Alzheimer’s doesn’t wait. Neither should a diagnosis.

Confirming amyloid positivity with CSF testing helps unlock new therapies for more patients.

Elecsys® CSF for amyloid pathology confirmation in cerebrospinal fluid (CSF)

Indication

Alzheimer's disease (AD) is a progressive, neurodegenerative disease associated with cognitive dysfunction and behavioral impairments. It represents the most common form of dementia, contributing to 50%–60% of cases.[1]

The accumulation of β-Amyloid and Tau are regarded as one of the earliest signs of the AD pathological cascade, taking place decades earlier than symptom onset.[2-4] β-Amyloid peptide arises by processing the amyloid precursor protein (APP). In AD, APP is abnormally processed, leading to excess production or reduced clearance of β-Amyloid protein and the extracellular accumulation of β-Amyloid plaques.[3]

Currently, two modalities can assess β-Amyloid 42 brain deposits: fluid (e.g., CSF biomarkers) and imaging (amyloid positron emission tomography (PET scan)). Historically, the diagnosis of AD, although suspected, was only confirmed post-mortem, during autopsy, by microscopic visualization of the beta-amyloid plaques and neurofibrillary tangles.

Although the clinical criteria for diagnosis has improved, many patients are still not diagnosed until their condition progresses to a late stage of AD. A diagnosis of Alzheimer's disease has been a diagnosis of exclusion, and the clinical criteria used offers only 70-80% diagnostic accuracy.[5] It is estimated that about 50% of patients with dementia are not formally diagnosed.[7] This has improved over recent years due to the availability of imaging and fluid biomarkers. The 2018 National Institute of Aging–Alzheimer's Association (NIA-AA) research framework introduced a paradigm shift in how AD is defined and diagnosed. The committee agreed that the detection by CSF and/or PET of the neuropathological changes of AD (i.e., the accumulation of β-Amyloid protein and Tau), can define and stage Alzheimer's disease biologically across its entire spectrum.[7]

Intended Use

Elecsys β-Amyloid (1-42) CSF II, Elecsys Phospho-Tau (181P) CSF and Elecsys Total Tau CSF (tTau) assays are in vitro electrochemiluminescence immunoassays for the measurement of the β-Amyloid (1-42) (Abeta42), Phospho-Tau (181P) (pTau181) and Total Tau (tTau) protein concentrations in cerebrospinal fluid (CSF) from adult patients aged 55 years and older being evaluated for Alzheimer's disease (AD) and other causes of cognitive impairment to generate a pTau181/Abeta42 or tTau/Abeta42 ratio value. A negative result, defined as a pTau181/Abeta42 ratio value below the cutoff or a tTau/Abeta42 value above the measuring range, is consistent with a negative amyloid positron emission tomography (PET) scan result.

A negative result reduces the likelihood that a patient's cognitive impairment is due to AD.

A positive result, defined as pTau181/Abeta42 or tTau/Abeta42 ratio value above the cutoff, is consistent with a positive amyloid PET scan result. A positive result does not establish a diagnosis of AD or other cognitive disorder. The pTau181/Abeta42 and tTau/Abeta42 ratio results are used as an adjunct to other clinical diagnostic evaluations.

A positive pTau181/Abeta42 ratio result in CSF does not establish a diagnosis of Alzheimer's disease (AD) and should always be interpreted in conjunction with clinical information.[4]

An early diagnosis supports early intervention

Alzheimer's disease (AD) is a public health crisis. The total number of people 65 and older living with AD is expected to nearly double from 6.7 million in 2023 to 13 million in 2050.[9] Between 50% and 75% of patients with dementia have no formal diagnosis.[7,10,11,12] Yet, 53% of family members report that they would have preferred an earlier diagnosis to help prepare for the future[12] and potentially provide access to new therapies.

