

Alzheimer's Disease Expert Meeting

November 23, 2024 (六) | 18:00-21:00

Meeting Objectives

- Understand the role of biomarkers in Alzheimer's Disease (AD), and the importance of early diagnosis
- Understand the key considerations in routine clinical practice, on biomarker's performance and result interpretation
- Understand the unmet needs and the gaps to routine CSF testing in Taiwan
- Learn from Singapore/Spain's experience to establish AD CSF testing service

Agenda

Time	Торіс	Speaker/Moderator
18:00-	Welcome and introduction	Dr. Hu Chaur-Jong
18:10		Taipei Medical University-
		Shuang Ho Hospital
18:10-	Dinner	All
18:30		
18:30-	Clinician considerations on Alzheimer's	Dr. Pablo Martinez-Lage
19:00	disease biomarkers & clinical utility along	Fundacion CITA-alzheimer
	patient journey	Fundazioa
19:00-	Discussion	Moderated by Dr Hsu Jung-
19:45		Long
19:45-	Setting up the CSF Alzheimer's disease	Assoc. Prof. Ng Kok Pin
20:10	biomarker service in Singapore	National Neuroscience
		Institute
20:10-	Taiwan case sharing	Dr. Hu Chaur-Jong
20:20		Taipei Medical University-
		Shuang Ho Hospital
20:20-	Discussion	Moderated by Dr. Hsu Jung-
20:50		Long
20:50-	Closing	Dr. Hsu Jung-Long
21:00		Chang Gung Memorial
		Hospital

Guest Speakers



Dr. Pablo Martínez-Lage Fundación CITAalzheimer Fundazioa



Assoc. Prof. Ng Kok Pin National Neuroscience Institute



Dr. Hsu Jung-Long 土城長庚醫院



Dr. Hu Chaur-Jong 雙和醫院

Participating Experts (依姓名筆劃順序排列)

姓名	單位
官怡君 醫師	雙和醫院
林詠萱 醫師	臺北榮總
洪于珺 醫師	土城長庚
孫瑜 醫師	恩主公醫院
陳怡君 醫師	林口長庚
陳培豪 醫師	馬偕醫院
陳達夫 醫師	臺大醫院
傅中玲 醫師	臺北榮總
黃瓊瑰 部長	林口長庚
劉子洋 醫師	新光醫院
劉議謙 醫師	耕莘醫院
鄭又禎醫師	輔大醫院

Executive summary

Clinician considerations on Alzheimer's disease biomarkers' & clinical utility along patient journey

- Alzheimer's disease (AD) diagnosis is frequently delayed and inaccurate.
 - A study from Spain revealed that over 50% of patients are at a moderate dementia stage when diagnosed. Another study found that more than 30% of patients with a probable AD diagnosis do not have AD.
- To improve diagnostic accuracy, the approach should shift from clinical pathology to biological diagnostics.
 - Previously, brain atrophy was identified through magnetic resonance imaging (MRI) and computed tomography (CT), while positron emission tomography (PET) imaging was used to assess brain metabolism and synaptic activity.
 - Amyloid PET, introduced in the early 21st century, offers approximately 95% sensitivity and accuracy by measuring amyloid plaque density.
 - Tau PET demonstrates the spread of tau protein in the brain, providing similar accuracy and assisting in disease progression confirmation.
- Lumbar puncture (LP) is a safe diagnostic method; however, patients on anticoagulants require special consideration.
- Cerebrospinal fluid (CSF) biomarkers are integral to improving diagnostic accuracy and personalizing AD management. Thus, they should be included in diagnostic workflows.
 - $\circ~$ Decreased levels of CSF amyloid beta 42 (A β 42) are linked to dementia due to AD.
 - $\circ~$ Levels of CSF AB42, t-tau and p-tau correlate with amyloid pathology and neurofibrillary tangles.
 - $\circ\,$ CSF biomarker ratios (e.g., A $\beta42/40$ and p-tau/A $\beta42$) are more reliable than individual markers, reducing the risk of false-negative and false-positive results
- Effective communication, and accurate and timely diagnosis can provide patients and their families with critical information about the disease, helping to alleviate anxiety and stress, thereby improving their quality of life.
- Early diagnosis of AD, particularly during the mild cognitive impairment (MCI) stage, not only offers patients the opportunity to receive prophylaxis treatments but also allows them to make informed decisions about their care and future arrangements while they still retain cognitive abilities.

