February 20, 2023

Pharmacologic Treatments

FDA-approved and dietary supplements

Tom Ala, MD

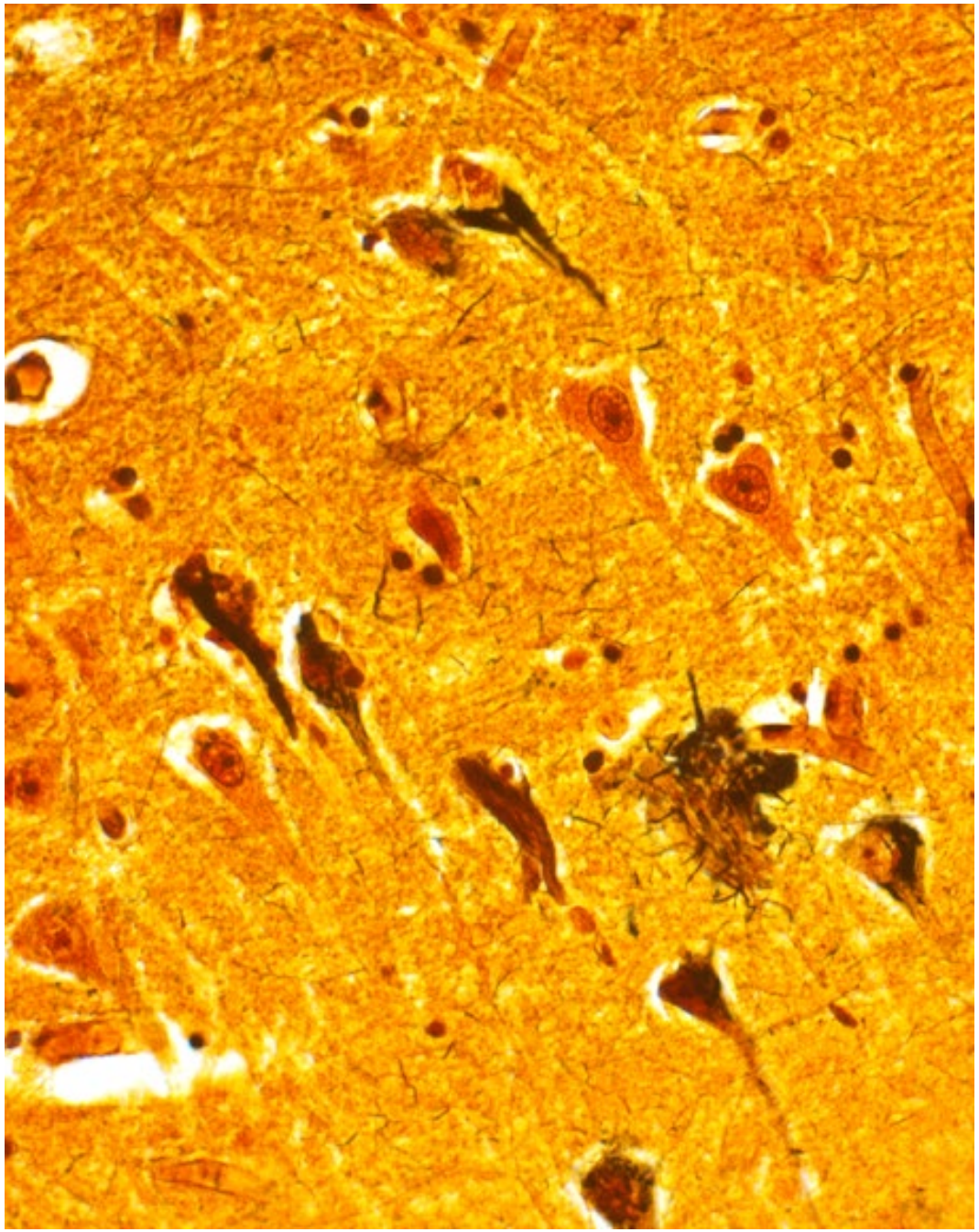
SIU MEDICINE
FORWARD. FOR YOU.

OBJECTIVES TODAY

- What is Alzheimer's disease?
- Explain its disease trajectory.
- Explain how the FDA-approved drugs affect its trajectory.
- Review donepezil, rivastigmine, galantamine, and memantine.
- Review aducanumab and lecanemab.
- Explain what dietary supplements are.

ALZHEIMER'S IS A DEGENERATIVE DISEASE

- The brain cells are dying off.
- The patient's thinking ability fades away.
- The exact cause is uncertain.
- There are no treatments proven to heal or halt the degeneration.



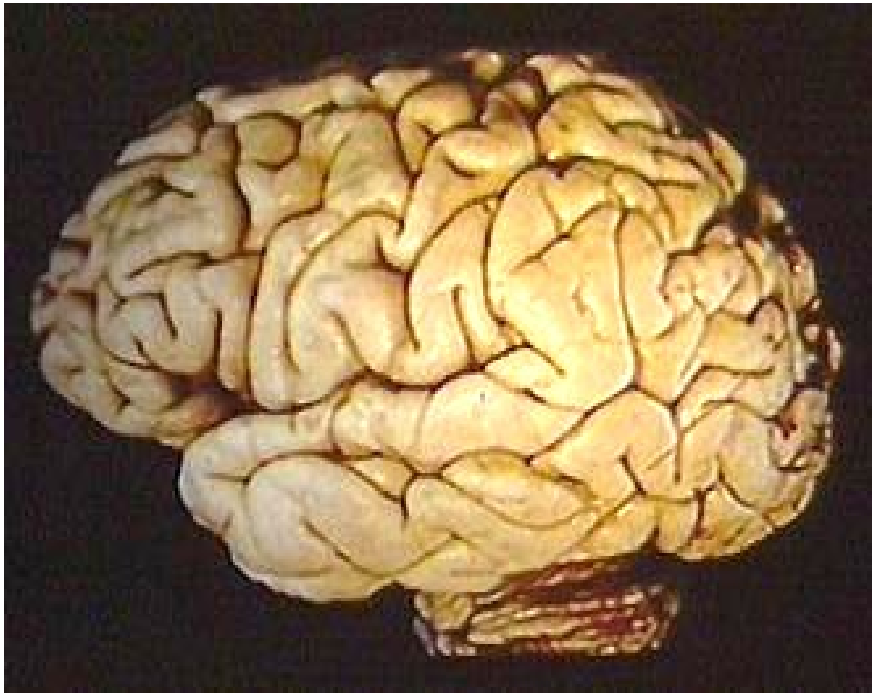
Neurofibrillary tangles

Amyloid plaques

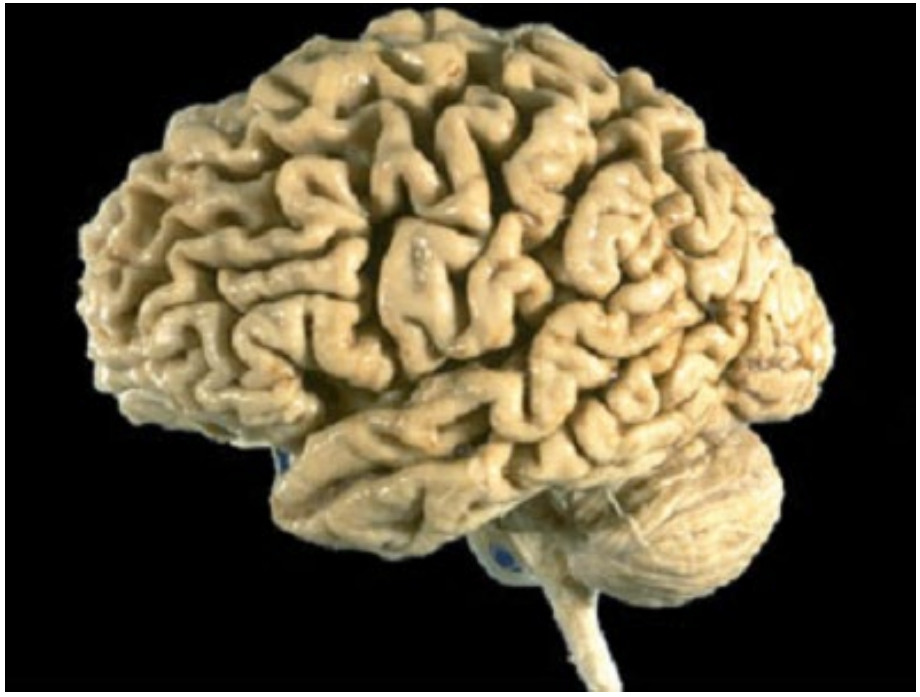
Loss of brain cells

Neurotransmitter imbalances

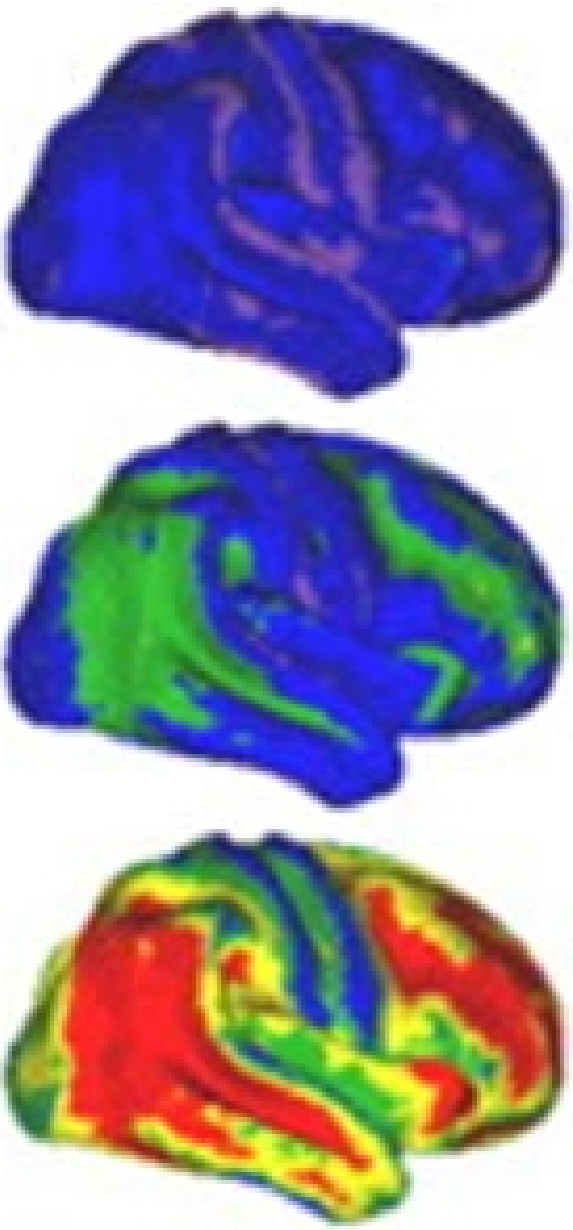
BRAIN ATROPHY



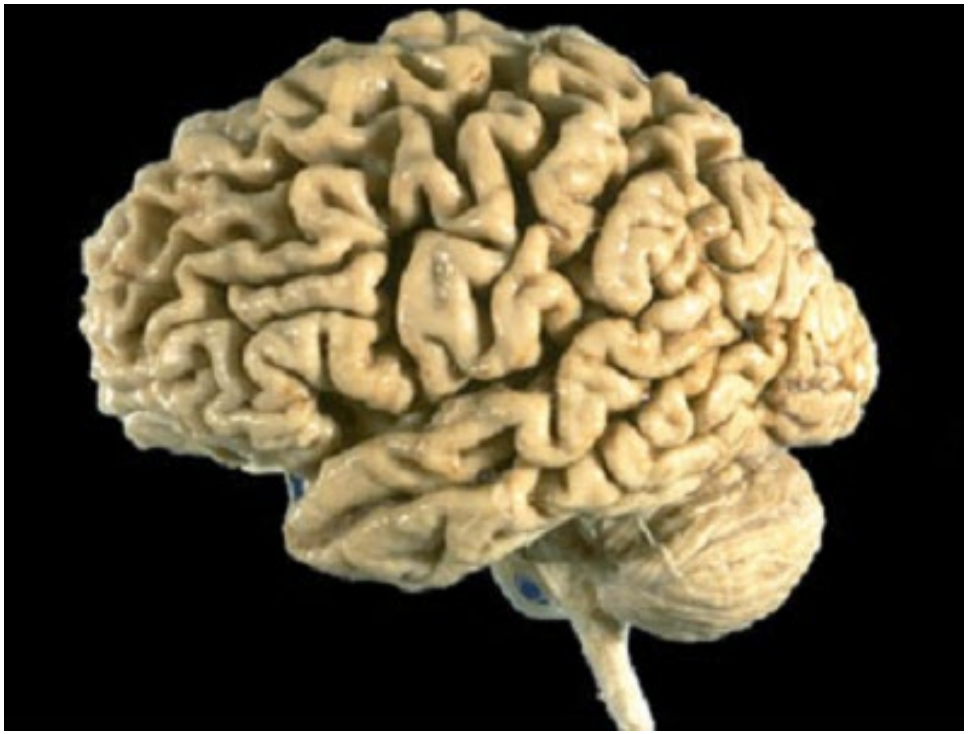
Normal brain



Alzheimer’s brain

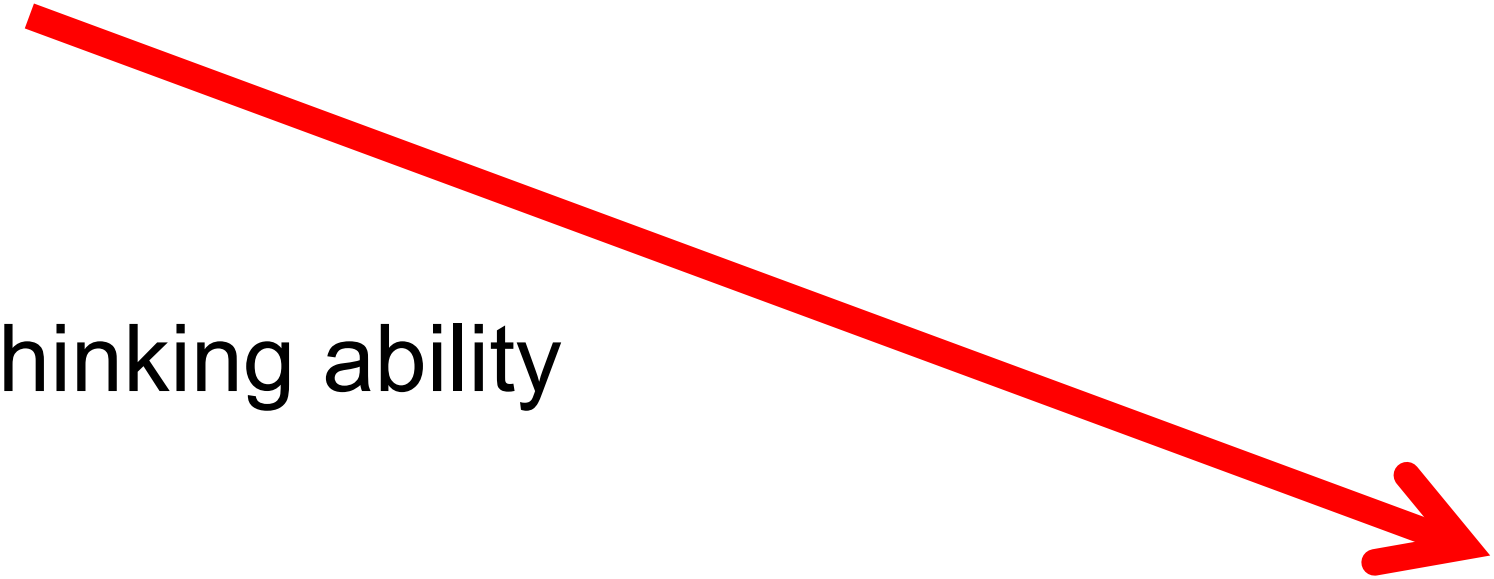


The protein amyloid accumulates in the brain.



