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Novel Monoclonal Antibodies for the Treatment of Alzheimers Disease using KISUNLA Drug

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Abstract: *For persons with early-stage sympathetic Alzheimer's disease (AD), including those with mild cognitive impairment and mild congitive dementia stages of the disease with confirmed amyloid pathology, KISUNLA (donanemab-azbt) is a disease-modifying treatment. Nearly half of research participants finished their course of treatment with Kisunla within a year, making it the first and only amyloid plaque targeting medication that uses a limited duration treatment regimen based on amyloid plaque elimination. For those with early-stage sympathetic Alzheimer's disease who desperately require an efficient therapeutic alternative, Kisunla shows extremely significant results.*

Keywords: Alzheimers Disease, dementia, monoclonal antibodies, Neurodegenarative disease

I. INTRODUCTION

Alzheimer's disease is a condition that gradually impairs memory and other aspects of cognition. Amyloid beta peptide buildup in the form of amyloid plaques is believed to be the origin of the sickness. Donanemab azbt, a humanized IgG1 antibody found in KISUNLA, targets N3 PG, a modified form of beta amyloid plaque. It is believed that KISUNLA helps the body eliminate an excessive accumulation of amyloid plaques in the brain, which could causeto cognitive and memory problems linked to Alzheimer's disease.The body naturally produces the protein amyloid, which can aggregate to form amyloid plaque. Alzheimer disease-related memory and cognitive problems may result from the brain's excessive accumulation of amyloid plaque. KISUNLA can assist the body in eliminating the excessive accumulation of amyloid plaque and slowing the deterioration that could impair people's memory for new knowledge, crucial dates and appointments, planning, organizing, making plans, using household appliances, managing finances, and being left alone. KISUNLA is used to treat early-stage sympathetic Alzheimer's disease in adults, including mild dementia and male cognitive impairment.

What is drug for?

Alzheimer's patients are treated with KISUNLA, an amyloid beta-directed antibody.Alzemers disease is a prevalent degenerative brain disease that begins with mild cognitive, judgment, and memory issues before progressing to dementia and eventual death.Patients who are in the moderate cognitive impairment or mild dementia stages of the disease should begin KISUNLA medication.

II. LITERATURE REVIEW

1. **Alex Philippidis**
GEN Edge 6 (1), 608-611, 2024
The FDA has approved Eli Lilly's Kisunla™(donanemab-azbt), a once-monthly injection treatment indicated for adults with early symptomatic Alzheimer's disease (AD), including mild cognitive impairment (MCI) or mild dementia stage of diseasewith confirmed amyloid pathology. Kisunla is the first amyloid plaque-targeting therapy with evidence to support stopping therapy when amyloid plaques are removed, which according to Lilly can reduce both the number of infusions needed as well as the treatment cost.[Eli Lilly] he FDA today approved Eli Lilly's early Alzheimer's disease drug Kisunla™(donanemab-azbt), a once-monthly injection treatment indicated for adults with early symptomatic

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Alzheimer's disease (AD), including mild cognitive impairment (MCI) or mild dementia stage of disease with confirmed amyloid pathology.

2. Connie Kang
Drugs, 1-6, 2024
Donanemab (donanemab-azbt; Kisunla TM) is an amyloid β-directed antibody developed by Eli Lilly and Company for the treatment of Alzheimer's disease. Donanemab recently received approval in the USA for the treatment of adults with early symptomatic Alzheimer's disease (patients with mild cognitive impairment or mild dementia stage of disease). This article summarizes the milestones in the development of donanemab leading to this first approval for Alzheimer's disease.

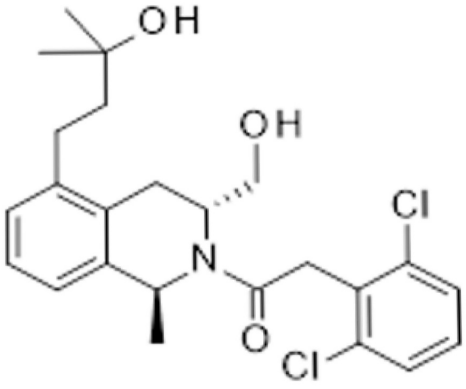
3. Diane S Aschenbrenner
AJN The American Journal of Nursing 124 (11), 18-19, 2024The Food and Drug Administration has approved donanemab (Kisunla) as a treatment for Alzheimer disease. Donanemab is an amyloid beta–directed monoclonal antibody that reduces amyloid beta plaques in the brain.

4. New England Journal of Medicine 384 (18), 1691-1704, 2021
Donanemab in early Alzheimer's disease

5.Tanya Song, Yunfei Wang, Bret David Silverglate, George T Grossberg
Expert Opinion on Drug Metabolism & Toxicology, 2024
Donanemab is a humanized monoclonal antibody that significantly reduces cerebral amyloid plaques in Alzheimer's Disease (AD). It can delay disease progression and cognitive decline, making it one of the most promising disease-modifying treatments in the current treatment landscape.

