AMYPAD

Amyloid Imaging to Prevent Alzheimer's Disease

In 5 years time….we want to have:

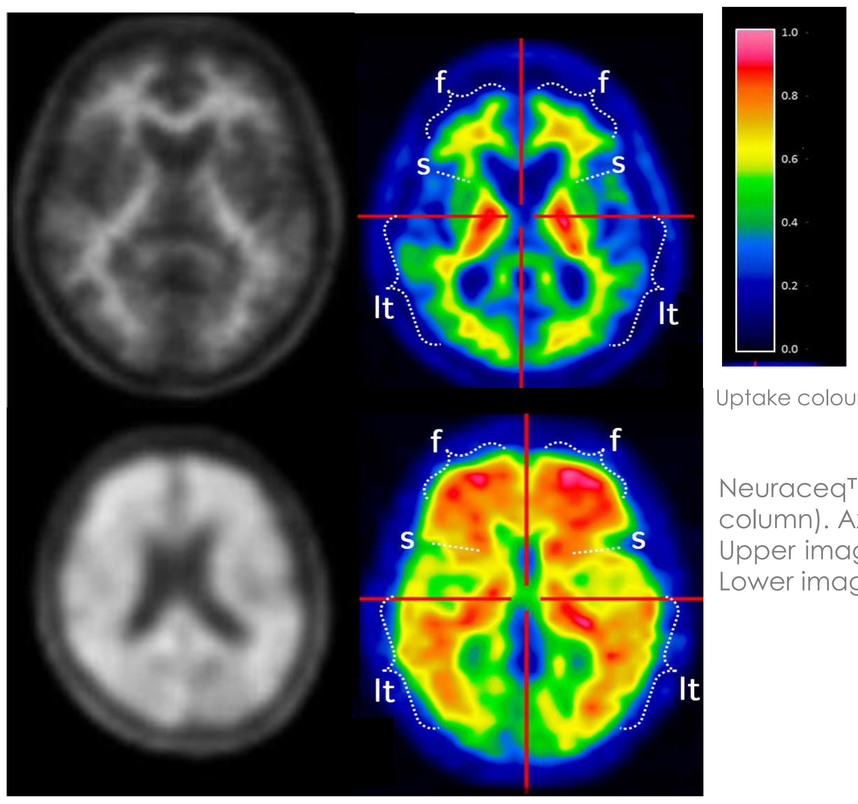
- demonstrated the value of amyloid imaging as a diagnostic marker for AD.
- determined the value of quantitative analysis of amyloid PET for selecting and following subjects in AD intervention trials
- determined the most sensitive methods of acquisition and analysis for longitudinal quantitative amyloid PET

^{18}F-amyloid PET imaging agents:

- Neuraceq™ /[^{18}F]florbetaben (Piramal)
- Vizamyl™ /[^{18}F]flutemetamol (GE Healthcare)

2 studies, 6000 doses:

- ~8 Clinical Partners + 12 affiliates
- ~20 PET centres in total
- ~200 subjects per site
- 4000 scans @t=0, 2000 scans @t=2yrs



Uptake colour map

Neuraceq™ (left column) and Vizamyl™ (right column). Axial images.
Upper images depict amyloid negative scans, Lower images depict amyloid positive scans.