Discussion 1

- Careful consideration should be given to selecting the appropriate diagnostic tools at an appropriate timing.
- In certain circumstances, confirming a diagnosis with diagnostic tools allowing patients to know whether they have AD—can provide reassurance.
- LP should be performed based on clinical judgment and the presence of signs consistent with AD. If cognitive decline or AD is suspected after neuropsychological testing, CSF analysis is recommended.
- Conversely, if subjective cognitive decline (SCD) is diagnosed with normal

neuropsychological results, CSF testing may be deferred, and follow-up monitoring is advised.

- Patient education and trust in physicians are crucial for the acceptance of procedures like LP.
- Physicians should provide comprehensive information about the available diagnostic tools, emphasizing the importance of identifying the underlying cause of the condition.
- Additionally, physicians may explain that a LP is similar to an epidural, which carries a low risk of side effects, such as headaches.

Setting up the CSF Alzheimer's disease biomarker service in Singapore

- AD is the most common form of dementia. In early-onset cases with atypical presentations, diagnostic biomarkers can significantly improve diagnosis and management.
- The 2018 National Institute on Aging and Alzheimer's Association (NIA-AA) guidelines defined the role of biomarkers in AD diagnosis, shifting the focus from clinical evaluations to biological evidence.
- Clinical significance of AD biomarkers:
 - Biomarkers support accurate AD diagnosis, going beyond symptoms-based assessments.
 - Biomarker confirmation enables clinicians to develop definitive management plans for patients
 - Biomarkers boost confidence in emerging treatments like lecanemab and donanemab, which target amyloid plaques and slow cognitive decline in early dementia.
- Experience in Singapore:
 - The high cost of amyloid PET remains a limitation, making CSF testing a more affordable alternative.
 - Singapore's compact geography facilitates the efficient transport of CSF samples to laboratories, reducing costs and improving convenience for patients.
 - According to a study conducted in Singapore, LP is a safe and effective diagnostic method. For some patients, the diagnosis and treatment plan were adjusted and modified after undergoing the procedure.
 - It is recommended to choose patients with MCI/dementia and <65 years old for LP and CSF testing.
 - The National Neuroscience Institute (NNI) and other countries have implemented automated diagnostic platforms to provide clinical testing services, ensuring quality care for patients.
 - Public awareness campaigns, such as newspaper articles, have helped disseminate information about CSF testing.
 - Physicians are encouraged to explain the benefits and limitations of amyloid PET and CSF testing to help patients and families make informed decisions.

Taiwan case sharing

• Biomarkers such as CSF analysis and amyloid PET are crucial in differentiating AD from other causes of cognitive decline, providing a more accurate diagnosis.

- However, amyloid PET readings can be subjective, depending on the interpreter, particularly near the cutoff point of approximately 30 centiloids.
- If amyloid PET results are negative, CSF testing is recommended, as it can detect biomarker changes earlier than amyloid PET abnormalities appear.
- The high or low level of CSF biomarker can directly confirm or exclude AD, reducing reliance on amyloid PET.
- For grey zone or borderline cases, combining the results of amyloid PET and CSF testing can offer more comprehensive clinical insights, facilitating clinical decision-making.

Discussion 2

- Establishing a CSF testing laboratory requires strict protocols to maintain sample integrity.
 - Rapid processing within two hours of collection and minimizing freezethaw cycles are essential to prevent degradation, especially for preserving p-tau proteins.
 - Specialized collection tubes are necessary to ensure biomarker stability.
- Laboratories must conduct validation and accuracy testing with a minimum of 20 clinical samples to meet international standards.

Discussion – Closing

- It is hoped that CSF testing will be covered by National Health Insurance (NHI) in the future.
- Health economic studies are needed to evaluate the cost-effectiveness of CSF testing and support its coverage under NHI reimbursement for CSF testing.
- Collaboration between medical societies, such as the Neurological Society and the Clinical Laboratory Medicine Society, along with cross-functional collaboration between different medical departments, is essential to ensure accurate diagnoses for AD.