P255

Effects of EDG-5506, a Fast Myosin Modulator, on Function and Biomarkers of Muscle Damage in Adults with Becker Muscular Dystrophy (BMD)

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Background

Fast (Type II) muscle fibers are affected early and disproportionately in BMD and Duchenne muscular dystrophy (DMD) [1]

EDG-5506 is an orally administered, once daily, investigational product that modulates fast skeletal muscle myosin and, in DMD disease models, decreased muscle damage biomarkers and fibrosis while increasing muscle strength and activity.

14 days of EDG-5506 in adults with BMD reduced biomarkers of muscle damage in a phase 1 study of safety, tolerability, and PK, 7 adults with BMD were treated for 14 days with 20 mg once-daily EDG-5506 or placebo, resulting in reduction in CK and TNNI2 (fast muscle troponin).

EDG-5506 Prevents Contraction-Induced Damage and Fiber Breakdown in Mouse Dystrophic Muscle [2]

Methods

Study Design

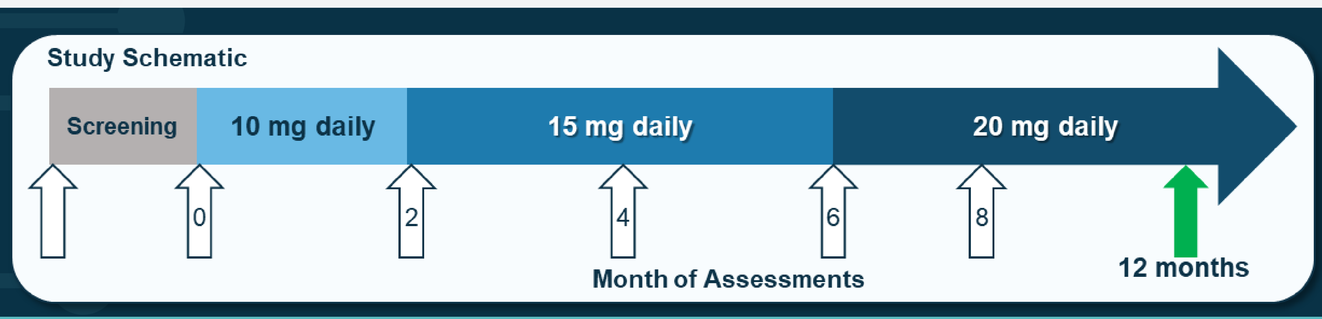
The ARCH study (NCT05160415) is a phase 1b open-label study of safety, PK and biomarkers in 12 adults with BMD.

Biomarker sampling and functional assessments, including North Star Ambulatory Assessment (NSAA), 100m test and rise from supine, were assessed at regular intervals (below)

Key Inclusion Criteria

- Ambulatory male aged 18 to 55 years (completes 100m)
- Confirmed mutation in DMD gene with BMD phenotype
- Not on corticosteroids

7 participants were enrolled from the EDG-5506-001 phase 1 study.



Results

EDG-5506 was well-tolerated

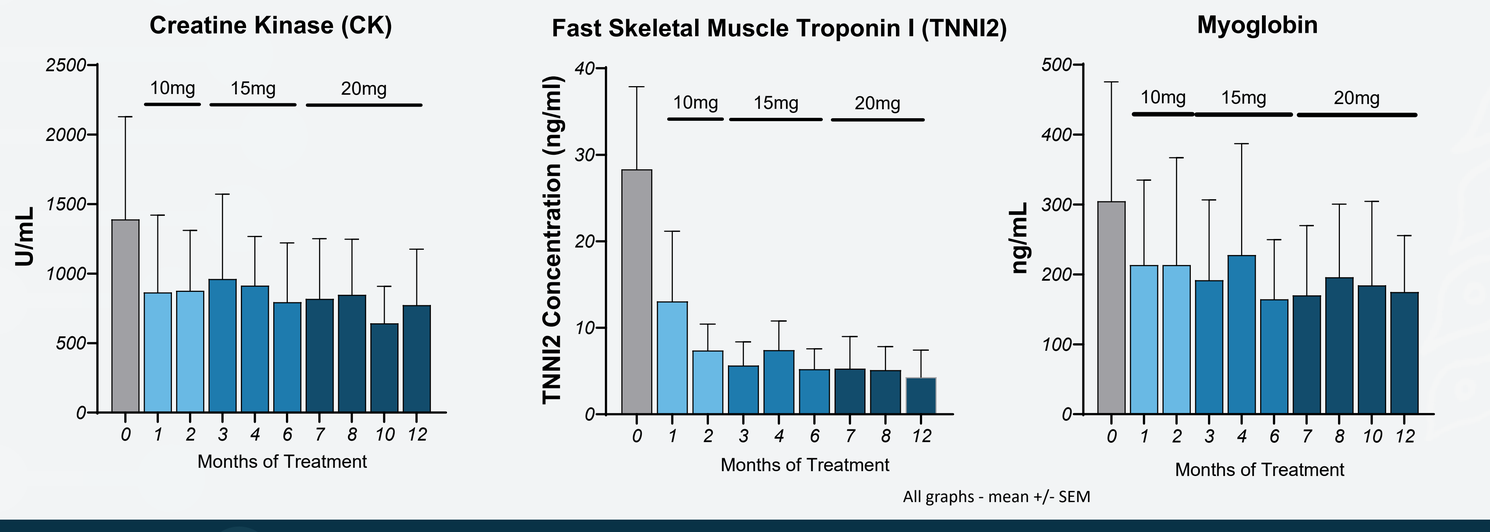
There were no serious adverse events and no withdrawals or dose reductions due to AE. Consistent with the phase 1 study, dizziness (n=4, 33%) and somnolence (n=3, 25%) were among the commonest AE. These occurred early in dosing/dose escalation, generally resolved within a few days and were mitigated by dosing at night.

