'Intervention' was defined as an increase in DA dose, addition of another DA, L-dopa or other dopaminergic therapy, or withdrawal due to lack of efficacy. Safety was assessed by an independent safety monitoring board.

**Results:** Of the 270 patients enrolled in the 6-month study, 232 entered the 12-month extension study, and 187 completed 18 months' treatment. At the end of the 6-month study, safinamide (50–100 mg/day) significantly improved motor symptoms, activities of daily living, quality of life and cognition compared with placebo; there was no incremental benefit with the high (150–200 mg/day) dose (Stocchi et al., AAN 2007). Preliminary results from the extension study, including an analysis of the pooled safinamide dose groups and post-hoc analyses by dosing group, will be presented.

**Conclusion:** These studies show promising information on the sustained improvement in efficacy that may be provided by safinamide, a potential new therapy for the treatment of patients with Parkinson's disease.

## 2.210 Determining the benefit of levodopa/carbidopa/entacapone (Stalevo®) on the pharmacokinetic profile of levodopa: a randomized, crossover, multicentre study in patients with Parkinson's disease

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**Objective:** To demonstrate that higher levodopa minimum concentration (Cmin) values are maintained following repeated doses of levodopa/carbidopa/entacapone (LCE; Stalevo®) compared with conventional levodopa/carbidopa (LC) in patients with Parkinson's disease (PD).

**Method:** This is an open-label, randomized, active-controlled, two-period, cross-over, pharmacokinetic (PK) trial. Dosing schedules were 100/25/200 or 150/37.5/200 mg LCE, or equivalent LC, four-times daily with 3.5-hourly intervals, in Groups I and II, respectively. In each group, patients were randomized to receive either LCE or LC during Period 1, before crossing to Period 2, following a washout period of 3–7 days. Blood samples for PK analysis were taken before the first dose (0 hr) and thereafter for up to 16 hr. Pharmacokinetic values determined for levodopa in plasma included: Cmin (primary variable), area under the curve of dose interval, maximum concentration and elimination half-life. For safety assessments, blood pressure, heart rates, 12-lead electrocardiogram and laboratory safety variables were measured at baseline and study end, with adverse events assessed throughout the study.

**Results:** A total of 10 patients have been randomized to Group I. The study with Group II is ongoing with 5 randomized patients. Primary evaluation compared Cmin values obtained following repeated doses of LCE and LC; mean Cmin values of each dose interval from 0–14 hours were also compared. Primary and secondary variables were evaluated using analysis of variance. In Group I, the geometric mean of the levodopa Cmin values were significantly higher ($p < 0.05$) after LCE administration compared with LC. Data for the efficacy and safety of study treatments for Groups I and II will be presented at the meeting.

**Conclusion:** We confirmed that higher Cmin values, and hence reduced troughs in levodopa levels, were maintained following repeated doses of LCE four-times daily at 3.5-hourly intervals compared with conventional LC treatment in patients with PD.

## 2.211 The SENSE study: An open-label, single-arm, multicentre, 6-week study evaluating the efficacy and safety of levodopa/carbidopa/entacapone (Stavelo) in Parkinson's disease patients experiencing early re-emergence of symptoms due to wearing-off with conventional medication

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**Objective:** To evaluate the benefits of direct transition from levodopa/carbidopa (LC) or levodopa/benserazide (LB) to levodopa/carbidopa/entacapone (LCE; Stalevo®) in patients with idiopathic Parkinson's disease (PD) experiencing early re-emergence of symptoms due to wearing-off.

**Method:** This was a Phase IV, multinational, multicentre, open-label, single-arm study in PD patients experiencing symptom re-emergence due to wearing-off while receiving 3–4 daily doses of LC or LB. Wearing-off was defined as $\geqslant$1 positive symptom in the 9-item Wearing-Off Questionnaire (WOQ-9). Patients were stratified 50:50 according to previous therapy (LC or LB) and switched to equivalent doses of LCE 3–4-times daily for 6 weeks. The primary outcome was patients' Clinical Global Impression of Change (CGI-C) at Week 6. Secondary outcomes included change from baseline in Unified Parkinson's disease Rating Scale (UPDRS) parts II and III; investigator-assessed CGI-C; quality of life (visual analogue scale); WOQ-9 and daily levodopa dose. Adverse events and vital signs were also recorded.

**Results:** A preliminary analysis of baseline data included 115 PD patients (71 males, 44 females) with a mean age of 70.1 years and Hoehn and Yahr stage 1–3. Mean duration of PD was 5.3 years and mean duration of levodopa treatment was 4.2 years. Previous therapy was LC in 41% of patients and LB in 59%. The mean daily levodopa dose was 333 mg; the number of daily doses was 3 in 56% of patients and 4 in 44%. Mean UPDRS part II score was 11.4, and part III 24.7. All patients had $\geqslant$1 motor symptom and 83% had $\geqslant$1 non-motor symptom (Table). Study results will be presented at the meeting.

**Conclusion:** A preliminary analysis of baseline data from the SENSE study indicates that most PD patients with early wearing-off experience re-emergence of both motor and non-motor symptoms when assessed using a structured questionnaire, such as WOQ-9.

## 2.212 Improved adherence to levodopa/carbidopa/entacapone (Stalevo®) or levodopa/carbidopa and entacapone as separate tablets reduces medical care utilization and costs among Parkinson's disease patients

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**Objective:** Previous studies have demonstrated that levodopa/carbidopa/entacapone (LCE; Stalevo®) is associated with improved adherence to treatment compared with separate levodopa/carbidopa and entacapone (LC and E) tablets in Parkinson's disease (PD) patients. This analysis aimed to assess the association between treatment adherence and medical care utilization/costs.

**Method:** A retrospective observational cohort was designed using health-insurance claims databases, spanning Jan 2000–Dec 2005, representing >50 million beneficiaries in the United States. Subjects included PD patients (ICD-9-CM 332 excl. 332.1) switched from LC to LCE or added E to existing LC. Date of first prescription for LCE or E was designated the index date. Patients with <365 days of enrolment prior and subsequent to index date were excluded. Adherence was determined from patients' medication possession ratio (MPR) during follow up (365 days post-index), calculated as the percentage of days with supply of LCE or LC and E, based on pharmacy refills. Satisfactory adherence was defined as MPR $\geqslant$80%. The association between adherence and medical care utilization/costs was