North Star (NSAA and NSAD) Functional Assessments in Individuals with Becker Muscular Dystrophy

James MacDougall[1] ,Meredith James[2], Craig McDonald[3], Han Phan[4], John Vissing[5], Michelle Eagle[6], Linda Lowes[7], Lindsay Alfano[7], Joanne Donovan[1]

[1] Edgewise Therapeutics, Boulder, CO, USA | [2]The John Walton Muscular Dystrophy Research Centre, Newcastle Upon Tyne, UK I [3]University of California Davis, Sacramento, CA I [4]Rare Disease Research, Atlanta, GA, USA I [5]Rigshospitalet, University of Copenhagen, Copenhagen, DK I [6]ATOM International, Newcastle upon Tyne, UK I [7]Nationwide Children's Hospital, Columbus, OH, USA

Background

Becker muscular dystrophy (Becker) is characterized by contraction-induced injury leading to muscle replacement with fat and fibrosis, with consequent loss of ambulatory functions.

The North Star Ambulatory Assessment (NSAA) and North Star Assessment for Limb-Girdle type muscular dystrophies (NSAD) are multi-item scales utilized in muscular dystrophy natural history studies to longitudinally assess functional measures. The NSAA has been well-characterized and widely used in Duchenne muscular dystrophy, but in Becker, neither the NSAA or NSAD has been validated.

NSAA & NSAD Functional Measures

- ❑ *Lifts head*
- ❑ *Hand to opposite shoulder**
- ❑ *Hip flexion supine**
- ❑ *Bridging in supine**
- ❑ *Rolling supine to prone**
- ❑ *Gets to sitting*
- ❑ *Reaches forward**
- ❑ *Stand up from chair*
- ❑ *Stand to sit on chair**
- ❑ *Stand*
- ❑ *Walk*
- ❑ *Stand on R-leg, ❑ on L-leg*
- ❑ *Climb box step R, ❑ step L*
- ❑ *Descend box step R, ❑ step L*
- ❑ *Touches floor from standing**
- ❑ *Rise from floor*
- ❑ *Stands on heels*
- ❑ *Jump*
- ❑ *Hop R-leg, ❑ L-leg*
- ❑ *Squat down**
- ❑ *Rise from squat**
- ❑ *High knee to stand R-leg lead*, ❑ L-leg lead**
- ❑ *Tiptoes**
- ❑ *Run (timed = 10 MWR)*

***NSAD only**

Objectives

- To characterize reproducibility of repeated pre-treatment NSAA and NSAD assessments in three clinical trials of EDG-5506, an investigational orally administered fast skeletal muscle myosin inhibitor designed to prevent contraction-induced muscle damage.
- To examine patterns of compensation and loss of individual functions over a range of baseline NSAA/NSAD scores for 4 groups of individuals with NSAA in the ranges of 0-9, 10-19, 20-29, and 30-34.

Methods

Participants included patients with Becker from the following studies:

- **EDG-5506-002 ARCH (NCT05160415):** N=12 (baseline only)
- **EDG-5506-201 CANYON & GRAND CANYON (NCT05291091):** N=70 (screening and baseline); Additional N=8 with screening or baseline
- **EDG-5506-202 DUNE**: N=10 (baseline only)

Key Inclusion Criteria:

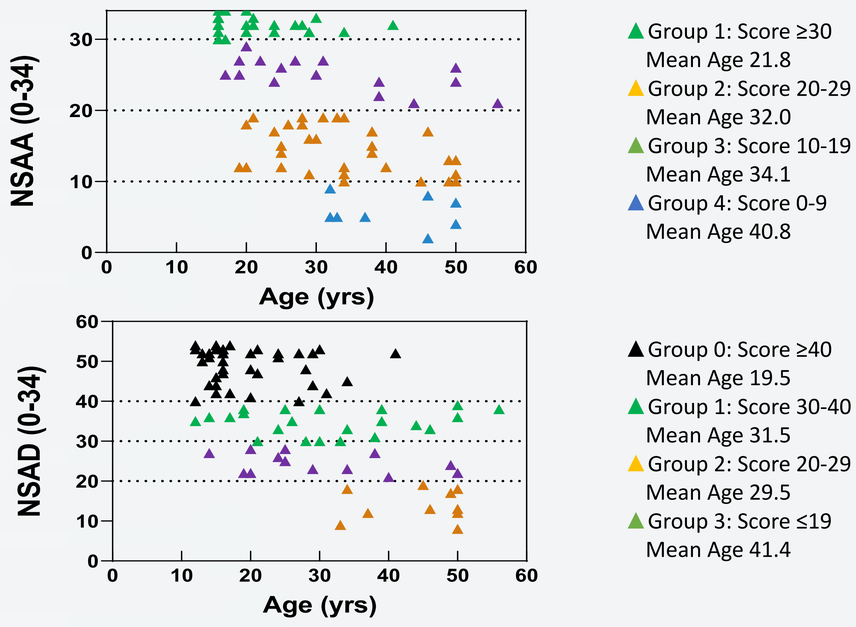
- Age ≥ 18 years old for ARCH, 12-50 years old for CANYON and GRAND CANYON, and 18-65 years old for DUNE
- A mutation in the dystrophin gene with a phenotype of Becker, ie. ambulatory past 16 years, or 18 years if on corticosteroids
- Ambulatory, able to perform the 100-meter timed test

