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A Comparison of Representative Drugs Under Two Existing Treatment Strategies for Alzheimer's Disease

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Abstract: This paper introduces two primary therapeutic approaches for Alzheimer's disease: symptom-improving drugs and disease-modifying treatments by comparing the specific drugs Donepezil and Aducanumab. Aducanumab, as the first disease-modifying treatment for Alzheimer's disease approved in more than two decades, marks the beginning of Aβ monoclonal antibody therapy efforts. Introducing this "pioneer" provides a fitting context to discuss symptom-improving treatments. Donepezil is a drug commonly used to relieve symptoms. It is considered to be more suitable for patients with earlier stages of the disease than similar drugs such as memantine. Therefore, it was the better choice when comparing the two drugs in this review. By comparing these two treatments, we can better assess their effectiveness in treating Alzheimer's disease and their suitability for different clinical situations. This comparison helps to identify common treatment strategies for Alzheimer's disease.

Keywords: Alzheimer's Disease, Donepezil, Aducanumab, Symptomatic Treatment, Disease-Modifying Treatment

1. Introduction

1.1. Fundamental pathological features

The exact cause of Alzheimer's disease (AD) is currently unclear, and there is no clear research on the etiology of the complex pathological phenomena that occur during its development. The two important neural markers of Alzheimer's disease (AD) are beta-amyloid (A β) plaques and neurofibrillary tangles (NFT) [1]. Although NFTs are caused by the continuous accumulation of highly phosphorylated tau proteins in neurons, the main influencing factors of these changes are the hippocampus and cerebral cortex, which are believed to play an important role in cognitive decline and memory loss.

Multiple pathogenic mechanisms have been proposed as a result of continuous research on the neuropathological mechanisms of Alzheimer's disease (AD). In addition to known factors, neuroinflammation and oxidative stress are also important factors that trigger AD. The immune cells of the central nervous system, microglia, are activated and trigger inflammatory responses, thereby exacerbating neuronal damage [2]. In addition, the increasing oxidative stress in the aging brain can lead to neuronal damage and rapidly increase the accumulation of A β and tau proteins.

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1.2. Pharmacological treatment strategies and research progress

1.2.1. Symptomatic treatments

The traditional treatment methods for Alzheimer's disease include cholinesterase inhibitors (such as donepezil, rivastigmine, and galantamine) and NMDA receptor antagonists (such as memantine). These drugs improve cognitive function and memory by enhancing neurotransmission or modulating the effects of glutamate, but they cannot halt or reverse the advancement of the condition.

1.2.2. Disease-modifying therapies

Recently, the US Food and Drug Administration has approved multiple monoclonal antibody drugs targeting A β plaques and tau protein, including Aducanumab, Lecanemab, and Donanemab. Aducanumab works by reducing amyloid plaques in the brain to slow cognitive decline, although its clinical trial results have been controversial. Lecanemab has demonstrated efficacy in slowing disease progression in clinical trials, particularly in early-stage AD patients, by clearing Aβ fibrils and reducing the accumulation of related biomarkers. Meanwhile, Donanemab is aimed at a particular variant of Aβ, demonstrating significant effectiveness in removing amyloid plaques.

1.2.3. Emerging strategies

Immunotherapy is becoming a focal point in AD research (disease-modifying therapies are a form of immunotherapy), including vaccine-based approaches such as UB-311. This strategy aims to stimulate the immune system to reduce Aβ plaques. Future research directions include multi-target drugs designed to address several pathological processes of AD simultaneously, such as mitochondrial dysfunction, autophagy impairment, and neuroinflammation.

2. Donepezil as a symptomatic treatment representative

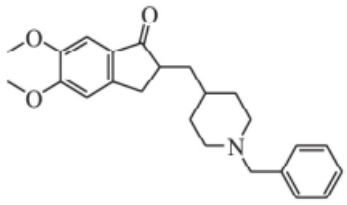

Figure 1: Structure of donepezil

2.1. Mechanism of action of drugs

One of the earliest theories to trace the pathogenesis of Alzheimer's disease (AD) is the hypothesis of cholinergic system damage, which plays an important role in AD research. Acetylcholine (ACh), a crucial excitatory neurotransmitter in the brain, is linked to complex behaviors like learning and memory. The central cholinergic system controls acetylcholine synthesis and release, thereby affecting its concentration in the nervous system [3].

