



Innovative Medicines Initiative

Public-Private Partnerships Boost Alzheimer's Disease Drug Discovery

IMI Official Satellite Symposium
at the 10th International
Conference on Alzheimer's and
Parkinson's Diseases
(AD/PD 2011)

9 March 2011 – Barcelona, Spain





Innovative Medicines Initiative

About the event

This half-day symposium was organised by the Innovative Medicines Initiative (IMI), the largest public-private partnership (PPP) in the health sciences area, to communicate its activities in the area of Alzheimer's disease (AD) research and development (R&D) in the context of European-funded research and similar initiatives in the United States. The symposium was attended by approximately 75 delegates.

Keywords

- Biomarkers and their qualification
- The importance of pre-symptomatic diagnosis of AD
- Personalised treatments
- The key role of patients
- The need for novel collaborative research models including all stakeholders to boost Alzheimer's disease drug discovery.

Setting the scene

The symposium started with a talk by **Professor Rivka Ravid** (Brain Bank Consultants, Dutch Royal Academy of Sciences, Amsterdam, the Netherlands) on the importance of the harmonisation of brain banks' standard operating procedures in the discovery of novel candidate biomarkers for Alzheimer's disease (AD).

Human specimens supplied by brain/tissue/bio (BTB) banks are a rich source of adequately collected and preserved specimens of the human body in health and disease. These specimens form an essential bridge between the clinic, basic science, post-mortem tissue banks and industry resulting in translational medicine and research. It is crucial to build the bridge between population banks, clinical banks and post-mortem banks to ensure the flow of clinical /genetic information available at the population banks to the post-mortem banks and create a global database.

This database should be accessible to the international scientific community. This is critical to create the roadmap for understanding the pathology of disease and identifying valid biomarkers. It is clear that the 'signatures' generated from anatomical, imaging and biochemical biomarkers are the most powerful tools, with the caveat that it is the neuropathological findings that decide the final diagnosis.

The activities of brain banks are multidisciplinary and have to tackle several scientific, legal and policy, and logistics issues. To be successful, brain-banking must adhere to the following 7 'Gold Standards':

1. a well-established local donor system;
2. rapid autopsies;





Innovative Medicines Initiative

3. compatibility of protocols;
4. a generally accepted consensus on the clinical and neuropathological diagnostic criteria ;
5. quality control of the disseminated samples;
6. adhering to internationally accepted guidelines for ethical and legal aspects;
7. monitoring of proper safety procedures.

In addition, they must be adequately funded and there needs to be integration of national and international efforts.

Professor Mony de Leon (New York University School of Medicine, New York, US) presented evidence that imaging (FDG-PET and high resolution MRI) is a powerful tool for detecting AD in its pre-symptomatic stages. However, while imaging biomarkers show sensitivity for early features of AD at both normal and mild cognitive impairment (MCI) stages of cognition and show good correlation with clinical progression, these measures are neither diagnostically nor pathologically specific for AD.

AD specific biomarkers are for example cerebro-spinal fluid (CSF) measures of hyperphosphorylated (P) P-tau, and CSF and positron emission tomography (PET) measurements of amyloid beta (AB). However, AD-specific biomarkers lack sensitivity and do not show useful progression effects. A combination of both sensitive (imaging) and specific biochemical markers is the most useful approach for advanced diagnosis at pre-symptomatic stages of AD.

A key objective for imaging and biomarkers is the identification of mechanisms explaining AD risk in pre-symptomatic subjects. Knowledge to this end is starting to be generated and will be of very high value in the light of developing a personalised medicine approach to AD.

Longitudinal studies suggest two candidate mechanisms. Firstly, pre-symptomatic subjects with a maternal history of AD show reduced glucose metabolism that progresses longitudinally, as well as excess brain amyloid deposits. This suggests an inheritance of mitochondrial DNA mutations.

Secondly, magnetic resonance imaging arterial spin labelling (MRI-ASL) shows that normal elderly people with elevated plasma AB40 levels show impaired CO₂-induced vasodilation of hippocampal blood vessels. This impaired reactivity suggests an AB-related vasoconstriction. Validation studies are underway.

New European Research Models to Boost Progress in AD Research

After these introductory talks, **Elisabetta Vaudano** (IMI, Brussels, Belgium) presented the mission and objectives of IMI. IMI is Europe's largest initiative to boost pharmaceutical innovation in Europe and aims to speed up the development of better and safer medicines for patients. IMI has a budget of





Innovative Medicines Initiative

€2 billion; €1 billion comes from the European Commission's Seventh Framework Programme (FP7), and this is matched by mainly in kind contributions worth at least another €1 billion from member companies of the European Federation of Pharmaceutical Industries and Associations (EFPIA).

Ejner K. Moltzen (H. Lundbeck, Copenhagen, Denmark) presented the reasons for the engagement of industry as a partner in IMI. The pharmaceutical industry is under enormous pressure for its future, in a health care environment that is undergoing significant changes and is becoming more and more challenging. This is particularly the case for CNS R&D where innovation is hampered by the lack of a proper understanding of disease biology, which is necessary to develop biomarkers for identification of sub-group specific end-points and new drug targets.

