CANYON Trial Results: Sevasemten, an Investigational Fast Skeletal Myosin Inhibitor, Reduced Muscle Damage Biomarkers and Stabilized Function in BMD

Craig McDonald[1], Hani Kushlaf[2], Diana Castro[3], Katherine Mathews[4], Arun Varadhachary[5], Anne M. Connolly[6], Michela Guglieri[7], Doris Leung[8], Jeffrey Statland[9], Erik H. Niks[10], Rosaline Quinlivan[11], Varun Sreenivasan[12], Aravindhan Veerapandiyan[13], Nicholas Johnson[14], Han Phan[15], Brenda Wong[16], Roxana Donisa Dreghici [17], James MacDougall[17], Alan Russell[17], Joanne Donovan[17]

[1]University of California - Davis, Davis, California, USA [2]University of Cincinnati College of Medicine, Cincinnati, Ohio, USA [3]Neurology Rare Disease Center, Denton, Texas, USA [4]University of Iowa, Iowa City, Iowa, USA [5]Washington University, St. Louis, Missouri, USA [6]Nationwide Children's Hospital, Columbus, Ohio, USA [7]Newcastle University, Newcastle upon Tyne, England, UK [8]Kennedy Krieger Institute, Baltimore, Maryland, USA [9]University of Kansas Medical Center, Kansas City, Kansas, USA [10]Leiden University Medical Center, Leiden, Netherlands [11]University College London, Queen Square Institute of Neurology, London, England, UK [12]University of Colorado – Denver, Denver, Colorado, USA [13]Arkansas Children's Hospital, University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA [14]Virginia Commonwealth University, Richmond, Virginia, USA [15]Rare Disease Research, Atlanta, Georgia, USA [16]UMass Medical Center, Worcester, Massachusetts, USA [17]Edgewise Therapeutics, Boulder, Colorado, USA

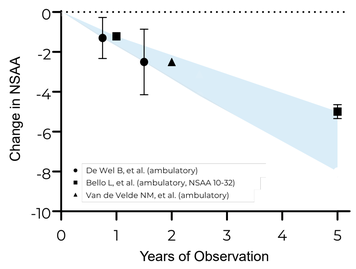
Background

Becker muscular dystrophy (BMD) is a serious, rare, neuromuscular disorder with no currently approved therapies.

Individuals with BMD experience contraction-induced muscle damage, which is the primary driver of muscle loss and impaired motor function in muscular dystrophies.[1,2,3,4] Fast muscle fibers are disproportionately injured by contraction in BMD.[5,6] Multiple natural history studies in individuals with BMD demonstrate the North Star Ambulatory Assessment (NSAA) average score decline of 1.0 to 1.8 points annually (shown right). [2,4,7,8]

Sevasemten is an investigational, novel, oral, fast skeletal myosin inhibitor designed to protect muscle against contraction-induced damage while preserving function.[9] Sevasemten is currently being investigated in BMD and Duchenne muscular dystrophy.

Natural History of BMD



Methods

Study Design

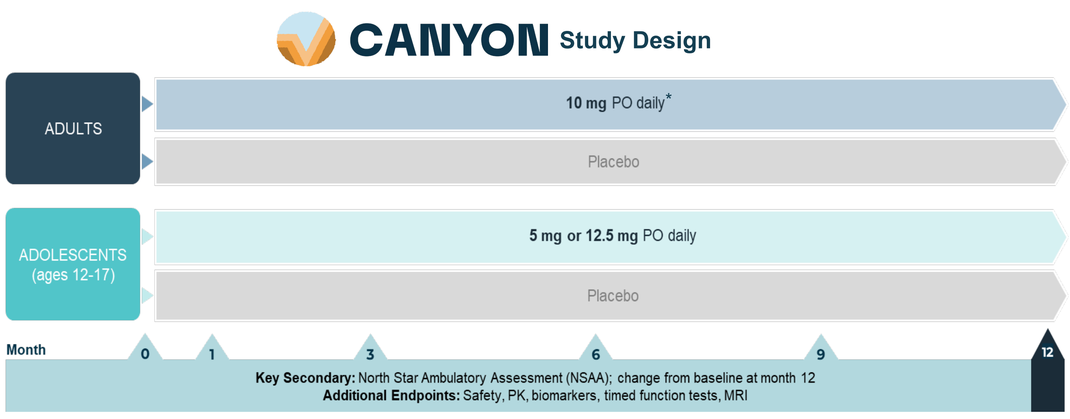
The CANYON study (NCT05291091) is a Phase 2, double-blind, placebo-controlled study of sevasemten, assessing safety, pharmacokinetics, biomarkers of muscle damage, and functional measures in adults and adolescents with BMD. Forty adults and 29 adolescents with BMD were enrolled. Analysis included the adult population (n=40).

Primary endpoint was change from baseline in serum creatine kinase (CK) over 6-12 months for adults. Key secondary endpoint was change from baseline in the North Star Ambulatory Assessment (NSAA) total score in adults at month 12.

Key Inclusion Criteria

Ambulatory males aged 12 to 50 years with a dystrophin mutation and a BMD phenotype, not on corticosteroids, with a NSAA between 5-32. Adolescents were not selected based on NSAA.

CANYON Study Design



*Originally, participants were randomized to 10mg or 15mg of sevasemten daily, but after completion of the ARCH trial, participants all received 10mg.

Baseline Characteristics

There was a notable imbalance between adult participants in the sevasemten and placebo groups, with the sevasemten group having more advanced disease at baseline based on all functional measures and MRI.

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

NSAA, North Star Ambulatory Assessment; 4SC velocity, 4-stair climb velocity; RFF, rise from floor; 10MWR, 10-minute walk/run; 100 MTT, 100-meter timed test

Results

Sevasemten was found to be well-tolerated.

No new safety concerns were observed in either the adult or adolescent populations. Headache and dizziness were the most commonly reported adverse events.

	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)

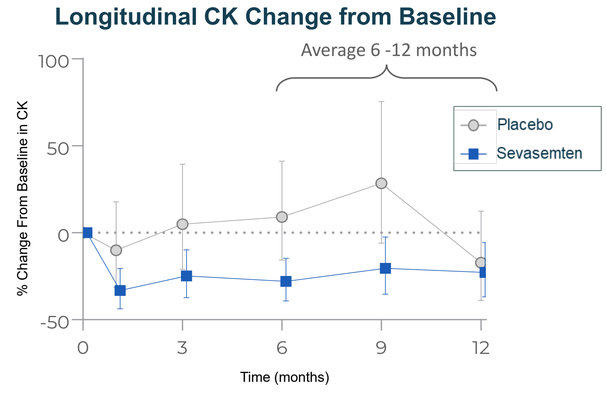
TEAE, treatment emergent adverse event

Results (Continued)

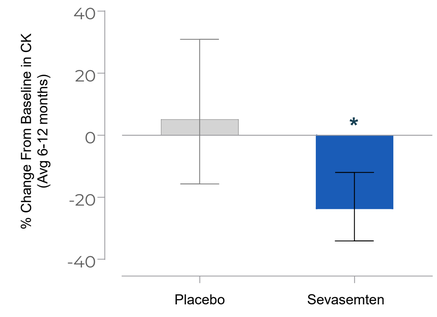
The CANYON trial met its primary endpoint of change from baseline in CK over the treatment period.

CK showed a rapid and sustained statistically significant decrease from baseline in CK in the sevasemten-treated group. The CK between-group difference LSMean was -28% (95% CI -44% to -6%); *p-value =0.02.

