



Innovative Medicines Initiative

Coalition Against Major Diseases

*Regulatory Science can Accelerate Drug
Development for Neurodegeneration*

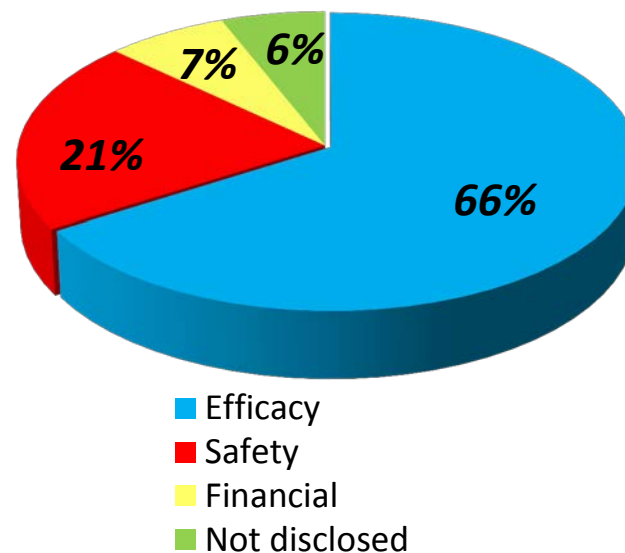
Diane Stephenson, PhD
Executive Director, CAMD
Critical Path Institute

Collaborating for Cures – March 7, 2013- Brussels

After recent AD Phase III failures... What's next?



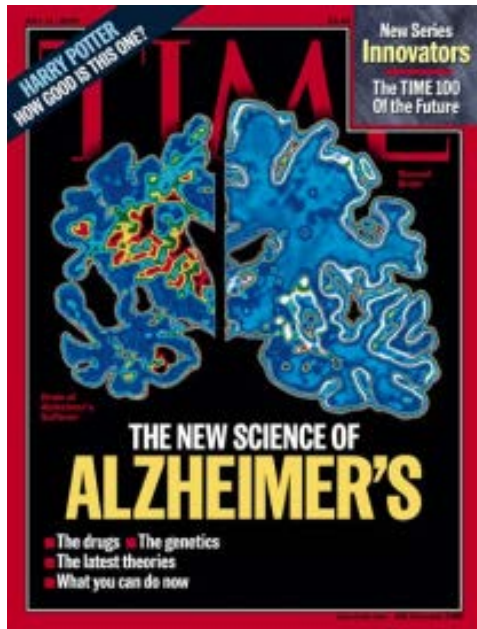
Reasons for Phase III & Submission Failures: 2007-2010



