Baseline Characteristics of Patients Enrolled in PolarisDMD, a Phase 3 Trial of Edasalonexent for Duchenne Muscular Dystrophy

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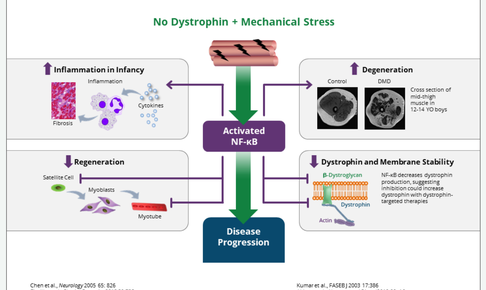
Background

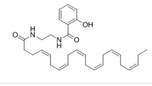
Activation of NF-κB in Duchenne Muscular Dystrophy Is a Key Factor in Disease Progression



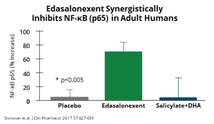
Chen et al., *Neurology* 2005 65: 826
Fiorillo et al., *Physiol Genomics* 2018 50:735
Kumar et al., FASEB J 2003 17:386
Akima et al., *Neuromuscul Disord* 2012 22: 16

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

- **Edasalonexent is an orally-administered small molecule**

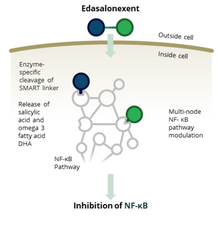


- **Edasalonexent has a unique pharmacological profile that inhibits NF-κB better than its individual components**



Donovan et al. J Clin Pharmacol 2017 57:627-639

- **Edasalonexent is a unique molecule delivering salicylic acid DHA into cells by using SMART Linker Technology**



Edasalonexent Clinical Development Program

- **Edasalonexent is being developed as a foundational therapy for Duchenne for all patients, regardless of mutation.**

MoveDMD
- The Phase 2 MoveDMD trial and open-label extension showed slowing of disease progression on MRI and functional measures and supported design of a pivotal Phase 3 trial, PolarisDMD, in a similar population.
- This Phase 2 trial was conducted at 5 sites in the US

POLARIS
- The Phase 3 trial is a one-year randomized, double-blind, placebo-controlled study to assess edasalonexent efficacy and safety and is fully enrolled.
- This Phase 3 trial is being conducted at 37 sites in 8 countries.

- The Phase 3 PolarisDMD trial is based on the MoveDMD trial, which showed improvements in MRI and functional measures compared to an off-treatment control period.
- The goal of this analysis was to compare baseline demographic and functional characteristics of the two trials.

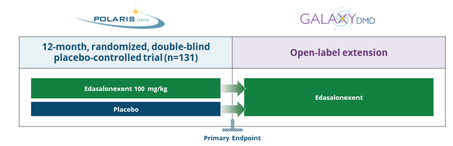
Study Design

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

Design
- **Study population**
  - Age 4 to 7 (up to 8th birthday); off steroids for ≥6 months
  - Able to swallow placebo capsules at the Screening Visit
- **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

Edasalonexent Phase 3 PolarisDMD Trial Designed for Global Registration



Eligibility:
- All mutations
- Age 4 to 7 (up to 8th birthday); off steroids for ≥6 months
- Able to swallow placebo capsules at the Screening Visit

Endpoints measured at Screening and Baseline, with Primary Endpoint at 52 Weeks:
- Primary: Change in North Star Ambulatory Assessment (NSAA)
- Key secondary: Velocity of age-appropriate timed function tests
- Additional assessments include growth, cardiac and bone measures

Top-line results expected in Q4 2020

Study Design

Entry Criteria of Phase 2 MoveDMD and Phase 3 PolarisDMD Trials Were Similar

MoveDMD
- Age 4 to 7 (up to 8th birthday)
- Not on corticosteroids for at least 6 months
- Diagnosis of Duchenne based on a clinical phenotype with increased serum CK and the presence of a mutation in the dystrophin gene known to be associated with a Duchenne phenotype
- Ability to walk independently
- No other prior or ongoing significant medical conditions
- No exposure to another investigational drug

POLARIS
- Age 4 to 7 (up to 8th birthday)
- Not on corticosteroids for at least 24 weeks
- Diagnosis of Duchenne based on a clinical phenotype with increased serum CK and the presence of a mutation in the dystrophin gene known to be associated with a Duchenne phenotype
- Ability to walk independently, perform the 4-stair climb and perform the stand from supine in ≤ 10 seconds
- No other prior or ongoing significant medical conditions
- No exposure to another investigational drug
- Stable eteplirsen allowed