Initial research identified significant damage to the cholinergic system in the brains of Alzheimer's patients. In memory-related experiments involving the cholinergic system, mice administered cholinergic antagonists exhibited impaired recognition abilities and memory deficits, manifesting as cognitive dysfunction. Subsequently, the administration of cholinergic agonists alleviated these symptoms [4], further establishing a connection between cholinergic system dysfunction and memory decline.

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Based on this, restoring acetylcholine levels in the brain became a clinical strategy for treating AD. Acetylcholinesterase (AChE) is the enzyme responsible for hydrolyzing ACh, leading to its inactivation by breaking down its normal physiological structure. Acetylcholinesterase (AChE) inhibitors act by blocking AChE activity, thereby prolonging the survival time of ACh in the synaptic cleft, increasing systemic ACh concentrations, and restoring cholinergic function to the system [5]. AChE inhibitors were among the earliest drugs approved for Alzheimer's treatment even remaining widely used in clinical practice. Donepezil, which inhibits the enzyme reversibly and non-competitively, is a key representative of this class.

2.2. Clinical data and efficacy

The cognitive benefits of donepezil were evaluated through the cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS Cog), which is a mature tool used in long-term Alzheimer's disease research. ADAS-cog assesses several aspects of cognition, such as memory, spatial awareness, attention, problem-solving, language, and practical skills. The score range is from 0 to 70, and the results are opposite. An increase in the value indicates a decrease in cognitive ability. Most healthy elderly individuals score around 0 or 1, but slightly higher scores may be observed in non-dementia adults.

In a large-scale, multicenter trial conducted under double-blind conditions and involving a comparison with a placebo group, scientists explored the therapeutic potential of Donepezil for individuals in the initial phases of Alzheimer's disease. The study involved 96 participants who initially received 5 mg of Donepezil daily, with an increase to 10 mg after six weeks. The key metric used to evaluate the results was the ADAS-cog. Results showed notable improvements in ADAS-cog scores for those treated with Donepezil at 12 and 24 weeks, with reductions of 1.9 points (P = 0.03), 2.3 points (P = 0.008), and 2.3 points (P = 0.001) compared to the placebo group [6].

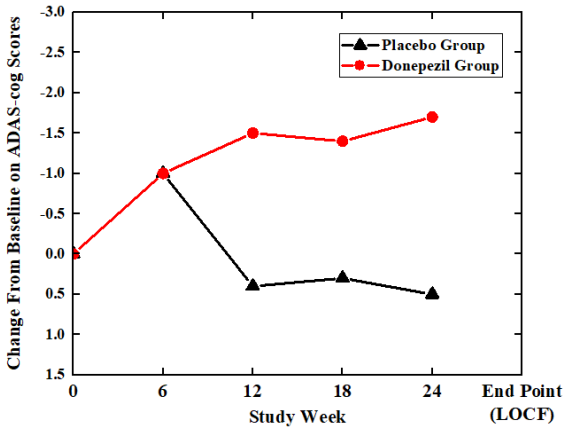

Figure 2: Over 24 weeks of treatment in the ADAS-cog total scores for both the Donepezil and placebo groups [6]

2.3. Limitations of the drug

2.3.1. Side effects

Typical adverse effects associated with Donepezil involve digestive system issues and neurological disturbances. Gastrointestinal issues, such as nausea, vomiting, and diarrhea, are often observed during the initial stages of treatment and may improve as therapy progresses [7]. Neurological

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symptoms, including dizziness, headaches, and drowsiness, are also frequently reported, and some patients may experience insomnia or abnormal dreams [8].

Although most side effects are relatively mild for the majority of patients, more serious health concerns can still arise in certain cases. These include cardiac issues, such as bradycardia and syncope [9], as well as severe allergic reactions characterized by difficulty breathing and facial swelling. It is crucial to monitor for these adverse effects during clinical administration.