Arrowsmith J. *Nature Reviews Drug Discovery* Feb 2011

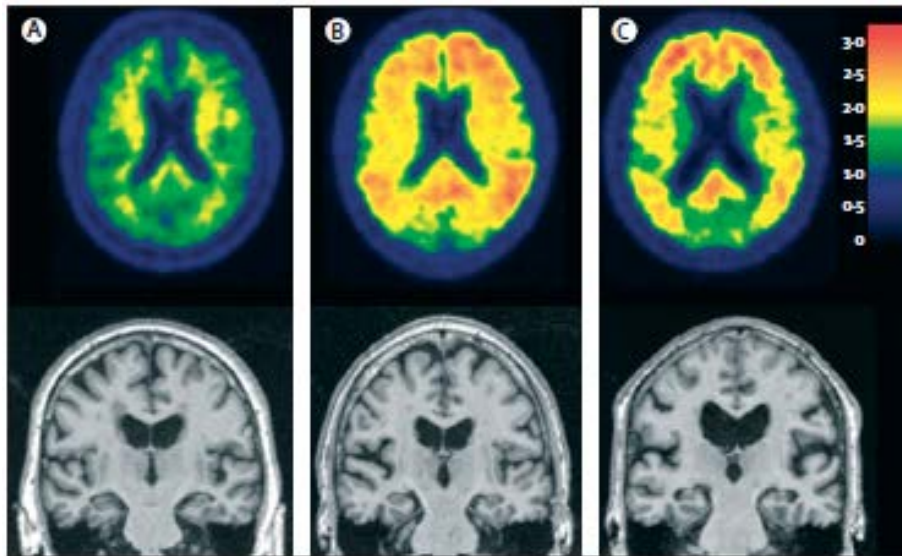
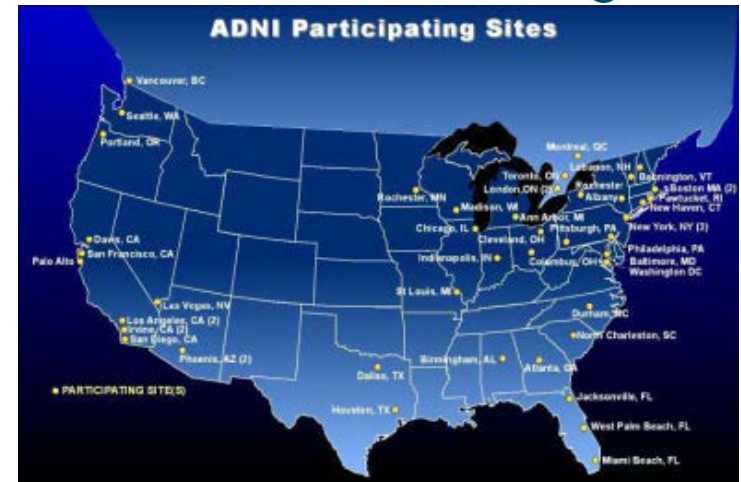
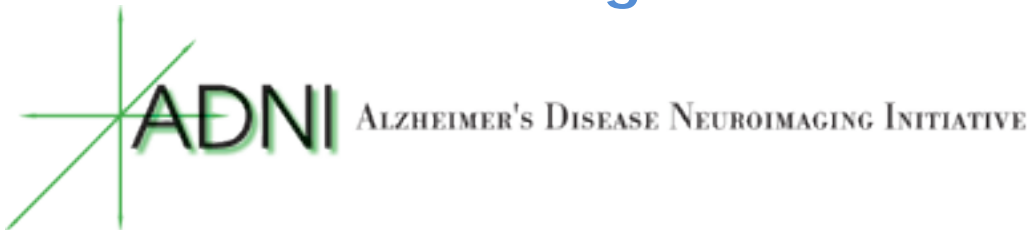
The Solution...Collaborations

that enable



- Sharing knowledge
- Learning from failures
- Public-Private Partnerships

Our Knowledge of Alzheimer's
Disease has been
Transformed through PPPs



- ADNI provided seminal new information concerning the pathophysiology of AD
- Defined early detection methods for Identification of risk
- Improved treatment trials for assessing predictors and outcomes
- Accelerated a path leading to the treatment and prevention of AD

Biomarker staging of AD

CAMD

The mission of CAMD is to advance innovative tools and technologies through a regulatory path that accelerates development of medical products for brain diseases.

Firsts:

- **Therapeutic Area clinical data standards published by CDISC (AD and PD)**
- **Unified CDISC database of Alzheimer's disease clinical trial information provided by multiple pharmaceutical companies**
- **Clinical trial modeling and simulation tool advanced for a regulatory decision**
- **Neuroimaging biomarker for Alzheimer's Disease qualified by a regulatory agency (EMA)**

CAMD: Tools to Advance Effective Treatments for Alzheimer's and Parkinson's Disease



Government/Regulatory participants



EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

FDA

National Institute on Aging ■ ♦ ★ *

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Industry members



Abbott
A Promise for Life

AstraZeneca

Bristol-Myers Squibb

Eisai

Forest Laboratories, Inc.

Genentech
A Member of the Roche Group

Takeda

GE Healthcare

Boehringer Ingelheim

gsk
GlaxoSmithKline

Johnson & Johnson

Lilly

NOVARTIS

MERCK

ORION
BUILDING WELL-BEING

Pfizer

Roche

SANOFI

TEVA

Non-profit research members



Alliance
FOR AGING RESEARCH

alzheimer's
association

CAFA
ALZHEIMER'S FOUNDATION OF AMERICA

FOX
THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

NATIONAL HEALTH COUNCIL

US Against Alzheimer's
we can stop it by 2020.

