

Dementia update

Joseph Quinn, MD

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agenda

- Update on diagnosis
 - Amyloid PET scans
 - Blood test for Alzheimer’s
- Update on treatment
 - Cholinesterase inhibitors – higher doses
 - Memantine-changes in manufacture
 - Vitamin E for preservation of ADLs
 - Depakote for symptom management
 - Prazosin for symptom management

Diagnosis of dementia

History, including collateral historian
 Examination, including mental status
 (Neuropsych if MMSE/MOCA/SLUMS is high)



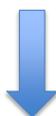
Diagnosis of dementia



Rule out treatable causes of cognitive decline:
 CBC, chem, B12, TSH
 structural brain imaging (CT or MRI)



Alzheimer’s



Vascular dementia



Lewy body



Frontotemporal

Imaging AD pathology in living patients

Use of Florbetapir-PET for Imaging β -Amyloid Pathology

Christopher M. Clark, MD

Julie A. Schneider, MD

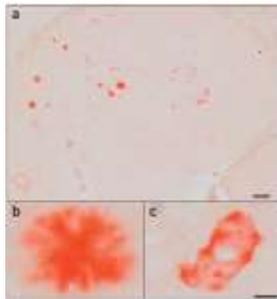
Barry J. Bedell, MD, PhD

Thomas G. Beach, MD, PhD

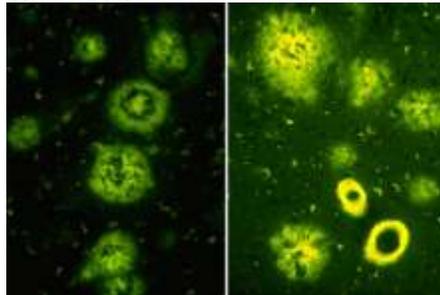
Context The ability to identify and quantify brain β -amyloid could increase the accuracy of a clinical diagnosis of Alzheimer disease.

JAMA. 2011;305(3):275-283

ission tomographic (PET) imaging
ice of β -amyloid in the brain at au-

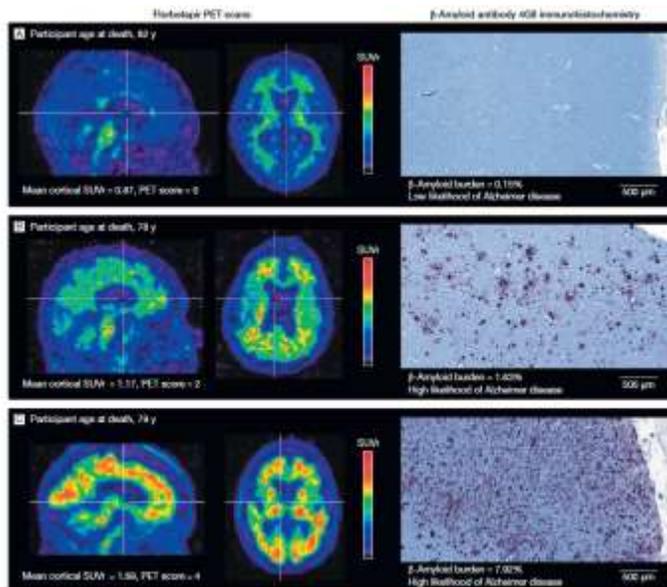


Congo red



Thioflavin S

Imaging AD pathology in living patients



Imaging AD pathology in living patients

- Florbetapir for PET scans was approved by the FDA April 2012
- Flutemetamol also recently approved (October 2013)
- CMS will not cover them, so no other insurance will cover them, including the VA

FDA statement on amyloid imaging:

- A negative florbetapir scan:
 - indicates sparse to no neuritic plaques.
 - is inconsistent with a neuropathological diagnosis of Alzheimer's disease at the time of image acquisition.
 - reduces the likelihood that a patient's cognitive impairment is due to Alzheimer's disease.

SOURCE INFORMATION

From the Division of Medical Imaging Products (L.Y., D.R.), Office of New Drugs and the Office of Drug Evaluation IV (C.G.), Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD.

FDA statement on amyloid imaging:

- A positive florbetapir scan:
 - indicates moderate to frequent amyloid neuritic plaques.
 - may be observed in older people with normal cognition and in patients with various neurologic conditions, including Alzheimer's disease.

SOURCE INFORMATION

From the Division of Medical Imaging Products (L.Y., D.R.), Office of New Drugs and the Office of Drug Evaluation IV (C.G.), Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD.

FDA statement on amyloid imaging:

- Important florbetapir scan limitations:
 - A positive scan does not establish a diagnosis of Alzheimer's disease or other cognitive disorder.
 - The scan has not been shown to be useful in predicting the development of dementia or any other neurologic condition, nor has usefulness been shown for monitoring responses to therapies.

SOURCE INFORMATION

From the Division of Medical Imaging Products (L.Y., D.R.), Office of New Drugs and the Office of Drug Evaluation IV (C.G.), Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD.

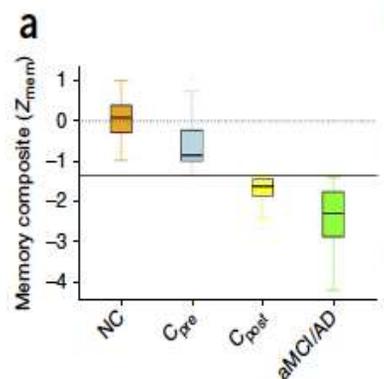
Blood test for Alzheimer's disease

Plasma phospholipids identify antecedent memory impairment in older adults

Mark Mapstone¹, Amrita K Cheema^{2,3}, Massimo S Fianadaca^{4,5}, Xiaogang Zhong⁶, Timothy R Mhyre⁵, Linda H MacArthur⁵, William J Hall⁷, Susan G Fisher^{8,14}, Derick R Peterson⁹, James M Huley¹⁰, Michael D Nazar¹¹, Steven A Rich¹², Dan J Berlau^{13,14}, Carrie B Peltz¹³, Ming T Tan⁶, Claudia H Kawas¹³ & Howard J Federoff^{4,5}

Received 27 August 2013; accepted 9 January 2014; published online 9 March 2014; doi:10.1038/nm.3466

nature
medicine



methods

- Enrolled 525 individuals in a 5 year study
- Divided into AD/MCI, Converters, Normal Controls
- 74 were AD/MCI
- in year 3, compared plasma metabolites in 53 AD/MCI and 53 matched control subjects to identify differences
- Then tested the hypothesis with 21 AD/MCI and 21 matched controls

Untargeted “LASSO” analysis:

Table 1 Putative metabolite markers resulting from binary comparison of the study groups

Metabolite	LASSO coefficient	Comparison groups	Mode	Mass/charge ratio
Phosphatidylinositol (18:0/0:0)	↓ (-0.674)	NC versus Converter _{pre}	NEG	599.3226
Proline-asparagine dipeptide	↑ (0.192)	NC versus aMCI/AD	POS	230.1146
Glycoursodeoxycholic acid	↑ (0.107)	NC versus aMCI/AD	POS	450.3196
Malic acid	↓ (-0.024)	NC versus aMCI/AD	POS	134.0207

