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VENLAFAXINE AND CYP2D6 IN CLINICAL PRACTICE: WORK IN PROGRESS

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Objective: Venlafaxine (V) is a SNRI metabolized primarily by the highly polymorphic cytochrome P4502D6 enzyme (CYP2D6) in O-desmethylvenlafaxine (ODV), the main active metabolite. Four CYP2D6 metabolizer phenotypes have been identified: poor (PM), intermediate (IM), extensive (EM) and ultrarapid (UM). Approximately 5-10% Caucasians are PMs; in these individuals metabolism of substrate is decreased and adverse clinical effects may be expected. The effectiveness of pharmacogenetic tests is controversial because the association between plasma levels of V/ODV and side effects is not attested.

We discuss the association between CYP2D6-genotype and Venlafaxine clinical effects.

Methods: We will recruit Caucasian patients aged 18 to 65, eligible for Venlafaxine treatment, satisfying DSM-IV criteria for major depressive episode, dysthymia or depressive adjustment disorder. Exclusion criteria will be: pregnancy, acute suicidality, alcohol/substance abuse, concomitant/prior antidepressive treatment in the previous 3 months. We will assess patients' age, gender, DSM-IV diagnosis, Venlafaxine dose, concomitant pharmacological treatment, BMI, BP, tobacco use, liver and kidney functionality. Clinical response and side effects will be monitored using CGI, HAM-D and SIDE at T0 (onset), T1 (1 week later) and T2 (6 weeks later).

The patients will be analyzed for the presence of 16 CYP2D6-genotype variants by INFINITI^{TM} CYP2D6 assay which utilizes AutoGenomics proprietary film-based microarray technology.

Results: We expect to find out a correlation between CYP2D6-genotype, Venlafaxine dose and clinical response to treatment.

Conclusions: We will investigate whether a pharmacogenetic test prior to treatment can be useful in clinical practice to detect a proper Venlafaxine dosage or to switch to a different drug.

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