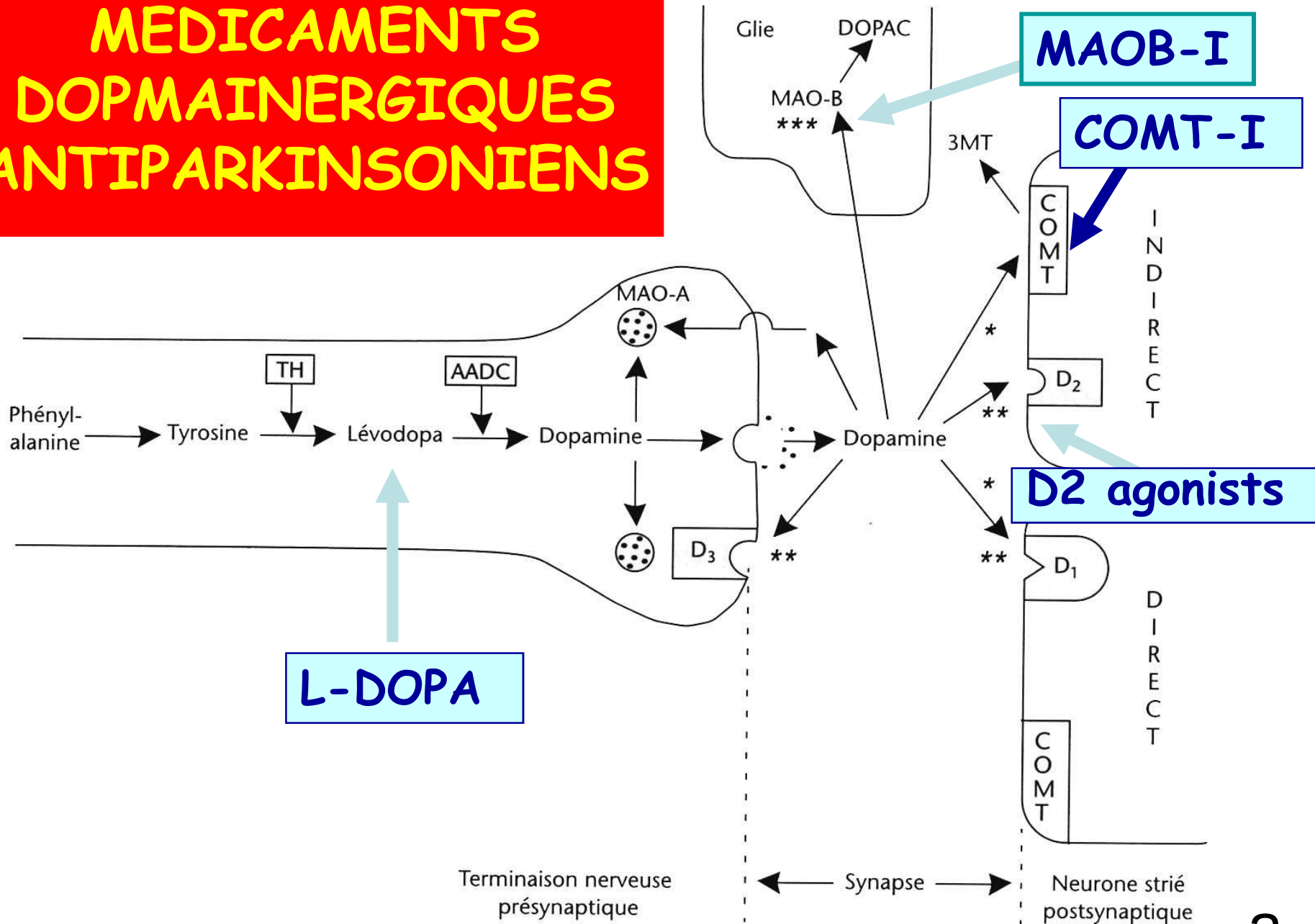


MEDICAMENTS DOPAMINERGIQUES ANTIPARKINSONIENS



a

➤ Trois « nouveaux » agonistes dopaminergiques:

- Rotigotine (NEUPRO[®])
- Ropinirole LP (REQUIP LP[®])
- Pramipexole LP (SIFROL LP[®])

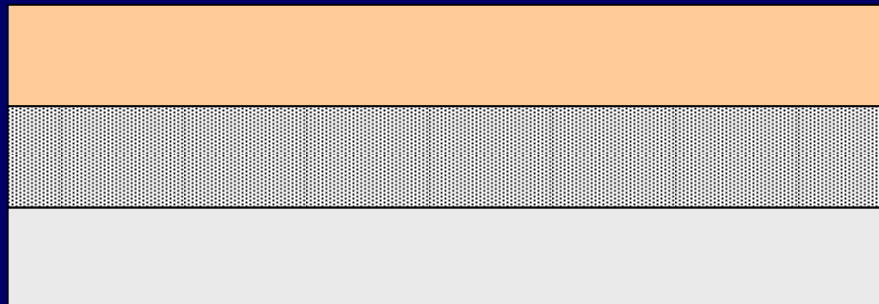
Une efficacité antiparkinsonienne avérée et une simplification des prises journalières

Quel autres avantages ?

(ASMR=5)