Nearly 2,000 patients progress from mild to moderate dementia every day, meaning time is of the essence.[13]

Patients want to know if their symptoms are due to AD[14]

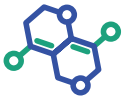
Confirming a diagnosis is important as it can reduce anxiety and may provide a sense of reassurance to patients and families that their symptoms are finally given a name.[16] In addition, a confirmed diagnosis at the early stage of the disease may qualify patients for new amyloid-targeting therapies.

Early diagnosis can bring substantial cost savings for healthcare systems[8,16]

An early diagnosis empowers patients and caregivers as they understand the cause of their symptoms, learn about disease evolution, plan for their future, and begin therapy and lifestyle changes that could prolong cognitive functions.[8,17] A study run by the Alzheimer's Association revealed that an early diagnosis at the mild cognitive impairment (MCI) stage could potentially save approximately $7 trillion in medical and long-term costs in the U.S. alone.[8]

Early diagnosis allows for appropriate and timely intervention[16]

With an early AD diagnosis, patients are empowered to make decisions and plan ahead.[18] Measures that individuals can start include[16,18,21]:



Gain access to new amyloid removal therapies.

Plan for financial support and care

Manage comorbidities (e.g., hypertension)

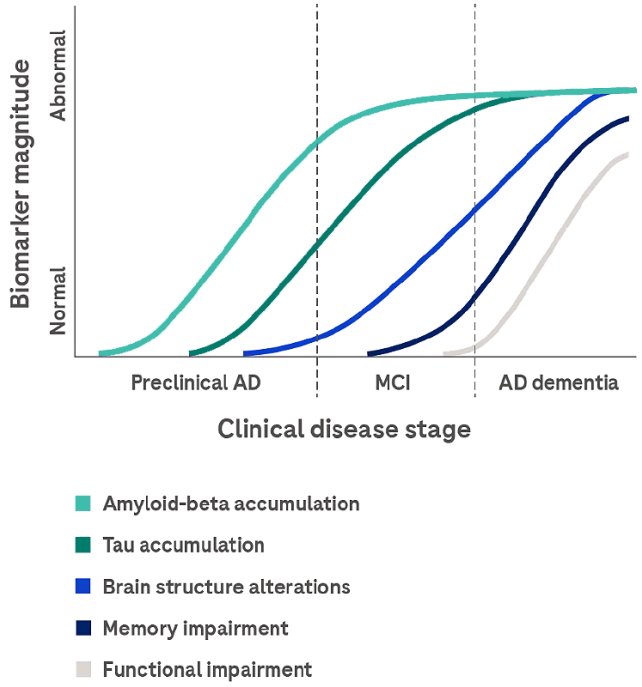
Begin preventive activities (e.g., social engagement)

The clinical utility of biomarkers in Alzheimer's disease diagnosis

Biomarkers for Alzheimer's disease can be an early indicator of change[2,3,4,22]

The accumulation of abnormal amyloid beta in plaques and tau in neurofibrillary tangles are regarded as the pathological hallmarks of AD.[6] Changes in both amyloid and tau proteins start decades before symptom onset and can be detected by fluid (e.g., CSF) or imaging (amyloid/tau PET) biomarkers.[6,7] In patients presenting with cognitive decline, a positive Elecsys pTau181/Abeta42 CSF ratio or Elecsys tTau/Abeta42 CSF ratio result is consistent with a positive amyloid PET scan result. A positive result does not establish a diagnosis of AD and should always be interpreted in conjunction with clinical information.[1]

