Baseline Characteristics in Part 2 of "MOXIe" Trial: A Study of the Efficacy and Safety of Omaveloxolone in Patients with Friedreich's Ataxia

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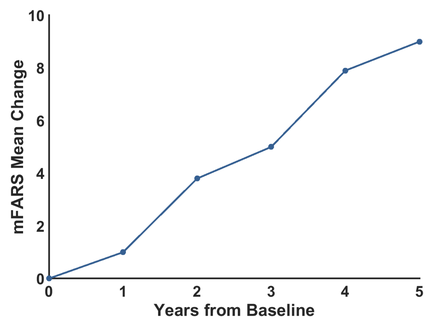
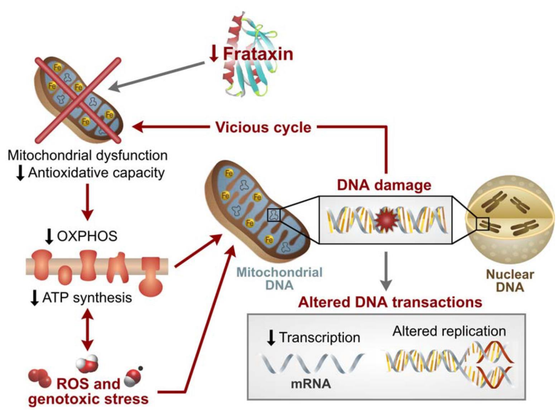
OMAVELOXOLONE IN FRIEDREICH'S ATAXIA

- Omaveloxolone (Omav) and analogs are potent activators of Nrf2[1]
- Nrf2 activation induces the transcription of hundreds of antioxidant genes to combat oxidative stress, mitochondrial dysfunction, and inflammation[2]
- Friedreich's ataxia (FA) leads to the phenotype of mitochondrial iron overload, disruption of Fe-S cluster biosynthesis, and oxidative stress due to reduced frataxin levels[3]
- There are no effective or approved therapies for FA currently[4]
- Nrf2 is impaired in cells isolated from patients with FA[4, 5]
- Omav has the potential to improve symptoms of FA by increasing mitochondrial function and reducing oxidative stress[6]
- Longitudinal data of the FA Rating Scale (FARS) and modified FARS (mFARS) changes have been well characterized and are significantly correlated with ataxia stage and activities of daily living (ADL)[7]



FARS Correlations (n=812)[7]	
Disease Stage	0.84 (p<0.0001)
ADL	0.84 (p<0.0001)



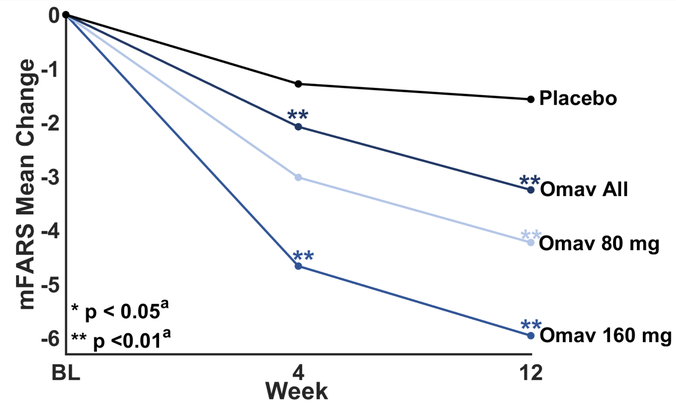
MOXIe PART 1 RESULTS AND CONCLUSIONS

MOXIe Part 1 was a 12-week dose-ranging study with patients randomized 3:1 to either Omav or placebo

RESULTS

- 160 mg patients had an mFARS placebo-corrected change of -2.3 (p=0.06)
- Primary endpoint of mFARS change was more robust in patients without pes cavus (-4.4 points in 160 mg dose group, placebo corrected)
- Omav was well-tolerated

mFARS Change in Patients without Pes Cavus (MOXIe Part 1)[8]



[a] Values are LS MEAN estimates at Week 12 vs. baseline using mixed-model repeated measures and p-values represent comparison to zero

CONCLUSIONS THAT INFORMED MOXIe PART 2

- Significant improvement seen in mFARS in Omav-treated patients without pes cavus
- (62%) of the patients had pes cavus
- Part 2 study enrollment capped at 20 patients with pes cavus
- mFARS changes correlate with disease progression
- Optimal dose determined to be 160 mg

