# Safety and Efficacy of Vatiquinone Treatment in Friedreich Ataxia Patients from MOVE-FA

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# Disclaimer

**David Lynch:** Participation in clinical trials for PTC Therapeutics

**Antoine Duquette**: Consultant for Reata Pharmaceuticals, Pfizer, and Actelion Pharmaceuticals Canada. Participation in clinical trials for AbbVie, PTC Therapeutics, Wave Life Sciences, Vaccinex, Roche and Novartis

**Marcondes Cavalcante França Jr**: Consultant for PTC, Biogen, Astellas. Speaker for PTC Therapeutics, Biogen

**Alexandra Durr**: Paris Brain Institute receives grants and consulting fees on Dr Durrs behalf from the National Institute of Health, French National Hospital Clinical Research Program (PHRC), Agence National de Recherche (ANR), Fondation de la recherche Médicale (FRM), Biogen, AskBIo, Servier, UCB, Genome Quebec and Brain-Team

**Elodie Petit:** Consultant for Biogen

**Katherine Mathews**: Consultant for Sarepta and edgewise. Participation in clinical trials for Reata, PTC Therapeutics, Lexeo

**Ludger Schöls**: Consultant for Vico Therapeutics and Novartis

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**Alana Salvucci**: Former employee of PTC Therapeutics. Employed by Acadia Pharmaceuticals

**Bert Yao:** Former employee of PTC Therapeutics, current shareholder of PTC stock

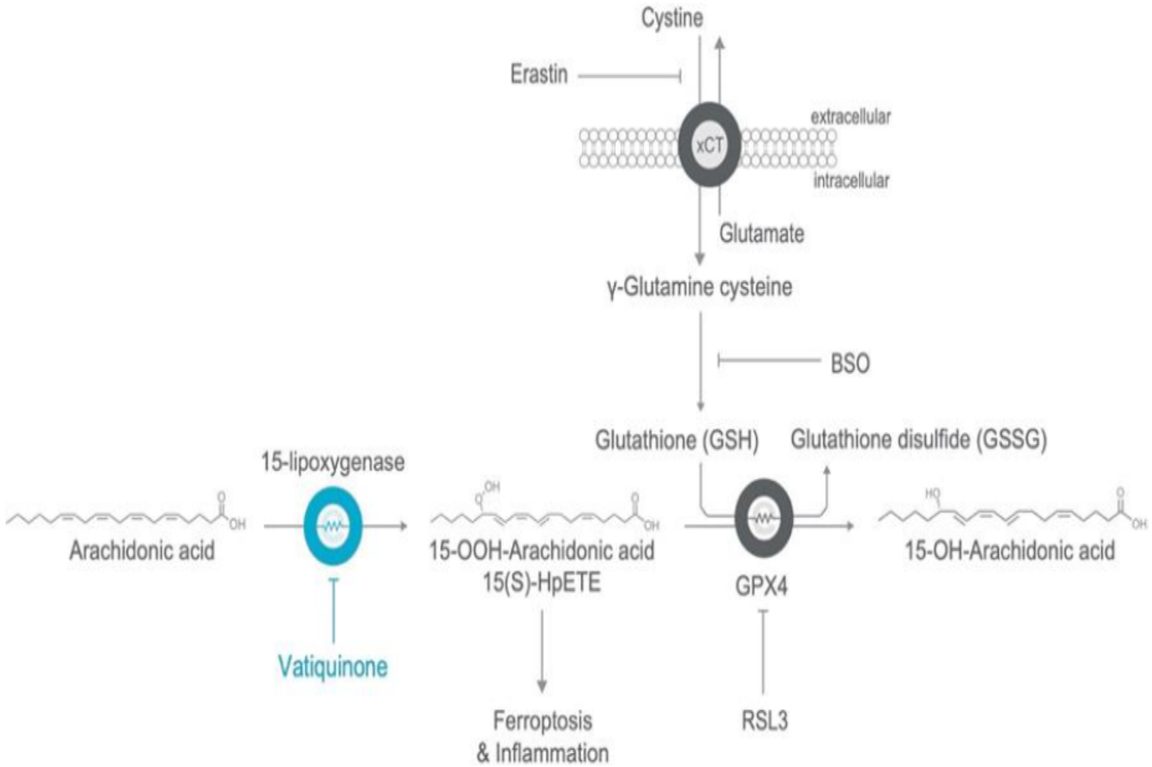
**Olivia Zhang, Jonathan Cherry, and Lee Golden**: Employees of PTC Therapeutics

**The MOVE-FA study is funded by PTC Therapeutics, Inc.**

# VATIQUINONE

- Vatiquinone is a small-molecule therapeutic in development for the treatment of mitochondrial diseases and disorders characterized by elevated oxidative stress and impaired energy metabolism.
- Administered orally, vatiquinone is able to cross the blood-brain barrier, reaching the central nervous system to exert its effects.
- Its primary mechanism involves targeting critical enzymes that play a role in energy metabolism, oxidative stress, and inflammation—key pathways involved in the progression of mitochondrial and neurological diseases.
- Through these combined mechanisms—targeting enzyme pathways linked to oxidative stress and inflammation, inhibiting lipid oxidation, and indirectly reducing ferroptosis—vatiquinone offers a novel and multi-faceted approach to treating mitochondrial and oxidative stress-related disorders.