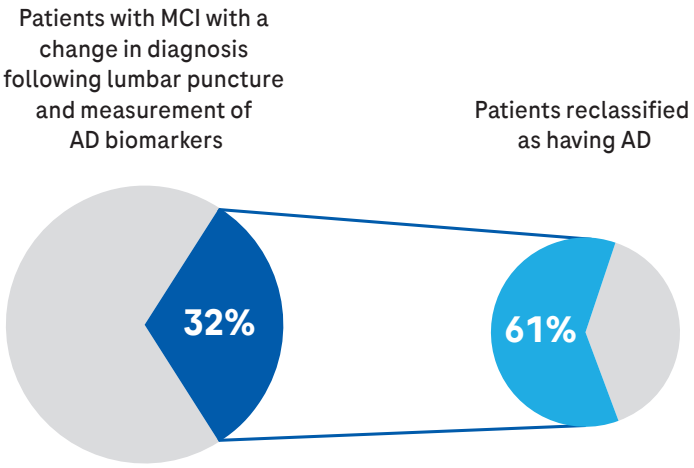
Dynamic biomarkers of the Alzheimer's pathological cascade[3]



CSF biomarkers for Alzheimer's disease increase specificity and confidence[5]

In patients presenting with cognitive decline, biomarkers detecting the abnormal amyloid and tau proteins enhance diagnostic accuracy and physician confidence in early diagnosis.[5,22]

A prospective, multicenter study evaluating physician surveys demonstrated the value of CSF testing in informing clinical decisions and optimizing patient management. In clinical cases where CSF results were considered, management was modified for 46.4% of patients (71/153), including 36 (23.5%) enrolled in clinical trials. Additionally, the inclusion of CSF testing modified diagnoses, increased AD diagnoses and improved clinician confidence in the diagnosis.[22]



Nearly one-third of patients had a change in diagnosis; of those patients, 61% were reclassified as having AD[23]

The most complete portfolio of Alzheimer's cerebrospinal fluid biomarker assays

The Elecsys AD CSF portfolio includes three assays[23]

- Elecsys β-Amyloid (1-42) CSF II (Abeta42) assay
- Elecsys Phospho-Tau (181P) CSF (pTau181) assay
- Elecsys Total-Tau CSF (tTau) assay

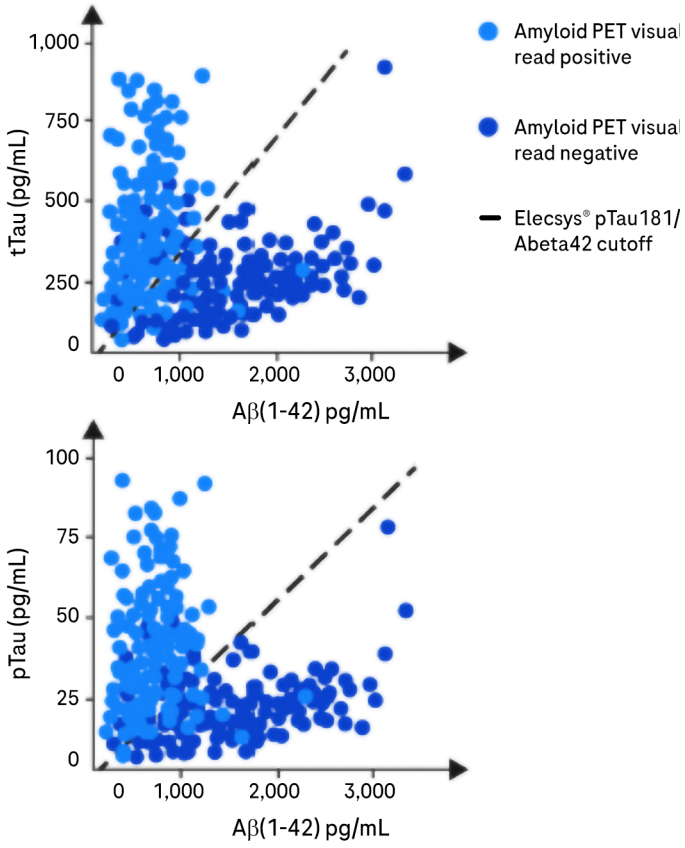
Roche's FDA-cleared CSF assays detect proteins involved in the three main Alzheimer's pathologies – amyloid plaques, tau neurofibrillary tangles and neurodegeneration.

