

What is the minimal clinical important improvement (MCIC) in the International Restless Legs Syndrome Rating Scale [IRLS] severity scale under dopaminergic treatment in clinical studies?

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Objective: Determine the minimal clinically important change (MCIC) in IRLS total score in patients with moderate to severe restless legs syndrome (RLS).

Background: The 6-month randomised, double-blind, placebo-controlled European study (SP790; NCT00136045) established the efficacy of rotigotine vs. placebo using the IRLS total score (primary endpoint) and CGI global change score (secondary endpoint). The mean (SD) change from baseline in rotigotine IRLS total score was: 1 mg, -13.2 (10.0); 2 mg, -15.6 (9.5); 3 mg, -16.1 (10.9). The mean (SD) change from baseline in IRLS total score for placebo (n=101) was -8.0 (9.7).

Design/Methods: Patients diagnosed with moderate to severe idiopathic RLS were randomised to receive rotigotine or placebo. Mean changes (SD) from baseline to end of maintenance (EoM) in IRLS total score were calculated for each CGI score. Pearson's correlation coefficients evaluated the relationship between CGI and changes in the IRLS total scores at EoM. An anchor-based approach and receiver operating characteristic (ROC) curves determined the MCIC for the IRLS total score based on CGI scores using the full analysis set (without LOCF).

Results: 307 randomised patients receiving rotigotine with baseline and EoM IRLS and CGI scores were included in the analysis. The mean (SD) change from baseline to EoM in IRLS total score in the CGI categories of minimally worse, no change, minimally improved, much improved, or very much improved was -4.2 (7.0), -3.8 (5.4), -8.2 (6.7), -12.4 (7.2), and -22.8 (7.2), respectively; a 29.6% change in mean IRLS total score from baseline to EoM was consistent with minimal improvement. IRLS total scores generally improved from baseline with improvements in the CGI ($r = 0.67$). The MCIC ROC cut-off for IRLS total scores was -6 points (sensitivity = 0.69; specificity = 0.65).

Conclusion: In patients with moderate to severe RLS, a 6-point reduction in the IRLS total score is felt to be clinically meaningful.
