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Background: Current pharmacologic treatment for Alzheimer's Disease(AD) is unable to prevent long-term clinical deterioration. TNF-alpha, a proinflammatory cytokine, has been implicated in the pathogenesis of AD. We investigated the use of a biologic TNF inhibitor, etanercept, for mild to severe AD, given by perispinal extrathecal administration. **Objective(s):** To explore the feasibility of the use of a biologic TNF inhibitor, etanercept, given by perispinal extrathecal administration, for treatment of Alzheimer's Disease. **Methods:** Patients were treated open-label with perispinal extrathecal etanercept, with a total weekly dose ranging from 25mg to 50mg. The primary efficacy variables were the change from baseline in three standard measures of cognition: the MMSE for all patients; the ADAS-Cog for patients with mild-moderate AD; and the Severe Impairment Battery (SIB) for patients with more severe AD. 15 patients were treated and evaluated through six months. **Results:** The average age was 76.7. The mean baseline MMSE was 18.2 (n=15); the mean baseline ADAS-Cog was 20.8 (n=11); the mean baseline SIB was 62.5 (n=5). There was significant improvement with treatment, as measured by all of the primary efficacy variables, through six months: MMSE increased by 2.13Â±2.23; ADAS-Cog improved(decreased) by 5.48Â±5.08; and SIB increased by 16.6Â±14.52. **Conclusions:** Increasing basic science and clinical evidence implicates excess TNF-alpha in the pathogenesis of Alzheimer's Disease. This small, open-label pilot study suggests that TNF-alpha modulation may hold promise as a potential new treatment approach. Further study of perispinal extrathecal etanercept in randomized, placebo-controlled clinical trials is merited.

P2-404 RESISTANT DEPRESSION IN ALZHEIMER'S DISEASE(AD)

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Background: Depression symptoms are common at the onset of AD and most studies concur that depressive symptoms become increasingly common with disease progression. **Objective:** To evaluate the efficacy, safety and tolerability between sertraline, mirtazapinum, venlafaxinum ER 150 and Carbamazepine in AD with resistant depression. **Methods:** 75 patients with AD diagnosis by DSM IV criteria, and resistant depression, treated with Donepezil 10 mg , with moderate Mini-Mental State Examination(MMSE) scores = 20-11. We divided 75 patients in 3 group -"A" 25 patients treated with sertraline medium dose 100mg/day, "B" 25 patients treated with mirtazapinum 30 mg/day, "C" 25 patients treated with venlafaxinum ER 150 mg/day. All 75 patients received Carbamazepine 400mg/day. We evaluated all 3 groups at baseline,after 2 week,3 week,1 month, 2 month using Hamilton Rating Scale for Depression HAMD-17, Clinical Global Impression Scale Severity and Improvement (CGI), MMSE. **Results:** This association was efficient after 3 weeks from group "C" and after 4 weeks from group "A" and "B", with 25% decrease of HAMD score. The recovery was predominant at 1 month from "C" group, and after 2 month from "A" and "B" group. At the endpoint from "A" group 15 patient responders, 5 partial/non-responders, 5 drop out; "B" group 18 responders, 4 partial/non-responders, 3 drop out; "C" group 23 responders, 1partial/non-responders, 1 drop out. MMSE scores were most improved at the endpoint from "C" group. **Conclusions:** 1. Venlafaxinum ER 150mg/day + Carbamazepine 400mg/day seems to be a better solution in resistant depression in AD. 2. The safety difference between groups was non-significant.

KEYWORDS: depression, antidepressants, mental state

P2-405 ACHEI EFFICACY IN FAMILIAL ALZHEIMER'S DISEASE

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Background: Alzheimer's disease (AD) is a progressive neurodegenerative disease for which no causative therapies are available. Acetylcholinesterase inhibitors (AcheEIs) are the current symptomatic approach largely used to enhance cholinergic function and hence cognitive performances. Nevertheless, drug response shows a large variability and is poorly predictable. It probably relies on the AD great genetic and phenotypic heterogeneity. 30% of AD cases display familiarity and 5% is caused by genes mutations. AD is particularly aggressive showing early onset and brief duration in the Calabrian families segregating PS1-Met146Leu mutation. To date, no studies on AChEis efficacy have been performed taking into account the presence of genes mutations and more generally the familiarity for AD. **Objective(s):** To evaluate AChEis response in a group of familial AD patients (with and without PS1Met146Leu) and to individuate possible predictors of response. **Methods:** Forty AD patients with familiarity (16 males, 24 females; mean age at onset 60.4+14,2 range 33-83) were diagnosed through NINCDS-ADRDA criteria, neuropsychological and neuroradiological assessment. Ten belonged to a PS1-Met146Leu family; 30 were familial cases not mutated (FADnm) whose familiarity was established through history. MMSE score measured degree of cognitive decline at T0, T3, T9, T15, T21 and T27 months. T0 was at about 4 years from onset, MMSE value at T0 was 15.6+3.7. Inquired predictors were: sex, education, age at onset, rate progression, MMSE score at T0, APOE4+, PS1 Met146Leu+, CYP46 polymorphism. Pearson/Spearman and the single t-test were used to compare to the expected decline (4.4 points for year). **Results:** All patients had a good response to AchEI: MMSE score improved of 1.3 point in mean at T3 (p=0.001) and patients maintained cognitive benefit up to 27 months (p=0.000). No predictors of drug response were identified. When stratified dataset for PS1 Met146Leu we observed that genetic patients were the worst responders in mean (at T3, MMSE score difference was not significant) but response was highly individual: T3 score varying from +4 to -2. **Conclusions:** We demonstrate a favourable effect of AChEIs in familial AD patients more evident in patients without genetic mutations. The genetic group efficacy was individual and not predictable.

P2-406 EFFICACY AND SAFETY OF MEMANTINE IN MODERATE TO SEVERE ALZHEIMER'S DISEASE - A META-ANALYSIS

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Background: The European Commission recently granted an extension of the indication for memantine, which is now indicated for the treatment of moderate to severe Alzheimer's disease (AD) in Europe. Six Phase III clinical studies that examined the efficacy and safety of memantine across the moderate to severe disease spectrum were analyzed in a meta-analysis. This meta-analysis was part of the material that was submitted to support the request for an extension of the memantine indication to include the moderate AD patient group. **Methods:** The six Phase III studies were randomized, placebo-controlled trials and included patients treated with memantine (20 mg per day) either as monotherapy or as an addition to existing stable acetylcholinesterase inhibitor treatment (n=2,311). This post hoc meta-analysis was conducted in the subgroup of patients (n=1,826) with moderate to severe AD (defined by baseline MMSE scores <20;). The three main domains of global status (Clinician's Interview-