Why Dementia is Associated with Poor Morbidity and Novel Treatments: An In-Depth Discussion about Alzheimer's Disease

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Abstract. One of the most common forms of dementia around the world is Alzheimer's. By 2022, it is estimated one out of every three seniors diagnosed with Alzheimer's will eventually die due to complications from the disease [1]. There are several biological and physical markers of Alzheimer's that may indicate that one has the disease, with symptoms all relating to a decline in cognitive function. The general development of Alzheimer's is ascribed to two factors, genetic and environmental. Along with the growth of an aging population and the absence of a definitive cure, the search for novel treatments has gained significant momentum. Some promising treatments include: immunotherapies targeting amyloid-beta plaques, such as the monoclonal antibody 'donanemab'; precision medicine for personalized therapies, namely deep brain stimulation (DBS); and TRIM11 as a biological target for the slowing of the decline in cognitive abilities. Despite progression in the development of novel treatments, the pathophysiological mechanism of the disease is yet to be understood, accounting for various trial-and-error type experiments. Continued research and a comprehensive approach are vital for the development of effective therapies for Alzheimer's disease.

Keywords: Alzheimer's disease, β-amyloid peptide, neurofibrillary tangles, dementia, novel treatments.

1. Introduction

Dementia is an umbrella term for a range of diseases that cause a decline in cognitive abilities such as memory loss. It can become so severe that the patient will lose all basic functions of life including ability to take care of themselves, unable to communicate and many more. This also causes problems for the patient's carer or family where a lot of time is dedicated to the patient. Some symptoms of dementia include difficulty with language and motor skills, lack of control with body muscles disabling them to swallow, control their bladder or bowel movements.

Dementia can be divided into many subtypes, with the most prevalent subtype being Alzheimer's disease (AD), constituting between 60-70% of all dementia cases [2]. It is a progressive neurodegenerative disease, where the degeneration of neurons leads to a multitude of symptoms. AD most commonly affects people over the age of 65, where 1 in 14 people in the UK will eventually get diagnosed. It is associated with a bad prognosis of 7 years, where patients ultimately die from complications of AD [3]. The pathophysiology and hence the treatments of AD are still not well understood and researched into. Therefore, this paper will discuss how AD affects the human body, how it can be diagnosed and managed. Finally, novel treatments for AD as well as associated challenges will also be analysed.

2. How Does AD happen

Although what triggers the development of AD is not completely understood, it is attributed to a combination of genetic and environmental risk factors. Genetic risk factors include a family history of inherited diseases - these include AD itself and Down's syndrome. This means that if a close family relative has had these diseases, the patient is also more likely to genetically inherit these diseases. Other risk factors range from general comorbidities such as diabetes and high blood cholesterol, to

more environmental and lifestyle-based factors such as low physical and cognitive activity, depression and loneliness. Unhealthy habits such as smoking and drinking alcohol can also increase risk as they are known to cause brain atrophy - loss and shrinkage of brain tissue [4].

The physiological mechanism that leads to AD is somewhat understood – it is caused by the build-up of an abnormal amount of proteins in the brain. The primary proteins include beta-amyloid peptide – a by-product of the amyloid precursor protein breakdown, which is expressed as a membrane protein on neuron synapses, and tau proteins – a protein expressed in neuronal axon microtubules. The pathological build-up of these two proteins is known as amyloid plaques and neurofibrillary tangles respectively [5]. As these proteins build up, they damage existing brain tissue leading to the loss of neurotransmitters such as acetylcholine, hence affecting neuronal transmission and causing cognitive decline. Some parts of the brain that are most commonly affected are those to do with memory formation such as the hippocampus; the temporal lobe which is in charge of language and emotional associations; and the subcortical nuclei which help coordinate movement [6].

3. Symptoms of AD

There are several symptoms linked with AD that are consistent with progressive cognitive decline. These symptoms can be divided based on the severity and staging of AD. However, one must note that these are symptoms that are not specific to AD as they may also be seen in other types of dementia.