Drug Profile:
Ellie Lilly and company developed KISUNLA, a monoclonal antibody used to treat Alzheimer's disease. Based on the findings of the TRAILBLAZER ALZ 2 Phase 3 research, a double blind, placebo control study designed to assess the safety and effectiveness of donanemabazbt in participants with early sympathetic Alzheimer disease who also had confirmed amyloid pathology, the FDA approved KISUNLA.

Chemical and physical data
Formula :- C6452H10038N1708O2013S42



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Structure of Donanemab

Molar mass:- 145089.74 g·mo

Drug class: beta-amyloid-directed antibody

Drug form: solution given as an intravenous (IV) infusion.

A single-use vial contains the solution known as Kisunla. There is only one strength available, which is 350 mg per 20 mL of solution (17.5 mg/mL).Kisunla is typically started at a dose of 700 mg (two vials) every infusion. You will be given three dosages of one infusion every four weeks.Following that, 1,400 mg (four vials) of Kisunla is the usual continuous dosage per infusion. You will still get one infusion every four weeks.

Active ingredient: donanemab-azbt

Inactive ingredients: anhydrous citric acid, polysorbate 80, sodium citrate, sucrose, and Water for Injection, USP

KISUNLA (donanemab-azbt) injection is a sterile, preservative-free, clear to opalescent, Colorless to slightly yellow to Slightly brown solution. KISUNLA is supplied in one vial per Carton as follows:

350 mg/20 mL (17.5 mg/mL) single-dose vial

Storage and Handling :

Unopened Vial

• Store refrigerated at 2°C to 8°C (36°F to 46°F).

• Keep the vial in the outer carton to protect from light.

• Do not freeze or shake.

• If refrigeration is not available, may be stored at room temperature (20°C to 25°C [68°F to 77°F]) for up to 3 days.

Aim

Kisunla is intended to treat Alzheimer's disease in its early stages by delaying the onset of symptoms including thinking difficulties and memory loss.

Objective

To evaluate the effectiveness and side effects of the antibody donanemab-azbt, which is intended to remove amyloid plaque from the brain.

Plan of work

Patient Selection Patient Selection → Screening → Donanemab Administration → Dose Escalation → Monitoring → Assessments → Data Analysis → Results

1.Patient Selection*: Identify patients with early symptomatic Alzheimer's disease

2.Screening*: Conduct medical screening and assessments to determine eligibility

3. Donanemab Administration*: Administer Donanemab via intravenous infusion

4. Dose Escalation*: Gradually increase dose to optimal level

5. Monitoring: Regularly monitor patients for efficacy and safety

6. Assessment :Conduct regular cognitive and functional assessments

7. Data Analysis: Analyze data to determine treatment efficacy and safety

Mechanism of action:

Donanemab-azbt is a monoclonal antibody that targets insoluble N-truncated pyroglutamate amyloid beta in a harmonise immunoglobulin gamma 1 (IgG1) fashion. One of the hallmark pathophysiological characteristics of Alzheimer's disease is the buildup of amyloid beta plaques in the brain. Utilize phagocytosis mediated by microglia to eliminate the current cerebral amyloid plaque. Amyloid positron emission tomography shows that donanemab-azbt reduces amyloid beta plaque in a dose and time dependent manner when compared to the placebo.

A monoclonal antibody called donanemab targets the insoluble modified and Nturminal truncate form of B amyloid, known as pyroglutamate amyloid beta, which is only seen in brain amyloid plaque .When donanemab binds to pyroglutamate AB at position 3 (pGlu3-AB, ABpE3), it facilitates the clearance of plaques by microglial-mediated phagocytosis.The TRAILBLAZER-ALZ 2 clinical research confirmed its amyloid-targeting mechanism. The

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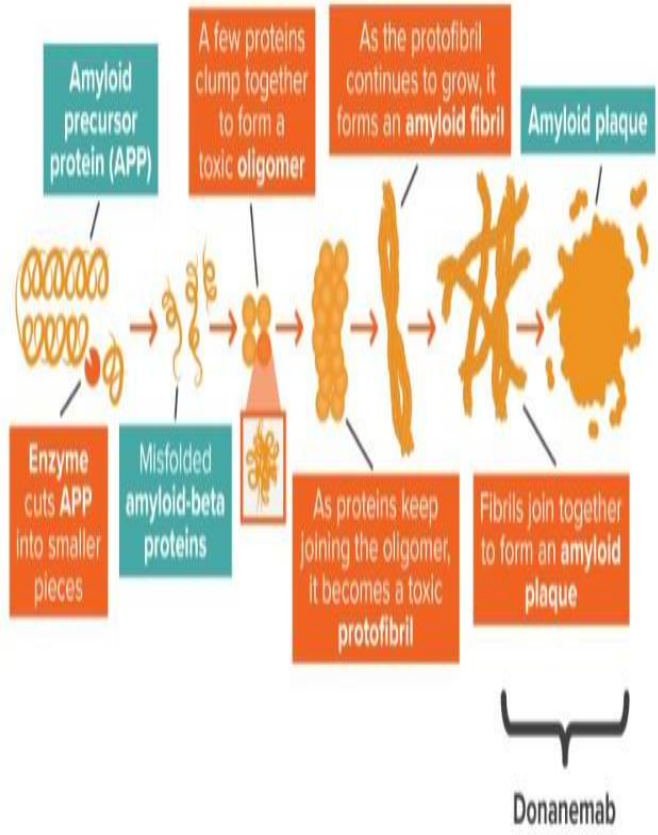
medication showed a decrease in amyloid beta plaques, a pathophysiological hallmark of Alzheimer's disease that is characteristic of the brain. Destroy them.

