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Re-analysis of the CSM-PROTECT Multicentre Randomized Controlled Trial Reveals a Global Treatment Benefit of Riluzole in Patients Undergoing Surgery for Degenerative Cervical Myelopathy

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Background: While the mJOA score (modified Japanese Orthopedic Association) currently serves as the prevailing measure for evaluating DCM (degenerative cervical myelopathy) outcomes, its limitations have recently raised concerns about its adequacy. A comprehensive representation of treatment outcomes in the DCM population remains underexplored.

Research Question: Can a global statistical test be used to represent the diverse aspects of recovery in DCM patients receiving perioperative riluzole therapy?

Design: This is a reanalysis of the prespecified secondary endpoints within the CSM-PROTECT trial.

Methods: We assessed clinical improvement at 1 year using five distinct assessment scales: SF-36 Physical Component Summary (PCS), Numeric Rating Scale for Neck and Arm pain, ASIA motor score and Nurick grade. A nonparametric global statical approach was used to evaluate treatment efficacy. The resulting global treatment effect (GTE, ranging from -1 to 1) measured the net gain in probability that one arm outperforms the other across multiple endpoints. A GTE >0 indicated a more favorable global treatment response to Riluzole than placebo.

Results: Our analysis included 290 patients [mean (SD) age of 59(10.1) years, 129 (44%) females]. Of these, 141 received Riluzole, and 149 received placebo. Riluzole demonstrated significantly higher GTE than placebo at 1 year [GTE = 0.08 (SD 0.04), p=0.02]. A similar favorable global response was identified at 35 days and 6 months (GTE = 0.07; p=0.04). Riluzole-treated patients had a 54% higher likelihood of improved outcomes at six months. The combination of ASIA Motor score, Neck and Arm pain NRS ratings yielded the best-fit parsimonious model for detecting Riluzole's greatest benefit [GTE = 0.11 (SD 0.05), p=0.007].

Conclusion: This global outcome reanalysis of the CSM-PROTECT trial data demonstrates a beneficial effect of riluzole on enhancing clinical outcomes in patients with DCM undergoing surgical treatment.

Fig. 1

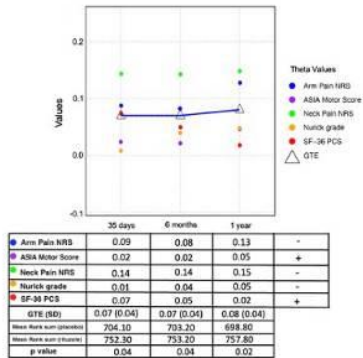


Figure 1. Application of a global statistical approach in the estimation of GTE (global treatment effect) and in significance testing at 35 days, 6 months, and 1 year. Each theta value (θ_p) quantifies the difference between the probability that treatment is better than control (p) and the probability that the control is better than the treatment (q). [i.e. $\theta_p = (p - q)$] The GTE represents the mean of the five theta values at each time-point. p -values were derived using O'Brien's rank sum type test with variance adjustment for testing the general nonparametric Behrens-Fisher hypothesis. The sign indicates that larger values were deemed better (+), while smaller values were better for (-)