3.1. Early Stage Symptoms

With early stage AD, patients may experience a decline in verbal abilities and cognitive functions. Examples include failing to recall earlier events and conversations, frequently losing items and asking questions repetitively. Specifically, the frontal and temporal lobe is impacted here which are in charge of verbal communication (Broca's area) and processing sensory input. The patient might also experience anosognosia, a condition where one lacks self-awareness and insight into the problems engendered by the disease. Again a frontal or temporal lobe lesion could be responsible for the anosognosia, or a parietal lobe lesion can also be responsible – it is well known for integrating our sensory information into our awareness which is held responsible by a section of the brain called the somatosensory cortex [7]. Hence with a decline in cognitive functions, the patient can show poor judgement or find it difficult to make decisions, as well as become less flexible and increasingly hesitant in their behaviours.

3.2. Middle Stage Symptoms

As AD worsens further into the middle stage, symptoms are aggravated. For instance, delusions and paranoia, disturbed sleep and increasing disorientation such as loss of spatial awareness happen. This is because the lesions within the brain are becoming larger, which cause more memory loss and muddled decision making. Their speech and communication can also worsen to the point where it is unusable. This is because they have developed aphasia which means the patient is unable to formulate or comprehend language whatsoever. Aphasia is divided into two types: expressive aphasia, which is also known as Broca's aphasia, is an inability to produce speech due to damage in Broca's area. The other type is receptive aphasia which is also known as Wernicke's aphasia. This describes patients as not being able to understand speech due to damage in Wernicke's area (located between the temporal and parietal lobe). In addition, the patient would need constant support to aid them in daily activities such as washing, getting dressed and most general activities. This is because they have lost motor control due to damage within the basal ganglia, a region of the cerebellum that is in charge of movement coordination. Certain regions within the brainstem such as nuclei within the midbrain and pons that control the neck muscles as well as respiratory function and eating may also be affected [9].

3.3. Late Stage Symptoms

In the late stages of AD, the symptoms become increasingly severe to the extent that it can be distressing for those around them as well. It becomes progressively harder for the patient to move, as the muscles become spastic and rigid which are consistent with an upper motor neuron lesion. Eventually, the muscles are not used and become wasted. This can result in difficulties with eating, swallowing and controlling the passing of urine and stools. The chances of contracting pneumonia are also greatly increased due to increased risk of aspiration. Aspiration pneumonia is a common cause of death in individuals with AD due to the inability to swallow, meaning that food and drink or foreign objects are able to enter the lungs and cause infection. Other common causes of death in individuals with AD include dehydration, malnutrition, falls and certain infections. Speech is most certainly lost at this point due to extensive damage within the frontal and temporal lobe, making it challenging for the patient to communicate with others [10]. At this point, the patient would need full-time care and assistance with essentially every activity. Evidently, this puts stress on those close to the patient. If a family member was to take care of a loved one with AD, the majority of their time would be dedicated towards aiding the patient in their daily life, which can be very time-consuming as well as draining. It can also mean that the role of the breadwinner within the family is affected, negatively impacting family finances.

4. Diagnosis of AD

There is no confirmatory test that can diagnose AD; therefore, the diagnosis is made clinically with several examinations. By thoroughly examining the patient's medical history and neurological status, as well as conducting physical examinations and scans, the patient's behavioural and cognitive changes over time can be understood. The typical "clinical picture" of AD is often described as a progressive and prominent decline in cognitive abilities including attention, memory, logic, reasoning, and processing [11].

4.1. History and Physical Examinations

During a medical workup, the patient's medical history will be reviewed by the physician. The patient's family history, such as whether his/her close relatives have had AD or other dementias are also inquired, as AD can be inherited. The physician may also inquire about environmental and lifestyle risk factors such as dietary habits, nutrition, and alcohol consumption. Special neurological tests can also be conducted accordingly to examine for features of dementia. Tests such as the mini mental state examination (MMSE) are common neurological tests used to detect cognitive impairment in older patients in clinical practice. MMSE is a structured way of assessing a patient's current mental state and is composed of two main components: a historic report from the patient and the physician's observational data obtained throughout the patient encounter [11].

General comorbidities that are risk factors for AD such as diabetes, high blood pressure, and heart disease; are also checked. The physician may choose to listen to the heart and lungs to check for certain abnormalities, or perform other procedures to assess the patient's overall health. Other physical tests, such as taking routine bloods, urine tests, and cerebrospinal fluid (CSF) samples can also be taken to check for AD proteins and, at the same time, gain a better understanding of the patient's status, thus allowing the medical professional to make a more accurate diagnosis [11].

