ON-DEMAND TREATMENT PREFERENCES OF PATIENTS WITH PARKINSON'S DISEASE AND "OFF" EPISODES: HETEROGENEITY ACROSS PATIENT SUBGROUPS

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KEY FINDINGS

- In an online discrete-choice experiment (DCE) survey evaluating patient preferences for theoretical on-demand treatments of Parkinson's disease (PD)-related "OFF" episodes, results demonstrated that 4 participant subgroups displayed largely homogeneous preferences for the treatment attributes and levels presented
- There were a few key differences in preferences for theoretical mode of administration with possible adverse events (AEs) among 2 participant subgroups
  - Both participants with a spouse/partner caregiver or no caregiver and those without on-demand "OFF" episode treatment experience preferred a sublingual film with AEs over an inhaled medication with AEs, and both subgroups also preferred the sublingual film and inhaled medication over an injected medication with AEs
- Theoretical cost was relatively more important than other attributes among those who reported waiting to address their "OFF" episodes compared with those who reported actively responding to "OFF" episodes
- The frequency of "OFF" episodes had no statistically significant impact on preferences for theoretical on-demand "OFF" episode treatment attributes

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INTRODUCTION

- Nearly all patients with PD receiving oral carbidopa/levodopa experience "OFF" episodes, defined as periods during the day when symptoms reappear or worsen[1]
- "OFF" episodes may have a significant negative impact on patient quality of life[2]
- Little is known about patient preference for different features of on-demand treatments of "OFF" episodes and whether preferences vary by patient characteristics or treatment experience
- Currently, there are 3 treatments approved by the US Food and Drug Administration for the on-demand treatment of "OFF" episodes (**Table 1**)

Table 1. Approved On-Demand Treatments for "OFF" Episodes

Treatment	FDA Approval
APOKYN® (apomorphine hydrochloride injection), for subcutaneous use[3]	2004
INBRIJA® (levodopa inhalation powder), for oral inhalation use[4]	2018
KYNMOBI™ (apomorphine hydrochloride) sublingual film[5]	2020

FDA, US Food and Drug Administration.

OBJECTIVE

- To quantify preference heterogeneity for theoretical on-demand treatments among patients with PD and "OFF" episodes

METHODS

Study Design

- Participants were recruited for an online DCE survey from September–October 2019
  - DCEs are based on the principle that products or services comprise multiple attributes and that the choice of a product or service is a function of the utility of each attribute
  - DCEs have been used to elicit patients' preferences for a wide range of health care topics[6,7]
- In each DCE question, participants selected between a pair of experimentally designed profiles for theoretical on-demand "OFF" episode treatments that varied by the attributes shown in **Table 2**
  - Attributes were selected based on qualitative interviews with 15 participants and were based on characteristics of existing on-demand treatments for "OFF" episodes; the survey instrument was then evaluated and revised based on pretest interviews with an additional 15 participants
- A full fractional design containing 72 DCE questions was used to create 8 blocks of 9 DCE questions each; participants were randomly assigned to 1 of these blocks

Table 2. DCE Attributes and Levels[a] of Theoretical Treatments

Mode of Administration; Possible AEs	Time to FULL "ON"	Duration of FULL "ON"	Out-of-pocket Cost Per 30 Doses
• Inhaled; no AEs • Inhaled; cough or mild respiratory infection • Injected; no AEs • Injected; injection-site reaction • Dissolvable sublingual film; no AEs • Dissolvable sublingual film; mouth or lip sores	• 15 minutes • 30 minutes • 60 minutes	• 1 hour • 1.5 hours • 2 hours	• $0 (no cost) • $10 • $30 • $90

[a]Values or categories used to characterize the theoretical treatment profiles in the DCE questions.
AE, adverse event; DCE, discrete-choice experiment.