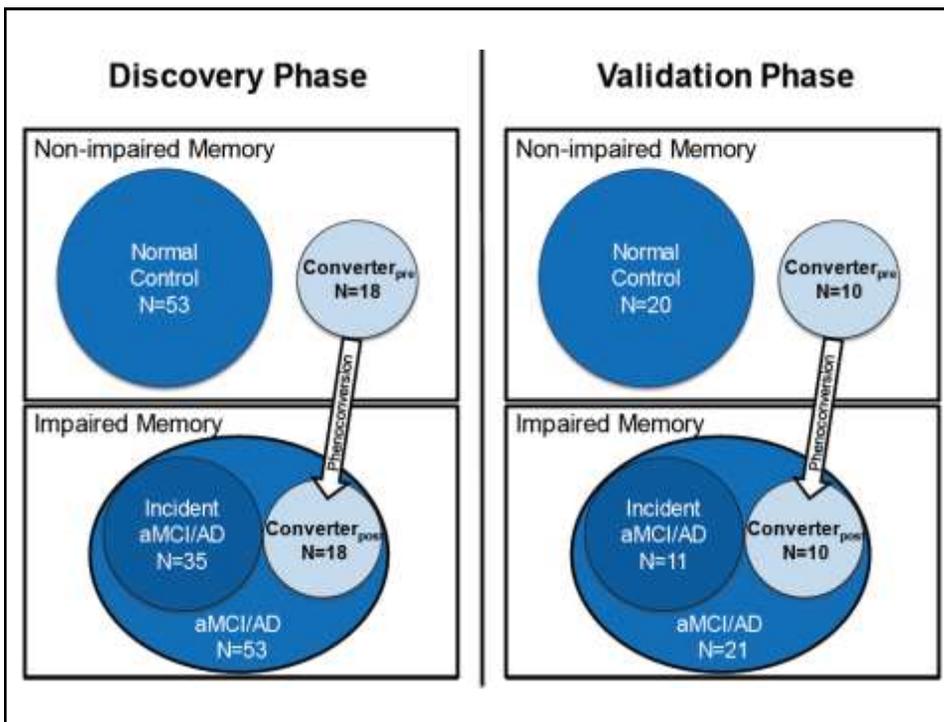
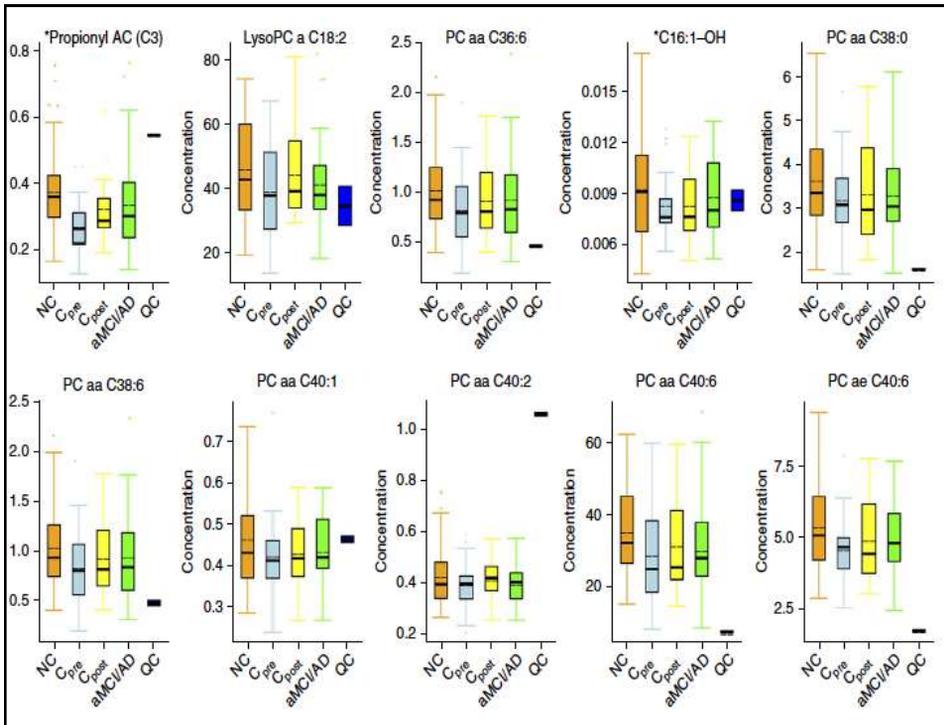
The markers were chosen on the basis of significant predictive value as determined by LASSO coefficient analysis. The positive estimated LASSO coefficient suggests elevation in corresponding comparison group (aMCI/AD and Converter_{pre}) compared to NC participants. Arrows indicate upregulation or downregulation in the comparison group as compared to the NC participants. NEG, negative; POS, positive.

Targeted analysis:

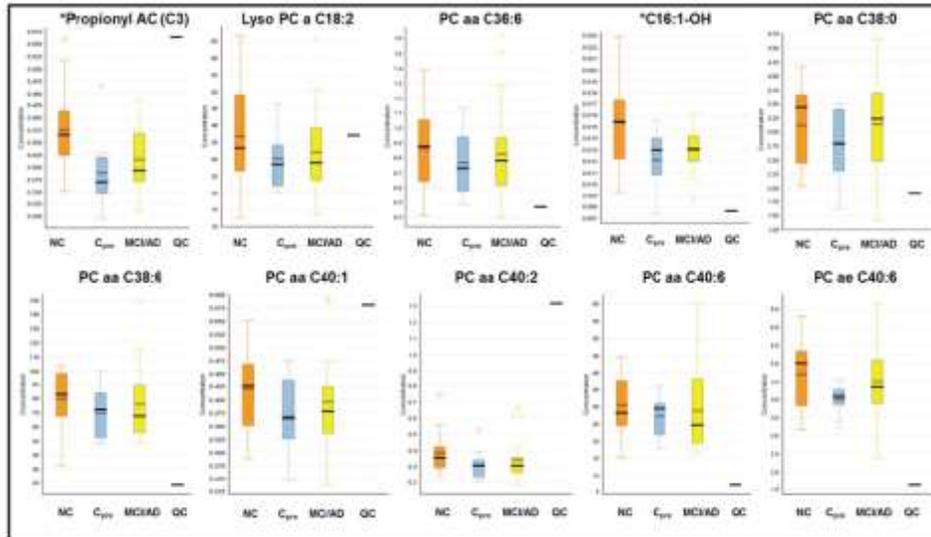
Table 2 Difference detection of putative metabolites using SID-MRM-MS

Metabolite	Fold change	Comparison groups	Mode	P value
PC ae C38:4	↓	NC versus Converter _{pre}	POS	0.00417
Proline	↓	NC versus Converter _{pre}	POS	0.00003
Lysine	↓	NC versus Converter _{pre}	POS	0.0020
Serotonin	↓	NC versus Converter _{pre}	POS	0.0160
Taurine	↓	NC versus Converter _{pre}	POS	0.0030
DOPA	↑	NC versus Converter _{pre}	POS	0.0001
Phenylalanine	↓	NC versus Converter _{pre}	POS	0.00001
Acylcarnitine C7-DC	↓	NC versus aMCI/AD	POS	0.0001

The arrows indicate upregulation or downregulation in the comparison group as compared to the NC participants. DOPA, dihydroxyphenylalanine; C7-DC, pimelyl-L-carnitine.



Validation phase:



Supplementary Figure 4. Trend plots for the ten metabolite panel- Validation phase. This figure shows the results of the internal c

Blood test for AD: conclusions

- Promising initial results from unbiased metabolomics study.
- Still a long way to a validated blood test for AD.

Update on dementia diagnosis:

- New PET studies FDA-approved but not covered by insurance
- Blood test results encouraging but very preliminary.
- Dementia diagnosis continues to be highly dependent on history and exam.

