'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

examined using multivariate regression to control for pre-index MPR with LC and other patient characteristics.

Results: Satisfactory adherence (n = 617) compared with unsatisfactory adherence (MPR < 80%, n = 598) was associated with a 39% reduction in PD-related hospitalization (95% confidence interval [CI]: 20–54%; $p < 0.001$), a 47% reduction in all-cause inpatient costs (95% CI: 18–65%; $p = 0.004$) and an 18% reduction in all-cause total costs (95% CI: 11–24%; $p < 0.001$). On an adjusted basis, patients with satisfactory adherence had costs of $3508 less than those with unsatisfactory adherence. Results were qualitatively similar in those receiving LCE or LC and E.

Conclusion: Better adherence to therapy is associated with reduced PD-related and all-cause medical care utilization and lower treatment costs. Strategies to improve treatment adherence, may result in substantial cost savings.

2.213 Improved antiparkinsonian effects during the night with levodopa/dopa decarboxylase inhibitor and entacapone compared with levodopa/dopa decarboxylase inhibitor in Parkinson's disease patients experiencing symptom re-emergence due to wearing-off

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Objective: To evaluate the effect of levodopa/dopa decarboxylase inhibitor (DDCI) and entacapone therapy on parkinsonian symptoms during the night in levodopa-treated Parkinson's disease (PD) patients with symptom re-emergence due to wearing-off.

Method: A retrospective, pooled analysis of four double-blind, placebo-controlled Phase III studies conducted in PD patients with wearing-off. Patients receiving levodopa/DDCI were randomized to either entacapone or placebo and followed for 24 weeks. Antiparkinsonian effect during the night was assessed by Unified Parkinson's disease Rating Scale (UPDRS) part II question (Q)12 (turning in bed and adjusting bed clothes) scores at Week 24. Data were available for 673 patients (entacapone: 382, placebo: 291) for intention to treat-observed case analysis (ITT-OC) and 773 patients (entacapone: 454, placebo: 319) for ITT-last observation carried forward (LOCF).

Results: At baseline (ITT-OC), mean age was 62.8 versus 62.6 years, PD duration was 9.5 versus 10.5 years, duration of levodopa treatment was 8.1 versus 8.6 years and mean daily levodopa dose was 675 versus 696 mg in levodopa/DDCI and entacapone and levodopa/DDCI and placebo groups, respectively. The majority of patients in both treatment groups (82.2 vs 83.5%) had difficulties (severity class 1) in turning in bed and adjusting bed clothes as assessed by UPDRS part II Q12. At Week 24, improvement from baseline in Q12 was more frequent (28.0 vs 15.5%) and worsening was less frequent (14.7 vs 20.3%) with levodopa/DDCI and entacapone versus levodopa/DDCI and placebo ($p < 0.001$, ITT-OC). Similarly, significant superior benefit with levodopa/DDCI and entacapone was observed regardless of treatment with ($p = 0.04$) or without ($p < 0.01$) concomitant controlled-release levodopa. Comparable findings were seen in the ITT-LOCF analysis ($p < 0.001$ for the total population).

Conclusion: In PD patients with symptom re-emergence due to wearing-off, levodopa/DDCI and entacapone provides superior benefit in night-time parkinsonian symptoms compared with conventional levodopa/DDCI therapy as measured by UPDRS part II Q12.

2.214 Tolcapone treatment fluctuating patients with Parkinson's disease who did not benefit from entacapone

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Objective: Prospective clinical follow-up of non-demented switched to tolcapone because persisting off periods during entacapone. Background: Several studies indicate that tolcapone reduces off time as well as levodopa requirements in advanced PD. Despite proven effectiveness, tolcapone prescription in clinical setting is currently limited to few patients. It is marginally mentioned in treatment algorithms and many patients come to DBS, apomorphine or duodenal levodopa without trying tolcapone. Finally there are no data in patients who did not benefit from entacapone (EMEA guidelines).

Method: Sixty-six consecutive fluctuating non-demented PD patients were evaluated at 6 and 12 months after initiation of tolcapone. All were "unresponsive" to entacapone according to EMEA indications. All patients were treated with tolcapone 100 mg t.i.d. Patients with liver disease were excluded. All were evaluated with UPDRS part II, III and IV in "on" state (in the morning, 90 minutes after first levodopa intake). We used off-time (Item 39) as main outcome measures to monitor tolcapone effect. Evaluations were conducted at baseline and after 6 and 12 months of therapy blind to treatment conditions. Concomitant medications did not change.

Results: The mean age was 64.0±9.7 yrs. Mean PD duration was 15.9±5.7 yrs (age at PD onset 52.4±8.7). Levodopa dose and off-time had been significantly reduced during follow-up; dyskinesia duration and UPDRS-III didn't change. 16% withdrew tolcapone all during the first month of treatment: 8% due to no benefit on fluctuations, 3% had liver enzyme above the upper limit of normal, one patient complained about diarrhea and abdominal pain, one referred severe dyskinesia and one case had dizziness.

Conclusion: Tolcapone is effective in the majority of entacapone resistant patients who fulfil current strict European prescription guidelines of the drug. We suggest that tolcapone should be considered before patients are referred for infusion or surgery procedures.

2.215 Efficacy and tolerability of rasagiline in routine clinical practice

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Objective: Rasagiline has been proven to be effective in early and advanced Parkinson's disease (PD) patients by controlled clinical trials. We performed an open prospective study to evaluate its efficacy and tolerability in routine clinical practice.

Method: 412 patients with PD (Hoehn–Yahr 1–3, mean 1.9) were followed up in 98 outpatient departments after introduction of rasagiline as a monotherapy or add on therapy. Intensity of tremor, bradykinesia, rigidity, postural instability and CGI were examined, as well as a record of adverse reactions. During the study adverse reactions were recorded as well as doses of levodopa and other antiparkinsonian medication.

Results: Mean age of this PD population was 69 (age range 40–91). The duration of the follow up period was 12 weeks. After 12 weeks of rasagiline treatment tremor was improved in 77% of patients, rigidity in 84%, bradykinesia 89% and postural instability in 34% of patients. Patient's global impression on efficacy was very good or good for 75%, only 0.3% of all patients felt worse. Adverse reactions were overall rare (3%). The most common were gastrointestinal complaints 1.6%, palpitations 0.4% and somnolence 0.2%. Only in 3 cases was rasagiline withdrawn due to adverse reactions and another 3 patients preliminary stopped follow up because of insufficient collaboration.

Conclusion: This study suggests that rasagiline is an effective and well-tolerated medication. The majority of patients showed improvement in tremor, rigidity and bradykinesia. Overall frequency of adverse reactions reported by neurologists in outpatient departments was markedly lower than the reactions reported in phase III controlled clinical trials.