PMID: 22108203
Vlassenko. *Biochimica Biophysica Acta* 2012;1822:370

THE TRAJECTORY OF ALZHEIMER'S DISEASE



MEDICATIONS TO TREAT ALZHEIMER'S

MEDICATIONS TO TREAT ALZHEIMER'S

- Symptomatic drugs
- Disease-modifying drugs

SYMPTOMATIC DRUGS

- treat the **symptoms**

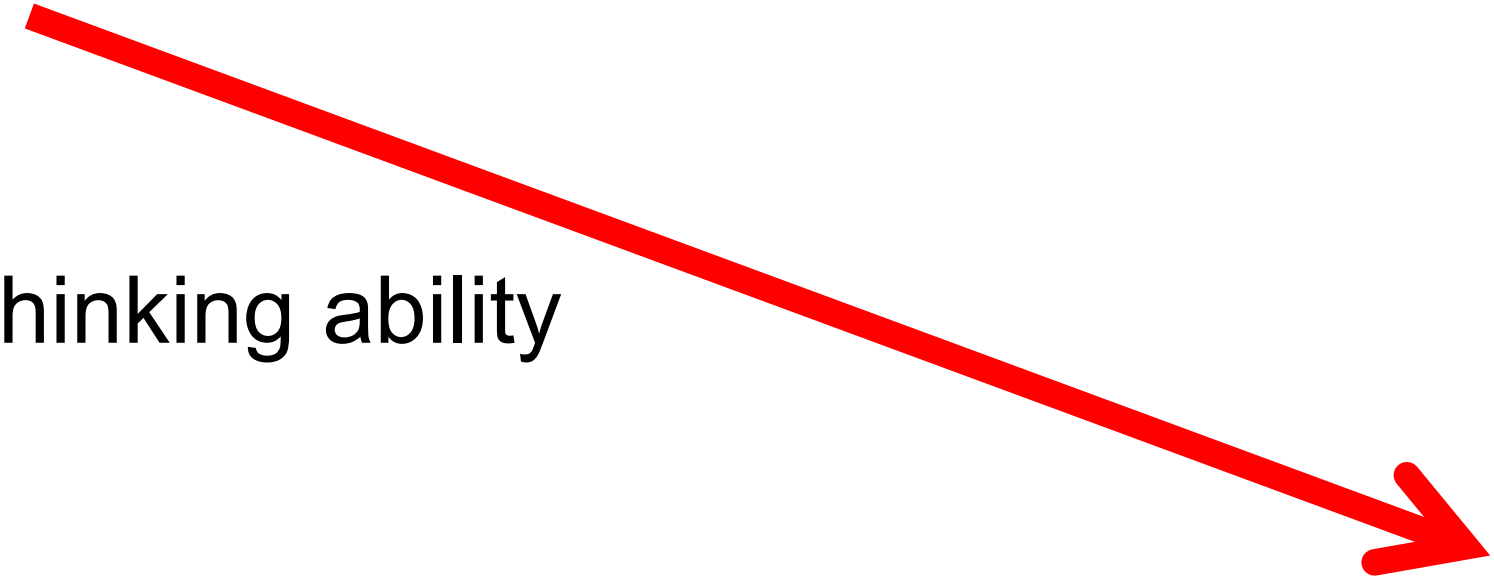
SYMPTOMS OF ALZHEIMER'S

- Memory loss
- Behavioral problems
  - Delusions
  - Hallucinations
  - Anxiety
  - Depression
  - Agitation
  - Apathy
- Disordered sleep
- Etc.

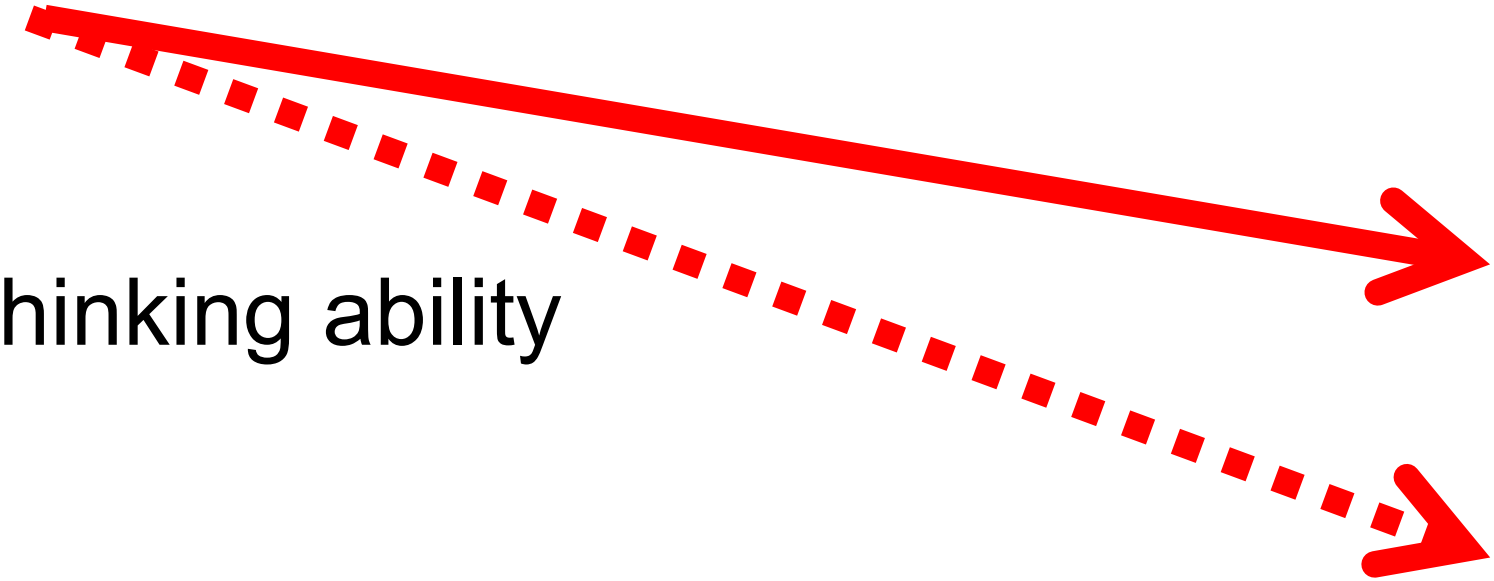
DISEASE-MODIFYING DRUGS

- treat the disease itself

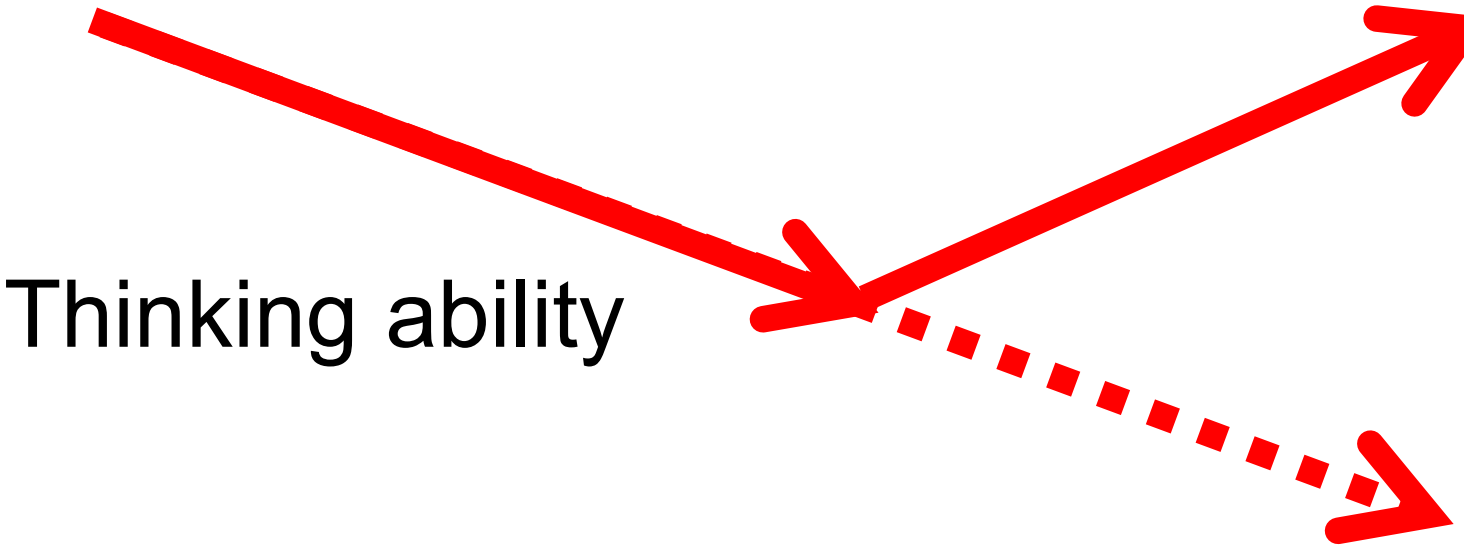
THE TRAJECTORY OF ALZHEIMER'S DISEASE



THE TRAJECTORY OF ALZHEIMER'S DISEASE



THE TRAJECTORY OF ALZHEIMER'S DISEASE



We wish!

TREATMENT OF ALZHEIMER'S

- Up until 2021, there had been no new FDA-approved drugs to treat AD in the preceding 18 years.

FDA-APPROVED DRUGS FOR ALZHEIMER'S DISEASE

donepezil

rivastigmine

galantamine

memantine

donepezil +
memantine

FDA-APPROVED DRUGS FOR ALZHEIMER'S DISEASE

- donepezil
- rivastigmine
- galantamine

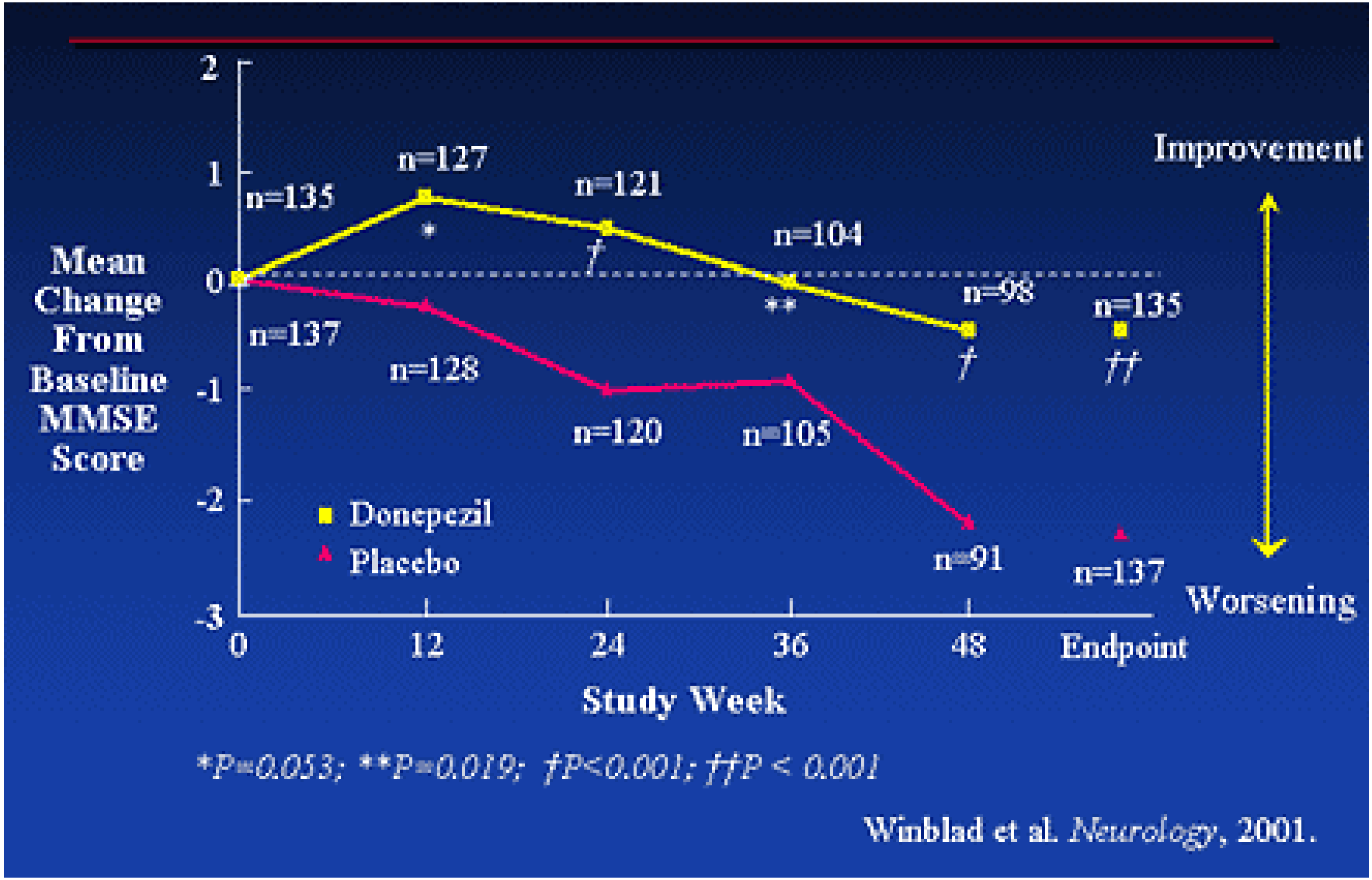
} increase acetylcholine acetylcholine esterase inhibitors (AChEIs)

- memantine — interferes with glutamate

FDA-APPROVED DRUGS FOR ALZHEIMER'S

- Alter the balance of neurotransmitters in the brain
  - donepezil (Aricept®)
  - galantamine (Razadyne®)
  - rivastigmine (Exelon®)
  - memantine (Namenda®)