Neupro® patch

Schematic Cross Section



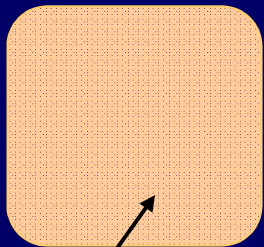
Backing Film 30 μ m

Self-adhesive

Drug Loaded Matrix 50 μ m

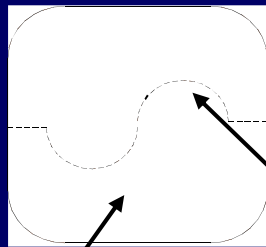
Release Liner 70 μ m

Front View



Backing Film

Back View

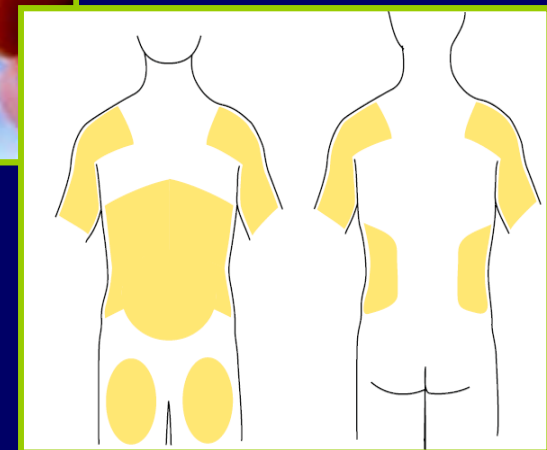


Release Liner

**S-cut
(peel-off aid)**



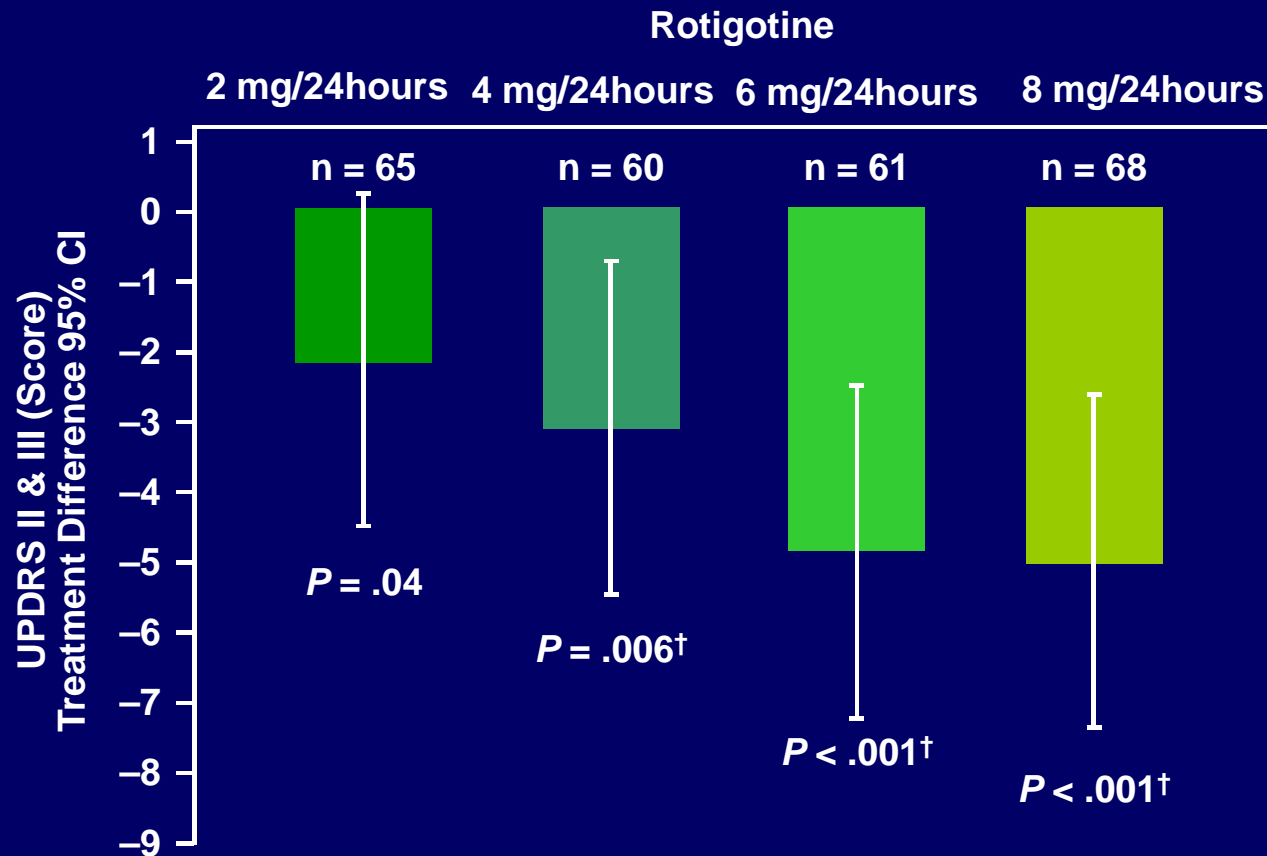
Application sites*



* Use a different site each day for 14 days. Press for 20 to 30 seconds to ensure adhesion. May be worn during exercise, in shower or pool

SP 506 – Results (*early stage PD*)

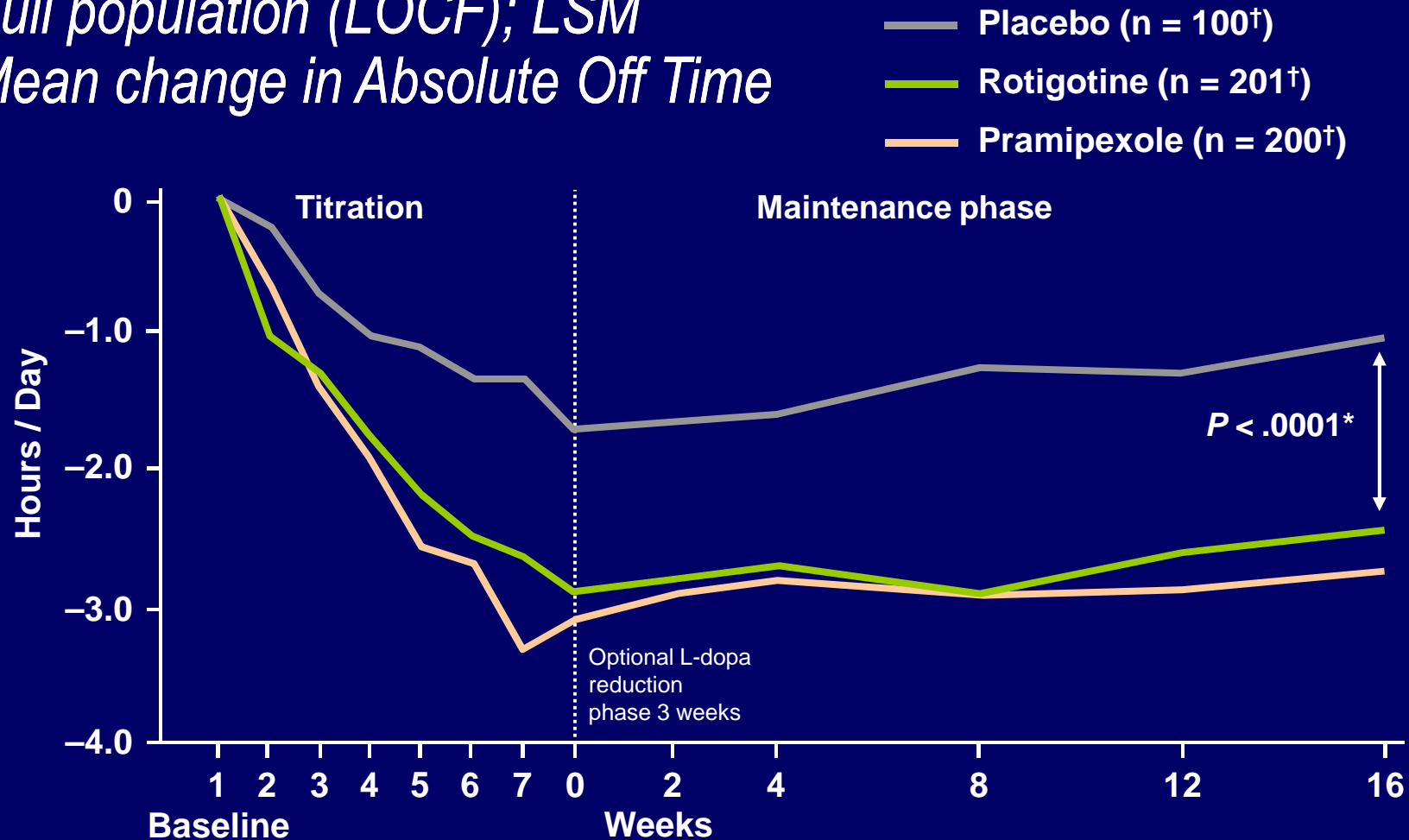
Intent to treat population – difference over placebo



