Edasalonexent Treatment in Young Boys with Duchenne Muscular Dystrophy Is Associated with Age-Normative Growth and Normal Adrenal Function

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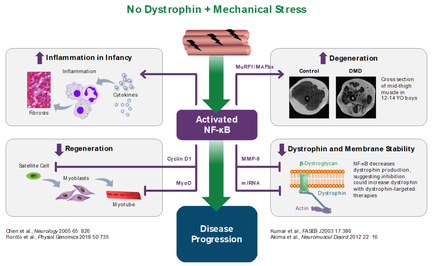
NF-κB Inhibition and Edasalonexent Mechanism of Action

Activation of NF-κB in Duchenne Muscular Dystrophy Is a Key Factor in Disease Progression

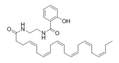


Chen et al., *Neurology* 2005 65: 826
Fiorillo et al., *Physiol Genomics* 2018 50:735

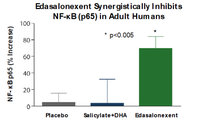
Kumar et al., *FASEB J* 2003 17:386
Akima et al., *Neuromuscul Disord* 2012 22: 16

Edasalonexent Inhibits NF-κB, a Key Driver of Muscle Disease in DMD

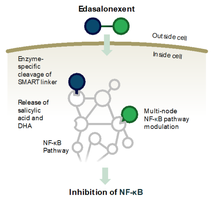
- Edasalonexent is an orally-administered small molecule



- Edasalonexent has a unique pharmacological profile that inhibits NF-κB better than its individual components



- Edasalonexent is a unique molecule delivering salicylic acid and the omega-3 docosahexaenoic acid (DHA) into cells by using SMART Linker Technology



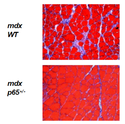
Donovan et al. JClin Pharmacol 2017 57:627-639

Inhibition of NF-κB Slowed Disease Progression in Preclinical Models of DMD

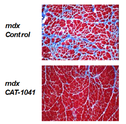
Genetic disruption of NF-κB slowed disease progression in *mdx* mice
- *mdx*/p65+/- mice with 50% reduction in NF-κB activity

Pharmacological inhibition of NF-κB also slowed disease progression in animal models of DMD
- Oral administration of edasalonexent analog (CAT-1041) reduced muscle inflammation and improved function in *mdx* mice and GRMD dog

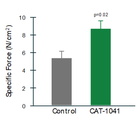
Reduced Muscle Fibrosis *(Gastrocnemius)*



Reduced Muscle Fibrosis *(Quadriceps)*



Improved Muscle Function *(Diaphragm Specific Force)*



Yin, et al. Muscle & Nerve 2017 56:759-767

Hammers, et al. JCI Insight 2016 1(21): e90341

Mean ± SEM shown

Study Design and Capsule Swallowing Ability

Design of MoveDMD®, a Phase 1/2 Trial with Open-Label Extension

- **Study Objectives**
  - Safety and PK in pediatric patients with Duchenne
  - Proof of concept using MRI to assess changes in muscle health
  - Long-term safety and effects on age-appropriate functional measures to enable design of Phase 3 study
- **Study Population**
  - Age 4 up to 8th birthday not currently being treated with corticosteroids
  - Able to perform timed function tests and MRI
- **Design**
  - Phase 1: 1-week open-label to assess safety and PK, with initial assessments of function and MRI
  - Off-treatment period of ~6 months prior to Phase 2
  - Phase 2: 12-week placebo-controlled period of 67 mg/kg and 100 mg/kg doses of edasalonexent
  - Open-label extension up to 150 weeks

- **Prespecified Analysis Plan**
  - 12-week placebo-controlled period evaluated MRI T2, North Star Ambulatory Assessment, timed-function tests, and safety
  - Additional comparison of rates of change during off-treatment control period versus on edasalonexent treatment

Experience with Edasalonexent Demonstrates Ability of 4 to 7-year-old Boys with DMD to Take Soft-gel Capsules in Clinical Trials

