S15-03

HOW TO INTERPRET EFFICACY AND SAFETY DATA OF ANTIDEPRESSIVE DRUGS AND PLACEBO RESPONSE RATES?

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During the process of drug development, the sponsoring pharmaceutical manufacturers conduct numerous clinical trials to demonstrate the therapeutic efficacy and safety of new antidepressive agents. These trials are required to provide 'substantial evidence of effectiveness' in accordance to terms and conditions codified by law. Accordingly, the design and conduct of clinical studies of new antidepressants are strongly impacted by the need to comply with scientific standards as well as by regulatory requirements for approval. Regulatory requirements are typically published in standard 'Guidance documents', but in practice the 'one size fits all' approach has room for interpretation for specific indications and clinical trials. Detailed statistical criteria applied for the regulatory evaluation of individual drug trials are typically not available in the standard medical literature, but are accessable via the FDA's Summary Basis of Approval Documents (SBAs). This presentation will examine SBA materials and published scientific literature to gain insight into factors that were considered for the establishment of substantial evidence of effectiveness from a statistical perspective. Specifically, the presentation will investigate critical elements considered for the evaluation of results of controlled trials of new antidepressive agents. Such elements include the measurement of relevant clinical outcomes, definition of endpoints, effect sizes, multiple inferences, and principal trial design choices such as placebo- or active-controlled trials. In addition, the presentation will review the contribution of placebo response to the frequent negative results in antidepressant clinical trials, and discusses the implicatons of this knowledge of the placebo response for future trials and clinical practice.

https://doi.org/10.1016/S0924-9338(09)70312-8 Published online by Cambridge University Press