



# **"EVIDENCE BASED MEDICINE"**

**nella gestione della Malattia di Parkinson con  
dopamino-agonista**

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DEI MEDICINALI E DELLA FARMACOVIGILANZA

**2**

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# clinical evidence

*conciso*  
**edizione italiana**

LA FONTE DELLE MIGLIORI  
PROVE DI EFFICACIA  
PER LA PRATICA CLINICA



CONTIENE CD  
CON L'EDIZIONE INTEGRALE

Reviews

- Bromocriptine for levodopa-induced motor complications in Parkinson's disease
- Bromocriptine versus levodopa in early Parkinson's disease (Bromocriptine/levodopa combined versus levodopa alone for early Parkinson's disease)
- Cabergoline for levodopa-induced complications in Parkinson's disease
- Cabergoline versus bromocriptine for levodopa-induced complications in Parkinson's disease
- Lisuride for levodopa-induced complications in Parkinson's disease
- Lisuride versus bromocriptine for levodopa-induced complications in Parkinson's disease
- Pergolide for levodopa-induced complications in Parkinson's disease
- Pergolide versus bromocriptine for levodopa-induced complications in Parkinson's disease
- Pramipexole for levodopa-induced complications in Parkinson's disease
- Pramipexole versus bromocriptine for levodopa-induced complications in Parkinson's disease
- Ropinirole for levodopa-induced complications in Parkinson's disease
- Ropinirole versus bromocriptine for levodopa-induced complications in Parkinson's disease

Protocols

- Early combination therapy with levodopa and dopamine agonist for preventing motor fluctuations in Parkinson's disease (Cochrane Protocol)



## SHORT REPORT

# Duration of amantadine benefit on dyskinesia of severe Parkinson's disease

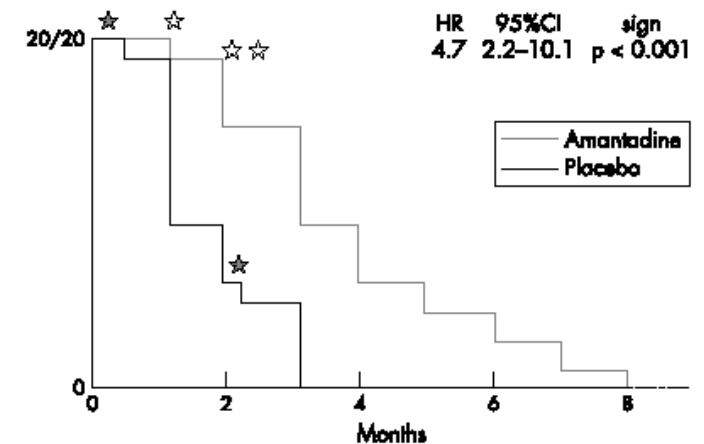
A Thomas, D Iacono, AL Luciano, K Armellino, A Di Iorio, and M Onofri

