MoveDMD®: Positive Effects of Edasalonexent, an NF-κB Inhibitor, in 4 to 7-Year Old Patients with Duchenne Muscular Dystrophy in Phase 2 Study with an Open-Label Extension

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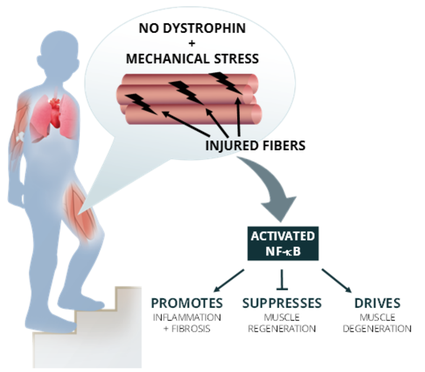
Background

NF-κB Is Activated in Duchenne Muscular Dystrophy following Mechanical Stress



- The absence of dystrophin is necessary but not sufficient to drive the disease process in DMD
- The lack of dystrophin combined with mechanical stress activates NF-κB which then promotes muscle degeneration and suppresses muscle regeneration
- Edasalonexent is an oral NF-κB inhibitor in development for all patients with DMD regardless of mutation type

Kumar, et al. FASEBJ 2003 17(3):17: 386-96.
Peterson, et al. Curr Top Dev Bio. 2011; 96: 85-119.

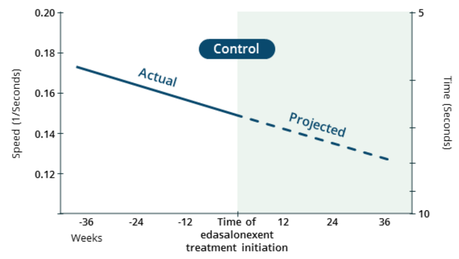
Study Design

MoveDMD Phase 2 Trial Design

- **Enrolled 31 boys ages 4 to 7 with confirmed DMD not on corticosteroids**
- **After 12-week Phase 2 data analysis showed safety and trend toward greater improvement for 100 mg/kg dose, patients on 67 mg/kg dose were transitioned to 100 mg/kg dose**
- **Data analysis performed after all boys reached 24 weeks after start of edasalonexent treatment**
  - Week 0 is from commencement of dosing with edasalonexent, either at the beginning of Phase 2 or in the case of placebo, in the open-label extension
  - Includes all boys participating in initial 100 mg/kg/day treatment group: n=16 at weeks 0 and 12, n=14 at week 24, n=11 at week 36 (2 remaining boys to be measured)
  - Discontinuations: 2 from 100 mg/kg/day treatment group between 12 and 24 weeks

Analysis Approach to Open-Label Assessments of Muscle Function

- **Changes during the control period were measured prior to commencing edasalonexent, either prior to the initiation of Phase 2 or in the placebo group, for time periods averaging 39 weeks**
- **Comparison of control period to on-treatment period assumes that the rate of decline remains linear**
  - However, DMD natural history data indicates a more rapid decline as boys get older

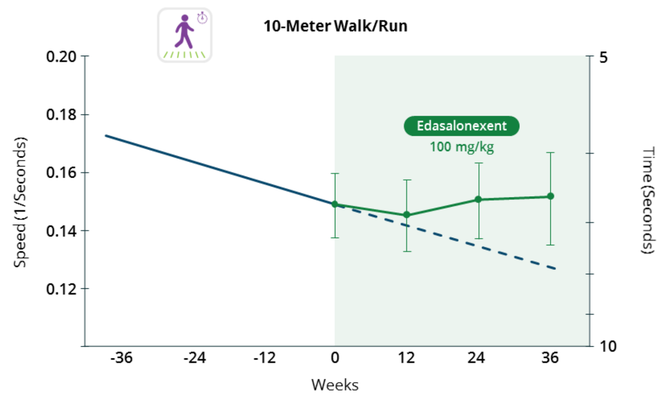


Solid line represents average of actual control period observations for boys in the 100 mg/kg treatment group (n=12)

Dashed line represents extension of control period observations

Results

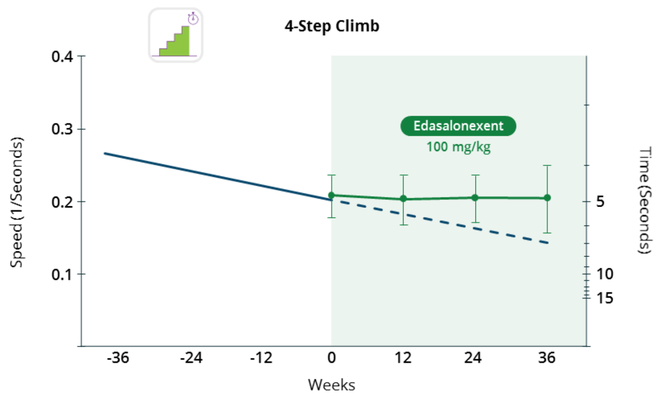
10-Meter Walk/Run Speed Stabilized with Edasalonexent Treatment



