



Impact of earlier use of NEUPRO[®] (rotigotine transdermal patch) in Parkinson's disease patients discussed at first EAN congress

- Presentation of pooled data from a post-hoc analysis of two pivotal 6-month double-blind Phase 3 studies of rotigotine transdermal patch in early Parkinson's disease (PD), and their 6-year open-label extension studies.¹
- The data recently published online¹ in a [peer reviewed journal](#), suggest that a 6-month earlier initiation of rotigotine may be associated with greater long-term benefits in patients with early PD with mild symptom severity and disability at baseline.
- Data suggest earlier rotigotine treatment initiation in patients with minimal or no functional disability or impairment may lead to extended clinical benefit for the patient.¹

Brussels (Belgium), 23rd of June 2015 – 07:00 CET – Results of the post-hoc analysis investigating the impact of 6-month earlier versus postponed initiation of NEUPRO[®] (rotigotine transdermal patch) in patients with early-stage Parkinson's disease (PD) with mild symptom severity were presented during the UCB Neurology Corporate Satellite Symposium at the 1st Congress of the [European Academy of Neurology \(EAN\)](#), in Berlin. The presentation was given by Professor Lars Timmermann, MD, from Department of Neurology, University Hospital Cologne, Germany and first author of a recently peer reviewed article published in *Expert Opinion on Pharmacotherapy*¹.

“The starting point of our investigation was to explore if time of treatment initiation impacts the outcome of patients living with early Parkinson's disease” explained Professor Timmermann. *“The initiation of treatment is often delayed until symptoms begin to limit the patient's ability to function. The results of our analysis suggest that initiation of rotigotine in Parkinson's patients during the early stages of this disease, when patients are presenting minimal or no functional disability or impairment, may be associated with additional long-term clinical benefit; postponing treatment may result in loss of functional ability that cannot be regained. Considering earlier rotigotine treatment initiation in patients with minimal or no functional disability or impairment may improve the patient journey.”* said Professor Timmermann.

Results are based on data from a pooled analysis of two pivotal 6-month, double-blind placebo-controlled Phase 3 studies of rotigotine in patients with early-stage PD, and their respective 6-year long-term open-label extension studies. Post-hoc analysis focused only on patients with mild symptom severity and disability at study baseline (as defined by the Hoehn and Yahr [HY] stage 1-2) and on the timing of rotigotine initiation. Results show that 6-month earlier initiation of rotigotine in early PD patients with mild symptom severity and disability at HY stage 1-2 may improve their activities of daily living and their motor function for longer (45 months) compared to postponing treatment for 6 months (21 months).¹

About this post-hoc analysis

Post-hoc analysis of pooled data from two pivotal 6-month, Phase 3, multicenter, randomized, double-blind, placebo-controlled study of rotigotine in patients with early-stage PD (SP512² and SP513³), and their respective long-term open-label extension studies of up to 6 years' treatment with rotigotine (SP702⁴ and SP716⁵), investigated the impact of 6-month earlier double-blind initiation of treatment with rotigotine transdermal patch in patients with mild symptom severity and disability, as defined by the HY scale. The analysis was restricted to a subgroup of patients at HY stage 1-2 (n=346) to focus specifically on the timing of rotigotine initiation in patients with minimal/no functional disability or impairment. Patient groups were defined by the double-blind study treatment:

- “Rotigotine-Rotigotine” group (n=221; mean [SD] age at baseline: 60.9 [9.7] years) received rotigotine in the 6-month double-blind study (ie 6-month earlier rotigotine initiation)
- “Placebo-Rotigotine” group (n=125; mean [SD] age at baseline: 63.0 [10.3] years) received placebo in the 6-month double-blind study (ie rotigotine in open-label extension only).

The effect of 6-month earlier double-blind initiation of rotigotine on long-term efficacy (the total score of the activities of daily living [ADL] section and motor examination section of the Unified Parkinson's Disease Rating Scale [UPDRS]) in patients with PD at HY stage 1-2 was investigated.

Results¹

- In the 6-month double-blind studies phase, the improvement in UPDRS ADL and motor examination total score from baseline to end of maintenance was greater in the subgroup of patients receiving rotigotine compared with placebo; treatment difference (95% CI): -5.01 (-7.28, -2.75), p<0.001 (exploratory analysis). The magnitude of the effect of rotigotine observed in this subgroup of patients living with PD is notable.
- At the start of open-label rotigotine maintenance period, mean (\pm SD) change from double-blind baseline in UPDRS ADL and motor examination total scores were improved in both groups.
- After this initial improvement, mean scores gradually increased (i.e. worsened) with worsening of mean UPDRS ADL and motor examination total scores relative to double-blind baseline
- At the time mean ADL and motor examination total scores for “Placebo-Rotigotine” had worsened relative to baseline (open-label week 84; ~21 months), mean scores were still improved relative to baseline in patients who had initiated treatment with rotigotine 6 months earlier (“Rotigotine-Rotigotine”); treatment difference (95%CI): -3.89 (-6.94, -0.84), p=0.013 (exploratory analysis).
- It is important to note that no apparent differences between both groups were observed in terms of the dose of rotigotine, number of patients who received concomitant levodopa, time to levodopa or levodopa dose, suggesting that these factors did not contribute to the observed numerical differences in UPDRS ADL and motor examination total scores over time.

