Malattia di Parkinson
Basi generali della malattia

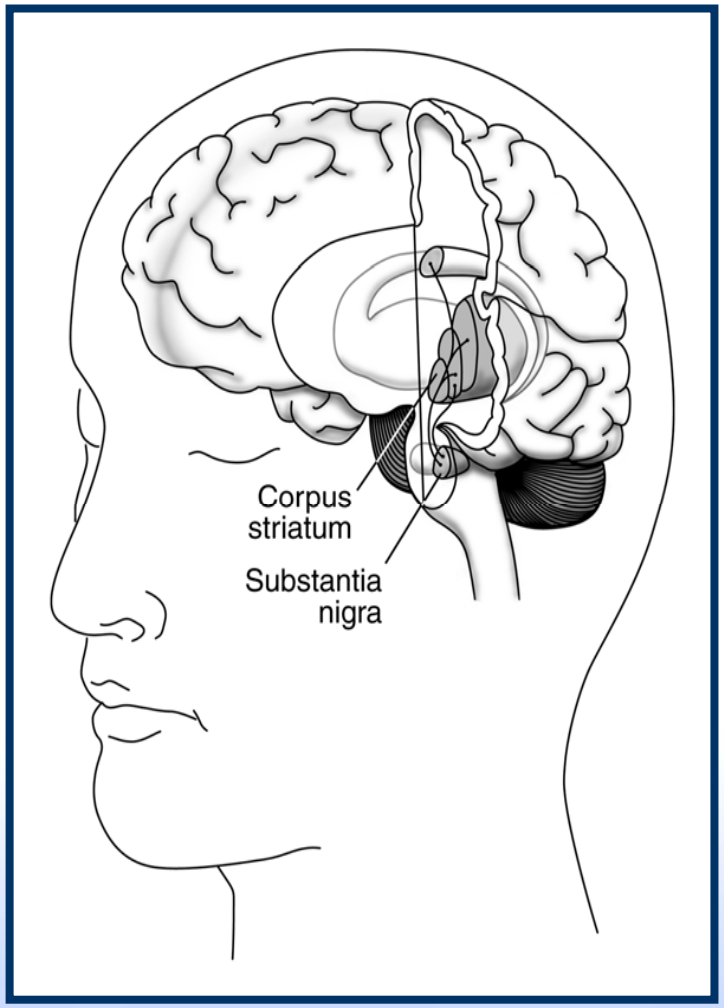
www.fisiokinesiterapia.biz

Malattia di Parkinson

Mdp hv#Sdunlqvrq#qho4;4:#ghvfulvvh ol#
p dolwwld qhodeur ŠDq#Hvvd|#rq#wkh#
Vkdnlqj#Sdov|õ=

ŠWuhp rullqyrorqwdul/#dffrp sdjqdwlgd
glp lqx}lrqh ghoo iru}d p xvfroluh/#lq#sduwl
gh#frusr qrq#lp shjqdwh qhop ryip hqwr
dqfkh vh#vruuhwwh>#whqghq}d dg#lqfdqduh lo
wurqfr lq#dydqwlhg d#sdvvduh gdofdp p lqr
dol fruvd/#p hqwuh ol#vhqvlelow< h#o#
ixq}lrqllqwhonwwlyh uhvwdqr lqdovhudwhõ1

Aree cerebrali del sistema extrapiramidale



Malattia di Parkinson
Realtà clinica e terapeutica

- P dolwwld qhxurorjlfd ghjhqhudwlyd=
  - Ù fdxvd lqrwd
  - Ù lqvrujhq}d lqvlgrvd
  - Ù ghfruvr judgxdoh hqwh surjuhvvlyr

- Wudwwdp hqwr idup dfrorjlfr=#vlqwrp dwlfr

Marsden, Olanow Ann Neurol 1998

Criteri Diagnostici

- Suhvhq}d#gh#vhjqh#p rwru#fdugqdd=

  WUHP RUH#0ULJGWDÚ0DFQHVD

  . #HVRUGLR#DVP P HWUFR#

- Yhulilfd#ghoo#uhvsrqvlylw< doo#whudslh#idup dfrorjlfd# +dyrgrsd,

- Hvfoxvlrqh#gl#vlqwrp l#Ñdwlslfl Ú=

  lqvwdelow< srvwxudo#suhfrfh/#judyh#glvdxwrqrp ld/# iuh}lqj suhfrfh/#doxflqd}lrq#qrq#DG #fruhodwh/## ghfdgp hqwr#lqwhonwwlyr#suhfrfh/#sduddv#yhuwlfdo# ghor#vjxdugr/#p ryp hqw#lqyrorqwdu#dwlslfl

Hughes AJ, Brain 2002

Sintomi all'esordio %

wuhp ruh	8 3 19
eudgliqhvld/#uljlgl w</#p lfurjudiid	6 9 19
groruh#duwlfrodu h	5 3 16
ghsuhvvlrqh	4 3 1<
htxlbeulr#ulgrwwr	4 19
glvwrqlh	3 1:
p dufld#d#slffrd#sdvvl	3 19
srvwxud#lq#idhvvlrqh	3 15
dowur	6 18

DATABASE Centro Parkinson CTO; Antonini comunicazione personale

Principali anomalie biochimiche

- P dufdwd#ulgx}lrqh#ghoo#grsdp lqd#vwuldwdh
- Dq#ghfhvvr#shugwd#gl#grsdp lqd#A #< 3 (
- Shugwh#lqihulruh#dq#8 3 (#vrqr#
  dvlqwrp dwlfkh
- Judylw< gl#shugwd#grsdp lqhujlfd fruwhoo#dq#
  p hjdr#frq#lo#vlqwrp r#eudgllqhvld

Jellinger KA Mol Chem Neuropath 1991

Epidemiologia

- Suhydodqq}d
  - Flufd#5 3 3 24 3 3 13 3 3 #Lwdod=#flufd#4 5 3 13 3 3 #sd}lhqwl,
- Lqfldhq}d
  - 5 3 24 3 3 13 3 3 #shu#SG #6 6 3 24 3 3 13 3 3 #rowuh l#9 3 #dqql,
  - Lqfldhq}d dxp hqwd surjuhvvlydp hqwh frq# dOlqyhffkduh ghood srsrod}lrqh
  - 4 3 (05 3 (#ghlfdvlgldjqrvwlfdwlvrcr#grsr dofxql dqql
- Hw< gllqvrujhq}d
  - 8 ; #e 4 3 #dqql>#dp elwr gd 5 3 #d#; 7 #dqql

Morgante L. et al.: Neurology 1992; 42: 1901-1907

Mortalità nella m. di Parkinson

- Ulgrwwd#dvshwwdwlyd#gl#ylwd
  - Vrsudyylyhq}d#p hgld#4 8 04 ; #dqql
  - P djjlruh#lq#vrjjhwwl#fkh#qrq#vyllussdqr#ghp hq}d
  - Surxqjdwd#gdóÍkvr#gl#hyrgrsd h#idup dfl# grsdp lqhujlfl
- Vrsudyylyhq}d#shu#SG #A A #fkh#shu# sdunlqvrqlvp l
- Oh#fdxvh#gl#ghfhvvr#vrqr=
  - lqih}lrq#srp rqdul/#lqih}lrq#yhvflfdd/#hp erdd# srp rqduh#h#frp sdfd}lrq#gl#fdgxwh#h#iudwwxuh

Mortalità nella malattia di Parkinson

Dxwkruv	Qxp ehuv ri sdwlhqwv	Irorz xs |hduv	P ruwdodw| Udwlr	Ohyrgrsd
Krhkq/4<9:	574	<17	51<3	qr
Gldp rqg/#4<;:	;4	0	31<8	|hv
\dku/#4<:9	8<:	441;	4179	|hv
Vkdz /#4<;3	4:;	4713	4179	|hv
Krhkq/#4<9;	498	0	4153	|hv
GDWDWRS/#4<<;	;33	;15	31;3	|hv
SGUJ0XN/#5334	:;5	<15	41:;	|hv

Causa della malattia

- Vfrqrvflxwd#qhoo#p djjlru#sduwh#gh#fdvl
- Jhqhwlfd
  - Ù p xwd}lrq#gh#jhqh#ghÚDskd v|qxfdnqd +furp rvrp d#7t,#ghqwlifdwd#q#xqd#dp sl#idp ljdd# lwddqd#Frqwxuvl,#h#8#idp ljdh#juhfkh#wudvp lvlrqh# dxwrvrp lfd grp lqdqwh,
  - Ù p xwd}lrq#gh#jhqh#sdunqd q#xqd#irup d#dxwrvrp lfd0 uhfhvvlyd uhvsrqvdeln#gl#flufd#d#53063 (#gh#fdv#dg# hvrugr#vrwwr#d#73#dqql
- Dp elhqwdln
  - Ù Hvsrvl}lrqh#dg#gurfduexu#sxrÚqwhuihuuh#frq#d# fruvr#ghoo#p dolwwl

Loci e geni nel Parkinson familiare

Orfxv	Srvl}lrqh	Jhqh	Wudvp lvvlrqh
SDUN4	7s5416	α0V|qxfohlq	DG
SDUN5	9t5815 05:	Sdunlq	*DU*
SDUN6	5s46		DG
SDUN7	7s48		DG
SDUN8	7s47	XFK004	DG
SDUN9	4s680s69		*DU*
SDUN:	4s69	GM04	*DU*
SDUN;	45s4415 0t4614		DG
SDUN<	4s69		*DU* +NxiruUdnhe v|qgurp h,
SDUN#43	4s65		Jhqh#fkh suhglvsrqh dg# hvruglr wdugly r

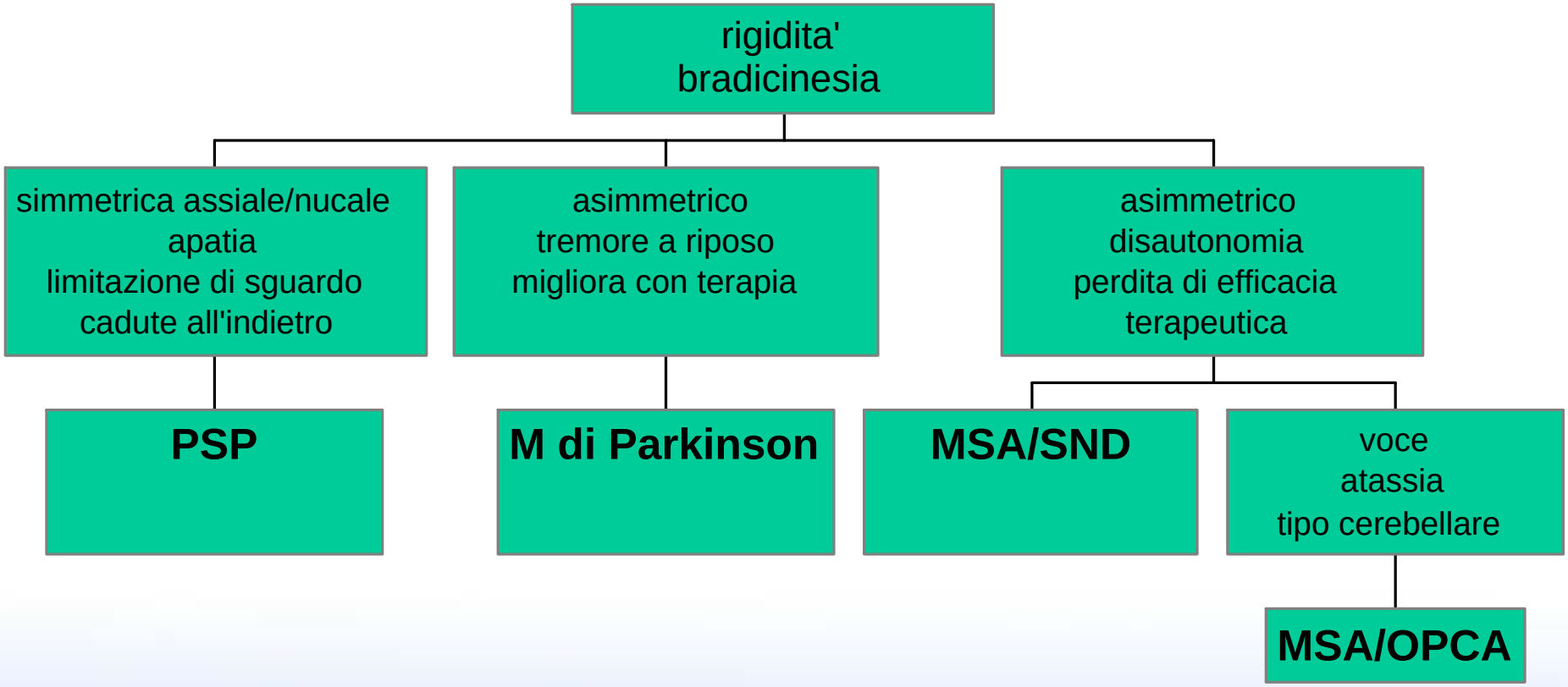
Malattia di Parkinson
Diagnosi differenziale

Diagnosi Differenziale

- Wuhp ruh#hvvhq}dodh
- Sdunlqvrqlvp l#vhfrqgdul
- Dwurid#P xowlvlvwhp lfd
- Sduddvl#Vrsudqxfohduh#Surjuhvvlydd
- Ghjhqhud}lrqh#Fruwlfr0Edvdoh
- P dodwwd#gd#frusl#gl#Ohz |#
- Ghp hq}h
- P dodwwh#huhgwduh

Hughes AJ Brain 2001

Schema Diagnostico Parkinsonismi



Diagnosi Differenziale: Neuroimmagini

- Wuhp ruh#hvvhq}ldo=#VSHFW#frq#GDWVFDQ
- Sdunlqvrqlvp l#vhfrqgdul=#dwurjhqh/#ydvfrodu#VSHFW#frq#GDWVFDQ/#UP Q#fhuhebudo
- Dwurilo#P xowlvwhp lfd/#Sduddvl#Vrsudqxfohduh#Surjuhvvlyd/#Ghjhqhud}lrqh#Fruwlfr0Edvdo=#VSHFW#frq#E]P /#UP Q#fhuhebudo
- P dodwwld#gd#frusl#gl#Ohz |=#VSHFW#ixxvvr/#UP Q#fhuhebudo

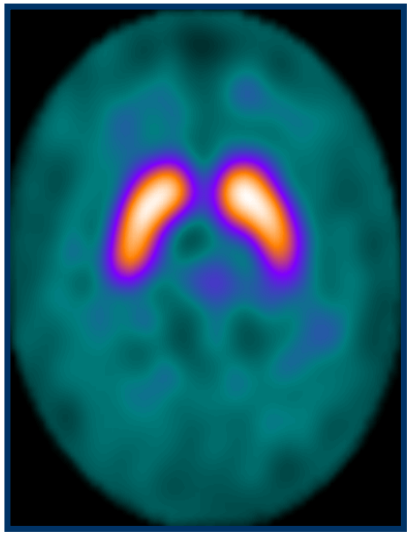
Diagnosi Differenziale: Risonanza Magnetica Cerebrale (meglio se 1 T o 1,5 T)

- Qhoh#P VD=#Jdrvl#ghh#sxwdp hq#edqgd#lshulqwhqvd#lq#W5#hg#lq#ghqvlwdÚsurwrqlfd,># Dwurilo#ghh#fhuyhohwwr
- Qhool#SVS=#Dwurilo#P hvhqfhidor
- Qhh#Sdunlqvrq#ydvfroduh=#Ohvlrqlp xovlsh#lq#W5# ghool#vrvwdq}d#eldqfd#shulyhqwulfroduh#h#ghl# jdqjd#ghool#edvh

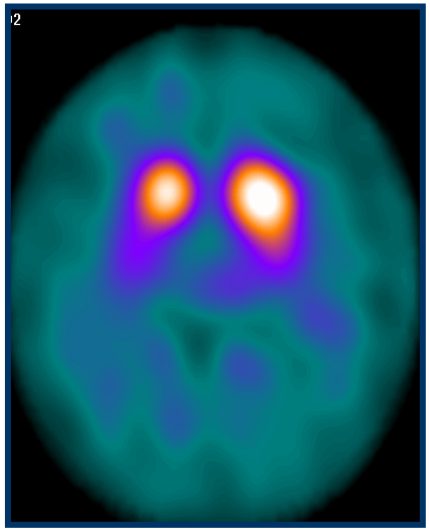
Diagnosi Differenziale: Neuroimmagini funzionali

- VSHFW#frq#GDWVFDQ=#P dunhu#shu#wwhup lqdd#grsdp lqhujlf#qhor#vwuldwr
- VSHFW#frq#E]P =#P dunhu#uhfhwwru#grsdp lqd frqwhqxw#qh#qhxurq#jdedhujlf#vwuldwdd
- VSHFW#ixvvr=#P dunhu#gl#ixq}lrqdd wdÚqhxurqddh#qrq#vshflilfr

Il trasportatore della dopamina nella malattia di Parkinson

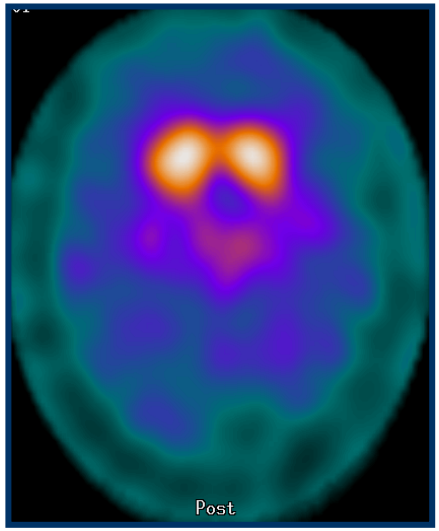


Frqwurœr



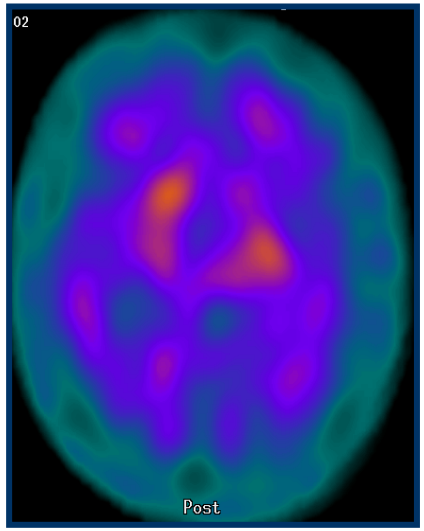
SG

K)\#L



SG

K)\#L



SG

K)\#Y

Antonini A Neurol Sci 2002

Malattia di Parkinson
Terapia della fase iniziale
Strategie terapeutiche e farmaci disponibili

Trattamento della MP

Farmaci più utilizzati

- Ohyrgrsd -vwdqgdug/#ubdvflr#p rglilfdwr/#p hwlbnvwhuh,
- Grsdp lqr#djrqlvwl=
  - 0 Dsrp ruilqd
  - 0 Hujrdqlfl=#Fdehujrdqd/#Eurp rfulswlqd/#Shjrdgh#
  - 0 Q rq0hujrdqlfl=#Sudp lsh{rcr/#Urslqurcr
- Lqlelwrul#ghoo P DR=#vhdnjlbqd
- Dp dqwdglqd
- Dqwlfrdqhujlfl
- FRP W#lqlelwrul=#Hqwdfdsrqh

Amantadina

- Frqrvflxwr frp h#djhqwh#dqwlyluda/#sx¿#dqfkh#dyhuh# dwwlylw< dqwlsdunqvrqldqd1
- Lp hffdqlvp r#gÚd}lrqh frp h#idup dfr#dqwlsdunqvrq qrq#· ghp#wxwwr#fkldur/#wxwwdyld · qrwr#fkh#ÓÚp dqwdglqd#lqlelvfh od#ulfdswd}lrqh#ghod#grsdp lqd/#vwlp rol l#uhfhwwrul# grsdp lqhujlfl#idyruhqgr#h#ulodvflr#gl#grsdp lqd/#h# suredelp hqwh#hvsdfd#xqÚd}lrqh#dqwlfrdqhujlfd#shulihulfd
- Uhfhqwhp hqwh · vwdwr#ulfrqrvflxwr#doÓÚp dqwdglqd# xqÚd}lrqh#dqwdjrqlvwd d#dyhor ghp#uhfhwwruh Q 0p hwlb0G 0 dvsduwdwr hg#hiilfdfld#qhp#frqwuror#ghoh#glvflqhvlh/#d}lrqh# fkh#suredelp hqwh#vl#hvsdfd##shu#lh#eorffr#ghod# wudvp lvvlrqh#jxwdp dwhujlfd#grvdjjlr#gd 4 3 3 #d#6 3 3 #p j,1

Anticolinergici

- Vrqr#vwdwl#sup l#idup dfl#dg#hvvhuh#vwdwl#
  lp slhjdwl#qh#wudwwdp hqwr#gl#txhvwd#sdwrorjld

- Lp hffdqlvp r#gÚd}lrqh · txhor#gl#dqwdjrqlvp r#
  p xvfdulqlfr d#dyhor#ghjd#lqwhuqhxurql#
  qljurvwuldwdd

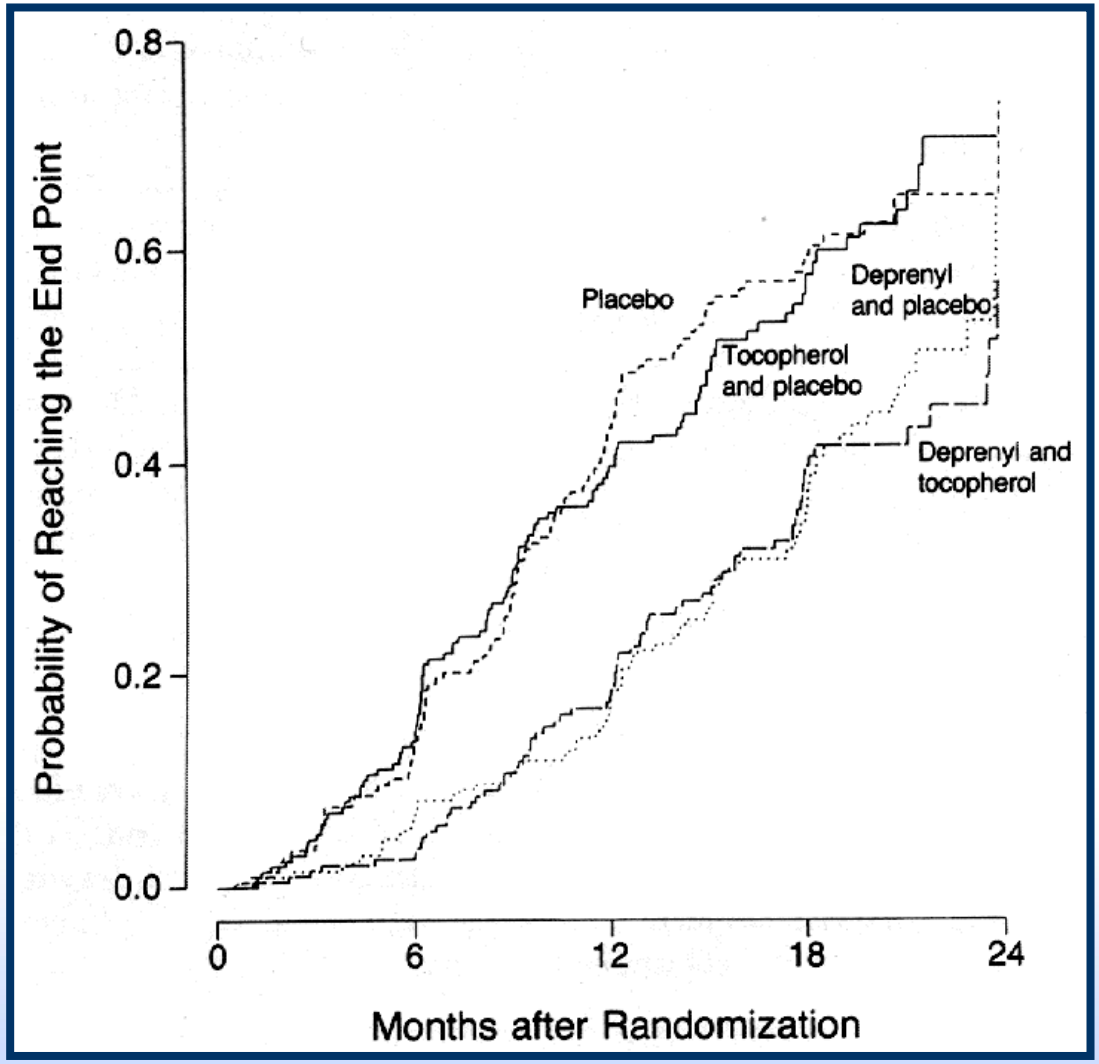
- Lp#eorffr#p xvfdulqlfr#vl#hvhuflwd#dqfkh lq#dowuh#
  duhh gh#VQF#h#vxo#vlvwhp d#qhuyrvr#dxwrqrp r/#
  frq#frqvhjxhqwh#hiihwwl#frodwhudd#fhqwuddh#
  shulihulfl

- OÚhiilfdfld#ghjd#dqwlfrdqhujlfl · p rghvwd#h#
  suhydh#vxo#wuhp ruh h#uljglw<1#

Inibitori MAO - Selegilina

- Oh#P DR#vrqr#hq}lp l#fkh#vyrojrqr xq#uxror#
  lp sruwdqwh#qho#fdwderodvp r#lqwudqhxurqdoh#gh l#
  qhxurwudvp hwwlwrul
- Oh#P DR0E#udssuhvhqwdqr flufd#ÓJ; 3 (#ghoh P DR#h#
  ghdp lqdqr ol#grsdp lqd/#surgxfhqgr#vrvwdq}h#
  wrvvlfkh##txdd l#udglfdo#behul
- Od#vhohj lbqd##· xq#P DR0E#luuhyhuvleh frq#xq#
  p rghudwr#hiihwwr#vlqwrp dwlfr
- Iud l#vxrl#p hwderdwl#vl#dqqryhudqr ol#O0dqihwdp lqd/#h#
  ol#O0p hwdqihwdp lqd/#vrvwdq}h#idflbwdqwl#lbuhohdvh#gl#
  grsdp lqd/#vhssxu lq#p lvxud#p lqruh#ulvshwwr#dool G0
  dqihwdp lqd

