Lecanemab: Looking before we leap

Alzheimer Disease creates an enormous burden for patients, families and society. Thus, the search for effective AD therapies has been pursued urgently for decades with mostly disappointing results. Recently, though, the Clarity AD trial demonstrated a significant improvement in cognition amongst patients treated with a novel amyloid-lowering agent, lecanemab, and vastly greater levels of amyloid lowering compared to prior amyloid lowering agents. On the basis of this trial the FDA recently granted accelerated approval for lecanemab with a label targeting mild cognitive impairment or mild AD. Yet, while lecanemab has been hailed as a breakthrough, we should be cautious before widely adopting this new medication without additional data for three reasons: 1. Its effect is modest and may be overestimated 2. Its real world harms are unknown are likely to be considerably higher than observed in the trial and 3. Its cost-effectiveness is uncertain and its aggregate societal cost ahs the potential to dwarf expenditures on all other medications.

A Bayesian perspective requires evaluating new evidence in the context of prior evidence. For novel therapeutics, its oftentimes difficult, to meaningfully quantify the realistic distribution of treatment effects before trial results are known. In the case of lecanemab, however, a fairly clear cut prior exists — many other amyloid-lowering treatments, including other monoclonal antibodies, have targeted AD. Prior work has identified that greater degrees of amyloid lowering are associated with modest slowing of cognitive decline. Given that lecanemab