 24 hours after exercise compared to baseline (**p<0.001).

Becker, Becker muscular dystrophy; LGMD2I, Limb Girdle Muscular Dystrophy; McArdle, McArdle Disease; CK, creatine kinase; TNNI2, fast skeletal troponin I; PBO, placebo

Stemmerik MG, et al. Poster presented at WMS 2024. #732LBP

DUNE Summary

- Sevasemten decreased CK and TNNI2 significantly compared to placebo during a period of normal activity.
- 12 weeks of treatment with sevasemten resulted in significant reductions in the post-exercise increases in multiple biomarkers of muscle injury, including CK and TNNI2.
- Sevasemten was generally well tolerated.

Becker, Becker muscular dystrophy; CK, creatine kinase; TNNI2, fast skeletal troponin I
Stemmerik MG, et al. Poster presented at WMS 2024. #732LBP

CANYON

A multi-center, randomized, double-blind, placebo-controlled, Phase 2 study to evaluate the safety, pharmacokinetics, biomarkers, and functional measures of sevasemten

NCT05291091

CANYON A Phase 2 Multi-Center Study to Assess Sevasemten Safety and Effect on Biomarkers in Adults with Becker

ADULT PRIMARY EFFICACY ENDPOINT

Change from baseline in CK averaged across Months 6, 9 and 12

KEY INCLUSION CRITERIA

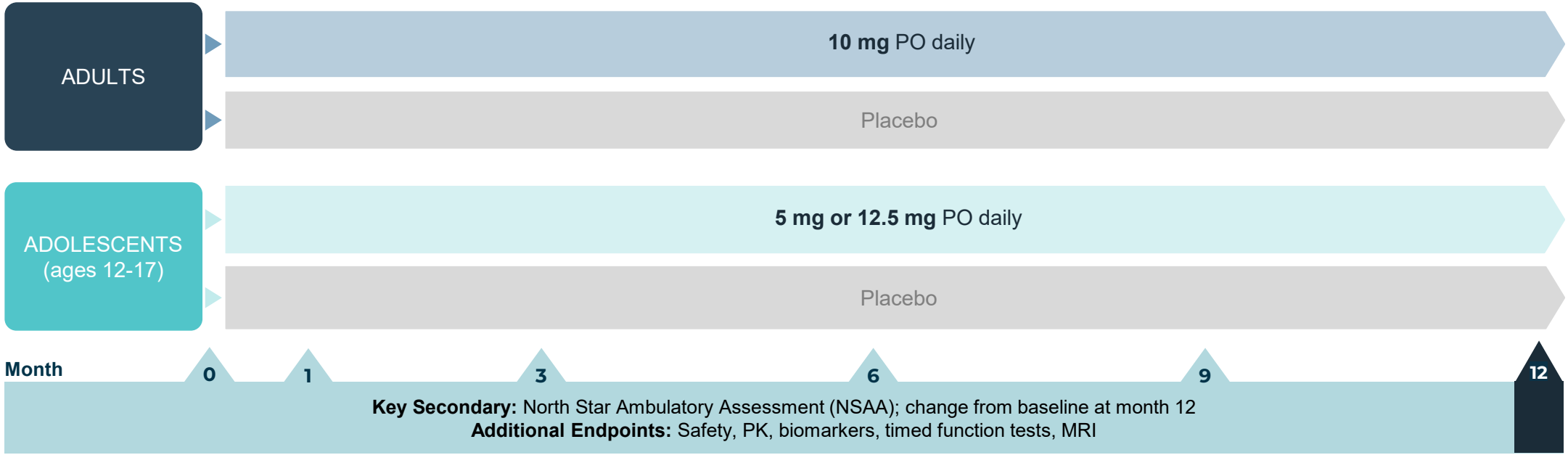
Ambulatory males aged 12 to 50 years with a dystrophin mutation and a Becker phenotype, not on corticosteroids, with a **NSAA between 5-32***

PATIENTS ENROLLED

Adults: **40**

Adolescents: **29**

Study design - 12 months



*Adolescents were not selected based on NSAA

CK, creatine kinase; NSAA, North Star Ambulatory Assessment; PK, pharmacokinetics

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Becker Mutation Overview: Slow Progression Genotypes were Largely Excluded with Functional Cut-Off Criteria

Mutation type	Adults (N=40)	Adolescents (N=29)
Becker mutations associated with progression	**39**	**26**
45-x	20	11
Other	19	15
None/very slow progression Becker mutations	**1**	**3**
X-51	1 (sevasemten)	2 (sevasemten)
Del 48	0	0
45-55 (associates with late myopathy)	0	1 (sevasemten)

