Aricept®

Donepezil HCl 5mg & 10mg Tablets

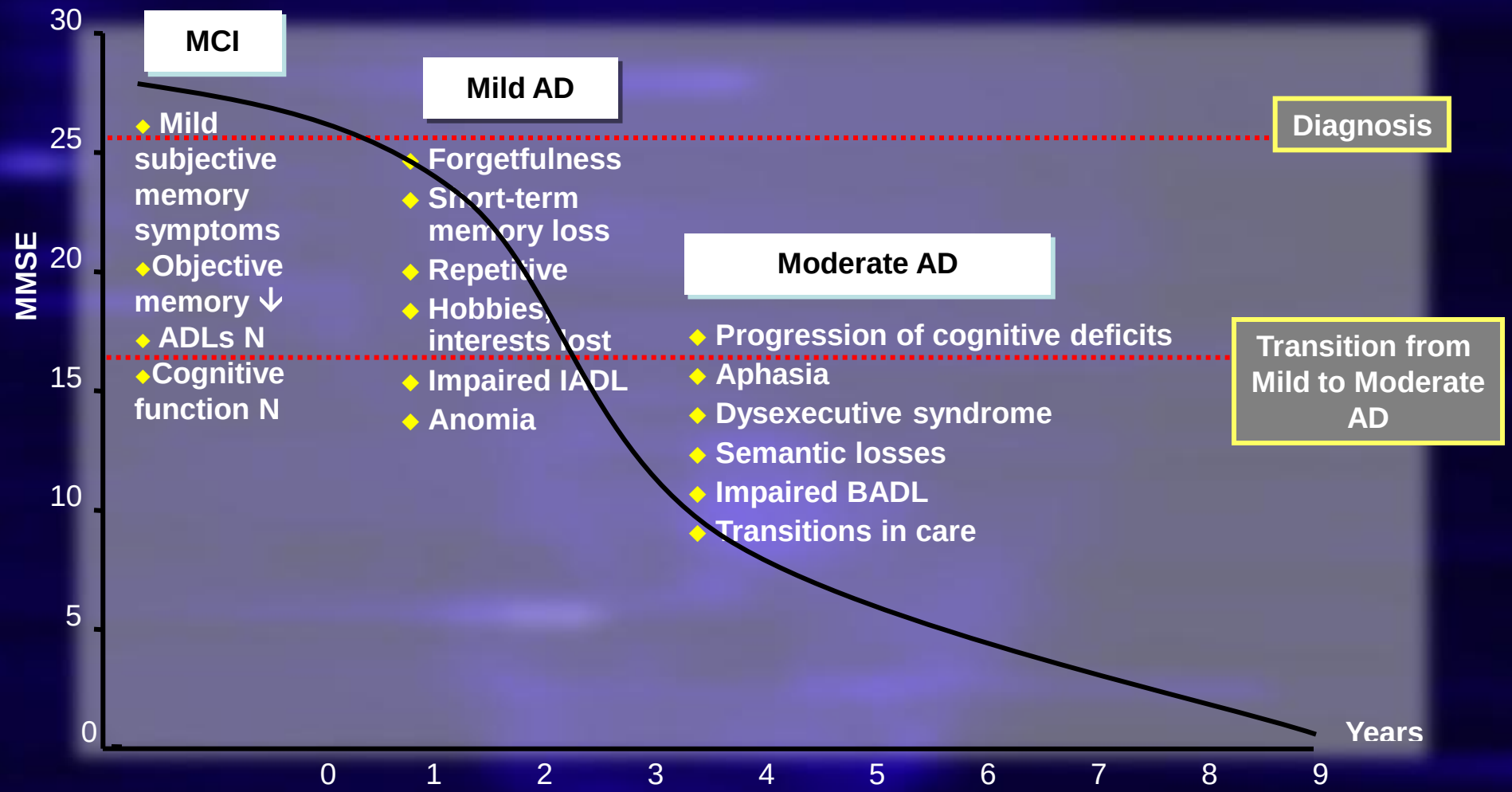
Eisai Korea Inc.

What is Alzheimer's disease?

- **A progressive, degenerative disease**
- **Its core symptoms are:**
  - Cognitive decline
  - Functional decline
  - Behavioral disturbances
- **Neurofibrillary tangles and plaques may lead to loss of cholinergic neuronal function**
- **Cholinergic hypothesis**
- -cholinergic deficit in cerebral cortex triggered Alzheimer's disease

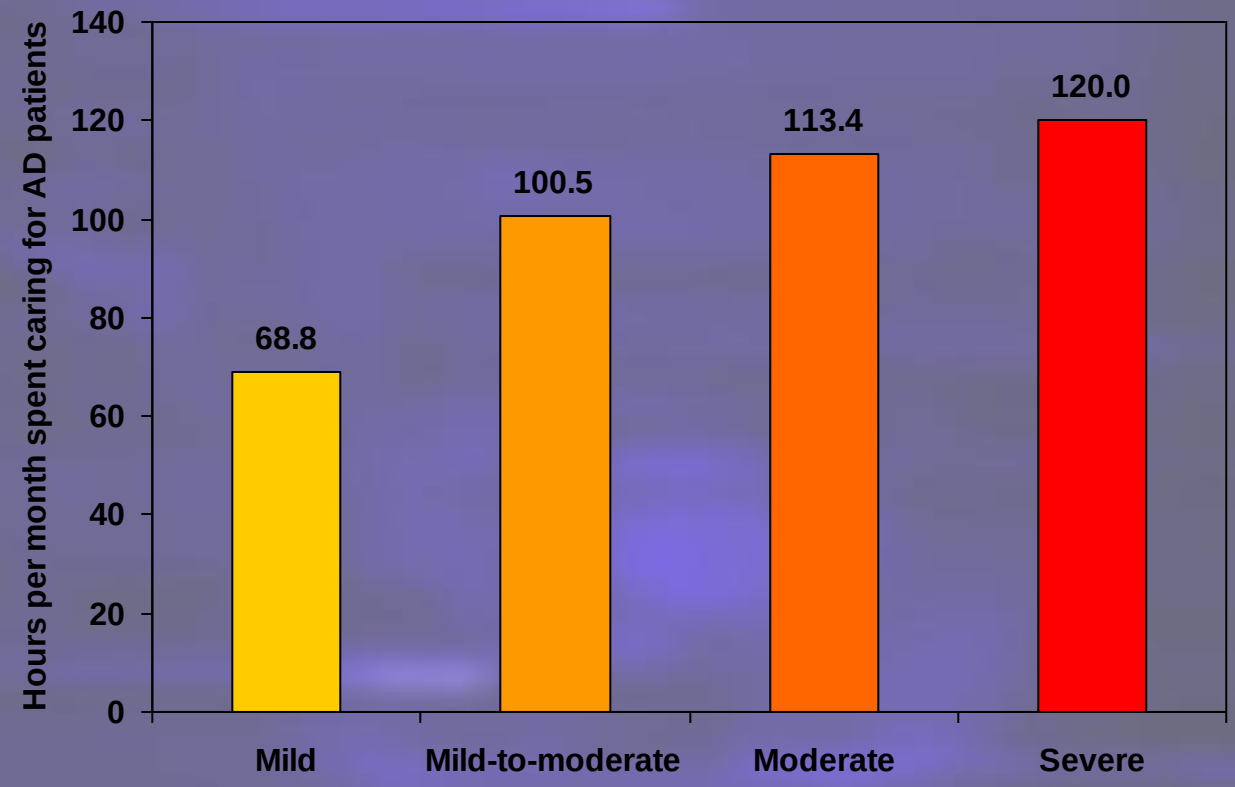
J Kor Med Assoc. 2002;45(4) : 356-360; JAMA. 1989;262(18):2251-6

Symptom Progression in AD



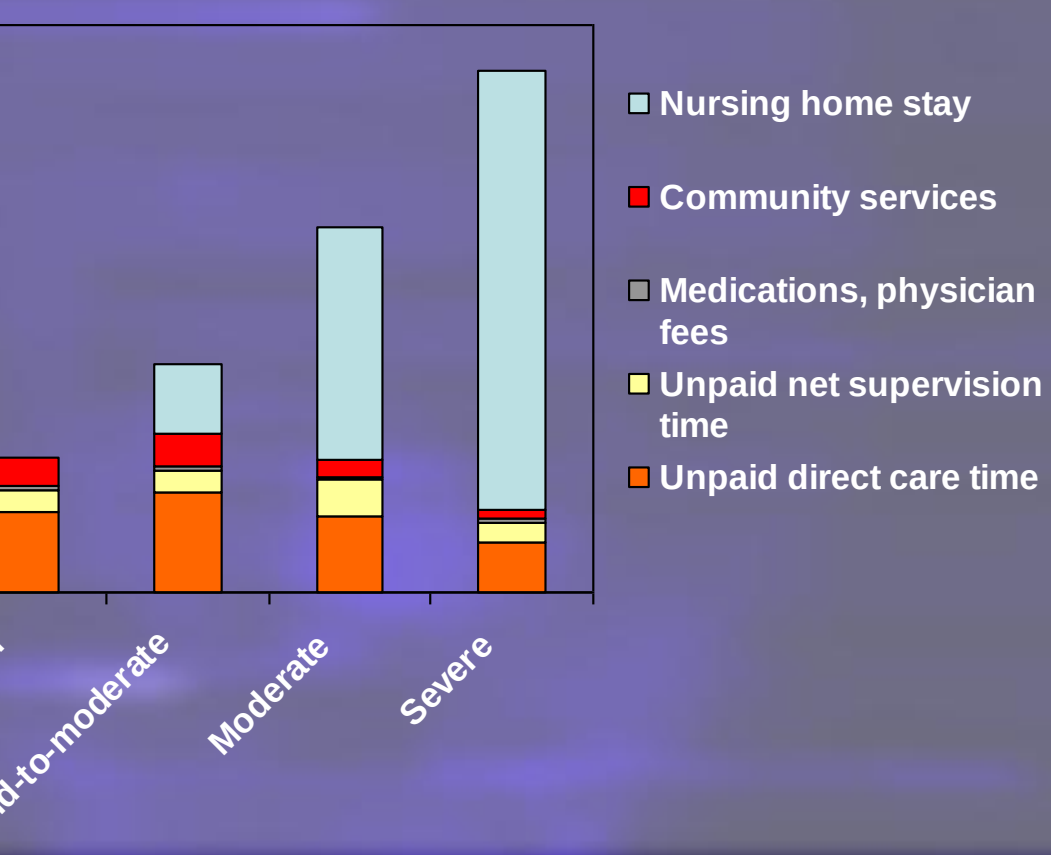
Modified from Feldman HH & Woodward M. *Neurology.* 2005;65:S10-17

AD Caregiver Time by Disease Severity



Hux et al. CMAJ, 1998.

Mean Annual Cost of AD by Disease Severity



Hux et al. CMAJ, 1998.

ARICEPT (Donepezil HCl)

- Donepezil 5mg & 10mg Tablet
- High bioavailability
- Long half life(70h) and Once daily
- No titration to reach effective dose
- Selective to CNS AChE (AChE>BuchE, IC50 Ratio = 1252/1)
- May be taken with or without food
- Aricept® is the only AChE inhibitor indicated for mild to severe Alzheimer's disease and Vascular Dementia treatment

ARICEPT (Donepezil HCl)

All Stage of AD

아리셉트는 Mild to Severe Alzheimer's Disease에 처방하실 수 있는 치매증상치료제입니다.

