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Sustained Clinically Meaningful Improvement in Quality of Life at 24 months After Initiation of Carbidopa/Levodopa Enteral Suspension (CLES) in Advanced Parkinson's Disease (APD) Patients in USA: Interim Results from the PROviDE Study

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CONCLUSIONS

- These results show that CLES treatment provides sustained clinically meaningful reduction in 'OFF'-time in the real-world US setting that is similar to improvements reported in clinical trials.[4,5]
- Clinically meaningful improvements in QoL are observed early and are maintained over 24 months after initiation of treatment with CLES; these are similar in magnitude to the improvement observed in a meta-analysis of other published CLES studies.[14]
- Despite changing their treatment regimen from oral to a device-aided therapy (i.e., CLES), patients feel more satisfied with CLES treatment than their previous treatment regimens, and there is a possible trend for increasing satisfaction with more prolonged use of CLES.
- This evidence suggests that CLES has sustained effects in controlling motor fluctuations and improving patient's QoL in the real-world.

INTRODUCTION

Background

- Patients with advanced Parkinson's disease (APD) have severe motor and non-motor symptoms that have a greater impact in reducing quality of life (QoL) than in patients with earlier stage PD.[1,2]
- Carbidopa/levodopa enteral suspension (CLES; also known as levodopa/carbidopa intestinal gel or LCIG outside USA) has been approved by FDA since 2015 for the treatment of motor fluctuations in APD patients.
- Clinical trials and observational studies have shown that CLES significantly reduces motor fluctuations, dyskinesia, non-motor symptoms, and improves QoL.[3-8] Most of the published real-world evidence on the long-term effectiveness of CLES stems from Europe and evidence from USA is emerging.[9]
- The Pursuing Real-world Outcomes via Duopa Ecosystem (PROviDE) study[10] was designed to evaluate the real-world, long-term effectiveness of CLES in patients with APD in the USA.

Objectives

- To examine the long-term impact of CLES on QoL in patients with APD in the real world.

METHODS

- The PROviDE study has been described previously.[10] In summary, it is a 3-year prospective, longitudinal, observational home-based study, to measure the impact of CLES on patient-reported outcomes such as 'OFF'-time, QoL, and treatment satisfaction in the USA.
- Assessments are made at baseline (when CLES treatment is initiated), and after 3, 6, 12, 18, 24, 30 and 36 months.
  - This is an interim analysis at 24 months.

Participant eligibility criteria

- English-speaking, adult patients diagnosed with Parkinson's disease who were enrolled in the patient support program and gave informed consent were included in the study.
- Exclusion criteria included:
  - Current or previous enrollment in a clinical or observational study of CLES.
  - Incapable of understanding or cooperating with the requirements of the study or not able to participate for the 3-year duration.
  - In hospice care.

Outcome measures

- The primary outcome for the PROviDE study is change in self-reported 'OFF'-time per day compared with baseline. 'OFF'-time is measured as the number of hours spent in 'OFF' state, normalized to a 16-hour waking day.
- Secondary outcomes included change in several variables, but this analysis focuses on QoL (as measured by Parkinson's Disease Questionnaire; PDQ-8) and treatment satisfaction (as measured by Treatment Satisfaction Questionnaire for Medication; TSQM-9).

Sample

- This interim analysis is based on patients who met the following criteria:
  - Completed both baseline and 24-month assessment.
  - Had baseline normalized 'OFF'-time from 3 to 12 hours/day.
  - Had CLES supply for at least 80% of the 24-month follow-up period.

Statistical analysis

- Mixed effect models were used to examine the impact of CLES on 'OFF'-time, QoL, and treatment satisfaction over a period of 24-months while controlling for age, gender, ability to walk, number of years since PD, and previous deep brain stimulation (DBS) treatment.

RESULTS

Patient characteristics

- The analytical sample consisted of 38 patients.
- In the study sample, the baseline mean (SD) normalized 'OFF'-time was 6.2 (2.2) hours, mean (SD) PDQ-8 score was 43.4 (19.6), and mean (SD) TSQM-9 Global Satisfaction score was 44.9 (15.5) (Table 1).