MOXIe PART 2 STUDY DESIGN

- Patients enrolled in Part 1 are ineligible for Part 2
- 103 patients were enrolled in Part 2 (NCT02255435)
- Patients enrolled in Part 2 were randomized 1:1 to receive Omav 150 mg or placebo once-daily for 48 weeks (follow-up at week 52)
- Patients with pes cavus, a musculoskeletal foot deformity characterized by high arch of the foot that does not flatten with weight-bearing, comprise approximately 20% of patients enrolled in Part 2
- Part 1 and Part 2 patients may participate in an open-label extension study (Omav 150 mg)

Key Inclusion Criteria

- Have genetically confirmed FA
- mFARS score ≥ 20 and ≤ 80
- Ability to complete exercise testing

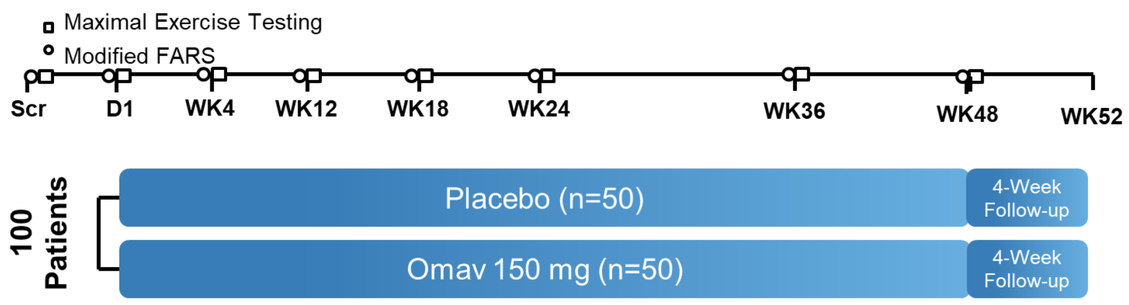
Key Exclusion Criteria

- Brain natriuretic peptide >200 pg/mL
- Clinically significant cardiac disease, with the exception of mild to moderate cardiomyopathy associated with FA

MOXIe PART 1 & 2 BASELINE CHARACTERISTICS

	MOXIe Part 1 N=69	MOXIe Part 2 N=103
Age (years), Mean ± SD	25.6 ± 6.5	23.7 ± 7.0
< 18, n (%)	7 (10.1%)	24 (23.3%)
Male, n (%)	32 (46.3%)	55 (53.3%)
White, n (%)	67 (97.0%)	100 (97.1%)
Pes cavus present, n (%)	32 (46.4%)	20 (19.4%)
BMI (kg/m^2), Mean (SD)	23.7 ± 4.7	23.0 ± 4.9
Age at FA onset (years) , Mean ± SD	15.3 ± 4.8	15.1 ± 5.5
Years since onset (years, Mean ± SD	10.3 ± 5.1	8.7 ± 5.0
Ambulatory, n (%)	62 (90.0%)	95 (92.2%)
GAA1 repeat length		
Mean ± SD	741.1 ± 284.7	705.8 ± 240.5
Range (min, max)	216, 1350	170, 1270
≥ 675, n (%)	38 (55.1%)	47 (45.6%)
Prior Scoliosis Surgery, n (%)	9 (13.0%)	26 (25.2%)
History of Areflexia, n (%)	55 (79.7%)	98 (95.1%)
Baseline Modified FARS, Mean ± SD	41.1 ± 11.5	39.4 ± 10.5
Baseline Peak Work (W/kg), Mean ± SD	1.06 ± 0.65	1.15 ± 0.59

PART 2 SCHEMA AND DOSING



CONCLUSION

- Part 2 of MOXIe, a pivotal Phase 2 trial intended to support registration, has completed enrollment to examine the effect of Omav on mFARS
- Enrolled patients were an average age of 23.7 years old and 92.2% were ambulatory

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DISCLOSURES

DL receives grant funds from Reata Pharmaceuticals, as the PI of the MOXIe trial and for other projects from the NIH and FARA
CJM, MC, AG and MO are employees of Reata Pharmaceuticals

Omaveloxolone is an investigational drug. Safety and efficacy have not been established by any agency.

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