

Substance abuse does not compromise improvements in Spanish patients with schizophrenia treated with risperidone long-acting injection

JM Olivares¹, A Lam², K Akhras³, A Jacobs⁴ on behalf of the e-STAR study group

¹Servicio de Psiquiatría, Hospital Meixoeiro Complejo, Hospitalario Universitario de Vigo, Spain; ²Janssen-Ortho Inc., Toronto, Canada; ³Johnson & Johnson Pharmaceutical Services, Raritan, NJ, USA; ⁴Johnson & Johnson Pharmaceutical Services, Beerse, Belgium

BACKGROUND

- Up to half of schizophrenia patients may exhibit comorbid drug or alcohol abuse, with younger age, male gender and earlier onset of schizophrenia being associated with a greater risk of substance abuse in these patients.¹
- Comorbid substance abuse is an obstacle to the effective management of schizophrenia because it is associated with poorer symptomatic outcomes and medication adherence.^{1,2}
- Strategies to minimize these poorer outcomes are needed to improve the prognosis for these patients.

OBJECTIVES

- To report the prevalence of substance abuse in schizophrenia patients enrolled in the electronic Schizophrenia Treatment Adherence Registry (e-STAR) in Spain.
- To determine if there are differences in long-term outcomes in patients with schizophrenia with and without a history of substance abuse (SA) treated with RLAI.

e-STAR

- e-STAR is an international, long-term, prospective, observational study to establish a large database about the outcome of treatment in patients with schizophrenia who commence treatment with RLAI during the course of their routine clinical management.
- e-STAR uses secure web-based data collection technology^{3,4} to allow a broad inclusion of centres and participants in both in- and outpatient settings under naturalistic conditions that reflect normal clinical practice.
- Data accrual is ongoing and results are being reported as they accrue.⁵⁻¹⁰

PATIENTS AND METHODS

- In the Spanish e-STAR study, patients with schizophrenia who start a new antipsychotic drug during their routine clinical management are eligible for enrolment in e-STAR. In order to reflect real-life treatment conditions, no formalised diagnostic procedures, randomisation, treatment decisions, or clinical assessments requiring extensive training, were specified in the protocol.
- For each patient, demographics, illness characteristics and reasons for initiating the new antipsychotic drug are recorded at baseline. Treatment and hospitalisation history are collected retrospectively for the 24 month period immediately preceding the start of the new antipsychotic (baseline) and prospectively at 3 monthly intervals for 24 months after baseline.
- Clinical effectiveness is evaluated prospectively as changes from baseline in Clinical Global Impression of Illness Severity (CGI-S), and Global Assessment of Functioning (GAF) scale scores. Other prospective outcome measures include the use of concomitant non-antipsychotic medication, and patients and investigator satisfaction with treatment.
- Information on all adverse events (AEs) and serious AEs (SAEs) were recorded.
- The present analysis focuses on the relative changes in outcomes in patients with schizophrenia with and without reported substance abuse at baseline, enrolled in e-STAR in Spain who initiated treatment with RLAI and completed 24 months of follow-up.

RESULTS

Patient population

- This analysis included a total of 843 patients enrolled in e-STAR in Spain, who initiated treatment with RLAI, and had 24 months of follow-up data.
- Of these, 334 (39.6%) had a history of substance abuse including alcohol, prescription medication and recreational drugs; the remainder (509, 60.4%) had no such history.
- Gender distribution, age, and years since diagnosis were the only demographics features that significantly differed between the 'substance abuse' and 'no substance abuse' cohorts at baseline (Table 1).

