Minocycline vs Placebo for Mild Alzheimer Disease

Alzheimer disease (AD) affects an estimated 50 million people worldwide, but there are no known disease-modifying treatments available. The anti-inflammatory tetracycline antibiotic minocycline inhibits microglia, reduces neuropathology and deficits in transgenic mouse AD models, and is a credible candidate for repurposing in AD modification. In a double-blind randomized clinical trial including 544 participants with very mild AD based in the UK National Health Service, Howard and coauthors found that 2 years of treatment with the highest tolerable minocycline doses (400 mg/d) gave no benefits on cognitive or functional decline and was poorly tolerated in this population. Despite promising preclinical data, minocycline should not be investigated further as a treatment for symptomatic AD. Editorial perspective is provided by Schneider.

Vascular Risk in Adulthood and Brain Pathology in Late Life

Cardiovascular risk factors are known to influence dementia risk, but the timing and mechanisms are unclear. In a prospective longitudinal cohort study from the Insight 46 study of 463 individuals born in a single week in 1946 and observed prospectively, Lane and coauthors calculated the Framingham Heart Study–cardiovascular risk scores at ages 36, 53, and 69 years and assessed associations with β-amyloid load, white matter–hyperintensity burden, and brain volumes at approximately 70 years. Higher risk scores—especially at age 36 years—were associated with higher white matter–hyperintensity load and smaller brain volume but not β-amyloid load. Addressing cardiovascular risk factors may need to start in the 30s or earlier to optimize brain health in later life. Editorial perspective is provided by Seshadri.

Infection Risks Associated With Treatments for MS

The risk of infections is important among patients with multiple sclerosis (MS) treated with newer disease-modifying therapies in clinical practice, and it is not clear if infection risk differs by treatment. In a nationwide register-based cohort study of 6421 patients with MS starting treatment in Sweden from 2011 to 2017, Luna and coauthors compared rates of infection-specific hospitalizations and drug use by therapy with general population rates. Patients with MS were found to be at increased risk of infections, with the lowest rates observed in patients using injectable therapies (interferon beta and glatiramer acetate). Rituximab use was associated with the highest rate of serious infections but less use of herpes antiviral medications compared with fingolimod and natalizumab use.

Lanabecestat for Treatment of Early and Mild AD

In 2 randomized clinical trials, AMARANTH (n = 2218 patients) and DAYBREAK-ALZ (n = 1722 patients), patients aged 55 to 85 years who met National Institute on Aging–Alzheimer’s Association criteria for early Alzheimer disease (AD) or mild AD were randomized to either daily doses of lanabecestat (20 mg or 50 mg), an oral beta-site amyloid precursor protein–cleaving enzyme 1 (BACE1) inhibitor, or placebo. Wessels and coauthors found that neither cognitive nor functional decline was slowed in patients who took lanabecestat at either dose, leading both studies to be terminated early. Although lanabecestat was a promising preclinical AD compound, it failed to meet a positive end point in large trials.