Study details: N=329. Data adjusted – adjusted for baseline and country. Percentage (of safety set) completers by dose (P,2,4,6,8): 84, 82, 89, 85, 84. † One-tailed t-test at .025 level of significance. Data on file at UCB. Partial cohort reported in: Parkinson Study Group. Arch Neurol. 2003;60:1721-1728.

SP 515 – Results (advanced PD)

Full population (LOCF); LSM
Mean change in Absolute Off Time



**P* value for LS means. † Five patients did not complete both BL and at least one post-BL endpoint measurement.
Median dose: RTG 16 mg / 24 h; PRM 3 mg / d. Completers (PBO, RTG, PRM): 74.3%, 88.7%, 85.6%; AE d/c: 5.9%, 5.4%, 7.0%
Adapted from Poewe, W. et al. (2007) Lancet Neurology 6:513-201; Poewe et al. WPC 2006 poster

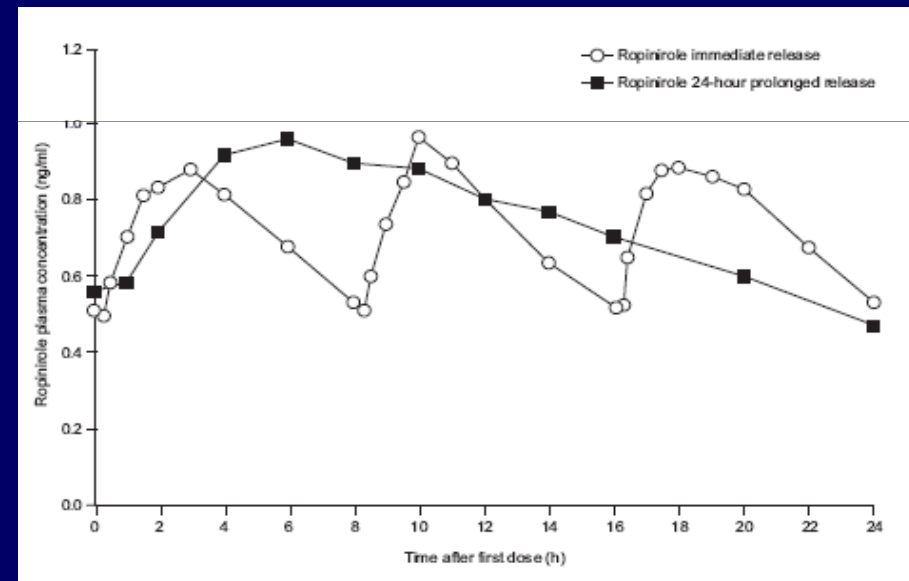
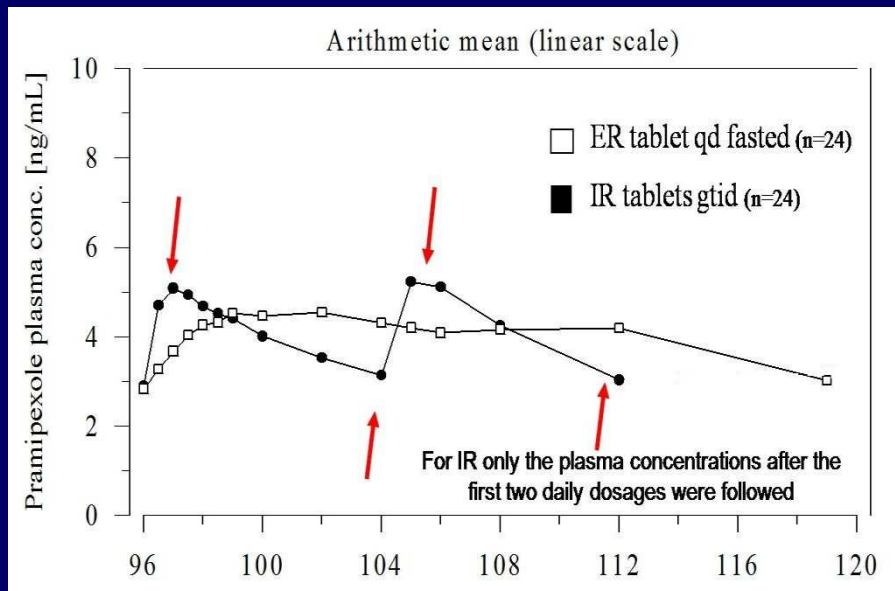
SP 515 - Most common adverse events

