



For the attention of Accredited Medical Writers Only

New data presented at the American Academy of Neurology meeting showed that Neupro® (rotigotine) improved both motor and non-motor symptoms of Parkinson's disease

- Analysis of RECOVER – first multinational study in a controlled setting to address the non-motor symptoms of Parkinson's disease – presented at major North American neurology congress
- Rotigotine provided sustained efficacy and tolerability in long term studies of early and late stage idiopathic Parkinson's disease

Brussels (Belgium), 14th April 2010, 1430 CET – Evidence of Neupro® (rotigotine) improving motor as well as non-motor symptoms of Parkinson's disease were presented at the 62nd American Academy of Neurology annual meeting in Toronto, Canada^{1,2}.

"The new data reported this week showed that treatment with rotigotine controlled early morning motor function and improved non-motor symptoms, as judged by the validated non-motor scale, in patients with Parkinson's disease and these effects translated into improvements in quality of life for our patients. RECOVER is the first study carried out in a controlled setting that addresses the non-motor symptoms of Parkinson's disease, such as sleep, mood, cognition and pain which can be just as debilitating to patients as the more obvious movement disorder." said Professor Ray Chaudhuri, Consultant Neurologist and Professor in Neurology and Movement Disorders at Kings College NHS Foundation Trust, and Kings Health Partners, London, UK.

These new findings were reported in extensive analyses of data from RECOVER - a multicentre, multinational, double-blind, placebo-controlled study designed to assess the effects of rotigotine in controlling early morning motor function and non-motor symptoms that affect the everyday lives of people with Parkinson's disease.



Of the 287 Parkinson's patients in RECOVER, 190 were randomized to rotigotine and 97 to placebo. The dose of rotigotine or placebo was tailored to individual patient need (2-16mg/24h or placebo) during a titration period lasting up to 8 weeks, followed by a 4 week maintenance period.

Early morning motor function was assessed using the Unified Parkinson's Disease Rating Scale (UPDRS) Part III (Motor Examination) and sleep quality was assessed using the Parkinson's Disease Sleep Scale (PDSS). Patients were hospitalized for two nights before assessment at baseline and again at the end of the maintenance period. The co-primary efficacy endpoints were the mean change from baseline to end of maintenance in PDSS and UPDRS Part III scores. Non-motor symptoms were assessed as secondary outcomes.

Key primary and secondary outcomes from baseline to end of maintenance were^{1,2}:

Motor symptoms and primary efficacy endpoints

Rotigotine provided significantly greater improvement in early morning motor symptoms than placebo (-7.0 vs -3.9 points; treatment difference -3.55; $p=0.0002$) as measured by the UPDRS Part III (Motor Examination), a comprehensive widely used evaluation of motor symptoms as well as cognition, behaviour and mood. Rotigotine also provided significantly greater improvement than placebo in sleep quality scores as measured by the PDSS (-5.9 vs -1.9 points; difference -4.26; $p<0.0001$).

Non-motor symptoms

- Overall patients experienced greater improvements in non-motor symptoms with rotigotine than placebo (-11.4 vs -6.3 points; treatment difference -6.65; $p=0.015$), as measured by the Parkinson's disease Non-Motor Symptoms assessment scale total (NMST), which measures the severity and frequency of nine categories of non-motor symptoms, including cardiovascular, sleep/fatigue, mood/cognition and attention/memory
- Rotigotine provided greater improvement than placebo in sleep/fatigue (treatment difference -2.03; $p=0.002$) and in mood/cognition (treatment difference -3.40; $p=0.0003$) as measured by the NMST
- Rotigotine provided greater improvement than placebo in mood (treatment difference -2.01; $p=0.011$) as measured by the Beck Depression Inventory (BDI-II), a widely used questionnaire developed to measure the intensity, severity and depth of depression



- Rotigotine provided greater improvement than placebo in quality of life (treatment difference -5.74, $p=0.0002$) as measured by PDQ-8, a short form Parkinson's disease questionnaire
- Rotigotine provided greater improvement than placebo in pain (treatment difference - 0.77, $p=0.004$) as measured by the Likert scale
- There was no change in the number of nocturias (excessive urination at night) in either the rotigotine or placebo group

Tolerability

The most frequently reported adverse events were nausea (rotigotine 21%, placebo 9%), application site reactions (rotigotine 15%, placebo 4%), and dizziness (rotigotine 10%, placebo 6%).

Tolerability and efficacy of rotigotine up to 6 years demonstrated in early stage Parkinson's disease

Rotigotine was generally well tolerated and provided sustained improvement in movement symptoms in patients with early Parkinson's disease treated for up to 6 years, according to new data from an open label extension of an earlier double blind trial, also presented at the congress³.

