Optimizing Delivery of Carbipoda/Levodopa via the Accordion Pill: Comparative Pharmacokinetics and Safety From 2 Randomized Studies in Healthy Volunteers

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BACKGROUND
Carbidopa/levodopa (CD/ LD) is the gold-standard treatment for Parkinson’s disease (PD). Long-term LD treatment is associated with motor fluctuations, with progressively longer OFF periods over time. Improving the stability of LD plasma levels should improve efficacy, reduce adverse events (AEs), and may even delay disease progression. The Accordion® CD/ LD is a novel drug delivery system based on gastric-retention multiple-unit films containing immediate-release CD and both immediate and controlled-release LD.

OBJECTIVE
To evaluate the pharmacokinetics (PK) and safety of AP-CD/LD versus immediate-release IR-CD/LD (Sinemet®) and under different meal conditions in healthy adults.

RESULTS
Demographics
A total of 18 and 30 healthy volunteers were enrolled in IN 11 005 and IN 14 001, respectively (Table 1).

Participants
One participant discontinued due to an AE of nausea and vomiting following AP-CD/LD 50mg/50mg. Five participants had the second dose of IR-CD/LD withheld due to ongoing AEs of nausea and vomiting, though they were not removed from the study.

Methods
In study IN 11 005, AP-CD/LD produced more consistent mean LD plasma concentrations over time, with attenuated peak-trough differences compared with IR-CD/LD (Sinemet®) and under different meal conditions in healthy adults. No serious AEs or deaths occurred in either study.

Serial blood samples for PK assessments were obtained at baseline and on days 3 through 10 days following the final dose of study drug. Serial Blood Samples

PK and Safety
PK populations included all participants with sufficient plasma drug concentration to measure the concentration-time profile at least at two points; safety populations included all volunteers who received at least one dose of study drug.

Table 3: Food Effects on PK Profile of AP-CD/LD (IN 14 001)

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<tr>
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<tbody>
<tr>
<td>Tmax (hr)</td>
<td>2.00 (0.500 ‑ 5.000)</td>
<td>2.00 (0.500 ‑ 7.000)</td>
<td>0.00 (0.00 ‑ 5.000)</td>
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<tr>
<td>Cmax (ng/mL)</td>
<td>1,288 (32.9%)</td>
<td>1,362 (32.4%)</td>
<td>2,544 (44.5%)</td>
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<tr>
<td>AUC0‑t (ng‑hr/mL)</td>
<td>765 (38.9%)</td>
<td>785 (33.9%)</td>
<td>1,649 (39.7%)</td>
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<tr>
<td>AUC0‑inf (ng‑hr/mL)</td>
<td>1,015 (51.9%)</td>
<td>1,011 (51.9%)</td>
<td>1,832 (53.7%)</td>
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CONCLUSIONS
- The effects of food on the PK of AP-CD/LD are shown in Table 3, in particular, residence time Tlag is largely dependent on the presence of a recent meal.
- The safety of AP-CD/LD was similar to the historic safety of CD/LD.
- AP-CD/LD should be taken with meals.
- The safety of AP-CD/LD was similar to the historic safety of CD/LD.

DISCLOSURES
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