Table 1. Selected baseline characteristics of the sample (n=38)

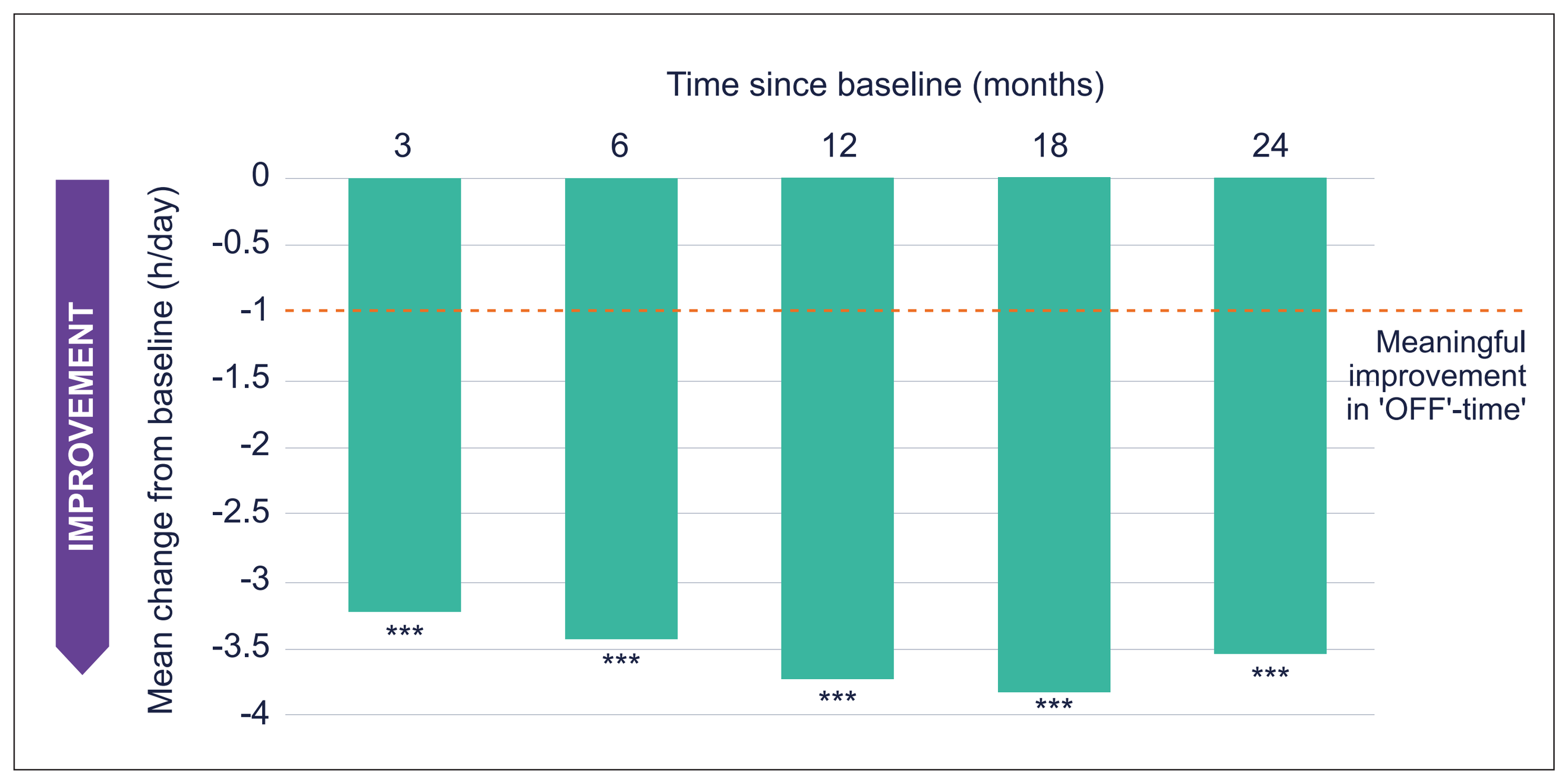
Baseline characteristic†	n (%)*
Mean (SD) age, years	66.6 (8.0)
Gender	
Male	25 (65.8)
Female	13 (34.2)
Mean (SD) time since PD diagnosis, years	11.5 (6.0)
Mean (SD) 'OFF'-time (normalized to 16 h waking day), hours/day	6.2 (2.2)
Mean (SD) PDQ-8 score	43.4 (19.6)
Mean (SD) TSQM-9 score	
Global Satisfaction	44.9 (15.5)
Effectiveness	44.0 (15.0)
Convenience	48.0 (21.9)
Previous DBS	11 (29.0)
Ability to walk	
Able to walk without support	10 (26.3)
Usually use a walking aid, such as cane or walker	20 (52.6)
Usually use the support of another person	2 (5.3)
Limited ability to walk and primarily use a wheelchair	6 (15.8)

