First one-year real-life study to assess management of augmentation of restless legs syndrome by switching to rotigotine patch

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Background: Augmentation (worsening of RLS symptoms) can be major complication of long-term dopaminergic therapy. Clinical studies indicated low augmentation rates with RTG (only long-acting dopaminergic approved for RLS); transdermal delivery maintains stable plasma levels over 24h.

Objective: We sought to assess the effect of switching to rotigotine (RTG) patch on the severity of restless legs syndrome (RLS) in patients who experienced augmentation with prior oral dopaminergics.

Methods: Eligibility criteria for this 13-month non-interventional study (AURORA; NCT01386944) in German neurology centers included moderate-to-severe RLS and augmentation with oral dopaminergics (judged by a physician). Decision to switch to RTG was made independently by the physician according to routine practice. Primary outcome: Clinical Global Impression severity score (CGI-1; 7-point scale). Secondary outcome: treatment regimen for switch assessed to day 28. Other: RLS-6, International RLS Rating Scale (IRLS), Augmentation Severity Rating Scale (ASRS), adverse events (AEs). To evaluate RLS severity and augmentation over time in patients who tolerated RTG, study completers were assessed for effectiveness.

Results: 102 patients were enrolled, 99 (mean age±SD:64.2±11.1 years; female:68) received RTG. 46 patients completed ~13 month study; 3 were excluded from effectiveness analyses due to concomitant Parkinson's disease. Most common reasons for premature withdrawal were AEs (26 [mainly application site reactions]) and lack of effectiveness (14); 8 patients lost to follow-up. Among 43 study completers (~13 months), prior dopaminergics were: benserazide/l-dopa (19); pramipexole (19); ropinirole (7); carbidopa/l-dopa (2); l-dopa (1). At final visit, median change in CGI-1 (Hodges Lehman estimate [95%CI]) was -2.0 [-2.5,-1.5)(baseline mean±SD:5.3±0.7). 16/43 patients were CGI-1 responders (≥50% improvement). 5 patients switched to RTG after >1-day drug holiday, 23 switched overnight, 9 had overlapping switch, and 6 received ongoing oral dopaminergics with RTG on day 28. IRLS and RLS-6 decreased

with RTG (Table 1). At final visit, patients had median ASRS of 0=no worsening/occurrence of augmentation (mean±SD:1.2±2.7). AEs shown in Table 2.

Conclusion: In this first long-term study of augmentation management, switching to 24h therapy with RTG patch (continuous dopaminergic stimulation) was effective in improving RLS severity among severely affected patients who tolerated RTG and remained on this therapy for 13 months.

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Table 1: CGI-1, RLS-6 and IRLS scores

	Baseline (n=43)* mean±SD	Final visit (n=43) mean±SD	Change from baseline, mean±SD
CGI-1	5.3±0.7	3.4±1.1	-1.9±1.3
RLS-6 items			
Item 1: Satisfaction with sleep	6.9±2.3	3.5±2.6	-3.5±3.3
Item 2: Severity when falling asleep	6.4±2.8	2.6±2.7	-3.8±3.4
Item 3: Severity during night	5.8±2.8	2.2±2.7	-3.6±4.1
Item 4: Severity during day when at rest	5.4±2.5	1.7±2.1	-3.7±2.8
Item 5: Severity during day when active	2.3±2.5	0.9±1.6	-1.4±2.2
Item 6: Daytime sleepiness/tiredness	5.9±2.6	3.2±2.8	-2.7±2.9
IRLS	29.2±5.4	16.6±9.7	-12.7±7.5
*No washout of prior dopaminergic medications was performed.			

Table 2: Adverse events

Preferred term	Patients (n=99)
Adverse events reported by ≥5 patients	
Application site reaction*	33
Nausea	13
Fatigue	9
Depression	7
Headache	6
Serious AEs	9
*MedDRA high-level term “application and instillation site reactions”; data are number of patients reporting at least 1 AE.	