<i>% of patients with AE (total safety set) (advanced PD)</i>	PRM N=201	RTG N=204	Placebo N = 101
Nausea	13	17	11
Erythema	4	9	5
Pruritus	2	9	4
Back pain	8	6	4
Somnolence	12	12	8
Dyskinesia	15	12	3
Dizziness	10	6	4
Headache	7	4	5
Hallucinations	7	5	1
Orthostatic hypotension	5	3	5

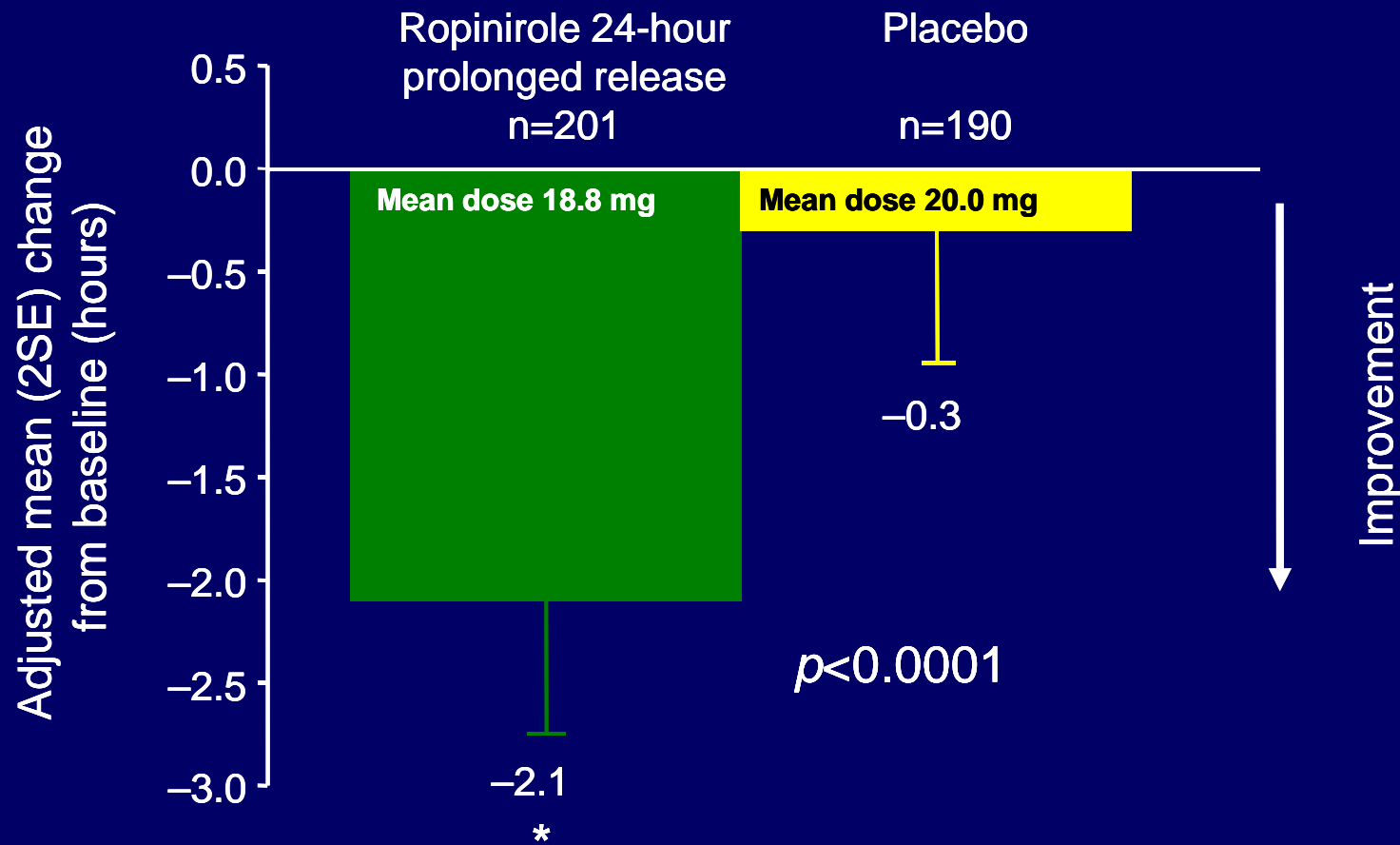
PRM: pramipexole; RTG: rotigotine

Pramipexole(SIFROL^o) LP et Ropinirole (REQUIP LP^o)

Une seule prise par jour

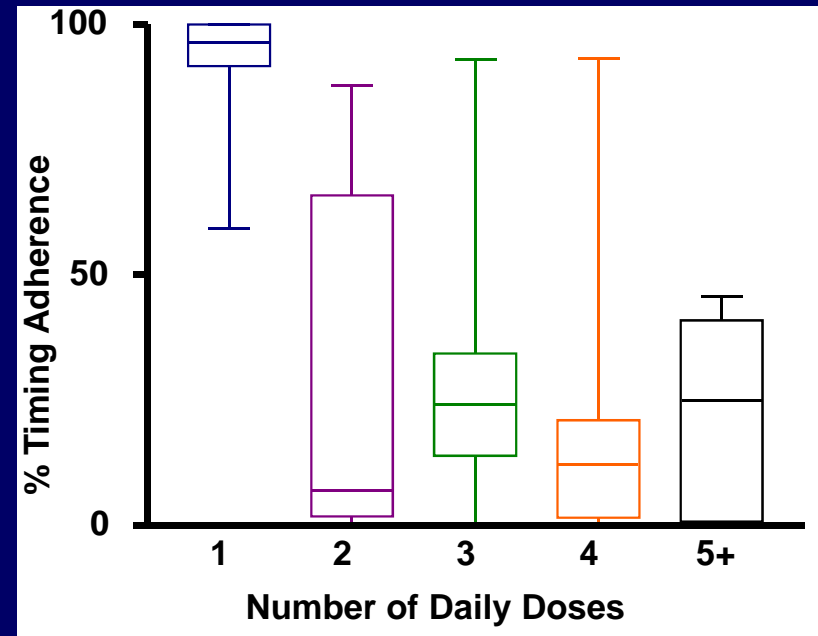


Adjusted mean change from baseline in daily awake time spent “off” at Week 24 LOCF (ITT population)



AVANTAGE POTENTIEL DES AGONISTES LP EN PRATIQUE

Une seule prise:
Plus pratique
Meilleure adhésion
Meilleure observance



Meilleure observance avec les agonistes à prise unique comparés aux agonistes avec prises multiples

(Grosset *et al. Mov Disord* 2007;22(15):2294)

Syndrome de “dysregulation dopaminergique” et troubles impulsifs

- Incidence estimée entre 1 et 10%
- Facteurs prédisposants (jeune age, sexe masculin, dépendance à l'alcool, agonistes dopaminergiques...)

