MoveDMD: Phase 1/2 Trial of Edasalonexent, an NF-κB Inhibitor, in 4 to 7-Year Old Patients with Duchenne Muscular Dystrophy

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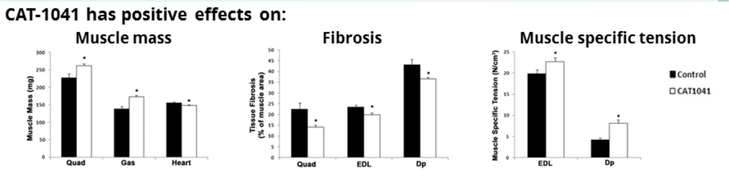
Background and Objective

- **NF-κB is activated from infancy in DMD, driving inflammation, muscle degeneration and inhibiting muscle regeneration. Edasalonexent, an oral small molecule that inhibits NF-κB, has shown positive preclinical effects on skeletal muscle, including the diaphragm, and heart in DMD models.**
- **Objective of the study:**
  - **To assess safety and efficacy of edasalonexent (CAT-1004) in boys with Duchenne muscular dystrophy (DMD) not yet on steroids**

Conflict of interest: Joanne Donovan, Maria Mancini, Pradeep Bista and Andrew Nichols are employees of Catabasis

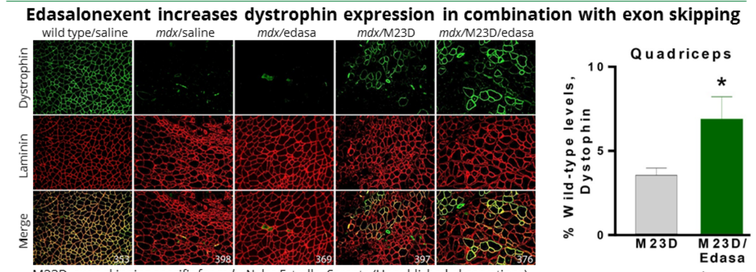
Positive Effects of NF-κB Inhibitors, CAT-1041 and Edasalonexent (CAT-1004), Observed in *mdx* Mice

CAT-1041 has positive effects on:



Hammers et al, JCI Insights (2016) *p<0.05

Edasalonexent increases dystrophin expression in combination with exon skipping

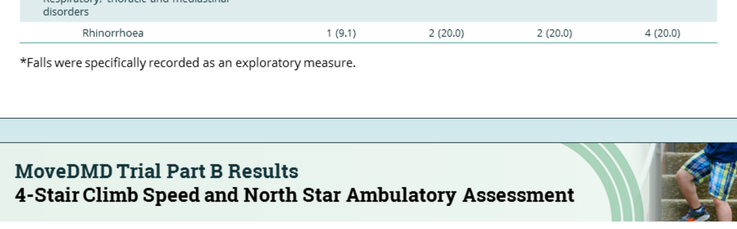


M23D: exon skipping specific for *mdx*; Nelsa Estrella, Sarepta (Unpublished observations)

*p<0.05

MoveDMD Trial Design

Study Population: All DMD mutations, ages 4 – 7, steroid naïve or off steroids for ≥6 months



- Assess the safety and PK of edasalonexent in ~18 boys with Duchenne
- Showed positive PK, NF-κB biomarker effects, safety and tolerability

- Assess the safety and efficacy of edasalonexent versus placebo using MRI as an early biomarker; trial was powered only for the primary end point of change from baseline in MRI T2 of composite of lower leg muscles
- Other measures: timed function tests (10-meter walk/run, 4-stair climb, time to stand), NSAA, muscle strength, PODCI and MRI fat fraction

- Measure the same safety and efficacy parameters as in Part B of the trial to assess treatment effects over a longer time

Part B Key Study Metrics and Efficacy End Points

Key Study Metrics

- Enrolled total of 31 boys at 5 sites for Part B of the trial, 16 of whom also participated in Part A. In Part B, patients were randomized to:
  - Edasalonexent 67 mg/kg/day given as twice per day dosing
  - Edasalonexent 100 mg/kg/day given as three times per day dosing
  - Placebo
- All 31 patients who enrolled completed the trial

Primary Efficacy End Point

- Average change from baseline to week 12 in MRI T2 relaxation time (milliseconds) for the composite of lower leg muscles:
  - Soleus (Sol)
  - Medial gastrocnemius (MG)
  - Tibialis posterior (TP)
  - Tibialis anterior (TA)
  - Peroneals (Per)

Additional Efficacy End Points

- Speeds and times for timed function tests (TFTs):
  - Completing the 10-meter walk/run (10MWR)
  - Climbing 4 stairs (4SC)
  - Standing from supine (time to stand: TTS)
- North Star Ambulatory Assessment (NSAA)
- Other MRI/MRS measures in lower and upper leg muscles
- Muscle strength testing
  - Knee extension
  - Plantar flexion
- Pediatric outcomes data collection instrument (PODCI)

