Diagnose

Lilly ConnectAD™

Welcome to ConnectAD™, a clinical case series created by the Eli Lilly and Company Neuroscience medical education team. This series is intended to connect healthcare professionals to resources that help them understand biomarkers and biomarker testing for Alzheimer's disease.

Disclaimer

The content for this clinical case was developed in collaboration between a group of global clinicians who care for patients with Alzheimer's disease and Eli Lilly and Company.

A variety of cognitive and diagnostic tests can reasonably be used in the detection and diagnosis of Alzheimer's disease. Inclusion of specific cognitive and/or diagnostic tests in this case reflects some of the options available to clinicians, but the use of particular diagnostic tools does not imply endorsement or recommendation by Lilly.

Learning Objectives

By completing this course, you will have a deeper understanding of:

1. The clinical presentation of Alzheimer's disease

2. The role clinical and biomarker assessments can play in diagnosing early symptomatic Alzheimer's disease

Lilly ConnectAD™

Connect *with Elena*

Diagnose

The clinical case presented here is entirely fictional and is not based on any real patient.

Our Patient Elena

- 72 years old
- Female
- Hispanic
- Married, lives with husband
- High school valedictorian, master’s degree in biochemistry
- Biochemical researcher in biotech industry (retired)
- Family history:
  - Dementia (mother)

Clinical Information and History

Elena reports the onset of impaired cognitive symptoms related to short-term memory over the past 6-12 months. Symptoms include:

- Getting lost while driving familiar routes, although she eventually finds her way
- Difficulty remembering the ingredients of her favorite dishes

She also mentions that lately, she has trouble falling asleep.

Elena's husband has noticed her symptoms.

Clinical Information and History

Clinical history

- Hypertension
- Gastroesophageal reflux disease

Current medication (class)

- Angiotensin-converting enzyme (ACE) inhibitor
- Proton pump inhibitor

Vital signs

- Heart rate: 70 bpm
- Blood pressure: 125/80 mmHg

Physical exam

- Normal (no tremors or gait dysfunction)

bpm=Beats Per Minute; mmHg=Millimeters of Mercury.

Initial Clinical Assessment

General neurological exam

- Normal

Mental status

- Alert and responsive
- Oriented to person, time, and place
- Independent in all activities of daily living
- GDS: 1/15 (not depressed)

Cognition

- MoCA: 24/30 (normal ≥26)

GDS=Geriatric Depression Scale; MoCA=Montreal Cognitive Assessment.

Additional Findings: Routine Labs and Further Assessments

Blood work within normal limits, including:

- Complete blood count (CBC)
- Electrolytes
- Glucose
- Creatinine
- Thyroid stimulating hormone (TSH)
- Vitamin B12

Based on the differential diagnosis, the following were also ordered:

Brain MRI

- Age-appropriate atrophy

Blood biomarker assay

- P-tau217 test negative

MRI=Magnetic Resonance Imaging; P-tau217=Phosphorylated Tau at Position 217.

Given the Patient Information Presented, What Are Possible Diagnoses the HCP Could Consider?

1. Generalized anxiety
2. MCI due to AD
3. Preclinical AD
4. Vascular cognitive impairment
5. Other

Elena

AD=Alzheimer's Disease; HCP=Healthcare Professional; MCI=Mild Cognitive Impairment.

Given the Patient Information Presented, What Is the HCP's Diagnosis?

1. Generalized anxiety
2. MCI due to AD
3. Preclinical AD
4. Vascular cognitive impairment
5. Other

Elena

AD=Alzheimer's Disease; HCP=Healthcare Professional; MCI=Mild Cognitive Impairment.

Why Is Elena Unlikely to Have AD?

For the past few months, Elena has noticed lapses in her short-term memory when driving or cooking. She also reports poor sleep. Elena schedules a visit with her PCP.

After optimizing her sleep hygiene, there still remains a concern for cognitive impairment. Therefore, Elena and her provider decide to pursue testing for the early symptomatic stages of AD, including a P-tau217 blood biomarker analysis.

The results of her P-tau217 blood biomarker analysis are inconsistent with the presence of AD pathology. Specifically, the low levels of P-tau217 indicate that she is unlikely to have amyloid pathology and AD.[1]

Referral to a neurologist and further testing rule out AD. The neurologist concludes LBD may be the cause of her cognitive impairment. The blood biomarker test helped enable the neurologist to eliminate AD as a potential cause of the symptoms and arrive at the LBD diagnosis faster.

AD=Alzheimer's Disease; LBD=Lewy Body Dementia; PCP=Primary Care Provider; P-tau217=Phosphorylated Tau at Position 217.

1. Hazan J, et al. *Alzheimers Dement*. 2025;21(3):e70113.

Key Learnings in Elena's Case (1 of 2)

Blood biomarker tests, including those that measure P-tau217, can rule out evidence of amyloid pathology as a potential cause of cognitive symptoms due to AD.[1-4]

The two hallmark pathological features of AD are[2]:

- Extracellular β-amyloid plaques
- Intracellular neurofibrillary tangles, which are composed of abnormally hyperphosphorylated tau protein, like P-tau217

Soluble $A\beta_{42}$ and P-tau217 appear at roughly the same time early in the disease process.[3]

- As AD progresses, $A\beta_{42}$ levels decline in CSF and blood (reflecting plaque formation), while P-tau markers rise in CSF and blood[1,5-7]

$A\beta_{42}$=42-Amino-Acid Version of Amyloid Beta; AD=Alzheimer's Disease; CSF=Cerebrospinal Fluid; P-tau=Phosphorylated Tau; P-tau217=Phosphorylated Tau at Position 217.

1. Teunissen CE, et al. *Alzheimers Dement.* 2025;21(1):e14397. 2. Palmqvist S, et al. *Alzheimers Dement.* 2025;21(7):e70535. 3. Arnsten AFT, et al. *Alzheimers Dement.* 2025;21(8):e70404. 4. Palmqvist S, et al. *JAMA.* 2024;332(15):1245-1257. 5. Sunderland T, et al. *JAMA.* 2003;289(16):2094-2103. 6. Padala SP, Newhouse PA. *Metab Brain Dis.* 2023;38(1):185-193. 7. Graff-Radford NR, et al. *Arch Neurol.* 2007;64(3):354-362.

Key Learnings in Elena's Case (2 of 2)

Comprehensive assessment involves: Medical evaluation, neurological exam, cognitive testing, laboratory assessment of potentially reversible etiologies of cognitive impairment, and structural neuroimaging.[1]

- Cognitive symptoms often have multiple causes, and misdiagnosis may result in delayed care, inappropriate treatment, and inaccurate prognoses[1]
- Many conditions other than AD can cause or exacerbate cognitive impairment; therefore, a comprehensive assessment should be used to identify the potential alternative etiologies[1]

AD biomarker testing is not intended as a standalone diagnostic test for symptomatic AD; it should always be used in the context of a comprehensive assessment.[1]

AD=Alzheimer's Disease.

1. Schindler SE, et al. *Nat Rev Neurol.* 2024;20(7):426-439.

Lilly ConnectAD™

Thank you for Connecting *with Elena*

Diagnose