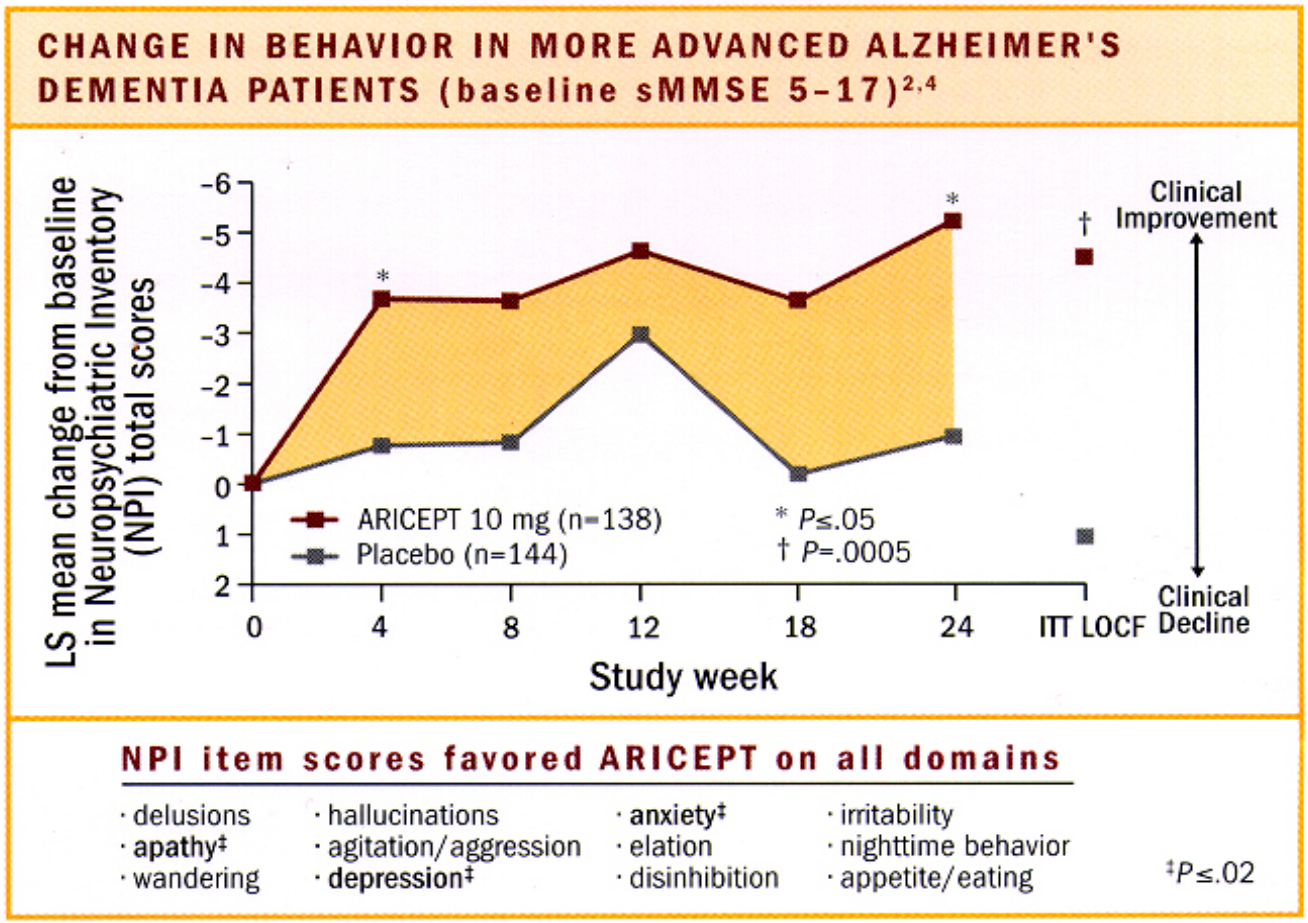
THESE DRUGS CAN IMPROVE COGNITION IN ALZHEIMER'S



PMID: 11502918

Winblad. *Neurology* 2001:14:489

THESE DRUGS CAN IMPROVE BEHAVIOR IN ALZHEIMER'S

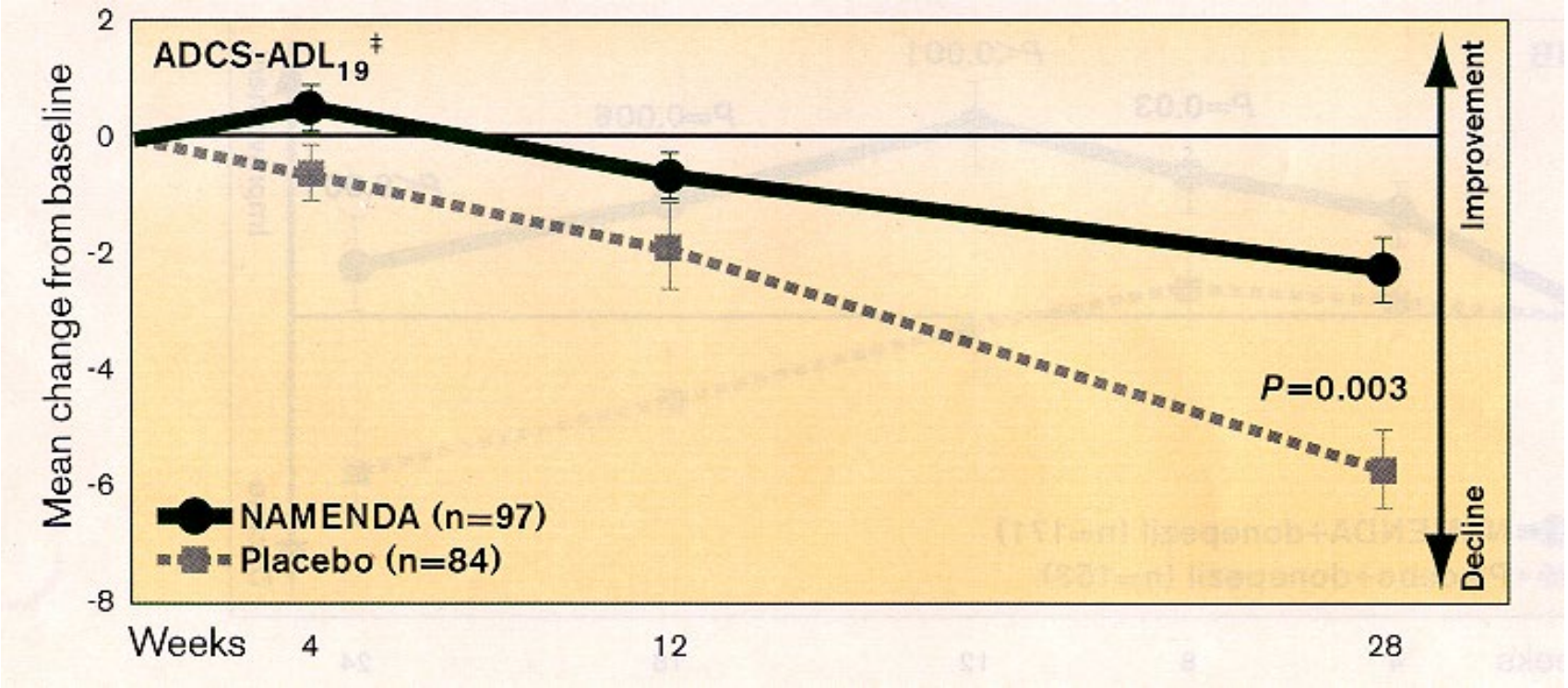


Neuropsychiatric Inventory Scale

PMID: 11524468

Feldman. *Neurology* 2001;57:613

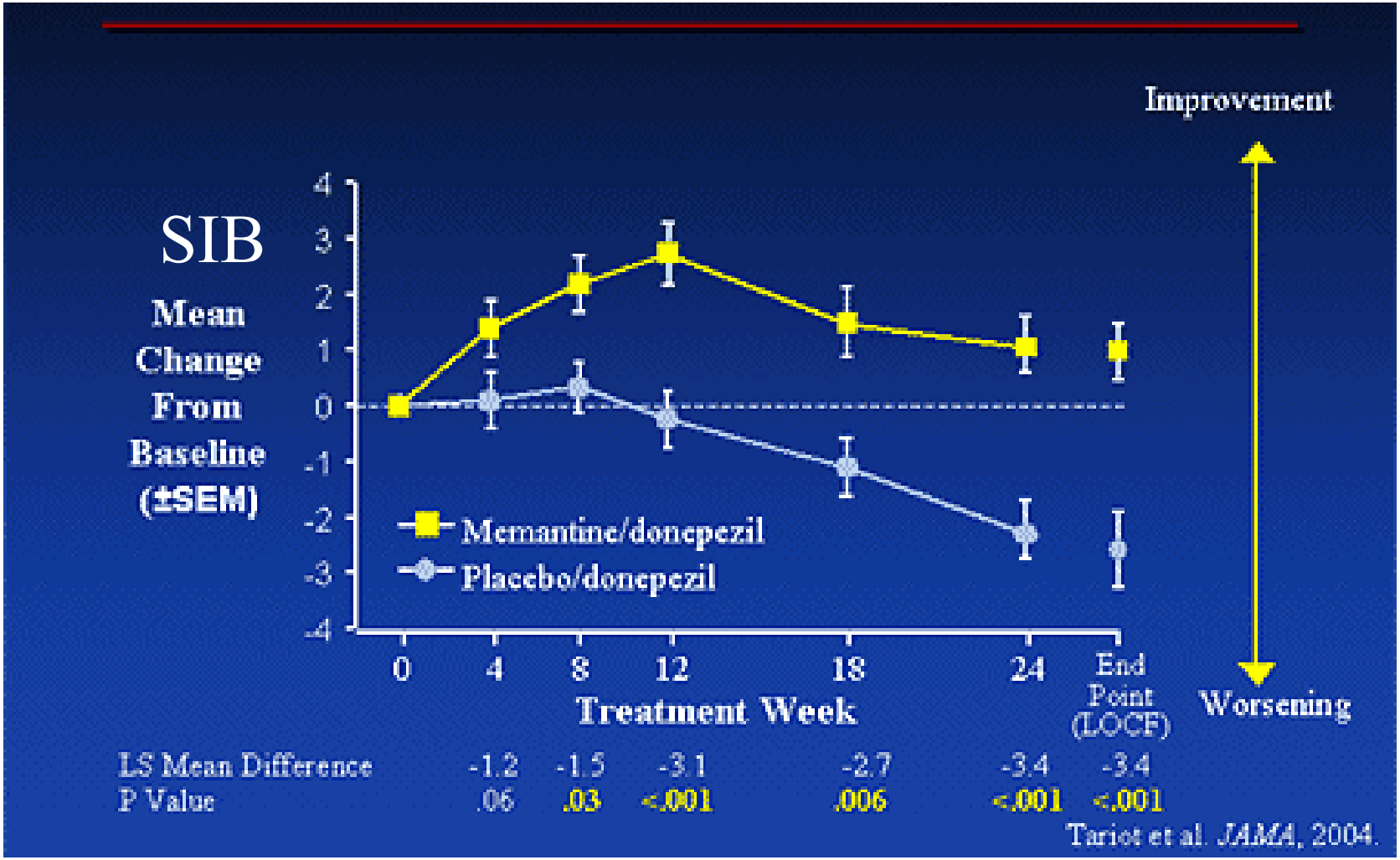
THESE DRUGS CAN IMPROVE ACTIVITIES OF DAILY LIVING IN ALZHEIMER'S



PMID: 12672860

Reisberg. *NEJM* 2003;348:1333

COMBINATION THERAPY



PMID: 14734594

Tariot. *JAMA* 2004;291:317

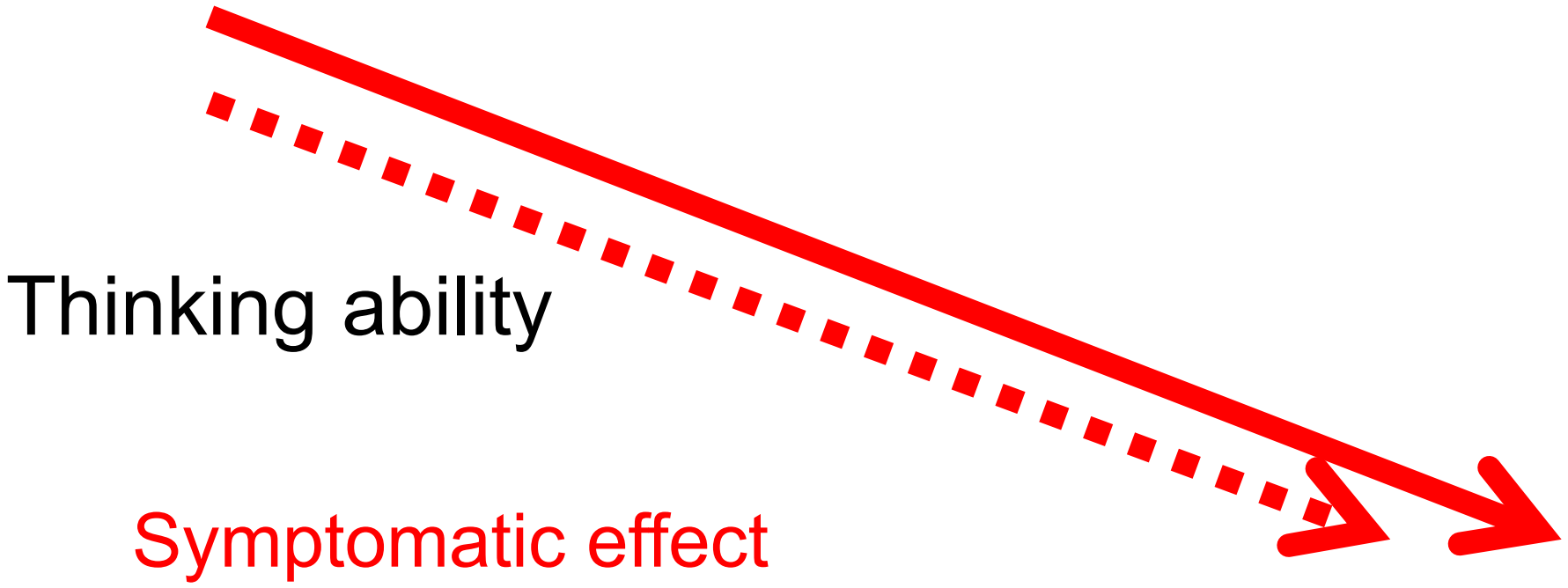
TREATMENT OF ALZHEIMER'S

- Up until 2021, there had been no new FDA-approved drugs to treat AD in the past 18 years.
- The drugs that had been approved offer modest *symptomatic* benefit.

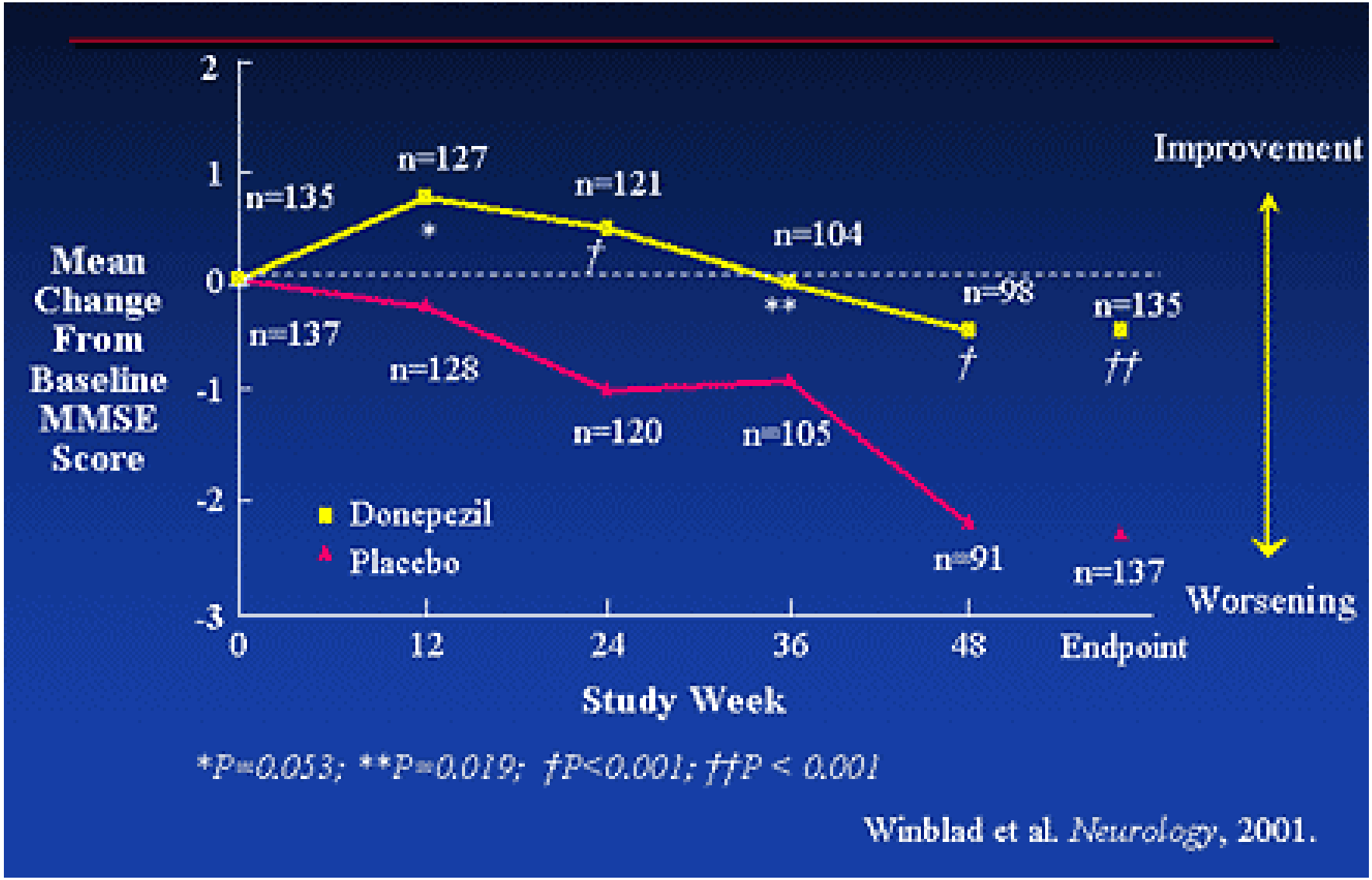
TREATMENT OF ALZHEIMER'S

- Up until 2021, there had been no new FDA-approved drugs to treat AD in the past 18 years.
- The drugs that had been approved offer modest *symptomatic* benefit.
- The drugs approved prior to 2021 do not slow or stop the progression of Alzheimer's.

