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Treatment satisfaction and effectiveness of Lurasidone on quality of life and functioning in adult patients with schizophrenia in the real-world Italian clinical practice: a prospective 3-month observational study

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Abstract

Background Although second-generation antipsychotics (SGAs) have proven to be effective therapeutic options for patients with schizophrenia, there is a notable lack of evidence on patients' subjective perspectives regarding their well-being, quality of life, and satisfaction with these medications. This study aimed to evaluate the treatment satisfaction and effectiveness of lurasidone on quality of life and functioning in adult patients with schizophrenia in real-world Italian clinical practice.

Methods This was a multicentre, national, non-interventional, single-arm, 3-month prospective study. Patients who were naive to lurasidone treatment and whose treating physician had decided to start them on this medication were enrolled and evaluated over a 3-month period. Eligible patients were adults (≥ 18 years of age) with a primary diagnosis of schizophrenia who were being treated with lurasidone (for the first time [i.e., they were lurasidone naive]) as part of routine clinical practice. Efficacy endpoints were changes in patient/caregiver treatment satisfaction (seven-point Likert scale from the Treatment Satisfaction Questionnaire for Medication), patient quality of life and functioning (QLS), investigator-rated global assessment of functioning (CGI-S, IAQ) after 6 weeks and 3 months of lurasidone, and number of relapses and hospitalizations.

Results Sixty-one patients were enrolled and 59 completed the study. The median dosage of lurasidone at baseline was 37.00 mg/day. The median duration of titration was 86.0 days (Min 28; Max 115 days); the median number of

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dosage changes was 1.0. At the end of 3-month observation period, the median dose of lurasidone was 74.00 mg/day. QoL and Functioning Score showed a trend of improvement over time, reaching a mean change from baseline of 9.8 at the end of the study. According to the CGI-S, the percentage of patients who were "markedly or severely ill" showed a continuous decrease from baseline to 3 months, from 62.29% to 8.20%. Patient satisfaction increased over time, with 80.32% of patients reporting that they were somewhat, fairly, or very satisfied (including 63.93% who were completely or very satisfied) at the end of the study. No relapses/hospitalizations for psychiatric reasons were reported. Lurasidone was well tolerated with no safety concerns or discontinuations due to AEs.

Conclusions Lurasidone represents a valid option for the treatment of schizophrenia and positively affects subjective well-being, quality of life and satisfaction.

Trial registration NCT06527885 retrospectively registered (01/08/2024).

Keywords Schizophrenia, Lurasidone, Second-generation antipsychotics (SGAs), Quality of life, Patient's satisfaction, Real-world, Observational, Prospective

Background

Schizophrenia is a chronic, debilitating disorder associated with increased morbidity and mortality and with a pervasive impact on personal, occupational, family and social life [1–5].

While relapse prevention has been the primary goal of schizophrenia treatment, increasing attention is being paid to a broader, patient-centred approach that includes patient functioning and quality of life (QoL) as key outcome measures [6–9].

Long-term antipsychotic treatment, particularly second-generation antipsychotics (SGAs), has been shown to significantly improve outcomes in patients with schizophrenia, including symptom control, relapse prevention, and improvement in cognitive function, social functioning, and quality of life [10, 11].

Lurasidone is an atypical antipsychotic drug approved for the treatment of schizophrenia in adults (2010 by FDA, 2014 by EMA) and in adolescents ≥ 13 years of age (2015 by FDA, 2020 by EMA).

Lurasidone has been extensively evaluated in several RCTs against placebo and active comparators, demonstrating good short- and long-term safety and efficacy with respect to several important outcomes, including symptom control, relapse prevention, improvement in social functioning, quality of life, and cognitive domains in adult patients with schizophrenia. [12, 13].

However, data on patient-reported outcomes (e.g., QoL, treatment satisfaction) and functioning in adult patients with schizophrenia treated with lurasidone as part of standard clinical practice are limited. Therefore, real-world, prospective studies are needed to provide the above evidence.

The present multicentre, non-interventional, prospective study with a 3-month follow-up period was conducted to describe the efficacy of lurasidone, focusing on patient-reported outcomes (e.g., QoL, treatment satisfaction) and functioning data, other than the safety/tolerability profile, in Italian patients with schizophrenia.

Methods

This multicentre, national, non-interventional, single-arm, 3-month, prospective, observational study was designed to describe the treatment satisfaction and efficacy of lurasidone on QoL and functioning in adult patients with schizophrenia in real-world Italian clinical practice.

All patients included in the study were assigned to lurasidone therapy prior to and independent of the decision to enrol in the study. Eligible patients were adults (aged ≥ 18 years) with a primary diagnosis of schizophrenia who were being treated with lurasidone (for the first time [i.e., they were naïve to lurasidone therapy]) according to routine clinical practice. As an observational study, patients could be recruited after a physician had decided to initiate treatment with lurasidone independently of this study and followed prospectively for a period of 3 months. Informed consent was obtained from all patients, and the study was approved by the local ethics committees.

Effectiveness endpoints

Primary endpoints were changes in patient and caregiver treatment satisfaction (via a seven-point Likert scale derived from the Treatment Satisfaction Questionnaire for Medication), patient QoL and functioning (via the Quality of Life Scale, QLS) after 6 weeks of lurasidone therapy.

Secondary endpoints were patient/caregiver treatment satisfaction, investigator-rated overall efficacy (via Clinical Global Impression – Severity of Illness, CGI-S, and Investigator's Assessment Questionnaire, IAQ) after 6 weeks and 3 months of lurasidone therapy, relapses and hospitalizations.

Patient's satisfaction with efficacy, safety, ease of use, and overall impression of medication was measured using seven-point Likert scales derived from the Treatment Satisfaction Questionnaire for Medication [14]. **Caregiver's satisfaction** with efficacy, safety, ease of use,

and overall impact on patient management was assessed using seven-point Likert scales derived from the Treatment Satisfaction Questionnaire for Medication [14].

