Sperimentazione sponsorizzata in ambiente accademico

IRCCS San Raffaele
Pisana

Finanziamenti dell'industria e risultati delle ricerche

- Nel 2006 sul *Journal of the American Medical Association (JAMA)*, **una ricerca di Ridker e Torres** ha voluto verificare se questa situazione fosse cambiata negli anni 2000, in particolare negli studi inerenti l'ambito cardiovascolare.

- Dopo avere fatto una revisione di 303 trial di superiorità, pubblicati tra il 2000 e il 2005 su *JAMA, NEJM* e *Lancet* e per i quali era indicata la fonte di finanziamento, gli autori trovarono che su 137 trial finanziati dall'industria 92 (**67%**) ebbero un risultato favorevole al nuovo trattamento ($P<.001$), mentre ciò accadde solo in 51 (**49%**) dei 104 trial finanziati da organismi non profit ($P=.80$).

Author's Conclusion

- **What is already known on this topic**
  - When a pharmaceutical company funds research into drugs, studies are likely to produce results favourable to the sponsoring company's product
- **What this study adds**
  - Research funded by drug companies was more likely to have outcomes that favour the sponsor's product than research funded by other sources
  - This cannot be explained by the reported quality of the methods in research sponsored by industry
  - The result may be due to inappropriate comparators or to publication bias

BMJ (326; may 2003)

Initiating Levodopa/Carbidopa Therapy With and Without Entacapone in Early Parkinson Disease

The STRIDE-PD Study

Fabrizio Stocchi, MD,[1] Olivier Rascol, MD,[2,3,4] Karl Kieburtz, MD,[5]
Werner Poewe, MD,[6] Joseph Jankovic, MD,[7] Eduardo Tolosa, MD,[8]
Paulo Barone, MD,[9] Anthony E. Lang, MD,[10] and C. Warren Olanow, MD[1,11]

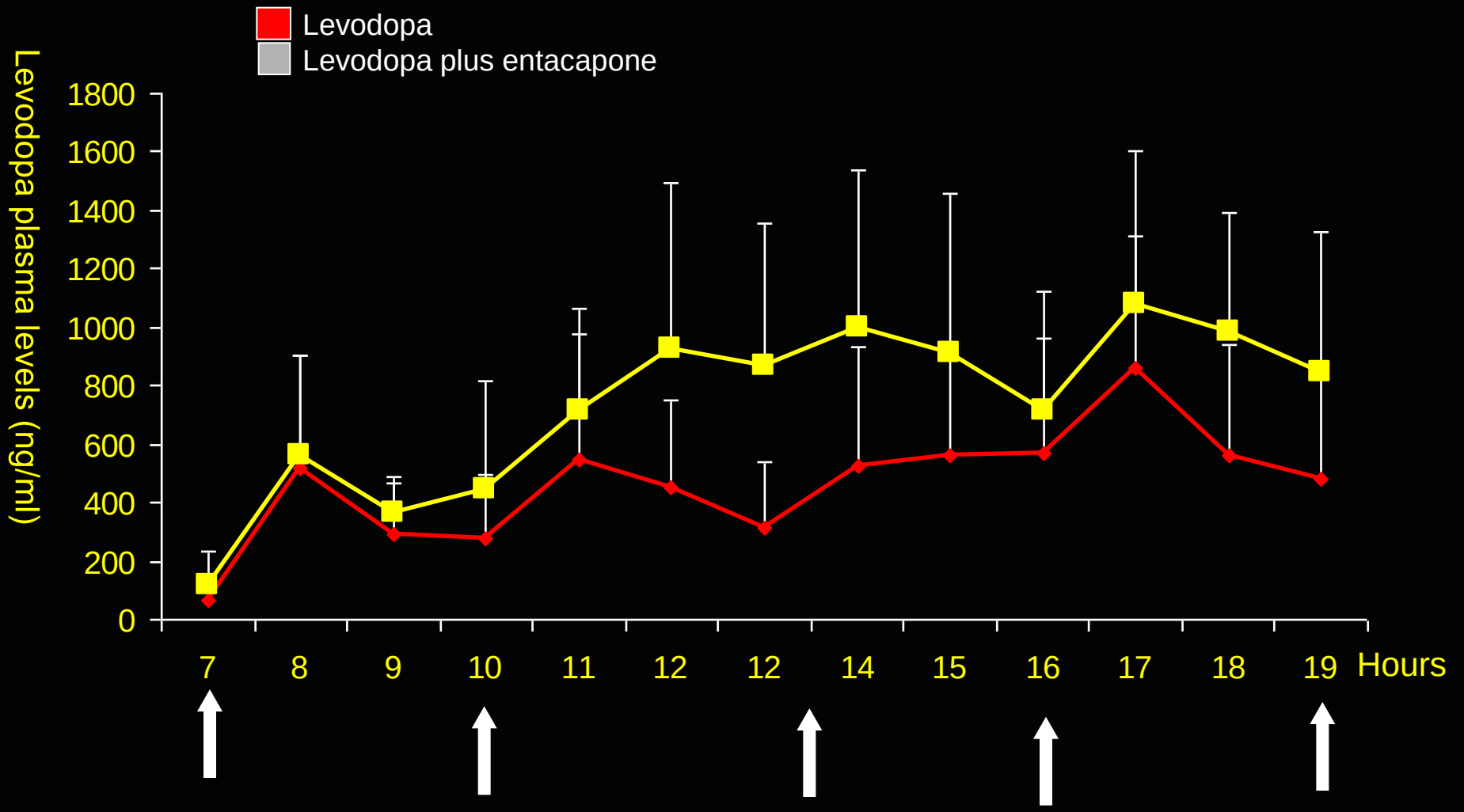
STRIDE PD – Hypothesis

- SNc neurons fire continuously, striatal dopamine is relatively continuous, and striatal dopamine receptors are continuously activated
- Motor complications are associated with intermittent delivery of a short-acting dopaminergic agent
- The concept of CDS proposes that continuous delivery of a dopaminergic drug will prevent or reverse motor complications
- In all studies perfomred in MPTP monkeys or PD patients, continuous administration of a dopaminergic agent is associated with a reduction in motor complications in comparison to continuous delivery of the same agent

STRIDE PD – Hypothesis

- Administration of levodopa in combination with a COMT inhibitor would achieve CDS and therefore delay the time to dyskinesia

100mg Levodopa @ 3 Hourly Group Mean (n=7)

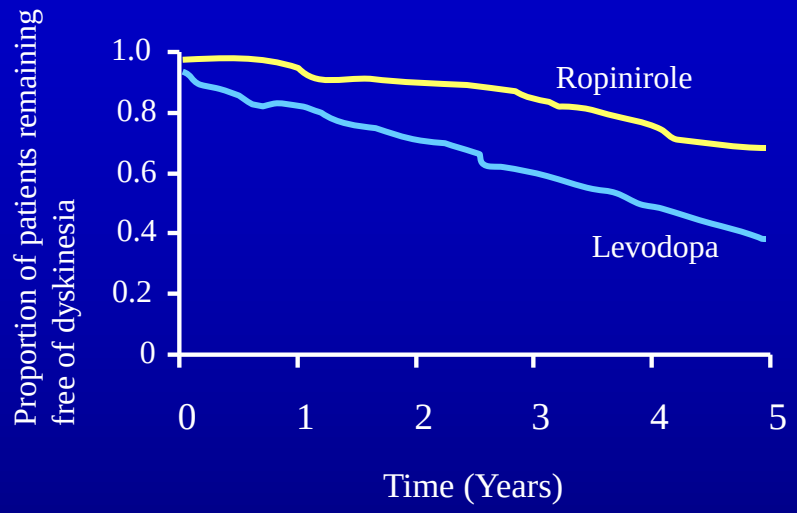


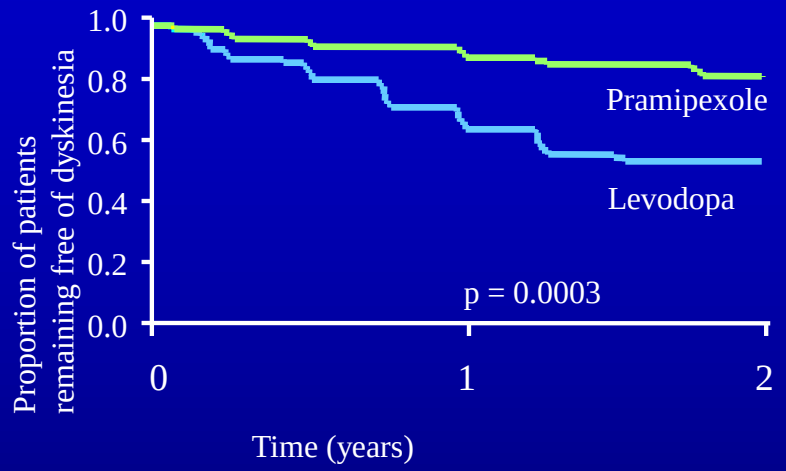
STRIDE PD – Study design

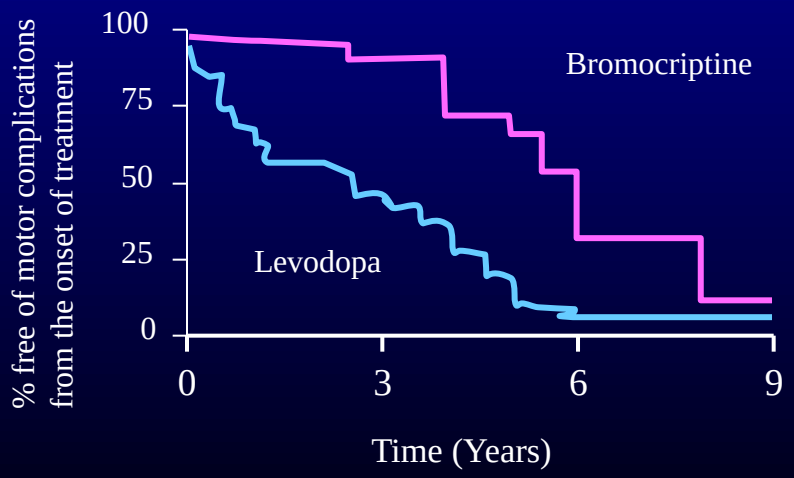
- **Objective:** Stalevo delays the onset of dyskinesia compared to standard formulation carbidopa/levodopa in PD patients requiring initiation of L-dopa

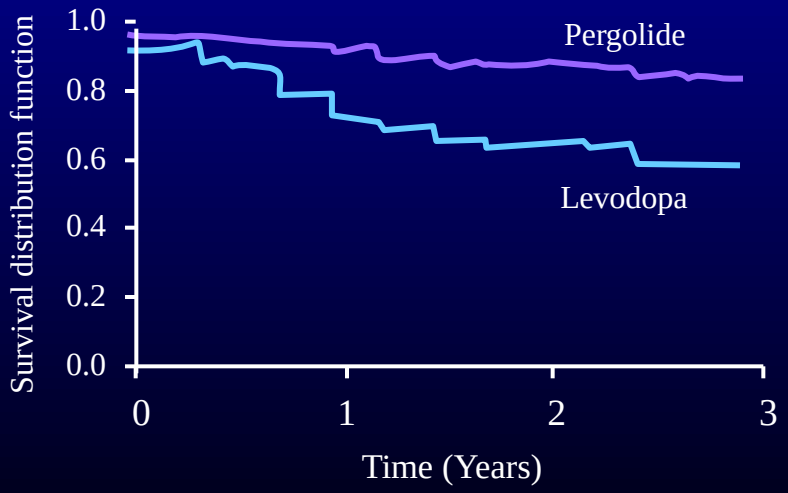
- **Study Design**
  - Multicenter, double-blind, randomized, parallel-group, active-controlled,
  - Stalevo vs. standard formulation carbidopa/levodopa
    - L-dopa dose range 200-1000 mg/day (target 400 mg/day)
    - Administered in 4 equal doses at 3.5 hour intervals
  - Treatment duration ~2.7 years to ~4 years
  - n=747 patients randomized
- **Clinical endpoints**
  - Primary: time to onset of dyskinesia
  - Secondary: UPDRS (non-inferiority, superiority), incidence and time to wearing-off, incidence of dyskinesia, QoL, safety/tolerability, PG

