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Long-term vatiquinone treatment slows FA disease progression relative to FACOMS natural history

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1. Introduction

- FA is a rare neurodegenerative condition characterized by progressive neurological damage[1]
  - The mean (SD) age at disease onset is 15.5 (8) years[2,3]
  - Nearly all patients eventually experience loss of ambulation and become wheelchair bound[4]
- FA is caused by biallelic mutations in the *FXN* gene, which lead to frataxin deficiency. This affects iron homeostasis, which activates 15-lipoxygenase, thereby increasing lipid peroxidation and ferroptosis-mediated cell death[5]
  - Inhibition of 15-lipoxygenase reduces lipid peroxidation and therefore inhibits ferroptosis[6]
- Vatiquinone is an orally bioavailable, first-in-class, selective inhibitor of 15-lipoxygenase that was developed for the treatment of FA
- The efficacy and safety of vatiquinone have been assessed in phase 3 (MOVE-FA, NCT04577352)[7] and phase 2 studies (EPI-2010-006, NCT01728064),[8] both of which included LTE periods
- Long-term data from clinical trials can be compared with natural history studies, such as FACOMS, to assess the clinical efficacy of investigational therapies[9]
  - FACOMS began in 2001 and is ongoing; it is the largest natural history database of patients with FA[10]

2. Objectives

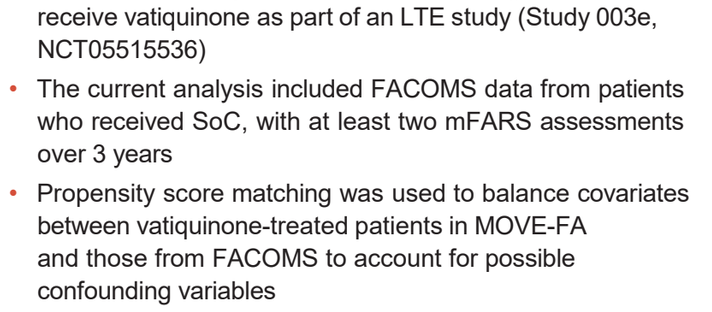
- To evaluate the long-term benefit and tolerability of vatiquinone treatment in patients with FA versus a natural history cohort from FACOMS

3. Methods

MOVE-FA and Study 003e

- MOVE-FA was a global, randomized, double-blind, placebo-controlled study of vatiquinone in patients with FA aged ≥ 7 years (**Figure 1**)
- Patients who completed MOVE-FA were eligible to receive vatiquinone as part of an LTE study (Study 003e, NCT05515536)
- The current analysis included FACOMS data from patients who received SoC, with at least two mFARS assessments over 3 years
- Propensity score matching was used to balance covariates between vatiquinone-treated patients in MOVE-FA and those from FACOMS to account for possible confounding variables
  - Baseline age, sex, mFARS and gait score, and age at FA onset were included in the primary propensity score model
  - ATT weighting was the primary propensity score weighting method and was applied to the natural history cohort
  - For sensitivity analyses, GAA repeats were included in the list of matching covariates
- The primary endpoint was the change in mFARS from baseline to 36 months
- The frequency and severity of TEAEs in MOVE-FA were also assessed

Figure 1. MOVE-FA and Study 003e design



The star indicates the primary endpoint for the 3-year data.
[a]Dependent on age and weight.

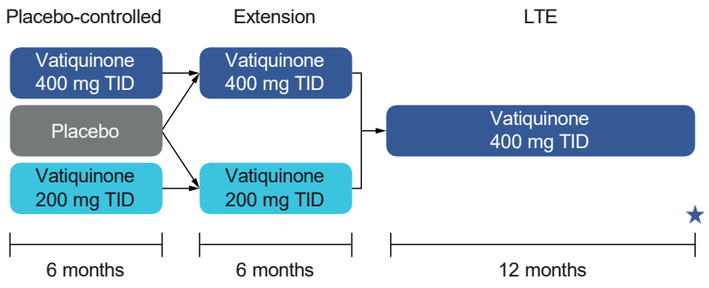
EPI-2010-006

- EPI-2010-006 was a multicenter, randomized, double-blind, placebo-controlled study of vatiquinone in ambulatory and non-ambulatory patients with advanced FA aged 18–45 years (**Figure 2**)
- The current analysis included FACOMS data from patients who received SoC, with at least two mFARS assessments over 2 years