Selegilina, Vitamina E e Parkinson
DATATOP



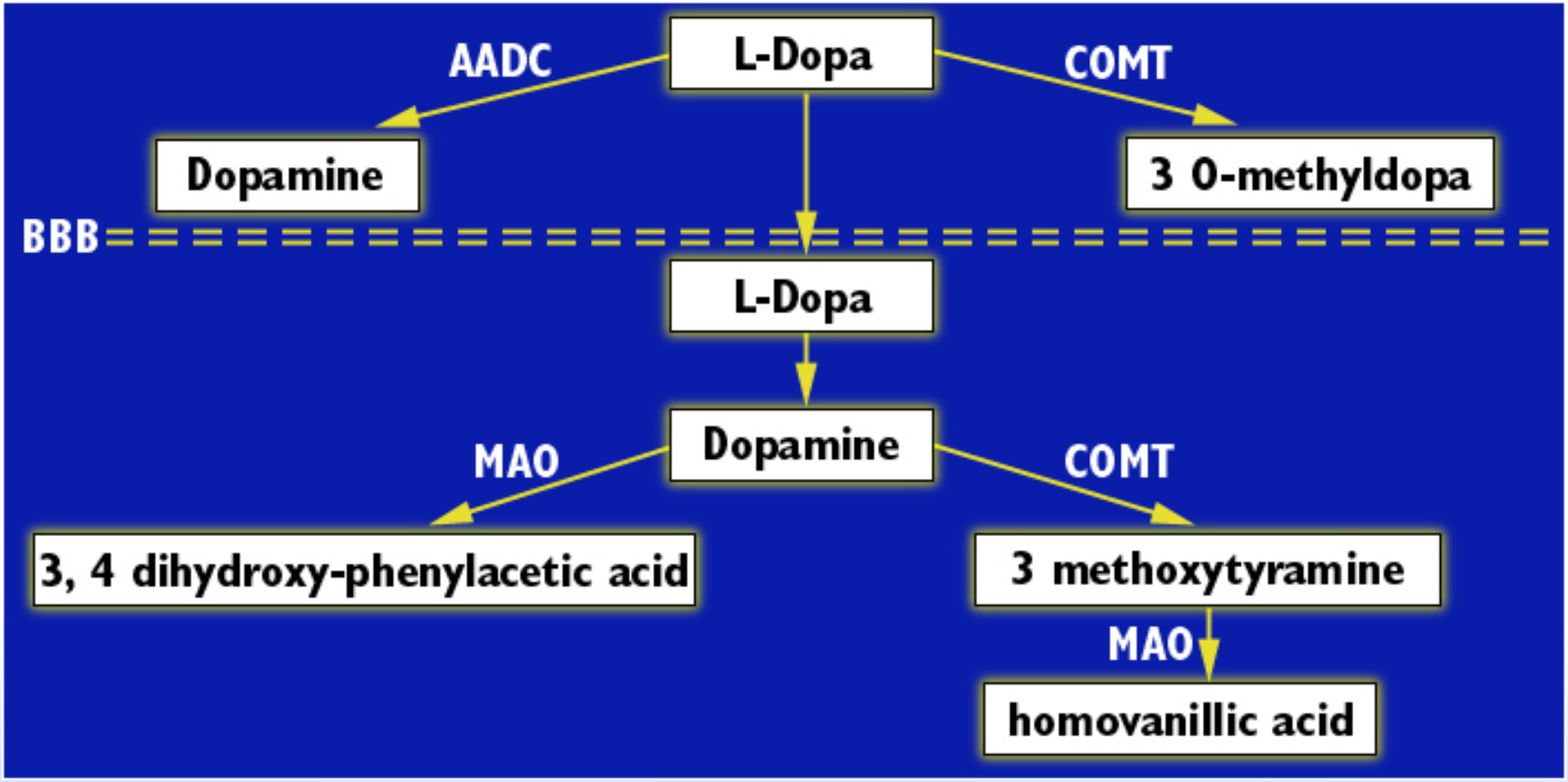
NEJM 1993

Levodopa

- Vylxssr#whup lqdwr#qhjd#dqqlÑ93>#glyhqqh# udslgdp hqwh#le#idup dfr#slxÚxwld}}dwr#qhœl# whudsld#ghœl#p dœlwwl
- HÚxq#dp lqrdflgr#qhxwur>#ulfklhgh# wudvsruwr#dwwlyr#dwwudyhuvr#ÓÍqwhvwlqr h# shu#vxshuduh œl#eduulhud#hp dwr0hqfhiddfd
- Udslgd#ghfduervvlœl}lrqh lq#shulihuld vh# qrq#vl#xwld}}dqr#lqelwrul#ghœh#grsd0 ghfduervvlœlvl+fduelgrsd/#ehqvhud}lgh,

Cotzias GC Engl J Med 1967; 276: 374-379
Nutt JG Clin Neuropharmacol 7: 35-49
Le Witt et al. Neurology: 39 Suppl 1: 45-53

Metabolismo della L-Dopa e Dopamina



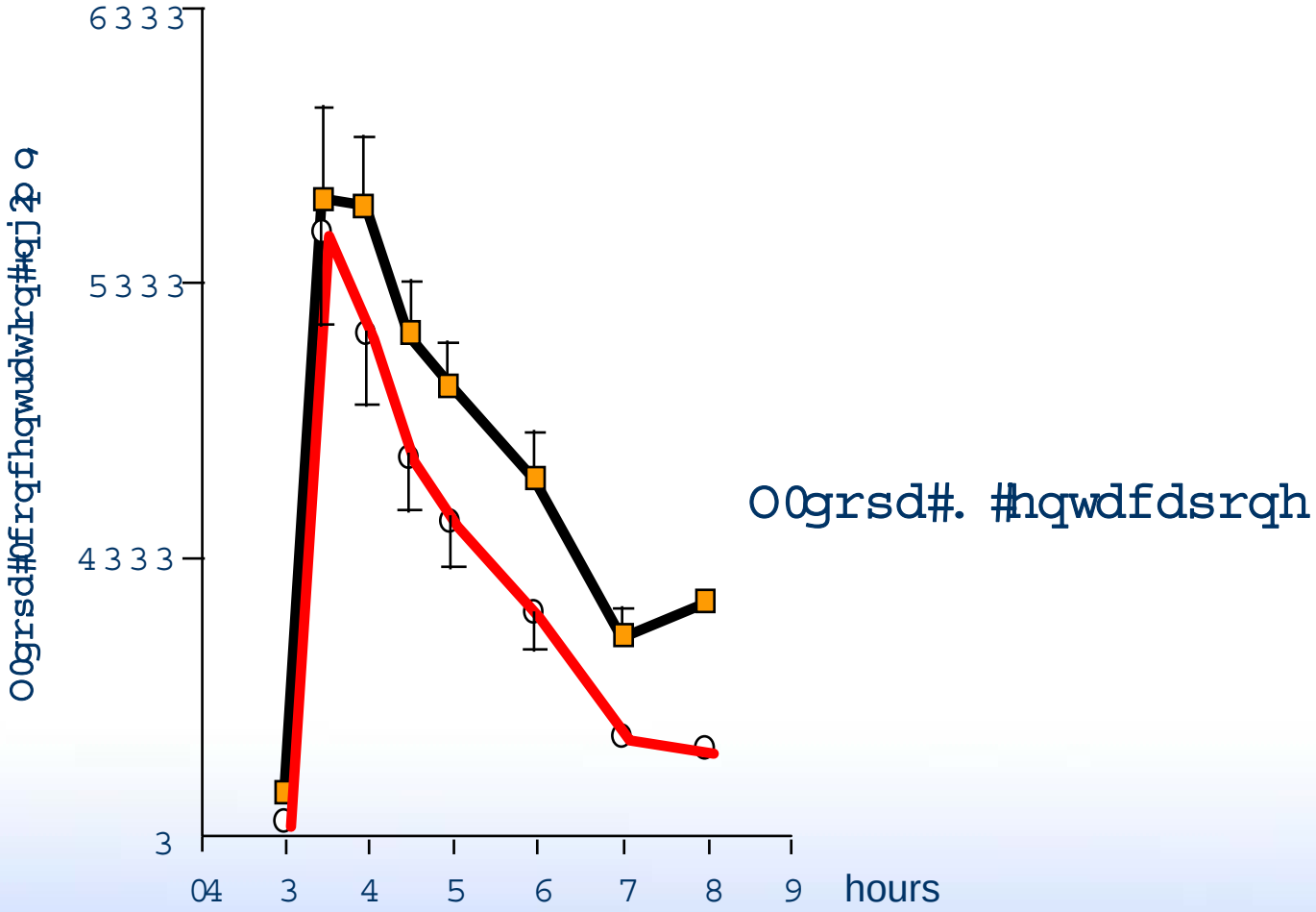
Inibitori COMT - Entacapone

- Lqlelwruh#shulihulfr#uhyhuvleln/#frq#xqÚ‚p lylwd#
  sodvp dwlfd#gl4/8#ruh1

- Hqwdfdsrqh#dxp hqwd#ÚÍhp lylwd#gl#hqp lqd}lrqh#ghoœl
  O0grsd/#vhq}d#dxp hqwduh ol#Fp d{/#lqrwuh#ubgxfh l#
  dyhol#sodvp dwlf l#gl*6 0R 0P hwlgrsd*/#p hwderdwd#
  srwhq}lln#frp shwlwruh#ghœl O0grsd shu#lofduuhu#d#
  dyhor#ghœl#eduuhud#hp dwr0hqfhiddfd1

- Vwxgl#kdqqr#hylghq}lwr#fkh#ÚÍdxp hqwr#ghoÚÍhp lylwd#
  sodvp dwlfd#ghœl O0grsd/#vl#dvvrfld dg#xqd#
  glp lqx}lrqh ghœ*z hdubqj0rii* frq#lqfuhp hqwr Šrqõ gl
  flufd#4#rud2jlruqr1

Effetto dell'entacapone sull'emivita della levodopa



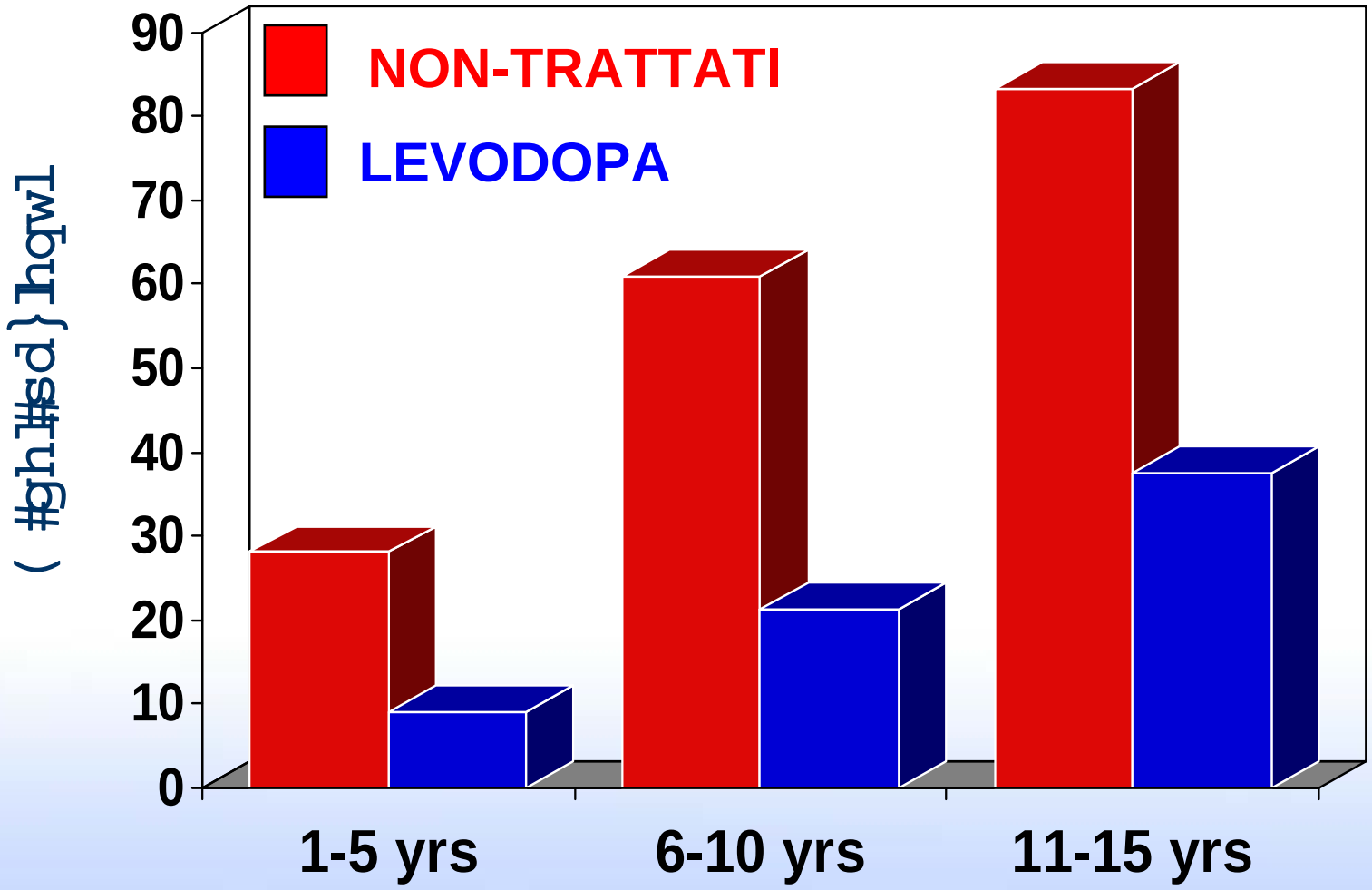
Caratteristiche farmacocinetiche delle diverse formulazioni di L-dopa

Wp d{=#whp sr#lq#fxl#ylhqh#udjjlxqwd#dl#p dvvlp d#frqfhqwud}lrqh#scdvp dwlfd>

W4 25=#hp lylwd#scdvp dwlfd

Idup dfr	Wp d{ +p lq,	W4 25 # +ruh,	Ohj1# surwhlqh#+(,	Elrglvsrqleldw< +(,
O0grsd###	q1g1	3 /9 03 /<	q1g1	<<
O0grsd. IGG	6 3 04 5 3	4 06	q1g1	<<
O0grsd. fduelgrsd FU#####	4 5 3 04 ; 3 ##########	7 08	q1g1	: 3
O0grsd. ehqvhud}lghKEV	4 5 3 05 7 3	9 0;	q1g1	9 3
O0grsd#p hwlhvwhuh##########	5 7 09 3	3 /5 03 /9	q1g1	<<
Iqlelwruh#ghoo#grsdghfduervvldvl1				
Ehqvhud}lgh##############	9 3	? 5	q1g1	q1g1
Fduelgrsd##################	6 3 06 3 3 ###########	5	q1g1	q1g1

Percentuale pazienti con grave disabilità in epoca pre- verso post-levodopa



Hoehn, 1983

Levodopa: Farmacodinamica

ORQJ#GXUDWLRQ#UHVSRQVH=

˘Vlp dqlhvwd#grsr#jlruqlr#vhwwlp dqh#glwudwwdp hqwr#frq#OO Grsd#h#ulfklhgh#xq#dowuhwwdqwr#xqjr#shulrgr#glwhp sr#shu# hvdxuluvl#dwhup lqh#ghoodl#vrp p lqlvwud}lrqh#ghoh#idup dfr

˘Suhydoh#qhoh#idvl#lqlzldl#glp dolwwld

VKRUW#GXUDWLRQ#UHVSRQVH=

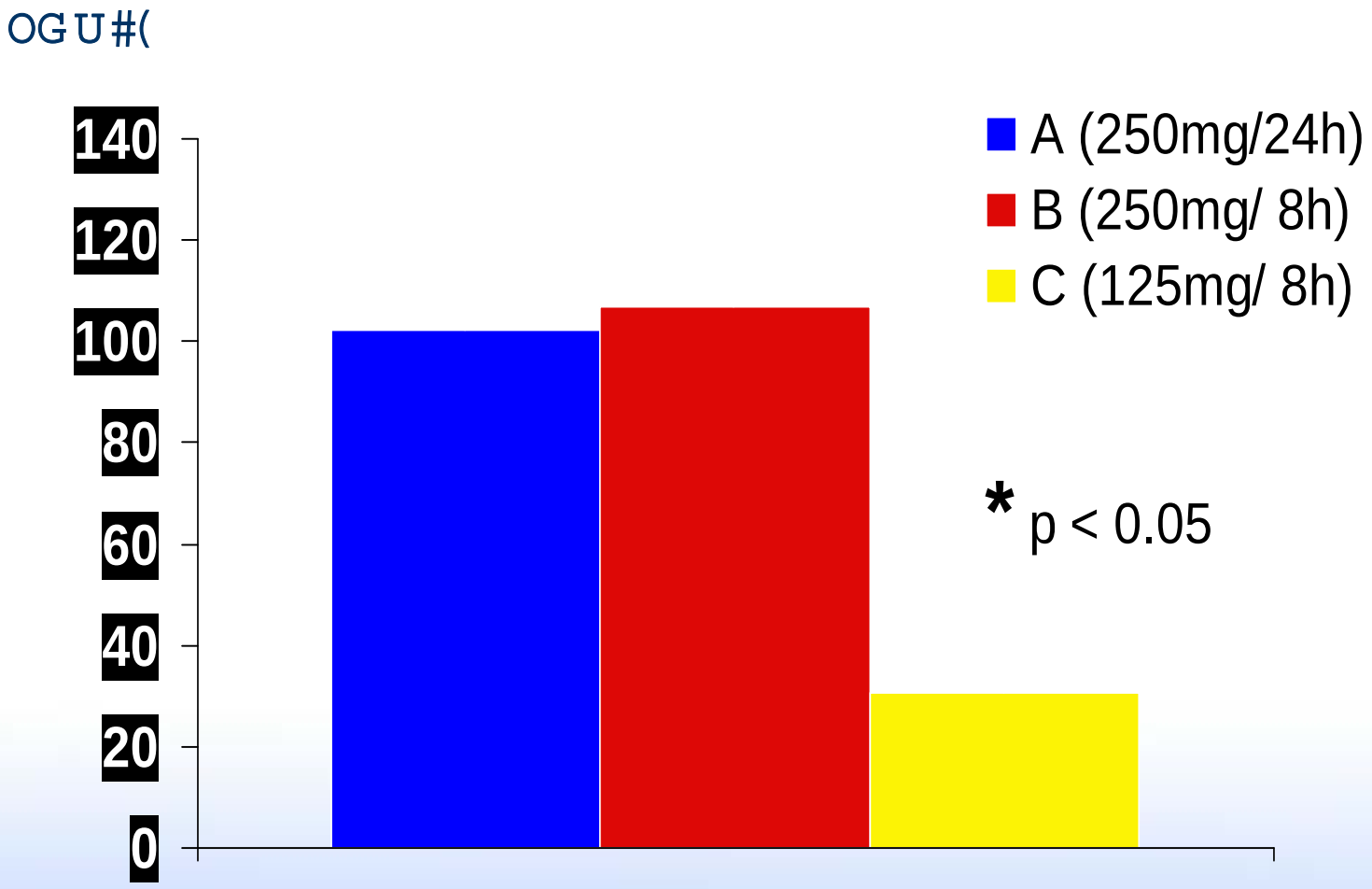
˘P ljdrudp hqwr#ghl#vlqwrp l#fkh#gxud#p lqxwlr#ruh>#vlp dqlhvwd# grsr#xqd#vlqjrodl#vrp p lqlvwud}lrqh#glOO Grsd/#lq#idvh#frq#h# frqfhqwud}lrql#sodvp dwlfkh#ghoh#idup dfr1#

˘Suhydoh#qhoh#idvl#dydq}dwh#glp dolwwld

Mauter MD et al. Mayo Clin Proc 46: 231-239 Nutt JG Ann. Neurol. 39: 561-573 Zappia M et al. Neurology 1999; 52: 763-767

Impiego della L-dopa

Importanza della singola dose per la LDR



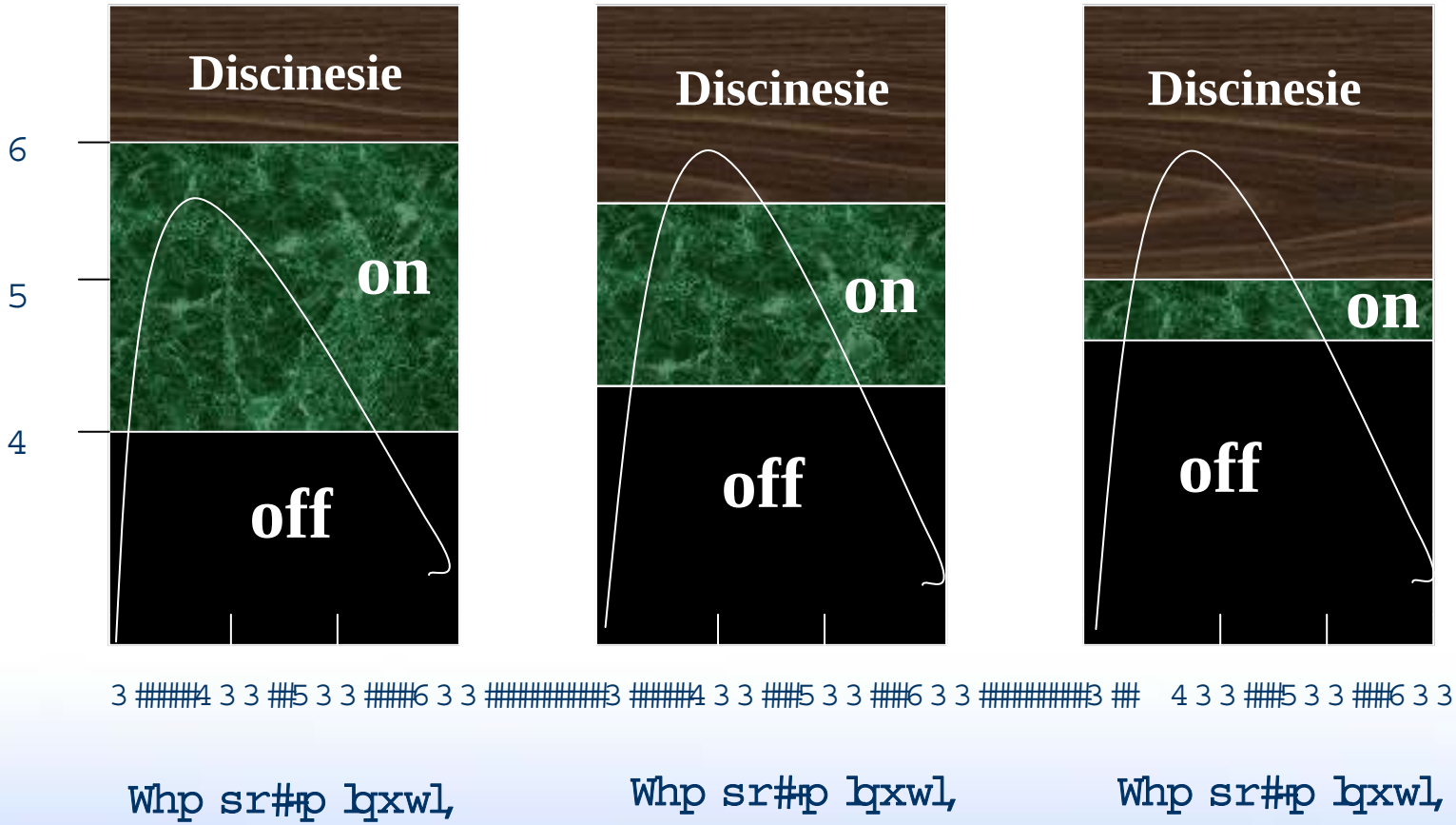
Zappia et al Neurology 2000

USO DELLA L-DOPA NELLA MALATTIA DI PARKINSON

VYDQWDJJL

- Q rq#hiilfdfh#shu#Šiuhh}lqjõ/#lqvwdeldw< srvwxudoh/# glvdxwrqrp ld h#ghp hq}d1
- Q rq#duuhvwd#ol#surjuhvvlrqh#ghoo#p dodwwld1
- Euhyh#hp lylwd#solvp dwlfd frq#dvvruelp hqwr# glshqghqwh#gdor#vyxrwdp hqwr#jdvwulfr1
- Ulfklhgh#wudvsruwr#dwwlyr#dwwudyhuvr#ólqwhvwlqr#h# shu#vxshuduh#ol#eduulhud#hp dwrhqfhiddfd1
- Vylxssr#gl#frp sdfdq}h#p rwruh1

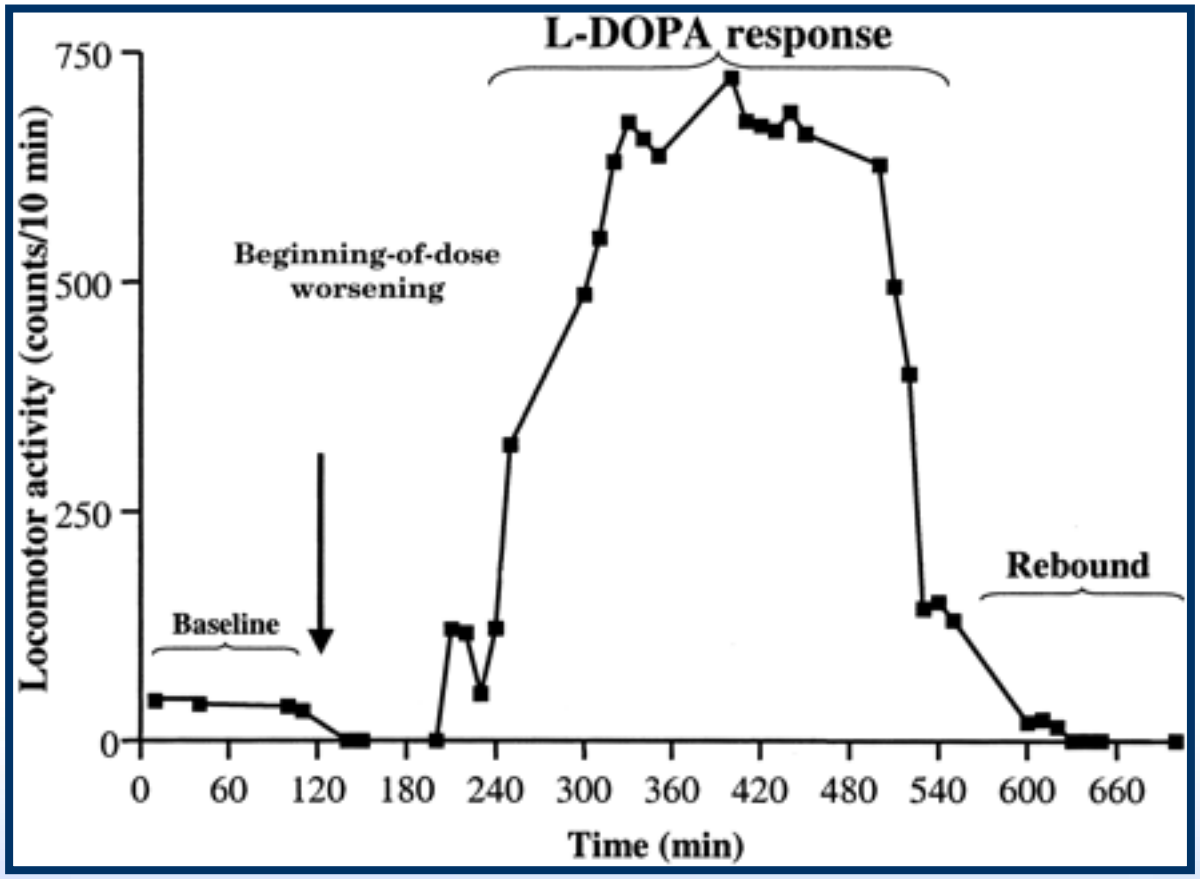
Effetto della progressione della malattia sulla finestra terapeutica della L-dopa



Levodopa (μg ml)

