PHARMACOGENETIC ANALYSIS

This genetic analysis includes the following sections:

- **Results Report**
- **Additional genetic information**
- **Annex**

PATIENT IDENTIFICATION

NFG_00011

REQUESTING DOCTOR:	Dr
Hospital/Clinic:	Instituto Inv. Neuropsiquiátricas López-Ibor

Results Report

Genetic analysis carried out at AB-BIOTICS S.A.
Parc Científic i Tecnològic de la UdG - c/Pic de Peguera 11 - 17003 Girona.
Healthcare authorization registration code E17867643.

Our laboratory has a Quality Management System certified by IQNet
which fullfills the requirements of the ISO 9001:2008 standard (ER-0788/2013).

Patient identification	NFG_00011	**Analysis #**	389
Sample Code:	ABL_DNA	**Entry date:**	08/10/2012

SUMMARY TABLE

An initial interpretation of the results obtained from the patients genetic profile is displayed in a table below. For each drug examined, the result is indicated according to the following code:

- Standard — No genetic variants relevant to the treatment have been found. Use as directed.
- Need for drug dose monitoring and/or less likelihood of positive response.
- Increased likelihood of positive response and/or lower risk of adverse drug reactions.
- Increased risk of adverse drug reactions.

Antidepressants					
Amitriptyline		**Citalopram**		**Clomipramine**	
Escitalopram		**Fluoxetine**		**Fluvoxamine**	
Imipramine		**Mianserin**		**Mirtazapine**	
Nortriptyline		**Paroxetine**		**Venlafaxine**	

Antipsychotics					
Aripiprazole		**Clozapine**		**Haloperidol**	
Olanzapine		**Perphenazine**		**Quetiapine**	Standard
Risperidone		**Ziprasidone**	Standard	**Zuclopenthixol**	

Stabilizers and anticonvulsants					
Carbamazepine		**Clobazam**	Standard	**Clonazepam**	Standard
Lamotrigine	Standard	**Levetiracetam**	Standard	**Lithium***	Standard
Oxcarbazepine	Standard	**Phenobarbital**	Standard	**Phenytoin**	Standard
Pregabaline	Standard	**Topiramate**	Standard	**Valproic Acid**	Standard
Vigabatrin	Standard				

Others					
Atomoxetine		**Methadone**	Standard	**Naloxone**	Standard
Naltrexone	Standard	**Pramipexol**	Standard		

Report reviewed and verified by		**Date**	08/17/2012

Dr

** According to the ATC code, Lithium is considered an antipsychotic (N05AN01). By request of the physicians the classification of lithium in the table has been modified and it is shown in the mood stabilizers section.*

RESULTS REPORT

This section lists the drugs for which the genetic analysis suggests that the patient will behave differently from the average population (colour box from the previous table), as well as a series of recommendations for guidance purposes. When different genetic results indicated in different colours coexist for a given drug, the resulting colour in the summary table will follow this safety priority rule: risk of adverse drug reactions (red) > dose monitoring and/or less likelihood of positive response (amber) > increased likelihood of positive response (green) and/or lower risk of adverse drug reactions. The final evaluation of the analysis is at the physician´s discretion.

PATIENT´S METABOLISING PROFILE

Gene	Genotype	Phenotype
CYP1A2	*1/*1F	Extensive (normal) metaboliser
CYP2C9	*1/*1	Extensive (normal) metaboliser
CYP2C19	*1/*1	Extensive (normal) metaboliser
CYP2D6	*4/*4	Poor metaboliser

DRUG — RECOMMENDATIONS FOR GUIDANCE PURPOSES

Amitriptyline

Analysis result:

- Higher likelihood of positive response to treatment (ABCB1)
- Poor metabolizer of the drug (CYP2D6)

Recommendation:

The analysis indicates there is a higher likelihood of positive response to treatment (ABCB1). Moreover, the analysis indicates that the patient is a CYP2D6 poor metaboliser of this drug. Consider an alternative drug not metabolized by this pathway. If this drug is warranted, consider a 50% reduction of the recommended starting dose.[1] Use therapeutic drug monitoring to guide dose adjustments[2].

