Patient-Reported Improvement in Quality of "OFF" Time, Severity of Non-Motor Fluctuations, and Medication Satisfaction in the OPTI-ON Study

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Peter LeWitt,[1] Olga Klepitskaya,[2] Michael Serbin,[2] Eric Jen,[2] Stacy Rattana,[3] Jeff Trotter,[3] Grace Liang[2]

[1]Departments of Neurology, Wayne State University School of Medicine and Henry Ford Hospital, Detroit, MI; [2]Neurocrine Biosciences, Inc., San Diego, CA; [3]Worldwide Clinical Trials, Morrisville, NC

BACKGROUND

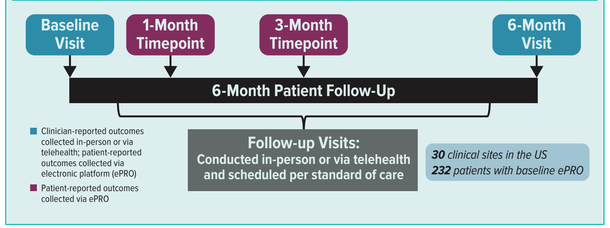
- For the development of better symptomatic treatments for Parkinson's disease (PD), patient-reported outcomes (PROs) are increasingly being used to understand the impact of motor- and non-motor fluctuations[1]
- Opicapone is an oral long-acting catechol-*O*-methyltransferase (COMT) inhibitor, approved as a once-daily adjunctive treatment to levodopa/carbidopa (LD/CD) in patients with PD experiencing "OFF" episodes
- Regulatory approval of opicapone was based on results from two double-blind, placebo-controlled, international Phase 3 studies: BIPARK-1 (NCT01568073) and BIPARK-2 (NCT01227655)
- These Phase 3 studies showed that adding opicapone to LD/CD was associated with significant mean reductions in absolute "OFF" time and significant mean increases in "ON" time without troublesome dyskinesia[2,3]
- OPTI-ON (**Op**icapone **T**reatment **I**nitiation **O**pe**n**-Label Study) was a real-world observational Phase 4 study for patients with PD experiencing motor fluctuations, as determined by study investigators (PD specialists)
- This US study was designed to describe safety/tolerability and treatment outcomes after opicapone was added to LD/CD regimens in real-world clinical settings
- This analysis focuses on PROs from OPTI-ON, including the severity of PD-related symptoms during both "ON" and "OFF" times, the severity of non-motor fluctuations, and patients' medication satisfaction at 3- and 6-month intervals following the addition of opicapone

METHODS

STUDY DESIGN

- OPTI-ON was an open-label, single-arm, multicenter, observational, prospective, longitudinal study conducted from March 2021 through August 2022 by PD specialists at 30 sites in the United States (**Figure 1**)
- This study enrolled patients who were newly prescribed opicapone in addition to their current LD/CD therapy as per clinician judgement and approved prescribing guidelines

Figure 1. Study Design



STUDY PARTICIPANTS

- Key inclusion criteria: male or female, aged ≥18 years; PD diagnosis with "OFF" episodes as per clinician judgment; new initiation of opicapone as an adjunctive treatment to LD/CD
- Key exclusion criteria: history of moderate or severe hepatic impairment; end-stage renal disease; concomitant use of non-selective monoamine oxidase inhibitors or COMT inhibitors (e.g., entacapone, tolcapone); current or previous treatment with opicapone
  - Patients entering the study could be switched from other COMT inhibitors to opicapone

STUDY ASSESSMENTS

- Patients completed the following assessments using an electronic platform (ePRO):
  - Patient Global Impression of Severity during "ON" times (PGI-S ON) and "OFF" times (PGI-S OFF)
  - Patient Global Impression of Change (PGI-C)
  - Patient Global Impression of Severity for Non-Motor Fluctuations (PGI-S NMF)
  - Medication Satisfaction Questionnaire (MSQ)
- Outcomes were analyzed descriptively at baseline (before initiating opicapone) and at 3 and 6 months after initiating opicapone