Clinical assessors underwent training and certification of proficiency. Repeat measures (screening and baseline) of NSAA and NSAD were conducted within 28 days. The NSAA and NSAD were conducted in sequence, with the NSAA measured first.

Results

NSAA and NSAD Scores and Age

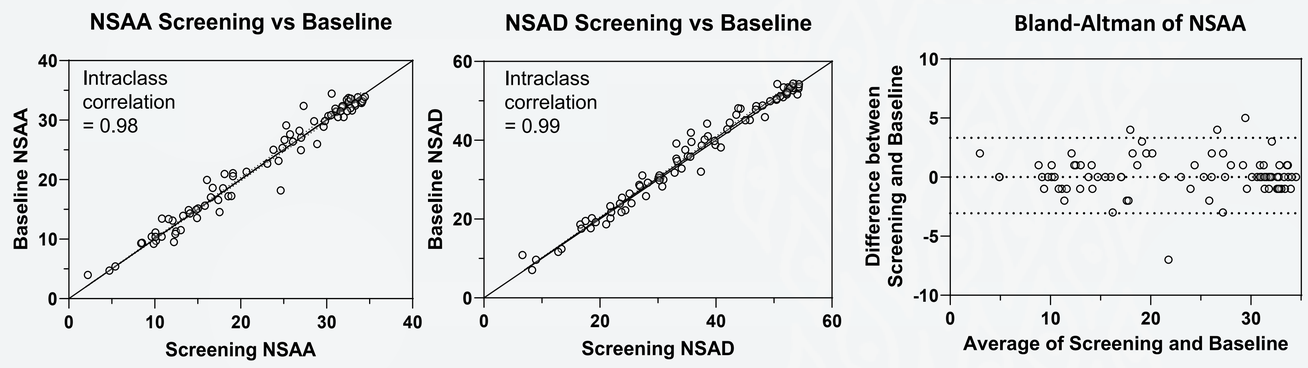
While scores decline with age, age is a poor predictor of NSAA and NSAD scores in Becker patients.



Results (Continued)

NSAA and NSAD Reproducibility

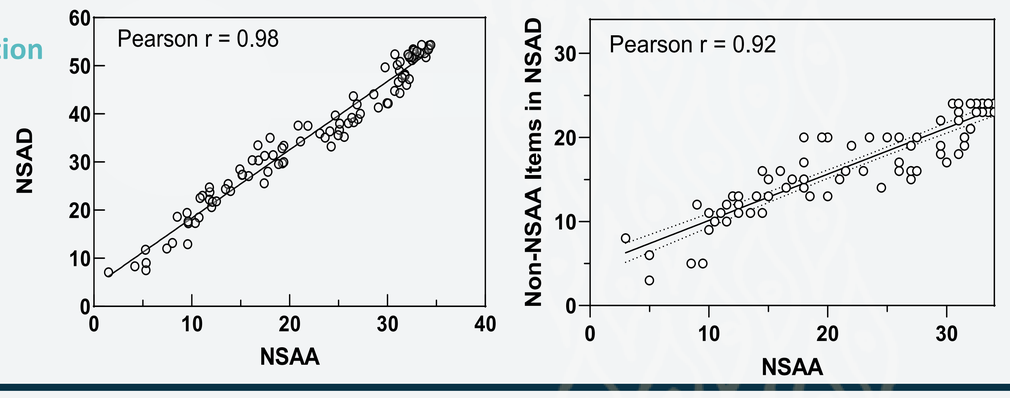
NSAA and NSAD were found to be highly reproducible, regardless of baseline scores.



