Advance reports

Included in this report are the highlights of the XIX World Congress on Parkinson's Disease and Related Disorders, Shanghai, China.

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PD MED Study: Quality of life results

Results from the PD MED study were recently presented at the XIX World Congress on Parkinson's Disease and Related Disorders, Shanghai, China.

PD Med is a large, simple, "real-life" trial that aims to determine much more reliably which class of drugs provides the most effective control, with the fewest side-effects, for both early and later Parkinson's disease. Patients with early Parkinson's disease were randomised between dopamine agonists, monoamine oxidase type B (MAOB) inhibitors and levodopa alone, with the option to omit either the MAOB inhibitor or levodopa alone arm. Those with later Parkinson's disease were randomised between catechol-O-methyltransferase (COMT) inhibitors, dopamine agonists and MAOB inhibitors, with the option to omit either the dopamine agonist or the MAOB inhibitor arm.

The main outcome measure was patient-rated quality of life, using the PDQ-39 scale, which assesses all aspects of the patient's life, and is sensitive to changes considered important to patients but not identified by clinical ratings.

PD MED Early study

In the PD MED Early study[1] 1620 newly diagnosed Parkinson's disease patients were randomised 2:1 between levodopa-sparing therapy (dopamine agonist or MAOB inhibitor) and levodopa alone. The primary outcome was mobility dimension on the patient rated PDQ-39 QoL scale and secondary outcomes included other dimensions of PDQ-39, EQ-5D, motor complications, dementia and mortality. Repeated measures regression and survival analyses were used.

The study found that PDQ-39 mobility scores were 1.8-points better in patients randomised to levodopa than levodopa-sparing, who also had better PDQ-39 ADL dimension, PDQ-39 summary index and EQ-5D scores. More motor complications were reported with levodopa (57% versus 45% at 5-years; $p = 0.0001$), with similar rates of dementia and mortality. PDQ-39 mobility scores were 1.5-points better with MAOB inhibitors than dopamine agonists. PDQ-39 cognition dimension and summary index were also better, with no difference in motor complications, dementia or mortality.

The authors concluded that patient-rated quality of life was slightly better in patients receiving levodopa than levodopa-sparing therapy, but these improvements need to be balanced against increased motor complications. MAOB inhibitors appeared more effective than dopamine agonists as levodopa-sparing therapy.

PD MED Later Study

In the PD MED Later[2] study 500 patients with advanced PD (ie. patients with motor complications) were randomised between dopamine agonist and dopamine degradation inhibitor (DDI) therapy (MAOB inhibitor or COMT inhibitor). The primary outcome was mobility dimension on the patient-rated PDQ-39 QoL scale and the secondary outcomes were other dimensions of PDQ- 39, EQ-5D, dementia and mortality. Repeated measures regression and survival analyses were used.

There were no differences between dopamine agonists and DDI therapy for patient-rated quality of life, dementia or mortality. PDQ-39 mobility scores were 2.9-points better with MAOB inhibitors than COMT inhibitors. There were also borderline significant differences on the PDQ-39 ADL, emotional well-being and social support

dimensions together with the summary index (favouring MAOB inhibitors). A similar trend was observed for EQ-5D. More patients developed dementia in the COMT inhibitor arm, but there was no difference in mortality.

The authors concluded that there was no difference in patient-rated quality of life between dopamine agonist and DDI therapy. However, a comparison of DDI therapy, found that quality of life was slightly better in patients receiving MAOB inhibitors.

1. Gray R, et al. A large randomised trial assessing quality of life in patient with early PD: results form PD Med Early. Abstract 1.091 XIX World Congress on Parkinson's Disease and Related Disorders December 11–14, 2011, Shanghai, China
2. Clarke CE, et al. A large randomised trial assessing quality of life in patient with later PD: results form PD Med Later. Abstracts 1.092 WFN XIX World Congress on Parkinson's Disease and Related Disorders December 11–14, 2011, Shanghai, China

Efficacy of rasagiline in combination with dopamine agonist therapy

In a subgroup analysis of a post-marketing, observational study conducted in patients with PD, four months treatment with rasagiline improved symptom control and quality of life when given in combination with dopamine agonist therapy.

The efficacy of rasagiline as monotherapy and as adjunct to levodopa is well established; however there is little clinical trial data on its efficacy when given in combination with dopamine agonists. This study, also presented at the World Congress, evaluated the efficacy and tolerability of rasagiline as sole adjunct to dopamine agonist therapy in Parkinson's disease patients.

Subjects were assessed at baseline and after an average of about four months treatment using the Columbia University Rating Scale (CURS), and the PD Questionnaire (PDQ-39). In addition, patients were asked to rate the efficacy and tolerability of rasagiline at the final study visit.

Results found that 57 PD patients (mean age 61.1 years; disease duration 3.8 years) were treated with rasagiline 1mg/day in combination with their current dopamine agonist medication. After a mean of four months treatment with rasagiline, Total-CURS scores significantly improved from 14.0±6.4 at baseline to 11.1±6.2 ($p<0.001$); motor-CURS scores improved from 5.2±1.7 to 4.0±1.8 ($p<0.001$); non motor-CURS scores improved from 8.8±5.1 to 7.1±4.9 ($p<0.001$) and Total-PDQ-39 scores improved from 24.0±15.8 to 19.5±14.3 ($p<0.001$).

