Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive, neurodegenerative, and fatal syndrome involving both upper and lower motor neurons, throughout which ubiquitinated proteinaceous inclusions may be found. Although the disease is characterized primarily by motor symptoms, cognitive and/or behavioral deficits may also occur in up to 50% of patients with ALS. There is generally a significant variation in clinical presentation, site of onset, and distribution of upper and lower motor neuron involvement.[1,2]

The incidence of ALS is about 1 to 2 individuals per 100,000 per year, and the prevalence is about 4 to 8 individuals per 100,000.[3,4] The prevalence is projected to increase by 69% by 2040.[5] The lifetime risk of an individual developing ALS is about 1 in 400.[6] Men are impacted more commonly than women, and the peak age at which the disease presents is in the 50s and 60s.[3,4] The impact of this disease is demonstrable, as individuals with ALS progressively lose many of their functional abilities, and their lifespan is truncated.[7]

Screening and Diagnosis

ALS is underrecognized and underdiagnosed, and it may take 10 to 16 months between symptom onset and definitive diagnosis.[1] A prompt referral to an ALS specialist is appropriate for patients who present with progressive and asymmetric muscle weakness in the absence of pain or sensory loss. The ALS Association provides an efficient tool, ThinkALS, to aid clinicians in recognizing and referring suspected cases of ALS for further evaluation and diagnosis.[9] While awaiting referral to an ALS specialist, it is vital that clinicians provide symptomatic treatment to improve patient quality of life.[10]

Treatment Options

The management of ALS is comprehensive, multifaceted, and holistic. A treatment plan may be comprised of symptomatic management, disease-modifying therapy (DMT), interprofessional/multidisciplinary care, and clinical trial enrollment, all of which may improve quality of life, prolong survival, and reduce hospitalization for patients with ALS.[1,2,10] In addition, the American Academy of Neurology recommends that cognitive and behavioral screening, interventions for respiratory insufficiency, fall interventions, end-of-life planning, communication support, and nutritional interventions be incorporated into the treatment plan as well.[11]

To date, 3 DMTs have been approved by the United States Food and Drug Administration (FDA) for the treatment of ALS: riluzole, edaravone, and tauroursodeoxycholic acid/sodium phenylbutyrate (TUDCA/NaPB), all of which have demonstrated significant benefit and acceptable safety in patients with ALS.[12-14] In addition, dextromethorphan/quinidine is FDA-approved for the treatment of pseudobulbar affect, a potential symptom of ALS.[15]

Key Considerations

Interprofessional, multidisciplinary, team-based care is the standard of care for managing patients with ALS. Symptomatic management is a cornerstone of treatment for patients with ALS. However, DMTs are also incorporated into the treatment plan.[10,17,18] Rational polypharmacy, that is, the combined use of DMTs, may be considered to optimize outcomes for patients with ALS.[18]

Access to an ALS clinic providing multidisciplinary, team-based, and specialized care is a critical challenge for patients affected by the disease, with approximately half of patients living more than 50 miles from an ALS specialty center. Telemedicine and remote monitoring may mitigate this problem and should be considered for some patients.[11,19]

REFERENCES

1. Goutman SA, Hardiman O, Al-Chalabi A, et al. Recent advances in the diagnosis and prognosis of amyotrophic lateral sclerosis. *Lancet Neurol.* 2022;21(5):480-493.
2. Hardiman O, Al-Chalabi A, Chio A, et al. Amyotrophic lateral sclerosis. *Nat Rev Dis Primers*. 2017;3:17071.
3. Longinetti E, Fang F. Epidemiology of amyotrophic lateral sclerosis: an update of recent literature. *Curr Opin Neurol.* 2019;32(5):771-776.
4. Miller C, Apple S, Paige JS, et al. Current and future projections of amyotrophic lateral sclerosis in the United States using administrative claims data. *Neuroepidemiology.* 2021;55(5):275-285.
5. Arthur KC, Calvo A, Price TR, Geiger JT, Chio A, Traynor BJ. Projected increase in amyotrophic lateral sclerosis from 2015 to 2040. *Nat Commun*. 2016;7:12408.
6. Ryan M, Heverin M, McLaughlin RL, Hardiman O. Lifetime risk and heritability of amyotrophic lateral sclerosis. *JAMA Neurol.* 2019;76(11):1367-1374.
7. Stages of ALS. ALS Association. Accessed June 6, 2023. https://www.als.org/understanding-als/stages
8. Mitsumoto H, Kasarskis EJ, Simmons Z. Hastening the diagnosis of amyotrophic laterals. *Neurology.* 2022;10.1212/WNL.0000000000200799.
9. thinkALS Tool. ALS Association. 2022. Accessed April 27, 2023. https://www.als.org/thinkals/thinkals-tool
10. Chen JJ. Overview of current and emerging therapies for amyotrophic lateral sclerosis. *Am J Manag Care.* 2020;26(9 Suppl):S191-S197.
11. Miller RG, Brooks BR, Swain-Eng RJ, et al. Quality improvement in neurology: amyotrophic lateral sclerosis quality measures: report of the quality measurement and reporting subcommittee of the American Academy of Neurology. *Neurology.* 2013;81(24):2136-2140.
12. Radicava. Prescribing information. MT Pharma America. May 2017. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209176lbl.pdf
13. Relyvrio. Prescribing Information. Amylyx Pharmaceuticals Inc. Rilutek. September 2022. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/216660s000lbledt.pdf
14. Rilutek. Prescribing information. Covis Pharmaceuticals Inc. April 2016. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020599s017lbl.pdf
15. Nuedexta. Prescribing information. Avanir Pharmaceuticals, Inc. June 2019. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021879s014lbl.pdf
16. Smith R, Pioro E, Myers K, et al. Enhanced bulbar function in amyotrophic lateral sclerosis: The Nuedexta treatment trial. *Neurotherapeutics.* 2017;14(3):762-772.
17. Hogden A, Foley G, Henderson RD, et al. Amyotrophic lateral sclerosis: improving care with a multidisciplinary approach. *J Multidiscip Healthc.* 2017;10:205-215.
18. Weiss MD, Weydt P, Carter GT. Current pharmacological management of amyotrophic [corrected] lateral sclerosis and a role for rational polypharmacy. *Expert Opin Pharmacother.* 2004;5(4):735-746.
19. Haulman A, Geronimo A, Chahwala A, Simmons Z. The use of telehealth to enhance care in ALS and other neuromuscular disorders. *Muscle Nerve*. 2020;61(6):682-691.