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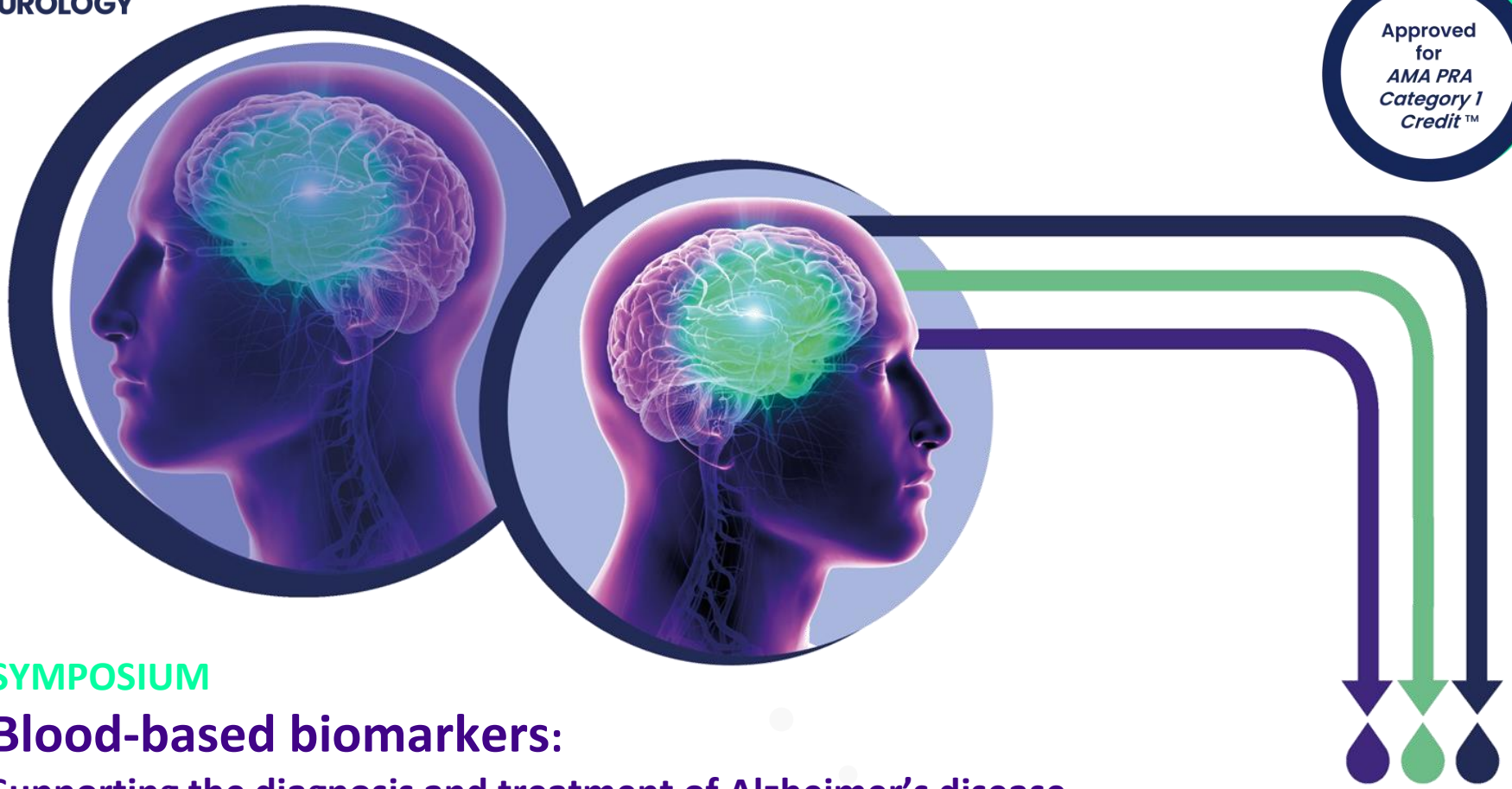

SYMPOSIUM

Blood-based biomarkers:

Supporting the diagnosis and treatment of Alzheimer's disease

Moving towards a biological diagnosis of Alzheimer's disease: The time is now

Prof. Liana Apostolova
Indiana University School of Medicine,
Indianapolis, IN, USA

Audience questions for discussion

1. Biomarkers should be a way to profile a patient and identify different potential biological mechanisms eventually to target combination therapeutic strategies
2. What are the major missing elements of the ATN approach? Are there other aspects of AD pathology that require biomarkers?
3. Do you think blood-based biomarkers can replace imaging studies in clinical trials?
4. How soon will the US FDA accept a plasma biomarker as diagnostic of AD? — on par with CSF and PET. If so, which one?
5. What about NfL?
6. To what extent do you see these biomarkers expanding into the diagnosis of preclinical and prodromal AD?
7. What is the biggest no-go with lumbar punctures? Invasiveness? Ability to assess the samples in the right labs? Patient resistance?
8. How will amyloid-beta treatments work if they rely on A+T+N+ diagnosis, where trials require earlier treatment?
9. How will amyloid depletion with amyloid-beta therapies affect ATN assessment for combination therapies?
10. In countries where CSF and amyloid PET are not available yet, is FDG-PET still helpful?
11. What are some ways that you see industry and scientific societies can collaborate to drive forward the biomarkers to be clinically robust enough to use as soon as possible?
12. Are there any imaging biomarkers for tauopathies other than AD?