Dopamine agonists vs levodopa
Effect on dyskinesia









Stocchi F – personal correspondence

RQM/BRD/08/36248/1

Study design

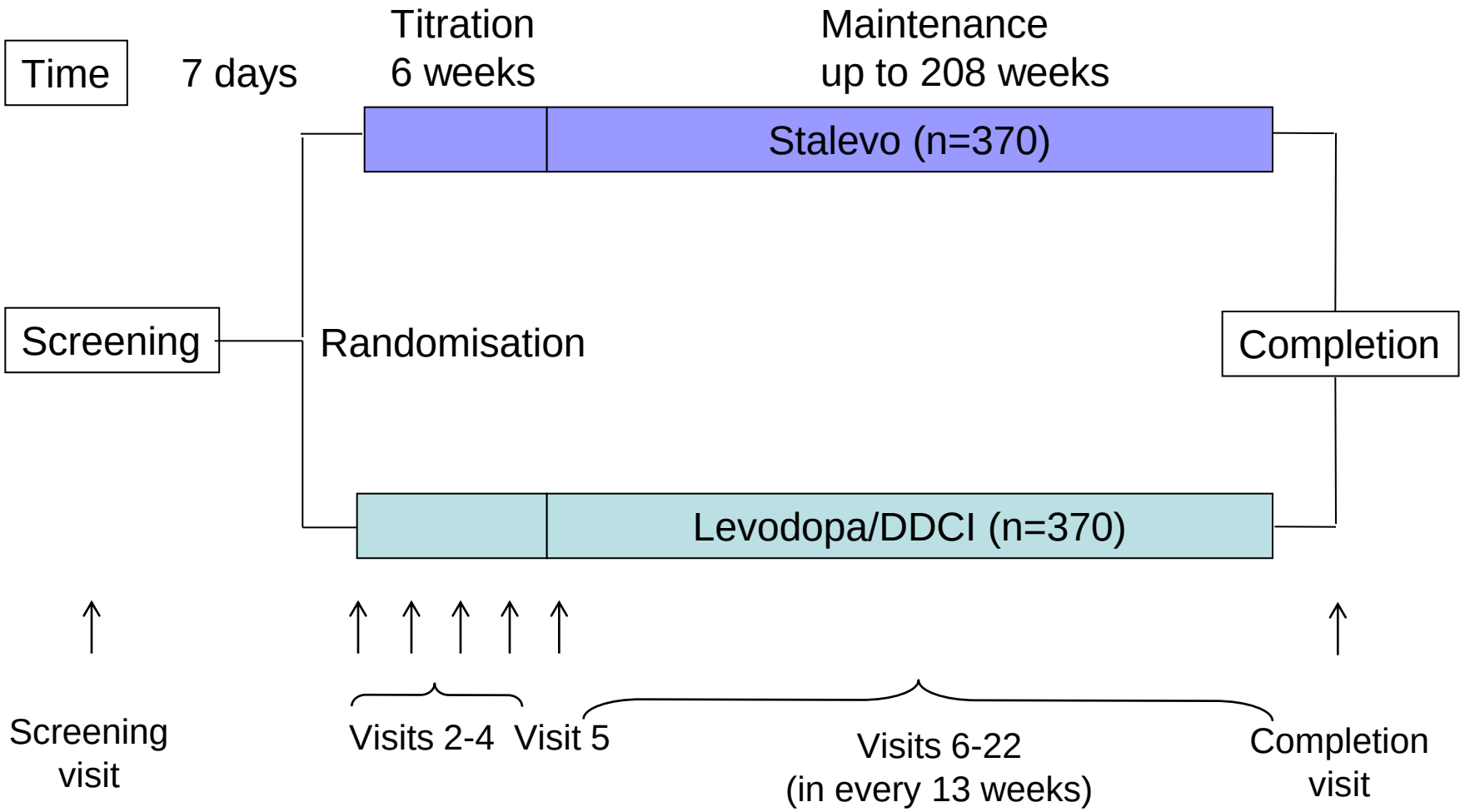


TABLE 2: Baseline Demographics by Treatment (Intention to Treat Population)

Variable	LCE, n = 373	LC, n = 372	Total, N = 745
Age, mean yr	60.6 ± 8.7	59.8 ± 8.2	60.2 ± 8.4
Men, No. (%)	245 (65.7%)	222 (59.7%)	467 (62.7%)
Caucasian	352 (94.4%)	357 (96.0%)	709 (95.2%)
Weight, kg	79.7 ± 15.8	79.1 ± 16.9	79.4 ± 16.4
Mean duration of PD, yr	2.0 ± 1.6	2.0 ± 1.7	2.0 ± 1.7
UPDRS total (II + III)	32.7 ± 12.6	31.5 ± 11.9	32.1 ± 12.3
UPDRS, Part II (ADL)	9.6 ± 4.3	9.1 ± 4.2	9.4 ± 4.2
UPDRS, Part III (motor)	23.1 ± 9.5	22.4 ± 9.0	22.8 ± 9.3
Hoehn & Yahr stage	1.9 ± 0.5	1.9 ± 0.5	1.9 ± 0.5
Schwab & England score	86.4 ± 7.3	86.3 ± 8.6	86.4 ± 7.9
PDQ-39	25.2 ± 15.0	22.9 ± 13.7	24.1 ± 14.4
Previous antiparkinson medication, No. (%)	263 (70.5%)	266 (71.5%)	529 (71.0%)
Dopamine agonist use, No. (%)	217 (58.2%)	217 (58.3%)	434 (58.3%)

LCE = L-dopa/carbidopa/entacapone; LC = L-dopa/carbidopa; PD = Parkinson disease; UPDRS = Unified Parkinson Disease Rating Scale; ADL = activities of daily living; PDQ-39 = Parkinson Disease Questionnaire.

TABLE 3: Baseline Demographics by Treatment and Dopamine Agonist Exposure (Intention to Treat Population)

Variable	DA Exposure at Baseline		No DA Exposure at Baseline	
	LCE, n = 217	LC, n = 217	LCE, n = 156	LC, n = 155
Age, mean yr	59.1	58.4	62.6	61.9
Men, No. (%)	151 (69.6)	132 (60.8)	94 (60.3)	90 (58.1)
Weight, mean kg	79.9	81.0	79.3	76.5
Duration of PD, mean yr	2.4	2.6	1.4	1.2
Hoehn & Yahr stage, mean	1.9	1.9	1.9	1.9
UPDRS Parts II + III, mean	33.0	31.1	32.2	32.2
UPDRS Part II, mean	9.7	9.2	9.4	9.0
UPDRS Part III, mean	23.3	21.9	22.8	23.2

DA = dopamine; LCE = L-dopa/carbidopa/entacapone; LC = L-dopa/carbidopa; PD = Parkinson disease; UPDRS = Unified Parkinson Disease Rating Scale.

Results

- Efficacy
  - Time to dyskinesia
  - Graph of time to dyskinesia
  - Occurrence of dyskinesia

Time to occurrence of dyskinesia (ITT population)

	Stalevo N=373 n %	C/L N=372 n %
Patients with dyskinesia	144 (38.6)	123 (33.1)
Survival time (weeks) –raw*		
Mean (SD)	74.2 (47.9)	79.1 (51.5)
Median	73.6	78.3
Survival time (weeks) –estimates**		
Q1 (95% CI)	90.7 (65.3, 104.0)	117.1 (92.1, 132.6)
P-value***	0.038	
Hazard ratio (95% CI)	1.29 (1.0, 1.65)	

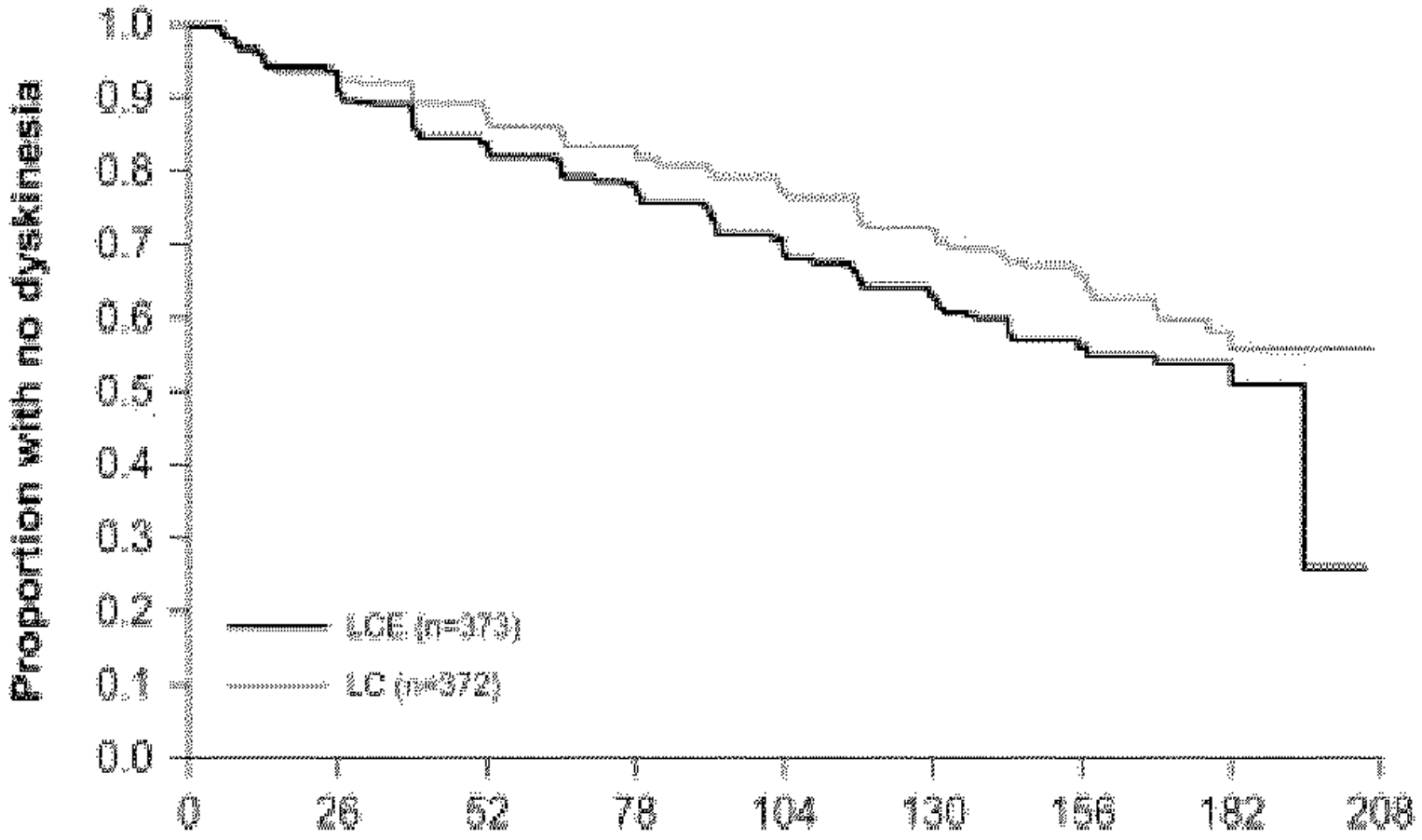
*Calculated only using subjects who had at least one occurrence of dyskinesia