Nonmember participants: Academic key opinion leaders, CROs



First CDISC Therapeutic Area Data Standard



COALITION AGAINST MAJOR DISEASES



Alzheimer's Disease-specific Therapeutic Area Supplement to the Study Data Tabulation Model User Guide

Prepared by the
Coalition Against Major Diseases (CAMD)

http://www.cdisc.org/stuff/contentmgr/files/0/464c32d97e58d1e0640c77ab2809f0ef/misc/sdtmug_alzheimer__s_2011_09_23_final_revised.pdf

Published Sept 2011



efpia



- **Nine companies remapped and pooled data from 24 trials for ~6500 patients**
- **Database open to >200 qualified research teams in 35 countries**



Data and Modeling & Simulation tools

A	C	D
1 Study #	MMSE	ADAS-cog
2		
3		
4		
5		
6		
7		

A	B
1 Study Number	Visit Num
2	
3	
4	
5	

A	C	D
1 Study Number	MMSE	ADAS-cog
2		
3		
4		
5		

A	B	C	D
1 Study Number	Visit Number	ADAS-cog	MMSE
2			
3			
4			
5			

Mixed Legacy Data



Data Standards

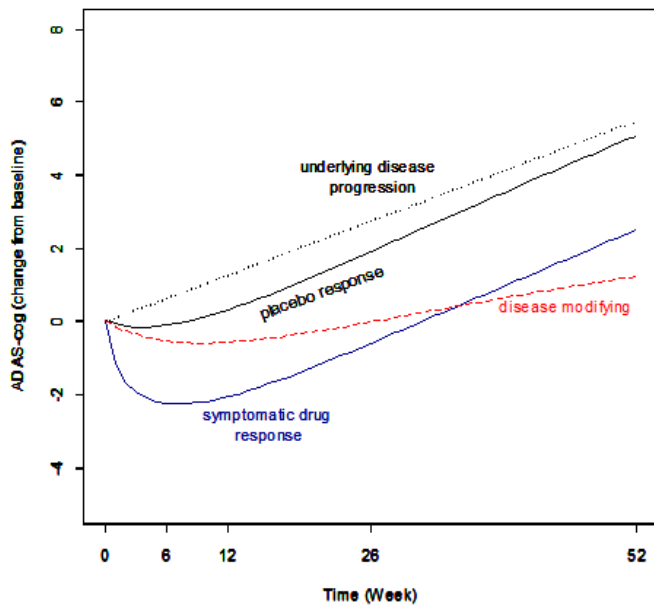


A	B	C	D
1 Study Number	Visit Number	MMSE	ADAS-cog
2			
3			
4			
5			

A	B	C	D
1 Study Number	Visit Number	MMSE	ADAS-cog
2			
3			
4			
5			

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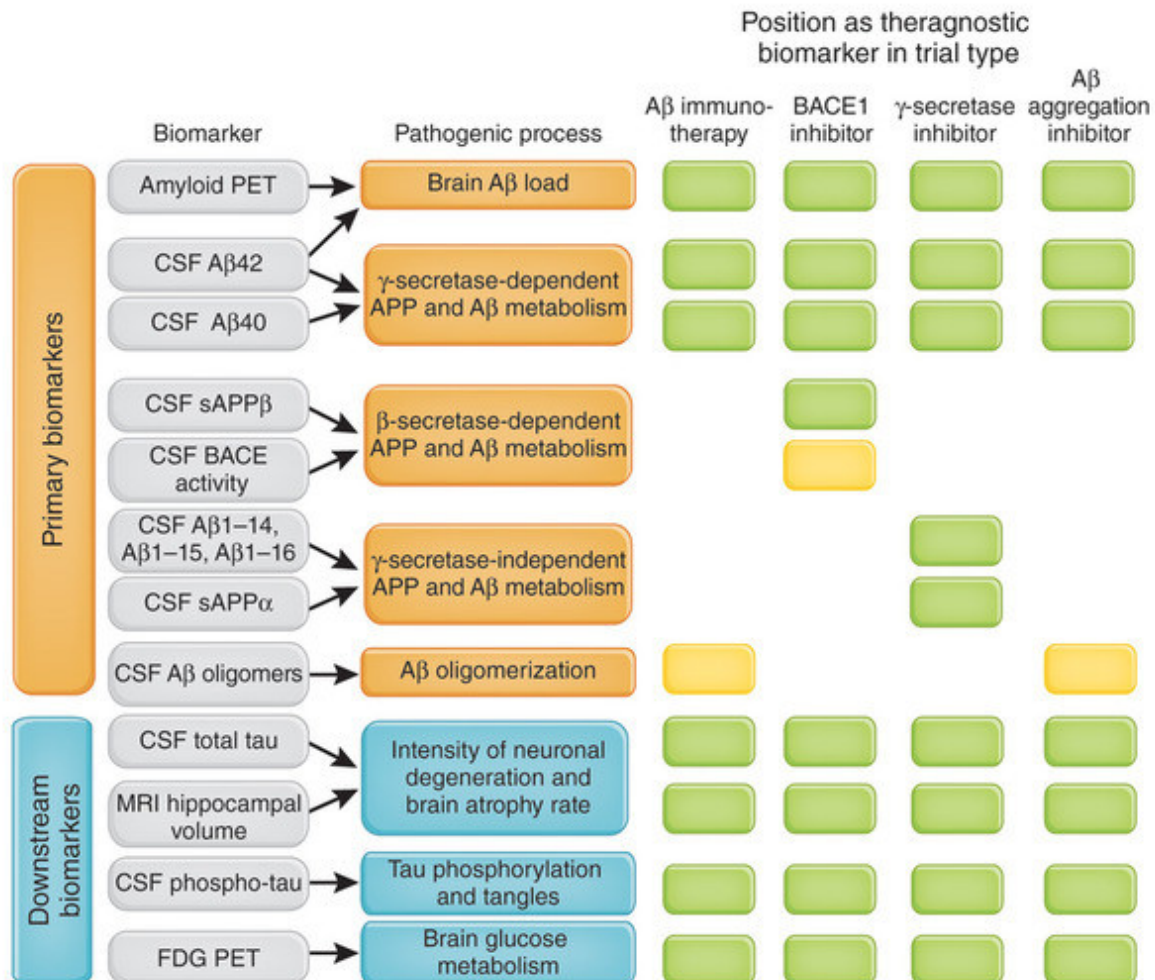
Integrated Data



