Survey Report

Perception mapping of clinicians on usage pattern of olanzapine and fluoxetine combination in treating psychotic depression patient

Version No.: 1.1

The study was conducted according to the approved protocol and in compliance with the protocol, Good Clinical Practice (GCP), and other applicable local regulatory requirements.

Table of content

1 INTRODUCTION

Psychotic depression is defined as a condition characterized solely by severe impairment, with or without the presence of delusions and hallucinations, which are traditional defining features of psychosis [1]. Severe depression accompanied by hallucinations had a different response to treatment than major depression without delusions, and the diagnostic and statistical manual of mental disorders DSM-III changed the criteria for psychotic depression to include delusions, hallucinations or depressed stupor [2]. A trait termed psychosis can be present in many different disorders, such as schizophrenia, bipolar disorder, schizoaffective disorder, MDD, and possibly other conditions that are complicated by psychotic features, like delusional disorder, PTSD, and certain personality disorders. The psychotic trait can be passed down apart from other characteristics like mood or thinking dysregulation [3].

Bipolarity is a powerful predictor of psychosis during a mood illness [4]. 48.5% of persons with psychotic depression in community samples were diagnosed with bipolar I disorder, and 10.5% with bipolar II illness [5]. Psychotic depression differs from non-psychotic depression in terms of severity, incapacity, diminished placebo response, prolonged duration of episodes, and recurrence of psychotic symptoms [6]. According to treatments, antipsychotics counter psychosis while antidepressants counter depression. Consequently, it would appear reasonable to use an antipsychotic to treat psychotic symptoms and an antidepressant to treat depressive symptoms in cases of psychotic depression.

Management of Psychotic depression can be done efficiently by combination therapy of two drugs olanzapine and fluoxetine combination (OFC) is the most efficient way to tackle psychotic depression. OFC is an approved treatment for certain mood disorders, including psychotic depression and bipolar I depression. This combination leverages the antipsychotic properties of olanzapine and the antidepressant effects of fluoxetine to address both the psychotic and depressive symptoms in patients. olanzapine/fluoxetine combination (OFC) is effective in treating bipolar depressive episodes and major depression with psychotic features. In several trials, the OFC treatment resulted in rapid reductions in Montgomery-Asberg depression rating scale scores, indicating significant improvements in depressive symptoms [7].

OFC combination therapy has been validated for its safety and efficacy through various clinical studies [8]. Successful treatment of treatment-resistant depression (TRD) with OFC is associated with changes in brain metabolism similar to those observed in treatment-responsive major depression, highlighting its biological impact on the brain. The FDA has approved OFC in capsule form for adult patients, ensuring it meets rigorous safety and efficacy standards. This approval underscores its reliability as a treatment option for clinicians managing psychotic depression [9].

This study employs a questionnaire-based survey conducted among physicians across India to gather insights into their perspectives on the effectiveness, safety and utilization patterns olanzapine and fluoxetine combination in treating psychotic depression patient. Physicians' clinical experiences, patient outcomes, and adherence to treatment protocols are critical factors in assessing the real-world applicability of this drug. By evaluating these perspectives, the study aims to provide valuable data that can inform clinical practice and guide treatment strategies tailored to the management of psychotic depression.

2 RATIONALE OF THE STUDY

The rationale for this study was to gather comprehensive insights into the clinical use and efficacy, safety and utilization patterns of olanzapine and fluoxetine combination in treating psychotic depression patient among Indian patients. Understanding the prescribing patterns, utilization patterns, treatment preferences, and perceived efficacy among physicians will aid in optimizing therapeutic strategies and improving patient outcomes.

The purpose of this study was to evaluate the utilization pattern of olanzapine and fluoxetine combination in Indian patients affected with threatened abortion. This investigation aims to assess understand the usage, patterns of prescribing improving patient compliance, and determining its long-term safety profile..

3 STUDY OBJECTIVE

The primary objective of this study was to evaluate the protective effects and utilization patterns of olanzapine and fluoxetine combination in Indian patients suffering with psychotic depression.

4 METHODS

This cross-sectional, questionnaire-based study aimed to gather insights from Indian physicians managing patients with psychotic depression regarding their experiences and practices with the olanzapine and fluoxetine combination. The study was designed to capture data on physicians' clinical experiences, prescribing practices, and perceptions of this medication regimen. A total of 90 physicians were targeted to ensure a representative sample for meaningful statistical analysis.

Physicians were identified and invited to participate through professional networks and medical associations. Prior to participation, they received detailed information about the study's purpose and procedures. The survey, consisting of 15 questions, was administered electronically to facilitate ease of participation. Responses were collected and securely stored to maintain confidentiality.

Data analysis involved both descriptive and inferential statistics. Descriptive statistics summarized demographic information and response frequencies, providing an overview of the participants' characteristics and general trends. Inferential statistics, including chi-square tests and logistic regression, were employed where appropriate to explore associations between physician characteristics and their perceptions and prescribing behaviors regarding the olanzapine and fluoxetine combination.

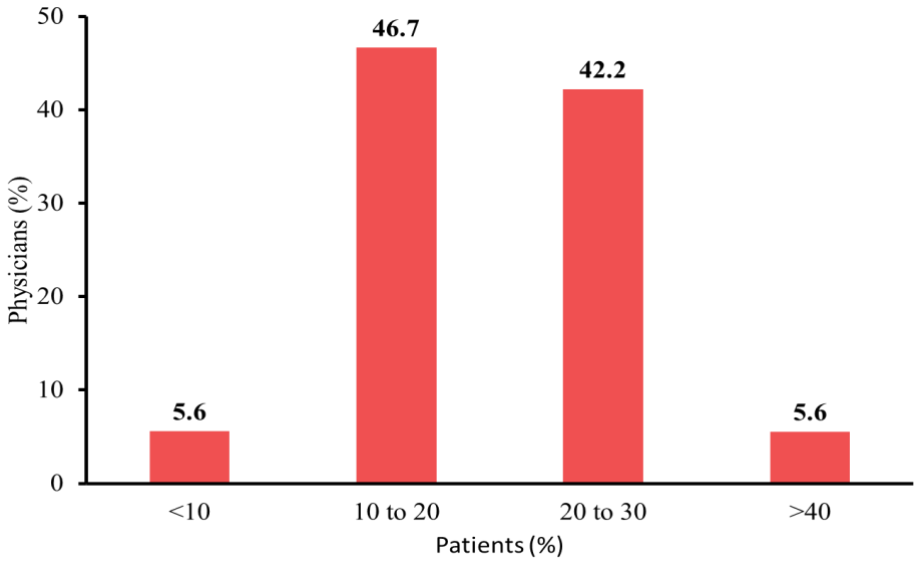
No treatment was administered as part of the study; the focus was solely on collecting and analyzing physicians' perspectives and practices. The findings were compiled into a comprehensive report, which was subsequently shared through scientific publications and/or presented at relevant conferences, if deemed suitable. The study adhered to ethical principles outlined in the Declaration of Helsinki, with ethical approval obtained from an Independent Ethics Committee, and all responses were anonymized to ensure participant confidentiality.

