Fondazione Istituto San Raffaele
G. Giglio di Cefalù

Congresso Regionale
SIN SICILIA

Innovazione Terapeutica: Demenze

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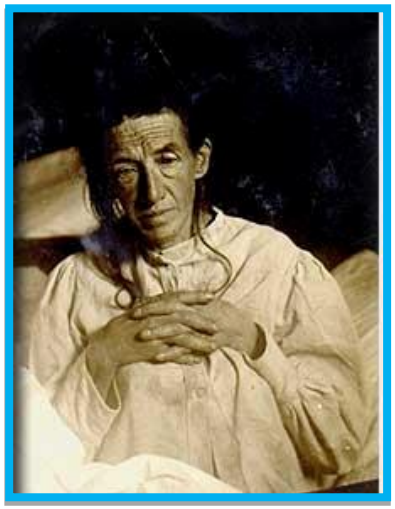
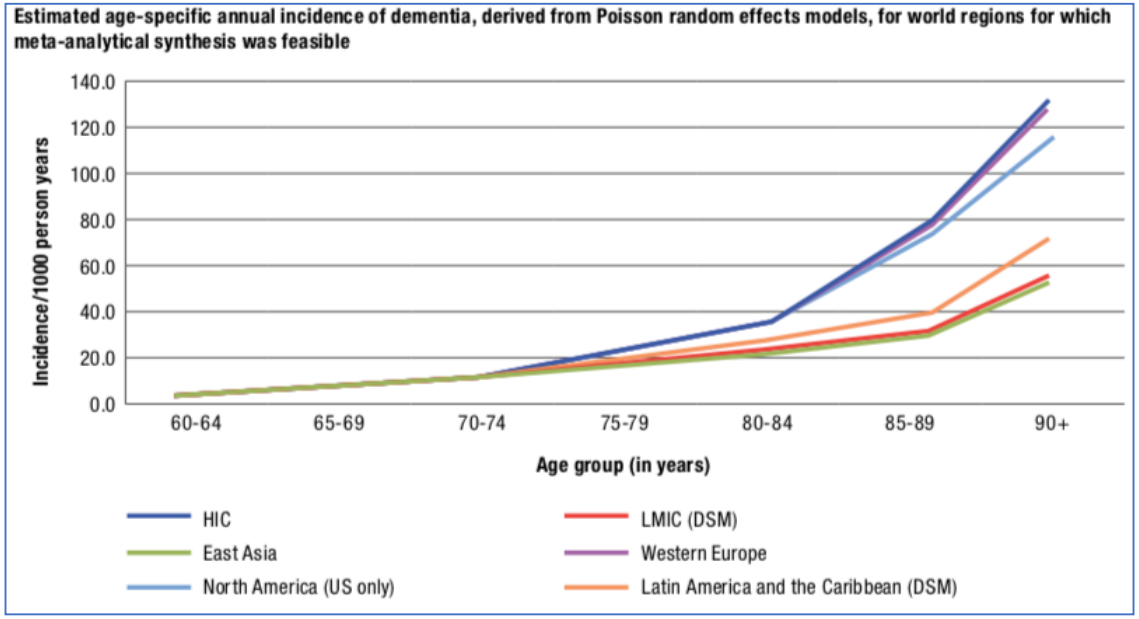
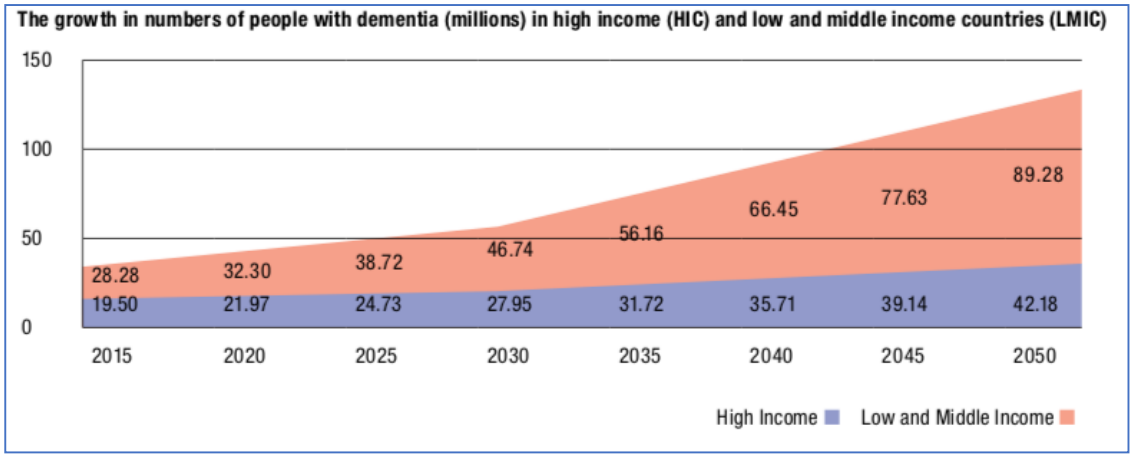


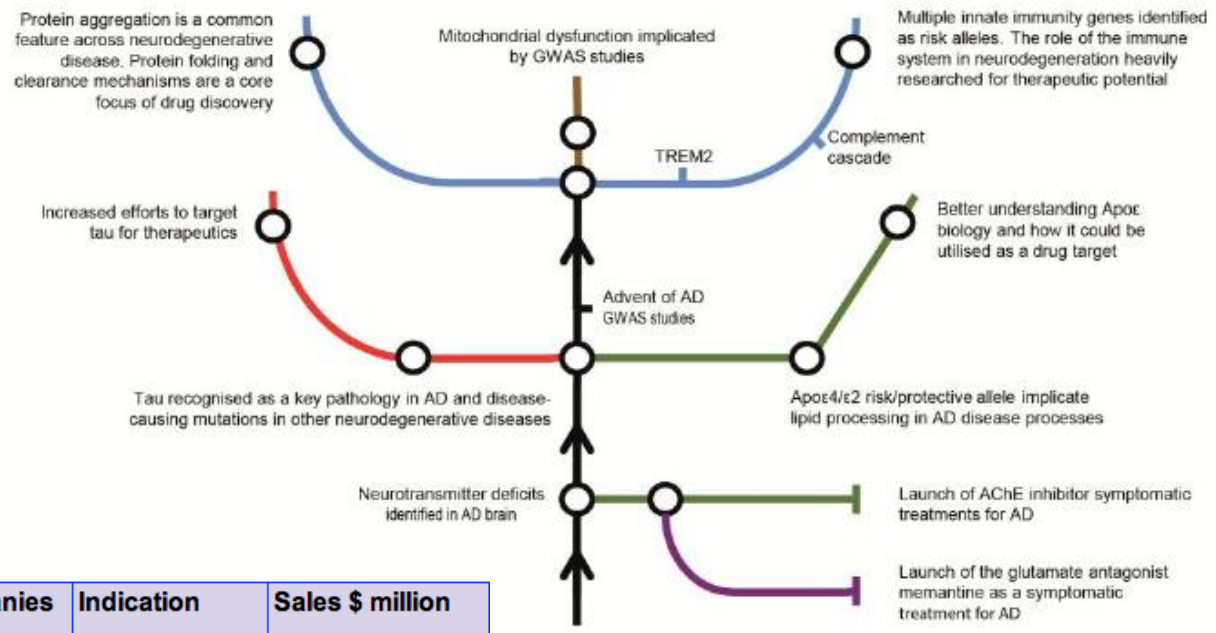
Catania, 15 febbraio 2019

Seicentomila malati di Alzheimer in Italia, il 4% degli over 65





Lo sviluppo delle terapie per l'AD (1980 - ad oggi)

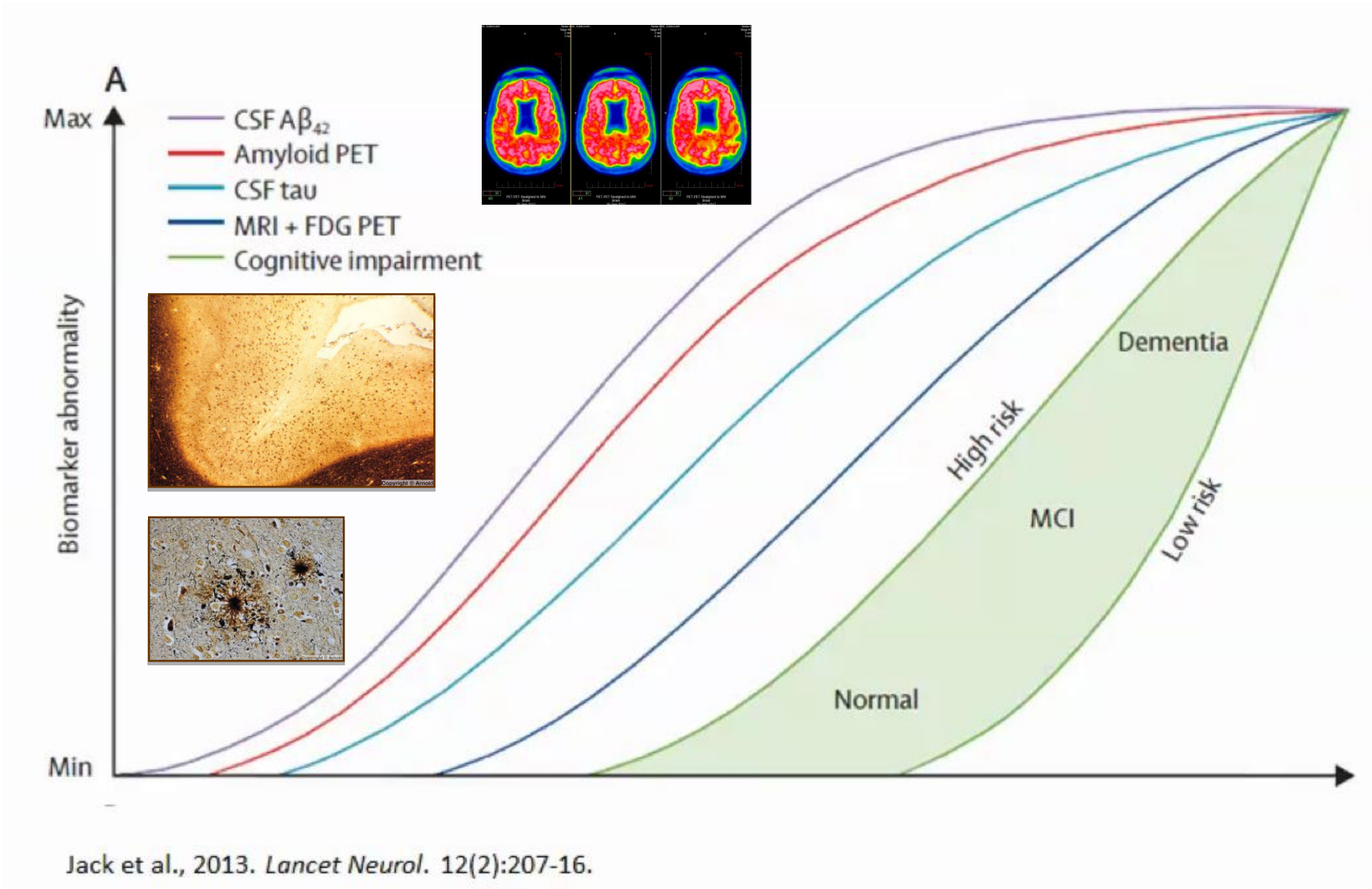


Generic Name	Brands	Companies	Indication	Sales $ million 2009
Donepezil	Aricept®	Eisai, Pfizer	AD	3430
Memantine	Namenda®, Ebixa®, Abixa®, Axura®, Akatinol®, Memox®	Forest, Lundbeck, Merz, Uniform	AD	1850
Rivastigmine	Exelon Patch®	Novartis	AD	954
Galantamine	Razadyne®	J&J	AD	415

Proteinopathies associated with neurodegenerative diseases

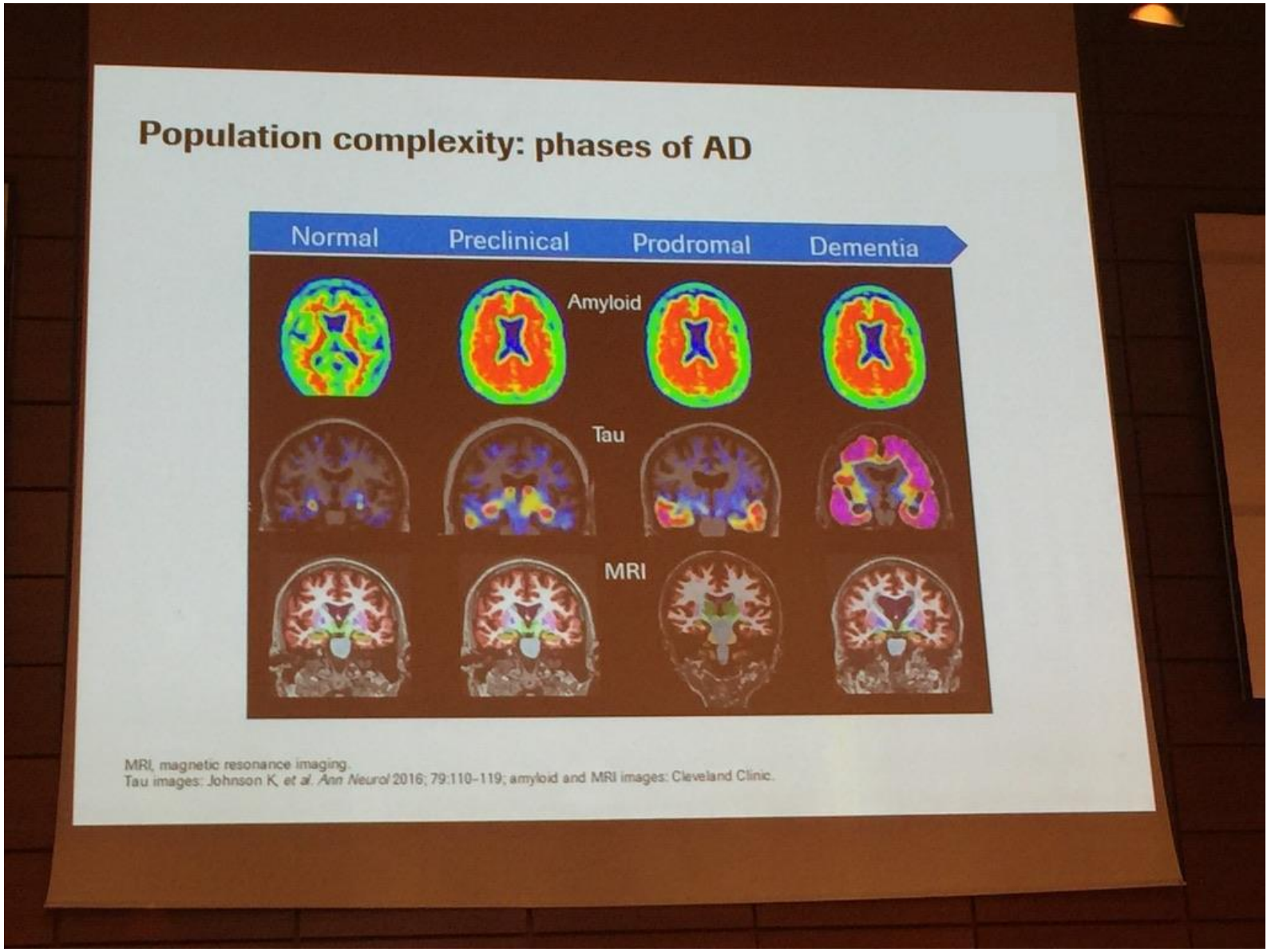
Disease*	Aggregating protein(s)	Propagation of pathology *in vitro* and *in vivo*
Alzheimer disease	Amyloid-β, tau[147]	• Seeding (amyloid-β[236,237] and tau[121–123,137]) • Spreading (amyloid-β[238,239] and tau[136,138,147,240])
Parkinson disease dementia with Lewy bodies	α-Synuclein	Seeding[241–243] and spreading[244–246]
Amyotrophic lateral sclerosis	SOD1, TDP43, FUS	• Seeding (SOD1 (REF. 247) and TDP43 (REFS 248,249)) • Spreading (SOD1 (REF. 247))
Frontotemporal dementia	Tau, TDP43, FUS	Spreading (TDP43 (REFS 250,251) and FUS[252])
Huntington disease	Huntingtin	Seeding[253–255] and spreading[256,257]
Prion diseases‡	PrP	Seeding[258–260] and spreading[261,262]

