Rotigotine in patients with restless legs syndrome and end-stage renal disease requiring hemodialysis

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Background: Restless legs syndrome (RLS) occurs in ~20% of end-stage renal disease (ESRD) patients and is linked to increased morbidity and mortality. RLS may be particularly bothersome when patients are immobile during dialysis. Periodic limb movements (PLMs) in sleep frequently occur in RLS. PLM Index (PLMI; PLMs/h in bed) is an objective severity measure.

Methods: Double-blind polysomnographic (PSG) study (RenaLys: NCT01537042) of rotigotine (RTG) in patients with RLS (International RLS Rating Scale [IRLS] ≥15; PLMI ≥15) and end-stage renal disease requiring hemodialysis. Patients randomized to optimal dose (1-3mg/24h) RTG/placebo (PBO). Polysomnographic assessment was performed at baseline (BL) and at the end of 2-weeks maintenance (EoM). Primary efficacy outcome: PLMI, assessed by ratio EoM/Baseline. Other outcomes (*p*-values exploratory): IRLS, Clinical Global Impression severity (CGI-1). Patients with evaluable Baseline and EoM data assessed for efficacy.

Results: Of 30 randomized patients (RTG: 20; PBO: 10), 25 (15;10) completed the study with evaluable data. Mean ± SD PLMI ratio at EoM: 0.7±0.4 for RTG; 1.3±0.7 for PBO (ANCOVA RTG/PBO ratio: 0.44 [95%CI: 0.22,0.88], p=0.0232). Mean ± SD change in PLMI score: -23.7±38.7 for RTG (BL:81.8±37.5); 10.3±21.0 for PBO (BL:85.3±67.3). Mean ± SD change in IRLS: -15.9±9.1 (BL:25.7±5.0) for RTG; -8.6±7.2 for PBO (BL:24.4±5.1); LS-mean treatment difference (RTG vs. PBO): -6.08 [95%CI: -12.18,0.02], p=0.0508. 10/15 RTG and 2/10 PBO patients were CGI-1 responders (≥50% improvement). LS-mean treatment difference for CGI-1: -0.81 [95%CI: -1.94,0.33], p=0.1534. Hemodialysis did not impact unconjugated RTG concentrations. Adverse events were typical of dopaminergic stimulation.

Conclusion: RTG improved PLMs and RLS symptoms in ESRD patients requiring hemodialysis.