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A Post-Authorisation Safety Survey Evaluating Risperidone Long-Acting Injectable in Romania

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Abstract

Background: The main treatment objectives for schizophrenia, a chronic disease, include clinical response and symptom resolution, relapse prevention, and recovery.

Objectives: The primary aim of this prospective survey is to confirm the safety of Risperidone Long-Acting Injectable (RLAI) under marketed conditions. Secondary objectives are to investigate the reasons for the initiation of treatment, effectiveness, and quality of life of patients on RLAI, alongside with compliance, clinical outcome and patients' and clinicians' satisfaction with treatment.

Methods: In total, 1354 subjects were recruited by 253 investigational sites in Romania. All patients treated with RLAI, as decided after agreement between the physician and the patient, were eligible for inclusion in this survey. Subjects were either patients requiring a switch from previous antipsychotic medication, or patients at onset of schizophrenia. Data was collected at baseline and at one or more data collection moments. The analysis focussed on the 6 and 12 month timepoints.

Results: After intake of RLAI, one third of the patients experienced a treatment-emergent AE. The most common reported AEs were psychiatric disorders related to the underlying disease (insomnia, anxiety, depression and psychotic disorder). Other reported AEs included extrapyramidal symptoms, weight gain, and endocrine disorders (amenorrhea, galactorrhea). The frequencies of these AEs were overall in agreement with those described in the current Summary of Product Characteristics. All parameters assessing drug efficacy showed a statistical significant improvement except for the number and the duration of hospitalizations which increased compared to the 6 months pre-study period.

Conclusion: Treatment-emergent AEs observed during this study were consistent with the established safety profile of RLAI. In addition, treatment with RLAI resulted in the expected, statistically relevant improvement of psychiatric status in subjects eligible for such treatment, in most cases subjects diagnosed with schizophrenia and schizoaffective disorders.

Keywords: Schizophrenia; Risperidone long-acting injectable; Safety; Clinical outcome

Introduction

Schizophrenia is a chronic disease that benefits from complex, personalized therapeutic strategies during acute exacerbations and maintenance treatment over the long term. The main objectives of the treatment of schizophrenia are: clinical response and symptoms resolution, relapse prevention, and recovery [1,2]. So far, psychopharmacological approaches, e.g. antipsychotics, constitute the mainstay of treatment for schizophrenia. Among these, atypical antipsychotics are the first line option in acute phases and in maintenance [3,4]. In spite of the various therapy approaches, the course of schizophrenia is still unsatisfactory, with high relapse rates (over 75% within 5 years) [5], due to the natural course of the disease itself, poor response on different psychopathology dimensions, inadequate treatment strategies and psychosocial services [6], health care delivery, reimbursement issues [7] and non-adherence. Non-adherence rates, estimated to be 40-60% in schizophrenia patients [8], could be a barrier to the achievement of the treatment goals, resulting in relapses, re-hospitalisations, supplementary costs [9] and poor outcomes. The consequences of relapses are unpredictable, disrupting social adjustment, presenting various risks and impacting outcomes (time and degree of recovery) [6]. Aside from being a public health challenge, prevention of relapses is a reliable measurement of outcomes [10], achieved mainly by continuous treatment, controlling symptoms, reducing morbidity, personal, family and society burden, and cost savings [11]. Data suggested that patients treated with conventional depot antipsychotics were less often admitted to psychiatric facilities than those on oral conventional neuroleptics [12,13]. The trend of prescription in the last 15 years, especially for the maintenance phase, favoured the atypical antipsychotics due to similar efficacy, lower extrapyramidal symptoms and other adverse effects risk, on-need adjustments, compared with first generation antipsychotics (FGA) and depot FGA [14]. The advantages of depot FGA over neuroleptics were obvious in relapse prevention [13].