Review of dementia treatment: “cognitive enhancers”

- Cholinesterase inhibitors:
 - Donepezil
 - Galantamine
 - Rivastigmine
- NMDA antagonist
 - Memantine

Review of cognitive enhancers

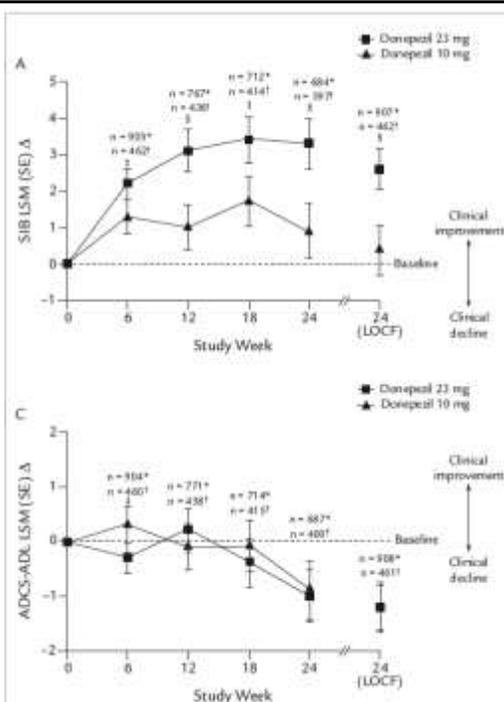
	MCI	Mild-moderate AD	Moderate-severe AD
Cholinesterase inhibitors	Optional	FDA approved	FDA approved
memantine	Not approved	Not approved	FDA approved

Update on treatment

- Cholinesterase inhibitors-23 mg donepezil
- Memantine
- Vitamin E
- Symptomatic treatments

Effectiveness and Tolerability of High-Dose (23 mg/d) Versus Standard-Dose (10 mg/d) Donepezil in Moderate to Severe Alzheimer's Disease: A 24-Week, Randomized, Double-Blind Study

Martin R. Farlow, MD¹; Stephen Salloway, MD, MS²; Pierre N. Tariot, MD³; Jane Yardley, PhD⁴; Margaret L. Moline, PhD⁵; Qin Wang, PhD⁵; Elimor Brand-Schieber, PhD⁵; Heng Zou, MS⁵; Timothy Hsu, MD⁵; and Andrew Satlin, MD⁵



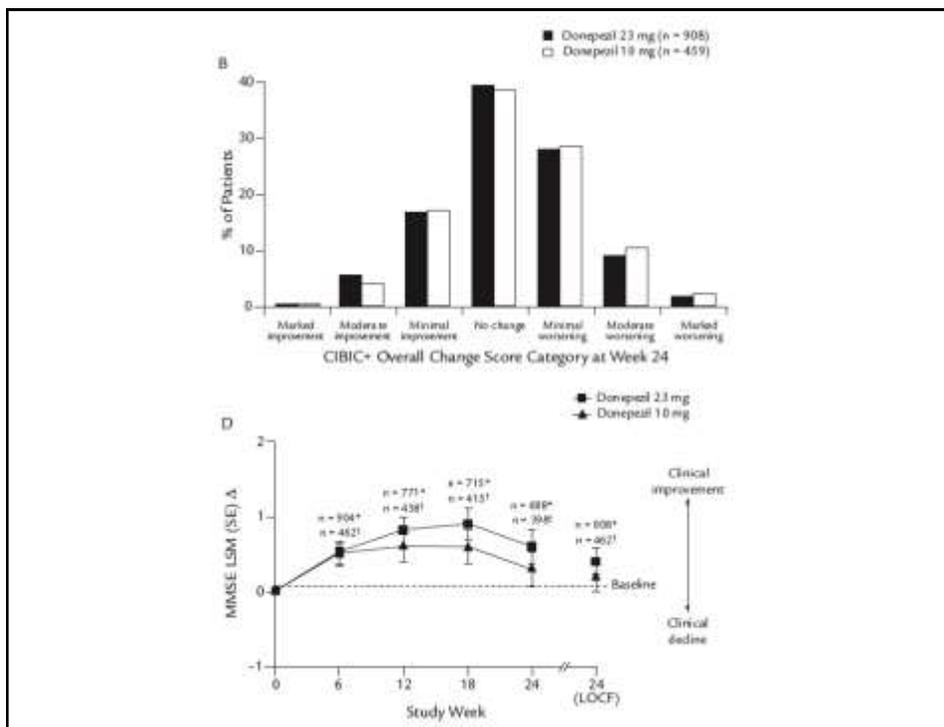


Table IV. Treatment-emergent adverse events* (TEAEs) in patients with moderate to severe Alzheimer's disease who received ≥1 dose of treatment with donepezil 23 or 10 mg/d. Data are number (%) of patients.

Parameter	Donepezil 23 mg/d (n = 963)	Donepezil 10 mg/d (n = 471)
Patients with ≥1 TEAE	710 (73.7)	300 (63.7)
TEAE		
Nausea	114 (11.8)	16 (3.4)
Vomiting	89 (9.2)	12 (2.5)
Diarrhea	80 (8.3)	25 (5.3)
Anorexia	51 (5.3)	8 (1.7)
Dizziness	47 (4.9)	16 (3.4)
Weight decrease	45 (4.7)	12 (2.5)
Urinary tract infection	42 (4.4)	19 (4.0)
Headache	41 (4.3)	15 (3.2)
Fall	39 (4.0)	18 (3.8)
Agitation	38 (3.9)	18 (3.8)
Insomnia	33 (3.4)	11 (2.3)
Bradycardia and sinus bradycardia	27 (2.8)	3 (0.6)
Aggression	26 (2.7)	12 (2.5)
Urinary incontinence	24 (2.5)	6 (1.3)
Fatigue	23 (2.4)	4 (0.8)
Asthenia	20 (2.1)	3 (0.6)
Somnolence	20 (2.1)	5 (1.1)
Contusion	20 (2.1)	1 (0.2)

*Medical Dictionary for Regulatory Activities preferred terms.¹³ TEAEs that occurred in ≥2% of patients who received donepezil 23 mg/d and that occurred at a higher frequency with donepezil 23 mg/d than with donepezil 10 mg/d are shown.

18.6% on 23 mg discontinued due to adverse events compared to 7.9% on 10 mg

DATE: July 22, 2010

FROM: Director
Division of Neurology Products/HFD-120

TO: File, NDA 22-568

SUBJECT: Action Memo for NDA 22-568, for Aricept (donepezil hydrochloride extended release) 23 mg Sustained Release

For these reasons, I believe that the 23 mg dose might be useful in patients who do not respond adequately to the 10 mg dose, although I believe labeling should make explicitly clear that this dose is associated with a significant increase in the incidence of adverse events that can have significant clinical sequelae.

The sponsor submitted this application for the 23 mg dose to be considered a modified release formulation. However, despite the formulation having some manufacturing aspects designed to produce a modified release preparation, the product's in vivo performance does not establish it as such a formulation (for instance, it is not given less frequently than the currently available immediate release formulations). Indeed, the plasma levels achieved with the 23 mg tablet are about twice those achieved with the 10 mg tablet. In other words, in our view, the new formulation is rightly seen simply as an increased dosage.

How does Aricept 23 compare to 10?

- Marginally greater efficacy on cognition
- No demonstration of benefit on global measures
- More side effects
- Higher cost
- Not available in VA

Namenda/Memantine

- Forest recently announced that they will no longer make the immediate-release tablets that have been the most commonly used form.
- They will continue to make the oral solution and sustained release formulation.