**Overview of the Ferroptosis Pathway and Role of 15-Lipoxygenase as a Central Regulator of Lipid Oxidation, Inflammation, Glutathione Depletion, and Cell Death**




**Abbreviations**: BSO, L-buthionine sulfoximine; GSH, glutathione; GSSG, glutathione disulfide; GPX4, glutathione peroxidase 4; HpETE, hydroperoxyeicosatetraenoic acid; RSL3, RAS-selective lethal

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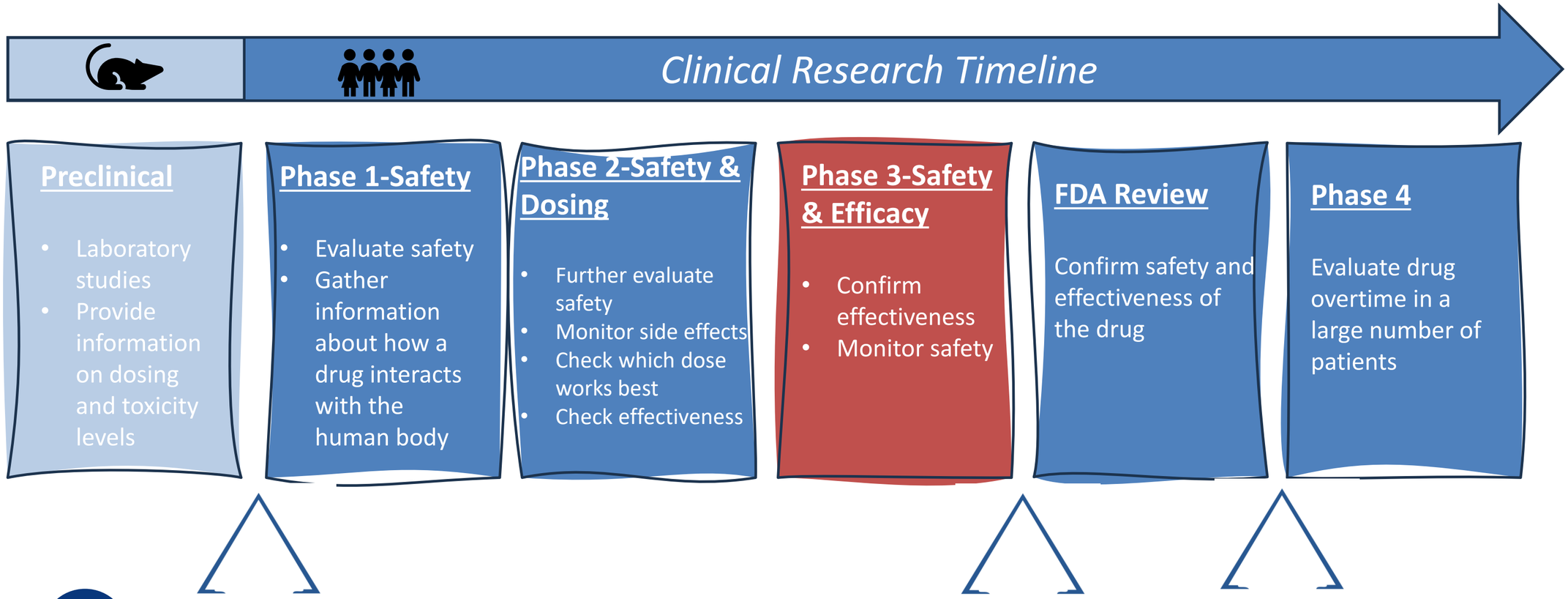
# STUDY DESIGN

- Phase 3_ Double blind_ Placebo controlled trial

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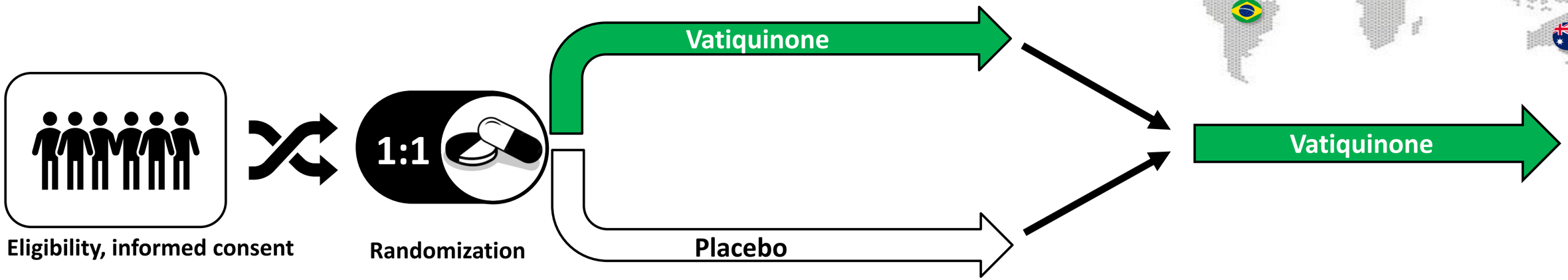
# STUDY DESIGN




- **Primary endpoint**
  - Change from baseline in mFARS at 72 weeks
- **Other Key Endpoints**
  - Change from baseline at 72 weeks :
    - FARS-ADL
    - 1 minute walk test
    - Upright Stability Subscale
    - Modified Fatigue Impact Scale