Antibodies found in donanemab attach to the protein amyloid, which accumulates in the brain during the early stages of Alzheimer's disease. Kisunla is a protein type known as a monoclonal antibody. To aid in the body's defense against some dangerous substances, such viruses or cancer cells, a monoclonal antibody is made to recognize and bind to them. Imagine it as a targeted missile that focuses on a particular adversary, increasing the accuracy and efficacy of therapies Kisunla targets and binds to brain amyloid-beta plaques in Alzheimer's disease. These plaques are collections of protein fragments that are thought to be crucial to the onset and course of the illness. Kisunla helps remove these plaques from the brain by attaching to them, which may lessen their negative cognitive effects.



Dosage schedule:-

Intravenous infusion every 4 weeks	KISUNLA Dosage administered over 30 min
Infusion 1,2,3	700mg
Infusion 4 and beyond	1400mg

Expected outcomes:

Safety and efficacy:-

According to research, donanemab has a good safety record. The most frequent side effects include infusion-related responses and abnormalities in imaging caused by amyloid. Clinical trials have shown that donanemab is effective in delaying the cognitive decline of patients with early-stage Alzheimer's disease.

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II. CONCLUSION

Donanemab is a novel monoclonal antibody that has shown promising results in the treatment of Alzheimer's disease. Its unique mechanism of action, targeting N3pG, offers a new approach to treating this devastating disease.

REFERENCES

[1]. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC.
[2]. Kisunla (donanemab-azbt). Medication Guide. Lilly USA, LLC. Sims JR, Zimmer JA, Evans CD, et al. Donanemab in Early Symptomatic Alzheimer Disease: The TRAILBLAZER-ALZ 2Randomized Clinical Trial. JAMA. 2023;330(6):512-527. Doi:10.1001/jama.2023.13239.
[3]. Ross EL, Weinberg MS, Arnold SE. Cost-effectiveness of Aducanumab and Donanemab for Early Alzheimer Disease in the US. JAMA Neurol. 2022;79(5):478-487. Doi:10.1001/jamaneurol.2022.0315.
[4]. Boustani M, Doty EG, Garrison LP Jr, et al. Assessing the Cost-effectiveness of A Hypothetical Disease-modifying TherapyWith Limited Duration for the Treatment of Early Symptomatic Alzheimer Disease. Clin Ther. 2022;44(11):14491462.Doi:10.1016/j.clinthera.2022.09.008.
[5]. Mattke S, Ozawa T and Hanson M. Implications of Treatment Duration and Intensity on the Value of Alzheimer'sTreatments. Clinical Trials on Alzheimer's Disease. Oct. 24-27, 2023.
[6]. Porsteinsson AP, Isaacson RS, Knox S, et al. Diagnosis of early Alzheimer's Disease:clinical practice in 2021. J Prev
[7]. Alzheimer's Association. 2023 Alzheimer's disease facts and figures. Alzheimers Dement. 2023;19(4):1598-1695 Wessels AM, Dennehy EB,
[8]. Dowsett SA, et al. Meaningful clinical changes in Alzheimer disease measured With the iADRSAnd illustrated using the donanemab TRAILBLAZER-ALZ study Findings. Neurol Clin Pract. 2023;13(2):e200127.Doi:10.1212/CPJ.0000000000200127
[9]. Bucci M, Chiotis K, Nordberg A; Alzheimer's Disease Neuroimaging Initiative. Alzheimer's disease profiled by fluid andImaging markers: tau PET best Predicts cognitive decline. Mol Psychiatry. 2021 Oct;26(10):5888-5898. Doi:
[10]. Boccalini C, Ribaldi F, Hristovska I, Arnone A, Peretti DE, Mu L, Scheffler M, Perani D, Frisoni GB, Garibotto V. The impactOf tau deposition and Hypometabolism on cognitive impairment and longitudinal cognitive decline. Alzheimers Dement.2023 Aug 9. Doi: 10.1002/alz.13355.
[11]. Data on File. Lilly USA, LLC. DOF-DN-US-0053.
[12]. Data on File. Lilly USA, LLC. DOF-DN-US-0055.
[13]. Data on File. Lilly USA, LLC. DOF-DN-US-0029