Randomized clinical trial double blind of lithium carbonate as association therapy in amyotrophic lateral sclerosis (Phase II)

We had proposed a phase II add on randomized coordinated double blind clinical trial with a placebo arm including 140 patients in 2 years involving 5 centres. The trial was designed with an initial Phase2a dose-selection with 3 different doses of lithium carbonate (200 mg, 400 mg and 600 mg) followed by a second Phase (2b) with a follow up of the patients in the selected dose for 24 months. The primary objective of the study was to compare the efficacy of the drug on ALS-disability measured by ALS-FRS. Other secondary objectives were to establish its effects on survival, adverse events and quality of life.

During the clinical trial the negative results of another international study LiCALS with the same drug were published (UKMND-LiCALS Study Group, Morrison KE, Dhariwal S, Hornabrook R, Savage L, Burn DJ, Khoo TK, Kelly J, Murphy CL, Al-Chalabi A, Dougherty A, Leigh PN, Wijesekera L, Thornhill M, Ellis CM, O'Hanlon K, Panicker J, Pate L, Ray P, Wyatt L, Young CA, Copeland L, Ealing J, Hamdalla H, Leroi I, Murphy C, O'Keeffe F, Oughton E, Partington L, Paterson P, Rog D, Sathish A, Sexton D, Smith J, Vanek H, Dodds S, Williams TL, Steen IN, Clarke J, Eziefula C, Howard R, Orrell R, Sidle K, Sylvester R, Barrett W, Merritt C, Talbot K, Turner MR, Whatley C, Williams C, Williams J, Cosby C, Hanemann CO, Iman I, Philips C, Timings L, Crawford SE, Hewamadduma C, Hibberd R, Hollinger H, McDermott C, Mils G, Rafiq M, Shaw PJ, Taylor A, Waines E, Walsh T, Addison-Jones R, Birt J, Hare M, Majid T. Lithium in patients with amyotrophic lateral sclerosis (LiCALS): a phase 3 multicentre, randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2013 Apr;12(4):339-45. doi: 10.1016/S1474-4422(13)70037-1. Epub 2013 Feb 27. Erratum in: Lancet Neurol. 2013 Sep;12(9):846. PMID: 23453347; PMCID: PMC3610091). This fact affected negatively the recruitment in our clinical trial, due to the low rate of recruitment we decided to stop the study.

Seventeen patients were included of which 13 completed the study. We performed an statistical analysis and we did not find any difference in disability measured by ALS-FRS nor survival (including use of mechanical ventilation and gastrostomy). We also did not find any difference in adverse events. A death occurred in the treated group that was reported to the Spanish Agency of Drugs AEMPs and finally considered as not related to the treatment but to the disease itself.