## Rotigotine

Novel dopamine agonists (pramipexole, ropinirole, rotigotine), catecholmethyltransferase inhibitors (entacapone), and monoamine oxidase B inhibitors (rasagiline) have been developed to provide more continuous oral delivery of dopaminergic stimulation in order to improve motor outcomes <sup>1)</sup>.

A post hoc analysis suggests that rotigotine may be efficacious across a broad range of progressive stages of PD symptom severity and functional disability (HY stages 1-4)<sup>2)</sup>.

Rotigotine, delivered over 24 h by a once-daily transdermal patch, has been investigated in several clinical trials. Continuous delivery of rotigotine showed to provide 'true' CDS in animal models. The potential of true CDS therapy to prevent or reduce long-term motor and non-motor complications requires investigation in appropriately designed clinical trials <sup>3)</sup>.

In a post hoc analyses, adjunctive treatment with rotigotine in patients already receiving an MAO-B inhibitor improved UPDRS II+III score; this appeared to be largely driven by improvements in the motor aspects of PD  $^{4)}$ .

Dropped head syndrome is a phenomenon of disproportionate neck anteflexion that has been reported in patients with Parkinson disease (PD). Antiparkinsonian medications such as dopamine agonists (DAs) have been implicated in the onset of DH episodes. Deep brain stimulation (DBS) is an important therapeutic option after the failure of conventional treatments such as DA therapy in patients with PD.

Mano et al. report the case of a patient with rigid-akinetic parkinsonism who developed DH syndrome after the initiation of DA treatment. Dopaminergic agonist treatment was required to stabilize motor dysfunction during a period of 5 years; yet, the patient experienced no improvements in DH during this time. Thus, they initiated DBS as an alternative therapy and gradually withdrew DA therapy. The patient recovered from long-term DH after the discontinuation of rotigotine treatment. Accordingly, this case highlights DA treatment as a possible cause of DH and the use of DBS to allow the discontinuation of DA treatment while preserving motor function in patients with PD<sup>5)</sup>.

## **Restless legs syndrome**

A study provides Class I evidence that for patients with moderate to severe restless legs syndrome RLS, rotigotine at optimal dose (1-3 mg/24 h) reduced PLM-associated nocturnal SBP elevations <sup>6)</sup>.

Idiopathic restless legs syndrome (RLS) can severely affect quality of life and disturb sleep, so that pharmacological treatment is necessary, especially for elderly patients. Treatment guidelines recommend initiation of therapy with dopamine agonists (pramipexole, ropinirole or the rotigotine transdermal patch, all approved in most countries) or  $\alpha$ -2- $\delta$  ligands (gabapentin enacarbil, approved

in the USA and Japan), depending on the country and availability.<sup>7)</sup>.

In a 13-month observational study, adults with moderate-to-severe RLS and augmentation were switched to rotigotine per the physician's independent decision. Assessments included Clinical Global Impression severity score (CGI-1); (primary), treatment regimen for switching (secondary), RLS-6, International RLS Study Group Rating Scale (IRLS), and augmentation severity rating scale (ASRS).

A total of 99 patients received rotigotine, of whom 46 completed observational period, and 43 were assessed for effectiveness. A total of 5 patients switched to rotigotine after a >1-day drug holiday, 23 switched overnight, 9 had an overlapping switch, and 6 received ongoing oral dopaminergics with rotigotine for  $\geq$ 28 days. Of the 99 patients, 57 took concomitant RLS medications (excluding switching medications) on at least 1 day. At the final visit, median change in CGI-1 (Hodges-Lehman estimate [95% CI]) was -2.0 (-2.5, -1.50); 37 of the 43 patients improved by  $\geq$ 1 CGI-1 category, and 16 of 43 were responders ( $\geq$ 50% improvement). RLS-6 and IRLS scores also improved. Patients had median ASRS of 0 at the final visit indicating "no worsening/occurrence of augmentation." ASRS item 1 showed a shift in mean time of symptom onset (24-h clock) from 12:38 (baseline) to 18:25 (final visit). Most common reasons for withdrawal of rotigotine were adverse events (26 patients) and lack of efficacy (14 patients).

Switching from oral therapies to rotigotine was effective in improving RLS symptoms in 37 of the 43 patients (from the original population of 99 patients) who remained in the study over 13 months<sup>8)</sup>.

1)

4)

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