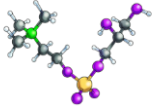


CHOLINE ALPHOSCCERATE ATTENUATES BRAIN ATROPHY AND IMPROVES BEHAVIOURAL SYMPTOMS IN MILD COGNITIVE IMPAIRMENT: ONE-YEAR OUTCOMES OF THE CARL STUDY

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Effect of treatment of the cholinergic precursor choline alphosccerate in mild cognitive dysfunction (CARL) trial



Choline Alphosccerate

Study design: Phase IV , explorative, non-profit, monocentric, randomized, double-blind and controlled vs placebo.

Study duration: 12 months

EU CT number : 2025-520685-21-00 SM-1

Pharmacological Treatment:

Treatment 1: Choline alphosccerate 2 x 600 mg/day in drinkable vials.

Treatment 2: Placebo

INCLUSION CRITERIA

- Patient able to understand and sign informed consent and by family member/caregiver.
- Age ≥ 65 years.
- Memory disorders presence evaluated by Neuropsychological Testing:
 - Mini Mental State Evaluation (MMSE): score ≥ 24.
 - Clinical Dementia Rating (CDR) = 0.5.
- Sufficient education to enable the patient to read, write and communicate effectively.
- Cooperative patient, able to complete all aspects of the study alone or with the help of a family member.
- MRI performed within 6 (six) months prior to enrolment.
- Presence of at least 2 (two) vascular risk factors listed below:
 - systemic arterial hypertension
 - diabetes mellitus
 - obesity
 - heart disease (e.g. atrial fibrillation)
 - dyslipidaemia
 - hyperhomocysteinaemia
 - tobacco addiction
 - previous cerebrovascular events
 - family history of cardio-cerebrovascular diseases.

EXCLUSION CRITERIA

- Overt Alzheimer's disease.
- All decompensated cardiac disorders.
- Chronic renal failure.
- Severe hepatic insufficiency
- Incorrect dystyroidism
- Serious ongoing developmental systemic pathologies (e.g. malignancies).
- Psychiatric disorders or mental retardation (Severe Depression, Psychosis, Dissociative Syndrome), Alcohol/drug/substance abuse or dependence.
- Diagnosis of Major Depression according to DSM V.
- Any contraindication to treatment or intolerance to choline alphosccerate.
- Patient involved in other clinical trials.

Demographics of patients recruited for the trial CARL

Sex (M/F)	♂ 37 (61%) / ♀ 23 (39%)	
Age	76 ± 5	76 ± 5
	Min 63	Max 96
	10 ± 4	Median 78
Education	Min 2	Max 18
	26 ± 2	Median 8
MMSE at baseline	Min 24	Max 30
	26 ± 2	Median 27

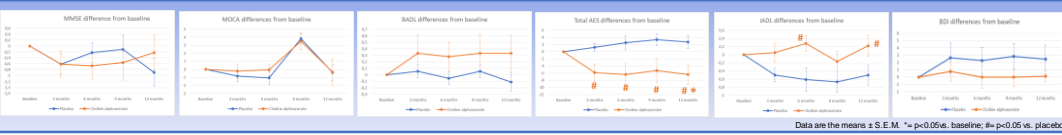
Demographics of patients recruited for the trial CARL (continued)

	Placebo	Choline alphosccerate
Sex (M/F)	♂ 60% / ♀ 40%	♂ 65% / ♀ 35%
Age	76 ± 5	75 ± 5
Education	9 ± 5	11 ± 4
MMSE at baseline	27 ± 2	27 ± 2

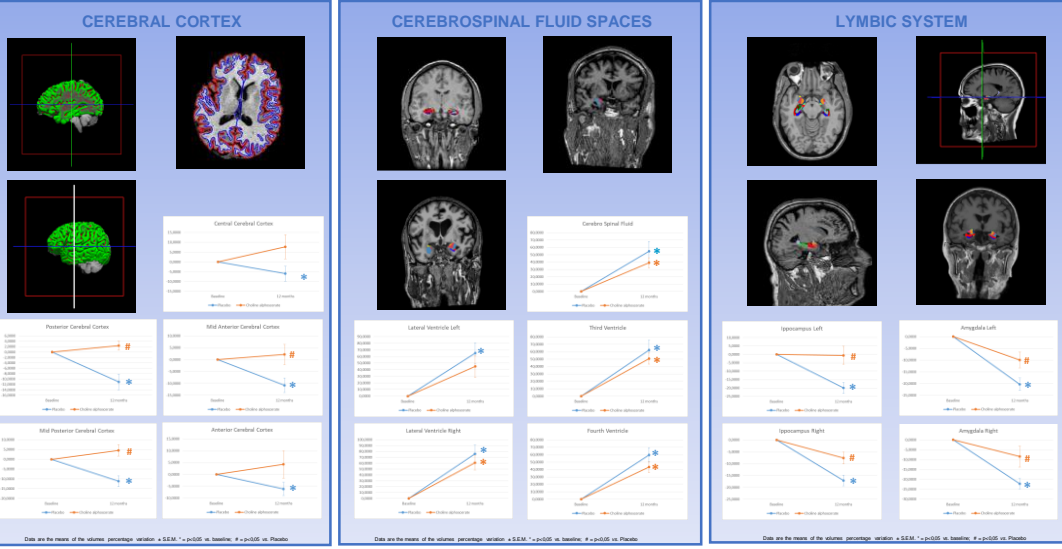
Patient withdrawals after one year of treatment

Therapy	No.	Placebo	No.	Choline alphosccerate
Causes of withdrawal				
Total		7		7
Lack of efficacy	2	Conversion to AD	2	1 Conversion to AD 1 Conversion to VAD
Non compliance	1	Not adhering to therapy	0	
Lack tolerability	1	Hypertension and asthma	0	
Other reasons	3	1 Problems in reaching the hospital 1 Family issues 1 Patient's choice	5	1 Problems in reaching the hospital 2 Family issues 1 Patient's choice

NEUROPSYCHOLOGICAL EVALUATION



NEUROMORPHOLOGICAL EVALUATION



CONCLUSIONS

- Analysis of brain volumes has shown that after one years, therapy with choline alphosccerate slows cortical atrophy in the cerebral cortex, hippocampus, and amygdala, compared to placebo in MCI patients
- Choline precursor therapy was not effective in counter the increase in the volume of CSF spaces.
- Choline alphosccerate has proven to be effective in limiting behavioral disorder (mainly apathy) and functional loss, during the year of treatment.
- Cognitive impairment does not manifest during the first year of study, it need more time to evaluate the effect of choline alfosccerate on MCI patients' cognition.
- Waiting for better therapeutic strategies, choline alphosccerate, could represent a therapeutic option to be considered in the treatment of Mid Cognitive Impairment associated with cerebrovascular damage.