Society for Advancement of Bipolar Affective Disorder
雙　相　情　緒　學　會

Identifying Treatment Goals and Barriers to Using a Long-Acting Injectable Antipsychotic in Patients with Bipolar Disorder

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Introduction

Bipolar I disorder (BD) is commonly misdiagnosed as depression, and it sometimes takes up to 10 years for patients to be correctly diagnosed with BD.[1,2] In a focus group interview conducted in Hong Kong, participants with BD previously thought that they were suffering from depression, and it took an average of 5 years to obtain a correct diagnosis.[3] In a roundtable meeting held by the Society for Advancement of Bipolar Affective Disorder (SABAD), on 18th April 2023, a panel of experts discussed the treatment landscape of BD, with a focus on facilitating the use of long-acting injectable (LAI) antipsychotics. This article summarises their discussion, which included the treatment goals of BD, the role of LAI antipsychotics as long-term maintenance therapy, the meaning and importance of functional recovery, and the barriers to using LAI antipsychotics.

Take-home messages

- Psychoeducation is important for both patients and caregivers to gain knowledge about LAI antipsychotics and the disease course of BD, highlighting the importance of compliance with maintenance therapy.
- Although the definition of functional recovery depends on the sociocultural context, most adult patients in Hong Kong focus on occupational and social recovery.
- The key barriers to prescribing LAI antipsychotics include an obsolete, negative image of injections among members of the public, and treatment cost.
- Patients and caregivers should be educated about the clinical benefits and cost-effectiveness of LAI antipsychotics.
- The risk of relapses should be discussed with patients, particularly those with a relevant family history and experience of relapses, and caregivers to enhance their expectation and willingness to use LAI antipsychotics.
- Compared with other LAI antipsychotics, aripiprazole once-monthly (AOM) appears to be associated with a less significant weight gain and lower risks of sedation and extrapyramidal side effects; therefore, it could facilitate functional recovery, particularly in patients whose occupation requires fine motor skills, as well as older male patients.

Treatment goals

Nine expert panellists (Table 1) participated in the meeting, which began with a discussion of treatment goals in patients with BD. Five (56%) and four (44%) panellists considered relapse prevention and functional recovery, respectively, as goals of maintenance treatment for patients with BD who have achieved symptom control. The panellists noted that, to achieve the treatment goals, psychoeducation is crucial to equip both patients and family members with insights and knowledge about medications and the disease course of BD, which includes unpredictably manic and depressive phases, highlighting the importance of compliance with maintenance therapy. They also recognised that patients should be reassured that depressive episodes are part of the natural course of BD and necessitate maintenance therapy.

Case sharing on the use of AOM

Dr. Raymond Wong shared the following case in which a female patient who experienced multiple relapses achieved a number of clinical benefits after switching to treatment with LAI aripiprazole once-monthly (AOM).

Medical history

A 34-year-old woman developed her first manic episode during the second year of university study at the age of 22. She presented with elated mood, inflated self-esteem, racing thoughts, reduced need for sleep, and a delusion of love towards a professor.

Oral medications and side effects

She received treatment with quetiapine XR 300 mg at night, achieved remission for 6 months, then suffered from her second manic episode. For 5 years, she experienced recurrent depression and elation. She had poor insight and stopped her medications during manic episodes. Quetiapine 500 mg/day, sodium valproate, lithium, and olanzapine were used, but were not tolerated because of side effects including weight gain and sedation. Notably, current clinical guidelines have recommended against the use of sodium valproate in any female able to have children.

Stabilisation and recurrence

Her condition was stabilised on treatment with brexpiprazole 2 mg plus lamotrigine 200 mg/day. However, in December 2022, her mood became elated before a trip to Japan. She later fell for an internet love scam.

Table 1. List of the expert panellists.

Chairman	Dr. Michael Ming-Cheuk Wong
Speaker	Dr. Raymond Ka-Yau Wong
Panellists	Dr. Chun Lam
	Dr. Ki-Yan Mak
	Dr. Yan-Ming Ip
	Dr. Rico Ching-Kwok Li
	Dr. Alfred Hin-Tat Pang
	Dr. Gregory Kai-Lok Mak
	Dr. Ching-Ping Cheung

Use of AOM and clinical outcomes

The patient was switched to treatment with AOM 400 mg plus lamotrigine 200 mg/day. She secured a full-time job and began providing private tutoring on weekends. She has also achieved symptom remission, functional recovery, alleviation of weight gain and sedation, and relapse prevention.