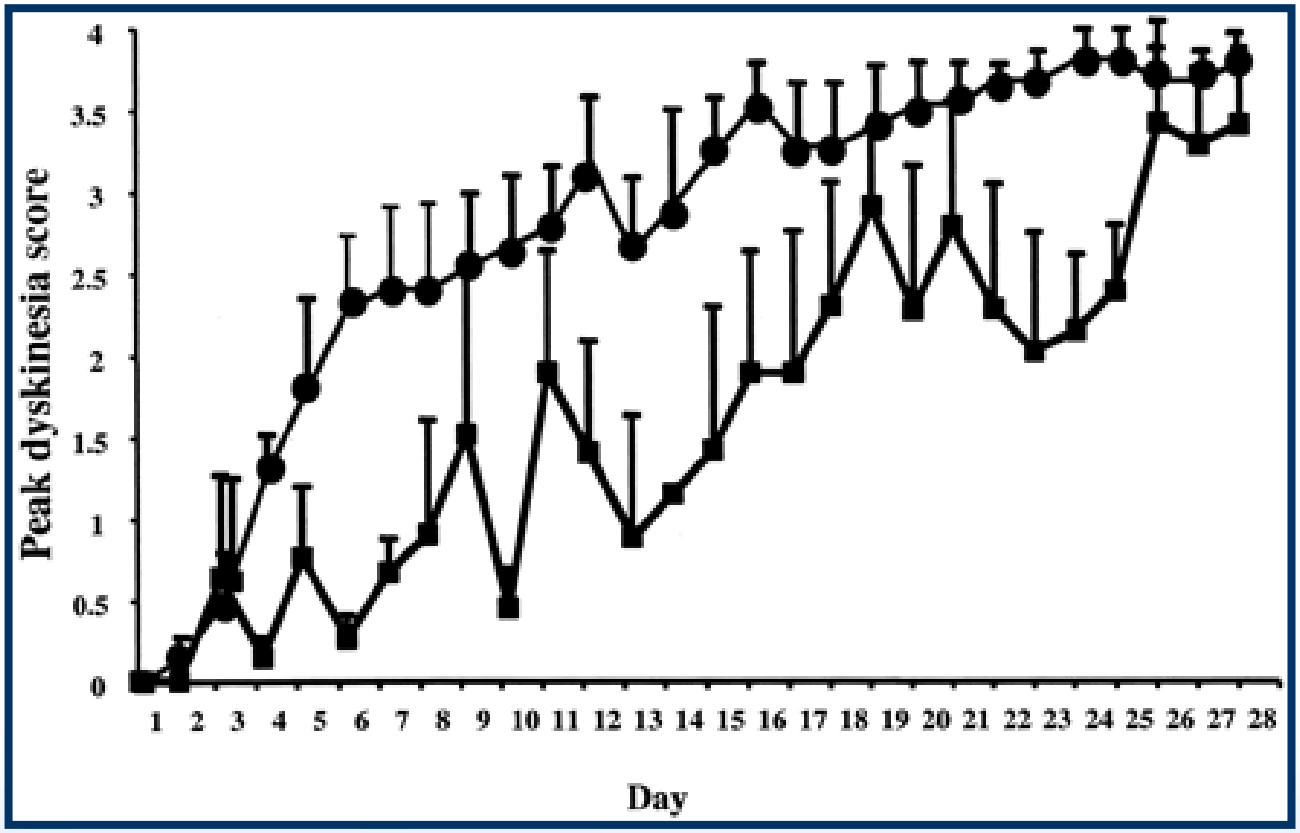
Obeso JA, Olanow W, Nutt JG. Levodopa motor complications in Parkinson's disease. Trends Neurosci 23 (Suppl. Basal ganglia, Parkinson's disease and levodopa therapy), S2-S7

Risposta acuta alla levodopa nella scimmia trattata con MPTP



Jenner P Neurology 2003

Crescente incidenza delle discinesie nella scimmia lesionata con MPTP dopo inizio terapia con levodopa



ol#vrp p lqlvwud}lrqh#gl#gxh#grvl#+0o 0, ghwhup lqd glvfinhvlh#sI udslgdp hqwh#ghoo#vlqjrol#grvh#0q 0

Jenner P Neurology 2003

Discinesie e Fluttuazioni

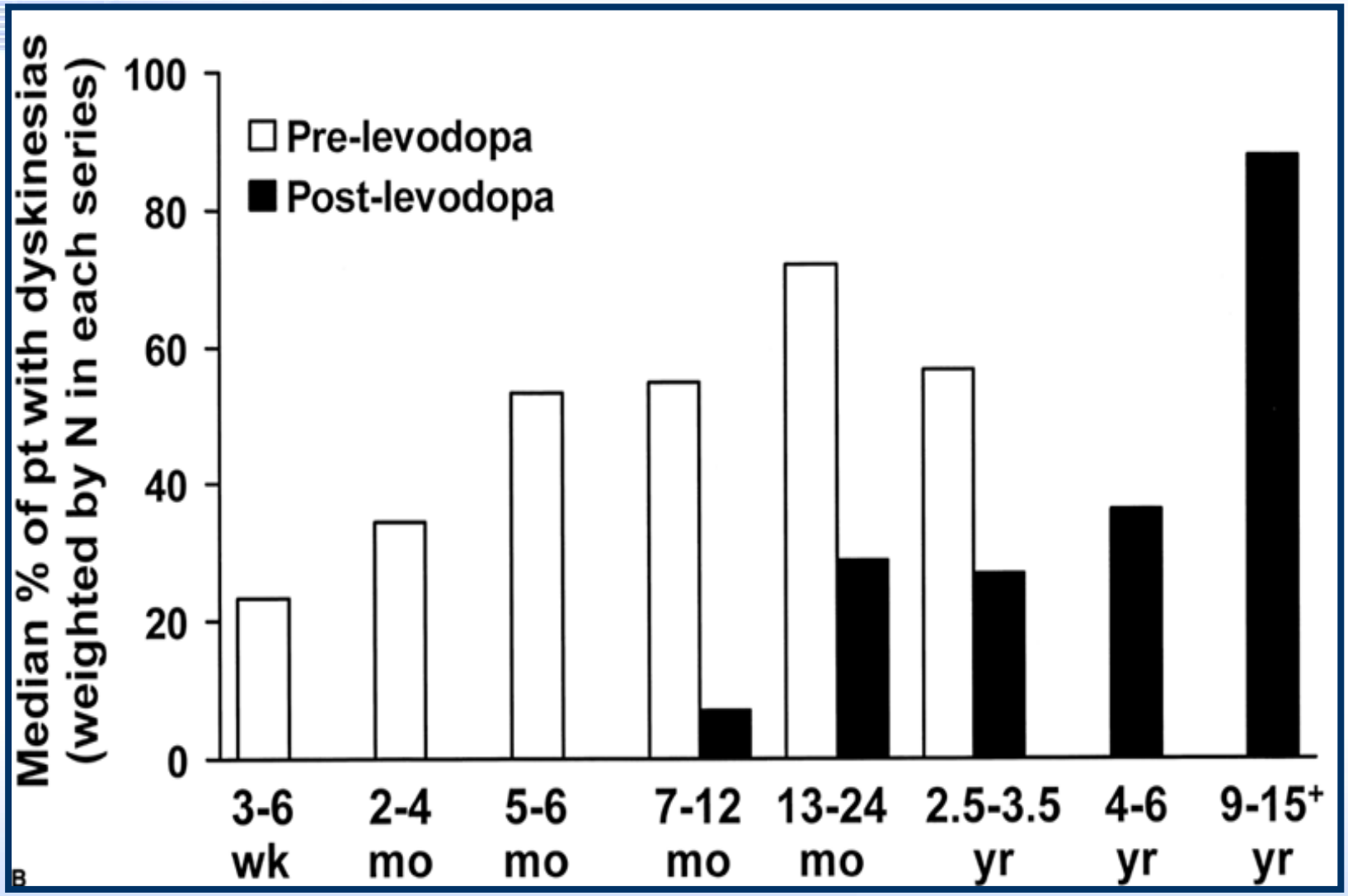
- P hq}lrqdwh#gd#Frw}bdv#qhoQ #HqjoM#P hg#4<9:

- Lqwhuydor#wud#bl}lr#wudwwdp hqwr frq#bhyrgrsd h#
  hvrugr#ghoh#glvfqhvh bq#449#sd}lhqwl

Ù 4##p hvh#	53(
Ù 5##p hvl	6<(
Ù 6##p hvl	79(
Ù 9##p hvl	86(
Ù <##p hvl	9:(
Ù 45#p hvl	;4(

Duvoisin Neurology 1974

Discinesie e Fluttuazioni



Ahlskog, Muenter Mov Dis 2001

Complicazioni motorie e sindrome da trattamento a lungo termine con levodopa

- Lqfoxgrqr=#ixwwxd}lrqh#p rwruh +z hdubqj0rii/# rq0rii,#h#glflqhvh#
- Frp sdfdq}h#p rwruh#kdqqr xq#lqflghq}d#gl# flufd#lo#43 (#shu#dqqr#qhoh#wudwwdp hqwr#d# oxqjr#whup lqh#frq#ohyrgrsd##
- Grsr 8#dqqlglwhudsld frq#ohyrgrsdflufd#lo 83 (#gh#sd}lhqwh#suhvhqwd z hdubqj0rii
- Od#vwlp rod}lrqh#sxovdwlh#frq#idup df# grsdp lqhujlf#d#euhyh#hp lylwd +hv1#ohyrgrsd,# vhp eud#hvvhuh#lo#p hffdqlvp r#uhvsrqvdelh

Koller WC et al, 1999. Poewe WH, 1994. Fahn S, 1992

Razionale per Stimolazione Dopaminergica Continua

- OÚlqixvlrqh#frqwlqxd#gl#hyrgrsd#sxrÚulgxuh#p dufdwdp hqwh#h#ixwwxd}lrql#p rwruh

- Vwudwhjlh#shu#rwwhqhuh#vwlp rol}lrqh#grsdp lqhujlfd frqwlqxd#srvvrqr#ulgxuh#h#ixwwxd}lrql#p rwruh# hvlvwhqwl#dg#hvhp slr#grsdp lqr#djrqlvwl#d#xqjd#hp lylwd# frp h#fdehujrdqd,

- Vwlp rol}lrqh#frqwlqxd#grsdp lqhujlfd/#vh# ql}lwd#dolÚl}lr#ghh#wudwwdp hqwr#sxrÚulgxuh# dÚlqflghq}d#gl#frp sdfd}lrql#p rwruh

Levodopa a rilascio modificato

IPOTESI: Formulazioni di levodopa a rilascio modificato, se iniziate all'inizio, potrebbero ridurre il rischio di complicazioni motorie

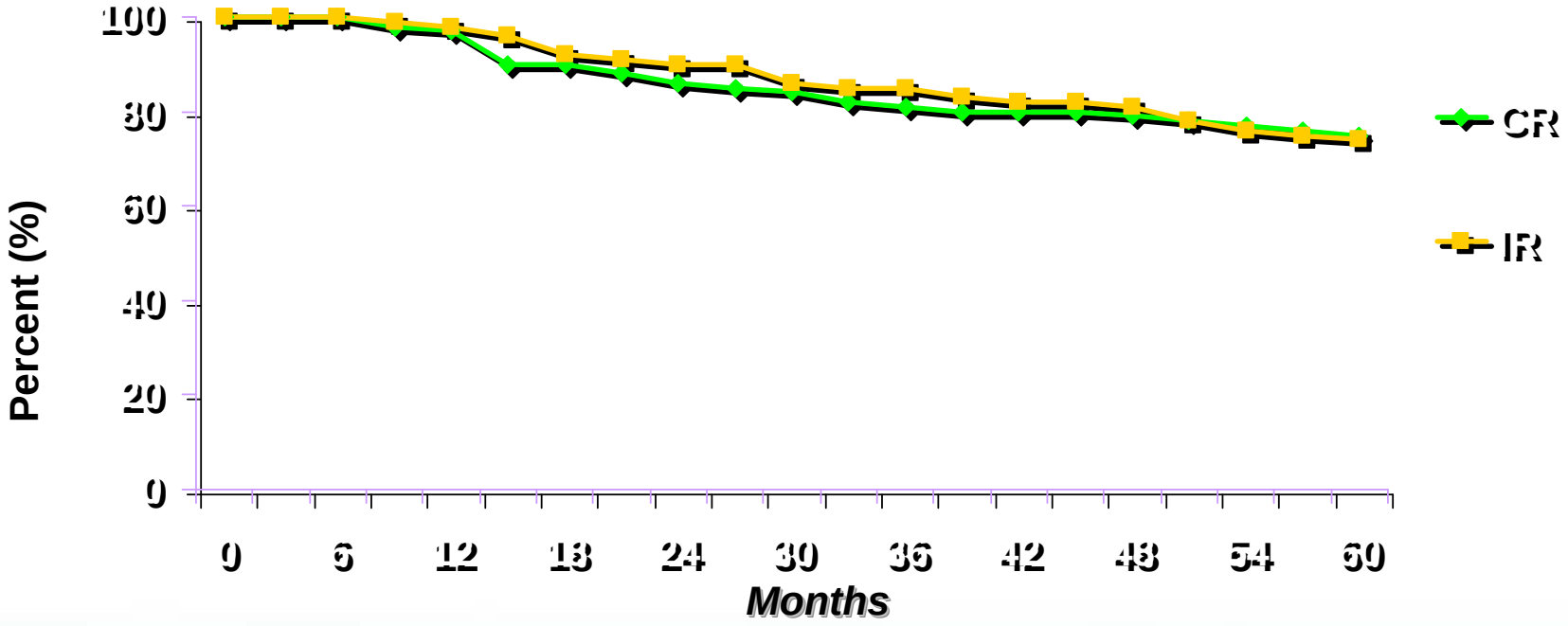
IIUVW#Vwxq|

- 94;#SG#sdwlhqwv/#bhyrgrsd#qdlyh=
  - Ù 639#fduelgrsd2bhyrgrsd IU
  - Ù 645#fduelgrsd2bhyrgrsd FU
- Grxeh0edqg/#udqgrp l}hg/#sdudoohoh#vwxg|
- 8#|hduv wuhdwp hqw
- Sulp du|#hqgsrlqw È wlp h#wr#rqvhw ri#p rwru# ixfwxdwlrqv

Block et al, 1997.

Non ci sono differenze nel rischio di complicanze motorie tra levodopa standard e levodopa a rilascio modificato

Kaplan-Meier Survival Distribution per fluttuazioni motorie



- Erwk#LU#dqg#FU#irup xodwlrqv#p dlqwdlqhg#d#vlp lodu#hyhd#ri#frqwurd#q#SG#diwhu#8#|hduv
- Diwhu#8#|hduv/#wkhuh#z dv#qr#vljqlilfdqw#gliihuhqfh#ehwz hhq#jurxsv#rq#p rwru# ioxfwxdwlrqv#hlwkhu#e|#gldu|#ru#txhvwlrqqdluh

Block et al. 1997

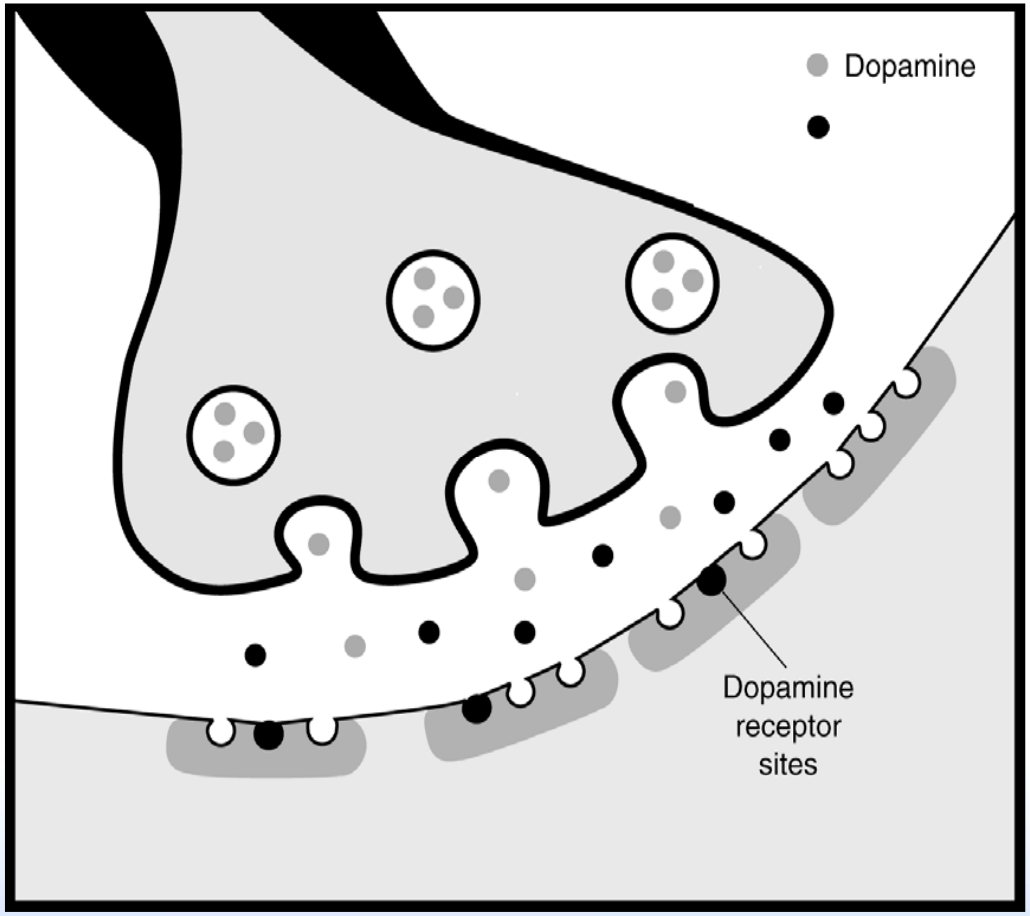
Prevenzione delle complicanze motorie

Evidenza clinica da studi controllati in pazienti con MP iniziale

Guxjv##	Gxudwlrq ri#wuhdwp hqw#+|u,######	Hiilfdf|
Surorqjhg#ohyrgrsd#devruswlrq		
Ohyrgrsd2fduelgrsd FU	8	Idlxuh
Ohyrgrsd2ehqvhud}lgh KEV	8	Idlxuh
FRP W#lqklelwlrq Hqwdfdsrqh	0	Wr eh#whvwhg
Wrfdsrqh	Wuldo#lqwhuuxswhg################	Wr eh#whvwhg
P DR0E#lqklelwlrq Vhohjhqh	8	Idlxuh
Ohyrgrsd . #grsdp lqh#djrqlvw		
Ohyrgrsd . #eurp rfulswlqh	8	Hiihfwlyh
Gluhfw#grsdp lqh0uhfhswru#vwlp xodwlrq		
Sudp lsh{rdh	5Ù7	Hiihfwlyh
Urslqlurdh	8	Hiihfwlyh
Fdehujrdqh	6Ù8	Hiihfwlyh
Shujrdgh	6	Hiihfwlyh

Barone Neurology 2003

Meccanismo d'azione dei farmaci dopaminergici



Dopamino agonisti: Ipotesi di lavoro

Wudwwdp hqwr#bqlzbdn frq#grsdp bqr djrqlvwl

Ulgxfrqr#bdnulvfklr#gl#frp sdfd}lrqlp rwruh

Gdqqr#ehqhilf#fdqf#vlp bdnd#bnyrgrsd

Kdqqr xq#suriior#gl#wrohudebwdÚdffhwwdebn

Sviluppo dei dopamino agonisti: Storia

Dgg0rq#d#dmyrgrsd

↓

P rqrwhudsld sup d#ghoo#dmyrgrsd

↓

Whudsld#lq}lbn frq#ehqhilfld#xqjr#whup lqh

↓

Whudsld#lq}lbn frq#ehqhilfld#xqjr#whup lqh

↓

Q hxursurwh}lrqh

Dopamino agonisti

- Vwlp rolqr#gluhwwdp hqwh#uhfhwwruh#grsdp lqhujlfl srvw0vlqdswlfl#p lp dqgr#Íd}lrqh#ghoo#grsdp lqd
- Surfxudqr#xq#ehqhilflr#vlqwrp dwlfr#vlo#lq#djjlxqwd# doo#D0grsd/#fkh#qhoh#idvl#lqlzldd#lq#p rqrwhudslo1
- Grsr#406#dqqlgl#p rqrwhudslo frq#grsdp lqrdjrqlvwl h#frq#lo#surjuhgluh#ghoo#p dodwwl/#lo#frqwurorr#ghoo# vlqwrp dwrorjlo#ulfklhgh#Íd}djjlxqwd#ghoo#D0grsd
- Srvvrqr#suryrfduh#qdxvhd/yrp lwr/lsrwhqvlrqh# ruwrvwdwlfd/#p hqwuh#d#dyhor#fhqwudo#srvvrqr# fdxvduh#lqfxel/#doxflqd}lrqlr#vrqqrohq}d

Dopamino Agonisti: Dosi medie

Hujrdqlfl=

- 0 Eurp rfulswlqd : /8 048 #p j
- 0 Shujrdgh 5 06 #p j
- 0 Fdehujrdqd 6 07 #p j

Q rq#Hujrdqlfl=

- 0 Sudp lsh{rcr 4 /8 06 #p j
- 0 Urslqlurcr 9 045 #p j

Dopamino Agonisti: Dosi equivalenti

Hujrdqlfl=

- 0 Shujrdgh 4 #p j
- 0 Fdehujrdqd 4 /8 #p j

Q rq#Hujrdqlfl=

- 0 Sudp lsh{ror 4 #p j
- 0 Urslqlurr 8 #p j

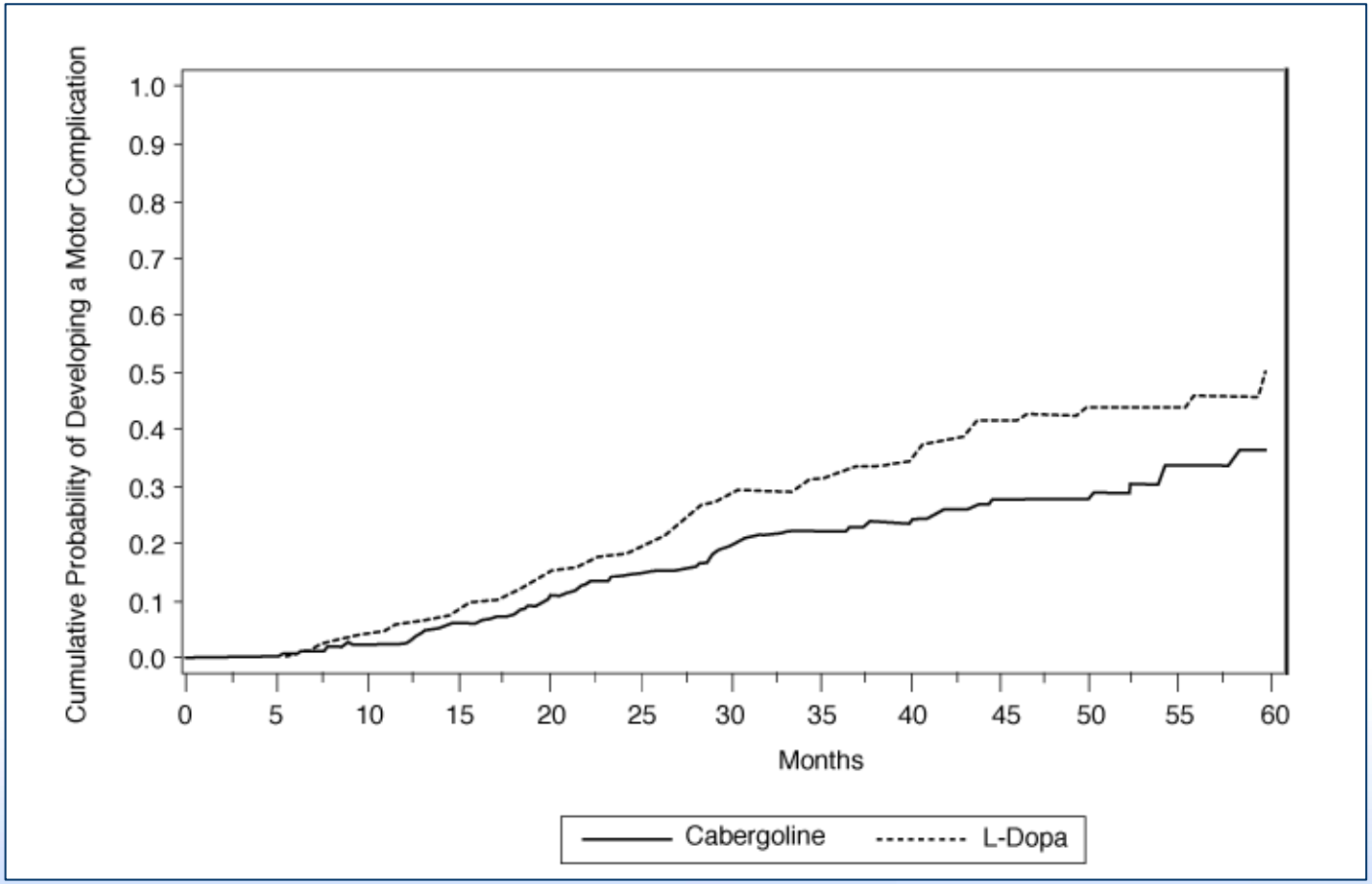
Il trattamento precoce con dopamino agonisti riduce il rischio di complicazioni motorie

Vwxg/	Gxudwlrq	*P hdq#Grvh Ohyrgrsd*	*P rwru# Frp sdfdwlrq*	*P rwru Frp sdfdwlrq Iuhtxhqf/*
OOGrsd#yv# urslqluroor Udvfro/#5333	8#|hduv	URS=#75:#p j OOGRSD=#:86#p j	G|vnlqhvld	OOGRSD=#78(URS=#53(
OOGrsd#yv# fdehujrdqd Ulqqh/#4<<;	8#|hduv	FDE=#765#p j OOGRSD=#:;7#p j	G|vnlqhvld ru P rwru#Lxfwxdwlrq	OOGRSD=#67(FDE=#55(
OOGrsd#yv# sudp lsh{ror SVJ/#5333	5#|hduv	SS[=#597#p j OOGRSD=#83<#p j	G|vnlqhvld ru P rwru#ixfwxdwlrq	OOGRSD=#84(SS[=#5;(

- Hduo|#wuhdwp hqw#z lwk#grsdp lqh#djrqlvwv#kdv#ehhq#vkrz q#wr# uhvxow#lq#orz hu#iuhtxhqf|#ri#p rwru#frp sdfdwlrqv#
- Lqfuhdvlqj#grvhv#ri#ohyrgrsd ryhu#h{whqghg#shulrgv#uhvxowv lq#kljkhu#iuhtxhqf|#ri#p rwru#frp sdfdwlrqv

