Integrated safety summary from Phase 3 clinical trials of IPX203, an extended-release carbidopa-levodopa formulation, in Parkinson's disease

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Background

- IPX203 is an investigational oral extended-release carbidopa-levodopa (CD-LD)
- IPX203 is designed to produce prolonged therapeutic LD plasma concentrations
- IPX203 has shown improvement in "Good On" time compared to immediate-release CD-LD

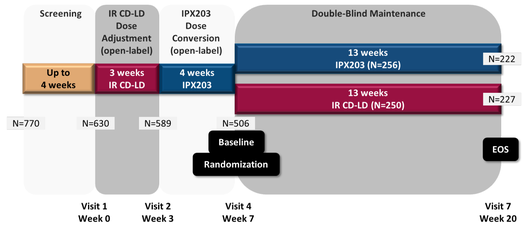
Objective

- To present the adverse event (AE) profile of IPX203 in the Phase 3 clinical trials in patients with Parkinson's disease (PD) experiencing motor fluctuations

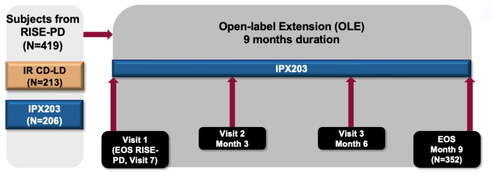
Methods

- Safety data from a multicenter, double-blind, randomized, active-controlled Phase 3 study and an open-label extension (OLE) Phase 3 study were combined and analyzed

RISE-PD Study Design



OLE Study Design



Majority of TEAEs with IPX203 are mild or moderate and had a first onset within 3 months of continuous drug exposure

Table 1. Overall Summary of AEs*

Any TEAE (whole population)	IPX203 Number of patients with AEs (%)	IPX203 Number of AEs (%)	IPX203 Number of AEs/patient (n/N)	Immediate-release LD Number of patients with AEs (%)	Immediate-release LD Number of AEs (%)	Immediate-release LD Number of AEs/patient (n/N)
Any TEAE	397/589 (67.4)	1355	2.3 (1355/589)	176/630 (27.9)	328	0.5 (328/630)
Treatment-related (TR) TEAE	205/589 (34.8)	471/1355 (34.8)	0.8 (471/589)	47/630 (7.5)	66/328 (20.1)	0.1 (66/630)
Maximum severity of TEAEs						
Mild	163/589 (27.7)	837/1355 (61.8)	1.4 (837/589)	109/630 (17.3)	230/328 (70.1)	0.4 (230/630)
Moderate	174/589 (29.5)	419/1355 (30.9)	0.7 (419/589)	54/630 (8.6)	82/328 (25.0)	0.1 (82/630)
Severe	60/589 (10.2)	99/1355 (7.3)	0.17 (99/589)	13/630 (2.1)	16/328 (4.9)	0.03 (16/630)
Treatment-related serious AEs	9/589 (1.5)			0		

***Patients were on IPX203 much longer (~52 weeks) compared to immediate-release LD (~16 weeks).**

Table 2. Most Common AEs (≥4% in TEAEs)

Any TEAE, n (%)	IPX203 TEAEs (N=589)	IPX203 Treatment-related TEAEs (N=589)
Dyskinesia	63 (10.7)	60 (10.2)
Dizziness	29 (4.9)	20 (3.4)
Hallucination	26 (4.4)	17 (2.9)
Nausea	44 (7.5)	32 (5.4)
Dry mouth	28 (4.8)	19 (3.2)
Constipation	25 (4.2)	10 (1.7)
Fall	35 (5.9)	6 (1.0)
Urinary tract infection	31 (5.3)	0

Table 3. Overall Summary of AEs by "Duration of Continuous Exposure" (at first onset of AE)

First onset of AEs over time, n/N (%)	IPX203 Any TEAE
<3 months	324/589 (55.0)
3 to <6 months	41/429 (9.6)
6 to <9 months	23/384 (6.0)
9 to <12 months	7/307 (2.3)
≥12 months	2/180 (1.1)

Results

- The safety population consisted of 630 patients with PD experiencing motor fluctuations
  - Mean age was 66.5 years (±9.0)
  - Mean duration of disease was 8.5 years (±4.9)
- Average total daily dose (TDD) of IPX203 was 1520.97 mg (±587.78)
- 83.0% of subjects received IPX203 at an average TDD between 800 mg and <2400 mg of LD
- Average daily dosing frequency of IPX203 was 3.08 times/day
- Mean (range) treatment duration was 242.9 (2 to 553) days
- Data includes 388.34 person-years of exposure to IPX203
- 65.9% (385/584) were exposed to IPX203 for ≥6 months
  - 30.7% (179) were exposed for ≥12 months
- In the Phase 3 studies pool, 397 (67.4%) IPX203 subjects experienced 1355 treatment-emergent AEs (TEAEs; **Table 1**)
  - Of these, 85% had a maximum severity of mild to moderate
  - Patients receiving IPX203 for the analysis could have had treatment for ~52 weeks vs treatment of ~16 weeks with immediate-release LD
- 205 of 580 (34.8%) TEAEs were treatment-related
- The most commonly reported TEAEs were dyskinesia, nausea, fall, and urinary tract infection (**Table 2**). These are all expected in an older PD population
- An analysis of TEAEs by duration of exposure to study treatment showed that most IPX203 subjects (55.0%) experienced first onset TEAEs within the first 3 months (**Table 3**)
  - The occurrence of TEAEs remained stable over time
- There were no deaths in the RISE-PD study. Six subjects died during the OLE study; all the fatal SAEs were deemed not related to the study drug, except for one subject who had a severe SAE of drowning that was considered related to the study drug.

Conclusions

- Considering the disease duration and presence of motor fluctuations in the PD cohort enrolled in the Phase 3 trials, IPX203 was generally safe and well tolerated
- The safety profile was stable over time and consistent with the known effects of other levodopa formulations

Disclosures

Hubert H. Fernandez has received personal compensation serving as a consultant and on the Speakers Bureau of Amneal. Dr. Fernandez has received personal compensation serving as a consultant for AbbVie and Cerevel. Dr. Fernandez has received personal compensation for serving as an editor, associate editor, or editorial advisory board member for Elsevier. The institution of Dr. Fernandez has received research support from Biogen, Michael J Fox Foundation, Parkinson Foundation, Roche, and UCB. Dr. Fernandez has received publishing royalties from a publication relating to healthcare. **Dr. Fernandez has received personal compensation for serving as a steering committee/advisory committee member with Parkinson Study Group. Robert A. Hauser has received personal compensation serving as a consultant and on the Speakers Bureau for Amneal. The institution of Vanessa Hinson has received research support from Amneal. Nirav Pavasia has received personal compensation for serving on a Speakers Bureau for Amneal. Eric Molho has received personal compensation serving as a consultant to Amneal. Hester Visser and Richard D'Souza have received personal compensation for serving as employees of Amneal.**

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