Treatment of dementia: beyond cognitive enhancers:

- Vitamin E
- Symptomatic therapies
 - Valproic acid
 - prazosin

Original Investigation

Effect of Vitamin E and Memantine on Functional Decline in Alzheimer Disease

The TEAM-AD VA Cooperative Randomized Trial

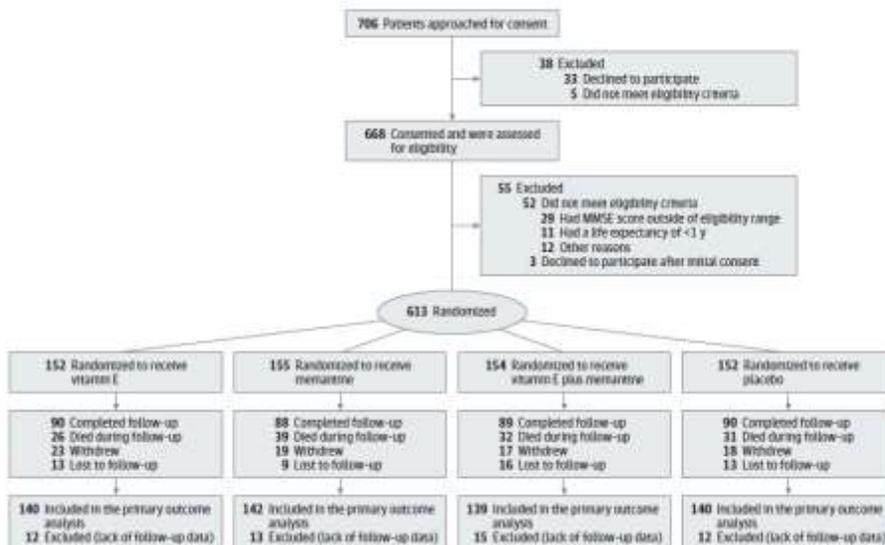
JAMA. 2014;311(1):33-44. doi:10.1001/jama.2013.282834

VA patients with mild to moderate AD on stable dose of CEI randomized to one of four groups:

- placebo
- memantine 10 bid
- vitamin E 2000 IU per day
- memantine plus vitamin E

Duration of intervention = 48 weeks

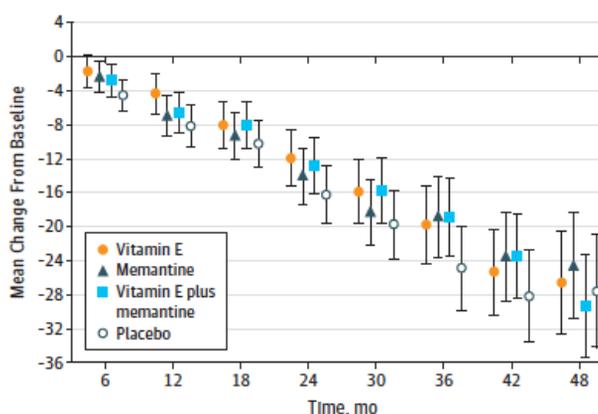
Figure 1. Flow of Participants in the Study



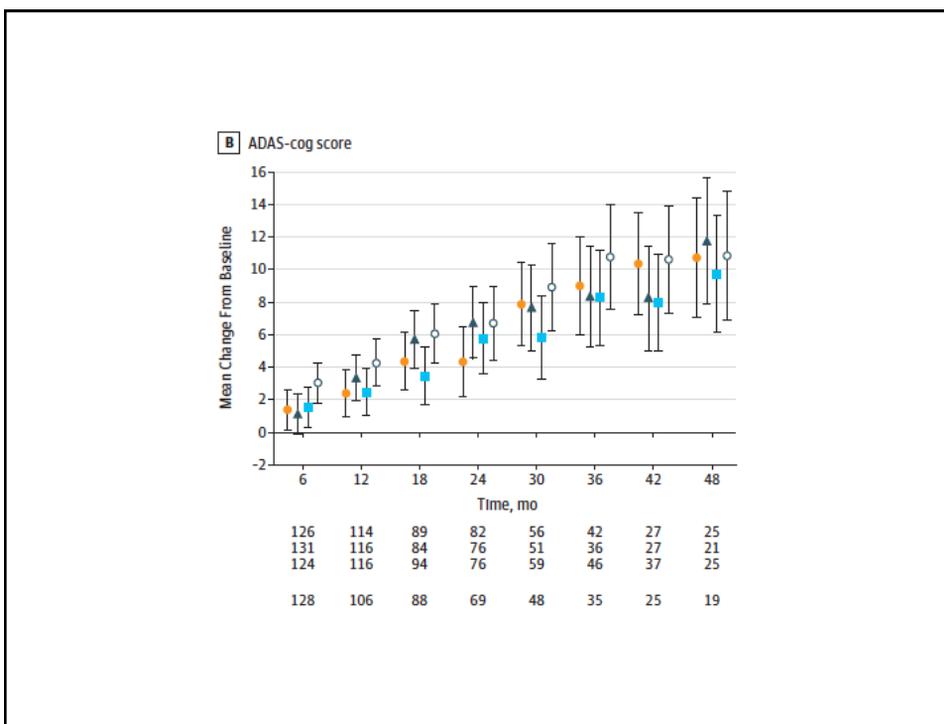
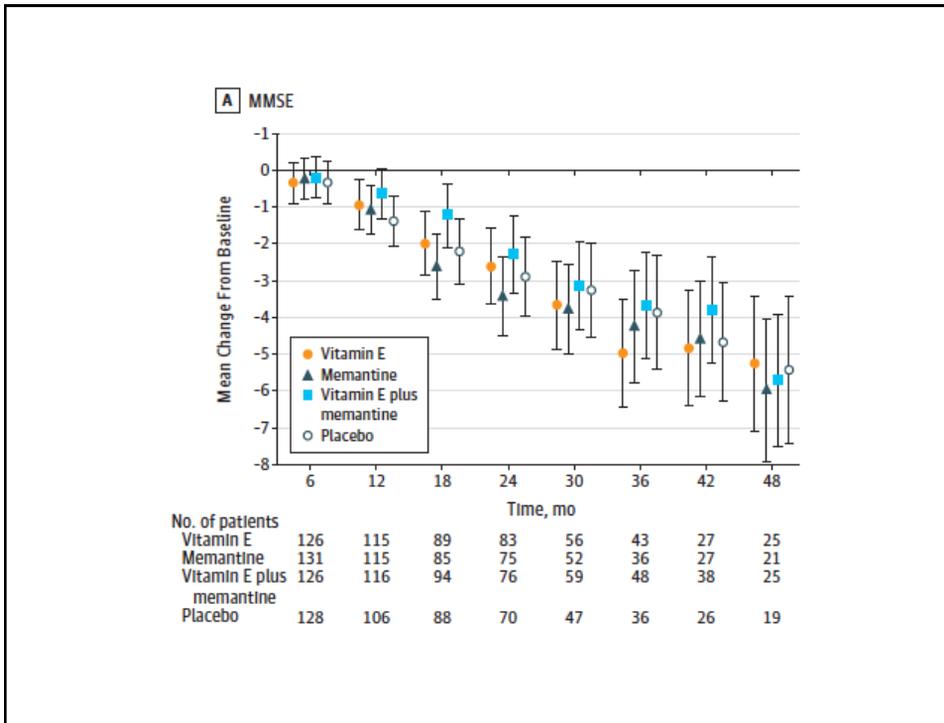
Groups were well matched on:

- Age (about 78 years old)
- Gender (96-98% male)
- MMSE (about 20)
- Cholinesterase inhibitors (all were on CEI, 65% donepezil, 30% galantamine, 5% rivastigmine)

Figure 2. Changes in Primary Outcome (ADCS-ADL Inventory Score) During the 4-Year Study Period, Compared With Baseline



