

Gispert JD, Lopes Alves I, Gray K, Buckley C, Collij L, Heeman F, Salvadó G, David Vázquez García, Peter Connelly, Claire Boutoleau-Bretonniere, Florence Pasquier, Julien Dumurgier, Audrey Gabelle, Bruno Dubois, Pierre Payoux, Oriol Grau, Pablo Martinez-Lage, Merce Boada, Marta Marquie, Rik Vandenberghe, Bernard Hansseuw, Miia Kivipelto, Michael Schöll, Scheltens P, Frisoni G; Ritchie CW; Vellas B, Stephens AW, Ford L, Molinuevo JL, Visser PJ, Farrar G, and Barkhof F, *on behalf of the AMYPAD Consortium*

## Background

Understanding the role of amyloid imaging in the earliest stages of Alzheimer's Disease (AD) becomes increasingly relevant for secondary prevention. In this context, the AMYPAD Prognostic and Natural History Study (PNHS) is an open-label, prospective, multi-centre cohort study (<http://amypad.eu/>) aiming to establish the value of quantitative amyloid PET imaging to determining AD dementia risk. The study recruits from several European cohorts and aims at enrolling 2000 non-demented individuals with a particular focus on those with emerging amyloid pathology.

## Results

- Centiloid values ranged from -32.6 to 116.2 (Mean±SD: 19.0±28.0 CL).
- Quantitatively, 227/417 (54%) of scans were categorized as negative (CL≤12), 133/417 (32%) in the gray-zone (12<CL≤50), and 57/417 (14%) as positive (CL>50).
- 69/338 (20%) of the baseline scans were visually rated as positive and 269/338 (80%) as negative.
- As expected, higher CL values were associated with higher age ( $r = 0.366$ ;  $p < 0.001$ ) and APOE-ε4 carriership ( $t = 6.53$ ;  $df = 288$ ;  $p < 0.001$ ).
- Of the negative group by CL quantification, 8/179 (4%) were visually rated as positive, as compared to 20/116 (17%) of the 'gray-zone' group and 41/43 (95%) of the positive one.
- Higher baseline CL value was associated with lower MMSE scores ( $t = -2.73$ ;  $p = 0.007$ ), CDR SOB ( $t = 3.82$ ;  $p < 0.001$ ), RBANS Immediate Recall ( $t = -6.43$ ;  $p < 0.001$ ) and RBANS Delayed Recall ( $t = -5.92$ ;  $p < 0.001$ ).

## Methods

- As of June 15th, 2021, AMYPAD PNHS had 17 actively recruiting sites across Europe, and 1027 non-demented participants (>95% cognitively unimpaired) had consented to participate in the study.
- Of those, 536 are from EPAD LCS, 165 from FACEHBI, 140 from ALFA+, 139 from EMIF-AD Twin 60+, 34 from FPACK, 10 from the UCL-2010-412 cohort and 3 from Microbiota.
- Within AMYPAD PNHS, 790 subjects have been scanned with either [18F]flutemetamol or [18F]florbetaben so far.
- Of them, 285 have undergone a follow-up scan within AMYPAD PNHS, while 478 already had a previous scan available.
- The primary outcome measure is the Centiloid (CL) quantification approach, with the whole cerebellum as reference region.
- Subjects were categorized as amyloid-negative (CL≤12); as in a "gray-zone" (12<CL≤50) or amyloid-positive (CL>50) and a Gaussian Mixture Model was used to assess the population's Centiloid distribution.
- In addition, PET scans have been visually assessed by local raters according to product guidelines, classifying subjects as amyloid negative or positive.
- In total, 417 of the 790 baseline PET scans have been quantified with IXICO's LEAP pipeline and passed Quality Control, thus rendering valid CL values.
- Visual assessment had been completed in 338 of these 417 scans.
- Associations between baseline CL values and MMSE, CDR SOB, RBANS Immediate and Delayed Recall have been sought in 536 participants from the EPAD LCS.

## Conclusion/Discussion

- ✓ **Preliminary quantitative results indicate that AMYPAD Prognostic and Natural History Study (PNHS) is being successful in recruiting its intended target population:**
  - ✓ **A cohort mostly composed of cognitively unimpaired individuals who are enriched for both early and established amyloid abnormalities.**
- ✓ **The AMYPAD PNHS cohort is therefore a highly valuable resource for future (early) secondary prevention trials, aimed at intervening on amyloid accumulation in a preclinical population.**

### Academic partners



### SMEs



### Industrial partners



### Patient organisation



### Contact:

[jdgispert@barcelonabeta.org](mailto:jdgispert@barcelonabeta.org)  
[info@amypad.org](mailto:info@amypad.org)  
[www.amypad.eu](http://www.amypad.eu)