2.3.2. Limitations of the treatment approach

The effects of Donepezil are limited to symptom management and do not alter the progression of Alzheimer's disease. Research has demonstrated that while Donepezil can temporarily slow cognitive decline, it neither stops nor reverses the fundamental pathological processes of the disease, including the accumulation of β-amyloid plaques and the development of tau tangles. Therefore, although patients may experience short-term improvements in memory and daily functioning, the long-term progression of AD remains unaffected [6].

3. Aducanumab as a disease-modifying treatment representative

3.1. Aβ cascade hypothesis

As mentioned earlier, the accumulation of beta-amyloid protein (A β) outside neurons and the formation of neurofibrillary tangles (NFT) inside neurons are two key pathological indicators of Alzheimer's disease (AD).

Aβ is a peptide produced by amyloid precursor protein (APP) through multiple complex mechanisms. APP is a membrane protein discovered in humans [10]. Under the action of β - secretase 1 (BACE-1), APP undergoes cleavage to form soluble APP β fragments (sAPP β) [11]. Gamma secretase is then used to process APP and produce A β monomers [12]. According to the cleavage site, gamma-secretase produces A β peptides of different lengths, such as A β (1-37), A β (1-40), and. A β (1-42) [13] and A β (1-42) play the most important roles in amyloid formation and disease progression [14].

When Aβ is produced in cells, it is released into the extracellular space. After aggregation of individual monomers, extracellular A β monomers aggregate to form A β oligomers (A β O), which then form fibers (A β fibrils), and finally form A β plaques [15]. Aβ storage fibrils. a key component of neurodegeneration and cognitive decline in Alzheimer's patients. However, this sequence of events can be explained by the famous "Aβ cascade hypothesis" [16].

3.2. Mechanism of action of drugs

Building on the Aβ hypothesis, researchers have suggested various approaches aimed at lowering Aβ concentrations in the brain. These strategies include:

3.2.1. Prevention or reduction of A β formation

This method mainly targets proteases in APP processing, such as B. BACE-1 and γ-secretase modulator (GSM), which inhibit or reduce Aβ production [17].

3.2.2. Enhancement of A β clearance

This approach aims to identify and regulate key enzymes responsible for Aβ degradation in the brain, such as neprilysin, to improve Aβ clearance [18].

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3.2.3. A β receptor antagonists

These drugs block the downstream pathways of Aβ, thereby preventing Aβ that cannot be effectively and safely cleared from exerting its neurotoxic effects. An example is TTP-488, which functions as an Aβ receptor antagonist [19].

3.2.4. Immunotherapy (passive or active)

This approach aims to clear existing amyloid deposits. Immunotherapy has shown the most promise among the proposed strategies, which is precisely the mechanism behind Aduzumab. Aducanumab works through indirect immunization, where intravenous injection of monoclonal antibodies (mAbs) targeting A β is used to treat Alzheimer's disease (AD) and mild cognitive impairment (MCI) associated with AD.

While the first three approaches have encountered various challenges, the fourth approach has demonstrated some success, as evidenced by the therapeutic mechanism of Aducanumab.

3.3. Clinical trial data

A 2016 study found that aducanumab was effective in two main areas: reducing amyloid plaques and slowing cognitive decline [20]. A study found that aducanumab reduced the number of plaques (microorganisms depending on the dose and treatment involved). At week 54, the standardized uptake ratio (SUVR) in the 3 mg/kg, 6 mg/kg, and 10 mg/kg groups decreased significantly and approached baseline. Positive and negative amyloid conversion

The use of the Total Cell Rating Scale (CDR-SB) in the Clinical Dementia Rating Scale to assess cognitive function showed that the treatment group experienced a dose-dependent decline in cognitive ability after one year. There is a statistically significant difference within the same group compared to the 10mg/kg group. The Mg/kg group showed a 10mg/kg group in the 10mg/kg group. Compared with the placebo group, the difference followed statistical significance ($P<0.05$). In addition, the scores of the Mini-Mental State Examination (MMSE) in the 3 mg/kg and 10 mg/kg groups significantly increased.