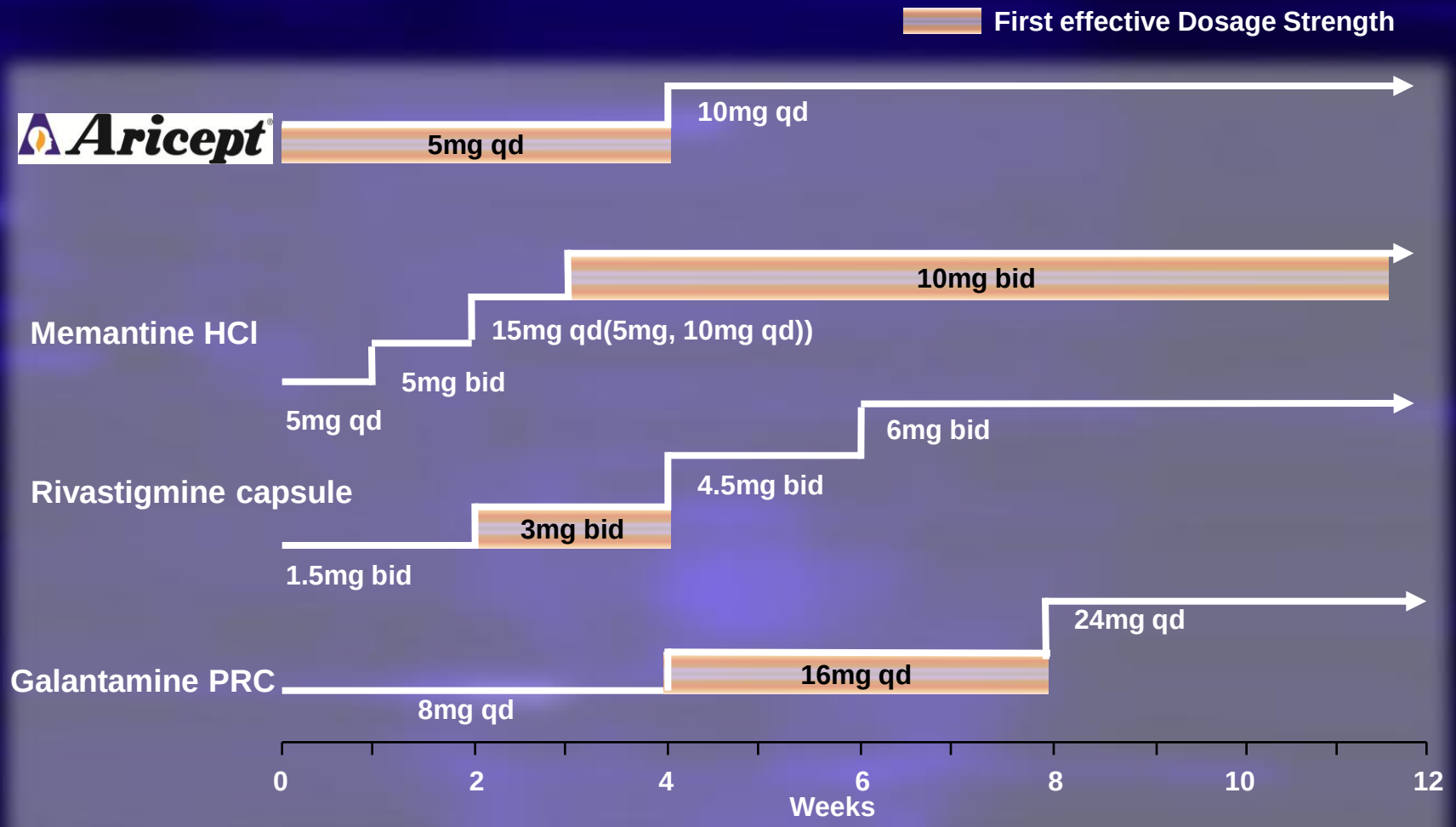
The 1st Choice of Dementia Treatment

아리셉트는 Alzheimer's Disease, Vascular Dementia에 처방하실 있는 치매증상치료제입니다.

Convenience

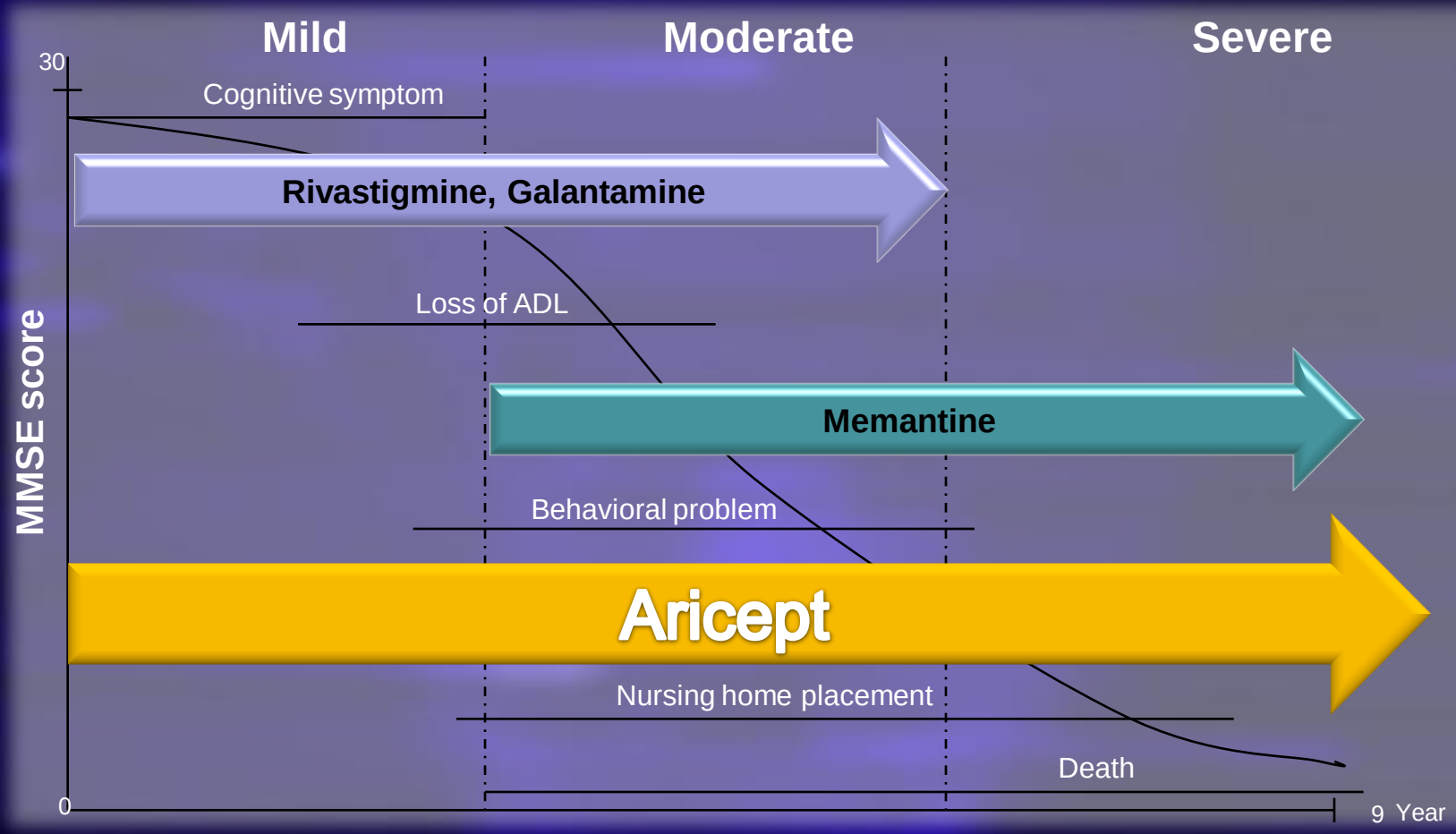
아리셉트는 임상적으로 유효약용량에 도달하기 위한 titration 기간이 필요 없는 치매증상 치료제입니다.

Mechanism of ARICEPT
Dose escalation schedule

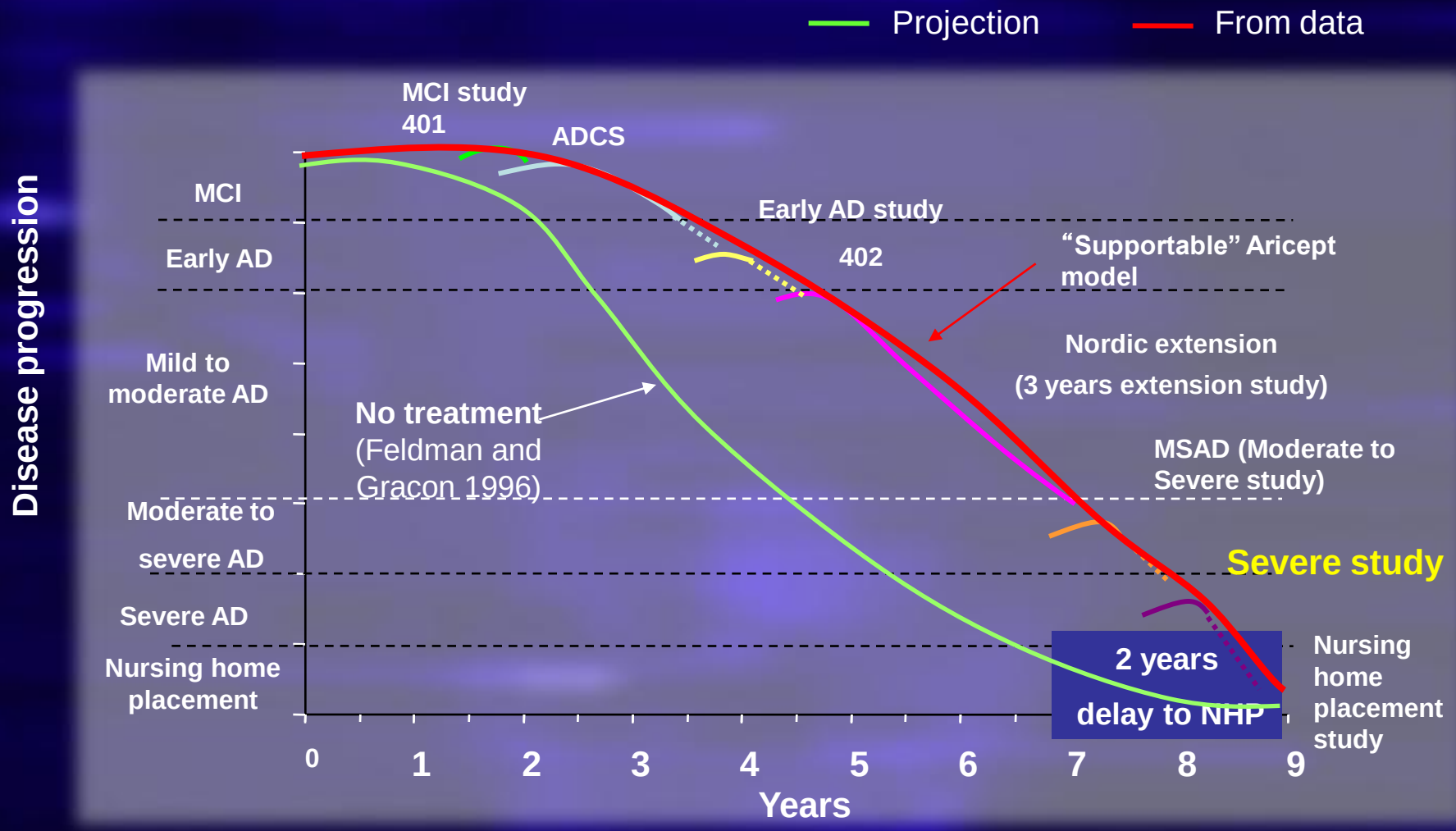


- Minimum titration intervals from respective package inserts.
- Rivastigmine should be administered with food. It is preferable to administer Galantamine with food.

