News

For the attention of Accredited Medical Writers Only

New post hoc analyses examined the effects of Neupro® (rotigotine) on daytime functioning, daytime symptoms, pain and mood in Restless Legs Syndrome

Brussels (Belgium), 10th June 2011, 0070 CET – Results from new post hoc analyses assessing the effects of Neupro® (rotigotine) in Restless Legs Syndrome (RLS) and utilizing novel surrogate markers suggested improved daytime functioning and daytime symptoms, reduced RLS-related pain and improved mood and depressive symptoms in patients with moderate to severe RLS [1-3]. The data were presented at the 15th International Congress of Parkinson's disease and Movement disorders in Toronto, Canada.

Daytime functioning and daytime symptoms in RLS patients

RLS has been mainly associated with symptoms occurring in the late evening and at night. However, epidemiological studies and this post hoc analysis suggested that patients may also experience daytime symptoms and report impairment of daytime functioning[1,2].

Results of a post hoc analysis of a six month double blind study of rotigotine in 458 patients suggested improvement in daytime functioning and daytime symptoms in patients treated with rotigotine (1, 2 and 3 mg/24h, pooled data) than placebo[2].

"Daytime functioning symptoms, such as symptoms in the afternoon, sleepiness and tiredness due to bad sleep are a problem for many patients with moderate to severe RLS, and can adversely affect their ability to carry out everyday activities. While additional studies are needed, this post hoc analysis suggested that patients treated with rotigotine for 6 months may experience improvements in daytime functioning and daytime symptoms compared to those treated with placebo. These effects may be explained by the 24 hour coverage of symptoms, whenever they occur, with the application of transdermal rotigotine, " said Dr Ralf Kohnen, University of Erlangen-Nuremberg, Germany.

Significant improvements with rotigotine versus placebo (from baseline to end of maintenance) were seen in a series of measures of RLS symptom severity on the International Restless Legs Syndrome Study Group Severity Rating Scale (IRLS) and the Restless Legs Syndrome-6 (RLS-6) scale, and quality of life on the Quality of Life Questionnaire for RLS patients (QoL-RLS):

Daytime functioning

- QoL-RLS Item 6 "mood impairment due to daytime sleepiness": ($p<0.0001$)[2]
- IRLS Item 5 "severity of tiredness/sleepiness during the day due to RLS symptoms": ($p<0.0001$)[2]
- IRLS Item 9 "impact of RLS symptoms on ability to carry out daily affairs": ($p<0.0001$)[2]
- RLS-6 Item 6 "sleepiness/tiredness during the day" : ($p<0.0001$)[2]

Daytime symptoms

- RLS-6 Item 4 "RLS symptom severity during the day at rest" : ($p<0.0001$)[2]
- RLS-6 Item 5 "RLS symptom severity during the day when active" : ($p<0.0062$)[2]

Pain in RLS patients

Results of the post hoc analysis suggested that treatment with rotigotine (1, 2, and 3 mg/24hours) for six months may improve impairment due to pain. More than half of the patients in the study experienced moderate to extreme impairment of daily activities due to pain at baseline[3]. Significant improvement with rotigotine versus placebo (from baseline to end of maintenance) was seen in the QoL-RLS Item 8 score, i.e. the degree to which pains in arms or legs impair wellbeing or normal daily activities ($p=0.0018$)[3].

Mood disturbance and depressive symptoms in RLS patients

Results of the post hoc analysis suggested that treatment with rotigotine (1, 2 and 3 mg/24 hours) for six months may improve mood disturbance and depressive symptoms[4]. Significant improvement with rotigotine versus placebo (from baseline to end of maintenance) was seen in the QoL-RLS Item 3, i.e. the degree to which RLS symptoms impair mental health/mood ($p<0.0001$) and in IRLS Item 10, i.e. the severity of mood disturbance due to RLS symptoms ($p<0.0001$)[4]. Significant improvement with rotigotine versus placebo (from baseline to end of maintenance) was also seen in the Self-rating Depression Scale (SDS-Index), i.e. patient reporting of moderate to definite severe depression ($p<0.0001$).

Notes to Editors

About Restless Legs Syndrome[5,6]

Restless Legs Syndrome (RLS) is a neurological disorder characterized by an uncontrollable urge to move the legs during periods of inactivity and rest. These urges are usually accompanied by uncomfortable or unpleasant sensations in the legs. Prevalence in the general population is between 3% and 10% and treatment is needed only in the moderate to severe form of the disorder. Dopaminergic treatment is the first choice in idiopathic restless legs syndrome.

About Neupro® in European Union[7]

Neupro® is approved in the European Union for the symptomatic treatment of moderate to severe idiopathic restless legs syndrome in adults. Neupro® (rotigotine) is also 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® in Europe Important Safety Information

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
Neupro® European Summary of Product Characteristics (Approved February 2011)
http://ec.europa.eu/health/documents/community-register/html/alfregister.htm

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. Neupro® is not FDA approved for the treatment of Restless Legs Syndrome.

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.

Neupro® in the U.S. - Important Safety Information
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®. Please go to http://www.neupro.com/documents/Neupro_PI_071207.pdf for US Full Prescribing Information.

About rotigotine transdermal system in Canada

Rotigotine transdermal system is not authorised for sale in Canada.

References

1. Allen RP, Walters AS, Montplaisir J et al. Restless Legs Syndrome, Prevalence and Impact. Arch Intern Med 2005; 165; 1286-92
2. Kohnen R, García-Borreguero D, Allen R, Grieger F, Bauer L, Schollmayer E, Trenkwalder C. Transdermal rotigotine improved daytime functioning and daytime symptoms in patients with

idiopathic restless legs syndrome. Presented at the 15th International Congress of Parkinson's disease and Movement disorders, Toronto, Canada, June 5-9 2011
3. Kohnen R, García-Borreguero D, Moran K, Bauer L, Grieger F, Schollmayer E, Allen R, Stiasny-Kolster K. Transdermal rotigotine reduced impairment due to pain in RLS patients: a post hoc analysis of patients with moderate to extreme impairment due to pain. Presented at the 15th International Congress of Parkinson's disease and Movement disorders, Toronto, Canada, June 5-9 2011
4. Beneš H, Trenkwalder C, Grieger F, Schollmayer E, Moran K, Bauer L, Allen R, Kohnen R. Transdermal rotigotine improved mood disturbance and depressive symptoms due to restless legs syndrome (RLS) symptoms in patients with idiopathic RLS. Presented at the 15th International Congress of Parkinson's disease and Movement disorders, Toronto, Canada, June 5-9 2011
5. http://www.ninds.nih.gov/disorders/restless_legs/detail_restless_legs.htm (accessed May 27th 2011)
6. Trenkwalder C, Paulus W, Walters AS. The restless legs syndrome. Lancet Neurol 2005; 4: 465
7. Neupro® European Summary of Product Characteristics (Approved February 2011) http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000626/WC500026397.pdf

For further information

Nancy Nackaerts, External Communications, UCB
T +32.473.864.414, nancy.nackaerts@ucb.com

Eimear O'Brien, Associate Director, Global CNS Communications UCB
T +32.2.559.9271,eimear.obrien@ucb.com

Andrea Levin, Senior Manager, Communications & PR, U.S.
T +770.970.8352, andrea.levin@ucb.com

About UCB

UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With more than 8 500 people in about 40 countries, the company generated revenue of EUR 3.2 billion in 2010. 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.