Table 1. Baseline patient characteristics

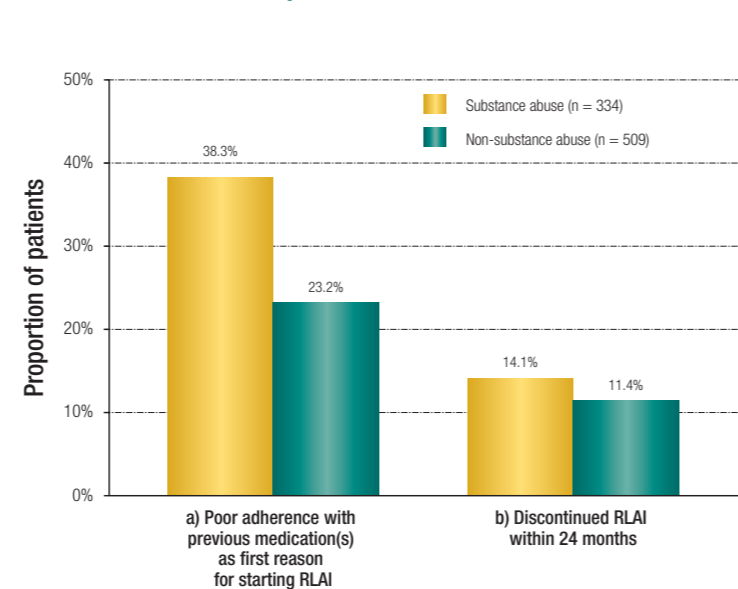
Parameter	Substance abuse	No substance abuse
Number of patients (%)	334 (39.6)	509 (60.4)
Male gender; n (%)	278 (83.2)	255 (50.1)*
Age, years; mean (SD)	35.6 (9.9)	40.8 (11.5)*
Diagnosis, n (%)		
• Schizophrenia	287 (85.9)	439 (86.2)
• Schizoaffective disorder	47 (14.1)	70 (13.8)
Years since diagnosis; mean (SD)	11.7 (8.7)	13.9 (10.3)*

*p<0.0001

Adherence and patient disposition

- At baseline the proportion of patients in whom poor adherence with previous medication(s) was the primary reason for initiating treatment with RLAI was higher in the substance abuse group (38.3%) than in the non-substance abuse group (23.2%) (Figure 1a).
- At 24 months, based on the Kaplan-Meier estimate the probability of still being maintained on RLAI treatment was 85.9% in the substance abuse group and 88.6% in the non-substance abuse group (Figure 1b).

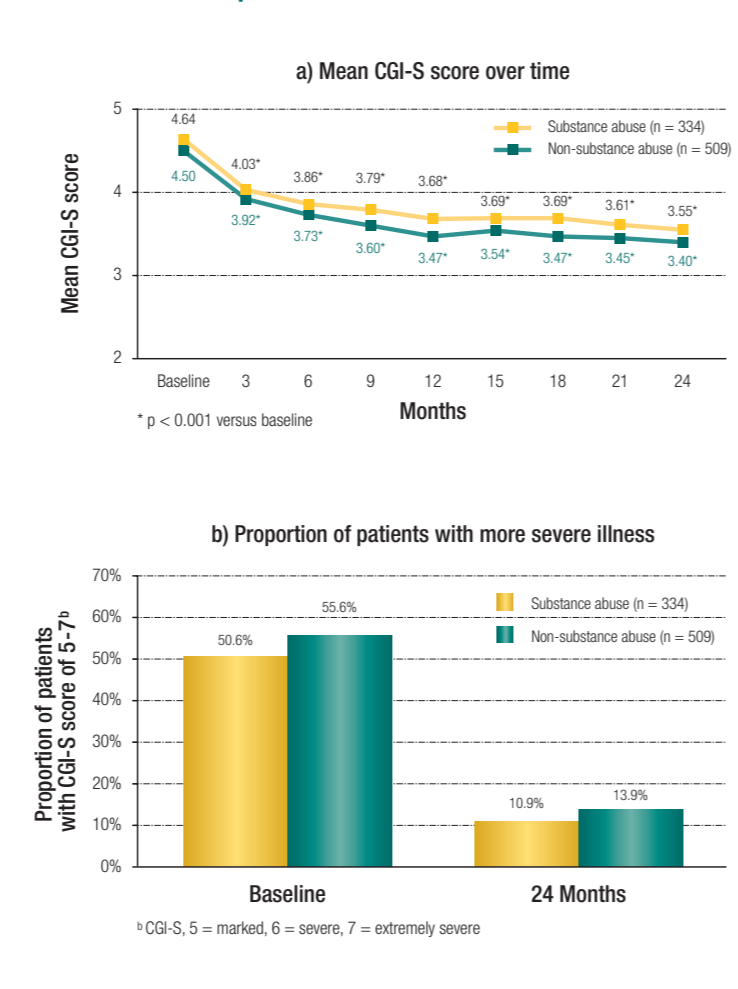
Figure 1. Difference in a) adherence history and b) patient disposition at 24 months between substance abuse and non-substance abuse patients treated with RLAI