Cabergolina: Studio a 5 anni

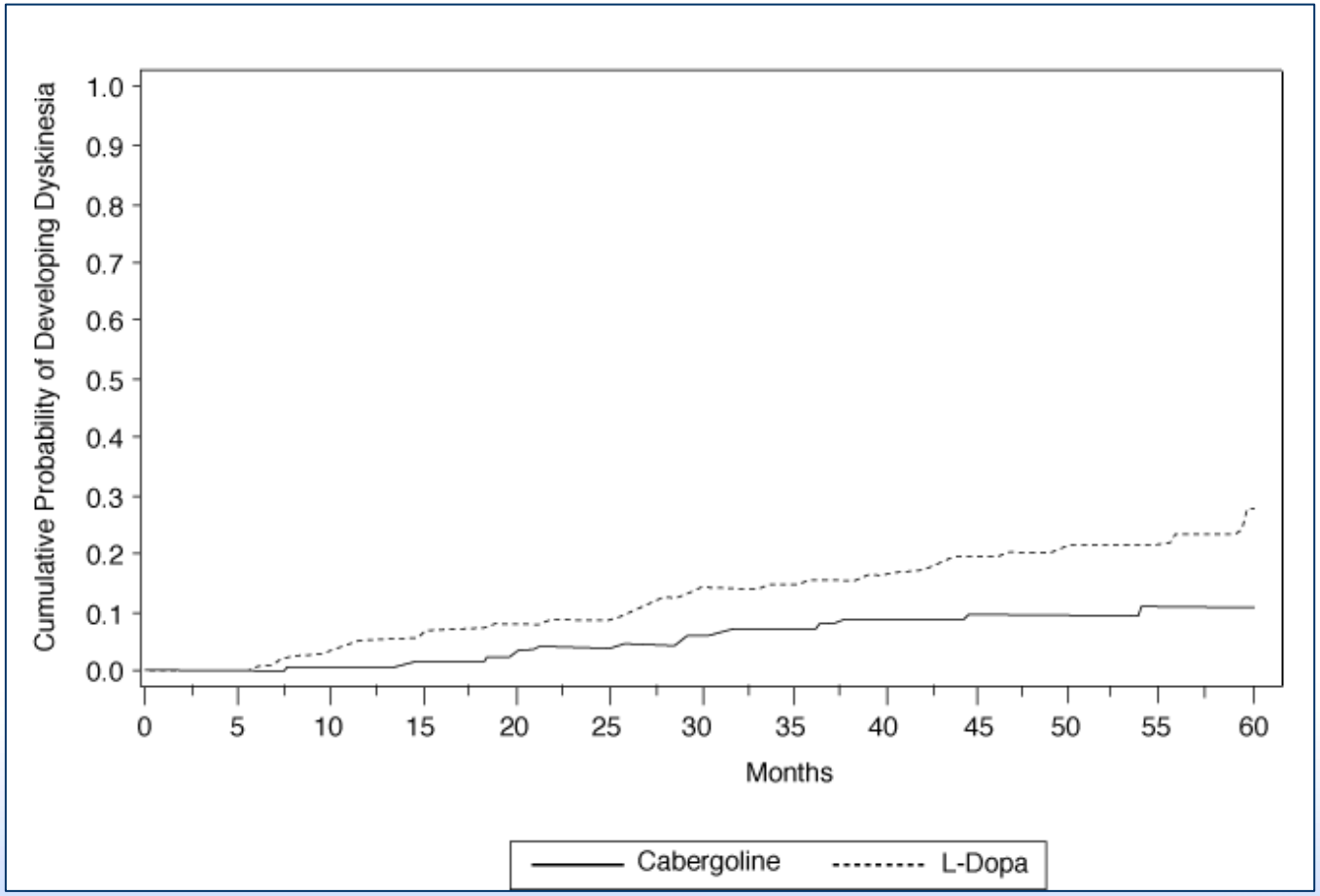
Rischio di sviluppare complicanze motorie



Bracco et al Drugs 2004

Cabergolina: Studio a 5 anni

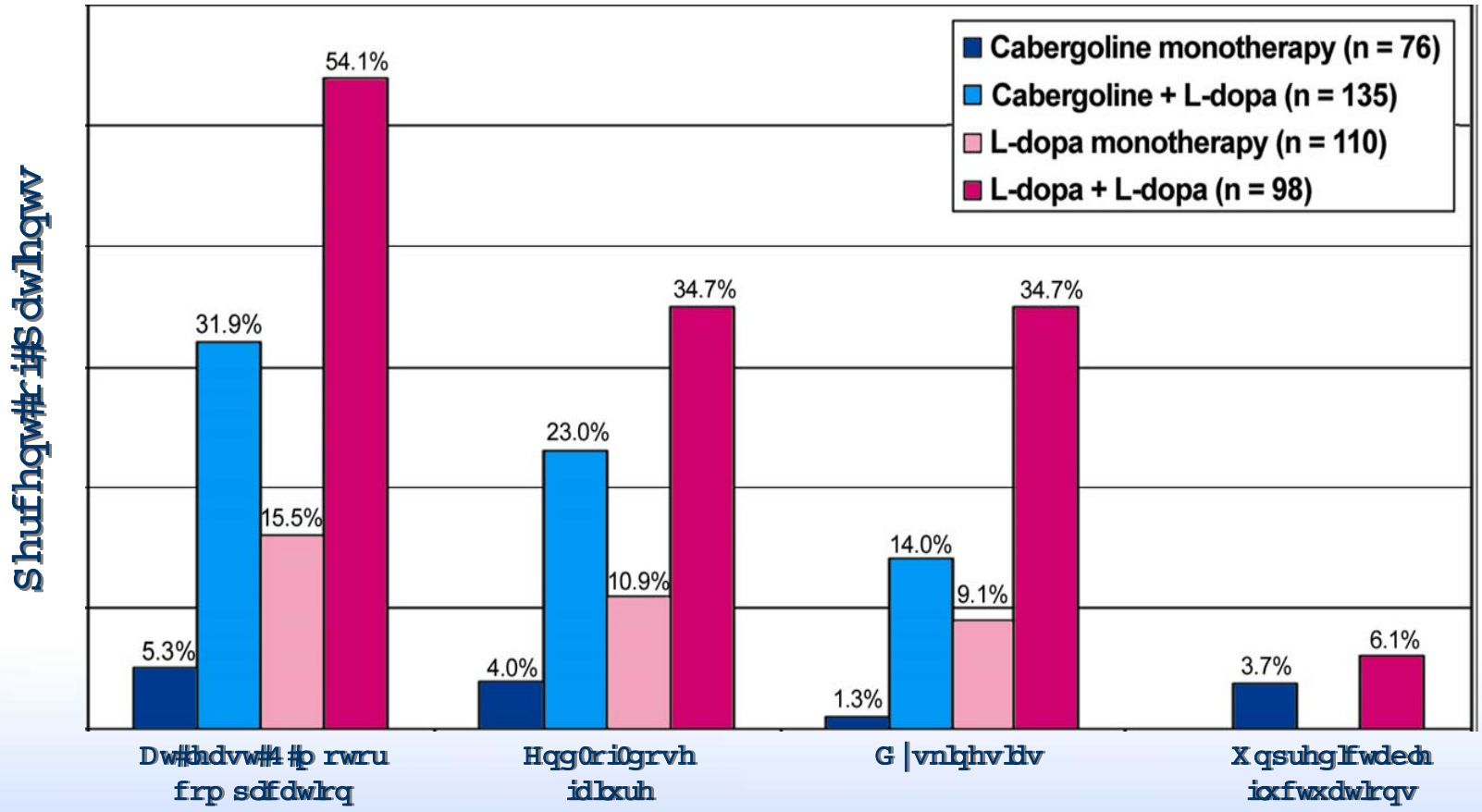
Rischio di sviluppare discinesie



Bracco et al Drugs 2004

Cabergolina Studio a 5 anni

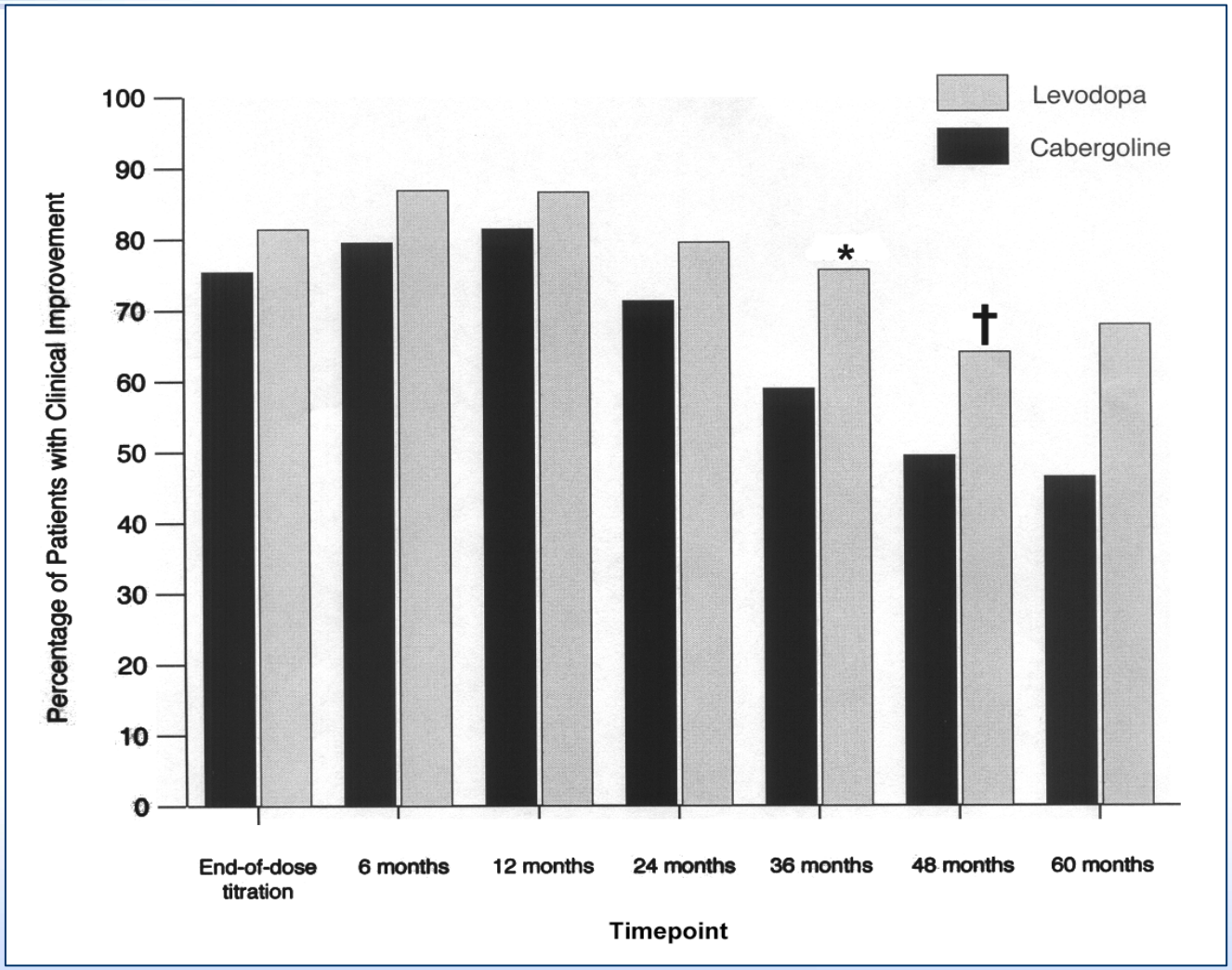
Comparsa di complicanze motorie



Bracco et al. Drugs in press

Cabergolina: Studio a 5 anni

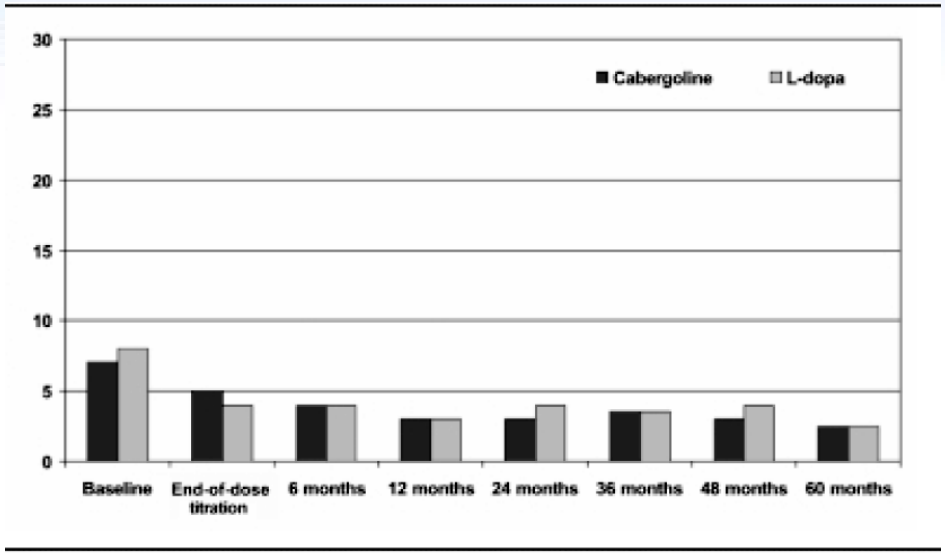
% Pazienti con miglioramento clinico



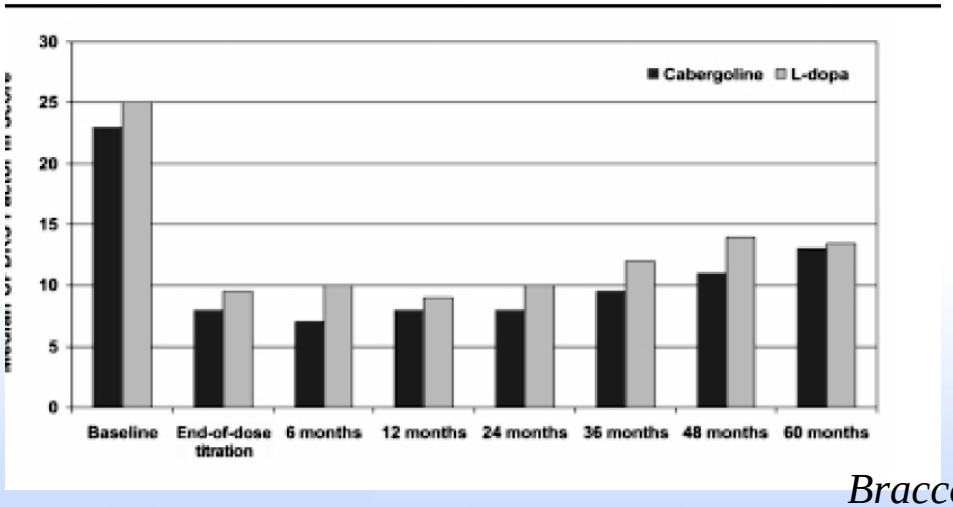
Bracco et al. Drugs in press

Cabergolina: Studio a 5 anni

XSGUV0IL
DGO

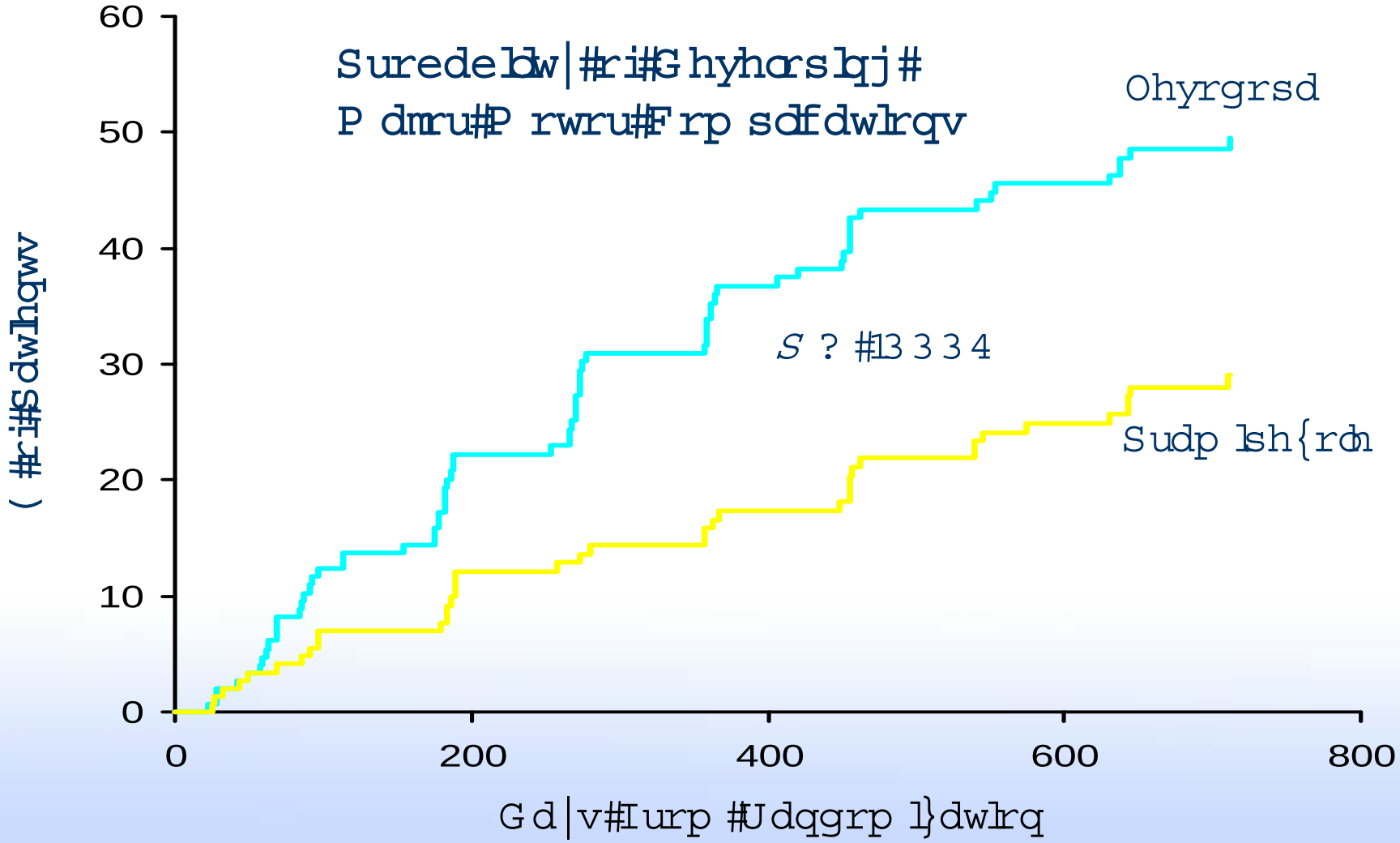


XSGUV0IIL
P rwrulb

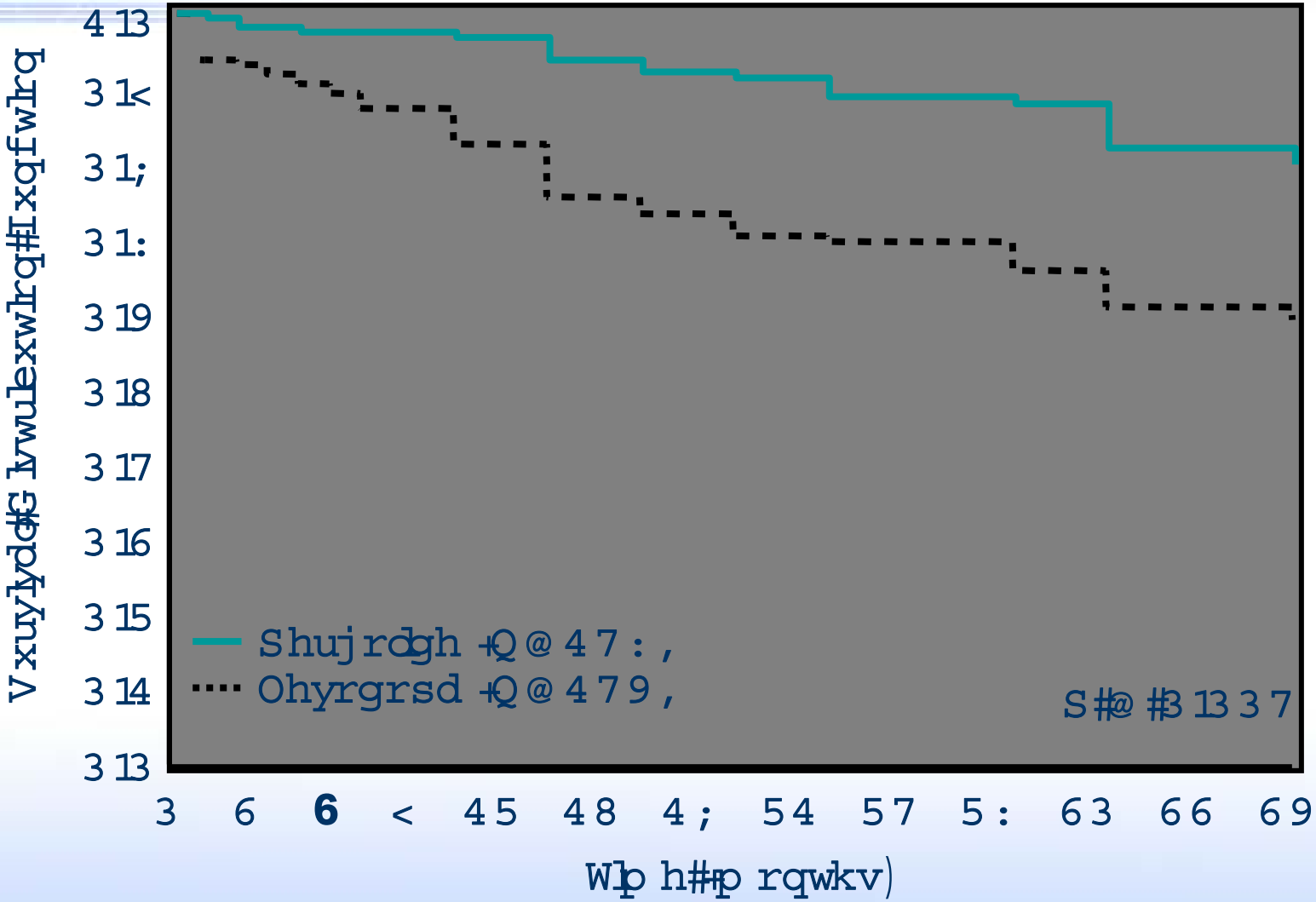


Bracco et al. Drugs in press

CALM-PD: Pramipexolo vs Levodopa

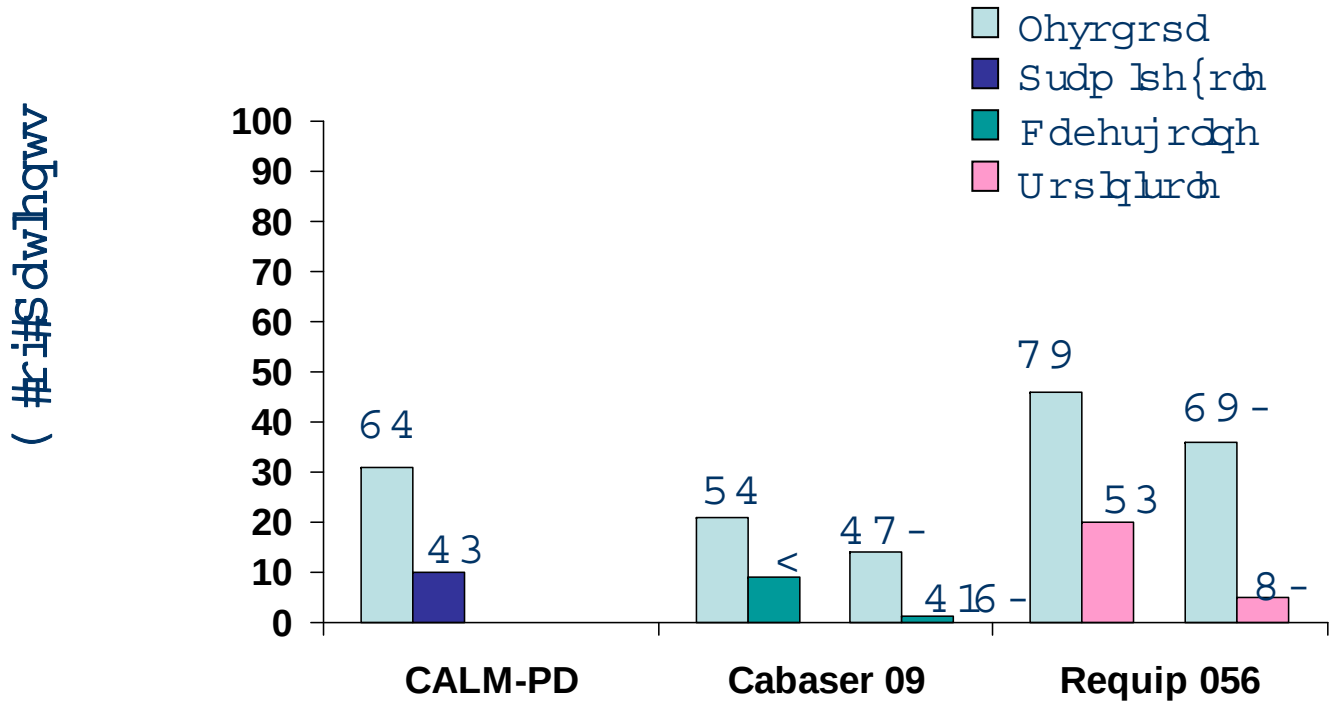


Tempo all'esordio di discinesie
(UPDRS Part IV A)



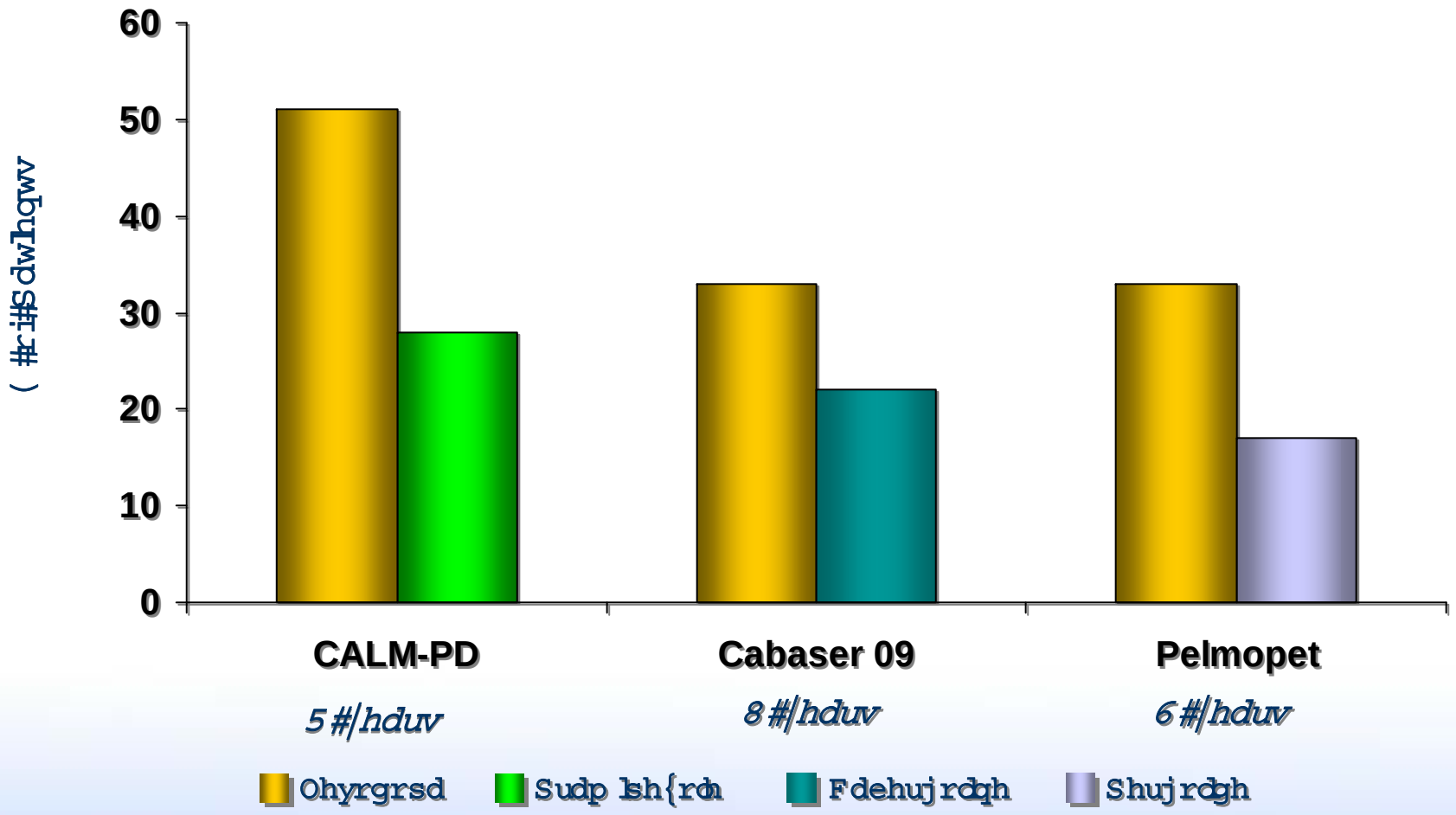
Oertel et al. (abstr) Mov Disorder 2000

Effetti sulle Discinesie: Risultati



*Monotherapy.

