Alzheimer Europe's involvement in three novel collaborative initiatives

We present a brief overview of AMYPAD, MOPEAD and ROADMAP, sponsored by Horizon 2020 under the auspices of IMI and EFPIA. The perspectives of both the academic and pharmaceutical partners are presented, regarding the rationale behind the projects and the concrete actions being undertaken

AMYPAD (Amyloid imaging to prevent Alzheimer's disease)

AMYPAD officially started on 1 October 2016 and has a duration of five years. The project has a budget of EUR 27.3 million distributed across a total of 15 partners. The Consortium is led by Stichting VUmc and GE Healthcare Life Sciences (on behalf of EFPIA).

In this project, Alzheimer Europe will co-lead the work package dedicated to ethics, communication and dissemination in close collaboration with GE Healthcare Life Sciences. It will include all communication related-activities as well as a guidance document on ethical issues. Alzheimer Europe is also involved in the overall project governance and management.

Gill Farrar, Project Co-lead

Gill Farrar and Frederik Barkhof, the two main project leaders present the overall vision of AMYPAD

What is the problem you are aiming to address with AMYPAD?

Gill Farrar: AMYPAD will help determine the value of β-amyloid as a diagnostic and therapeutic marker for AD, which represents an untreatable illness estimated to cost society 1% of the global GDP. Since the deposition of β-amyloid is an early and necessary step on the path towards the development of AD, the possibility of assessing levels of β-amyloid *in vivo* by means of Positron Emission Tomography (PET) presents great potential. In fact, it is already recognised that β-amyloid PET can improve early diagnosis and, if recognised in a pre-symptomatic population, has also the potential for secondary prevention in AD.

Currently, great efforts are being undertaken in order to develop effective disease-modifying therapies aimed at lowering β-amyloid burden. However, a more detailed understanding of the sequence of events on the path towards AD is needed, especially for determining the optimal window of opportunity for possible intervention in the β-amyloid pathway. AMYPAD is set out to contribute to these efforts by developing optimal generation and utilisation of β-amyloid PET data. In that process, AMYPAD will improve the chances of 1) detecting specific changes in β-amyloid deposition, and 2) accurately measuring the impact of novel therapies in clinical trials. For that purpose, AMYPAD will be carefully and thoroughly studying a large cohort of subjects from early stages of β-amyloid deposition, providing a unique opportunity to select patients for proof-of-concept treatment trials aiming to reduce, revert, and eventually prevent β-amyloid burden.

What are the concrete objectives and actions which will be undertaken by AMYPAD?

Frederik Barkhof: AMYPAD aims at better understanding the role of β-amyloid for the diagnosis, the patient management, and the current and future therapies targeting β-amyloid deposition. For that purpose, AMYPAD plans to: 1) make early diagnosis more accurate and cost-effective, 2) improve patient selection for clinical trials, and 3) enable proper quantification of the impact of novel therapies, improving the chance of clinical trials to detect specific changes in β-amyloid deposition.

In line with the first goal, AMYPAD will first scan a large population cohort (n=4100) suspected of possible AD at different time points within a diagnostic setup. There, AMYPAD will help determine the value of β-amyloid PET imaging regarding diagnostic confidence, change in diagnosis and/or patient management, and healthcare resource utilisation.

In order to achieve the second goal, AMYPAD will leverage a Europe-wide network in close collaboration with EPAD to study the earliest stages of AD in a longitudinal fashion (n= 1900). In that process, AMYPAD will contribute to building a trial-readiness cohort while improving the understanding of AD pathophysiology. As a result, the natural history of the early stages of AD will be better understood, allowing to determine and explore the optimal window of opportunity for secondary prevention of AD.

Finally, AMYPAD will perform full quantitative analysis of dynamic PET data and go beyond currently applied metrics and towards model disease progression. Therefore, AMYPAD will work towards achieving high quality standards for both acquisition and quantitative analysis of β-amyloid PET data. As a result, the third goal will be met by improving statistical power and minimising technical and biological factors affecting β-amyloid PET measurements.