Improvement in illness severity

- At baseline the mean CGI-S score in the substance abuse and non-substance abuse groups were similar (4.64 and 4.50, respectively) indicating that, on average, patients were experiencing moderate-to-marked illness severity before the start of RLAI (Figure 2a).
- At 24 months, illness severity was reduced significantly in both the substance abuse and non-substance abuse groups (CGI-S score 3.55 in the substance abuse group and 3.40 in the non-substance abuse group; both p<0.001 vs. baseline) indicating a mean reduction to mild-to-moderate severity in both groups following the initiation of RLAI. Significant improvements were apparent by month 3 in both the substance abuse and non-substance abuse group (4.03 and 3.92, respectively, p<0.001 vs. baseline) and continued to improve to 24 months (Figure 2a).
- The improvement in CGI-S score between baseline and 24 months was similar in both groups (p=0.2671) (Figure 2a).
- Moreover, the proportion of patients with a CGI-S score of 5-7 (marked, severe, or extremely severe illness) was reduced by over 70% between baseline and 24 months in both the substance abuse (50.6% vs. 10.9%, respectively) and non-substance abuse (55.6% vs. 13.9%, respectively) groups (Figure 2b).

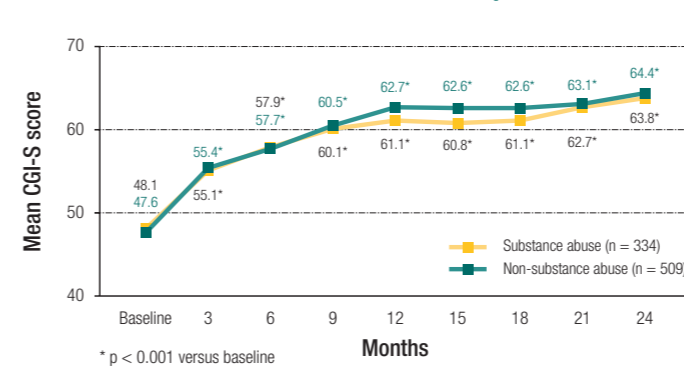
Figure 2. Changes in illness severity (measured by CGI-S) from baseline to 24 months in substance abuse and non-substance abuse patients treated with RLAI



Improvement in patient functioning

- Mean GAF scale scores at baseline indicated a moderate level of functional impairment in both the substance abuse (47.6) and non-substance abuse (48.1) patients (Figure 3).
- At 24 months after the start of RLAI, patient functioning improved significantly in both groups (63.8 and 64.4 in the substance abuse and non-substance abuse groups, respectively, both p<0.001 vs. baseline). Significant improvements in GAF scores were apparent by month 3 in both the substance abuse and non-substance abuse group (55.1 and 55.1, respectively, p<0.001 vs. baseline) indicating that improvements in global functioning occurred early and continued to improve long-term (up to 24 months) (Figure 3).
- The improvement in GAF score between baseline and 24 months was similar in both groups (p=0.5422).