Delivery by Work Packages

WP1	WP2	WP3	WP4	WP5	WP6
Overall project governance and management	Tracer delivery, PET scanning and Image analysis	Diagnostic and Patient Management Study (n=900)	Risk stratification: Natural history and enrichment strategies	Monitoring treatment: Quantifying patient-specific efficacy	Ethics, communication and dissemination
Carlos Díaz (SYNAPSE) Gill Farrar (GE)	Juan Domingo Gispert (BBRC) Chris Foley (GE)	Giovanni Battista Frisoni (UNIGE) Andrew Stephens (Piramal)	Craig Ritchie (UEDIN) Serge Van der Geyten (JPNV)	Frederik Barkhof (VUmc) Mark Schmidt (JPNV)	Jean Georges (AE) Anja Mett (GE)
• Project governance and management structure, in alignment with EPAD (European Prevention of Alzheimers Disease) • Work plan integration and monitoring • Reporting, financial and legal management • Risk management **CHALLENGES** • Balanced Interaction with EPAD • Managing large scale initiative with multiple partners • Facilitation between work packages	• Tracer distribution strategy and site selection • Management of tracer production (GMP) and effective batch delivery • Site qualification and scan protocols and imaging manuals • Determine standardized methods of image analysis for scans across tracers • Refinement of amyloid quantification methods • Biological factors affecting amyloid load (incl. demographics, lifestyle, diet) • Image transfer, storage, QC and quantification. Data reconciliation with EPAD • Data sharing and dissemination Leverage EPAD, informatics platform **CHALLENGES** • Optimal tracer batch utilisation: 5 subjects per batch • SUVr stability over longitudinal timepoints • Ensuring image quality and transfer across large imaging network • Raw and processed data storage and synchronization • ROI and reference region selection • Reconstruction, PVC, motion correction etc	• Prospective Amyloid PET Study • Study protocol, health authority buy-in, operations, enrolment, data collection • Impact on patient management • Health economic outcome measures/cost effectiveness • Developing a regulatory pathway for use of amyloid-PET in a diagnostic setting **CHALLENGES** • High burden of admin tasks to initiate study • Sufficient patient recruitment into study • Availability of quality hospital records for health economics analysis	• Add on study to EPAD LCS, selection for repeat imaging • Site selection from the EPAD network • Implementation to collect ≈3100 baseline scans • Relation with other AD markers – understanding confounders • Analysis of other variables for optimal enrichment of trials • Establish trial readiness population to target **CHALLENGES** • Regulatory Authority challenges • Recruitment into EPAD-LCS • Massive data handling and analysis	• Longitudinal modelling of quantitative β-amyloid • Model of longitudinal change/accumulation, thresholds for 2nd scan, • Inclusion of perfusion data + static scan • Advanced disease modelling • Spatio-temporal analysis, brain reserve, atrophy • Planning intervention studies • Developing a regulatory pathway for inclusion of amyloid-PET in the future routine use of approved amyloid targeted therapeutics (incl. reimbursement) **CHALLENGES** • Clear delineation of 'core' and 'advanced' analysis • Regulatory work could involve multiple interactions + many partners	• Report and provide guidance on ethical issues • Communication Plan and Tools • Dissemination, networking and outreach activities • Scientific, review and information sharing • Liaison with external stakeholders of wider dementia community (IMI-AD platform) • Public data access and posting • Evaluation of short- and long-term psychological, behavioural and social consequences of disclosing PET results **CHALLENGES** • Ethics of disclosure: IRB & HA issues Local vs central • 'Core' vs 'advanced' communication outlined • EPAD vs AMYPAD communication clear • Policies for access rights

PARTNERS

Academia

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UNIVERSITÉ DE GENÈVE
UCL
Radboudumc
University of Cologne
Karolinska Institutet
Hôpitaux de Toulouse

EFPIA

janssen PHARMACEUTICAL COMPANIES OF Johnson&Johnson
GE Healthcare
Piramal knowledge action care

Patient Organization

Alzheimer Europe

SMEs

IXICO
SYNAPSE

SUMMARY

AMYPAD aims to complement our current understanding of the relevance of amyloid deposition, and to answer the following key questions with regards to improved patient management and the development of disease modifying drugs:

- **Does amyloid PET imaging have a role in routine patient work-up for cognitive impairment-related management?**
- **How can amyloid PET imaging inform clinicians and drug developers about progression to AD?**
- **Is it advantageous to quantify results for longitudinal comparison, and can clinical trials leverage the analysis with confidence?**

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