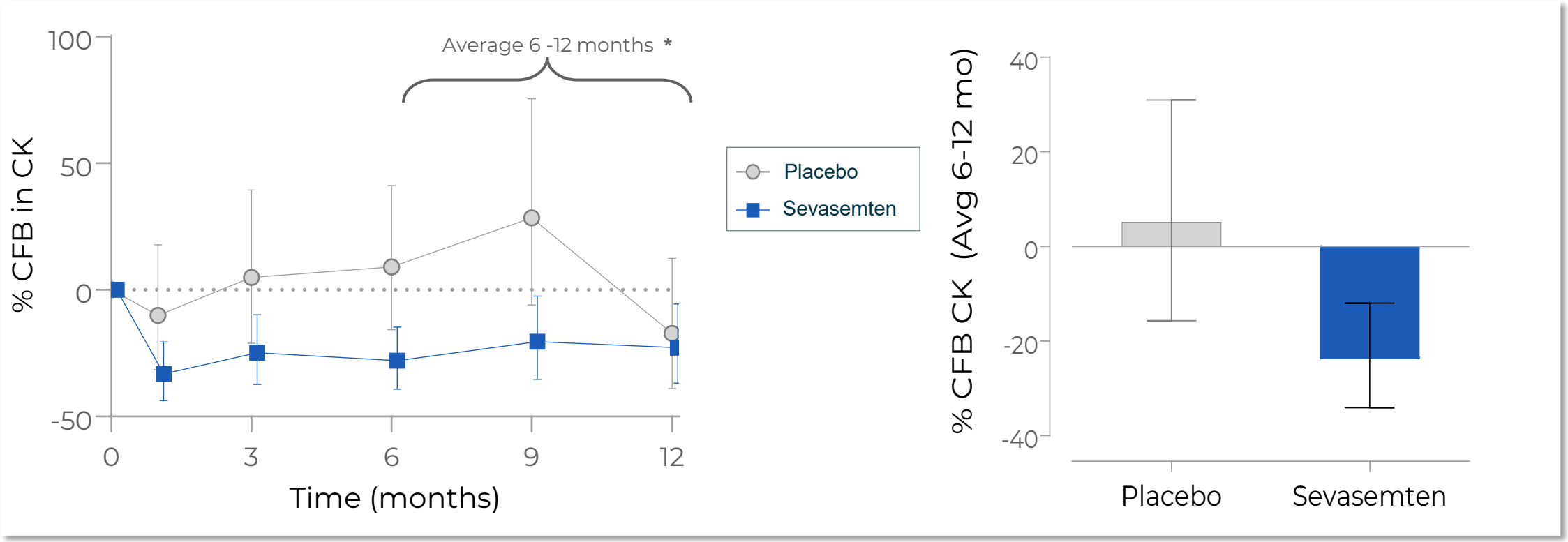
CANYON Functional Measures Not Well Matched at Baseline; Patients in Sevasemten Group had Lower Baseline NSAA

Functional test	Adults Sevasemten (n=28)	Adults Placebo (n=12)	Difference (from placebo)	P-value vs. Placebo
Mean total NSAA score, points (SD)	18.4 (7.66)	24.2 (8.19)	**-5.8**	**0.04**
Mean 4SC velocity, 1/seconds (SD)	0.22 (0.128)	0.34 (0.173)	**-0.12**	**0.02**
Mean RFF velocity, 1/seconds (SD)*	0.14 (0.114)	0.21 (0.128)	**-0.07**	**0.09**
Mean 10MWR velocity, meters/second (SD)	1.52 (0.731)	2.00 (0.884)	**-0.48**	**0.08**
Mean 100MTT velocity, meters/second (SD)	1.50 (0.856)	1.78 (0.782)	**-0.28**	**0.32**

*At baseline, 1 placebo and 9 sevasemten treated participants were unable to rise from floor
100MTT, 100-meter timed test; 10MWR, 10-meter walk/run; 4SC, 4-stair climb; NSAA, North Star Ambulatory Assessment; SD, standard deviation

CANYON Statistically Significant Decrease in the Primary Endpoint of CK: 28% Reduction vs. Placebo

CK between-group difference LSMean: **-28%**
(95% CI -44% to -6%); **p-value = 0.02**

