Gill Farrar: EFPIA Lead, GE Healthcare, UK

Frederik Barkhof: Academic Lead, VUMC, Netherlands and UCL, UK
Amyloid Imaging to Prevent Alzheimer’s Disease (AMYPAD)

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

Will end Sept 22

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AMYLOID Pathology: Integral to the diagnosis of Alzheimer’s Disease
ADUHELM is indicated for the treatment of Alzheimer’s disease. Indication approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with ADUHELM.
1) Diagnostic Study: Examining influence of amyloid PET scan in diagnosis, confidence and patient management

2) Prognostic Study: Understanding the evolution of amyloid deposition in the brain. Capturing earlier subjects who may be ‘developing’ the pathology
# AMYPAD: Outputs

1) Curated Data and Image Repository (>ADDI Platform)

<table>
<thead>
<tr>
<th>Projected Asset (DPMS)</th>
<th># Data</th>
<th>Projected Asset (PNHS)</th>
<th># Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET Images</td>
<td>900</td>
<td>Unique subject scans (baseline + follow-up)</td>
<td>1046</td>
</tr>
<tr>
<td>Patient Diaries (0,3,6, 13mts)</td>
<td>2600</td>
<td>+ Other cohort scans (baseline+ follow up)</td>
<td>1247</td>
</tr>
<tr>
<td>Clinical evaluations (0,3,6, 13mts)</td>
<td>3200</td>
<td>Total scans</td>
<td>2293</td>
</tr>
</tbody>
</table>

Recruitment status (as 1 June, 2021)

- **844** Diagnostic Study
- **1,001** Prognostic Study
## 2) Network of Study Cohorts, Investigators & Collaborators

<table>
<thead>
<tr>
<th>Site</th>
<th>Site Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>010</td>
<td>UEDIN, Edinburgh</td>
</tr>
<tr>
<td>020</td>
<td>CHUT, Toulouse</td>
</tr>
<tr>
<td>030</td>
<td>BBRC, Barcelona</td>
</tr>
<tr>
<td>040</td>
<td>VUmc, Amsterdam</td>
</tr>
<tr>
<td>060</td>
<td>UNIGE, Geneva</td>
</tr>
<tr>
<td>050</td>
<td>KI, Stockholm</td>
</tr>
<tr>
<td>015</td>
<td>Tayside, Scotland</td>
</tr>
<tr>
<td>021</td>
<td>Nantes, France</td>
</tr>
<tr>
<td>022</td>
<td>Lille, France</td>
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<tr>
<td>023</td>
<td>Paris Nord, France</td>
</tr>
<tr>
<td>024</td>
<td>Montpellier, France</td>
</tr>
<tr>
<td>025</td>
<td>Paris la Pitié, France</td>
</tr>
<tr>
<td>031</td>
<td>CITA, San Sebastien, Spain</td>
</tr>
<tr>
<td>032</td>
<td>Fundació ACE, Barcelona</td>
</tr>
<tr>
<td>041</td>
<td>UZ Leuven, Belgium</td>
</tr>
<tr>
<td>043</td>
<td>UC Louvain, Belgium</td>
</tr>
<tr>
<td>051</td>
<td>UGOT, Gothenburg, Sweden</td>
</tr>
</tbody>
</table>

Inclusion of additional cohorts

DELCODE
FPACK
FACEHBI

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3) Diagnostic Study: Design endorsed by European Medicines Agency (EMA)
4) Health Economic (cost:benefit) data from Diagnostic Study (DPMS)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 Months</th>
<th>6 Months</th>
<th>13 Months</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collected Diaries</td>
<td>705</td>
<td>660</td>
<td>635</td>
<td>600</td>
<td>2600</td>
</tr>
</tbody>
</table>

Example questions include....