Dopamino Agonisti
Complicazioni motorie



Dopamino agonisti e neuroprotezione

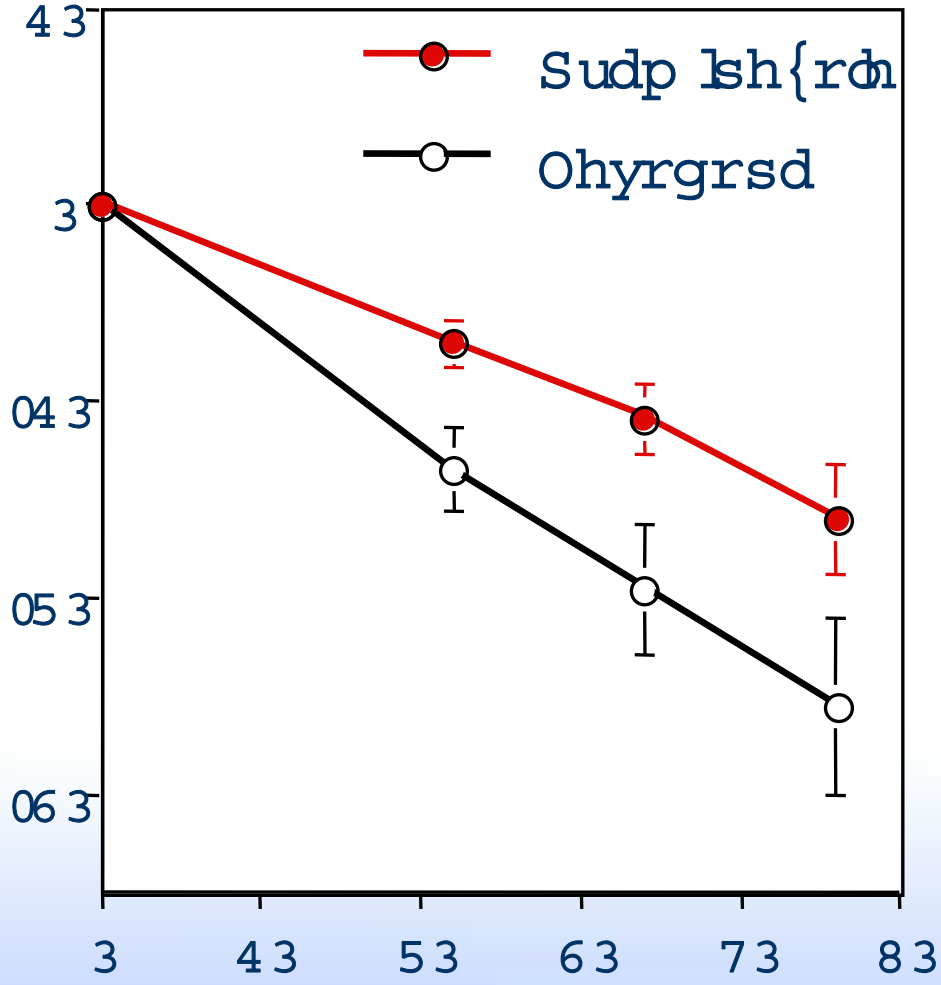
Progressive loss of Striatal DAT measured by ß-CIT Uptake

Merek et al JAMA 2002

CALM-PD

Neuroprotezione

% Change in Striatal ß-CIT Uptake from Baseline



Merek et al JAMA 2002

REAL PET
Ropinirolo nella MP iniziale

% Cambiamento nella captazione della Fluorodopa/PET

	Ropinirolo	Levodopa
N Pazienti	68/93	54/93
% Discinesie	3,3	25,3
% Riduzione FDOPA uptake nel Putamen	**- 13,43**	**- 20,28**

Whone et al. Ann Neurol 2003

Dose di levodopa supplementare nei pazienti con trattamento precoce con dopamino agonista

Vwxg|	Gxudwlrq	Qr1#Sdwlhqwv Dvvljqhg#wr Djrqlvw	Sdwlhqwv#Frp sdwlqj Vwxg|#rq#Grsdp lqh Djrqlvw#P rqrwkhuds| +(	Sdwlhqwv#Uhtxluqj Ohyrgrsd Vxssdp hqwdwlrq
L- Dopa vs ROP Rascol, 2000. (Requip 056)	5 years	179	29/179 (16%)	ROP = 56/179 (31%) L-Dopa = 16/89 (18%)
L- Dopa vs CAB Rinne, 1998 (Cabaser 09)	5 years	211	76/211 (36%)	CAB = 135/211 (64%) L-Dopa = 98/208 (47%)
L- Dopa vs PPX PSG, 2000 (CALM-PD)	2 years	151	48/151 (32%)	PPX = 80/151 (53%) L-Dopa = 58/158 (39%)

Dopamino agonisti
Conclusioni

- Ghwhup lqdqr#xqd#vwlp rol}lrqh#
  grsdp lqhujlfd frqwlqxd#xqjd#hp lylwd,#

- Ulgxfrqr#lqulvfklr#gl#ixwxd}lrqlp rwruh

- Srvvrqr#udoohqwduh ol#surjuhvvlrqh#gl#
  p dolwwld vh#ql}lwl#suhfrfhp hqwh

Come e quando iniziare il trattamento nel paziente con M. di Parkinson

- Lq#wudwwdp hqwr#vlqwrp dwlfr#gryuheeh#bqlzlduh qrq# dsshqd l#vlqwrp l#fdqlf#glyhqwdqr#hylghqwl
- L#grsdp lqr#djrqlvw#gryuheehur#hvvhuh#suhihulwl# dooólqlzlr#frqvlghudwr#lo#srwhqzldh#hiihwwr#vxoo# surjuhvvlrqh#gl#p dodwwld hg#lo#ulgrwwr#ulvfklr#gl# frp sdfdzlrq#p rwruh
- Od#ohyrgrsd#sx¿#hvvhuh#djjlxqwd#vxffhvvlydp hqwh p d# l#grvdjj l#gryuheehur#hvvhuh#p rghudwl+? #833#p j2gl h,

TERAPIA DELLA FASE INIZIALE

IDWWRUL#FKLDYH=

0 Frqgl}lrq#frjqlwlyh

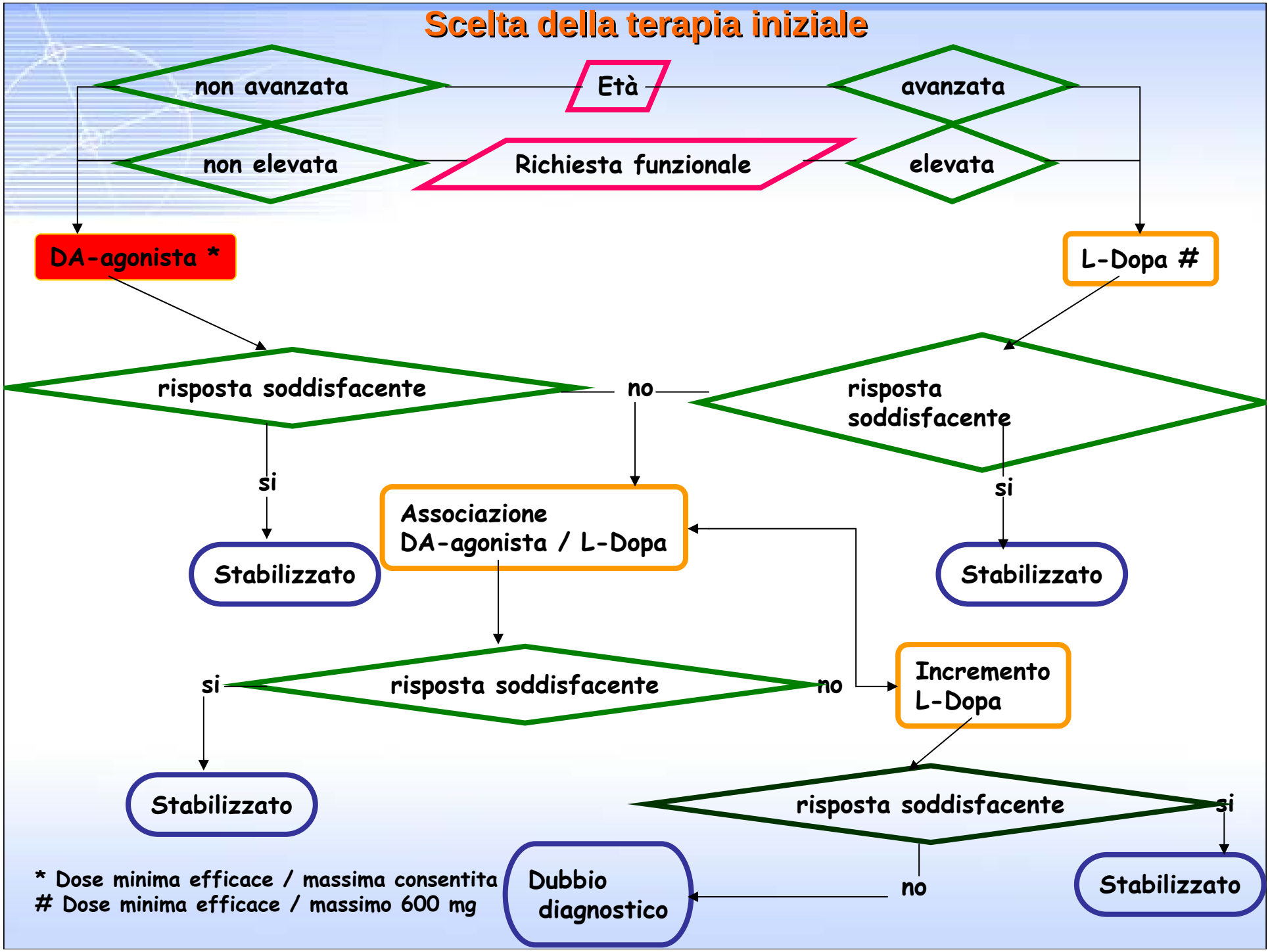
0 Hw< gh#sd}lhqwh

0 Ulfklhvwd#ixq}lrqdoh

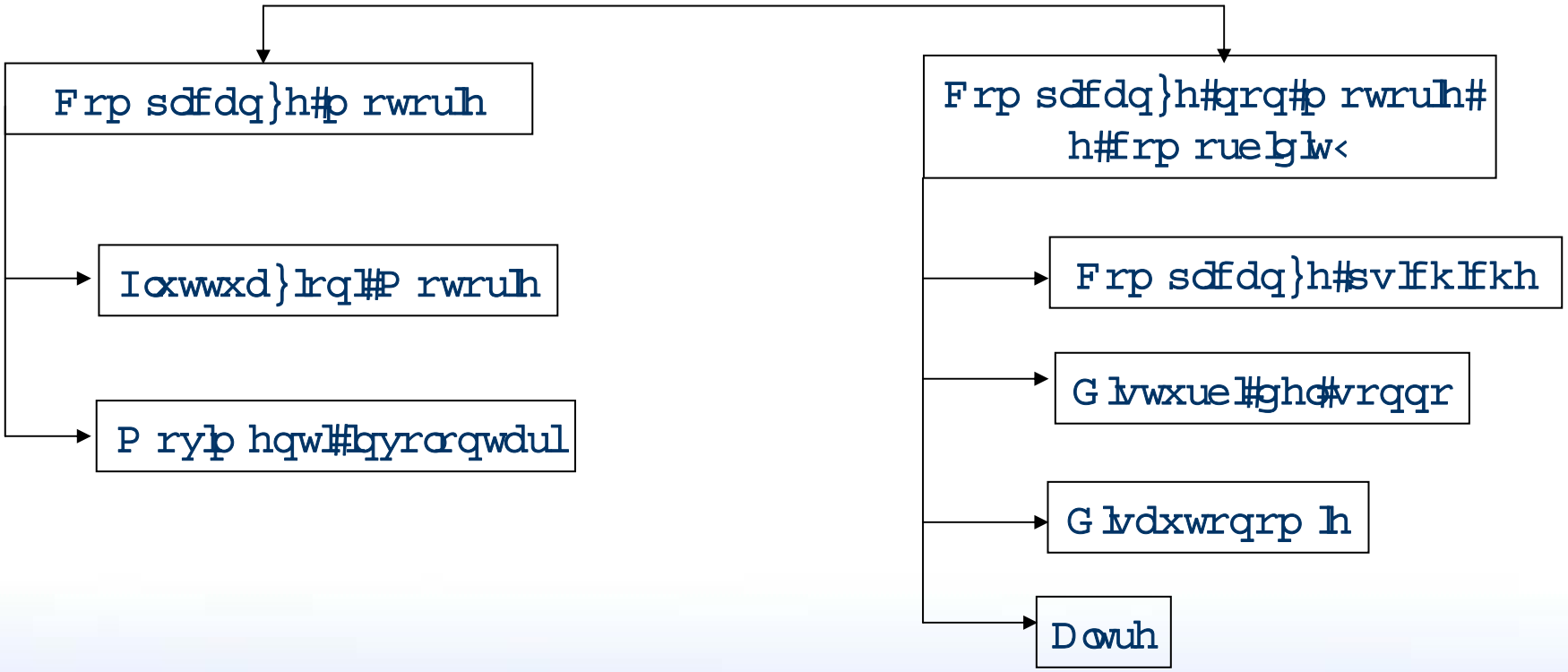
Linee guida per il trattamento della MdP: Neurological Science 2002 Suppl. 23

Malattia di Parkinson
Terapia della fase avanzata
Strategie terapeutiche

Scelta della terapia iniziale



Malattia di Parkinson in fase avanzata



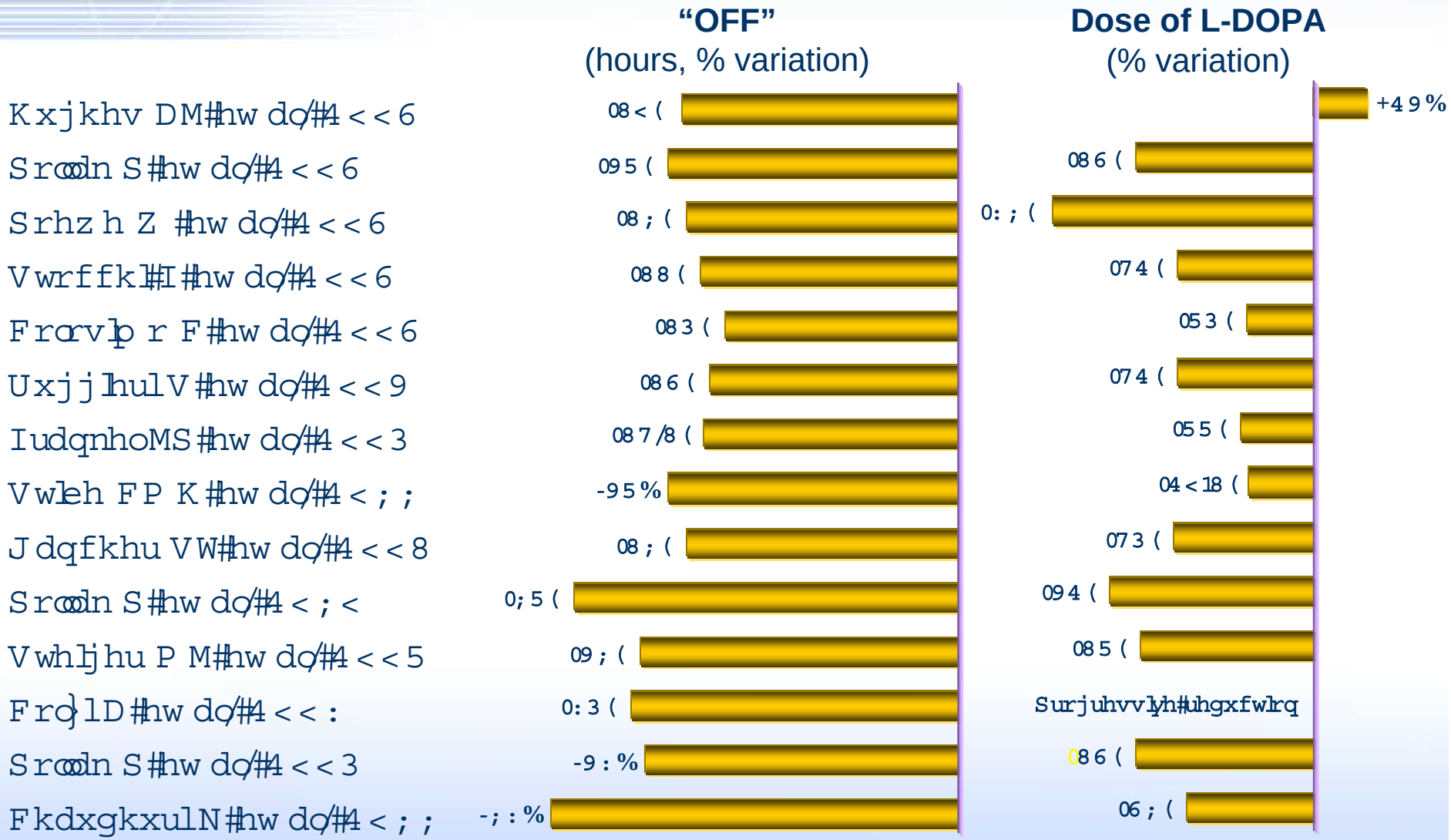
Linee guida per il trattamento della MdP: Neurological Science 2002 Suppl. 23

M di Parkinson avanzata

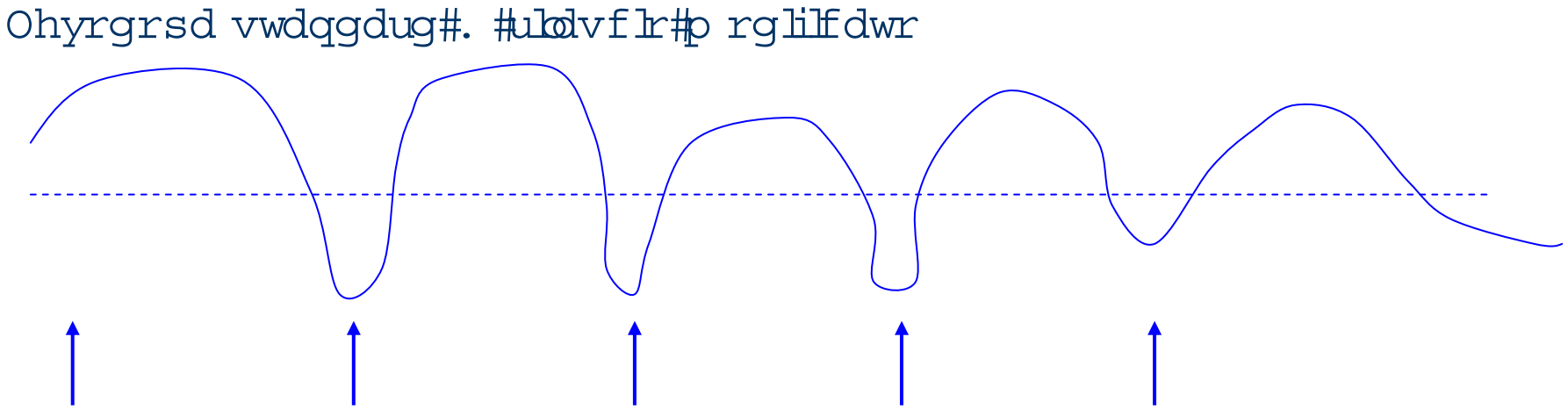
- OÚdjjlxqwd#gl#grsdp lqr#djrqlvwd lq# sd}lhqwl lq#p rqrwhudsld frq#hyrgrsd# frqvhqwh#gl=

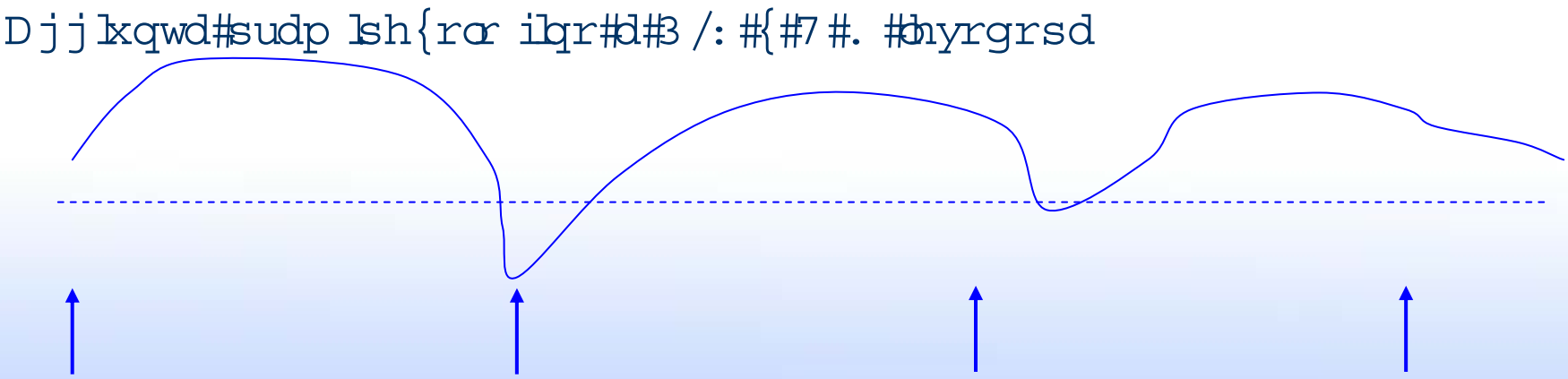
  - Ù Ulgxuuh l#grvdjjl#gl#hyrgrsd
  - Ù Ulgxuuh oh#ruh#glrii#glxuqr h#qrwwxuqr
  - Ù P ljdruduh od#txddw< glylwd

L'infusione sottocutanea di apomorfina



Effetto dell'aggiunta di pramipexolo sulle fluttuazioni motorie





Pramipexolo come add-on

Vwxgllq#sd}hqwlfrq#p dodwwld#dydq}dwd

Vwxglr	Sxeedfd}lrqh	Qr1#Sd}lhqwl
343#	*Qhxurorj*//4<<:	693
+yv sodfher,		
369	*Qhxurorj*//4<<:	579
+yv1#eurp rfulswlqd h# sodfher,		

Pramipexolo come add-on nella MP avanzata

Studio 010: Metodi

- P xovlfhqwhu/#grxeh0edqg/ solfher0frqwurodqg/#sdudoh0jurxs
- Sulp du|#hqg#srlqwv
  - XSGUV#sduwv#L#dqg#LL
- Vhfrqgdu|#hqg#srlqwv
  - P hdq#(#Šriiõ wlp h
  - P hdq#vhyhulw|#Šriiõ wlp h
  - Ohyrgrsd grvh#uhgxfwlrq
  - Sdunqvrq#G |vnqhvld Vfdoh

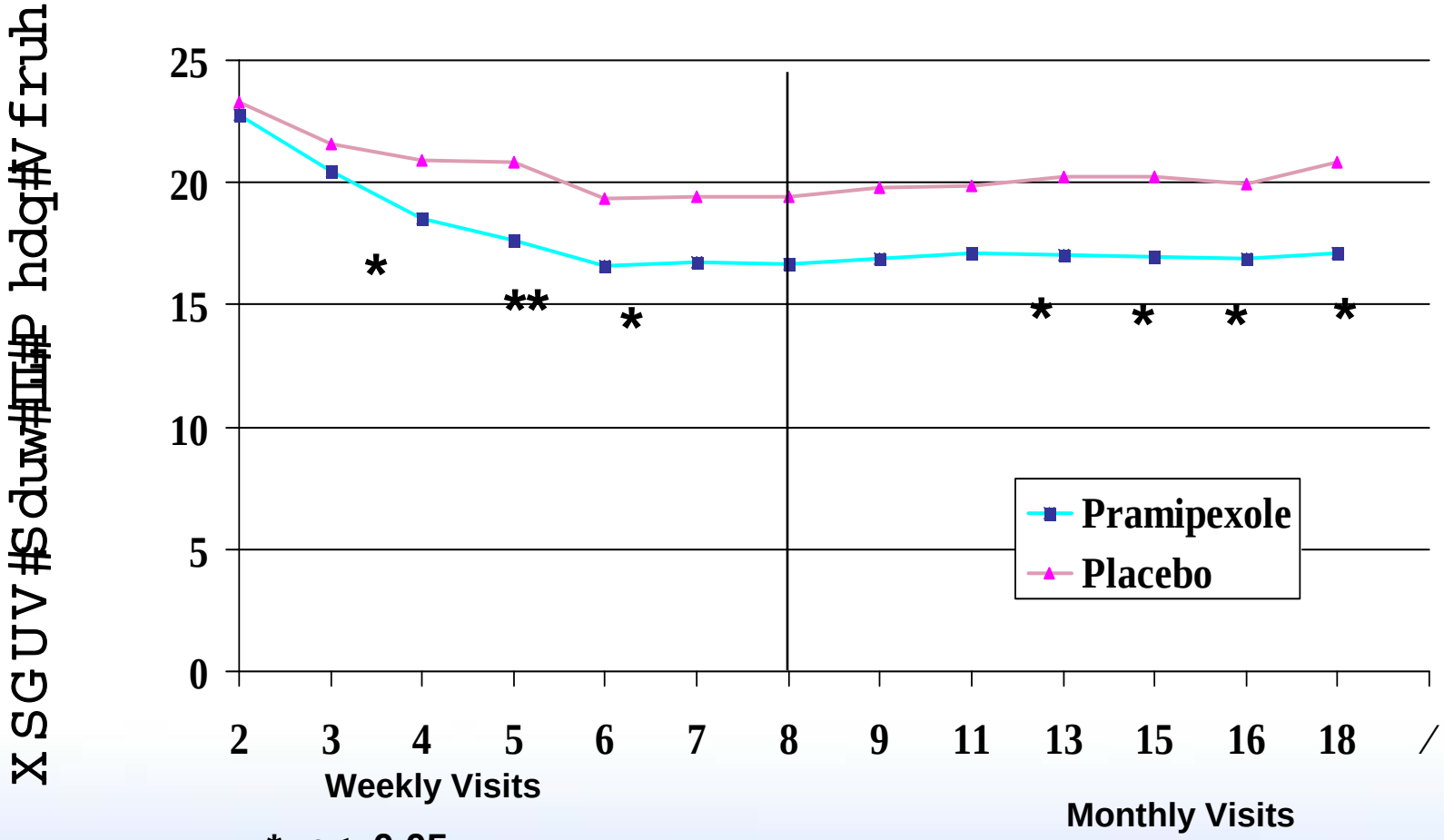
Pramipexolo come add-on nella MP avanzata

Studio 010: Risultati

	Sodfher	Sudp lsh{rdn
Qr1#hqwhuhg	4 : ;	4 ; 4
Qr1#frp sdwhg####	4 7 3 #(+: ; 15 (,	4 8 4 #(+; 6 17 (,
SG #z ruvh	< #(+8 13 (,	6 #(+4 1: (,
Dgyhuvh#hyhqw####	4 ; #(+4 3 14 (,	5 4 #(+4 4 19 (,
Qr#hiilfdf|	3	3
Surwrfrq#ylrodwlrq	3	4 #(+3 19 (,
Orvw#wr#I2X	5 ##(+4 14 (,	3
Z lwkgurz #frqvhqw###	6 #(+4 1: (,	7 #(+5 15 (,