*J Neurol Neurosurg Psychiatry* 2003;000:1-4

### Follow-up evaluations for Ama and placebo group

	Baseline	15 days	30 days	Before withdrawal 60-240 days	1 week after withdrawal	1 month after withdrawal
<b>AMA</b>						
"On" time (hours)	8.9 (2.4)	9.6 (2.1)	9.9 (1.9)	9.0 (2.3)	9.4 (2.0)	9.1 (2.3)
"Off" time (hours)	6.4 (2.9)	5.6 (2.5)	4.8 (2.0)	6.1 (2.4)	6.2 (2.1)	6.9 (2.3)
UPDRS I-III	52.9 (8.5)	48.1 (7.8)	47.2 (7.7)	49.7 (7.9)	51.1 (8.8)	51.5 (9.2)
UPDRS IV 32-34	6.7 (2.8)	2.0 (1.1)	2.3 (1.0)	6.1 (2.8)	7.0 (2.9)	6.8 (2.9)
IGA reduction %	-	100	100	0	0	58
unchanged %	-	0	0	6	35	35
increase %	-	0	0	94	65	7
DRS	19.6 (1.2)	10.5 (1.3)	10.3 (1.6)	18.4 (1.5)	22.2 (3.4)	20.4 (1.4)
<b>PLACEBO</b>						
"On" time (hours)	9.1 (2.1)	9.2 (2.0)	9.1 (2.2)	9.0 (1.9)	9.0 (2.1)	9.0 (1.8)
"Off" time (hours)	6.2 (2.4)	6.1 (2.1)	6.2 (2.2)	6.3 (2.1)	6.3 (2.3)	6.3 (2.2)
UPDRS I-III	52.7 (8.2)	52.5 (8.3)	52.7 (8.2)	52.8 (8.1)	52.8 (8.2)	52.4 (8.0)
UPDRS IV 32-34	6.6 (2.6)	6.1 (2.4)	6.4 (2.6)	6.7 (2.6)	6.8 (2.4)	6.8 (2.3)
IGA reduction %	-	11	11	0	0	28
unchanged %	-	83	61	61	72	61
increase %	-	6	28	39	28	11
DRS	20.4 (1.9)	20.2 (1.6)	20.0 (1.6)	20.2 (1.5)	20.4 (1.7)	20.9 (1.7)

The patients who withdrew because of side effects other than dyskinesia, (shown in the figure) are omitted from calculations. (Ama, n=17; placebo, n=18)  
Values are mean (SD).



**Figure 1** Kaplan-Meier curve indicating the probability of dyskinesia worse than or equal to that recorded before initiation of treatment. Stars indicate drop outs because of side effects unrelated to dyskinesia. Black stars: placebo; white stars: amantadine.

# *Movement* **Disorders**

*Official Journal of the Movement Disorder Society*

## Management of Parkinson's Disease: An Evidence-Based Review

Produced by a task force commissioned  
by The *Movement* Disorder Society

Volume 17/Supplement 4, 2002

 **WILEY-LISS**  
ISSN 0885-3185

<b>Indication</b>
<ul style="list-style-type: none"> <li>• Prevention of disease progression</li> <li>• Symptomatic control of parkinsonism</li> <li>• Prevention of motor complications</li> <li>• Control of motor complications</li> <li>• Control of non-motor complications</li> </ul>
<b>Type of intervention</b>
<p><b>Drug treatment</b></p> <ul style="list-style-type: none"> <li>• Amantadine</li> <li>• Anticholinergics</li> <li>• Levodopa</li> <li>• MAO-B inhibitors</li> <li>• COMT inhibitors</li> <li>• DA agonists               <ul style="list-style-type: none"> <li>* Ergot-compounds                   <ul style="list-style-type: none"> <li>- Bromocriptine</li> <li>- Cabergoline</li> <li>- Dihydroergocryptine</li> <li>- Lisuride</li> <li>- Pergolide</li> </ul> </li> <li>* Non-ergot compounds                   <ul style="list-style-type: none"> <li>- Apomorphine</li> <li>- Piripeditil</li> <li>- Pramipexole</li> <li>- Ropinirole</li> </ul> </li> </ul> </li> <li>• Drugs used to control autonomic dysfunction               <ul style="list-style-type: none"> <li>- Hypotension</li> <li>- Urinary dysfunction</li> <li>- Gastrointestinal dysfunction</li> </ul> </li> <li>• Drugs used to control neuropsychiatric dysfunction               <ul style="list-style-type: none"> <li>- Treatment of depression</li> <li>- Treatment of dementia and psychosis</li> </ul> </li> </ul> <p><b>Surgical treatment</b></p> <ul style="list-style-type: none"> <li>• Deep brain surgery</li> <li>• Neural transplantation</li> </ul> <p><b>Physical and psychosocial treatment</b></p> <ul style="list-style-type: none"> <li>• Physical therapy</li> <li>• Psychosocial counseling</li> <li>• Speech therapy</li> </ul>

<b>Level of Evidence</b>	<b>Definition</b>
Level-I studies	Randomized, controlled trials
Level-II studies	Controlled clinical trials or observational controlled studies such as cohort or case-control studies
Level-III studies	Non-controlled studies like case series