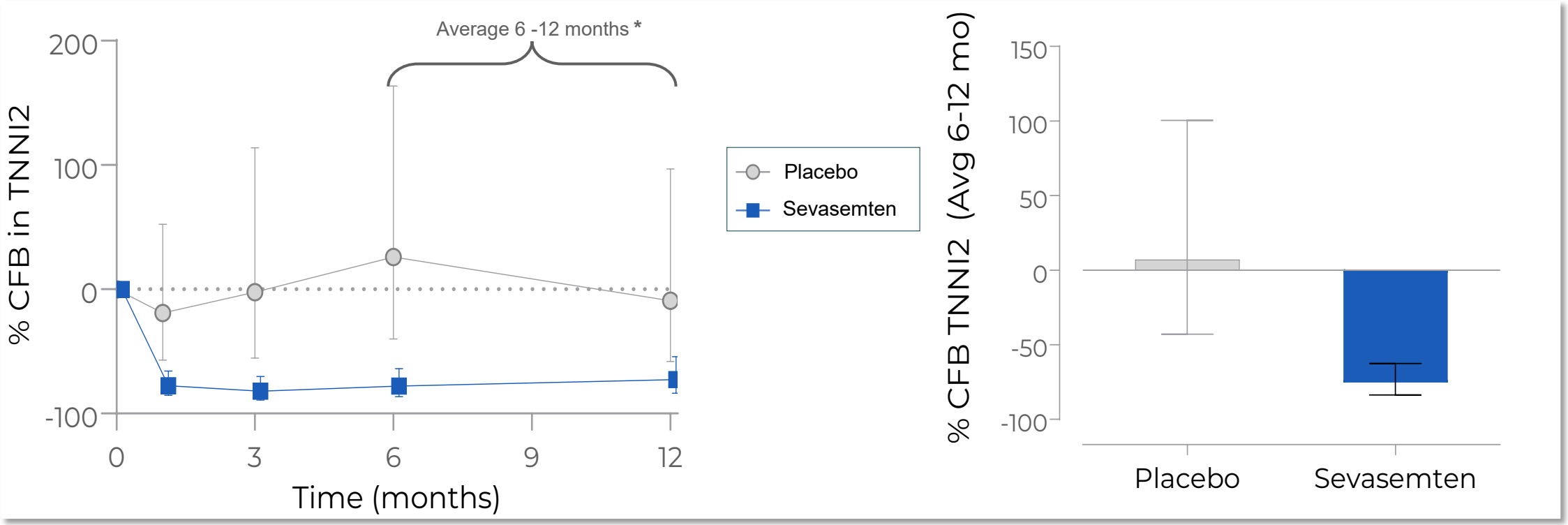


CK showed rapid and sustained decreases with sevasemten treatment

*p<0.05; CK values are log-transformed. LS (least squares) means, LS mean differences and CIs were back-transformed to percent scale
CFB, change from baseline; CI, confidence interval; CK, creatine kinase

TNNI2 Decreased 77% from Baseline in the Sevasemten Treatment Group vs. Placebo

Fast skeletal troponin I (TNNI2) between-group difference LSMean: **-77%**
(95% CI -89% to -51%); **p-value < 0.001**

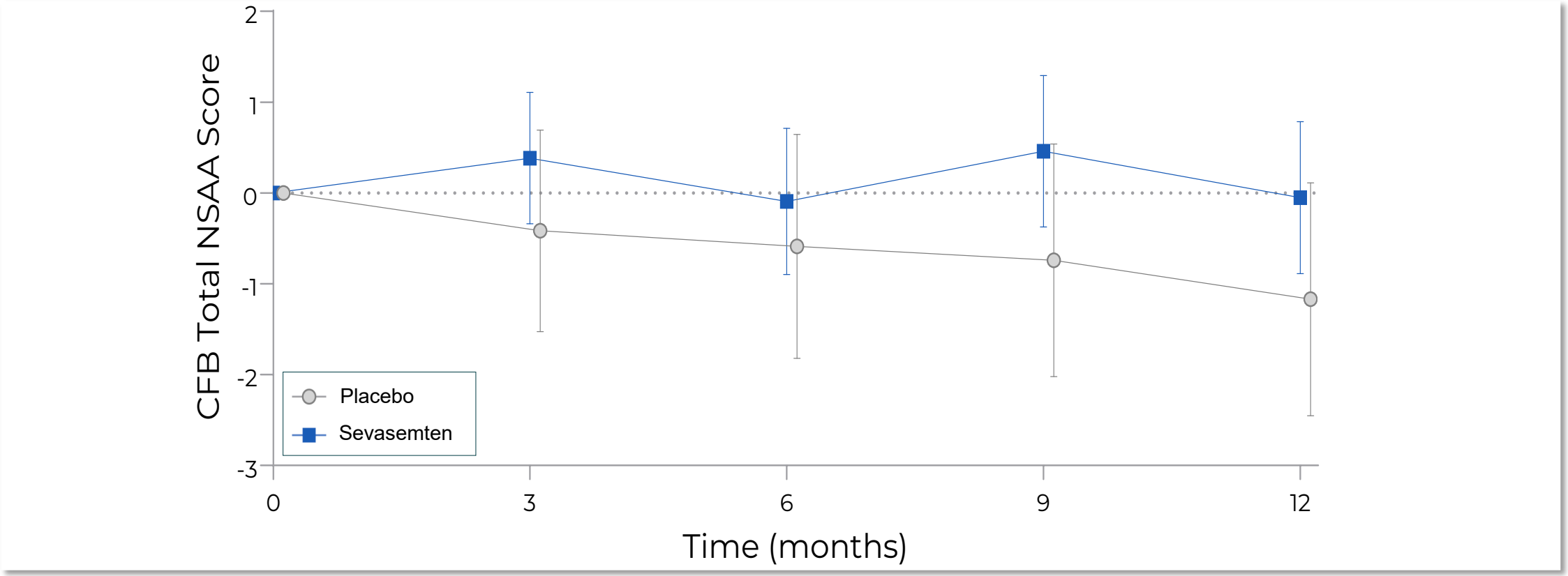


TNNI2, an on-target biomarker of fast muscle fiber damage, also demonstrated rapid and sustained decreases with sevasemten treatment