Elecsys AD CSF assays can detect amyloid positivity, aiding clinical decisions[25,26]

Amyloid PET detects amyloid pathology but has several limitations for clinical routine implementation: expensive technique, requires specialist unit equipment, and it confers a radioactive burden to the patient.[19,26]

The Elecsys pTau181/Abeta42 and the tTau/Abeta42 CSF ratio assays have clinically validated cutoffs and the performance of the Elecsys pTau181/Abeta42 and tTau/Abeta42 ratios demonstrate ~90% concordance with β-Amyloid PET scan results. A result above the cutoff is consistent with a positive amyloid PET visual read.[23,25]

Amyloid PET read classification



The performance of the test for African American, Asian, and other races had high uncertainty due to the limited number of patients studied.[23]

A positive pTau181/Abeta42 or tTau/Abeta42 ratio result does not establish a diagnosis of AD or other cognitive disorders and should always be interpreted in conjunction with clinical information.[23]

Your results are reliable with Elecsys

The Elecsys Abeta42 assay has been standardized against the three certified reference materials (CRMs): ERM®-DA480/IFCC, ERM®-DA481/IFCC, and ERM®-DA482/IFCC.[24]

The Elecsys pTau181 assay has been standardized against a purified reference material Tau(172-205) [pThr181] amide, absolutely quantified via amino acid analysis.[24]

The Elecsys tTau assay has been standardized against a reference method. Calibrator values are based on weighted purified reference tTau material, traceable to National Institute of Standards and Technology (NIST) amino acid reference calibrators.

Elecsys pTau181/ Abeta42 [24] * †

		Within-run		Between-run		Between-day		Within laboratory	
	Mean	SD	CV	SD	CV	SD	CV	SD	CV
Sample 1	0.021	0.0005	2.3%	0.0003	1.5%	0.0005	2.6%	0.0008	3.8%
Sample 2	0.028	0.0006	2.0%	0.0006	2.1%	0.0003	1.1%	0.0009	3.1%
Sample 3	0.038	0.0006	1.6%	0.0004	1.0%	0.0008	2.1%	0.001	2.8%
Sample 4	0.041	0.0008	2.0%	0.0004	0.9%	0.0008	1.8%	0.001	2.8%
Sample 5	0.054	0.0009	1.6%	0.0008	1.4%	0.0007	1.3%	0.001	2.5%

Elecsys tTau/ Abeta42 [24] * †

	Mean	SD	CV	SD	CV	SD	CV	SD	CV
Sample 1	0.24	0.004	1.7%	0.005	2.1%	0.003	1.3%	0.009	3.6%
Sample 2	0.38	0.010	2.7%	0.010	2.6%	0.006	1.7%	0.017	4.5%
Sample 3	0.47	0.006	1.3%	0.007	1.4%	0.002	0.4%	0.012	2.5%
Sample 4	0.49	0.010	1.9%	0.005	0.9%	0.002	0.3%	0.011	2.3%
Sample 5	0.51	0.010	1.9%	0.007	1.4%	0.0	0.0%	0.013	2.5%
Sample 6	0.30	0.004	1.2%	0.005	1.7%	0.002	0.8%	0.010	3.2%

* Elecsys pTau181/Abeta42 ratio precision data determined on the **cobas e** 601 analyzer.

† Precision in human CSF samples.

The performance of the test for African American, Asian and other races had high uncertainty due to the limited number of patients studied.