4.2. Brain Imaging

Brain imaging, via CT or MRI is also a reliable method of determining whether or not a patient has AD. CT scans are able to demonstrate certain characteristic patterns of cortical atrophy – the brain's outer layer will show slow and persistent degeneration, whereas MRI detects alterations more accurately and is better able to rule out alternative types of dementia, hence it is the more preferred modality [12]. Aside from structural imaging, PET molecular imaging is becoming more practical in the detection of AD. Braak staging, a semiquantitative measure of the severity of NFT pathology on

imaging, reveals the association of numerous formations as follows: Stages I and II saw the initial involvement of the entorhinal cortex; Stages III and IV saw the limbic system and hippocampus involved; Stages V and VI saw the involvement of the cortex—more specifically, the precuneus—with the temporal lobes [12]. The measurement of volume change in distinctive brain regions serves as the primary function of MRI (and CT) in the diagnosis of AD, yielding up to 87% sensitivity [12]. However in the early on, such decline in volume is not prominent. Ultimately, there are two main bases for the diagnosis: mesial temporal lobe atrophy (the hippocampus, entorhinal cortex and perirhinal cortex, in particular); and temporoparietal cortical atrophy. Brain volume measurements, along with segmentation assessments, signify that AD patients have brain volume loss at accelerated rates, typically approximately double the normal individual (1% vs ~0.5%/year) [12]. The difference is especially distinguishable in the hippocampus, with affected individuals displaying three times the shrinkage in volume each year (~4.5% vs ~1.5%/year) [12].

The best way to ascertain how memory and other cognitive capacities are evolving over time is to repeat such tests and scans over a certain period of time. Once the disease progression of the patient n has been documented properly, treatments such as therapies or drugs can be prescribed accordingly, depending on factors such as severity and the patient's pre-existing conditions.

5. Current AD Treatments and Prevention Methods

While there is currently no definite treatment or specific methods to prevent or slow down the progression of AD since the exact cause and mechanism behind it is still unknown, current treatments aim to temporarily reduce the symptoms and delay the disease. These treatments are separated into two categories: lifestyle modifications and medical treatment.

5.1. Physical Therapies

Physical therapies and activities have also proven to be effective as a method of mitigating symptoms. The main focus of physical therapy sessions is to improve the patient's quality of life by helping them cope with AD, rather than temporarily improving symptoms through medications. Cognitive stimulation therapy (CST) requires the patient to take part in group activities and exercises that are designed to improve cognitive skills - skills such as reading, learning and memorization. Sessions strive to engage and actively stimulate AD patients amid providing an optimal learning environment as well as the social benefits of collaborating as a group. Alternatively, cognitive rehabilitation involves the patient working with a healthcare worker or friend to reach a goal. The goal can be relatively simple, for instance using a mobile phone or brushing their teeth. This rehabilitation technique enables the AD patient to use the areas of their brain that are unaffected [13].

5.2. Prevention of AD

The optimal choice is to prevent AD from developing early on rather than treating and reducing symptoms at a later stage. Lifestyle modifications aim to mitigate the risk factors of AD. These modifications are given first to a patient at risk of dementia or AD, since they are easily implementable and require minimal effort. These modifications are also prophylactic, meaning they prevent one from getting AD. This is done by avoiding the disease's risk factors which is one of the simplest and most advocated methods of prevention that can lower the chances. Modifiable risk factors that are associated with lifestyle habits include smoking, consuming excessive alcohol and dietary fat that may lead to obesity. It is recommended for one to have a healthy, balanced diet, and engage in physical activity for at least 150 minutes per week. This keeps the metabolism up as well as encourages active cognitive behaviour. There are also social and psychological risk factors in developing AD, including depression, loneliness or social isolation. Several ways to avoid these risk factors include increasing social interactions, seeking professional help or getting medications such as antidepressants. By avoiding or modifying the risk factors one has control over, the risk of developing AD could be significantly reduced.

5.3. Pre-existing Medications

Furthermore, there is also medical treatment that targets certain biochemical mechanisms, which aim to improve and reduce symptoms of AD.

