



For the attention of accredited medical writers only

Neupro[®] (rotigotine) showed significant benefit on early morning motor control, sleep and nocturnal symptoms in patients with Parkinson's disease

- Detailed RECOVER trial analysis presented at major international congress

Brussels (Belgium), 17th June 2010, 1430 CET – New data presented this week at the 14th International Congress of Parkinson's Disease and Movement Disorders in Buenos Aires, Argentina (June 13-17, 2010) showed that Neupro[®] (rotigotine) provided significantly greater improvement in early morning motor symptoms and sleep quality, compared with placebo, and as measured by the Unified Parkinson's Disease Rating Scale and the Parkinson's Disease Sleep Scale. ^{1,2}

The latest data come from an analysis from the RECOVER study - 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.

"Sleeping without being restless, uncomfortable or immobile during the night may be just as important to people with Parkinson's disease, as being able to move around during the day" said Professor Claudia Trenkwalder from the Paracelsus-Elena Hospital, Kassel, Germany. "Findings from the RECOVER study showed that rotigotine was an effective treatment option for patients with Parkinson's disease having beneficial effects on both motor and non-motor symptoms."

About the RECOVER trial analysis

Of the 287 patients with idiopathic Parkinson's disease and unsatisfactory early morning motor control 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. Patients were hospitalized for two nights before assessment at baseline and again at the end of the maintenance period.



Early morning motor function was assessed from baseline to the end of maintenance using the Unified Parkinson's Disease Rating Scale (UPDRS) Part III (Motor Examination), a comprehensive, widely used evaluation of motor symptoms. Additional exploratory endpoints were the UPDRS Part II (Activities of Daily Living) and Part II+III scores, assessed from baseline to end of treatment. Responder rates were also assessed, with responders defined as people with a) $\geq 20\%$ and b) $\geq 30\%$ improvements in UPDRS Part III score from baseline to end of maintenance.

Sleep quality was assessed using the modified Parkinson's Disease Sleep Scale (PDSS-2) from baseline to end of maintenance. The PDSS-2 assesses sleep disturbance, nocturnal motor and non-motor symptoms. Mean changes in PDSS-2 domain and individual item scores were additional exploratory endpoints.

The co-primary efficacy endpoints were the mean change from baseline to end of maintenance in PDSS-2 and UPDRS Part III scores.

Primary efficacy endpoints^{1,2}

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). Rotigotine also provided significantly greater improvement than placebo in sleep quality scores as measured by the PDSS-2 total score (-6.08 vs -2.45 points; treatment difference -4.26; $p<0.0001$).

Additional exploratory endpoints^{1,2}

- Improvement in PDSS-2 score for disturbed sleep was significantly better with rotigotine than placebo (treatment difference -1.4 points; $p=0.0009$), and within this domain, scores were better for difficulty falling asleep (treatment difference -0.46 points; $p=0.0008$) and feeling tired and sleepy in the morning (treatment difference -0.4 points; $p=0.0036$). No significant differences were seen for poor sleep quality, difficulty staying asleep or need to get up and pass urine.
- PDSS-2 scores for motor symptoms at night were significantly better with rotigotine than placebo (treatment difference -1.54 points; $p<0.0001$), and within this domain, scores were better for restlessness of legs or arms (treatment difference -0.36 points; $p=0.0025$), urge to move legs or arms (treatment difference -4.3 points; $p=0.0003$), painful posturing in the morning (treatment difference -0.34 points); $p=0.0027$) and



tremor on waking (treatment difference -0.33 points; $p=0.0153$). The only item not to show a significantly greater improvement with rotigotine was distressing dreams.

- Patients had fewer PD symptoms at night with rotigotine than placebo, according to PDSS-2 domain scores (-1.41 points; $p<0.0001$), and within this domain, scores were better for feeling uncomfortable and immobile (-0.49 points; $p<0.0001$), pain in arms or legs (-0.36; $p=0.001$), muscle cramps in arms or legs (-0.31; $p=0.0067$), and breathing difficulties or snoring (-0.24; $p=0.0064$). Only scores for distressing hallucinations showed no difference between the two groups.
- Patients experienced significantly greater improvements in UPDRS Part II (Activities of Daily Living) with rotigotine than placebo (-2.6 vs -1.3 points; treatment difference -1.49; $p=0.0005$), and significantly greater improvements in Part II+III scores (-9.6 vs -5.2 points; treatment difference -4.95; $p<0.0001$).
- UPDRS Part III responder rates were higher with rotigotine than placebo ($\geq 20\%$ improvement: rotigotine 52%, placebo 33%; $\geq 30\%$ improvement: rotigotine 38%, placebo 19%).

In the RECOVER study, 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%).³

For further information

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About Neupro[®] in Europe⁴

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 Information⁴

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) 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. Recently the U.S. Food and Drug Administration (FDA) has recommended that UCB reformulate Neupro[®] patches and UCB is working on the development of a new formulation. Patients and physicians with questions about the status of Neupro[®], or about UCB's Patient Access program for Neupro[®], may contact UCB Medical Information at 1-866-822-0068 (option 9).



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 a registered trademark of the UCB Group of companies.

Neupro[®] is not available in Argentina for the treatment of Parkinson's disease.

References

1. Trenkwalder C, Kies B, Rudzinska M, Fine J, Niki J, Hill DL, Anderson T, Surmann E, Whitesides J, Boroojerdi B, Chaudhuri KR, on behalf of the RECOVER study group. Effect of rotigotine on control of early morning motor function in Parkinson's disease. RECOVER study. *Poster session II, June 15th 2010, 0900-1800*. Presented at the 14th International Congress of Parkinson's Disease and Movement Disorders, Buenos Aires, Argentina .
2. Trenkwalder C, Kies B, Rudzinska M, Fine J, Niki J, Hill DL, Anderson T, Surmann E, Whitesides J, Boroojerdi B, Chaudhuri KR, on behalf of the RECOVER study group. Effect of rotigotine on sleep and nocturnal symptoms in Parkinson's disease. RECOVER study. *Poster session III, June 16th 2010, 0900-1800*. Presented at the 14th International Congress of Parkinson's Disease and Movement Disorders, Buenos Aires, Argentina .
3. 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).
4. 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.