AMYPAD
Amyloid Imaging to Prevent Alzheimer’s Disease

Alzheimer Europe Conference- October 2019

José Luis Molinuevo

www.amypad.eu
Amyloid Imaging to Prevent Alzheimer’s Disease

Part of Innovative Medicines Initiative (IMI) program, a joint undertaking between the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA)

A 5-year programme with a budget of €27.3M distributed across a total of 15 partners.

www.amypad.eu
Two studies to deliver on objectives

**Diagnostic Study**

**Diagnostic Value:** Usefulness of β-amyloid imaging in diagnostic certainty and patient management

**Risk Stratification:** Natural history of disease and methods to enrich secondary prevention studies

**Monitoring Treatment:** Quantifying treatment-induced changes and patient-specific efficacy

**Prognostic study**

**Disease Modelling**

<table>
<thead>
<tr>
<th>Study/objective</th>
<th>Cohort</th>
<th>Baseline PET</th>
<th>Follow-up PET</th>
<th>Total scans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic</td>
<td>Memory clinic</td>
<td>900</td>
<td>300</td>
<td>1200</td>
</tr>
<tr>
<td>Prognostic</td>
<td>Natural history</td>
<td>2000</td>
<td>1000</td>
<td>3000</td>
</tr>
<tr>
<td>Disease Modelling</td>
<td>All subjects</td>
<td>2900</td>
<td>1300</td>
<td>4200</td>
</tr>
</tbody>
</table>
Diagnostic & Patient Management Study

**Aim:** to determine the impact of amyloid PET imaging on diagnostic thinking in the workup of patients with SCD-plus, MCI, and dementia

**Primary objective:** To test the hypothesis that an etiologic diagnosis with very high confidence (≥90%) is reached earlier if amyloid PET imaging is performed early in the diagnostic workup

**Secondary objectives:** diagnosis and confidence, patient management, HTA, quantitative PET

**Novel features:** randomized design & inclusion of SCD-plus
Randomization, SCD value & cost-effectiveness

(Across Europe, n=900)

Randomised design
Close adherence to clinical practice
Less observer bias (e.g. IDEAS, ABIDE)
Longitudinal observations

EudraCT NUMBER: 2017-002527-2

Recruitment status: 523 randomized
## Secondary endpoints

<table>
<thead>
<tr>
<th>Diagnosis and Confidence</th>
<th>Patient Management</th>
<th>Health Economics Outcomes</th>
<th>Quantitative Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to communicate an etiological diagnosis</td>
<td>Patients randomised to DMD or other AD clinical trials</td>
<td>Impact of patient reported outcomes (eg coping skills)</td>
<td>Analysis of local image read results</td>
</tr>
<tr>
<td>Changes in etiological diagnosis over time</td>
<td>Change in patient management plans</td>
<td>Cost of diagnostic work up to high confidence Dx</td>
<td>Measurement of Suvr and Centiloid units across tracers and patient subgroups</td>
</tr>
<tr>
<td>Changes in diagnostic confidence over time</td>
<td></td>
<td>Differences in use of medical resources</td>
<td>Comparison of global &amp; visual read results to quantitative measures across tracers &amp; subgroups</td>
</tr>
<tr>
<td>Likelihood patients symptoms due to AD over time</td>
<td></td>
<td>Subject withdrawals/costs</td>
<td></td>
</tr>
<tr>
<td>Changes over time in use of amyloid in free choice arm</td>
<td></td>
<td></td>
<td>Early Arm will get 2nd scan: measurement of longitudinal change</td>
</tr>
</tbody>
</table>
Recruitment ongoing, balancing strata

AMYPAD DPMS Recruitment Status

<table>
<thead>
<tr>
<th>Site</th>
<th>SCD</th>
<th>MCI</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNIGE</td>
<td>33</td>
<td>81</td>
<td>33</td>
</tr>
<tr>
<td>VUmc</td>
<td>20</td>
<td>37</td>
<td>45</td>
</tr>
<tr>
<td>CHUT</td>
<td>26</td>
<td>40</td>
<td>19</td>
</tr>
<tr>
<td>BBRC</td>
<td>24</td>
<td>22</td>
<td>2</td>
</tr>
<tr>
<td>UKK</td>
<td>5</td>
<td>34</td>
<td>19</td>
</tr>
<tr>
<td>UCL</td>
<td>10</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td>CHUV</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>KI</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>119</td>
<td>240</td>
<td>123</td>
</tr>
</tbody>
</table>
From early diagnosis to secondary prevention
Aim: to understand the role of amyloid PET imaging in predicting progression within each domain of a so-called AD risk probability spectrum

Primary objective: quantitatively assess amyloid burden using PET to complement the extensive assessment of Parent Cohorts and enable risk assessment and updated disease models

Secondary objectives: determine and assess the utility of rate of amyloid accumulation, CBF proxy measures, advanced PET analyses and several risk factors in predicting cognitive and other AD-related decline

Novel features: dynamic & quantitative PET, adaptive inclusion, effective resource utilization and collaborative framework

Risk Stratification: Natural history of disease and methods to enrich secondary prevention studies

Prognostic study
Large scale amyloid PET in preclinical/prodromal AD

- ~ 20 sites across Europe
- 2,000 cognitively unimpaired subjects
- Focus on “gray-zone” of amyloid build up

Study design

- Dynamic scans as preference
- Longitudinal PET in at least 50%

Recruitment status: 319 enrolled
Focus on “gray-zone” of amyloid build up

Initial amyloid accumulation, even prior to current abnormality thresholds

Select 80% of target subjects based on risk factors available (20% at random):
- Previous PET/CSF
- Age
- APOE4 status
- Family history
- etc

AMYPAD PNHS Scan #1

Re-select enrolled participants for follow-up (50%) based on:
- previous info + AMYPAD PNHS scan results
Ongoing recruitment of participants and Parent Cohorts

<table>
<thead>
<tr>
<th>Cohort</th>
<th># participants</th>
<th>Inclusion (expected)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPAD</td>
<td>&gt;1500</td>
<td>October 2018</td>
</tr>
<tr>
<td>EMIF-AD</td>
<td>190</td>
<td>May 2019</td>
</tr>
<tr>
<td>ALFA+</td>
<td>200</td>
<td>November 2019</td>
</tr>
<tr>
<td>F-PACK</td>
<td>180</td>
<td>Q4 2019</td>
</tr>
<tr>
<td>GAP</td>
<td>150</td>
<td>Q1 2020</td>
</tr>
<tr>
<td>FACEHBI</td>
<td>130</td>
<td>Q1 2020</td>
</tr>
<tr>
<td>BIOFINDER</td>
<td>350</td>
<td>Q2 2020</td>
</tr>
<tr>
<td>Others?</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Earlier and etiological diagnosis & improving risk profiling

Early diagnosis (AMYPAD Diagnostic Study)
- Positive and negative predictive value in real-life setting
- Actual change in management
- Cost-effective implementation and reimbursement possibilities

Natural history and risk stratification (AMYPAD Prognostic Study)
- Value of quantitative PET in preclinical/prodromal AD
- Who is at most risk of developing dementia and when can we intervene
- How can we best measure the impact of treatment
Thank you

The project leading to this application has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 115952. This Joint Undertaking receives the support from the European Union’s Horizon 2020 research and innovation programme and EFPIA