plasticity (Castillo et al. Neuron 2012;76,70-81). The endocannabinoid system appears to play an important role in some clinical presentations of autism, such as socialization. Indeed, Autism Spectrum Disorder seems to be characterized by a hypofunctionality of the endocannabinoid system (Aran et al. Mol Autism 2019;10, 2).
Objectives: The present work aims to describe the current state of the art regarding the possible role of cannabinoids in the modulation of the excitatory and inhibitory systems in individuals with ASD.
Methods: We carried out a search on PubMed concerning the randomized clinical trials on the modulating effect of excitatory and inhibitory cannabinoid systems in autism. Three eligible articles were found according to the purpose of the present study.
Results: The results of the three articles considered highlighted a cannabinoid (CBD)-related increase in glutamate in subcortical regions (basal ganglia) and a decrease in cortical regions (dorsomedial prefrontal cortex), both in subjects with and without ASD. CBD increased GABA transmission in the subcortical regions of neurotypical subjects, while it decreased it in the same areas of the ASD group. Furthermore, CBD modulated low-frequency activity, used as a measure of brain activity and functional connectivity in the brains of adults with ASD.
Conclusions: Data from the three functional MRI studies demonstrated that CBD influences cortical and subcortical connectivity on an adult sample. This effect was notable only in the ASD group but not in the controls. However, further studies are needed to confirm the results obtained so far.

Disclosure of Interest: None Declared

EPP0346

Anti-amyloid-β Monoclonal Antibodies as Promising Disease-Modifying Therapies in Alzheimer's Disease: A Focus on Aducanumab, Lecanemab, Crenezumab, Gantenerumab and Solanezumab

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Introduction: Alzheimer's disease (AD) is the most prevalent form of age-related dementia in the world. The body of evidence suggesting that its main pathological features consist of amyloid-β (Aβ) plaque deposits and neurofibrillary tangles formed by hyperphosphorylated tau protein is robust. The drugs currently on the market have no effect on disease progression and provide only partial symptomatic relief, which creates a large unmet medical need. Anti-Aβ monoclonal antibodies (mAbs) have been shown to reduce amyloid plaques. Therefore, passive immunization is a major hope for treatment of AD.
Objectives: This review aims to summarize the up to date knowledge and experience with Anti-Aβ mAbs with positive clinical or biomarker effects in long-duration trials.
Methods: A narrative review was conducted based on a search in *Google Scholar* and *Pubmed*, using the following terms or combinations "anti-aβ protofibril antibody"; "early alzheimer's disease"; "immunotherapy for Alzheimer's disease". Peer-reviewed literature published between 2016 and April 2022 was screened on full-text for this purpose.
Results: Aducanumab surpassed a successful Phase 1B trial demonstrating a dose and time dependency for Aß reduction with a beneficial impact on some clinical measures after 1 year of treatment. Two large Phase 3 clinical trials were initiated and already discontinued based on futility analysis done and not based on safety concerns. Further analyses including participants exposed for longer periods of time at higher doses indicated that aducanumab reduced brain amyloid and decreased the rate of decline.
Lecanemab (BAN2401) completed a Phase 2 trial (2018) with evidence of amyloid reduction and slowing of cognitive decline and has now entered Phase 3. Aducanumab and BAN2401 showed significant efficacy on both clinical and biomarker outcomes.
Crenezumab Phase 2 trial results suggested efficacy in mild AD; a Phase 3 program was recently halted due to futility. This mAb is currently being assessed in a prevention trial involving a Colombian kindred with autosomal dominant AD.
Gantenerumab showed significant biomarker effects, with no clinical efficacy reported to date and is being assessed in Phase 3 trials after a trial in prodromal disease stopped for futility suggested that higher doses might be efficacious. Gantenerumab and solanezumab showed no drug-placebo differences in clinical outcomes of specific studies included in this review.
Conclusions: Therapies with anti-Aβ mAbs have been developed successively and conducted in clinical trials signaling a promising new era for AD drug development and providing compelling evidence for the prominent role of neurotoxic soluble amyloid oligomers in the pathogenesis of AD and as therapeutic targets. Lessons learned from these studies may also be a bridge to more efficacious, safe drugs in AD.

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Others 02

EPP0348

Cariprazine's efficacy in treating depressive symptoms – pooled data from schizophrenia, bipolar depression and major depression trials

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Introduction: Depressive symptoms are a common feature of schizophrenia (SCH) and define bipolar disorder and major depressive disorder (MDD). Their emergence is related to altered neurotransmission at the serotonin receptors and potentially at dopamine D3 receptors.
Objectives: The aim of this analysis was to examine the efficacy of cariprazine (CAR) in treating depressive symptoms in SCH, bipolar depression (BD) and MDD.
Methods: Clinical trials with randomised, double-blind, placebo (PLB)-controlled designs were included in these analyses. Data from 3 SCH [NCT00694707, NCT01104766, NCT01104779; 1.5-9 mg/d] and 3 BD [NCT01396447, NCT02670538, NCT02670551; 1.5-3