EXHIBIT E

Update on Lecanemab treatment for early-stage Alzheimer's disease

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Lecanemab approval (full approval July 2023)

- Lecanemab was approved based on a multicenter, double-blind, randomized, placebo-controlled trial (CLARITY-AD) that assessed the efficacy and safety in patients 50 to 90 years of age with early Alzheimer's disease.

- Lecanemab slowed the rate of disease progression by about 20–30% after 18 months of therapy

van Dyck et al N Engl J Med 2023

UAMS protocol for Lecanemab

Main Eligibility or Inclusion Criteria
Diagnosis of Mild Cognitive Impairment (MCI) or early-stage Dementia consistent with AD Demonstrated through clinical assessments and neurocognitive performance (MMSE 22-30 or MoCA >15)
Positive biomarkers for brain amyloid pathology Demonstrated through positive amyloid PET scan **or** positive CSF studies (pTau/amyloid ratio) indicative of AD

These eligibility criteria are based on Approved Use Recommendations by Cummings et al (2023).
At UAMS we have incorporated increased safety features, especially for older age groups and those with co-morbid conditions.

Cummings, J. et al (2023). Lecanemab: Appropriate Use Recommendations. *The journal of Prevention of Alzheimer's disease*, https://doi.org/10.14283/jpad.2023.30

Biomarker confirmation of AD

If we suspect memory problems are due to Alzheimer's disease, how can we be more certain that it is Alzhemier's?

Perform either test of Amyloid biomarkers

Amyloid PET scan

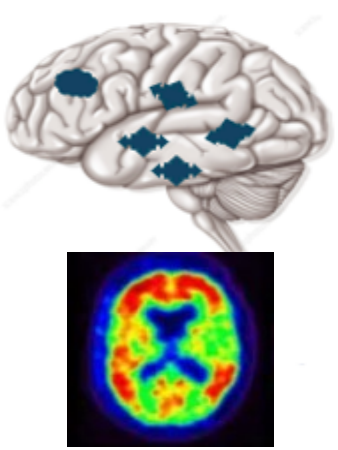
To look for amyloid protein deposits in the brain

CSF Spinal Tap

To look for amyloid and tau protein in the cerebrospinal fluid (CSF)

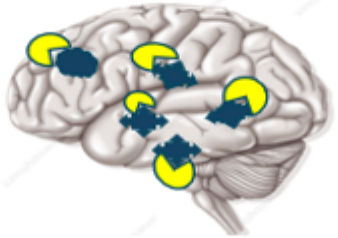
If either test is positive

Patients could be eligible for therapy with monoclonal antibody infusions

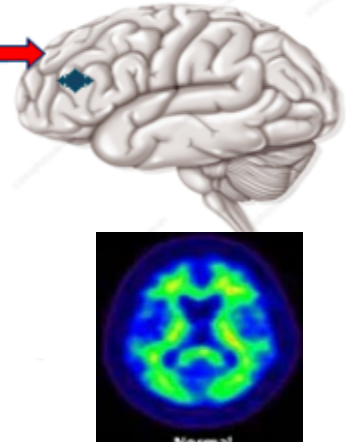


Amyloid excess in brain blocking normal function

Anti-Amyloid antibodies



Reduced amyloid in brain with better function

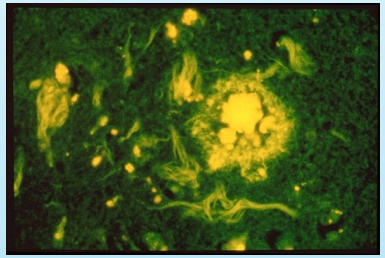


Lecanemab binds to amyloid in the brain

Amyloid PET scan is now available in Highland Oncology, Springdale, AR

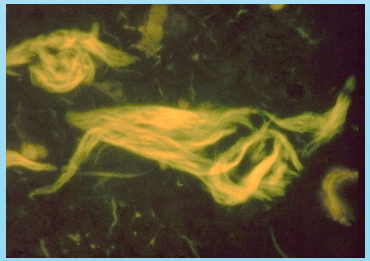
Diagnosis of AD using CSF Biomarkers

Amyloid



ß Amyloid plaques

Tau



Tau-based Neurofibrillary tangles

Diagnostic lumbar puncture or spinal tap is performed under fluoroscopic guidance at UAMS and CSF results are available within 3-4 weeks

CSF result interpretation

If the ratio of pTau/ Aβ42 is > 0.028, then it is most likely Alzheimer's disease.

Other concurrent pathologies might still be present in the brain.