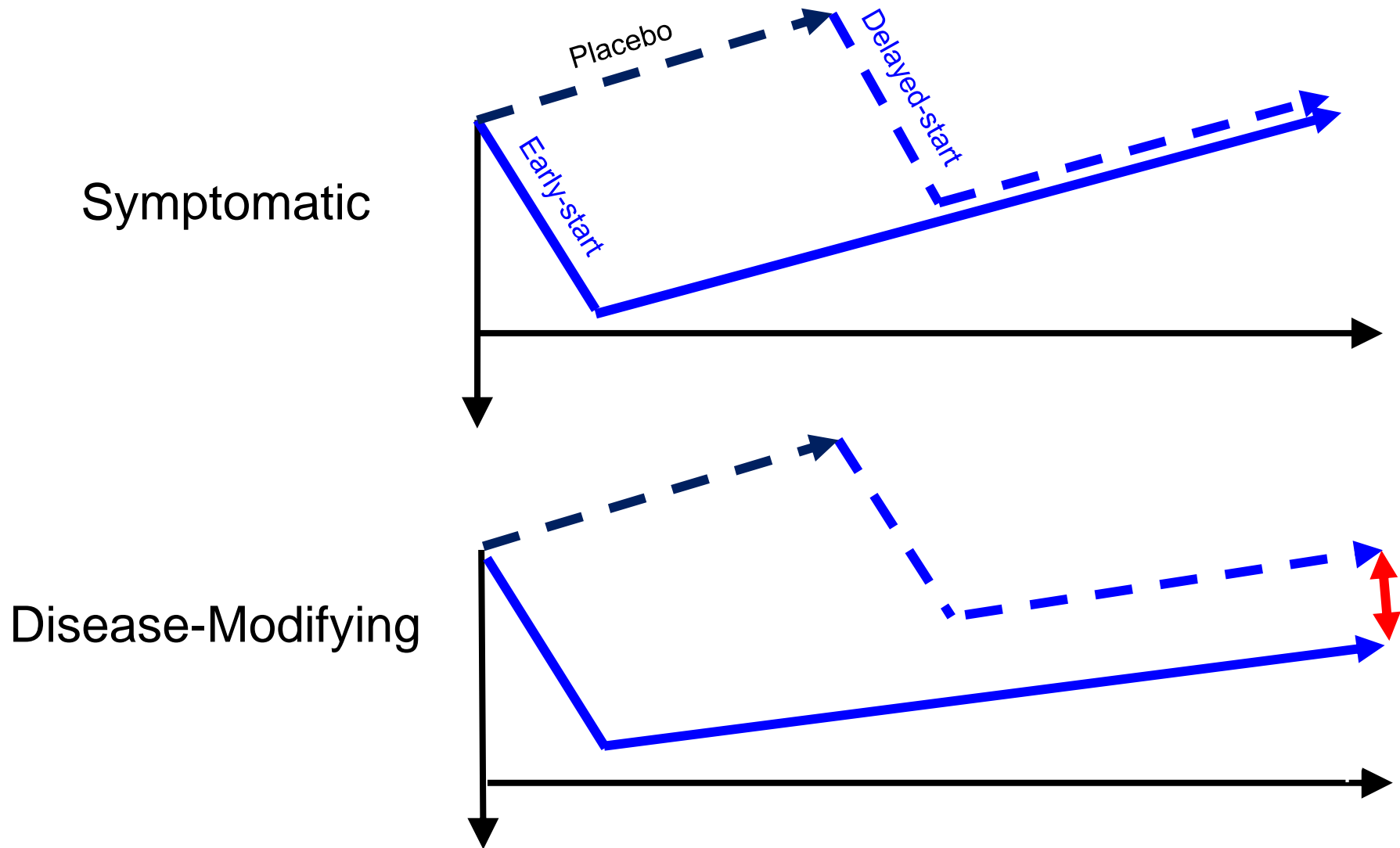


➤ **Un nouvel IMAO-B: Rasagiline (AZILECT[®])**

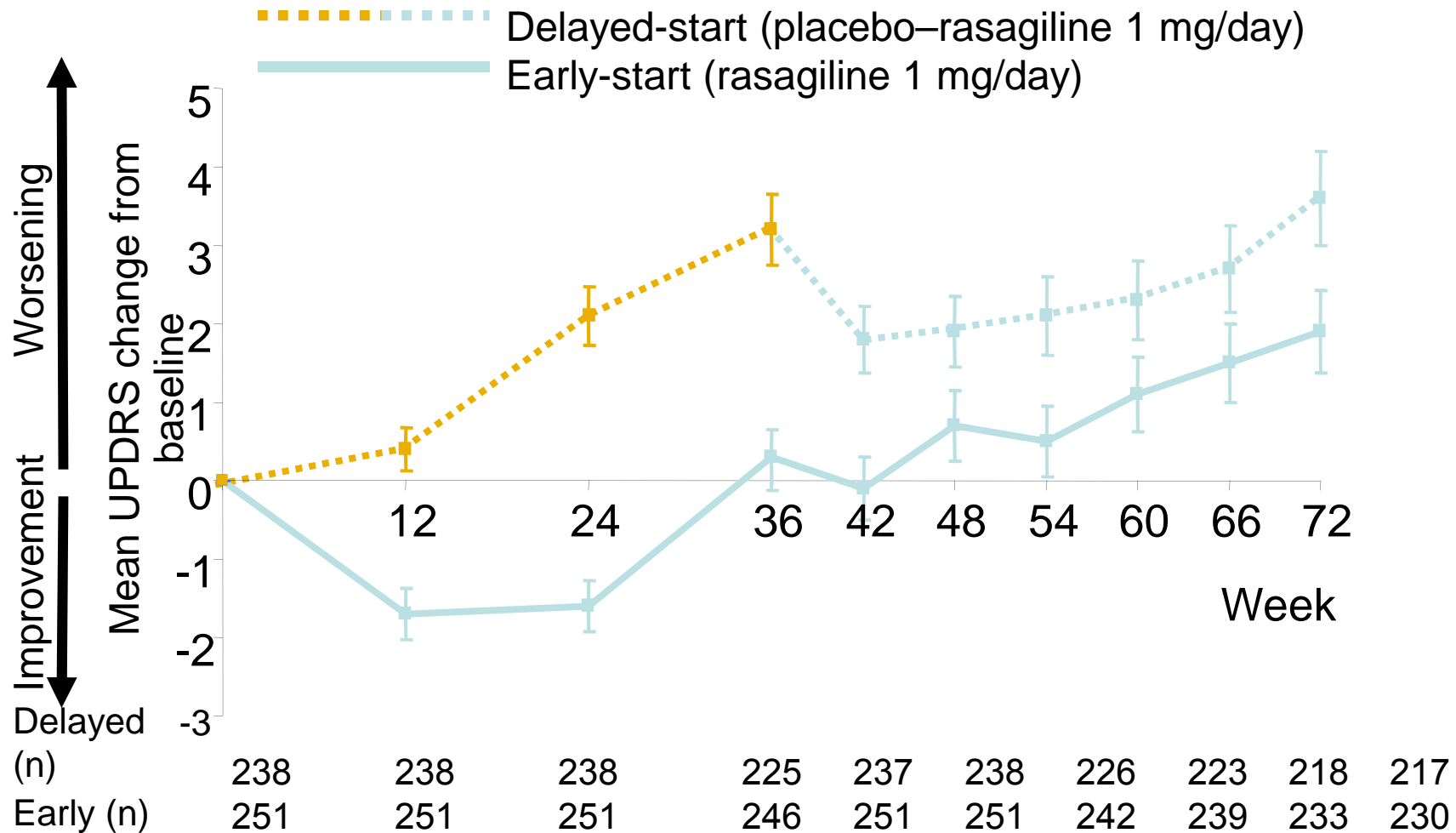
- Un antiparkinsonien à l'efficacité démontrée mais modeste
- Une dose (1mg/j), une prise/j, pas de titration
