THE JOURNAL OF
CLINICAL PSYCHIATRY
THE OFFICIAL JOURNAL OF THE AMERICAN SOCIETY OF CLINICAL PSYCHOPHARMACOLOGY

Supplementary Material

Article Title: Generalizability of the Results of Efficacy Trials in First-Episode Schizophrenia: Comparing Outcome and Study Discontinuation of Groups of Participants in the Optimization of Treatment and Management of Schizophrenia in Europe (OPTiMiSE) Trial

Author(s): Lyliana G. Nasib, MSc; Inge Winter-van Rossum, PhD; Nicolaas P. A. Zuithoff, PhD; Zimbo S. R. M. Boudewijns, PhD; Stefan Leucht, MD, PhD; and René S. Kahn, MD, PhD

DOI Number: https://doi.org/10.4088/JCP.22m14531

List of Supplementary Material for the article

1. **Appendix 1** Sensitivity analyses premature study discontinuation
2. **Appendix 2** Baseline comparisons of individual comorbidity groups
3. **Appendix 3** Overview of missing data of baseline characteristics and symptom severity
4. **Appendix 4** Serious adverse events (SAEs)

Disclaimer

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary Appendix 1: Sensitivity analyses premature study discontinuation

A sensitivity analyses was conducted on the premature study discontinuation outcome in the study sample including patients who met remission criteria at baseline. The sample contained 404 patients; 288 non-comorbid patients and 116 comorbid patients; the latter group was further divided in the following three individual comorbidity groups; 47 patients with suicidality only, 59 patients with SUD only and 10 patients with suicidality and SUD. In total, 66 patients (17%) did not complete the four week amisulpride treatment period; 46 of the non-comorbid patients (16%) and 20 comorbid patients (17%); 5 patients (11%) with suicidality only, 11 patients with SUD only (17%) and 4 patients (40%) with suicidality and SUD. No significant differences in the likelihood to discontinue the study prematurely were found when comparing comorbid patients versus non-comorbid patients at end of treatment (OR 1.157, 95% CI 0.626 – 2.137, p=0.64). When comparing the individual comorbidity groups with the non-comorbid group at end of treatment, no significant differences in the likelihood to discontinue the study prematurely were found for patients with suicidality only (OR 0.647, 95% CI 0.230 – 1.815, p=0.41) nor for patients with SUD only (OR 1.277, 95% CI 0.585 – 2.789, p=0.54), nor for patients with suicidality and SUD (OR 4.639, 95% CI 1.149 – 18.725, p=0.03, significant effect is lost after Bonferroni correction for multiple testing (3 tests; p<0.017)) when compared to non-comorbid patients.

Supplementary Appendix 2: Baseline comparisons of individual comorbidity groups

In the individual comorbidity analyses, when comparing suicidality only patients with non-comorbid patients, suicidality only patients had significantly more severe depressive symptoms (8.7 versus 4.1; p<0.001), more severe psychosis symptoms (as measured with PANSS total)(86.9 versus 79.2; p=0.007), more severe PANSS positive symptoms (22.2 versus 20.4; p=0.035), more severe PANSS general symptoms (43.9 versus 38.9; p=0.001). Significant differences were found when comparing SUD only patients with non-comorbid patients; SUD patients were younger (24.0 versus 26.4; p=0.001) and were more likely to be male (90 versus 66%; p<0.001). When comparing the suicidality and SUD patients with non-comorbid patients significant differences were found as well; suicidality and SUD patients had more severe depressive symptoms (8.1 versus 4.1; p=0.006) and more impaired social functioning (37.7 versus 49.1; p=0.02).

Supplementary Appendix 3 – Overview of missing data of baseline characteristics and symptom severity

Missing data of continuous variables in Table 1: Comparisons of baseline characteristics between comorbid and non-comorbid patient groups

		Comorbid patients			
			Subgroups distinguished by comorbidity		
Variable	Non-comorbid	Suicidality and/or SUD	Suicidality only	Substance use only	Suicidality and substance use
Education	247/254	104/106	45/45	51/52	8/9
PSP	249/254	104/106	43/45	52/52	10/9

outcomes

Missing outcome data Table 3: Symptom severity outcomes at end of treatment

		Comorbid patients			
			Subgroups distinguished by comorbidity		
Variable	Non-comorbid (n = 212)	Suicidality and/or SUD (n = 88)	Suicidality only (n = 41)	Substance use only (n = 42)	Suicidality and substance use (n = 5)
PANSS	212/212	88/88	41/41	42/42	5/5
CDS	205/212	85/88	38/41	42/42	5/5
PSP	205/212	82/88	36/41	41/42	5/5
CGI severity and improvement	209/212	86/88	40/41	41/42	5/5

Supplementary Appendix 4: Serious adverse events (SAEs)

In total, for 26 patients (7%) adverse events meeting one of the SAE criteria were reported during the four week amisulpride treatment period. The majority of the SAEs occurred in the non-comorbid group (n=22; 8%); 14 patients were hospitalized due to psychotic exacerbation, two patients were hospitalized due to suicidal ideations, one patient committed suicide, one patient was hospitalized for social reasons, one patient was hospitalized due to side-effects, one patient was hospitalized due to acute dystonia, one patient attempted suicide and one patient was diagnosed with cerebellar glioma. The remaining SAEs (n=4; 4%) occurred in the comorbidity groups; one hospitalization in the suicidality only group was due to psychotic exacerbation, two hospitalizations in the SUD only group were due to psychotic exacerbation and one severe epileptic seizure occurred in the suicidality and SUD group.