THE TRAJECTORY OF ALZHEIMER'S DISEASE



THESE DRUGS CAN IMPROVE COGNITION IN ALZHEIMER'S



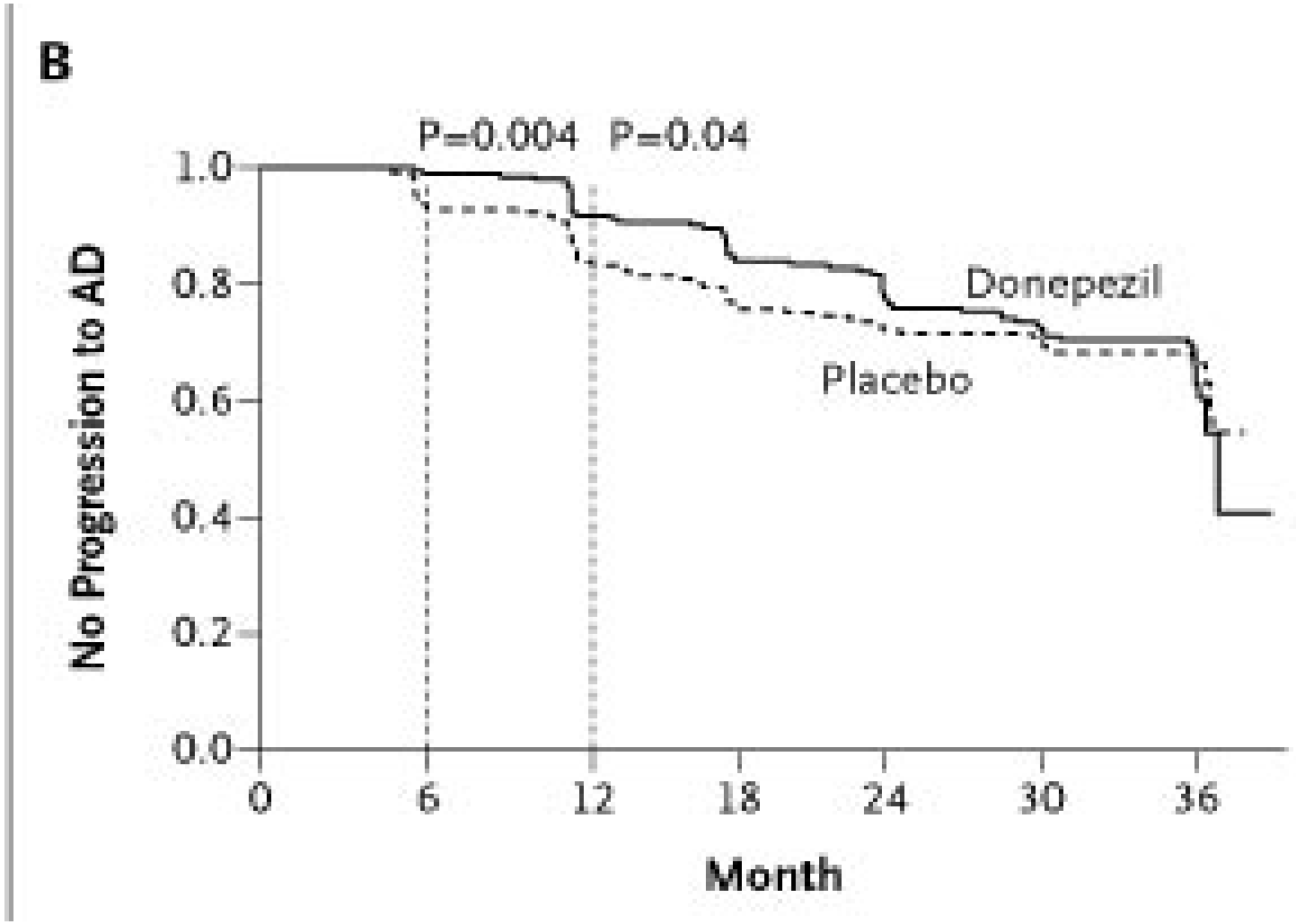
PMID: 11502918

Winblad. *Neurology* 2001:14:489

THE BENEFIT OF THESE DRUGS

- The average patient functions a little better.
- A few patients do significantly better.
- They delay the conversion to Alzheimer's disease.
- They help keep the patient out of the nursing home.

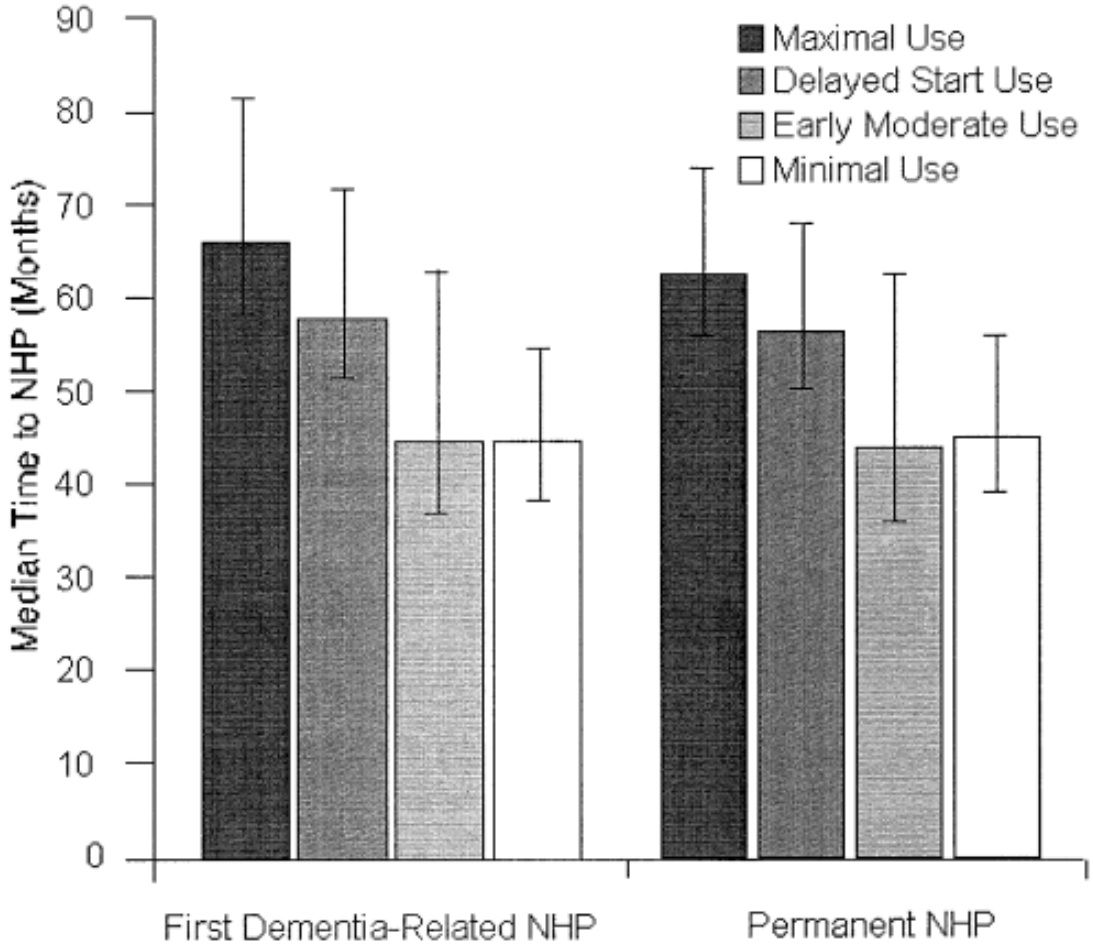
DELAYING CONVERSION TO ALZHEIMER'S



PMID: 15829527

Petersen. *NEJM* 2005;352:2379

DELAYING NURSING HOME PLACEMENT



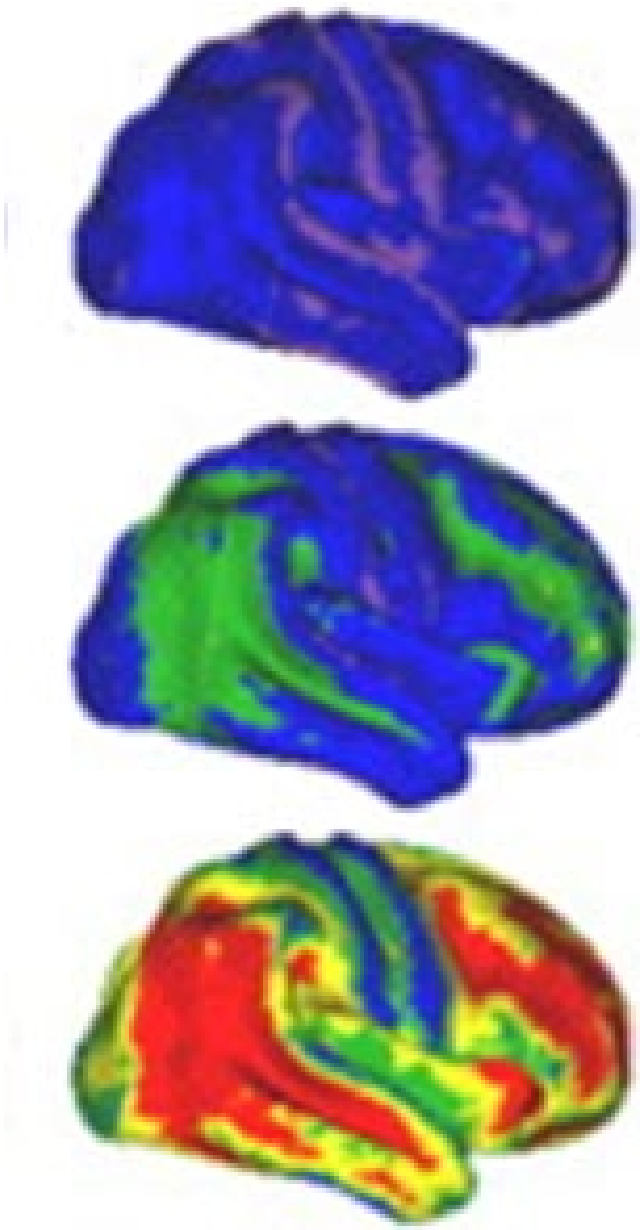
When donepezil was taken at an effective dose for at least 9 to 12 months, conservative estimates of the time gained before NHP were 21.4 months for first dementia-related NHP and 17.5 months for permanent NHP.

PMID: 12834513

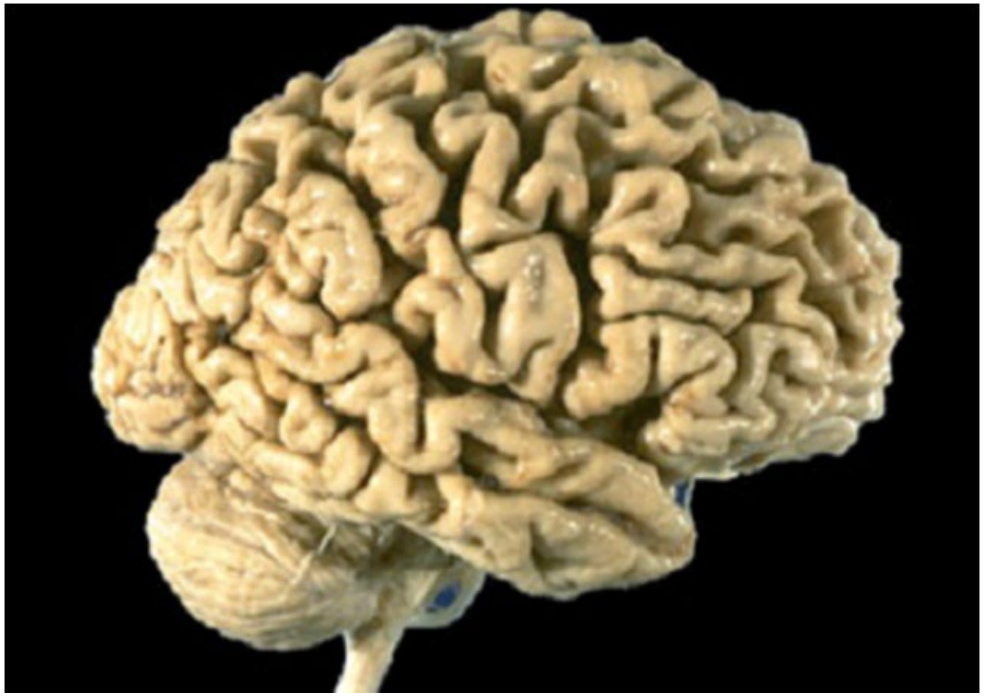
Geldmacher. *JAGS* 2003;51:937

THE BENEFIT OF THESE DRUGS

Like using a crutch if we have severe leg pain...



The protein amyloid accumulates in the brain.

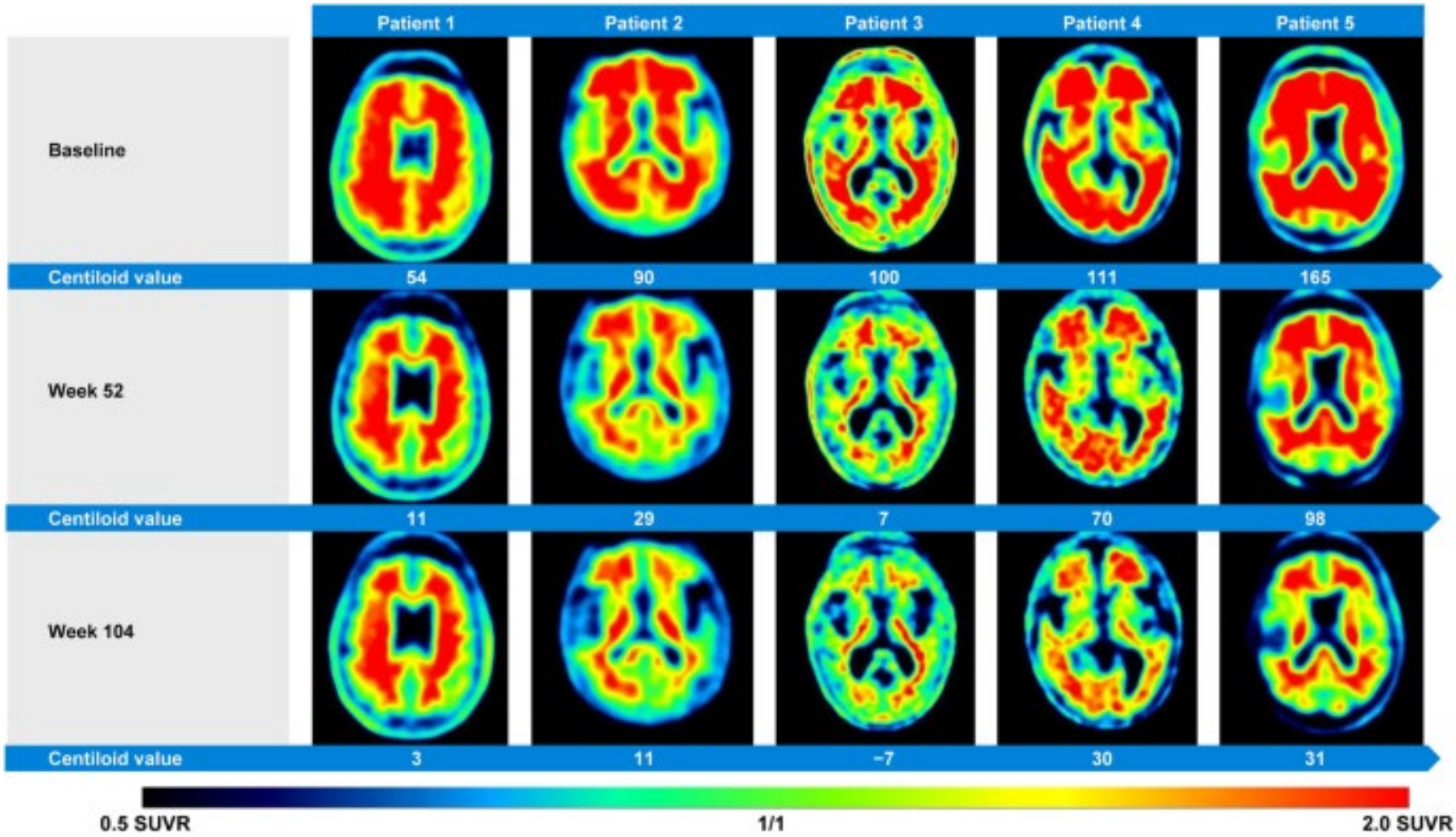


PMID: 22108203
Vlassenko. *Biochimica Biophysica Acta* 2012;1822:370.

