Publishable Summary

In this deliverable, we report on the progress of the disease modeling activities of the AMYPAD Prognostic and Natural History study, especially with respect to the processing of the prospective data being collected in the study, as well as the access to the multiple Parent Cohorts that will share data with AMYPAD for the purposes of our main modeling analyses.

In short, the overall progress in the study was successful until March 2020, when the COVID-19 pandemic resulted in a halt in subject enrollment across sites, and only a small recovery in recruitment activities has been seen since. Nonetheless, this idle period in site activity saw progress in the quantification of scans already performed, as well as in the set-up of the infrastructure for the access to the complementary non-imaging data from the Parent Cohorts. As a result, we have been able to perform a first descriptive analysis of the population being enrolled in the study, which is reported in this deliverable, which will be the cornerstone of future modeling analyses.

First, we see that there is an over-representation of the [18F] flutemetamol tracers in relation to the [18F]florbetaben in this study. This was a known risk, and became more pronounced with the addition of Parent Cohorts which had already scanned their participants in the past with the first tracer. Nonetheless, this imbalance is being monitored and shall not compromise the results of the study, as the two ligands are demonstrated to be interchangeable for the purposes of our analyses (more details to be reported in a deliverable within WP2). More importantly, the quantitative results from the amyloid PET scans already quantified show that AMYPAD PNHS is successfully enrolling the targeted population, i.e. subjects with low-to-intermediate levels of amyloid burden, at the beginning of the pathological process. This includes a considerable proportion of “gray-zone” individuals (32%) with Centiloid values between 12-50. The continued enrollment of subjects in that range of amyloid burden will ensure the study is well equipped to understand the first stages of Alzheimer’s disease.

In addition to the EPAD cohort, we currently have 5 other Parent Cohorts which are actively enrolling into AMYPAD PNHS, with 2 additional ones coming in within Q4 2020. The difference in mean age between the cohorts will allow AMYPAD PNHS to cover a wide age range across the preclinical AD spectrum for its future analyses. Across all enrolled subjects, the mean age is 67.9 ± 7.5 years. Further, the current (limited) availability of APOE genotyping shows the AMYPAD PNHS population is comprises a substantial proportion of APOE-ε4 carriers (30.7%), again confirming the desired enrichment.

Finally, our first approach at creating a global cognitive composite that can serve as outcome across Parent Cohorts seems effective, showing that relationships between amyloid burden and longitudinal cognitive changes (in a limited sample) are behaving similarly across cohorts. Pending confirmation of these findings, this indicates AMYPAD PNHS will be able to successfully pool subject-specific information across cohorts and analyse the effects of this pathology on overall cognitive performance.

For more information: info@amypad.org

Acknowledgement: This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 115952. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.