†Based on patient self-reporting; *Unless otherwise stated in left-hand column.
Abbreviations: DBS, deep-brain stimulation. PDQ-8, Parkinson's Disease Questionnaire. TSQM-9, Treatment Satisfaction Questionnaire for Medication.

Effectiveness of CLES at follow-up

- After initiation of CLES, the normalized hours of 'OFF'-time per day (adjusted for variables in the mixed effect model) were reduced significantly by 3 hours or more from baseline at all timepoints up to 24 months (p<0.0001; Figure 1).
  - After 24 months of treatment with CLES, the mean (SD) 'OFF'-time per day was 2.7 hours compared with 6.2 hours before starting CLES treatment (p<0.0001).
  - A reduction by 1 hour of 'OFF'-time is considered clinically meaningful improvement.[11]
  - This clinically meaningful improvement in 'OFF'-time is sustained over a period of 24-months after CLES initiation.

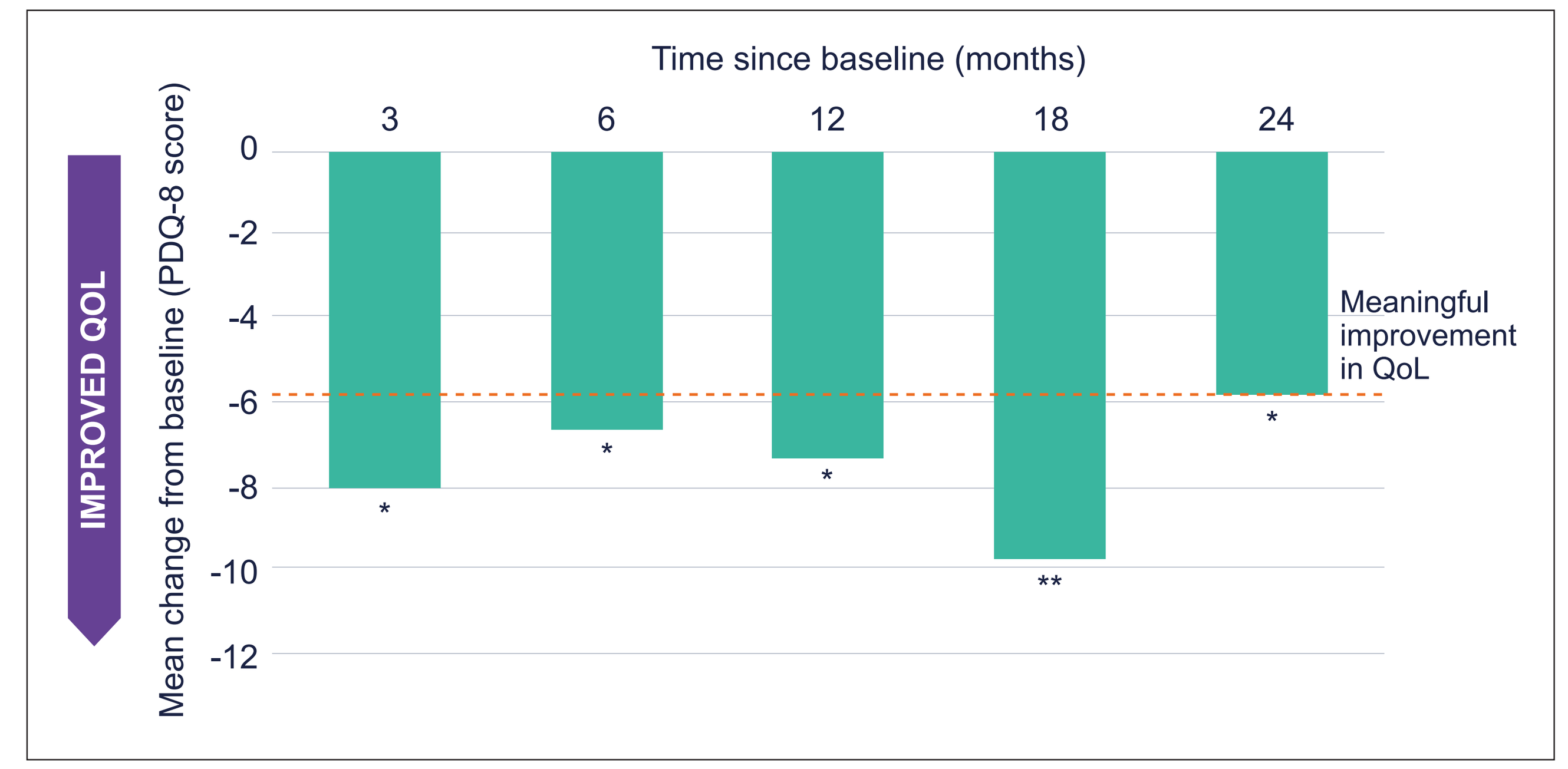
Figure 1. Reduction in 'OFF'-time per day (normalized to 16 h waking day) for up to 24 months after initiation of CLES treatment (adjusted for age, gender, ability to walk, number of years since PD diagnosis, and previous DBS treatment)



