An open-label, randomized, crossover, comparative bioavailability study of Levodopa Cyclops® and Inbrija® in healthy adult subjects

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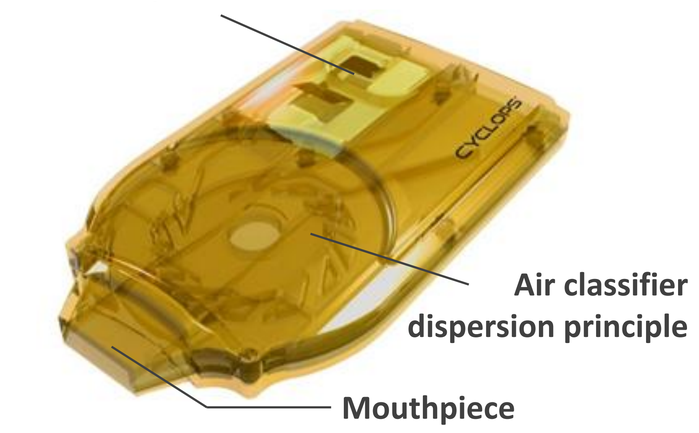
Introduction

- Many Parkinson's disease (PD) patients experience **OFF episodes** that require medication with a predictable and fast onset of effect.
- This unmet medical need was addressed by **apomorphine-based products** and **Inbrija®**, but these products still have limitations.
- **Levodopa Cyclops®** is a **pre-filled**, **ready-to-use**, **single-use** dry powder inhaler (DPI) that offers PD patients **excellent ease-of-use**.
- Previous studies in PD patients have shown **Levodopa Cyclops®' fast efficacy** (< 20 min.), ease-of-use during OFF episodes, and **tolerability**.[1,2]

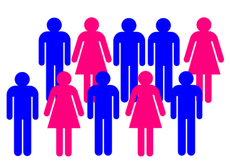
Objective

Primary objective was to determine the comparative bioavailability between **Levodopa Cyclops®** and **Inbrija®**.

Most important secondary objective was to determine the safety and tolerability of **Levodopa Cyclops®**.



Methods



26 healthy volunteers

Levodopa Cyclops®
- 45 mg (1 DPI)
- 90 mg (2 DPIs)
- 135 mg (3 DPIs)

Inbrija®
- 84 mg (2 capsules)

+

Carbidopa
- 50 mg
- 1 h. pre-dose

→

- **Blood sampling:** -60, -30, -15, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 40, 60 minutes, 1:30, 2:00, 4:00 and 8:00 hours
- **PK endpoints:** C_{max}, T_{max}, AUC_{0-4}, AUC_{0-t}, $AUC_{0-\infty}$, $t_{½}$
- **Safety endpoints:** adverse events, vital signs and clinical and laboratory examination