The QLS is a validated measure of health-related quality of life and functioning in schizophrenia [15] that focuses on intrapsychic, social, and negative symptoms and their impact on functioning in schizophrenia. In addition to overall quality of life, the QLS total score reflects functioning, richness of personal experience, quality of interpersonal relationships, and productivity in occupational roles in patients with schizophrenia. The questionnaire consists of 21 items in 4 domains: Interpersonal Relations (8 items), Instrumental Role (4 items), Intrapsychic Foundations (7 items), and Common Objects and Activities (2 items). Each item is scored on a 7-point Likert scale ranging from 0 (severe impairment) to 6 (normal or unimpaired functioning). A score is calculated for each domain, and the total score ranges from 0 to 126. It is a clinician-rated scale derived from a semi-structured patient interview that is widely used in the psychopharmacological evaluation of treatments for schizophrenia. The IAQ is a validated, clinician-rated scale designed to assess the relative effectiveness (efficacy, safety, and tolerability) of antipsychotic medications in patients with schizophrenia [16]. The IAQ consists of 12 equally weighted items: positive symptoms, negative symptoms, other efficacy symptoms, somnolence, weight gain, signs and symptoms of prolactin elevation, akathisia, other extrapyramidal symptoms, other safety or tolerability issues, cognition, energy and mood. For each item, current medication was compared with previous antipsychotic medication on a five-point scale from 1 (much better) to 5 (much worse). Total IAQ scores range from 12 to 60, with lower total IAQ scores indicating better relative treatment efficacy. Permission was granted by the authors.

The CGI-S measures the clinician's impression of the patient's current state of mental illness on a 7-point scale ranging from 1 (normal-not at all ill) to 7 (among the most severely ill patients) [17]. Although the CGI-S is considered a very simple and synthetic tool for assessing the severity of schizophrenia, it has been shown to be reliable and its indications are consistent with other more sophisticated scales such as the Global Assessment of Functioning (GAF) and the Positive and Negative Syndrome Scale (PANSS) [18]. The CGI-S requires knowledge of the patient's clinical history; for this reason, the patient was always assessed by the same clinician to detect any change in the patient's condition. The CGI-S is a public domain document. Relapses (acute episodes, i.e., the number of acute episodes since the last assessment, defined as any new-onset or recurrent psychotic symptom requiring either initiation of new antipsychotic treatment, change in existing treatment, or hospitalization [19]) were recorded. Hospitalizations lasting>24 h for psychiatric reasons (number, diagnosis, duration) were also collected.

Safety endpoints

Tolerability via IAQ (investigator) after 6 weeks and 3 months of lurasidone treatment; AEs, SAEs, ADRs and SADRs; hospitalizations for non-psychiatric reasons (number, diagnosis, duration); if available, metabolic parameters (body weight, HDL-C, LDL-C, total cholesterol, triglycerides, glycemia, prolactin) and ECG QTc values were collected. According to clinical practice, these laboratory tests were routinely performed by the investigators at the start of a new treatment/change in therapy and repeated every 3 months. Blood count e HbA1c, liver and kidney function: if available according to routine practice, values were collected corresponding to the start of lurasidone treatment and the end of the observation period.

Pharmacological treatment

Current treatment and treatment history were recorded. A post hoc analysis was performed to describe, for all psychotropic medications, whether they were started before or after the start of lurasidone and the mean/median duration during the study (calculated from the start of lurasidone). Patient setting at initiation of lurasidone (inpatient or outpatient) and titration details were recorded. Treatment adherence was assessed by specific questions to the patient at the 6-week and 3-month visits to determine if the patient had discontinued any dose since the last visit and to collect details (discontinued dose, reasons), if any.

Statistical analysis

Due to the non-interventional nature of this study, the statistical analyses were purely descriptive. All data collected in the eCRF were used in the statistical analysis. Categorical variables were summarized by frequency and percentage of patients, whereas continuous variables were summarized by number of non-missing observations, mean and standard deviation, median, minimum and maximum values. Due to the descriptive nature of the study, no statistical test was performed. As the study population also included young adult patients (aged 18 to 25 years), a sub-analysis was performed to describe patient and caregiver treatment satisfaction, patient functioning and quality of life, efficacy and tolerability of lurasidone treatment in this patient group (aged 18 to 25 years), in addition to describing these outcomes in the overall population.

Results

Sixty-one (61) patients from 3 Italian centres met the inclusion criteria and were enrolled between October 2022 and June 2023. The observation period was 3 months, and the study was completed in September 2023. Two patients (3.28%) discontinued lurasidone permanently. One patient decided to discontinue treatment and study participation during the titration phase, approximately 3 weeks after starting lurasidone; the second patient discontinued lurasidone 1 week after starting the medication at the discretion of the investigator (no adverse events). There were no temporary interruptions of lurasidone.

Patient characteristics at baseline

The median age was 44.0 years, ranging from 18 to 74 years. The sexes were almost equally represented (52.46% female). Approximately 40% were employed or students; most patients (73.77%) lived with cohabiting relatives, although only one patient reported caregiver support (family caregiver); approximately 32% were married or engaged; almost 80% reported no physical activity. The median time since the onset of schizophrenia was about 12 years, with a family history in 36.07% of patients (Table 1).

Metabolic disorders were reported by 11.48%, while hypertension was reported by 8.20% of patients. The most commonly used non-psychiatric treatment category was antihypertensives.

Psychiatric comorbidities were reported by 22.95% of patients. A description of pharmacologic management, including prior and concomitant psychiatric medications, is provided in "Additional file 1" (See supplementary information).