Sequenza patologica dell'AD (2019)

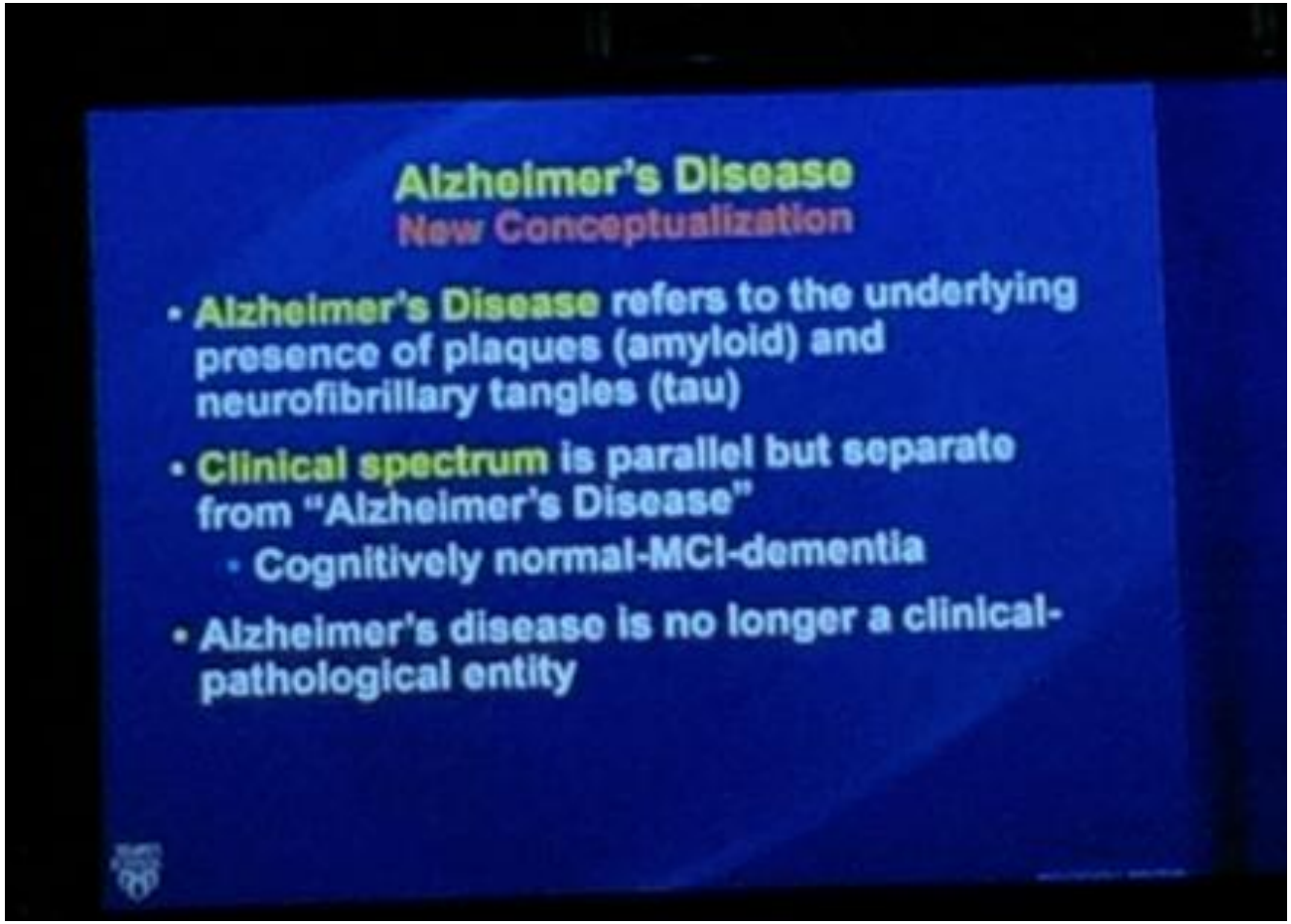


Jack et al., 2013. *Lancet Neurol.* 12(2):207-16.

PET amiloide e tau



AAN San Diego, 2018



Nuova definizione di malattia di Alzheimer (2018)

ELSEVIER

CrossMark

Alzheimer's & Dementia 14 (2018) 535-562

Alzheimer's & Dementia

2018 National Institute on Aging—Alzheimer's Association (NIA-AA) Research Framework

NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease

Clifford R. Jack, Jr.,[a,*], David A. Bennett[b], Kaj Blennow[c], Maria C. Carrillo[d], Billy Dunn[e], Samantha Budd Haeberlein[f], David M. Holtzman[g], William Jagust[h], Frank Jessen[i], Jason Karlawish[j], Enchi Liu[k], Jose Luis Molinuevo[l], Thomas Montine[m], Creighton Phelps[n], Katherine P. Rankin[o], Christopher C. Rowe[p], Philip Scheltens[q], Eric Siemers[r], Heather M. Snyder[d], Reisa Sperling[s]

Contributors[†]**:** Cerise Elliott, Eliezer Masliah, Laurie Ryan, and Nina Silverberg

Diagnosi di AD: Classificazione AT(N)

A

T

N

AT(N) biomarker grouping

A: Aggregated Aβ or associated pathologic state
CSF $A\beta_{42}$, or $A\beta_{42}/A\beta_{40}$ ratio
Amyloid PET
T: Aggregated tau (neurofibrillary tangles) or associated pathologic state
CSF phosphorylated tau
Tau PET
(N): Neurodegeneration or neuronal injury
Anatomic MRI
FDG PET
CSF total tau

Abbreviations: Aβ, β amyloid; CSF, cerebrospinal fluid.

NOTE. See section 9.4 for explanation of (N) notation.

Diagnosi di AD: markers biologici

Biomarker profiles and categories

AT(N) profiles	Biomarker category	
A-T-(N)-	Normal AD biomarkers	
A+T-(N)-	Alzheimer's pathologic change	Alzheimer's continuum
A+T+(N>	Alzheimer's disease	
A+T+(N)+	Alzheimer's disease	
A+T-(N)+	Alzheimer's and concomitant suspected non Alzheimer's pathologic change	
A-T+(N)-	Non-AD pathologic change	
A-T-(N)+	Non-AD pathologic change	
A-T+(N)+	Non-AD pathologic change	

Abbreviation: AD, Alzheimer's disease.

Demenza amnesica non-AD

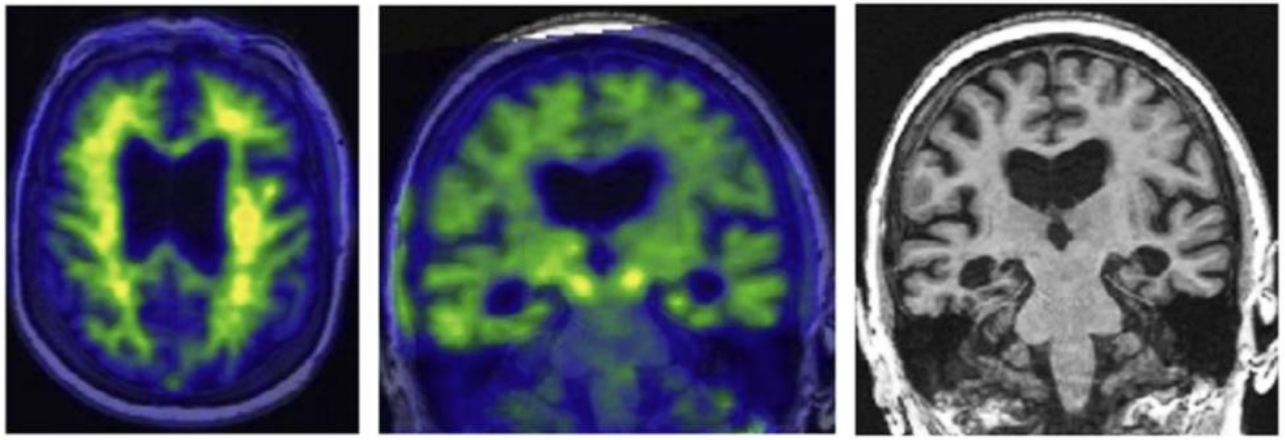


Fig. 5.
Non-Alzheimer's pathologic change with dementia. An 86-year-old female with progressive amnestic dementia. The patient had been diagnosed clinically (i.e., without biomarkers) as "Alzheimer's disease dementia" by several physicians before enrolling in the Mayo Alzheimer's Disease Research Center. Imaging performed for research purposes revealed a normal amyloid PET (Pittsburgh compound B, left), normal tau PET with flortaucipir (middle), and severe medial temporal atrophy on MRI (right). The biomarker profile [A–T–(N)+] suggests the patient has non-Alzheimer's pathologic change. Based on her biomarker profile, hippocampal sclerosis was suspected antemortem, and hippocampal sclerosis with TDP43 (and without Alzheimer's disease) was later confirmed at autopsy.

A+T-(N-)

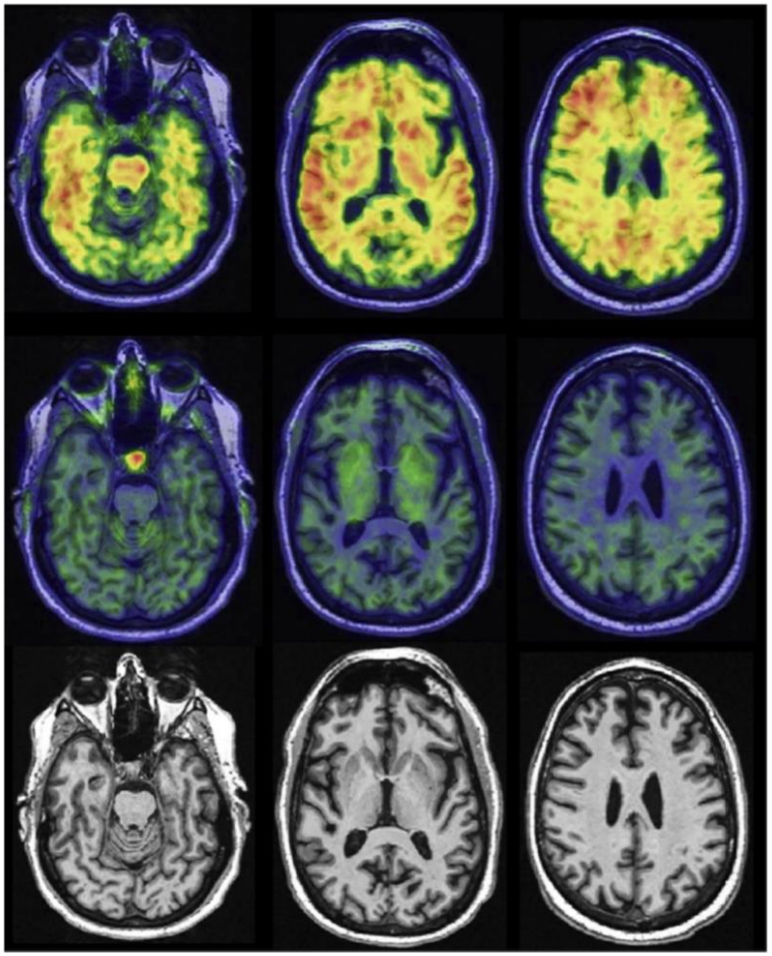


Fig. 2.
Preclinical Alzheimer's pathologic change. A cognitively unimpaired 67-year-old man. Participant in the Mayo Clinic Study of Aging. Abnormal amyloid PET (Pittsburgh compound B, top row), no uptake on tau PET (with flortaucipir, middle row), no atrophy on MRI (bottom row). Biomarker profile A+T−(N)−.

A+T+(N+)

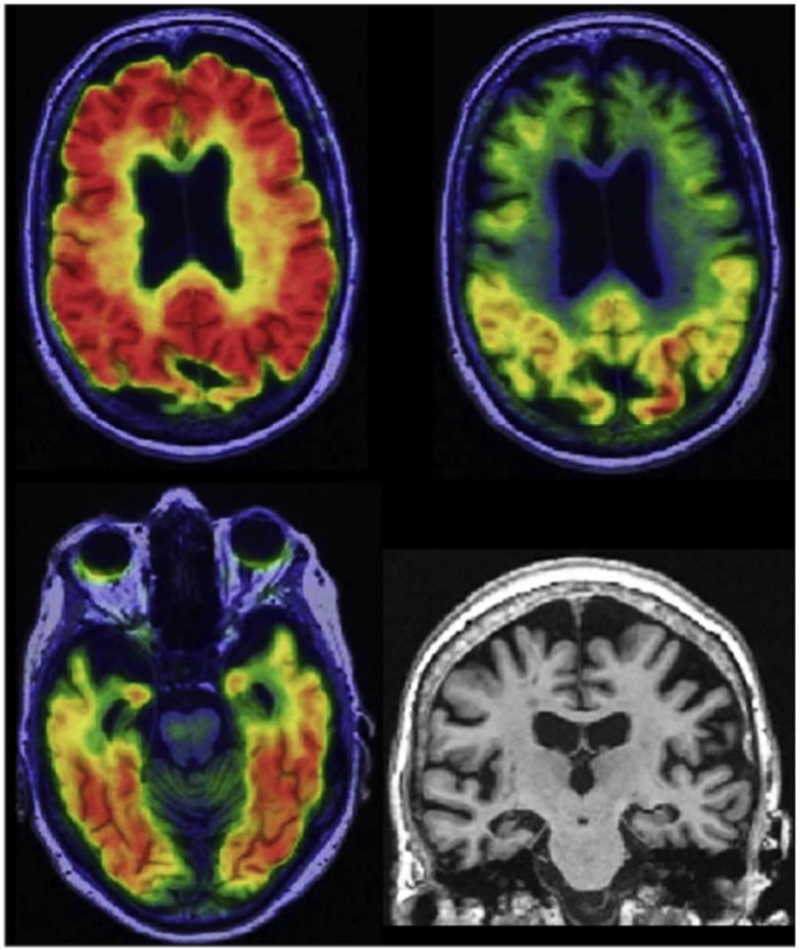


Fig. 1.
Alzheimer's disease with dementia. A 75-year-old woman with amnestic multidomain dementia. Participant in the Mayo Alzheimer's Disease Research Center. Abnormal amyloid PET with Pittsburgh compound B (top left), tau PET with flortaucipir (top right and bottom left), and atrophy on MRI (bottom right). Biomarker profile A+T+(N)+.