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# BASELINE CHARACTERISTICS

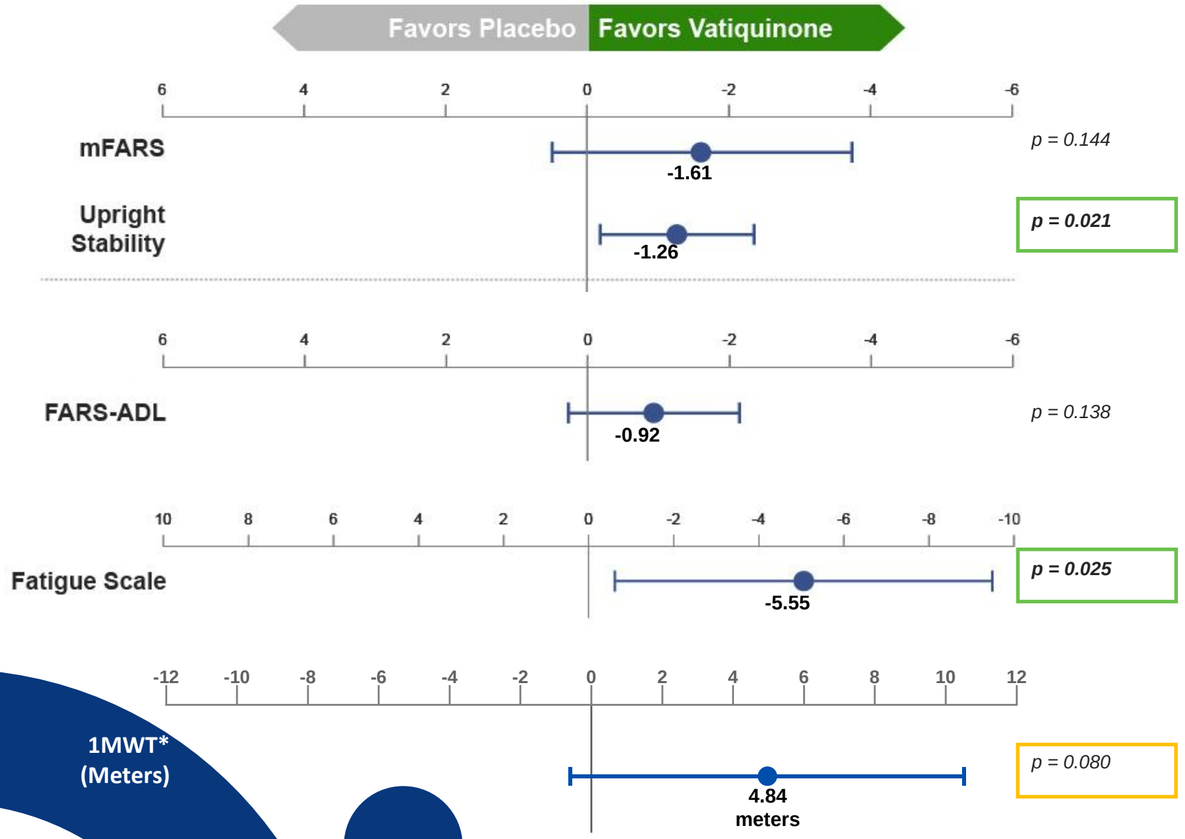
| | Primary Analysis Population (7-21 years old) | | | Overall Enrolled Population (≥7 years old) | | |
|---|---|---|---|---|---|---|
| | Placebo n (%) | Vatiquinone n (%) | Total n (%) | Placebo n (%) | Vatiquinone n (%) | Total n (%) |
| **Subject Number** | 62 | 61 | 123 | 73 | 70 | 143 |
| **Mean Age at Baseline [min,max]** | 14.3 [8,21] | 15.0 [9,21] | 14.6 [8,21] | 18.2 [8,68] | 19.1 [9,68] | 18.7 [8,68] |
| **Age at Onset** | | | | | | |
| **<8** | 28 (45.2) | 27 (44.3) | 55 (44.7) | 28 (38.4) | 27 (38.6) | 55 (38.5) |
| **8 to <14** | 30 (48.4) | 26 (42.6) | 56 (45.7) | 34 (46.6) | 28 (40.0) | 62 (43.4) |
| **14 and over** | 4 (6.5) | 8 (13.1) | 12 (9.8) | 11 (15.1) | 15 (21.4) | 26 (18.2) |
| **mFARS at Baseline [min, max]** | 43.3 [20, 68] | 41.6 [22, 69] | 42.5 [20, 69] | 43.3 [20, 68] | 42.5 [22, 69] | 42.9 [20,69] |
| **Region – n (%)** | | | | | | |
| **Asia Pacific** | 3 (4.8) | 5 (8.2) | 8 (6.5) | 3 (4.1) | 5 (7.1) | 8 (5.6) |
| **European Union** | 19 (30.6) | 16 (26.2) | 35 (28.5) | 19 (26) | 16 (22.9) | 35 (24.5) |
| **North America** | 31 (50) | 33 (54.1) | 64 (52) | 42 (57.5) | 42 (60) | 84 (58.8) |
| **Latin America** | 9 (14.5) | 7 (11.5) | 16 (13) | 9 (12.3) | 7 (10) | 16 (11.2) |