Study Population

- Carbidopa/levodopa-treated adults (age 18–75 years) from the US with a self-reported diagnosis of PD for ≥5 years or <5 years but with "OFF" episode experience were recruited through a health care research recruiting firm (Global Perspectives, Norwich, England) using online research panels and other ad hoc recruiting sources (ie, recruiters' patient databases, physician referrals, online support groups, and targeted advertising on social media)

Statistical Analyses

- Data were analyzed for 4 subgroups (**Table 3**) using separate random parameters logit models with interaction terms that identified participants in each subgroup
  - The model related participants' choices to the differences in attribute levels across the alternative levels in each DCE question[8]
  - Variables for mode of administration, time to FULL "ON," and duration of FULL "ON" were effects-coded categorical variables
  - Cost was modeled as a continuous linear variable adjusted for the participant's income
  - The parameter on each interaction term was the difference between the 2 subgroups' preference weights for the corresponding attribute level
  - The overall relative importance of each attribute was calculated as the utility difference between the most and least preferred levels and was conditional on the levels selected for the survey
- Differences in preferences between subgroups were tested through a log-likelihood χ^2 test of joint statistical significance of all interaction terms (P<0.05), and a 1-sample t test was used to determine the significance of differences between adjacent attribute levels (P<0.05) for each attribute

RESULTS

- Among the 300 participants, 294 (98%) had experience with "OFF" episodes
- Interaction terms for the "caregiver," "participant response to 'OFF' episodes," and "on-demand 'OFF' episode treatment experience" subgroups were jointly statistically significantly different from the main effect, suggesting that preferences for theoretical on-demand "OFF" episode treatment attributes were different between these 3 subgroup pairs (**Table 3**)
- The joint test was not significant for the "'OFF' episode frequency" subgroup, indicating that the frequency of "OFF" episodes had no significant impact on preferences for on-demand "OFF" episode treatment attributes

Table 3. Subgroup Descriptions, Sample Sizes, and Joint Test of Significance

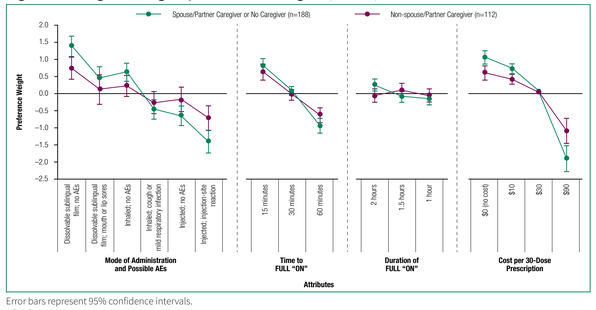
Subgroup Pair	Subgroup Description	n	*P* Value
Caregiver	• Those who had a caregiver who was a non-spouse/partner • Those who had a caregiver who was a spouse/partner or had no caregiver	112 188	<0.001
Participant response to "OFF" episode[b]	• Exclusively waited until the symptoms went away or waited until it was time for the next dose of their regular PD maintenance medication when they had an "OFF" episode • Those who did something when they had an "OFF" episode[c] (ie, took maintenance medication off schedule [n=171], called their doctor [n=56], took an "OFF" episode medication [n=25], or other [n=5])	82 212	0.005
On-demand "OFF" episode treatment experience	• Those who had experience with on-demand "OFF" episode treatments[d] (apomorphine subcutaneous injection[3] [n=54] or levodopa inhalation powder[4] [n=54]) • Those who did not have experience with on-demand "OFF" episode treatments	77 223	<0.001
"OFF" episode frequency[b]	• Those who experienced at least 1 "OFF" episode per day (ie, multiple times a day [n=74] or once a day [n=77]) • Those who experienced "OFF" episodes less frequently than once a day (ie, every few days [n=91], about once a week [n=28], every few weeks [n=17], or about once a month or less [n=7])	151 143	0.344

[a]Values or categories used to characterize the theoretical treatment profiles in the discrete-choice experiment questions.
[b]Includes only those participants with "OFF" episode experience (n=294).
[c]Participants could have reported more than one action taken when they had an "OFF" episode.
[d]Participants could have reported experience with more than one treatment.
PD, Parkinson's disease.

