Clinical Pharmacogenomics in Depression Treatment

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PGY-2 PSYCHIATRIC PHARMACY RESIDENT
CENTRAL TEXAS VETERANS HEALTH CARE SYSTEM

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGI-S</td>
<td>Clinical Global Impression – Severity Scale</td>
</tr>
<tr>
<td>CKD</td>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>DSM-V</td>
<td>Diagnostic and Statistical Manual of Mental Disorders, 5th edition</td>
</tr>
<tr>
<td>DSM-IV</td>
<td>Diagnostic and Statistical Manual of Mental Disorders, 4th edition</td>
</tr>
<tr>
<td>HAM-D</td>
<td>Hamilton Rating Scale for Depression</td>
</tr>
<tr>
<td>MAOI</td>
<td>Monoamine oxidase inhibitor</td>
</tr>
<tr>
<td>MDD</td>
<td>Major depressive disorder</td>
</tr>
<tr>
<td>NNT</td>
<td>Number needed to treat</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>PGI-I</td>
<td>Patient global impression of improvement</td>
</tr>
<tr>
<td>PGx</td>
<td>Pharmacogenetics</td>
</tr>
<tr>
<td>RR</td>
<td>Risk ratio</td>
</tr>
<tr>
<td>SSRI</td>
<td>Selective serotonin reuptake inhibitor</td>
</tr>
<tr>
<td>SNRI</td>
<td>Serotonin/norepinephrine reuptake inhibitor</td>
</tr>
<tr>
<td>TAU</td>
<td>Treatment as usual</td>
</tr>
<tr>
<td>TCA</td>
<td>Tricyclic antidepressant</td>
</tr>
<tr>
<td>VA/DoD</td>
<td>Veterans Affairs/Department of Defense</td>
</tr>
</tbody>
</table>
Question

How likely would you order a pharmacogenetic report for a patient with depression who returns to clinic after failing fluoxetine?
A. Sure thing
B. Likely
C. Not likely
D. No chance

Objectives

Discuss epidemiology, pathology, and standard of care of depression
Identify how differences in phenotypes and medication characteristics affect variability in response to antidepressants
Assess whether primary literature adequately justifies the use of pharmacogenetic reports in depression treatment
Major Depressive Disorder

Characterized by “persistent low mood or lack of interest in activity plus impairment in functional areas of life”

People ≥12 Years Old with Depression

7.6%

Suicide deaths in 2015

44,193

The Management of Major Depressive Disorder Working Group, 2016.
National Center for Health Statistics, 2016.
Depression Etiology

- Genetic
- Biochemical
- Psychodynamic
- Socioenvironmental

Biological Theories of Depression Etiology

- Neurotransmitters
- Signal transduction / gene expression

Depression Rating Scales

Several rating scales exist, including:

- Hamilton Depression Rating Scale (HAM-D, HDRS)
- Patient Health Questionnaire
- Quick Inventory of Depressive Symptomatology
- Beck Depression Inventory
- Montgomery-Asberg Depression Rating Scale
- Zung Self-Rating Depression Scale

**HAM-D Scoring**

<table>
<thead>
<tr>
<th>17 item, range 0-53</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-7: no depression</td>
</tr>
<tr>
<td>8-16: mild depression</td>
</tr>
<tr>
<td>17-23: moderate depression</td>
</tr>
<tr>
<td>&gt;23: severe depression</td>
</tr>
</tbody>
</table>

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Treatment Goals and Outcomes

Goals of therapy: “alleviating functional impairments and improving quality of life in addition to achieving symptom resolution and episode remission”

- **Non-response**: <26% severity reduction
- **Partial Response**: 26-49% severity reduction
- **Response**: 50+% severity reduction
- **Remission**: Absence of symptoms

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Treatment Guidelines

American Psychiatric Association
- First line
  - Psychotherapy +/-
  - SSRI
  - SNRI
  - Bupropion
  - Mirtazapine
- After treatment failure
  - Increase dose
  - Change medication
  - Augment with pharmacotherapy
  - Augment with psychotherapy