MRS: Magnetic Resonance Spectroscopy

MoveDMD Trial Part B Baseline Demographics and Values

Treatment Group	Placebo	Edasalonexent 67 mg/kg/day	Edasalonexent 100 mg/kg/day	Overall Edasalonexent
	(n =11)	(n =10)	(n =10)	(n =20)
Age at Week 0 (years)[1]	6.3	6.0	6.0	6.0
Age at Symptom Onset (years)[2]	3.7	3.0	2.0	2.5
Age at Diagnosis (years)[2]	4.6	3.5	3.0	3.3
Weight at randomization (kg)	21.4	22.1	22.0	22.1
10-meter walk/run (10MWR in seconds)[1]	6.9	6.3	6.8	6.6
4-stair climb (4SC in seconds)[2]	5.0	4.5	6.3	5.4
Time to stand (TTS in seconds)[2]	6.5	7.0	12.0	9.4

Values shown are means
Patients were all male and steroid-naive and predominantly Caucasian

[1]Patient randomization was stratified for baseline age and 10-meter walk/run

[2]On average, patients in the edasalonexent 100 mg/kg/day group were symptomatic at a younger age and did not perform as well on the 4-stair climb and the time to stand function tests at baseline; characteristics consistent with more advanced disease

All 31 patients completed the study and were included in the per protocol population.

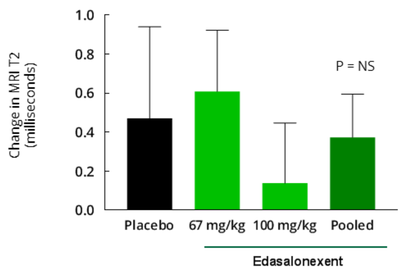
MoveDMD Trial Part B Results Adverse Events

Treatment Group	Placebo	Edasalonexent 67 mg/kg/day	Edasalonexent 100 mg/kg/day	Overall Edasalonexent
Adverse events in >10% of edasalonexent patients	(n =11)	(n =10)	(n =10)	(n =20)
Subjects with any TEAEs	10 (90.9)	9 (90.0)	8 (80.0)	17 (85.0)
Gastrointestinal disorders				
Diarrhea	0 (0.0)	3 (30.0)	4 (40.0)	7 (35.0)
Vomiting	1 (9.1)	1 (10.0)	3 (30.0)	4 (20.0)
Abdominal Pain Upper	0 (0.0)	2 (20.0)	2 (20.0)	4 (20.0)
Nausea	0 (0.0)	1 (10.0)	2 (20.0)	3 (15.0)
General disorders				
Pyrexia	3 (27.3)	0 (0.0)	0 (0.0)	0 (0.0)
Injury, poisoning and procedural complications				
Fall*	3 (27.3)	4 (40.0)	2 (20.0)	6 (30.0)
Skin abrasion	0 (0.0)	2 (20.0)	1 (10.0)	3 (15.0)
Metabolism and nutritional disorders				
Decreased appetite	0 (0.0)	1 (10.0)	2 (20.0)	3 (15.0)
Respiratory, thoracic and mediastinal disorders				
Rhinorrhoea	1 (9.1)	2 (20.0)	2 (20.0)	4 (20.0)

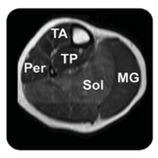
*Falls were specifically recorded as an exploratory measure.

MoveDMD Trial Part B Results Primary Efficacy End Point

Change in MRI T2 from Baseline to Week 12 in Composite of 5 Lower Leg Muscles



Smaller increase in MRI T2 correlates with less muscle inflammation

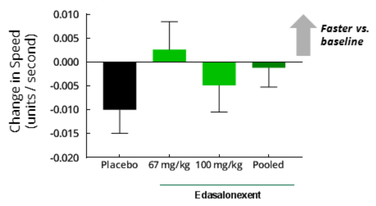


- No significant change in the primary end point, average change from baseline to Week 12 in the MRI T2 measure for a composite of lower leg muscles for the pooled edasalonexent treatment groups vs. placebo.