Lurasidone dosages and titration pattern

Dosages and titration pattern were determined as per clinician's decision, on the basis of individual needs, in line with clinical practice and labelling guidelines. The median duration of lurasidone titration was 86.0 days (Min 28; Max 115 days); the mean changes in lurasidone dosages were 0.9 (median 1.0). At baseline, at 6-week and at 3-month follow-up, the mean (median) dosages were 42.46 (37.00) mg/day, 61.14 (37.00) mg/day and 72.75 (74.00) mg/day.

Patient's reported outcomes (treatment satisfaction and quality of life)

After 6 weeks of lurasidone, 65.57% of patients reported being "somewhat," "quite," or "extremely" satisfied with symptom relief and treatment; among these, the rate of "quite" or "extremely" satisfied was 39.34%. On the other hand, the rate of "extremely", "quite" or "somewhat" dissatisfied was 8.20%, with 3.28% being "quite" dissatisfied

Table 1 Social-demographic characteristics at baseline and schizophrenia history

	Total (*N* = 61)
Age (years)	
Mean (SD)	42.5 (16.41)
Median (Q1; Q3)	44.0 (26.0; 55.0)
Min; max	18.0; 74.0
Gender, n (%)	
Male	29 (47.54)
Female	32 (52.46)
Education, n (%)	
Primary or lower secondary school	16 (26.23)
Secondary school	37 (60.66)
University degree	7 (11.48)
Not known	1 (1.64)
Marital status, n (%)	
Single	32 (52.46)
Married	14 (22.95)
Widowed	2 (3.28)
Divorced/separated	6 (9.84)
Engaged	6 (9.84)
Not known	1 (1.64)
Professional status, n (%)	
Student	6 (9.84)
Employed	19 (31.15)
Unemployed	20 (32.79)
Retiree	9 (14.75)
Unemployable	6 (9.84)
Not known	1 (1.64)
Need of caregiver's support, n (%)	
Yes	1 (1.64)
Not known	1 (1.64)
Type of caregiver, n (%)[1]	
Family caregiver	1 (100.00)
Smoke, n (%)	
Yes	32 (52.46)
Not known	3 (4.92)
Number of cigarettes per day, n (%)[1]	
<=10	13 (40.63)
>10	19 (59.38)
Alcohol consumption, n (%)	
No	48 (78.69)
Occasional consumption	10 (16.39)
Regular consumption	2 (3.28)
Not known	1 (1.64)
Substance abuse, n (%)	
No	56 (91.80)
Yes	4 (6.56)
Not known	1 (1.64)
Physical activity, n (%)	
No physical activity	48 (78.69)
Moderate physical activity (1–2 times/week)	9 (14.75)

Table 1 (continued)

	Total (*N*=61)
Regular physical activity (on alternate days or daily)	3 (4.92)
Not known	1 (1.64)
Co-habitation, n (%)	
Live alone	15 (24.59)
Live with a cohabitant relative	45 (73.77)
Time from onset of schizophrenia (months)	
Mean (SD)	185.2 (163.41)
Median (Q1; Q3)	142.0 (49.5; 340.5)
Number of suicidal attempts within the last 12 months, n (%)	
0	58 (95.08)
1	2 (3.28)
3	1 (1.64)
Patients' setting at lurasidone treatment start, n (%)	
Inpatient	19 (31.15)
Outpatient	42 (68.85)
Family history of psychiatric disorder, n (%)	
Yes	22 (36.07)
Degree of kinship, n (%)[1]	
Mother	12 (54.55)
Father	2 (9.09)
Brother/sister	3 (13.64)
Uncle/aunt	4 (18.18)
Other	1 (4.55)

ENR: Enrolled population

Q1: 1st Quartile

Q3: 3rd Quartile

SD: Standard Deviation

Notes:

Percentages are calculated relative to the total number of patients in the ENR

[1]Percentages are calculated relative to the number of patients who need a caregiver's support in the ENR

Information about how many hours in a week of caregiver's support was not collected

and 4.92% being "somewhat" dissatisfied. The remaining patients were "neither satisfied nor dissatisfied" (24.59%). At 3 months (secondary objective), 80.32% of patients reported being "somewhat", "quite" or "extremely" satisfied; the rate of "quite" or "extremely" satisfied was 63.93%. On the other hand, the rate of "extremely", "quite" or "somewhat" dissatisfied was 4.92%, with 3.28% "quite" dissatisfied and 1.64% "extremely" dissatisfied. The remaining patients reported being "neither satisfied nor dissatisfied" (Fig. 1).

When looking at the age groups (N=13 for 18–25 years; N=48 for 25+years), the rate of patients who were "somewhat", "quite" or "extremely" satisfied with the way the medication relieved symptoms at 6 weeks was 53.85% in the 18–25 years group and 68.75% in the 25+years group. Of these, 23.08% and 43.75%, respectively, reported being "quite" or "extremely" satisfied. Conversely, the rate of "somewhat" or "quite" dissatisfied was similar: 7.69% in the younger group vs. 8.34% in the other group (no patient was extremely dissatisfied). At 3 months, the proportion of patients who were "somewhat", "quite" or "extremely" satisfied with the way the medication relieved symptoms was 76.93% in the 18–25 years old group and 81.25% in the 25+years old group; of these, the rate of "quite" or "extremely" satisfied was 53.85% in the younger group and 66.67% in the other. Conversely, the rate of "somewhat" or "quite" or "extremely" dissatisfied was: 7.69% in the younger group vs. 4.16% in the other.

QoL & Functioning were assessed in almost all enrolled patients (N=61 at baseline, N=60 at 6 weeks). At baseline, the total QLS score was 61.2±19.86. After 6 weeks of lurasidone treatment, the mean absolute change in QLS total score was 4.4±11.97, the relative change was 9.5±23.47%. At 3 months, the QLS absolute (relative) change was 9.8±14.49 (18.8±30.06%), showing a trend of improvement during the observation period. Looking at the data by age group, the baseline mean total score values were 58.1±17.19 for 18–25 years old (N=12) and 62.0±20.61 for 25+years old (N=48).