ARICEPT is the only AChE-I for all stage of AD



Proven efficacy of ARICEPT through all dementia course



MCI study (Neurology 2004;63:651-657)

CME

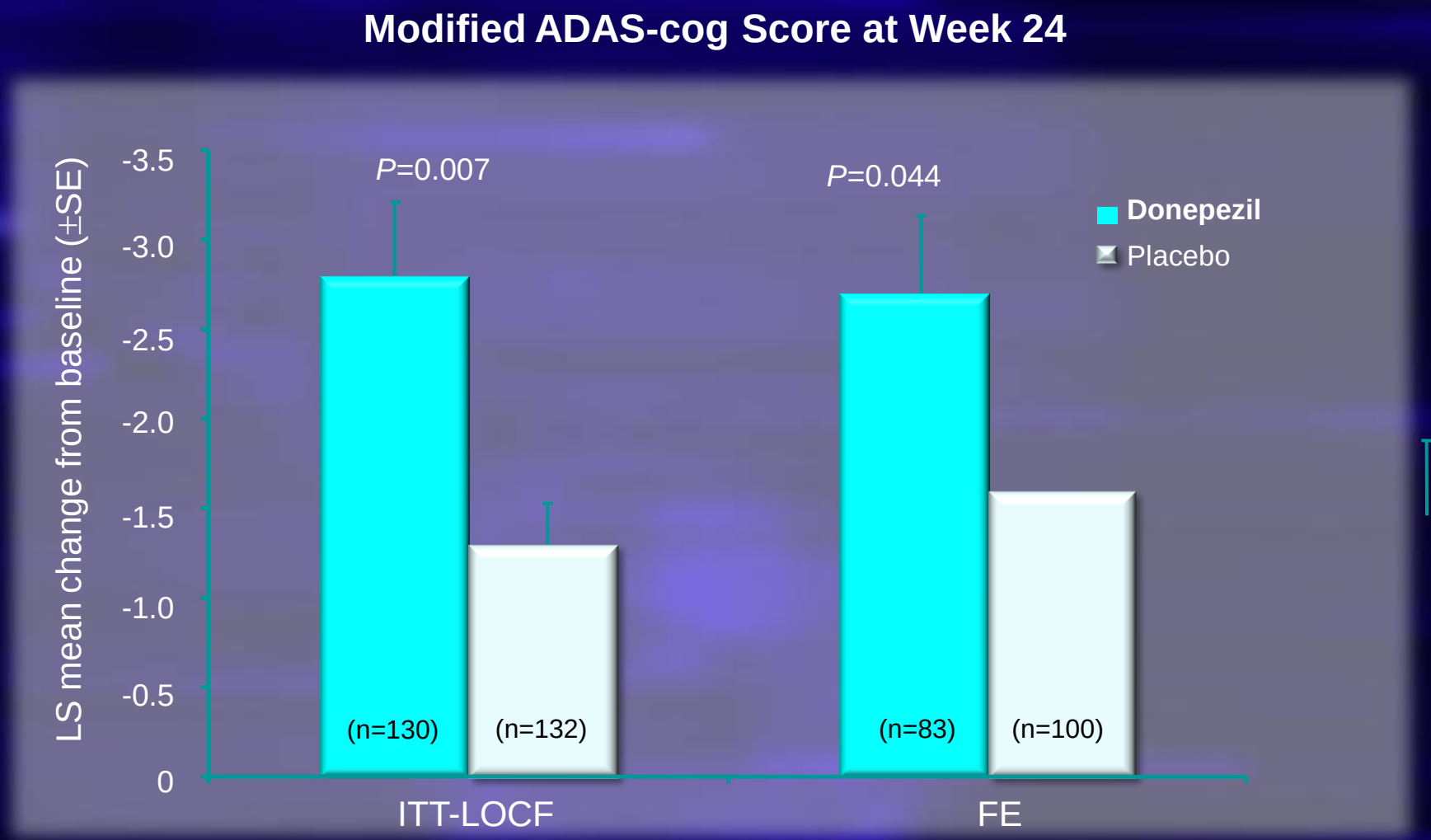
Efficacy of donepezil in mild cognitive impairment

A randomized placebo-controlled trial

S. Salloway, MD, MS; S. Ferris, PhD; A. Kluger, PhD; R. Goldman, PhD; T. Griesing, PhD; D. Kumar, MS; and S. Richardson, PhD, for the Donepezil "401" Study Group*

- *Design*: 24-week, multicenter, randomized, double-blind, placebo-controlled study
- *Patients*: A total of 270 patients with MCI (24≤MMSE score) were enrolled and randomized to receive either donepezil or placebo

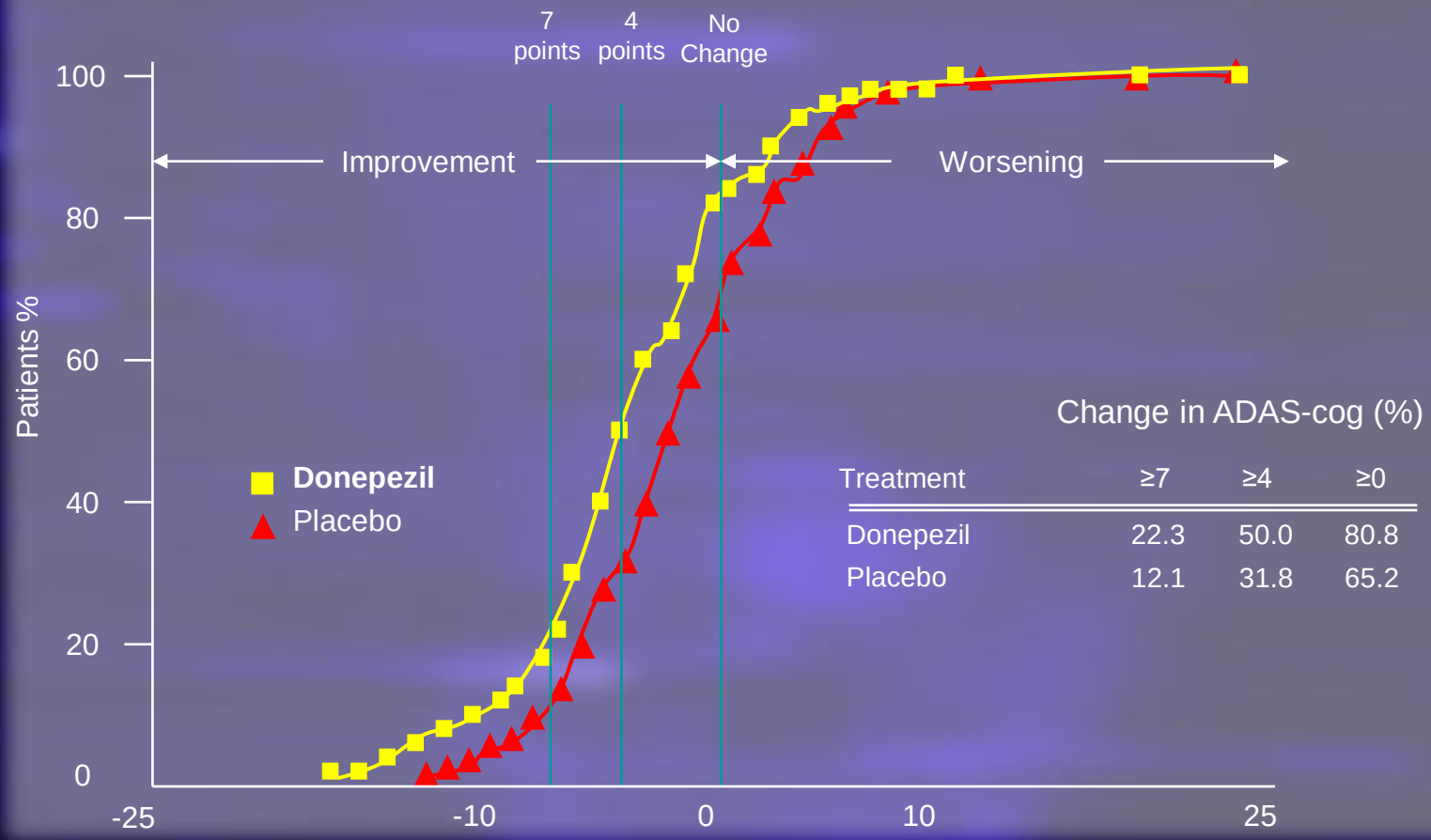
Result of MCI study (1)



Neurology 2004;63;651-657

Result of MCI study (2)

Cumulative percentage of patients with specified changes from baseline in ADAS-cog

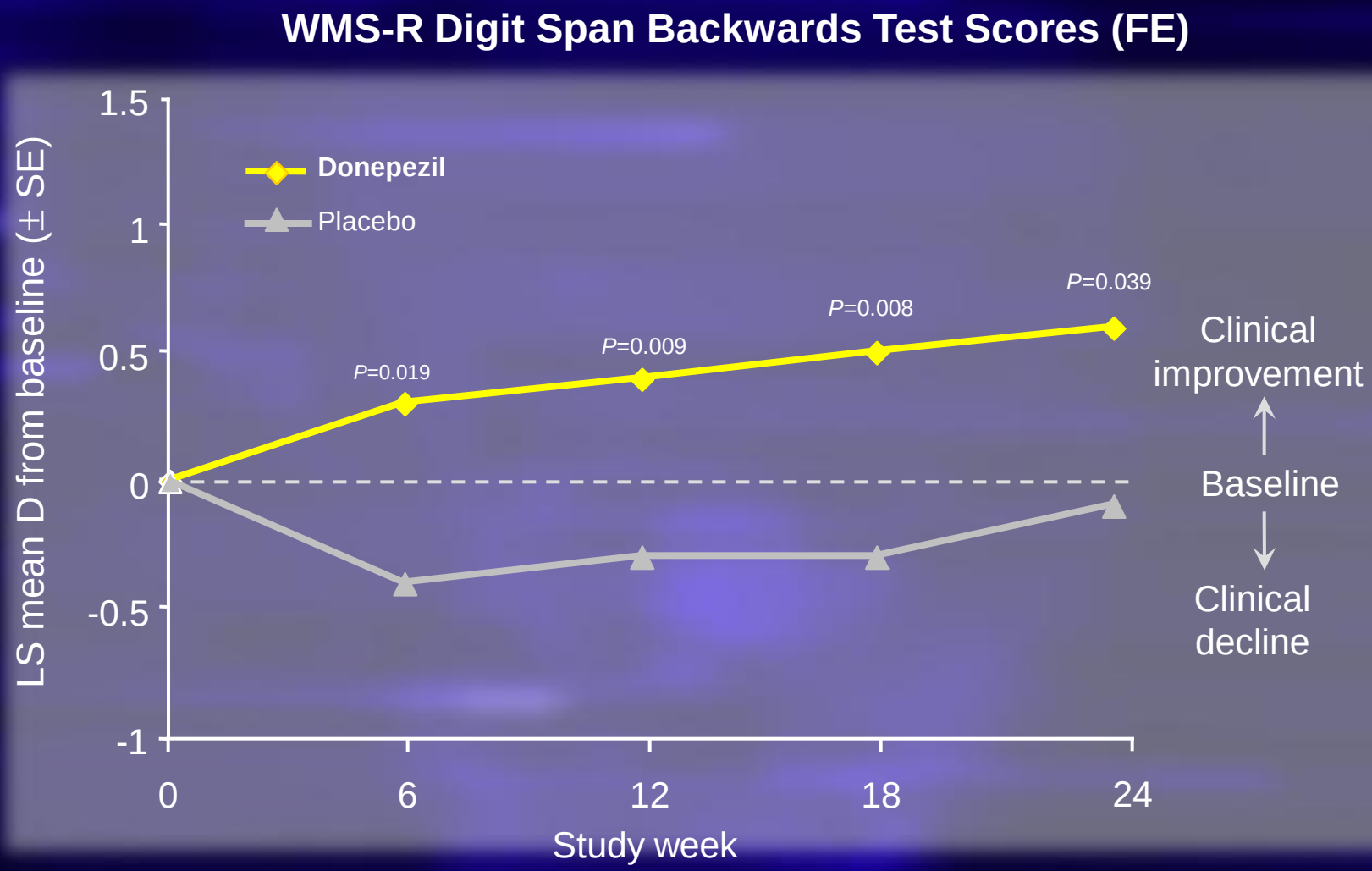


Change in ADAS-cog (%)