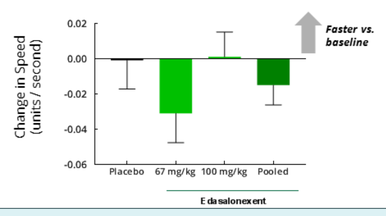
Error bars in chart denote SEM

MoveDMD Trial Part B Results 10-meter Walk/Run Speed and Time to Stand Speed

Change in 10-meter Walk/Run Speed from Baseline to Week 12



Change in Time to Stand Speed from Baseline to Week 12

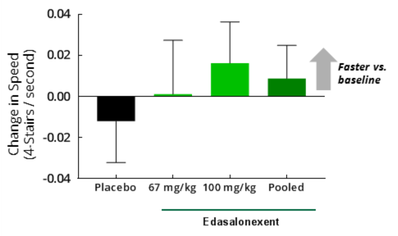


- Change in timed function test Speed at Week 12 was a pre-defined end point
- Speed is the reciprocal of the time to perform the function test. In contrast to Time, Speed allows for accounting for boys who are unable to perform tests
- Change in 10-meter walk/run Speed and change in time to stand Speed numerically better for edasalonexent 100 mg/kg/day vs. placebo although neither was statistically significant

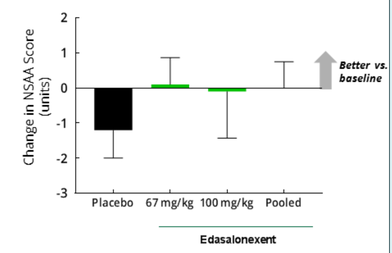
Error bars in chart denote SEM

MoveDMD Trial Part B Results 4-Stair Climb Speed and North Star Ambulatory Assessment

Change in 4-Stair Climb Speed from Baseline to Week 12



Change in Total NSAA Score from Baseline to Week 12



- Changes in 4-stair climb Speed and North Starr Ambulatory Assessment were numerically better for edasalonexent vs. placebo, although not statistically significant

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Error bars in chart denote SEM

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MoveDMD Trial Part B Results Muscle Strength

Change in Plantar Flexion Strength from Baseline to Week 12

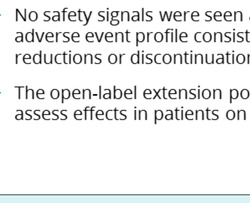
Change in Knee Extension Strength from Baseline to Week 12

- Assessed by Biodex at Baseline and Week 12 in 26 of 31 boys
- Changes not statistically significant

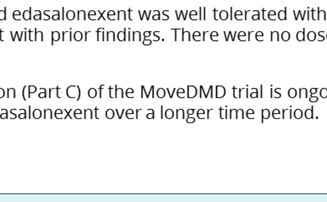
Error bars in chart denote SEM

MoveDMD Trial Part B Results Pediatric Outcomes Data Collection Instrument

Change in PODCI BL Part B to Week 12 (transfer & basic mobility)



Change in PODCI BL Part B to Week 12 (upper extremity & physical function)



Change in PODCI BL Part B to Week 12 (global function)

- Of the PODCI subscores, the Transfer and Basic Mobility Score generally correlates best with loss of milestones over time (McDonald, 2010).
- For all PODCI subscores, there were numerical improvement for the treatment groups compared with placebo, although not statistically significant.

Error bars in chart denote SEM

MoveDMD Trial: Observations During Control Period from Baseline of Part A to Baseline of Part B

- The period from Baseline of Part A to Baseline of Part B was defined as the control period. During this period of approximately 8 months, patients were off-treatment except for the initial week of dosing in Part A.
- Declines in TFT's and NSAA were evident during the control period.
- Muscle strength was stable

*p<0.05
◊ For reference, shown for Baseline of Part A are the times corresponding to the average speed.

Error bars in chart denote SEM

Comparison of Rate of Change During Control and Active Treatment Periods

- For the 12 boys who crossed over to edasalonexent in Part B, there was numerical improvement in the rate of decline in timed function tests, NSAA and PODCI when comparing the active treatment period to the control period, although these changes were not statistically significant.
- The time periods for the control period between Part A and Part B differ, so weekly rates of change are shown.
- For perspective, during the control period there was at least an 8% decline in the timed function tests.

MoveDMD Trial Part B Conclusions

- No significant change was observed in the primary end point of change from baseline in MRI T2 of the composite of lower leg muscles for pooled edasalonexent doses vs. placebo.
- In functional exploratory endpoints, edasalonexent treatment groups generally showed numerical improvement vs. placebo across multiple measures although the changes were not statistically significant:
  - 3 age-appropriate timed function tests: 4-stair climb, 10-meter walk/run and time to stand
  - NSAA, PODCI and muscle strength
- For the 12 boys who crossed over to edasalonexent in Part B, there was numerical improvement in the rate of decline in timed function tests, NSAA and PODCI when comparing the active treatment period to the control period, although these changes were not statistically significant.
- No safety signals were seen and edasalonexent was well tolerated with an adverse event profile consistent with prior findings. There were no dose reductions or discontinuations.
- The open-label extension portion (Part C) of the MoveDMD trial is ongoing to assess effects in patients on edasalonexent over a longer time period.

Thank you

- Patients and families
- Patient groups
- ImagingDMD Staff
- Catabasis team

Jett Foundation
Cure Duchenne
Parent Project Muscular Dystrophy — LEADING THE FIGHT TO END DUCHENNE
MDA Fighting Muscle Disease

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