# TOLERANCE

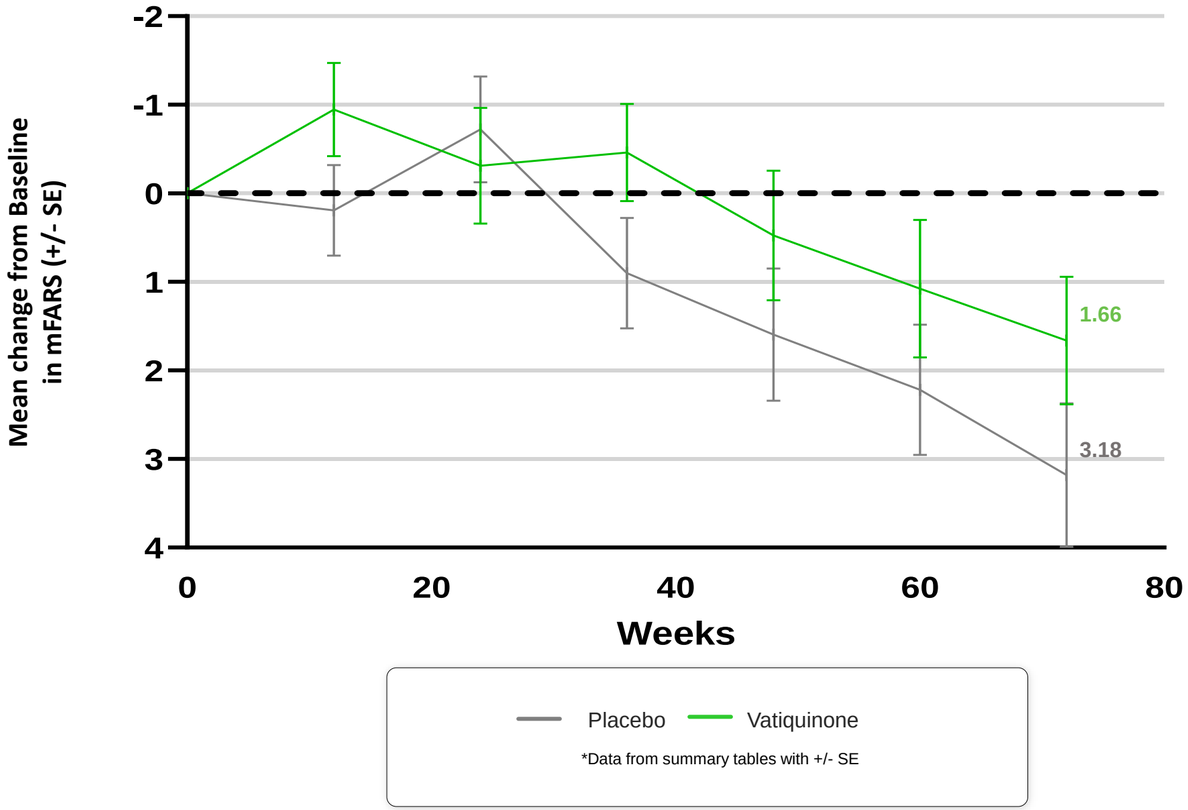
| | Placebo (n=73) | | | Vatiquinone (n=73) | | |
|---|---|---|---|---|---|---|
| | Events (n) | Subjects (n) | Subjects (% of placebo arm) | Events (n) | Subjects (n) | Subjects (% of treatment arm) |
| **Headache** | 62 | 26 | 35.6% | 43 | 25 | 34.2% |
| **Diarrhea** | 17 | 14 | 19.2% | 32 | 22 | 30.1% |
| **Nausea** | 25 | 13 | 17.8% | 19 | 15 | 20.5% |
| **Abdominal pain** | 8 | 7 | 9.6% | 15 | 10 | 13.7% |
| **Epistaxis** | 4 | 3 | 4.1% | 10 | 8 | 11% |
| **Pruritus** | 1 | 1 | 1.4% | 5 | 5 | 6.8% |
| **Dyspepsia** | 4 | 4 | 5.5% | 10 | 5 | 6.8% |
| **Decreased appetite** | 4 | 4 | 5.5% | 6 | 5 | 6.8% |
| **International Normalized Ratio Increased** | 0 | 0 | 0% | 4 | 4 | 5.5% |
| **Musculoskeletal stiffness** | 0 | 0 | 0% | 3 | 3 | 4.1% |
| **Chest pain** | 1 | 1 | 1.4% | 2 | 2 | 2.7% |

# VATIQUINONE TREATMENT DEMONSTRATED IMPROVEMENT VS PLACEBO ON MFARS AND IN KEY SUBSCALES

**Primary Analysis (mITT) Population**
(LS Mean with 95% CI)




**Primary Analysis population (mITT)**

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# Upright Stability Subscale captures Primary Drivers of Disease Progression and is Most Sensitive to Capturing Treatment Effect

