Effectiveness of Opicapone Added to Different Levodopa Doses in Parkinson's: *Post-Hoc* Analysis of the ADOPTION Trials

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Introduction

- Increasing levodopa (L-DOPA) dose and/or frequency is commonly used to manage first OFF symptoms in Parkinson's Disease (PD), but often leads to further treatment adjustments.[1,2]
- Opicapone (OPC), a catechol-O-methyltransferase inhibitor, is widely used to optimise L-DOPA therapy and reduce OFF time.[1-3]
- The **e**A**r**ly levo**D**opa with **O**picapone in **P**arkinson's pa**T**ients w**I**th mot**O**r fluctuatio**N**s (ADOPTION) clinical program showed that OPC 50 mg significantly reduced OFF time compared to an additional 100 mg L-DOPA dose in patients experiencing early wearing-off.[4]

Objective

- This *post-hoc* analysis of the ADOPTION studies aimed to assess if baseline L-DOPA dose impacts the efficacy of OPC 50 mg versus +100 mg L-DOPA in reducing OFF time in PD patients with early wearing-off.

Methods

- The ADOPTION clinical program included two open-label, phase 4 studies conducted in *South Korea* and *Europe*.
- PD patients with early wearing-off were randomised to receive OPC 50 mg or +100 mg L-DOPA for 4 weeks, added to baseline L-DOPA/dopa decarboxylase inhibitor (DDCI).
  - Key inclusion criteria: idiopathic PD, age >30, modified Hoehn & Yahr (H&Y) 1-3 (at ON state), stable L-DOPA/DDCI regimen (<600 mg/day; 3-4 intakes/day, >4 weeks); early signs of wearing-off (OFF time >1 h/day for >4 weeks but <2 years).
  - Patients were excluded if experienced severe and/or unpredictable OFFs or OFF time >5h/day.
- Primary endpoint: change from baseline in absolute OFF time.

In this exploratory *post-hoc* analysis, efficacy (change in absolute OFF and ON time, % of OFF time responders and Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale [MDS-UPDRS] part III) was evaluated in two subgroups:

- Patients receiving ≤400 mg/day of L-DOPA at baseline

- Patients receiving >400–≤650 mg/day of L-DOPA at baseline

Results

Patient population:

- Baseline characteristics were comparable between patients randomised to OPC 50 mg or +100 mg L-DOPA in both subgroups.
  - Patients with <400 mg/day L-DOPA at baseline were in general younger, had shorter PD duration, and lower mean H&Y stage than those with >400 mg/day L-DOPA at baseline (Table 1).

Table 1. Baseline characteristics (safety set)

Characteristic	≤400 mg/day L-DOPA at baseline		>400 mg/day L-DOPA at baseline	
	OPC 50 mg (n=73)	+100 mg L-DOPA (n=63)	OPC 50 mg (n=52)	+100 mg L-DOPA (n=55)
Age, mean (SD) years	63.1 (8.7)	63.3 (10.0)	65.4 (7.5)	66.1 (7.8)
PD duration, mean (SD) years	4.6 (3.0)	4.8 (3.6)	5.7 (4.1)	5.9 (3.4)
H&Y stage, mean (SD)	1.9 (0.5)	1.9 (0.5)	2.2 (0.5)	2.2 (0.5)
OFF time at baseline, mean (SD) h	3.4 (1.1)	3.3 (1.0)	3.5 (0.9)	3.5 (1.0)
L-DOPA dosage, mg/day				
Mean (SD)	317.8 (66.7)	318.6 (62.0)	513.5 (67.9)	519.8 (68.2)
Minimum, maximum	150, 400	150, 400	425, 600	450, 650

H&Y, Hoehn and Yahr; L-DOPA, levodopa; OPC, opicapone; PD, Parkinson's disease; SD, standard deviation

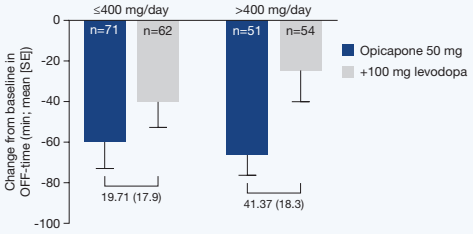
Efficacy:

- **OFF time reduction mean** (95% confidence interval [CI]) **was consistently greater with OPC 50 mg than with +100 mg L-DOPA, regardless of L-DOPA dose at baseline (Figure 1):**

<u>≤400 mg/day L-DOPA at baseline:</u>
- -60.1 (-85.8, -34.5) vs -40.40 (-65.0, -15.8) minutes, for OPC 50 mg and +100 mg L-DOPA, respectively.
- Between-group difference of 19.7 (17.9) minutes favouring OPC 50 mg.

<u>>400 mg/day L-DOPA at baseline:</u>
- -66.3 (-86.3, -46.2) vs -24.9 (-55.2, 5.4) minutes, for OPC 50 mg and +100 mg L-DOPA, respectively.
- Between-group difference was 41.4 (18.3) minutes, favouring OPC 50 mg.

Figure 1. Mean (SE) change from baseline to end of study treatment in absolute OFF-time



SE, standard error; min, minutes

Table 2. Change from baseline to week 4 in efficacy outcome measures

Outcome measures	≤400 mg/day L-DOPA at baseline		>400 mg/day L-DOPA at baseline	
	OPC 50 mg (n=71)	+100 mg L-DOPA (n=63)*	OPC 50 mg (n=51)	+100 mg L-DOPA (n=54)
Change in absolute OFF time, mean (SE)	-60.1 (12.8)	-40.4 (12.2)	-66.3 (9.9)	-24.9 (15.0)
OFF time responders, %(n/N)	58 (41/71)	48 (30/62)	55 (28/51)	44 (24/54)
Change in absolute ON time, mean (SE)	58.4 (13.7)	56.0 (15.3)	72.3 (11.8)	28.2 (18.0)
Change in MDS-UPDRS part III, mean (SE)	-4.6 (0.7)	-2.5 (6.4)	-3.3 (0.9)	-2.5 (1.0)

*One patient did not deliver the Hauser Diary required at Visit 4. L-DOPA, levodopa; MDS-UPDRS, Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale; OPC, opicapone; SE, standard error

Efficacy:

- **OFF time responders (>1-hour reduction)** were more frequent with OPC 50 mg in both subgroups:
  - 58% (41/71) vs 48% (30/62) for OPC 50 mg and +100 mg L-DOPA, respectively, in patients with <400 mg/day L-DOPA at baseline.
  - 55% (28/51) vs 44% (24/54) for OPC 50 mg and L-DOPA +100 mg, respectively, in those with >400 mg/day L-DOPA at baseline.
- **ON time increase** and **MDS-UPDRS part III scores improvements** were numerically greater with OPC 50 mg than with +100 mg L-DOPA in both subgroups.
- While **OPC 50 mg maintained consistent efficacy across L-DOPA dose ranges, +100 mg L-DOPA showed a trend toward lower efficacy** at higher baseline doses.

CONCLUSION

Opicapone consistently reduced OFF time by ~1h across all L-DOPA doses at baseline and was more efficacious than an increased L-DOPA dose of 100 mg.

Opicapone is an effective strategy to manage early wearing-off in PD patients instead of increasing L-DOPA dosage.

References

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Conflicts of Interest

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