- Peu d'effets indésirables (interactions ?)
- Un effet possible pour modifier le cours évolutif de la maladie de Parkinson ?

(ASMR = 5)

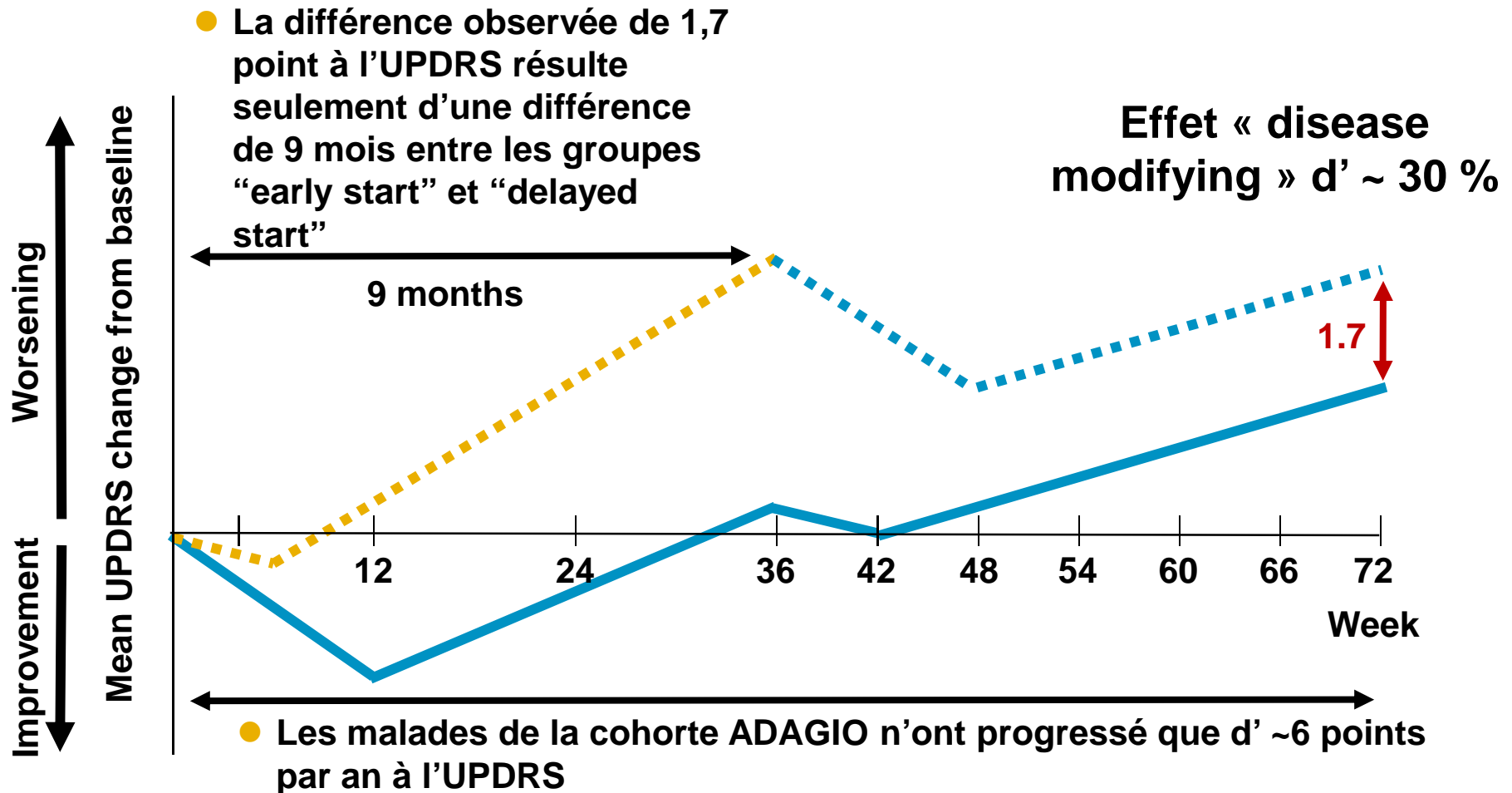
DELAYED START DESIGN:



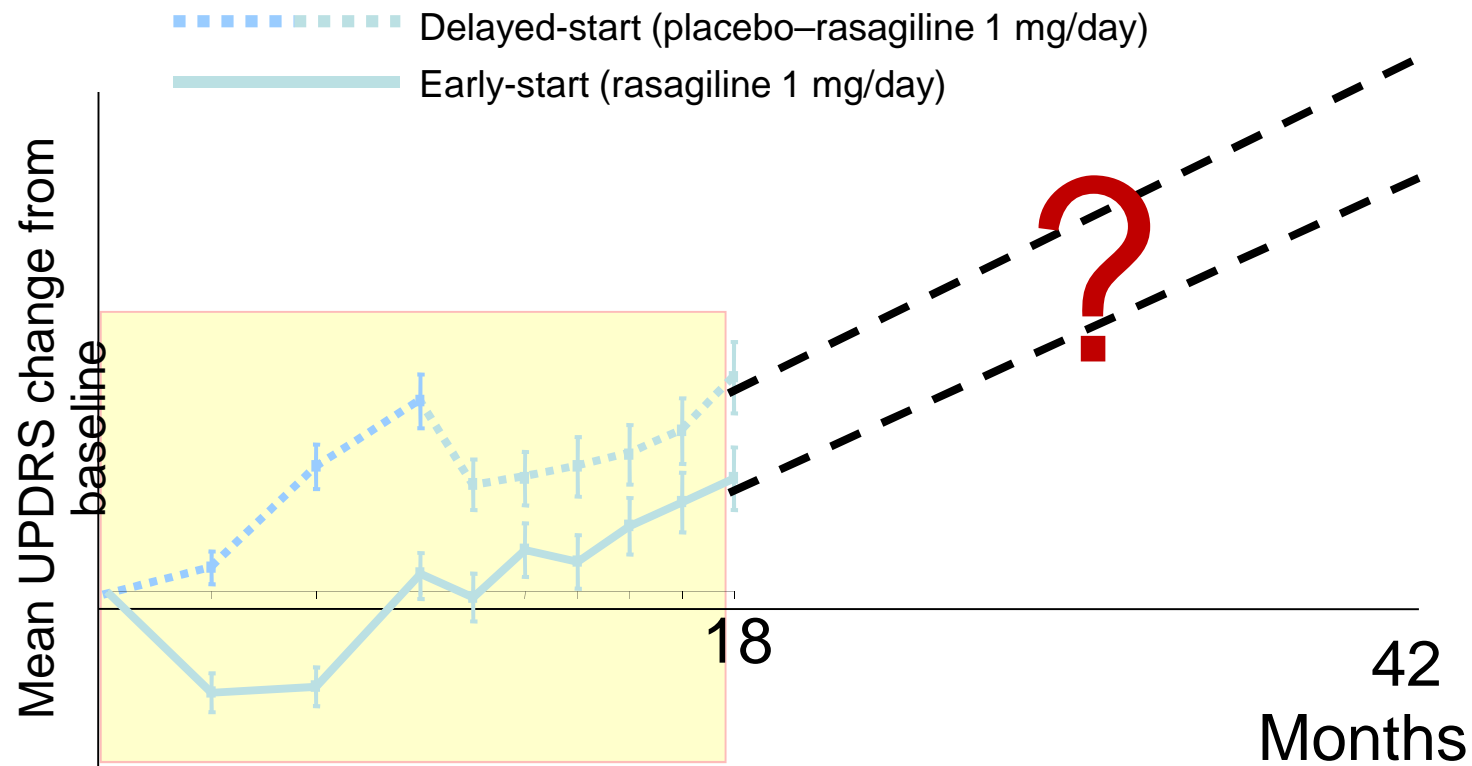
ADAGIO: mean UPDRS change from baseline, rasagiline 1 mg/day



ADAGIO: bénéfice de 1.7 points UPDRS en faveur du groupe "early start". Quelle importance pour la pratique?