3. Methods (continued)

- Propensity score matching was used to balance covariates between vatiquinone-treated patients in EPI-2010-006 and those from FACOMS to account for possible confounding variables
  - Baseline age, sex, mFARS and gait score, and shortest GAA repeats were included in the primary propensity score model
  - ATT weighting was the primary propensity score weighting method and was applied to the natural history cohort
  - For sensitivity analyses, GAA repeats were included in the list of matching covariates
- The primary endpoint was the change in mFARS from baseline to 24 months
- The frequency and severity of TEAEs in EPI-2010-006 were also assessed

Figure 2. EPI-2010-006 study design



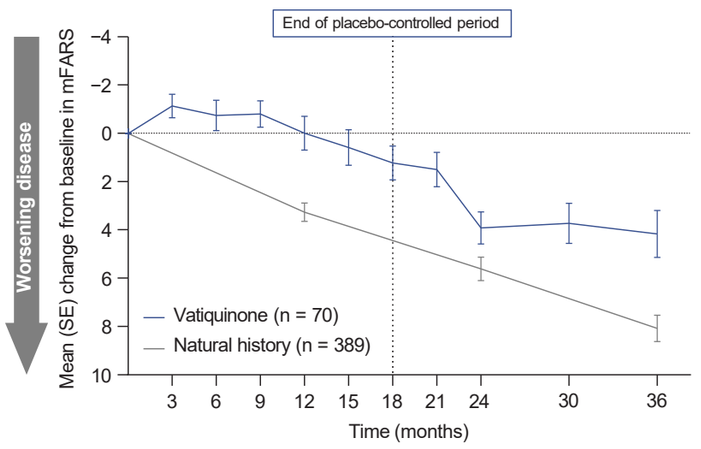
The star indicates the primary endpoint for the 2-year data.

4. Results

Vatiquinone treatment in patients with FA potentially slowed disease progression, as measured by mFARS score, relative to a matched FACOMS natural history cohort

- Based on the analysis of patients in MOVE-FA and Study 003e receiving vatiquinone (n = 70), treatment potentially slowed FA disease progression (as measured by the mFARS) by 50% over 3 years relative to the matched FACOMS cohort (**Figure 3**)
  - At month 36, vatiquinone-treated patients had an LS mean 3.75-point increase in mFARS score versus a 7.48-point increase in the matched FACOMS cohort
  - Vatiquinone was associated with a treatment benefit of 3.73 points versus the matched FACOMS cohort ($p < 0.0001$)
    - A statistically significant benefit was observed for both the upper and lower limb coordination subscales of mFARS versus the matched FACOMS cohort (2.00 points [$p < 0.0001$] and 1.35 points [$p < 0.0001$], respectively)

Figure 3. mFARS change from baseline over 3 years in MOVE-FA and Study 003e vatiquinone recipients versus the matched FACOMS cohort

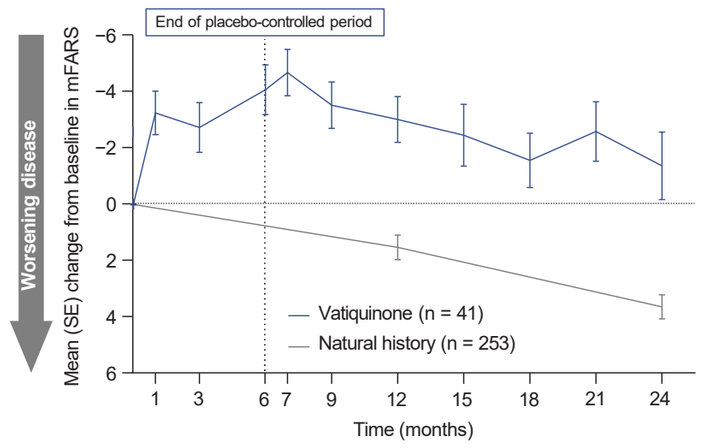


- Vatiquinone treatment showed a potential association with the slowing of disease progression based on the analysis of patients in EPI-2010-006 receiving vatiquinone (n = 41) relative to FACOMS (**Figure 4**)
  - After 24 months, vatiquinone-treated patients had an LS mean 0.92-point decrease (improvement) in mFARS score versus a 3.89-point increase in the matched FACOMS cohort
  - The treatment benefit of vatiquinone was 4.81 points versus the matched FACOMS cohort ($p < 0.0001$)

4. Results (continued)

  - Statistically significant benefits were observed for both upper (3.58 points [$p < 0.0001$]) and lower (1.29 points [$p = 0.0005$]) limb coordination scores versus the matched FACOMS cohort
- The results of the sensitivity analyses were consistent with the main analyses