Table 3 Rating Scale for Quality of Evidence

	Yes	Unclear/ Possibly	No	N/A
<b>RESULTS</b>				
1. Is an estimate of the treatment effect given	2	1	0	N/A
2. Is it of clinical importance	2	1	0	N/A
3. Is the estimate of treatment effect sufficiently precise	2	1	0	N/A
<b>VALIDITY: SELECTION</b>				
4. Was the spectrum of patients well defined?	2	1	0	N/A
5. Was the diagnosis of the disease well defined?	2	1	0	N/A
6. If pragmatic, were suitably broad eligible criteria used?	2	1	0	N/A
7. If explanatory, were eligibility criteria suitably narrow?	2	1	0	N/A
<b>MEASUREMENT</b>				
8. Was assignment to treatments stated to be random?	2	1	0	N/A
9. If yes, was the method of randomization explained?	2	1	0	N/A
10. Were all patients accounted for after randomization?	2	1	0	N/A
11. Were losses to follow-up low (<10)?	2	1	0	N/A
12. Were the treatment groups similar in important factors at the start of the trial?	2	1	0	N/A
13. Were all patients otherwise treated alike?	2	1	0	N/A
14. Were patients, health care workers and investigators "blind" to treatment?	2	1	0	N/A
15. Was assessment of outcome "blind"?	2	1	0	N/A
16. Was the occurrence of side effects explicitly looked for?	2	1	0	N/A
17. If yes, were estimates of their frequency/severity given?	2	1	0	N/A
<b>STATISTICAL ANALYSIS</b>				
18. Was the main analysis on "intention to treat"?	2	1	0	N/A
19. If no, was a sensitivity analysis performed?	2	1	0	N/A
20. Were additional clinically-relevant factors allowed for?	2	1	0	N/A
21. Were appropriate statistical methods used?	2	1	0	N/A
22. Were any "unusual" methods used?	2	1	0	N/A
23. If subgroup analyses were done, were they explicitly presented as such?	2	1	0	N/A
<b>UTILITY</b>				
24. Do the results help me choose treatment?	2	1	0	N/A
TOTAL (add ringed scores above):	(A)			
No. of questions which actually applied to this article (maximum=24):	(B)			
Maximum possible score (2 X B)	(C)			
OVERALL RATING (A/C expressed as a percentage)	%			

N/A=not applicable establishing conclusions

**Table 4. Definitions for specific recommendations**

<b><u>Efficacy Conclusions</u></b>	<b><u>Definition</u></b>	<b><u>Required Evidence</u></b>
Efficacious	Evidence shows that the intervention has a positive effect on studied outcomes	Supported by data from at least one high-quality (score $\geq$ 75%) RCT without conflicting Level-I data
Likely efficacious	Evidence suggests, but is not sufficient to show, that the intervention has a positive effect on studied outcomes	Supported by data from any Level-I trial without conflicting Level-I data
Unlikely efficacious	Evidence suggests that the intervention does not have a positive effect on studied outcomes	Supported by data from any Level-I trial without conflicting Level-I data
Non-efficacious	Evidence shows that the intervention does not have a positive effect on studied outcomes	Supported by data from at least one high-quality (score $\geq$ 75%) RCT without conflicting Level I data
Insufficient evidence	There is not enough evidence either for or against efficacy of the intervention in treatment of Parkinson's disease	All the circumstances not covered by the previous statements
<b><u>Safety</u></b>		
Acceptable risk without specialized monitoring		
Acceptable risk, with specialized monitoring		
Unacceptable risk		
Insufficient evidence to make conclusions on the safety of the intervention		
<b><u>Implications for Clinical Practice</u></b>		
Clinically useful	For a given situation, evidence available is sufficient to conclude that the intervention provides clinical benefit	
Possibly useful	For a given situation, evidence available suggests, but insufficient to conclude that the intervention provides clinical benefit	
Investigational	Available evidence is insufficient to support the use of the intervention in clinical practice, but further study is warranted	
Not useful	For a given situation, available evidence is sufficient to say that the intervention provides no clinical benefit	
Efficacy unlikely	Evidence suggests that the intervention does not have a positive effect on studied outcomes. Supported by data from any Level-I trial without conflicting Level-I data	

