in scores on the Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB), the Alzheimer’s Disease Assessment Scale, the Alzheimer’s Disease Cooperative Study-Instrumental Activities of Daily Living Inventory, and the MMSE. The researchers assessed for adverse events and obtained laboratory studies.

Results

The study enrolled 257 participants with a mean age of 75.0 years in the donanemab group and 75.4 years in the placebo group. The donanemab group showed a smaller reduction in iADRS score at 76 weeks than the placebo group (−6.86 vs. −10.06), indicating less cognitive and functional decline over that period. Between-group differences in scores on the CDR-SB and the other secondary outcome measures were not statistically significant, however.

By 24 weeks, the donanemab group showed a reduction in amyloid plaque level that was 67.83 centiloids greater than the reduction in the placebo group. At week 76, the difference favoring donanemab had increased to 85.06 centiloids, the researchers reported. There was no association between reduction in amyloid plaque level and clinical outcomes, however.

The researchers stated they had sought a reduction of at least half in progression of Alzheimer’s disease as measured by the iADRS, but that goal was not reached.

There were no significant between-group differences in the prevalence of serious adverse events. The incidence of amyloid-related imaging abnormalities with edema or effusions was significantly higher in the donanemab group, and two donanemab patients were hospitalized as a result of this phenomenon.

Implications

The researchers stated they had sought a reduction of at least half in progression of Alzheimer’s disease as measured by the iADRS, but that goal was not reached. They added that the study did not show an effect of treatment on global tau load, possibly because the study period was not long enough to detect such changes. Other limitations of the study included enrollment of few non-white participants.

“Longer and larger trials are required to study the efficacy and safety of donanemab in early Alzheimer’s disease,” the study’s authors wrote in conclusion.

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Mintun MA, Lo AC, Evans CD, et al. Donanemab in early Alzheimer’s disease. N Engl J Med 2021; published online Mar 13; doi: 10.1056/NEJMoA2100708. Correspondence to: Mark A. Mintun, M.D., Eli Lilly, Lilly Corporate Center, Indianapolis, IN 46285; Email: mintun@lilly.com.

Nursing homes’ prescribing of psychotropics higher in pandemic

The imposition of safety-related lockdowns in nursing homes during the COVID-19 pandemic raised concerns about the mental health of residents and possible increases in the prescribing of psychotropic drugs. A cross-sectional study conducted in Ontario, Canada examined monthly trends in the prescribing of psychotropic medications to nursing home residents relative to the prescribing of other drugs in the period between April 2018 and September 2020 (COVID-related restrictions on activities in Ontario’s nursing homes began in March 2020). The researchers examined prescribing patterns for antipsychotics, antidepressants, benzodiazepines, and trazodone, comparing these to trends in the prescribing of metformin and statins. They examined the proportion of nursing home residents receiving a psychotropic drug prescription in periods just before the pandemic (January to February 2020) and during the pandemic (March to September 2020). They reported absolute increases in the proportion of residents receiving prescriptions for antipsychotics, antidepressants, and trazodone in the March to September period. Benzodiazepine prescribing was down slightly in the same period but was higher than a pattern of declines that had been observed between April 2018 and February 2020. Decreases in the proportion of residents receiving prescriptions for metformin and statins were reported in the pandemic period. A lack of information on indications for the prescribing was cited as a limitation of the study. “Overall, the study’s findings highlight the importance of balancing infection prevention and control measures in nursing homes with the well-being of residents during the COVID-19 pandemic,” the study’s authors wrote. [Stall N, et al. JAMA Intern Med 2021; published online Mar 15; doi: 10.1001/jamainternmed.2021.0224]

Ezogabine falls short in trial measuring brain response in depression

Dysfunction in the brain reward system has emerged as a core feature of depression, with many patients experiencing deficits in response to pleasure that manifest as anhedonia. Voltage-gated potassium channels in brain regions associated with depression regulate cell membrane excitability and have been identified as potential treatment targets. A placebo-controlled trial evaluated the effects of the KCNQ2/3 channel opener ezogabine, originally developed as an anticonvulsant and also known as retigabine, on brain response during reward anticipation in patients with depression. Adults aged 18 to 65 meeting DSM-5 criteria for depression, not taking any psychotropic medication at randomization, and exhibiting clinically significant anhedonia were eligible. Participants were randomized to 5 weeks of treatment with ezogabine or placebo, with dosing titrated to 900 mg/day at week 4. Participants received magnetic resonance imaging scans at baseline and week 5. The primary outcome measure was change in activation during reward anticipation in the left and right ventral striatum. Several measures of depression and anhedonia were used to evaluate changes in symptoms. Forty-five participants were enrolled. The researchers found no significant