

A Randomized Clinical Trial of Lithium Carbonate with Riluzole versus Placebo with Riluzole in ALS Shows No Benefit

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In February 2008, Dr. Francesco Fornai and colleagues at the University of Pisa, Italy, reported in a pilot study that lithium carbonate at dosages of 300-450 mg daily (titrated to a plasma level of 0.4-0.8 mEq/liter) combined with riluzole showed a large positive effect in people with ALS (Fornai, F., et al., Lithium delays progression of amyotrophic lateral sclerosis. PNAS, 2008.105(6): p. 2052-2057).

To further investigate lithium carbonate as a possible treatment for ALS, a randomized, blinded, multicenter trial of lithium carbonate with riluzole versus placebo with riluzole was conducted in people with ALS in the U.S. and Canada. The study used similar dosing to the Italian study. The study was conducted by the Northeast ALS (NEALS) and Canadian ALS (CALs) Consortia and was sponsored by the National Institute of Neurological Disorders and Stroke (NINDS) of the National Institutes of Health, the ALS Association and the ALS Society of Canada. This unique collaboration between investigators and funding organizations resulted in a novel study design and expeditious execution of the trial to efficiently answer a critically important clinical question. Study leaders included Drs. Swati Aggarwal, Lorne Zinman, Jeremy Shefner and Merit Cudkowicz.

An interim analysis was conducted after enrollment of the 84th subject and presented to the NINDS Data and Safety Monitoring Board in September 2009. Based on the interim analysis the trial was stopped for futility. This study did not show the same beneficial effect of lithium carbonate on the progression of ALS as the prior pilot study conducted in Italy.

Although the results are disappointing, it was very important for the ALS community to quickly and efficiently determine if the large benefit first observed for lithium could be replicated in a well controlled trial. With the ongoing assistance and commitment of patient volunteers, researchers can now focus on other promising therapeutics for patients with ALS.