EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

CPAD's 2018 Annual Meeting

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Discuss the need to create global consortia like CAMD

In the US, and EU the cost has been estimated at $225 billion per year and is expected to rise to $1 trillion by 2050.

The lack of sensitive measures to detect decline or a slowing of decline in the early stages of disease, and inadequate clinical trials infrastructure to identify.

Identifying the appropriate study subjects and defining the critical window for preventing AD and has also proved difficult, particularly since different treatments that target different pathological manifestations of the disease may have different critical windows.

Comment on EMA's Efforts to Advance Alzheimer's Disease Guidelines for Clinical Trials.

Increased alignment between FDA, EMA, PMDA , Health Canada and industry sponsors on the use of biomarkers and cognitive measures in prevention studies: AD Data sharing exercise.

Creation of New AD guidelines by the CHMP.

As success in the Qualification of novel methodologies since inception, major milestones for CPAD include;

A qualification opinion granted by the European Medicines Agency (EMA) for the use of low-baseline hippocampal volume (HV) for patient enrichment in pre-dementia trials (2011)

Development and publication of the first Clinical Data Interchange Standards Consortium (CDISC) therapeutic area user guide for AD (v1.0 in 2011; v2.0 update in 2013) in partnership with CDISC.

The first drug-disease trial model and clinical trial simulation tool endorsed by the U.S. Food and Drug Administration (FDA) and qualified by the EMA for mild and moderate AD (2013)

Recognition of the consortium, in FDA Letters of Support encouraging the further study and use of cerebrospinal fluid (CSF) analytes $A\beta_{1-42}$, Total-Tau, Phospho-Tau, and low-baseline HV, measured by magnetic resonance imaging (MRI), as exploratory prognostic biomarkers for enrichment in AD trials (2015)

EMA Letter of Support encouraging industry sponsors to share the patient-level data from completed phase II and III clinical trials, including active and control arms, with CPAD, allowing CPAD to complete development and validation of a proposed quantitative novel methodology in drug development and encouraging dissemination and access to the current version of the CPAD model for implementation by sponsors actively designing clinical trials in amnestic Mild Cognitive Impairment.

In addition, CPAD recently added four datasets, to the Critical Path Institute Online Data Repository (CODR): Critical Path for Alzheimer's Disease (CPAD) Consortium Database.

The challenges ahead

Prevention trials face multiple challenges due to the high degree of heterogeneity among individuals with dementia.

The lack of sensitive measures to detect decline or a slowing of decline in the early stages of disease, and inadequate clinical trials infrastructure to identify earlier populations.

Recruit, and retain sufficient numbers of participants to carry out long duration and lengthy trials.

The challenges ahead

Identifying the appropriate study subjects and defining the critical window for preventing AD and has also proved difficult.

Particularly since different treatments that target different pathological manifestations of the disease may have different critical windows.

Thus, treatment with drugs with different mechanism of actions at different stages of AD will be need it.

What efficacy end points will need cognition, function, ADL.

How long patients need to be treated it in different states of the AD disease.

What biomarkers will be relevant for showing efficacy.

What biomarkers will be relevant for safety.

The challenges ahead

A major limitation is that studies done on research cohorts or in specific geographical areas may not be generalizable to the entire population.

In addition, patients and caregivers may be reluctant to join prevention studies in the absence of a proven treatment that slows progression of the disease.

Nonetheless, the impact of AD on individuals, families, the public health, and the financial health of governments worldwide demands and international collaborative response.

Comment on recent workshop "EMA Regulatory Science to 2025" and how trends for future are applicable to the work CPAD is undertaking.

The five key goals of the strategy include:

- catalysing the integration of science and technology in medicine development;

- driving collaborative evidence generation - improving the scientific quality of evaluations;

Comment on recent workshop "EMA Regulatory Science to 2025" and how trends for future are applicable to the work CPAD is undertaking.

- advancing patient-centred access to medicines in partnership with healthcare systems;
- addressing emerging health threats and availability/therapeutic challenges;
- enabling and leveraging research and innovation in regulatory science.

EMA guidance for companies requesting SA or PA

http://www.emea.europa.eu/pdfs/human/sciadvice/426001en.pdf

Qualification of novel methodologies for drug developments

http://www.emea.europa.eu/pdfs/human/biomarkers/7289408en.pdf

Scientific guidelines

Http://www.emea.europa.eu/htms/human/humanguidelines/background.htm