**Taken from Kaplan-Meier analysis including all subjects and censoring those without dyskinesia

*** Taken from the log-rang test

Table 14.2-1.1.3

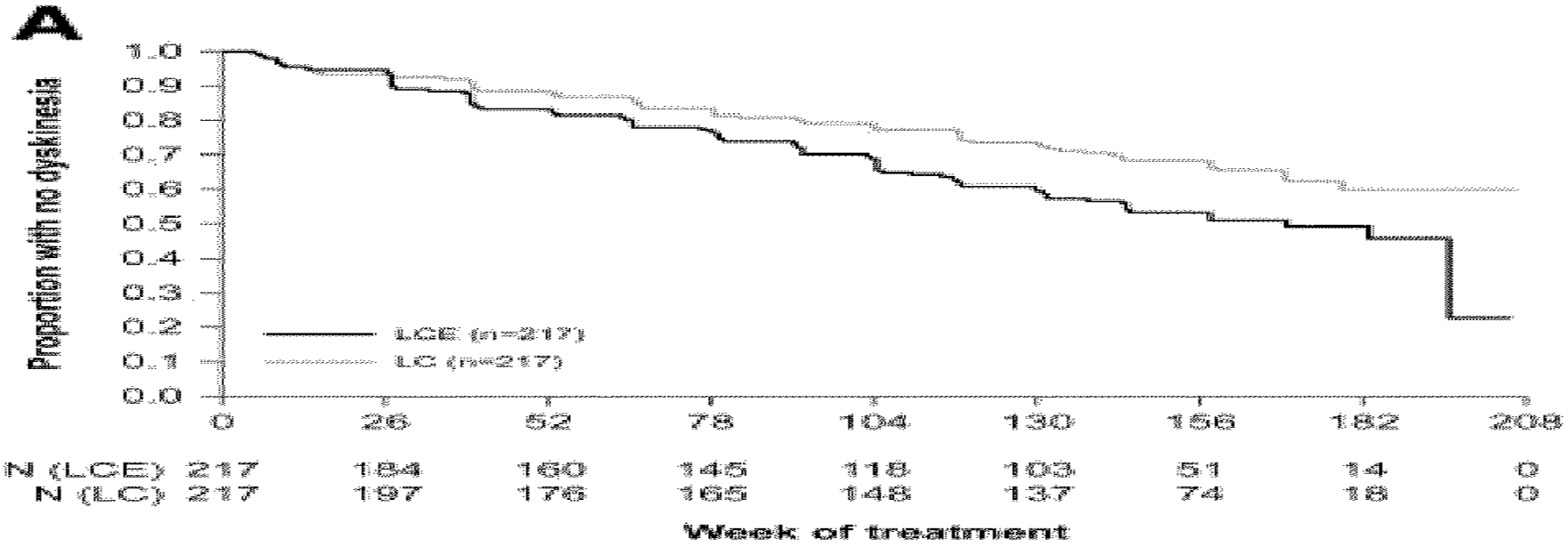
Stocchi et al: L-dopa/Carbidopa in PD

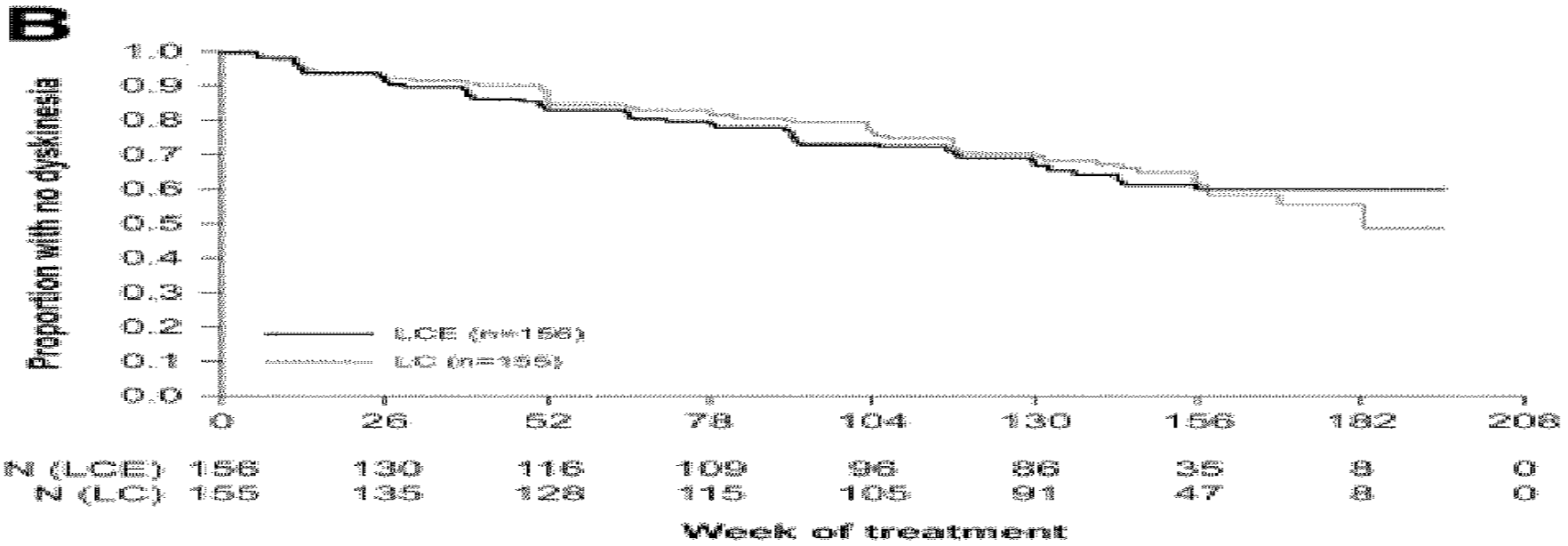


Time to first occurrence of dyskinesia by Dopamine Agonists exposure at baseline

	DA exposure		No DA exposure	
	Stalevo N=217	C/L N=217	Stalevo N=156	C/L N=155
Patients with dyskinesia n (%)	91(41.9)	68 (31.3)	53 (34.0)	55 (35.5)
Time to dyskinesia - raw				
Mean (weeks)	76.5	76.6	70.3	82.2
Median (weeks)	78.1	72.4	65.1	82.1
Survival time- estimates				
Q1	78.9	117.4	92.1	105.1
P-value	0.006		0.957	
Hazard ratio (95% CI)	1.55 (1.13, 2.13)		0.99 (0.68, 1.45)	

Table 14.2-1.4.3


A
Proportion with no dyskinesia
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
LCE (n=217)
LC (n=217)
0
26
52
78
104
130
156
182
208
N (LCE) 217 184 160 145 118 103 51 14 0
N (LC) 217 197 176 165 148 137 74 18 0
Week of treatment


B
Proportion with no dyskinesia
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
LCE (n=156)
LC (n=155)
0
26
52
78
104
130
156
182
208
N (LCE) 156 130 116 109 96 86 35 8 0
N (LC) 155 135 128 115 105 91 47 8 0
Week of treatment

Side Effects

	LCE	LC	TOTAL
Myocardial infarction	7 (1.9)	0 (0.0)	7 (0.9)
Prostate cancer	9 (2.4)	2 (0.5)	11 (1.5)
Skin cancer	7 (1.9)	12 (3.2)	19 (2.6)
Basal cell carcinoma	6 (1.6)	5 (1.3)	11 (1.5)
Squamous cell carcinoma	0	4 (1.1)	4 (0.5)
Melanoma	0	1 (0.3)	1 (0.1)

Cardiovascular and Mortality Risks in Parkinson's Disease Patients Treated With Entacapone

David J. Graham, MD, MPH,[1] James R. Williams, PhD,[1‡] Ya-Hui Hsueh, PhD,[2] Katlyn Calia, BA, BS,[3] Mark Levenson, PhD,[2] Simone P. Pinheiro, ScD, MSc,[1] Thomas E. MaCurdy, PhD,[3,4] David Shih, MD, MS,[1] Chris Worrall, BS,[5] and Jeffrey A. Kelman, MD, MMSc[5]

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Movement Disorders, Vol. 00, No. 00, 2013

Cardiovascular and Mortality Risks in Parkinson's Disease Patients Treated With Entacapone

- This study was restricted to the approximately 21 million elderly beneficiaries enrolled in fee for-service Medicare Part A (hospitalization), Part B (outpatient medical care), and Part D (prescription drugs), because claims from these sources were necessary for research purposes.
- Among patients with PD who were treated with L-dopa, a new user, inception cohort design was employed to compare the effect of the initiation of entacapone (either as a single agent or in fixed combination with L-dopa/carbidopa) versus either dopamine agonist (DA) or a selective monoamine oxidase type-B inhibitor (MAOBI) on the occurrence of AMI, stroke, or death

Cardiovascular and Mortality Risks in Parkinson's Disease Patients Treated With Entacapone

- Cohort follow-up began on the date of the first qualifying study drug prescription and continued until the occurrence of a study end point.
- In total, 8776 entacapone-treated patients and 23,408 DA-MAOBI-treated patients met study eligibility criteria.
- Within the DA-MAOBI cohort, 73% of patients received a DA (primarily pramipexole or ropinirole), and 27% eceived a MAOBI,(primarily rasagiline).
- About 45% of patients in both cohorts stopped their study drug after the first month; and, during follow-up, 99% of entacapone patients and 92% of DA-MAOBI patients also took L-dopa.

Cardiovascular and Mortality Risks in Parkinson's Disease Patients Treated With Entacapone

During follow-up, there were 106 AMIs, 89 strokes, and 201 deaths among cohort members.

TABLE 4. Event counts, incidence rates, and adjusted hazard ratios with 95% confidence intervals for acute myocardial infarction, stroke, and death in elderly medicare beneficiaries with Parkinson's disease treated with entacapone compared with dopamine agonists or monoamine oxidase type-b inhibitors

	Event Counts		Rate per 100 Person-Years		
Event	Entacapone	DA/MAOBI	Entacapone	DA/MAOBI	Adjusted HR (95% CI)
Acute myocardial infarction	31	75	1.21	1.39	0.86 (0.57–1.30)
Stroke	26	63	1.01	1.17	0.85 (0.54–1.35)
Death	55	146	2.14	2.71	0.79 (0.58–1.07)

DA, dopamine agonist; MAOBI, monoamine oxidase type-B inhibitor; HR, hazard ratio; CI, confidence interval.

Cardiovascular and Mortality Risks in Parkinson's Disease Patients Treated With Entacapone

- With advanced age and the associated comorbidity burden that accompanies it, patients in our study were at substantially *higher baseline risk* of experiencing a cardiovascular event than the patients enrolled in STRIDE-PD.

- In conclusion, in a population of more than 26,000 elderly patients with PD who were treated with either entacapone or a DA-MAOBI, entacapone was not associated with increased risk of AMI, stroke, or death.