VA/DoD
- Psychotherapy +/-
  - SSRI
  - SNRI
  - Bupropion
  - Mirtazapine
- Increase dose
- Change medication
- Augment with pharmacotherapy
- Augment with psychotherapy

Texas Medication Algorithm Project
- SSRI
- SNRI
- Bupropion
- Mirtazapine
- Increase dose
- Change medication
- Augment with pharmacotherapy
- Augment with psychotherapy

Antidepressants
Antidepressants

MAOIs
• Isocarboxazid, phenelzine, selegiline, tranylcypromine

TCAs
• Amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine

SSRIs
• Fluoxetine, sertraline, paroxetine, (es)citalopram, vilazodone, vortioxetine

SNRIs
• Duloxetine, levomilnacipran, (des)venlafaxine

Miscellaneous
• Bupropion, mirtazapine, trazodone, nefazodone

Work Group on Major Depressive Disorder. 2010.

Antidepressant pharmacodynamics

MAO-I

SSRI

SNRI, TCA

Mirtazapine

https://accesspharmacy.mhmedical.com/data/books/2249/m_katzung14_ch30_f002-1.png
Antidepressant Pharmacokinetics

<table>
<thead>
<tr>
<th></th>
<th>1A2</th>
<th>2B6</th>
<th>2C9</th>
<th>2C19</th>
<th>2D6</th>
<th>3A4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>++</td>
<td></td>
<td></td>
<td>++</td>
<td></td>
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<tr>
<td>Escitalopram</td>
<td></td>
<td></td>
<td>++</td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>++</td>
<td>+</td>
<td></td>
<td>++</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Sertraline</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td></td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

+ minor substrate  ++ major substrate

Work Group on Major Depressive Disorder. 2010

Antidepressant Side Effects

- Gastrointestinal
- Insomnia/sedation
- Sexual side effects
- Cardiovascular
- Anticholinergic
- Serotonin Syndrome

Work Group on Major Depressive Disorder. 2010
Development of Clinical Pharmacogenomics

Candidate genes code for pharmacodynamic, pharmacokinetic, and downstream pathway targets

## Drug-Gene Pharmacodynamic Interactions

<table>
<thead>
<tr>
<th>Drug</th>
<th>BDNF</th>
<th>COMT</th>
<th>FKBP5</th>
<th>HTR1A</th>
<th>HTR2A</th>
<th>SLC6A2</th>
<th>SLC6A4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion</td>
<td></td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>Citalopram</td>
<td>+</td>
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<td>+++</td>
<td></td>
</tr>
<tr>
<td>Duloxetine</td>
<td>+</td>
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<td>+</td>
<td>+++</td>
<td></td>
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<tr>
<td>Escitalopram</td>
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<td>Fluoxetine</td>
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<tr>
<td>Mirtazapine</td>
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<tr>
<td>Paroxetine</td>
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<td></td>
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<tr>
<td>Sertraline</td>
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</tr>
<tr>
<td>Venlafaxine</td>
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<td></td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSRIs</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Number of gene variants**

|       | 6  | 2  | 4  | 3  | 5  | 1  | 3  |

**Level of Evidence:**
- + low
- ++ moderate
- +++ high


## Drug-Gene Pharmacokinetic Interactions

<table>
<thead>
<tr>
<th>Drug</th>
<th>ABCB1</th>
<th>CYP1A2</th>
<th>CYP2B6</th>
<th>CYP2C19</th>
<th>CYP2D6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>+</td>
<td></td>
<td>+++</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Duloxetine</td>
<td></td>
<td></td>
<td>+++</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Escitalopram</td>
<td>+</td>
<td></td>
<td>+</td>
<td>++</td>
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<tr>
<td>Fluoxetine</td>
<td></td>
<td></td>
<td>+++</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Mirtazapine</td>
<td></td>
<td></td>
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<td>+</td>
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</tr>
<tr>
<td>Paroxetine</td>
<td>+</td>
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<td>+++</td>
<td></td>
</tr>
<tr>
<td>Sertraline</td>
<td></td>
<td></td>
<td>+</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Venlafaxine</td>
<td></td>
<td></td>
<td></td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>SSRIs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Number of gene variants**

|       | 15 | 9  | 5  | 8  | 14 |

**Level of Evidence:**
- + low
- ++ moderate
- +++ high

Marketed Pharmacogenetic Clinical Decision Support Tools for Antidepressant Selection

