The Desire for Pre Symptomatic Treatment in the At Risk Genetic ALS and FTD Community

Swidler [J*1], Olson [T1], Edelstein [AL1] , Granning [J1], Haddad [C1], Uhrlaub [M1], Wicks [P2]

[1] Genetic ALS & FTD: End the Legacy; [2] Wicks Digital Health; *Jean.swidler@gmail.com

Introduction

We are a group of people at risk of genetic ALS/FTD organized as “Genetic ALS & FTD: End The Legacy” under the ALS Hope Foundation, a 501(c)(3).

We organized Genetic ALS & FTD: End the Legacy to provide educational and support resources to, encourage and promote research about, and advocate for the Genetic ALS & FTD community.

We sought to understand how our community felt about access to taking presymptomatic therapies and to explore the risks (e.g. genetic information being in the medical record) and inconveniences we would tolerate for different efficacy profiles.

Methods

- Anonymous survey on Google Forms for 3 weeks September - October 2022
- Inclusion criteria: participants age 18 and at risk for genetic ALS and/or FTD.
- Exclusion criteria: people already diagnosed with ALS/FTD, or tested negative for their family’s mutation.
- The survey was advertised via email and social media including Twitter, Reddit, private Facebook groups for Familial ALS and C9orf72, and message forums for ALS and dementia.

Results - Participants

- 197 total survey responses; 174 after exclusion criteria (see Figure 1)
- Respondents ranged in age from 18-86+, with most between the ages of 36-55.
- 72.9% of respondents identified as female and 95.3% White/Caucasian.
- 72% from US, followed by the UK (10%), Canada (9.4%), Europe (3.5%), Australia (2.9%), and the rest of the world (1.7%).

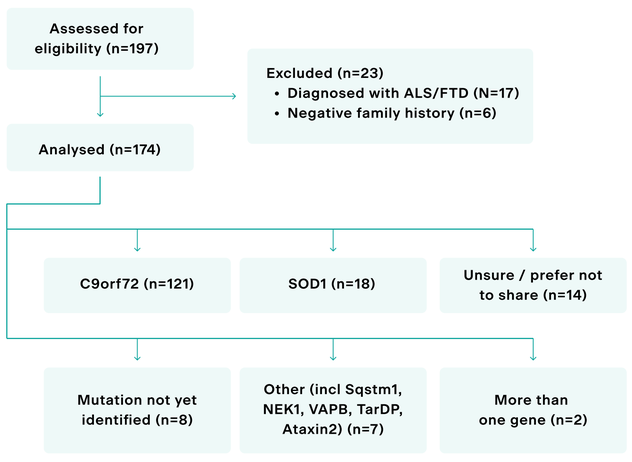

Figure 1: CONSORT diagram including ALS/FTD Variant in family (where known)

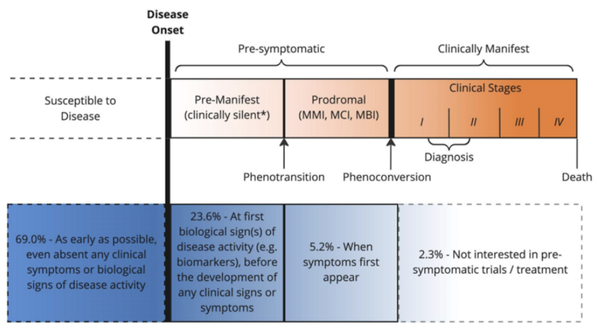

Figure 2: Comparison of Benatar et al. (2022) overview of presymptomatic genetic ALS/FTD with survey of N=174 people at risk.

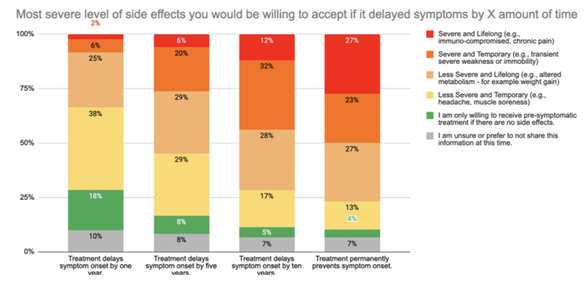

Figure 3: Highest level of side effect burden that respondents would be willing to tolerate across different potential treatment profiles

“How frequently, if at all, would you be willing to accept treatment by differing methods below if it delayed symptoms by the amount listed:”