LE PLAN EXPERIMENTAL DU DELAYED-START EST DE NATURE EXPLICATIVE ET NON PAS PRAGMATIQUE

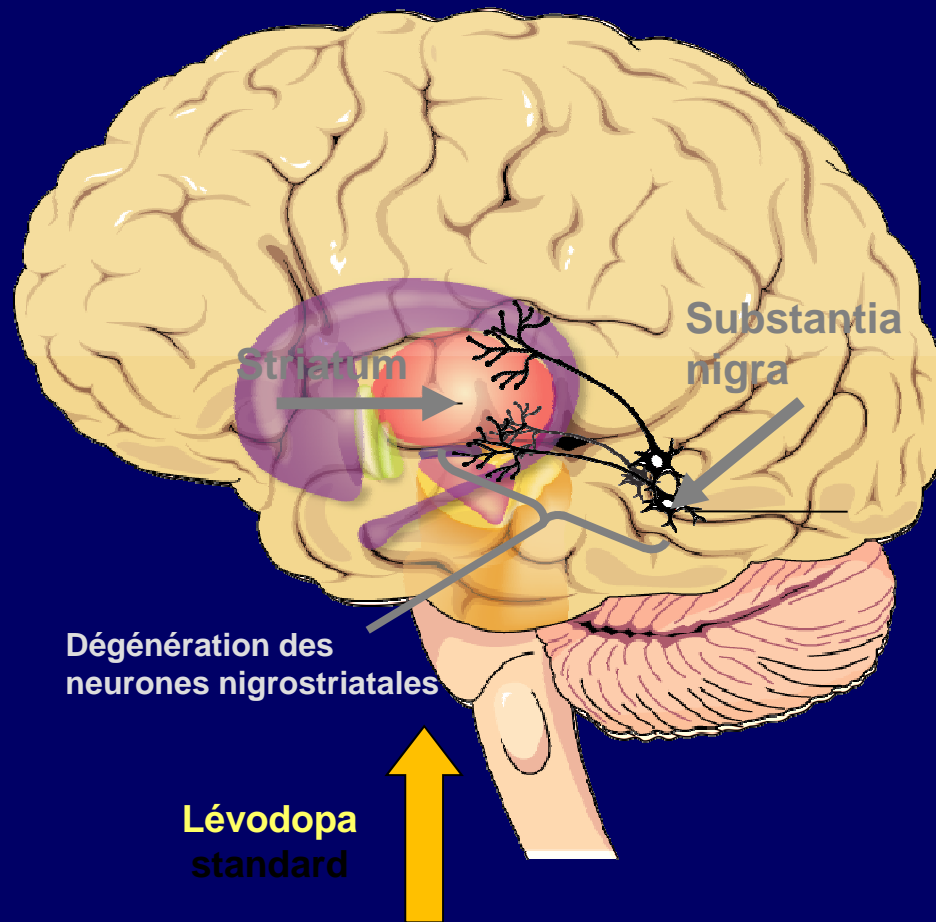


⇒ Suivi au long cours de la cohorte ADAGIO

➤ STRIDE-PD:

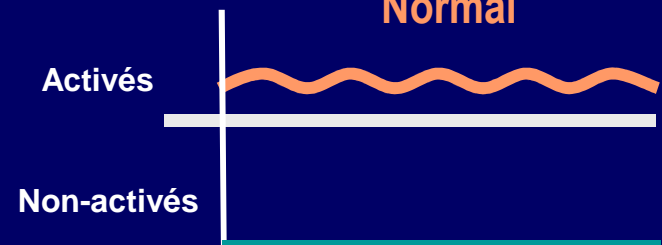
- Une stimulation dopaminergique théoriquement moins « pulsatile » devrait diminuer le risque de survenue de dyskinésies
- Mais dans l'étude STRIDE-PD, l'usage précoce de L-DOPA + Carbidopa + entacapone (STALEVO[®]) a augmenté le risque de dyskinésies !...

Administration (dis)continue des médicaments et pulsatilité de la stimulation des récepteurs dopaminergiques

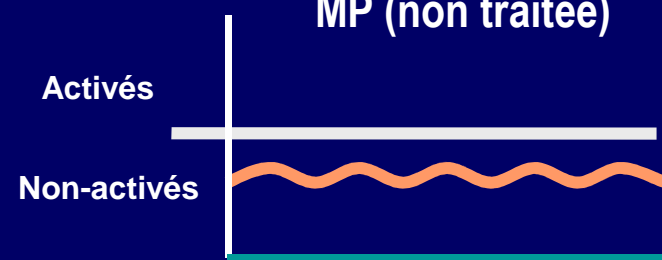


Etat des récepteurs dopaminergiques

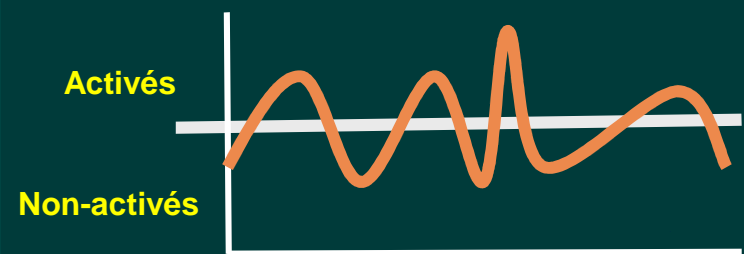
Normal



MP (non traitée)

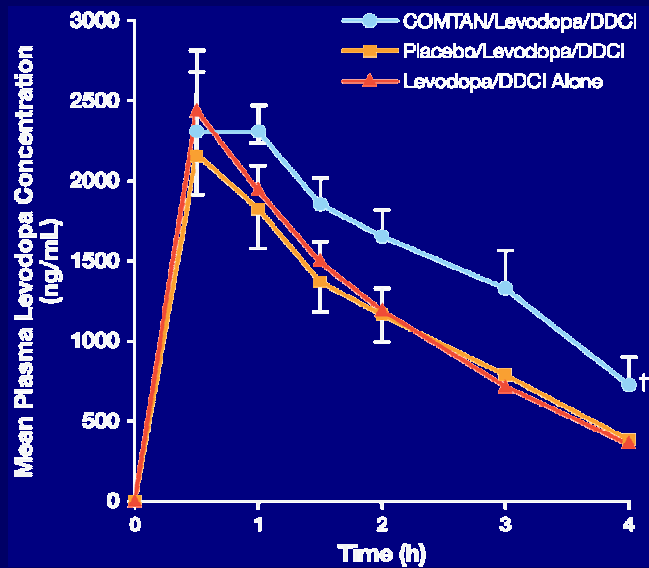


Levodopa standard

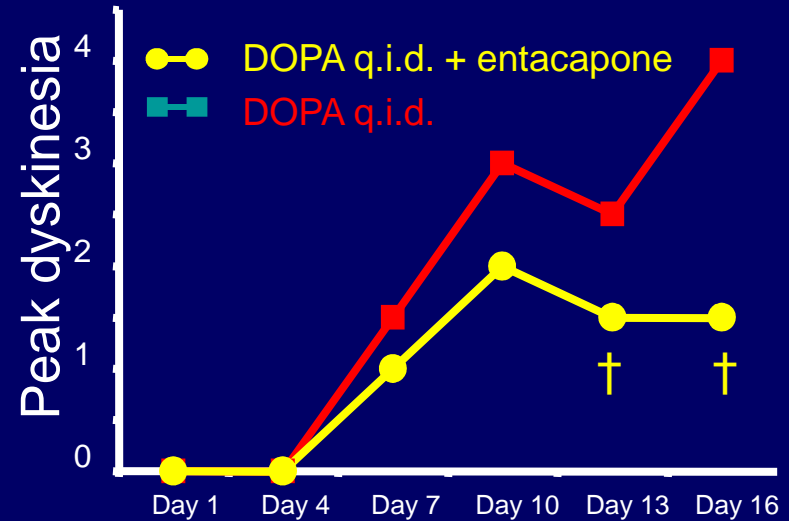


EARLY COMBINATION OF L-DOPA + ENTACAPONE

PK: Entacapone prolongs L-DOPA elimination half-life



MPTP-marmoset: Less dyskinesia when entacapone is associated early with L-DOPA



STRIDE-PD:
More dyskinesias on early combination (L-DOPA + entacapone)