Disease progression on edasalonexent improved compared with rate of change on control

Means ± SEM shown

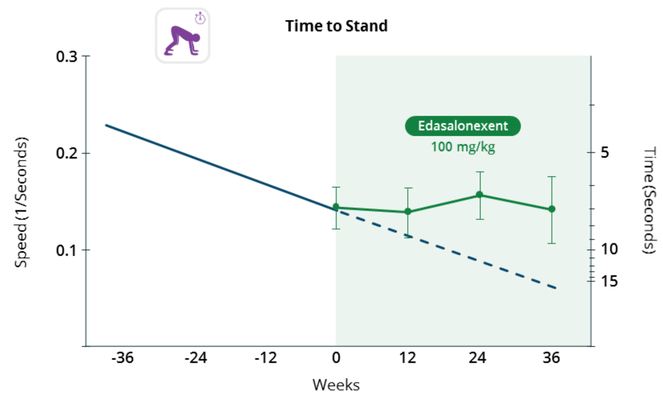
4-Stair Climb Speed Stabilized with Edasalonexent Treatment



Disease progression on edasalonexent improved compared with rate of change on control

Means ± SEM shown

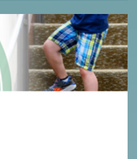
Time to Stand Speed Stabilized with Edasalonexent Treatment

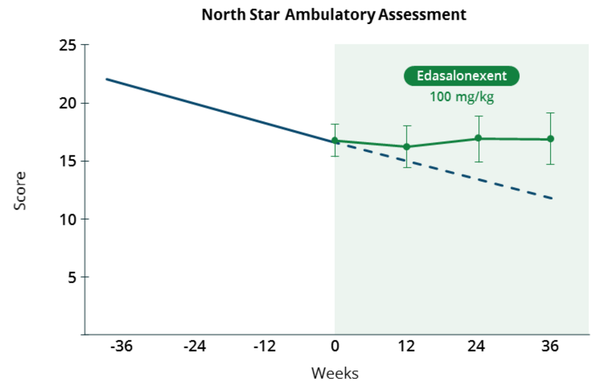


Disease progression on edasalonexent improved compared with rate of change on control

Means ± SEM shown

North Star Ambulatory Assessment Score Stabilized with Edasalonexent Treatment





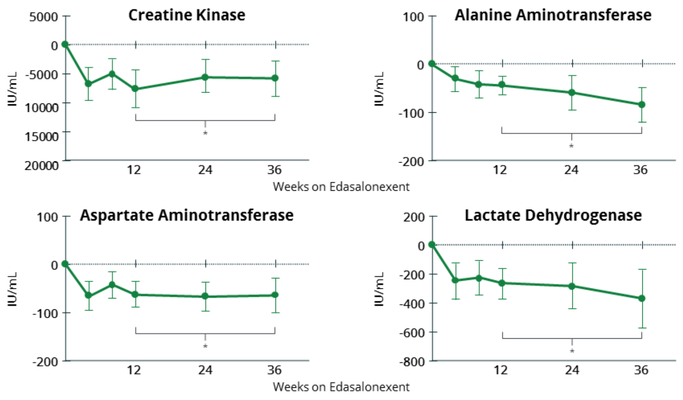
North Star is a composite endpoint evaluating physical function across 17 tests

Disease progression on edasalonexent improved compared with rate of change on control

catabasis Means ± SEM shown

Muscle Enzymes Significantly Decreased from Baseline on Edasalonexent

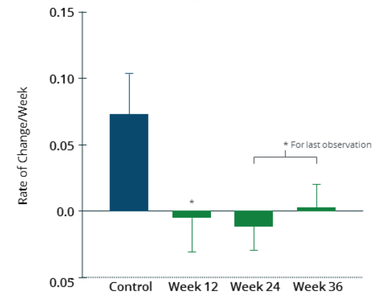
- **Consistent with positive impact on muscle, and supportive of a benefit of edasalonexent**



Means ± SEM shown; * p<0.05 for change from baseline after 12 weeks

Edasalonexent Significantly Improved Rate of Change of MRI T2 Lower Leg Composite of 5 Muscles Compared with Control Period

