

## CSF Biomarkers in Alzheimer's Disease (AD), a descriptive classification scheme (A/T/N):

|                                 | CSF<br>cut-off values <sup>1</sup> | CSF<br>ATN classification                                                                                              | ATN classification <sup>2</sup><br>presence of:                                                                             |
|---------------------------------|------------------------------------|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|
| <b>Aβ Ratio Aβ1-42 / Aβ1-40</b> | > 0,069 pg/ml                      | Pathological if lower<br><br>→ <b>A+</b><br><br><small>priority is ratio over single<br/>measured value Aβ1-42</small> | <b>Amyloid</b><br><br><b>decrease</b> in CSF Aβ ratio or Aβ1-42<br>in absence of Aβ1-40<br><br>(Or presence in amyloid PET) |
| <b>Aβ1-42</b>                   | > 600 pg/ml                        |                                                                                                                        |                                                                                                                             |
| <b>P-Tau181</b>                 | < 56,5 pg/ml                       | Pathological if higher<br><br>→ <b>T+</b>                                                                              | <b>Tangles</b><br><br><b>increase</b> in CSF P-Tau181                                                                       |
| <b>T-Tau</b>                    | < 404 pg/ml                        | Pathological if higher<br><br>→ <b>N+</b>                                                                              | <b>Neurodegeneration</b><br><br><b>increase</b> in CSF T-Tau<br><br>(or presence of atrophy on structural MRI, FDG PET)     |
|                                 | > 1200 pg/ml                       |                                                                                                                        | See below T-Tau / P-Tau remark                                                                                              |

<sup>1</sup> ref. Alcolea et al., 2019 ACTN; cfr. Perugia data, Lumipulse cut-off values

<sup>2</sup> ref. Jack et al., 2016 Neurology

|                                                          |                                            |                                                                                                                                                                                                                                                                                                                                                            |
|----------------------------------------------------------|--------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Ratio T-Tau / P-Tau</b><br><br>or<br><br><b>T-Tau</b> | <b>≥ 14,025</b><br><br><b>≥ 1200 pg/ml</b> | <b>Remark:</b> if T-Tau/P-Tau ratio ≥14,025 <sup>(3)</sup> or if T-Tau ≥1200pg/ml and if clinically relevant in context of differential diagnosis Creutzfeldt-Jakob disease (diagnostic criteria 'possible CJD' according to WHO/ECDC), contact <a href="mailto:biomarkers@uantwerpen.be">biomarkers@uantwerpen.be</a> for further PrPsc RT-QuIC analysis. |
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<sup>3</sup> ref. Foucault-Fruchard et al. 2020 J. Neurol Sci

## Summary of consensus comments for interpretation of biochemical profiles of Alzheimer's disease (AD) biomarkers in CSF

| <b>A</b> | <b>T</b> | <b>N</b> | consensus comment on CSF<br>biochemical profile <sup>4</sup>                                                                                                       | possible co-occurring pathology <sup>3</sup> |
|----------|----------|----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| +        | +        | +        | consistent with AD                                                                                                                                                 | See above T-Tau / P-Tau remark               |
| +        | +        | -        | atypical, consistent with AD                                                                                                                                       |                                              |
| +        | -        | +        | atypical, may be consistent with AD                                                                                                                                | See above T-Tau / P-Tau remark               |
| +        | -        | -        | compatible with early neuropathological<br>changes of AD and increased risk to clinically<br>develop AD; consider other causes of current<br>cognitive complaints. |                                              |
| -        | -        | -        | not consistent with AD                                                                                                                                             |                                              |
| -        | +        | +        | atypical, not consistent with AD                                                                                                                                   | See above T-Tau / P-Tau remark               |
| -        | +        | -        | atypical, not consistent with AD                                                                                                                                   |                                              |
| -        | -        | +        | not consistent with AD, may be consistent with<br>other neurodegenerative disease and/or<br>neural damage                                                          | See above T-Tau / P-Tau remark               |

<sup>4</sup> ref. Jack et al., 2018 Alzheimers Dement; Delaby et al., 2021 Alzheimers Dement