Integrazione gruppi AT(N) nella diagnosi di malattia di Alzheimer

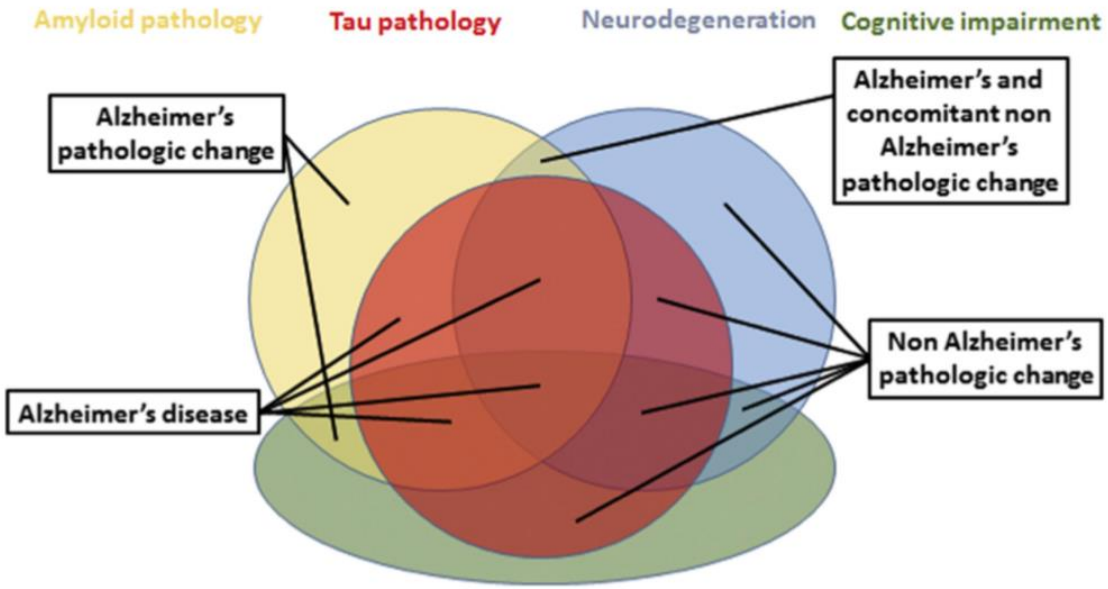
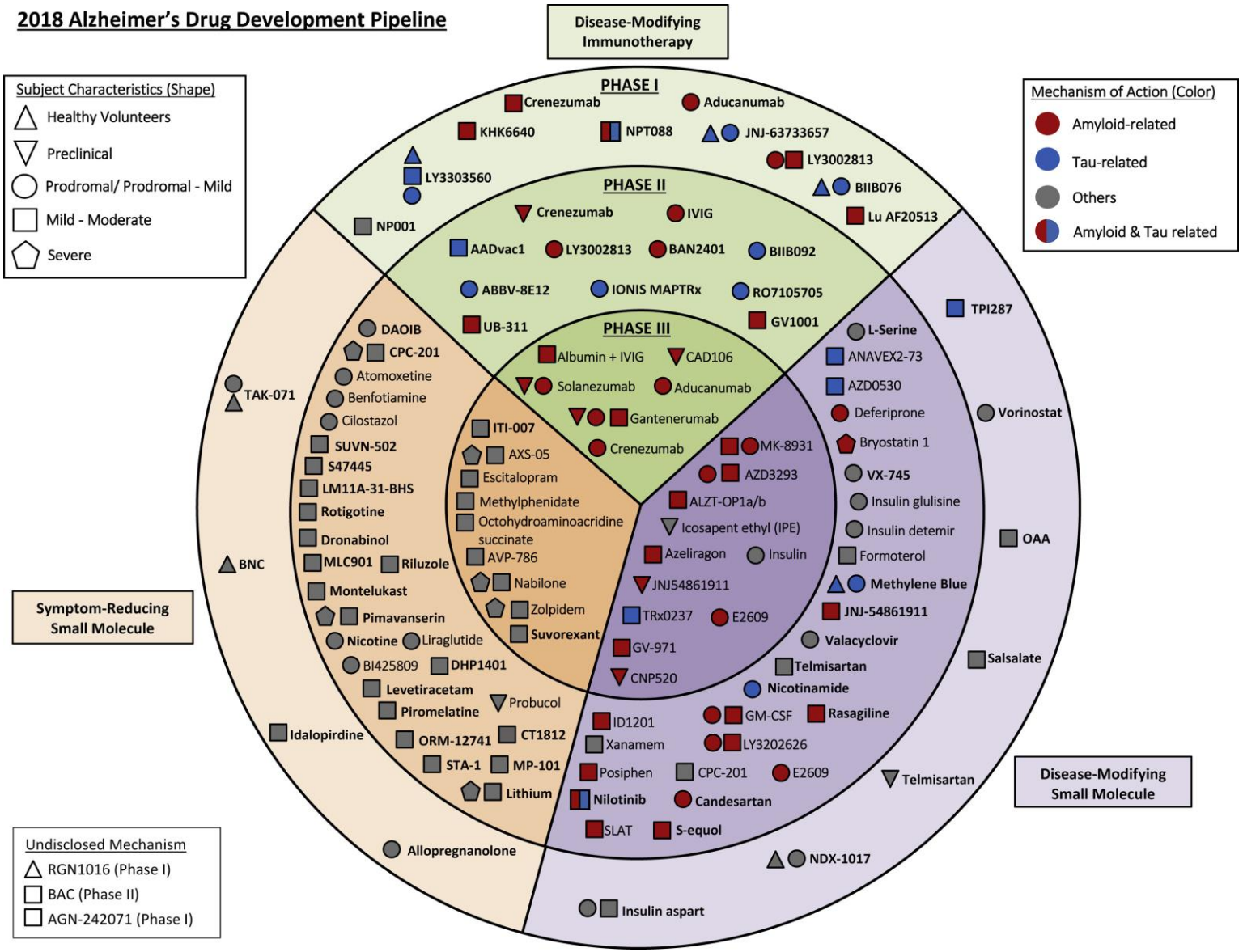
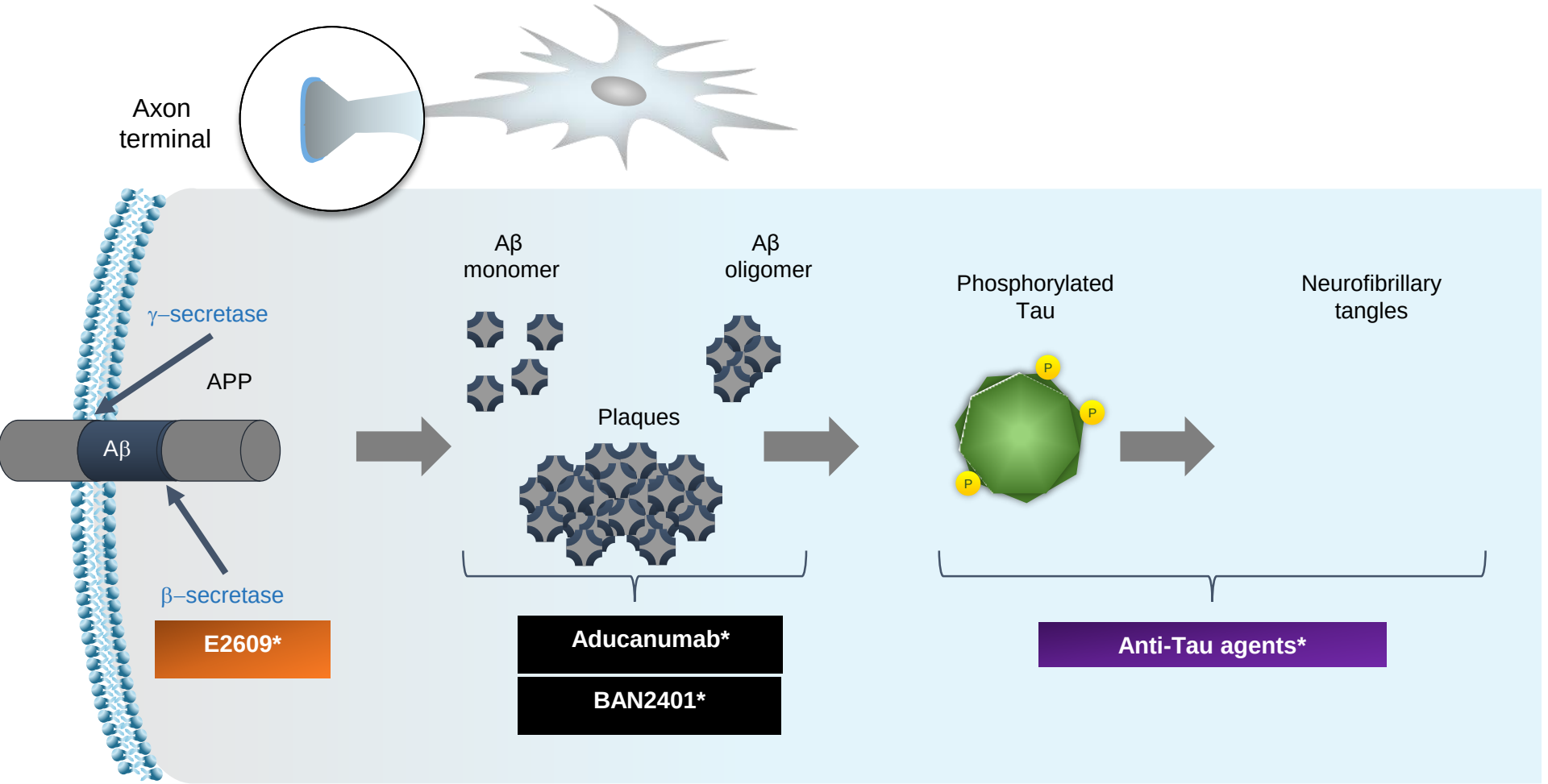


Fig. 4.
Descriptive nomenclature Venn diagram. As an adjunct to Table 4, we illustrate how AT(N) biomarker grouping and cognitive status interact for classification of research participants in this Venn diagram. For simplicity, MCI and dementia are combined into a single (cognitively impaired) category and the A−T−(N)− groups are not shown. Also "Alzheimer's and concomitant non-Alzheimer's pathologic change" [A+T−(N)+] in cognitively impaired is not shown in this figure. Abbreviation: MCI, mild cognitive impairment.

Farmaci in sviluppo per l'Alzheimer (2018)



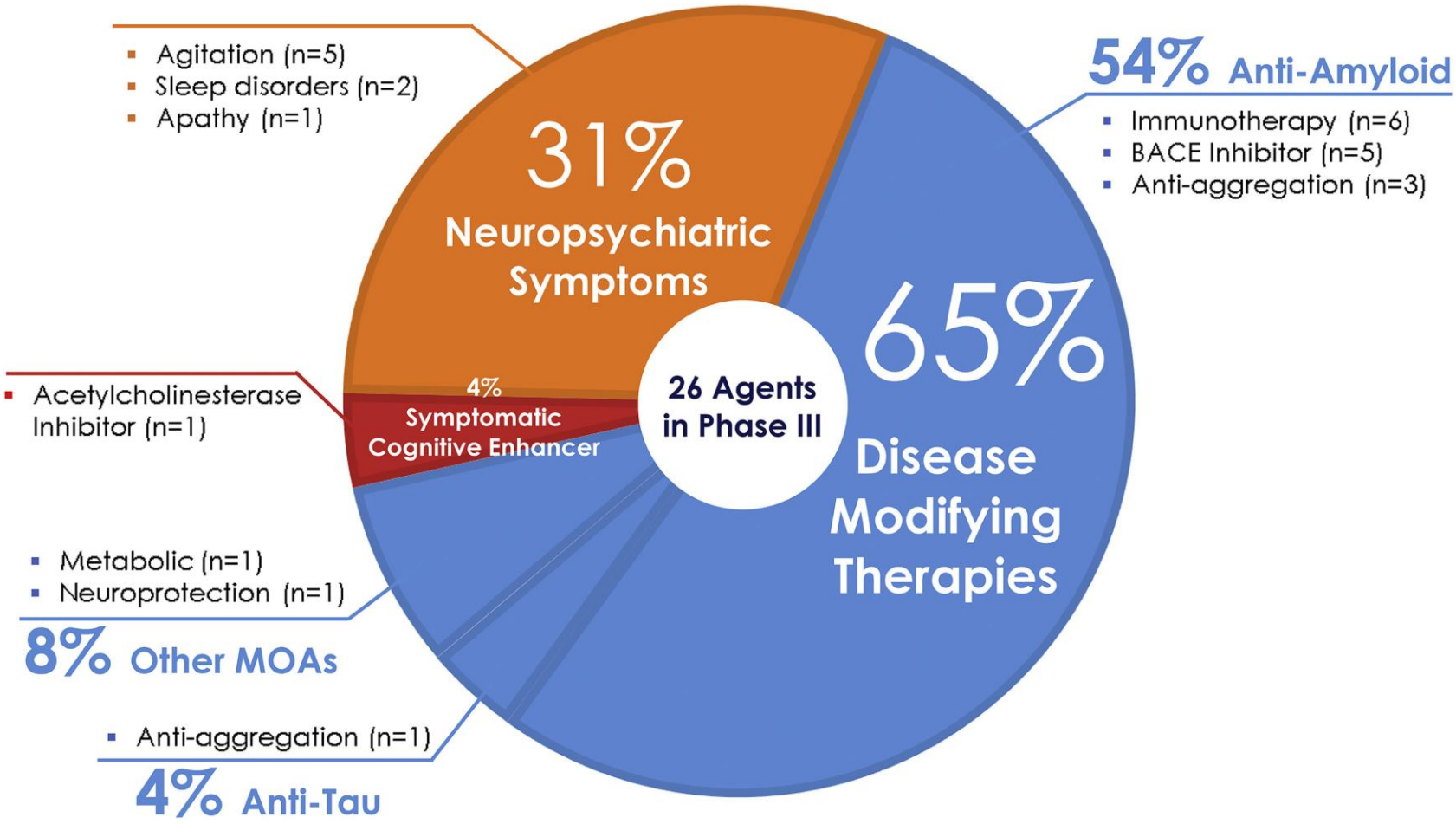
Target terapeutici nella cascata proteino-patologica dell'AD



* Collaboration program.

Figure adapted from Jia et al. *BioMed Res Int.* 2014; 2014:837157; O'Brien and Wong. Annu Rev Neurosci. 2011; 34:185-204.; Scangos Presented at: J.P. Morgan 2016 Health Care Conference; January 2016; San Francisco, CA.