Pramipexolo come add-on nella MP avanzata

Studio 010: UPDRS Part III-- Score motorio

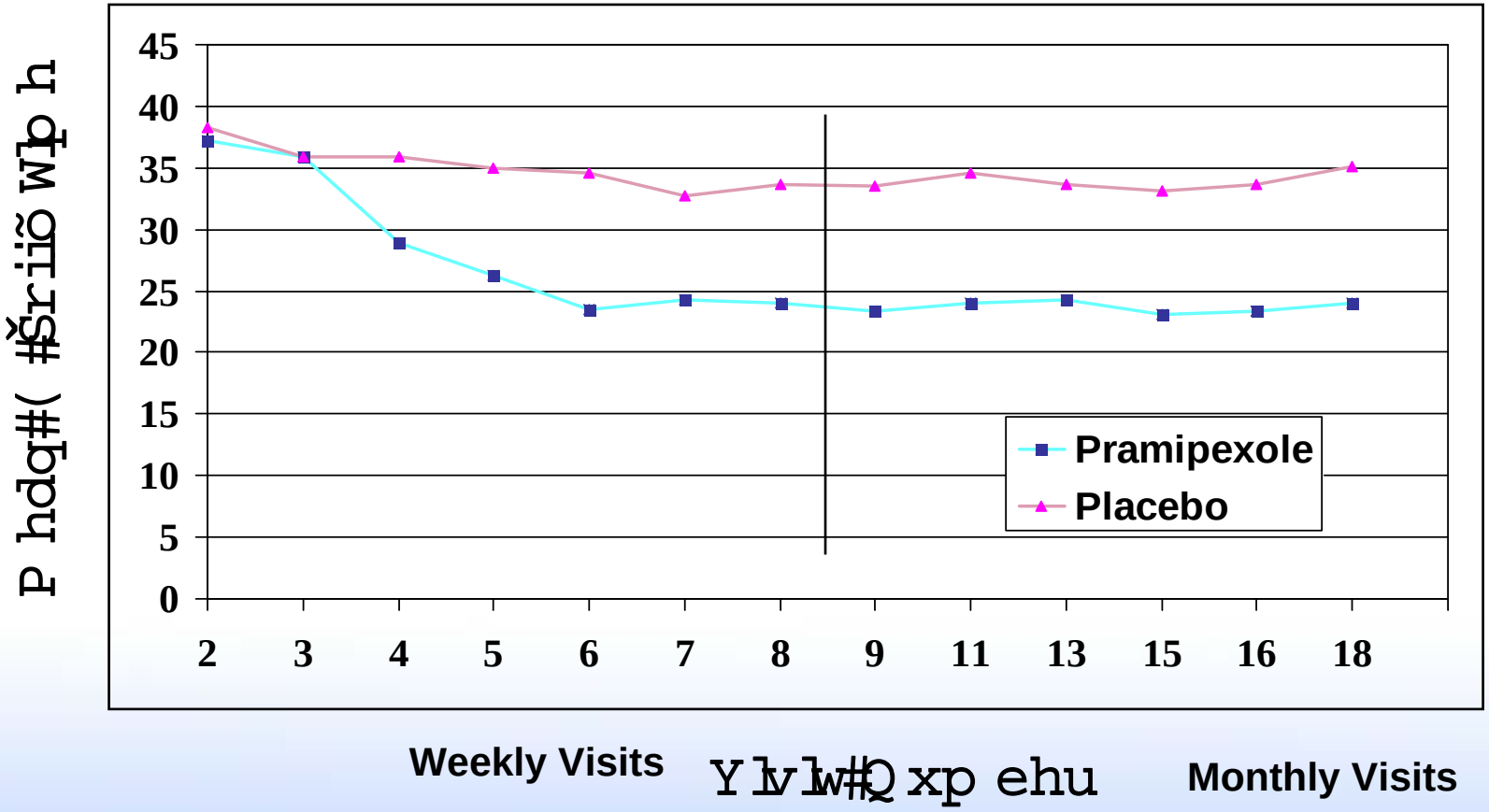


* p<=0.05

** p<=0.01

Pramipexolo come add-on nella MP avanzata

Studio 010: % tempo in off giornaliero



Pramipexolo come add-on nella MP avanzata

Conclusioni Studio 010

- Sudp lsh{ror#vxshulruh d#sodfher=
  - 0XSGUV#LL#Ù LL
  - 0Ulgrwwr Šriiõ wlp h
  - 0Ulgrwwd#judylw< ghl#shulrgl#glŠriiõ
  - 0Ulgrwwh#grvl#gl#hyrgrsd

- Edvvd#lqflghq}d#gl#hyhqwl#dyyhuvl=#glvflqhvlh/# doxflqd}lrql

Pramipexolo come add-on nella MP avanzata

Studio 036: Metodi

- P xovl0fhqwhu/#frqwurodhg/#survshfwlyh/#grxeoh0edqg/#udqgrp l}hg/#sdudoohoj urxs#wr#frp sduh#vdihw|/#wrohudqfh/#dqg#hiilfdf|#ri#sudp lsh{rohn +? @ #7 18 #p j2gd|,#dqg#eurp rfulswlqh +? @ #6 3 #p j#2gd|,#yv solfher

Pramipexolo come add-on nella MP avanzata

Studio 036: Popolazione

	Sudp lsh{rdh	Eurp rfulswlqh	Sodfher	Wrwdo
Qxp ehu#ri Sdwlhqwv	:<	;7	;6	579
Vh{##+(,				
P ddh	7;#+94(,	88#+99(,	86#+97(,	489#+96(,
Ihp ddh	64#+6<(,	5<#+67(,	63#+69(,	<3#+6:(,
Djh#+|hduv,				
+p hdq,	951<	9418	961:	951:
SG#gxudwlrq#+|,				
+p hgldq,	9	:14	:19	:

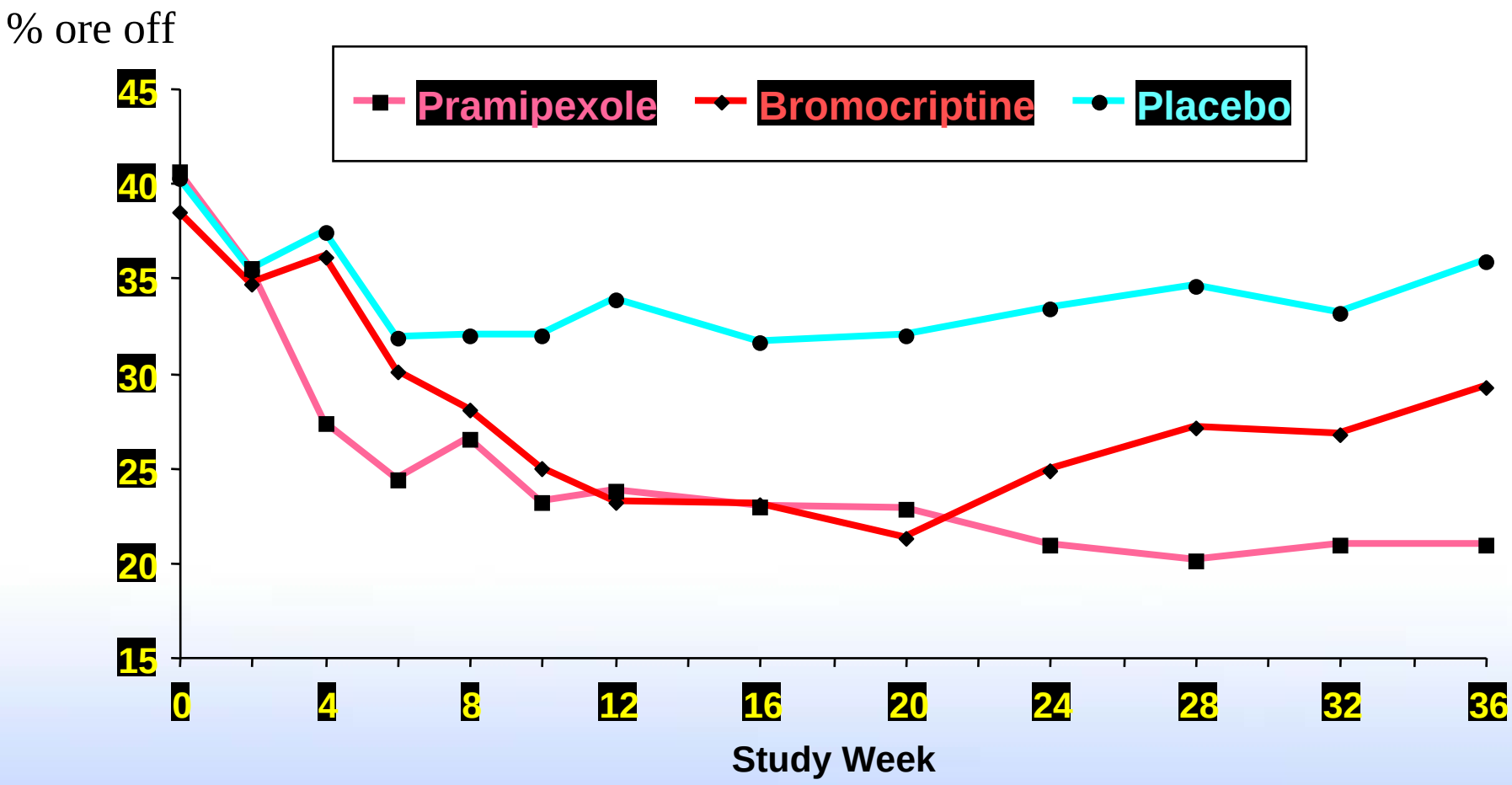
Pramipexolo come add-on nella MP avanzata

Studio 036: UPDRS Part III – Motor Score

	Sudp lsh{rdn	Eurp rfulswlqh	Solfher
Qxp ehu#ri#Sdwlhqwv	:<	;7	;6
P hgldq#fkdqjh#urp edvhdqh#xqlwv,#	09 13	08 13	05 13
P hgldq#fkdqjh#urp edvhdqh#+(,	06 7 1; ;	05 6 1; 6	08 1: 4
s#ydoxh#frp sduhg# z lwk#solfher	3 13 3 3 9	3 13 4 4 6	

Pramipexolo come add-on nella MP avanzata

Studio 036: % tempo in off medio settimanale



Pramipexolo come add-on nella MP avanzata

Conclusioni (a) Studio 036

D, Hqg#srlqw#sup dur

- Hqwudp ell#grsdp lqr#djrqlvwl#p ljdrudqr DGO#h# Vfruh#p rwrulr#ulvshwwr d#sodfher
- Lq#p ljdrudp hqwr · p djjlruh h#sI gxudwxur shu# sudp lsh{ror#ulvshwwr d#eurp rfulswlqd

Dopamino agonisti nella MP avanzata

Considerazioni Finali

- Frp h#shu#sudp lsh{rqr#Óodjjlxqwd#gl#grsdp lqr#djrqlvwl# ghwhup lqd#ehqhilflp rwrul#frqvlvwhqwl#qhoo#sd}lhqwh lq# p rqrwhudsld frq#bhyrgrsd
- Od#wrohudelow< ghl#grsdp lqr#djrqlvwl· lq#jhqhudoh# frp sdudelh d#txhoo#ghoo#bhyrgrsd#hffhwwr shu#lo# p djjlru#ulvfklr#gl#dxflqd}lrql
- OÚhiihwwr#ghl#grsdp lqr#djrqlvwl#vl#p dqwlhqh#qhowhp sr
- Grsdp lqr#djrqlvwld#p djjlru#hp lylwd +dg#hv1# fdehujrdqd,#srvvrqr#jdudqwluh#xqd#sÚ hiilfdfh# vwlp rol}lrqh#grsdp lqhujlfd frqwlqxd

Pramipexolo come add-on nella MP avanzata

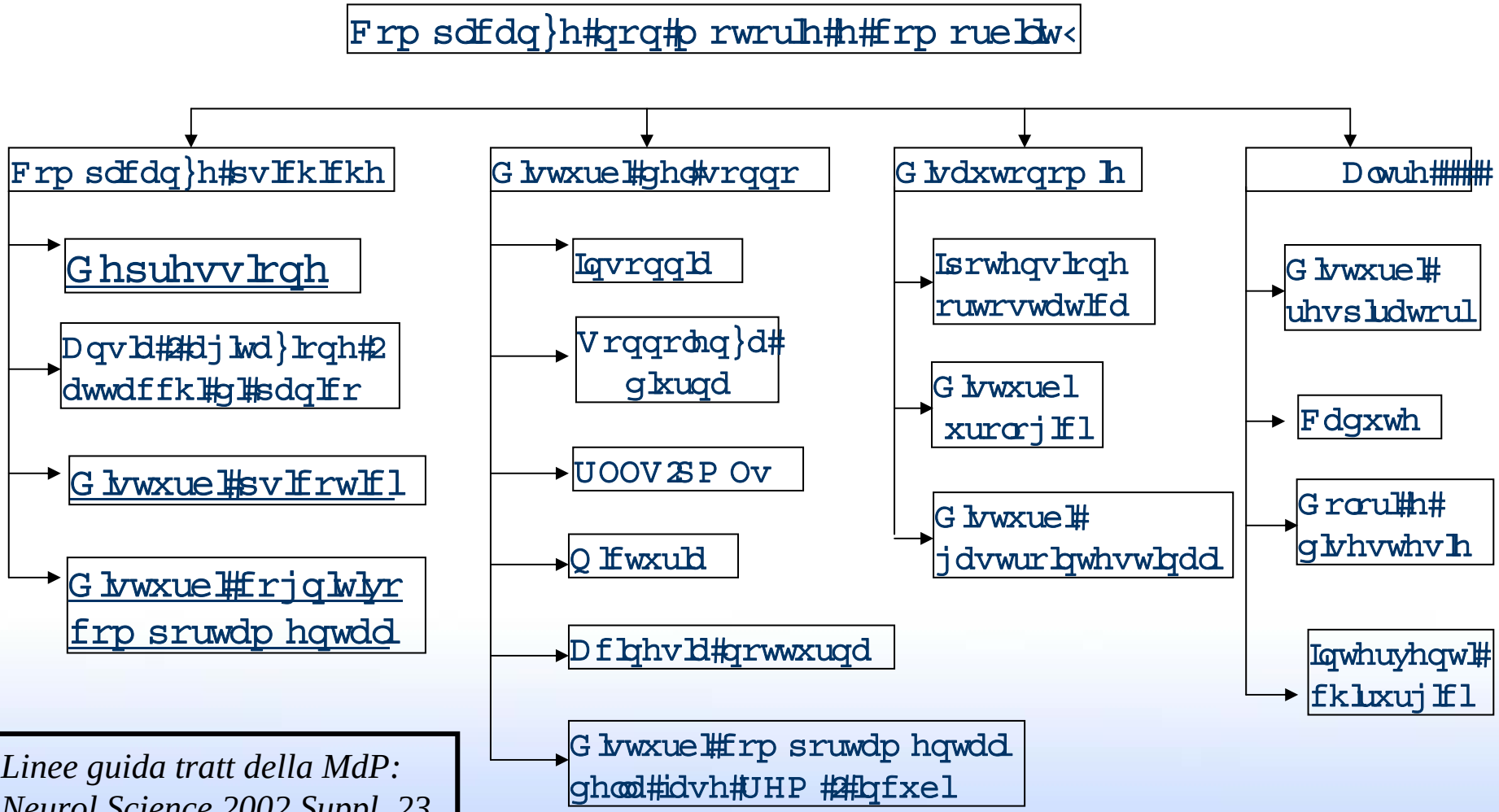
Conclusioni (b) Studio 036

E ,#Hqq#Srlqw#vhfrqgdulr @ #Whp sr#lq#ŠR iiõ

- Sudp lsh{ror#ulgxfh#vljqlilfdwlydp hqwh ďŠriiõ wlp h/#h# ghwhup lqd xq#lqfuhp hqwr#p hglr ghďďrqõ gl##5 18 #ruh# dq#j lruqr
- Q hvvxq#fdp eldp hqwr#vljqlilfdwlyr frq#eurp rfulswlqd
- OÍhiihwwr#p dvvlp r#gl#sudp lsh{ror#v#udjjlxqjh# udslgdp hqwh#hqwur 7 #vhwwlp dqh +eurp rfulswlqd =#; # vhwwlp dqh,
- OÍhiihwwr#gl#sudp lsh{ror · frqvhuydwr shu#ďÍqwhur# shulrgr +dq#frqwudulr#gl#eurp rfulswlqd,

Malattia di Parkinson
Complicanze non-motorie

Malattia di Parkinson in fase avanzata - *Complicanze non motorie e comorbilità*



Disturbi del sonno nella malattia di Parkinson

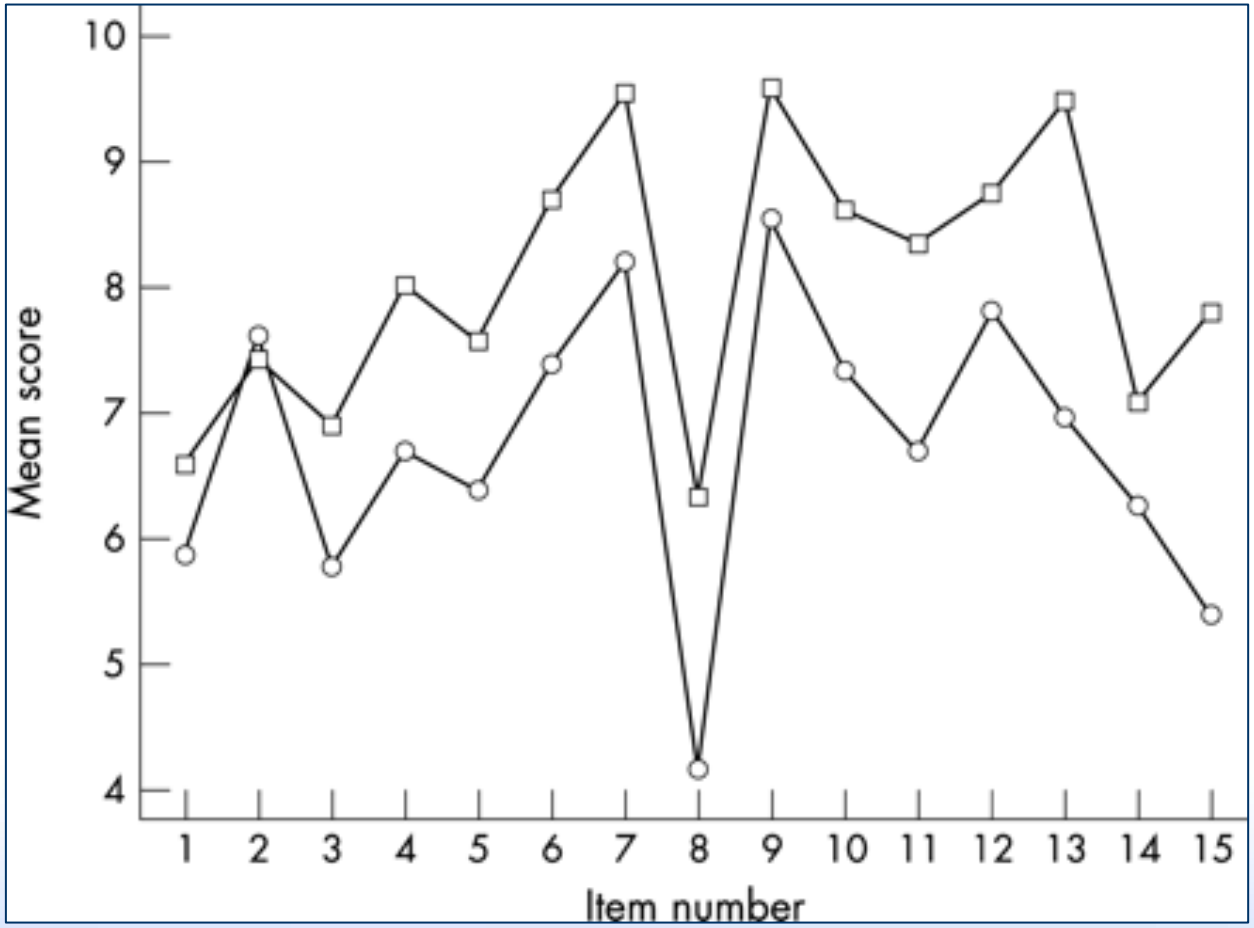
Ulgrwwd#txddw< gl#ylwd#hjdwd#dod#txddw< ghq#vrqqr

- Sd}lhqwl#lq#idvh#lq}lddn
  - Gliilfrow< dg#dggrp p hqwduvl
  - Ulvyhjdr#suhfrfh#dq#p dwwlqr
- Sd}lhqwl#lq#idvh#p rghudwd0judyh
  - Dflqhvld#qrwwxuqd
  - Iudp p hqwd}lrqh#gh#vrqqr
  - Glvwrqld#h#Fudp sl#grorurvl
  - Qlfwxuld

Disturbi del sonno nella malattia di Parkinson

- Fdxvh=
  - Shjjlrudp hqwr#gh#vlqwrp #sdunlqvrqldq#gxudqwh ol#qrwwh#txdqgr #sd}lhqwlqrq#dvvxp rqr ol#whudsld
  - G liilfrow< uhvsludwruh
  - Surjuhvvlrqh#ghoo#p dolwwld
  - Suhvhq}d#g#glvwxue#ghoo#idvh UHP #UEG ,#
  - Hw<

Parkinson's disease Sleep Scale nei pazienti con MP e nei controlli



C

MP

Chaudhuri et al JNNP 2002;73:629-635

Parkinson's disease Sleep Scale

Parkinson's Disease Sleep Scale (PDSS)

How would you rate the following, based on your experience during the past one week.
(Place a cross at the appropriate point on the line)

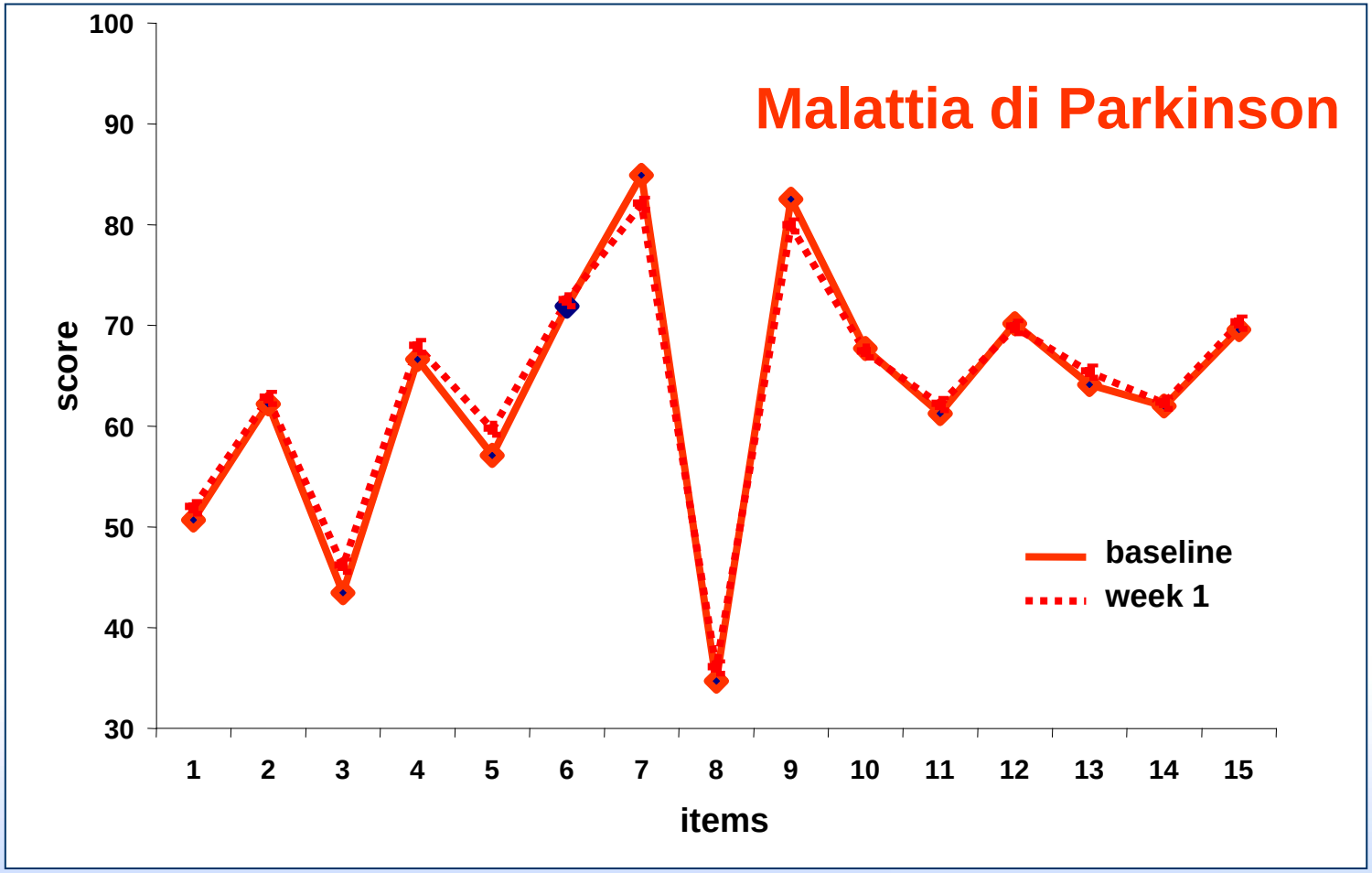
1.	The overall quality of your night's sleep is:	AWFUL	EXCELLENT
2.	Do you have difficulty falling asleep each night?	ALWAYS	NEVER
3.	Do you have difficulty staying asleep?	ALWAYS	NEVER
4.	Do you have restlessness of legs or arms at night or in the evening causing disruption of sleep?	ALWAYS	NEVER
5.	Do you fidget in bed?	ALWAYS	NEVER
6.	Do you suffer from distressing dreams at night?	ALWAYS	NEVER
7.	Do you suffer from distressing hallucination at night (seeing or hearing things that you are told do not exist)?	ALWAYS	NEVER
8.	Do you get up at night to pass urine?	ALWAYS	NEVER
9.	Do you have incontinence of urine because you are unable to move due to "off" symptoms?	ALWAYS	NEVER
10.	Do you experience numbness or tingling of your arms or legs which wake you from sleep at night?	ALWAYS	NEVER
11.	Do you have painful muscle cramps in your arms or legs whilst sleeping at night?	ALWAYS	NEVER
12.	Do you wake early in the morning with painful posturing of arms or legs?	ALWAYS	NEVER
13.	On waking do you experience tremor?	ALWAYS	NEVER
14.	Do you feel tired and sleepy after waking in the morning?	ALWAYS	NEVER
15.	Have you unexpectedly fallen asleep during the day?	FREQUENTLY	NEVER