**Quality scores (%)**

**Based on Table III**

**Dixon, Munro, Silcocks**

**Checklist for Critical Approval**

**The EBM workbook**

**Butterworth Heineman 1997, Appendix I**

<b>PRINCIPIO ATTIVO</b>	<b>efficacia</b>					<b>sicurezza</b>
	<i>Prevenzione della progressione della malattia</i>	<i>Controllo complicanze motorie</i>	<i>Prevenzione delle complicanze motorie</i>	<i>Controllo del PD sintomatico</i>		
<b>Bromocriptina</b>	Dati inadeguati		Piuttosto efficace	Pochi dati	Molto efficace	Accettabile senza un monitoraggio specializzato
<b>Cabergolina</b>	Dati inadeguati	Efficace	Efficace	Pochi dati	Poche evidenze	Accettabile senza un monitoraggio specializzato
<b>Pergolide</b>	Dati inadeguati	Efficace	Pochi dati	Efficace	Efficace	Accettabile senza un monitoraggio specializzato
<b>Pramipexolo</b>	Dati inadeguati	Efficace	Efficace	Efficace	Efficace	Accettabile, seppur bisogna tener conto degli "sleep attacks"
<b>Ropirinolo</b>	Dati inadeguati	Efficace	Efficace	Efficace	Dati insufficienti	Accettabile senza un monitoraggio specializzato
<b>Apomorfina</b>	Dati inadeguati	Pochi dati	Efficace	Pochi dati	Efficace	Accettabile
<b>Lisuride</b>	Dati inadeguati	Pochi dati	Pochi dati	Efficace	Efficace	Accettabile
<b>Piribedil</b>	Dati inadeguati	Pochi dati	Pochi dati	Efficace	Efficace	Non ci sono molti dati significativi