STRIDE-PD SECONDARY ANALYSIS

W.OLANOW F. STOCCHI

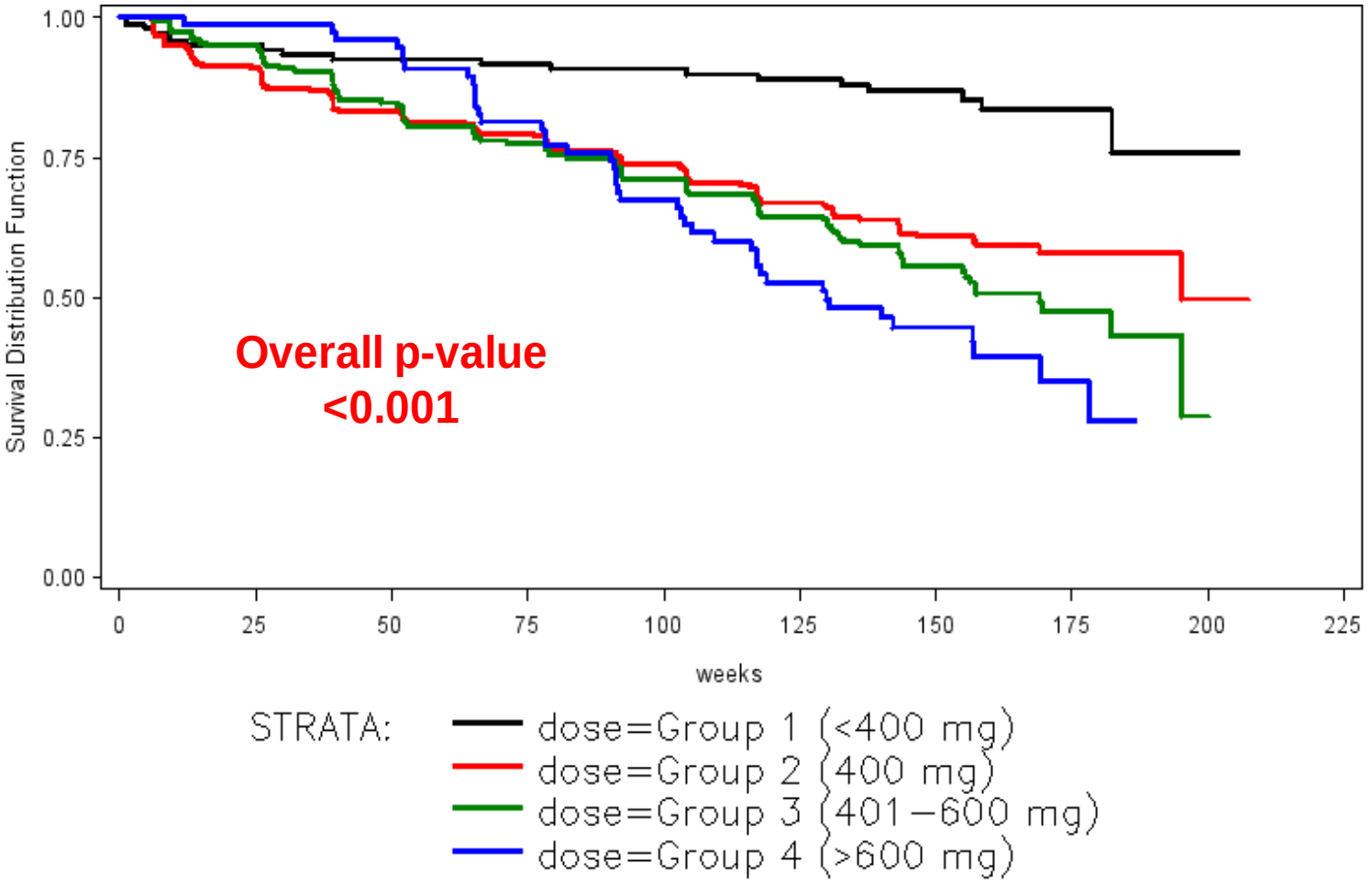
Table 1 **Demographic and baseline characteristics classified by nominal levodopa dose[1] - (Mean (standard deviation) or percentage**

Variable	Group 1: <400 mg/day (N=157)	Group 2: 400 mg/day (N=310)	Group 3: >400-600 mg/day (N=201)	Group 4: >600 mg/day (N=77)	Total (N=745)	p-value[2]
Age (years)	60.6 (9.2)	60.4 (8.0)	59.9 (8.6)	59.4 (8.0)	60.2 (8.4)	0.651
Men (%)	64.3	55.2	67.2	77.9	62.7	<0.001
Weight (kg)	79.1 (14.8)	75.8 (15.8)	82.6 (16.3)	86.4 (18.4)	79.4 (16.4)	<0.001
Duration of Parkinson's disease (years)	2.0 (1.6)	2.0 (1.7)	1.9 (1.7)	1.9 (1.6)	2.0 (1.6)	0.754
Hoehn & Yahr staging	1.9 (0.5)	1.8 (0.5)	2.0 (0.5)	2.1 (0.4)	1.9 (0.5)	<0.001
UPDRS total (II+III) at baseline	31.3 (12.5)	29.7 (11.5)	34.4 (12.3)	37.5 (12.3)	32.1 (12.3)	<0.001
UPDRS part II	8.7 (3.9)	8.5 (3.7)	10.4 (4.7)	11.2 (4.2)	9.4 (4.2)	<0.001
UPDRS part III	22.6 (9.7)	21.2 (8.8)	23.9 (9.1)	26.3 (9.4)	22.8 (9.3)	<0.001
Use of dopamine agonist (%)	59.9	60.3	52.2	62.3	58.3	0.237

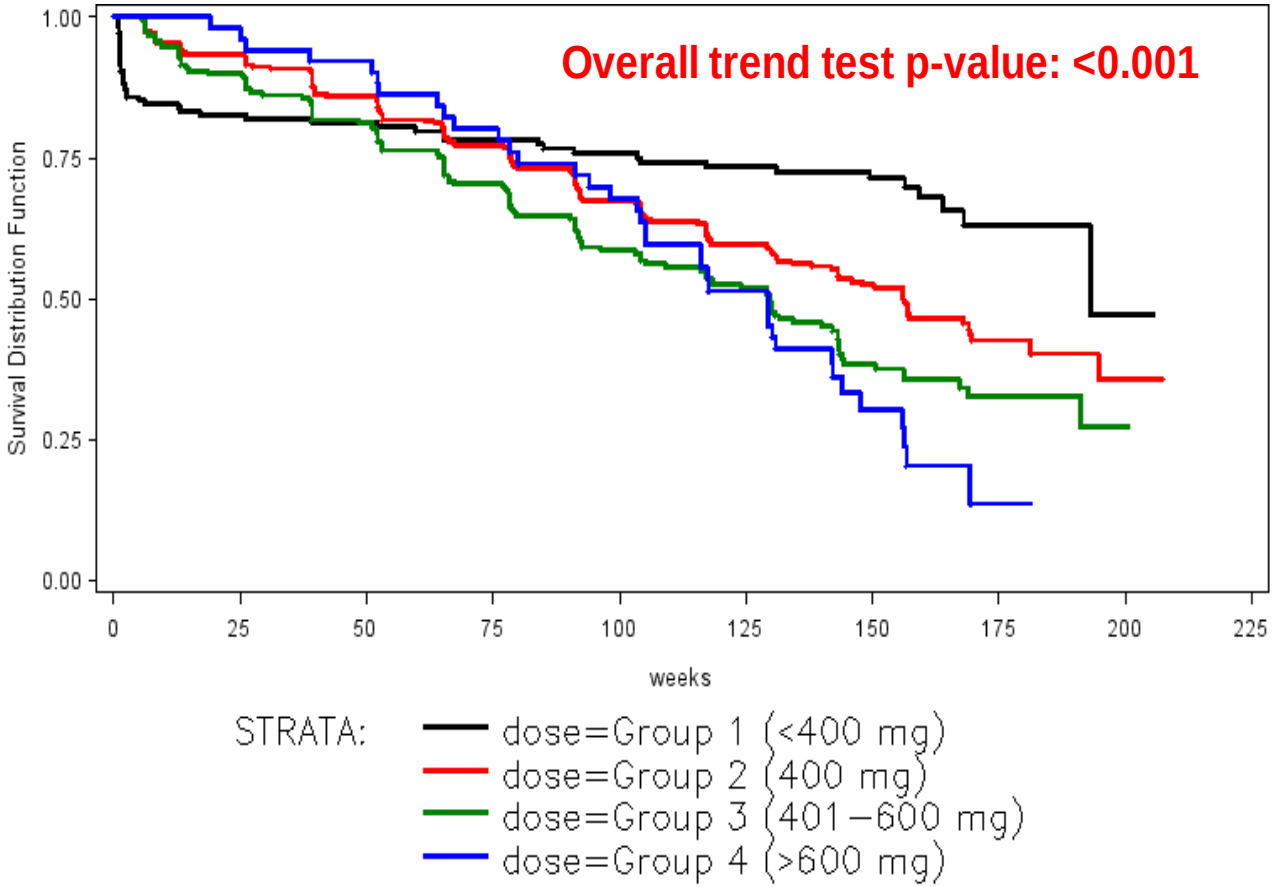
[1]Nominal levodopa dose at time of onset of dyskinesia or at time of study conclusion (if no dyskinesia)

[2]Difference between the four groups based on analysis of variance for continuous variables or chi-squared test for categorical variables (gender, use of dopamine agonists)

Time to to Dyskinesia



Time to Wearing Off



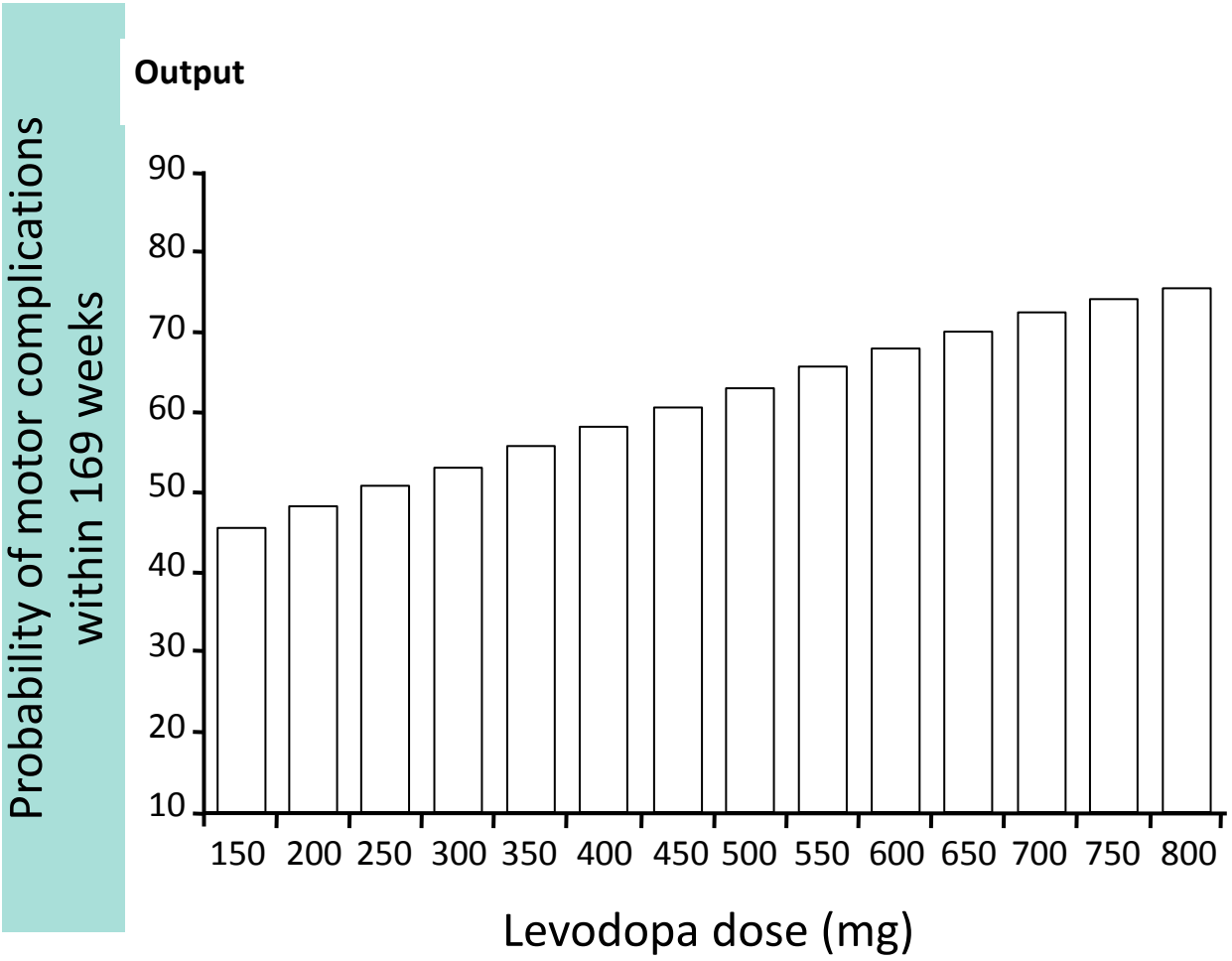
Summary of multivariate model for predictive factors: time to dyskinesia and time to wearing off