If pTau/ Aβ42 ratio is negative, then the individual has some other reason for cognitive impairment, but not Alzheimer's disease

Plasma biomarkers are available but not approved for eligibility

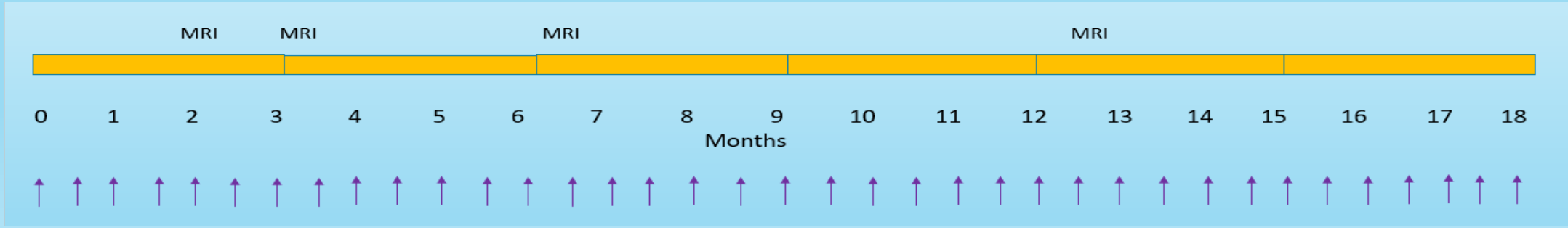
Treatment considerations when staring Lecanemab therapy (Leqembi)

Shared Decision Making with Patients and Caregiver/partners

An interdisciplinary team headed by a dementia-expert (e.g., geriatrician, neurologist, or another clinician with expertise in dementia with a social worker, APN, PA, nurse and pharmacist) will engage in shared decision-making with the patient and caregiver(s) throughout the diagnosis and treatment of AD.

Caregivers/partners will be an integral part of the team throughout the process and will be required to be present at every infusion visit.

Leqembi infusion schedule



Additional Inclusion criteria for lecanemab therapy
MCI and Early AD: Mini-Mental Status Examination (MMSE) of 22-30 or equivalent performance on other commonly provided screening measures (e.g., MoCA >15, Bergeron et al., 2017)
Have a willing and able care partner who can provide support as needed for treatment and appropriate monitoring at home
Brain MRI within the preceding 12 months of screening without contraindications for initiating anti-amyloid therapy
Body Mass Index (BMI) >17 and <35*
Age 50-90*
Baseline EKG with sinus rhythm
Agreeable to monitoring brain MRIs prior to 5th, 7th and 14th and 26th infusion and to possibly unscheduled brain MRIs, based on signs or symptoms
Agree to pregnancy tests and use of contraception if of childbearing age.

- Pat Walker Memory Clinic might use a different upper and lower age and BMI cut-offs based on evaluation on a case-by-case basis, with special attention paid to any increased risk.

Main Exclusion Criteria for Lecanemab therapy
Non-AD, MCI or dementia
Moderate or Severe AD at screening
Medical, neurologic, or psychiatric condition that is significantly contributing to their cognitive impairment
More than 4 **microhemorrhages** (<10mm in diameter)
A single macrohemorrhage (>10mm in diameter)
Any significant superficial siderosis (iron deposition in brain)
Evidence of vasogenic edema
More than 2 lacunar infarcts or **strokes** involving major vascular territory
Severe subcortical hyperintensities consistent with Fazekas score of 3
Evidence of amyloid beta-related angiitis (ABRA)
Cerebral amyloid angiopathy-related inflammation (CAA-ri)
Evidence of **cerebral contusion, encephalomalacia**, brain aneurysm, major **vascular malformation**, CNS infections, and brain **tumors** other than meningiomas or arachnoid cysts
Any major intracranial pathology that may cause cognitive impairment
Any patients where MRIs can't be performed due to patient factors or choice.
History of stroke or TIAs within past 12 months
Any history of **epilepsy**/seizing disorder or status epilepticus
Mental illness that interferes with comprehension of requirements, benefits, and harms and is judged to render patients unable to comply with treatment requirements. Additionally, any patient for whom disclosure of positive biomarkers may trigger suicidal ideation.

Additional Exclusion Criteria

Immunologic disease or systemic treatment with immunosuppressants, immunoglobins, or monoclonal antibodies or their derivatives

Patients with **bleeding disorders** (platelet count <80,000 or INR >1.5 for participants not on an anti-coagulant)

Patients on warfarin, vitamin K antagonists, direct oral anticoagulants, or heparin

Any additional **medical conditions** determined to create undue risk to the patient by the treatment team. These could include conditions such as:

- Unstable hemodynamic status pre-Leqembi infusion
- Atrial fibrillation or another serious arrhythmia
- Heart Failure with New York Heart Association (NYHA) stage 3-4 heart failure with shortness of breath on minimal exertion or shortness of breath at rest
- Receiving chemotherapy or have received chemotherapy within the past 6 months
- Active liver disease or cirrhosis*
- Moderately severe kidney failure with GFR <45

Women who are pregnant or are currently breastfeeding.