	Studio	Overall Quality (%)	Durata (mesi)	Tipo di studio	N. Pz	End points	Staging	Metodi di valutazione	Follow-up	Dose Media (mg /die)	Effetti indesiderati e collaterali
Bromocriptina	Montastruc 1994	69	60	L-Dopa-controlled, parallel, open-label	60 de novo	< complicanze motorie a lungo termine	PD iniziale	CURS UPDRS H/Y	UPDRS Brom 10.6 L-Dopa 11.0	10.652	Allucinazioni
	Korczyń 1998	89		Ropi vs Brom	335					8.5	Sonnolenza, disturbi psichiatrici
Cabergolina	Rinne 1998	75	12	Open-label con L-Dopa	413 de novo	<30% UPDRS	EoPD in monoterapia	UPDRS CGI	81% pz con CAB 88% pz con L-Dopa	4mg+ 600 L-Dopa	Edema, gastrite, disturbi sonno, ipotensione, confusione, allucinazioni
	Hutton 1996	80	6	Randomized, parallel, placebo-controlled	188 con deterioramento fine dose	<UPDRS II-III (-16% vs -6%) <mg/die L-Dopa	Combinazione tardiva cab/L-Dopa	UPDRS ADL	<UPDRS-III (13.7 vs 16.3) <mg/die L-Dopa (175mg vs 25.5mg)	3.2	Disturbi SNA e neuropsich.
Pergolide	Onalow 1994	83	6	Randomized, parallel, placebo-controlled	376 con discinesia moderata, deterior. fine dose	<mg/die L-Dopa >ADL scores	Combinazione tardiva con L-Dopa	ADL; Scala discinesie q.tà ("off")	<25% vs 5% >ADL (22.1 vs 30.8)	2.94	Discinesie, allucinazioni, insonnia, sonnolenza
	Barone 1999	95	3	Randomized, parallel, double-blind, placebo-controlled	105 de novo	<30% UPDRS-III	Monoterapia	UPDRS CGI ADL	UPDRS (57% vs 17)	2	Nausea, vomito, sonnolenza (15% vs 6%)
Pramipexolo	Shannon 1997	75	24	Randomized, parallel, placebo-controlled	335	Variazioni % UPDRS-III	EoPD in monoterapia	UPDRS ADL	UPDRS 8.7	3.8	Sedazione (18% vs 9%) Allucinazioni
	P. Study Group 2000	95	24	Randomized, L-Dopa-controlled	151 Pram, 150 L-Dopa	Complicazioni motorie >mg/die L-Dopa <uptake SPECT	Monoterapia	UPDRS SPECT	53% vs 39% con L-Dopa	2.78 vs 406	(10% vs 2%)
Ropinirolo	Rascol 2000	90	60	Randomized, parallel, double-blind, L-Dopa controlled	268 de novo	Comparsa discinesie		UPDRS ADL		16.5+ 427 L-Dopa; 753	Allucinazioni (17% vs 6%)
	Whone, REAL PET Study Group 2003	95	24	Randomized, parallel, L-Dopa-controlled, double-blind	186	<UPDRS %discinesie <degenerazione striatale	H/Y 1-2.5 esordio<2 aa no L-Dopa	UPDRS PET	<UPDRS (67.8%Rop, 74.4%L-Dopa); %discinesie; <uptake PET in putamen	9 vs 458.8; A 2 aa: 12.2 vs 558.7	Nausea, sonnolenza, allucinazioni, confusione
Apomorfin	Pietz 1998		3-66		60	<"off" <mg/die L-Dopa <<discinesie	50% "off" Obeso: 2.2 intensità 1.7 durata	H/Y, SCHWAB Obeso (discinesie intens. 0-4, durata 0-3)	<25% "off" 450mg/die L-Dopa Obeso: 1.9 intensità 1.5 durata	116inf. cont. o sottocute; 900L-Dopa	
Lisuride	Allain 2000	73	60	Randomized, parallel, L-Dopa-controlled	82		EoPD <3aa; Baseline: 446.7 mg/die L-Dopa, UPDRS 38.37	<mg/die L-Dopa >UPDRS in "on"	52% pz. 387.5mg/die L-Dopa =UPDRS		
Piberidil	Rondot 1992	70	3	Randomized, placebo-controlled	113 de novo	<%Webster scale	EoPD	WEBSTER	41% WEBSTER	207	Nausea, vomito, insonnia

## Implications for Clinical Practice

<b>Bromocriptine</b>	Clinically Useful		<b>Dose</b>	<b>Equivalence</b>
	1 y of therapy	30% 3 years	20-40 mg/die	1
<b>Cabergoline</b>	Clinically Useful	20 % 3-5 years	2 – 5mg/die	?
<b>Lisuride</b>	Possible Useful	?	1.5 –3.5mg/die	?
<b>Pergolide</b>	Clinically Useful	3 months	1.5 – 4.5mg/die	1/10
<b>Pramipexole</b>	Clinically Useful	?	2.0 – 4.5mg/die	?
<b>Ropinirole</b>	Clinically Useful	6 months	8.0 –18.0mg/die	?
		L-Dopa>Ropinirole		
		Ropinirole>Bromocriptine		

## IMPLICATIONS FOR CLINICAL RESEARCH

A number of important issues remain to be discussed with ropinirole and should be addressed in future studies. Some of these include:

- The antiparkinsonian efficacy of ropinirole in L-dopa-treated PD patients should be better evaluated.
- Comparative trials need to be done with other DA agonists (eg. pergolide, pramipexole) as bromocriptine is not widely used anymore in many countries.
- Ropinirole should be compared to MAO-B inhibitors and COMT inhibitors in patients with advanced PD who have fluctuations.
- The true benefit/risk ratio of ropinirole regarding sleep problems needs to be better investigated, both through large epidemiological studies and specific pharmacodynamic sleep studies. Further studies are required to assess if such cases simply correspond to somnolence, which is frequently observed in clinical trials with ropinirole (and many other dopaminergic agents), if this is a specific problem of some DA agonists like ropinirole, if this is a dose-related effect, and if some patients exhibit a special susceptibility to somnolence.
- Longer follow-up studies (up to and more than 10 years) should be conducted to assess if patients morbidity, mortality and quality of life is improved by ropinirole.
- Pharmacoeconomic trials should be conducted to assess if it is justified to use an expensive DA agonist, like ropinirole, instead of a cheaper one, like bromocriptine.
- The role of ropinirole on non-motor symptoms, depression for example, should be studied.

## IMPLICATIONS FOR CLINICAL RESEARCH

- Since bromocriptine has been available clinically for a long time, most of the reported studies to date were done prior to current standards used for clinical research. Consequently, quality scores are lower than what is normally seen with more recent studies conducted with newer compounds, like pramipexole and ropinirole. Because bromocriptine is less expensive (generic formulations are available in many countries), and there is little evidence that bromocriptine is markedly less effective or less potent than other newer dopamine agonists, modern comparative trials and pharmacoeconomic trials are needed to compare these agents to verify or negate clinical similarities or differences among these agents.
- Bromocriptine is empirically recommended in younger rather than older patients due to the risk of associated adverse reactions. Well designed trials should be conducted to confirm this practice and to define what is the optimal dose range.
- There is a need to assess if initial bromocriptine monotherapy, with late levodopa supplementation is equivalent regarding long-term efficacy (10 years), safety, and costs as compared to combined early L-dopa and bromocriptine treatment in de novo patients with PD (early combination strategy).
- Additional studies are also needed to assess if patients should be started on initial bromocriptine monotherapy (in an effort to delay the start of L-dopa therapy), or if patients should be started with L-dopa and supplemented with bromocriptine once motor complications appear.
- Further long-term studies are necessary to assess the impact of bromocriptine on quality of life and mortality.

## IMPLICATIONS FOR CLINICAL RESEARCH

In the literature there are few reports on the efficacy and safety of cabergoline. Additional studies are needed including:

- Well-designed, short-term, placebo-controlled study in L-dopa naïve PD-patients to properly assess the magnitude of the effect of cabergoline on parkinsonian symptoms.
- Appropriate comparisons with other antiparkinsonian agents (other dopamine agonists, MAO-B and COMT-inhibitors).
- Studies comparing the risk of fluctuations and dyskinesias in patients treated with cabergoline versus treatment with other shorter-acting dopamine agonists (e.g. lisuride). The prolonged elimination half-life of cabergoline offers an advantage of once-daily dosing, but possible disadvantages with this treatment regimen are not well understood. For example, the prolonged elimination half-life might be a handicap in terms of wash-out of adverse events (like psychosis). These benefits vs. risks need to be further evaluated in prospective, controlled trials.
- Studies on the long-term quality of life impact of cabergoline, effects on mortality, and pharmacoeconomic benefits.

## IMPLICATIONS FOR CLINICAL RESEARCH

- Pergolide effects on long-term clinical outcomes and disease progression are needed (ie. The PELMO-PET study is ongoing).
- Active comparator trials evaluating the relative efficacy of pergolide to other DA agonists and other antiparkinsonian agents, like MAO-B and COMT inhibitors are needed.
- Pharmacoeconomic studies are needed to compare the cost benefits between the different DA agonists.
- Long-term data on the impact of pergolide on quality of life and mortality are needed.