Target terapeutici farmaci AD in fase III

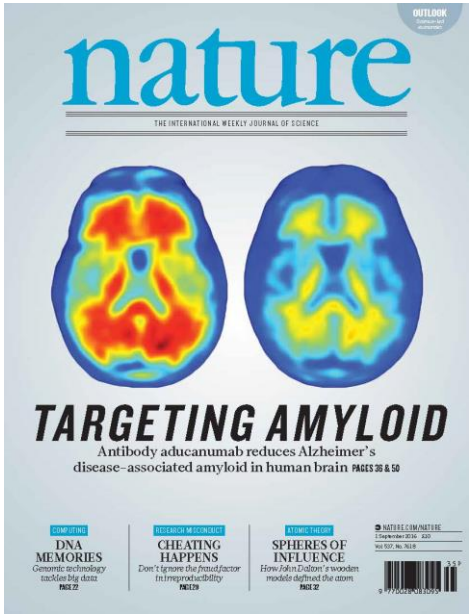


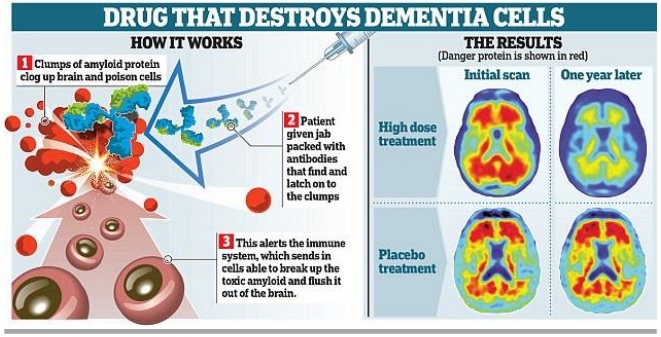
Monoclonali anti-amiloide in sviluppo

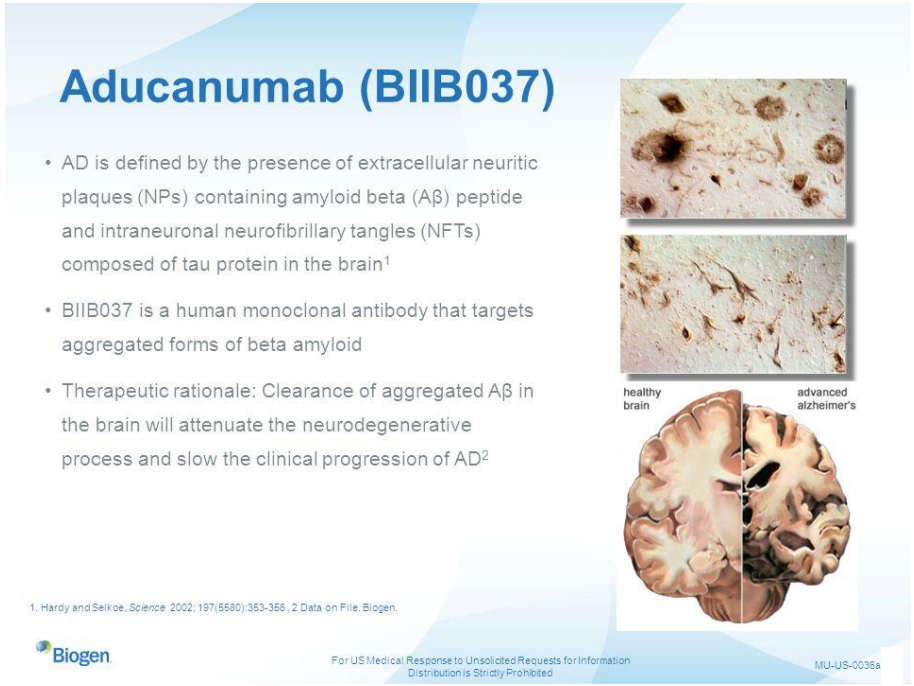
	Manufacturer	Epitope	Origin	Isotype	Target	Possible mechanism of action	Outcomes in latest stage trial	Amyloid biomarker inclusion criteria in trials	Trials planned or in progress	Rate of amyloid-related imaging abnormalities
Solanezumab (NCT0760005, NCT01900665)	Eli Lilly	Mid-domain	Humanised	IgG1	Soluble, monomeric, non-fibrillar Aβ	Sequestration of soluble monomeric Aβ	Negative clinical outcomes in two phase 3 trials in mild-to-moderate Alzheimer's disease; possible slowing of cognitive decline in mild disease	None	Phase 3 trials underway in mild, preclinical, and autosomal-dominant Alzheimer's disease	Low
Bapineuzumab (NCT00575055, NCT00574132)	Pfizer/Johnson & Johnson	N-terminus	Humanised	IgG1	All forms of Aβ (fibrillar, oligomeric, monomeric)	Microglia-mediated clearance	Negative clinical outcomes in two phase 3 trials despite significant decrease in amyloid PET and phosphorylated tau concentrations in cerebrospinal fluid	None	–	Related to dose and APOE ε4 carrier status
Crenezumab (NCT 01397378, NCT01723826, NCT01998891)	Roche/ Genentech	Mid-domain	Humanised	IgG4	All forms of Aβ (fibrillar, oligomeric, monomeric)	Microglia-mediated clearance	Negative clinical outcomes in phase 2 trials in mild-to-moderate Alzheimer's disease; possible cognitive slowing in mild disease in patients given high doses	None in ABBY trial; amyloid PET in BLAZE trial	Phase 3 trial in autosomal-dominant Alzheimer's disease underway	Low
BAN2401 (NCT01767311)	Eisai/Biogen	N-terminus	Humanised	IgG1	Fibrillar and oligomeric Aβ	Microglia-mediated clearance	No phase 2 trials yet completed	Amyloid PET	Phase 2 trial underway in mild cognitive impairment	–
Gantenerumab (NCT01224106, NCT02051608)	Roche/ Genentech	N-terminus and mid-domain	Human (phage display library and affinity maturation)	IgG1	Fibrillar and oligomeric Aβ	Microglia-mediated clearance	Negative clinical outcomes in phase 3 trial for prodromal Alzheimer's disease	Cerebrospinal fluid Aβ	New phase 3 trial in planning phase	Related to dose and APOE ε4 carrier status
Aducanumab (NCT02484547, NCT02477800)	Biogen/ Neurimmune	N-terminus	Human (RTM)	IgG1	Fibrillar and oligomeric Aβ	Microglia-mediated clearance	Dose-dependent decrease in amyloid PET and cognitive decline in early Alzheimer's disease (mild cognitive impairment and mild disease) in interim analysis of phase 1b trial	Amyloid PET	Phase 1 trial in prodromal or mild Alzheimer's disease and phase 3 trial of early disease underway	Related to dose and APOE ε4 carrier status

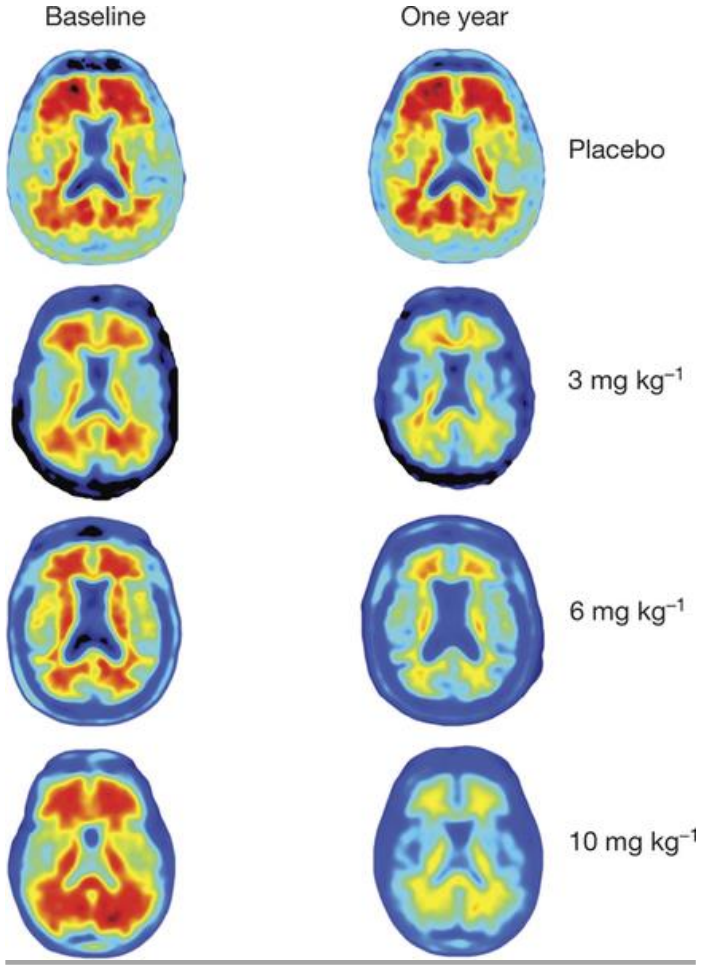
Aβ=amyloid β. –=not applicable. RTM=reverse translational medicine.

Table: **Anti-amyloid monoclonal antibodies in clinical development**


nature
THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE
TARGETING AMYLOID
Antibody aducanumab reduces Alzheimer's disease-associated amyloid in human brain PAGES 35 & 50
DNA MEMORIES
Genomic technology tackles big data
CHEATING HAPPENS
Don't ignore the fraud factor in irreproducibility
SPHERES OF INFLUENCE
How John Dalton's wooden models defined the atom

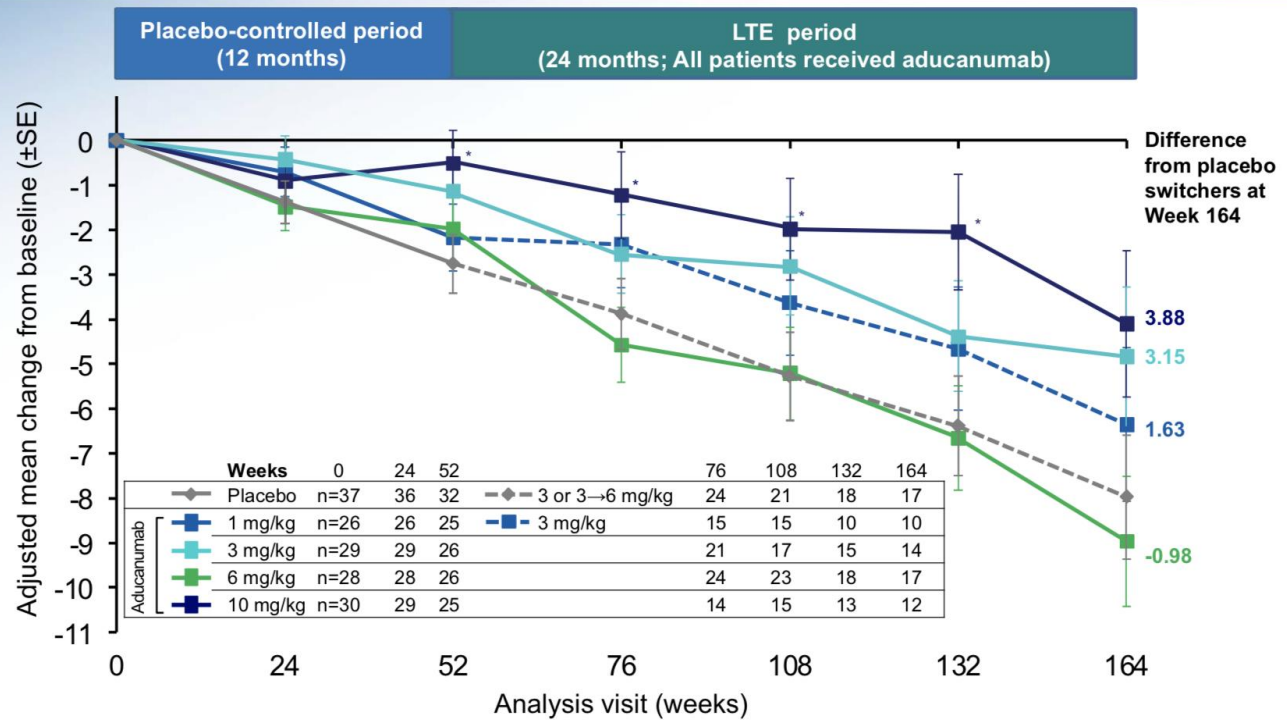

DRUG THAT DESTROYS DEMENTIA CELLS
HOW IT WORKS
1 Clumps of amyloid protein clog up brain and poison cells
2 Patient given jab packed with antibodies that find and latch on to the clumps
3 This alerts the immune system, which sends in cells able to break up the toxic amyloid and flush it out of the brain.
THE RESULTS
(Danger protein is shown in red)
Initial scan
One year later
High dose treatment
Placebo treatment


Aducanumab (BIIB037)
• AD is defined by the presence of extracellular neuritic plaques (NPs) containing amyloid beta (Aβ) peptide and intraneuronal neurofibrillary tangles (NFTs) composed of tau protein in the brain[1]
• BIIB037 is a human monoclonal antibody that targets aggregated forms of beta amyloid
• Therapeutic rationale: Clearance of aggregated Aβ in the brain will attenuate the neurodegenerative process and slow the clinical progression of AD[2]
healthy brain
advanced alzheimer's
1. Hardy and Selkoe. Science 2002; 197(5580):353-356. 2 Data on File. Biogen.
Biogen
For US Medical Response to Unsolicited Requests for Information Distribution is Strictly Prohibited
MU-US-0036a


Baseline
One year
Placebo
3 mg kg⁻¹
6 mg kg⁻¹
10 mg kg⁻¹

Studio PRIME: aducanumab in AD (fase II)

Effect of Aducanumab on Clinical Decline as Measured by MMSE (Exploratory Endpoint)



Nominal *$P<0.05$ vs placebo in the placebo-controlled period and vs placebo switchers in the LTE period. MMSE is an exploratory endpoint. Results based on MMRM, fitted with change from baseline as a dependent variable, and included fixed effects for categorical treatment, categorical visit and treatment-by-visit interaction, continuous baseline value, and laboratory ApoE ε4 status (carrier and non-carrier). LTE, long-term extension; MMRM, mixed model for repeated measures; MMSE, Mini-Mental State Exam; SE, standard error.

ARIA !

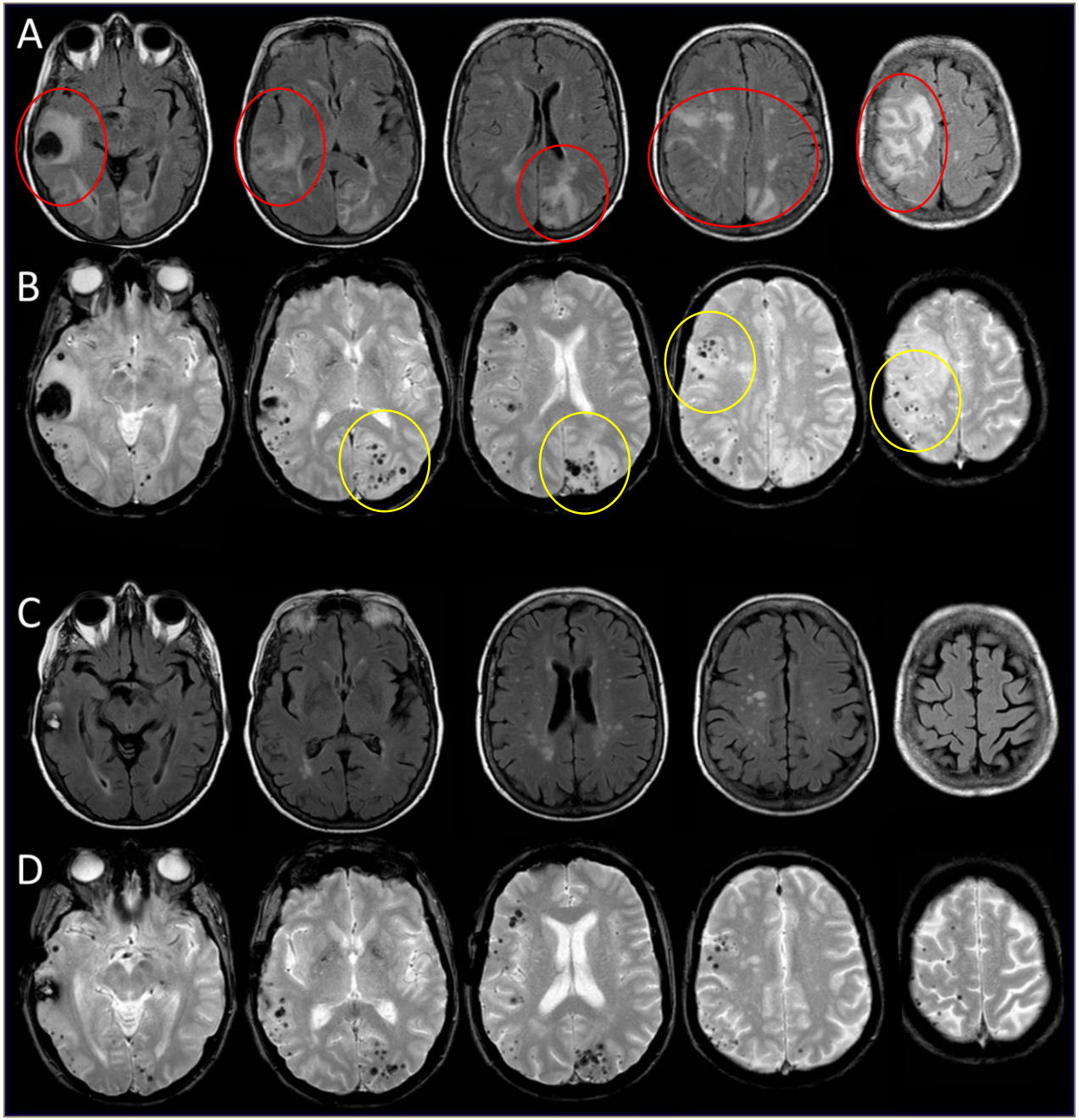
(Amyloyd Related
Imaging Abnormalities)

NIH Public Access
Author Manuscript
Alzheimers Dement. Author manuscript; available in PMC 2013 June 26.

