Poor Patient Benefit in Clinical Trials in Restless Legs Syndrome

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Almost all clinical trials with dopaminergic drugs in restless legs syndrome (RLS) have been shown to be successful according to standard statistical criteria (denoting success as $p<0.05$). The majority of these trials have demonstrated that active short-term treatment is clinically more effective than placebo in improving RLS symptoms—symptom severity, sleep dissatisfaction, impairment of quality of life—compared to baseline. However, in general, at the end of most RLS trials the study patients still have “moderate” RLS according to the International RLS (IRLS) severity rating scale. If we look at the distribution of individual benefit of the study patients, more than one-third of those treated with active therapies are not “responders” (defined as a 50% improvement on the severity scale between the start and the end of treatment). In long-term trials, patients may experience loss of efficacy (tolerance or relapse) or augmentation.

In the current RLS literature, there is a lack of awareness of the virulent problem of patients who do not benefit at all, or only very slightly from dopaminergic therapies in clinical trials. Besides augmentation, long-term complications such as tolerance or loss of efficacy (relapse) are not considered in trials that run for more than 6 months.

In our presentation, we propose a model for defining poor treatment outcome, both after commencing a new treatment and during long-term treatment. This model is based on changes in the IRLS severity scale.