Biomere

COMMUNITY BLOG

HOW ADUHELM'S APPROVAL IS CHANGING THE ALZHEIMER'S DISEASE DRUG DEVELOPMENT LANDSCAPE

Finding new therapies for neurological diseases has always posed challenges, and while there has been some drug success stories, neurological diseases no longer attract much pharma or venture capital investment[1]. There is no doubt that a neurodegenerative disease like Alzheimer's disease (AD) has enormous unmet clinical needs but repeated clinical trial failures have reduced pharma interest in developing disease-modifying therapies[2]. Additionally, the pathophysiology of diseases like AD are very complicated since symptoms like memory loss, cognitive dysfunction etc. manifest in later stages. Because the early stages of the disease are asymptomatic, it is almost impossible to identify patients with very early-stage disease who can be enrolled in clinical trials for disease-modifying therapies. Due to the complexity and high failure rate in the clinic, many pharma companies like Pfizer, Amgen and Astra Zeneca backed away from neuroscience drug development1, likely due to the fact that there were no short-term gains to be had. Biogen, however, went against the trend and continued working on a drug called aducanumab that targeted β-amyloid plaques that are a hallmark of AD. Aducanumab is a monoclonal antibody that enters the brain at low concentrations where it binds to the β-amyloid plaques and triggers immune-mediated clearance of the plaques. The hypothesis is that if the plaques reduce, cognitive decline will also slow down and may even reach a plateau.

The initial phase I and II clinical trial data on aducanumab looked promising but an interim analysis of a phase III trial in early-stage AD patient with mild symptoms, predicted that the drug would not meet the primary endpoints[3]. Aducanumab seemed to be destined to join the scrap heap of failed AD drugs, but in an surprising reversal, Biogen announced that after analyzing a larger data set, the drug did reduce clinical decline in AD patients when given at high doses[4]. Expectedly, this *volte face* triggered a great deal of discussion as to how the larger data set showed a completely different outcome compared to the interim readouts. Nevertheless, in June 2021, the FDA approved aducanumab for the treatment of Alzheimer's disease[5] and the drug is now available under the brand name Aduhelm. The approval is conditional in that ongoing post-approval studies are ongoing and need to demonstrate clinical benefits. If these shows do not show definitive clinical benefit, the FDA may revoke approval. Understandably, the approval is quite controversial and many clinicians are not ready to prescribe the drug and payors like Medicare are not willing to pay the steep price[6].

While Aduhelm is receiving both positive and negative attention, the approval decision has triggered renewed interest in Alzheimer's disease drug programs. For example, Eli Lilly is filing for approval of their AD drug candidate, donanemab and companies like Bristol Myers Squibb (BMS) and GlaxoSmithKline (GSK) are signing deals to bring new AD drug candidates[7]. BMS is working on licensing in a new anti-tau therapy from Prothena and GSK signed a deal with Alector Pharmaceuticals to develop drug candidates for Alzheimer's disease and Parkinson's disease[8]. Aduhelm's accelerated approval could pave the way to overcoming other challenges as well. The regulatory approval path that Biogen took could potentially serve as a blueprint for the next-generation of AD therapies. If payors are willing to accept the high price point of Aduhelm (estimated at $56,000 a year), it will likely set a precedent for other AD therapies. Additionally, if the post-approval studies show that plaque clearance does improve cognition and has clinical benefits, this will open the doors for innovative new drugs that can clear plaques efficiently in early- and even mid-stage AD patients. If Aduhelm and the next-generation of AD drugs are shown to work, the benefits to millions of AD patients and their families will be incalculable.

References:

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