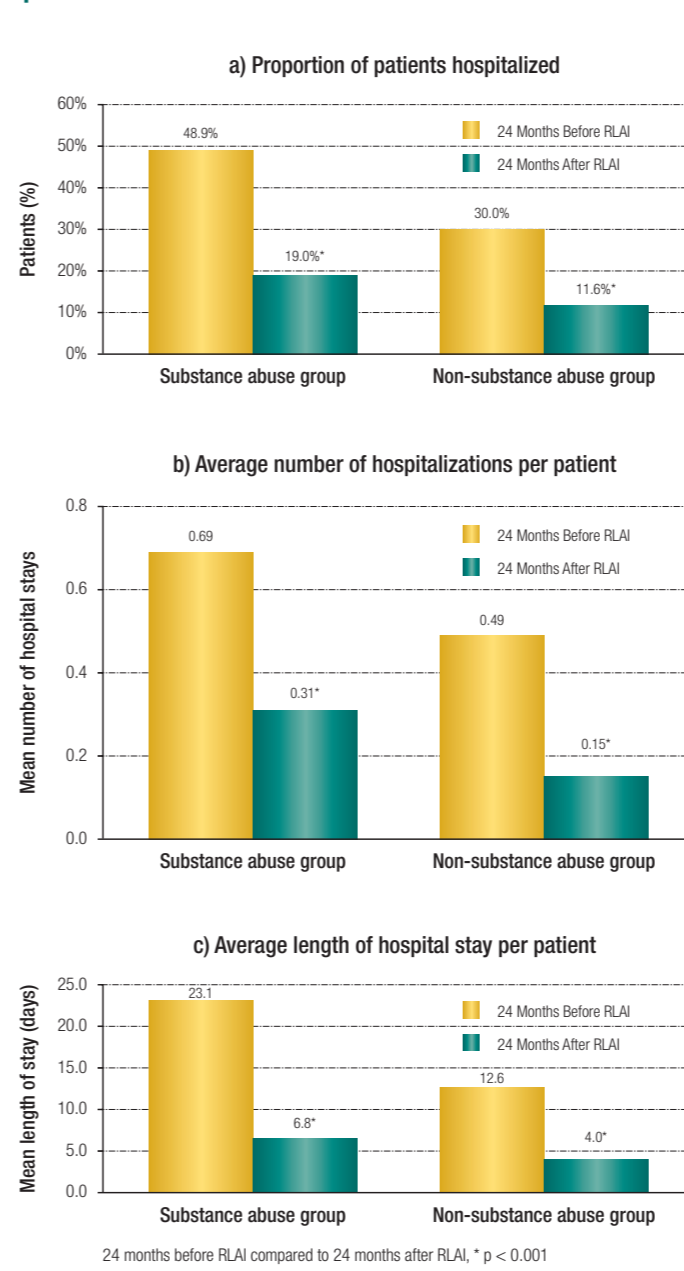
Figure 3. Changes in patient functioning (measured by GAF) from baseline to 24 months after initiation of RLAI in substance abuse and non-substance abuse patients



Reduction in hospitalization

- During the 24 months before the start of RLAI, a significantly higher proportion of substance abuse compared to non-substance abuse group had been hospitalized at least once (48.9% and 30.0%, p<0.0001, respectively).
- Compared with the 24 month retrospective period, the proportion of patients who had been hospitalized during the 24 months after the start of RLAI was significantly lower in both the substance abuse (48.9 vs. 19.0%, p<0.001) and non-substance abuse (30.0% vs. 11.6%, p<0.001) group (Figure 4a).
- Compared with the 24 months before the start of RLAI, the mean number of hospital stays per patient was significantly lower during the 24 months after the start of RLAI in both the substance abuse (0.69 to 0.31; p<0.001, 55% reduction) and the non-substance abuse (0.49 to 0.15; p<0.001, 67% reduction) group (Figure 4b).
- The mean length of stay in hospital per patient decreased by approximately 70-80% between the 24 months before and after the start of RLAI in both the substance abuse (23.1 vs. 6.8 days, p<0.0001, 71% reduction) and the non-substance abuse (12.6 vs. 4.0 days, p<0.001, 68% reduction) group (Figure 4c).