About Parkinson's Disease⁶

Parkinson's disease is a progressive and chronic neurological disease characterized by the physical motor symptoms of resting tremor, muscle rigidity and slowness of movement. Symptoms not related to movement (non-motor symptoms) can also occur and include pain, sleep disturbances and depression. It is estimated that 6.3 million people are living with Parkinson's disease worldwide. The

age of onset is usually over 60 years. Although it is estimated that 1 in 10 people are diagnosed before the age of 50.

About NEUPRO in the European Union⁷

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 occur (end of dose or on-off fluctuations).

NEUPRO is also approved in the European Union for the symptomatic treatment of moderate to severe idiopathic Restless Legs Syndrome in adults.

NEUPRO in the European Union Important Safety Information⁷

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 to avoid skin burns.

It is recommended to monitor blood pressure, especially at the beginning of treatment, due to the risk of postural/orthostatic hypotension associated with dopaminergic therapy and reported during NEUPRO treatment. NEUPRO has been associated with somnolence and episodes of sudden sleep onset. Patients treated with dopamine agonists, including NEUPRO, have been reported to exhibit behavioural symptoms of impulse control disorders such as pathologic gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating. Symptoms suggestive of neuroleptic malignant syndrome have been reported with abrupt withdrawal of dopaminergic therapy. Therefore it is recommended to taper treatment.

Patients should be informed that manifestations of abnormal thinking and behaviour such as paranoid ideation, delusions, hallucinations, confusion, psychotic-like behaviour, disorientation, aggressive behaviour, agitation and delirium 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. Exposure of a skin rash or irritation to direct sunlight could lead to changes in the skin colour. Application site reactions lasting more than a few days, spreading outside the area of the patch, or that increase in severity should lead to risk/benefit balance re-assessment. If a generalised skin reaction (eg, 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.

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. NEUPRO should not be used during pregnancy. Breast-feeding should be discontinued.

In Parkinson's disease, 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.

In restless legs syndrome, augmentation may occur. Augmentation refers to the earlier onset of symptoms in the evening (or even the afternoon), increase in severity of symptoms, and spread of symptoms to involve other body parts.

At the beginning of therapy, dopaminergic adverse reactions, such as nausea and vomiting, may occur. These are usually mild or moderate in intensity and transient, even if treatment is continued.

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. The majority of the application site reactions are mild or moderate in intensity.

Adverse drug reactions reported in more than 10% of RLS patients treated with NEUPRO are nausea, application site reactions, asthenic conditions (including fatigue, asthenia, malaise) and headache. The majority of the application site reactions are mild or moderate in intensity.

Please refer to the European Summary of Product Characteristics for full prescribing information <http://www.ema.europa.eu/ema/> (Date of final CHMP opinion of the EU Product Information: 26 February 2015)

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For further information

Corporate Communications

France Nivelles,
Global Communications, UCB

T +32.2.559.9178,
france.nivelles@ucb.com

Laurent Schots,
Media Relations, UCB
T+32.2.559.92.64,
Laurent.schots@ucb.com

Investor Relations

Antje Witte,
Investor Relations, UCB

T +32.2.559.94.14,
antje.witte@ucb.com

Brand Communications

Bahar Etratti,
Global Communications, UCB

T +32.2.559.96.78,
bahar.etratti@ucb.com

References

1. Timmermann L *et al.* Impact of 6-month earlier versus postponed initiation of rotigotine on long-term outcome: post-hoc analysis of patients with early Parkinson's disease with mild symptom severity. *Expert Opin Pharmacother.* 2015 May 22:1-11. [Epub ahead of print]
2. Watts RL *et al.* Randomized, blind, controlled trial of transdermal rotigotine in early Parkinson disease. *Neurology.* 2007 Jan 23;68(4):272-276

3. Giladi N *et al.* Rotigotine transdermal patch in early Parkinson's disease: a randomized, double-blind, controlled study versus placebo and ropinirole. *Mov Disord.* 2007;22(16):2398-2404
4. Elmer LW *et al.* Long-term safety and tolerability of rotigotine transdermal system in patients with early-stage idiopathic Parkinson's disease: a prospective, open-label extension study. *Parkinsonism Relat Disord.* 2012 Jun;18(5):488-493
5. Giladi N *et al.* The safety and tolerability of rotigotine transdermal system over a 6-year period in patients with early-stage Parkinson's disease. *J Neural Transm.* 2013;120(9):1321-1329
6. European Parkinson's Disease Association. Accessed 1st April 2015 from <http://www.epda.eu.com/en/parkinsons/in-depth/parkinsonsdisease>
7. NEUPRO[®] Summary of Product Characteristics. Accessed 1st April 2015 from http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000626/WC500026397.pdf

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 8500 people in approximately 40 countries, the company generated revenue of €3.3 billion in 2014. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

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This press release contains forward-looking statements based on current plans, estimates and beliefs of management. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, political, regulatory or clinical results and other such estimates and results. By their nature, such forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and assumptions which could cause actual results to differ materially 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, the inability to obtain necessary regulatory approvals or to obtain them on acceptable terms, costs associated with research and development, changes in the prospects for products in the pipeline or under development by UCB, effects of future judicial decisions or governmental investigations, product liability claims, challenges to patent protection for products or product candidates, changes in laws or regulations, exchange rate fluctuations, changes or uncertainties in tax laws or the administration of such laws and hiring and retention of its employees. UCB is providing this information as of the date of this press release and expressly disclaims any duty to update any information contained in this press release, either to confirm the actual results or to report a change in its expectations.

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Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement.