CANYON: THE LARGEST INTERVENTIONAL TRIAL IN BECKER MUSCULAR DYSTROPHY TO DATE

Sevasemten is an investigational agent that is currently not approved for use by any regulatory authority in any territory. The publication of this Infographic was funded by Edgewise Therapeutics.
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BACKGROUND

Becker muscular dystrophy is a rare, progressive, debilitating neuromuscular disease with no currently approved therapies.[1]

In muscular dystrophies, excessive contraction-induced damage of muscle fibers can occur, with fast muscle fibres being most susceptible to injury.[2,3]

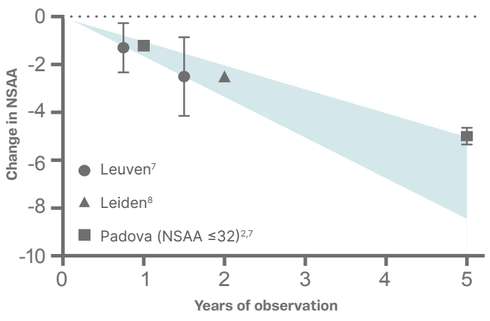
Fiber breakdown leads to the release of muscle proteins (such as creatine kinase and fast skeletal muscle troponin I) into the circulation, where they can be measured as disease-related biomarkers.[4]

Sevasemten is an investigational, novel, oral, fast skeletal myosin inhibitor designed to protect muscle against contraction-induced injury while preserving function.[5]

BECKER NATURAL HISTORY

- Individuals with Becker experience progressive muscle degeneration and weakness, leading to eventual loss of muscle function.[1]
- The NSAA is a clinically meaningful measure utilised in natural history studies of muscular dystrophy to longitudinally assess global function.[6-9]
- Multiple natural history studies in individuals with Becker demonstrate a consistent and irreversible decline in NSAA average score of 0.9 to 1.7 points annually.[6-9]

Consistent rate of functional decline



95% CI shown for Bello L et al. 2016[6] (note within 1 year point) and De Wel B et al. 2024[8]; not available for van de Velde NM et al. 2018.[9]

THE CANYON TRIAL[10]

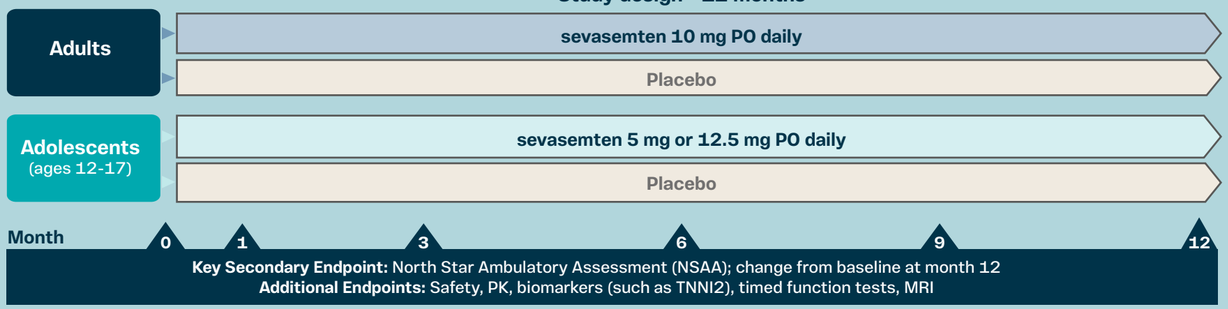
- The CANYON trial (NCT05291091) is a Phase II, double-blind, placebo-controlled study of sevasemten.
- CANYON assessed safety, pharmacokinetics, biomarkers of muscle damage (CK), and functional measures, in adults and adolescents with Becker (with data currently available for the adult dataset only).
- There was a notable imbalance between adult participants in the sevasemten and placebo groups at baseline, with the sevasemten group having more advanced disease based on all functional measures and MRI.

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 an Becker phenotype, not on corticosteroids, with a NSAA between 5-32

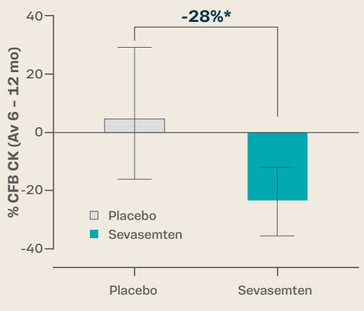
PATIENTS ENROLLED
Adults: **40**
Adolescents: **29**

Study design - 12 months



EFFICACY RESULTS[10]

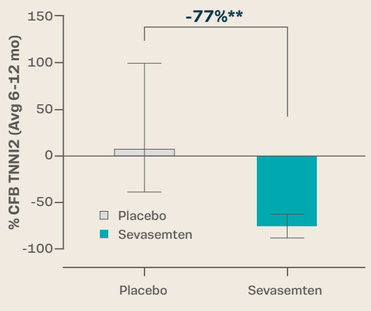
Primary Endpoint: CK % Change from Baseline



* p=0.02

The CANYON trial met its primary endpoint, with a **28% average decrease in CK** in sevasemten-treated patients vs placebo (p=0.02).

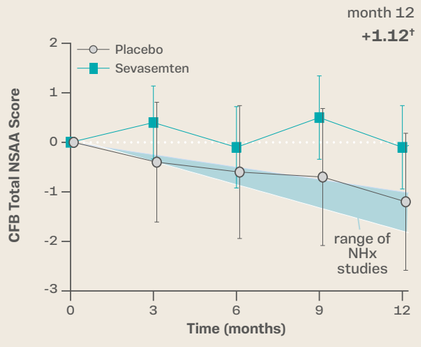
TNNI2 % Change from Baseline



** p<0.001

Another biomarker of muscle damage, **TNNI2, decreased 77%** from baseline vs placebo (p<0.001).

NSAA Score Change from Baseline at 12 months



† p=0.16

Sevasemten-treated patients showed **stabilisation of NSAA**, while the placebo group declined in line with natural history.

SAFETY[10]

- Sevasemten was well tolerated in the CANYON study, with no new safety concerns observed.
- 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)

KEY MESSAGES

CANYON is the largest interventional trial in Becker to date and the first to achieve its primary endpoint, reduction in circulating levels of creatine kinase.

Sevasemten-treated patients showed trends toward stabilisation of NSAA at 12 months compared to placebo, a key secondary endpoint.

Sevasemten was well-tolerated, with no new safety concerns identified.

Research with sevasemten in Becker is ongoing with the GRAND CANYON trial[11] and MESA, an open-label extension study.[12]

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Abbreviations
Becker: Becker muscular dystrophy; CFB: change from baseline; CK: creatine kinase; NHx: natural history; NSAA: North Star Ambulatory Assessment; PO: orally; TEAE: treatment-emergent adverse event; TNNI2: fast skeletal muscle troponin I; vs: versus.