DISEASE-MODIFYING DRUGS?

- aducanumab (Aduhelm®)
- lecanemab (Leqembi®)
- donanemab
- ~~gantenerumab~~

Gantenerumab reduces amyloid-β plaques in patients with prodromal to moderate Alzheimer's disease

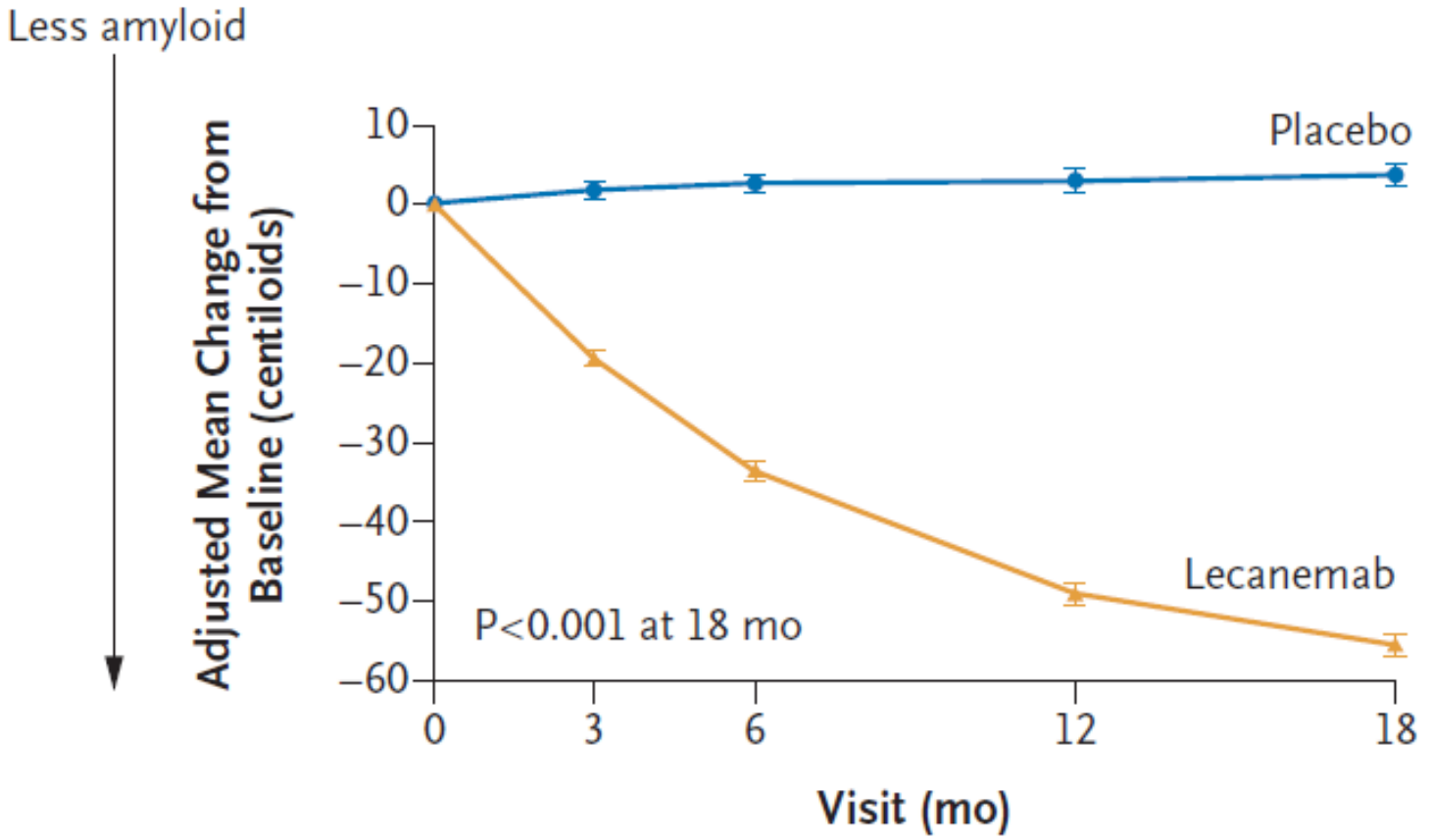


PMID: 31831056

Klein. *Alz Res Ther* 2019;11:101

LECANEMAB

Amyloid burden on PET



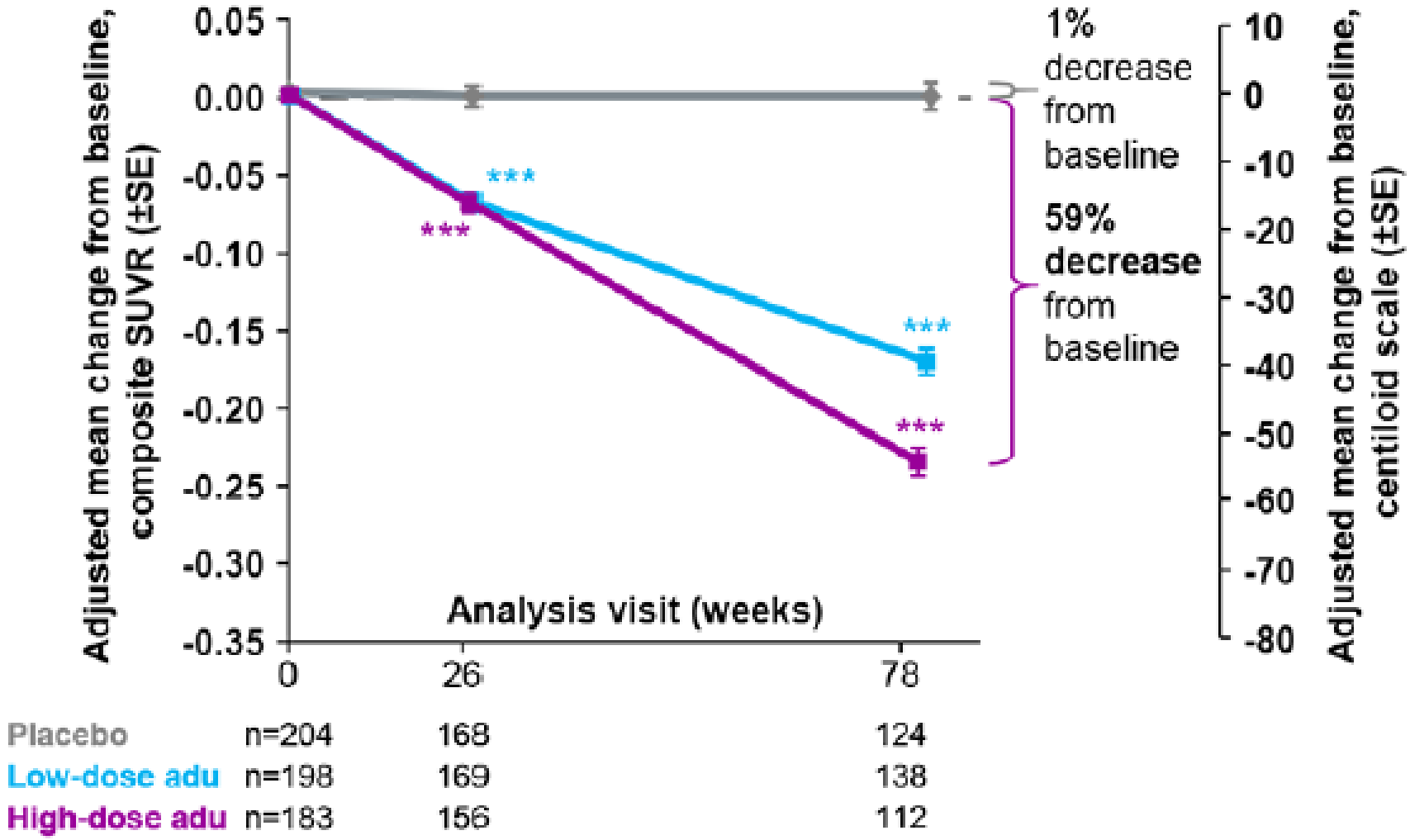
No. of Participants					
Lecanemab	354	296	275	276	210
Placebo	344	303	286	259	205