## Primary Analysis Population (mITT)

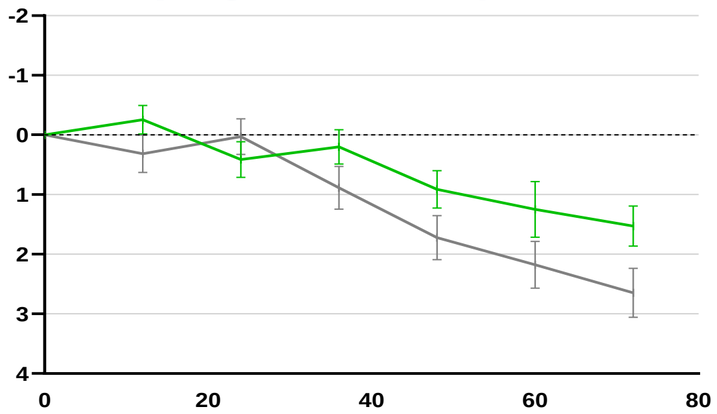
Placebo

Vatiquinone

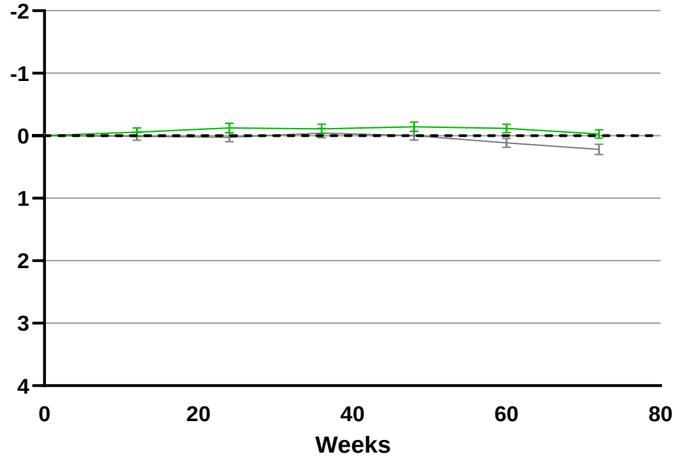
Data from summary tables with +/- SE

Mean Change from Baseline in mFARS sub scores (+/- SE)