3.4. Efficacy, limitations, and risks of Adu

One of the main limitations of aducanumab is that subsequent phase III clinical trials produced conflicting results in two studies of identical design [21]. In addition, the results of the escalating dose study arm were inconclusive. This has raised concerns about the long-term effectiveness of the drug, especially in large-scale clinical trials where it has had long-term effects, particularly on cognitive function.

Additionally, the safety profile of Aducanumab warrants careful consideration. Previous studies have reported amyloid-related imaging abnormalities (ARIA), such as vasogenic edema and/or microhemorrhages (ARIA-E and ARIA-H) detected on brain MRI scans, with incidence rates of 35% and 36%, respectively. About one-quarter of participants with imaging abnormalities exhibited symptoms, particularly those carrying the APOEε4 allele [22]. This highlights the need for ongoing monitoring of safety concerns in the broader clinical use of Aducanumab.

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4. Comparison of symptomatic and disease-modifying treatments

4.1. Efficacy comparison

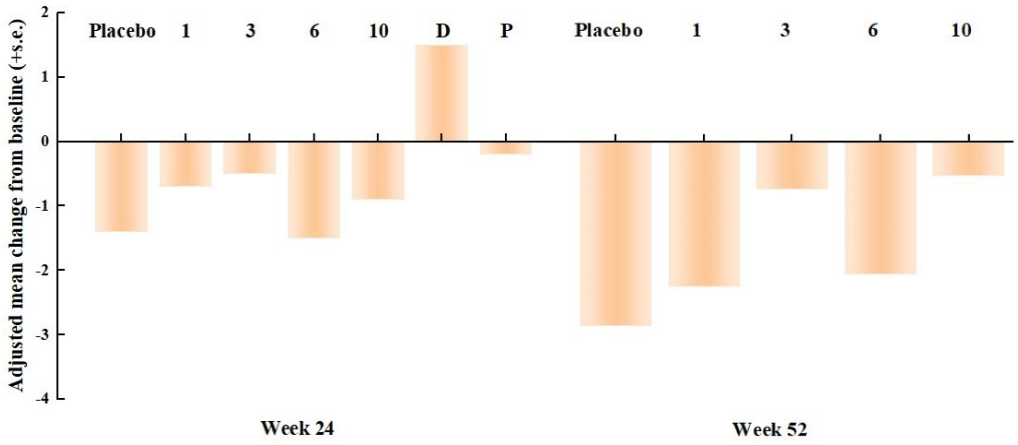

Figure 3: Clinical progression of patients on the Mini-Mental State Examination (MMSE) under treatments with Aducanumab, Donepezil, and placebo (note: this figure is based on reanalyzed and newly compiled data.) [6,20]

The numbers represent the doses of aducanumab (mg/kg), while the letters "D" and "P" represent clinical trial data for donepezil and its placebo control group (The dosage began with 5 mg/day for the initial 6 weeks, then was increased to 10 mg/day, or a placebo was administered.).

The figure illustrates the mean changes from baseline in cognitive performance, adjusted for patient differences. Upon observation, Donepezil shows significant cognitive improvement at week 24, depicted in the figure as a positive change. Aducanumab, on the other hand, exhibits a dose-dependent improvement, with the 3 mg/kg and 10 mg/kg doses demonstrating the most pronounced effects compared to the placebo. As time progresses, by week 52, all patient groups exhibit varying degrees of decline in MMSE scores, with the placebo group experiencing the most pronounced decline, indicating the progression of Alzheimer's disease. At this point, the efficacy of Aducanumab, especially in the 3 mg/kg and 10 mg/kg groups, becomes even more significant compared to its effects at week 24.

This further underscores the potential of Aducanumab as a disease-modifying treatment, particularly in early intervention, which is something Donepezil, as a symptomatic drug, cannot achieve. This difference is fundamentally driven by the distinct therapeutic strategies of the two drugs.