At 6 weeks, the absolute (relative) change in mean total score was 7.0±13.61 in the 18–25 group and 3.7±11.59 in the 25+group (18.3±35.76% vs. 7.4±19.17%). At 3 months, the mean absolute (relative) change in total score was 12.0±15.27 (28.1±41.01%) in the 18–25 group and 9.2±14.40 (16.5±26.63%) in the 25+group.

Figure 2 shows the mean values of the QLS total score over the study period (2A) in the total population; the individual domains in the total population (2B) and per age subgroup: 18–25 (2C) and 25+ (2D); an almost linear trend of improvement can be seen for all groups. The baseline status appears to be worse in the younger group, which shows a more pronounced change compared to the 25+group.

The absolute mean change after 6 weeks of lurasidone treatment in the Interpersonal Relations domain was 2.7±4.10 in the 18–25 age group (N=12), 1.4±5.29 in the 25+age group (N=48) (relative change 15.1±24.08% vs. 10.3±31.15%); the absolute mean change in the Instrumental Role domain was 1.6±3.85 (N=12) in the 18–25 age group (mean at baseline 5.8±7.10) and 0.1±2.75 (N=48) in the 25+age group (mean at baseline 11.5±6.38), the relative change was 56.7±89.81% (N=6) vs. 4.9±29.29% (N=44), respectively; the absolute change from baseline in the Intrapsychic Foundations was 2.8±5.28 in the 18–25 age group and 1.6±3.73 in the 25+age group (relative change 27.3±63.97% vs. 11.9±30.05%). The absolute (relative) change from baseline in the Common Objects and Activities domain

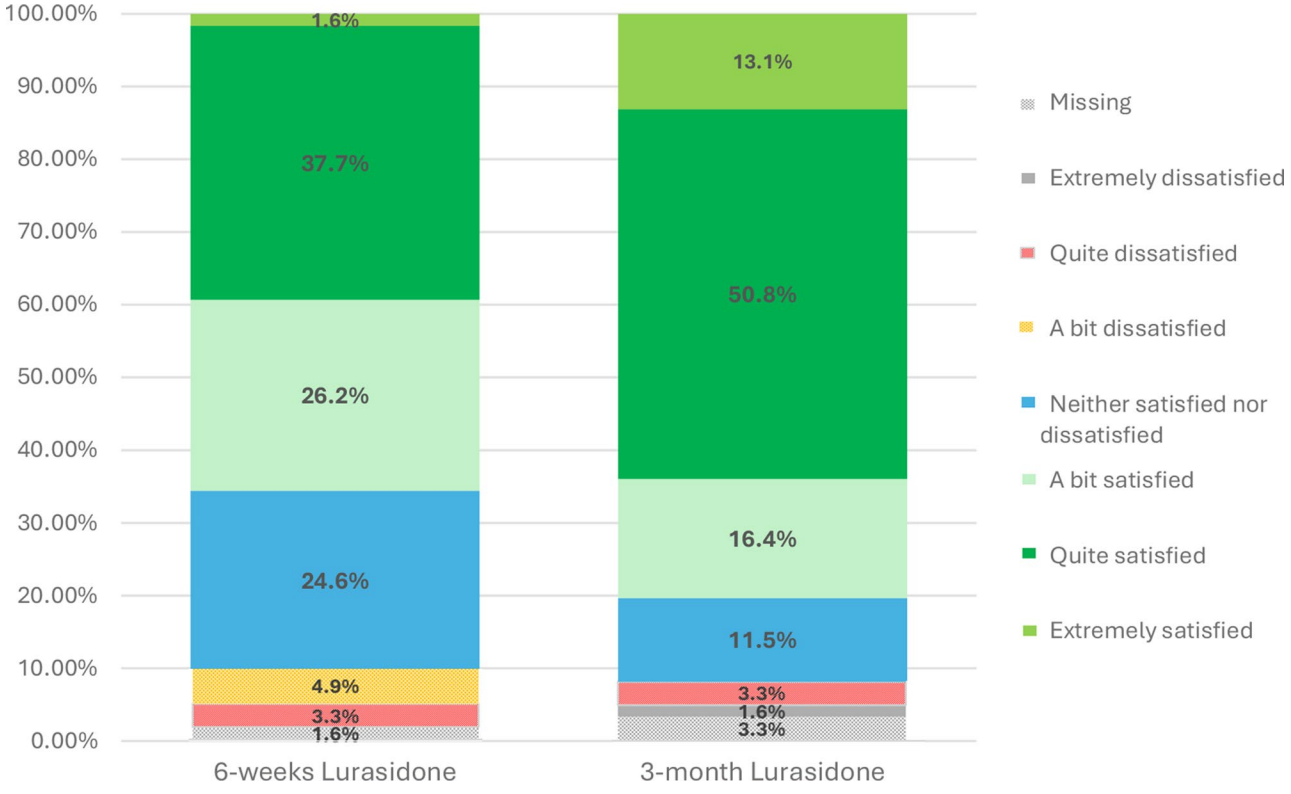

Fig. 1 Patient satisfaction with treatment and symptom relief after 6 weeks and 3 months treatment

was 0.0±2.59 vs. 0.5±1.30 (9.1±50.10% (*N*=12) vs. 8.4±20.32% (*N*=48)). It should be noted that many patients did not answer the occupational domain, especially in the younger group.

Figure 2 C and D show the individual domains over the course of the study by age group, with the same trend of improvement in mean total scores for both classes, more evident for both classes in the Interpersonal Relations and Intrapsychic Foundations domains. It should be noted that the baseline instrumental role domain is lower in the 18–25 class, probably due to the low occupational level, but the improvement trend is similar to that of the 25+class; the baseline scores of the social and intrapsychic domains appear slightly higher in the younger class.