Deterioration ↑

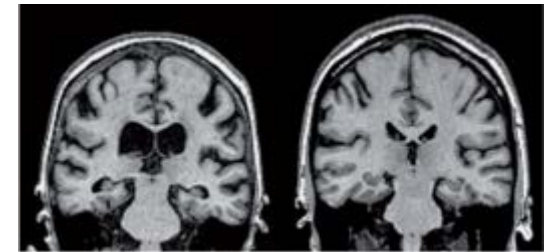


Biomarkers are being actively employed in AD therapeutic trials



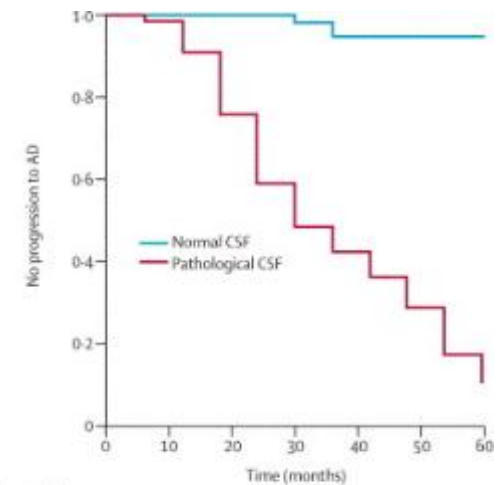
Biomarkers for Choosing the Right Patients

Baseline hippocampal volume



Jack et al, Brain 33:3336-48, 2010

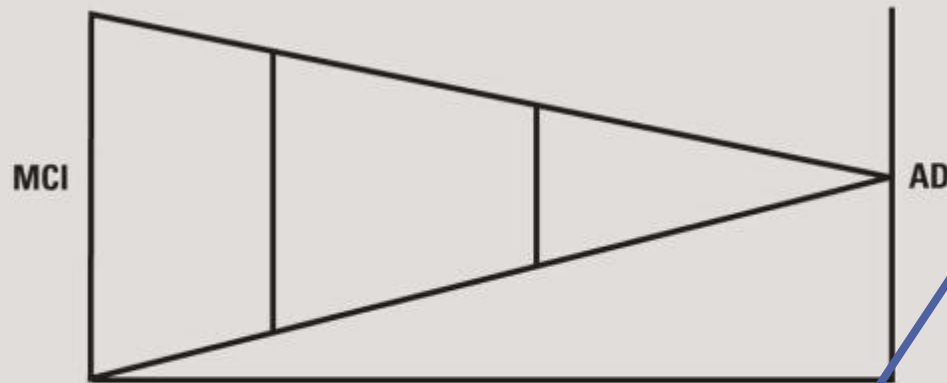
CSF biomarkers



	0	10	20	30	40	50	60
Numbers at risk							
Total	134	131	111	87	74	55	31
Normal CSF	67	66	62	56	47	40	28
Pathological CSF	67	65	49	31	27	15	3

SLIDE 3

Conceptual Model Depicting the Approach to Earlier Alzheimer's Disease Diagnosis



Clinical Factors

Episodic memory
Vascular risk factors
Depression

Biomarkers

ApoE4 status
Structural imaging
CSF A β /tau/phosphotau
Functional imaging

MCI=mild cognitive impairment; AD=Alzheimer's disease; ApoE4=apolipoprotein E4; CSF=cerebrospinal fluid; A β =amyloid β .