Published in final edited form as:
Alzheimers Dement. 2011 July ; 7(4): 367–385. doi:10.1016/j.jalz.2011.05.2351.

Amyloid Related Imaging Abnormalities (ARIA) in Amyloid Modifying Therapeutic Trials: Recommendations from the Alzheimer's Association Research Roundtable Workgroup

Reisa A. Sperling[a,i,*], Clifford R. Jack[b,*], Sandra E. Black[c], Matthew P. Frosch[d], Steven M. Greenberg[e], Bradley T. Hyman[f], Philip Scheltens[g], Maria C. Carrillo[h], William Thies[h], Martin M. Bednar[i], Ronald S. Black[j], H. Robert Brashear[k], Michael Grundman[l], Eric R. Siemers[m], Howard H. Feldman[n,*], and Rachel J. Schindler[o,*]

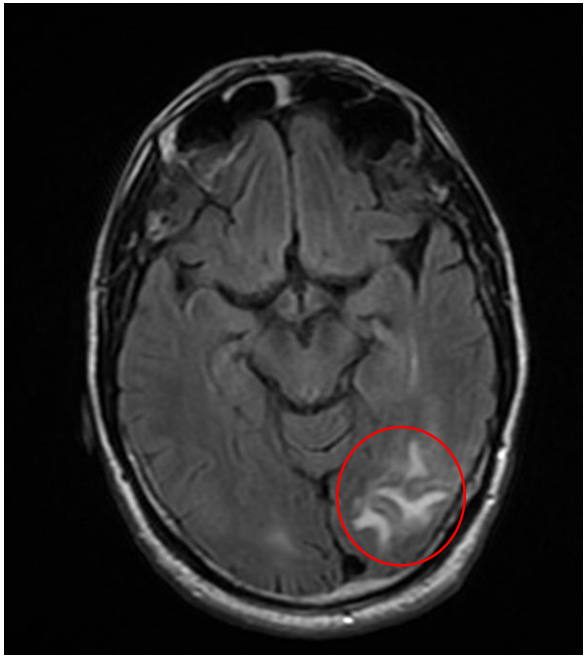


Le ARIA sono associate a una buona risposta clinica?

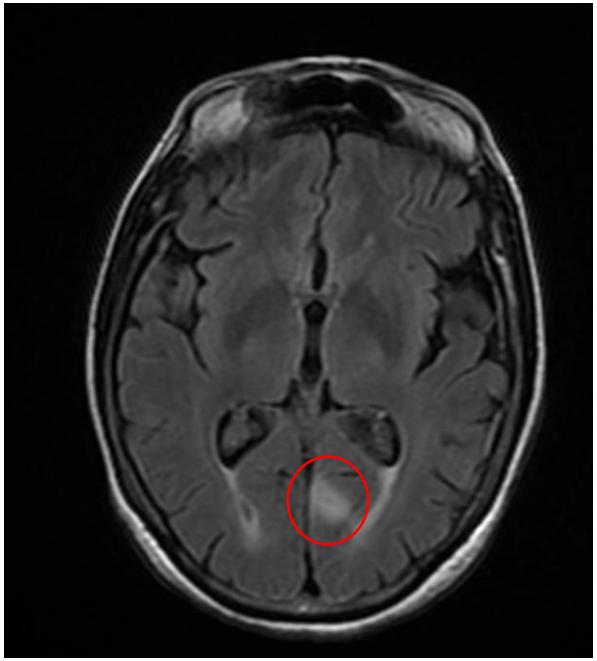
engage ENGAGE / 221AD301

Regional Enrollment Targets

	Mild AD				MCI due to AD				Total Randomized Target
	In screening	Randomized	Final Randomization slots open	Final Randomization cap	In screening	Randomized	Final Randomization slots open	Final Randomization target	
North America	25	103	94	197	57	613	46	659	856
Europe	26	97	21	118	53	332	61	393	511
Asia-Pacific	7	28	7	35	6	103	13	116	151
Japan	5	14	12	26	21	52	9	61	87
Global	63	242	134	376	137	1100	74	1229	1605



Paz.03



Paz.08

E2609 – elenbecestat

(inibitore della BACE)

ALZHEIMER'S NEWS TODAY

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Alzheimer's Therapy Elenbecestat Reduces Brain Amyloid Levels, is Safe and Well-Tolerated, Trial Shows

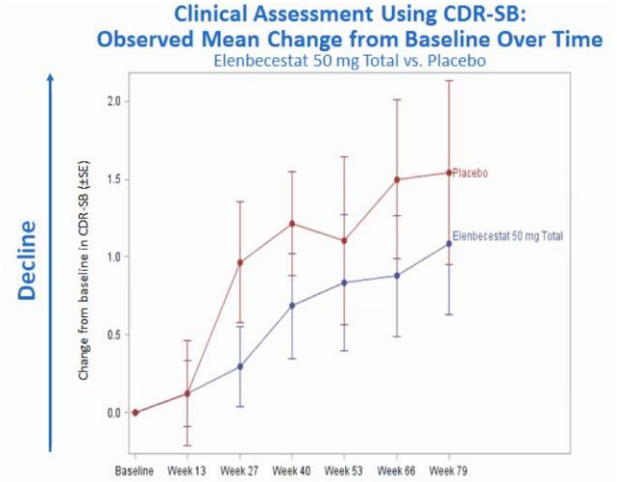
JUNE 8, 2018 BY JOSE MARQUES LOPES IN NEWS.

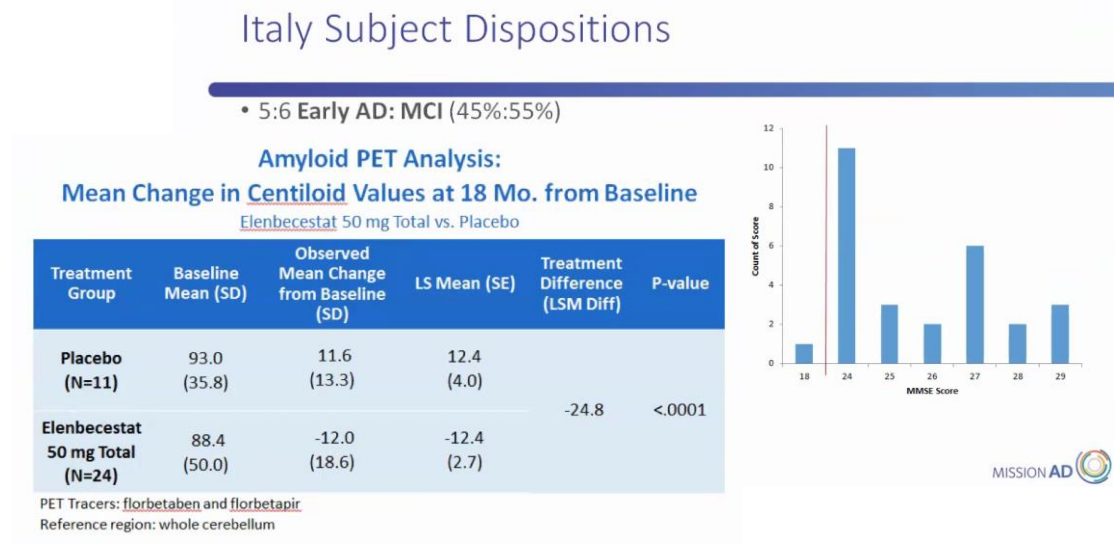
Eisai and Biogen Announce Positive Topline Results of the Final Analysis for BAN2401 at 18 Months

July 5, 2018 at 11:30 PM UTC

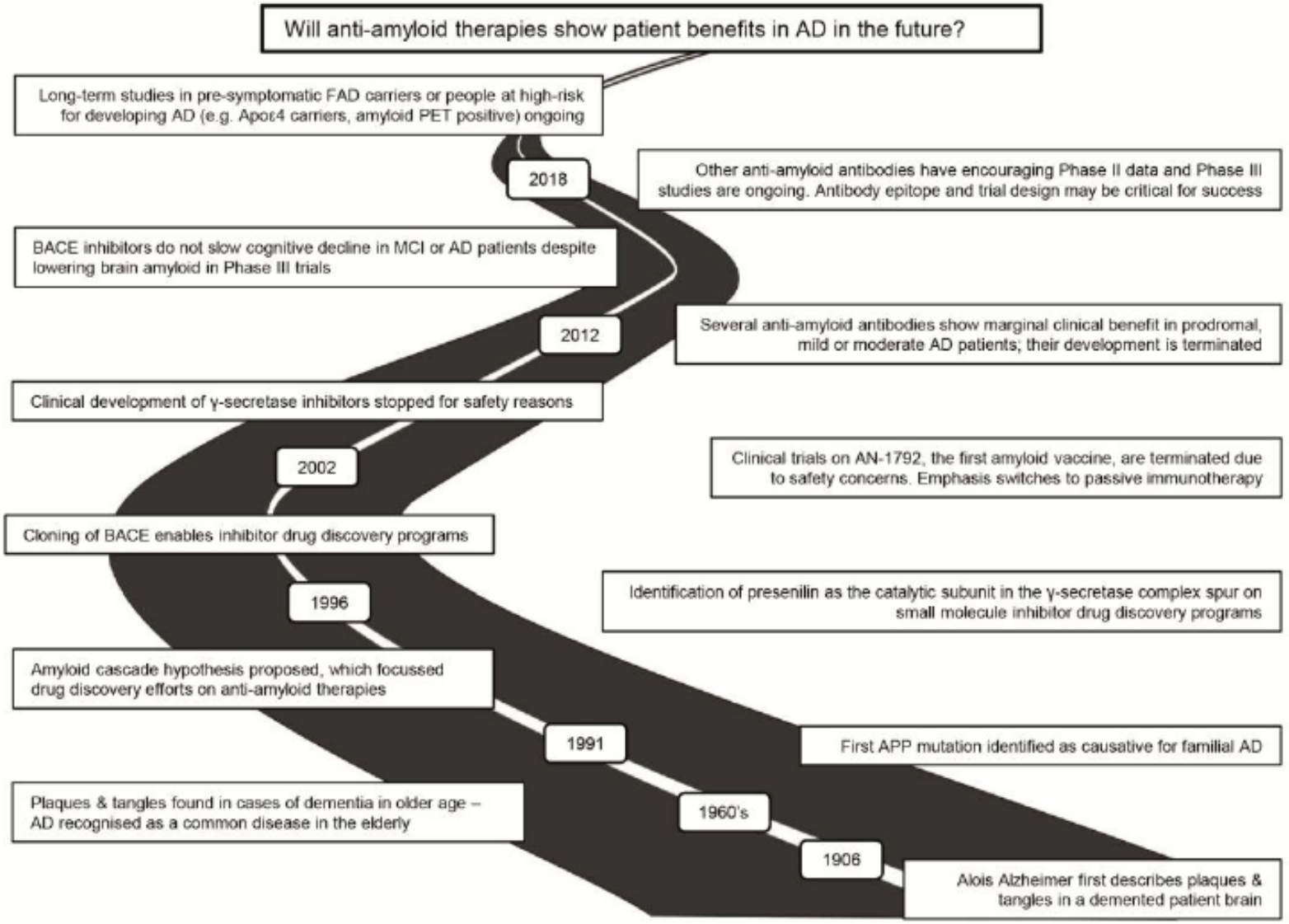
- *The final analysis at 18 months of the 856 patient Phase II clinical study in early Alzheimer's disease demonstrated statistically significant slowing in clinical decline and reduction of amyloid beta accumulated in the brain*
- *First late-stage study data successfully demonstrating potential disease-modifying effects on both clinical function and amyloid beta accumulation in the brain*
- *New data provide compelling evidence to further support amyloid hypothesis as a therapeutic target for Alzheimer's disease*

TOKYO and CAMBRIDGE, Mass., July 05, 2018 (GLOBE NEWSWIRE) -- Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") and Biogen Inc. (NASDAQ:BIIB) (Headquarters: Cambridge, Massachusetts, United States, CEO: Michel Vounatsos, "Biogen") announced positive topline results from the Phase II study with BAN2401, an anti-amyloid beta protofibril antibody, in 856 patients with early Alzheimer's disease. The study achieved statistical significance on key predefined endpoints evaluating efficacy at 18 months on slowing progression in Alzheimer's Disease Composite Score (ADCOMS) and on reduction of amyloid accumulated in the brain as measured using amyloid-PET (positron emission tomography).

