Real-World Experience with Omaveloxolone Treatment in Friedreich's Ataxia

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Background: Friedreich's ataxia (FRDA) is the most common hereditary ataxia worldwide and is a progressive, disabling disease. Omaveloxolone, a novel Nrf2 activator, is the first specific treatment for FRDA and has shown promise in stabilizing symptoms in clinical trials patients. However, real-world data on its use remains limited. We aimed to assess the real-world tolerability and preliminary outcomes of omaveloxolone in a single-centre cohort.

Materials and Methods: Twenty-one FRDA patients initiated treatment with omaveloxolone at our center. Patients were monitored for adverse events, adherence, and clinical outcomes. Clinical scales including SARA, mFARS, and FA-ADL were assessed at baseline, at 3- and 6-month follow-ups. Median values and interquartile ranges (IQRs) were calculated.

Results: Median age was 42.0 (IQR 31.0-51.0), median age at onset was 18.0 (IQR 11.0-30.5). Median baseline scores were SARA 24.0 (IQR 17.75–29.0), mFARS 58.5 (IQR 49.75–69.5), and FA-ADL 19.0 (IQR 14.25–23.0). After 3 months, scores changed to SARA 25.0 (IQR 17.0–28.0), mFARS 64.5 (IQR 49.62–69.37), and FA-ADL 19.5 (IQR 15.0–23.0). After 6 months, scores improved to SARA 23.0 (IQR 17.0–26.0), mFARS 57.0 (IQR 42.0–65.5), and FA-ADL 16.0 (IQR 13.0–21.0). One patient (4.8%) discontinued treatment due to acute heart failure. No other serious adverse events were reported. Asymptomatic elevations in liver transaminases were observed in 6 patients for AST and in 7 patients for ALT while total bilirubin remained stable. One patient (4.8%) experienced a maximum ALT elevation ≥3× the upper limit of normal (ULN) at 3 months. Elevated transaminase levels in all patients returned to normal by T6 following dose reduction. Common adverse effects included headache (n=3), abdominal pain (n=3), nausea (n=2), and fatigue (n=1). Subjective clinical improvements were reported by several patients: three noted increased strength and endurance during physiotherapy, one reported reduced pain, and one experienced improved trunk control. Caregivers of two patients reported enhanced speech intelligibility.

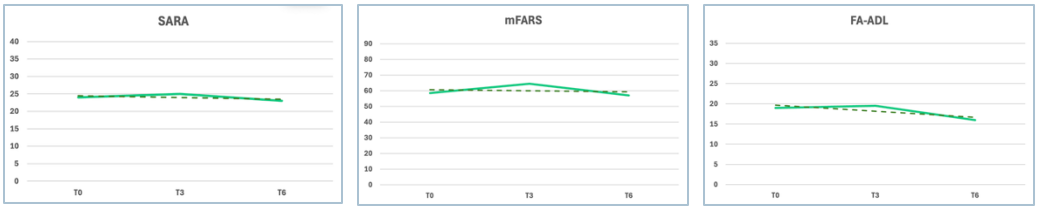

Fig. 1 Median scores for SARA, mFARS, and FA-ADL at baseline (T0), 3 months (T3), and 6 months (T6)

Discussion: Our findings are consistent with those reported in the MOXIe study, where omaveloxolone demonstrated slowing of neurological decline. Although our cohort is small and follow-up limited to six months, we observed mild improvements or stabilization across multiple clinical scales, suggesting a potential functional benefit even in more advanced disease stages. Importantly, omaveloxolone was generally well tolerated. The asymptomatic liver enzyme elevations we observed were expected and manageable. In addition, most of the patients reported subjective improvements in motor function, endurance, and speech, which may reflect clinically meaningful, patient-centered outcomes not fully captured by rating scales.

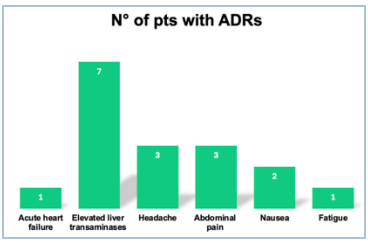

Fig. 2 Frequency of adverse events reported during the study

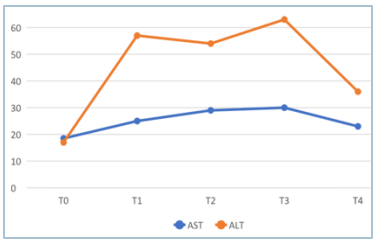

Fig. 3 Mean change from baseline (T0) for transaminases of patients receiving omaveloxolone treatment at 1 month (T1), 2 months (T2), 3 months (T3), 4 months (T4)

Conclusions: Omaveloxolone was generally well tolerated and may offer functional benefits in FRDA. Further studies are needed to confirm its long-term safety and efficacy.

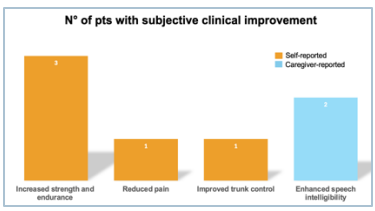

Fig. 4 Subjective clinical improvements reported by patients and caregivers

References

1. Lynch DR, Chin MP, Delatycki MB, et al. Safety and Efficacy of Omaveloxolone in Friedreich Ataxia (MOXIe Study). Ann Neurol. 2021 Feb;89(2):212-225. doi: 10.1002/ana.25934. Epub 2020 Nov 5.
2. Lynch DR, Chin MP, Boesch S, Delatycki MB, Giunti P, Goldsberry A, Hoyle JC, Mariotti C, Mathews KD, Nachbauer W, O'Grady M, Perlman S, Subramony SH, Wilmot G, Zesiewicz T, Meyer CJ. Efficacy of Omaveloxolone in Friedreich's Ataxia: Delayed-Start Analysis of the MOXIe Extension. Mov Disord. 2023 Feb;38(2):313-320. doi: 10.1002/mds.29286.