Frederick Barkhof, Project Coordinator

MOPEAD (Models of Patient Engagement for Alzheimer's disease)

MOPEAD officially started on 1 October 2016 and has a duration of 33 months with a budget of EUR 4.0 million. The Consortium consists of 14 partners and is led by Fundació ACE (FACE) and Eli Lilly & Company Ltd (ELI).

Alzheimer Europe will contribute to this project by providing a guidance document on the ethical implications of the project and will be engaged in the communication and dissemination activities. A special symposium will be organised in October 2018 at Alzheimer Europe's Annual Conference to present the outcomes and recommendations developed in the project.

Laura Campo and Mercè Boada who are leading the project present the idea behind MOPEAD

What is the problem you are aiming to address with MOPEAD?

Laura Campo The clinical paradigm for Alzheimer's disease (AD) largely engages patients in the later clinical stages of disease, with the majority of patients and their caregivers not seeking and/or receiving care until moderate or severe dementia has ensued. This approach does not support or emphasize the need for early detection, diagnosis or action when symptoms of AD first begin. To compound the issue, many physicians are reluctant to provide a diagnosis, because they perceive AD as an incurable disease without adequate treatment and supports.

This lack of urgency compromises the quality of patient care and also robs patients of access to available support resources and services. The field must shift to greater public awareness of the importance of an early diagnosis and improved medical efficiency in identifying AD as soon as clinical symptoms emerge.

Not only could these efforts improve clinical access to treatment and support resources and patient engagement earlier in the stages of disease, but they would also help widen the funnel for clinical trial recruitment and earlier treatment development.

The magnitude and complexity of the issue is such that it can only be addressed by a major public-private-partnership involving a variety of stakeholders. This is a programme that cannot be accomplished by an individual research group or company, and will require a strong collaborative effort to be successful. This effort can only be achieved through a consortium of industry, academia, practitioners, advocacy groups, and other committed stakeholders who are willing to test new solutions.

Ultimately, MOPEAD will respond to the urgency of finding interventions to halt AD by stimulating a faster recruitment of patients into clinical trials.

Laura Campo, Project Leader

Mercè Boada, Project Coordinator

What are the objectives and actions taken when implementing the MOPEAD project?

Mercè Boada: In Alzheimer's disease (AD), it has been shown that patient involvement and engagement improves the accuracy of diagnosis and care. Yet one of the main causes of delayed AD diagnosis is the lack of awareness in the general population of how cognitive decline is manifested. The MOPEAD objective is to clarify the meaning of cognitive decline and to raise awareness of the early signs and symptoms of AD. MOPEAD aims to identify efficient approaches for early diagnosis by comparing different models of patient engagement (Runs) across Europe.

In order to achieve the latter, MOPEAD will test, examine and prove the efficiency of four different models of patient engagement within the partnering institutions of the consortium. These four models will be implemented in four different scenarios and will be directed to four different target populations, as described in more detail below.

One of the features of the applied models includes a pre-screening procedure in order to identify the reasons for which the patient will be included in a more extensive neurodegenerative set of tests. Consequently, the patient will undergo an immediate diagnostic process, and as a result, we will be able to offer them important resources: pharmacological and non-pharmacological interventions, experimental medicine (e.g. taking part in clinical trials), and recommendations that would improve their quality of life.

We will try to recreate similar conditions in each one of the scenarios in order to get the most accurate results across five Europeans countries. The process will include recruiting the same number of patients for each of the models, to then include them as part of the process of diagnosis. MOPEAD clinical core has been designed in two stages, pre-screening and diagnosis, working as a funnel-shaped.