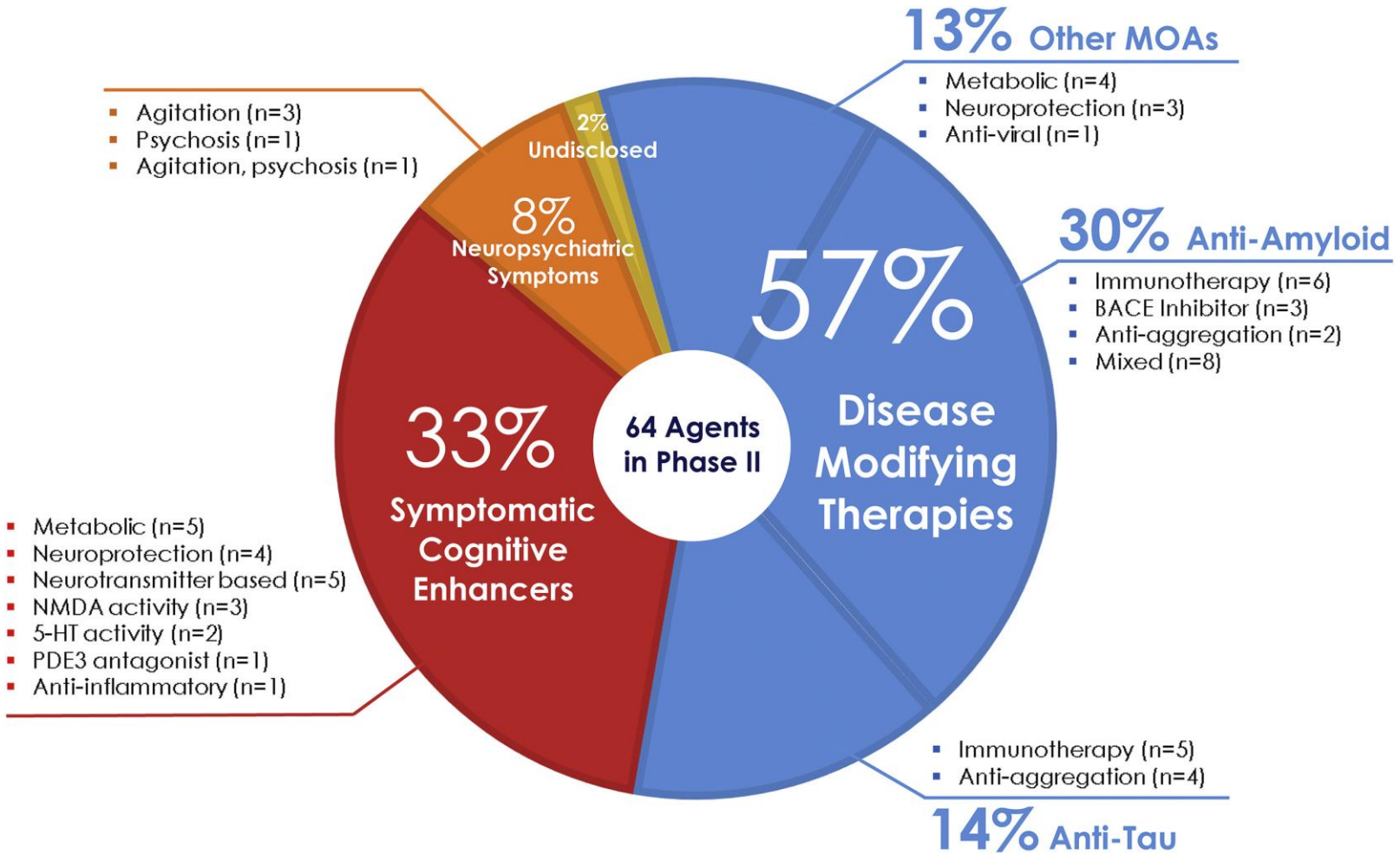




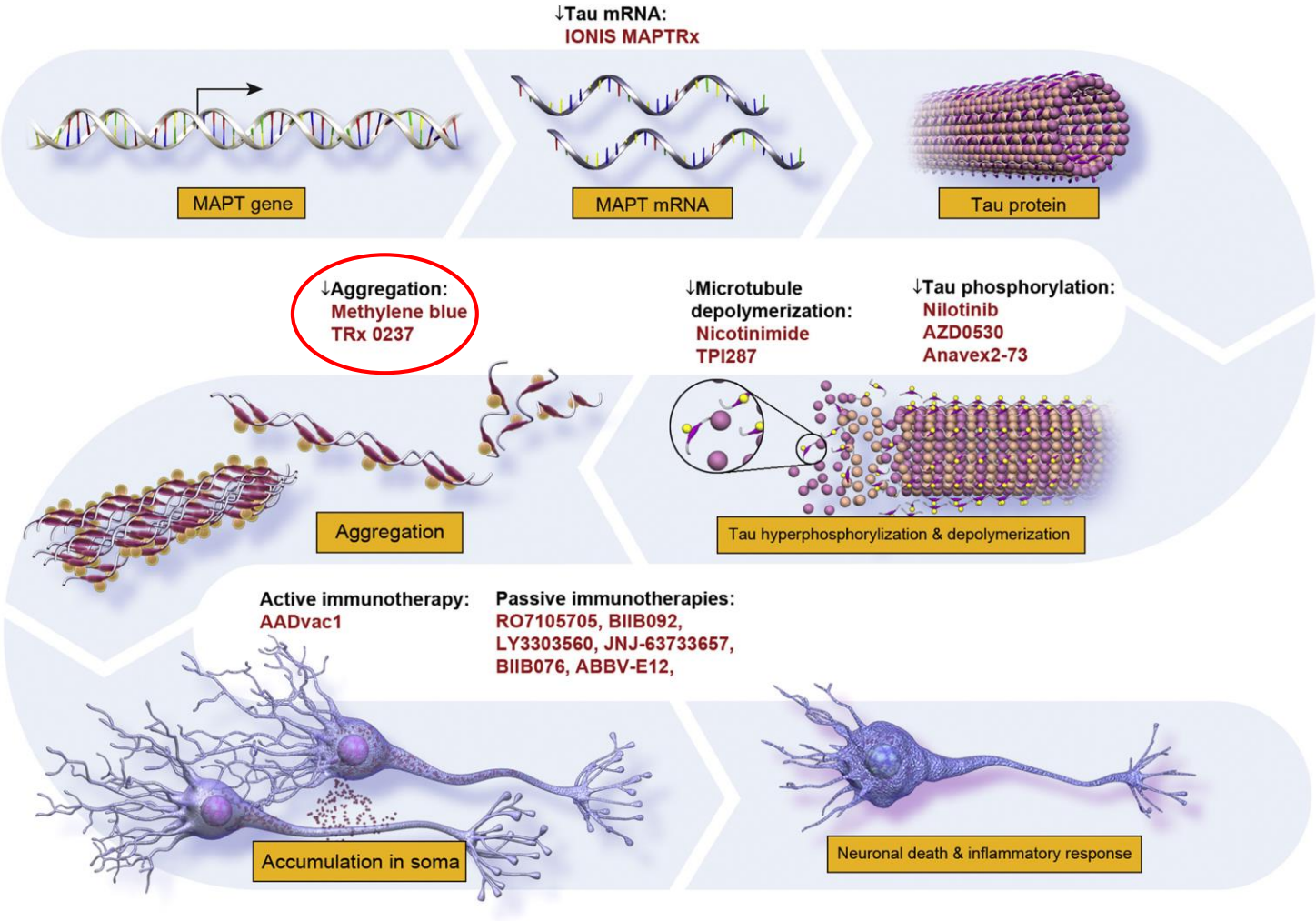
The long road to anti-amyloid therapies



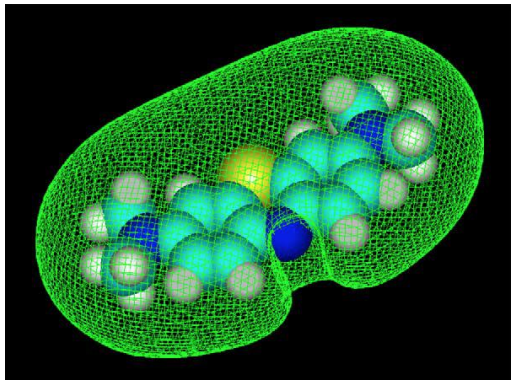
Target terapeutici farmaci AD in fase II



Siti d'azione farmaci anti-tau



Il Blu di metilene inibisce la formazione degli oligomeri Ab42 promuovendo quella di fibrille

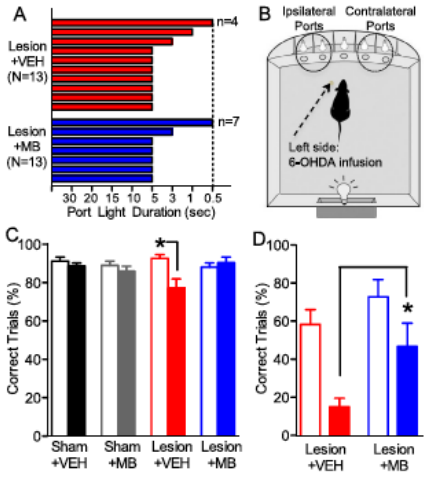


Neuroscience 359 (2017) 8–16

DAILY CONSUMPTION OF METHYLENE BLUE REDUCES ATTENTIONAL DEFICITS AND DOPAMINE REDUCTION IN A 6-OHDA MODEL OF PARKINSON'S DISEASE

ELIZABETH S. SMITH, MADELINE E. CLARK, GWENDOLYN A. HARDY, DAVID J. KRAAN, ELISA BIONDO, F GONZALEZ-LIMA, LAWRENCE K. CORMACK, MARIE MONFILS AND HONGJOO J. LEE*

The University of Texas at Austin, Department of Psychology, United States



Biochemical Pharmacology 78 (2009) 927–932

Contents lists available at ScienceDirect

Biochemical Pharmacology

journal homepage: www.elsevier.com/locate/biochempharm

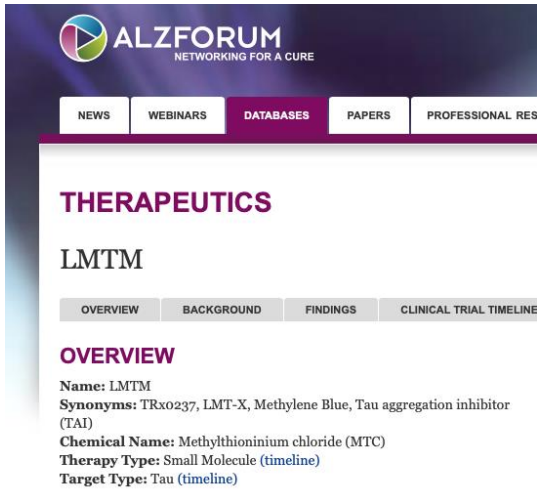
Commentary

Methylene blue and Alzheimer's disease

Murat Oz [a,b,*], Dietrich E. Lorke [c], George A. Petroianu [b]

[a] Integrative Neuroscience Section, Intramural Research Program, National Institute on Drug Abuse, NIH, DHHS, Balt
[b] Department of Pharmacology, Faculty of Medicine and Health Sciences, UAE University, Al Ain, United Arab Emirat
[c] Department of Anatomy, Faculty of Medicine and Health Sciences, UAE University, Al Ain, United Arab Emirates

In risposta alla richiesta dei familiari di un farmaco per cercare di arginare la progressione di malattia si segnala come il blu di metilene, un vecchio antisettico urinario attualmente ancora utilizzato come antidoto per gli avvelenamenti da metaemoglobina, è in sperimentazione per le sue capacità antiaggreganti proteiche proprio per la demenza di Alzheimer, in genere a dosaggi variabili tra 125 e 250mg al giorno per via orale. Tale farmaco potrebbe essere preparato in modo galenico da un farmacista e la sua assunzione richiederebbe un controllo medico attento in quanto ha una sua neurotossicità intrinseca e, per esempio, non consente l'uso contemporaneo di anti-depressivi o neurolettici (in uso per calmare questi pazienti, es. olanzapina, quetiapina, risperidone, etc.).



TRx 0237 (LMTX™) is a second-generation tau protein aggregation inhibitor for the treatment of Alzheimer's disease (AD) and frontotemporal dementia

Protocollo: TRx-237-039
N. EUDRACT 2017-003558-17

TauRx Therapeutics Ltd.

09 novembre 2018

1 SINOSSI

Nome dello sponsor/dell'azienda: TauRx Therapeutics Ltd (TauRx)
Nome del prodotto finito: LMTM (TRx0237) compresse rivestite con film, 4 mg
Nome dell'ingrediente attivo (sostanza farmaceutica): idrometiltionina mesilato
Numero e titolo dello studio: TRx-237-039: Studio randomizzato, in doppio cieco, controllato con placebo, a tre bracci, della durata di 9 mesi, con esame diagnostico per immagini del cervello, sulla sicurezza e sull'efficacia di leuco-metiltioninio bis (idrometansulfonato) (LMTM) in soggetti con malattia di Alzheimer precoce

Frequenza relativa geni associati all'AD

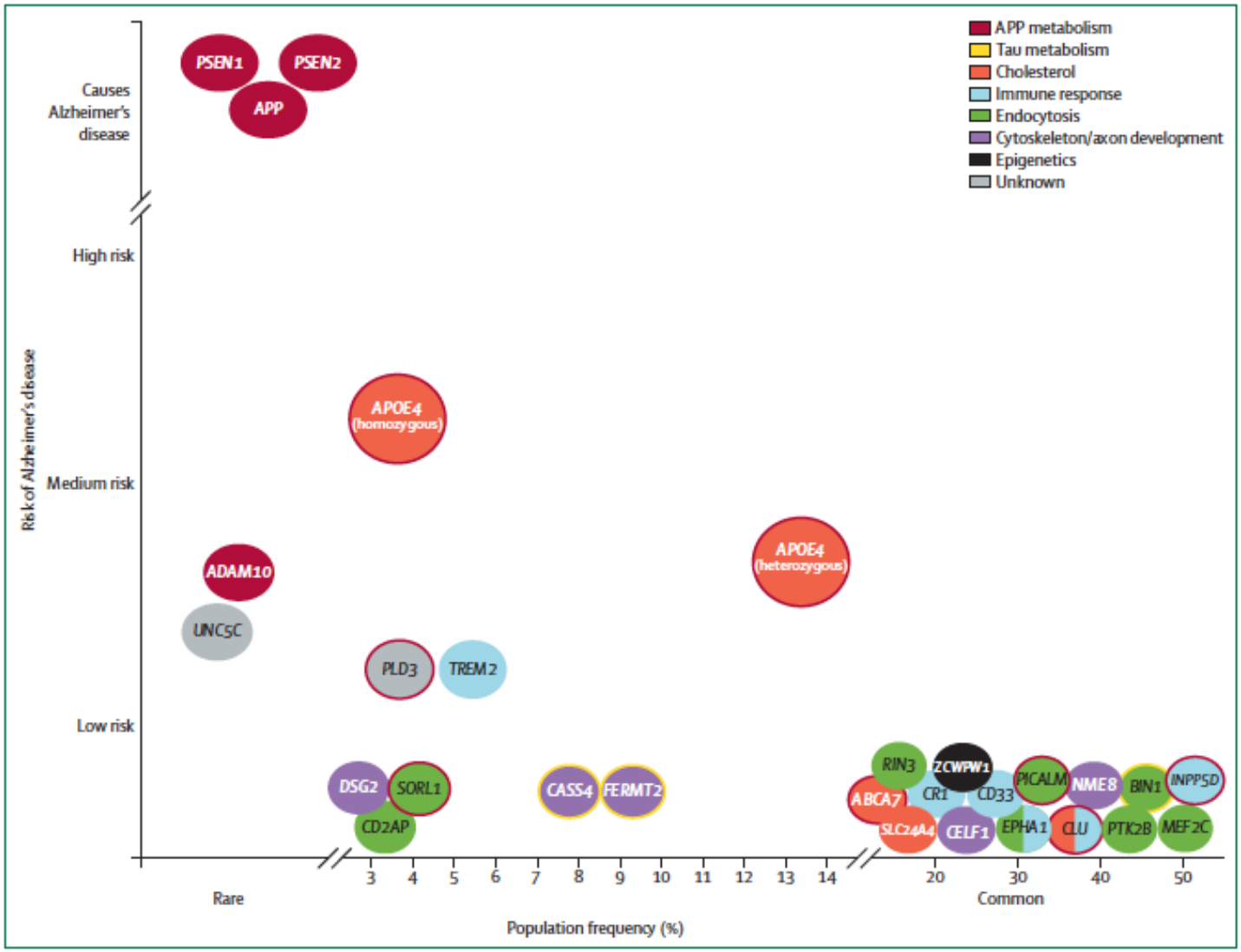
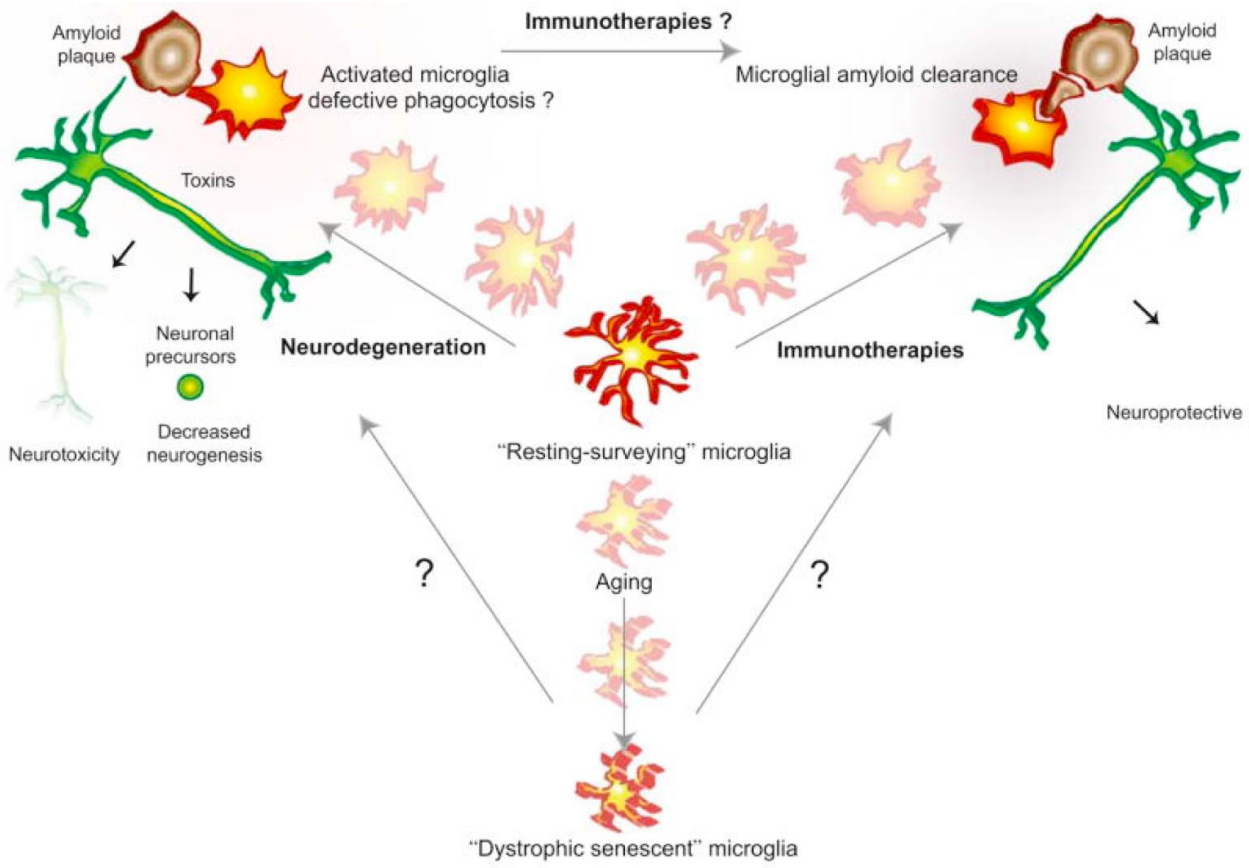