Panellist's comments

One panellist commented that LAI antipsychotics are underused in Hong Kong. He noted that oral risperidone is often the first-line treatment regimen for BD in the public healthcare setting; however, it is associated with increased prolactin levels, especially in females. He added that, although not the most potent agent, oral aripiprazole offers a promising safety profile, and that its use has increased in recent years.

Reasons for switching from oral antipsychotics to LAI antipsychotics

The panellists highlighted that traditional injections were perceived as punishment with poor chemicals, whereas contemporary LAI antipsychotics should be considered as a prestigious therapeutic product with multiple clinical benefits. They discussed the different perspectives on switching from oral medications to LAI antipsychotics for the long-term treatment of BD (Table 2).

Best times for switching from oral antipsychotics to LAI antipsychotics

The panellists recommended that patients with BD who experience relapses, unstable conditions, or non-compliance issues on oral medications to consider switching to LAI antipsychotics, which is a modern treatment paradigm. However, they noted that many patients do not believe in

Table 2. Reasons for switching to a long-acting injectable (LAI) antipsychotic based on the panel discussion.

Physician perspective	• LAI antipsychotics can reduce the risk of relapses and preserve cognitive function by improving treatment compliance. • Earlier use of LAI antipsychotics may reduce the risk of mood swings. • LAI antipsychotics can reduce the severity and facilitate recovery in cases of relapses.
Patient perspective	• There are patients who prefer to receive LAI antipsychotics. • Some patients reported that AOM was associated with less fatigue and lower weight gain compared with oral aripiprazole. • Compared with other LAI antipsychotics, AOM appears to be associated with a less significant weight gain and lower risks of sedation and extrapyramidal side effects.
Family member perspective	• Family members can avoid the annoyance and conflict involved in monitoring the patient's treatment compliance.

Table 3. Risk factors for cognitive decline in a cohort of patients with bipolar I disorder (N = 128).[4]

	Univariate logistic regression analysis			Multivariate logistic regression analysis		
	Odds ratio	95% CI	P value	Odds ratio	95% CI	P value
Manic episode density	**10.02**	**1.35–74.57**	**0.024**	NA	NA	NA
Episode with psychotic features density	**26.90**	**2.44–297.13**	**0.007**	**25.21**	**2.15–259.61**	**0.010**

CI, confidence interval; NA, not applicable.

the necessity or benefits of earlier use of LAI antipsychotics; therefore, psychoeducation remains important. One panellist shared that patients are often willing to take nutritional supplements that are promoted as neuroprotective; however, what patients should be educated about is the benefit of preserving the cognitive functioning through relapse prevention with LAI antipsychotics.

Functional impairment of BD

Dr. Michael Wong shared the evidence for the association between experience of relapse and neurocognitive impairment in patients with BD. A retrospective study of patients with BD showed that the density of episodes with psychotic features was an independent risk factor for cognitive decline after adjusting for age, gender, and dose of mood stabiliser (Table 3).[4] Another study demonstrated that, compared with BD patients with relapses (N = 24) and healthy controls (N = 143), no-relapse BD patients (N = 18) had neurocognitive improvements.[5]

In a focus group interview (N = 11) conducted by the Hong Kong Mental Health in Action Foundation, participants believed that BD mostly affected their ability to work and socialise, making them feel at a loss.[3] The panellists noted that the definition of functional recovery depends on the sociocultural context. Different age groups and genders may see functional recovery differently. To most adult patients in Hong Kong, functional recovery brings to mind the ability to work.

Key barriers to prescribing LAI antipsychotics

The panellists emphasised that there remains a traditional concept among members of the public that injections are intended for severe disease only, and contain low-quality medication. Indeed, international clinical guidelines have recommended modern LAI antipsychotics for the maintenance treatment of BD. The panellists noted that treatment cost remains another major barrier; however, the overall cost-effectiveness of LAI antipsychotics is favourable and

comparable to oral medications. They agreed that, built on the vibration, resonance and trust between the treating physician and the patient, effective psychoeducation can help to boost the acceptance of LAI antipsychotics (Figure 1).