Caregiver Subgroup Analysis

- Participants with a non-spouse/partner caregiver had fewer statistically significant differences in preferences among the theoretical modes of administration compared with the rest of the study sample (**Figure 1**)
  - These participants ranked the overall importance of an improvement in mode of administration with possible AEs, time to FULL "ON," and cost as equally important attributes of an on-demand treatment for "OFF" episodes
- Participants with a spouse/partner caregiver or no caregiver had stronger preferences for theoretical sublingual and inhaled modes of administration without AEs over the other choices
  - These participants ranked the overall importance of an improvement in mode of administration with possible AEs and cost as relatively more important than improvements in the other attributes, followed by time to FULL "ON"

Figure 1. Caregiver Subgroup Preference Weights (N=300)

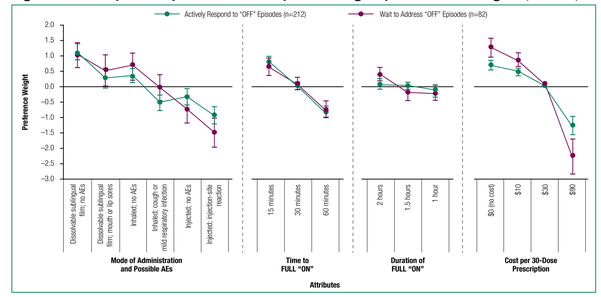


Error bars represent 95% confidence intervals.
AE, adverse event.

Participant Response to "OFF" Episode Subgroup Analysis

- Preferences between these 2 groups were similar; however, participants who waited to address their "OFF" episodes had statistically significant differences in preference for theoretical levels of duration of FULL "ON," whereas those who actively responded to their "OFF" episodes did not differentiate between these levels (**Figure 2**)
  - Those who waited to address their "OFF" episodes ranked the overall importance of an improvement in cost as relatively more important than improvements in other attributes of an on-demand treatment for "OFF" episodes
  - Those who actively responded to their "OFF" episodes ranked the overall importance of an improvement in mode of administration with possible AEs, time to FULL "ON," and cost as equally important

Figure 2. Participant Response to "OFF" Episode Subgroup Preference Weights (N=294[a])

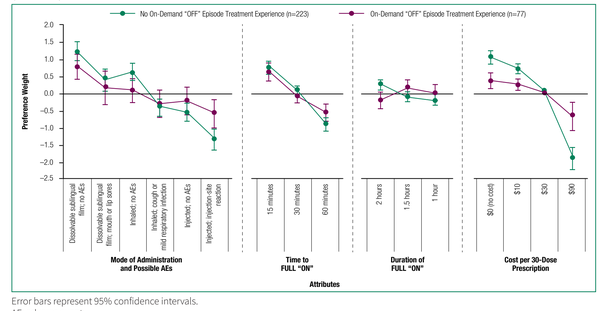


Error bars represent 95% confidence intervals.
[a]Includes only those participants with "OFF" episode experience.
AE, adverse event.

On-Demand "OFF" Episode Treatment Experience Subgroup Analysis

- Those with on-demand "OFF" episode treatment experience had fewer statistically significant differences in preferences among the theoretical modes of administration with AEs (**Figure 3**)
  - These participants ranked the overall importance of an improvement in mode of administration with possible AEs, time to FULL "ON," and cost as equally important attributes of an on-demand treatment for "OFF" episodes
- Participants with no on-demand "OFF" episode treatment experience had stronger preferences for theoretical sublingual and inhaled modes of administration without AEs over other choices and for theoretical treatments that lasted 2 hours versus 1 or 1.5 hours
  - These participants ranked an improvement in mode of administration with possible AEs and cost as the most important attributes

Figure 3. On-Demand "OFF" Episode Treatment Experience Subgroup Preference Weights (N=300)



Error bars represent 95% confidence intervals.
AE, adverse event.

LIMITATIONS

- Study sample may be subject to selection bias based on the online nature of the survey and that it was not designed to be representative of the overall US population of patients with PD
- Participants self-reported demographic and disease information
- Data were based on theoretical choice profiles; therefore, differences can arise between stated and actual choices in the real world

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