64

What change to expect in duration of benefit per dose when switching from immediate-release CD-LD to IPX203 (extended-release CD-LD)

Robert A. Hauser[1], Simon Allard[2], Ghazal Banisadr[2], Stanley Fisher[2]

[1]USF Parkinson's Disease and Movement Disorders Center/Parkinson Foundation Center of Excellence, Tampa, FL, USA; [2]Amneal Pharmaceuticals, Bridgewater, NJ, USA

Objective

- To investigate if duration of benefit ("Good On" time) per dose during immediate-release (IR) CD-LD treatment predicts response to IPX203 dose conversion based on clinical trial experience from the phase 3 RISE-PD study in patients with Parkinson's disease (PD)

Background

- IPX203 is an oral extended-release carbidopa-levodopa (CD-LD) that was developed to address the limited absorption window and short plasma half-life of LD
- 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 randomized study
- IPX203 showed statistically significant improvement in "Good On" time per day and "Good On" time per dose compared to IR CD-LD
- The average duration of efficacy per dose is a key metric to assess the benefit of a long-acting formulation.

Methods

- RISE-PD was a multicenter, randomized, double-blind, double-dummy, active-controlled phase 3 study conducted at 105 sites across the United States and Europe (NCT03670953)
- All patients underwent 3 weeks of IR CD-LD dose adjustment, and a 4-week open-label conversion to IPX203, followed by randomization (at Visit 4/baseline) to a 13-week double-blind treatment with either IR CD-LD or IPX203 (**Figure 1**)
- Post hoc analyses were performed on Hauser diary data from the 495 subjects that completed the RISE-PD clinical trial
  - The patient population was rank-ordered and then divided into quartiles based on their "Good On" time per dose at the end of the IR CD-LD dose optimization phase
  - The mean end-of-study "Good On" time per dose values were then compared between IPX203- and IR CD-LD–treated groups for each quartile
- "Good On" time was defined as the sum of "On" time without dyskinesia and "On" time with nontroublesome dyskinesia, equivalent to "On" time without troublesome dyskinesia

Regardless of the duration of benefit per dose observed with IR CD-LD, the improvement in duration of benefit per dose observed with IPX203 remained similar, with an overall mean of 1.58 hours more "Good On" time per dose compared to IR CD-LD

Figure 1. RISE-PD Study Design

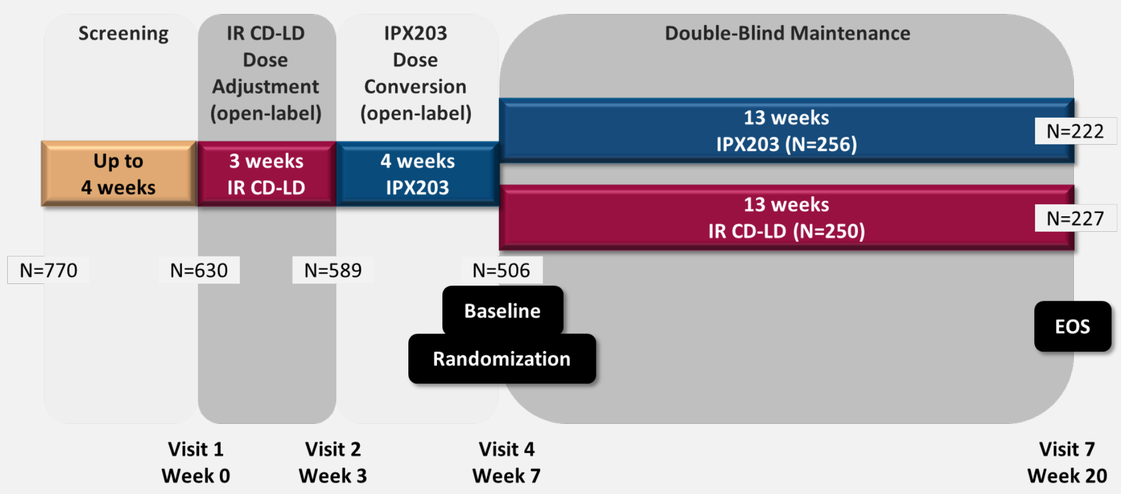
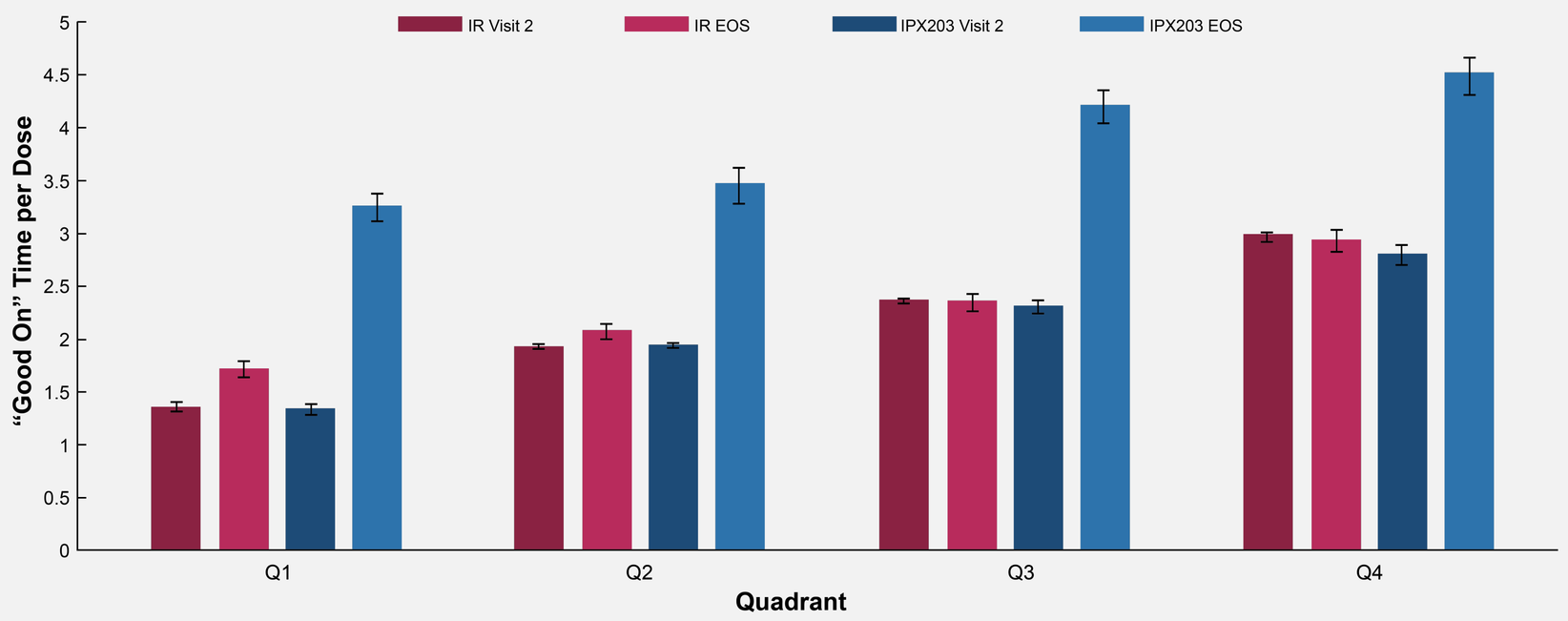