5 RESULTS

A total of 90 physicians participated in the survey. Below is the summary of the responses.

Question 1: In your clinical practice, what is the percentage of patients with bipolar disorder?

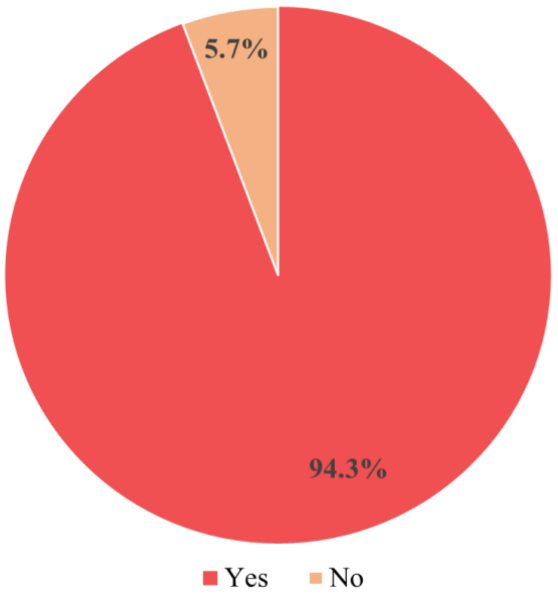
Options	Number of physicians (N=90)
<10%	5 (5.6)
10-20%	42 (46.7)
20-30%	38 (42.2)
>40%	5 (5.6)
Data presented as n (%).	



- About 46.7% of physicians reported, that 10-20% of their patients have bipolar disorder.
- A significant portion (42.2%) reported that 20-30% of their patients have bipolar disorder. Only a small number of physicians (5.6%) reported that less than 10% of their patients have bipolar disorder.
- Similarly, another small group (5.6%) reported that more than 40% of their patients have bipolar disorder.

Question 2: In your clinical practice, do you consider Olanzapine and Fluoxetine combination is first line of treatment option for acute bipolar disorder?

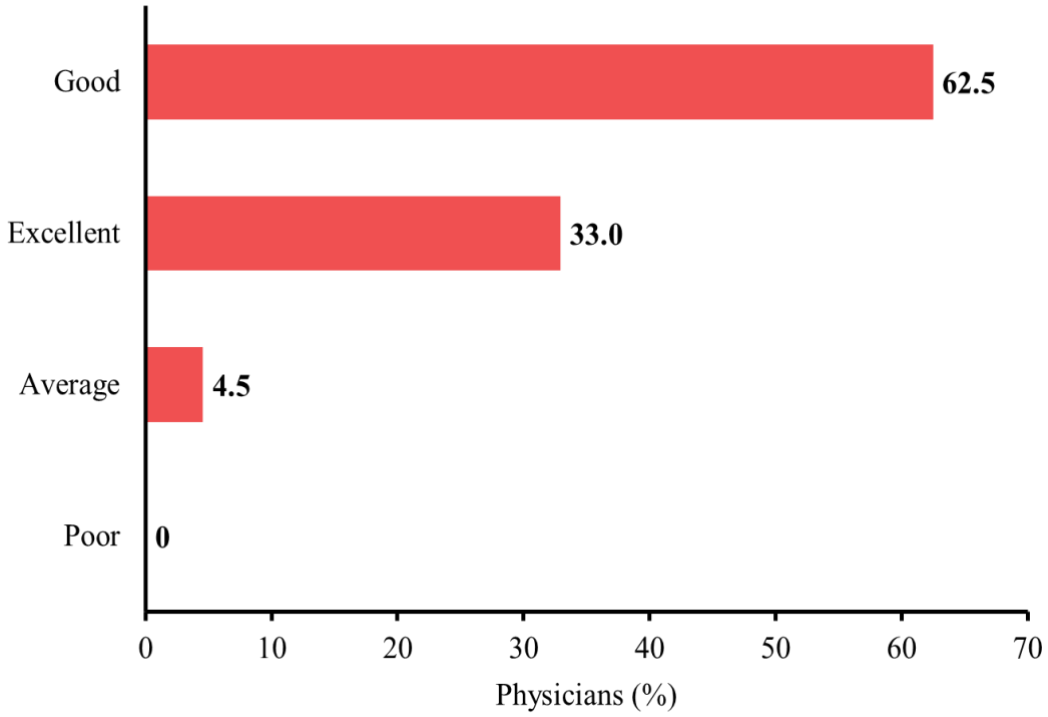
Options	Number of physicians (N=88)
Yes	83 (94.3)
No	5 (5.7)
Data presented as n (%).	



- A majority of physicians (94.3%) consider the combination of olanzapine and fluoxetine as a first-line treatment option for acute bipolar disorder.
- Only a small percentage of physicians (5.7%) do not consider this combination as a first-line treatment option.

Question 3: In your clinical practice, how do you rate Olanzapine and Fluoxetine combination therapy in the management bipolar disorder in terms of safety?

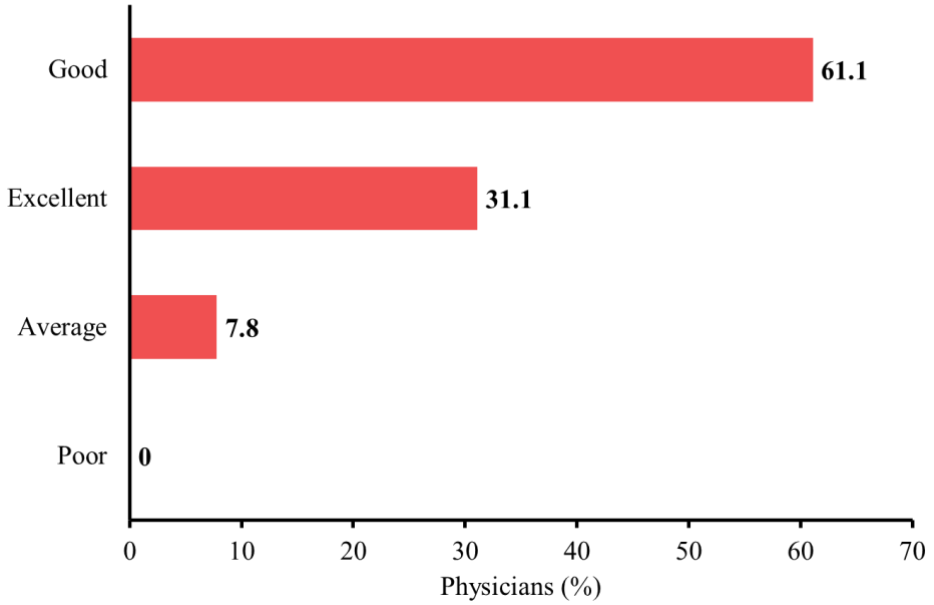
Options	Number of physicians (N=88)
Good	55 (62.5)
Excellent	29 (33)
Average	4 (4.5)
Poor	0
Data presented as n (%).	