The first model, Run1, will consist of a citizen-science based web page, aimed at the general public. Run2 will be conducted by neurologists and neuropsychologists at memory unit offices, and will aim to identify cognitive disorders. The third model, Run3, will be conducted by primary-care physicians who will work to identify vascular risk factors, which are a risk factor for AD. Lastly, Run4 will be conducted by endocrinologists specialised in treating type 2 diabetes, as it represents another of the risk factors to developing AD.

The beneficiaries of this project will not only be the patients, but also healthcare professionals and the public at large. The MOPEAD project works with a true spirit of collaboration and aspiration to bring value to the people living with AD, their loved ones and health care systems

ROADMAP (Real world outcomes across the Alzheimer's disease spectrum for better care: multi-modal data access platform)

ROADMAP officially started on 1 November 2016 and has a duration of two years with a budget of EUR 7.7 million. The consortium consists of 24 partners and is led by the University of Oxford and Novartis (on behalf of EFPIA).

Alzheimer Europe is leading the communication and dissemination activities throughout the project in close cooperation with Eli Lilly. It will also include the perspectives of people with dementia and their carers for the definition of relevant outcomes and on patient attitudes towards the specific platform and data integration proposed by ROADMAP, and contribute to a review on ethical, legal and social issues in the real world evidence.

Frederic de Reydet de Vulpillieres, Project leader and John Gallacher Project coordinator present the overall vision of ROADMAP

What is the problem you are aiming to address with ROADMAP?

Frederic de Reydet de Vulpillieres: Alzheimer's Disease (AD) and related dementias affect nearly 50 million individuals worldwide with prevalence projected to double over the next twenty years. Recent scientific progress indicates the potential for the first round of effective therapies for AD in the near-term. Successfully delivering these therapies to the tens of millions in need will depend on building a sustainable approach that addresses the challenges and opportunities around treatment access at time of approval. In AD this will very much depend on the integration of Real World Evidence (RWE) within health care systems to support evidence for approval as well as Health Technology Assessment and funding allocation. But are health care systems prepared? And what can we do to help be prepared?

AE: What can we do to help be prepared? By 2018, the ROADMAP public private consortium with its 24 EU partners, coordinated by the University of Oxford and Novartis, aims to deliver guiding principles and recommendations on incorporating RWE in healthcare systems. In this manner, the project will help to better inform consensus and decisions in support of better care for people with AD.

What are the concrete objectives and actions which will be undertaken by ROADMAP?

John Gallacher: ROADMAP aims to build a EU-wide database with Real World Evidence (RWE) outcomes for better care. To accomplish this, data will be used from 6 EU Member States involving 75 national databases and clinical registries.

During the project, the partners will involve diverse stakeholders (patients, carers, regulators, HTA bodies, payers, industry and researchers) to identify and prioritise possible outcomes of clinical trials with regard to their individual relevance but also health-economic importance. Using the information from the different cohorts and databases, new and ground laying analyses will be developed and realised.

This will lead to the creation of theoretical disease models of Alzheimer's disease, starting from no evidence of impairment (cognitively healthy), through subjective memory complaint and mild cognitive impairment (MCI) diagnosis, to AD and dementia diagnosis. Using and comparing different models throughout the project's progression, it will be possible to identify biomarkers for the disease which can inform clinical decision making.

In addition, ROADMAP will explore how different treatment pathways affect disease progression in different groups, allowing treatments to be more closely linked to patient response. In order to estimate the overall societal impact of treating dementia, ROADMAP will also model the long-term economic impacts of different disease trajectories and treatment pathways.

Definitive responses to these complex questions cannot be sought within the duration of the project. Therefore, information on the analyses and the stakeholder engagement (with special emphasis on patients, HTA, regulators and payers) will be used to identify data and knowledge gaps. This information will be used to lay the foundation for the development of phase 2 of the ROADMAP initiative for a long-term European based world-leading RWE environment.

Frederic de Reydet de Vulpillieres, Project Leader

John Gallacher, Project Coordinator

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