CRITICAL PATH
INSTITUTE

Neuroimaging as a drug development tool for patient enrichment



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

- 1 10 October 2011
- 2 EMA/CHMP/SAWP/809208/2011
- 3 Committee for Medicinal Products for Human Use (CHMP)

- 4 Qualification opinion of low hippocampal volume
- 5 (atrophy) by MRI for use in regulatory clinical trials - in
- 6 pre-dementia stage of Alzheimer's disease
- 7

Agreed by Scientific Advice Working Party	1 September 2011
Adoption by CHMP for release for consultation	22 September 2011
End of consultation (deadline for comments)	1 November 2011

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CAMD Aligns with Relevant PPPs



Public-Private Partnerships



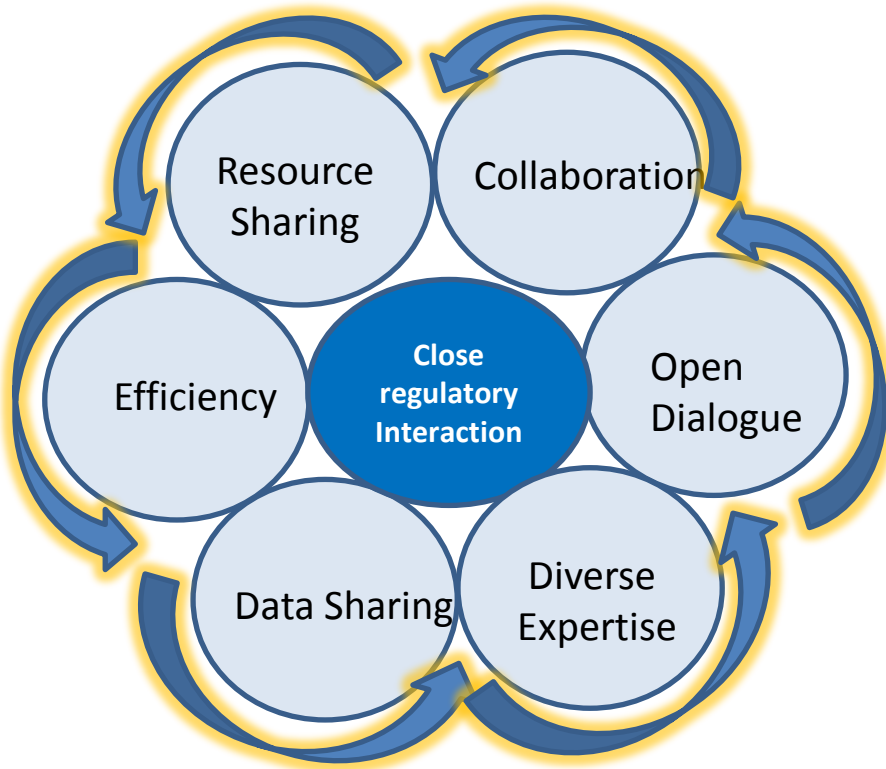
Research Roundtable

Banner
Alzheimer's
Institute
Alzheimer's Prevention
Initiative

Global Standardization
Biomarkers Consortium



Global CEO
initiative



- Resource constraints at all levels
- Consortia fatigue
- Organizational Structure and Governance
- Data Sharing
- Communication among partners
- Culture
- Financing
- Incentives
- Risk Mitigation
- Respect for confidentiality

- Given the CAMD and IMI summarizes of work-scope just presented do you see the gaps that are not being addressed, but would be critical to advancing the Alzheimer's disease initiatives?
- What opportunities do you see for synergy/ leveraging both efforts?
Given the global scale of this disease we all agree that information and data "sharing" is critical. (Whether it is sharing across companies or PPP's).
- Do you view sharing of information as a continued challenge and if so what can be done to improve the environment?
- What do you see as the regulatory impact of these efforts and/or areas of future focus; "harmonization of efforts"
Have we done enough to empower/include/enthuse the public/patients/caregivers and if not how might we?
- Data sharing and joint-working seems to be working really well with clinical studies and human-data. How about preclinical and animal studies?