- The majority of physicians (62.5%) rated good, to olanzapine and fluoxetine combination therapy in the management bipolar disorder in terms of safety.
- A substantial portion of physicians (33.0%) rated the safety as Excellent, reflecting a high level of confidence in the therapy's safety.
- Contrast, a smaller percentage of physicians (4.5%) rated the safety as Average. None physicians rated the therapy's safety as Poor.

Question 4: In your clinical practice, how do you rate Olanzapine and Fluoxetine combination therapy in the management bipolar disorder in terms of efficacy?

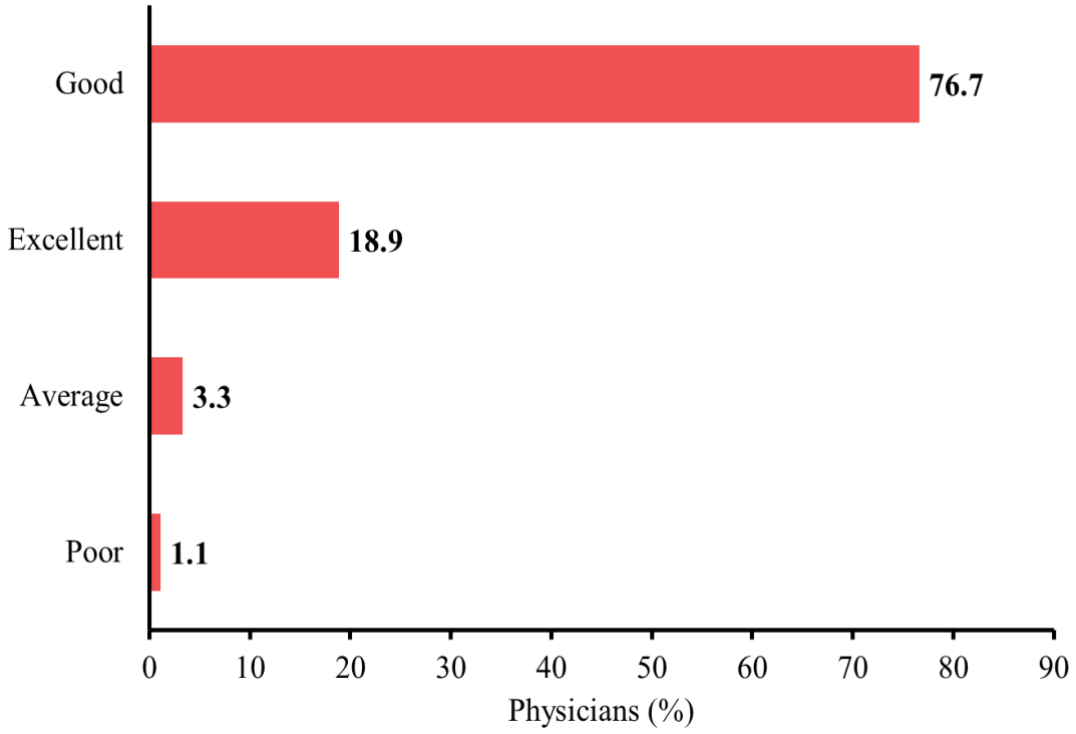
Options	Number of physicians (N=90)
Good	55 (61.1)
Excellent	28 (31.1)
Average	7 (7.8)
Poor	0
Data presented as n (%).	



- The majority of physicians (61.1%) rated the efficacy of the olanzapine and fluoxetine combination therapy as good during their clinical practices.
- About 31.1% of physicians rated it as Excellent, indicating high satisfaction with the therapy's performance. While, a smaller percentage 7.8% rated its efficacy as Average.
- None physicians rated the therapy's efficacy as Poor, which underscores a general agreement that the olanzapine and fluoxetine combination therapy is effective and beneficial for most patients.

Question 5: In your opinion, how is the tolerability of Olanzapine and Fluoxetine combination?

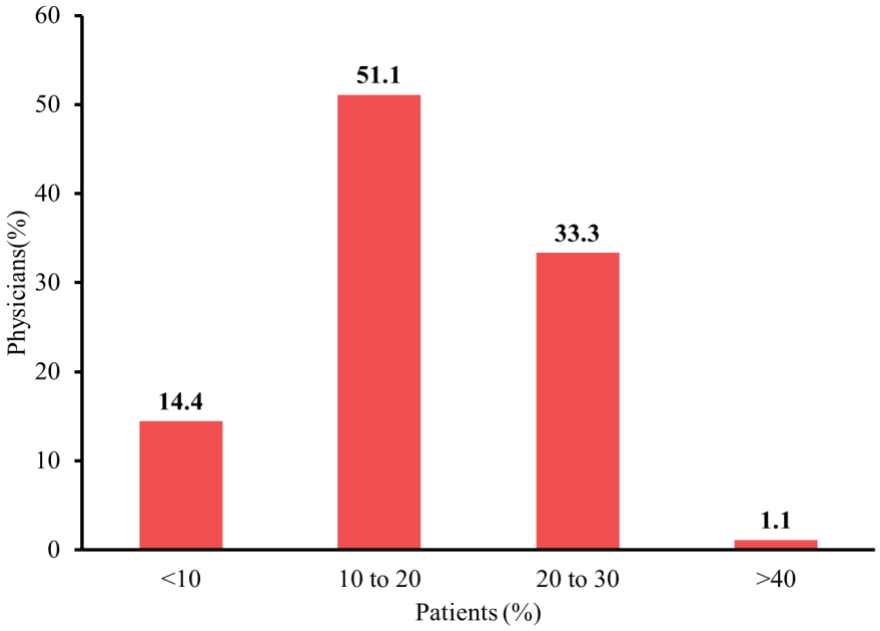
Options	Number of physicians (N=90)
Good	69 (76.7)
Excellent	17 (18.9)
Average	3 (3.3)
Poor	1 (1.1)
Data presented as n (%)	



- A majority (76.7%) rated good for the tolerability of the olanzapine and fluoxetine combination therapy indicating that most physicians find the therapy.
- About, 18.9% of physicians rated it as excellent. However, a small percentage (3.3%) rated the tolerability as average.
- Notably, only 1 physician (1.1%) rated the tolerability as poor, reflecting that very few physicians observed significant tolerability concerns with the therapy.