Patients with current substance or alcohol abuse disorders

Visit schedule

Visit 1: Screening Memory evaluation, past history, medication review, social history, clinical physical exam, labs, MRI. Discussion of all factors influencing memory

Visit 2: If MCI or early dementia, discussion of Biomarker evaluation CSF or amyloid PET. Other brain scans, FDG-PET or DAT might be ordered.

Visit 3: Discussion of biomarker results – inclusion/exclusion criteria for Leqembi, APO-E 4

Visit 4: Treatment plan discussion - alternatives, potential risks, expected benefits, and anticipated costs.
If a patient agrees with lecanemab therapy, then they will be registered with Alz-Net per CMS requirements.

If a patient is not eligible for lecanemab, other options for management and continuity of care will be discussed.

Infusions Visits (1-18 months) Infusions will be given at the Winthrop P. Rockefeller Cancer Institute, UAMS.
Patient's caregiver will be required to be present at every infusion

Patients will be observed and monitored for 3 hours after their first infusion.
If a patient has no infusion reaction, then monitoring will be reduced to 1-2 hours for subsequent infusions

Side-effects of Lecanemab

- **Common side-effects**, infusion reactions, rash, headaches, dizziness, visual changes, confusion, nausea, flu-like symptoms, gait problems
- **Serious side-effects** are associated with more symptoms, including epilepsy, stroke, encephalopathy, stupor and might require admission and transfer to an intensive care unit.
- **Amyloid-related imaging abnormalities (ARIAs)** are seen in MRI brain scans

ARIA stands for **Amyloid Related Imaging Abnormalities**. There are 2 kinds of ARIA:

ARIA-E is a temporary increase in fluid in the brain. The E stands for **edema**, or swelling.

ARIA-H is small spots of bleeding in the brain or on its surface. The H stands for **hemosiderin**, a protein with iron that is related to bleeding.

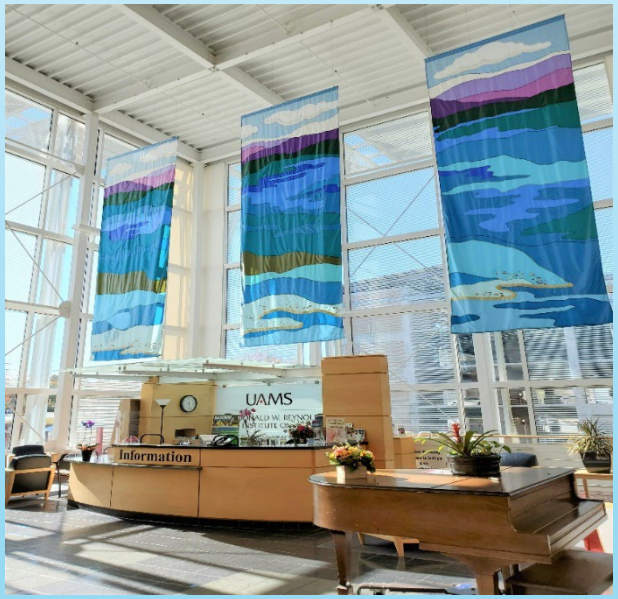
- Symptomatic ARIA occurred in 3% of patients treated with Leqembi. Serious symptoms were reported in 0.7% patients.
- ARIA-E was observed in 13% of patients on Leqembi vs 2% on placebo.
- ARIA-H was observed in 17% of patients on Leqembi vs 9% on placebo.

Hypersensitivity to Lecanemab and increased genetic risk for side-effects

- Leqembi is contraindicated in patients with serious hypersensitivity to lecanemab -irmb or to any of the excipients of Leqembi.

- **ApoE ε4 Carrier Status and Risk of ARIA**
- Approximately 15% of Alzheimer's disease patients are ApoE ε4 homozygotes.
- ARIA was 45% in ApoE ε4 homozygotes on Leqembi vs 22% on placebo.
- ARIA was 19% in ApoE ε4 heterozygotes on Leqembi vs 4% on placebo.
- **Serious events of ARIA occurred in 3% of ApoE ε4 homozygotes**, and approximately 1% in heterozygotes

The field of Alzheimer's disease is rapidly evolving hence, this protocol might be modified based on the experience with Leqembi and any new guidelines or information issued by the FDA, Alzheimer's Association, or the National Institute of Health (NIH).



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