Figure 4. mFARS change from baseline over 2 years in EPI-2010-006 vatiquinone recipients versus the matched FACOMS cohort



Vatiquinone treatment was generally well tolerated in all age groups studied

- In the placebo-controlled period of MOVE-FA, the most common TEAEs occurred at a similar or lower frequency in the vatiquinone group compared with the placebo group[11]
- Only one serious TEAE in MOVE-FA was considered possibly related to the study drug (a hospitalization for gastroenteritis that resolved on its own without dose modification)[11]
- Adverse reactions reported in > 5% of patients treated with vatiquinone and with a greater incidence than with placebo included diarrhea, nausea, headache, abdominal pain and dizziness[12]

5. CONCLUSIONS

- The results of Study 003e provide further evidence for the benefit of vatiquinone for the treatment of FA as observed in MOVE-FA
- EPI-2010-006 provides evidence for the efficacy of vatiquinone in adult patients with advanced disease
- The pre-specified endpoints for both extension studies were met, with statistically significant evidence of durable treatment benefit in potentially slowing disease progression in ambulatory and non-ambulatory pediatric and adult patients
- Vatiquinone demonstrates the potential to fulfill the high unmet need for pediatric patients with FA, and to provide a well-tolerated and effective therapy for adult patients with FA

ABBREVIATIONS

ATT, average treatment effect on the treated; FA, Friedreich's ataxia; FACOMS, Friedreich Ataxia Clinical Outcome Measures Study; LS, least-squares; LTE, long-term extension; mFARS, modified Friedreich's Ataxia Rating Scale; SD, standard deviation; SE, standard error; SoC, standard of care; TEAE, treatment-emergent adverse event; TID, three times daily.

REFERENCES

1. Keita M *et al. Neurodegener Dis Manag* 2022;12:267–83.
2. Bürk K. *Cerebellum Ataxias* 2017;4:4.
3. Indelicato E *et al. Orphanet J Rare Dis* 2020;15:1–8.
4. Rummey C *et al. eClinicalMedicine* 2020;18:100213.
5. La Rosa P *et al. Biomolecules* 2020;10:1551.
6. Kahn-Kirby AH *et al. PLoS One* 2019;14:e0214250.
7. Lynch D *et al*. Muscular Dystrophy Association, 2025. Poster S79.
8. Zesiewicz T *et al. Neurodegener Dis Manag* 2018;8:233–42.
9. Liu J *et al. J Clin Pharmacol* 2022;62 Suppl 2:S38–55.
10. Rummey C *et al. Ann Clin Transl Neurol* 2024;11:129000.
11. Lynch D *et al*. International Congress of Parkinson's Disease and Movement Disorders, 2024. Oral.
12. Data on file, PTC Therapeutics.

DISCLOSURES

JJC, **MR**, **OZ**, **JB**, **ED** and **LG** are employees of PTC Therapeutics. **ADuq** is a consultant for Actelion Pharmaceuticals Canada, Pfizer and Reata Pharmaceuticals, and participates in clinical trials for AbbVie, Novartis, PTC Therapeutics, Roche, Wave Life Sciences and Vaccinex. **MCF** is a consultant for Astellas, Biogen and PTC Therapeutics, and is a speaker for Biogen and PTC Therapeutics. **SP** and **DL** participate in clinical trials for PTC Therapeutics. **ADur** receives grants and consulting fees from the NIH, redirected to their institution, and is affiliated with the Agence Nationale de la Recherche, AskBio, Biogen, BRAIN-TEAM, Fondation pour la recherche Médicale, French National Hospital Clinical Research Program and Servier. **EB** participates in advisory board meetings for Biogen and PTC Therapeutics. **KM** is a consultant for Edgewise and Sarepta, and participates in clinical trials for Lexeo Therapeutics, PTC Therapeutics and Reata Pharmaceuticals. **LS** is a consultant for Novartis and Vico Therapeutics. **AF** participates in clinical trials for PTC Therapeutics, receives research funds from CIHR and has research projects on transition (pediatric to adult care). **MD** is an employee of Victorian Clinical Genetics Services. **SS** receives research funding from Avidity, Biogen, Biohaven, PTC Therapeutics, Reata Pharmaceuticals and Vertex, as well as the FARA, FDA, MDA, NAF and NIH. **RR** is a consultant for Biogen, Larimar Therapeutics and Roche. **TZ** does not have any disclosures.

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