In summary, the chart provides comparative data on the cognitive performance of Alzheimer's patients treated with Aducanumab and Donepezil, highlighting Aducanumab’s dose-dependent effects and Donepezil's short-term cognitive improvements. Although overall cognitive function declines over time, high-dimensional aducanumab continues to show some level of disease-modifying impact, which is important for long-term treatment strategies for Alzheimer's disease.

4.2. Safety comparison

Scientifically speaking, donepezil has more frequent and more serious side effects. These are mainly caused by gastrointestinal and nervous symptoms. Although long-term use is considered relatively safe and tolerable, aducanumab has caused more serious side effects. Starch-like protein-related imaging shows severe abnormalities (ARIA). This is especially true for patients with the APOEε4 allele, who are at higher risk.

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Due to this long-term risk, patients taking aducanumab should be closely monitored. This includes MRI for the prevention and treatment of acute respiratory viral infections and other serious side effects. It was one of the first drugs. However, the toxicological details remain unclear.

Overall, Donesil is milder and better suited for long-term use. However, aducanumab's serious side effects and potential long-term risks require special caution when using it.

5. Future directions and challenges

The approval of aducanumab represents a major breakthrough as it is the first approved disease-relief drug specifically designed for the treatment of atopic dermatitis. It has demonstrated significant effects on pathological biomarkers, such as a reduction in the number of B. beta-amyloid plaques; its long-term effects on improved cognitive function are controversial. The mild side effects of ARIA suggest that aducanumab is not an ideal solution. It has opened up new treatment options and paved the way for the development of new drugs, such as lecanemab and donanemab (adjuvants to aducanumab), which have been identified as very important areas of research in this field. They are also currently included in the list of the top ten scientific achievements in 2023 by Science magazine.

Donepezil is likely to be used in combination with other medicines. Used to treat Alzheimer's disease, especially memantine, which has been studied as an example. The goal of this combination treatment is to reduce cognitive decline. And improve patients' quality of life By relying on the synergistic effect of different methods. Donepezil and memantine are thought to enhance cholinergic and glutamatergic neurotransmission. This results in better control of symptoms in the middle and late stages of Alzheimer's disease. This combination therapy has been shown to improve cognitive function and daily functioning. It is particularly beneficial for patients with advanced Alzheimer's disease [23], leading to a deeper understanding of the pathological mechanisms of Alzheimer's disease. Future research directions may include combining donepezil with other new drugs. For example, the combination of donepezil with a disease-modifying drug can provide a double benefit for the patients; drugs can slow down the development of the pathology. This combination may be particularly suitable for patients with early and intermediate-stage disease as it reduces symptoms and slows disease progression. However, there may be a risk of drug interactions if these medications are used together. This is especially true because different drugs affect neural transmission through different mechanisms. Further research is needed to evaluate whether the different mechanisms of action of different drugs may lead to safety issues.

6. Conclusion

This article compares the two main approaches to treating Alzheimer's disease with donepezil and aducanumab: symptomatic treatment and supportive care. Donepezil is a cognitive enhancer that provides short-term benefits, particularly in the early and middle stages of Alzheimer's disease. However, its effect is limited to increasing acetylcholine levels and cannot stop or reverse the progression of the disease. Meanwhile, aducanumab, a new disease-modifying drug, aims to reduce β-amyloid plaques and slow the progression of the disease. However, the cognitive benefits remain controversial and, like ARIA, carry significant risks.

Comparing these two drugs reveals their strengths and weaknesses. And demonstrates how symptom relief and disease intervention can complement each other in the treatment of Alzheimer's disease, representing a significant advance in disease-modifying therapies. However, the long-term efficacy and safety of the drug require further study. At the same time, it has been reported that drugs with known symptoms, in combination with drugs such as memantine, could be used more widely. And could expand the scope of treatment. Future research in Alzheimer's disease will likely focus on

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combination treatments that combine symptom control and disease modification. This provides patients with greater treatment options.