- As part of the eligibility criteria, Phase 2 MoveDMD trial required boys to demonstrate ability to swallow at least one capsule size in order to meet eligibility
- In the Phase 2 MoveDMD trial, 97% of boys screened were able to swallow capsules
- Edasalonexent capsules were well-accepted in boys with DMD
  - Site experience, clinical trial personnel confidence and initial capsule size presentation had the most significant impact in selection.
  - Age did not appear to be a major determinant of ability to take capsules
  - Soft-gel capsules were successfully be used in this phase 2 clinical trial of boys as young as 4 years with appropriate support

Phase 2 Safety Experience

In Phase 2 MoveDMD Trial and Open-Label Extension:

Safety: Edasalonexent was Well-Tolerated

- Well tolerated for up to 150 weeks
- Majority of adverse events mild in nature
  - Most common related adverse event was diarrhea, generally mild and transient
  - No serious adverse events on treatment (one on placebo)
- No adverse trends in chemistry and hematology

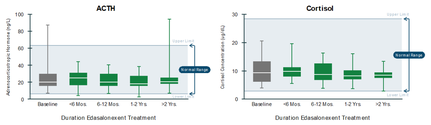
Treatment-Related Adverse Events >5%	Edasalonexent Overall (N=31)
System Organ Class/ Preferred Term	n %
Subjects with any treatment-emergent adverse event	31 (100%)
Subjects with any treatment-emergent adverse event related to study treatment	19 (61.3)
Gastrointestinal disorders	
Diarrhoea	16 (51.6%)
Abdominal pain upper	7 (22.6%)
Nausea	3 (9.7%)
Vomiting	3 (9.7%)
Abdominal discomfort	2 (6.5%)
Abdominal pain	2 (6.5%)
Faecal incontinence	2 (6.5%)
Faeces soft	2 (6.5%)
Metabolism and nutrition disorders	
Decreased appetite	4 (12.9%)

In Phase 2 MoveDMD Trial and Open-Label Extension:

Safety: Edasalonexent was Well-Tolerated

- Edasalonexent is not a steroid and does not impact the glucocorticoid receptor
- High-dose steroids are associated with adverse effects related to bone health, growth and adrenal suppression, among other side effects
- There was no evidence of adrenal insufficiency for up to 150 weeks, with no clinically significant changes in either cortisol or ACTH

Pituitary gland → ACTH Production → Adrenal Gland → Cortisol Production



Box plot error bars indicate range of results

Phase 2 Bone Health and Growth Curves

Potential for Bone Preservation with Edasalonexent

- Both myopathy and glucocorticoid (GC) therapy lead to reduced bone density and bone strength in DMD

- Unlike GC, edasalonexent treatment in a *mdx* mouse model preserves bone length and bone density

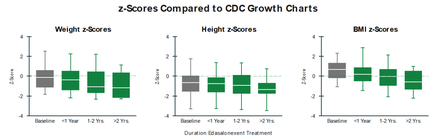
- Increased fracture risk is apparent in boys with DMD with or without GC*
  - In this retrospective study, fracture incidence in glucocorticoid naïve boys was 2.5%/year
  - In the same study, fracture incidence in first 2 years of glucocorticoids was 11.6%
- In MoveDMD, fracture incidence was 3.2%/year with neither long bone nor minimal trauma fractures
  - In over 60 patient-years of exposure, only two fractures were reported (radius and metatarsal), none with minimal trauma

Donovan 2019 Bone Symposium oral presentation, Salzburg, Austria

In Phase 2 MoveDMD Trial and Open-Label Extension:

Safety: Growth Continues as Expected Compared to Standard Growth Charts

- Boys on edasalonexent grew similarly to growth curves for unaffected boys up to 150 weeks
  - Height increased along expected growth curves for unaffected boys, while weight increase was less than the mean for unaffected boys, resulting in overall normalized BMIs
- BMI is typically elevated in these boys and on edasalonexent treatment, BMI trended down