RESULTS

- In total, 232 patients were initiated on once-daily opicapone 50 mg and had ≥1 PRO assessment at baseline; 148 (63.8%) patients completed the study
- Patient characteristics are presented in **Table 1**

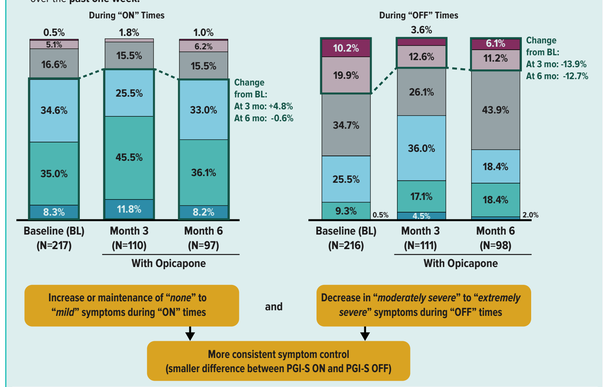
Table 1. Baseline Characteristics

	All Patients (N=232)
Age, mean (SD), years	67.6 (9.0)
Age at PD diagnosis, mean (SD), years[a]	60.1 (9.9)
Time since PD diagnosis, mean (SD), years[a]	8.1 (5.0)
Time since MF onset, mean (SD), years[b]	3.8 (4.2)
Male, n (%)	148 (63.8)
Race, n (%)	
White	213 (91.8)
Asian	10 (4.3)
Black / African American	2 (0.9)
Multiple	4 (1.7)
Native Hawaiian / Pacific Islander	1 (0.4)
Unknown / missing / not reported	2 (0.9)
Not Hispanic or Latino, n (%)	208 (89.7)
PD Status Questionnaire, n (%)[c]	
1 – mild Parkinson's	4 (1.7)
2 – mild to moderate Parkinson's	57 (24.6)
3 – moderate Parkinson's	118 (50.9)
4 – moderate to advanced Parkinson's	29 (12.5)
5 – advanced Parkinson's	6 (2.6)
Not assessed	18 (7.8)

[a]n=231; [b]n=228; [c]PD Status Questionnaire is a single-item, clinician-rated assessment based on the PD Foundation's 5 stages of disease progression.
MF, motor fluctuation; PD, Parkinson's disease; SD, standard deviation.

- PGI-S ON and PGI-S OFF ratings indicated more consistent symptom control at 3 and 6 months after opicapone was initiated (**Figure 2**)
  - "ON" times with "*none*" to "*very mild*" PD symptoms were maintained, while "OFF" times with "*moderately severe*" to "*extremely severe*" PD symptoms were reduced

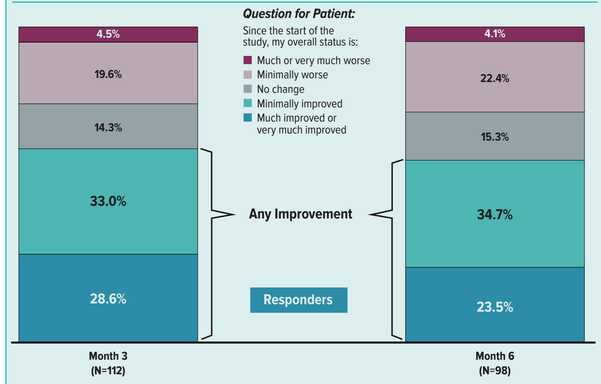
Figure 2. PGI-S ON and PGI-S OFF Scores at Baseline, 3 Months, and 6 Months



BL, baseline; mo, month; PD, Parkinson's disease; PGI-S OFF, Patient Global Impression of Severity during "OFF" times; PGI-S ON, Patient Global Impression of Severity during "ON" times.