All tools listed include: Serotonin transporter, CYP1A2, CYP2C19, CYP2D6, CYP3A4

<table>
<thead>
<tr>
<th>Company/Tool</th>
<th>Total Genes Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>cnsdose</td>
<td>24</td>
</tr>
<tr>
<td>GENECEPT ASSAY</td>
<td>19</td>
</tr>
<tr>
<td>genesight</td>
<td>13</td>
</tr>
<tr>
<td>IDgenetiX</td>
<td>17</td>
</tr>
<tr>
<td>neuropharXen</td>
<td>30</td>
</tr>
</tbody>
</table>


Guidance and Guidelines

FDA Guidance for Industry (2013)

- Recommends labeling appropriate doses based on pharmacogenomics

Clinical Pharmacogenetics Implementation Consortium (2015, 2016)

- Dosing recommendations for SSRIs and TCAs based on existing pharmacogenomic data

Royal Dutch Association for the Advancement of Pharmacy, Pharmacogenetics Working Group (2011)

- Dosing recommendations for medications based on existing pharmacogenomic data

U. S. Department of Health and Human Services. 2013
Question

A patient comes to your clinic for depression, and an antidepressant is indicated. The patient has already been genotyped for CYP2C19 and CYP2D6. What is the standard of care regarding the approach toward antidepressant selection?

A. Ignore pharmacogenetic data and select medication based on clinical factors
B. Use the existing pharmacogenetic data and select medication taking into account other clinical factors
C. Order additional pharmacogenetic data and select medication taking into account other clinical factors
Fabbri 2018, Qualitative Analysis

Identified 21 clinical trials with search strategy in accordance with PRISMA

6 RCTs: Genesight, CNSDose, Genelex, Neuropharmagen, NeuroIDgenetix

6 non-randomized case control study

9 observational studies without comparator group

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Randomized Control Trial Summary

<table>
<thead>
<tr>
<th>Tool</th>
<th>Study Design</th>
<th>Blinding</th>
<th>Population</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genesight (Winner 2013)</td>
<td>Prospective, double-blind, randomized, 10 weeks</td>
<td>Patient and rater blinded, provider unblinded</td>
<td>51 patients with MDD or depressive disorder</td>
<td>OR=2.14 for response (CI 0.59-7.69) OR=2.75 for remission (CI 0.48-15.80)</td>
</tr>
<tr>
<td>CNSDose (Singh 2015)</td>
<td>Prospective, double-blind, randomized, 12 weeks</td>
<td>Patient and rater blinded, provider unblinded</td>
<td>148 patients with MDD</td>
<td>RR= 2.52 for remission (CI 1.71-3.73) RR= 0.88 for intolerability (CI 1.01-1.25)</td>
</tr>
<tr>
<td>Neuropharmagen (Perez 2017)</td>
<td>Prospective, double-blind, randomized, 12 weeks</td>
<td>Patient and rater blinded, provider unblinded</td>
<td>280 patients with MDD</td>
<td>OR=1.19 for sustained response (CI 0.74-1.92) OR= 1.62 for response (CI 1.00-2.61)</td>
</tr>
<tr>
<td>NeuroIDgenetix (Bradley 2018)</td>
<td>Prospective, double-blind, randomized, 12 weeks</td>
<td>Patient and rater blinded, provider unblinded</td>
<td>685 patients with depression or anxiety</td>
<td>None reported for entire sample</td>
</tr>
</tbody>
</table>
Singh 2015

Improved Antidepressant Remission in Major Depression via a Pharmacokinetic Pathway Polygene Pharmacogenetic Report


Study Basics

Objective
- “[I]nvestigate the clinically utility of a... pharmacogenetic interpretive report...”

