Biomarker testing may inform diagnosis and change patient care\(^1\)

The IDEAS Study, a longitudinal study of 11,409 patients, investigated whether biomarker testing via positron emission tomography (PET) imaging changed the diagnosis and management of patients with mild cognitive impairment (MCI) or dementia of uncertain etiology.

Over 60% of patients experienced a change in clinical management after biomarker testing\(^1\)

**Primary endpoint:** Change in patient management* between pre- and post-PET imaging.

Over 35% of patients received a change in diagnosis after biomarker testing\(^1\)

**Secondary endpoint:** Proportion of changes in diagnosis from AD to non-AD and vice versa between pre- and post-PET imaging.

### Change in Management

<table>
<thead>
<tr>
<th>Disease State</th>
<th>MCI [95% CI: 59.1-61.4]</th>
<th>Dementia [95% CI: 62.1-64.9]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>60.2%</strong></td>
<td><strong>63.5%</strong></td>
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</tbody>
</table>

N=11,409; P<0.001

- Results significantly exceeded the target of 30.0% composite change in each group (P<0.001, 1-sided)

*As assessed by a composite outcome that included Alzheimer’s disease drug therapy, other drug therapy, and counseling about safety and future planning.*

### Change in Diagnosis

<table>
<thead>
<tr>
<th>Disease State</th>
<th>AD to non-AD [95% CI: 24.3-25.9]</th>
<th>Non-AD to AD [95% CI: 10.0-11.1]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>25.1%</strong></td>
<td><strong>10.5%</strong></td>
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</tbody>
</table>

Alzheimer's disease is a clinical and biological disease. Recent IWG recommendations state:

"The diagnosis of Alzheimer's disease is clinical–biological. It requires the presence of both a specific clinical phenotype of Alzheimer's disease and biomarker evidence of Alzheimer's disease pathology."

Classifying and evaluating biomarkers of AD pathology

The ATN Classification System

The ATN Classification System categorizes AD biomarkers into three groups used to evaluate neuropathologic changes. AD-specific biomarkers are useful because neurodegeneration and injury may occur in non-AD conditions, particularly in elderly individuals with comorbidities.

ATN Biomarker Grouping

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>T</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aggregated Aβ or associated pathologic state</td>
<td>Aggregated tau (neurofibrillary tangles) or associated pathologic state</td>
<td>Neurodegeneration or neuronal injury*</td>
<td></td>
</tr>
<tr>
<td>CSF Aβ₄₂, or Aβ₄₂/Aβ₄₀ ratio</td>
<td>CSF phosphorylated tau</td>
<td>Anatomic MRI</td>
<td></td>
</tr>
<tr>
<td>Amyloid PET</td>
<td>Tau PET</td>
<td>FDG PET</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CSF total tau</td>
<td></td>
</tr>
</tbody>
</table>

Evaluating AD Biomarkers with PET imaging

PET imaging uses radiotracers to bind to amyloid plaques or tau in the brain. It offers high diagnostic accuracy and localized information, provides an opportunity to visually assess AD pathology in the brain, and may be used to establish biomarker relationships with changes in cognition and neurodegeneration.

Evaluating AD biomarkers with CSF testing via lumbar puncture

CSF analysis enables assessment of brain pathology and can measure Aβ and tau biomarkers from the same collection. Levels of Aβ in CSF are inversely related to the extent of cerebral Aβ deposits. CSF phosphorylated tau is a biomarker of the abnormal pathophysiology specifically associated with neurofibrillary tangles in AD. It is not elevated in primary tauopathies, head injury, or stroke. CSF total tau is a biomarker of neuronal degeneration; it is not specific for AD.

CSF is collected between the L3 and L4 or L4 and L5 vertebrae.

Studies have shown a strong correlation between CSF biomarkers and PET scan results.

References:

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