Clinician reported outcomes

The percentage of patients rated by the investigator as "markedly" or "severely" ill on the CGI-S was 62.29% at baseline, 24.59% at week 6, and 8.20% at month 3. The percentage of "mildly ill" patients was 3.28% at baseline, 16.39% at week 6, and 27.87% at month 3. The percentage of "borderline mentally ill" patients was 0% at baseline, 4.92% at week 6, and 14.75% at month 3. The percentage of patients classified as "normal" was 0% at baseline, 0% at week 6, and 4.92% at 3 months (Fig. 3).

The total IAQ score also showed a decreasing trend, with a mean score of 32.3 at 6 weeks (median=33) and 29.7 (median=31) at 3 months (the lower the score, the better the relative treatment efficacy compared to the previous treatment).

Finally, there were no relapses or psychiatric hospitalizations during the observation period. It should be noted that at baseline, 40% of patients started treatment with lurasidone in an inpatient setting.

Safety

During the 3-month observation period, 3 adverse events were recorded, occurring in 2 patients out of 61 enrolled (3.28%). The 3 events occurred in 3 different SOCs: tachycardia (cardiac disorders), somnolence (nervous system disorders), affective disorders (psychiatric disorders); none of them were judged to be related to lurasidone.

No ADR, SAE, SADR or any AE leading to discontinuation of lurasidone occurred.

No changes in metabolic parameters were observed during the study. In addition, no hepatic, renal or ECG changes or relevant abnormalities in blood count parameters were observed.

In addition, after 6 weeks and 3 months of treatment with lurasidone, investigator assessment of the most common antipsychotic-associated signs/symptoms (somnolence, akathisia, other extrapyramidal symptoms (EPS), weight gain, prolactin elevation) compared to previous antipsychotic treatment was collected by IAQ.

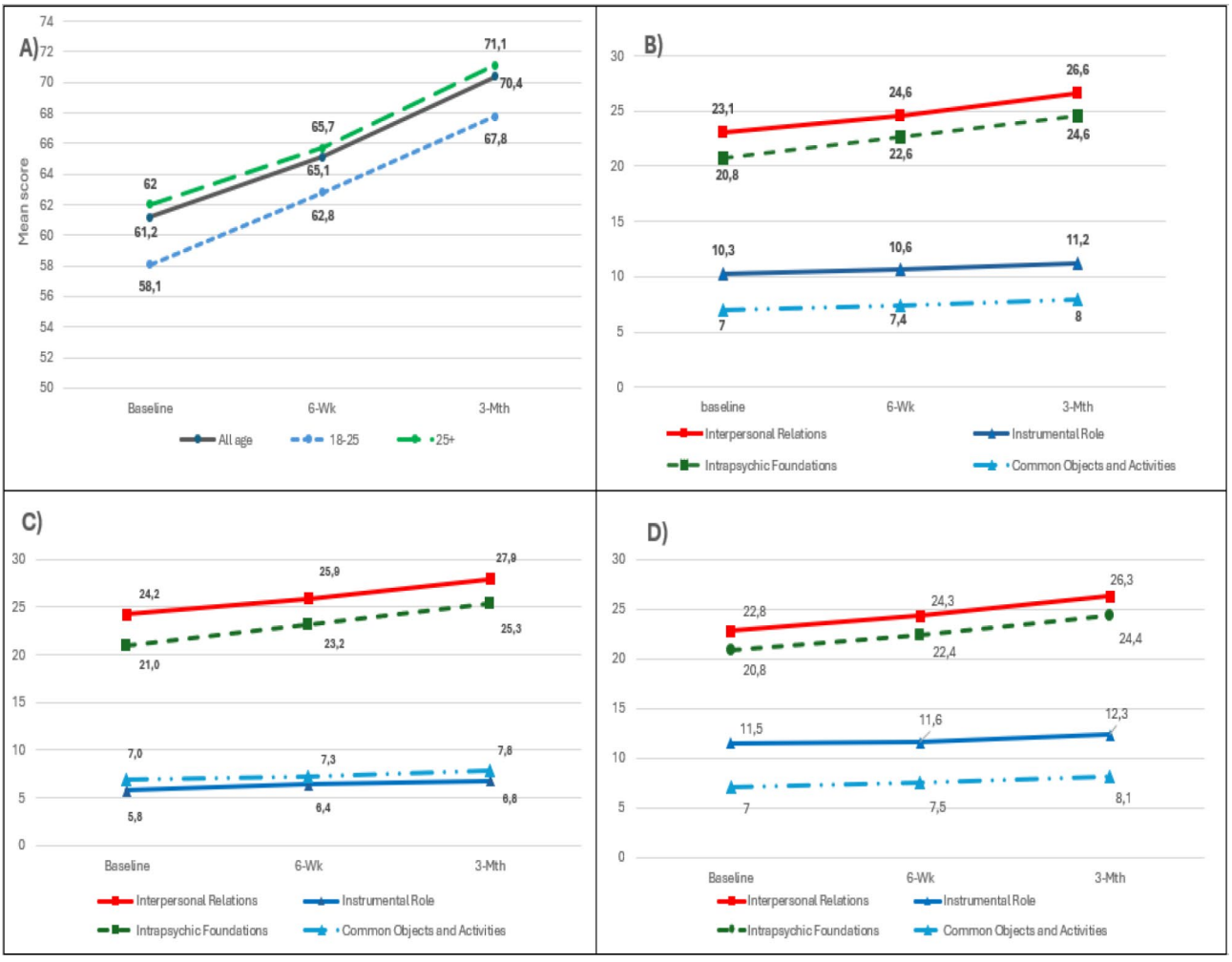

Fig. 2 QLS mean total and QLS functioning domains score during the study. QLS mean scores are shown at each study time-point [at baseline (lurasidone start), at 6-week lurasidone treatment (6-Wk) and 3 month-lurasidone treatment (3-Mth)]: (**A**) QLS total score overall population (black line), 18–25 ys old subgroup (blue line), 25+ys old subgroup (green line); (**B**) QLS Functioning domains; (**C**) QLS Functioning domains in 18–25 ys old subgroup; (**D**) QLS Functioning domains in 25+ys old subgroup. Functioning domains are: Interpersonal Relations (red line), Intrapsychic Foundations (green line), Instrumental Role (blue line) and Common Objects and Activities (light blue line)

None of the signs/symptoms were judged to have significantly worsened.

