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Comparative analysis of opicapone and entacapone in the management of motor fluctuations in patients with Parkinson's disease, from clinical trials to healthcare resource usage

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BACKGROUND

- Opicapone (OPC, Ongentys®) and entacapone (ENT) are catechol-O-methyltransferase (COMT) inhibitors developed as adjunct therapies to levodopa (LD) to improve the bioavailability of LD and decrease peak-trough fluctuations

OBJECTIVE

- To compare the extent of COMT inhibition, efficacy and tolerability of two COMT inhibitors, OPC and ENT

METHODS

- A review of OPC pharmacokinetics/pharmacodynamics and phase 3 studies that included an ENT arm was conducted to compare the extent of COMT inhibition, clinical efficacy, and safety profiles of OPC and ENT in the management of motor fluctuations in Parkinson's disease

RESULTS

- A randomized, double-blind study in healthy subjects showed that OPC, when compared to ENT, provides prolonged and enhanced LD bioavailability associated with more pronounced, long-lasting, and sustained COMT inhibition[1] (**Figure 1**)
- OPC has a favorable safety profile compared to ENT
  - ENT treatment is associated with severe diarrhea and urine discoloration[2]
  - No treatment-related diarrhea has been observed with OPC[3]
  - Urine discoloration is uncommon with OPC (only two cases of chromaturia were considered to be related to study drug in the pivotal phase 3 trials in patients taking OPC 25 mg)[3]

REFERENCES

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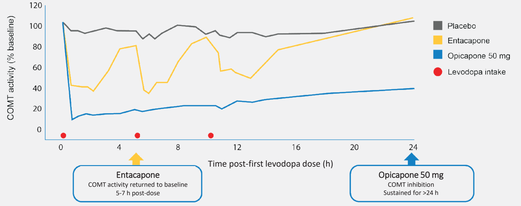
Opicapone once daily provides greater and more sustained COMT inhibition, favorable efficacy, and safety profiles vs entacapone

PHARMACOKINETICS/PHARMACODYNAMICS STUDY

Figure 1. Opicapone provided more pronounced and sustained COMT inhibition vs entacapone[1]



BIPARK I PHASE 3 STUDY

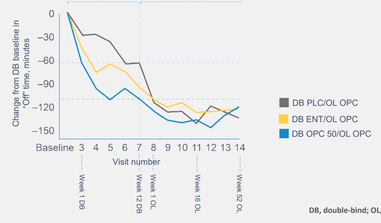
Table 1. Opicapone once daily provided greater magnitude of reduction in "Off" time from baseline to end of study compared to entacapone

Treatment	Adjusted LS Mean Change in "Off" Time (95% confidence intervals)
Opicapone 50 mg	−116.8 (−144.2, −89.4) minutes
Entacapone 200 mg	−96.3 (−122.6, −70.0) minutes
Placebo	−56.0 (−82.3, −29.7) minutes

LS, least squares

BIPARK I OPEN-LABEL PHASE

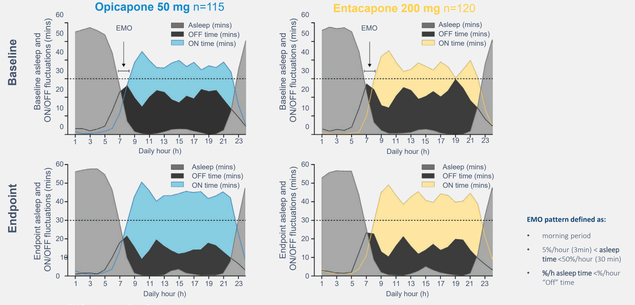
Figure 2. Switching from entacapone to opicapone significantly reduced "Off" time



DB, double-bind; OL, open-label

POST-HOC ANALYSIS OF BIPARK I STUDY

Figure 3. Opicapone led to increased proportion of patients waking up "On," reduced morning "Off" vs entacapone, and no EMO pattern in contrast to entacapone



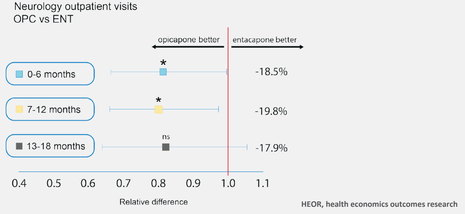
EMO, early morning "Off"

Opicapone has a favorable safety profile compared to entacapone

- Entacapone treatment is associated with severe diarrhea and urine discoloration[2]
- No treatment-related severe diarrhea has been observed with opicapone[3]
- In the opicapone EU Summary of Product Characteristics, chromaturia is listed as an 'uncommon' adverse reaction[3]

HEOR STUDY

Figure 4. Opicapone led to fewer outpatient neurology visits compared to entacapone



HEOR, health economics outcomes research

RESULTS

- A phase 3 clinical trial, BIPARK I, established the noninferiority of OPC 50 mg vs ENT 200 mg[5]
  - OPC dosed once daily reduced "Off" time with greater magnitude vs multiple daily doses of ENT (least square [LS] mean change of –116.8 minutes vs –96.3 minutes, respectively) (**Table 1**)
  - A higher proportion of patients on OPC vs ENT showed minimally, much, or very much improved Clinician (73% vs 50.9%, respectively, *p*=0.0070) and Patient (72.1% vs 52.5%, respectively, *p*=0.0091) Global Impression of Change scores[5]
  - The open-label phase showed that patients who switched from ENT to OPC had an additional 39.3 minutes reduction in "Off" time (*P*=0.006) and an additional 45.7 minutes increase in "On" time without dyskinesia (*p*=0.015) (**Figure 2**)[5]
  - A post-hoc analysis showed that treatment with OPC, in comparison to ENT, led to a greater increase in the proportion of patients who woke up "On" and a greater decrease in time-to-"On" from first morning levodopa intake[6] (**Figure 3**)
  - Due to a substantial reduction in morning "Off" time, no early morning "Off" (EMO) pattern was found for patients treated with OPC, in contrast to ENT (**Figure 3**)
- A health economics outcomes research (HEOR) study showed OPC treatment resulted in 18.5% fewer neurology outpatient visits compared to ENT, after 6 months of COMT treatment (**Figure 4**)[7]

CONCLUSIONS

- Opicapone's sustained COMT inhibition, convenience of once-daily dosing, and favorable efficacy and safety profiles distinguish it from ENT, potentially offering improved patient outcomes, treatment adherence and reduced healthcare cost

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Data from Amneal Pharmaceuticals LLC