

A Multicentre, Multinational, Phase III, Randomised, Double-Blind, Double-Dummy, 3-Arm Parallel Group, Placebo- and Pramipexole-Controlled Trial of the Efficacy and Safety of Rotigotine Patch in Subjects With Advanced-Stage, Idiopathic Parkinson's Disease who are not Well Controlled on Levodopa

Short title: Rotigotine for the Treatment of Advanced Parkinson's Disease in Adults

Background¹

- Parkinson's disease is a disorder of the nervous system that worsens over time. The main symptoms include uncontrollable shaking, stiffened muscles, slowness of movement, and loss of spontaneous movement.
- In the early stages of Parkinson's disease, so-called early Parkinson's disease, patients' ability to do daily activities is affected. In advanced stage of Parkinson's disease, so-called advanced Parkinson's disease, the movement-related problems get worse and the patients are severely disabled.

Purpose of the study

- To determine if rotigotine (Neupro[®]) transdermal patch decreases 'off-time', which is a time period with loss of treatment effect, and decreases dyskinesia (involuntary movements) in patients with advanced Parkinson's disease.
- To determine if rotigotine is well tolerated by these patients.

Study participants

- The study included 506 female and male patients aged 30 years or more with advanced idiopathic (i.e. unknown cause) Parkinson's disease. These patients were not adequately controlled with their current medicine, thus facing 'off-time' equal or superior to 2.5 hours per day.

Study design and research methodology

- The study was conducted in 77 centres across Austria, Belgium, Croatia, Czech Republic, Denmark, Finland, France, Germany, Hungary, Italy, Netherlands, Norway, Poland, Spain, Sweden, Switzerland, UK, Israel, South Africa, Australia and New Zealand between March 2004 and July 2005. Patients participated in the study for a maximum of 8 months.
- The study participants were randomly divided into 3 groups:
 - The first group received rotigotine skin patch and placebo tablet orally.
 - The second group received pramipexole (another medicine used for the treatment of advanced Parkinson's disease) tablet orally and placebo applied as skin patch.
 - The third group received placebo as tablet orally and as skin patch.
- After 6 months of medicine exposure, the decrease in daily 'off time' periods was measured; and the number of 'responders', who are defined as patients showing at least 30% decreased 'off time', was calculated. The decrease in the amount of time spent without involuntary movements was measured.
- Side effects were also studied.

Key findings

- More patients treated with either rotigotine or pramipexole compared with placebo showed:
 - Decrease in their daily 'off-time' periods.
 - Increase in the amount of time spent without involuntary movements.
 - Improvement in the symptoms of advanced Parkinson's disease.
- There were more 'responders' in both rotigotine and pramipexole groups compared with placebo group.
- Rotigotine and pramipexole showed similar improvement in symptoms of advanced Parkinson's disease.
- Similar percentage of patients in all the groups showed side effects. Most of the side effects were mild to moderate.
 - Side effects most commonly seen in at least 5% of patients in any of the groups were skin problems at the site of application of the patch, nausea, somnolence (drowsiness), dyskinesia (involuntary movements), back pain, and dizziness.
- Patients who completed this study were followed for an additional period of up to 5 years to further assess the long-term safety of rotigotine [NCT00501969].

Peer-reviewed publication

Poewe WH, Rascol O, Quinn N, et al. Efficacy of pramipexole and transdermal rotigotine in advanced Parkinson's disease: a double-blind, double-dummy, randomised controlled trial. *Lancet Neurol.* 2007;6:513-520.

Peer-reviewed publication of follow-up trial

LeWitt P, et al. Rotigotine transdermal system for long-term treatment of patients with advanced Parkinson's disease: results of two open-label extension studies, CLEOPATRA-PD and PREFER. *J Neural Transm.* 2013; 120(7):1069-1081.

References:

1. Blandini F, Armentero MT. Dopamine receptor agonists for Parkinson's disease. *Expert Opin Investig Drugs.* 2014;23(3):387-410.

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