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# Duration of Continuous “Good On” Intervals and Number of Motor Fluctuations: IPX203 (Extended-Release Carbidopa-Levodopa) vs Immediate-Release Carbidopa-Levodopa in Parkinson’s Disease Patients with Motor Fluctuations


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## Background

- IPX203 is an oral extended-release (ER) carbidopa-levodopa (CD-LD) formulation
- IPX203 was compared with immediate-release (IR) CD-LD in patients with Parkinson’s disease (PD) experiencing motor fluctuations in RISE-PD, a phase 3, double-blind, randomized study
- IPX203 showed statistically significant improvement in “Good On” time per day and “Good On” time per dose compared to IR CD-LD
- Continuous “Good On” time is a critical metric for comparing the effects of ER LD formulations with shorter-acting IR LD formulations and has important implications for patients’ ability to plan and engage in daily activities

## Objective

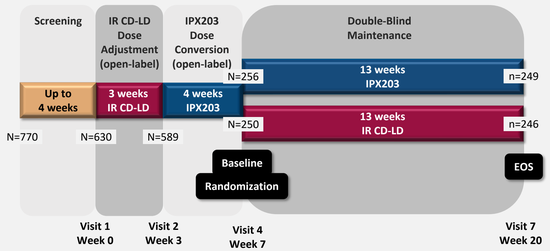
- To compare the duration of continuous “Good On” intervals and number of motor fluctuations per day in patients with PD treated with IPX203 vs IR CD-LD

## Methods

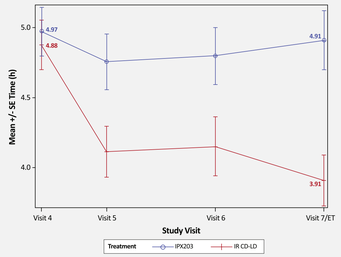
- RISE-PD study design is shown in **Figure 1**
- The average duration of continuous “Good On” intervals and average daily number of motor fluctuations were assessed using data from patient PD diaries
- “Good On” time was defined as the sum of “On” time without dyskinesia and “On” time with non-troublesome dyskinesia, equivalent to “On” time without troublesome dyskinesia
- For each 3-day PD Diary, continuous intervals of “Good On” state were identified. Average duration across the diary for each visit when PD Diaries are collected were calculated
- A motor fluctuation was defined as a change from “Off” to “On” state (with or without dyskinesia) or from “On” to “Off” state
- Analysis:
  - Average duration of each continuous “Good On” episode and its change from baseline was summarized descriptively by post-randomization visit and treatment group. The endpoint was analyzed using a mixed model for repeated measures (MMRM).

# IPX203 increased the average duration of continuous “Good On” intervals by 0.92 hours and decreased the number of daily motor fluctuations by 1.35 compared to IR CD-LD

### Figure 1. RISE-PD Study Design

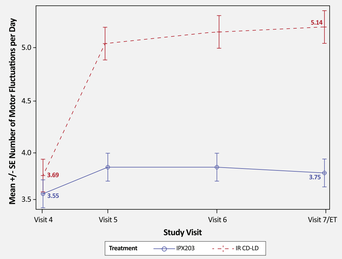



### Figure 2. Patients on IPX203 showed a longer duration of continuous "Good On" intervals compared to patients on IR CD-LD (*P*=0.0002)




**LS mean difference from Visit 4 to Visit 7/ET, IPX203 vs IR CD-LD: 0.92 ± 0.247 (95% CI 0.44, 1.41; *P*=0.0002)**

### Figure 3. Patients on IPX203 had significantly lower numbers of motor fluctuations per day compared to patients on IR CD-LD (*P*<0.0001)




**LS mean difference from baseline to Visit 7/ET, IPX203 vs IR CD-LD: -1.35 ± 0.190 (95% CI -1.72, -0.97; P<0.0001)**

### Table 1. Change from baseline in average duration of continuous “Good On” interval (h)

| | | IPX203 (N=249) | | IR CD-LD (N=246) | |
|---|---|---|---|---|---|
| Visit | Statistic | At Visit | Change from Baseline | At Visit | Change from Baseline |
| Visit 4 (Baseline) | N | 249 | | 246 | |
| | Mean (SD) | 4.97 (2.757) | | 4.88 (2.725) | |
| Visit 7/ET | N | 234 | 234 | 241 | 241 |
| | Mean (SD) | 4.91 (3.184) | -0.07 (3.114) | 3.91 (2.821) | -0.98 (3.182) |

### Table 2. Change from baseline in average number of motor fluctuations per day

| | | IPX203 (N=249) | | IR CD-LD (N=246) | |
|---|---|---|---|---|---|
| Visit | Statistic | At Visit | Change from Baseline | At Visit | Change from Baseline |
| Visit 4 (Baseline) | N | 249 | | 246 | |
| | Mean (SD) | 3.55 (1.790) | | 3.69 (1.901) | |
| Visit 7/ET | N | 235 | 235 | 241 | 241 |
| | Mean (SD) | 3.75 (2.065) | 0.17 (1.812) | 5.14 (2.666) | 1.47 (2.573) |

CI, confidence interval; ET, end of treatment; IR CD-LD, immediate-release carbidopa-levodopa; LS, least squares.

- Analysis (Continued):
  - The model included baseline (Visit 4) value as a covariate, treatment (IPX203 or IR CD-LD) and visit (5, 6, or 7/ET) as fixed effects, pooled center as random effect, and a treatment-by-visit interaction
  - Similar analysis was used for the change in the number of motor fluctuations per day

## Results

- 506 patients (IPX203, n=256; IR CD-LD, n=250) who successfully completed dose conversion, were randomized. Of those, 249 IPX203 and 246 IR CD-LD patients completed the double-blind period (**Figure 1**)
- Patients in the modified intent-to-treat (mITT) population who received IPX203 showed significantly greater improvement in average duration of continuous “Good On” interval from Visit 4 (double-blind baseline) to Visit 7/ET vs IR CD-LD (*P*=0.0002) (**Figure 2, Table 1**)
- Mean change from baseline to Visit 7/ET for continuous “Good On” interval was -0.07 for IPX203 and -0.98 for IR CD-LD (LS mean difference: 0.92)
- Patients who received IPX203 showed a significantly greater improvement in the average number of motor fluctuations per day from Visit 4/baseline to Visit 7/ET vs IR CD-LD (*P*<0.0001) (**Figure 3, Table 2**)
- At the end of study, mean number of motor fluctuations per day was 3.75 for IPX203 and 5.14 for IR CD-LD (LS mean difference: 1.35)

## Conclusions

- IPX203 was associated with significantly greater improvements in average duration of continuous “Good On” intervals and a greater improvement in the average number of motor fluctuations per day as compared with IR CD-LD
- The longer duration of continuous “Good On” intervals and decreased number of daily motor fluctuations may allow PD patients to better plan and engage in their daily activities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