Design
- Randomized, prospective, double-blind

Intervention
- CNSDose

Patient Selection

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>• DSM-V diagnosed MDD</td>
<td>• Comorbid psychiatric disorders</td>
</tr>
<tr>
<td>• HAM-D ≥18</td>
<td>• Pregnancy/breastfeeding</td>
</tr>
<tr>
<td>• Caucasian</td>
<td>• Hepatic or renal impairment</td>
</tr>
<tr>
<td></td>
<td>• CYP2D6, CYP2C19, ABCB1 inducers/inhibitors</td>
</tr>
<tr>
<td></td>
<td>• Tobacco smoking</td>
</tr>
</tbody>
</table>

Methods

<table>
<thead>
<tr>
<th>Assessment and Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcomes</strong></td>
</tr>
<tr>
<td>• Remission rates at 12 weeks per HAM-D</td>
</tr>
<tr>
<td>• Adverse events</td>
</tr>
<tr>
<td>• Number of sick days taken due to depression</td>
</tr>
<tr>
<td><strong>Statistics</strong></td>
</tr>
<tr>
<td>• T-tests used to compare between group differences</td>
</tr>
</tbody>
</table>

Study Design

Visit with report available

Randomization & sample collection

Visit without report available

Week 0

HAM-D

Week 4

HAM-D, etc.

Week 8

HAM-D, etc.

Week 12

HAM-D, etc.

Study Sample

Patient Characteristics

- 148 patients completed study
- Mean age 44.2 years, ~60% female
- Mean MDD duration of ~8.5 months
- Baseline mean HAM-D 24.7
- Average 2.2 previous MDD episodes
- No statistically significant differences between groups
Results

- 65% of patients in treatment group changed therapy based on PGx report
- No statistically significant differences between groups regarding proportion on certain antidepressants (p>0.05)

Most frequently used medications
- Sertraline
- Agomelatine
- Escitalopram
- Venlafaxine
- Fluoxetine
- Paroxetine


<table>
<thead>
<tr>
<th>Outcome</th>
<th>PGx (n=74)</th>
<th>TAU (n=74)</th>
<th>Risk Ratio</th>
<th>P-value</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission at 12 weeks</td>
<td>72%</td>
<td>28%</td>
<td>2.52</td>
<td>&lt;0.001</td>
<td>3</td>
</tr>
<tr>
<td>Tolerability problems</td>
<td>4%</td>
<td>15%</td>
<td>0.88</td>
<td>0.0272</td>
<td>10</td>
</tr>
<tr>
<td>Percentage of patients with sick leave</td>
<td>4%</td>
<td>15%</td>
<td>0.88</td>
<td>0.0272</td>
<td>10</td>
</tr>
</tbody>
</table>

## Study Assessment

### Strengths
- Guidelines supported primary outcome
- Randomization and double blind design

### Limitations
- Extensive exclusion criteria
- No adverse event report
- No defined statistical analysis

## Implications
- CNSDose shown to improve remission rates, tolerability to treatment, and patient functionality for select patients with moderate-severe depression
- External validity limited by sample characteristics

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**Perez 2017**

Efficacy of prospective pharmacogenetic testing in the treatment of major depressive disorder: results of a randomized, double-blind clinical trial

Study Basics

Objective
• "[E]valuate the effectiveness of pharmacogenetic (PGx) testing for drug therapy selection in major depressive disorder patients"

