Introduction

In clinical practice and in the literature differing subtypes of bipolar disorder have been characterized. Greenwood et al (2013) identified clinical phenotypes associated with elated (elevated) and irritable subtypes. Others (e.g., Sato et al, 2002) have identified similar phenomenological subtypes and suggested that there are differences in treatment response.

This study (NCT01567527) used data from a randomized, double-blind, placebo-controlled trial to assess the time to recurrence of any mood episode in subjects with bipolar I disorder who have maintained stability on aripiprazole IM depot for at least 8 weeks. It was required at study entry that the patients were currently experiencing a manic episode with a YMRS score of ≥ 20. Because in this study the diagnostic criteria was for bipolar I disorder and had no specific indication of which DSMVTR criteria were used and we were not able to determine irritable versus elevated subtype.

We used the proxy of specific YMRS items to make the distinction. In clinical practice and in the literature differing subtypes of bipolar disorder have been characterized. Greenwood et al (2013) identified clinical phenotypes associated with elated (elevated) and irritable subtypes. Others (e.g., Sato et al, 2002) have identified similar phenomenological subtypes and suggested that there are differences in treatment response.

Subjects included in the analysis were those that completed a screening visit and continued to the week 6 visit. All subjects in this phase of the trial were on oral aripiprazole and being cross titrated from their previous oral antipsychotic following a manic episode. The criteria for subgroup membership were the following:

- Irritable Subtype: Irritability item score greater than 4 and Elevated Mood item score less than 3 at screening.
- Elevated Mood Subtype: Elevated Mood item score greater than 2 and Irritability item score less than 4 at screening.
- No subtype: All other YMRS item presentations.

These criteria are supported by factor analytic studies of the YMRS identifying subtypes and different factor structures (e.g., Hanwella & de Silva, 2011). The criteria are also supported by phenomenological subtypes identified in the literature (Sato et al., 2002). There is no precedent for the severity score cutoffs however, and this is based on the logic of the scale and severity score anchors.

Table 1: YMRS item and total score effect sizes and mean change from screening to week 6 across subtypes.

- Elevation item score: µ∆ = 15.64, p = 0.003
- Irritability item score: µ∆ = 14.63, p = 0.000
- Speech (rate and amount) item: µ∆ = 2.09, p = 0.046
- Disruptive-Aggressive Behavior item: µ∆ = 1.59, p = 0.019
- Irritability item score: µ∆ = 15.88, p = 0.003
- Total score: µ∆ = 3.30, p = 0.000

No subtype: All other YMRS item presentations.

Results

Using the design criteria we found that the elevated mood subtype at screening included 100 of 367 subjects (27% of the sample). Irritable mood subtype at screening included 40 subjects (11% of sample). There were 227 subjects (62%) that belonged to no subtype according to the analysis criteria.

There was a not a significant difference between YMRS total score rates of improvement (decrease in YMRS score) between these subtypes and with respect to belonging to no subtype.

- Irritable subtype (n=40): µ∆ to week 6 = 14.63
- Elevated subtype (n=100): µ∆ to week 6 = 15.64
- No subtype (n=227): µ∆ to week 6 = 15.88

A by-item analysis for each subtype (see Table 1) was conducted and in the irritable subtype there were very notable changes on the irritability item (µ∆ to week 6 = 3.30), the Speech (rate and amount) item (µ∆ to week 6 = 2.35), the Content item (µ∆ to week 6 = 2.18) as well as the Disruptive-Aggressive Behavior item (µ∆ to week 6 = 2.30). The elevated mood subtype differences were more pronounced around the Elevated Mood item (µ∆ to week 6 = 2.09) and Speech (rate and amount) item (µ∆ to week 6 = 3.04). It is notable that the Elevated Mood item mean change from screening for the irritable subtype group was just .60 and the no subtype group was 1.44.

Conclusion

In the course of the trial we identified the presence of differing subtypes of bipolar disorder. We found that there were similar mean changes from screening to the week 6 visit as well as comparable effect sizes (see Table 1 above) in response to oral aripiprazole: this means that despite belonging to a given subtype, rates of response were similar. Clinically, this is important in deciding which medication may be appropriate for a given symptom presentation. The findings may have especially important implications for the treatment of the irritable subtype as these individuals are often considered more at risk and present different challenges in treatment.

References