What is needed is research able to create the link between the patient (the clinical world) and drug discovery (the molecular world) via an approach of forward and back translation. To achieve this, collaboration among all stakeholders is mandatory. Industry is enthusiastic about IMI because it aims to tackle issues of fundamental industry interest.

The **European Commission** (Directorate-General for Research and Innovation) provided a presentation on the support provided to research on the brain and in particular on neurodegeneration. A significant budget from the FP7 Health programme has been allocated to neurodegeneration, with support available to different types of initiatives. The most recent initiative is the Joint Programming of Research Activities in the field of Neurodegenerative Diseases, which aims to support the direct engagement of the Member States in this important area of research.

PharmaCog: Tackling the bottlenecks in AD drug discovery

The symposium continued with a session featuring presentations from representatives of the IMI PharmaCog Project: **Alexandra Auffret**, PharmaCog Project Manager (University of Marseille, France), **Michael O'Neil**, PharmaCog work package leader (Eli Lilly, UK) and **Jean Georges**, PharmaCog work package leader (Alzheimer Europe, Luxembourg).

The speakers presented the scientific approach being taken by PharmaCog investigators and explained how this initiative differs from other ongoing research activities and how this will provide direct benefit to Alzheimer's patients in Europe.

Despite the increase in translational medicine activities in recent years, there is a lack of agreement regarding the predictive value of behavioural, neuroimaging, and electrophysiological markers to be used for AD drug discovery, and the number of successful new drugs reaching patients is still very low.

The launch of the five year €20 million PharmaCog project funded through IMI marks the beginning of the most ambitious European project aimed at





Innovative Medicines Initiative

improving the success rate in AD drug discovery. This ambitious project brings together leading scientists from 30 organisations comprising public institutions, corporate partners as well as the patients' association Alzheimer Europe. PharmaCog will also work closely with the European Medicines Agency (EMA), as an associate partner of this project, to share project progress and discuss the implications for drug development in Europe.

This is a truly unique opportunity bringing together world leaders with a diverse range of expertise and experience to work together to improve our ability to assess the potential clinical value of a new drug candidate. It is anticipated that such a concerted effort will minimise the risk of progression of unsuitable compounds and accelerate the development of promising new medicines for AD.

Getting the broad picture: from Europe, to US and beyond

The symposium was concluded by **Dr Marc Cantillon**, Executive Director of the Coalition Against Major Diseases (CAMD) of the Critical Path Institute (C-Path). C-Path is an independent, non-profit institute, unaffiliated with any single entity or interest group, which was created in 2005 by the University of Arizona and the US Food and Drug Administration (FDA).

As a neutral party, C-Path is uniquely positioned to establish an overarching framework for collaboration between stakeholders to foster the development of new evaluation tools to inform medical product development. The objective is to develop a scientific consensus on which methods are 'qualified for use' in drug development among those who will use the methods (industry), and those who will accept the methods (the regulatory authorities).

To foster these developments, C-Path has currently five initiatives running, one of which is the CAMD. In neurodegenerative conditions such as AD and Parkinson's disease, predictive biomarkers are needed for early identification, at the pre-symptomatic stage, to allow for early intervention. The development of diagnostic tools with high specificity will increase the likelihood of successful intervention and pave the way to shorter clinical studies with smaller sample size and more uniform patient populations. This will decrease the costs and duration of drug development, and increase the chances for novel effective and safe drugs to benefit patients.

Conclusions

The symposium was perceived by all delegates as a very welcome opportunity to learn more about the progress of PPP initiatives, and IMI in particular, in the area of Alzheimer's disease drug research and development.

It was also an opportunity for raising some key issues.





Innovative Medicines Initiative

- If real progress is to be achieved, the patient's perspective has to be integrated in the drug discovery and development process.
- The tasks to be undertaken to overcome the hurdles hampering AD drug discovery are such that they can only be tackled by a joint collaborative effort between all public and private stakeholders working together pre-competitively and openly.
- Currently, efforts of this kind are still fragmented geographically. Since Alzheimer's disease is a global issue it is necessary to find ways to make these initiatives global as well.
- In order to achieve maximal impact and long-term value, ways have to be found to ensure the standardisation and harmonisation of data between initiatives, and their long-term sustainability.

Useful links and references

IMI: www.imi.europa.eu

PharmaCog: www.pharmacog.org

Alzheimer's Europe: www.alzheimer-europe.org

C-Path: www.c-path.org

CAMD: www.c-path.org/CAMD.cfm

AD/PD 2011: <http://www2.kenes.com/adpd2011/Pages/Home.aspx>

Goldman, M. (2011) Reflections on the Innovative Medicines Initiative, Nat. Rev. Drug Discov. 10 (5): 321-2. DOI: 10.1038/nrd3434.

<http://www.nature.com/nrd/journal/v10/n5/full/nrd3434.html>

Presentations

All presentations given at the event can be downloaded from the IMI website at:

<http://www.imi.europa.eu/events/2011/04/14/imi-symposium-alzheimer's-disease-drug-discovery>

Contact IMI

Postal mail: IMI JU, TO 56, Office 6/5, 1049 Brussels, Belgium

Visiting address: Avenue de la Toison d'Or, 56-60, 1060 Brussels, Belgium

Tel: +32 (0)2-221 81 81

Fax: +32 (0)2-221 81 74

E-mail: infodesk@imi.europa.eu

Website: www.imi.europa.eu