Treatment	≥7	≥4	≥0
Donepezil	22.3	50.0	80.8
Placebo	12.1	31.8	65.2

Neurology 2004;63;651-657

Result of MCI study (3)



Neurology 2004;63;651-657

MCI long term study (comparison with VitE & Placebo)

The NEW ENGLAND JOURNAL of MEDICINE

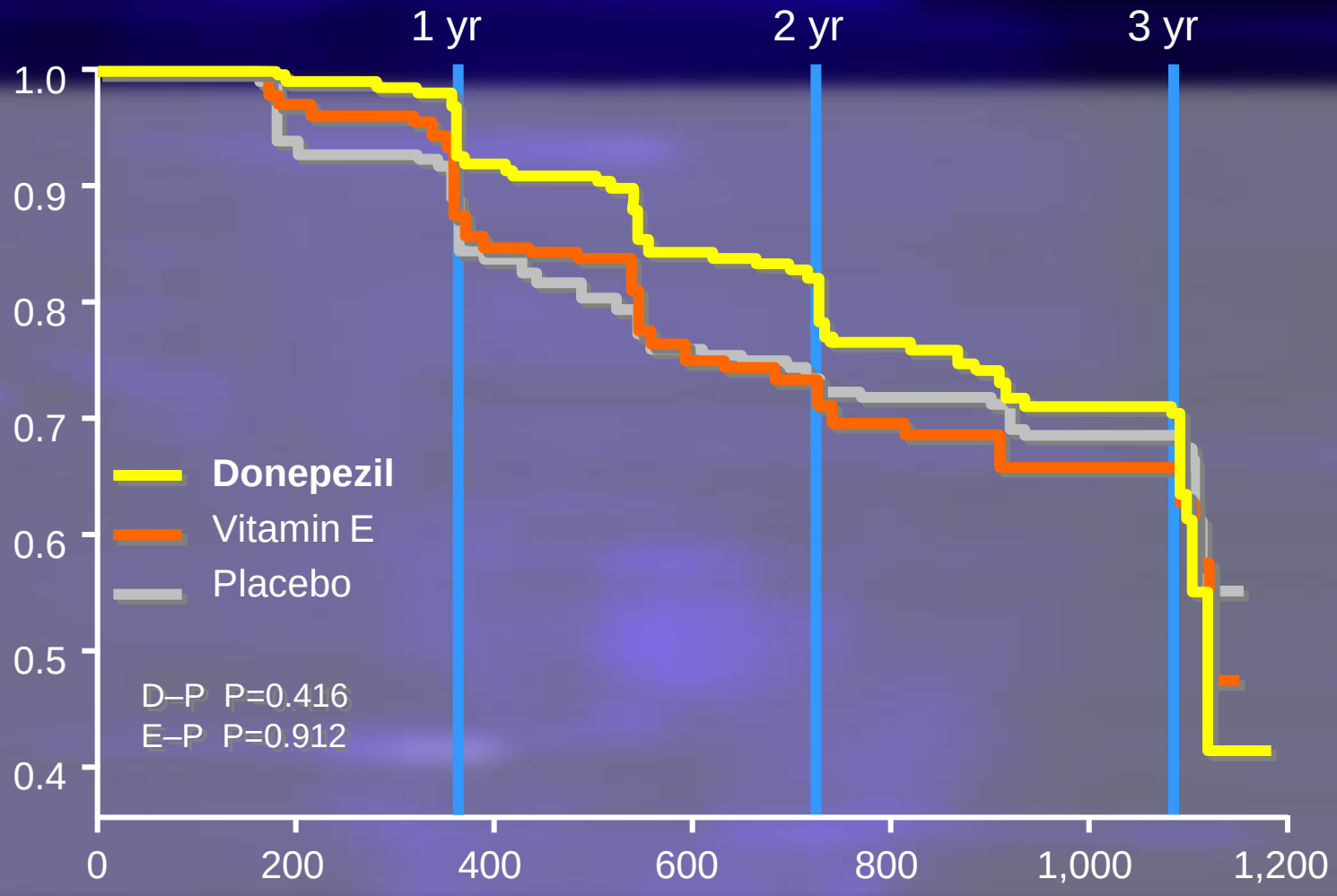
ESTABLISHED IN 1812 JUNE 9, 2005 VOL. 352 NO. 23

Vitamin E and Donepezil for the Treatment of Mild Cognitive Impairment

- *Design*: 3 years, randomized, multicenter, randomized, double-blind, placebo-controlled, parallel study

  (→ Open-label donepezil after conversion to AD)

ARICEPT delays conversion to dementia



N Eng J Med 352;23

Benefit for early stage AD patients

Efficacy of Donepezil in Early-Stage Alzheimer Disease

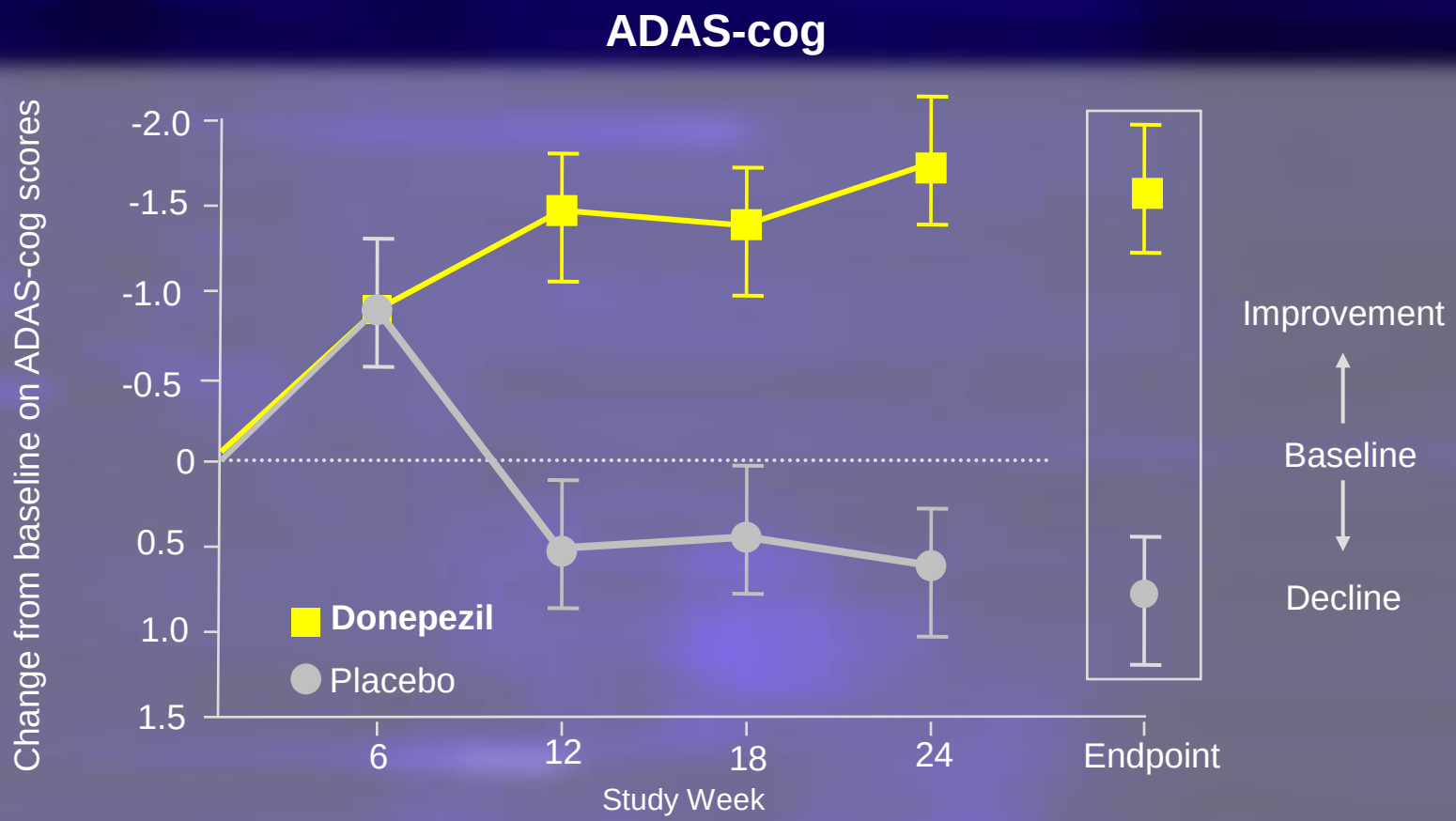
A Randomized Placebo-Controlled Trial

Ben Seltzer, MD; Parvaneh Zolnouni, MD; Margarita Nunez, MD; Robert Goldman, PhD; Dinesh Kumar, MA; John Ieni, PhD; Sharon Richardson, PhD; for the Donepezil "402" Study Group

Arch Neurol. 2004;61:1852-1856

- *Design*: 24-week, multicenter, randomized, double-blind, placebo-controlled study
- *Patients*: A total of 153 patients with early AD (21≤ MMSE score ≤26) were enrolled and randomized to receive either donepezil or placebo

Result of Early AD study (1)

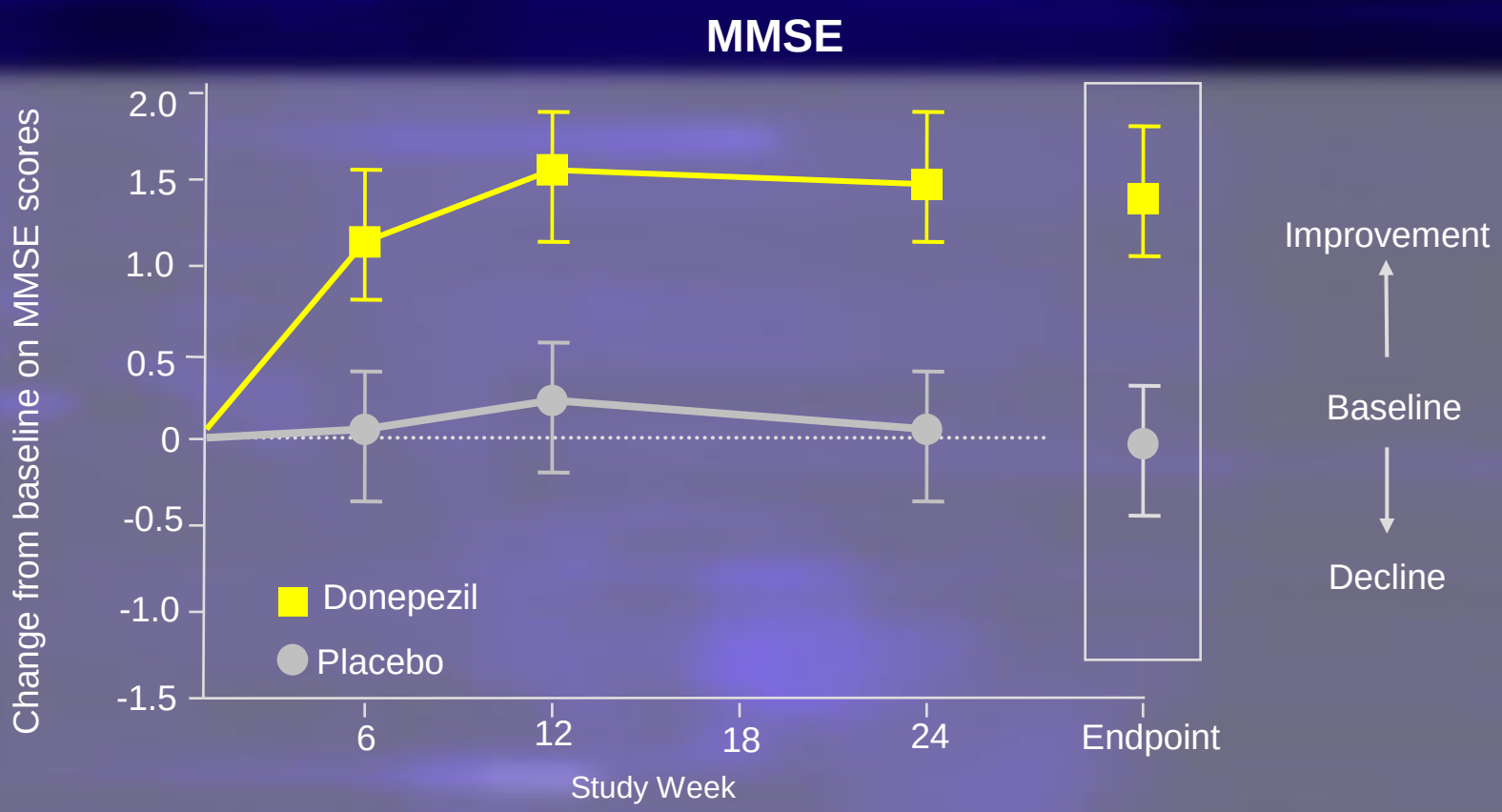


*Improvement ≥4 points : 16% placebo, 37% donepezil

*Improvement ≥7 points : 7% placebo, 10% donepezil

Arch Neurol. 2004;61:1852-1856

Result of Early AD study (2)