No. of patients								
Vitamin E	134	122	103	88	66	51	39	31
Memantine	139	119	95	80	64	45	38	30
Vitamin E plus memantine	131	120	102	84	64	55	46	32
Placebo	135	112	96	77	54	41	33	25



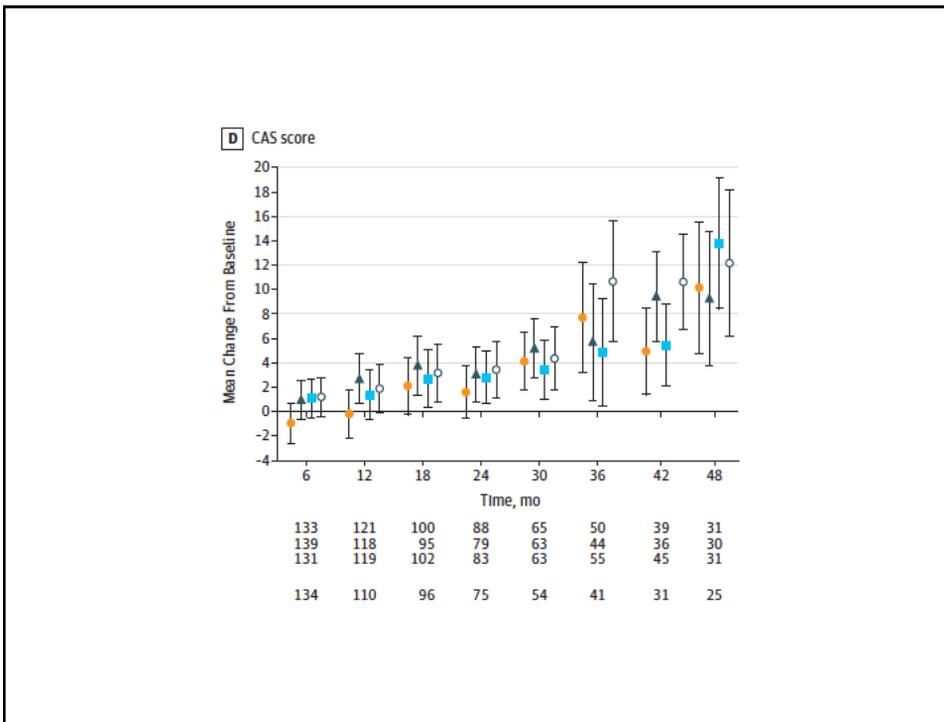
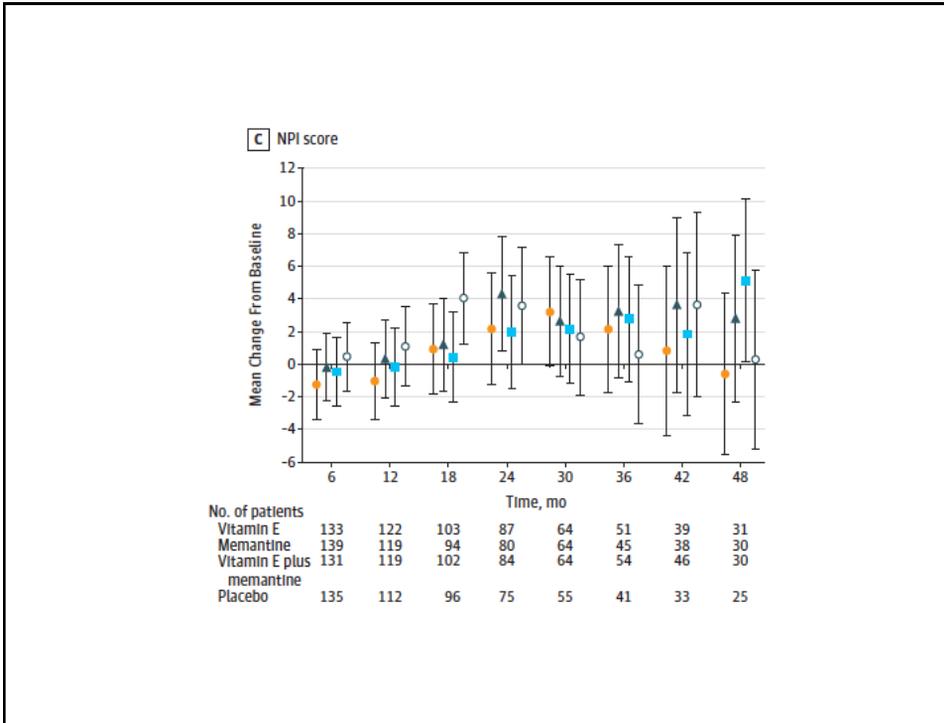
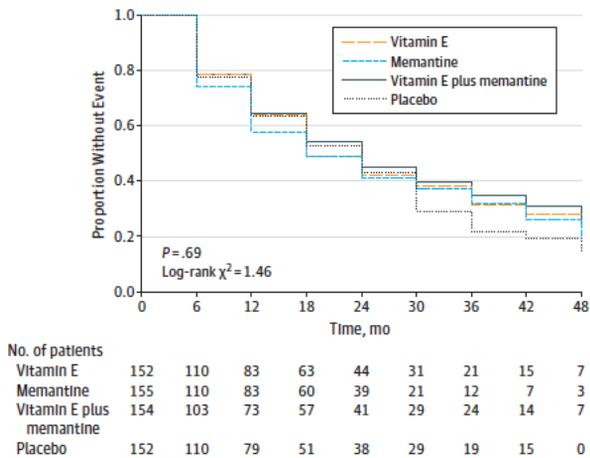


Figure 4. Dependence Scale Score Time-to-Event Analysis



VA Vitamin E study conclusions:

- Vitamin E associated with slowing of functional decline
- No effect on cognitive measures
- How does this compare with previous literature?

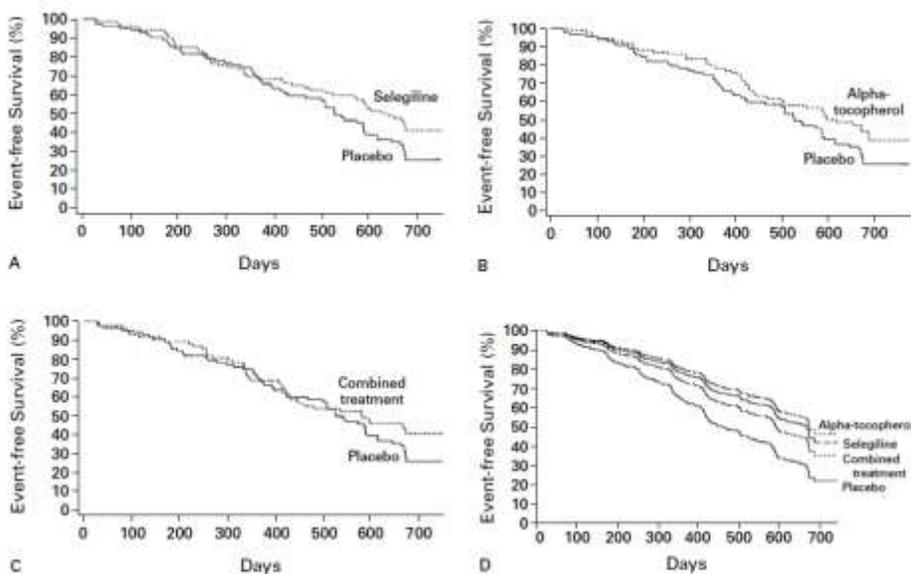
A CONTROLLED TRIAL OF SELEGILINE, ALPHA-TOCOPHEROL, OR BOTH AS TREATMENT FOR ALZHEIMER'S DISEASE