## IMPLICATIONS FOR CLINICAL RESEARCH

- Randomized, controlled trials testing the efficacy and tolerability of pramipexole should be done including comparative trials to other dopamine agonists and to other antiparkinsonian agents such as MAO-B and COMT inhibitors.
- Additional studies are needed concerning the incidence of sleep attacks in patients taking pramipexole. The relative frequency of this adverse reaction needs to be compared to other treatments in this class of medication.
- Long-term studies that specifically investigate the low propensity of pramipexole for inducing dyskinesia in L-dopa-naïve (non-primed) patients with PD are needed.
- The role of pramipexole on prevention of disease progression (or neuroprotective effects) needs to be further studied.
- Future long-term, follow-up studies (10 years) are necessary to clearly assess the usefulness of the early use of pramipexole on patient's functioning, life expectancy, and quality of life.
- Pharmacoeconomic studies are needed to assess the benefits of this relatively expensive drug compared with less expensive DA agonists (eg, older medications like bromocriptine).
- The effects of pramipexole on non-motor symptoms, like depression, should be tested in clinical trials.

**Table 3.**  
List of equivalence dosages of all dopamine agonists which are on the German market

Pergolide	0,5	1	1,5	2	2,5	3	3,5	4	4,5	5
$\alpha$ Dihydrocriftine	30	60	90	120						
Lisuride	0,5	1	1,5	2						
Cabergoline	0,8	1,5	2,25	3	3,75	4,5	5,25	6		
Pramipexole	0,5	1	1,5	2	2,5	3	3,5	4	4,5	
Ropinirole	2	4	6	8	10	12	14	16	18	20
Bromocriptine	5	10	15	20	25	30				

All medication is given in milligrams

**Table 4.**  
Characteristics of dopamine agonists

Dopamine agonist	D1	D2	D3	$\alpha$ 1	$\alpha$ 2	$\beta$	5-HT	HLT (h)
Bromocriptine	-	++	+	+	+	?	+	6
Cabergoline	+	+++	++	+	+	?	+	68
$\alpha$ Dihydroergocriptine	$\pm$	+++	?	+	+	0	+	16
Lisuride	$\pm$	+++	+++	$\pm$	$\pm$	?	$\pm$	2-3
Pergolide	+	+++	+++	$\pm$	++	+	+	16
Pramipexole	0	+++	+++	0	+	0	0	8-12
Ropinirole	0	+++	++	0	0	0	0	6-9

$\alpha$ 1, $\alpha$ 2, adrenergic receptor subtypes,  $\beta$  adrenergic receptor, D1,D2 are dopamine receptor subtypes which are important for motor function, D3 dopamine receptor which may be associated with mood, 5-HT serotonergic receptor,, HLF plasma half life time.

- antagonist, + agonist with low affinity, ++ agonist with medium affinity, +++ agonist with high affinity,  $\pm$  partial agonist, 0 agonist with very low affinity, ? no information available.  
(adapeted from Gerlach et al. 2001)

**Table 5.**  
Which dopamine agonists should be combined?

- an ergot derivative with a non-ergot derivative
- a dopamine agonist with a long plasma half-life with one with a short plasma half-life
- two dopamine agonists with different receptor profiles
- two dopamine agonists with different side effects
- a dopamine agonist patch and an orally applicable agonist



NEW TRENDS IN

CLINICAL NEUROLOGY

SERIES

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# PARKINSON'S DISEASE

## The Role of Dopamine Agonists

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Edited by A. Lieberman and X. Lataste

### CONCLUSIONS

- (1) Only a small proportion of *de novo* parkinsonian patients maintain a sustained antiparkinson effect when they are treated with dopamine agonists alone.
- (2) However, patients treated with dopamine agonists alone have far less fluctuations and dyskinesias as compared to patients receiving levodopa.
- (3) Long-term studies show that the early combination of low doses of levodopa and a dopamine agonist (bromocriptine, pergolide or lisuride) not only improves parkinsonian disability, but also inhibits the development of fluctuations (especially end-of-dose disturbances) and dyskinesias.
- (4) Combined treatment with a dopamine agonist and low-dose of levodopa offers a better long-term effect than high-dose levodopa, presumably by maintaining the striatal dopamine neurotransmission normally for a longer time than levodopa alone.
- (5) The combination of a dopamine agonist with low doses of levodopa can be started early in the disease and can reduce the
- (6) It appears advisable that the new policy of treatment of parkinsonian patients should begin early with a dopamine agonist combined with a low dose of levodopa.