At the end of the study, a slight worsening of somnolence and akathisia was reported in 2 patients each (3.28%). However, somnolence was rated as significantly improved in 18.03% of patients ($n=11$) and slightly improved in 26.23% of patients ($n=16$). Akathisia was rated as slightly improved in 9.84% ($n=6$) of patients; other EPSs were rated as much improved in 3.28% ($n=2$) and slightly improved in 4.92% ($n=3$) of patients. Weight gain was rated as much improved in 13.11% ($n=8$) and slightly improved in 14.75% ($n=9$) of patients. Signs and symptoms of prolactin elevation were rated as much improved in 1.64% ($n=1$) and slightly improved in 6.56% ($n=4$) of patients.

In the Patient Satisfaction Questionnaire, after 6 weeks of lurasidone treatment, 62.30% of patients reported "not at all" bothersome side effects, with an additional 31.15% reporting "just a little" or "somewhat" bothersome side effects. Similar results were seen after 3 months of lurasidone, with 65.57% reporting "not at all" bothersome side effects, and an additional 26.23% reporting "just a little" or "somewhat" bothersome side effects. At both visits, a total of 3 patients (4.92%) reported "quite" or "moderately" bothersome side effects. No patient reported very or extremely bothersome side effects.

Considering the age groups, the percentage of patients who reported "not at all" or "just a little" or " somewhat " bothersome side effects at week 6 was 76.92% (10/12) in the 18–25 years old group and 97.91% (47/48) in the 25+years old group, of which the rate of patients who reported "not at all bothersome" was 30.77% ($N=4$) and 70.83% ($N=34$) respectively in the two groups. For the remaining patients, in the younger group, 2 patients

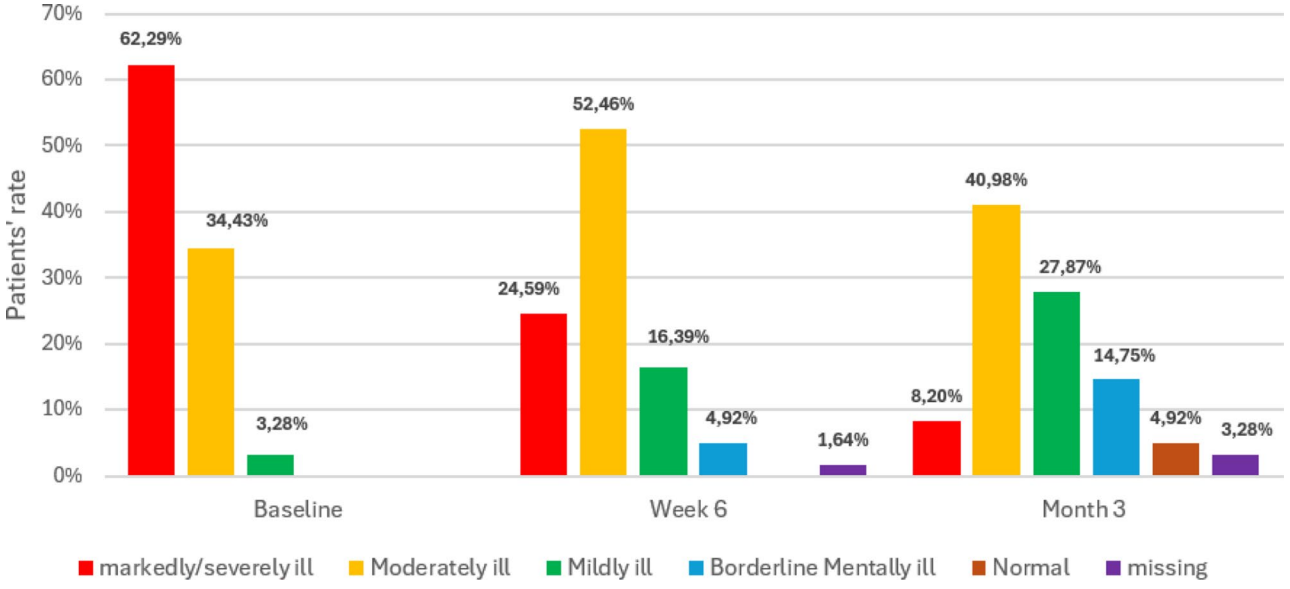

Fig. 3 CGI-S during study

reported "moderate" ($N=1$, 7.69%) and "quite" bothersome ($N=1$, 7.69%) side effects, respectively. In the 25+group, 1 patient (2.08%) reported moderately bothersome side effects. Similar rates were observed after 3 months of lurasidone treatment.

Discussion

Although second-generation antipsychotics (SGAs) have been proven to be useful therapeutic options used in clinical practice for the treatment of schizophrenia for almost thirty years, the focus on the subjective perspective of patients regarding their satisfaction, well-being and quality of life in relation to the administration of these drugs is partially lacking, despite the fact that quality of life represents a central element in selecting the appropriate treatment for people with schizophrenia [20].

The aim of this study was to evaluate treatment satisfaction and effectiveness of lurasidone on quality of life and functioning in adult patients with schizophrenia treated in real Italian clinical practice. Patients should be naive to lurasidone treatment. The QLS score, based on the patient's response to specific questions on different domains, showed a trend of improvement over time. In our study, the mean change from baseline was 4.4 at 6 weeks and 9.8 at 3 months: QLS total score ranges from 0 to 126, and a change of ≥5.3 points is considered clinically relevant [21].