Aripiprazole

Analysis result:

- Poor metabolizer of the drug (CYP2D6)

Recommendation:

The analysis indicates that the patient is a CYP2D6 poor metabolizer of this drug. Consider reducing the starting dose to 50%, and proceed to titrate dose in response to efficacy (do not exceed the maximum dose of 10mg/day).

Atomoxetine

Analysis result:

- Poor metabolizer of the drug (CYP2D6)

Recommendation:

The analysis indicates that the patient is a CYP2D6 poor metabolizer of this drug. Treatment should be initiated at a daily dose of 0.5 mg/kg and only increase to the usual target dose of 1.2 mg/kg/day if symptoms fail to improve after 4 weeks and the initial dose is well tolerated.

Carbamazepine

Analysis result:

- Faster detoxification of the drug (EPHX1)

Recommendation:

The analysis indicates that a higher dose than standard may be necessary to achieve therapeutic effects (EPHX1).

Citalopram

Analysis result:

- Higher likelihood of positive response to treatment (ABCB1)

Recommendation:

The analysis indicates the presence of factors associated with a higher likelihood of positive response to treatment (ABCB1), and therefore, if applicable, use of this drug is recommended in preference to other similar alternatives.

Clomipramine

Analysis result:

- Poor metabolizer of the drug (CYP2D6)

Recommendation:

The analysis indicates that the patient is a CYP2D6 poor metabolizer of this drug. Consider an alternative drug not metabolized by this pathway. If this drug is warranted, consider a 50% reduction of the recommended starting dose.[1] Use therapeutic drug monitoring to guide dose adjustments[2].

Clozapine

Analysis result:

- Poor metabolizer of the drug (CYP2D6)
- Increased risk of metabolic syndrome (HTR2C)

Recommendation:

The analysis indicates that the patient is a CYP2D6 poor metabolizer of this drug. However, there is no evidence suggesting a clinical effect of this phenotype; therefore use as directed and titrate dose in response to efficacy and adverse drug events. Moreover, the analysis indicates that there is an increased risk of metabolic syndrome (HTR2C), and therefore, if applicable, consider selecting an alternative drug or increase medical surveillance.

Escitalopram

Analysis result:

- Higher likelihood of positive response to treatment (ABCB1)
- Slight increase in the likelihood of positive response (HTR2A)

Recommendation:

The analysis indicates the presence of factors associated with a higher likelihood of positive response to treatment (ABCB1, HTR2A), and therefore, if applicable, use of this drug is recommended in preference to other similar alternatives.

Fluoxetine

Analysis result:

- Poor metabolizer of the drug (CYP2D6)

Recommendation:

The analysis indicates that the patient is a CYP2D6 poor metabolizer of this drug. However, there is no evidence suggesting a clinical effect of this phenotype; therefore use as directed and titrate dose in response to efficacy and adverse drug events.

Fluvoxamine

Analysis result:

- Poor metabolizer of the drug (CYP2D6)

Recommendation:

The analysis indicates that the patient is a CYP2D6 poor metabolizer of this drug. If needed, consider monitoring plasma concentrations and dose adjustments.

Haloperidol

Analysis result:

- Poor metabolizer of the drug (CYP2D6)

Recommendation:

The analysis indicates that the patient is a CYP2D6 poor metabolizer of this drug. Reduce dose by 50% or select an alternative drug.

Imipramine

Analysis result:

- Poor metabolizer of the drug (CYP2D6)

Recommendation:

The analysis indicates that the patient is a CYP2D6 poor metabolizer of this drug. Consider an alternative drug not metabolized by this pathway. If this drug is warranted, consider a 50% reduction of the recommended starting dose.[1] Use therapeutic drug monitoring to guide dose adjustments[2].

