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Impact of concomitant therapy with a dopamine agonist on converting patients with Parkinson's disease from immediate-release carbidopa-levodopa to CREXONT® (IPX203)

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Background

- Extended-release (ER) carbidopa-levodopa (CD-LD) and concomitant medications like dopamine agonists (DA) are routinely used to manage motor fluctuations in Parkinson's disease (PD).
- CREXONT® (IPX203) is a novel oral ER CD-LD formulation.
- In the RISE-PD clinical trial, CREXONT has demonstrated a significant increase in "Good On" time (GOT) vs immediate-release (IR) CD-LD, in PD patients with motor fluctuations.[1]

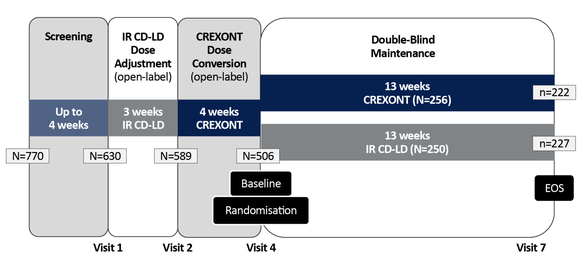
Objective

- To assess the effect of dopamine agonists on the efficacy of CREXONT.

Methods

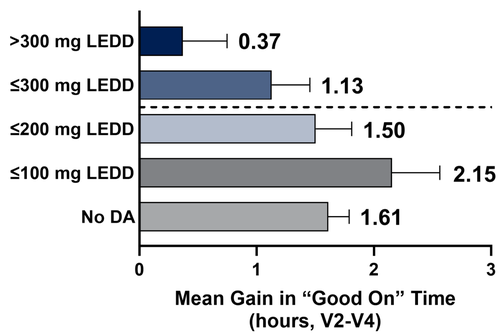
- RISE-PD was a randomized, double-blind, active-controlled, phase 3 study examining the safety and efficacy of CREXONT vs IR CD-LD (**Figure 1**).
  - The trial included a 4-week open-label dose-conversion from IR CD-LD to CREXONT.
- To evaluate the impact of concomitant DA therapy on CREXONT's efficacy, we analyzed GOT in subgroups based on their levodopa equivalent daily dose (LEDD) of DA, comparing GOT values at the end of the CREXONT conversion period to the end of IR CD-LD Dose Adjustment (Visit 2).

Figure 1. RISE-PD Study Design[1]



In all subgroups, CREXONT improved "Good On" time vs IR CD-LD. Greatest benefit was observed with ≤200 mg DA levodopa-equivalent daily dose

Figure 1. "Good On" Time Means and Standard Errors for Individual Dopamine Agonist Groups (Visit 2 to Visit 4)

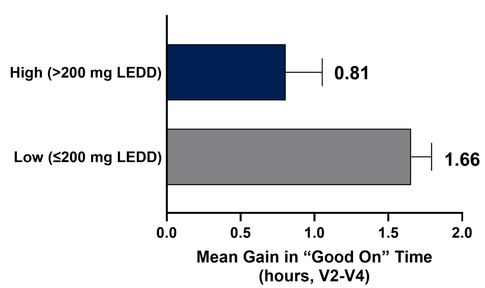


Dotted line indicates the threshold between low vs. high dopamine agonist dosing

Table 1. Conversion Factor for Calculating Total LEDD[2]

Agonist	Conversion Factor
Piribedil	1 LEDD = 1 mg
Apomorphine	10 LEDD = 1 mg
Ropinirole	20 LEDD = 1 mg
Rotigotine	30 LEDD = 1 mg
Pramipexole	100 LEDD = 1 mg

Figure 2. "Good On" Time Means and Standard Errors for Low vs High Dopamine Agonist Groups From Visit 2 (Optimized IR) to Visit 4 (End of CREXONT Conversion)



DA, dopamine agonist; LEDD, levodopa equivalent daily dose.

Results

- In the full patient population (n=493) , conversion from IR CD-LD to CREXONT improved GOT by 1.74 hours while reducing average dosing frequency from 5 to 3 times/day.
- Subgroup analysis showed reductions in GOT from visit 2 to visit 4 as LEDD increased (**Figure 1**).
  - The group without DA (n=237) demonstrated increases in GOT of 1.61 hours
  - DA LEDD ≤100 mg led (n=47) to 2.15 hours GOT gain
  - DA LEDD 101-200 mg led (n=87) to 1.5 hours GOT gain
  - DA LEDD 201-300 mg led (n=70) to 1.13 hours gain
  - DA LEDD >300 mg led (n=52) to 0.37 hours gain
- **Table 1** shows conversion factors for total daily dose of select drugs to the LEDD.[2]
- ANOVA revealed a significant effect of DA dose on GOT gain achieved by converting to CREXONT ($p<0.01$).
- An unbiased thresholding algorithm identified the impactful cutoff point at 200 DA LEDD. Using this threshold, we observed a significant difference between the groups with low (≤200 mg DA LEDD) and high (>200 mg DA LEDD) groups, with GOT gains of 1.66 hours and 0.81 hours, respectively ($p<0.01$) (**Figure 2**).

Conclusions

- Converting patients from IR CD-LD to CREXONT improved GOT in all subgroups, with the highest benefit in those receiving ≤200 mg DA LEDD.
- Patients on higher DA doses also benefited from conversion, but GOT gain was reduced by 51% compared to the low dose group.

REFERENCES

1. Hauser RA, et al. *JAMA Neurology*. 2023;80(10):1062-1069. 2. Schade S, et al. *Mov Disord Clin Pract*. 2020;7(3):343-345.

Disclosures

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