References

[1] Bibl, M., Mollenhauer, B., Esselmann, H., Lewczuk, P., Klafki, H. W., Sparbier, K., Smirnov, A., Cepek, L., Trenkwalder, C., Rüther, E., Kornhuber, J., Otto, M., & Wiltfang, J. (2006). CSF amyloid-beta-peptides in Alzheimer's disease, dementia with Lewy bodies and Parkinson's disease dementia. Brain: a journal of neurology, 129(Pt 5), 1177–1187. https://doi.org/10.1093/brain/awl063

[2] Bowen, D. M., Smith, C. B., White, P., & Davison, A. N. (1976). Neurotransmitter-related enzymes and indices of hypoxia in senile dementia and other abiotrophies. Brain: a journal of neurology, 99(3), 459–496. https://doi.org/10.1093/brain/99.3.459

[3] Budd Haeberlein, S., Aisen, P. S., Barkhof, F., Chalkias, S., Chen, T., Cohen, S., Dent, G., Hansson, O., Harrison, K., von Hehn, C., Iwatsubo, T., Mallinckrodt, C., Mummery, C. J., Muralidharan, K. K., Nestorov, I., Nisenbaum, L., Rajagovindan, R., Skordos, L., Tian, Y., van Dyck, C. H., ... Sandrock, A. (2022). Two Randomized Phase 3 Studies of Aducanumab in Early Alzheimer's Disease. The journal of prevention of Alzheimer's disease, 9(2), 197–210. https://doi.org/10.14283/jpad.2022.30

[4] Das, P., Howard, V., Loosbrock, N., Dickson, D., Murphy, M. P., & Golde, T. E. (2003). Amyloid-beta immunization effectively reduces amyloid deposition in FcRgamma-/- knock-out mice. The Journal of Neuroscience: the official journal of the Society for Neuroscience, 23(24), 8532–8538. https://doi.org/10.1523/JNEUROSCI.23-24-08532.2003

[5] Drachman, D. A., & Leavitt, J. (1974). Human memory and the cholinergic system. A relationship to aging?. Archives of Neurology, 30(2), 113–121. https://doi.org/10.1001/archneur.1974.00490320001001

[6] Drugs.com. (2022). Donepezil side effects. Drugs.com. Retrieved from https://www.drugs.com/sfx/donepezil-side-effects.html

[7] GoodRx. (2022). The 9 most common donepezil side effects. GoodRx. Retrieved from https://www.goodrx.com/classes/cholinesterase-inhibitors/donepezil-side-effects

[8] Hardy, J. A., & Higgins, G. A. (1992). Alzheimer's disease: the amyloid cascade hypothesis. Science (New York, N.Y.), 256(5054), 184–185. https://doi.org/10.1126/science.1566067

[9] Huang, Y., & Mucke, L. (2012). Alzheimer mechanisms and therapeutic strategies. Cell, 148(6), 1204–1222. https://doi.org/10.1016/j.cell.2012.02.040

[10] Jan, A., Gokce, O., Luthi-Carter, R., & Lashuel, H. A. (2008). The ratio of monomeric to aggregated forms of Abeta40 and Abeta42 is an important determinant of amyloid-beta aggregation, fibrillogenesis, and toxicity. The Journal of Biological Chemistry, 283(42), 28176–28189. https://doi.org/10.1074/jbc.M803159200

[11] Li, D. D., Zhang, Y. H., Zhang, W., & Zhao, P. (2019). Meta-Analysis of Randomized Controlled Trials on the Efficacy and Safety of Donepezil, Galantamine, Rivastigmine, and Memantine for the Treatment of Alzheimer's Disease. Frontiers in neuroscience, 13, 472. https://doi.org/10.3389/fnins.2019.00472

[12] NHS. (2023). Side effects of donepezil. National Health Service. Retrieved from https://www.nhs.uk/medicines/donepezil/side-effects

[13] Nilsberth, C., Westlind-Danielsson, A., Eckman, C. B., Condron, M. M., Axelman, K., Forsell, C., Stenh, C., Luthman, J., Teplow, D. B., Younkin, S. G., Näslund, J., & Lannfelt, L. (2001). The 'Arctic' APP mutation (E693G) causes Alzheimer's disease by enhanced Abeta protofibril formation. Nature Neuroscience, 4(9), 887–893. https://doi.org/10.1038/nn0901-887