Step[1]	Factor	Chi squared statistic	P-value	Effect on dyskinesia (Higher risk)
1	Age at onset of PD	36.09	<0.001	Lower age
2	Nominal levodopa dose	31.55	<0.001	Higher dose
3	Region (North America/Europe)	12.82	<0.001	North America
4	Weight	10.05	0.002	Lower weight
5	Treatment allocation (LCE/LC)	8.80	0.003	LCE
6	Gender	4.46	0.035	Females
7	UPDRS part II at baseline	3.88	0.049	Higher scores
Step[1]	**Factor**	**Chi squared statistic**	**P-value**	**Effect on wearing off (Higher risk)**
1	Age at onset of PD	63.04	<0.001	Lower age
2	UPDRS part II	21.72	<0.001	Higher score
3	Region (North America/Europe)	33.81	0.001	North America
4	Nominal Levodopa dose	25.04	<0.001	Higher dose
5	Gender	8.84	0.003	Females
6	UPDRS part III	3.98	0.05	Higher score

[1]Order in which the factors were selected to the model

Risk calculator example case: high-risk patient

Output



Input

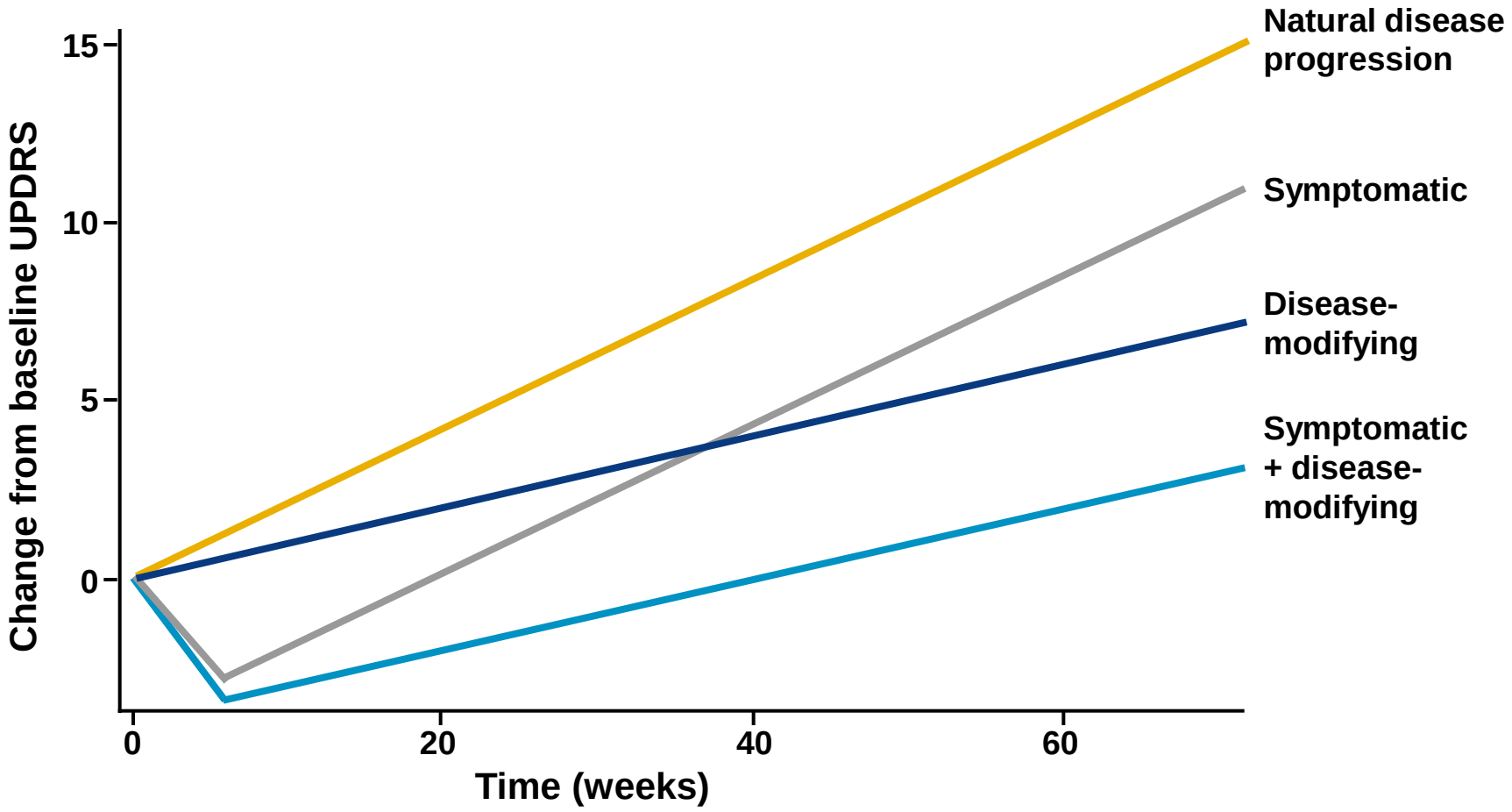
Age (years)	60
Gender	Male
Weight (kg)	75
UPDRS Part II	10
Hoehn & Yahr	2.5

Poewe et al. Poster at MDS 2012

Randomised neuroprotection trials in PD

Class	Agent	*n*	Primary outcome	Duration	Comments
Antioxidant/MAO inhibitor	Selegiline	800	Time to symptomatic treatment		DATATOP
	Selegiline	54	Time to symptomatic treatment	3 years	
	Selegiline	157	Time to symptomatic treatment	1–3 years	
	Selegiline	101	Change in UPDRS	14 months	2 month washout
	Selegiline	79	Change in UPDRS	60 months	1 month washout
	Lazabemide	321	Time to symptomatic treatment	12 months	
	Rasagiline	404	Change in UPDRS	12 months	Delayed start
	Selegiline	157	Change in UPDRS	7 years	With levodopa
Antioxidant	Vitamin E	800	Time to symptomatic treatment		DATATOP
	Coenzyme Q10	80	Change in UPDRS	16 months	QE2
	Coenzyme Q10	213	Change in UPDRS	12 months	Futility study
	Creatine	60	[^{123}I]-FP-CIT SPECT	24 months	
	Creatine	200	Change in UPDRS	12 months	Futility study
DA replacement	Pramipexole	82	[^{123}I]-β-CIT SPECT	46 months	CALM-PD
	Ropinirole	186	[^{18}F]-dopa PET	24 months	REAL-PET
	Levodopa	360	Change in UPDRS	40 weeks	ELLDOPA; 2 week washout
Glutamate antagonist	Riluzole	20	Change in UPDRS	6 months	
Trophic factor	GDNF	50	Change in UPDRS motor score	8 months	
	GDNF	34	Change in UPDRS motor score	6 months	
Neuroimmunophilin ligand	GPI-1485	300	Change in UPDRS motor score	6 months	
	GPI-1485	213	Time to symptomatic treatment	12 months	Futility study
Antiapoptotic agent	TCH346	301	Change in UPDRS	12–18 months	
	CEP-1347	806	Change in UPDRS	Average 21.4 months	PRECEPT
	Minocycline	200	Time to symptomatic treatment	12 months	Futility study