Question 6: In your clinical practice, what is the percentage of patients with treatment resistant depression?

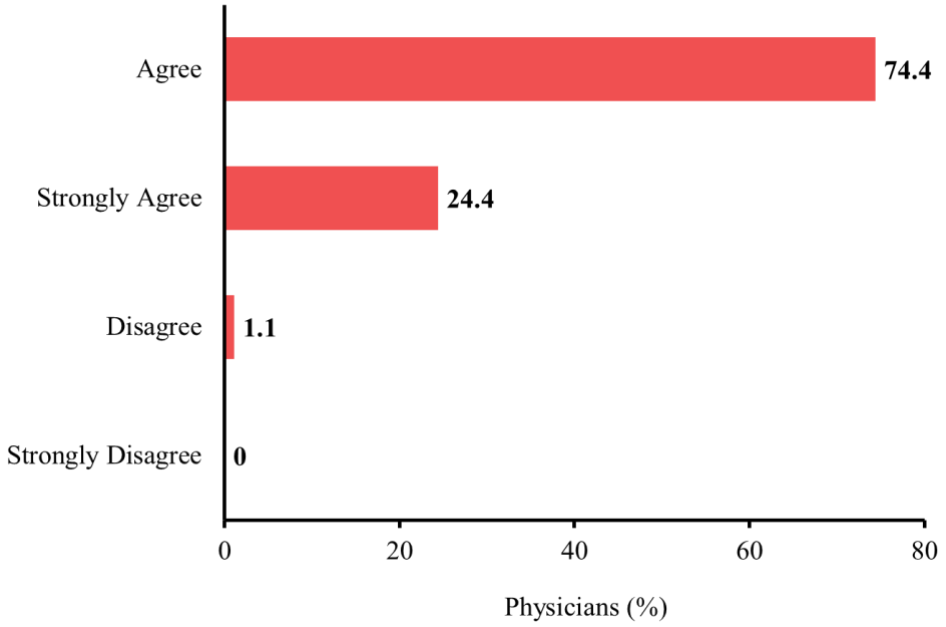
Options	Number of physicians (N=90)
<10%	13 (14.4)
10-20%	46 (51.1)
20-30%	30 (33.3)
>40%	1 (1.1)
Data presented as n (%).	



- The majority of physicians (51.1%) observed that 10-20% of their patients have treatment-resistant depression during their clinical practice.
- Around 33.3% of physician observed that 20-30% of their patients had treatment resistant depression.
- A smaller group 14.4% reports less than 10% of their patients as treatment-resistant.
- Very few 1.1% have a patient population with over 40% treatment-resistant depression.

Question 7: In treatment resistant depression, Olanzapine and Fluoxetine combination therapy offers higher remission and response rate than monotherapy. Do you agree?

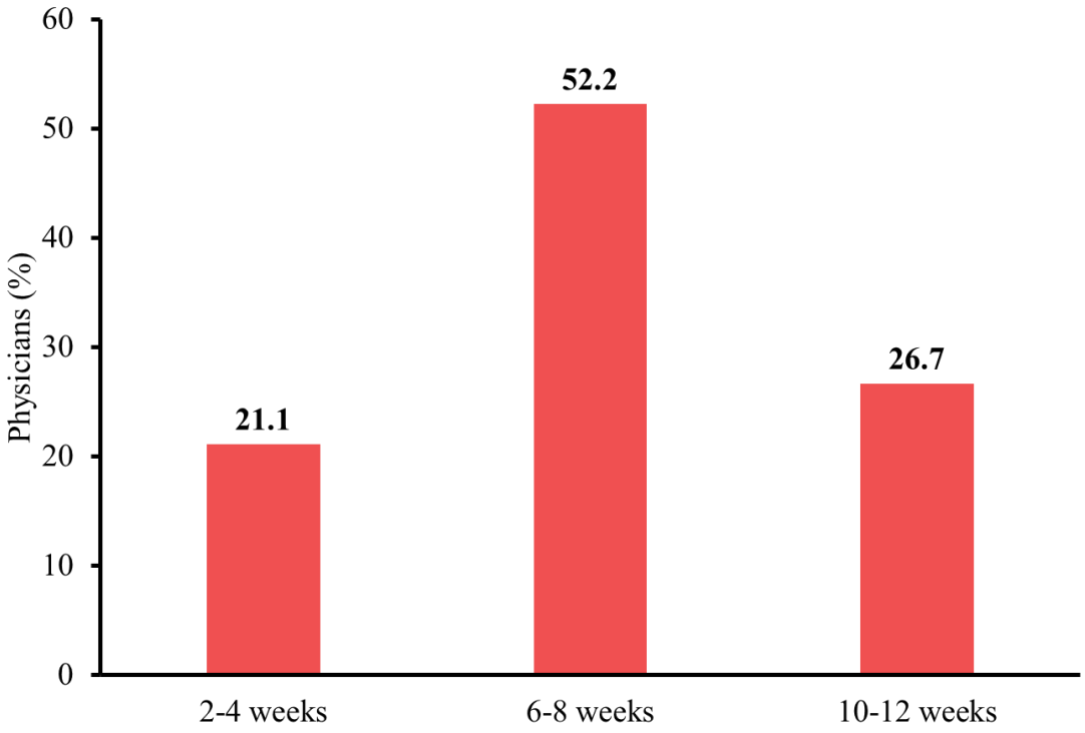
Options	Number of physicians (N=90)
Agree	67 (74.4)
Strongly Agree	22 (24.4)
Disagree	1 (1.1)
Strongly Disagree	0
Data presented as n (%).	



- Majority (74.4%) of physicians agree that olanzapine and fluoxetine combination therapy offers higher remission and response rates than monotherapy.
- About 24.4% of physicians strongly agree that olanzapine and fluoxetine combination therapy offers higher remission and response rates than monotherapy.
- Only 1 physician (1.1%) disagrees, and none strongly disagree that olanzapine and fluoxetine combination therapy offers higher remission and response rates than monotherapy.

Question 8: In your clinical practice, what is the duration of treatment with the combination of olanzapine and fluoxetine for patients with bipolar depression?

