## ROLE OF CITICOLINE ON THE TREATMENT ISCHEMIC STROKE: A FORMAL AND CUMULATIVE META-ANALYSIS

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Background: Citicoline is a neuroprotective/neurorestorative drug used in several countries for the treatment of acute ischemic stroke. Recently a large clinical study performed in Europe (ICTUS trial) has been published, with neutral results. Because the circumstances of the trial (external validity), these results only could be applied under the circumstances of the trial, that is, performed in Europe, in highly expertise stroke units and with a rate of use of rtPA over 46%, scenario that differs on the real practice. We can interpret the results of the ICTUS trial as a dilution of the effect of the drug in parallel with the improvement of the standard of care, thus, patients treated with rtPA in a stroke unit, could not need an additional treatment with citicoline.

Methods: A systematic search was performed on Medline, Embase, Cochrane Specialised Register of Clinical Trials, Clinicaltrials.gov and Ferrer Group database to identify all published, unconfounded, controlled clinical trials of citicoline initiated within 14 days of onset of acute ischemic stroke patients. Results: 10 controlled trials enrolling 4420 patients were identified. The studies used citicoline with doses ranging from 500 to 2000 mg administered by oral or intravenous route. Under the random-effects model, the meta-analysis shows an OR of 1.56 (95%CI, 1.12; 2.16) in favour of citicoline in the rates of death and disability, using as measure the mRS 0-2. Cumulative m-a will be also presented. Conclusion: Formal meta-analysis of trials of citicoline in acute and subacute ischemic stroke shows a beneficial treatment effect, without safety concerns.