PMID: 36449413

Van Dyck. *NEJM* 2023;388:9

ADUCANUMAB

Amyloid burden on PET

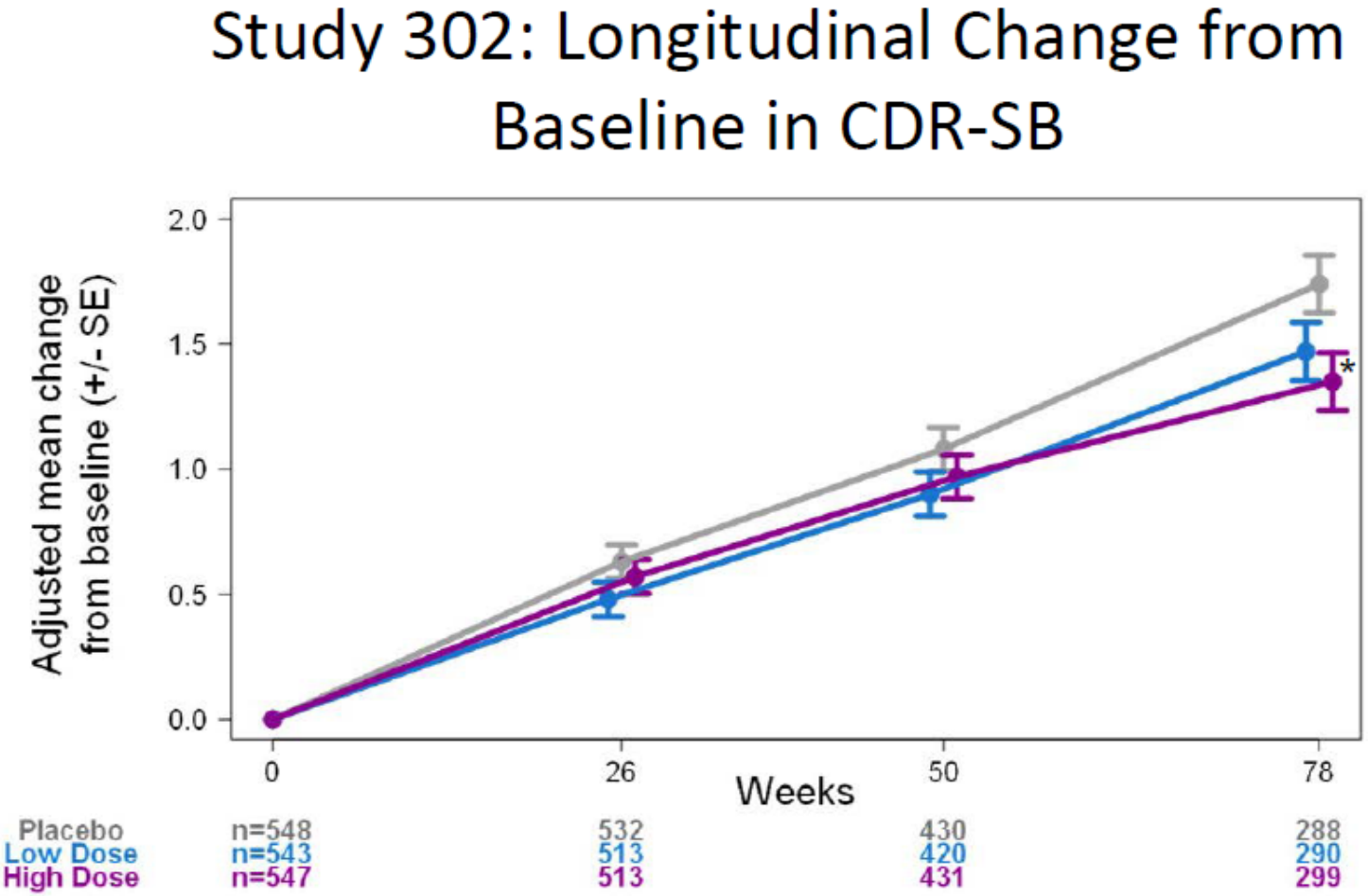


PMID: 35542991

Budd Haberlein. *J Prev Alz Dis* 2022; 2:197

ADUCANUMAB

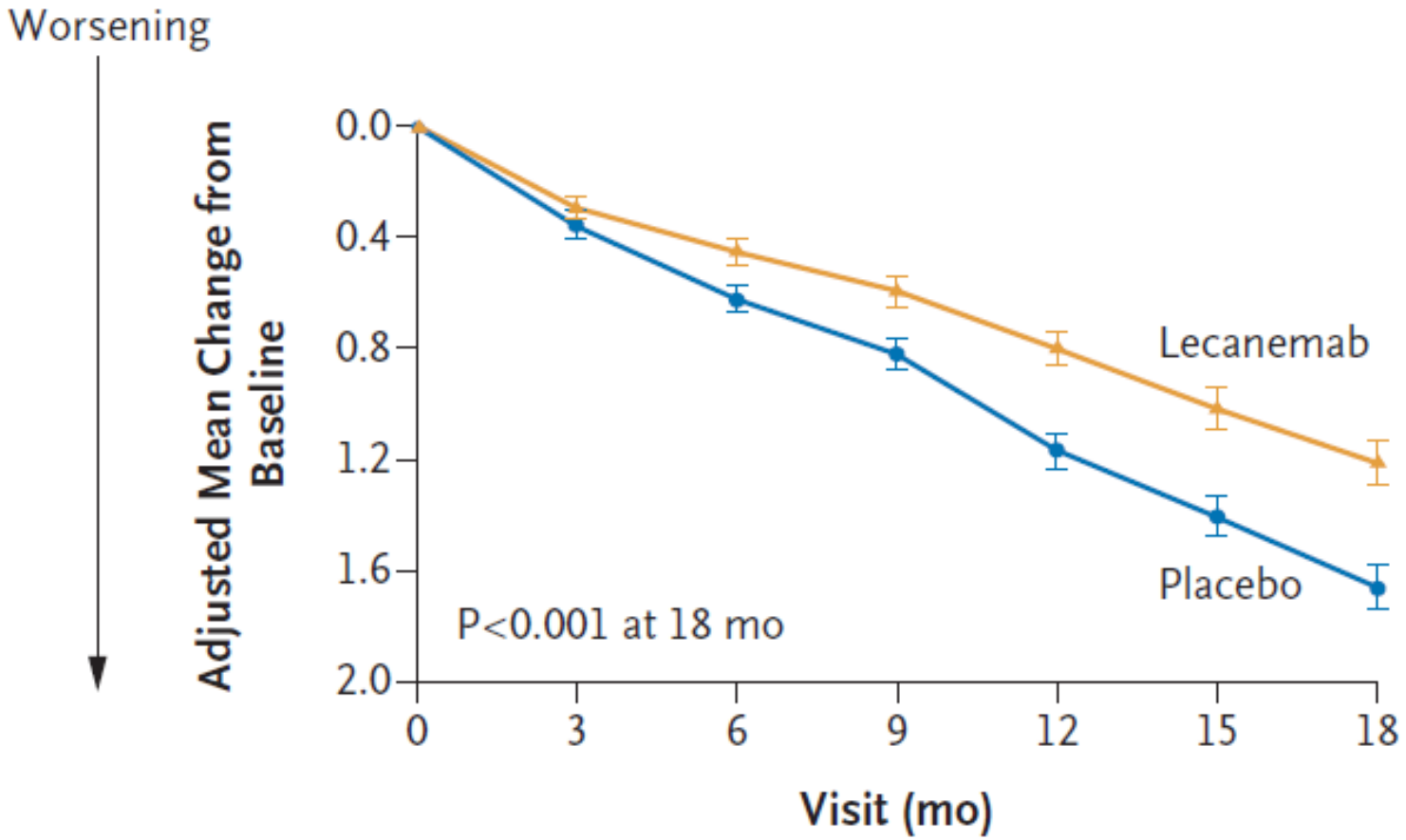
CDR-SB score



https://www.fda.gov/media/143504/download

LECANEMAB

CDR-SB score



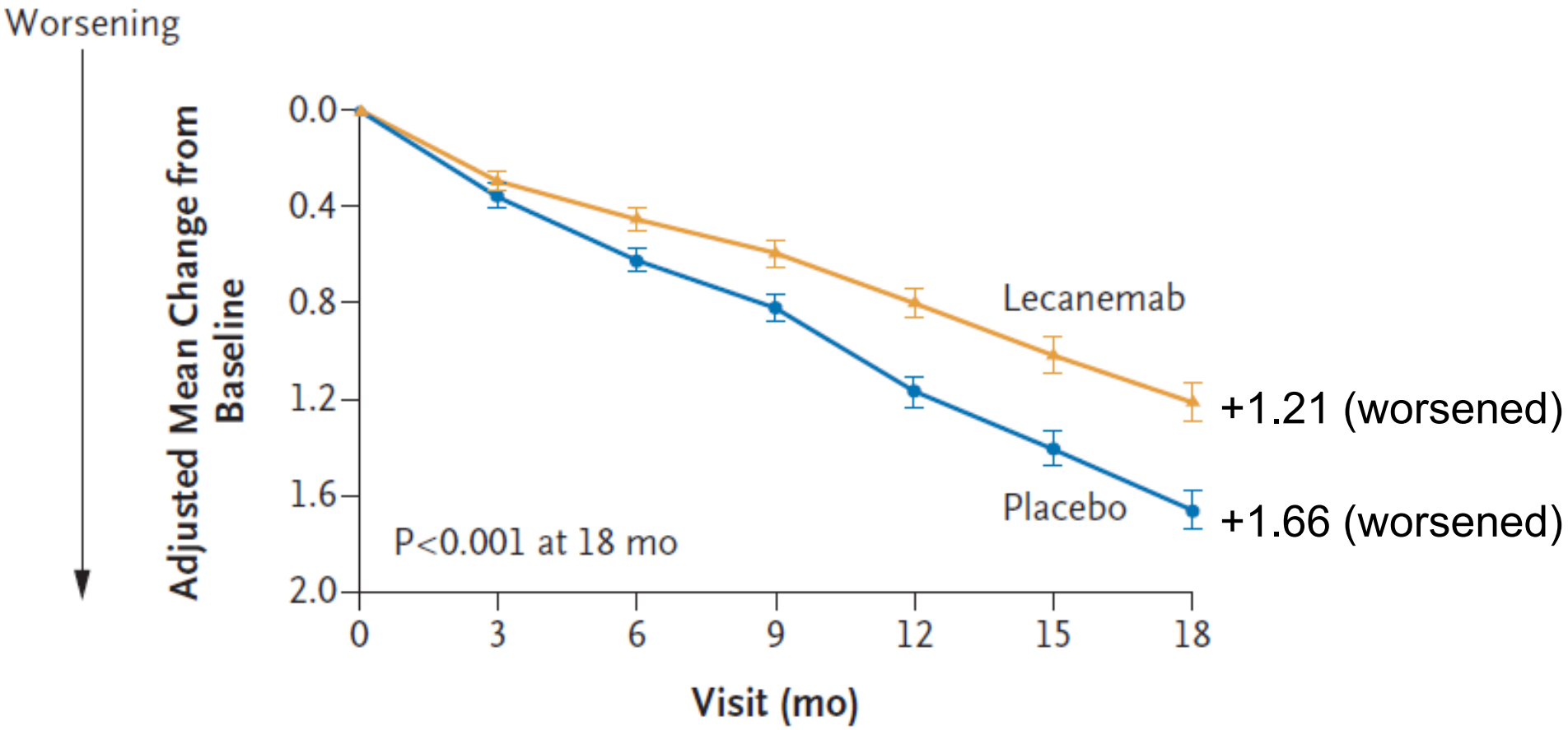
No. of Participants							
Lecanemab	859	824	798	779	765	738	714
Placebo	875	849	828	813	779	767	757

PMID: 36449413

Van Dyck. *NEJM* 2023;388:9

LECANEMAB

CDR-SB score



No. of Participants							
Lecanemab	859	824	798	779	765	738	714
Placebo	875	849	828	813	779	767	757

PMID: 36449413

Van Dyck. *NEJM* 2023;388:9

LECANEMAB

CDR-SB score

The placebo group worsened by 1.66 points
The lecanemab group worsened by 1.21 points

PMID: 36449413

Van Dyck. *NEJM* 2023;388:9

LECANEMAB

CDR-SB score

The placebo group worsened by 1.66 points
The lecanemab group worsened by 1.21 points
Difference = 0.45 points

PMID: 36449413

Van Dyck. *NEJM* 2023;388:9

LECANEMAB

CDR-SB score

The placebo group worsened by 1.66 points
The lecanemab group worsened by 1.21 points
Difference = 0.45 points

0.45 ÷ 1.66 = 0.27

PMID: 36449413

Van Dyck. *NEJM* 2023;388:9

LECANEMAB

CDR-SB score

The placebo group worsened by 1.66 points
The lecanemab group worsened by 1.21 points
Difference = 0.45 points

0.45 ÷ 1.66 = 0.27

During the 18 month trial, the subjects who received lecanemab experienced 27% less worsening than the subjects who received placebo.

PMID: 36449413

Van Dyck. *NEJM* 2023;388:9

LECANEMAB

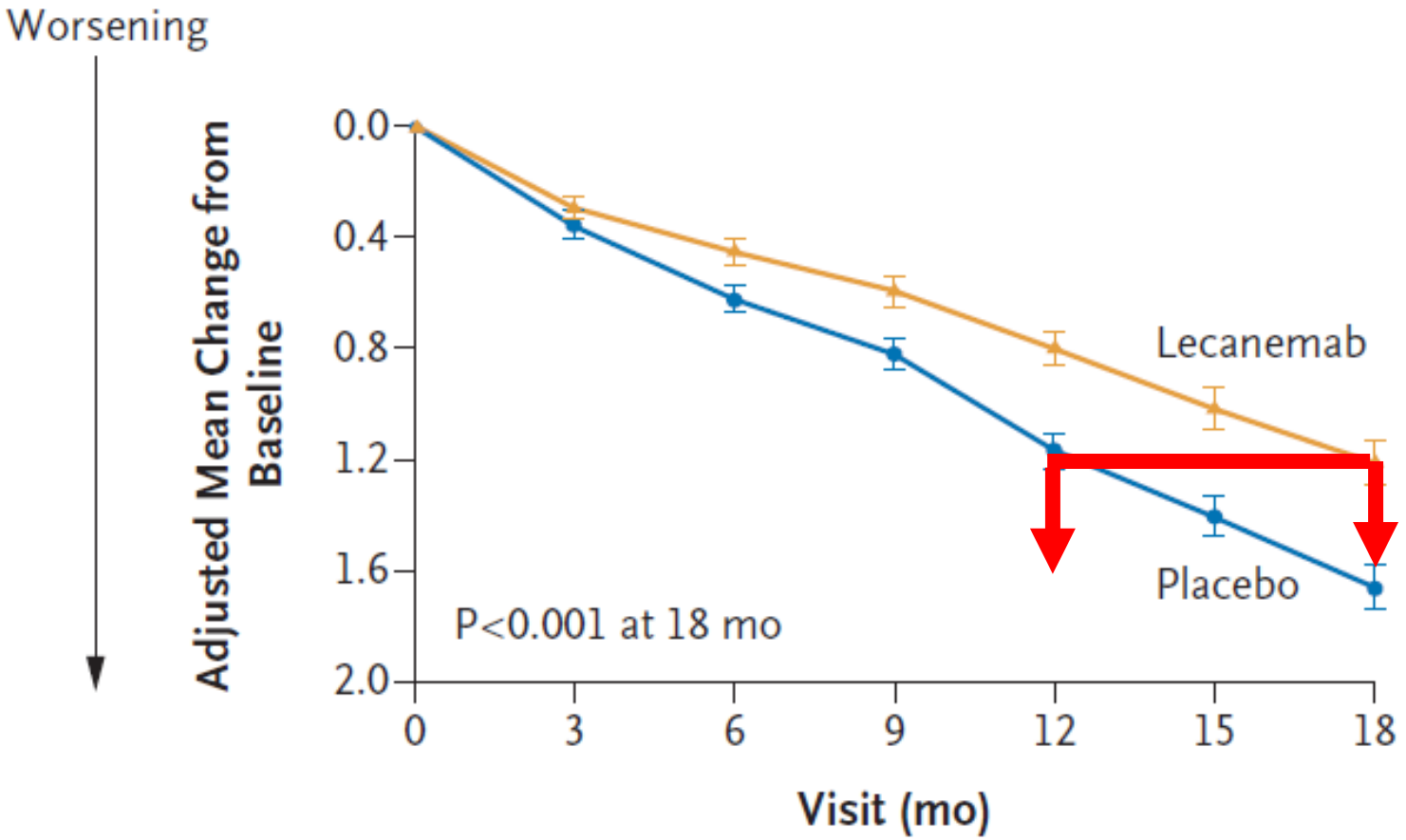
- What is the significance of a 27% slowing of progression?
  - The CDR-SB scale has a range of 18 points.
    - How noticeable is a change of 0.45 points?

LECANEMAB

- What is the significance of a 27% slowing of progression?
  - The CDR-SB scale has a range of 18 points.
    - How noticeable is a change of 0.45 points?
  - *Maybe* it means the clock was set back six months.

LECANEMAB

CDR-SB score



No. of Participants							
Lecanemab	859	824	798	779	765	738	714
Placebo	875	849	828	813	779	767	757

PMID: 36449413

Van Dyck. *NEJM* 2023;388:9

LECANEMAB

- What is the significance of a 27% slowing of progression?
  - The subjects worsened despite taking the treatment.
  - The trial was 18 months long.
    - What if they had taken it longer?
  - How long should lecanemab be taken?
  - The subjects in the trial were very selected.
    - Not all the Alzheimer's patients who applied were accepted.
  - What about side effects?
  - What about cost?

ADUCANUMAB AND LECANEMAB

- Aduhelm® and Leqembi® (brand names)
- Somewhat controversial: many experts disagree about their benefits.
- Administered by intravenous infusions (every 2 or 4 weeks).
- Very expensive, more than $20,000 per year for the drug itself, not including the cost of the infusions. Insurance coverage is uncertain at this time.
- At present Medicare will only cover the cost if the patient is in an approved study.
- Patient must have a test that shows that amyloid is accumulating in the brain, either by a spinal tap or an amyloid PET scan. Blood tests may be an option.
- Patient must have relatively mild Alzheimer's or only significant memory impairment.
- Unknown at this time how long the drug should be administered.
- 20-43% of patients may experience some degree of brain swelling or microhemorrhages.

DISEASE-MODIFYING DRUGS?

- aducanumab (Aduhelm®)
- lecanemab (Leqembi®)
- donanemab
- ~~gantenerumab~~

HAVE YOU SEEN ANY ADVERTISEMENTS FOR MEMORY PILLS LATELY?

ADS I HAVE SEEN IN THE PAST FEW MONTHS

- Prevagen
- Neuriva
- Focus factor
- Cognimax
- Cognium
- Ceremin
- Neuronol
- Neuro enhancer
- Brain Awake

THERE ARE MANY MORE…

- Procera AVH
- Alpha Brain
- NAD^{+}OVIM
- Brainjuice
- Cebria
- Excelerol
- NooCube
- US Doctor's Clinical Brain Power Advances
- Genius Consciousness
- Healthycell Pro
- Brain Awake
- LumUltra
- Lumonol
- Brain Armor
- brainMD (Brain & Memory Power Boost, Neurovite Plus)
- Clarity Brain Health Formula
- Percepta
- Qualia Mind
- OptiMind
- Neurofuse
- Etc, etc, etc

INGREDIENTS OF THE DIETARY SUPPLEMENTS

- Apoaequorin
- Huperzine A
- Vitamin B Complex
- L-Tyrosine
- L-Theanine
- Alpha Lipoic Acid
- Guarana
- Ginkgo Biloba
- Brahmi (Bacopa monnieri)
- Bacopa Extract (Bacopa monnieri)
- Rhodiola Rosea
- S-Adenosyl Methionine
- Cat's claw (Uncaria tomentosa)
- CoQ-10
- Lutein
- Omega-3 fatty acids (e.g., DHA and EPA)
- St. John's Wort
- l-Glutamine,
- DMAE (dimethylaminoethanol)
- Green Tea Extract
- Oolong Tea Extract
- Caffeine
- Vitamin B12
- Acetyl-L-Carnitine
- Phosphatidylserine
- Creatine
- Resveratrol
- Whole coffee cherry extract
- Choline
- Etc, Etc, Etc

INGREDIENTS OF THE DIETARY SUPPLEMENTS

- Apoaequorin
- Huperzine A
- Vitamin B Complex
- L-Tyrosine
- L-Theanine
- Alpha Lipoic Acid
- Guarana
- Ginkgo Biloba
- Brahmi (Bacopa monnieri)
- Bacopa Extract (Bacopa monnieri)
- Rhodiola Rosea
- S-Adenosyl Methionine
- Cat's claw (Uncaria tomentosa)
- CoQ-10
- Lutein
- Omega-3 fatty acids (e.g., DHA and EPA)
- St. John's Wort
- l-Glutamine,
- DMAE (dimethylaminoethanol)
- Green Tea Extract
- Oolong Tea Extract
- Caffeine
- Vitamin B12
- Acetyl-L-Carnitine
- Phosphatidylserine
- Creatine
- Resveratrol
- Whole coffee cherry extract
- Choline
- Etc, Etc, Etc

PubMed.gov

The apoaequorin Chewables Year Supply Sweepstakes x2

Enter for a chance to win a vear supply of apoaequorin Chewables for you and a friend!

ENTER NOW

https://prevagen.com/

What is apoaequorin?

apoaequorin was originally discovered in jellyfish. Apoaequorin is safe and uniquely supports brain function.*

® Selected as the **#1 Pharmacist Recommended Memory Support Brand in 2021** Pharmacy Times annual survey for third year in a row.

https://prevagen.com/

Apoaequorin is an over-the-counter supplement for healthy brain function and memory improvement.

Based on a clinical study of subgroups of individuals who were cognitively normal or mildly impaired.

https://prevagen.com/

Apoaequorin

Madison Memory Study

In a double-blinded, placebo-controlled trial, apoaeq..demonstrated the ability to improve aspects of cognitive function in subgroups of participants with either normal cognitive aging or very mild impairment, as determined by pre-trial screening. The group of participants taking apoaeq..improved certain aspects of cognitive function according to computer-based testing. The adults were over 40 years old and took one capsule daily (10 mg) for 90 days.

PMID: 26878676

Moran. *Adv Mind Body Med* 2016;30:4

https://prevagen.com/

Apoaequorin

Study details

A total of 218 participants, ages 40 to 91, with self-reported memory concerns were enrolled in the study. Two hundred and eleven (211) participants completed the study.