A1.2 Participant health care resource utilization
1. During the last 30 days, have you been admitted to a hospital for one or more nights?
   - Yes
   - No, go to question 4

2. How many times were you admitted to a hospital (for one or more nights)?
   _____ times, during the last 30 days

Each diary has approx. 40 data points

16. During the last 30 days, how many times did you receive care from a health care provider outside a hospital? Please specify the number of visits for each type of care received:

<table>
<thead>
<tr>
<th>Type of care</th>
<th>Number of visits during last 30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>General practitioner</td>
<td></td>
</tr>
<tr>
<td>Geriatrician</td>
<td></td>
</tr>
<tr>
<td>Practice nurse</td>
<td></td>
</tr>
</tbody>
</table>

19. Please specify the medications you are using:

<table>
<thead>
<tr>
<th>Name of medication</th>
<th>Strength</th>
<th>Frequency</th>
<th>Number of days taken over last 30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Example: Aspirin</td>
<td>500 mg</td>
<td>2 times a day</td>
<td>10 days</td>
</tr>
</tbody>
</table>
5) AMYPAD Studies: Early Results

1) Diagnostic Study

2) Prognostic Study:
6) Quantitation of brain amyloid: Discussion/interaction with EMA

Critical Assessment of Current Quantitative Methodologies

- Baseline
- Longitudinal
- Dynamic/Static scans
- Research participants
- Clinical patient subtypes

Amyloid Burden measured by the ‘Centiloid’ Unit
7) NiftyPET Software Platform

NiftyPET: High-throughput image reconstruction and analysis

NiftyPET is a software platform and a Python namespace package encompassing sub-packages for high-throughput PET image reconstruction, manipulation, processing and analysis with high quantitative accuracy and precision. One of its key applications is brain imaging in dementia.

https://niftypet.readthedocs.io

NiftyPET Example
Accessing and querying GPU devices
DICOM anonymisation
List-mode processing and motion detection
Basic PET image reconstruction
Dynamic image reconstruction
Corrections for quantitative PET

OPEN-SOURCE DATA
Raw brain PET data

c/o Pawel Markiewicz
p.markiewicz@ucl.ac.uk

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8) High quality publications in top-tier journals

Multitracer model for staging cortical amyloid deposition using PET imaging (2020)
Lyduine Collij & Fiona Heeman et al

https://amypad.eu/ managed by
Sustainability for the Future

9) AMYPAD will join the Gates Ventures funded ADDI workbench (+ aim to follow up via NEURONET)

About ADDI

The Alzheimer’s Disease Data Initiative (ADDI), a 501(c)(3) medical research organization (MRO), is dedicated to advancing scientific breakthroughs in the treatment of Alzheimer’s disease and related dementias.
And finally for AMYPAD:
😊 Talent Incubator 😊

- Understand the causes underlying discordance between PET and CSF markers of amyloid pathology
- Apply advanced statistical approaches to model biomarker discordance as a continuous feature, avoiding cut-off dependent inferences

Arianna Sala

- Set-up and management of both the AMYPAD DPMS/PNHS in Toulouse + other French centers

David Vallez Garcia

- Optimizing visual assessment of amyloid PET images
- Investigate the value of regional and quantitative amyloid PET measures within the context of the natural history of AD.

Lyduine Collij

- Define and implement optimal methodology for acquisition and analysis of dynamic PET data
- Analyses of all dynamic PET scans

Fiona Heeman

- Analyses of the AMYPAD-DPMS data
- Assessment of the utility of amyloid-PET in clinical practice

Daniele Altomare

- Improvement of the standardization of amyloid PET quantification
- Analyses of amyloid PET data from external cohorts

Gemma Blasco

- Set-up and management of a multi-center multi-national natural history study across 17 sites
- Scientific coordination of the disease modelling team and its scientific publications

Isadora Lopes Alves

- Data manager of AMYPAD-PNHS
- Senior researcher focused on quantitative PET methodology

Laure Saint-Aubert

- Analyses of amyloid PET data
- Methodological aspects of amyloid PET image quantification

Mahnaz Shekari

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