*p<0.05; TNNI2 values are log-transformed. LS (least squares) means, LS mean differences and CIs were back-transformed to percent scale
CFB, change from baseline; CI, confidence interval; TNNI2, fast skeletal troponin I

Key Secondary Endpoint: NSAA Remained Stable Over Time in Sevasemten Group

NSAA between-group difference LSMean: **1.12**
(95% CI -0.4 to 2.7); **p-value = 0.16**

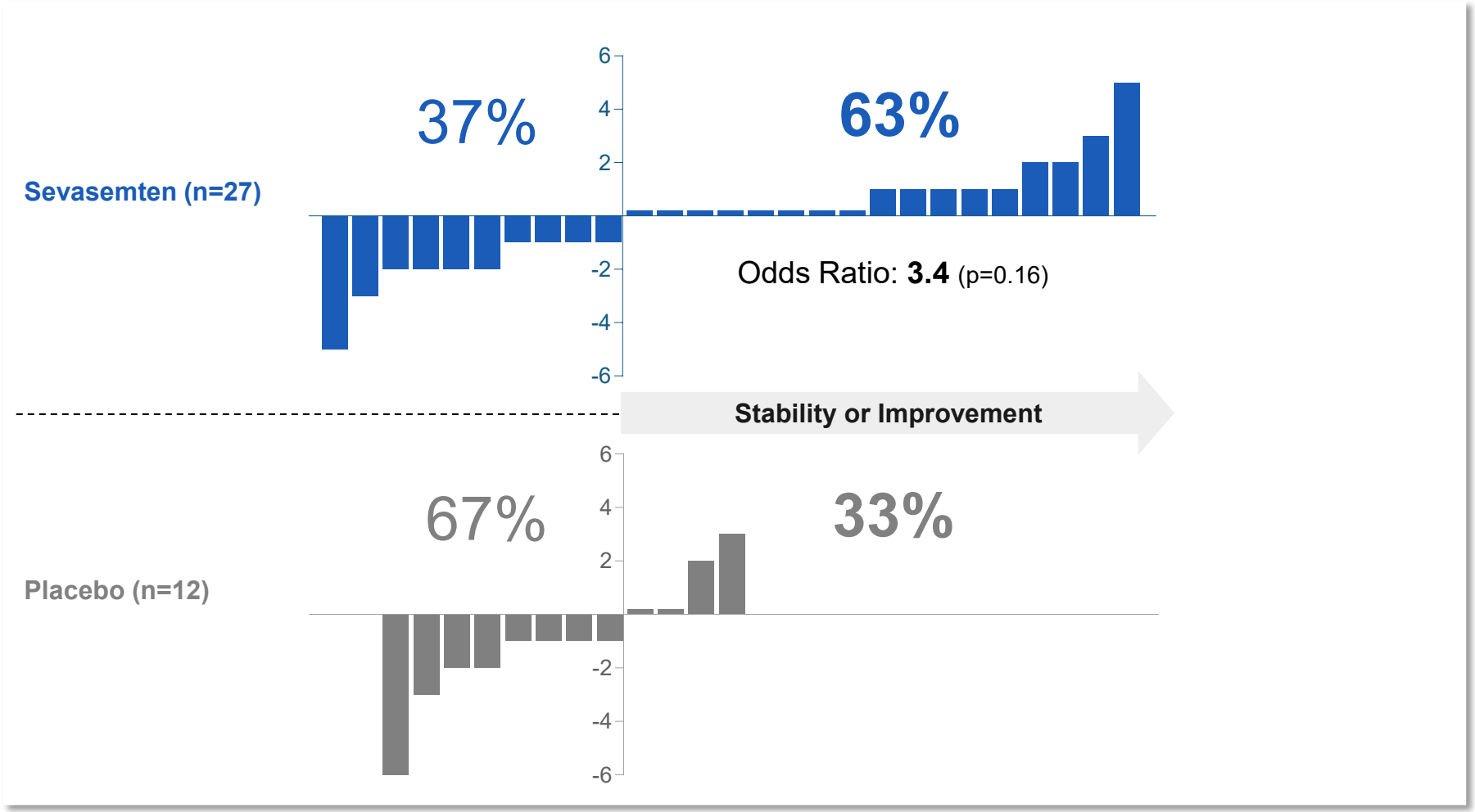


Positive trends in NSAA favoring sevasemten with placebo declining in line with natural history