Adverse Events

The Experimental and Control substances were very well tolerated. Two participants experienced adverse events during the study. Each group had a single adverse event, and there were no serious adverse events (SAEs) in the study.

https://prevagen.com/

AD8 test

AD8 Dementia Screening Interview

Patient ID#:_____
CS ID#:_____
Date:_____

Remember, "Yes, a change" indicates that there has been a change in the last several years caused by cognitive (thinking and memory) problems.	YES, A change	NO, No change	N/A, Don't know
1. Problems with judgment (e.g., problems making decisions, bad financial decisions, problems with thinking)			
2. Less interest in hobbies/activities			
3. Repeats the same things over and over (questions, stories, or statements)			
4. Trouble learning how to use a tool, appliance, or gadget (e.g., VCR, computer, microwave, remote control)			
5. Forgets correct month or year			
6. Trouble handling complicated financial affairs (e.g., balancing checkbook, income taxes, paying bills)			
7. Trouble remembering appointments			
8. **Daily** problems with thinking and/or memory			
TOTAL AD8 SCORE			

Adapted from Galvin JE et al, The AD8, a brief informant interview to detect dementia, Neurology 2005:65:559-564

Apoaequorin

Table 1 Computerized cognitive measurement tests

Task	Cognitive Domain Measured
International Shopping List (ISL)	Verbal Learning
International Shopping List - Delayed Recall (ISRL)	Memory
Groton Maze Learning (GML)	Executive Function
Groton Maze Learning - Delayed Recall (GMR)	Memory
Detection (DET)	Psychomotor Function
Identification (IDN)	Attention
One Card Learning (OCL)	Visual Learning
One Back (ONB)	Working Memory
Two Back (TWOB)	Working Memory

https://prevagen.com/

Apoaequorin

Study results

Table 3 The Score Differences in the Two Groups Before and After Treatment (AD8 0-1)

	Placebo		Within p	Apoaequorin		Within p	Between Group P value			
Tasks	Day 0	Day 90	value	Day 0	Day 90	value	Group	Time	Group x Time	Base
ISL	24.62 ± 3.499	25.19 ± 5.163	0.373	24.48 ± 6.162	27.25 ± 5.106	0.002*	0.125	0.040*	0.279	<.0001*
ISRL	8.208 ± 2.449	8.904 ± 2.947	0.030*	8.702 ± 2.654	9.277 ± 2.614	0.091	0.704	0.134	0.897	<.0001*
GML	61.83 ± 21.54	51.00 ± 21.54	0.003*	57.64 ± 18.97	44.58 ± 13.69	<0.0001*	0.103	<.0001*	0.491	<.0001*
GMR	9.208 ± 4.211	8.809 ± 5.182	0.296	9.324 ± 4.870	6.444 ± 3.691	0.000*	0.011*	0.065	0.078	<.0001*
DET	2.503 ± 0.066	2.557 ± 0.096	0.005*	2.543 ± 0.095	2.530 ± 0.082	0.561	0.015*	0.146	0.021*	<.0001*
IDN	2.733 ± 0.066	2.727 ± 0.059	0.965	2.725 ± 0.069	2.723 ± 0.059	0.854	0.246	0.979	0.460	<.0001*
OCL	1.016 ± 0.103	1.018 ± 0.119	0.836	1.017 ± 0.103	1.049 ± 0.093	0.057	0.010*	0.330	0.193	<.0001*
ONB	1.313 ± 0.145	1.404 ± 0.160	0.015*	1.356 ± 0.156	1.397 ± 0.145	0.214	0.220	0.013*	0.388	<.0001*
TWOB	1.220 ± 0.168	1.321 ± 0.157	0.021	1.244 ± 0.148	1.312 ± 0.134	0.019*	0.747	0.004*	0.474	<.0001*

Notes on Table 3
1 Time is the number of visits since the initial Baseline visit and was coded as a categorical variable.

https://prevagen.com/

Apoaequorin

Study results

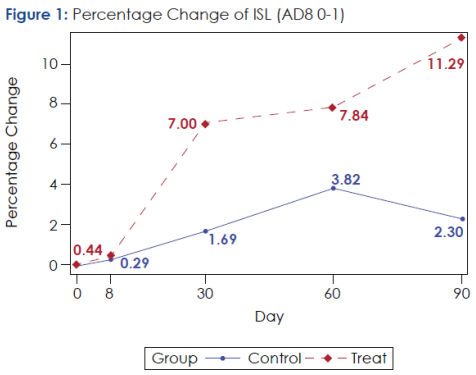
Table 4 The Score Differences in the Two Groups Before and After Treatment (AD8 0-2)

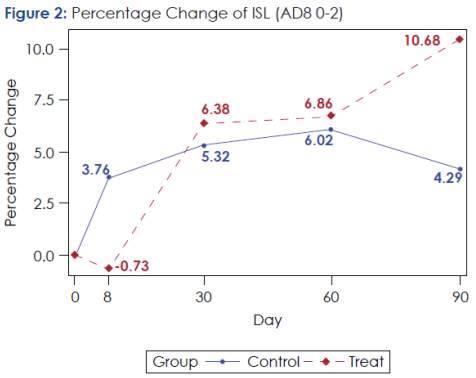
	Placebo		Within p	Apoaequorin		Within p	Between Group P value			
Tasks	Day 0	Day 90	value	Day 0	Day 90	value	Group	Time	Group x Time	Base
ISL	24.45 ± 4.075	25.50 ± 5.474	0.090	25.01 ± 5.434	27.68 ± 4.634	<0.0001*	0.324	0.000*	0.039*	<.0001*
ISRL	8.275 ± 2.385	9.000 ± 2.908	0.012*	8.762 ± 2.336	9.482 ± 2.400	0.002*	0.465	0.015*	0.703	<.0001*
GML	60.37 ± 21.08	50.02 ± 22.43	0.000*	58.59 ± 23.45	46.46 ± 18.78	<0.0001*	0.040*	<.0001*	0.463	<.0001*
GMR	9.400 ± 5.424	8.861 ± 5.938	0.229	8.898 ± 4.470	7.017 ± 4.722	0.001*	0.107	0.092	0.367	<.0001*
DET	2.500 ± 0.081	2.537 ± 0.099	0.045*	2.534 ± 0.104	2.533 ± 0.100	0.675	0.250	0.165	0.365	<.0001*
IDN	2.726 ± 0.068	2.732 ± 0.064	0.267	2.729 ± 0.072	2.725 ± 0.061	0.815	0.037*	0.780	0.108	<.0001*
OCL	1.005 ± 0.113	1.018 ± 0.121	0.292	1.013 ± 0.107	1.041 ± 0.100	0.046*	0.020*	0.437	0.357	<.0001*
ONB	1.298 ± 0.185	1.421 ± 0.156	<.0001*	1.356 ± 0.163	1.397 ± 0.140	0.081	0.944	0.000*	0.223	<.0001*
TWOB	1.223 ± 0.164	1.317 ± 0.176	0.002*	1.251 ± 0.114	1.302 ± 0.127	0.028*	0.934	0.000*	0.290	<.0001*

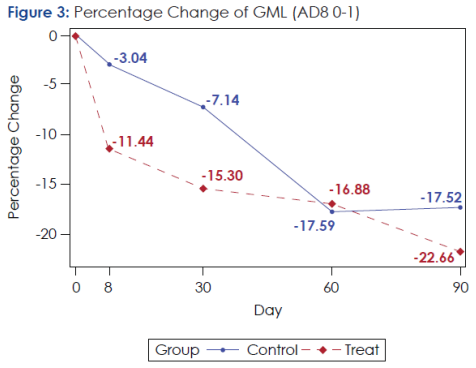
Notes on Table 4
1 Time is the number of visits since the initial Baseline visit and was coded as a categorical variable.

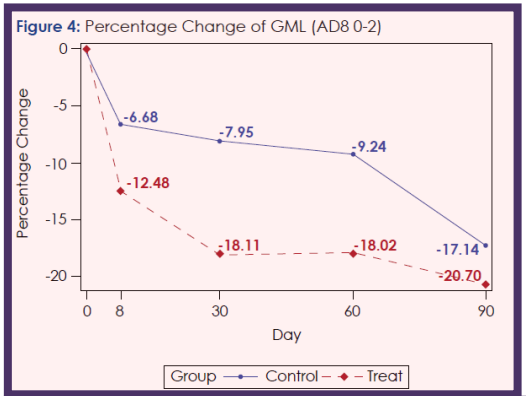
https://prevagen.com/

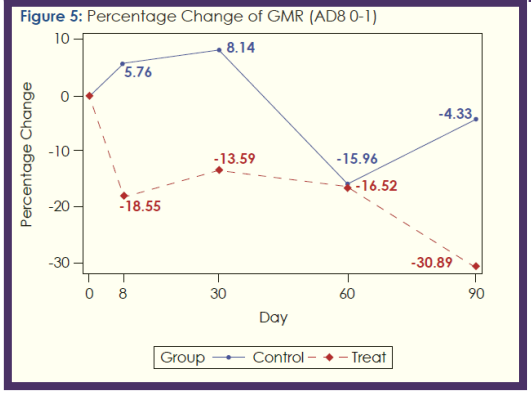
Apoaequorin

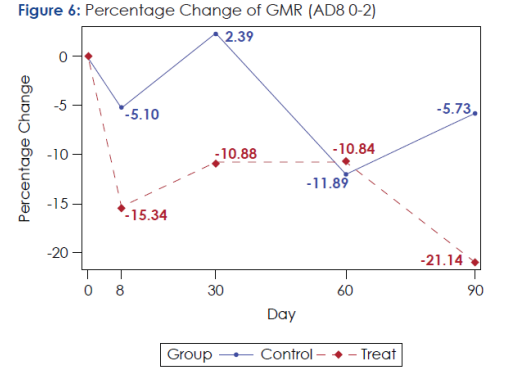


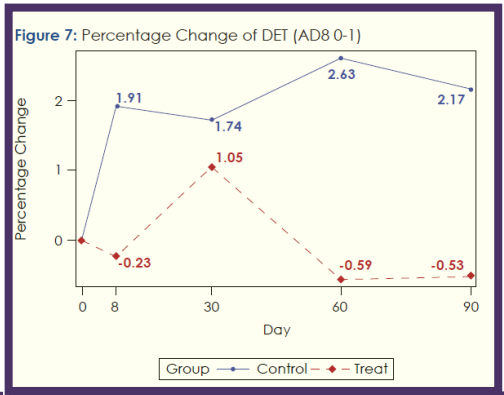


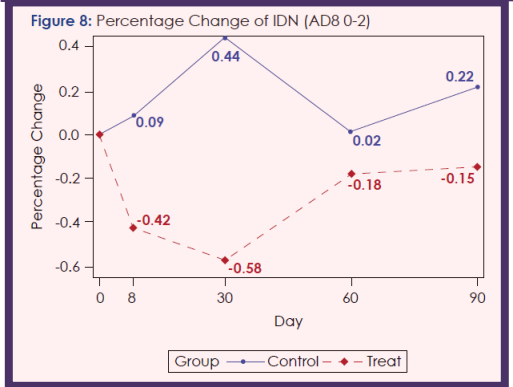


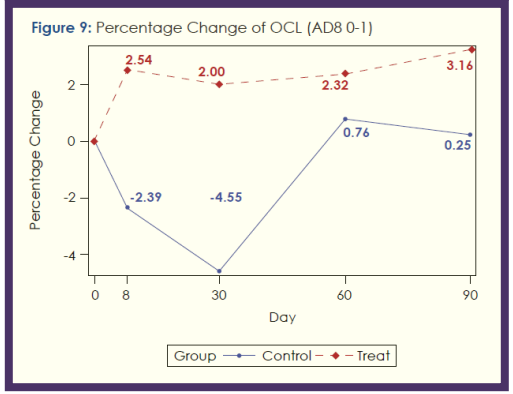


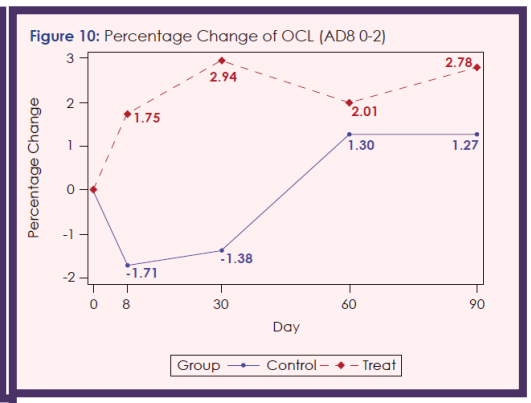












Study data

Significant difference between the AD8 0-1 groups

Significant difference between the AD8 0-2 groups

https://prevagen.com/

CONCLUSION

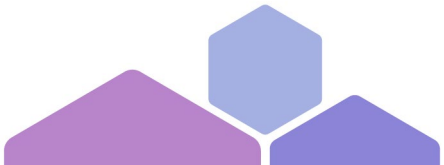
apoaequorin demonstrated the ability to improve aspects of cognitive function in older participants with either normal cognitive aging or very mild impairment, as determined by AD8 screening.

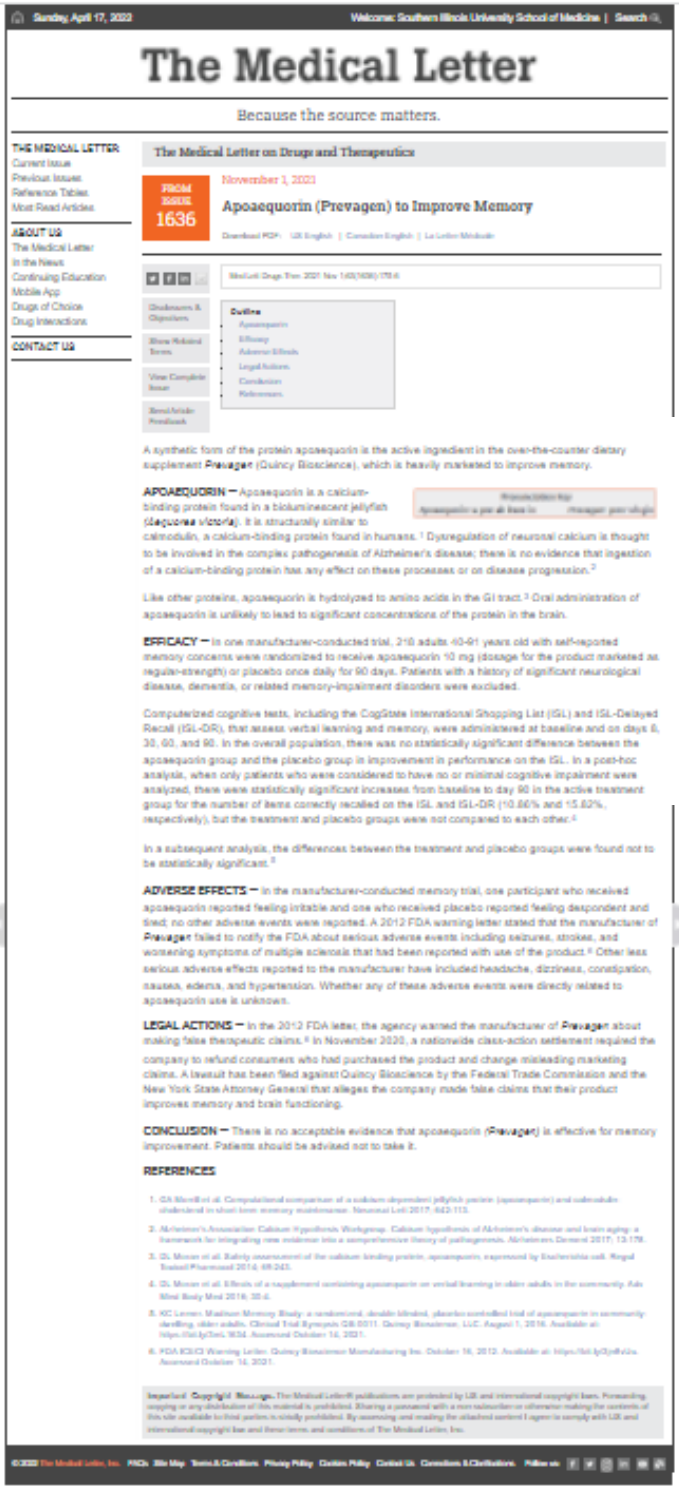
https://prevagen.com/

PMID: 26878676
Moran. *Adv Mind Body Med* 2016;30:4

HMMMM….

