Patients Preference of Olanzapine Orodispersible Tablet Compared with Olanzapine Conventional Oral Tablet

Introduction

Patient preference can have long-term implications in terms of patient's motivation and insight into their disease state and treatment necessities and this might have a direct impact on compliance and treatment adherence. Studies investigating patient preference can be used to support studies with traditional efficacy measures when drug compliance is an important issue. Poor adherence to antipsychotics is a major problem in long term treatment of schizophrenia, a relationship between poor adherence and relapse is well documented in the literature. One of the factors that may affect compliance is antipsychotic formulation.

Objective

The primary objective of the study was to compare patient preference for olanzapine conventional tablet (OCT) with orodispersible tablet (ODT) as measured by a formulation preference question. ODT and OCT tablets are bioequivalent, however ODT tablets have a more rapid onset of gastrointestinal absorption than the OCT tablet, which is likely due to its more rapid disintegration. The novel orodispersible formulation of olanzapine is a rapidly disintegrating freeze-dried tablet which starts to dissolve immediately upon contact with saliva.

Secondary objectives of the study assessed changes in compliance and drug attitude, as well as tolerability and safety. We also investigated weight changes, BMI changes, serum ghreline levels, and subjective appetite differences (measured by a visual analog scale (VAS)).Disease severity was measured by the Clinical Global Impression of Severity scale (CGI-S).

Methods

A 12-week open label, randomized, crossover, multinational study (Turkey, Romania, Israel, Brazil, Mexico) conducted to estimate the proportion of patients preferring OCT over ODT after 6 weeks of treatment with each formulation. Outpatients with stable schizophrenia (CGI-S<4) on OCT monotherapy for at least 1 month before study inclusion were randomized 1:1. Compliance, drug attitude were measured using DAI-10 and MAF scales; tolerability and safety by AMDP-5 questionnaire and adverse event summary.

Dosing

All patients started on a flexible dose 5-20mg/day. The dose could be adapted during study period II but needed to be stable after the switch to the new formulation in study period III. The mean dose throughout the study was 12.3 mg for ODT and 12.4 mg for OCT.

Results

From 265 randomized patients,207 were eligible for the analysis and 175 patients answered the preference question. Among patients who expressed preference 106(61%) patients preferred ODT, and 48(27%) preferred OCT (p<0.001 adjusted for treatment sequence); 21(12%) expressed no preference. Patients receiving OCT during period III preferred OCT with 39%; and those receiving ODT preferred ODT with 73%. This trend is seen in patients who liked ODT as well as OCT and was adjusted for in the primary analysis. Preference reasons provided by patients can be grouped into experience reasons (ease of use, taste of the formulation) and expectations for better effectiveness and weight loss or no weight gain.

Preference distribution table by periods **

	Randomized to ODT N (%)	*Randomized to OCT N (%)*	*All*
Preference period II Preference period III No preference expressed	40 (47%)* 33 (39%)* 12 (14%)	15 (17%)* 66 (73%)* 9 (10%)	55 (31%) 99 (57%) 21 (12%)
Total	85 (100%)	90 (100%)	175 (100%)

**p<0.001 from chi-square test for preference by treatment sequence association indicates difference in preference between formulations. Patients, who expressed no preference are excluded from the test.*
*** includes only patients who answered the preference question*

90% of patients were rated as almost always compliant on both formulations. The adverse event profiles of ODT and OCT were similar: most common (>1%) adverse events were weight increase, hypertriglyceridemia, and somnolence.

No significant association between formulation and BMI, body weight or subjective appetite was found after switching from OCT to ODT formulation.

Conclusions

Most of the patients who answered the preference question declared to prefer olanzapine orodispersible to conventional formulation. Given the importance of patient's preference as one of the factors for future compliance, olanzapine orodispersible tablet could be a good choice.

Excerpted from: Ciorabai EM, Oyffe I, Dilbaz N, Lozano S, Ruschel S, Salburg J, Dyachkova Y, Treuer T. Patients Preference of Olanzapine Orodispersible Tablet Compared with Olanzapine Conventional Oral Tablet in a Multinational, Randomized, Crossover Study.Poster presented at European Congress of Psychiatry, April 5-9, 2008,Nice France.