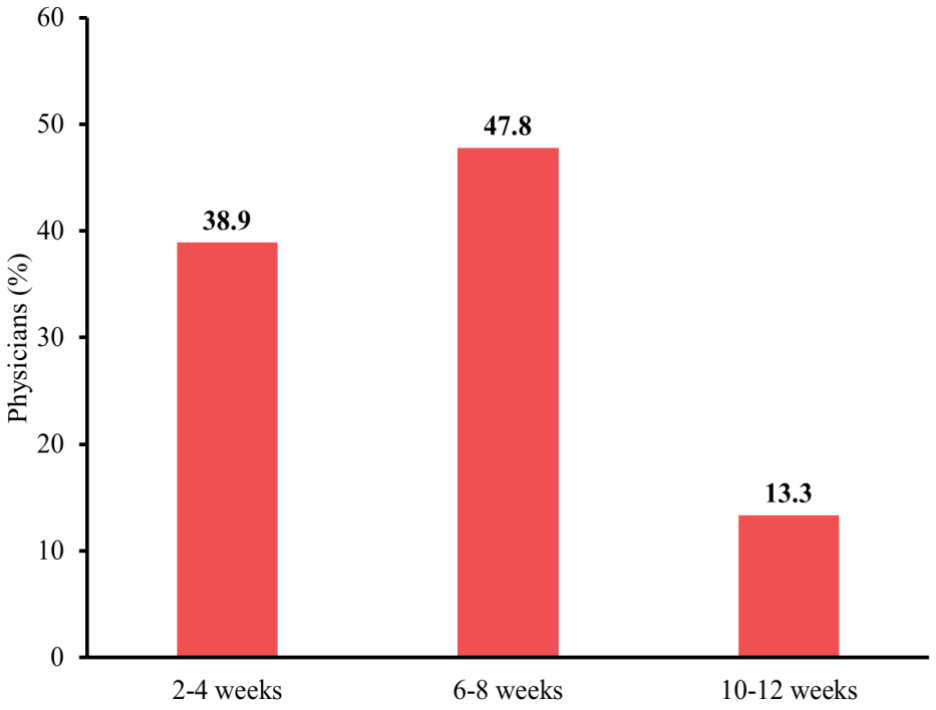
Options	Number of physicians (N=90)
2-4 weeks	19 (21.1)
6-8 weeks	47 (52.2)
10-12 weeks	24 (26.7)
Data presented as n (%).	



- The majority of physicians (52.2%) recommend a treatment duration of 6-8 weeks with the combination of olanzapine and fluoxetine for patients with bipolar depression.
- Around 26.7% of physician recommends a longer duration of 10-12 weeks. Meanwhile, a smaller group of physicians (21.1%) supports a shorter treatment duration of 2-4 weeks with combination of olanzapine and fluoxetine for patients with bipolar depression.

Question 9: In your clinical practice, what is the duration of treatment after which patient reports positive outcomes with the combination of olanzapine and fluoxetine for patients with bipolar depression?

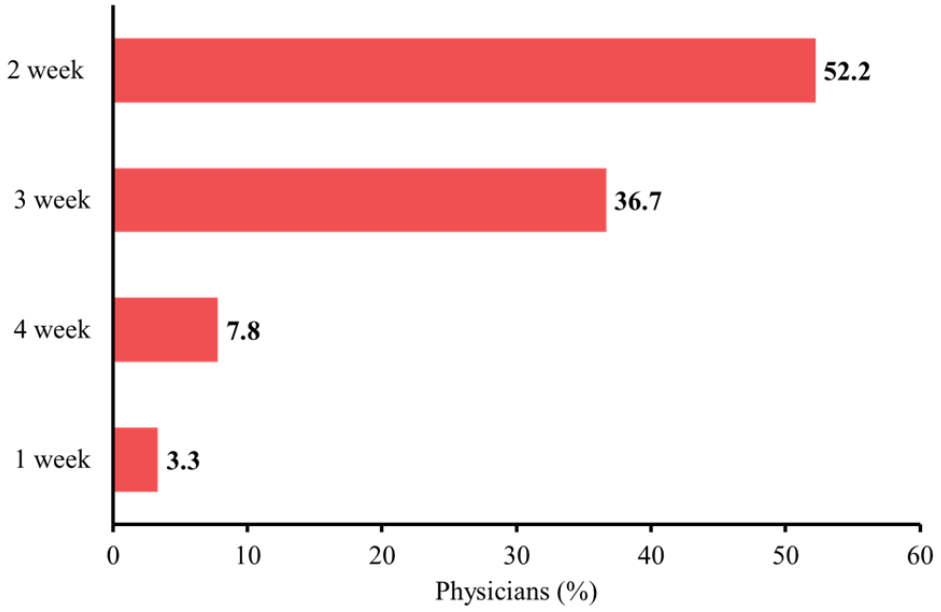
Options	Number of physicians (N=90)
2-4 weeks	35 (38.9)
6-8 weeks	43 (47.8)
10-12 weeks	12 (13.3)
Data presented as n (%).	



- The largest group of physicians (47.8%) reported that patients begin to see positive outcomes after 6-8 weeks of treatment.
- The largest group of physicians (47.8%) reported that patients begin to see positive outcomes after 6-8 weeks of treatment.
- A smaller percentage of physicians (13.3%) reported that patients see positive outcomes after 10-12 weeks of treatment.

Question 10: How long should a patient be stabilized on the initial dose of OFC before considering a dose increase?

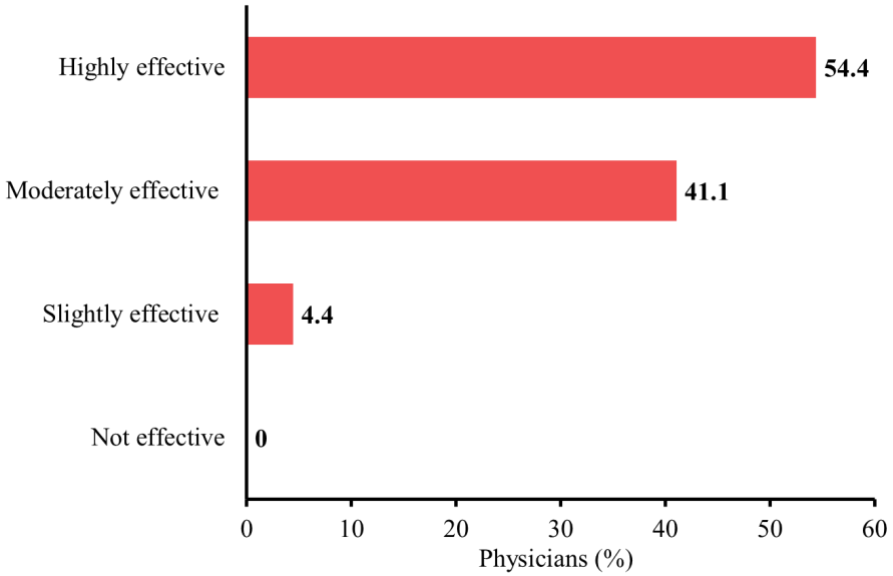
Options	Number of physicians (N=90)
2 weeks	47 (52.2)
3 weeks	33 (36.7)
4 weeks	7 (7.8)
1 weeks	3 (3.3)
Data presented as n (%).	