Mean difference (screening – baseline): 0.1 ± 1.6 *Mean difference (screening – baseline): -0.6 ± 2.1*

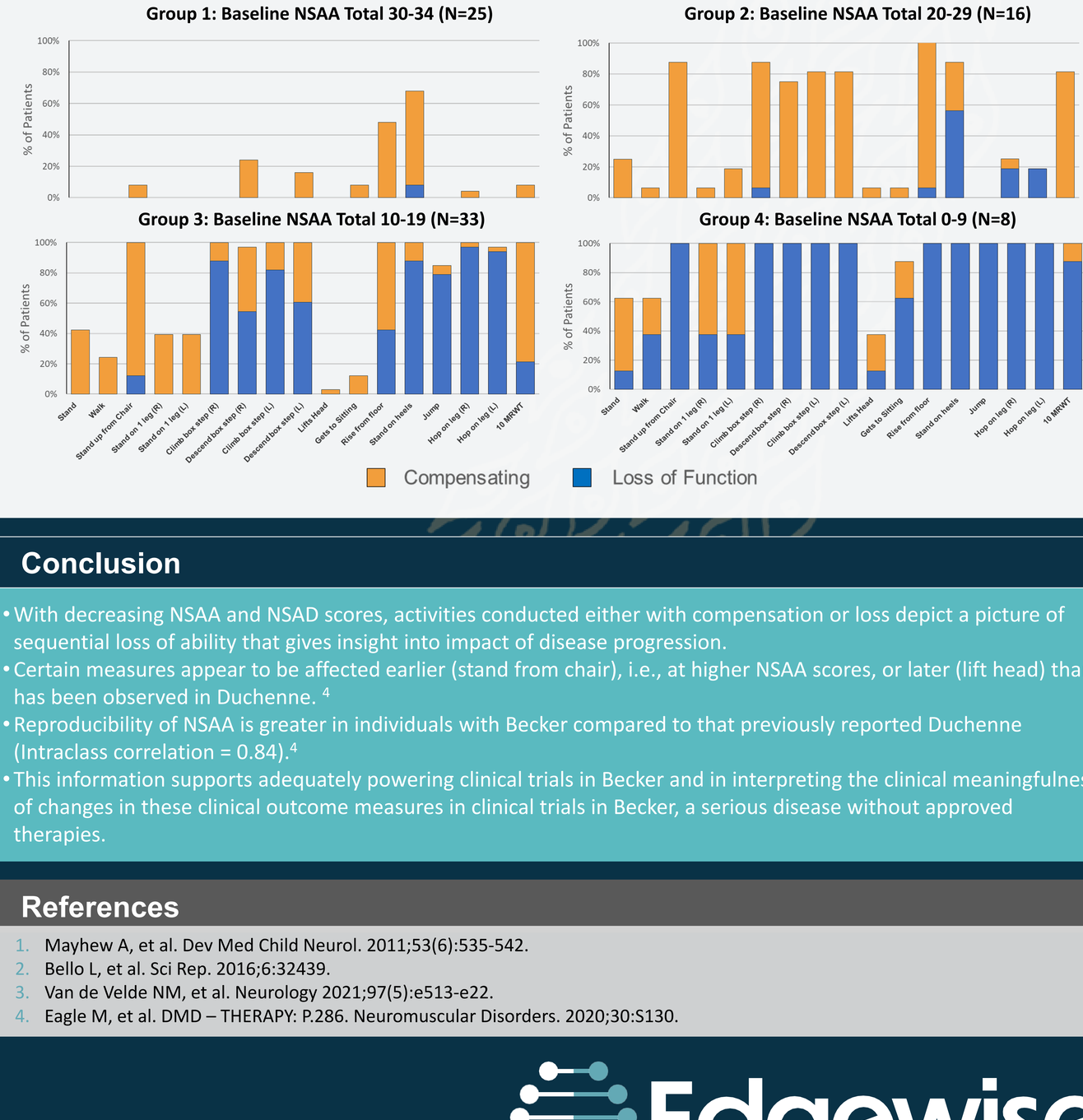
NSAA and NSAD Correlation

NSAA and NSAD were found to be highly correlated, while the score of items in the NSAD not included in the NSAA correlated less strongly.



Patterns of Compensation and Loss in Individual Functions: A Cross-Sectional Representation of Characteristics of Individuals Across a Range of NSAA Scores

Individual NSAA assessments are ordered in terms of difficulty as determined for Duchenne muscular dystrophy.[1] Based on natural history observations that found a decrease of approximately 1.2 NSAA points per year, it is anticipated that transitions between groups 2, 3, and 4 would be approximately 8-9 years.[2,3]



Conclusion

- With decreasing NSAA and NSAD scores, activities conducted either with compensation or loss depict a picture of sequential loss of ability that gives insight into impact of disease progression.
- Certain measures appear to be affected earlier (stand from chair), i.e., at higher NSAA scores, or later (lift head) than has been observed in Duchenne. [4]
- Reproducibility of NSAA is greater in individuals with Becker compared to that previously reported Duchenne (Intraclass correlation = 0.84).[4]
- This information supports adequately powering clinical trials in Becker and in interpreting the clinical meaningfulness of changes in these clinical outcome measures in clinical trials in Becker, a serious disease without approved therapies.

References

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Disclaimer
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