CI, confidence interval; NSAA, North Star Ambulatory Assessment

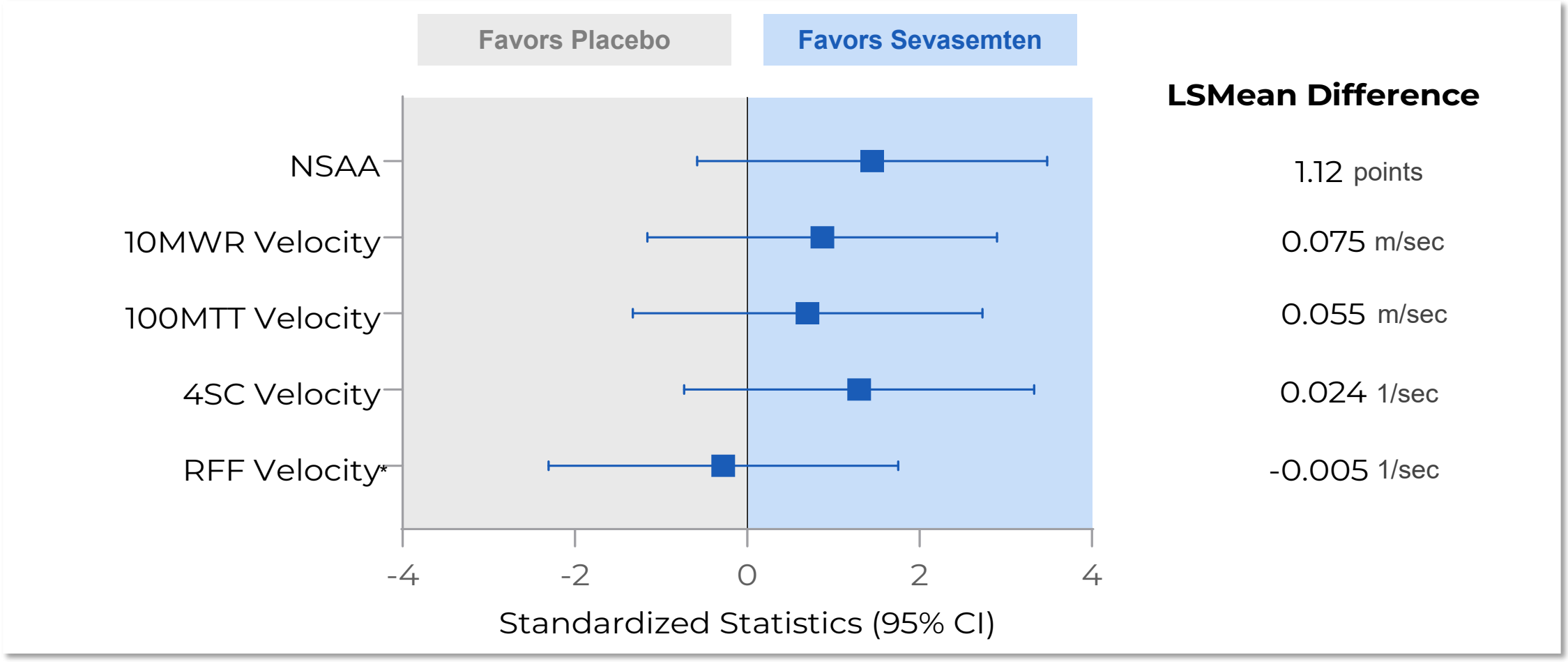
63% of Patients Treated with Sevasemten Showed Stable or Improved Function After 12 Months