Most patients rated the efficacy (49.1%) and tolerability (87.8%) of rasagiline as good/very good.

1. Reichmann H, et al. Efficacy of rasagiline in combination with dopamine agonist therapy: results from a post marketing observation study in patients with Parkinson's disease. Abstract 1272 XIX World Congress on Parkinson's Disease and Related Disorders December 11–14, 2011, Shanghai, China

The REST study: rasagiline improves the quality of sleep in patients with PD

Two months treatment with rasagiline improved night-time sleep experience in patients with Parkinson's disease according to another study presented at the Parkinson's disease and Related Disorders Congress.

Sleep dysfunction in Parkinson's disease (PD) is common affecting some 60–98% of patients. Sleep disorders include excessive daytime sleepiness, sleep attacks, advanced sleep phase syndrome, nocturnal awakenings, and REM sleep behaviour disorder—each having a significant impact on patient quality of life.

This study evaluated the impact of rasagiline treatment on sleep disturbances in PD. It was an open-label, multi-center, single-arm study in patients with Parkinson's disease who were considered suitable for treatment with rasagiline as monotherapy or adjunct therapy (0.5 or 1.0mg once daily per Canadian label). Subjects were assessed at baseline and after two months of treatment using the Parkinson's Disease Sleep Scale (PDSS) to assess overall sleep quality and Epworth Sleepiness Scale (ESS) to assess daytime sleepiness.

It found that of the 110 Parkinson's disease patients who were treated with rasagiline (mean age 67 years; disease duration 4.3 years), 97 completed the two visits. Most had a Hoehn and Yahr Stage of 2 and received rasagiline as adjunct therapy. Treatment with rasagiline improved mean ± SD PDSS scores from 96.2±21.6 at baseline to 105.5±21.93 at

two months (treatment effect 9.1±18.7 points, p=0.003 [n=97]), denoting an improvement in sleep experience. Analysis by item revealed significant differences from baseline in overall quality of sleep, nocturnal restlessness, nocturnal motor symptoms and sleep refreshment (p<0.05). Although there was a small improvement in ESS scores, it was not statistically significant.

1. Panisset M, et al. Rasagiline improves the quality of sleep in patients with Parkinson's disease: results of the rasagiline effect on sleep trial (REST) Abstract 124 XIX World Congress on Parkinson's Disease and Related Disorders December 11–14, 2011, Shanghai, China

Olfaction and profile of weight change in PD

Early assessment of olfaction may identify PD patients at the risk of weight loss according to a study presented at the World Congress on Parkinson's disease.[1]

The study was a prospective assessment of 99 PD patients for clinical parameters, olfaction using UPSIT and current and previous body weight. Patients were categorised as weight losers and nonweight-losers depending on change of weight from previous years. Olfaction was categorised into two groups at the cut-off of the median level of UPSIT scores.

Data was then analysed to study the relationship of olfaction on weight change and found that 39 were weight losers and 60 non-weight losers. Weight losers were significantly older (p=0.02), females (p=0.03) and had more severe impairment of olfaction (UPSIT 15±4 versus 19±5; p < 0.004).

Patients with more severe olfaction impairment were older (p=0.001) and had significantly lower weight, 75 versus 83kg (p= 0.01). There was no difference in the proportion of smokers, medication usage, difficult swallowing or calorie consumption in any group.

Patients below the median-UPSIT (more severe olfactory loss) had lost weight during follow-up whereas those above the median (less severe olfactory loss) had gained weight. Regression analysis revealed UPSIT at the median level to be the most significant variable (p<0.001) for weight loss.

It was concluded that as severe loss of olfaction is associated with weight loss in PD, this may represent a different phenotype predicting weight loss during follow-up since not all PD patients lose weight.

1. Sharma J, et al. Olfaction and profile of weight change in PD: identifying a phenotype. Abstract 37 XIX World Congress on Parkinson's Disease and Related Disorders December 11–14, 2011, Shanghai, China

Significance of body weight in PD

A weight related approach to the dose of levodopa therapy could be an easily modifiable factor to reduce the burden of levodopa related dyskinesia in PD according to another study at the World Congress.[1]

Patients with PD have a lower body mass index than the general population. Lower body weight may predispose PD patients to under-nutrition and osteoporosis. The objective of the study was to determine if body weight has an implication on dyskinesia.

A proportion of PD patients lose weight during the course of the disease. A number of factors might be related to weight loss such as increased energy utilisation, lower energy intake, excessive tremor or rigidity, older age and probably the degree of impaired olfaction. A significant relationship between body weight and levodopa related dyskinesia has been reported in observational studies and clinical trials. Patients with lower initial body weight and weight-losers during the course of the disease are at a significantly higher risk of developing dyskinesia.

The study found that there is a linear relationship between levodopa dose per kilogram body weight and the risk of dyskinesia; higher the levodopa dose per kilogram body weight, higher the risk of dyskinesia. This relationship is more significant than the absolute levodopa dose suggesting that higher body weight might be protective against dyskinesia.

The authors concluded that managing a PD patient in a way to adjust levodopa dose according to current body weight and reducing levodopa in weight-losers during follow-up, supplemented by other medications, may reduce the risk of developing dyskinesia.

1. Sharma J, et al. Significance of body weight in PD—relationship with dyskinesia Abstract 37 XIX World Congress on Parkinson's Disease and Related Disorders December 11–14, 2011, Shanghai, China