The history of depot antipsychotics is quit heterogeneous: being popular in many European countries, especially in Scandinavian countries and in the United Kingdom [15], and less prescribed in the United States of America [16] due to concerns of adverse effects and non-acceptance by patients [17,18]. Even though various second generation long-acting injections are available, their prescription rates attain only about 20% [19], in spite of their clear advantages such as relief of uncertainties about medication administration, reliable drug delivery [20], safety, and good overall acceptance [19]. The conservative stereotype of prescription of long-acting injectables refers to difficult to treat, non-adherent patients, more severe patients who failed to respond to previous treatment trials [21], with more than four re-exacerbations [19], with chronic course [20], and who were rarely initiated as inpatients [22]. Long-acting injectables are seen as a last resort medication rather than being routinely offered. More adequate

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candidates for long-acting injectables were identified: well informed, with good insight and previous good experience with depots [19]. Due to lack of sufficient studies [23,24], it is uncertain if first episode schizophrenia patients could benefit from long-acting injectables as they are more prone to relapses due to drug discontinuation. This national naturalistic multicentre single-arm prospective survey was initiated as there was a need for the post-authorisation assessment of the safety, efficacy and tolerability of RLAI in patients diagnosed with schizophrenia, schizophreniform disorder or schizoaffective disorder. It is in the interests of the community and of the patients that treating physicians know more about how the drug works in routine clinical use. To date, although clear advantages of risperidone long-acting injectable (RLAI) or other depot antipsychotic over non-depot formulations in terms of safety and efficacy (relapse) have been shown [18-20], RLAI or other depot drugs are not routinely prescribed to schizophrenic patients [18,19] due to concerns on the safety [17,18]. Therefore, the primary aim of the survey was to confirm the safety of RLAI under marketed conditions in routine clinical practice after switch from a previous treatment or at initiation in schizophrenia, schizophreniform disorder (recent onset and duration of less than 6 months), and schizo-affective disorder to support the use of RLAI in this patient population. Secondary objectives were to investigate the reasons of initiation of this treatment, effectiveness, quality of life of patients on RLAI, compliance, clinical evolution (severity of symptoms, hospitalizations, relapses) and the patients' and clinicians' satisfaction with the treatment.

Subjects and Methods

Subjects

All patients diagnosed with schizophrenia, schizophreniform disorder or schizoaffective disorder and treated with RLAI, as decided after agreement between the physician and the patient, were eligible for inclusion in this survey. Patients for whom RLAI was contraindicated (as per local label, e.g., hypersensitivity to the product) were excluded from the survey. Subjects were either patients requiring a switch from previous antipsychotic medication, or patients with onset of schizophrenia. All patients that completed the initial 6 months treatment duration within this study were eligible for the follow-up data collection. Subjects were withdrawn from the survey if RLAI treatment was stopped. In this Phase 4 study, 1354 subjects diagnosed with schizophrenia, schizophreniform disorder or schizo-affective disorder according to the DSM-IVTR criteria were recruited by 253 investigational sites in Romania. All subjects were Caucasian, with a median age of 38 years (overall range 18-82 years). A slight majority of subjects was female (N=687, 50.7%). Median body weight at baseline was 70 kg, resulting in a median Body Mass Index (BMI) of 24.4 kg/m^2. Data was collected for 6 months (at the start within 1 week and at 1, 3 and 6 months) and treatment was prescribed according to daily practice. Follow-up information was collected after 12 months of treatment, only from patients that completed the initial 6 months treatment. Subjects were withdrawn from the survey if the treatment with RLAI had been stopped. As this study was a naturalistic survey, no interventions were carried out, subjects did not receive any investigational medication (RLAI was used according to daily clinical practice) and data were collected anonymously (no name, date of birth or initials). Therefore, patients' explicit consent was not applicable. Patients could be informed that research would be carried out using coded data and that they had the opportunity to object to this. Only data from patients who had no objections were included, according to the local Code of Good Clinical Practice. This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and was consistent with Good Clinical Practices and applicable regulatory requirements.

All 1354 subjects received RLAI according to daily practice (doses of 25, 37.5 or 50 mg). Concomitant medications were allowed but had to be reported. In total, 1354 patient were included in this study of whom 1186 (87.6%) patients completed the 6 months observation period and 168 (12.4%) patients withdrew from the study. A total of 966 (71.3%) patients completed the follow-up phase of the study by attending the 12-month visit.

Methods

The following data was collected at baseline and at one or more data collection moments (at 1, 3, 6 and/or 12 months): demographic data, psychiatric history, previous antipsychotic treatment and reason(s) for initiating RLAI, effectiveness measured by Clinical Global Impression (CGI) severity of illness and CGI improvement versus baseline, SF-36 and Global Assessment of Functioning Scale (GAF), the number and durations of psychiatric hospitalizations in the previous 6 months and during RLAI treatment, patient's and physician's treatment opinion about the antipsychotic treatment, dates and dosages of all RLAI injections, any concomitant medication, any adverse events (AEs), and reason for stopping treatment with RLAI.