Results and discussion

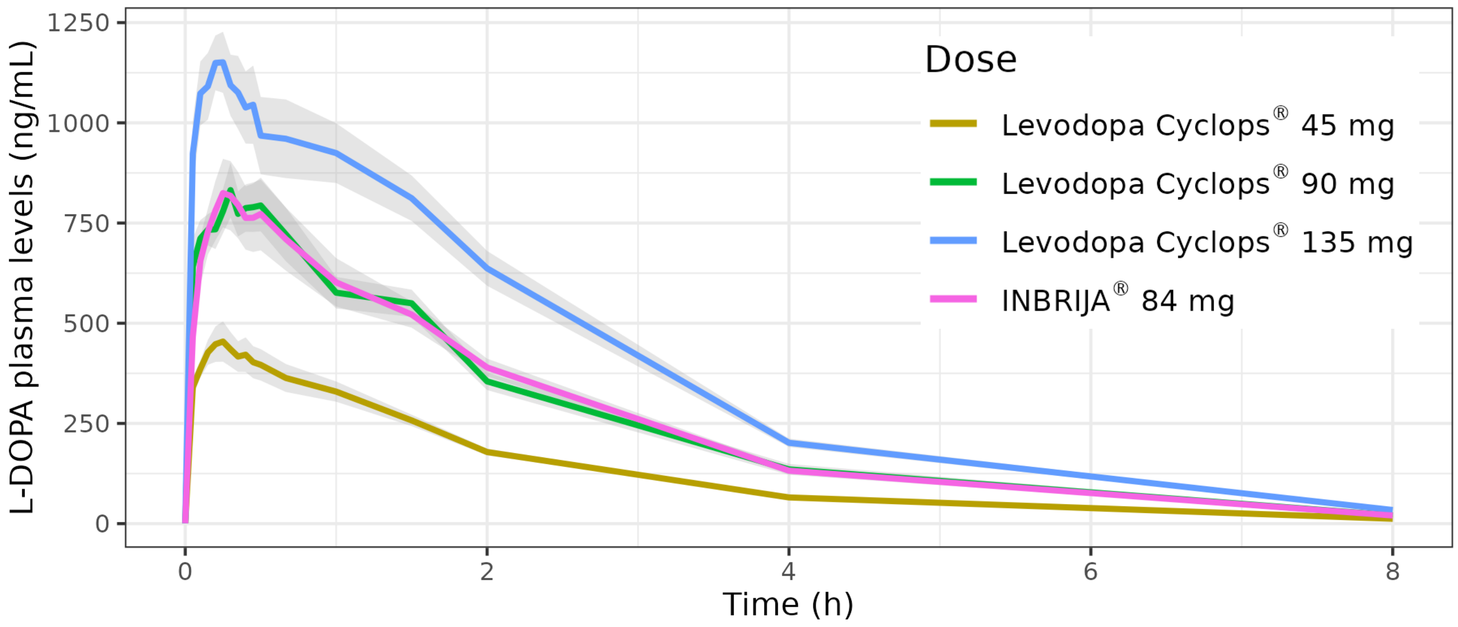


Figure 1: plasma levodopa concentration profiles following inhalation from Levodopa Cyclops® and Inbrija®.

Table 1: Pharmacokinetic results; geom. mean (geom. CV%).

	t_{max} (min)	C_{max} (ng/mL)	$AUC_{0-\infty}$ (ng*h/mL)
Cyclops® 45 mg	19.4	531 (40.6)	1041 (19.3)
Cyclops® 90 mg	19.6	1021 (32.7)	1973 (24.9)
Cyclops® 135 mg	17.2	1504 (28.4)	3120 (18)
Inbrija® 84 mg	23	969 (51.9)	1849 (55.9)

- **~2000 plasma samples** were analyzed by LC-MS/MS.
- **Therapeutic levodopa levels** were reached **within minutes**.
- **Linear increase** in concentration as the **Levodopa Cyclops®** dose increases.
- **Similar shape of the curves** of **Levodopa Cyclops® 90 mg** and **Inbrija®**.
- Only one case of levodopa-related diarrhea was reported as adverse event and **no reports of cough** for **Levodopa Cyclops®**.

Cyclops®Switch – for dual use

Conclusions

- **Levodopa Cyclops®** is safe and very well tolerated (**no cough**).
- Levodopa absorption from **Cyclops®** is comparable to **Inbrija®**, thereby, fulfilling the **bioequivalence** criteria.
- Results enable **abbreviated registration** routes with a limited - **PK-only** - clinical program.
- **Cyclops®Switch** for dual use is in development.
- **Levodopa Cyclops®** is **very easy to use** and systemic **absorption is fast**, so it will be a valuable asset to offer fast and reliable relief of debilitating OFF episodes.

References

1. Luinstra et al. (2019), International Journal of Pharmaceutics, p. 1-5, vol. 567
2. Luinstra et al. (2019), Therapeutic Advances in Chronic Disease, 204062231985761, vol. 10

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