***p-value <0.0001
Abbreviations: CLES, carbidopa/levodopa enteral suspension; PD, Parkinson's disease; DBS, deep brain stimulation

- QoL also significantly improved throughout the treatment period as demonstrated by the PDQ-8 score reductions from baseline at all time points (p<0.05; Figure 2).
  - A change of -5.7 points on PDQ-8 is considered clinically meaningful improvement in QoL.[12,13]
  - This clinically meaningful improvement in QoL is sustained over a period of 24-months after CLES initiation.

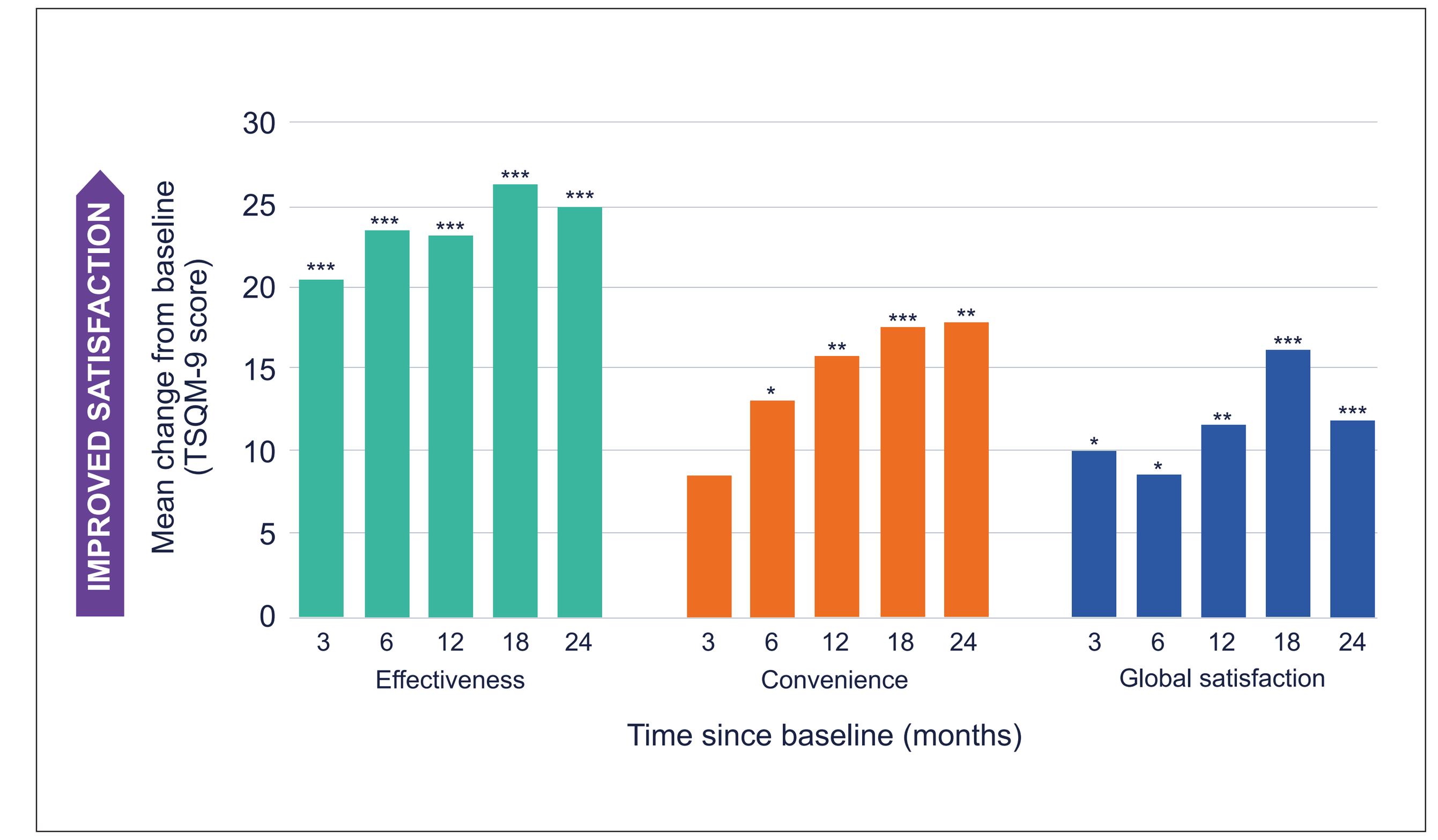
Figure 2. Change in QoL (measured by PDQ-8 score) for up to 24 months after initiation of CLES treatment (adjusted for age, gender, ability to walk, number of years since PD, and previous DBS treatment)



*p-value <0.05; **p-value <0.001
Abbreviations: CLES, carbidopa/levodopa enteral suspension; PD, Parkinson's disease; DBS, deep brain stimulation; PDQ, Parkinson's disease questionnaire; QoL, quality of life

- Treatment satisfaction significantly improved after initiation of CLES (Figure 3).
  - The greatest improvements were in satisfaction with the effectiveness of treatment (p<0.0001 at all timepoints). CLES treatment also significantly improved satisfaction with treatment convenience (p<0.05; except at 3 months when the improvement was non-significant) and global satisfaction with treatment (p<0.05).

Figure 3. Change in treatment satisfaction (measured by TSQM-9 score) for up to 24 months after initiation of CLES treatment (adjusted for age, gender, ability to walk, number of years since PD, and previous DBS treatment)



*p-value <0.05; **p-value <0.001; ***p-value <0.0001
Abbreviations: CLES, carbidopa/levodopa enteral suspension; PD, Parkinson's disease; DBS, deep brain stimulation; TSQM, treatment satisfaction questionnaire for medication

Strengths

- The PROviDE study has one of the largest US-specific cohorts of patients with APD receiving CLES with a long-term follow-up in the real-world.
- This is the first study examining treatment satisfaction with CLES over the long-term.

Limitations

- Limitations include the risk of self-reporting bias, the interim nature of the data, and the exclusion of patients with 'OFF'-time <3 hours or >12 hours/day.

DISCLOSURES

Author disclosures:
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- Thomas Marshall was an employee of AbbVie and may own stocks/shares in the company.
- Pavnit Kukreja and Jorge Zamudio are employees of AbbVie and may own stocks/shares in the company.

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