Statistical Analysis

Due to the explorative character of the survey, the sample size was not calculated. A total of 1500 patients were expected to enter the survey. This number was considered to be sufficient to describe the safety profile of RLAI.

All subjects who received at least one injection of RLAI were included in the analysis of demographic, baseline characteristics and safety data. An analysis of treatment-emergent adverse events was performed. The efficacy dataset for the entire study included only those patients who completed the follow up phase.

Statistical analysis was performed in SPSS v20. The changes from baseline to endpoint were tested for differences using the Wilcoxon signed rank test (ordinal/continuous data). For nominal data, the sign test was used. Statistical tests for differences between endpoint and baseline were interpreted at the 5% significance level (two-tailed).

Results

Baseline data

In total, 1354 patients were included in this study of whom 1186 (87.6%) completed the 6 months observation period and 168 (12.4%) patients withdrew. Reasons for discontinuation during the first 6 months were: lost to follow up (56.5%), insufficient response (8.3%), adverse events (6.5%), and other reasons (28.5%). A total of 966 (71.3%) patients completed the follow-up phase of the study by attending the 12-month visit.

The main diagnoses of subjects entering the study were schizophrenia (70.1%) or schizoaffective disorder (20.9%). The most common reasons for starting therapy with RLAI were insufficient efficacy (46.4%) and non-compliance (33.6%) with previous medication. Co-morbidities at baseline were reported by a large majority of patients (83.9%) and included obesity (8.7%), cardiovascular co-morbidities (2.6%), alcohol abuse (1.3%), drug abuse (0.9%), Type II diabetes (0.9%) and Type I diabetes (0.7%). In 84.7% of patients, previous

treatment with antipsychotics was recorded at baseline. The most frequent previous antipsychotic therapy was oral risperidone (28.2% of patients). Previous therapy was most often assessed as "moderate" by the physician as well as by the patient. The most frequently used other concomitant medications were the antiepileptic drug valproic acid (20.8%) and the antiparkinsonian drug trihexyphenidyl (7.6%).

Safety

After intake of RLAI, 31.2% of patients experienced a treatment-emergent AE (TEAE). An overview of AEs occurring in at least 7 patients (0.5%) is provided in Table 1. Most TEAEs were mild (32%) or moderate (48.6%) in intensity. The most common TEAE was insomnia in 5.9% of the patients participating in the study. Other common TEAEs occurring in more than 1% of the patients were extrapyramidal disorder, anxiety, psychomotor hyperactivity, weight increase, tremor, depression, psychotic disorder, galactorrhea, and amenorrhea. In addition, drug ineffectiveness was reported as an AE in 4.4% of the patients. The majority of most commonly reported AEs were psychiatric disorders, and were considered to be related to the underlying disease (insomnia, anxiety, depression, psychotic disorder, schizophrenia relapse). There were also AEs reported that are known to be possible adverse drug reactions to RLAI like extrapyramidal disorder, weight gain, and endocrine disorders (amenorrhea, galactorrhea). The frequencies of these AEs (between 1.0-2.2% of the patients) were overall in agreement with those described in the current SmPC. Forty-six subjects experienced a total of 73 serious treatment-emergent AEs (SAEs) (Table 1). The most common SAEs were related to psychotic disorder in 15 patients (1.1%) and schizophrenia relapse in 9 patients (0.7%). Three deaths occurred in the study population. Two of the AEs leading to death were considered not related to RLAI by the investigators. These events were a completed suicide (by hanging) and road traffic accident (patient walked over the railway line and was run over by a train). One fatal case of acute myocardial infarction was considered by the investigator to be very likely/certainly related to RLAI.

Treatment-Emergent Adverse Events, N (%)	TEAE	TEAE reported as SAE
Any treatment-emergent AE/SAE	**423 (31.2%)**	**46 (3.4%)**
Endocrine disorders		
Amenorrhea	16 (1.2%)	2 (0.1%)
Galactorrhea	15 (1.0%)	4 (0.3%)
Hyperprolactinaemia	5 (0.4%)	3 (0.2%)
General disorders and administration site conditions		
Drug ineffective	60 (4.4%)	0
Metabolism and nutrition disorders		
Weight increased	20 (1.5%)	0
Nervous system disorders		
Extrapyramidal disorder	30 (2.2%)	0
Psychomotor hyperactivity	25 (1.8%)	6 (0.4%)
Tremor	19 (1.4%)	1 (0.1%)
Headache	12 (0.9%)	0
Sedation	11(0.8%)	0
Tardive dyskinesia	10 (0.7%)	2 (0.1%)
Psychiatric disorders		
Insomnia	80 (5.9%)	4 (0.3%)
Anxiety	27 (2.0%)	0
Depression	18 (1.3%)	0
Psychotic disorder	16 (1.2%)	15 (1.1%)
Schizophrenia relapse	9 (0.7%)	9 (0.7%)
Delirium	6 (0.4%)	4 (0.3%)
Hallucination	2 (0.1%)	2 (0.1%)
Suicidal ideation	2 (0.1%)	2 (0.1%)