0 1 2 3 4 5 6 7 8 9 10

Chaudhuri et al JNNP 2002;73:629-635

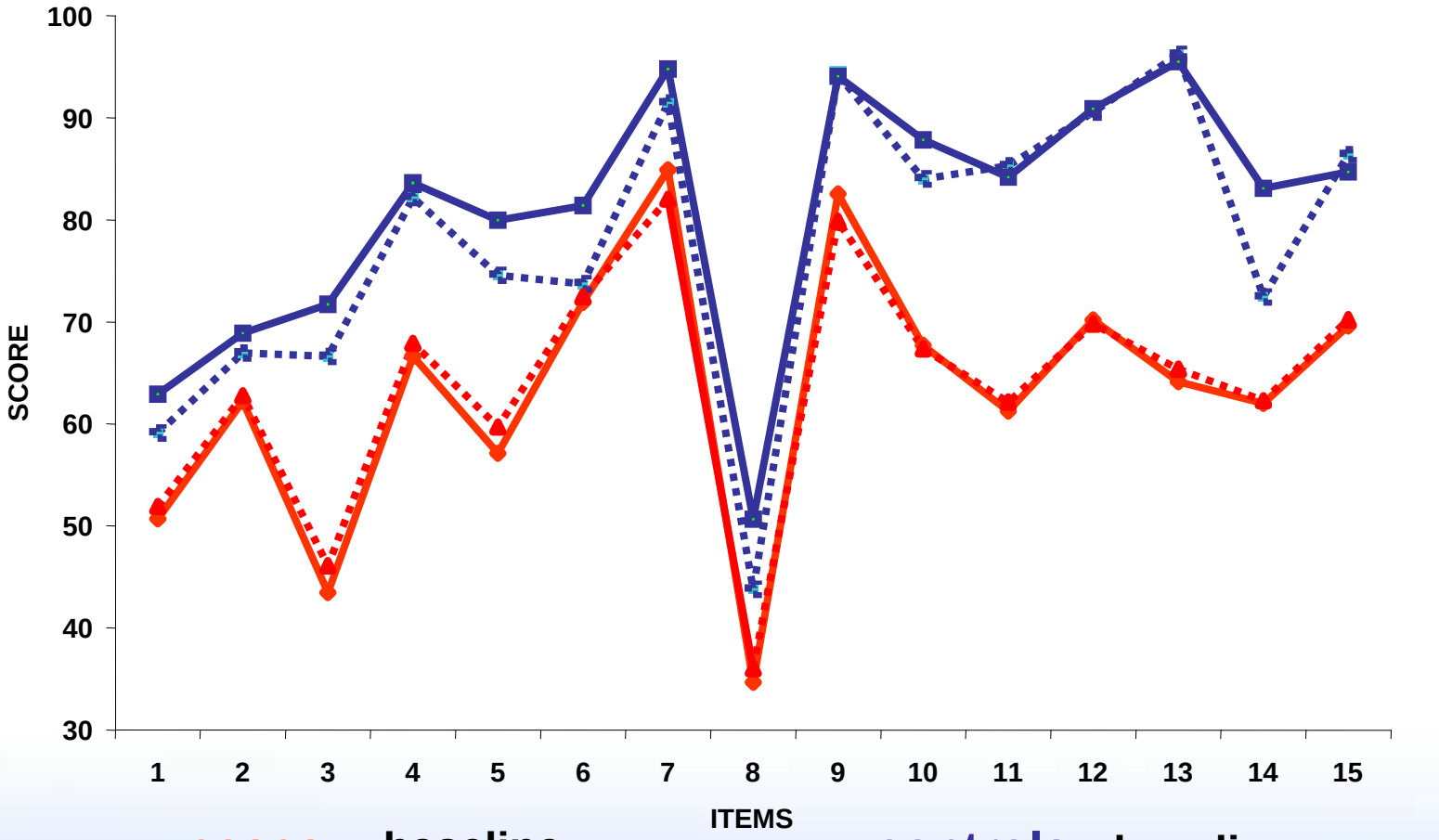
Parkinson's disease Sleep Scale

Progetto Morpheus (interim analisis)



Parkinson's disease Sleep Scale

Progetto Morpheus (interim analisis)



cases baseline ——— controls baseline ———

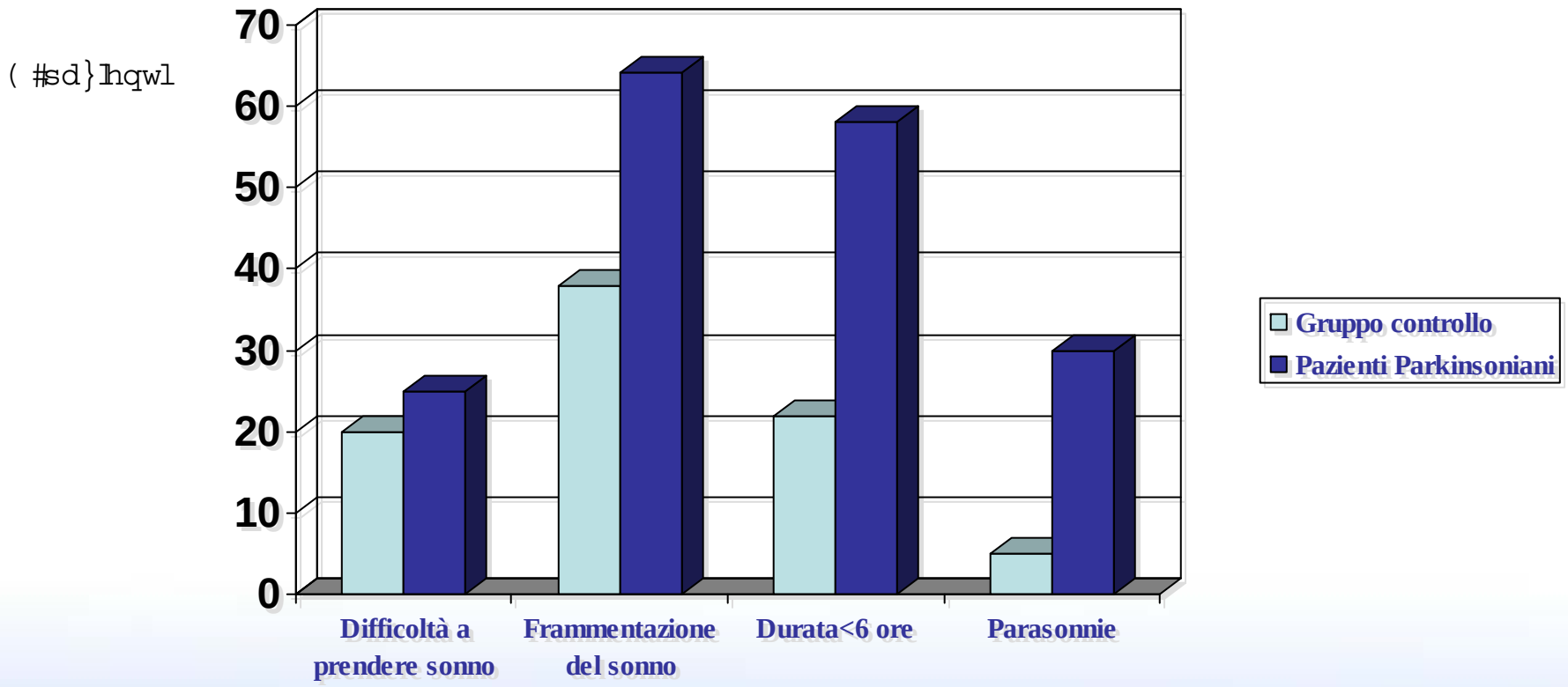
week 1 ..... week 1 .....

EPWORTH SLEEPINESS SCALE

- Vlwwlqj#dqg#uhdglqj
- Z dwfklqj#WY
- Vlwwlqj#lqdfwlyh#lq#d#sxedf#sodfh#h1j#d#wkhdwhu#ru#d#p hhwlqj,#
- Dv#d#sdvvhqjhu#lq#d#fdu#iru#dq#krxu#z lwkrxw#d#euhdn#
- O|lqj#grz q#wr#uhvw#lq#wkh#diwhuqrrq#z khq#flufxp vwdqfhv#shup lw
- Vlwwlqj#dqg#wdonlqj#wr#vrp hrqh#
- Vlwwlqj#txlhwo|#diwhu#d#xqfk#z lwkrxw#dfrkro#
- Lq#d#fdu/#z klh#vwrsshg#iru#d#ihz #p lqxwhv#lq#wudiilf#

Vfruh	3 #@ #qr#fkdqfh#ri#gr}lqj
	4 #@ #vdjkw#fkdqfh#ri#gr}lqj#
	5 #@ #p rghudwh#fkdqfh#ri#gr}lqj#
	6 #@ #kljk#fkdqfh#ri#gr}lqj

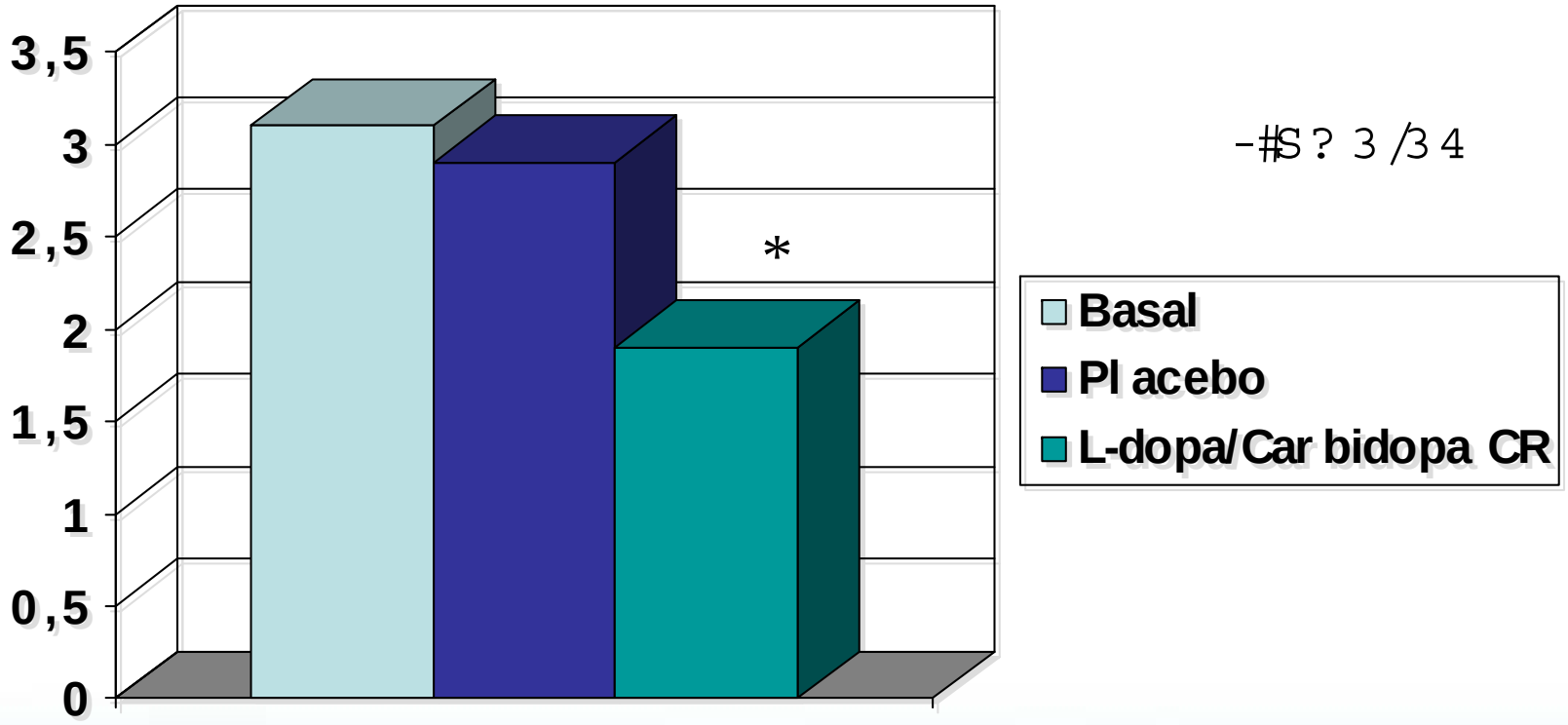
Disturbi del sonno nella malattia di Parkinson



Rubio P et al, Rev Neurol 23 (120),1995

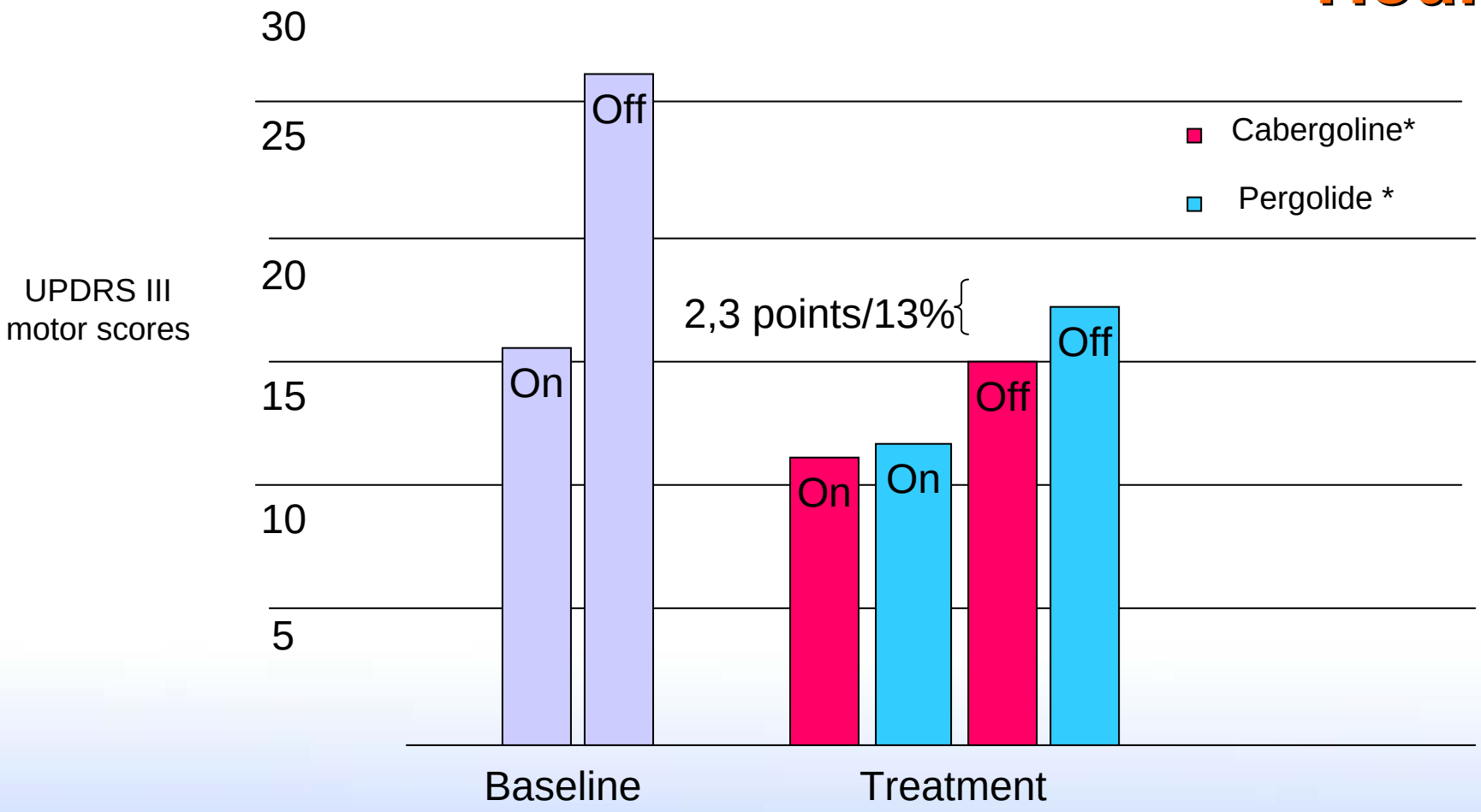
L-Dopa/carbidopa a rilascio controllato in pazienti con disturbi del sonno

Risultati



Stocchi et al: J Neurol 1998-245 (Suppl 1): S15-S18

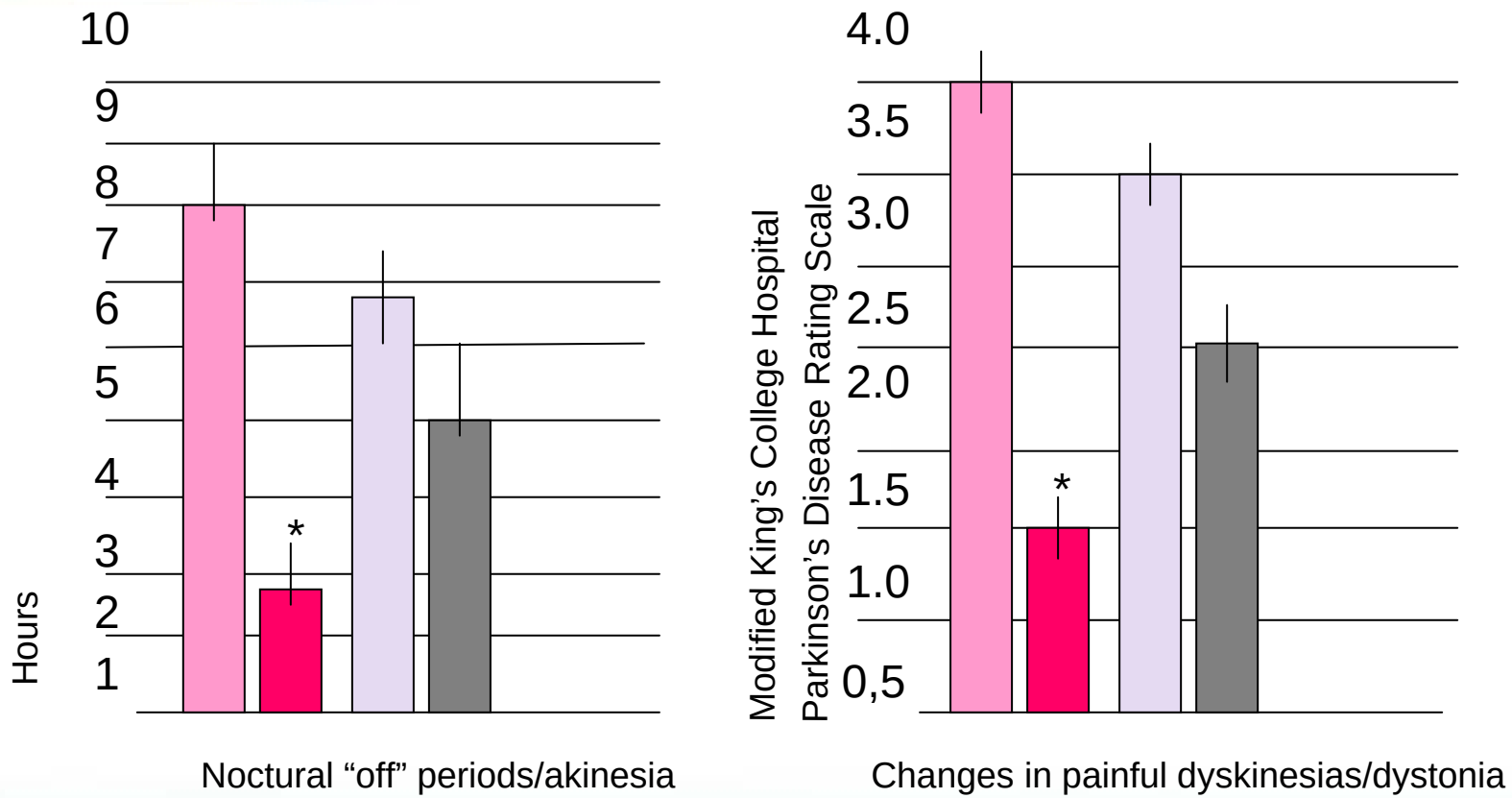
MODAC Study: Cabergoline Versus Pergolide - Motor Function During "On" and "Off" Hours*



* Blinded, primary endpoint.

Adapted from Ulm. G., et al. Akt Neurologie,1999

Cabergoline Versus Controlled-Release Levopada: Nocturnal Disabilities



- Pre-cabergoline (n=25)
- Cabergoline (n=25)
- Pre-controlled-release levodopa (n=15)
- Controlled-release levodopa (n=15)

* p< .05.

Adapted from Chaudhurl KR, et al. Eur J Neurol 1999,6 (suppl 5)

Levodopa Supplementation in Early PD Patients With Dopamine Agonist Monotherapy

Vwxg|	Gxudwlrq	No. Patients Dvvljqhg#wr Djrqlvw	Sdwlhqwv#Frp sdnwlqj Vwxg|#rq#Grsdp lqh Djrqlvw#P rqrwkhuds|	Sdwlhqwv#Uhtxluqj Ohyrgrsd +(,#Vxssdnp hqwdwlrq
L- Dopa vs ROP Rascol, 2000. (Requip 056)	5 years	179	29/179 (16%)	ROP = 56/179 (31%) L-Dopa = 16/89 (18%)
L- Dopa vs CAB Rinne, 1998 (Cabaser 09)	5 years	211	76/211 (36%)	CAB = 135/211 (64%) L-Dopa = 98/208 (47%)
L- Dopa vs PPX PSG, 2000. (CALM-PD)	2 years	151	48/151 (32%)	PPX = 80/151 (53%) L-Dopa = 58/158 (39%)

Rascol O et al: N Engl J Med,342:1484-1491;2000
Rinne UK et al, Drugs 1998; 55 Suppl. 1: 23-30

Parkinson Study Group: JAMA 2000; 284: 1931-1938

DA Studies to Prevent Motor Complications: Key Adverse Effects (%)

	FDOP 0SG	UTS#389	FEV#3<	Shqp rshw
Dgyhuvh#Hyhqwv	P S[	0G rsd	UTS	0G rsd	FEV	0G rsd	Shuj	0G rsd
Qdxvhd	6917	691:	6<	65	6:17	6515	73	53
Vrp qrdnqfh	6517	4:16	55	45	5918	-5;17	6	3
Kdodxflqdwlrq	<16	616	4:	9	716	71;	43	8

Rascol O et al: N Engl J Med,342:1484-1491;2000
Rinne UK et al, Drugs 1998; 55 Suppl. 1: 23-30
Parkinson Study Group: JAMA 2000; 284: 1931-1938
Oertel et al. Mov Disord 2000 Suppl 2

*Includes sleep disorders and insomnia.

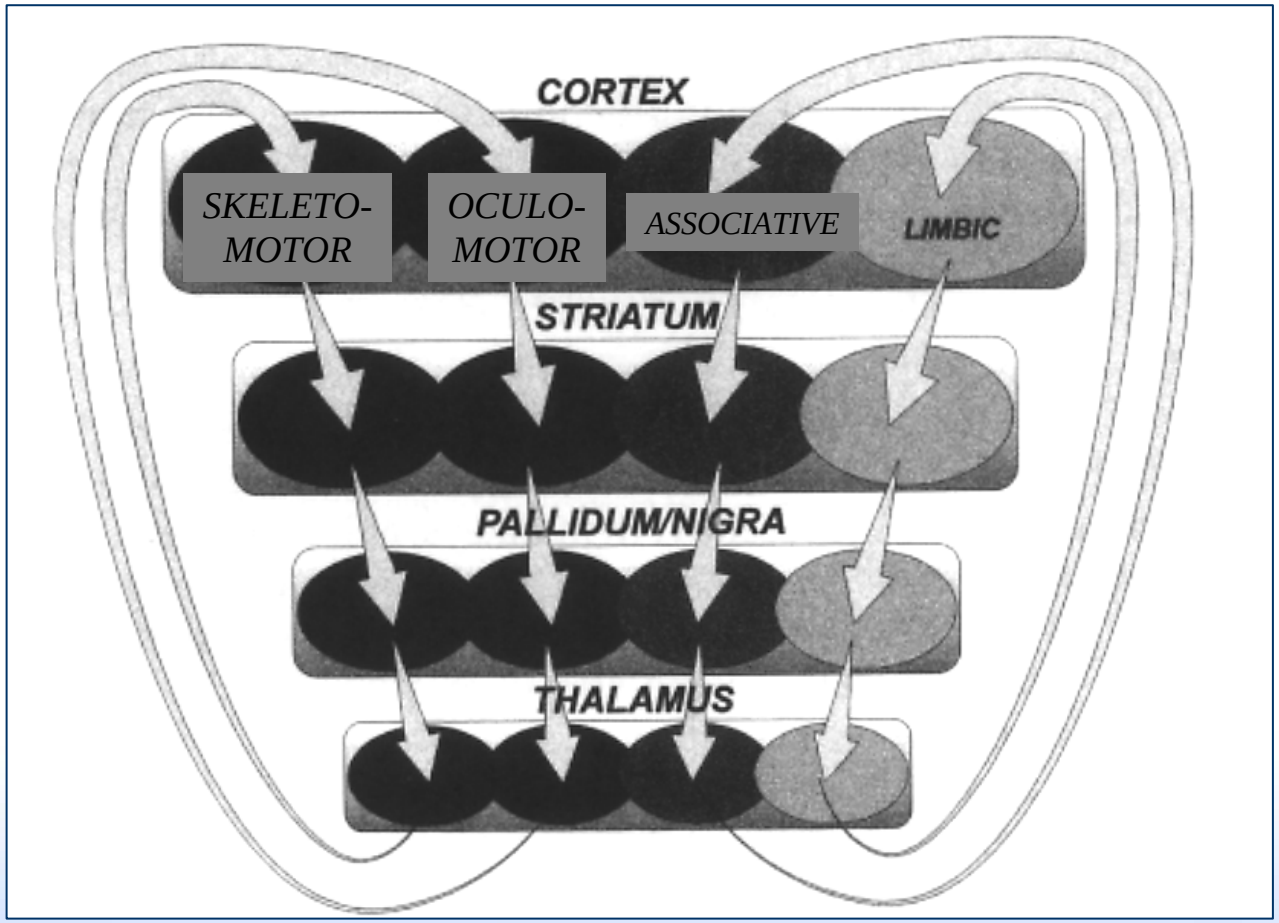
Depressione

Malattia di Parkinson

- Od#ghsuhvvlrqh#· lq#glvwxuer#svlfklfr#sl frp xqhp hqwh#dvvrfldwr#dood#P 1#gl# Sdunlqvrq=#ol#iuhtxhq}d#p hgld#gl#lqflghq}d# · sdul#dl#73 (#udqjh 70:3 (,