Mianserin

Analysis result:

- Poor metabolizer of the drug (CYP2D6)

Recommendation:

The analysis indicates that the patient is a CYP2D6 poor metabolizer of this drug. However, there is no evidence suggesting a clinical effect of this phenotype; therefore use as directed and titrate dose in response to efficacy and adverse drug events.

Mirtazapine

Analysis result:

- Poor metabolizer of the drug (CYP2D6)

Recommendation:

The analysis indicates that the patient is a CYP2D6 poor metabolizer of this drug. This phenotype has been associated with reduced clearance of the drug. Use as directed and titrate dose in response to efficacy and adverse drug events.

Nortriptyline

Analysis result:

- Higher likelihood of positive response to treatment (ABCB1)
- Poor metabolizer of the drug (CYP2D6)

Recommendation:

The analysis indicates there is a higher likelihood of positive response to treatment (ABCB1). Moreover, the analysis indicates that the patient is a CYP2D6 poor metaboliser of this drug. Consider an alternative drug not metabolized by this pathway. If this drug is warranted, consider a 50% reduction of the recommended starting dose.[1] Use therapeutic drug monitoring to guide dose adjustments[2].

Olanzapine

Analysis result:

- Increased risk of metabolic syndrome (HTR2C)

Recommendation:

The analysis indicates that there is an increased risk of metabolic syndrome (HTR2C), and therefore, if applicable, consider selecting an alternative drug or increase medical surveillance.

Paroxetine

Analysis result:

- Higher likelihood of positive response to treatment (ABCB1, HTR2A)

Recommendation:

The analysis indicates the presence of factors associated with a higher likelihood of positive response to treatment (ABCB1, HTR2A), and therefore, if applicable, use of this drug is recommended in preference to other similar alternatives.

Perphenazine

Analysis result:

- Poor metabolizer of the drug (CYP2D6)

Recommendation:

The analysis indicates that the patient is a CYP2D6 poor metabolizer of this drug. Therefore, there is a higher risk of adverse drug events. Consider dose adjustments in response to efficacy and ADE.

Risperidone

Analysis result:

- Poor metabolizer of the drug (CYP2D6)
- Increased risk of metabolic syndrome (HTR2C)

Recommendation:

The analysis indicates that there is an increased risk of metabolic syndrome (HTR2C). Moreover, the analysis indicates that the patient is a CYP2D6 poor metabolizer of this drug. Select an alternative drug or be extra alert to adverse drug events and adjust dose to clinical response.

Venlafaxine

Analysis result:

- Higher likelihood of positive response to treatment (ABCB1)
- Poor metabolizer of the drug (CYP2D6)

Recommendation:

The analysis indicates there is a higher likelihood of positive response to treatment (ABCB1). Moreover, the analysis indicates the patient is a CYP2D6 poor metabolizer of this drug. Select an alternative drug or adjust dose to clinical response.

Zuclopenthixol

Analysis result:

- Poor metabolizer of the drug (CYP2D6)

Recommendation:

The analysis indicates that the patient is a CYP2D6 poor metabolizer of this drug. Reduce dose by 50% or select alternative drug.

The following information applies only to tricyclic antidepressants, and as long as they are referenced in the text of the recommendation:

(1) Patients may receive an initial low dose of TCA, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.

(2) The dosing recommendations apply only to higher initial doses of tricyclics used for treatment of conditions such as depression. For conditions in which lower initial doses are used, such as neuropathic pain, no dose modifications for poor or intermediate metabolizers are recommended, but these patients should be monitored closely for side effects.

(3) The dosing recommendations apply only to higher initial doses of tricyclics used for treatment of conditions such as depression. For conditions in which lower initial doses are used, such as neuropathic pain, CYP2D6 ultrarapid metabolizers are at risk of failing TCA therapy, thus alternative agents should be considered.

For any further information about the analysis, please do not hesitate to contact us at: +34 900 102 016 o info@neurofarmagen.com