Table 1: Overview of adverse events in at least 7 subjects and/or serious adverse events in at least 2 subjects.

One pregnancy case was reported during the conduct of this study, with no relevant safety findings.

A statistically significant mean (SD) increase in the patient's weight compared to baseline values could be observed after 6 months (1.1 kg [4.4]) and after 12 months (2.0 kg [5.8]) of treatment (p=0.01 and p=0.001, respectively). The corresponding mean (SD) BMI showed an overall significant ($p \leq 0.01$) increase respect to baseline values of 0.39 (1.40) kg/m^2 and 0.69 (2.10) kg/m^2 at 6 and 12 months, respectively. A significant increase in BMI after 6 months of treatment was also observed when considering the different age groups; however after 12 months, this increase was only significant for the age group between 30-40 years (p=0.014).

Efficacy

GAF score improved significantly (p<0.001) from baseline to both 6 and 12 months, with an average increase of 22.8 and 39.7 points, respectively. An improvement on the GAF score after 6 months was observed in 94.3% of the patients, and 68.7% of the 966 patients who completed the follow up period showed an improvement on the GAF score at 12 months (Table 2). The rate of patients with improvement in CGI increased significantly (p<0.001) from baseline to both 6 and 12 months. At 6 months, 79.6% of the patients presented a CGI score rated as "very much improved" or "much improved" compared to baseline values. Of the 996 patients who completed the follow up period, 88.4% had a CGI score rated as "very much improved" or "much improved" at 12 months versus baseline score (Figures 1 and 2). The results of this study indicated that 328 patients were hospitalized for at least one day in the 6-month period previous to the study start, whereas 491 were hospitalized during the 12-month period of duration of the study. There was a median increase of 4 days in the length of hospitalization during the study with respect to the 6-month period previous to the study start (from 18 to 22 days). The physician's and patient's opinion on the antipsychotic treatment showed a statistically significant (p<0.001) improvement between baseline and both 6 months and 12 months. In 23.7% of the analysed patients, the opinion of the physician about the antipsychotic treatment at baseline was rated as "good" or "very good". This opinion increased up to 90.8% of the patients after 6 months of treatment (Figure 3). At 12 months, the physician's opinion of the antipsychotic treatment was rated as "good" or "very good" in 96.3% of the patients completing the study. Similar results were observed for the patient's opinion, which was rated as "good" or "very good" by 85.5% and 95.9% of the patients at 6 and 12 months, respectively, in comparison with 29.9% of the patients at baseline (Figure 4). Regarding the quality of life, both physical and mental component scores of SF-36 (Physical Component Summary [PCS] and Mental Component Summary [MCS], respectively) range from 0 to 100 with higher scores indicating better quality of life. The results indicated that for the PCS, the mean (SD) score significantly increased (p=0.001) over the 12-month treatment period with a change from baseline at endpoint of 37.8 (126.4), indicating better physical health. For the MCS there was a lower, but also significant (p=0.001) increase over the 12-month treatment period with a change from baseline at endpoint of 1.89 (20.5) indicating an improvement in mental health.

	Baseline	6 months	Baseline vs. Endpoint	12 months	Baseline vs. Endpoint
GAF score	**N=1354**	**N=1341**	**N=1341**	**N=966**	**N=966**
Mean (SD)	49.2 (14.8)	72.1 (13.7)	22.8 (15.2)	79.0 (12.1)	39.7 (40.6)
Median	50	73	20	80	28.8
Range	-	15-100	-30 to +85	30-100	-9 to +533
p-value			<0.001		<0.001
Individual change in GAF score			**N=1338**		**N=966**
Decreased	-		20 (1.4%)		72 (7.5%)
Stable	-		54 (4.3%)		230 (23.8%)
Increased	-		1264 (94.3%)		664 (68.7%)

Table 2: GAF scores at baseline, 6 months and 12 months.