Table. "Good On" Time per Dose at Baseline and End of Study by

	Q1	Q2	Q3	Q4
IR CD-LD				
n	53	58	60	69
Visit 2/Week 3, mean (SE), h	1.36 (0.043)	1.91 (0.019)	2.36 (0.017)	2.97 (0.041)
Visit 7/Week 20 (EOS), mean (SE), h	1.71 (0.074)	2.06 (0.071)	2.34 (0.077)	2.93 (0.099)
IPX203				
n	66	61	59	48
Visit 2/Week 3, mean (SE), h	1.33 (0.048)	1.92 (0.016)	2.30 (0.061)	2.80 (0.092)
Visit 7/Week 20 (EOS), mean (SE), h	3.25 (0.13)	3.44 (0.16)	4.19 (0.15)	4.49 (0.17)
Difference (IPX203 vs IR CD-LD) at Week 20, mean, h	1.53	1.38	1.85	1.56

EOS, end of study; h, hours; SE, standard error.

Figure 2. "Good On" Time per Dose at Baseline and End of Study by Quartile



Error bars: 95% confidence interval.

Results

- Mean "Good On" time per dose for each quartile (Q1 to Q4) of the IR CD-LD dose optimization phase was 1.36, 1.91, 2.36, and 2.97 hours, respectively. For patients randomized to IR CD-LD, the end-of-study mean "Good On" time per dose values were 1.71, 2.06, 2.34, and 2.93 hours, respectively (**Table, Figure 2**)
- In patients randomized to IPX203, the end-of-study mean "Good On" time per dose values for each quartile (Q1 to Q4) were 3.25, 3.44, 4.19, and 4.49 hours, respectively
- The mean differences in "Good On" time per dose between IPX203 and IR CD-LD were 1.53 hours for Q1, 1.38 hours for Q2, 1.85 hours for Q3, and 1.56 hours for Q4

Conclusions

- Regardless of the duration of efficacy observed with IR CD-LD, measured as "Good On" time per dose, the improvement in duration of benefit observed with IPX203 remained similar, with a range of approximately 1.38 to 1.85 hours for the four quartiles and an overall mean of 1.58 additional hours compared to IR CD-LD treatment
- These results may help guide health care providers when planning conversion regimens and anticipating clinical responses
- In addition, these results may allow PD patients to better plan and engage in their activities of daily living

Presented at the International Congress of Parkinson's Disease and Movement Disorders, August 27–31, 2023, Copenhagen, Denmark. Data from Amneal Pharmaceuticals LLC.