- Majority of physicians (52.2%) recommended stabilizing a patient on the initial dose of OFC for two weeks before considering a dose increase.
- A significant portion (36.7%) advised a stabilization period of three weeks. A smaller percentage of physicians (7.8%) recommended stabilizing for four weeks. While only a few (3.3%) suggested a stabilization period of one week.

Question 11: In your clinical practice, which of the following statements best describes the efficacy of olanzapine and fluoxetine combination in treating psychotic depression?

Options	Number of physicians (N=90)
Highly effective	49 (54.4)
Moderately effective	37 (41.1)
Slightly effective	4 (4.4)
Not effective	0
Data presented as n (%).	

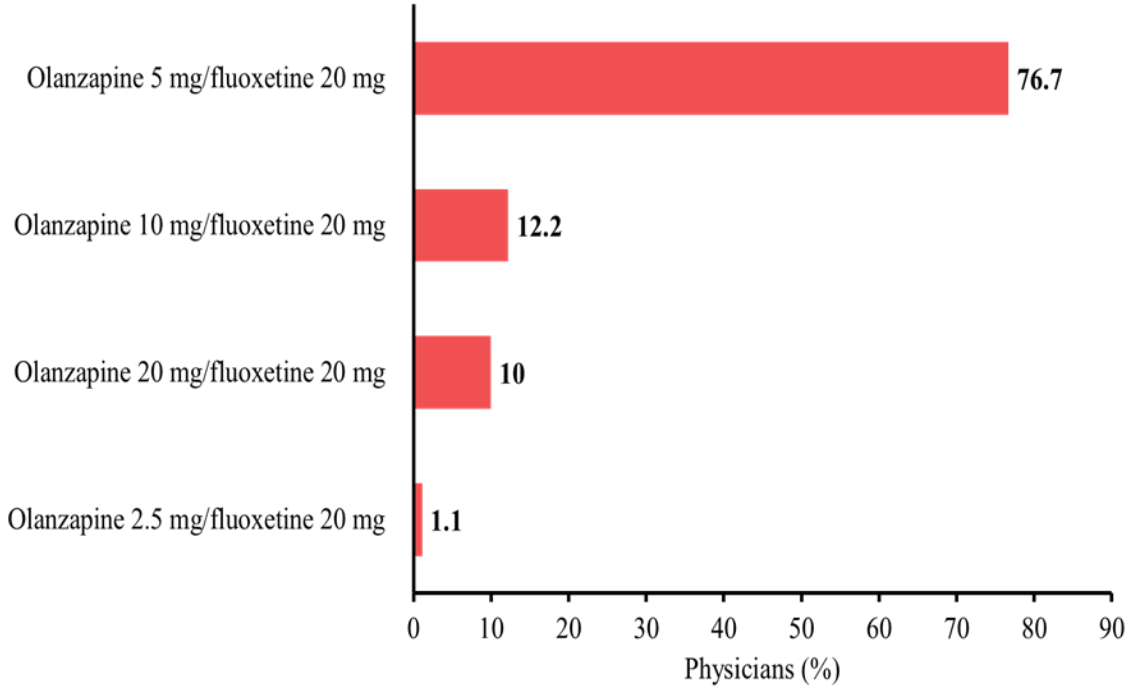


- The majority of physicians (54.4%) considered the olanzapine and fluoxetine combination to be highly effective in treating psychotic depression.
- Around 41.1% of physicians rated it as moderately effective. A small percentage (4.4%) deemed it slightly effective, and no physicians (0%) found it ineffective.

  This data indicates strong support among physicians for the combination's efficacy, with most regarding it as highly effective.

Question 12: In your clinical practice, what is the starting dose of olanzapine in the combination therapy?

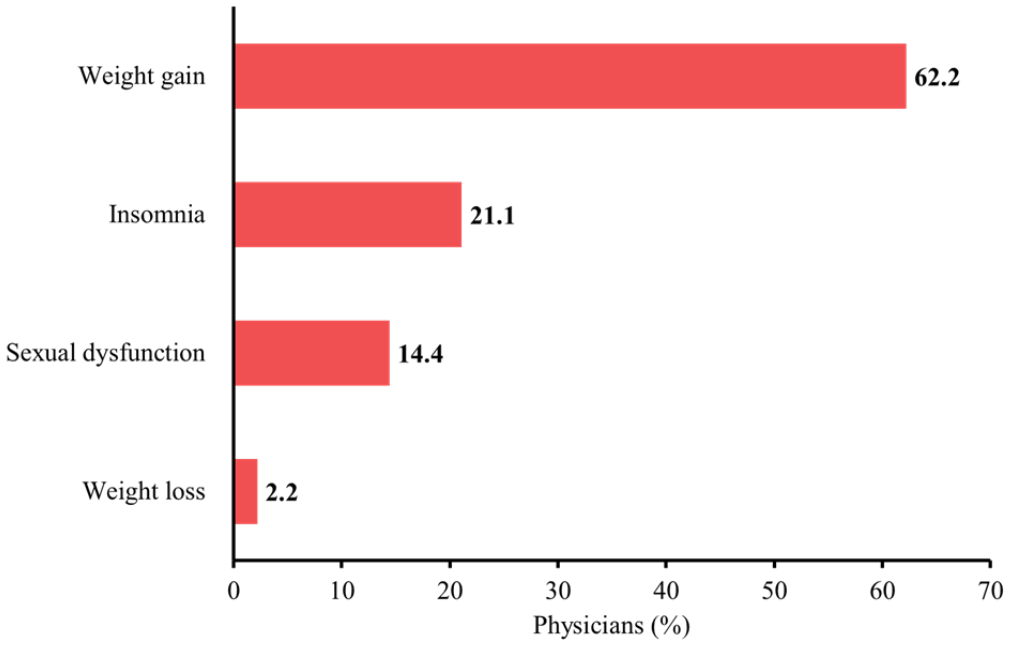
Options	Number of physicians (N=90)
Olanzapine 5 mg/fluoxetine 20 mg	69 (76.7)
Olanzapine 10 mg/fluoxetine 20 mg	11 (12.2)
Olanzapine 20 mg/fluoxetine 20 mg	9 (10)
Olanzapine 2.5 mg/fluoxetine 20 mg	1 (1.1)
Data presented as n (%).	



- The majority of physicians (76.7%) preferred the combination of olanzapine 5 mg with fluoxetine 20 mg as the starting dose.
- This was followed by 12.2% of physicians who selected olanzapine 10 mg with fluoxetine 20 mg.
- A smaller proportion, 10%, opted for olanzapine 20 mg with fluoxetine 20 mg. The least preferred starting dose was olanzapine 2.5 mg with fluoxetine 20 mg, chosen by only 1.1% of physicians.

