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BRIEF REPORT

The effectiveness and safety of amisulpride in Chinese patients with schizophrenia: An 8-week, prospective, open-label, multicenter, single-arm study

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Abstract

Introduction: This study evaluated the effectiveness and safety of amisulpride in Chinese schizophrenia patients.

Methods: A multicenter, single-arm Phase IV study (NCT01795183). Chinese patients with schizophrenia received amisulpride for 8 weeks. The primary endpoint was ≥50% decrease in Positive and Negative Syndrome Scale total score from Baseline to Week 8.

Results: A total of 316 patients were enrolled; 295 were included in the effectiveness analysis; 66.8% (197/295) achieved ≥50% decrease in Positive and Negative Syndrome Scale total score from Baseline to Week 8. Nine patients discontinued treatment because of adverse events.

Discussion: Amisulpride had clinical effectiveness and was relatively well tolerated in Chinese patients with schizophrenia.

Introduction

The majority of extant efficacy and safety data for amisulpride (Solian®) come from studies conducted in Western patients. In Asian populations, only a small number of relevant studies of amisulpride have been reported, and these included relatively small numbers of patients. Furthermore, the data available in Chinese patients are particularly scarce.(Hwang et al., 2003; Wang et al., 2008; Ahn et al., 2011; Lee et al., 2012) Therapeutic responses to amisulpride have shown significant inter-patient variability and will likely differ between geographic regions because of factors such as pharmacogenetics, and local standards of care and dosing recommendations.(Brandl et al., 2014; Lally & MacCabe, 2015) Therefore, the present study was

designed in order to assess the effectiveness and safety of amisulpride in Chinese patients with schizophrenia.

Methods

Study design and patients

This 8-week, prospective, multicenter, single-arm Phase IV study was conducted at 13 psychiatric-specialist Tier 1 hospitals in China between 30 October 2012 and 3 December 2013. Adults (18–65 years) who met the ICD-10 criteria for schizophrenia, and had a Positive and Negative Syndrome Scale (PANSS) total score ≥60, were eligible for inclusion. Enrollment included patients treated as inpatients and outpatients. The study was conducted in accordance with the principles of the declaration of Helsinki and received ethical approval from local institutional ethics review boards at all participating centers. Written informed consent was obtained from all study subjects. The study was registered at ClinicalTrials.gov (NCT01795183).

Treatment

After a screening phase, amisulpride tablets (50 mg/tablet) were administered orally for 8 weeks; dosing and titration were in accordance with the approved Chinese labeling (http://drugs.medlive.cn/drugref/html/15330.shtml. Accessed October 2015). In patients switching from other antipsychotics (because of suboptimal treatment response or unacceptable adverse events [AEs]), the dose of the previous medication was gradually reduced upon initiation of amisulpride, with the aim of complete discontinuation within 1 week.

Measurements

The primary effectiveness endpoint was a ≥50% decrease in PANSS total score from Baseline to Week 8. Two subgroup analyses were conducted: in treatment-naive patients versus patients who were switched to amisulpride, and in patients with predominantly positive versus predominantly negative symptoms. Safety data were continuously monitored from Baseline to the end of the study. Blood samples for prolactin level testing were taken from patients in the morning before breakfast.

Statistics

Using an estimate that 60% of patients would achieve a ≥50% improvement in PANSS total score after 8 weeks, enrolment of 300 patients would provide a 95% confidence interval of 53.64% to 66.12%, accounting for a 16% dropout rate.(Kuang et al., 2009)

All statistical analyses and treatment effects were tested at a two-sided significance level of 0.05. Statistical Analytic System software version 9.2 (SAS Institute, Cary, North Carolina, USA) was used to perform all statistical analyses.

Results

In total, 316 patients were enrolled, and 251 completed the 8-week study. Among patients in the effectiveness analysis, 66.8% (197/295) achieved the primary endpoint (Table 1). An early clinical response (≥20% improvement in PANSS total score after 2 weeks of treatment) was achieved by 56.6% of patients.

A similar proportion of the treatment-naive and previously treated patients achieved a ≥50% decrease in PANSS total score from Baseline to Week 8 (68.6% versus 66.2%) (Table 1). Among the 266 patients with predominantly positive symptoms, 68.4% achieved a ≥50% decrease in PANSS total score by Week 8. Of the 26 patients with predominantly negative symptoms, 50.0% achieved a ≥50% decrease in PANSS total score at Week 8.

A total of nine (3.1%) patients withdrew from the study because of an adverse reaction, and one patient experienced a serious AE (suicide attempt), which the investigator judged was not related to the study treatment. The incidence of drug-related, treatment-emergent AEs was 58.9% (186/316) (Table 1).

Discussion

The results of this single-arm study show that 8-week treatment with amisulpride effectively improved the clinical symptoms of Chinese patients with schizophrenia; approximately two thirds (66.8%) of patients achieved a ≥50% decrease in PANSS total score from Baseline to Week 8. In addition, a rapid response to amisulpride treatment was observed in the majority of patients; 56.6% of study subjects achieved a ≥20% improvement in PANSS total score from Baseline to Week 2. Interestingly, results of a subgroup analysis suggested that amisulpride is equally effective for treatment-naive schizophrenia patients and those who switch to amisulpride from other antipsychotics.