*** Improvements from week 6 (P=.02) through week 24 (P=.03)**

*** Difference 1.8 points (P = .002) at the end point**

Arch Neurol. 2004;61:1852-1856

Mild to Moderate AD (Nordic study 2001)

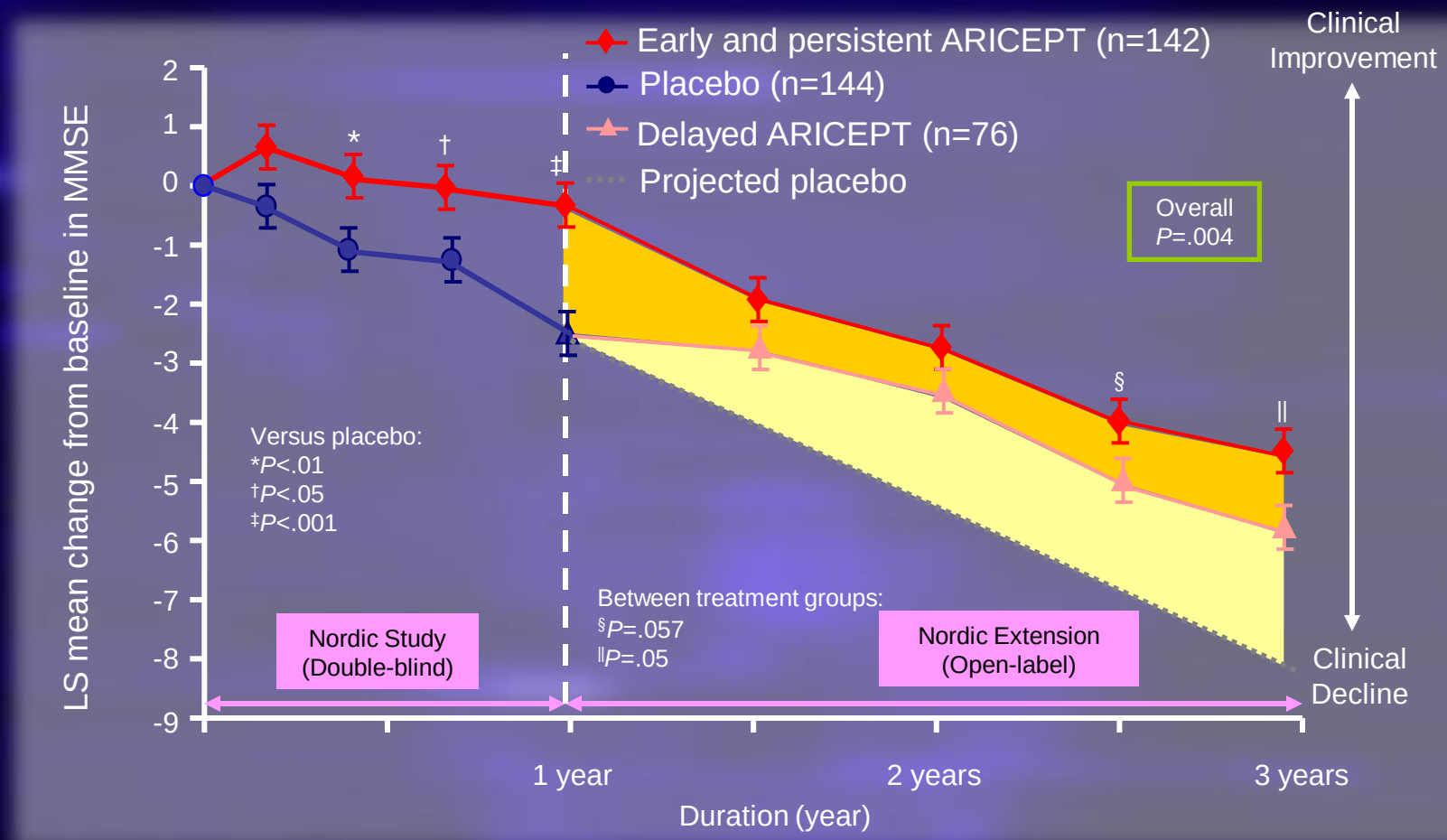
3-Year Study of Donepezil Therapy in Alzheimer's Disease: Effects of Early and Continuous Therapy

B. Winblad[a] A. Wimo[b] K. Engedal[c] H. Soininen[d] F. Verhey[e]
G. Waldemar[f] A.-L. Wetterholm[g] A. Haglund[g] R. Zhang[h] R. Schindler[h]
for the Donepezil Nordic Study Group

- *Design*: 52-week, double-blind phase (1 year)→ open-label extension (2 year)
  ☞ total 3 year nordic extension study
- *Patients*: N=286 with possible or probable AD (MMSE 10~26)

  - donepezil 5mg/day for 4 weeks, followed by 10mg/day

Benefit of early and persistent treatment



Neurology. 2001;57:489-495

Efficacy of ARICEPT for Moderate to Severe AD

A 24-week, randomized, double-blind study of donepezil in moderate to severe Alzheimer's disease

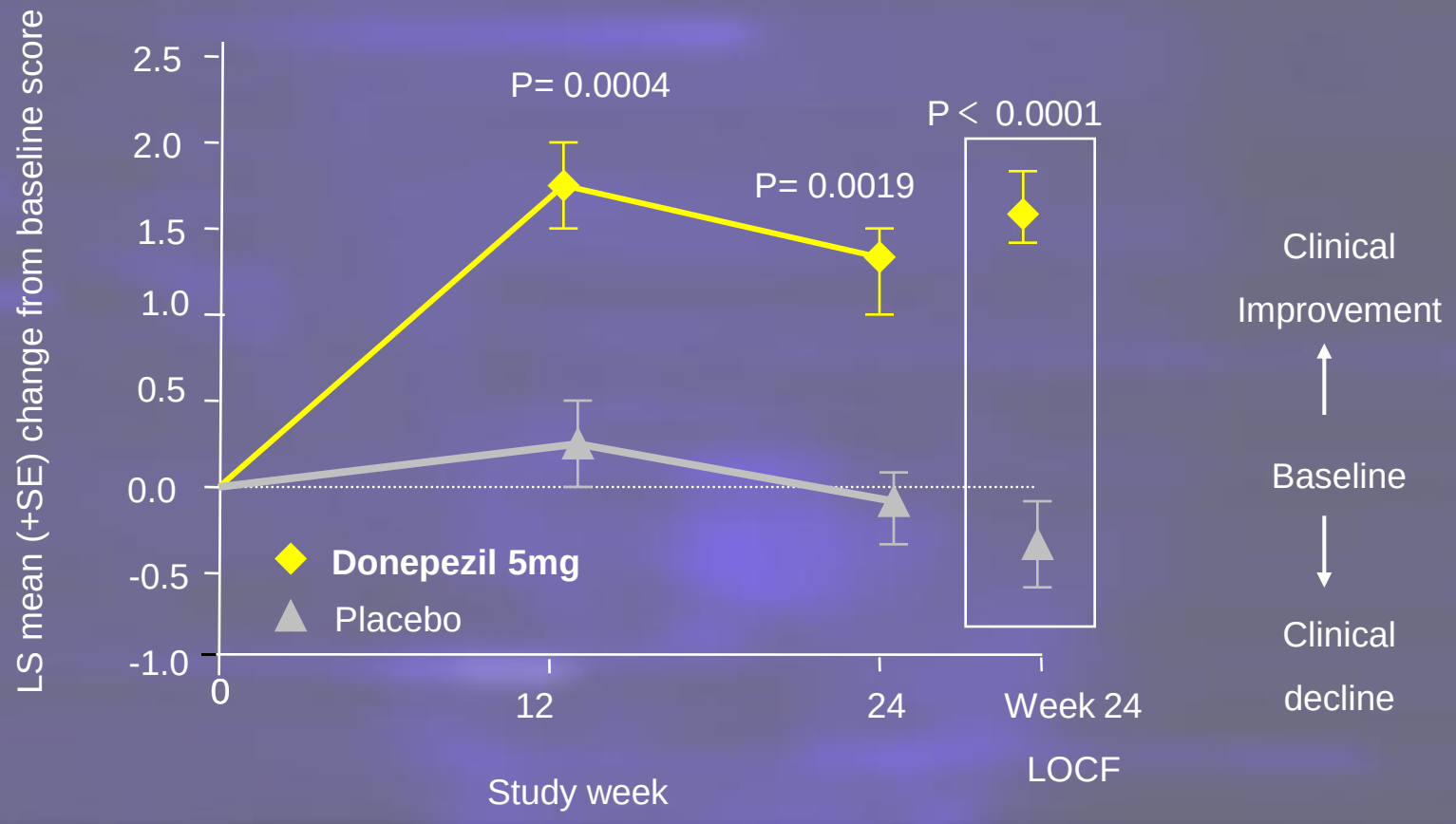
H. Feldman, MD; S. Gauthier, MD; J. Hecker, MD, B. Vellas, MD, PhD; P. Subbiah, MD; E. Whalen, PhD, and the Donepezil MSAD Study Investigators Group*

NEUROLOGY 2001;57:613–620

- *Design*: 24-week, multicenter, randomized, double-blind, placebo-controlled, parallel-group study
- *Patients*: 290 patients (sMMSE 5 to 17) were randomized to receive either donepezil or placebo