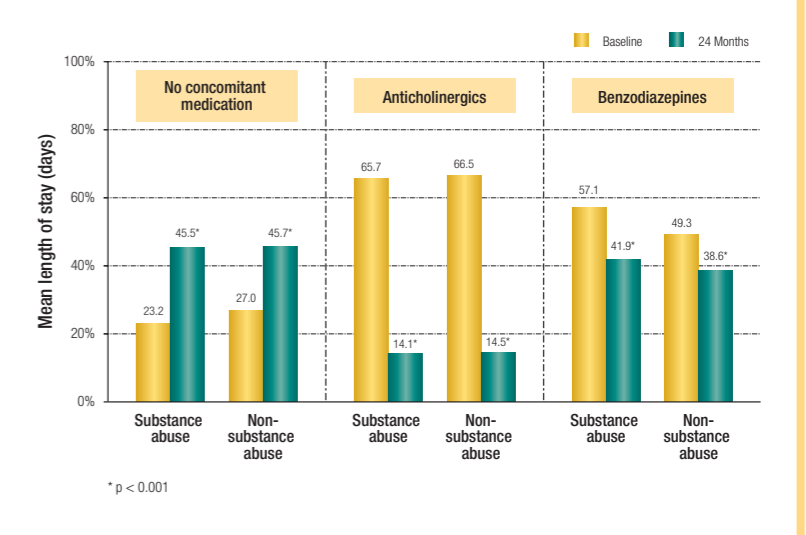
Figure 4. Change in a) the proportion of patients hospitalized, b) the average number of hospitalizations, and c) the average length of hospital stay per patient between the 24 month period before and after the initiation of RLAI



Changes in the use of concomitant medication

- At baseline, the majority of patients in both the substance abuse and non-substance abuse group were taking non-antipsychotic concomitant medication (77% and 73%, respectively) that included anticholinergics, antidepressants, mood stabilisers, benzodiazepines and somatic medications.
- At 24 months after the start of RLAI, the proportion of patients taking these concomitant medications reduced to 54% (p<0.001 vs. baseline) in each group (Figure 5).
- The most significant reductions from baseline were seen for benzodiazepines and anticholinergics in both the substance abuse and non-substance abuse groups (Figure 5).

Figure 5. Changes between baseline and 24 months in the proportion of substance abuse and non-substance abuse patients treated with RLAI and taking concomitant non-antipsychotic medication



Safety and tolerability

- Over the 24-month duration of the study, the number of reported adverse events was 70 (21.0%) and 105 (20.6%) in the substance abuse and non-substance abuse group, respectively.
- A total of 2 (0.6%) and 5 (1.0%) serious adverse events were reported in the substance abuse and non-substance abuse group, respectively.
- There were no unexpected tolerability or safety issues.

Limitations

- The analysis only included patients who completed 24 months of follow-up and who had a baseline and 24-month value for the effectiveness measures.
- The naturalistic design limits the ability to establish causal relationships between RLAI and improvements in effectiveness measures.

CONCLUSIONS

- Two in every five patients enrolled in e-STAR in Spain had a history of substance abuse, potentially compromising the effective management of their schizophrenia.
- Significant improvements in illness severity and functional ability as well as significant reductions in hospitalization were seen in both patients with and without a history of substance abuse.
- Symptomatic and functional improvements were accompanied by significant reductions in the use of non-antipsychotic concomitant medication in both groups, indicating that these improvements following treatment with RLAI were not a manifestation of differences in the use of other symptomatic medications.
- Although a history of substance abuse may predict poorer outcomes in schizophrenia^{1,2}, substance abuse patients treated with RLAI are similarly compliant and improve to a level comparable with non-substance abuse patients.

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DATA SOURCE

- e-STAR Statistical comparison: Consta patients with 24-month follow-up: substance abuse at baseline vs. no substance abuse at baseline. Country Report: Spain. Report date: 10 March 2009.
- e-STAR 24-month follow-up analysis. Country Report: Spain: Consta - Substance Abusers. Report date: 10 March 2009.
- e-STAR 24-month follow-up analysis. Country Report: Spain: Consta - No substance abuse. Report date: 10 March 2009.