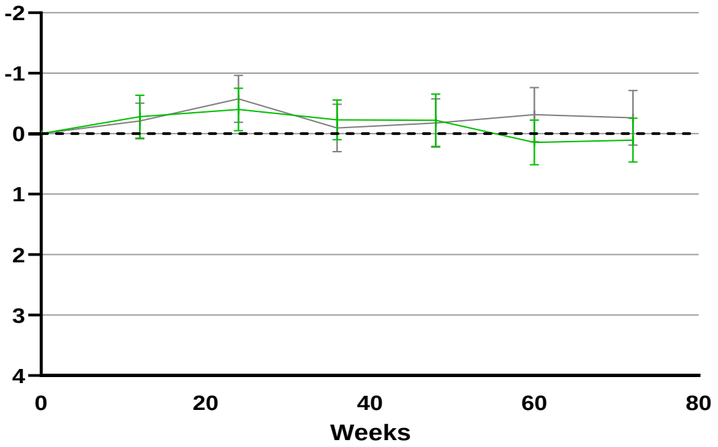
### Upright Stability



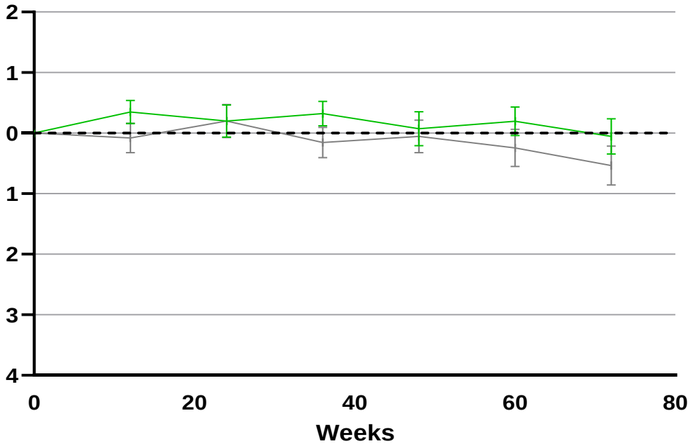

### Bulbar




### Upper Limb




### Lower Limb

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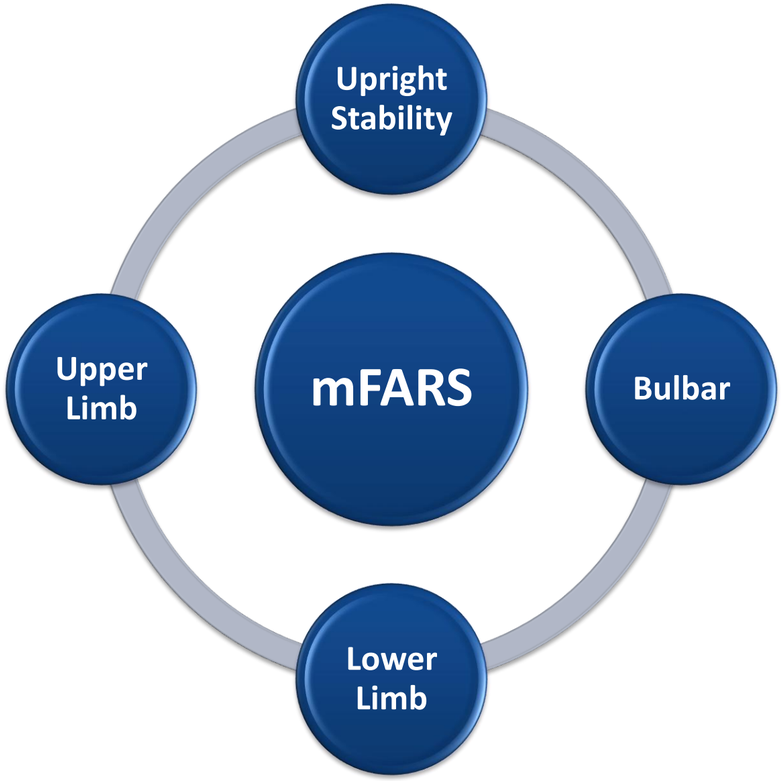
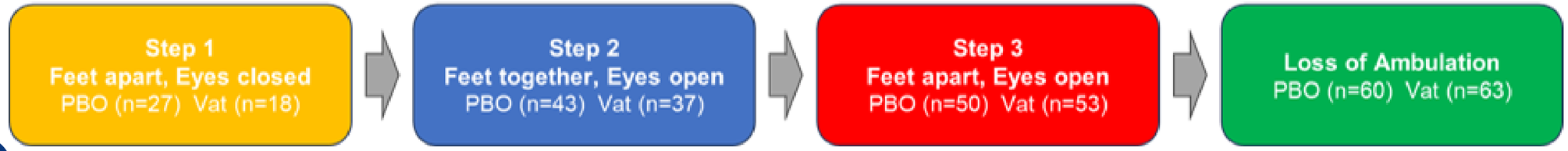
# UPRIGHT STABILITY SUBSCALE (USS)




- USS captures clinically relevant functional tasks that can be tied directly to the ability to ambulate independently
- USS includes 2 types of assessments:
  - stance/balance items
  - walking/sitting items

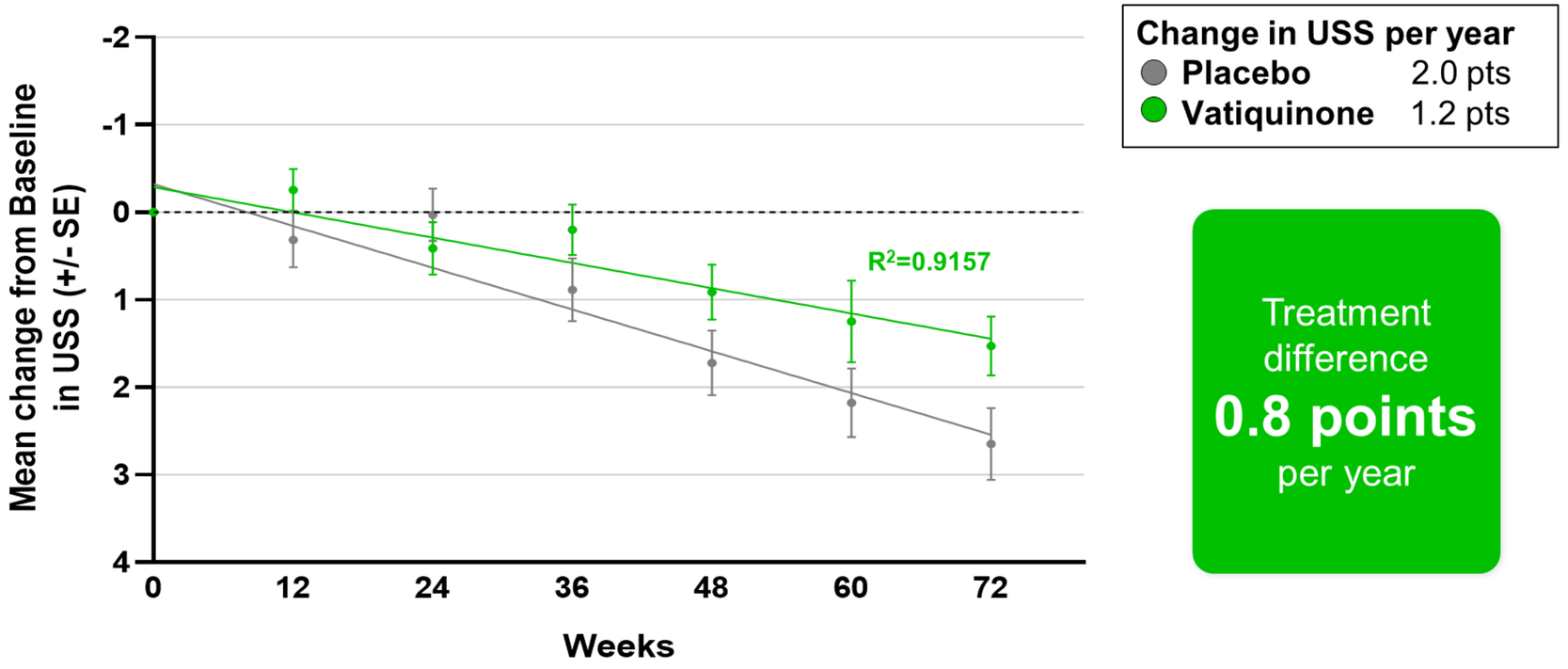
- There is a unique and reproducible pattern of functional loss in the USS stance/balance items during FA progression