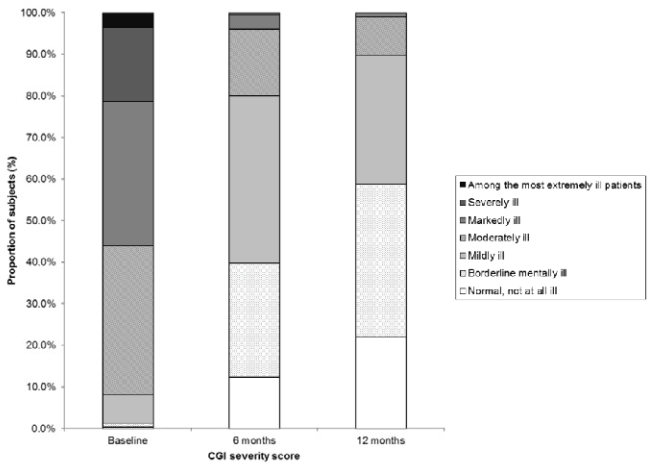

Figure 1: Effectiveness of treatment with risperidone long-acting injectable: CGI severity
Graphical presentation of the proportion of subjects per CGI severity score at baseline and after 6 and 12 months of treatment.

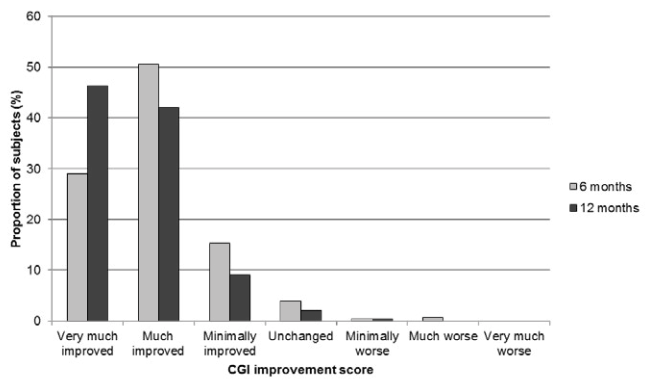

Figure 2: Effectiveness of treatment with risperidone long-acting injectable: CGI improvement.
Graphical presentation of the proportion of subjects per CGI improvement score after 6 and 12 months of treatment.

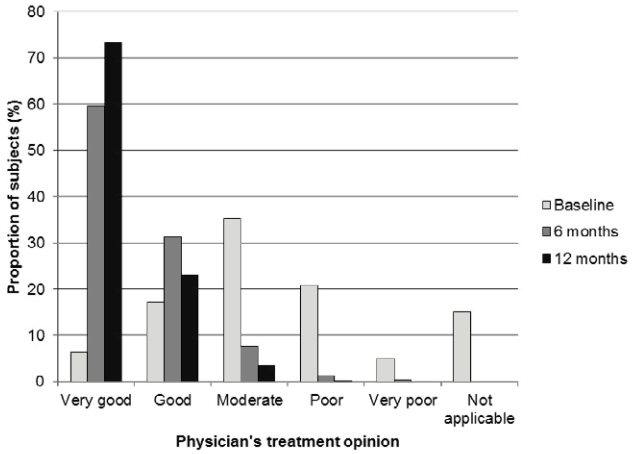

Figure 3: Long term effect of treatment on clinical outcome: physician's treatment opinion.
Graphical presentation of the proportion of subjects per physician's treatment opinion score at baseline and after 6 and 12 months of treatment.

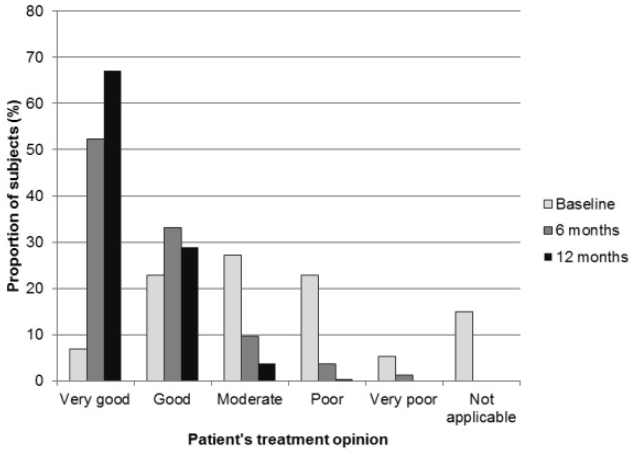

Figure 4: Long term effect of treatment on clinical outcome: patient's treatment opinion.
Graphical presentation of the proportion of subjects per patient's treatment opinion score at baseline and after 6 and 12 months of treatment.