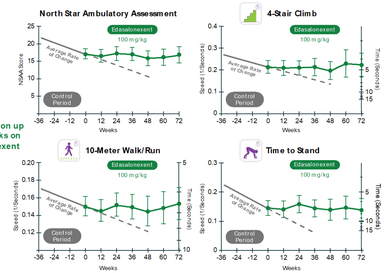
Means ± SEM shown
Box plot error bars indicate range of values
Comparison with CDC growth charts: https://www.cdc.gov/growthcharts/clinical_charts.htm

Phase 2 Functional Results

In Phase 2 MoveDMD Trial and Open-Label Extension:

Edasalonexent Demonstrated Clinically Meaningful Slowing of Disease Progression Compared to Off-Treatment Period

Sustained stabilization up to 72 weeks on edasalonexent



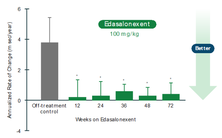
Means ± SEM shown. Includes data of all boys initially started on 100 mg/kg dose (n=16) with 11 boys participating through 72 weeks

Phase 2 MRI T2 Results

In Phase 2 MoveDMD Trial and Open-Label Extension:

Edasalonexent Improved Rate of Change of MRI T2 Compared to Off-Treatment Control Period

MRI T2: Composite of 5 Lower Leg Muscles



Means ± SEM; mixed model comparison with off-treatment period
* Week 12: p=0.002, n=16; Week 24: p=0.004, n=14; Week 36: p=0.032, n=13; Week 48: p=0.018, n=12; Week 72: p=0.052, n=9

- Composite of 5 lower leg muscles MRI T2 (soleus, gastrocnemius, anterior and posterior tibialis, peroneals) used to encompass muscles at various stages of disease progression and minimize variability
- MRI T2 is tightly correlated with fat fraction and functional measures
- 12-week Phase 2 MRI T2 primary endpoint for treated boys compared to boys in the placebo group was directionally positive although not statistically significant
- Following 72 weeks of edasalonexent, the rate of increase in the composite MRI T2 decreased as compared to the rate of increase during the off-treatment control period
- **Early and sustained response in annualized rate of change**

Phase 2 MoveDMD Trial Supports Phase 3 Trial Design

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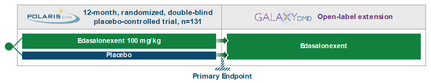
- The global PolarisDMD trial is fully enrolled across all 8 countries where the trial is active



- Enrolled 131 boys ages 4-7 (up to 8th birthday)
  - Not on corticosteroids for at least 6 months
- 2:1 randomization, 67% of boys receive drug initially, all boys have the option to receive drug after 12 months through GalaxyDMD
- Clinical trial site visits and key assessments every 3 months
- Safety measures including labs every 3 months
- Top-line results expected in Q4 2020

NCT03703882 and NCT03917719

Conclusion and Acknowledgements

Conclusion

- Treatment with edasalonexent was well-tolerated and associated with favorable growth patterns without negative impact on bone health or adrenal function
- Edasalonexent has the potential to be disease-modifying in DMD patients and in this Phase 2 trial did not have the adverse effects associated with high-dose steroids
- An ongoing Phase 3 trial of edasalonexent, PolarisDMD, is fully enrolled and is further assessing safety and efficacy in young boys with DMD
- Phase 3 PolarisDMD trial results are expected in Q4 2020

Acknowledgements

- Patients and families
- Patient groups
- Phase 3 PolarisDMD Site Staff
- Phase 2 MoveDMD Site Staff
- Catabasis team
- Thanks to PPMD and MDA for generous grant support for patient travel in the Phase 2 MoveDMD trial

Questions? MedInfo@catabasis.com

World Muscle Society, October 2020, Virtual Poster # 282

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- The clinical trial was sponsored by Catabasis Pharmaceuticals, Inc.
- Krista Vandenborne, H. Lee Sweeney, Erika Finanger, Gihan Tennekoon, Perry Shieh, and Sabrina Yum received research support from Catabasis. H. Lee Sweeney, Erika Finanger, and Perry Shieh received honoraria from Catabasis
- Maria Mancini, James MacDougall, and Joanne Donovan are employees or consultants of Catabasis and may hold stock in Catabasis
- Edasalonexent is an investigational agent that is not approved in any territory