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Role of the Sodium/Glutamate Blocker Riluzole in Enhancing Functional Outcomes in Patient Undergoing Surgery for Degenerative Cervical Myelopathy

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Introduction

Degenerative cervical myelopathy (DCM), which encompasses cervical spondylotic myelopathy and ossification of the posterior longitudinal ligament, is the most common cause of spinal cord impairment.

Decompressive surgery is the most effective treatment, however, most patients are left with residual neurological impairment and some experience neurological decline.

Based on strong preclinical basic science evidence and collateral evidence from trials in human spinal cord injury and amyotrophic lateral sclerosis, we sought to explore if the sodium-glutamate antagonist riluzole would enhance neurological recovery and reduce perioperative neurological decline.

Methods

This is a phase III multi-center, double-blind, placebo-controlled, randomized controlled trial. Between March 2012 and June 2017, 300 surgically naive patients with moderate to severe DCM were enrolled at 16 sites. Subjects were randomized 1:1 to either the 50 mg riluzole bid or placebo-controlled group, beginning the medications at 14 days pre-surgery and ending at 28 days post-operative. Follow-up was at 6- and 12-months to determine the primary endpoint, change in mJOA scores; and the secondary endpoints, change in SF-36v2, Neck Disability Index (NDI), Nurick grade, EQ-5D, ASIA motor and sensory scores, Bazaz scale, Visual Analog Scale (VAS) for Pain, grip strength and neurological compilations.

Statistical Design

Sample size of 270 subjects total will have 80% power to detect .35 Cohen's d effect size (i.e. 0.9 difference in mJOA). Study uses adaptive sequential design that allows sample size change during the interim analysis.

Statistical Design

Plan ID	Parameter
Type of the hypothesis	1-Sided
Type I Error (α)	0.025
Power (1 - β)	0.80
Randomization Ratio (Investigational vs. Control)	1:1
Planned Number of Interim Looks	2
Spacing of Looks	65%, 100%
Hypothesis to be Rejected	H0 or H1 (binding)
Boundary Family	Published Function
Boundary to Reject H0	O'Brien-Fleming
Boundary to Reject H1	Gamma (-2)
Difference of Means Assuming H_1	0.9
Standard Deviation (σ)	2.57
Sample Size	270 (135 per arm)

Results

Demographics

Demographics		N (%)
Age (N = 300)		58.0 (10.2)
Gender	Female	133 (55.7%)
	Male	167 (44.3%)
Race	White	242 (80.7%)
	African-American	29 (9.7%)
	Asian	15 (5.0%)
	Pacific Islander	1 (0.3%)
	Alaska Native	1 (0.3%)
	Unknown	4 (1.3%)
	Other	7 (2.3%)
	Did not answer	1 (0.3)
Surgery	Anterior	131 (45.3%)
	Posterior	150 (52.0%)
	Ant + Pos	8 (2.8%)

Outcomes

Outcome Measure		Mean (Standard Deviation)
mJOA (N = 300)		11.8 (1.5)
ASIA	Motor Total (N = 296)	95.3 (6.0)
	Sensory Light Touch (N = 293)	106.0 (10.8)
	Sensory Pin Prick (N = 293)	105.9 (10.4)
SF36v2 PCS (N = 296)		32.8 (9.5)
Pain VAS	Pain in Arm and Shoulder (N = 298)	4.7 (2.9)
	Pain in Neck (N = 298)	4.9 (3.0)
NDI (N = 297)		42.9 (20.7)
EQ-5D (N = 299)		0.6 (0.2)

Learning Objectives

The aim of this study is to explore if the sodium-glutamate antagonist riluzole would enhance neurological recovery and reduce perioperative neurological decline.

Conclusions

This study contributes Level I evidence concerning efficacy and safety of riluzole as an adjunct therapy to decompressive surgery for patients with DCM.

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