Longitudinal CK Change from Baseline



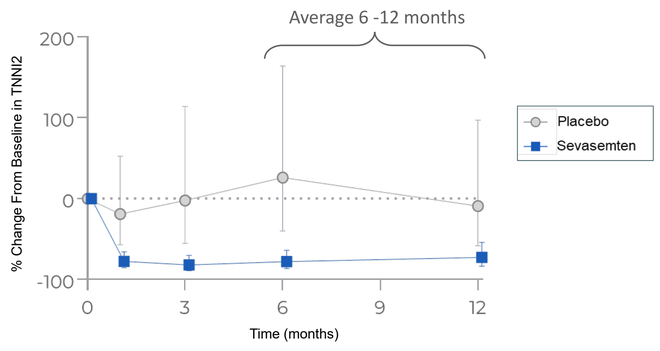
Average CK Change from Baseline



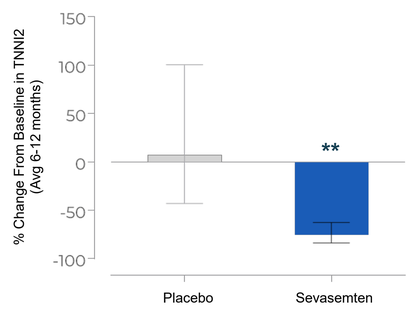
Fast skeletal troponin I (TNNI2) decreased 77% from baseline in the sevasemten treatment group compared to placebo, averaged over months 6 through 12.

TNNI2 also demonstrated rapid and sustained decreases with sevasemten treatment, with a between-group difference LSMean of -77% (95% CI -89% to -51%); **p-value < 0.001.

Longitudinal TNNI2 Change from Baseline



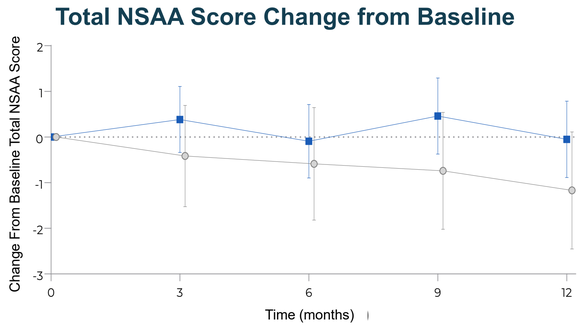
Average TNNI2 Change from Baseline



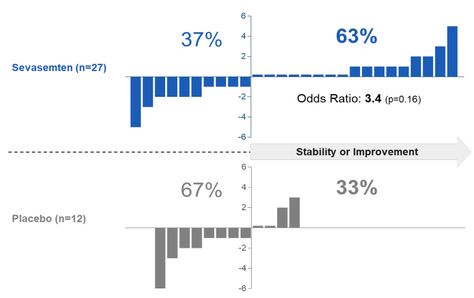
NSAA remained stable over time in the sevasemten treatment group.

The between-group difference was 1.1 points, favoring sevasemten; p=0.06 across all adult participants. NSAA remained stable over time in the sevasemten treatment group, similar to the observations in the ARCH study. Further, while the placebo group was small in number (n=12), NSAA declined similarly to that observed in previous natural history studies.

Total NSAA Score Change from Baseline



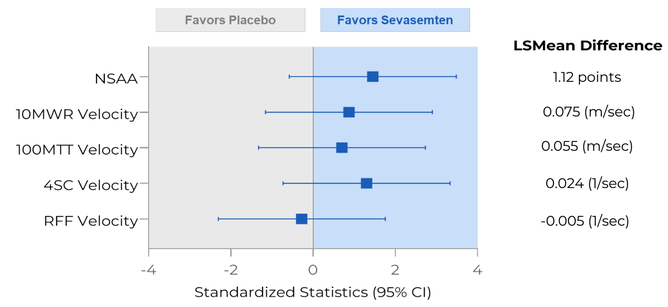
Sevasemten NSAA Responder Analysis



Trends in other functional measures favored 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 the floor.

For the figure to the right, 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).



NSAA, North Star Ambulatory Assessment; 4SC velocity, 4-stair climb velocity; RFF, rise from floor; 10MWR, 10-minute walk/run; 100 MTT, 100-meter timed test

Conclusions

- Sevasemten was well-tolerated at all doses in adults and adolescents, with no new safety concerns identified.
- The primary endpoints was achieved, with a 28% average decrease in CK versus placebo (p=0.02). An additional biomarker of muscle damage, TNNI2, decreased 77% from baseline versus placebo (p<0.001).
- Sevasemten-treated patients showed stabilization of NSAA, with trends toward improvement, while the placebo group (n=12) decline in line with natural history.
- CANYON is the largest interventional trial to date in BMD and the first to achieve its primary endpoint. A global pivotal cohort of adults in BMD, GRAND CANYON (NCT05291091), is fully enrolled with results expected in Q4 2026.

References

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