- MRI T2 increases over time in DMD, as shown for the control period
- Consistent with positive impact on muscle and a reduction in inflammation and supportive of a benefit of edasalonexent



MRI T2 was measured for the 5 muscles in the lower leg, and changes in the composite of these 5 muscles was the primary endpoint for Phase 2

Means ± SEM shown; * p≤0.05 for comparison with pre-treatment period

Safety

Safety

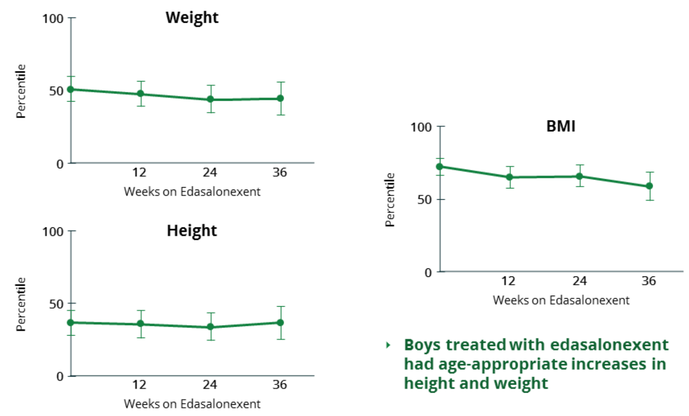
- **No safety signals**
  - 24 years of patient exposure
- **Well tolerated with majority of adverse events being mild in nature, mostly gastrointestinal**
  - Most common treatment-related adverse events were gastrointestinal and mild in severity
    - Diarrhea was transient, median duration 3 days
    - Vomiting was transient, median duration 1 day
  - No serious treatment-related adverse events or dose reductions
- **Vital Signs**
  - ECG heart rate decreased toward age-normative values
- **Growth: Weight, height and BMI changes age-appropriate**
- **No adverse trends in hematology, chemistry, renal or adrenal function, calcium and phosphate**

Adverse Events

Treatment Group	Edasalonexent 67 mg/kg/day	Edasalonexent 100 mg/kg/day
Adverse events in >10% of edasalonexent patients	(n =15)	(n =16)
Gastrointestinal disorders		
Diarrhea	6 (40.0)	8 (50.0)
Vomiting	5 (33.3)	7 (43.8)
Abdominal Pain Upper	2 (13.3)	2 (12.5)
Nausea	2 (13.3)	2 (12.5)
General disorders		
Pyrexia	4 (26.7)	6 (37.5)
Injury, poisoning		
Fall*	10 (66.7)	10 (62.5)
Contusion	3 (20.0)	4 (25.0)
Head Injury	2 (13.3)	2 (12.5)
Infections and infestations		
Nasopharyngitis	4 (26.7)	3 (18.8)
Ear infection	3 (20.0)	3 (18.8)
Gastroenteritis viral	1 (6.7)	5 (31.25)
Pharyngitis streptococcal	1 (6.7)	4 (25.0)
Respiratory disorders		
Cough	4 (26.7)	6 (37.5)
Rhinorrhoea	4 (26.7)	4 (25.0)
Metabolism and nutritional disorders		
Decreased appetite	1 (6.7)	4 (25.0)

*Falls were specifically recorded as an exploratory measure.

Age-Appropriate Growth Similar to Standard Growth Curves While on Edasalonexent



- **Boys treated with edasalonexent had age-appropriate increases in height and weight**

Conclusions

100 mg/kg Dose Selection

- **Safety profile similar at 67 and 100 mg/kg doses**
- **PK shows trough levels higher at 100 mg/kg dose**
  - Preclinical data support that efficacy is related to time above an efficacious level (unpublished data)
- **Patients on 100 mg/kg had a greater improvement in functional measures compared with control period than did patients on 67 mg/kg**

Open-Label Extension Results: Edasalonexent Substantially Slowed DMD Disease Progression

- **Disease progression on edasalonexent improved compared to rate of change in control period**
  - North Star Ambulatory Assessment
  - Timed function tests 10-meter walk/run, 4-stair climb and time to stand
- **Additional measures provide further support for positive edasalonexent treatment effects**
  - Lower leg muscle MRI T2 rate of change significantly improved compared to control period progression
  - Muscle enzymes decreased compared to baseline at 12 weeks and later time points
- **Safety profile**
  - No safety signal and well tolerated
  - Height, weight and BMI growth patterns continued to be similar to unaffected boys
- **Functional endpoints evaluated are anticipated to be used in the Phase 3 clinical trial expected to initiate in H1 2018**

Acknowledgments

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