

Prolonged release dopamine agonists in clinical practice: a comparative European multicentre survey of tolerability rates and impulse control behaviour trends in young and old PD.

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OBJECTIVES:

- To address **comparative tolerability/retention rates** (minimum 6 months use) of oral prolonged release (PR) dopamine agonists (DAs) and rotigotine skin patch (RTG) in an European real life population base in young (< 75 yrs) and old (≥ 75 yrs) PD
- To compare **impulse control disease/behaviour (ICD) rates** in cases with active DA intake, to dissociate ICD leading to discontinuation and managed by optimising DA therapy

BACKGROUND:

- Comparative tolerability/ retention rate of **prolonged release** DAs are unknown in patients over 75 years of age.
- Tolerability can be classified as suggested by Shulman et al.²
- ICDs are thought to be related to the use of immediate release DAs in PD (17.1% in DOMINION study³)

METHODS:

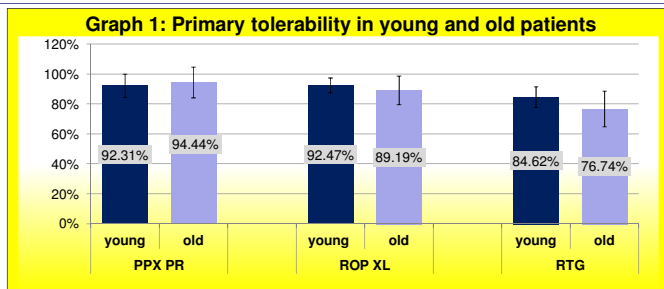
- Retrospective/ prospective clinic interview and case note survey (audit based questionnaire as per Appiah-Kubi et al.¹)
- 373 cases initiated on DA were included: RTG used in 152 (mean dose 8.6 mg), ROP XL in 150 (12.6 mg), PPX PR in 64 (2.8 mg).

Table 1: DEMOGRAPHICS	All cases		ICD cases
	No/ Mean/% (Distr./ Range)	% Distr./ Median (Range)	No/ Mean/% (Distr./ Range)
Patients (Male: Female)	373 (225M: 148F)	60.3%M: 39.7%F	52/ 13.9% (41M: 11F)
Age (yrs)	68.4	69.0 (37– 90)	62.0 (42– 85)
Age of PD onset (yrs)	60.6	62.0 (18– 85)	55.0 (34– 85)
Age of PD onset <50 Patients (Male: Female)	61/ 16.4% (46M: 15F)	75.4%M: 24.6%F	18/ 34.6% (14M: 4F)
Duration of Disease (yrs)	7.7	(0– 37)	7.2 (0–24)
Hoehn & Yahr Stage	2.7	2.5 (1.0– 5.0)	2.8

Results TOLERABILITY:

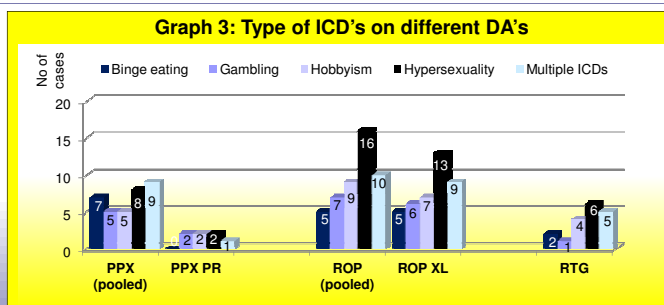
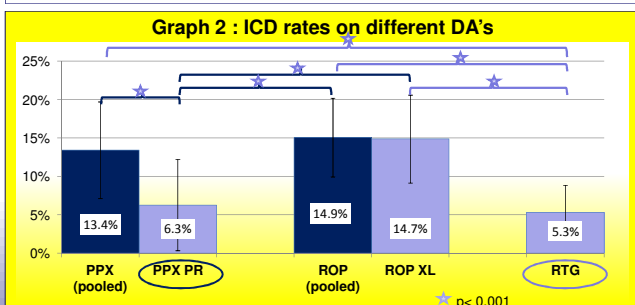
- 110 of 134 assessable patients (82.1%) on RTG tolerated the drug, 119/130 (91.5%) tolerated ROP XL and 53/57 tolerated PPX PR (93.0%).
- No significant differences of tolerability rates were observed between the age groups or the different PR DAs (p>0.09, chi² test, graph 1).
- 37 of the 373 evaluated cases (9.9%) report treatment with dual agonists (mostly oral with patch).
- 38/148 assessed patients (25.7%) suffered from swallowing difficulties, 81.0% of which tolerated transdermal patch therapy.

Table 2: Main reason for discontinuation (% / total on therapy)	PPX PR (n=64)		ROP XL (n=150)		RTG (n=152)	
	Young (n=45)	Old (n=19)	Young (n=108)	Old (n=42)	Young (n=104)	Old (n=48)
Age: young <75 yrs old ≥75 yrs						
Skin reaction	N/A	N/A	N/A	N/A	11.2%	3.3%
Lack of effect	0%	0%	2.0%	0%	4.6%	4.6%
Somnolence	3.2%	0%	1.4%	0.7%	0%	0.7%
Hallucination	1.6%	3.2	2.7%	2.0%	0.7%	1.3%
Confusion	0%	1.6	1.4%	0.7%	0.7%	2.0%



Results ICD:

- 52 cases (13.9%) reported impulse control disorders (ICD), of which 48 were exposed to oral DA.
- Rate of ICD with RTG, as well as with PPX PR was significantly lower (p<0.001, binomial probability test) than ICD rate with ROP XL, or with pooled ROP data (long acting +short acting) or pooled PPX (graph 2). No significant difference between RTG and PPX PR was observed.
- Discontinuation due to ICD was reported in 44.2% (23/52) of all ICD cases. This reflects 2.0% (3/152) of all cases treated with RTG, 5.3% (8/150) of ROP XL and 3.1% (2/64) of PPX PR.
- 6 cases with ICD on PPX /ROP reported attenuation of ICD when started on RTG patch.



REFERENCES:

- Appiah-Kubi L et al., J Applied Research 2003; 3: 356-362
- Shulman LM et al., Mov Disord 2000; 15(4): 661-668
- Weintraub et al., Arch Neurol 2010; 67(5): 589-595

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Table 3: ICDs (% / total on therapy)	Pooled PPX n=164	PPX PR n=64	Pooled ROP n=188	ROP XL n=150	RTG n=152
Incidence (%)	22 (13.4%)	4 (6.3%)	28 (14.9%)	22 (14.7%)	8 (5.3%)
Mean dose all (with ICD's)	2.7 mg (2.8 mg)	2.7 mg (2.9 mg)	12.7 mg (15.2 mg)	12.6 mg (14.1 mg)	8.6 mg (10.0 mg)
ICD leading to discontinuation	12 (7.3%)	2 (3.1%)	12 (6.4%)	8 (5.3%)	3 (2.0%)

CONCLUSIONS: This ongoing survey reveals

- Prolonged release DAs are well tolerated in younger (< 75yrs) and older (≥ 75yrs).**
- ICD rates are variable and RTG patch as well as PPX PR appears to have a significantly lower rate compared to other short acting or long acting DAs. The reason for this is unclear.**
- In some, reversal of ICD is reported after switching to RTG.**
- Our survey shows rates of swallowing difficulties similar to other published studies and in this group use of RTG patch is particularly useful.**
- Contrary to common belief, somnolence and hallucination rates are low with all observed PR DA.**