Sevasemten NSAA Responder Analysis



CI, confidence interval; NSAA, North Star Ambulatory Assessment

CANYON Trends in Other Functional Measures Favor Sevasemten Treatment Arm

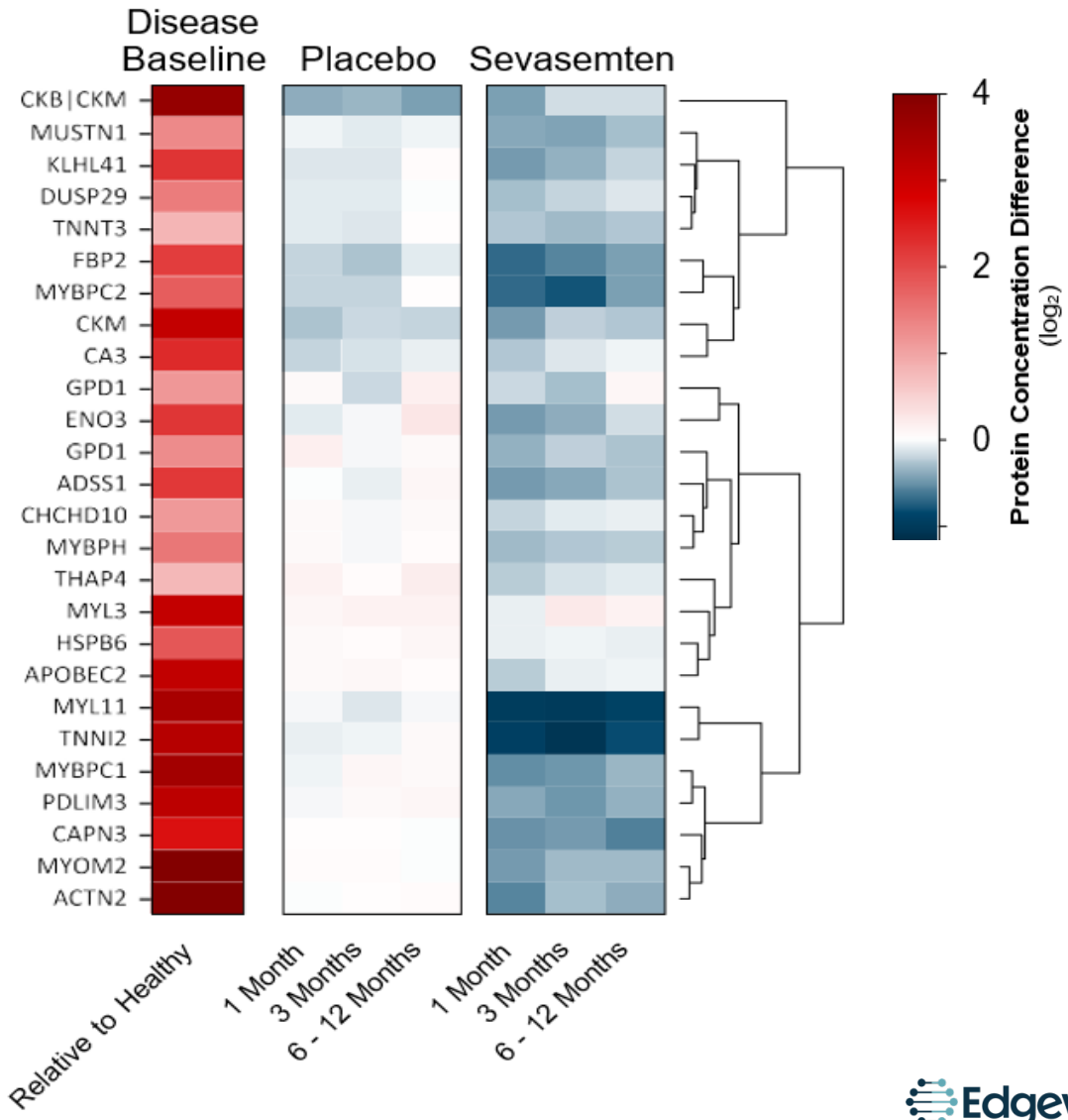


*At baseline, 9 sevasemten and 1 placebo treated participants were unable to rise from floor. At Month 12, 9 sevasemten and 2 placebo treated participants were unable to rise from floor. Note: For the figures, LSM differences and Cis were standardized by dividing by the SE. LSM differences presented on the right of the figure are on original scale (without SE adjustment).
CI, confidence interval; NSAA, North Star Ambulatory Assessment

Sevasemten Significantly and Robustly Reduced Muscle Injury Proteins Relative to Placebo

- All muscle injury proteins were generally elevated in CANYON BMD subjects relative to healthy samples.
- While placebo generally had little effect, daily treatment with 10 mg of sevasemten broadly reduced circulating levels by 1 month and maintained reduced levels through 6-12 months.

For more information, please see MDA poster LB432!



BMD, Becker muscular dystrophy

Sevasemten was Well Tolerated: Overview of Treatment Emergent Adverse Events (TEAE)

Functional test	Sevasemten (n=28) n (%)	Placebo (n=12) n (%)	Total (N=40) n (%)
Any TEAE	26 (92.9)	10 (83.3)	36 (90)
Severe TEAE	0 (0)	0 (0)	0 (0)
Serious Adverse Events	1 (3.6)	0 (0)	1 (2.5)
Any drug related TEAE	16 (57.1)	5 (41.7)	21 (52.5)
Discontinuation due to TEAE	1 (3.6)	0 (0)	1 (2.5)
Deaths	0 (0)	0 (0)	0 (0)