**Progression of Mini-milestones**



# VATIQUINONE TREATMENT SLOWED DISEASE PROGRESSION (TOTAL USS)

- USS changed at a rate of 2.0 points per year in the placebo group
- Vatiquinone treatment slowed progression by 0.8 points per year
- At week 72, the treatment benefit predicts a 40% reduction in disease progression and a delay in time to loss of ambulation of approximately 9 months




MOVE-FA

# VATIQUINONE DEMONSTRATED MEANINGFUL BENEFIT AND STRONG SAFETY PROFILE FOR YOUNGER AMBULATORY FA PATIENTS

Vatiquinone treatment resulted in a statistically significant treatment effect on **Upright Stability** and **Fatigue**

New data highlight that upright stability scale is the subscale that best captures disease progression and is most likely to capture treatment effect in ambulant FA patients

**Vatiquinone treatment was safe and well tolerated** with an adverse event profile similar to placebo

**A high unmet need for pediatric FA patients remains**

# THANK YOU

## to the patients and families

## who participated in the study

*and*

## to all the MOVE-FA Investigators

Enrico Bertini
Alejandra Darling
Martin Delatycki
Antoine Duquette
Alexandra Durr
Anne Fournier
Marcondes Cavalcante França Jr
David Lynch
Katherine Mathews
Susan Perlman
Richard Roxburgh
Ludger Schöls
Sub Subramony
Theresa Zesiewicz


euro ataxia

# Questions ?

# Improvement in Upright Stability Subscale of mFARS With Vatiquinone Treatment in MOVE-FA: A Phase 3, Double-blind, Placebo-controlled Trial

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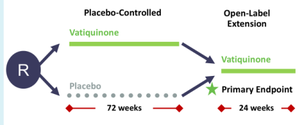
## 1. MOVE-FA Study Design

Friedreich Ataxia (FA), the most common inherited ataxia, is characterized by progressive neurological damage and loss of ambulation. Vatiquinone is an oral, first-in-class inhibitor of 15-lipoxygenase. MOVE-FA (NCT04577352), a global phase 3 trial, evaluated the safety and efficacy of vatiquinone in patients with FA. Here, we describe the results from the 72-week placebo-controlled phase.




Participating Countries

Australia, Brazil, Canada, France, Germany, Italy, Spain, New Zealand, USA

Primary Analysis Population (mITT; n=123)
**Ambulatory FA subjects 7-21 years old**

Overall Enrolled Population (ITT; n=143)
**Ambulatory FA subjects ≥ 7 years old**

**Dosing Regimen**
400mg TID (patients <25 kg)
200mg TID (patients >25 kg)

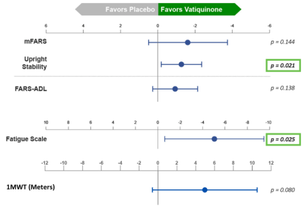
**Primary Endpoint**
Change from baseline in mFARS at 72 wks

**Other Key Endpoint**
*Change from baseline at 72 wks:*
Upright Stability Subscale
FARS-Activities of Daily Living
Modified Fatigue Impact Scale
1 minute walk test

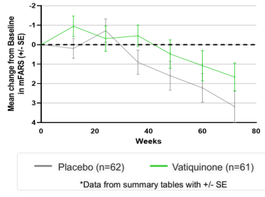
## 2. Topline Results from MOVE-FA

- Vatiquinone treatment benefit was observed across the primary, secondary, and exploratory endpoints.
- In the mITT population, there was a -1.61 (p=0.144) change in mFARS at 72-weeks relative to placebo.
- Notably, there were nominally significant benefits recorded in the Upright Stability subscale (USS/FARS E) of mFARS (-1.26 [p=0.021]), a relevant metric of disease progression in younger, ambulatory FA patients, and the Modified Fatigue Impact Scale (MFIS), -5.05 (p=0.025).

**Primary Analysis (mITT) Population**
(LS Mean with 95% CI)




**Primary Analysis (mITT) Population**
(change from baseline in mFARS)

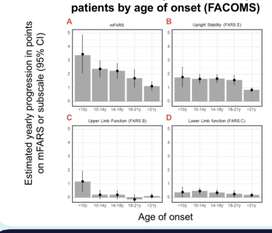



*Data from summary tables with +/- SE

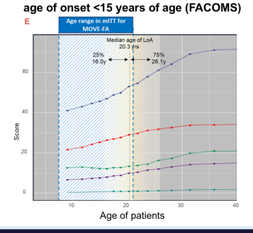
## 3. Disease Progression in Ambulatory FA Patients

- The FA Clinical Outcome Measures Study (FACOMS) represents the most comprehensive natural history database of patients with FA. It has enrolled more than 1300 participants to date, with data from over 6400 visits
- Patients with earlier disease onset are more likely to display rapid neurological progression as measured by mFARS. [1]
- USS assesses functions related to balance, stance, and mobility
- USS is the primary and most stable driver of decline in mFARS for ambulatory patients with age of onset between 10 and 21 years of age (*Figure 3a and 3b*)
- USS has the largest contribution to overall mFARS score in typical onset, ambulatory FA subjects and is relatively stable through loss of ambulation (LoA) (*Figure 3e*) [1]