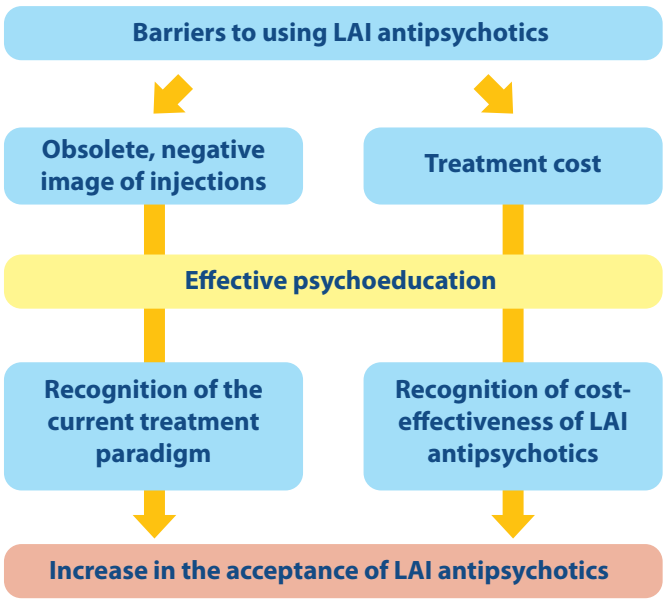

Figure 1. Psychoeducation helps to address barriers to using long-term injectable (LAI) antipsychotics.

What to do if patients prefer not to use LAI antipsychotics

The panellists noted that the risk of relapses should be discussed with patients and family members to enhance their preparedness and willingness to use LAI antipsychotics. Additionally, if patients have relapse risk factors, such as a strong family history and experience of relapse, they should be advised to switch to LAI antipsychotics. The panellists also suggested that, to enhance the acceptance of LAI antipsychotics, several measures can be considered (Figure 2): 1) dissemination of overseas data on the clinical use and popularity of LAI antipsychotics; 2) promotion of the notion that injections are the primary treatment for many other chronic diseases, such as diabetes mellitus; and 3) advocacy of the benefits of early use of LAI antipsychotics, which can act as a safety net to alleviate the severity and duration of relapses, if any. One panellist shared that, considering its safety profile, AOM is preferred over other LAI antipsychotics by patients whose occupation requires fine motor skills, as well as by older male patients, who are more susceptible to antipsychotic-related extrapyramidal side effects.

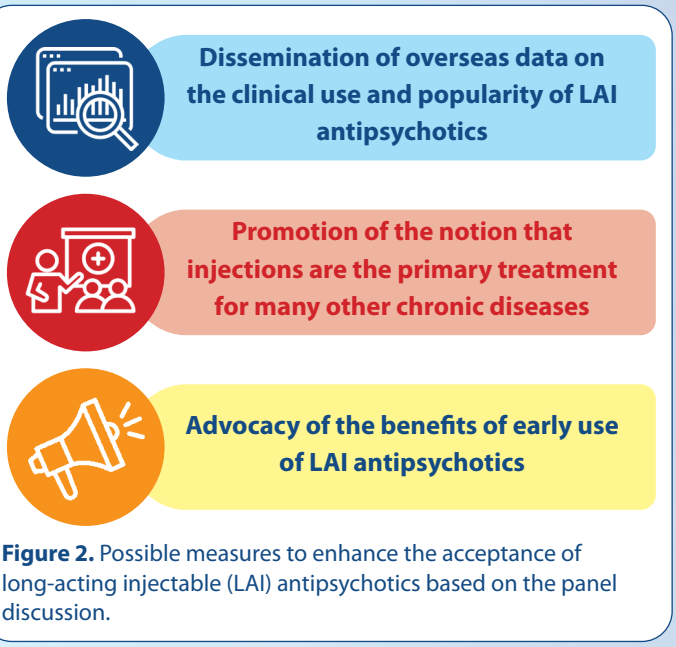

Figure 2. Possible measures to enhance the acceptance of long-acting injectable (LAI) antipsychotics based on the panel discussion.

Importance of functional recovery and closing remarks

All panellists agreed that relapse prevention helps with long-term maintenance and functional recovery in patients with BD, and that LAI antipsychotics should be introduced before a relapse occurs. Dr. Michael Wong closed the meeting with several remarks: 1) functional impairment is common among BD patients, and cognitive functioning may deteriorate with each relapse; 2) to improve functional recovery, it is of utmost importance to prevent relapses among BD patients; and 3) LAI antipsychotics can reduce the risk of relapses by addressing partial- or non-adherence problems.

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