Although a direct comparison of this study with previous research is difficult, because of variability in study duration, enrolment criteria, and assessment variables, the effectiveness results broadly support several prior studies conducted in other countries.(Carriere et al., 2000; Sechter et al., 2002; Mortimer et al., 2004) The incidence of extrapyramidal side effects reported in the present study (25.9%) is comparable with two

Table 1. Summary of study results

	Variable	
Baseline characteristics	Male, *n* (%)	148 (46.8)
(SS; *n* = 316)	Mean age (years ± SD)	32.6 ± 11.8
	Mean BMI (kg/cm^2 ± SD)	23.1 ± 4.0
	Type of schizophrenia defined by ICD-10, n (%)	
	Paranoid	192 (60.8)
	Undifferentiated	101 (32.0)
	Other	17 (5.4)
	Unspecified	6 (1.9)
	Received previous treatment for schizophrenia, *n* (%)	237 (75.0)
Treatment exposure (SS, *n* = 316)	Mean starting dose of amisulpride, mg ± SD	243.7 ± 115.6
	Mean daily dose of amisulpride over 8-week study duration, mg ± SD[†]	678.0 ± 224.6
	Use of any concomitant medication, *n* (%)	257 (81.3)
Effectiveness[‡] (ITT, *n* = 295)	Primary endpoint: ≥50% decrease in PANSS total score from	197 (66.8) [61.1–72.1]
	Baseline to Week 8, *n* (%) [95% CI]	
	Treatment naive patients (*n* = 70)	48 (68.6)
	Pre-treated patients switching to amisulpride (*n* = 225)	149 (66.2)
	Predominantly positive symptoms (*n* = 266)	182 (68.4)
	Predominantly negative symptoms (*n* = 26)	13 (50.0)
	Early response: ≥20% decrease in PANSS total score from	167 (56.6) [50.7–62.3]
	Baseline to Week 2, *n* (%) [95% CI]	
Safety[§] (*n* = 316)	≥1 AE, *n* (%)	187 (59.2)
	≥1 treatment-related AE, *n* (%)	186 (58.9)
	Nervous system, *n* (%)	107 (33.9)
	Extrapyramidal side effects	82 (25.9)
	Akathisia	15 (4.7)
	Dystonia	8 (2.5)
	Laboratory testing and electrocardiogram, *n* (%)	93 (29.4)
	Blood prolactin increase (>25 ng/mL)	82 (25.9)
	Weight gain (>7% increase from Baseline)	14 (4.4)
	Endocrine system, *n* (%)	26 (8.2)
	Hyperprolactinemia[¶]	26 (8.2)

AE, adverse event; BMI, body mass index; ICD-10, Tenth Revision of the International Classification of Diseases and Related Health Problems; ITT, Intention-to-Treat, the effectiveness analysis population defined as patients who received at least one dose of study medication and underwent at least one assessment of the primary effectiveness variable; PANSS, Positive and Negative Syndrome Scale; SD, standard deviation; SS, safety analysis population, defined as all patients who received at least one dose of study medication.

[†]In 305 patients with available data.

[‡]Last observation carried forward.

[§]Patients may have reported >1 adverse event.

[¶]blood prolactin increase with clinical symptoms.

[Corrections added on 16 May 2016, after first online publication: All occurrences of '% (*n*)' and the format of its corresponding data have been amended to '*n* (%)' throughout the above table for consistency.]

previous reports (23% and 13%) (Carriere et al., 2000; Colonna et al., 2000).

The primary limitation of this study was that patients with predominantly positive symptoms accounted for the majority of the patients included, which may limit the generalizability of the results.

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Contributorship statements

All authors drafted or revised the work for intellectual content and approved the final version. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately

investigated and resolved. Ying Liang: Conception and design of the work and the acquisition and interpretation of data, analysis of data. Changan Cao: Conception and design of the work and the acquisition and interpretation of data. Cheng Zhu: Conception and design of the work and the acquisition and interpretation of data. Chuanyue Wang: Conception and design of the work and the acquisition and interpretation of data. Congpei Zhang: Conception and design of the work and the acquisition and interpretation of data. Fang Dong: Conception and design of the work and the acquisition and interpretation of data. Fude Yang: Conception and design of the work and the acquisition and interpretation of data, Hong Deng: Conception and design of the work and the acquisition and interpretation of data. Jingjie Yu: Conception and design of the work and the acquisition and interpretation of data. Jisheng Tang: Conception and design of the work and the acquisition and interpretation of data. Lei Su: Conception and design of the work and the acquisition and interpretation of data. Limin Xin: Conception and design of the work and the acquisition and interpretation of data. Ling Hong: Conception and design of the work and the acquisition and interpretation of data. Minglong Gao: Conception and design of the work and the acquisition and interpretation of data. Muni Tang: Conception and design of the work and the acquisition and interpretation of data. Shiping Xie: Conception and design of the work and the acquisition and interpretation of data. Shuiping Lu: Conception and design of the work and the acquisition and interpretation of data. Tiebang Liu: Conception and design of the work and the acquisition and interpretation of data. Xiaojin Xu: Conception and design of the work and the acquisition and interpretation of data. Xijin Wang: Conception and design of the work and the acquisition and interpretation of data. Xuanzi Li: Conception and design of the work and the acquisition and interpretation of data. Xueyi Wang: Conception and design of the work and the acquisition and interpretation of data. Yi Li: Conception and design of the work and the acquisition and interpretation of data. Yong Zhang: Conception and design of the work and the acquisition and interpretation of data. Zhiyu Chen: Conception and design of the work and the acquisition and interpretation of data. Xin Yu: Conception and design of the work and the acquisition and interpretation of data, analysis of data.

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