Question 13: In your clinical practice, which adverse effect is commonly associated with olanzapine and fluoxetine combination therapy?

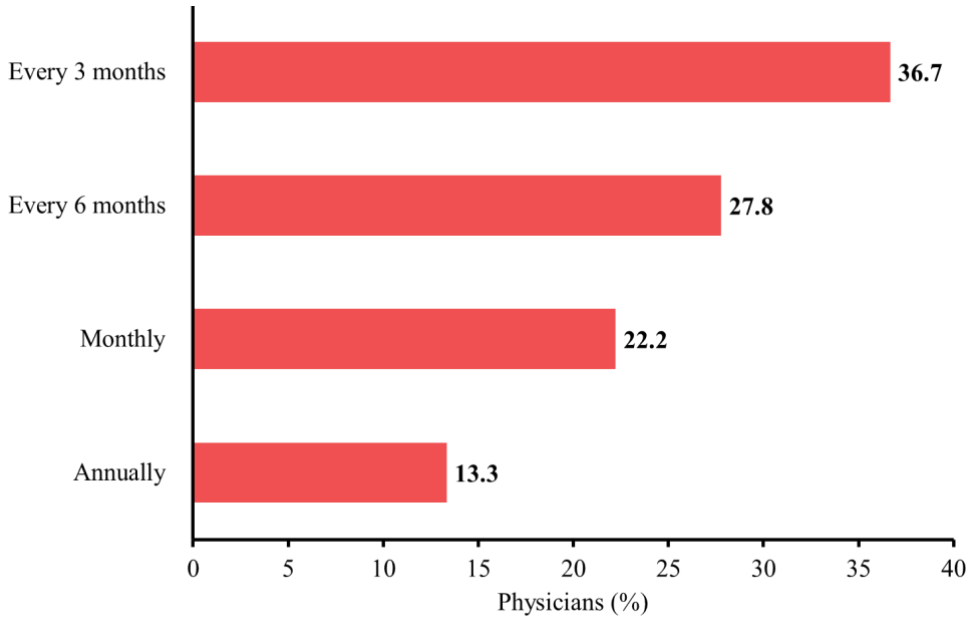
Options	Number of physicians (N=90)
Weight gain	56 (62.2)
Insomnia	19 (21.1)
Sexual dysfunction	13 (14.4)
Weight loss	2 (2.2)
Data presented as n (%).	



- In clinical practice, the most commonly associated adverse effect with olanzapine and fluoxetine combination therapy is weight gain, reported by 62.2% of physicians.
- Insomnia is the second most frequently mentioned adverse effect, reported by 21.1% of physicians. Sexual dysfunction is noted by 14.4% of physicians. Weight loss is the least commonly associated adverse effect, mentioned by only 2.2% of physicians.

Question 14: In your clinical practice, how often patients receiving olanzapine and fluoxetine combination therapy are monitored for metabolic side effects?

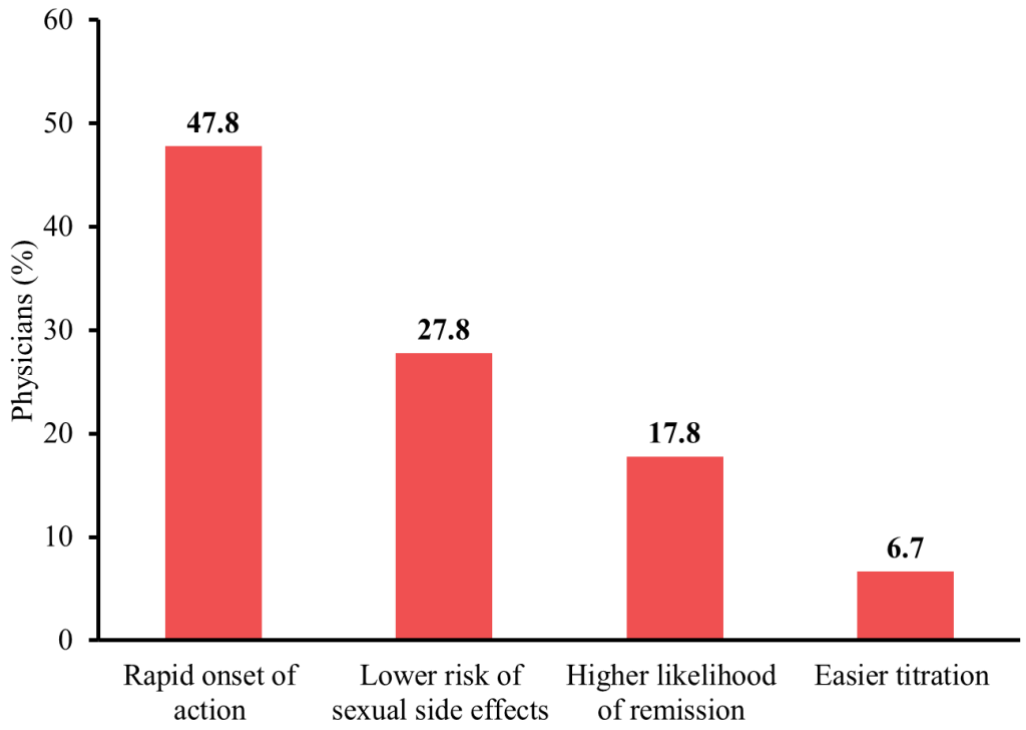
Options	Number of physicians (N=90)
Every 3 months	33 (36.7)
Every 6 months	25 (27.8)
Monthly	20 (22.2)
Annually	12 (13.3)
Data presented as n (%).	



- In clinical practice, 36.7% of patients receiving olanzapine and fluoxetine combination therapy are monitored for metabolic side effects every three months.
- Around 27.8% of patients are monitored every six months, while 22.2% undergo monthly monitoring. Only 13.3% of patients are monitored annually.

Question 15: What is the main advantage of using the combination of olanzapine and fluoxetine over other treatment options for treatment-resistant depression?

Options	Number of physicians (N=90)
Rapid onset of action	43 (47.8)
Lower risk of sexual side effects	25 (27.8)
Higher likelihood of remission	16 (17.8)
Easier titration	6 (6.7)
Data presented as n (%).	



- The main advantage of using the combination of olanzapine and fluoxetine over other treatment options for treatment-resistant depression, according to 47.8% of physicians, is the rapid onset of action.
- A lower risk of sexual side effects is noted by 27.8% of physicians as a significant benefit. Higher likelihood of remission is considered an advantage by 17.8% of physicians. Easier titration is seen as a primary advantage by 6.7% of physicians.