TEAE, treatment emergent adverse event

CANYON Sevasemten was Well Tolerated: TEAEs Occurring in ≥5% of Total

System Organ Class/Preferred Term	Sevasemten (n=28) n (%)	Placebo (n=12) n (%)	Total (N=40) n (%)
Any TEAE	**26 (92.9%)**	**10 (83.3%)**	**36 (90%)**
Eye disorders			
Vision blurred	1 (3.6%)	2 (17%)	3 (8%)
General disorders and administration site conditions			
Fatigue	5 (18%)	3 (25%)	8 (20%)
Infections and infestations			
COVID-19	6 (21%)	2 (17%)	8 (20%)
Nasopharyngitis	6 (21%)	2 (17%)	8 (20%)
Upper respiratory tract infection	5 (18%)	2 (17%)	7 (18%)
Influenza	4 (14%)	1 (8%)	5 (13%)
Injury, poisoning and procedural complications			
Fall	8 (29%)	2 (17%)	10 (25%)
Investigations			
Ejection fraction decreased	0 (0%)	2 (17%)	2 (5%)
Musculoskeletal and connective tissue disorders			
Back pain	3 (11%)	0 (0%)	3 (8%)
Nervous system disorders			
Headache	9 (32%)	2 (17%)	11 (28%)
Dizziness	9 (32%)	0 (0%)	9 (23%)
Somnolence	5 (18%)	1 (8%)	6 (15%)
Migraine	3 (11%)	1 (8%)	4 (10%)
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain	4 (14%)	0 (0%)	4 (10%)
Cough	3 (11%)	0 (0%)	3 (8%)

CANYON Summary of Trial Results

Safety

- Well-tolerated, at all doses, in adults and adolescents
- No safety concerns identified

Biomarkers

- Primary endpoint achieved: 28% average decrease in CK versus placebo (p=0.02)
- Plasma TNNI2 decreased 77% from baseline versus placebo (p<0.001)

Function

- Sevasemten treated patients (n=28) showed stabilization of NSAA with trends toward improvement
- Placebo group (n=12) declined in line with natural history

Secondary & Exploratory

- The imbalance between groups confounded interpretation of a few endpoints (e.g., MRI); evaluation of the full data set ongoing

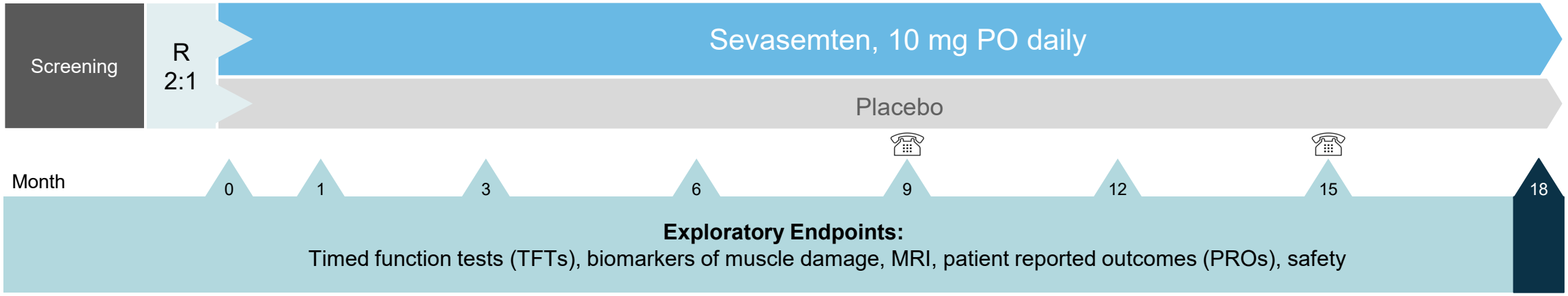
CK, creatine kinase; NSAA, North Star Ambulatory Assessment

Next Steps

Global, Multi-Center, Placebo-Controlled Study of Sevasemten; Pivotal Cohort and Potentially Registrational

- **Population:** Adults with Becker with NSAA 5-32, not on corticosteroids
- **Enrollment:** 175 patients (powered to show a difference in NSAA at 18 months)
- **Primary endpoint:** NSAA at 18 months
- **Secondary Endpoints:** 100 m timed test, biomarkers of muscle damage, MRI