High agreement with amyloid PET at the clinically validated cutoffs

The Elecsys pTau181/Abeta42 and tTau/Abeta42 ratios cutoffs that have been established and then validated in two separate studies: BIOFINDER, respectively Alzheimer's Disease Neuroimaging Initiative (ADNI).[26,24]

Performance of the Elecsys AD CSF ratios cutoff vs amyloid PET visual read[26,24]

	Elecsys pTau181/Abeta42 ratio	Elecsys tTau/Abeta42 ratio
Cutoff (+)*	> 0.023	> 0.28
Cutoff (-)†	≤ 0.023	≤ 0.28
PPA%	88.2 (84.4-91.2)‡	85 (80.9 – 88.4)
NPA%	92.6 (89.1-95.1)‡	94 (90.7 – 96.2)
OPA/TPA%	90.2 (87.7-92.3)‡	89.2 (86.5 – 91.3)

PPA, positive percent agreement; NPA, negative percent agreement

OPA, overall percent agreement; TPA: total percent agreement

* Consistent with positive amyloid PET scan result.

† Consistent with negative amyloid PET scan result.

‡ 95% CI are calculated using a Wilson score method for binomial proportions.

The performance of the test for African American, Asian, and other races had high uncertainty due to the limited number of patients studied.[26]

A positive pTau181/Abeta42 and/or tTau/Abeta42 ratio result does not establish a diagnosis of AD or other cognitive disorders and should always be interpreted in conjunction with clinical information.[26]

CSF collection protocols

Ordering the Alzheimer's CSF biomarkers requires careful adherence to pre-analytical sample handling procedures, which are based on recommendations from the Alzheimer's Association International guidelines.[23,28] Adherence to the pre-analytical protocol (below) is essential for the validity of results due to the particularities of the Abeta42 peptides, which are sticky and adsorb to the surfaces of certain types of plastic tubes. CSF exposed to polystyrene tubes leads to a 20–50% reduction in Abeta42 concentration due to adherence.

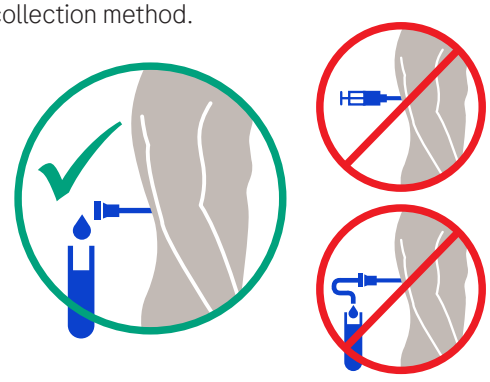
Procedure and handling

The Alzheimer's Association recommends a standardized protocol based on the drip collection method which reduces binding of Abeta42 to the syringe and instead **directly** collecting in a low bind tube.[24]

This protocol was the basis of the Elecsys CSF assays protocol recommended in the package inserts.

Step 1

Perform the lumbar puncture (LP) using gravity drip collection method.

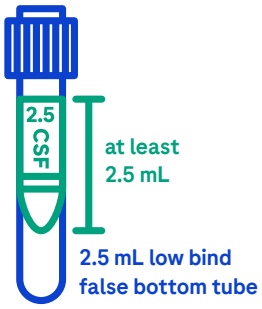


Step 2

Do not use the first 2 mL of CSF for Elecsys AD biomarker measurement.

Step 3

Subsequently collect at least 2.5 mL of CSF directly into the CSF tube (2.5 mL low bind false bottom tube).



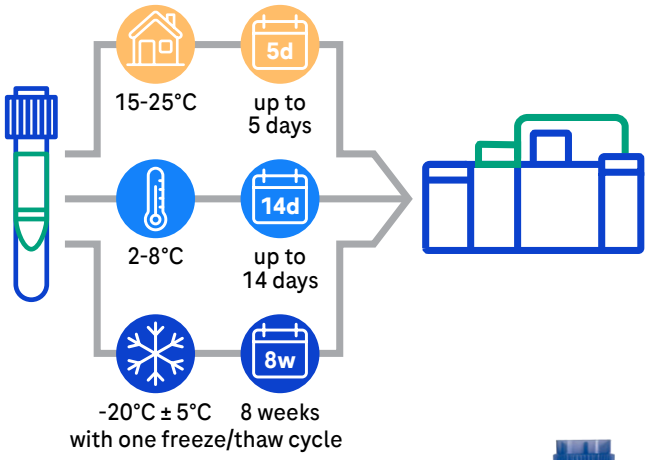
Step 4

Do not process the CSF sample before transport to the measuring site (e.g., no mixing/inverting, no tube transfers, no aliquoting, no freezing, and normally no centrifugation) until measurement.