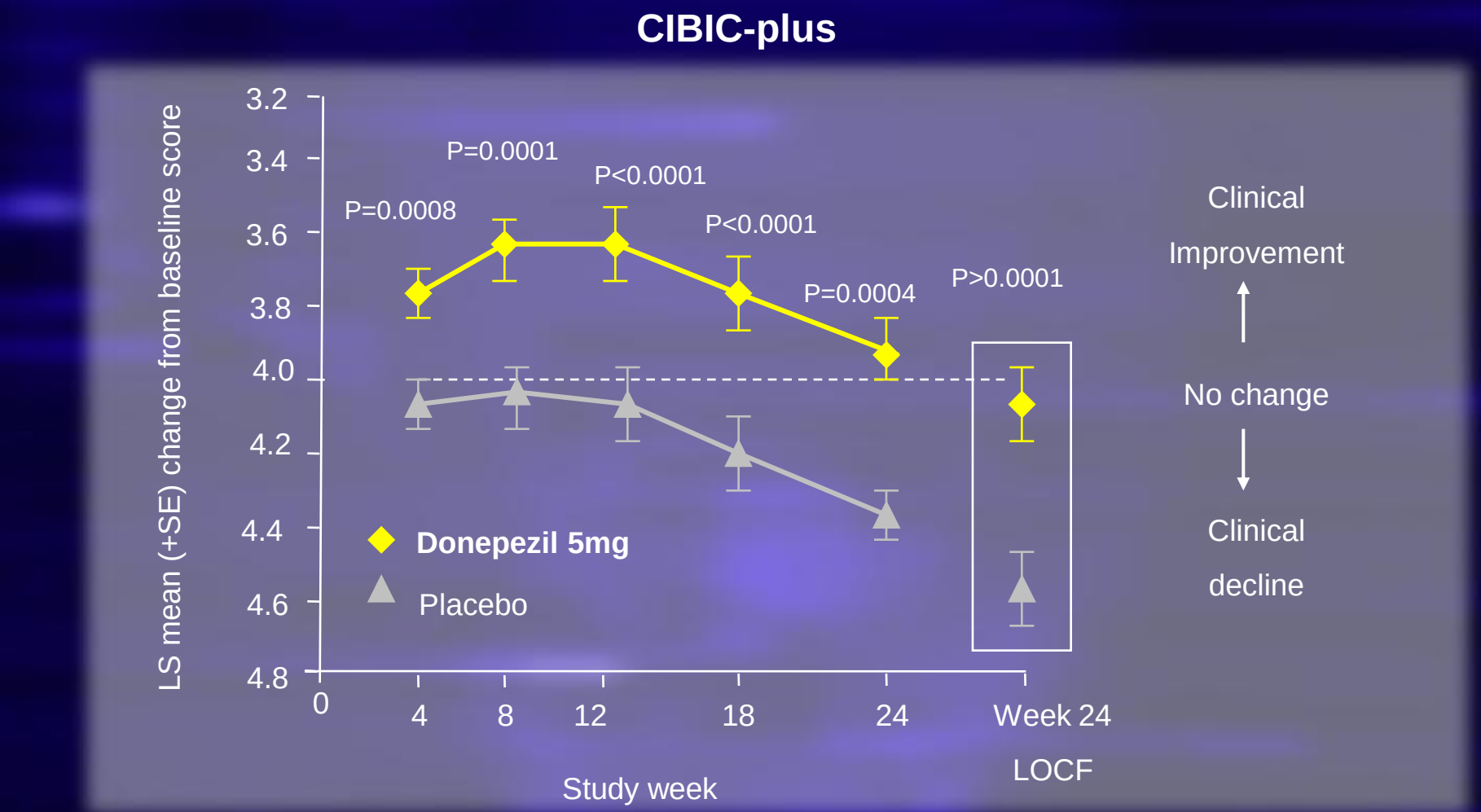
Result of Moderate to Severe AD (1)

sMMSE



Neurology 2001;57;613-620

Result of Moderate to Severe AD (2)



Neurology 2001;57;613-620

Efficacy of ARICEPT for Severe AD

Efficacy and safety of donepezil in patients with more severe Alzheimer's disease: a subgroup analysis from a randomized, placebo-controlled trial

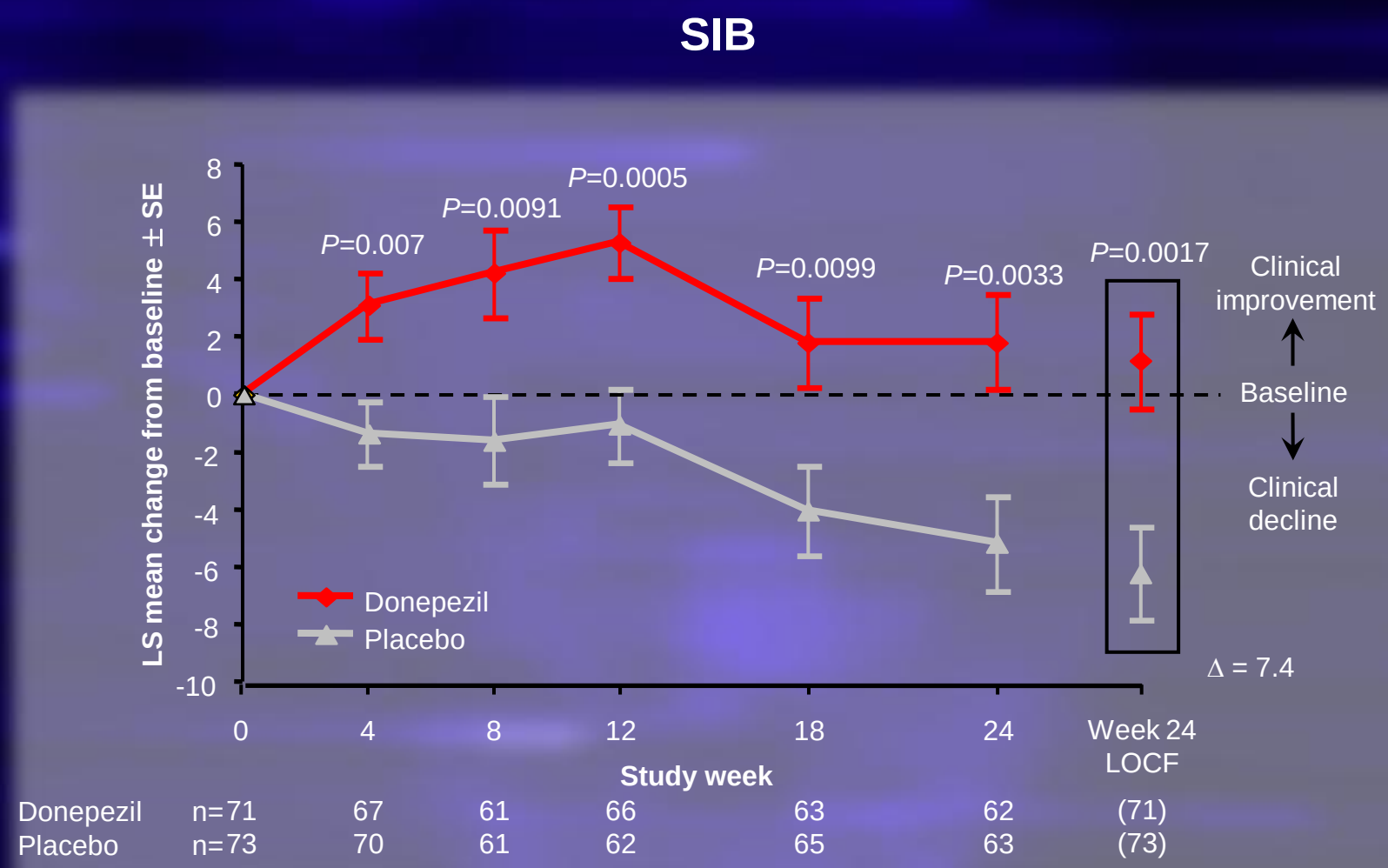
Howard Feldman[1]*, Serge Gauthier[2], Jane Hecker[3], Bruno Vellas[4], Yikang Xu[5], John R. Ieni[6], Elias M. Schwam[7] and the Donepezil MSAD Study Investigators Group

Int J Geriatr Psychiatry 2005; 20: 559-569

- ***Design***: 24-week, multicenter, randomized, double-blind, placebo-controlled study

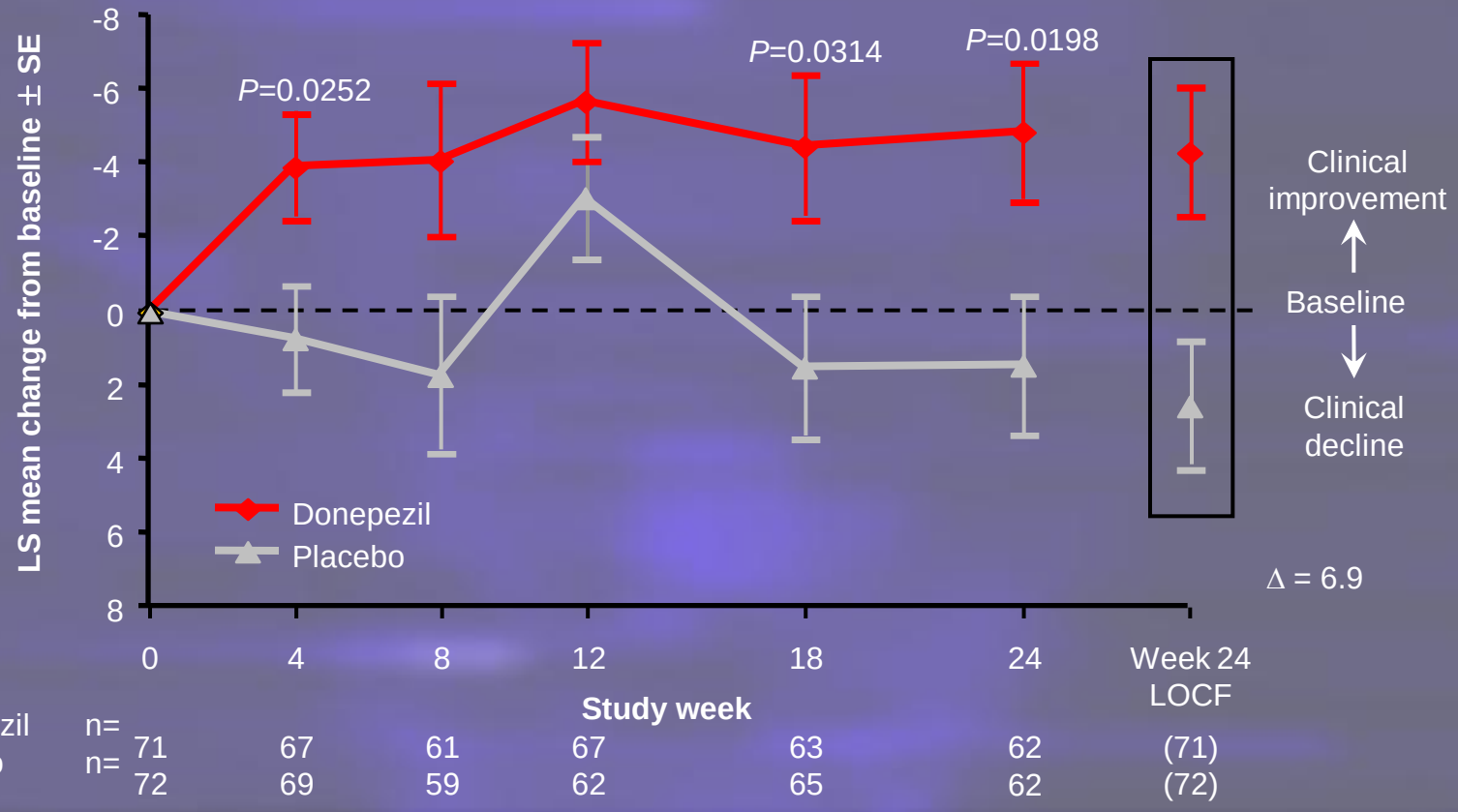
- ***Patients***: A total of 145 patients with more severe AD (sMMSE 5 to 12) were enrolled and randomized to receive either donepezil or placebo

Result: SIB


SIB
LS mean change from baseline ± SE
8
6
4
2
0
-2
-4
-6
-8
-10
P=0.007
P=0.0091
P=0.0005
P=0.0099
P=0.0033
P=0.0017
Clinical improvement
Baseline
Clinical decline
Donepezil
Placebo
Δ = 7.4
0
4
8
12
18
24
Week 24 LOCF
Study week
Donepezil n=71 67 61 66 63 62 (71)
Placebo n=73 70 61 62 65 63 (73)