AD, Alzheimer's disease; ATN, amyloid/tau/neurodegeneration; CSF, cerebrospinal fluid; FDG, fluorodeoxyglucose; NfL, Neurofilament light chain; PET, positron emission tomography.

Blood-based biomarkers in Alzheimer's disease: Advantages and limitations

Prof. Oskar Hansson
Lund University,
Lund, Sweden

Audience questions for discussion

1. With these biomarkers existing on a spectrum, how do you see FDA (and other regulatory agencies) dealing with the cut-off numbers for diagnosis?
2. P-tau is classified in ATN as “T”. However, it is better correlated to amyloid plaques than tau tangle pathology seen in tau PET. So is it really “A”?
3. Alzheimer co-pathology is frequent in dementia with Lewy bodies. Do biomarkers help with differentiating these two conditions?
4. Any thoughts on the use of p-tau231 versus p-tau217?
5. The prevalence of AD-pathology increases in the general population with age. Do you think we’ll be able to use blood based biomarkers in individuals 80+ years old?
6. Will blood-based biomarkers provide information that will help us to advise our patients meaningfully?
7. Are there measurable changes in p-tau biomarkers in normal ageing?

AD, Alzheimer’s disease; ATN, amyloid/tau/neurodegeneration; PET, positron emission tomography; p-tau, phosphorylated tau.

Integrating blood-based biomarkers in Alzheimer's disease: How and when?

Prof. Charlotte Teunissen
Amsterdam UMC
Amsterdam, Netherlands

Audience questions for discussion

1. *APOE4* genotyping is another available blood-based biomarker. Where does it sit in terms of blood-based biomarkers (BBMs)?
2. Once a patient is amyloid negative following treatment, are blood-based biomarkers for amyloid-beta still relevant, do you see ptau217 or 181 being used to follow treatment, to measure amyloid reduction in the brain by PET over time, to decide when to stop or re-initiate treatment?
3. Will the clinical data for blood-based biomarkers be translated to a real-world setting where there is higher variability in sample handling and testing as well as heterogeneity of patients who are ethically more diverse and with comorbidities etc?
4. You mentioned that we need to identify influencing factors before implementing the test in clinical care. Are there any factors in particular you are aware of besides possibly BMI?
5. Can you elaborate on the utility of ptau181 compared to ptau217 in the development of the disease?
6. How will ptau217 help PCPs in triaging patients to specialist centres? AD only accounts for 50% of dementia cases. Should we stop diagnosing FTD, DLB? Will patients not have to go to diagnostic evaluation, even with a negative test for AD?
7. You have discussed reduction in ptau217 in the donanemab trial. How much of that is the effect of the drug and how much of that can be attributed to assay variability?

AD, Alzheimer's disease; ATN, amyloid/tau/neurodegeneration; BBM, blood-based biomarker; BMI, body mass index; DLB, dementia with Lewy bodies; FTD, frontotemporal dementia; PET, positron emission tomography; p-tau, phosphorylated tau.

Panel discussion

Prof. Jeffrey Cummings
University of Nevada,
Las Vegas, NV, USA

Prof. Liana Apostolova
Indiana University School of Medicine, Indianapolis, IN, USA

Prof. Oskar Hansson
Lund University,
Lund, Sweden

Prof. Charlotte Teunissen
Amsterdam UMC,
Amsterdam, Netherlands

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Audience questions for discussion

1. We have p-tau217,181,231. Could there be others?
2. Thoughts on total tau vs p-tau levels? Does p-tau/total tau ratio increase accuracy vs p-tau alone?
3. I'm surprised that some of the panellists have advocated against screening in the general population. Can each elaborate on this in light of the ongoing preclinical trials?
4. What three biomarkers would you choose in a patient with early symptomatic disease?
5. What is the best blood-based biomarker to predict and track disease progression?
6. Does discovery work with highly multiplexed proteomics technologies suggest multi-marker algorithms that may out-perform the current markers? If so, do you see a future clinical path? Is it cost-effective?
7. What's the missing biomarker?

AD, Alzheimer's disease; BBM, blood-based biomarker; p-tau, phosphorylated tau.