Discussion

Long acting injectable antipsychotics proved to be effective and safe treatments for schizophrenia, considered an advance on long-term management of this disease [14,25], especially with regard to relapse prevention [26,27]. The meta-analysis by Leucht et al. [28], searching mainly Randomized Controlled Trials (RCT) with at least one year duration on out-patients with maintenance therapy, showed a significant reduction of relapses on antipsychotic depots in comparison to oral antipsychotics. Moreover, it has been established that antipsychotic maintenance therapy substantially reduced relapse risk up to 2 years, in single episodes or in remitted patients with a decrease in size over time [29].

Besides the decrease of the rater selection biases, which are strengths obtained through blinding and randomization [9], various limits of randomized control trials have been outlined such as: the inclusion of more adherent patients [30] due to frequent visits and prescription refills [9], less severely ill patients [31]. The comparisons of long-acting injectables versus oral antipsychotics in RCT support the idea of relapse reduction but less information is provided regarding the adherence style [28,29]. Authors acknowledged that RCT do not reflect usual care. This may be reflected rather by observational studies, which compare the course of illness before and after a given medication (mirror-image studies) [9,30,32]. Nevertheless, RCT failed to show superiority of long-acting injectables over other antipsychotics, even though adherence problems could be signalled earlier [31,33]. The current study is an observational study that may be in consonance with the prescription guidelines: to switch poorly adherent schizophrenia patients from oral antipsychotics to depots [4], that fits also the conservative prescription style of identification of patients who qualify for long-acting injectables [19]. The prescription of relatively new drugs respond to high expectations, being prescribed more often to more severe patients, treatment failures [34], this kind of selective prescribing being known as "the channelling effect" [21]. Comparing to the endpoint of the current study-12 months, 71.3% of patients completed the follow-up, while other studies, with a more strict protocol but with the same duration, completers were 52 to 55% [35] or 39.9% in a study with longer duration [36]. Several studies, focused on safety issues, synthesized by Möller [37], outlined the fact that RLAI is safe and well tolerated. Data suggest the more evident benefits of the switch from conventional antipsychotics to RLAI regarding lower extrapyramidal symptoms [38,39]. Patients included in the current study were previously frequently treated with oral atypical antipsychotics 64.9% (among them 28.2% on risperidone) and less often with typical oral (16.2%) or depot neuroleptics (14.5%). A special comment should be added: a switch strategy implies a change of treatment between antipsychotic drug groups but not between different formulations of the same drug [21], meaning that in fact 71.8% of the study population had major treatment changes. Reasons to initiate RLAI were insufficient efficacy (46.4%) and non-compliance (33.6%) with previous medication, which is similar or higher compared to other (observational) studies) [40,41]. As a primary objective of this study emphasized safety issues, appreciated by recording the most frequent TEAE, which were: insomnia (5.9%), extrapyramidal symptoms (more than 1%), anxiety (2.0%), weight gain with consecutive BMI increase (1.5%), amenorrhea (1.2%), and galactorrhea (1.0%). Compared to this study, Lindenmayer et al. [35], reported a higher incidence of psychiatric AEs (psychosis, headache, agitation) and extrapyramidal symptoms (22-33%) in an extension study in which patient received RLAI during 12 months. This was also observed in a relapse prevention trial in which patients received RLAI for 24 months where the incidence of psychiatric symptoms was 43.2% [42]. Several studies [42,43,44] also reported a higher incidence of weight increased AEs (7.0% and 5.0%, respectively) although mean change in body weight and/or BMI was similar or higher [43,44]. Nevertheless, the results of a meta-analysis of data from studies that included tolerability data for RLAI published between January 1994 and March 2006 presented by Möller [37] outlined the fact that in spite of a weight increase of 1-2 kg, there were no short term consequences on lipid and glucose metabolism. He also demonstrated that asymptomatic prolactin elevations decreased in time.