Design
• Randomized, prospective, double-blind, multicenter

Intervention
• Neuropharmagen

Patient Selection

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Age ≥18 years</td>
<td>• Primary psychiatric diagnoses</td>
</tr>
<tr>
<td>• DSM-IV diagnosis of major depressive disorder</td>
<td>• Pregnant/breastfeeding</td>
</tr>
<tr>
<td>• CGI-S ≥4 at screening and randomization (moderately ill or worse)</td>
<td>• Concurrent CYP2D6 strong inhibitors</td>
</tr>
<tr>
<td>• Required addition of or change to medications according to physician assessment</td>
<td></td>
</tr>
</tbody>
</table>

Pérez V, et al. BMC Psychiatry. 2017;17(1)
Methods

Assessment and Analysis

Outcomes

- **Primary**
  - Sustained response at 12 weeks (PGI-I ≤2 at 2 consecutive visits, and maintained at study end)
- **Secondary**
  - Response at 12 weeks (PGI-I ≤2)
  - Change in HAM-D, CGI-S, FIBSER, SATMED-Q, SDI
  - Adverse effects analyzed via FIBSER score

Statistics

- Chi-square and student t-tests used for comparisons according to data type
- 390 patients needed for 80% power to detect 15% difference in sustained response between groups
- Adjusted alpha = 0.0271

Study Design

- **Visit with medication change, report available**
  - Randomization & sample collection
  - **Visit with medication change, no report available**

- **Week 0**
  - DB PGI-I
  - SB HAM-D, etc.

- **Week 4**
  - SB PGI-I

- **Week 6**
  - DB PGI-I

- **Week 8**
  - SB and DB assessment

- **Week 12**

Study Sample

**Patient Characteristics**

- 316 patients randomized
- Mean age 51.2 years, 63.6% female, 92.4% Caucasian
- Median MDD duration of 14.1 months
- Baseline mean HAM-D 19.2
- 35.8% with comorbid anxiety, 12.6% comorbid substance abuse
- Average 2.6 previous medication trials
- No statistically significant differences between groups
- Patients prescribed medication in disagreement with Neuropharmagen report excluded in assessment (17 patients)

---

Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>PGx (n=155)</th>
<th>TAU (n=161)</th>
<th>Odds Ratio</th>
<th>P-value (α = 0.271)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustained response</td>
<td>47.8%</td>
<td>36.1%</td>
<td>1.62</td>
<td>0.0476</td>
<td>9</td>
</tr>
<tr>
<td>Response at 12 weeks</td>
<td>51.3%</td>
<td>36.1%</td>
<td>1.86</td>
<td>0.0135</td>
<td>7</td>
</tr>
<tr>
<td>FIBSER ≤2 at 12 weeks</td>
<td>68.5%</td>
<td>51.4%</td>
<td>2.06</td>
<td>0.0260</td>
<td>6</td>
</tr>
</tbody>
</table>

Larger effect size seen in patients with 1-3 treatment failures
Results

Change in HAM-D

Statistically significant

Study Assessment

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Inclusion of psychiatric comorbidity</td>
<td>• CGI-I not validated for depression</td>
</tr>
<tr>
<td>• Sample characterization</td>
<td>• Validated rating scales single-blinded</td>
</tr>
<tr>
<td>• Statistical methods</td>
<td>• Treatment group exclusion</td>
</tr>
</tbody>
</table>

Implications

• Neuropharmagen failed to show statistically significant benefit for primary outcome, but didn’t reach power
• Neuropharmagen likely show benefit for response and tolerability if assessed with more precise measures
• Benefit may be more robust for patients with medication failure
Improved efficacy with targeted pharmacogenetic-guided treatment of patients with depression and anxiety: A randomized clinical trial demonstrating clinical utility


Study Basics

Objective

• “[E]valuate the effect of pharmacogenetics-guided treatment on patients diagnosed with depression and/or anxiety... as compared to the standard of care”

