Personalising efficacy scales based on predominant symptoms at baseline

Submitter Danièle Laverdure-Dupont

Affiliation H. Lundbeck A/S

SUBMISSION DETAILS

What is the Methodological Question Being Addressed? Can clinical outcome assessments be adapted to capture effects on the most severe symptoms for the individual patient and demonstrate a better sensitivity to detect a drug effect in clinical trials?

Introduction The symptom presentation of patients with neurological or psychiatric disorders is heterogeneous, and to capture the complex manifestation of the conditions, clinical scales typically includes all aspects of the concept (symptom or impact) important to patients (content validity). However, since not all symptoms are expressed in all patients, the use of these assessment tools to support clinical trial endpoints can lead to decreased sensitivity to detect drug-induced changes (bias toward the null). We present here a quantitative approach to individualise broad symptom scales to support efficacy evaluations focused on the predominant symptoms at baseline for each patient. The concept was tested on data obtained with the Montgomery-Asberg Depression Rating Scale (MADRS) in clinical trials with vortioxetine. The MADRS assesses the severity of depressive symptoms and includes 10 items, each rated on a scale ranging from 0-6.

Methods For a symptom scale which includes several items each associated with a discrete symptom (such as the MADRS), the predominance of a symptom at baseline can be represented by indexing the individual item score at baseline with the total score at baseline for each patient (predominance index for symptom X = item score at baseline/total score at baseline). The predominance index for each item is used to weight the change at end of treatment for this specific item, leading to an increased contribution of the changes observed on the most severe symptoms for an individual, to the overall change from baseline in total score.

Results Datasets of 5 vortioxetine trials were used, and the changes from baseline in MADRS total score were recalculated after each item change were weighted with its predominance index. For all active treatments in all trials tested, the application of the predominance index increased the mean group difference to placebo in the change from baseline in MADRS total score, with improvements ranging from 0.06 to 1.47 normalised points on the weighted scale. The proportionality between the treatment arms was conserved, and no important impact on the normality of the distribution was observed. However, an increase in variance was noted on weighted outcomes, leading to similar p-values for the standard and weighted scales. The weighted MADRS was also used to recalculate the proportion of responders (defined as those who display an improvement of 50% or greater relative to baseline) in these studies; the results generally show a higher proportion of responders to active treatment with the weighted MADRS, which translated into lower p-values for responder analysis endpoint.

Conclusion The integration of the predominance of symptoms at baseline may represent an objective method to focus efficacy assessment on symptoms that are important to individual patient. This quantitative, data-driven approach could be applied to widely accepted symptom scales, so that outcome measures become tailored to each patient, while being maintained in a widely recognized, unified conceptual framework.

Co-Authors

* Presenting Author

First Name	Last Name	Affiliation
Danièle *	Laverdure-Dupont *	H. Lundbeck A/S
Mogens	Nielsen	H. Lundbeck A/S
Anna-Karin	Berger	H. Lundbeck A/S

Keywords

Keywords
predominant symptoms
patient-centricity
clinical scales

Guidelines I have read and understand the Poster Guidelines

Disclosures if applicable The authors report no conflicts of interest for this work.

Related tables <blank>