This looks half-way decent!





Sunday, April 17, 2022 Welcome: Southern Illinois University School of Medicine | Search

The Medical Letter

Because the source matters.

THE MEDICAL LETTER
Current Issue
Previous Issues
Reference Tables
Most Read Articles

ABOUT US
The Medical Letter
In the News
Continuing Education
Mobile App
Drugs of Choice
Drug Interactions

CONTACT US

The Medical Letter on Drugs and Therapeutics

FROM ISSUE 1636

November 1, 2021

Apoaequorin (Prevagen) to Improve Memory

Download PDF: US English | Canadian English | La Lettre Médicale

Outline

- Apoaequorin
- Efficacy
- Adverse Effects
- Legal Actions
- Conclusion
- References

A synthetic form of the protein apoaequorin is the active ingredient in the over-the-counter dietary supplement **Prevagen** (Quincy Bioscience), which is heavily marketed to improve memory.

APOAEQUORIN — Apoaequorin is a calcium-binding protein found in a bioluminescent jellyfish (*Aequorea victoria*). It is structurally similar to calmodulin, a calcium-binding protein found in humans.[1] Dysregulation of neuronal calcium is thought to be involved in the complex pathogenesis of Alzheimer's disease; there is no evidence that ingestion of a calcium-binding protein has any effect on these processes or on disease progression.[2]

Like other proteins, apoaequorin is hydrolyzed to amino acids in the GI tract.[3] Oral administration of apoaequorin is unlikely to lead to significant concentrations of the protein in the brain.

EFFICACY — In one manufacturer-conducted trial, 218 adults 40-91 years old with self-reported memory concerns were randomized to receive apoaequorin 10 mg (dosage for the product marketed as regular-strength) or placebo once daily for 90 days. Patients with a history of significant neurological disease, dementia, or related memory-impairment disorders were excluded.

Computerized cognitive tests, including the CogState International Shopping List (ISL) and ISL-Delayed Recall (ISL-DR), that assess verbal learning and memory, were administered at baseline and on days 8, 30, 60, and 90. In the overall population, there was no statistically significant difference between the apoaequorin group and the placebo group in improvement in performance on the ISL. In a post-hoc analysis, when only patients who were considered to have no or minimal cognitive impairment were analyzed, there were statistically significant increases from baseline to day 90 in the active treatment group for the number of items correctly recalled on the ISL and ISL-DR (10.86% and 15.82%, respectively), but the treatment and placebo groups were not compared to each other.[4]

In a subsequent analysis, the differences between the treatment and placebo groups were found not to be statistically significant.[5]

ADVERSE EFFECTS — In the manufacturer-conducted memory trial, one participant who received apoaequorin reported feeling irritable and one who received placebo reported feeling despondent and tired; no other adverse events were reported. A 2012 FDA warning letter stated that the manufacturer of **Prevagen** failed to notify the FDA about serious adverse events including seizures, strokes, and worsening symptoms of multiple sclerosis that had been reported with use of the product.[6] Other less serious adverse effects reported to the manufacturer have included headache, dizziness, constipation, nausea, edema, and hypertension. Whether any of these adverse events were directly related to apoaequorin use is unknown.

LEGAL ACTIONS — In the 2012 FDA letter, the agency warned the manufacturer of **Prevagen** about making false therapeutic claims.[6] In November 2020, a nationwide class-action settlement required the company to refund consumers who had purchased the product and change misleading marketing claims. A lawsuit has been filed against Quincy Bioscience by the Federal Trade Commission and the New York State Attorney General that alleges the company made false claims that their product improves memory and brain functioning.

CONCLUSION — There is no acceptable evidence that apoaequorin (**Prevagen**) is effective for memory improvement. Patients should be advised not to take it.

REFERENCES

1. GA Morrill et al. Computational comparison of a calcium-dependent jellyfish protein (apoaequorin) and calmodulin clustered in short-term memory maintenance. Neurosci Lett 2017; 642:113.
2. Alzheimer's Association Calcium Hypothesis Workgroup. Calcium hypothesis of Alzheimer's disease and brain aging: a framework for integrating new evidence into a comprehensive theory of pathogenesis. Alzheimers Dement 2017; 13:178.
3. DL Moran et al. Safety assessment of the calcium binding protein, apoaequorin, expressed by Escherichia coli. Regul Toxicol Pharmacol 2014; 69:243.
4. DL Moran et al. Effects of a supplement containing apoaequorin on verbal learning in older adults in the community. Adv Mind Body Med 2016; 30:4.
5. KC Lerner. Madison Memory Study: a randomized, double-blinded, placebo-controlled trial of apoaequorin in community-dwelling, older adults. Clinical Trial Synopsis CS-0011. Quincy Bioscience, LLC. August 1, 2016. Available at: https://bit.ly/3zL1K34. Accessed October 14, 2021.
6. FDA ICSO Warning Letter. Quincy Bioscience Manufacturing Inc. October 16, 2012. Available at: https://bit.ly/3jvBVUa. Accessed October 14, 2021.

Important Copyright Message. The Medical Letter® publications are protected by US and international copyright laws. Forwarding, copying or any distribution of this material is prohibited. Sharing a password with a non-subscriber or otherwise making the contents of this site available to third parties is strictly prohibited. By accessing and reading the attached content I agree to comply with US and international copyright law and these terms and conditions of The Medical Letter, Inc.

©2022 The Medical Letter, Inc. FAQs Site Map Terms & Conditions Privacy Policy Cookies Policy Contact Us Corrections & Clarifications Follow us

LEGAL ACTIONS — In the 2012 FDA letter, the agency warned the manufacturer of apoaeq about making false therapeutic claims.[6] In November 2020, a nationwide class-action settlement required the company to refund consumers who had purchased the product and change misleading marketing claims. A lawsuit has been filed against Quincy Bioscience by the Federal Trade Commission and the New York State Attorney General that alleges the company made false claims that their product improves memory and brain functioning.

CONCLUSION — There is no acceptable evidence that apoaequorin is effective for memory improvement. Patients should be advised not to take it.

PMID: 35085208

Med Lett Drugs Ther 2021;63:175

CONCLUSION

- There is no acceptable evidence that apoaequorin is effective for memory improvement. Patients should be advised not to take it.

PMID: 35085208

Med Lett Drugs Ther 2021;63:175

Apoaequorin

Pharmacists should not recommend a product with limited evidence to support its use.

Sr Care Pharm. 2022 Aug 1;37(8):335-338. doi: 10.4140/TCP.n.2022.335.

Prevagen®: Analysis of Clinical Evidence and Its Designation as a "#1 Pharmacist Recommended Brand"

Sara Grossman [1], Joseph P Nathan [1], Alicja Siuzdak [2], Jessica Liang [1], Christopher Sprycha [1]

Affiliations — collapse

Affiliations

1 1Long Island University, Arnold & Marie Schwartz College of Pharmacy and Health Sciences, Brooklyn, New York.

2 2Regeneron Pharmaceuticals, Inc., Medical Information Department, Tarrytown, New York.

PMID: 35879840 DOI: 10.4140/TCP.n.2022.335

Abstract

Prevagen® is a dietary supplement that is marketed to help with mild memory loss associated with older people. The manufacturer of the product notes that clinical evidence supports this use. Furthermore, the manufacturer notes that Prevagen® is a "#1 Pharmacist Recommended Brand." The authors' search of the literature identified one clinical study that evaluated the efficacy and safety of Prevagen®; however, this study possesses significant limitations and therefore one must question the merits of such clinical evidence. Prevagen®'s designation as a "#1 Pharmacist Recommended Brand" is based on a survey facilitated by *Pharmacy Times*® that is designed to identify the brand name over-the-counter products that pharmacists recommend most frequently. Because of the limited clinical data supporting Prevagen®'s efficacy, it is likely that the survey results reflect pharmacists' familiarity with this product, which may be influenced by extensive advertising techniques. As practitioners of evidence-based medicine, pharmacists should not recommend a product with limited evidence to support its use. Furthermore, pharmacists should proactively educate their patients, especially those who are most vulnerable, about the rational use of all pharmacologically active substances, including dietary supplements.

PMID: 35879840

Grossman. *The Senior care Pharmacist* 2022;37:335

Apoaequorin

Are there any side effects with Prevagen? –

If you are concerned with any side effects, you may want to talk with your doctor before beginning Prevagen use.

https://prevagen.com/

- Prevagen is a dietary supplement.
- Prevagen is not FDA-approved.

DIFFERENCE BETWEEN FDA-APPROVED DRUGS AND DIETARY SUPPLEMENTS.

- In order for a drug to be approved by the FDA, it must be proven to be safe and effective.
  - data on the drug's effects have been reviewed by the Center for Drug Evaluation and Research, and the drug is determined to provide benefits that outweigh its known and potential risks for the intended population.
- Unlike new drugs, dietary supplements are not reviewed and approved by the FDA based on their safety and effectiveness.
- When public health concerns arise about a dietary supplement after the product is on the market, the FDA evaluates the product's safety through research and adverse event monitoring.
- Promotional information about the supplement must include the phrase, "These statements have not been evaluated by the FDA and are not intended to diagnose, treat, cure or prevent any disease or health condition."

https://www.fda.gov/consumers/consumer-updates/it-really-fda-approved

DIFFERENCE BETWEEN FDA-APPROVED DRUGS AND DIETARY SUPPLEMENTS.

- In order for a drug to be approved by the FDA, it must be proven to be safe and effective.
  - data on the drug's effects have been reviewed by the Center for Drug Evaluation and Research, and the drug is determined to provide benefits that outweigh its known and potential risks for the intended population.
- Unlike new drugs, dietary supplements are not reviewed and approved by the FDA based on their safety and effectiveness.
- When public health concerns arise about a dietary supplement after the product is on the market, the FDA evaluates the product's safety through research and adverse event monitoring.
- Promotional information about the supplement must include the phrase, "These statements have not been evaluated by the FDA and are not intended to diagnose, treat, cure or prevent any disease or health condition."

https://www.fda.gov/consumers/consumer-updates/it-really-fda-approved

What is apoaequorin?

apoaequorin was originally discovered in jellyfish. Apoaequorin is safe and uniquely supports brain function.*

® Selected as the **#1 Pharmacist Recommended Memory Support Brand in 2021** Pharmacy Times annual survey for third year in a row.

These statements have not been evaluated by the FDA and are not intended to diagnose, treat, cure or prevent any disease or health condition

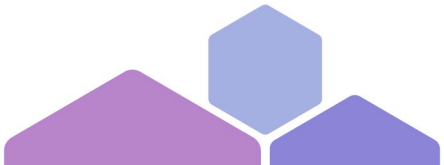
https://prevagen.com/

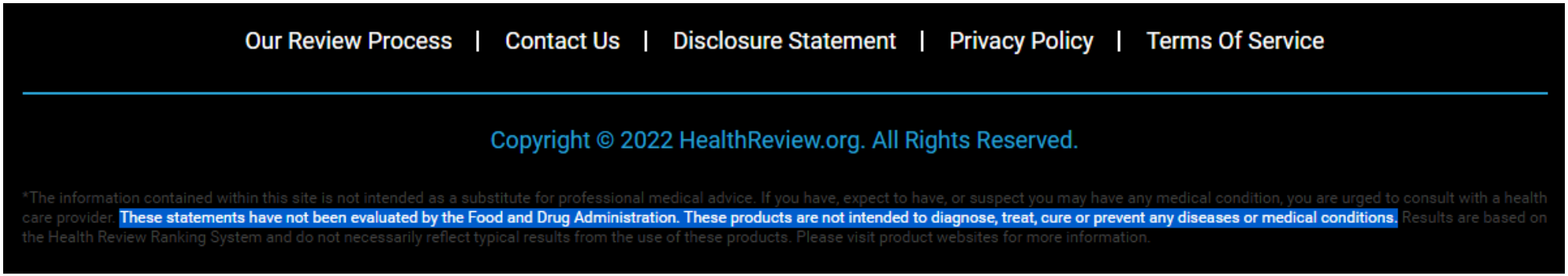
Citations

1. https://www.ncbi.nlm.nih.gov/pubmed/17182482
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3501277/
3. https://www.ncbi.nlm.nih.gov/pubmed/20182035
4. https://www.ncbi.nlm.nih.gov/pubmed/22300295
5. https://www.ncbi.nlm.nih.gov/pubmed/21731159
6. https://www.ncbi.nlm.nih.gov/pubmed/22549035
7. https://www.ncbi.nlm.nih.gov/pubmed/12093601
8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4772032/

https://healthreview.org/brain-supplements/neuronol/?gclid=EAIaIQobChMIwqW_tueg9wIV9vTjBx10tgPOEAAYASAAEgIfqfD_BwE

https://healthreview.org/brain-supplements/neuronol/?gclid=EAIaIQobChMIwqW_tueg9wIV9vTjBx10tgPOEAAYASAAEgIfqfD_BwE





These statements have not been evaluated by the FDA and are not intended to diagnose, treat, cure or prevent any disease or health condition.

https://healthreview.org/brain-supplements/neuronol/?gclid=EAIaIQobChMIwqW_tueg9wIV9vTjBx10tgPOEAAYASAAEgIfqfD_BwE

ALZHEIMER'S ASSOCIATION STATEMENT

- One of the biggest problem areas for unsubstantiated claims are dietary supplements, foods and products that claim to be beneficial for Alzheimer's or other dementia symptoms.

ALZHEIMER'S ASSOCIATION STATEMENT

- One of the biggest problem areas for unsubstantiated claims are dietary supplements, foods and products that claim to be beneficial for Alzheimer's or other dementia symptoms.
- These products are not approved by the FDA, and little is known about their effectiveness, quality and safety.

ALZHEIMER'S ASSOCIATION STATEMENT

- One of the biggest problem areas for unsubstantiated claims are dietary supplements, foods and products that claim to be beneficial for Alzheimer's or other dementia symptoms.
- These products are not approved by the FDA, and little is known about their effectiveness, quality and safety.
- But that hasn't stopped some outlets from touting their benefits for cognitive health.

Alz.org

ALZHEIMER'S ASSOCIATION STATEMENT

- One of the biggest problem areas for unsubstantiated claims are dietary supplements, foods and products that claim to be beneficial for Alzheimer's or other dementia symptoms.
- These products are not approved by the FDA, and little is known about their effectiveness, quality and safety.
- But that hasn't stopped some outlets from touting their benefits for cognitive health.
- In the past five years, the FDA has issued more than 40 warning letters to companies illegally marketing over 80 products claiming to prevent, treat or cure Alzheimer's disease.

Alz.org

DON’T FALL FOR FALSE HEALTH CLAIMS

YOU DON'T NEED TO BE A SCIENTIST TO THINK LIKE ONE — USE THESE TIPS TO NAVIGATE THE CONFUSING WORLD OF RESEARCH

- Be savvy
  - review research news with a critical eye.
- Supplement your awareness
  - Talk to your doctor.
  - Look for FDA-approved treatments.
- Be your own advocate
  - “The most important thing you can do is to demand evidence rigorously backed in science.”
- Think like a scientist
  - Is there sufficient evidence?
  - Who conducted the research?
  - How was the research conducted?
  - Does it sound too good to be true?
  - Where was the research announced?

Alz.org

BOTTOM LINE…

- Not recommended.

BOTTOM LINE…

- Not recommended.
- But use your judgment; it's up to you.
  - Is it OK with your primary MD?
  - No side effects?
  - Can you afford it?

The end

Thank you!

SIU MEDICINE
FORWARD. FOR YOU.