Of note, the absolute change in mean total score at 6 weeks was 7.0 in the 18–25 years old group (3.7 in the 25+years old group), with a relative change of 18.3% vs. 7.4%. At 3 months, the mean absolute change in total score was 12.0 in the 18–25 group and 9.2 in the 25+group, with relative changes of 28.1% and 16.5%, respectively.

When analysing individual domains, improvements in intrapsychic and relational functions were more evident than in occupational domains, possibly due to the fact that about 60% of the patients were unemployed.

Notably, baseline instrumental role domain scores were lower in the 18–25 years old group, probably due to lower occupational level, whereas baseline social and intrapsychic domain scores appeared slightly higher in the younger age group.

In addition, the continuous improvement trend from 6 to 12 weeks of treatment is consistent with the results of a double-blind, placebo-controlled study in which social functioning was measured by the PANSS in 478 patients treated with lurasidone [22]. During the 6-week double-blind period, social functioning improved compared to placebo ($p<0.01$) and continued to improve over the course of the 12-week extension treatment with lurasidone, with successively lower scores on the 4-item prosocial subscale of the PANSS (change of -3.0 from double-blind baseline to week 6; mean score change of -4.2 from double-blind baseline to week 12 of the extension phase). The effects of lurasidone on social functioning appeared to be comparable to those reported for other atypical antipsychotics.

Consistently, an improvement in the severity of schizophrenia according to the clinician-rated CGI-S was observed in this study, as highlighted by the decrease in the proportion of patients defined as markedly ill and severely ill, and the increase in the proportion of patients defined as normal, borderline mentally ill and mildly ill, after lurasidone therapy compared to before lurasidone

initiation, with an improvement trend from 6 weeks to 3 months of observation.

In parallel, the level of patient satisfaction shows an increase over time, with 65.57% and 80.32% of patients reporting somewhat, quite or extremely satisfied (of which 39.34% and 63.93% quite or very satisfied) at week 6 and 3 months, respectively. Similar results were observed for both age groups.

A continuous improvement was observed in all efficacy parameters measured after 3 months of treatment compared to baseline and the first 6 weeks of lurasidone treatment, which is consistent with the fact that the mean titration time of lurasidone was almost 90 days and that a better result was obtained once the optimal dosage was reached. This is also consistent with findings from long-term studies showing that lurasidone has the preventive effects on relapse and improves cognitive and functional performance in patients with schizophrenia, especially in long-term treatment [23].

The safety profile was also consistent with CTs: lurasidone was well tolerated with no lurasidone-related adverse events reported. Overall, three adverse events occurred in two patients out of 61 enrolled (3.28%), but none were considered related to lurasidone.

No change in metabolic parameters or weight gain was observed during the study, and no hepatic, renal, ECG changes or relevant abnormalities in blood count parameters were observed. No SAE, SADR, or AE leading to discontinuation of lurasidone occurred.

In addition, none of the most common antipsychotic-associated signs/symptoms (somnolence, akathisia, other EPS, weight gain, prolactin elevation) significantly worsened compared to the previous antipsychotic after 3 months of therapy, as assessed by investigator IAQ. At the end of the study, only a slight worsening of somnolence and akathisia was reported in 2 patients each (3.28%), which was not significant (no AEs reported). On the contrary, some improvement in most symptoms was noted: somnolence was rated as significantly or slightly improved in approximately 45% of patients. Akathisia was rated as slightly improved in approximately 10% of patients; other EPSs were rated as much improved in 3.28% of patients and slightly improved in 4.92% of patients. Weight gain was rated as much improved or slightly improved in approximately 25% of patients. Signs and symptoms of prolactin elevation were rated as much improved in 1.64% and slightly improved in 6.56% of patients. The investigator's assessment was consistent with the patients' responses to the question about bothersome side effects, with more than 90% of the subjects reporting that they were not bothered or only slightly bothered.

Despite the limited observation period of 3 months, treatment persistence was assessed and only 2 of 61 patients discontinued treatment (both in the first weeks of titration) after starting lurasidone, confirming the above clinician and patient judgments of efficacy, tolerability and safety.

However, there were some methodological concerns related to the assessment of satisfaction, subjective quality of life, and well-being. Validated instruments were used in this study, but there is still a lack of a gold standard assessment of patients' subjective perspective on antipsychotic treatments.

In addition, the study was conducted in 3 Italian sites, and the generalizability of our findings to other health care systems is difficult to ascertain. Nevertheless, our baseline QLS scores are very similar to other real-life studies: in a study conducted in Japan with 55 patients, which aimed to investigate clinical factors related to social functioning in people with schizophrenia, the QLS scores were overlapping (60.63±20.86 total score, 20.27±8.61 interpersonal relations; 11.34±5.84 instrumental role, 21.84±7.28 intrapsychic foundations; 7.18±2.39 common objects and activities) [24].

In addition, the sample size of the study was relatively small and the observation period limited to 3 months, which may have prevented the observation of persistence and the impact on it of variables (e.g. rare side effects) that occur infrequently. In particular, the sample in the 18–25 age group was very small, which limits any consideration of this subgroup.

Some other limitations in interpreting the results must be considered due to the nature of the study. This was an observational, non-interventional, non-randomized, non-controlled study, lacking of control group and/or comparison with other pharmacological regimens. Patients were recruited after a physician had already decided to prescribe lurasidone. Patients received the drug at a dose and titration schedule determined by the treating physician independent of the study. Treatment was recorded but not specified in the study protocol, and patients were allowed to receive any concomitant medication as determined by the treating physician. All of the above could have confounded the study results.

