Importance of timely diagnosis

What happened at AAIC?

① AD/PD ② CONy **③ AAIC**

Clinical data on blood-based biomarkers and amyloid-targeted therapies (ATTs) was presented, paving the way for earlier diagnosis and intervention.

Expert insights

- Timely diagnosis is essential for identifying patients with mild cognitive impairment (MCI) due to Alzheimer's disease (AD) and early AD, allowing for:
  - Identification of patients who may be eligible for disease-modifying therapies such as ATTs.
  - Advanced care planning and enhanced support systems.
  - Reduced stress for patients by providing clarity about their condition.
- Global shortages of specially trained primary care doctors, geriatricians, and neurologists are a significant barrier to timely diagnosis.
  - Resource limitations and current workflows also impact on ability to provide appropriate follow-up and care if a diagnosis is made.

Use of blood-based biomarkers in practice

What happened at AAIC?

① AD/PD ② CONy **③ AAIC**

Data was presented showing the promise of blood-based biomarkers in enhancing the triage process for AD. New clinical evidence shows that blood-based biomarkers have the potential to predict AD pathology and improve diagnostic accuracy in both primary and secondary care settings.

Expert insights

- Blood-based biomarkers have the potential to form an important part of a stepwise diagnostic work up for early-stage AD, but cautious implementation is required if they are approved.

  - They may be very useful for initial triaging – the current workflow requires a PET scan which is expensive and often not covered by insurance policies, or a lumbar puncture which is invasive.

  - Current studies lack diverse populations, which limits the generalizability of findings.

  - False positives and false negatives can occur therefore established biomarkers (e.g. PET) would still be required to confidently confirm a diagnosis.

- Combining various biomarkers in a multi-marker evaluation could support a personalized medicine approach, which identifies the specific pathology of each patient.

- Significant educational efforts are required for healthcare providers to understand and effectively use new blood-based biomarkers as part of new workflows.

  - They could prove useful in primary care for triaging patients who need to see specialists.

Implementation of amyloid-targeting therapies (ATTs)

What happened at AAIC?

① **②** **③**

AD/PD   CONy   **AAIC**

Updated efficacy and safety data on ATTs was presented. Experts looked at how results from clinical trials on ATTs can be translated into the clinic, focusing on efficacy, amyloid-related imaging abnormalities (ARIA) risk, and dosing.

Expert insights

- Appropriate use criteria are important to consider when determining eligibility for ATTs:
  - Only recommended for patients with MCI or early-stage AD; currently, no benefit observed after this point.
  - Vascular comorbidities and anticoagulant use are key contraindications.
  - *APOE4* testing is a topic of debate, and if used requires genetic counselling.
- Still unanswered questions, such as optimal treatment duration and whether treatment should be stopped if amyloid is cleared and restarted if it returns.
- Safe prescription of these therapies requires a complex infrastructure, including collaboration among several specialties, and comprehensive testing and patient monitoring.
  - May limit treatment access to those in under resourced areas, exacerbating healthcare disparities.
- Researchers are exploring other targets, such as tau and neuroinflammation markers, which may lead to a more comprehensive, multi-targeted approach to treatment.
  - The future may involve a more personalized medicine approach, combining anti-amyloid therapies with other targeted interventions, to tailor treatment based on individual patient pathologies.
- Shared decision-making is crucial and ongoing education for both healthcare providers and the public is essential to navigate the complexities of these emerging therapies effectively.

Amyloid-related imaging abnormalities (ARIA)

What happened at AAIC?

① AD/PD **②** CONy **③** AAIC

Clinical data on the safety of ATTs (e.g., donanemab, lecanemab) was discussed, including data on the risk of ARIA associated with these therapies.

Expert insights

- ARIA is a significant concern in patients on ATTs, due to the unknown long-term effects and clinical implications.

- Explaining the risks of ARIA, such as brain swelling or hemorrhages, can cause anxiety in patients even if symptoms are mild or they are asymptomatic.

- Effective management of ARIA requires rigorous MRI monitoring and careful record-keeping, posing operational challenges for healthcare systems.

- Accurately diagnosing ARIA requires skilled neuroradiologists, which may not be available at all healthcare facilities.
  - Artificial intelligence (AI) could potentially assist in this area, but current AI models are not yet reliable enough to ensure safety and further research is required.

- Establishing a standardized approach to ATT prescribing and monitoring is crucial for patient safety.

Summary

AAIC 2024 showcased significant advancements in blood-based biomarkers and ATTs that have the potential to improve outcomes for patients with early-stage AD. However, several key considerations are important for the implementation of these advances in practice:

Timely diagnosis

Timely of AD is crucial to allow for identification of eligible patients for ATTs and advanced care planning. However, shortages of trained healthcare professionals and cost are significant barriers to timely diagnosis, posing a global challenge requiring efficient use of healthcare resources.

Further research on blood-based biomarkers

Blood-based biomarkers could be valuable in diagnosing early-stage AD but require cautious implementation. They may aid initial triaging, complementing established methods like PET and CSF. However, current research lacks diversity and significant educational efforts are needed to ensure effective use.

Optimal implementation of ATTs

ATTs offer potential benefits for patients with early-stage AD, but they require careful patient selection, comprehensive monitoring, and shared decision-making between clinicians and patients. Further research is required to determine optimal treatment duration and workflows to ensure that access to ATTs is not limited to those in well-resourced centers. In the future, other targeted treatments could complement ATTs to form a personalized approach.

Optimization and standardization of ARIA monitoring

ARIA poses a challenge due to unknown long-term effects and clinical implications. Managing ARIA requires rigorous MRI monitoring by skilled neuroradiologists, which can be operationally demanding and not always available. Standardization of ATT monitoring is crucial for safety but may be limited by access disparities and the need for specialized expertise.

More resources

Read our **News Nuggets**

Detailed summaries of the data presented at AAIC.

Watch and listen to our **Breakfast Bites**

On-site interviews with delegates from AAIC share their insights on the data and topics presented.

Take-away our **Microdigests**

Summary of key developments presented at AAIC in downloadable infographics.