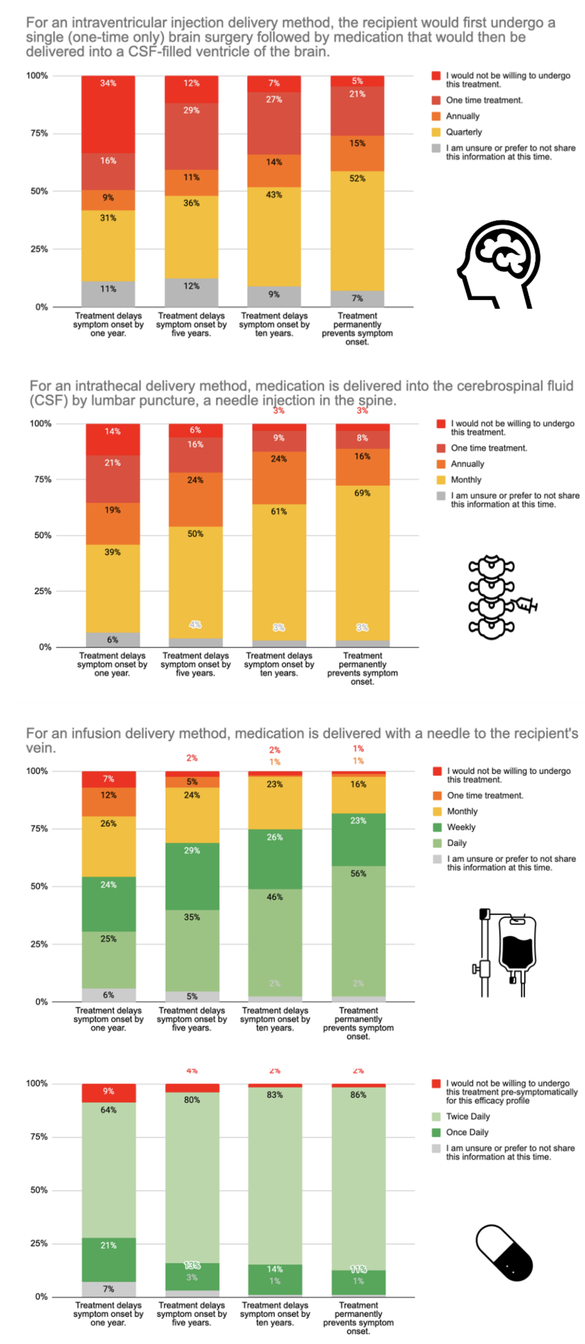

Figure 4: Highest acceptable frequency of administration for a.) oral pill, b.) IV infusion, c.) intrathecal delivery, d.) intraventricular delivery

Results - Treatment Preferences

Most respondents (120/174, 69%) were interested in treatment as early as possible, even absent any clinical symptoms or biological signs of disease activity (Figure 2). The community appears more willing to consider only trials in the prodromal phase.[1]

To understand the tradeoffs between efficacy, side effects, and treatment burden, respondents were shown four potential efficacy profiles for treatments that could delay major symptom onset for 1 year (A), 5 years (B), 10 years (C), or forever (D).

Specific questions were fielded to gauge sensitivity to side effects (Figure 3), mode of administration (Figure 4), and concerns over genetic results in the medical record (70% said it would not affect their decision).

Overall, respondents reported a higher willingness to tolerate side effects, take intrusive means of medication delivery, and travel longer distances in exchange for stronger profiles of efficacy. However, there was a degree of uncertainty expressed throughout, and a small subset of respondents who would not consider taking a pre-symptomatic profile with only modest efficacy (e.g., Profiles A + B).

Discussion

Those who are at risk for genetic ALS/FTD strongly desire pre-symptomatic treatment. As new therapies become available, it is important for those designing trials, regulating drug labels, and potential prescribing providers to accept the need and willingness of this population to tolerate genetic information being in their medical records, side effects and inconveniences of medical therapy for different levels of efficacy.

Limitations

- Small sample size; may not represent the opinions of all gene carriers.
- Barriers to genetic testing means many individuals don’t know their risk
- Our sample is likely biased to those most engaged and educated about ALS/FTD.

Acknowledgements

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References

[1] Benatar et al (2022) Mild motor impairment as prodromal state in amyotrophic lateral sclerosis: a new diagnostic entity. Brain. 145(10):3500-3508

[2] Swidler et al (2023) A new diagnostic entity must enable earlier treatment in gene carrier. Brain. Published Online May 18th 2023

Data Availability

Available on FigShare as “End the Legacy Q4 2022 Survey questionnaire and raw data”