Assessments

Assessments Performed During Clinical Visits, with NSAA as Primary Endpoint

Physical Function Outcomes

Primary Endpoint: North Star Ambulatory Assessment

Assessment measures*

Hop right leg	Climb box step right
Hop left leg	Climb box step left
Stand on heels	Stand on one leg right
Rise from floor	Stand on one leg left
Run	Get to sitting
Jump	Rise from chair
Lift head	Walk
Descend box step right	Stand
Descend box step left	

How measures are scored

2 Can perform | 1 Can perform with difficulty | 0 Unable to perform

3 Timed Function Tests
- Time to Stand
- 4-Stair Climb
- 10-Meter Walk/Run

Additional Outcomes Include:
- Growth
- Cardiac Health

- Functional measures assessed at screening and baseline, which were within 4 weeks apart
- Clinical assessors were trained and certified prior to screening visits

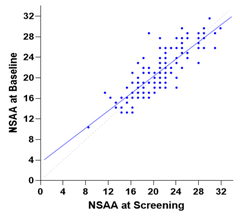
Overview of the North Star Ambulatory Assessment (NSAA)

NSAA is a validated scale specifically developed to measure physical performance of everyday activities in ambulatory boys with Duchenne

*These are tested individually on the left and right leg
Mazzone 2009, Mayhew 2011, FDA 2018, EMA 2016, Birnkrant 2018, MDA 2020 e-poster

Results

NSAA Reproducible Between Screening and Baseline Visits in Young Boys in PolarisDMD



- Boys completed the NSAA at the Screening Visit and at the Baseline Visit, which were up to 4 weeks apart, before treatment with edasalonexent
- During this time there were no changes in their treatment
- On average, there was very little difference (0.3 points) between scores at Screening and Baseline
- This consistency validates the use of the NSAA in boys of this age and shows that there is no learning effect from performing the test after the first time in the clinical trial setting

Reproducibility of Additional Functional Measures Between Screening and Baseline

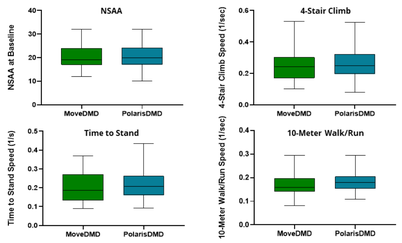
- **The NSAA and timed function tests were highly reproducible in the Phase 3 PolarisDMD study population**
- **NSAA was more reproducible than the timed function tests in this population**

	Pearson Correlation Coefficient
North Star Ambulatory Assessment (NSAA) score	0.84
10-Meter Walk/Run speed (1/s)	0.82
4-Stair Climb speed (1/s)	0.81
Time to Stand speed (1/s)	0.79

Results

Distribution of Functional Measures at Baseline Was Similar in MoveDMD and PolarisDMD Trials

- **Age, baseline NSAA, and speeds of timed function tests (time to stand, 4-stair climb, and 10-meter walk/run) were similar in both studies**



Medians, 25th and 75th percentiles and range shown
Mean differences NS, and differences between distributions tested by Kolmogorov-Smirnov test NS

Phase 3 PolarisDMD and Phase 2 MoveDMD Trials Have Similar Baseline Characteristics

- **Analysis shows that Phase 3 trial enrolled the expected patient population**
  - Comparison of baseline age and function (NSAA, time to stand, 4-stair climb, and 10-meter walk/run) were similar in both trials; there were no significant differences in baseline characteristics between the two trials*

	MoveDMD (n=23)	PolarisDMD (n=131)
Age (years)	6.0 ± 1.1	5.7 ± 1.0
% never previously on steroids	100%	98%
Baseline CK	19842	18964
Heart Rate	99	102
NSAA score	20.1 ± 5.5	20.8 ± 4.7
10-Meter Walk/Run velocity (1/s)	0.168 ± 0.045	0.181 ± 0.037
4-Stair Climb velocity (1/s)	0.254 ± 0.110	0.265 ± 0.097
Time to Stand velocity (1/s)	0.193 ± 0.080	0.212 ± 0.070

Means ± standard deviation shown
*Kolmogorov-Smirnov test used to assess for population distribution differences

Conclusion

Conclusions

- Boys enrolled in the PolarisDMD Phase 3 trial are similar to boys enrolled in the Phase 2 MoveDMD edasalonexent trial, without significant differences in baseline age or functional measures.
- NSAA is a consistent and reproducible measure of function of everyday activities in young boys with Duchenne, characteristics that are important for validity of clinical trial outcomes.
- The Phase 2 MoveDMD trial and open-label extension showed slowing of disease progression on MRI and functional measures compared with an off-treatment control period, and supported design of a pivotal Phase 3 trial, PolarisDMD.

Acknowledgements

- Patients and families
- Patient groups
- PolarisDMD Phase 3 Site Staff
- MoveDMD Phase 2 Site Staff
- Catabasis team
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Questions? MedInfo@catabasis.com
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