Of 216 patients who received treatment during the open label phase more than half (52%) received at least five years of rotigotine treatment. Overall, 24% of patients discontinued due to adverse events, of which the most frequently reported (rate per patient-year) were somnolence (23% per patient-year), peripheral edema (14% per patient-year), and fall (17% per patient-year). Treatment-emergent application site reactions were reported in 70 (32%) of patients during open label treatment (12% per patient-year). Mean UPDRS (II + III) scores after up to 6 years of rotigotine treatment remained within 4 points of patients' original double-blind baseline scores.

Long term efficacy and tolerability of rotigotine in advanced Parkinson's disease

Continued efficacy and tolerability were also reported in long term follow up studies of over 600 patients who enrolled in open label extensions of two previous double blind trials of rotigotine in advanced Parkinson's disease⁴.

A four year open label extension trial enrolled 395 patients. While UPDRS Activities of Daily Living (ADL) mean total score improved from double-blind baseline by -4.5 points



during the open label titration to rotigotine 4-16mg/24h, it gradually returned to baseline values (+0.8 points) over 4 years. The mean UPDRS Motor Score (MS) improved from double-blind baseline by -10.1 points during titration then gradually declined to -2.8 points of improvement.

Of 258 patients who entered the open label phase of a second study, 68 (26%) withdrew by the end of year 6 because of adverse events. The -4.9-point mean ADL score improvement achieved during titration declined to +4.1 points above baseline over 6 years, and the mean MS declined from an initial -11.4-point improvement to baseline values (-0.2 points). Treatment-emergent adverse effects were typically dose-related dopaminergic effects (such as insomnia, (5–7% per patient-year), dyskinesias (4–8% per patient-year), and hallucinations (4–8% per patient-year).

For further information

Onsite at meeting

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About Neupro® in Europe⁵

Neupro® (rotigotine) is approved in the European Union for the treatment of the signs and symptoms of early-stage idiopathic Parkinson's disease, as monotherapy (i.e. without levodopa) or in combination with levodopa, i.e. over the course of the disease, through to late stages when the effect of levodopa wears off or becomes inconsistent and fluctuations of the therapeutic effect occurs. Neupro® is also approved in the European Union for the symptomatic treatment of moderate to severe idiopathic restless legs syndrome in adults.

Neupro® in Europe Important Safety Information⁵

Neupro® is contraindicated in case of hypersensitivity to the active substance or to any of its excipients, and in case of magnetic resonance imaging (MRI) or cardioversion. Neupro® should be removed if the patient has to undergo MRI or cardioversion.

It is recommended to monitor blood pressure, especially at the beginning of treatment, due to the general risk of orthostatic hypotension associated with dopaminergic therapy.

Neupro® has been associated with somnolence episodes of sudden sleep onset episodes. Patients treated with dopamine agonists including Neupro®, have been reported as exhibiting signs of pathological gambling, increased libido and hypersexuality.

Symptoms suggestive of neuroleptic malignant syndrome have been reported with abrupt withdrawal of dopaminergic therapy. Therefore it is recommended to taper treatment.

Neupro® contains sodium metabisulphite, a sulphite that may cause allergic-type reactions including anaphylactic symptoms and life threatening or less severe asthmatic episodes in certain susceptible people.

Hallucinations have been reported, and patients should be informed that hallucinations can occur.



Cases of cardiopulmonary fibrotic complications have been reported in some patients treated with ergot-derived dopaminergic agents. Neuroleptics given as antiemetic should not be given to patients taking dopamine agonists. Ophthalmologic monitoring is recommended at regular intervals or if vision abnormalities occur.

External heat, from any source should not be applied to the area of the patch. Exposure of a skin rash or irritation to direct sunlight could lead to changes in the skin color. If a generalized skin reaction (e.g. allergic rash) associated with the use of Neupro[®] is observed, Neupro[®] should be discontinued.

Caution is advised when treating patients with severe hepatic impairment or acute worsening of renal function, a dose reduction might be needed.

The incidence of some dopaminergic adverse events, such as hallucinations, dyskinesia, and peripheral oedema generally is higher when given in combination with L-dopa. This should be considered when prescribing Neupro[®].

Neupro[®] should not be used during pregnancy. Breast-feeding should be discontinued.

Augmentation may occur in Restless Legs Syndrome patients. Augmentation refers to the earlier onset of symptoms in the evening (or early afternoon), increase in severity of symptoms, and spread of symptoms to involve other body parts.

Adverse drug reactions reported in more than 10% of Parkinson's patients treated with Neupro[®] are nausea, vomiting, application site reactions, somnolence, dizziness and headache.

