

ORIGINAL ARTICLE

## Antidepressant monotherapy compared with combinations of antidepressants in the treatment of resistant depressive patients: A randomized, open-label study

MARTIN BARES<sup>1,2</sup>, TOMAS NOVAK<sup>1,2</sup>, MILOSLAV KOPECEK<sup>1,2</sup>, PAVLA STOPKOVA<sup>1,2</sup>, JAN CERMAK<sup>1</sup>, JIRI KOZENY<sup>1,2</sup> & CYRIL HÖSCHL<sup>1,2</sup>

<sup>1</sup>Prague Psychiatric Center, Prague, Czech Republic, and <sup>2</sup>Department of Psychiatry and Medical Psychology, 3rd Faculty of Medicine, Charles University, Prague Czech Republic

### Abstract

**Objective.** This randomized, 6-week, open-label study compared efficacy of CAD and antidepressant monotherapies (ADM) that had been chosen according to clinical judgment of the attending psychiatrist. **Methods.** A total of 60 inpatients (intent-to-treat analysis) with depressive disorder ( $\geq 1$  unsuccessful antidepressant treatment) were randomly assigned to the interventions. The responders who completed the acute phase of study, were evaluated for relapse within 2 months of follow-up treatment. The primary outcome measure was change in the Montgomery-Åsberg Depression Rating Scale (MADRS) and response was defined as a  $\geq 50\%$  reduction of MADRS score. **Results.** Mean changes in total MADRS score from baseline to week 6 for patients in both treatment modalities were not different (ADM =  $13.2 \pm 8.6$  points; CAD =  $14.5 \pm 9.5$  points;  $P = 0.58$ ). The analysis of covariance performed for significantly higher value of imipramine equivalent dose in CAD group showed only a non-significant between-group difference for total MADRS change ( $P = 0.17$ ). There were also no differences between groups in response rate (ADM = 48%; CAD = 58%) and number of drop-outs in acute treatment as well as proportion of responders' relapses in the follow-up. **Conclusions.** Both treatment modalities produced clinically relevant reduction of depressive symptomatology in acute treatment of patients with resistant depression and their effect was comparable.

**Key Words:** Resistant depression, treatment, antidepressant monotherapy, combination of antidepressants

### Introduction

Major depressive disorder (MDD) is a chronic, recurrent illness associated with significant morbidity and mortality. Despite recent progress in psychopharmacology and treatment possibilities many (about 30%) patients do not respond to standard antidepressant monotherapy (ADM) [1,2]. The most frequent pharmacological methods to manage resistant depression are switching antidepressants (ADs), augmentation of ADs with various compounds (second-generation antipsychotics, triiodothyronine, lithium, pindolol, buspirone, etc.), and combinations of two distinctly different ADs. However, there is no clear consensus in current guidelines of treatment which strategy should be preferred [3–5]. Antidepressant combination (CAD)

is an often used strategy to overcome resistance to treatment in current clinical practice [6,7]. A combination of ADs might increase the number of patients who could benefit from treatment [8,9]. Synergy between various mechanisms of action might affect a wider range of neurotransmitter or neuromodulator systems that might lead to faster onset of action and potential avoidance of side effects [10,11]. There are plenty of possible combinations but the evidence supporting their efficacy ranges from nothing or case reports to randomized clinical trials [12–14]. CAD can be applied in two different approaches: (1) Continuing the first AD and adding the second one, (2) combining two new ADs from the initiation of treatment. Several double-blind studies demonstrated higher efficacy

Correspondence: Martin Bares, MD, Prague Psychiatric Center, Ustavní 91, Prague 8 – Bohnice, 181 03, Czech Republic. Tel: + 420 266003330. Fax: + 420 266003337. E-mail: bares@pcp.ifej.cuni.cz

(Received 22 November 2011; accepted 20 February 2012)

ISSN 1365-1501 print/ISSN 1471-1788 online © 2013 Informa Healthcare  
DOI: 10.3109/13651501.2012.674533

RIGHTS LINK