MARY SANO, PH.D., CHRISTOPHER ERNESTO, M.S., RONALD G. THOMAS, PH.D., MELVILLE R. KLAUBER, PH.D.,
 KIMBERLY SCHAFER, M.S., MICHAEL GRUNDMAN, M.D., M.P.H., PETER WOODBURY, JOHN GROWDON, M.D.,
 CARL W. COTMAN, PH.D., ERIC PFEIFFER, M.D., LON S. SCHNEIDER, M.D.,
 AND LEON J. THAL, M.D., FOR THE MEMBERS OF THE ALZHEIMER'S DISEASE COOPERATIVE STUDY*

TABLE 1. BASE-LINE DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF 341 PATIENTS WITH ALZHEIMER'S DISEASE RANDOMLY ASSIGNED TO RECEIVE PLACEBO, SELEGILINE, ALPHA-TOCOPHEROL, OR BOTH AGENTS.*

CHARACTERISTIC	PLACEBO (N=84)	SELEGILINE (N=87)	ALPHA-TOCOPHEROL (N=85)	SELEGILINE AND ALPHA-TOCOPHEROL (N=85)
Age (yr)	73.5±8.8	72.7±8.9	73.4±7.8	73.9±7.1
Education (yr)	12.2±3.1	12.4±3.7	12.6±3.3	12.7±3.3
Duration of illness (yr)	5.5±2.9	4.8±2.4	5.3±2.7	4.7±2.5
Female sex (% of patients)	65.5	67.8	65.9	60.0
Score on Mini-Mental State Examination†	13.3±4.9‡	12.7±5.0	11.3±5.7	12.9±5.7
Score on Blessed Dementia Scale§	6.1±2.1	6.3±1.9	6.6±2.1	6.4±2.3
Extrapyramidal signs (% of patients)	19.0	26.4	18.8	24.7
Clinical Dementia Rating¶	10.9±1.2	11.0±1.2	11.3±1.3	10.9±1.2

A CONTROLLED TRIAL OF SELEGILINE, ALPHA-TOCOPHEROL, OR BOTH AS TREATMENT FOR ALZHEIMER'S DISEASE



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Results Despite random assignment, the base-line score on the Mini-Mental State Examination was higher in the placebo group than in the other three groups, and this variable was highly predictive of the primary outcome ($P < 0.001$). In the unadjusted analyses, there was no statistically significant difference in the outcomes among the four groups. In analyses that included the base-line score on the Mini-Mental State Examination as a covariate, there were significant delays in the time to the primary outcome for the patients treated with selegiline (median time, 655 days; $P = 0.012$), alpha-tocopherol (670 days, $P = 0.001$), or combination therapy (585 days, $P = 0.049$), as compared with the placebo group (440 days).

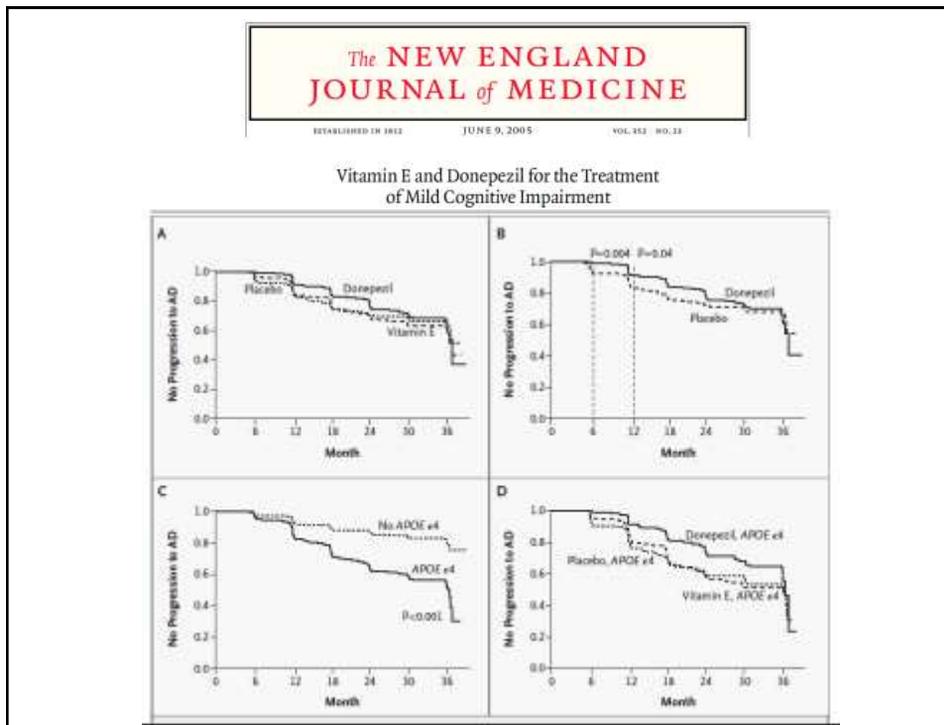
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 9, 2005 VOL. 352 NO. 23

Vitamin E and Donepezil for the Treatment of Mild Cognitive Impairment

Table 1. Baseline Characteristics of the Subjects.*

Variable	Placebo Group (N=259)	Donepezil Group (N=253)	Vitamin E Group (N=257)	All Subjects (N=769)
Age — yr	72.9±7.6	73.1±7.1	72.8±7.3	72.9±7.3
Female sex — no. (%)	121 (47)	112 (44)	119 (46)	352 (46)
APOE ε4 carrier — no. (%)	136 (53)	147 (58)	141 (55)	424 (55)
ADAS-Cog score				
Original	11.03±4.2	11.28±4.5	11.48±4.4	11.26±4.4
Modified	17.40±6.0	17.72±6.2	18.04±6.0	17.72±6.1
MMSE score	27.35±1.8	27.25±1.8	27.20±1.9	27.27±1.8
CDR sum-of-boxes score	1.87±0.8	1.80±0.8	1.78±0.8	1.82±0.8
Score on Global Deterioration Scale	2.72±0.6	2.66±0.6	2.64±0.6	2.67±0.6
Score on Activities of Daily Living Scale	45.87±5.2	46.49±4.3	45.82±4.6	46.06±4.7