The two main medicines generally prescribed to help improve symptoms of AD are acetylcholinesterase (AChE) inhibitors and memantine. AChE inhibitors assist in raising levels of acetylcholine [13], a key neurotransmitter that plays an important role in brain functions. AChE inhibitors prevent the cholinesterase enzyme from degrading acetylcholine, enhancing the magnitude and duration of the neurotransmitter activity. This improves communication between the nerve cells, which in turn can prevent cognitive functions from declining quickly, improving neurological symptoms of AD. Memantine is an alternative to AChE inhibitors, and is often prescribed to those who are not able to tolerate AChE inhibitors as a temporary mode of relief from the symptoms. It is licensed for use in helping with moderate and severe AD, and is also widely used off label for mild AD in the United States [14]. In Alzheimer's, a neurotransmitter named glutamate that is released from damaged nerve cells activates extrasynaptic NMDA receptors and triggers pro-apoptotic signalling, which overcomes synaptic NMDA-mediated survival signalling. As this signalling is already being undermined by several other mechanisms in AD, the glutamate released in this case can lead to further synaptic damage and ultimately neuronal death. As an antagonist of NMDA receptors, memantine provides protection to those nerve cells damaged by AD through blocking the effects of excess amounts of glutamate [13].

Other medicines used to target specific behavioural and psychological symptoms of dementia (BPSD) can also be prescribed. Risperidone and haloperidol are the only licensed antipsychotic medicines in relieving BPSD, and are prescribed to those with moderate to severe AD when there is a risk that the patient may harm themselves or others. Risperidone acts by blocking dopamine receptors in the brain, avoiding excessive dopamine activity, and assisting with psychosocial AD symptoms. Risperidone also increases dopamine and serotonin levels, which subsequently improves thinking, mood, and behaviour. However risperidone should be used at the lowest dosage and for the shortest time period possible, as there can be serious side effects such as problems standing or walking, seizures, as well as increased risk of stroke or heart attack. Antidepressants can also be given if depression is suspected as an underlying cause of anxiety [15].

6. Promising Novel Therapies

As the world's older population continues to grow, so does the number of AD cases. Around 1 in 9 people aged 65 and older are known to have or eventually develop AD [16]. As the incidence of AD is growing, it is slowly becoming a grave problem worldwide, and current treatments are only able to provide temporary relief. Hence, there is a need for novel treatments for AD to improve the patient's life quality, and reduce the burden on carers. The novel treatments discussed here aim to slow down the progression of or treat AD as opposed to symptom alleviation.

6.1. TRIM11 as a Biological Target

Tripartite motif-containing protein 11 (TRIM11) is a protein found in humans that is encoded by the TRIM11 gene [17]. The protein is also closely linked with the production of tau proteins, which are the pathological proteins in AD that are converted into insoluble fibrillar aggregates known as neurofibrillary tangles. Conventionally, TRIM11 acts as a protein quality control system for these protein aggregates by removing or preventing them. However, its role in AD and neurofibrillary tangles is unexplored. Hence, Zhang et al. have done a study to demonstrate TRIM11's relationship to AD. Thus, it may become a viable treatment target to treat the root cause of AD.

There are three mechanisms by which the TRIM11 protein prevents tau proteins from becoming pathological neurofibrillary tangles. Firstly, the turnover of mutant tau and excessive regular tau is regulated by the protein. This is accomplished by having the protein bind to tau, particularly mutant variants or hyperphosphorylated species, and enhance SUMOylation, which results in proteasomal

destruction. This demonstrates a critical link between tau and the TRIM11 proteasome. Secondly, TRIM11 prevents tau misfolding and aggregation – which are primary factors that lead to the development of neurofibrillary tangles – by functioning as a molecular chaperone for tau. Thirdly, the protein exists as a tau disaggregase, meaning that it dissolves pre-existing tau deposits, including the intractable fibrillar aggregates. [18].

To demonstrate TRIM11's relationship to AD, the post-mortem brain tissue of 23 AD individuals were compared to 14 healthy controls [19]. Results found that TRIM11 protein levels were significantly lowered in those with AD. This shows that TRIM11 is definitely involved in AD, and warrants further investigation. Hence, in order to establish the potential utility of TRIM11 for use as a plausible therapeutic agent, Zhang et al. used an adeno-associated viral vector (AAV) to deliver the TRIM11 gene into the brain of mouse models with tauopathies. It was found that in these mice the levels of neurofibrillary tangles were markedly decreased, and had much improved cognitive and motor abilities. This proves TRIM11 as a possible therapeutic target. However, it must be noted that these are results derived from an animal model; hence it may not completely translate well to human models.