Adverse drug reactions reported in more than 10% of RLS patients treated with Neupro[®] are nausea, application site reactions, asthenic conditions and headache.

All Neupro[®] supply should be stored in a refrigerator. There is no need for patients to transport Neupro[®] patches in special containers and they must not be stored in a freezer compartment.

Please refer to the European Summary of Product Characteristics for full prescribing information (Approved 15th March 2010): <http://www.emea.europa.eu/humandocs/PDFs/EPAR/neupro/emea-combined-h626en.pdf>

About Neupro[®] in the U.S.

Neupro[®] (Rotigotine Transdermal System) is indicated in the U.S. for the treatment of the signs and symptoms of early-stage idiopathic Parkinson's disease.

In April 2008, UCB recalled Neupro[®] from the U.S. market after ongoing monitoring revealed that specific batches of Neupro[®] had deviated from their approved specification. Neupro[®] is currently not available in the U.S. UCB is working with the U.S. FDA so that Neupro[®] can be available to patients with early-stage Parkinson's disease as soon as possible.

Important Safety Information – U.S.

Some patients treated with Neupro[®] reported falling asleep while engaged in activities of daily living, including operation of motor vehicles, which sometimes resulted in accidents. Some patients perceived no warning signs, such as excessive drowsiness. Hallucinations were reported in 2.0% of patients treated with Neupro[®] compared to 0.7% of patients on placebo. Neupro[®] contains metabisulfite. Neupro[®] should be used with caution in patients, especially those at risk for cardiovascular disease, because of the potential for symptomatic hypotension, syncope, elevated heart rate, elevated blood pressure, fluid retention, and/or weight gain. All Parkinson's disease patients are at a higher risk for melanoma and should be monitored regularly. The most commonly reported side effects in clinical trials were nausea, application site reactions, somnolence, dizziness, headache, vomiting, and insomnia. Some subjects who received Neupro[®] experienced a decline in blood hemoglobin levels (about 2% relative to subjects who received placebo). It is not known whether this change is readily reversible with discontinuation of Neupro[®].



Neupro® is not approved or available in Canada for the treatment of idiopathic Parkinson's disease or for the treatment of Restless Legs Syndrome

Neupro® is a registered trademark of the UCB Group of companies.

References

1. Chaudhuri KR, Rudzinska M, Kies B, Fine J, Hill DL, Anderson T, Surmann E, Whitesides J, Boroojerdi B, Trenkwalder C, on behalf of the RECOVER study group. Effect of rotigotine on non-motor symptoms in subjects with idiopathic Parkinson's disease. Presented at the 62nd American Academy of Neurology annual meeting, Toronto, Canada (April 10-17 2010)
2. Kies B, Chaudhuri KR, Anderson T, Fine J, Hill DL, Rudzinska M, Surmann E, Whitesides J, Boroojerdi B, Trenkwalder C, on behalf of the RECOVER study group. Effect of rotigotine on sleep quality and control of early morning motor function in subjects with idiopathic Parkinson's disease. Presented at the 62nd American Academy of Neurology annual meeting, Toronto, Canada (April 10-17 2010)
3. Watts RL, Boroojerdi B, Jankovic J. Open-label extension to the double-blind SP512 trial to assess the safety of long-term treatment of rotigotine in subjects with early-stage idiopathic Parkinson's disease. Presented at the 62nd American Academy of Neurology annual meeting, Toronto, Canada (April 10-17 2010)
4. LeWitt PA, Boroojerdi B, Poewe W. Long-term treatment of advanced Parkinson's disease with rotigotine. Presented at the 62nd American Academy of Neurology annual meeting, Toronto, Canada (April 10-17 2010)
5. Neupro® European Summary of Product Characteristics (Approved March 15th 2010) <http://www.emea.europa.eu/humandocs/PDFs/EPAR/neupro/emea-combined-h626en.pdf>

About UCB

UCB, Brussels, Belgium (www.ucb.com) is a biopharmaceutical company dedicated to the research, development and commercialization of innovative medicines with a focus on the fields of central nervous system and immunology disorders. Employing more than 9 000 people in over 40 countries, UCB produced revenue of EUR 3.1 billion in 2009. UCB is listed on Euronext Brussels (symbol: UCB).

Forward looking statement

This press release contains forward-looking statements based on current plans, estimates and beliefs of management. Such statements are subject to risks and uncertainties that may cause actual results to be materially different from those that may be implied by such forward-looking statements contained in this press release. Important factors that could result in such differences include: changes in general economic, business and competitive conditions, effects of future judicial decisions, changes in regulation, exchange rate fluctuations and hiring and retention of its employees.