**Mean annual change in ambulatory FA patients by age of onset (FACOMS)**



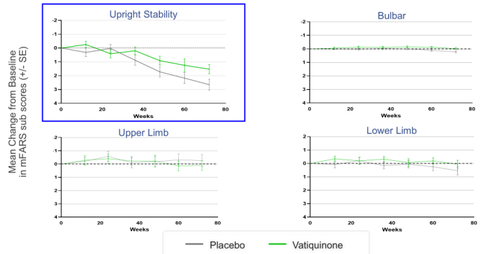

**Contribution of subscales in FA patients with age of onset <15 years of age (FACOMS)**




## 4. USS Subscale Is Only mFARS Component Sensitive to Treatment Effect in the MOVE-FA Patient Population

- USS was the only one of the four subscales of mFARS in which there was evidence of progression in the primary analysis population of MOVE-FA
- USS was the only component of the mFARS capable of registering treatment effect on the slowing of disease progression in this population

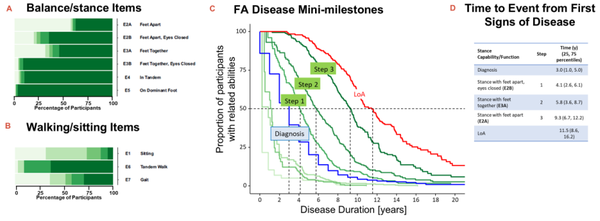
**Primary Analysis Population (mITT)**




*Data from summary tables with +/- SE

## 5. Topline Results from MOVE-FA

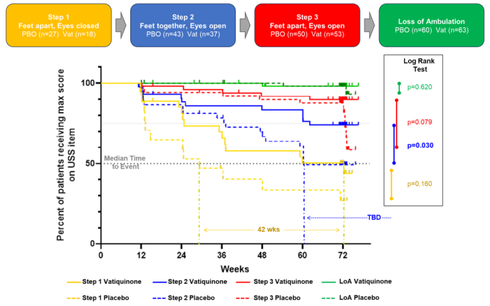
- USS captures clinically relevant functional tasks that can be tied directly to the ability to ambulate independently
- USS includes 2 types of assessments: 6 stance/balance items (E2A, E2B, E3A, E3B, E4, and E5) and 3 walking/sitting items (E1, E6, and E7).
- Stance items demonstrate a distinct bimodal distribution where patients transition between being able to performing a task and failing the task very quickly (*Figure 5a and 5b*) [2]
- There is a unique and reproducible pattern of functional loss in the USS stance/balance items during FA progression
- These 3 steps (E2B, E3A, and E2A) act as mini-milestones of disease progression and occur in a defined and reproducible pattern that predictably precede LoA (*Figure 5c ad 5d*) [2]




## 6. Loss of Mini-Milestones in the MOVE-FA Study

- Vatiquinone treatment delayed loss of two mini-milestones
  - Step 1 (E2B) and Step 2 (E3A)

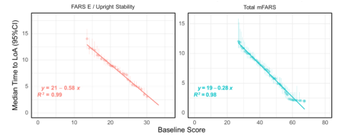
**Progression of Mini-milestones**




## 7. Predictive Relationship Between mFARS/USS Score and LoA

- Long term natural history data allow the correlation of time to LoA with a subject's mFARS and USS scores at enrollment.
- Median time to LoA was estimated based on subgroups of patients with specific disability ranges (USS or mFARS scores). The resulting times were plotted versus mean baseline scores.
- The resulting slope indicates a delay in time to loss of ambulation, achieved by preserving one point in USS (or mFARS, respectively).
- This suggests that preserving 1-point in USS delays LoA by 0.58 yrs (6.9 months)

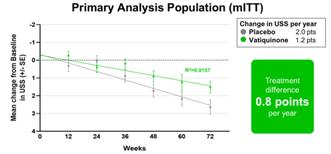
**Analysis of Total FACOMS Population (N=760)**




## 8. Vatiquinone Treatment Effect on USS Predicts 40% Yearly Reduction in Progression

- Extrapolations of the rate of change in the USS were performed with longitudinal data
- USS changed at a rate of 2.0 points per year in the placebo group. That change is consistent with the increase in USS observed in ambulatory patients <15 years for FACOMS [1]
- Vatiquinone treatment slowed progression by 0.8 pts per year and the 1.26 pt difference in USS at week 72 would corresponds to 9 month delay in loss of ambulation

**Primary Analysis Population (mITT)**




## Conclusions

- Upright Stability subscale (USS/FARS E) is the subscale of mFARS that is most sensitive to change in pediatric and adolescent ambulatory FA patients
- Vatiquinone demonstrated statistically significant treatment benefit on USS and delayed mini-milestones of disease progression associated with loss of ambulation
- The treatment benefit predicts a 40% reduction in disease progression and a delay in time to loss of ambulation of approximately 9 months

References

1. Rummey, C, Corben, LA, Delatycki, M, Wilmot, G, Subramony, SH, Corti, M, et al. Natural History of Friedreich Ataxia. Heterogeneity of Neurologic Progression and Consequences for Clinical Trial Design 2022;99(14):e1499-e1510
2. Rummey, C, Farmer, JM and Lynch, DR. Predictors of Loss of Ambulation in Friedreich's Ataxia. EClinicalMedicine 2020;18:100213.

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**International Congress of Parkinson's Disease and Movement Disorders 2024**
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