P-641 - THE IMPORTANCE OF RIGOR IN POST-BASELINE ASSESSMENTS IN CNS CLINICAL TRIALS

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Introduction: Inappropriate subjects may be enrolled in a study when enrollment pressures cause inflated baseline severity scores. An increasing number of studies now include methods such as blinded independent centralized ratings (CR) to ensure that appropriate subjects are entered into the trial. Post-baseline factors such as functional unblinding, expectation bias and rater drift can also affect outcomes.
Objectives: Independent raters, blind to study visit, can minimize functional unblinding and expectation bias. Continuous calibration of CR can minimize rater drift.
Aims: To examine studies with both site ratings (SR) and CR to determine how critical post-baseline blinding and continuous calibration are.
Methods: A trial of acute schizophrenia used CR for the PANSS and SR for the BPRS on the same subjects.
A Parkinson's psychosis study used CR in the US and SR ex-US to assess subjects using the SAPS.
A GAD trial used CR of subjects enrolled by SRs' SIGH-A evaluations.
Results: In the schizophrenia trial, CR separated the active comparator and one of two test arms. SR separated the active comparator but neither test arm.
In the Parkinson's psychosis study, pimavanserin showed greater separation with CR than SR.
In the GAD trial, CR had lower placebo response than SR, independent of subject selection.
Conclusions: Data from several studies support the continued importance of rater blinding and independence, post subject selection. Results suggest that precision of ratings beyond baseline can increase the sensitivity of findings in a clinical trial, decrease placebo response rates and potentially eliminate Type II errors.

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