6.2. Monoclonal Antibody Donanemab

Donanemab is a humanised IgG1 monoclonal antibody derived from mE8-IgG2a in mice [20]. Like numerous others in the most recent line of AD drugs, donanemab selectively targets and binds to N-terminal pyroglutamate amyloid beta (pGlu)-Aβ epitope, an amyloid protein thought to be particularly toxic to brain cells [21]. The beta-amyloid plaque is one of many defining pathological features of AD. The formation of these Aβ plaques in between neuron synapses damages existing brain tissue, leading to the loss of neurotransmitters, which affects neuronal transmission and causes further cognitive decline.

Donanemab's mechanism works by targeting and removing amyloid plaques through microglial-mediated clearance [20]. Donanemab binds specifically to pGlu-Aβ and triggers an immune response that leads to the clearance of beta-amyloids in the brain. Specifically, donanemab induces the activation of microglia – immune cells within the brain that aid in the clearing of beta-amyloid deposits. Activated microglia have the ability to bind to and phagocytose beta-amyloid plaques, removing them from the brain.

Taking donanemab during the onset stages of AD has been proven to be the most effective in slowing the progression of the disease. A 1,736-person clinical trial was recently conducted by Eli Lilly, US developer and producer of donanemab. Among participants who began taking the drug in the earliest stages, 47% showed no disease development on certain measures, in comparison with 29% who took a placebo. In participants with relatively minor cognitive impairment, the decline in cognitive abilities slowed by as much as 60% [22]. Once participants had relatively low levels of amyloid, the donanemab drug was switched with a placebo. In the year following this placebo replacement, participants who received donanemab initially declined at a more moderate pace as opposed to those who received a placebo. Overall, findings indicate that if diagnosed and treated with donanemab early, participants with AD are likely to have a better outcome.

However, there are still several regions of uncertainty as well as concerns with usage in clinical practice within the currently limited conclusion. For instance, it remains unclear whether doctors should mimic the original trials and stop giving patients the drug once amyloid is no longer present in their brains. Moreover, the drug has only been tested in individuals who had explicit biological markers of AD; thus, it may lack effectiveness in other individuals who do not share the same characteristics. It is also important to note that donanemab does not provide as much relief to individuals who have later stage AD or those with certain genetic variants that raise the risk of the disease. Donanemab, similar to lecanemab – a comparable monoclonal antibody drug that is amyloid beta-directed and currently used in the treatment of AD – along with the affiliated drug aducanumab, can lead to a condition known as amyloid-related imaging abnormalities (ARIA), and can occasionally result in fatal brain haemorrhage and seizures. In Eli Lilly's phase III trial of the drug,

approximately one-quarter of the participants developed ARIA, with three cases of fatalities from the condition [22]. It was also discovered that participants who carried the APOE4 genetic variation – a variation that increases risks of developing AD later on in life – were more likely to contract ARIA [22]. This might be one of the more severe flaws of monoclonal antibody drugs like donanemab. Since the drug can be resisted by certain genetic variants, and even proceed to develop into more serious conditions like ARIA, patients who possess such variants should find alternative treatment methods to this drug. Another major flaw that might make donanemab relatively inaccessible to the majority of general patients is its market price. John Sims, medical director of Eli Lilly has declined to provide an estimated price of the drug), however affiliated pre-existing monoclonal antibody drugs on the market aducanumab and lecanemab have been marketed in excess of $26,000 USD per year [22]. Additionally, there is risk of inherent bias within the results as the trial was conducted by the manufacturers themselves.

6.3. Deep Brain Stimulation

Deep brain stimulation (DBS) is a neuron activity modulating neurosurgical technique consisting of the application of electrodes. The electrodes are implanted in areas of the brain affected by the specific condition [23]. Electrical impulses are produced by the electrodes and act as abnormal impulse regulators which affect neurotransmitter release within the brain. A device, similar to that of a pace-maker, is also inserted under the skin and controls the magnitude of stimulation in DBS. This device is linked to the electrodes in the brain through a wire that runs under the skin [24]. Yet, the exact mechanisms of DBS in treating AD remain unclear. According to one theory, the stimulation helps to rebalance nerve networks that have gone out of sync. DBS, according to another theory, restores unstable nerve movements. A different theory states that the stimulation lowers levels of amyloid plaques that are toxic to nerve cells in affected regions of the brain [23]. All three theories mentioned above suggest possible explanations for improvements in physical condition in AD patients after undergoing DBS, however it should be kept in mind that they are only educated guesses.