Figure: Schematic overview of genes linked to Alzheimer's disease

Neuroinflammation in AD

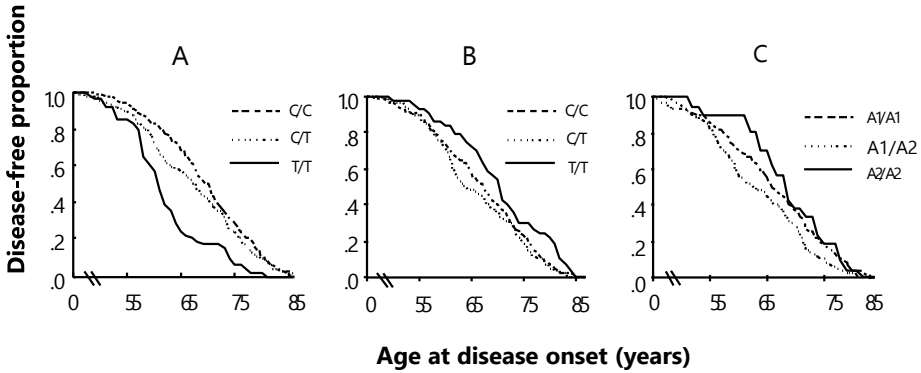


Association of Early-Onset Alzheimer's Disease with an Interleukin-1α Gene Polymorphism

Luigi M. E. Grimaldi, MD,*†‡
Valeria M. Casadei, MD,*† Cinzia Ferri, Msc,*†
Fabrizio Veglia, PhD,§§ Federico Licastro, MD,§
Giorgio Annoni, MD,‖ Ida Biunno, PhD,¶
Gianluca De Bellis, PhD,¶
Sandro Sorbi, MD,# Claudio Mariani, MD,**
Nicola Canal, MD,*† W. Sue T. Griffin, PhD,††
and Massimo Franceschi, MD‡‡

Overexpression of the pluripotent cytokine interleukin-1 (IL-1) by microglial cells correlates with formation of neuritic β-amyloid plaques in Alzheimer's disease (AD). We evaluated polymorphisms in the genes coding for the IL-1α, IL-1β, and IL-1 receptor antagonist cytokines, and tested their association with the occurrence and age at onset of sporadic AD. We found a strong association between the IL-1A T/T genotype and AD onset before 65 years of age (odds ratio, 4.86), with carriers of this genotype showing an onset of disease 9 years earlier than IL-1A C/C carriers. A weaker association with the age at onset was also shown for the IL-1B and IL-1RN genes. These data suggest either a direct effect of the IL-1 gene family, mainly IL-1A, on the clinical onset of AD, or a linkage dysequilibrium with an unknown locus relevant to AD on chromosome 2.

Grimaldi LME, Casadei VM, Ferri C, Veglia F, Licastro F, Annoni G, Biunno I, De Bellis G, Sorbi S, Mariani C, Canal N, Griffin WST, Franceschi M. Association of early-onset Alzheimer's disease with an interleukin-1α gene polymorphism. Ann Neurol 2000;47:361–365



Association of Interleukin-1 Gene Polymorphisms with Alzheimer's Disease

James A. R. Nicoll, MD,* Robert E. Mrak, MD, PhD,†‡
David I. Graham, MD, PhD,* Janice Stewart,*
Gordon Wilcock, DM, FRCP,§ Sian MacGowan, DM,§
Margaret M. Esiri, DM, FRCPath,‖
Lilian S. Murray, PhD,¶ Deborah Dewar, PhD,#
Seth Love, PhD, FRCP, FRCPath,§
Tim Moss, PhD, FRCPath,§
and W. Sue T. Griffin, PhD**††§§

Interleukin-1 (IL-1) is markedly overexpressed in Alzheimer's disease. We found the *IL-1A* 2,2 genotype in 12.9% of 232 neuropathologically confirmed Alzheimer's disease patients and 6.6% of 167 controls from four centers in the United Kingdom and United States (odds ratio, 3.0; controlled for age and for *ApoE* [apolipoprotein E] genotype). Homozygosity for both allele 2 of *IL-1A* and allele 2 of *IL-1B* conferred even greater risk (odds ratio, 10.8). IL-1 genotypes may confer risk for Alzheimer's disease through IL-1 overexpression and IL-1–driven neurodegenerative cascades.

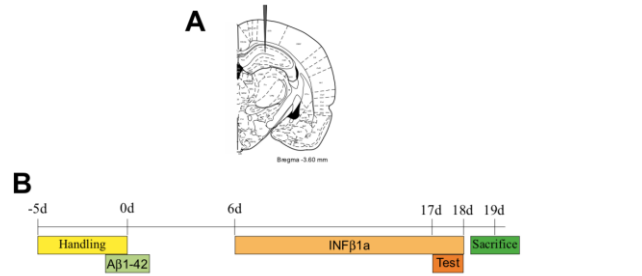
Nicoll JAR, Mrak RE, Graham DI, Stewart J, Wilcock G, MacGowan S, Esiri MM, Murray LS, Dewar D, Love S, Moss T, Griffin WST. Association of interleukin-1 gene polymorphisms with Alzheimer's disease. Ann Neurol 2000;47:365–368

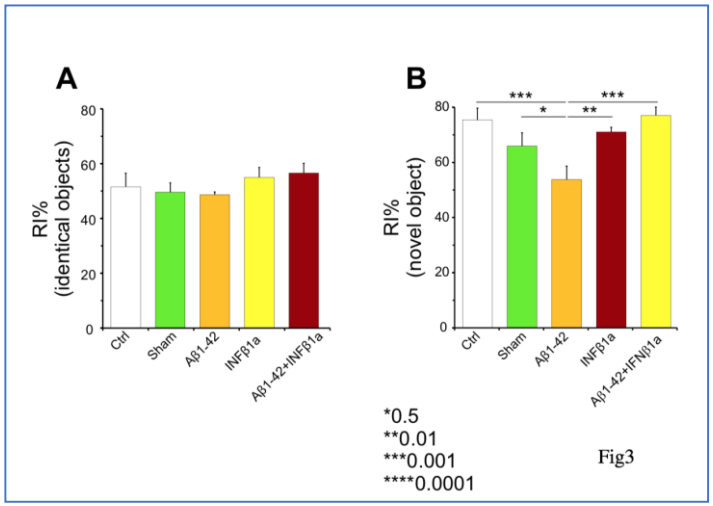
Journal of Neuroinflammation

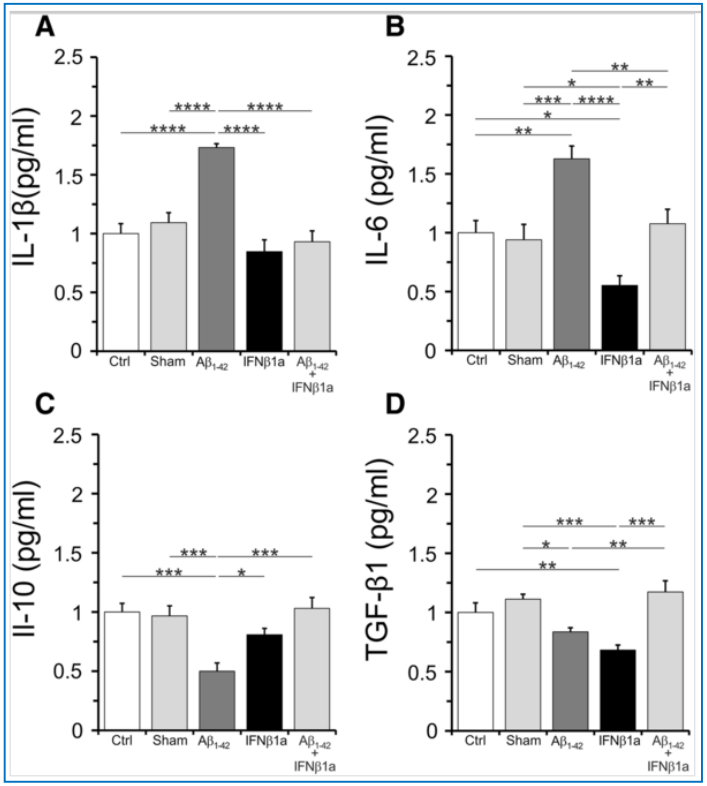
RESEARCH Open Access

Anti-inflammatory and cognitive effects of interferon-β1a (IFNβ1a) in a rat model of Alzheimer's disease

Giuseppa Mudò[1], Monica Frinchi[1], Domenico Nuzzo[2], Pietro Scaduto[1], Fulvio Plescia[3], Maria F. Massenti[3], Marta Di Carlo[2], Carla Cannizzaro[3], Giovanni Cassata[4], Luca Cicero[4], Maria Ruscica[5], Natale Belluardo[1*] and Luigi M. Grimaldi[5*]







Grimaldi et al. Journal of Neuroinflammation 2014, 11:30
http://www.jneuroinflammation.com/content/11/1/30

JOURNAL OF NEUROINFLAMMATION

RESEARCH Open Access

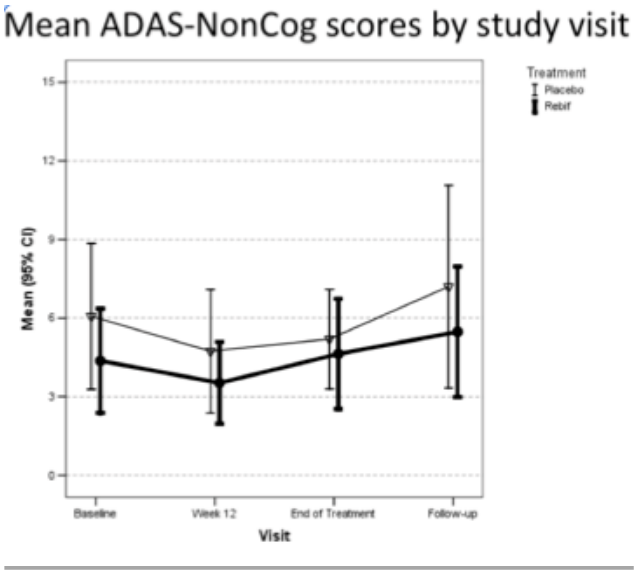
A pilot study on the use of interferon beta-1a in early Alzheimer's disease subjects

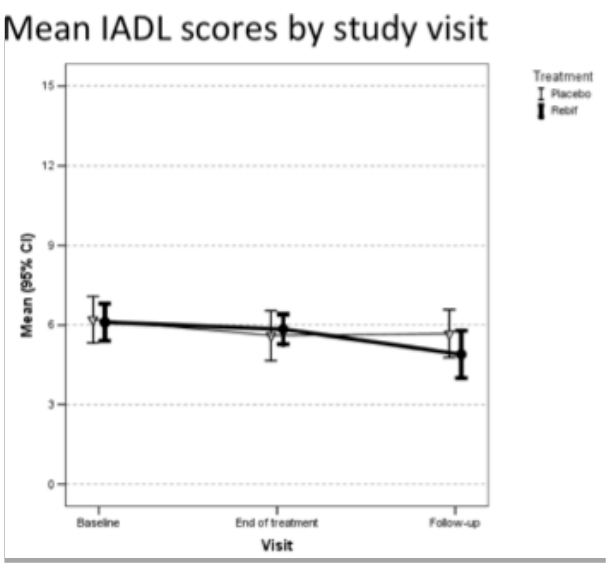
Luigi Maria Edoardo Grimaldi[1*], Giuseppe Zappalà[2], Francesco Iemolo[3], Anna Elisa Castellano[4], Stefano Ruggieri[3], Giuseppe Bruno[5] and Andrea Paolillo[6]

Abstract

Despite the fact that multiple sclerosis (MS) and Alzheimer's disease (AD) share common neuroimmunological features, interferon beta 1a (IFNβ1a), the well-established treatment for the prevention of disease progression and cognitive decline in MS patients, has never been used in AD. We evaluated the safety and efficacy of IFNβ1a in subjects affected by mild-to-moderate AD in a double-blind, randomized, placebo-controlled, multicenter pilot study. Forty-two early Alzheimer's patients were randomized to receive either a 22 mcg subcutaneous injection of IFNβ1a or placebo three times per week. A treatment period of 28 weeks was followed by 24 weeks of observation. IFNβ1a was well tolerated and adverse events were infrequent and mild to moderate. Although not statistically significant, a reduction in disease progression during follow-up was measured in IFNβ1a-treated patients by the Alzheimer's Disease Assessment Scale cognitive subscale. Interestingly, the treatment group showed significant improvements in the Instrumental Activities of Daily Living and Physical Self-maintenance Scale. This study suggests that IFNβ1a is safe and well tolerated in early AD patients, and its possible beneficial role should be further investigated in larger studies.