- Opicapone was associated with perceived improvements in overall PD severity, as indicated by the percentage of patients with PGI-C response (rating of *"much improved"* or *"very much improved"*) at 3 months (29%) and 6 months (24%) (**Figure 3**)
  - More than one-half of patients reported any improvement (rating of *"minimally improved"* or better) at both 3 months (62%) and 6 months (58%)

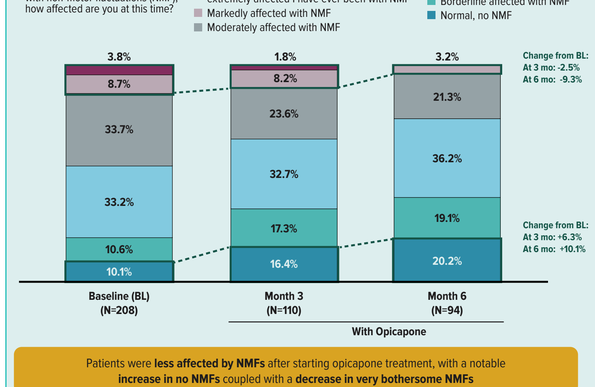
Figure 3. PGI-C Treatment Responders at Baseline, 3 Months, and 6 Months



PGI-C, Patient Global Impression of Change.

- The PGI-S NMF indicated that patients were less affected by NMFs after starting opicapone treatment (**Figure 4**)

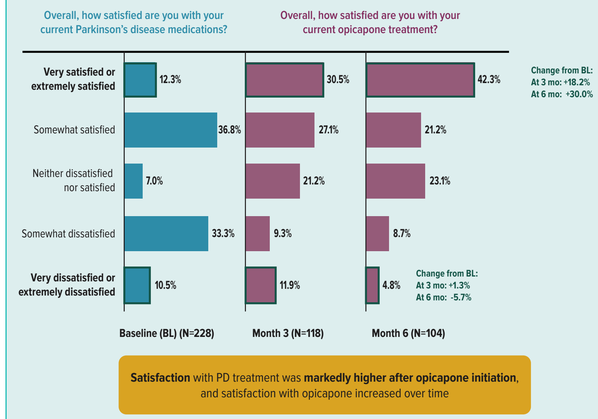
Figure 4. PGI-S NMF Score at Baseline, 3 Months, and 6 Months



BL, baseline; mo, month; PGI-S NMF, Patient Global Impression of Severity for Non-Motor Fluctuations.

- MSQ results indicate that opicapone was associated with higher medication satisfaction than patients' baseline PD medications (**Figure 5**)

Figure 5. MSQ Score at Baseline, 3 Months, and 6 Months



BL, baseline; mo, month; MSQ, Medication Satisfaction Questionnaire; PD, Parkinson's disease.

CONCLUSION

- At 3 and 6 months after adding once-daily opicapone 50 mg to their LD/CD regimen, patients maintained "ON" times with *"none"* to *"very mild"* PD symptoms (PGI-S ON) and experienced a decrease in "OFF" times with *"moderately severe"* to *"extremely severe"* PD symptoms (PGI-S OFF)
  - Together, these results indicate more consistent control of PD symptoms
  - Reports by patients of decreased fluctuations in the severity of motor symptoms is consistent with decreased levodopa fluctuations, which is a previously demonstrated impact of opicapone on levodopa pharmacokinetics[4]
- Patients also reported the following:
  - PGI-C improvements that were consistent with those in BIPARK-1 and BIPARK-2[2,3]
  - Decreased impact of non-motor fluctuations after starting opicapone (PGI-S NMF)
  - Higher satisfaction with opicapone compared to patients' baseline PD regimens (without opicapone), and higher satisfaction with opicapone over time (MSQ)
- Along with the mean reduction in absolute "OFF" time and increase in absolute "ON" time without troublesome dyskinesia demonstrated in BIPARK-1 and BIPARK-2,[2,3] these results from OPTI-ON suggest that adding once-daily opicapone to LD/CD reduces the severity of motor fluctuations and helps manage non-motor symptoms in patients with PD

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