Two of the 3 AEs leading to death were considered not related to RLAI by the investigator: road traffic accident and suicide. The latter is the leading cause of death observed in studies with patients on RLAI [45]. One fatal case of acute myocardial infarction was considered very likely/certainly related to RLAI by the investigator. The use of antipsychotic medications is associated with weight gain or glucose-metabolism related AEs which are risk factors for developing cardiovascular disease [46,47]. In addition to the possible risk of risperidone use, the patient was a smoker with a concurrent diagnosis of atherosclerosis. Myocardial infarction was also reported as adverse event in other studies that included risperidone (long-acting injectable) [48,49].

Remission criteria, proposed by the Remission in Schizophrenia Working Group, may not ascertain properly the broad range of dimensions and subjective impact of treatment, ignoring important variables of functional recovery [50]. Therefore, global functioning [36] and increased quality of life in schizophrenia patients achieving prolonged remission [51] may be more relevant. The secondary objectives of the current study were exactly the clinical evolution, functioning, and quality of life, assessed by CGI, GAF and SF-36, which recorded significant improvements at 6 and 12 months, with a more evident physical health component score and a lower but also significant mental health component score on SF-36. Functional remission has been defined by the two scales as follows: achievement of at least 60 points on GAF and a SF-36 mental component of at least 52 at 6, 18 months or other endpoint of observation [36]. There were substantial gains in these fields at 6 and 12 months (endpoint): GAF=72.1 (SD 13.7) at 6 months, GAF=79.0 (SD 12.1) at endpoint; SF-36 MCS at 12 months 74.1 (SD 6.7). Improvements in GAF score were greater than observed by Schreiner et al. [44]. CGI scores at 6 and 12 months indicated a greater proportion of "much" and "very much improved" than the Lindenmayer et al. results [35]. In spite of the global good outcome and safety of RLAI, there was an increase in the number and duration of hospitalizations on RLAI, in contrast to other studies that recorded a decrease of admittances [41,44,52]. A possible explanation of this finding could be the need for closer surveillance in a hospital setting at the transition to a new treatment as safety issues could arise if patients have not yet been exposed to that treatment and/or mental health care professionals do not have previous experience with it. In addition, RLAI treatment was initiated in a high proportion of subjects initiating due to ineffective previous treatment (46.4%) that could have required hospitalisation. Citrome et al. [22] recommended long-acting injectables also for inpatients due to daily drug administration struggles and during the critical transition phase from inpatient to outpatient status, establishing longer durations of hospitalization prior to and after RLAI.

The absence of comparators is a limitation of the open-label, single arm study design. Other limitations of the survey include the use of co-medication that may confound the assessment of TEAEs, as well as the lack of precise record of the number and kind of previous switches and treatment trials.

Conclusion

The spectrum of TEAEs observed in this survey could be expected from the composition of enrolled subjects comprising individuals with schizophrenia or schizo-affective disorder. The TEAEs that fell into the category of special interest regarding extrapyramidal syndrome, and endocrine disorders (amenorrhea, galactorrhea) or glucose-related AEs were reported but did not exceed the expected level.

In addition, treatment with RLAI showed the expected, statistically relevant improvement of psychiatric status in subjects

eligible for treatment with RLAI, in most cases subjects diagnosed with schizophrenia and schizoaffective disorders taking into account all parameters assessing drug efficacy (CGI, GAF, patient's quality of life, as well as the opinion on treatment by the investigator and patient). There was an increase in the number and the duration of hospitalizations compared to the 6 months pre-study period. A possible explanation could be that the transition in treatment regimen between old treatment and study medication required a closer surveillance of these subjects only feasible at the hospital.

In conclusion, the results of this study show that the safety and efficacy in patients treated with RLAI in a naturalistic setting are according to expectations, based on clinical studies thereby providing relevant information to psychiatrists initiating or optimizing an antipsychotic treatment. The results confirm that RLAI is safe and well tolerated as well as effective in subjects diagnosed with schizophrenia and schizoaffective disorder.

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Conflict of Interest

Prof. Dr. Micluța received honoraria as coordinating and principal investigator in the PASTEL study from Johnson & Johnson. She is consultant or member in advisory boards for Astra-Zeneca, BMS, Eli-Lilly, and Lundbeck and speaker for Angelini, Astra-Zeneca, BMS, Eli-Lilly, Ever, Glenmark, Lundbeck, Novartis, Pfizer, Sanofi, Servier, Terapia, and Torrent.

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Dr. Ciungu is a full time employee of Janssen, a division of Johnson & Johnson Romania.

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