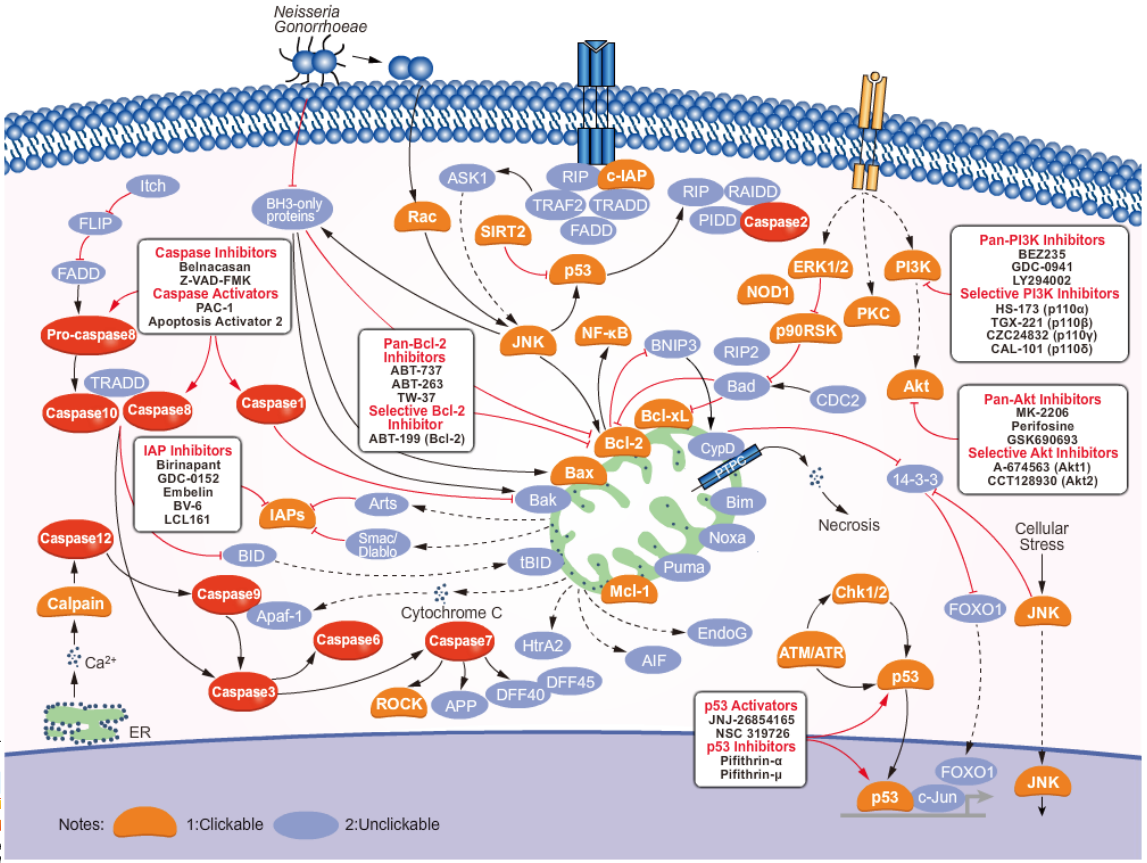
Keywords: Alzheimer's disease, clinical trials, randomized, controlled, multiple sclerosis, interferon





Caspasi 1

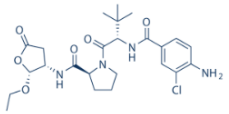
(IL-1β converting enzyme)



Belnacasan (VX-765)

Catalog No.S2228

Belnacasan (VX-765) is a potent and selective inhibitor of **caspase-1** with K_i of 0.8 nM



Size	Price	Stock	Quantity
10mg	EUR 137	In stock	0
50mg	EUR 461	In stock	0
Bulk Size	Bulk Discount		

Ac

Free Ov
Next da

Tel: +49-89-46148500 eu.info@selleckchem.com

Molecular Weight(MW): 509

Cited by 8 Publications

Cell, 2018, 175(2):442-457
Mucosal Immunol, 2016, 9(1):124-36
Mucosal Immunol, 2015, 9(1):124-36
Front Immunol, 2016, 7:536
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J Cell Mol Med, 2017, 21(7):1373-1387
Exp Cell Res, 2016, 10.1016/j.yexcr.2...
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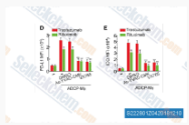
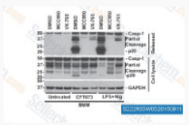
4 Customer Reviews





Purity & Quality Control

Batch: S222806 Purity:99.08 %

COA | NMR | HPLC | Microanalysis (Why microanalysis?) | MSDS | Datasheet | An article on Nature Medicine

Choose Selective Caspase Inhibitors

Name	Caspase	Caspase-1	Caspase-3	Caspase-8	Caspase-9	Caspase-4	Capase-7	Caspase-2	Caspase-5	Caspase-6	Caspase-10	Clinical Phase
Belnacasan (VX-765)		++++				++++						2
Ac-DEVD-CHO		+++	++++	++++	++	++	+++	+	++	+++	+++	
Q-VD-Oph		++	++	++	++							
Z-VAD-FMK	√											

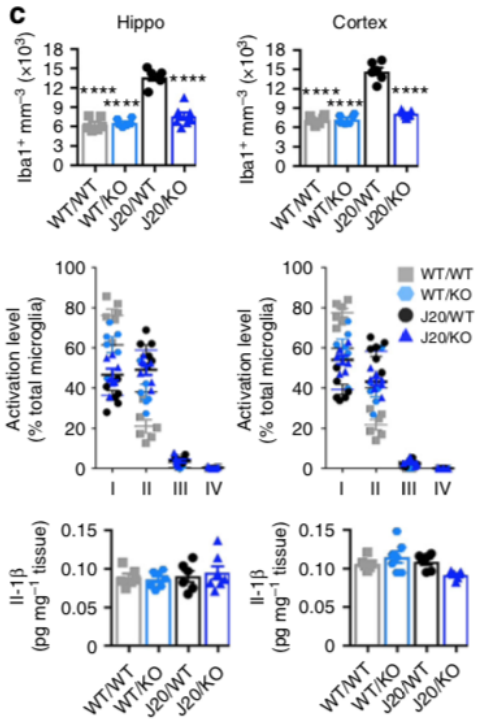
nature COMMUNICATIONS

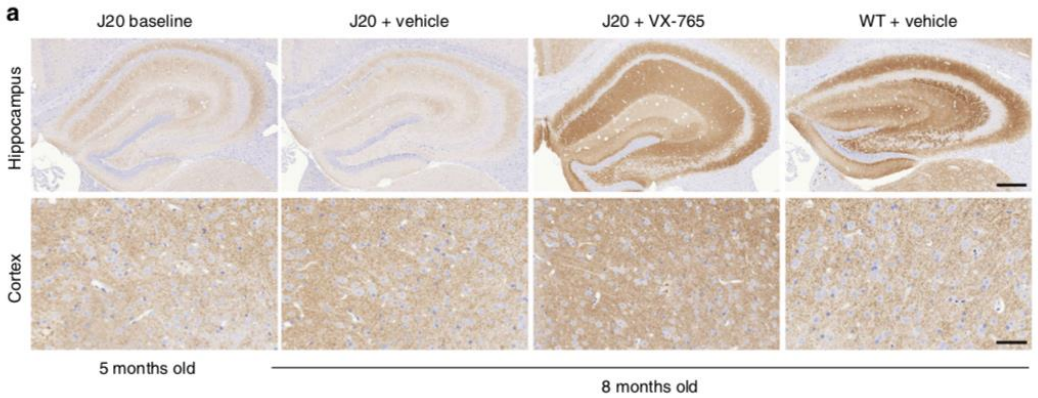
ARTICLE

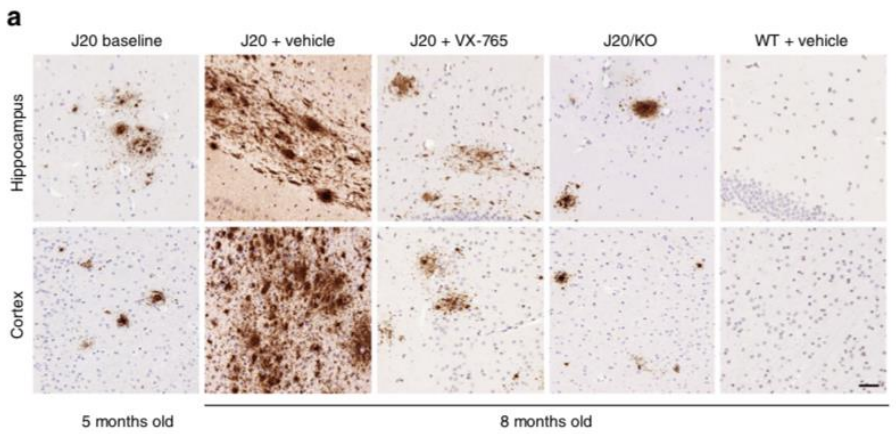
DOI: 10.1038/s41467-018-06449-x OPEN

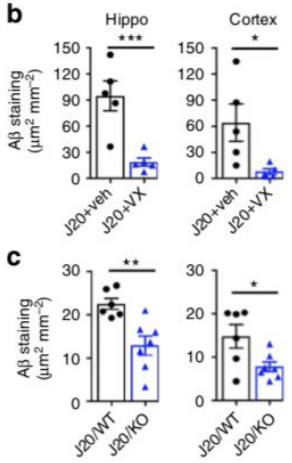
Caspase-1 inhibition alleviates cognitive impairment and neuropathology in an Alzheimer's disease mouse model

Joseph Flores[1,2], Anastasia Noël[1,2], Bénédicte Foveau[1], Jeffrey Lynham[1,3], Clotilde Lecrux[2] & Andréa C. LeBlanc[1,2,3]









Principali studi farmacologici in corso 2018 (1)

Product	Trial	Setting	Trial Start	Primary Completion
Solanezumab	~~EXPEDITION-3~~	~~Mild AD~~	~~Jul 2013~~	~~Oct 2016~~
	DIAN-TU	Pre-clinical to mild AD	Dec 2012	Sep 2023
	A4	Pre-clinical AD	Feb 2014	Jul 2022
	~~EXPEDITION-PRO~~	~~Prodromal / MCI~~	~~Jun 2016~~	~~Apr 2021~~
ALZT-OP1	AZT-001	Prodromal / MCI	Jun 2016	Mar 2018
TTP-488	STEADFAST A	Mild AD	Mar 2015	Nov 2018
	STEADFAST B	Mild AD	Mar 2015	Nov 2018
	STEADFAST EXT	Mild AD	Dec 2016	Nov 2020
AD-4833	TOMORROW	Pre-clinical AD	Aug 2013	Jul 2019
	TOMORROW EXT	Pre-clinical AD	Nov 2014	Apr 2021
Lanabecestat (AZD3293)	AMARANTH	MCI and mild AD	Sep 2014	Aug 2019
	~~DAYBREAK~~	~~Mild AD~~	~~Jun 2016~~	~~Sep 2019~~
	Additional P3 Trial	*MCI due to AD*	*Jun 2018*	*Jun 2023*
	AMARANTH EXT	MCI and mild AD	Mar 2017	Sep 2020
AGB-101	HOPE4MCI	aMCI	*Jan 2018*	*Mar 2021*
Elenbecestat (E2609)	MISSION AD1	MCI and mild AD	Oct 2016	*Jun 2020*
	MISSION AD2	MCI and mild AD	Dec 2016	Aug 2020
Verubecestat (MK-8931)	~~EPOCH~~	~~Mild to moderate AD~~	~~Dec 2012~~	~~Feb 2017~~
	APECS	MCI due to AD	Nov 2013	Feb 2019
	Additional P3 Trial	*MCI due to AD*	*Jun 2018*	*Jun 2023*
Masitinib	AB09004	Mild to moderate AD	May 2013	*Feb 2017*
	Additional P3 Trial	*Mild AD*	*Nov 2017*	*Nov 2021*

Principali studi farmacologici in corso - 2018 (2)(2/2)

Product	Trial	Setting	Trial Start	Estimate Primary Completion
Crenezumab	CREAD	MCI and mild AD	Mar 2016	Aug 2020
	CREAD2	MCI and mild AD	Mar 2017	Oct 2021
Gantenerumab	DIAN-TU	Pre-clinical to mild AD	Dec 2012	Sep 2023
	GRADUATE 1	Prodromal to mild	*Mar 2018*	*Aug 2022*
	GRADUATE 2	Prodromal to mild	*Mar 2017*	*Aug 2022*
TRx0237	*Monotherapy*	*Prodromal / MCI*	*Jan 2018*	*Jan 2023*
JNJ-54861911	EARLY	Pre-clinical AD	Nov 2015	Apr 2024
	DIAN-TU	Pre-clinical to mild AD	Dec 2012	Sep 2023
CNP-520	GENERATION S1	Pre-clinical AD	Nov 2015	Mar 2024
	GENERATION S2	Pre-clinical AD	Jun 2017	Jul 2024
ALZ-801	Planned P3 Trial	Mild to moderate AD	*Jul 2017*	*Jan 2021*
	Planned P3 Trial	Mild AD	*Oct 2017*	*Apr 2021*
Grifols	AMBAR	Mild to moderate AD	Mar 2012	Dec 2017
	Additional P3 Trial	*Mild AD*	*Jun 2018*	*Jun 2023*
CAD-106	GENERATION	Pre-clinical AD	Nov 2015	Aug 2023

FONDAZIONE ISTITUTO G. GIGLIO DI CEFALU'

Un modello di gestione integrata ospedale-territorio per pazienti con demenza finalizzata all'ottimizzazione dell'approccio diagnostico e terapeutico e alla creazione di una rete regionale

Luigi M.E. GRIMALDI

U.O. Neurologia

Rete regionale integrata per i pazienti a rischio demenza nell'ambito della quale si possa:

a. Individuare e caricare informazioni su un sistema informatico dedicato (MMG; **I livello**);

b. Effettuare uno screening iniziale clinico/neuropsicologico di conferma (rete Centri UVA; **II livello**);

c. Applicare tecnologie e competenze avanzate (PET, genomica, proteinomica) per definire diagnosi specialistica, trattamento neurologico (sia sperimentale che standard) e predisporre tramite il sistema informatico regionale il percorso terapeutico-gestionale personalizzato a livello dell'ASP di competenza territoriale, es. Case Sollievo, RSA, hospice (Centro o Centri Regionali ad elevata specializzazione; **III livello**);

d. Formare il personale coinvolto nella rete assistenziale (Centro o Centri Regionali; III livello);

e. Analizzare e rendicontare scientificamente i risultati sanitari, scientifici e gestionali (Centri Regionali; III livello);

f. Fornire supporto tecnico all'Assessorato per la gestione economica e l'appropriatezza terapeutica


Grazie