[14] Selkoe D. J. (2019). Alzheimer disease and aducanumab: adjusting our approach. Nature reviews. Neurology, 15(7), 365–366. https://doi.org/10.1038/s41582-019-0205-1

[15] Seltzer, B., Zolnouni, P., Nunez, M., et al. (2004). Efficacy of Donepezil in early-stage Alzheimer disease: A randomized placebo-controlled trial. Archives of Neurology, 61(12), 1852–1856. https://doi.org/10.1001/archneur.61.12.1852

[16] Sevigny, J., Chiao, P., Bussière, T., Weinreb, P. H., Williams, L., Maier, M., Dunstan, R., Salloway, S., Chen, T., Ling, Y., O'Gorman, J., Qian, F., Arastu, M., Li, M., Chollate, S., Brennan, M. S., Quintero-Monzon, O., Scannevin, R. H., Arnold, H. M., Engber, T., ... Sandrock, A. (2016). The antibody aducanumab reduces Aβ plaques in Alzheimer's disease. Nature, 537(7618), 50–56. https://doi.org/10.1038/nature19323

[17] Vassar, R., Bennett, B. D., Babu-Khan, S., Kahn, S., Mendiaz, E. A., Denis, P., Teplow, D. B., Ross, S., Amarante, P., Loeloff, R., Luo, Y., Fisher, S., Fuller, J., Edenson, S., Lile, J., Jarosinski, M. A., Biere, A. L., Curran, E., Burgess, T., Louis, J. C., ... Citron, M. (1999). Beta-secretase cleavage of Alzheimer's amyloid precursor protein by the transmembrane aspartic protease BACE. Science (New York, N.Y.), 286(5440), 735–741. https://doi.org/10.1126/science.286.5440.735

DOI: 10.54254/2753-8818/2025.24223

[18] *Walker, J. R., Pacoma, R., Watson, J., Ou, W., Alves, J., Mason, D. E., Peters, E. C., Urbina, H. D., Welzel, G., Althage, A., Liu, B., Tuntland, T., Jacobson, L. H., Harris, J. L., & Schumacher, A. M. (2013). Enhanced proteolytic clearance of plasma Aβ by peripherally administered neprilysin does not result in reduced levels of brain Aβ in mice. The Journal of neuroscience: the official journal of the Society for Neuroscience, 33(6), 2457–2464. https://doi.org/10.1523/JNEUROSCI.3407-12.2013*

[19] *Wang, H., & Zhang, H. (2019). Reconsideration of Anticholinesterase Therapeutic Strategies against Alzheimer's Disease. ACS Chemical Neuroscience, 10(2), 852–862. https://doi.org/10.1021/acschemneuro.8b00391*

[20] *Xia, W., Wong, S. T., Hanlon, E., & Morin, P. (2012). γ-Secretase modulator in Alzheimer's disease: shifting the end. Journal of Alzheimer's disease: JAD, 31(4), 685–696. https://doi.org/10.3233/JAD-2012-120751*

[21] *Yoshikai, S., Sasaki, H., Doh-ura, K., Furuya, H., & Sakaki, Y. (1990). Genomic organization of the human amyloid beta-protein precursor gene. Gene, 87(2), 257–263. https://doi.org/10.1016/0378-1119(90)90310-n*

[22] *Yuksel, M., & Tacal, O. (2019). Trafficking and proteolytic processing of amyloid precursor protein and secretases in Alzheimer's disease development: An up-to-date review. European journal of pharmacology, 856, 172415. https://doi.org/10.1016/j.ejphar.2019.172415*

[23] *Zhang, D. F., Xu, M., Bi, R., et al. (2019). Genetic analyses of Alzheimer's disease in China: Achievements and perspectives. ACS Chemical Neuroscience*, 10*(2), 890–901. https://doi.org/10.1021/acschemneuro.8b00435*