Regional Baseline Symptom Patterns in Major Depressive Disorder Trials

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RESULTS

- Mean scores by item and region:
  - Mean total scores and individual item scores for 9 of the 10 items differed significantly by region (item 7, Lassitude was the exception); although statistically significant, the effect sizes (eta squared) were small for the total score and individual items, with the exception of item 10 (Suicidal Thoughts). Post hoc regional comparisons (Tukey-Kramer) for these significant but small effect size findings (items 1, 2, 3, 4, 5, 6, 8, 9, and Total) were scattered; for individual items, no clear pattern by region emerged, and the numeric differences in means were less than 1 point for individual items and 3 points for total score (see Figure 1).

- Item 10, Suicidal Thoughts, showed a large effect size of region (p<0.17), as shown by Tukey-Kramer post hoc testing. Eastern Europe scores (mean=1.96) were significantly higher, and Western Europe scores significantly lower (mean=0.04) than US and Asia scores (means=0.89 and 1.0, respectively), which did not significantly differ from each other. Graphic depictions of the total and 10 individual mean scores by region are shown in Figure 1.

- Collapsed across region, the proportion of baseline item scores of 0 or 1 was low (approximately 5% or less) for all items except Reduced Appetite (47.3%) and Suicidal Thoughts (71.9%) (see Table 1).

- When examined by region, statistically significant differences in 0-1 scoring were found for items 4 (Reduced Sleep), 5 (Reduced Appetite), 6 (Concentration Difficulties), 7 (Lassitude), 9 (Pessimistic Thoughts), and 10 (Suicidal Thoughts) [χ2(5)] 162.2, 50.7, 15.3, 11.1, 33.0, 407.0, respectively, p's from .01 to .001. The effect sizes and numerical differences by region were small for all but items 10 (Suicidal Thoughts) and 5 (Reduced Appetite). For Suicidal Thoughts, 100% of scores in Asia and Western Europe were 0 or 1; in the US the number was 71%, and in Eastern Europe, in marked contrast to other regions, the number was 21.3% (see Figure 2). For Reduced Appetite, 51.5% of US scores were 0 or 1, in contrast to Asia (44%), Eastern Europe (31%), and Western Europe (33%) (see Figure 3).

FIGURE 1: Mean Scores by Region

FIGURE 2: MADRS Item 10: Suicidal Thoughts

FIGURE 3: MADRS Item 5: Reduced Appetite

CONCLUSIONS

- For most items of the MADRS, regional differences were small, suggesting that patients with similar levels of symptom expression are entering these multinational trials
- Overall, symptom ratings of 0 or 1 at baseline were infrequent, adding supporting to the scale’s utility in allowing demonstration of drug-related improvement.
- Reduced Appetite and Suicidal Thoughts were the items with the largest regional differences and were associated with the highest proportions of low endorsement.
- Of interest, these two items were the least frequently endorsed of all MADRS items almost 20 years ago in a US sample of hospitalized depressed patients.
- As actively suicidal patients are disallowed from most MDD protocols (and from all of the protocols included in this analysis), skewed scoring toward the less severe end is expected.
- Suicidal Thoughts endorsement was higher in Eastern Europe, suggesting greater severity and some potential for trial improvement on this item.
- Lower endorsement of Reduced Appetite may reflect the enrollment of less melancholic patients, the symptom was endorsed at lower levels in the US than in other regions.

REFERENCES


DISCLOSURES

Dr. Busner is a full-time employee of Bracket. Dr. Montgomery is a consultant, speaker and/or advisory board member to multiple pharmaceutical companies (all information available upon request).