6 SUMMARY

In a survey of 90 physicians, about 46.7% reported that 10-20% of their patients have bipolar disorder, and 42.2% indicated 20-30%. Only 5.6% noted less than 10%, while another 5.6% reported more than 40%. A majority (94.3%) consider olanzapine and fluoxetine combination therapy a first-line treatment for acute bipolar disorder, with 62.5% rating its safety as Good and 33% as Excellent. Similarly, 61.1% rated its efficacy as Good and 31.1% as Excellent. For tolerability, 76.7% rated it Good and 18.9% as Excellent. Regarding treatment-resistant depression, 51.1% of physicians reported that 10-20% of their patients fall into this category. Additionally, 74.4% agree that the combination therapy offers higher remission rates than monotherapy. Most physicians (52.2%) recommend a treatment duration of 6-8 weeks, and 47.8% observed positive outcomes after this period. For dose stabilization, 52.2% suggest 2 weeks before increasing. The combination is considered highly effective for psychotic depression by 54.4% of physicians. The preferred starting dose is olanzapine 5 mg with fluoxetine 20 mg (76.7%). The most common adverse effect is weight gain (62.2%), with insomnia and sexual dysfunction following. The most common monitoring frequency is every 3 months, and the rapid onset of action is seen as the greatest advantage.

7 DISCUSSION

The survey for the use of olanzapine and fluoxetine combination therapy for acute bipolar disorder, the survey reveals several key insights from physicians. A substantial portion of respondents, 46.7%, indicated that 10-20% of their patients have bipolar disorder, with another 42.2% reporting that 20-30% of their patients fall into this category. This prevalence underscores the significance of effective treatment options. The overwhelming majority (94.3%) of physicians consider the combination of olanzapine and fluoxetine a first-line treatment, reflecting confidence in its efficacy and safety profile. Indeed, 62.5% rated the safety of this combination as Good and 33% as Excellent, with no reports of it being Poor. Similarly, 61.1% rated its efficacy as Good and 31.1% as "Excellent," demonstrating strong clinical endorsement.

The tolerability of the combination therapy is also well-regarded, with 76.7% rating it as Good and 18.9% as Excellent. Physicians highlighted weight gain (62.2%) as the most common adverse effect, followed by insomnia (21.1%) and sexual dysfunction (14.4%). Monitoring practices varied, with the most common frequency being every 3 months (36.7%). Regarding treatment-resistant depression, 51.1% of physicians reported that 10-20% of their patients are affected, and 74.4% agreed that the combination therapy offers higher remission rates than monotherapy. The recommended treatment duration is typically 6-8 weeks, with 47.8% of physicians observing positive outcomes within this timeframe. Stabilization on the initial dose for 2 weeks before increasing is advised by 52.2% of respondents. The combination therapy's rapid onset of action (47.8%) and lower risk of sexual side effects (27.8%) are significant advantages, further solidifying its role in managing acute bipolar disorder and psychotic depression, where 54.4% consider it highly effective.

8 CONSULTANT OPINION

Based on the survey data, it is evident that the combination of olanzapine and fluoxetine is widely regarded as a first-line treatment option for acute bipolar disorder, with 94.3% of physicians endorsing its use. The combination therapy is highly rated in terms of safety, efficacy, and tolerability, with the majority of physicians rating it as Good or Excellent. The preferred starting dose is olanzapine 5 mg with fluoxetine 20 mg, chosen by 76.7% of physicians. While weight gain is the most commonly reported adverse effect, the rapid onset of action and lower risk of sexual side effects are significant advantages. The combination therapy is also deemed effective for psychotic depression by 54.4% of respondents. Regular monitoring every 3 months is common practice, reflecting the need for ongoing assessment. Overall, the combination of olanzapine and fluoxetine is a well-accepted and effective treatment for bipolar disorder and psychotic depression, offering higher remission rates and manageable side effects.

9 MARKET OPPORTUNITIES

The survey data presents several market opportunities for olanzapine and fluoxetine combination therapy in treating acute bipolar disorder. With a significant portion of physicians (94.3%) considering this combination as a first-line treatment and 62.5% rating its safety as "Good," there is a clear endorsement of its clinical utility. The preference for the starting dose of olanzapine 5 mg with fluoxetine 20 mg by 76.7% of physicians highlights a targeted dosage strategy that can be emphasized in marketing campaigns. The notable advantages, such as rapid onset of action (47.8%) and lower risk of sexual side effects (27.8%), offer strong selling points. Additionally, with weight gain being the most common adverse effect reported by 62.2% of physicians, there is potential for developing adjunctive treatments or lifestyle management programs to address this issue, thereby enhancing the overall treatment experience. Frequent monitoring, every 3 months as cited by 36.7% of physicians, suggests opportunities for follow-up services or digital health solutions to support ongoing patient management.

10 MARKET POSITIONING

- The olanzapine and fluoxetine combination therapy has emerged as a first-line treatment for acute bipolar disorder among physicians, reflecting its robust positioning in the psychiatric medication landscape. With 94.3% of surveyed physicians endorsing it as their primary choice, this combination therapy is highly trusted for its safety, efficacy, and tolerability.
- The majority of physicians (62.5%) rate the safety profile of this combination as "Good," with an additional 33% considering it "Excellent." This high level of confidence underscores its reliability as a treatment option. In terms of efficacy, the therapy is similarly well-regarded, with 61.1% rating it as "Good" and 31.1% as "Excellent." Its tolerability is particularly noteworthy, with 76.7% of physicians rating it as "Good" and 18.9% as "Excellent."
- In the challenging area of treatment-resistant depression, where 51.1% of physicians report that 10-20% of their patients are affected, the combination therapy offers a significant advantage. With 74.4% of physicians agreeing that this combination achieves higher remission rates compared to monotherapy, it is well-positioned as a superior alternative for difficult-to-treat cases.
- Physicians also appreciate the rapid onset of action as the therapy's greatest advantage, making it an appealing choice for achieving timely patient outcomes. The recommended treatment duration of 6-8 weeks, endorsed by 52.2% of physicians, and the observation of positive outcomes within this period by the same percentage of respondents, further solidify its practical utility in clinical settings.
- For dose stabilization, 52.2% of physicians suggest a 2-week period before dose escalation, providing a clear and manageable protocol for achieving optimal therapeutic levels. The preferred starting dose of olanzapine 5 mg with fluoxetine 20 mg, supported by 76.7% of physicians, aligns with this approach and facilitates ease of use in clinical practice.
- Despite the common adverse effect of weight gain reported by 62.2% of physicians, the combination therapy's overall profile—marked by its efficacy in psychotic depression (as noted by 54.4% of physicians) and high tolerability—positions it as a highly effective and reliable treatment option. The most

common monitoring frequency of every 3 months ensures that potential side effects are managed appropriately, further reinforcing its safety profile.

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