+Fxp p lqjv#1<<5,

Il sistema extrapirimidale



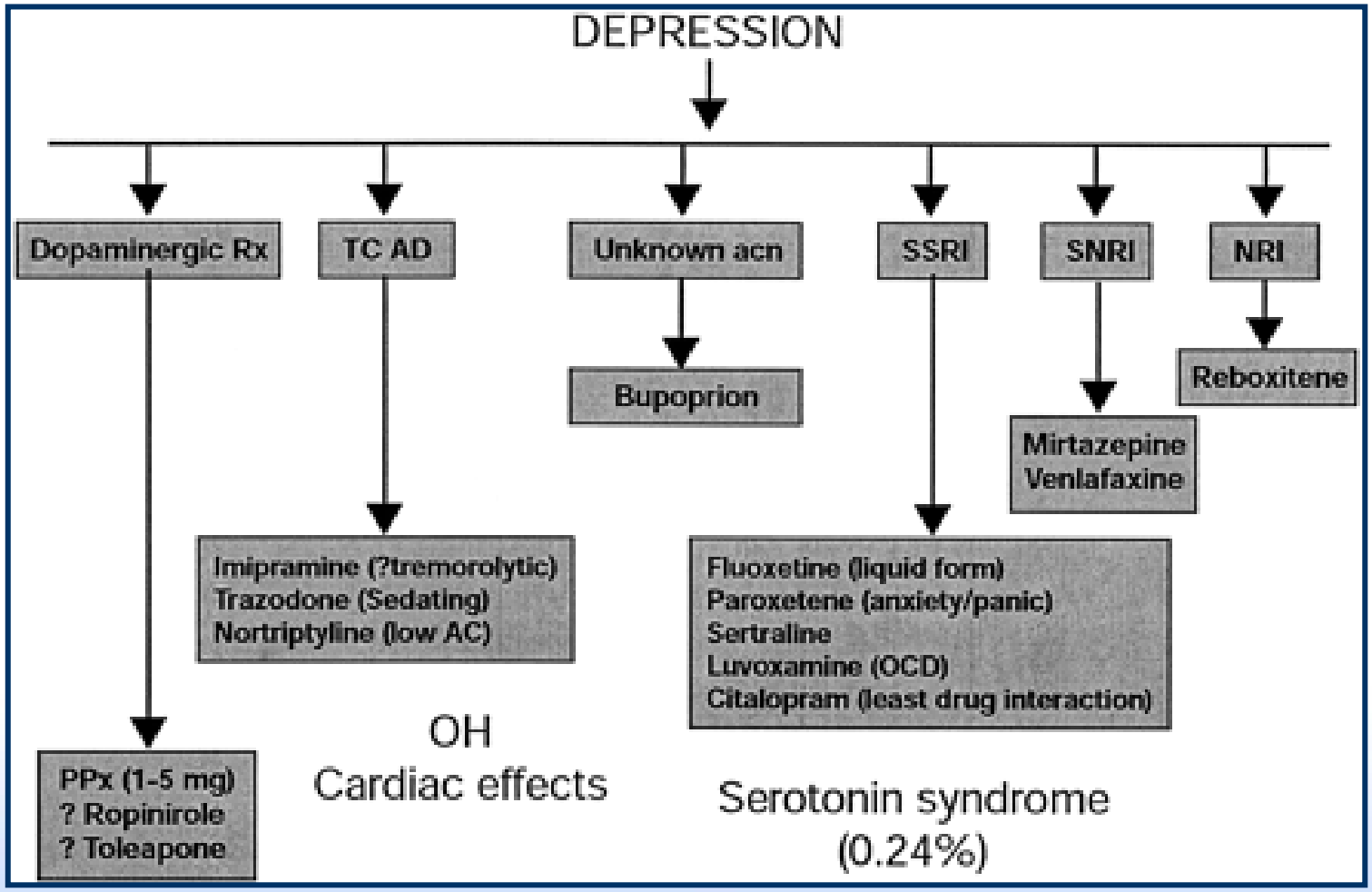
Alexander et al Prog Brain Res 1990

Tratti di personalità, depressione e stato di salute in gemelli monozigoti (6) e dizigoti (9) di MP

	P]	G]	Frqwurov	s#Ydoxh
Olih#vdwlvidfwlrq	8 16 #	8 1:	9 1;	3 14 5 #
Vrfldo#ruhqwdwlrq	8 14 #	8 17	8 1;	3 18 8 #
Dfklhyhp hqw#ruhqwdwlrq	6 15 -	8 14	8 1;	3 13 3 6 #
Lqkleluhgqhvv	8 16	8 1; -	6 1; #	3 13 7 < #
Lp sxovlyhqhvv	7 16	7 1;	7 17 #	3 18 ; #
Djjuhvvlyhqhvv	6 1:	8 14	8 13 #	3 13 5 #
Vrp dwlf#frp sodqwv	8 14 -	7 17	6 13 #	3 13 3 8 #
Khdowk#frqfhuq	7 14 -	7 17 -	9 14 #	3 13 3 5 #
Iudqnqhvv	6 1;	8 15 -	6 1< #	3 13 7 #
H{wudyhuvlrq	6 19 -	7 18	9 15 #	3 13 3 9 #
Hp rwlrqdo	7 1;	8 17 -	6 17 #	3 13 3 : #
Ghsuhvvlrq	**4 4 15**	**4 3 1; -**	**7 1< #**	**3 13 3 < #**
Vwdwh#ri#khdowk	**4 : 16**	**4 < 14 -**	**: 18 #**	**3 13 4**

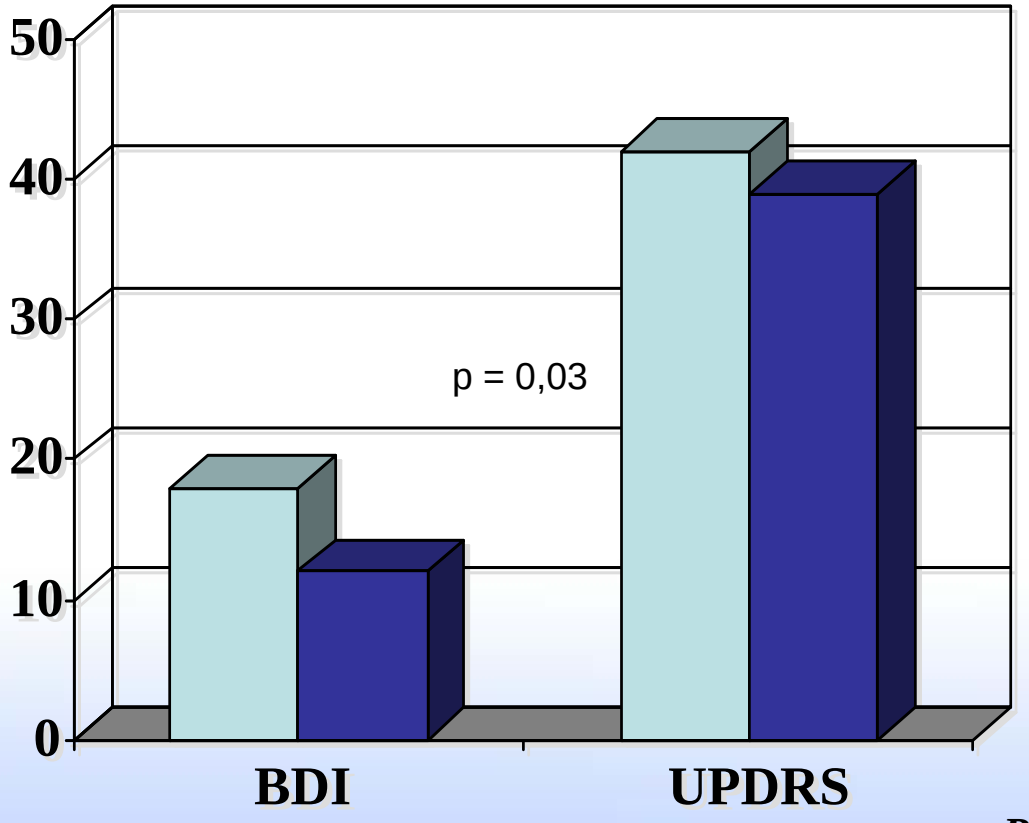
Heberlein JNNP 1998

Strategie Farmacologiche nel Trattamento per Depressione nella MP



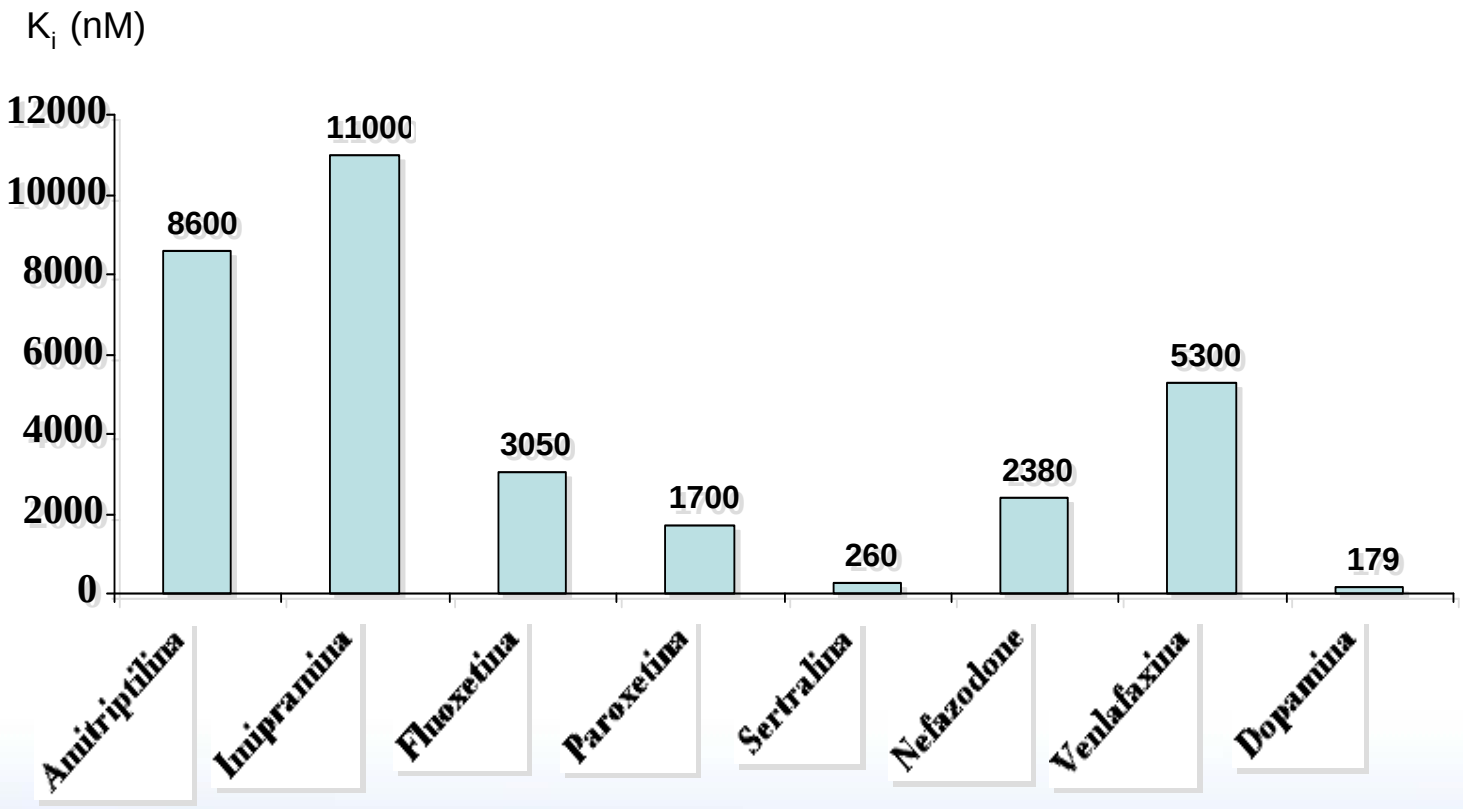
Chaudhuri Neurology 2003

Sertralina nei pazienti depressi con malattia di Parkinson: miglioramento della BDI senza variazioni significative alla UPDRS



RA Hauser e TA Zesiewicz, 1997

SSRI e inibizione del re-uptake della dopamina



C Boden-Watson e E. Richelson, 1993

Demenza e Malattia di Parkinson

- Od#ghp hq}d#udssuhvhqwd#xqd#ghoh#
  frp sdfdq}h#slxÚ iuhtxhqwl#ghoo P S#
- Sulp d#p hq}lrqh#gd#sduwh#gl#Iuhghulfk#
  Ohz |#qho4<56=#vx :3#sd}lhqwl#hvdp lqdwl
  87#hudqr#ghp hqwl+: :(,
- Q hoÍhsrfd srvw0hyrgrsd#ÚÍqflghq}d#yduld#
  wud#lo43(#h#lo73(

Rischio di Demenza nella MP

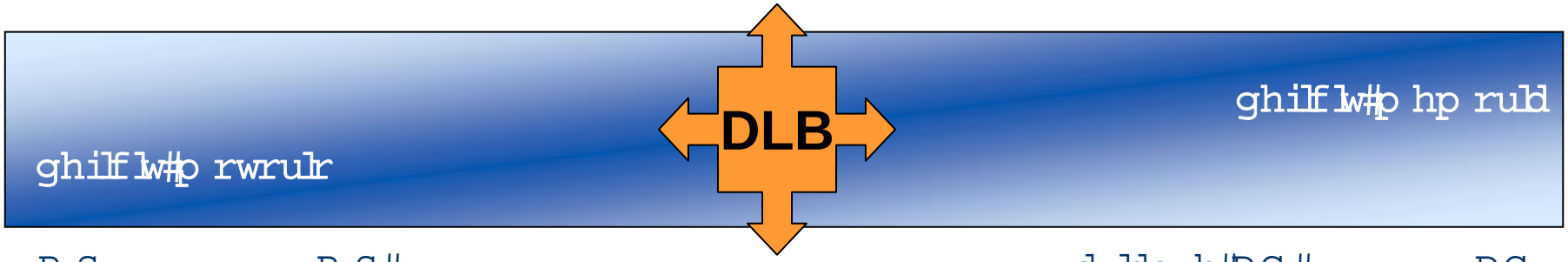
- Vwxglr#orqjlwxglqdoh#fdvr0frqwurorr=
  - Ù 463#sd}lhqwlqrq#ghp hqwlfrq#P S

  - Ù 76#dyhydqr#vyllussdwr#ghp hq}d +66 (,#
- Ulvfklr#gl#ghp hq}d 9#yrowh A #fkh#qhoodl#srsrodl}lrqh# frqwurorr
- Idwwruli#gl#ulvfklr=
  - Hw<
  - Judylw< ghh#glvwxuer#p rwrulr
  - P P VH#? #5<#d#edvdoh

Aarsland D Neurology 2001

Parkinson ed Alzheimer
Realta' clinica

glvwxuer#frp sruwdp hqwdoh



P S

P S#.
ghp hq}d

doxflqd}lrql
ylvlyh

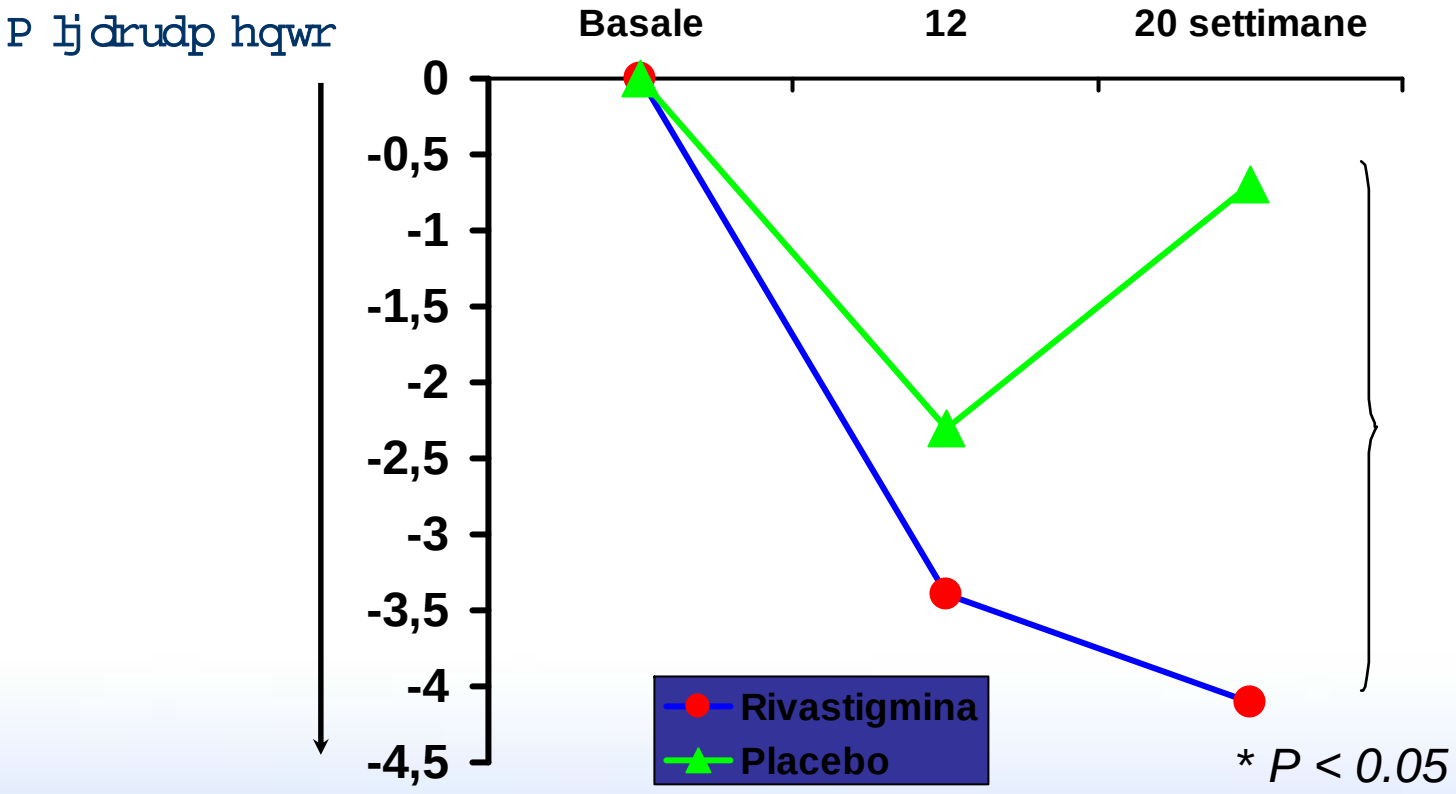
yduldqwh#DG#.
frusl#gl#Ohz |

DG

Galvin JE Arch Neurol 2001

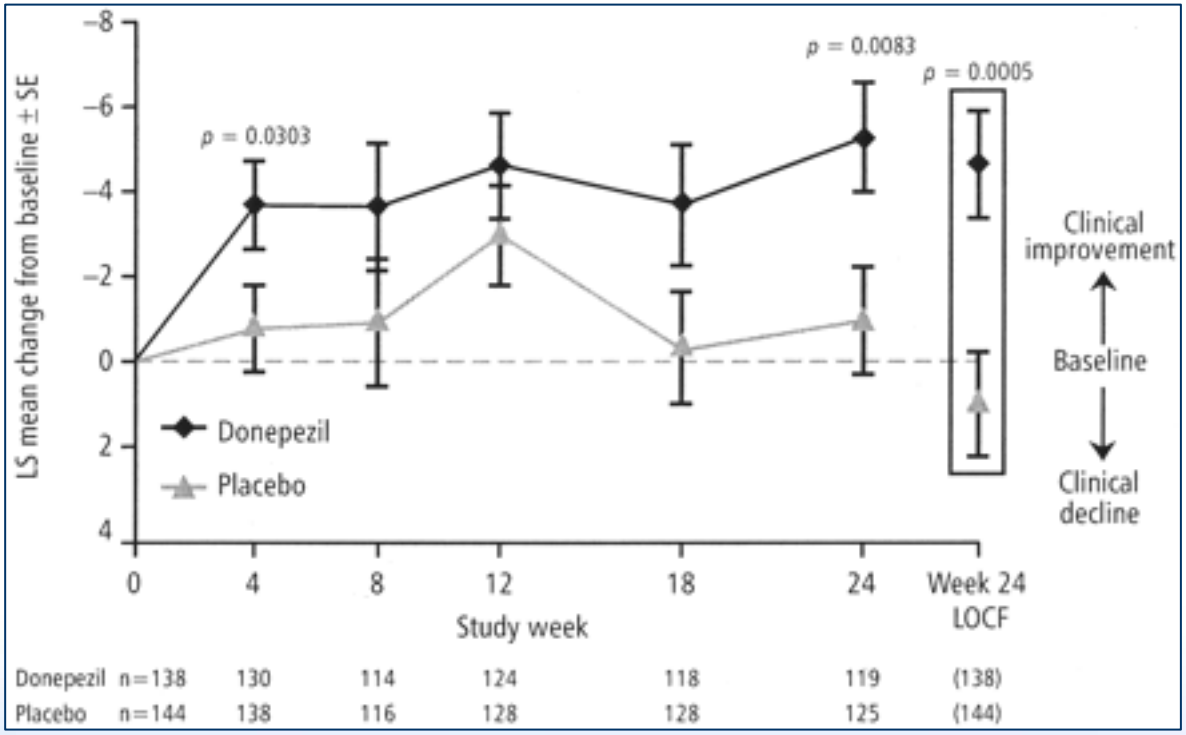
Rivastigmina
Demenza con corpi di Lewy

Variazione media NPI score vs basale



McKeith et al., Lancet , 2000

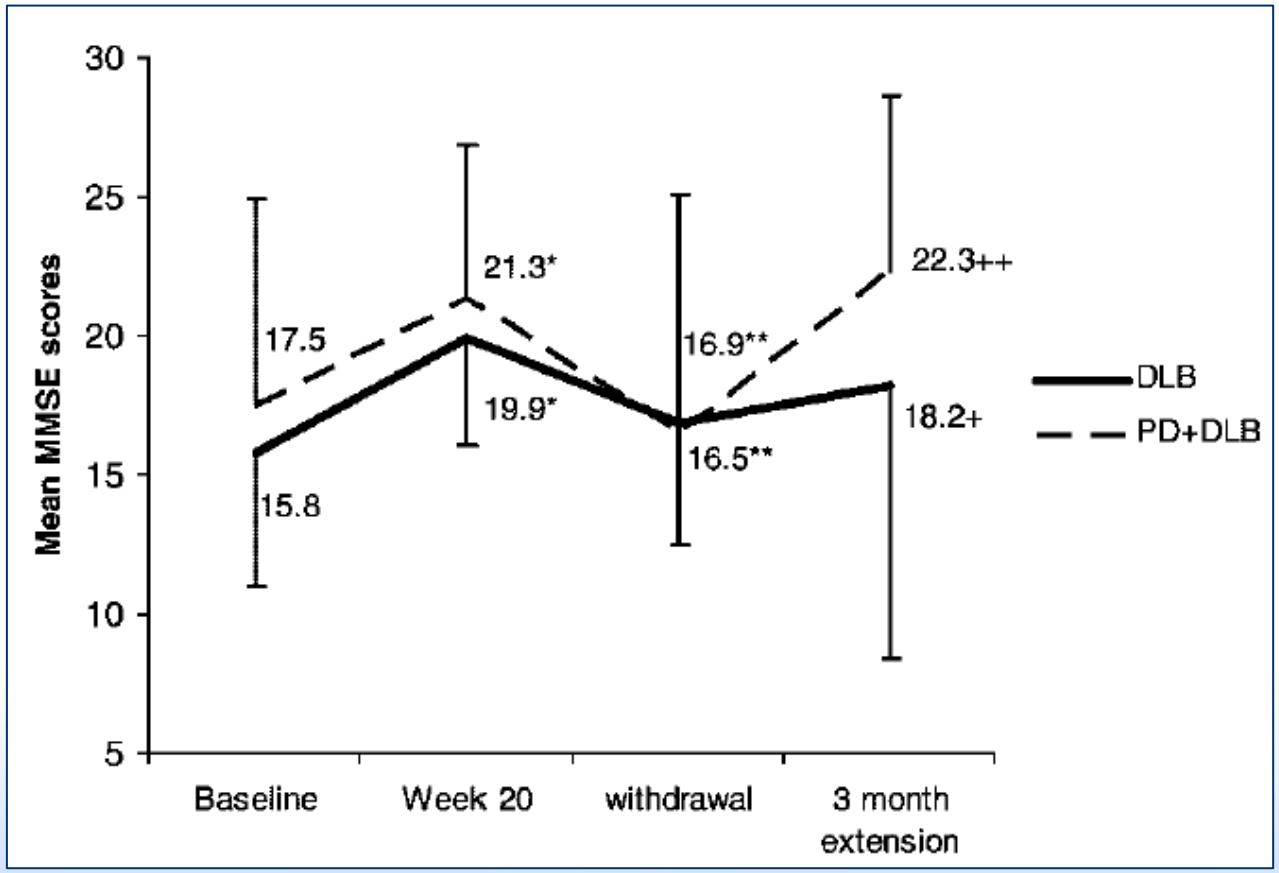
Donepezil e Indice Neuropsichiatrico (NPI) Miglioramento in pazienti con Alzheimer medio-grave



Feldman H Neurology 2001

Donepezil
Demenza con corpi di Lewy

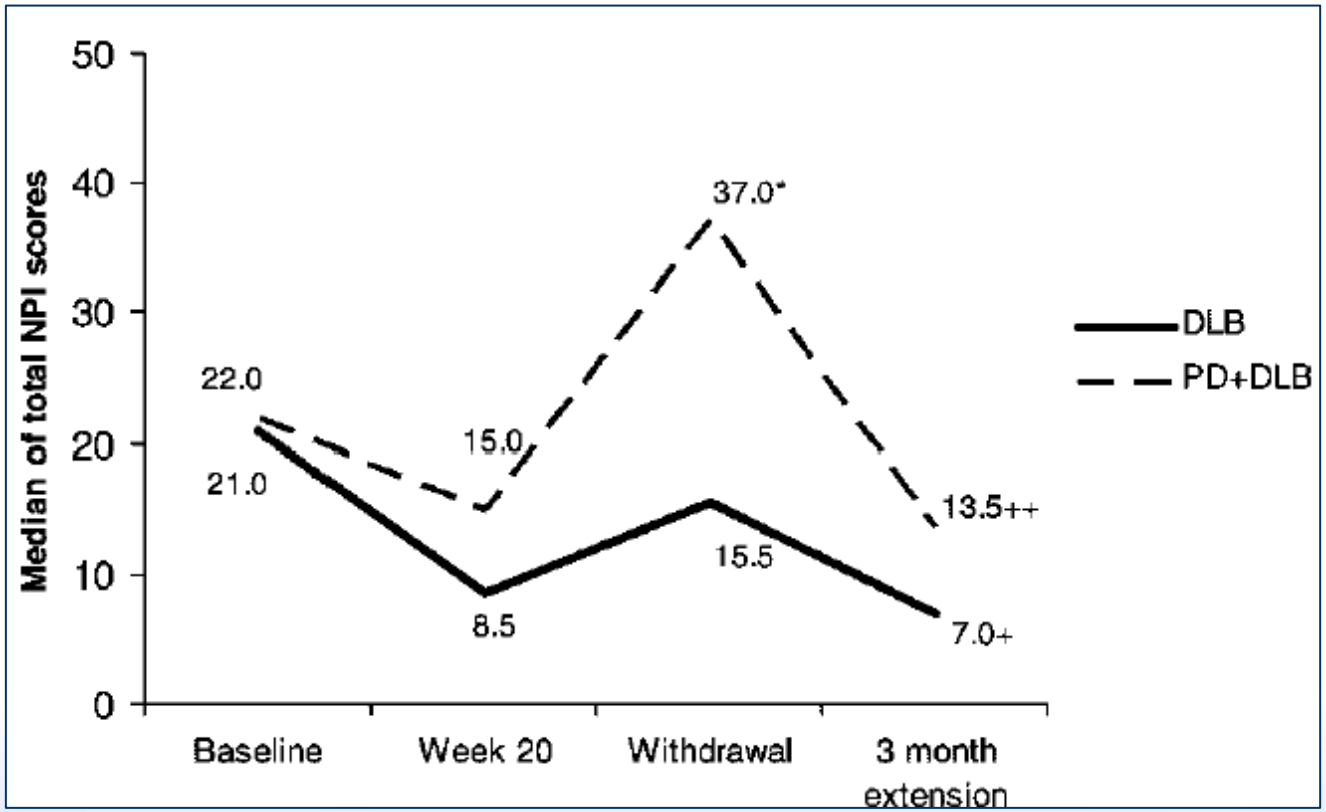
Variazione media MiniMental score



Minnet et al., Int J Geriatr Psychiatry, 2003

Donepezil
Demenza con corpi di Lewy

Variazione media NPI



Minnet et al., Int J Geriatr Psychiatry, 2003