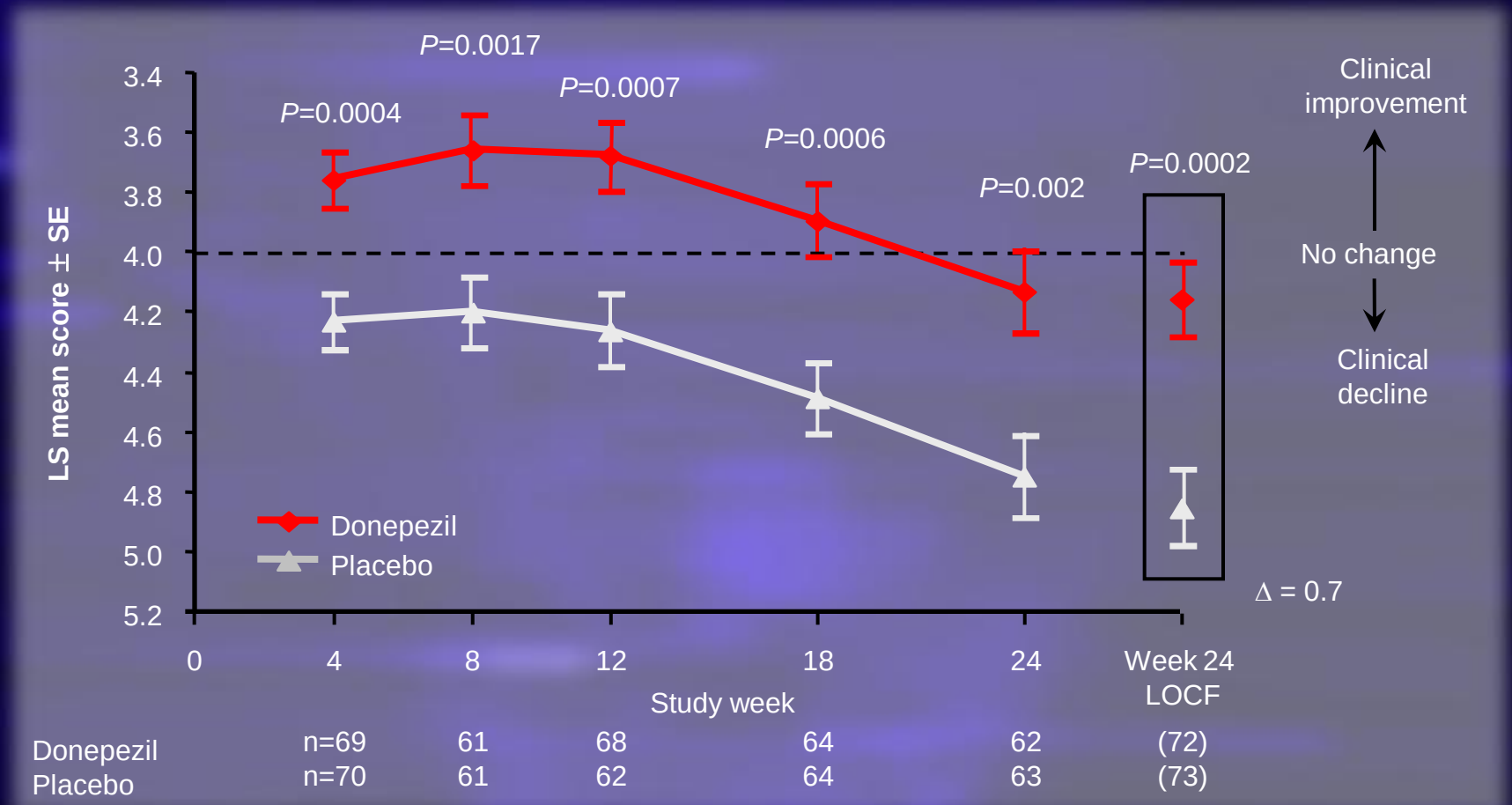
Result: NPI

12-Item NPI Total



Donepezil	n=	71	67	61	67	63	62	(71)
Placebo	n=	72	69	59	62	65	62	(72)

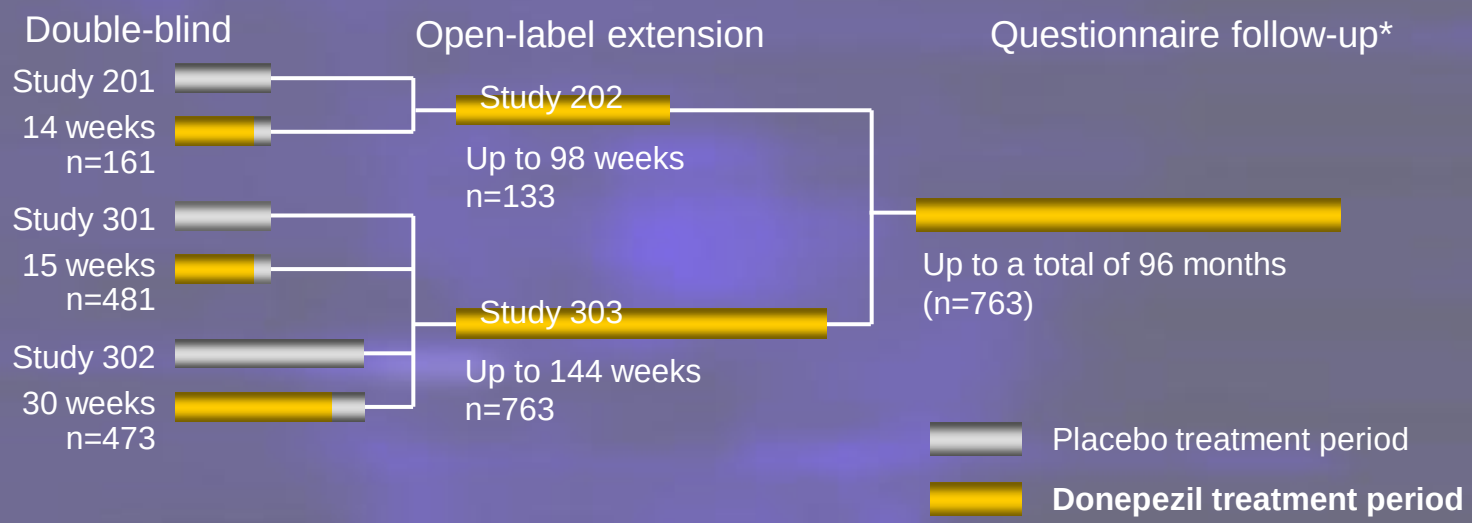
Result: CIBIC-plus



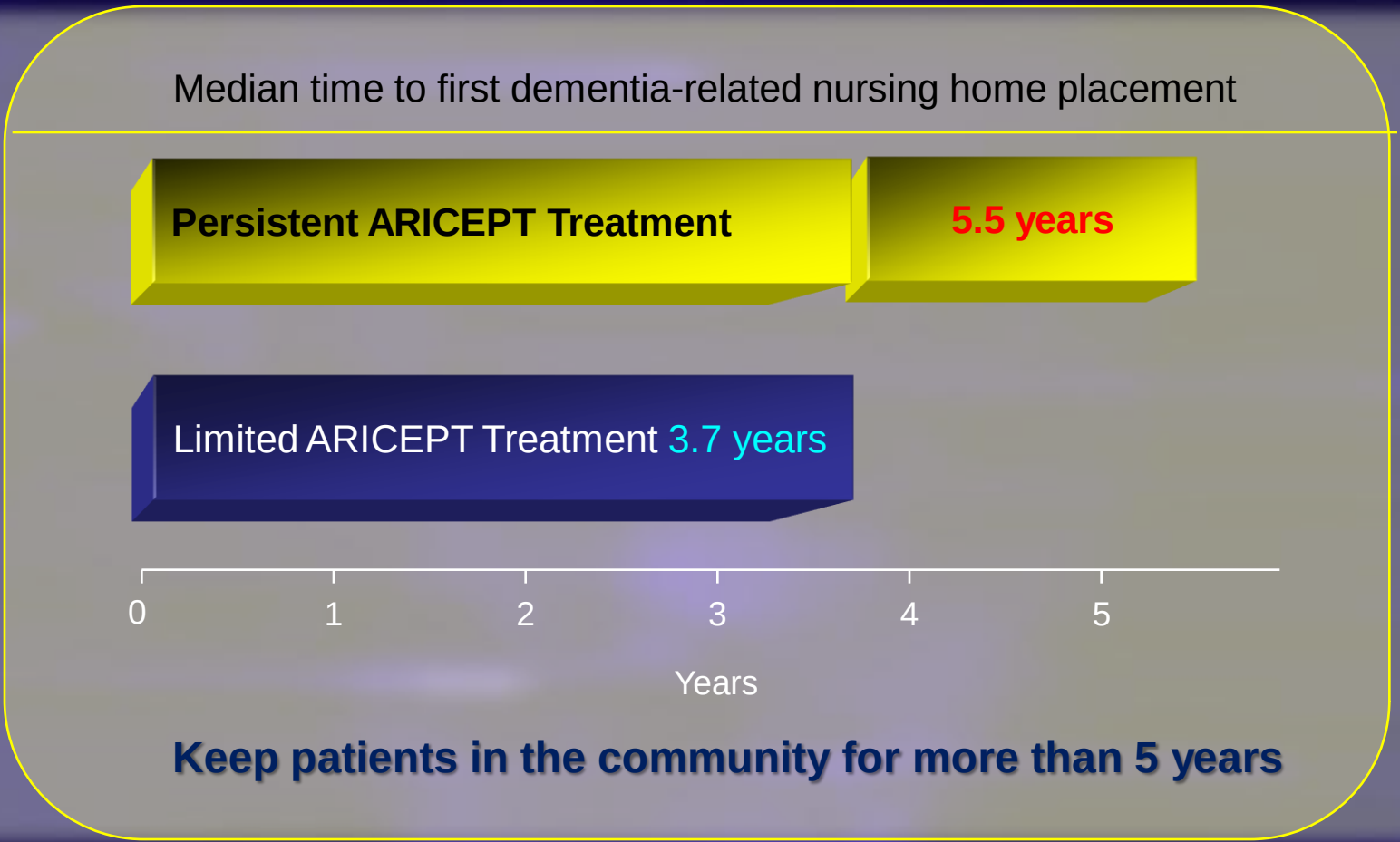
Efficacy of ARICEPT for DNHP

Donepezil Is Associated with Delayed Nursing Home Placement in Patients with Alzheimer's Disease

David S. Geldmacher, MD,[*†] *George Provenzano, PhD,*[‡] *Thomas McRae, MD,*[§] *Vera Mastey, MS,*[‖] *and John R. Ieni, PhD*[¶]



2 year delay to NHP



Keep patients in the community for more than 5 years

Geldmacher DS et al. J Am Geriatr Soc. 2003;51:937-944

Long-term efficacy of ARICEPT

ELSEVIER

European Neuropsychopharmacology 10 (2000) 195–203

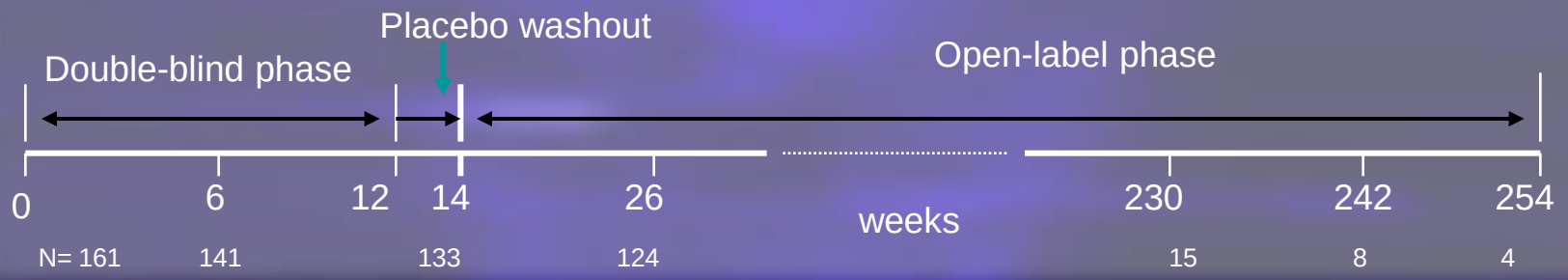
EUROPEAN NEURO-PSYCHOPHARMACOLOGY

www.elsevier.com/locate/euroneuro

Long-term efficacy and safety of donepezil in the treatment of Alzheimer's disease: final analysis of a US multicentre open-label study

S.L. Rogers[a,*], R.S. Doody[b], R.D. Pratt[c], J.R. Ieni[c]