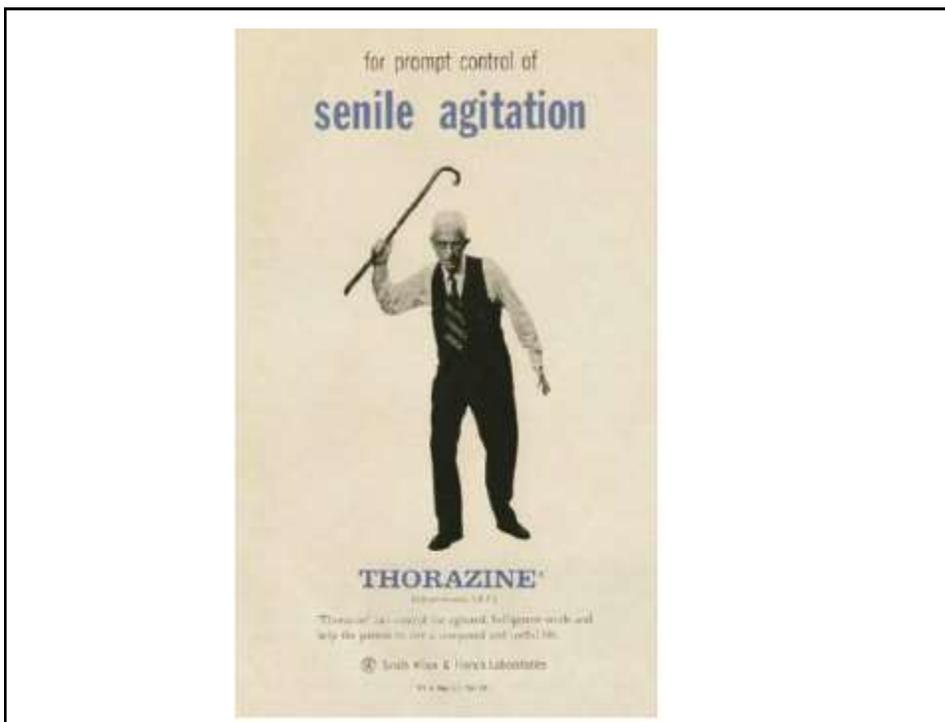


Vitamin E

- No benefit in MCI
- Questionable benefit in moderate AD
- Modest effect on ADLs in veterans with mild-moderate AD at 2000 IU per day
- IOM recommends a maximum dose of 1000 IU per day.

Symptomatic therapy for AD

- Depression
- Sleep disturbance
- Psychosis
- Anxiety
- Agitation



Symptomatic therapy for agitation

- Antipsychotic agents
 - associated with increased risk of mortality in dementia, “black box” warning in PDR, must be used with caution
- Valproic acid
 - is frequently used for agitation in dementia
- Prazosin
 - is being developed as an alternative

ORIGINAL ARTICLE

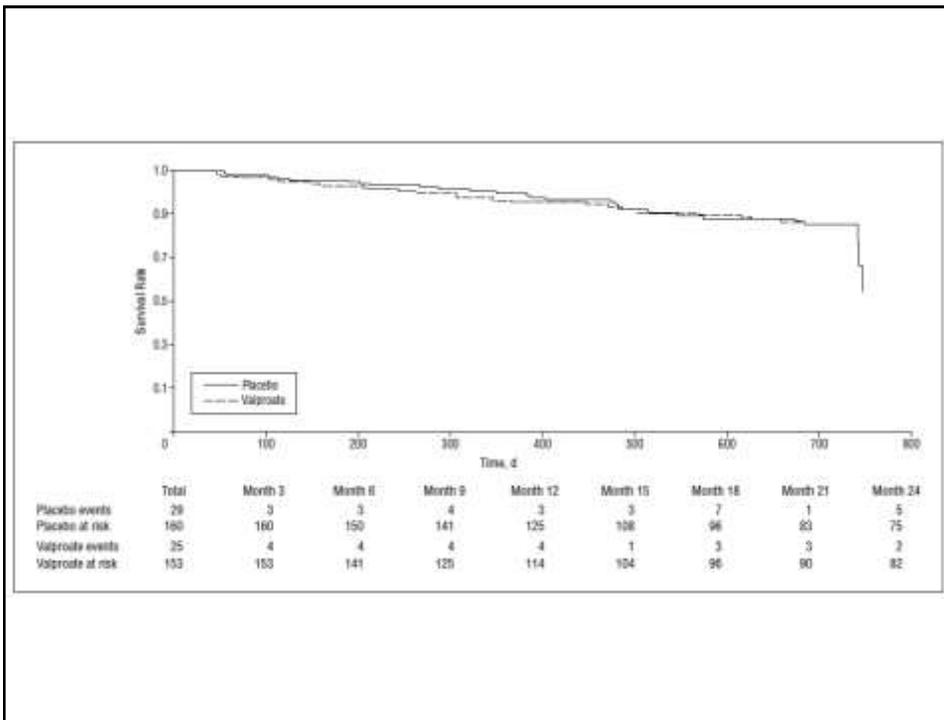
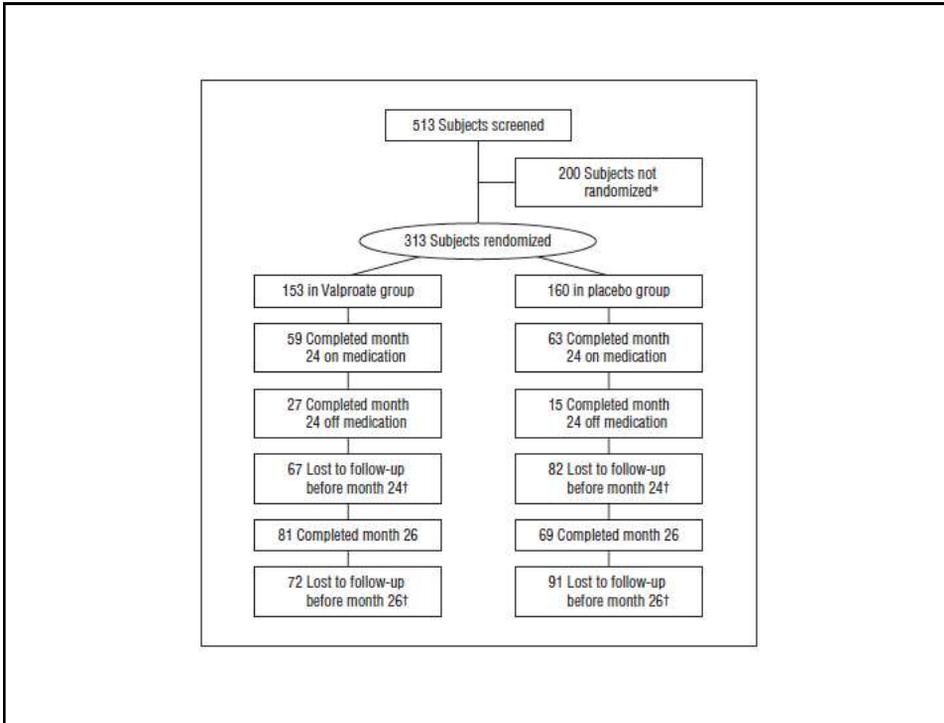
Chronic Divalproex Sodium to Attenuate Agitation and Clinical Progression of Alzheimer Disease

Pierre N. Tariot, MD; Lon S. Schneider, MD; Jeffrey Cummings, MD; Ronald G. Thomas, PhD; Rema Raman, PhD; Laura J. Jakimovich, RN, MS; Rebekah Loy, PhD; Barbara Bartocci, MPH; Adam Fleisher, MD; M. Saleem Ismail, MD; Anton Porsteinsson, MD; Michael Weiner, MD; Clifford R. Jack Jr, MD; Leon Thal, MD†; Paul S. Aisen, MD; for the Alzheimer’s Disease Cooperative Study Group

Table 1. Baseline Demographic and Clinical Characteristics

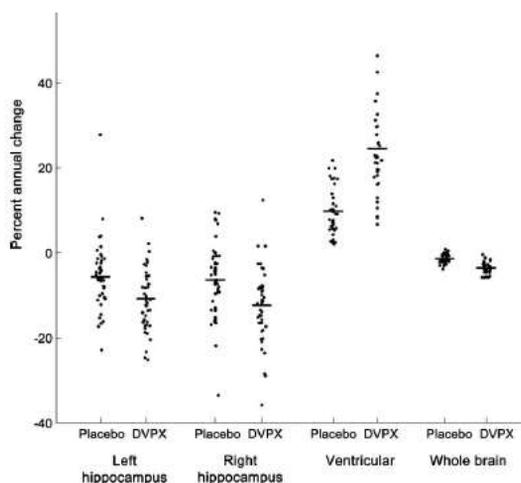
Characteristic	Placebo (n=160)	Valproate (n=153)
Age, mean (SD), y	76.6 (7.4)	74.9 (8.2)
Years of education, mean (SD)	13.6 (3.5)	14.0 (3.0)
Years since AD onset, mean (SD)	5.0 (2.5)	4.6 (2.4)
Female sex, No. (%)	101 (63.1)	83 (54.2)
Race, No. (%)		
Unknown	1 (0.6)	0
Asian	3 (1.9)	2 (1.3)
Black	8 (5.0)	8 (5.2)
White	148 (92.5)	141 (92.2)
>1 Race	0	2 (1.3)
Apolipoprotein E4, No. (%)		
No	39/136 (28.7)	40/132 (30.3)
Yes	97/136 (71.3)	92/132 (69.7)