Biomarkers of muscle damage were significantly reduced within 4 weeks of treatment

At 12 months, CK was reduced by a mean of 37% and TNNI2 – a specific marker of fast fiber damage, was reduced by 79%.

In addition, average pain scores were reduced across all doses.

Treatment with EDG-5506 was Associated with Rapid, Significant and Sustained Reduction in Biomarkers of Muscle Damage in Adults with BMD Treated for 12 Months

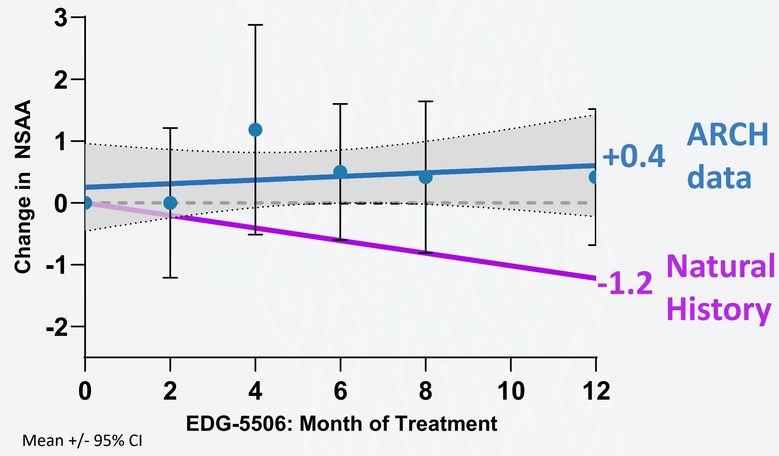


Results (Continued)

Baseline Characteristics

Mean age (SD)	32.8 y (8.1)
Mean NSAA (range)	15.5 (4-31)
Mean 10m walk/run	8.4 secs

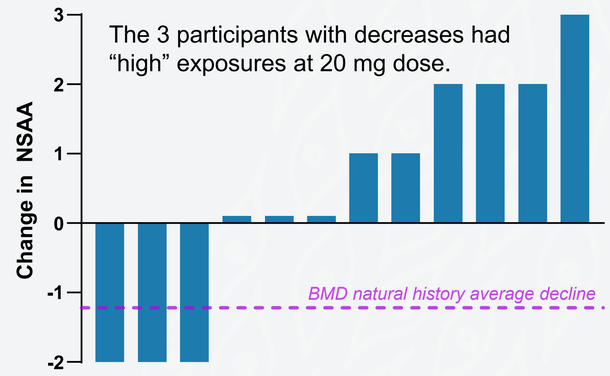
With EDG-5506 Treatment, NSAA Diverged from Natural History



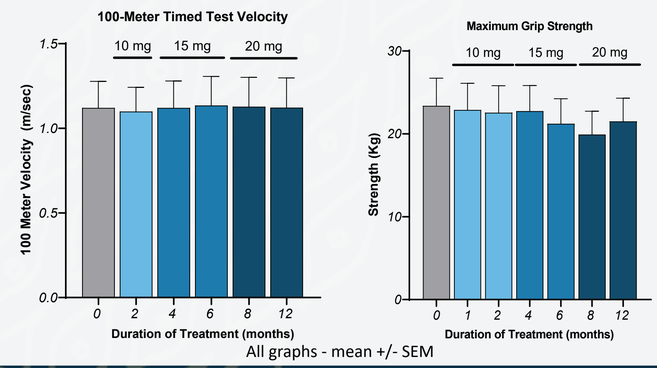
Mean +/- 95% CI

NSAA shows stabilization (mean increase 0.4 points) and divergence from expected natural history (1.2-point decline) [3, 4]

75% of Participants Had Stable or Improved Function at 12 Months



No Significant Change over 12 Months in Grip Strength or 100m Timed Test



All graphs - mean +/- SEM

GRAND CANYON

Potentially registrational cohort within ongoing phase 2 study - enrolling 2023

Approximately 120 ambulatory adults with BMD across US, EU & UK

Conclusions

EDG-5506 was well tolerated at 10 mg, 15 mg and 20 mg once-daily

10 mg produced rapid and significant decreases in multiple muscle damage biomarkers

Function trended towards improvement and diverged from expected natural history over 12 months

Data from the ARCH study supports a dose of 10 mg.

CANYON Phase 2 is currently enrolling and amended to be potentially registrational (GRAND CANYON)

References

1. Barthel *et. al*., Muscle and Nerve, March 2021
2. Russell *et al*., J Clin Invest 2023
3. Bello *et al*., Sci Rep 2016
4. van de Velde NM et. al., Neurology, 2021

Notes

- The authors are grateful to the participants in the trial and their families
- EDG-5506 is an investigational drug not approved in any territory.
- Han Phan is a consultant for Edgewise. Other authors are employees of Edgewise Therapeutics and may hold stock and/or stock options

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