Design

• Randomized, prospective, double-blind, multicenter

Intervention

• NeurolDgenetix
Study Sample

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
</table>
| • Age 19-87 years  
  • DSM-V diagnosis of depression and/or anxiety  
  • Either  
    • New to treatment  
    • Inadequately controlled | • Bipolar disorder  
  • Schizophrenia  
  • Personality disorder  
  • Traumatic brain injury  
  • Significant risk for suicide and hospitalization  
  • History of chronic renal dysfunction or CKD stage 4/5  
  • Malabsorption  
  • Pregnancy  
  • Abnormal hepatic function |

Methods

Assessment and Analysis

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Statistics</th>
</tr>
</thead>
</table>
| • Change in HAM-D at week 4, 8, 12 for patients with HAM-D scores ≥18  
  • Response (>50% reduction in HAM-D)  
  • Remission (HAM-D ≤7)  
  • Adverse drug events | • T-test for change in HAM-D  
  • Fischer’s exact test for response and remission rates  
  • Mixed model repeated measures performed for data at week 12  
  • Alpha not defined |
Bradley 2018

Visit with medication change, report available

Randomization & sample collection

HAM-D

Visit with medication change, no report available

Week 0

Week 4

Week 8

Week 12

HAM-D, adverse effects

HAM-D, adverse effects

HAM-D, adverse effects


Study Sample

685 Randomized

146 with depression only

204 with depression and anxiety

579 Completed

261 with HAM-D17 ≥18

Patient Characteristics

- Mean age 48 years
- 73% female
- No differences in phenotype distribution (p>0.05) between groups of randomized patients
- No report of previous medication trials

Results

• More medication changes in PGx group (81% vs 64%, p <0.0001)
• Alignment of medications with PGx report 70% vs 29%

<table>
<thead>
<tr>
<th>Outcome</th>
<th>PGx (n=140)</th>
<th>TAU (n=121)</th>
<th>Odds Ratio</th>
<th>P-value</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission at 12 weeks</td>
<td>35%</td>
<td>13%</td>
<td>3.54</td>
<td>0.02</td>
<td>5</td>
</tr>
<tr>
<td>Response at 12 weeks</td>
<td>73%</td>
<td>36%</td>
<td>4.72</td>
<td>0.001</td>
<td>3</td>
</tr>
<tr>
<td>Adverse events</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.21</td>
<td>-</td>
</tr>
</tbody>
</table>

• 94% adverse events not severe

Study Assessment

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Study design</td>
<td>• Selective reporting</td>
</tr>
<tr>
<td>• Validated measures</td>
<td>• Statistical significance not defined</td>
</tr>
<tr>
<td>• Randomized, double-blind</td>
<td></td>
</tr>
<tr>
<td>• Inclusion of treatment naïve patients</td>
<td></td>
</tr>
</tbody>
</table>

Implications

• NeurolDgenetix improves remission and response rates for select patients with moderate-severe depression
• Effect on tolerability not shown
• Selective reporting suggests results are not robust, limiting confidence in analysis
Literature Summary

- No strong evidence for benefit in mild depression or depression with comorbid psychiatric conditions
- Unclear of benefit for treatment naïve patients
- Improved remission rates and response to treatment has been shown for moderate to severe depression
  - Difference in measures used limits meta-analysis
  - Positive data has large effect sizes

- Criteria for ordering pharmacogenetic test and report
  - Uncontrolled moderate to severe depression
  - 1-3 treatment failures

Question

How likely would you order a pharmacogenetic report for a patient with depression who returns to clinic after failing fluoxetine?

A. Sure thing
B. Likely
C. Not likely
D. No chance
Future Considerations

Cost as limiting factor of implementation
• Would already be standard of care if cheap
• Cost effectiveness analyses inconclusive

Product changes over time
• Each product is continually changing based on public and private research
• Genome wide data may be available before a single product becomes regularly utilized


Thanks!
• Central Texas Psychiatric Pharmacists
• Dr. Jacqueline Meaney
References

- Fabini C, Zohar J, Sanetti A. Pharmacogenetic tests to guide drug treatment in depression: Comparison of the available testing kits and clinical trials. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2018;84:38-44.