MMSE=12-20



Chronic divalproex sodium use and brain atrophy in Alzheimer disease

Neurology® 2011;77:1263-1271



Valproic acid and dementia: summary

- Cochrane review (2009) finds no evidence of efficacy of valproate for agitation in dementia.
- Randomized clinical trial (2011) shows no evidence that valproic acid can prevent emergence of behavioral problems
- Randomized clinical trial (2011) suggests valproic acid may accelerate rate of brain atrophy in AD.

Prazosin for agitation in AD

- Developed by Drs Murray Raskind and Elaine Peskind at Puget Sound VA
- Based on evidence that the ascending noradrenergic system is over-active in AD
- Prazosin is an alpha-1 antagonist

Am J Geriatr Psychiatry. 2009 September ; 17(9): 744-751. doi:10.1097/JGP.0b013e3181ab8e61.

PRAZOSIN FOR THE TREATMENT OF BEHAVIORAL SYMPTOMS IN ALZHEIMER'S DISEASE PATIENTS WITH AGITATION AND AGGRESSION

Lucy Y. Wang, MD^{1,2,*}, Jane B. Shofer, MS², Kirsten Rohde, RN¹, Kim L. Hart, PA-C¹, David J. Hoff, PA-C¹, Yun H. McFall, RPh¹, Murray A. Raskind, MD^{1,2}, and Elaine R. Peskind, MD^{1,2}

- Possible or probable AD
- Score of 4 or more on the Brief Psychiatric Rating Scale in anxiety, tension, hostility, uncooperativeness, or excitement.
- Randomized to placebo vs prazosin, titrated to 6 mg per day
- (with each dose increase requiring pre-dose systolic BP of ≥ 110)

Pilot trial of prazosin pilot study population:

characteristic	Prazosin N=11	Placebo N=11
age	83.2±11.5	78.1±10.8
MMSE	9.3±6.6	14±12
Female/male	4/7	5/6
Nursing home/community dwelling	6/5	6/5

Pilot trial of prazosin-outcomes

scale	treatment	Group mean change	P value
NPI	prazosin	-19 ± 21	0.012
"	placebo	-2 ± 15	
BPRS	prazosin	-9 ± 9	0.036
"	placebo	-3 ± 5	
CGIC	prazosin	2.6 ± 1	0.011
"	placebo	4.5 ± 1.6	

Prazosin for dementia

- Larger clinical trial under way in Seattle
- Prazosin is available for open label use
- The primary morbidity is hypotension

Prazosin for dementia

- Medication initiation and each dose increase requires systolic BP of ≥ 110 :
 - 1 mg qhs x 3 days
 - 1 mg bid x 3 days
 - 1 mg qam, 2 mg qpm x 3 days
 - 2 mg bid x 3 days
 - 2 mg qam and 3 mg qpm x 3 days
 - 3 mg bid

Treatment of dementia: summary

- Cholinesterase inhibitor: 23 mg donepezil does not have a significant role
- Memantine: expect a change in formulation
- Valproic acid: use with caution, if at all
- Prazosin: consider for off-label use in agitated patients with sufficient blood pressure

Any questions before moving on to the case discussion?



Case study

- 70 year old man is brought in by his family with concerns about cognitive decline.
- No functional decline reported by spouse, but he is repetitive even during the visit, reinforcing impression of memory decline.
- MMSE=28/30
- No significant medical hx, meds, or fam hx
- Balance of general and neuro exams are unremarkable.

Diagnosis update

- Which test is most useful at this point?
- A) amyloid PET scan
- B) FDG PET scan
- C) blood test for Alzheimer's
- D) neuropsychological assessment

Preferred answer:

- D) neuropsychological assessment
- This is the only option that will help clarify whether this patient's memory complaint is in the range of normal aging or Mild Cognitive Impairment (MCI)

- Neuropsychological assessment confirms the presence of memory disorder outside the range expected for age, with relative preservation of other cognitive functions.
- In other words, the neuropsych results are consistent with a diagnosis of Mild Cognitive Impairment.

- You proceed to rule out treatable causes of cognitive decline with brain MRI, CBC, chem panel, vitamin B12 level, and TSH. The MRI shows “age-related changes” and the bloodwork is all negative. Your diagnosis at this point is Mild cognitive impairment.

What medications might be considered at this point?

- A) donepezil
- B) memantine
- C) valproic acid
- D) prazosin

Preferred answer

- A) donepezil
- Donepezil has shown modest (and somewhat transient) efficacy in amnesic MCI so is a viable option. Memantine is approved only for moderate to severe AD, and the other options are treatments for agitation, typically in moderate to severe dementia.

- Two years pass and the patient slowly declines on MMSE and in daily function. His MMSE is now 22/30 and he is dependent in managing finances, remembering medications, remembering appointments, and driving, but his basic ADLs (dressing, eating, toileting) are well preserved. He is also frustrated and irritable, snapping at his wife over little things.

What treatment options would you consider at this point:

- A) discontinue donepezil since it is not slowing the progression of disease.
- B) add memantine to donepezil.
- C) add prazosin for agitation
- D) trial of an SSRI

Preferred answer

- D) trial of an SSRI
- There is no absolute right or wrong answer here, but frustration and irritability in early dementia will often respond to an SSRI with relatively few risks.

- Three more years pass with continued gradual decline. The MMSE is now 14/30, and the patient now needs assistance with dressing and grooming, needs food cut up, is occasionally incontinent. He resists efforts to help with his care and he is frequently restless and pacing. He does not have any evidence of hallucinations or delusions.

What treatment options might be considered at this point?

- A) valproic acid
- B) thorazine
- C) quetiapine
- D) prazosin

Preferred answer

- Again, no clear standard of care here, but:
- Little data to support valproic acid use. No psychotic symptoms to justify antipsychotic use. Prazosin is an option, but it is clearly off label use and the published data to date is limited.

- Prazosin fails. The patient now begins to elaborate more clear-cut hallucinations, seeing people and animals which are quite distressing to him.

What treatment options might be considered at this point?

- A) haldol
- B) thorazine
- C) quetiapine
- D) risperdal
- E) avoid antipsychotics at all cost due to PDR black box warning regarding mortality in dementia.

Preferred answer:

- Quetiapine or risperdal.
- Since the patient is having distressing psychotic symptoms, antipsychotic use is justified. Older antipsychotic agents like haldol and thorazine produce significant extrapyramidal (parkinsonian) symptoms in elderly patients. Some older agents also have anticholinergic side effects which aggravate cognitive impairment.

Preferred answer:

- Quetiapine or risperdal.
- Quetiapine has the lowest incidence of extrapyramidal side effects of all the available antipsychotic agents, with the exception of clozaril, which is difficult to prescribe. Risperdal is also a reasonable option as long as the dose remains low; as extrapyramidal side effects begin to emerge at higher doses.

Any questions?