Untangling drugs with different effects

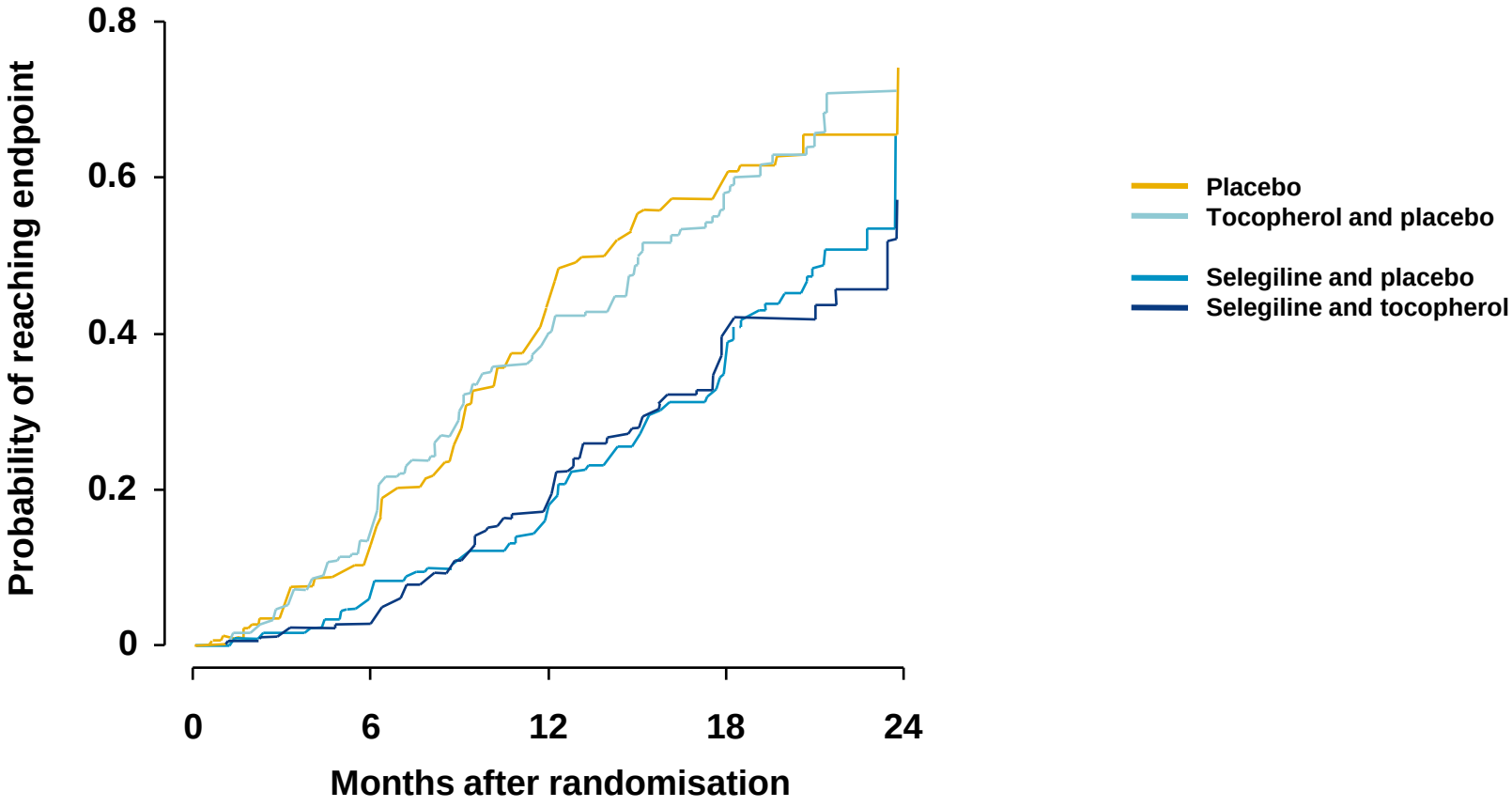


Bhattaram et al. AAPS J 2009; 11 (3): 456

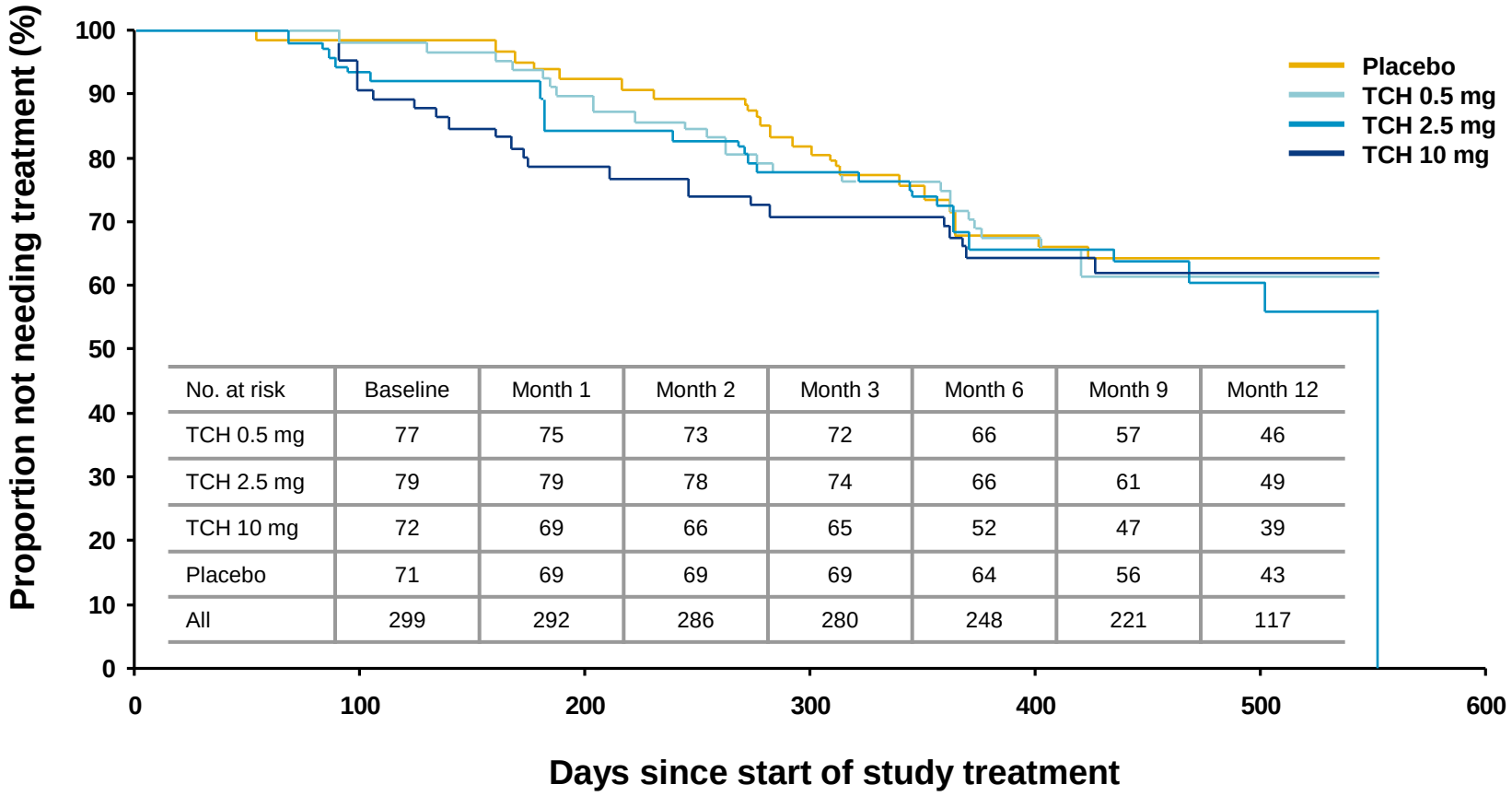
Clinical Trials

- Instruments: scales
- Lack of biomarkers
- Dose definition: the problem of U-shaped response
- Study population

Time to endpoint – e.g., DATATOP

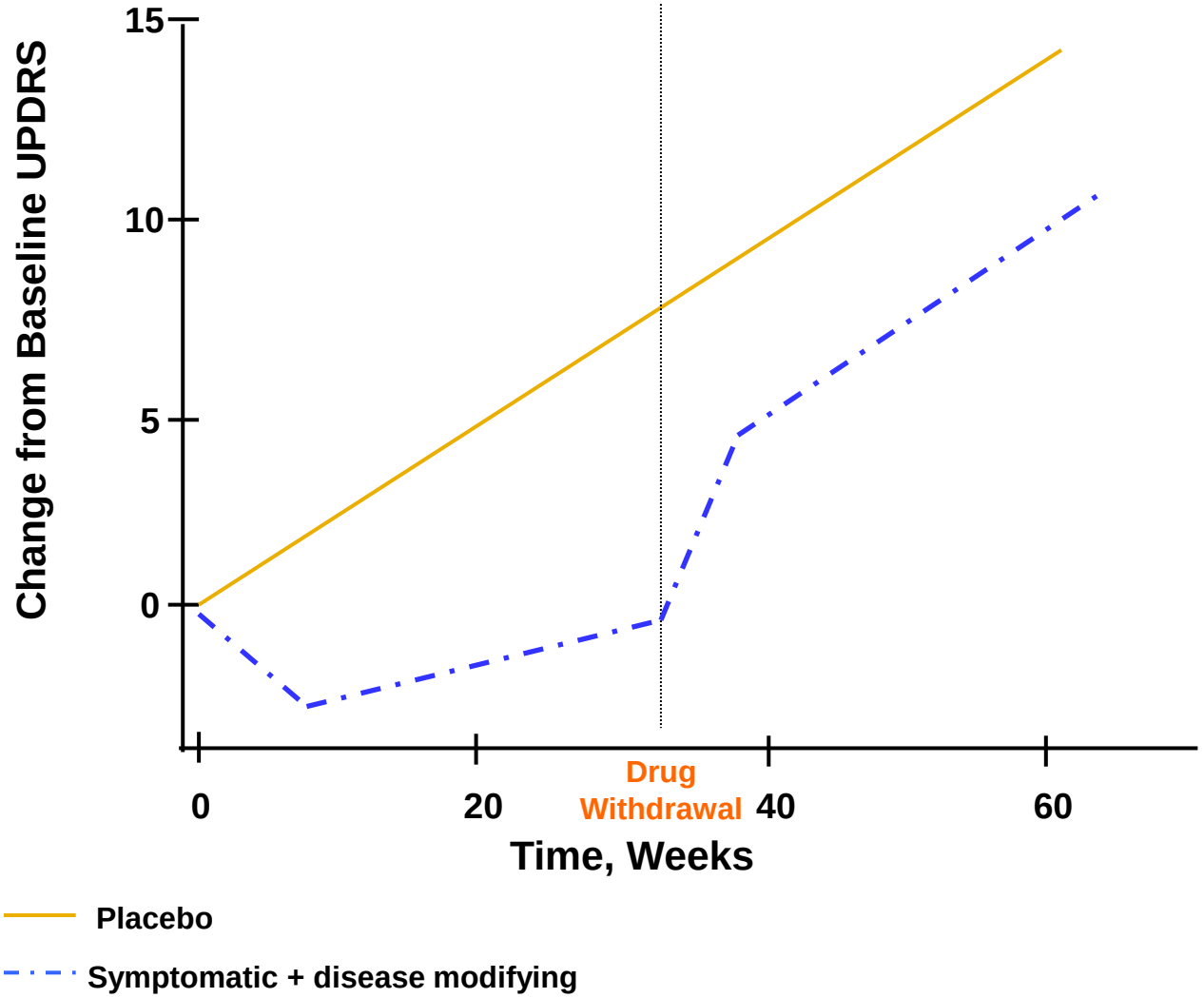


Time to endpoint – e.g., TCH346



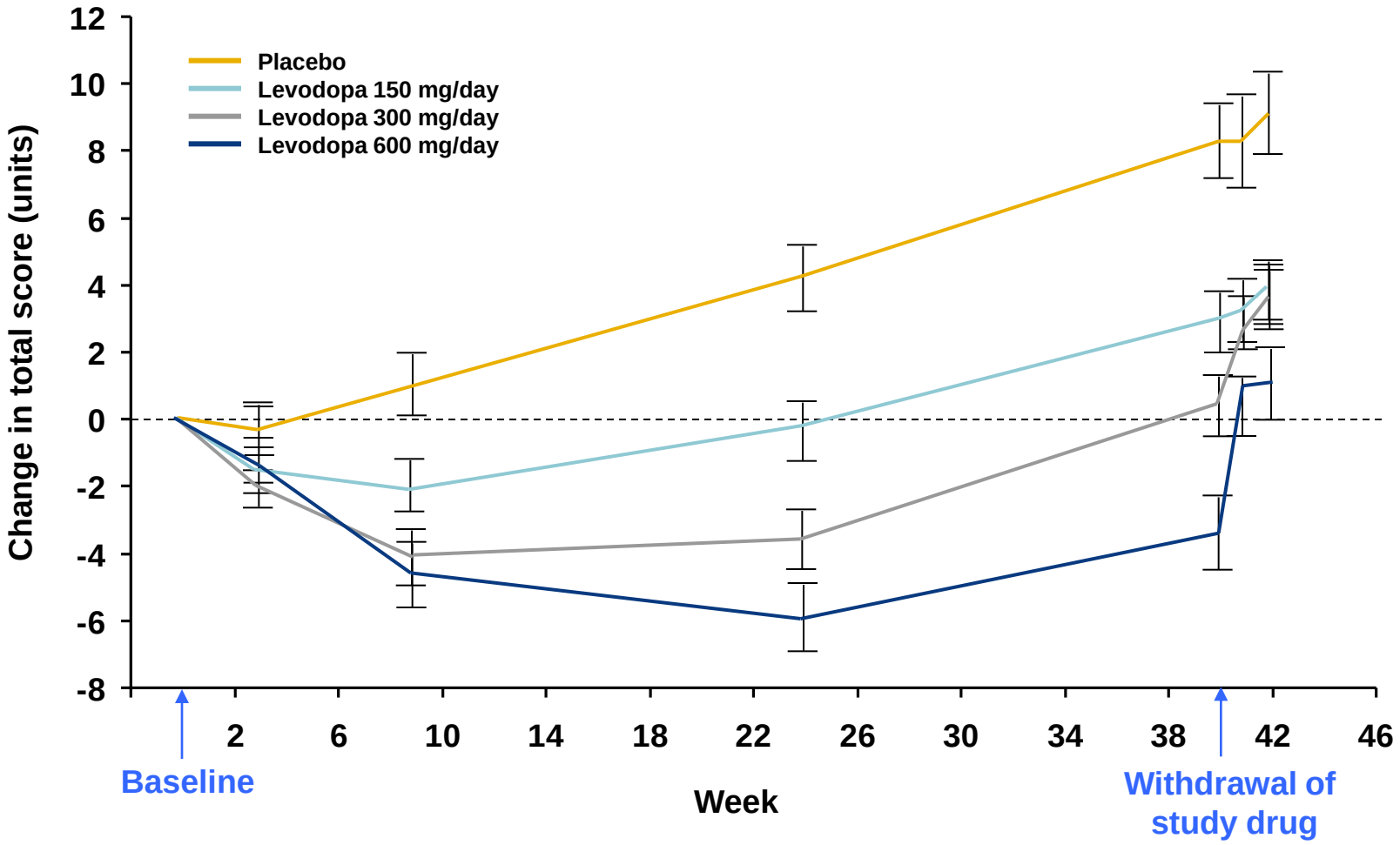
No. at risk	Baseline	Month 1	Month 2	Month 3	Month 6	Month 9	Month 12
TCH 0.5 mg	77	75	73	72	66	57	46
TCH 2.5 mg	79	79	78	74	66	61	49
TCH 10 mg	72	69	66	65	52	47	39
Placebo	71	69	69	69	64	56	43
All	299	292	286	280	248	221	117

