Detection, diagnosis, and drug treatment: What is the role of Alzheimer's disease biomarkers?

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Disclosures

• NIH R01AG037639
• NIH R01AG062285
• NIH R01AG059312
• NIH R01AG070883
• NIH R01AG070973
• Weston Family Foundation
• Research precursors and radiotracers from Avid Radiopharmaceuticals, subsidiary of Eli Lilly
Alzheimer’s dementia
Vascular dementia
Lewy Body dementia
Frontotemporal dementia
Parkinson’s disease dementia
Mixed dementia

DEMENTIA

• Memory and thinking skills
• Loss of function
• Behavioral

• Cause of symptoms
So, what is a biomarker and how do we use it?

A biomarker (short for biological marker) is a measurable substance or characteristic that indicates the presence or progression of a disease or condition in the body. Biomarkers can include a wide range of substances and characteristics, such as proteins, genes, antibodies, and imaging findings.

Biomarkers can be used to identify risk for disease, measure disease, and measure the efficacy of treatments.
To participate in an anti-amyloid drug trial, you must have elevated amyloid to qualify.
- Aducanumab
- Lecanemab
- Donanemab
- Monoclonal antibody
- Infusion therapy

Aducanumab impacts amyloid but clinical trials did not show an impact on cognition.

Lecanemab Impacts Amyloid

Amyloid is lower
Lecanemab Impacts Cognition

Results from Clarity AD research study

Decline is slower

May 4, 2023, Lilly announced positive top-line results for Trailblazer-ALZ2.

In this Phase 3 study, treatment significantly slowed decline on the primary outcome of Integrated Alzheimer’s Disease Rating Scale by 40 percent, and improved all secondary clinical endpoints.

Aducanumab and Lecanemab received accelerated FDA approval. Donanemab is expected to follow.

What are the risks?

Infusion reaction.

ARIA: Amyloid-Related Imaging Abnormalities.

Potential serious adverse events.
Are biomarkers helpful in people who don’t have a dementia diagnosis?

Alzheimer’s disease progression

Pre-Clinical ‘Window’
~10-30 years before dementia

Adapted from Dr. Sterling Johnson, the WRAP study
Amyloid scan

Tau scan (tangles)

Participant 1
Amyloid positive
Tau positive

Participant 2
Amyloid negative
Tau negative

Courtesy Sterling Johnson, the WRAP study

Betthauser, et al. 2020, Brain

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Amyloid accumulates in a predictable way but people develop amyloid at different ages

Average Time A+ Onset to Dementia: 24 years

Courtesy Sterling Johnson, the WRAP study

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What factors contribute to resilience?

Potentially modifiable factors account for 40% of dementia risk.

Among those with high amyloid, higher physical fitness = better memory performance.
Most pathologies are mixed


Vascular
TDP-43
α-synuclein

What about blood biomarkers?

PET scans and blood tests are closely related
Blood tests predict cognitive change

Your doctor can order blood tests

What are the caveats?

May work less well when:
- Early in the disease process
- Kidney disease
- Obesity
- Heart disease/stroke
- Other co-morbidities

Many are tests still in development.
What are the caveats?

Other considerations:

• Inclusion of biomarker results in medical record?
• Long term care insurance?
• Access to treatment?
• Commercial tests recommended for people with symptoms.
• Disclosure in research studies for people without symptoms.

Other considerations:

• Healthy adults ages 55-80.
• Not diagnosed with Alzheimer’s disease or another dementia.
• Have a study partner.
• Have elevated or intermediate amyloid found by imaging as part of the study.

Summary

• Biomarkers: brain imaging, CSF, and blood measures.
• Tell us what is happening in the brain.
• Identify people at risk for dementia.
• Tell us about cause of dementia.
• Help enroll people with disease into clinical trials.
• Can be used to monitor effect of therapies.
• Expected to become used more routinely in the future.