Step 5

Transport the samples to the measuring site (laboratory), where the sample is placed directly on the **cobas e** system for measurement.[29]

The CSF sample can be analyzed immediately after collection by directly placing the tube with false bottom CSF, 2.5 mL onto the analyzer. If storage and/or transport is necessary, samples can be transported/stored according to the graphic below.



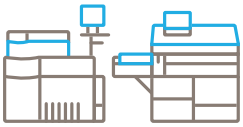
*** The tube required for CSF collection**
(but not available through Roche):

Product: 2.5 mL low bind false bottom tube
Order Number: 63.614.625
Vendor: Sarstedt

The Elecsys pTau181/Abeta42 and tTau/Abeta42 ratios are available for every size laboratory

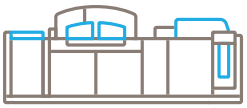
Efficiency through integration

With **cobas**®, you can run the Elecsys AD CSF assays on an instrument of your choice, from the smallest to the largest.[24]

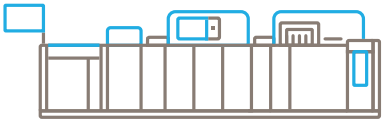


cobas 4000
analyzer series

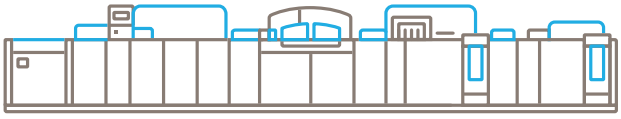
cobas pure
integrated solutions



cobas 6000
analyzer series



cobas pro
integrated solutions



cobas 8000
modular analyzer series

Ordering Information for Elecsys β-Amyloid (1-42)

Product	Catalog Number	Kit Configuration	Tests/Kit
Elecsys β-Amyloid (1-42) CSF II RackPack	08821909160	Rgnt kit for e411, e601/e602 only	60
Elecsys β-Amyloid (1-42) CSF II e-pack	08821941190	Rgnt kit for e801 and e402 only	100
CalSet β-Amyloid (1-42) II	08821976190	4 x 1.0 mL	n/a
PreciControl β-Amyloid (1-42) II	08821968190	6 x 1.0 mL	n/a
CalCheck β-Amyloid (1-42) II	06986854190	5 x 1.0 mL	n/a

Ordering Information for Elecsys Phospho-Tau (181P)

Product	Catalog Number	Kit Configuration	Tests/Kit
Elecsys Phospho-Tau (181P) CSF RackPack	08846693160	Rgnt kit for e411, e601/e602 only	60
Elecsys Phospho-Tau (181) CSF e-pack	08846715190	Rgnt kit for e801 and e402 only	100
CalSet Phospho-Tau (181P)	07357044190	4 x 1.0 mL	n/a
PreciControl Phospho-Tau (181P)	07357052190	6 x 1.0 mL	n/a
CalCheck Phospho-Tau (181P)	07546424190	5 x 1.0 mL	n/a

Ordering Information for Elecsys Total-Tau

Product	Catalog Number	Kit Configuration	Tests/Kit
Elecsys Total-Tau CSF RackPack	08846634160	Rgnt kit for e411, e601/e602 only	60
Elecsys Total-Tau CSF e-pack	08846685190	Rgnt kit for e801 and e402 only	100
CalSet Total-Tau	07357010190	4 x 1.0 mL	n/a
PreciControl Total-Tau	07357028190	6 x 1.0 mL	n/a
CalCheck Total-Tau	07546459190	5 x 1.0 mL	n/a

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