Disease modifying effect in washout design



Bhattaram V.A. et al. The AAPS Journal; Published online June 12, 2009

Washout – e.g., ELLDOPA



Delayed-start design

Alzheimer Disease and Associated Disorders
Vol. 10, Suppl. 1, pp. 31–35

Observations and Suggestions on Antidementia Drug Development

Paul Leber

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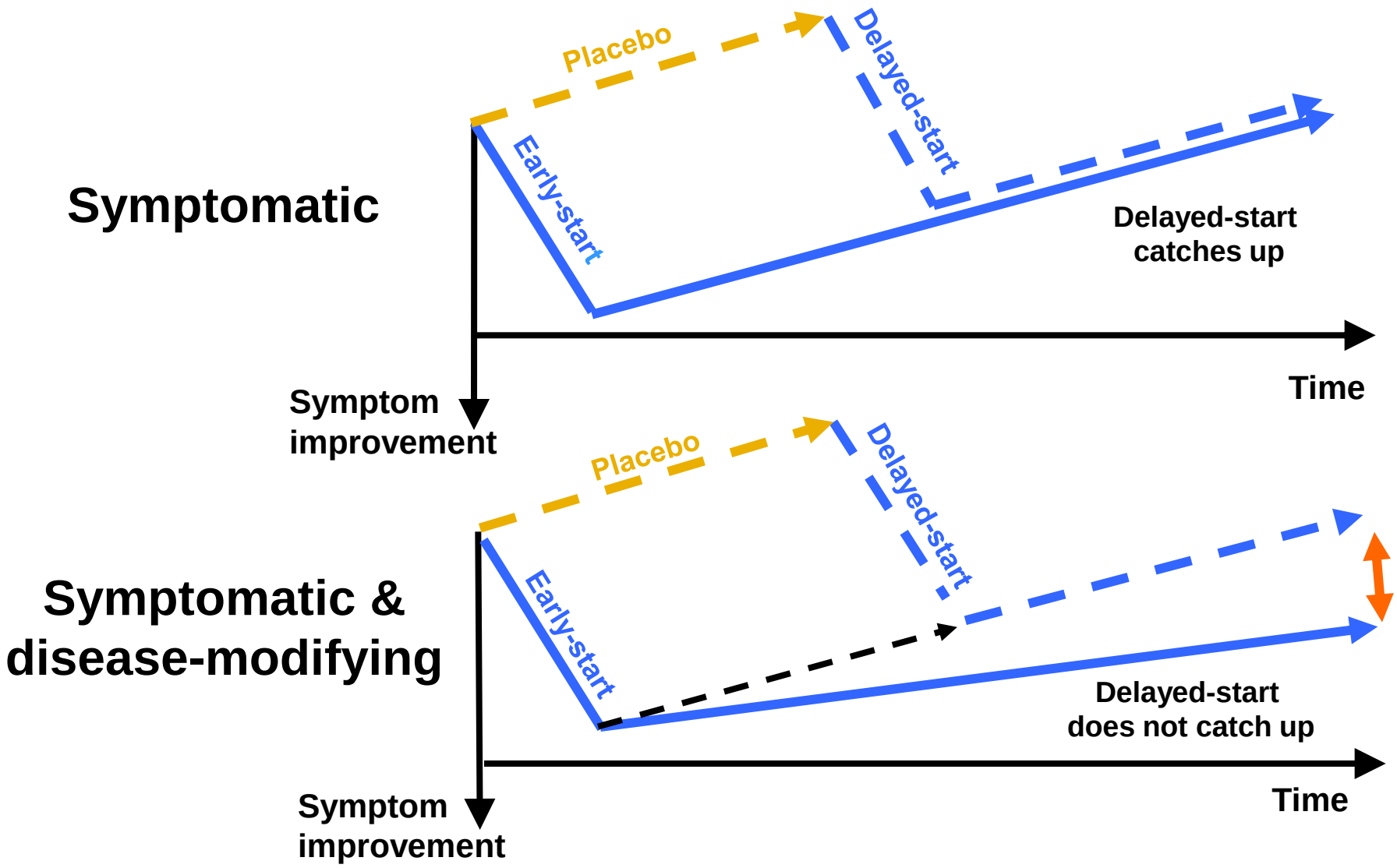
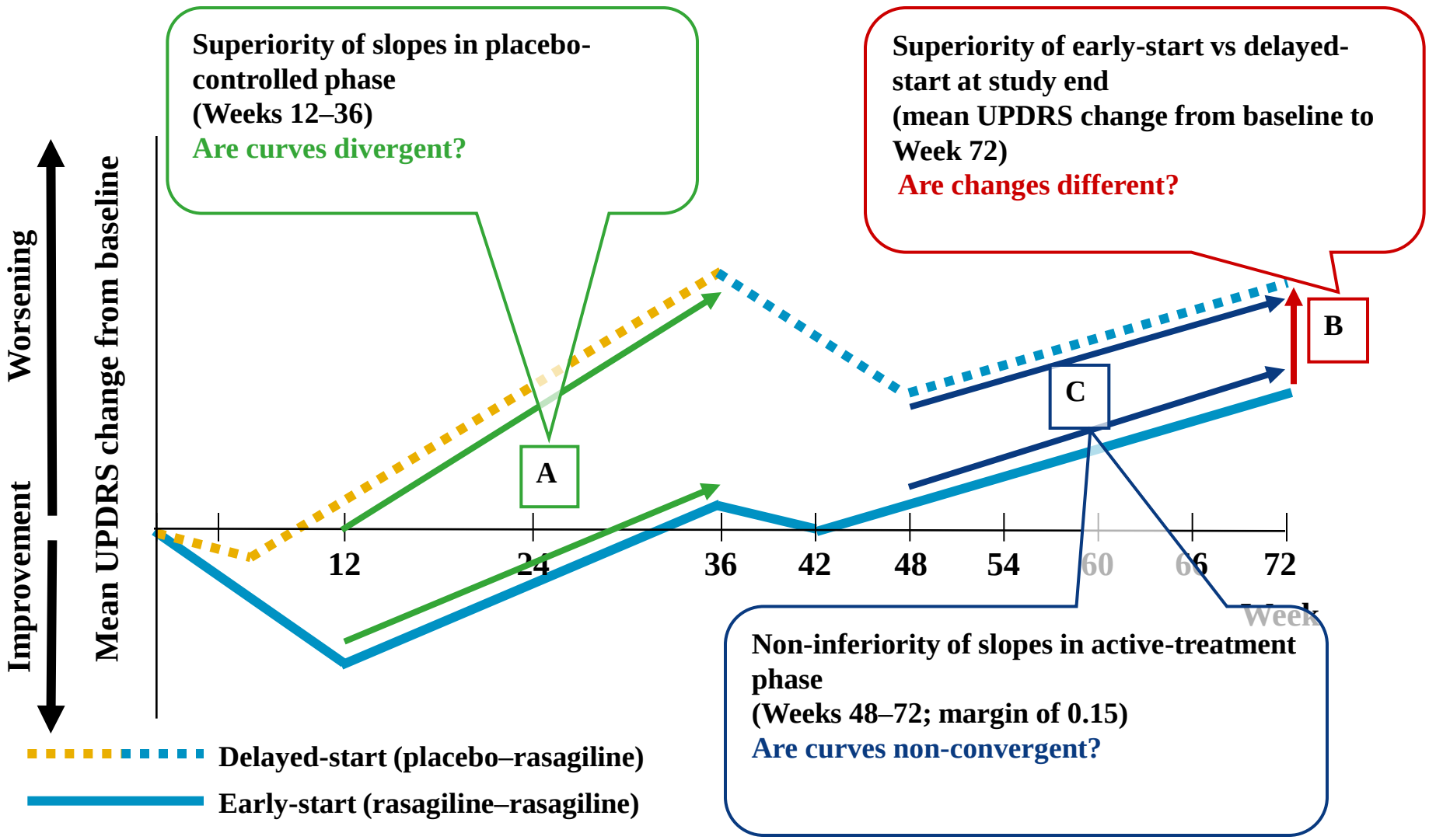
Summary: Recent advances in the theoretical neurosciences have suggested a number of novel strategies that might be applied to prevent and/or retard the progression of Alzheimer disease. Whether or not these interventions will succeed cannot be determined on theoretical grounds, however; the value of each new stratagem must be evaluated in patients with Alzheimer disease. How best to conduct clinical studies of disease-modifying treatments remains a controversial subject. The author reviews and compares two clinical trial designs that may prove useful in assessing whether or not a putative treatment actually modifies the course of dementia. **Key Words:** Dementia—Antidementia treatments—Drug product development—Clinical trials—Re-randomized design—Randomized start design.