DBS has been proven to be successful in symptom alleviation for several circuit disorders of the human brain, specifically obsessive-compulsive disorder, Parkinson's and so forth. DBS to the fornix – a white matter bundle positioned in the cerebral hemispheres' mesial aspect is currently an experimental treatment for individuals with mild AD, with the intention of regulating associative and limbic networks that promote memory function. However, researchers are still attempting to determine the optimal way of usage of DBS for AD, such as the most suitable parts of the brain to stimulate, the intensity of the stimulation, and the duration of the stimulation. Though, it is understood that general target areas of DBS for AD are: the ventral capsule/ventral striatum, which is involved in basic cognitive skills and behaviour; the intralaminar thalamic nucleus, involved in important cognitive functions; the midline thalamic nuclei, associated with memory; and the nucleus basalis of Meynert, a part of a critical pathway in relation to cognition and memory [23].

A case study that initially employed DBS in the treatment of obese patients rekindled interest regarding clinical application of DBS for AD patients. It was found that a patient with morbid obesity's memory was strengthened after fornix DBS treatment. The reason for such enhancement could have been due to DBS's marginal activity-regulating nature, meaning that electrical activity throughout the medial temporal lobe is induced during DBS stimulation [25]. Certain positive effects of the using DBS for AD have been shown through preliminary studies throughout the past 10 years, such as delaying deterioration in cognitive abilities and hippocampal atrophy, and boosting the metabolism of cerebral glucose and brain connectivity [25].

However, in addition to several uncertainties surrounding the fundamental mechanisms of DBS in the treatment of AD, DBS does not serve as an effective treatment method to certain individuals, thus is not a heavily reliable method to many. In a small trial conducted, 42 participants with mild early and late-onset AD had DBS devices implanted in a region in the brain in between the hippocampus and the hypothalamus. The participants consisted of 12 individuals under the age of 65 with early-onset AD and 20 over the age of 65. At the beginning of the first year, half the devices were turned

on; the other half of the devices were turned on after a year had passed. All devices delivered constant stimulation of 130 hertz between 3-3.5 volts. Two main methods were used to track the progression of the disease: two questionnaires that evaluated the participants' cognitive abilities, personal care, and judgement; and PET scans to oversee and track changes in their brain structure. Ultimately, researchers found that participants under the age of 65 did not benefit from DBS and showed no signs of having slowed cognitive decline. It is possible for participants over 65 to have benefitted from the stimulation in the sense that they seemed to be declining at a slower pace than those without the device turned on. Even so, a larger study is necessary for accurate conclusions to be drawn [26].

7. Conclusion

The search for novel treatments for AD presents a promising frontier in neurodegenerative research. The diverse range of relatively new approaches discussed above in the discussion, including immunotherapies, neurosurgical techniques, and upcoming drug based treatments all offer hope for improved outcomes in the management of AD.

Having TRIM11 as a biological target is promising in terms of looking to stop further decline in cognitive activity in AD, as it is able to completely mediate the build-up of harmful protein aggregates. However, there are major limitations, such as the fact that the experiment was done on animal models and thus might not translate well to human models; as well as the excessive amount of unconfirmed information surrounding its role in AD and neurofibrillary tangles.

Donanemab, a monoclonal antibody-based therapy developed by Eli Lilly, has been proven to be successful in slowing cognitive decline. Though it should be noted that AD-related complications such as brain haemorrhage and seizures have developed in several participants following the consumption of the drug. Such complications can pose serious obstacles, and should be screened for at-risk individuals in order for donanemab to be a considerable drug in the treatment of AD.

DBS, a more physical-based neurosurgical technique and therapy has shown somewhat favourable results, such as increasing cerebral glucose metabolism and brain connectivity. Yet, there are more uncertainties in comparison to positive outcomes. Rather than multiple anomalies distributed over a range of ages, DBS therapy appeared to be completely neutral and ineffective for individuals under the age of 65. However, a larger trial must be conducted to confirm and clarify the conclusions drawn.

While a definitive cure for AD remains elusive, the ongoing research and development of novel treatments provide a renewed sense of hope for individuals affected by the disease. Collaborative research is vital for advancing these treatments, eliminating ambiguities, and eventually improving the quality of life for those living with AD.

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