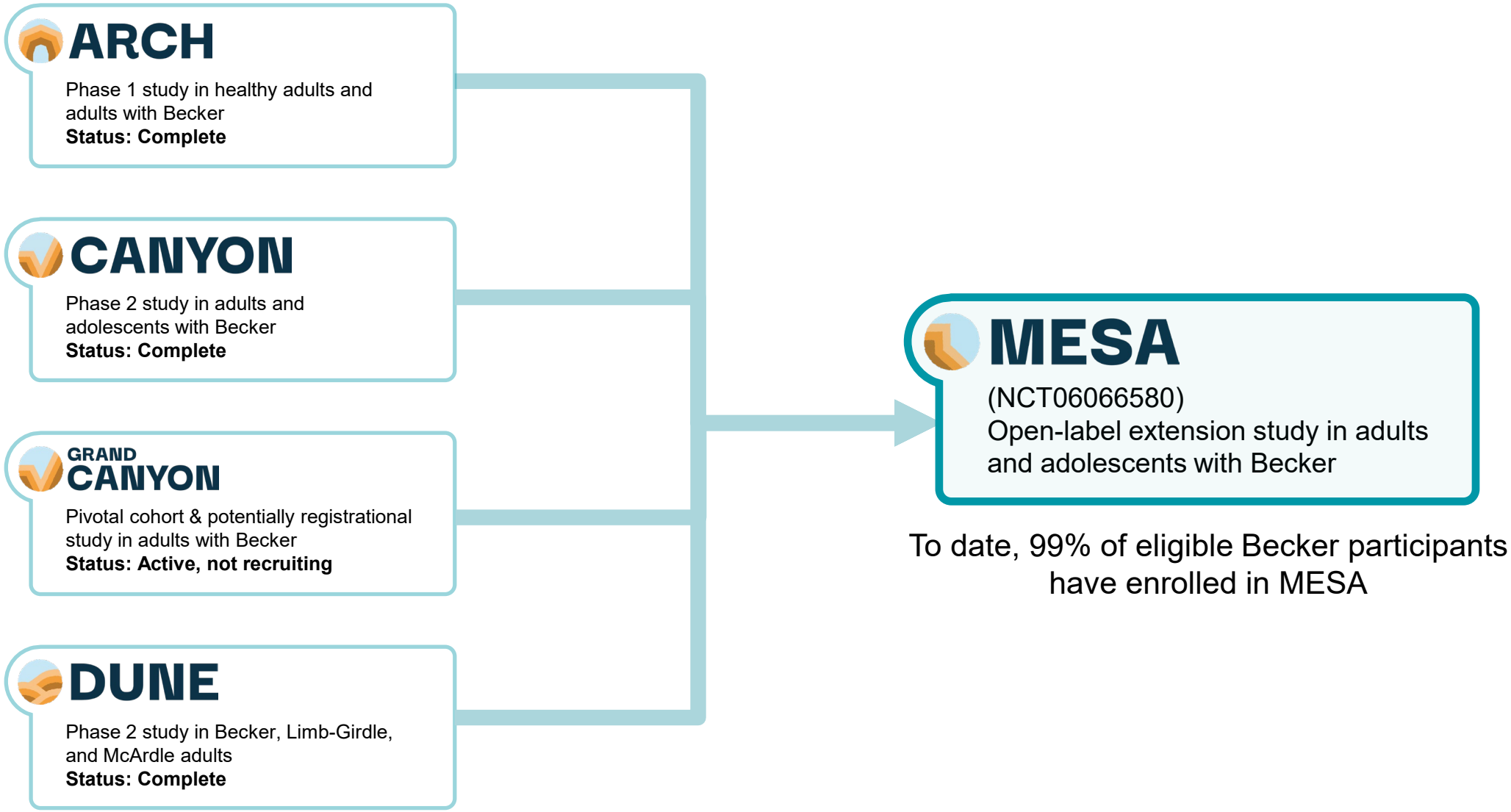
Study design - 18 months



R, randomization; NSAA, North Star Ambulatory Assessment.

1. ClinicalTrials.gov. NCT05291091. https://clinicaltrials.gov/ct2/show/NCT05291091. 2. Data on file.

Open-Label Extension Study MESA Enrolls Eligible Patients from ARCH, CANYON, GRAND CANYON, and DUNE



To date, 99% of eligible Becker participants have enrolled in MESA

Sevasemten Continues To Be Investigated In Becker

ARCH

- Sevasemten was found to be well-tolerated.
- Demonstrated rapid, sustained and significant decrease in multiple biomarkers of muscle damage at 24 months.
- Stabilization of functional assessments was seen.

DUNE

In enrolled BMD patients, sevasemten decreased CK and TNNI2 significantly compared to placebo during normal activity. 12 weeks of treatment also resulted in reductions in post-exercise increases in CK and TNNI2, with no effect on exercise capacity or strength.

CANYON

- Sevasemten was found to also be well-tolerated, with no safety concerns identified.
- The results demonstrated a significant change from baseline in CK in the sevasemten-treated group.
- NSAA remained stable over time in the sevasemten treatment group, similar to the observations in ARCH.
- Plasma TNNI2 decreased from baseline in the sevasemten-treated group compared to placebo, averaged over months 6-12 in adults.
- CANYON is the largest interventional trial to date in Becker and the first to achieve its primary endpoint.

GRAND CANYON

The functional observations from CANYON support that the GRAND CANYON pivotal cohort's primary endpoint is powered at >95% to demonstrate a statistically significant NSAA difference at 18 months.

MESA

Sevasemten continues to be investigated in an open-label extension trial to assess the long-term effects of sevasemten in individuals with Becker muscular dystrophy.

Thank you!

Thank you for joining us today!

Additionally, we would like to thank the patients, investigators, study site personnel, Edgewise Therapeutics personnel, and all of those helping to facilitate clinical trials and improve care.

To inquire about clinical trials, please email studies@edgewisetx.com or visit clinicaltrials.gov.

Connect with Edgewise at MDA!

Meet our team:
Booth #502

Hear our presentation:
Wed March 19th at 10:30am CST

Learn about our data
with our many posters!