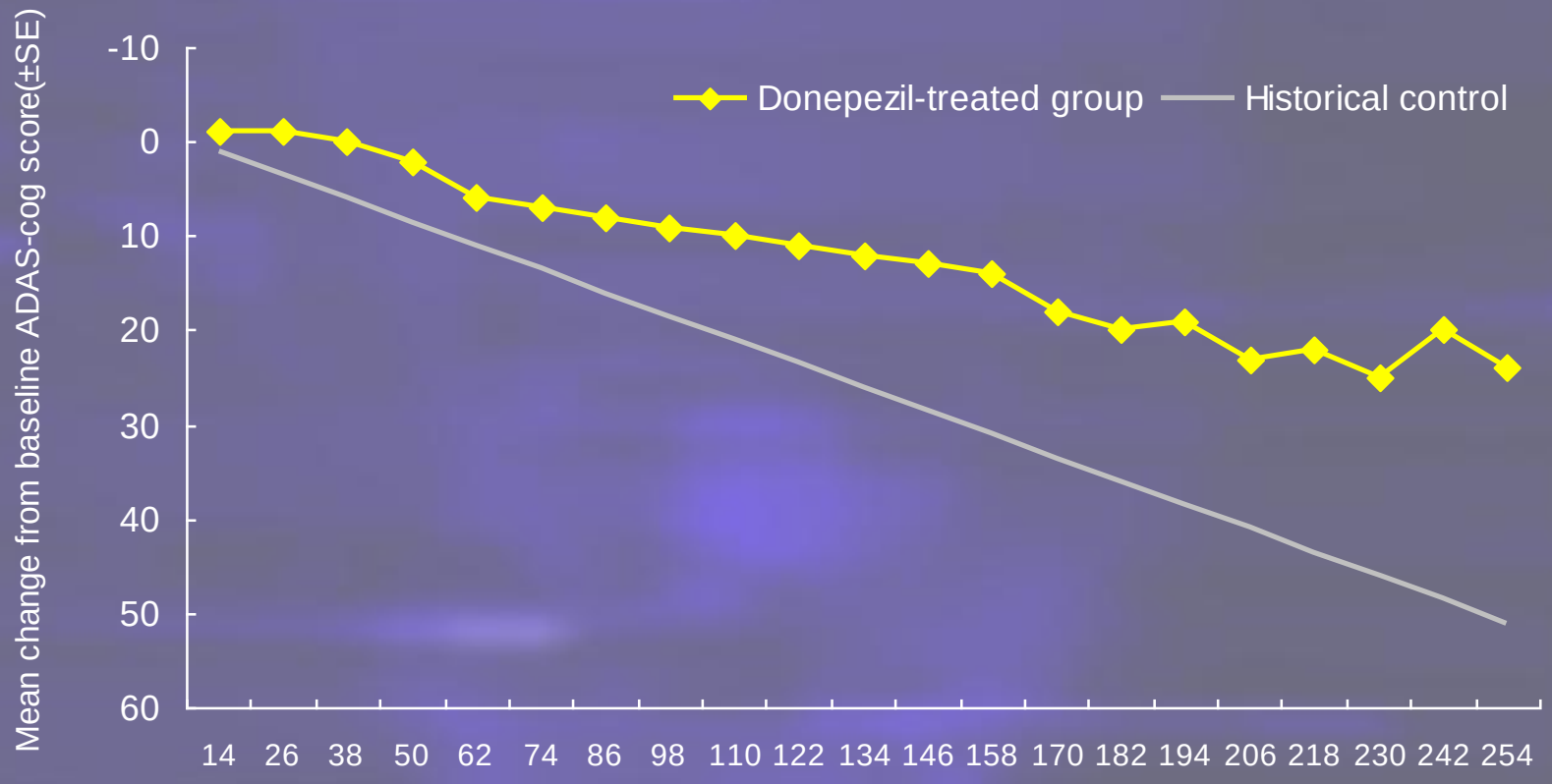
- *Design*: for up to cumulative 254 weeks *(4.9 years)*



Result of long-term efficacy of ARICEPT

ADAS-cog

→ *over 254 cumulative weeks*



ARICEPT for severe BPSD

Effects of Donepezil on Neuropsychiatric Symptoms in Patients With Dementia and Severe Behavioral Disorders

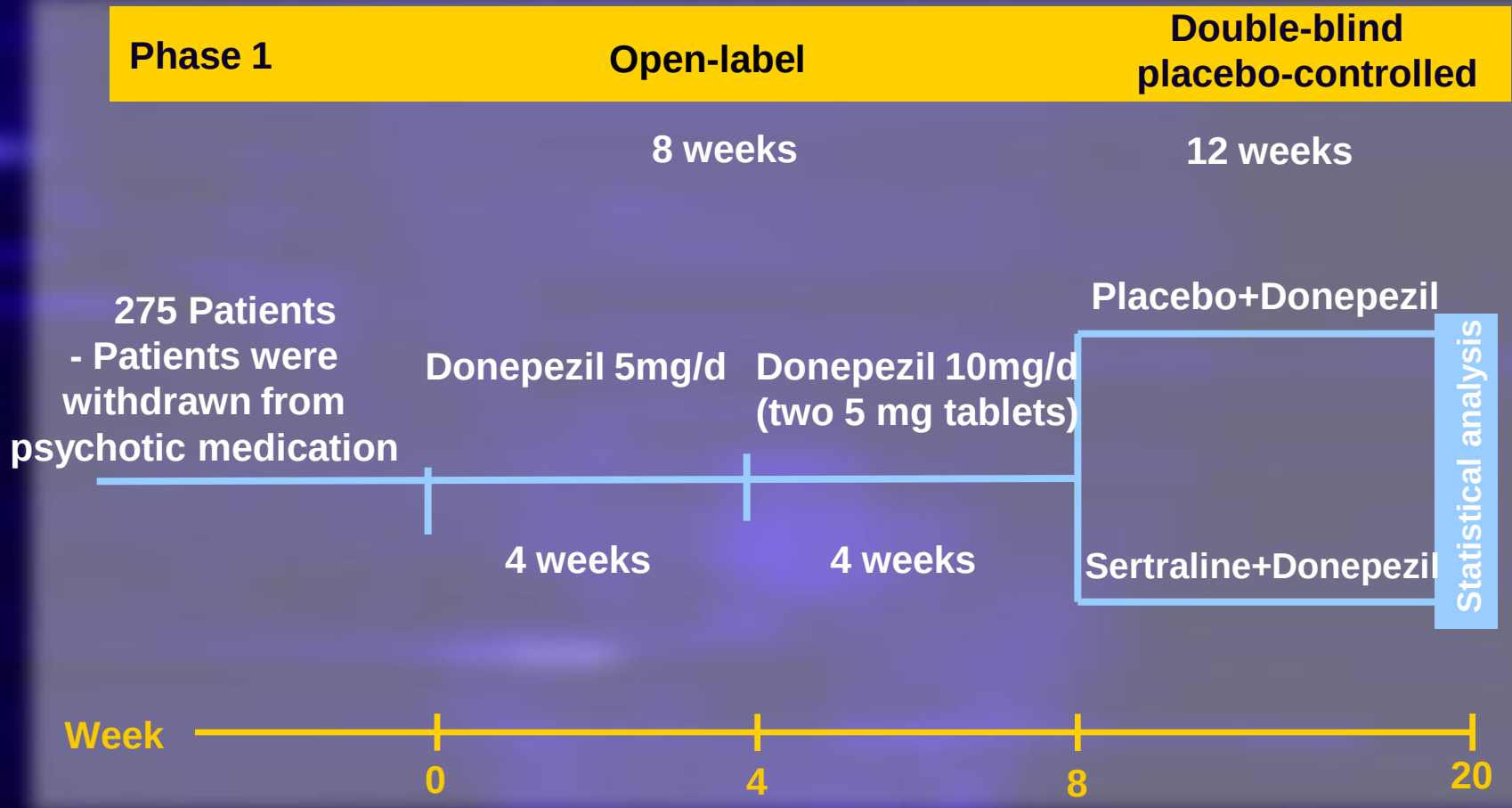
Jeffrey L. Cummings, M.D., Thomas McRae, M.D., Richard Zhang, Ph.D., The Donepezil–Sertraline Study Group

Am J Geriatr Psychiatry 2006; 14: 605

Design **:** 8-week open-label,
12-week double-blind, placebo-controlled study

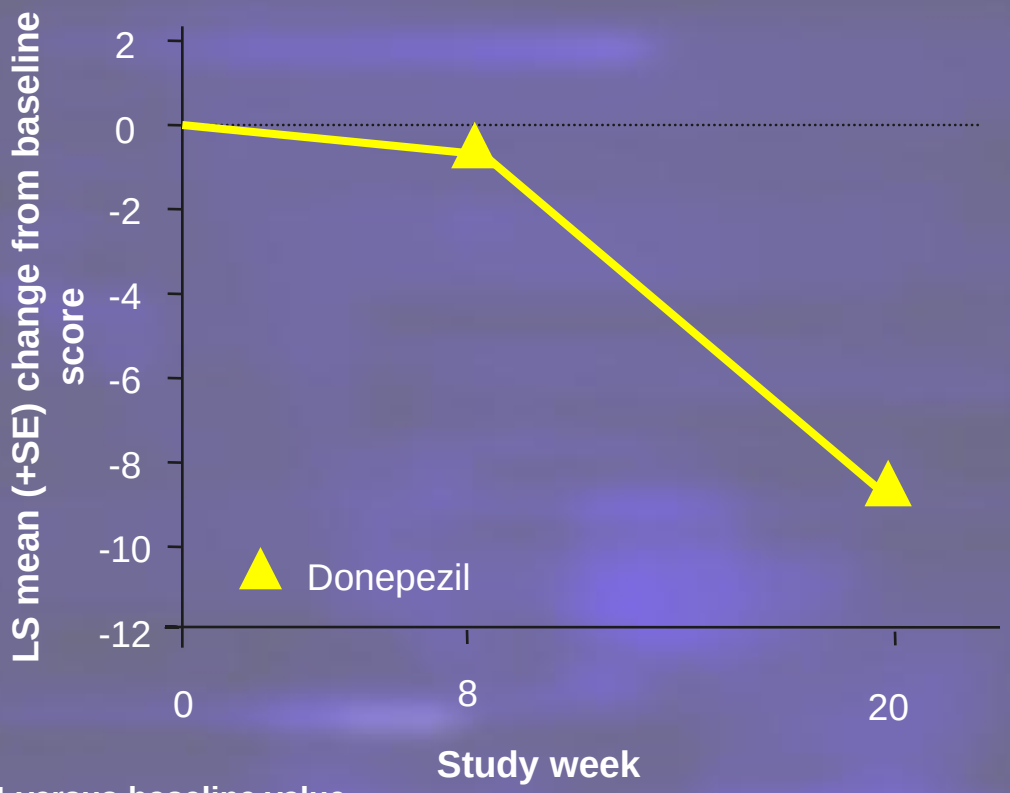
Patients **:** Probable or possible AD, according to NINCDS-ADRDA criteria, NPI ≥5
Open-label (n=275; mean age, 76.3 years)
Double-blind (n=120; mean age, 76.9years)

Study Design



Result: NPI

NPI-12



Clinical decline

Baseline

Clinical improvement

[a]p 0.001 versus baseline value.

[b]p 0.05 versus baseline value.

ARICEPT for Safety and Tolerability

Adverse Event	Placebo (n=392)	Aricept® (n=501)
% of patients with any AEs	73	81
Diarrhea	**4**	**10**
Nausea	**2**	**6**
Vomiting	4	8
Anorexia	4	8
Headache	3	4
Dizziness	1	2
Insomnia	4	5

* AEs reported in controlled Clinical Trials in ar Least 2% of patients receiving Aricept® and at higher frequency than placebo.

From data on Aricept product information

Summary

- ARICEPT® significantly improved cognition, global function and behavioral symptoms in patients with mild to severe AD.
- ARICEPT® shows the benefit in all course of AD patients
- ARICEPT® is safe and well tolerate in severe AD patients
- ARICEPT® is a only approved AChE-Inhibitors in severe AD and VaD

Aricept is the first choice of dementia treatment