Finally, although the lack of a control group limits the ability to attribute results to treatment and the ability to rule out a placebo effect, the improvement in all parameters considered over time from the start of lurasidone can be seen as an indicator of a treatment-related effect.

Conclusions

This study suggests that lurasidone is a treatment option for schizophrenia that can positively impact patients' subjective well-being, quality of life, functional capacity and satisfaction. There was a sustained improvement in all patient-reported outcomes measured after 3 months of treatment compared to baseline and the first 6 weeks

of lurasidone treatment. The safety profile of lurasidone was also consistent with previous clinical trials, with minimal effects on body weight, a low risk of clinically meaningful changes in glucose, lipids or electrocardiographic parameters, and a modest risk of extrapyramidal side effects, akathisia and prolactin elevation. However, it should be noted that the study had some limitations, such as the small sample size and the limited observation period of 3 months, which may have prevented the observation of rare side effects that occur infrequently. In addition, the study was observational and non-interventional, non-randomized and non-controlled, which may have influenced the study results. Future studies should address these limitations and further investigate the effects of lurasidone on subjective well-being, quality of life, and functional capacity in patients with schizophrenia. In addition, a gold standard assessment of patients' subjective perspective on antipsychotic treatment should be developed to better assess treatment satisfaction and effectiveness. Overall, lurasidone represents a valid treatment option for patients with schizophrenia, but further research is needed to fully understand its potential benefits and limitations.

Clinical implications

The results of this study underscore the potential of lurasidone as a valuable treatment option for adult patients with schizophrenia in real-world clinical settings. Over a 3-month observation period, lurasidone not only demonstrated a favourable safety profile, but also produced significant improvements in patient-reported outcomes, including treatment satisfaction, quality of life (QoL), and functional capacity. These improvements are particularly clinically relevant as they are consistent with a patient-centred approach that prioritizes subjective well-being and daily functioning in addition to symptom management.

The significant improvements in QoL and satisfaction suggest that lurasidone may effectively address the broader aspects of schizophrenia treatment, particularly for patients for whom improving daily functioning and life satisfaction are primary goals.

Lurasidone had minimal metabolic side effects, with no significant changes in body weight, glucose levels or lipid profiles. In addition, the low incidence of extrapyramidal symptoms, akathisia and prolactin elevation supports the favourable tolerability profile of lurasidone, potentially reducing the burden of side effects commonly associated with other antipsychotic medications.

The results of this observational study are consistent with those of randomized clinical trials and support the long-term safety and efficacy of lurasidone in the treatment of schizophrenia. Importantly, the real-world context of this study enhances its generalizability to routine clinical practice and provides confidence in the use of lurasidone in diverse patient populations.

Despite the promising results observed in this study, the relatively short follow-up period suggests that future research should explore longer-term effects, including relapse prevention and sustained functional recovery. In addition, further investigation of the effects of lurasidone on specific subgroups, such as younger patients and those with higher occupational demands, would be valuable.

In conclusion, lurasidone offers a clinically meaningful option for the treatment of schizophrenia, particularly for patients who prioritize improvements in quality of life and functional outcomes. Its safety and efficacy make it a versatile antipsychotic, particularly for individuals with metabolic concerns or those seeking to avoid other significant side effects, which are relatively low for lurasidone compared with some other antipsychotics.

Abbreviations

ADR	Adverse Drug Reaction
AE	Adverse Event
CGI-S	Clinical Global Impression-Severity
CT	Clinical Trial
ECG	Electrocardiogram
eCRF	electronic Case Report Form
EPS	Extrapyramidal Symptoms
GAF	Global Assessment of Functioning
HbA1c	Glycated Haemoglobin
HDL-C	High-Density Lipoproteins-Cholesterol
IAQ	Investigator's Assessment Questionnaire
IMP	Investigational Medicinal Product
LDL-C	Low-Density Lipoproteins -Cholesterol
PANSS	Positive and Negative Syndrome Scale
QLS	Quality of Life Scale
QoL	Quality of Life
SADR	Serious Adverse Drug Reaction
SAE	Serious Adverse Event
SGA	Second-Generation Antipsychotic

Supplementary Information

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Supplementary Material 1

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Author contributions

The authors M. M., M. A. M., N. F. are Angelini S.p.A. employees and they have conceptualised and coordinated the study. C. S. managed the study for the CRO Hippocrates Research S.r.l. delegated by Angelini S.p.A. in clinical operations. P. M. (Hippocrates Research S.r.l.) drafted the study protocol and the article in collaboration with the author A. F., who was appointed on behalf of Angelini on the study design and final review of results. He didn't participate as Investigator. All the remaining authors are Investigators belong to Hospital or University. A regular study contract has been signed for the specific activities envisaged. All authors revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the ethics committee at each participating centre (Comitato Etico Regione Toscana – Area Vasta Sud Est; Comitato Etico di Brescia; Comitato Etico Lazio 2) and performed in accordance with good clinical practice and local regulatory requirements. Written informed consent was obtained from all patients and consent could be withdrawn at any time.

Consent for publication
Not applicable.

Competing interests
Alessandro Cuomo is /has been a consultant and/or a speaker and/or has received research grants from Angelini, Boheringer Ingelheim, Italfarmaco, GSK, Lundbeck, Janssen, Otsuka, Pfizer, Recordati, Rovi, Sunovion, Teva, Viatris. Andrea Fagiolini is /has been a consultant and/or a speaker and/or has received research grants from Angelini, Boheringer Ingelheim, Idorsia, Italfarmaco, Lundbeck, Janssen, Medicamenta, Medifar, Otsuka, Pfizer, Recordati, Rovi, Sunovion, Teva, Viatris. Patrizia Mascagni and Claudia Santini are Hippocrates Research S.r.l. employees (CRO delegated for study conduction). Marco Micillo, Marta Antonia Manes, Nathalie Falsetto are Angelini S.p.A. employees. The other authors declare no conflict of interest.

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