Delayed-start design
symptomatic vs. disease-modifying effect



Primary efficacy analysis: composed of 3 hierarchical endpoints based on UPDRS-Total scores (Parts I, II and III) – *schematic*



Adapted from Olanow et al. Mov Disord 2008; 23 (15): 2194

The ADAGIO STUDY

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

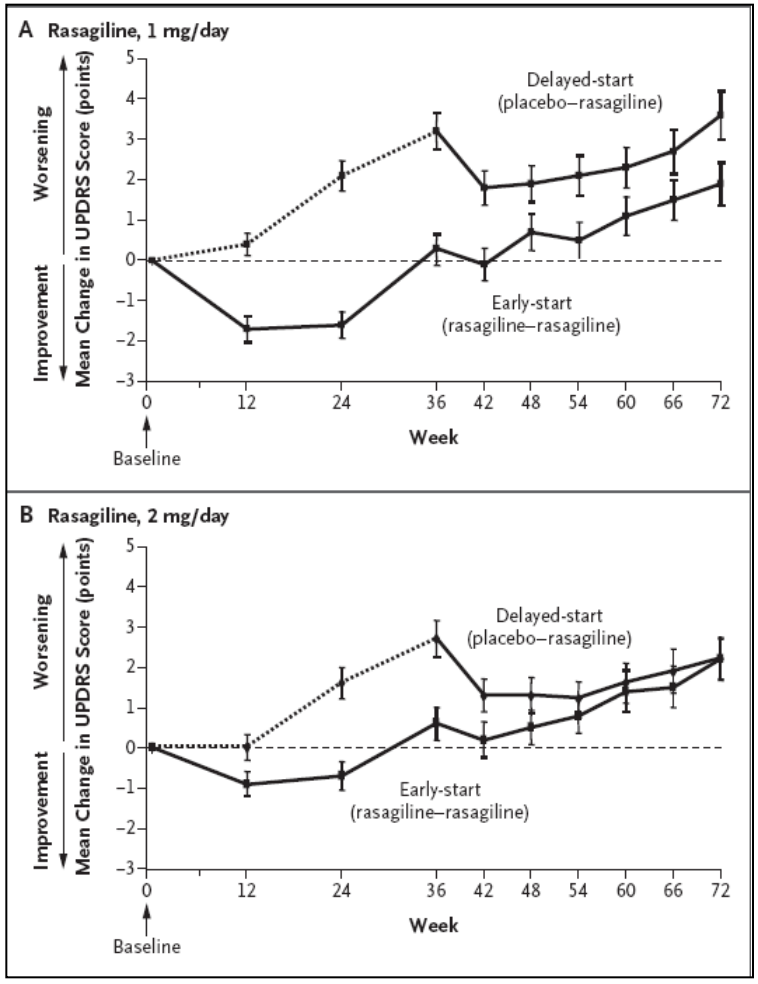
A Double-Blind, Delayed-Start Trial of Rasagiline in Parkinson's Disease

C. Warren Olanow, M.D., Olivier Rascol, M.D., Ph.D., Robert Hauser, M.D., Paul D. Feigin, Ph.D., Joseph Jankovic, M.D., Anthony Lang, M.D., William Langston, M.D., Eldad Melamed, M.D., Werner Poewe, M.D., Fabrizio Stocchi, M.D., and Eduardo Tolosa, M.D., for the ADAGIO Study Investigators*

The statistical model better demonstrates the DM effects of rasagiline 1mg/day vs. the descriptive graphs

Table 2. Results for the Primary and Secondary End Points.*

End Point	Estimated No. of Points	Confidence Interval†	P Value
First primary (estimated rate of change in UPDRS score/wk, wk 12–36)			
Placebo	0.14±0.01		
Rasagiline			
1 mg/day	0.09±0.02		
2 mg/day	0.07±0.02		
1 mg/day vs. placebo	−0.05±0.02	−0.08 to −0.01	0.01
2 mg/day vs. placebo	−0.07±0.02	−0.11 to −0.04	<0.001
Second primary (estimated change in total UPDRS score from baseline to wk 72)			
Rasagiline			
1 mg/day, early start	2.82±0.53		
1 mg/day, delayed start	4.50±0.56		
2 mg/day, early start	3.47±0.50		
2 mg/day, delayed start	3.11±0.50		
1 mg/day, early start vs. delayed start	−1.68±0.75	−3.15 to −0.21	0.02
2 mg/day, early start vs. delayed start	0.36±0.68	−0.99 to 1.70	0.60
Third primary (estimated rate of change in UPDRS score/wk, wk 48–72)			
Rasagiline			
1 mg/day, early start	0.085±0.02		
1 mg/day, delayed start	0.085±0.02		
2 mg/day, early start	0.094±0.01		
2 mg/day, delayed start	0.065±0.02		
1 mg/day, early start vs. delayed start	0.00±0.02	−0.04 to 0.04‡	<0.001
2 mg/day, early start vs. delayed start	0.03±0.02	−0.01 to 0.06‡	<0.001



Olanow et al, 2009

Clinical Trials

- Another approach is the long-term simple study, where subjects are randomized to active treatment or placebo, and then followed for a prolonged period of time (many years) in which the physician can manage the patient in any way they deem to be appropriate.
- A combination of the delayed start and long term simple studies offers assessments of mechanism and clinical significance

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Clinical Trials

- Adaptive design is another approach that can be of great value. Here, unannounced but predetermined interim analyses examine data accumulated during the course of the trial without compromising the blind or the integrity and validity of the study. Such an approach can permit early termination of a study for adverse events or futility, examination of large numbers of doses with rejection of those doses that are futile, re-estimation of sample size, and early planning and streamlining of next phase studies

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Costs

- The average drug development program for a CNS drug is approximately 15 years from the time the drug is first introduced to the clinic
- Cost of approximately 1.2 billion dollars

ISS (Investigator Sponsored Study)

Uno studio ISS è uno studio dove lo Sponsor dello studio è uno sperimentatore o altro soggetto ma non l'azienda Farmaceutica.

- *Sponsor: la persona, società, istituzione oppure organismo che si assume la responsabilità di avviare, gestire e/o finanziare una sperimentazione clinica*

IRCCS San Raffaele Pisana

ISS (Investigator Sponsored Study)

- **Uno studio ISS può essere:**

- **Interventistico**
  - E' lo studio che valuta un intervento (diagnostico, terapeutico, riabilitativo) non previsto dalla normale pratica clinica.

- **Osservazionale**
  - In questo caso il prodotto in studio è utilizzato secondo indicazione e il trattamento non è determinato dal protocollo dello studio.

IRCCS San Raffaele
Pisana

ISS (Investigator Sponsored Study)

… e l'azienda cosa fa?

- L'azienda supporta lo studio dello sperimentatore soltanto con supporto scientifico, sostegno economico e/o fornitura del farmaco.
- L'idea e il razionale dello studio devono essere sviluppati dall'investigatore e non dall'azienda. L'azienda può altresì fornire suggerimenti a riguardo ma non è autorizzata a modificare sostanzialmente il disegno.

IRCCS San Raffaele
Pisana

ISS (Investigator Sponsored Study)

- **…** Nel supportare un ISS, l'accordo con lo sperimentatore necessita di essere documentato in un contratto scritto
- *Le parti intendono definire il supporto economico e liberale di **XXXX**, ai sensi dell'art. 2 commi 6 e 7 del Decreto Ministero della Salute 17 dicembre 2004, per la realizzazione dello studio da parte dell'Ente e le responsabilità di quest'ultima*
- Per gli studi no-profit il valore del supporto economico non deve superare il 50% del valore totale dello studio.
- I risultati dello studio sono di proprietà dell'Ente e la loro utilizzazione sarà libera, con il solo obbligo di citare, nelle eventuali pubblicazioni, che essi sono scaturiti con il contributo di ***XXXX***. Inoltre l'Ente garantisce che tali risultati non saranno impiegati per scopi commerciali di terze parti.

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Criticità

I dati non possono essere utilizzati a fini registrativi

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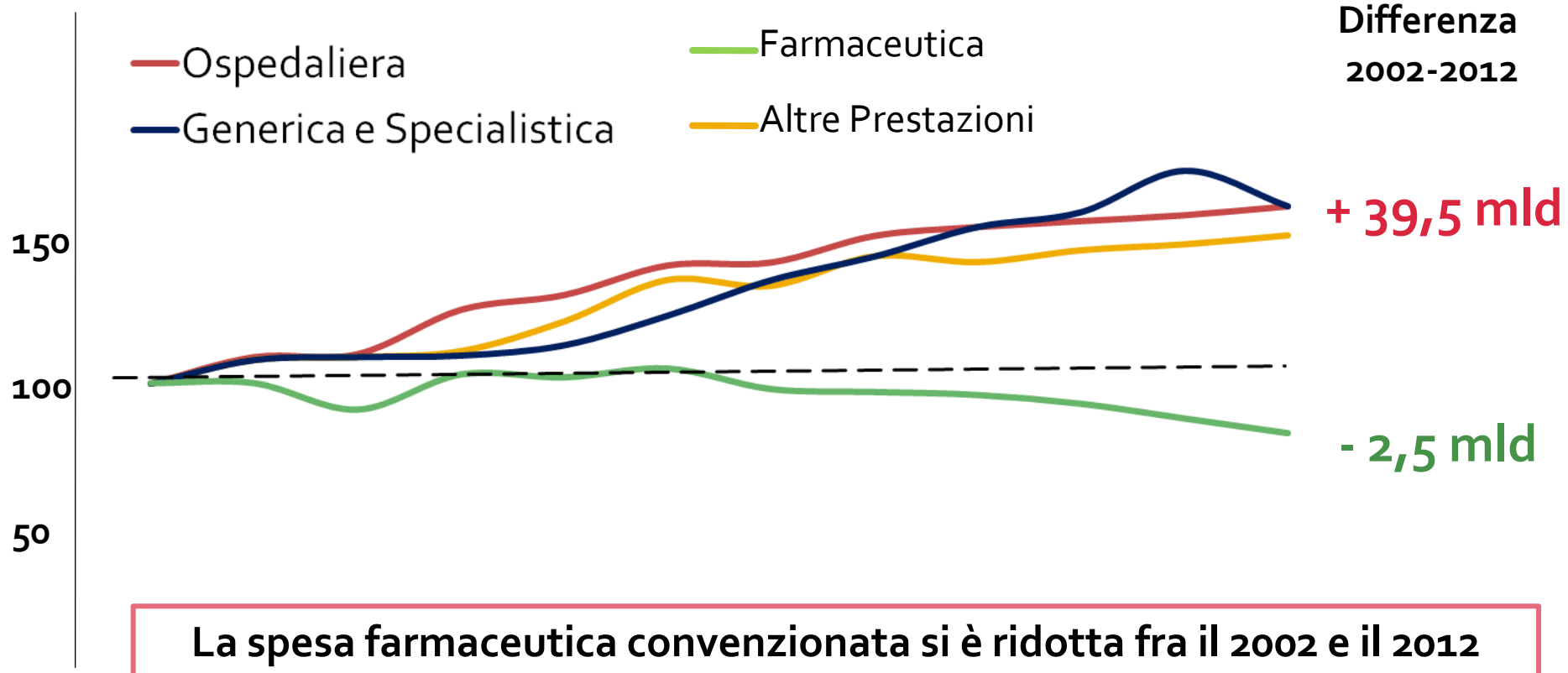
Critiche

- Roma, 17 mar 2014 - La legge sugli studi clinici spontanei va cambiata quanto prima. E i risultati delle sperimentazioni non sponsorizzate devono essere utilizzati a fini registrativi: è la richiesta contenuta nella lettera inviata oggi al Ministro della Salute, Beatrice Lorenzin, dall'Associazione Italiana di Oncologia Medica (AIOM) e dal Collegio Italiano Primari Oncologi Medici Ospedalieri (CIPOMO).

IRCCS San Raffaele Pisana

Evoluzione delle principali voci della spesa sanitaria pubblica

(indice 2001 =100), 2001-2012



La spesa farmaceutica convenzionata si è ridotta fra il 2002 e il 2012 passando dal 14,8% all'8,3% della spesa sanitaria pubblica

Fonte: The European House-Ambrosetti su dati Corte dei Conti,"Rapporto 2012 sul coordinamento della finanza pubblica", maggio 2012; Farmindustria, "indicatori Farmaceurici 2012", giugno 2012